

UNITED EUROPEAN
GASTROENTEROLOGY

ueg journal

October 2024

Volume 12, Issue S8

ISSN 2050- 6414 (Online)

onlinelibrary.wiley.com/toc/20506414/2024/12/S8

12

**An international forum for
clinical practice and research
in digestive health**

Abstract issue

32nd United European Gastroenterology Week 2024

Find out more at ueg.eu/journal/

@UEGJournal
@my_UEG

WILEY

UNITED EUROPEAN
GASTROENTEROLOGY

uegeducation

Ingest the best

Online Courses

15,000 users, 40 courses
Be part of the learning
community



Learn. Advance. Excel
ueg.eu/education

Letter of Thanks for UEG Week 2024 Reviewers

United European Gastroenterology Journal
2024, Vol 12 (S8) | © Author(s) 2024
Reprints and permissions: wiley.com/en-gb/permissions
DOI: 10.1002/ueg2.12610 | onlinelibrary.wiley.com/toc/20506414/2024/12/S8

UNITED EUROPEAN
GASTROENTEROLOGY
ueg journal
WILEY

Dear Colleagues,

On behalf of the UEG Scientific Committee, I would like to express our deepest gratitude for your invaluable contributions as abstract reviewers for the UEG Week 2024 original programme. Your efforts in the abstract reviewing process are vital to maintaining the high scientific quality and relevance of UEG Week. I am aware of the significant time and dedication required for this task, and without your expertise, we could not have achieved the exceptional standards of our abstract-based sessions. Your hard work ensures that UEG Week continues to be the premier international meeting in the field of digestive diseases

Thank you once again for your dedication and support!

We received a total of **3,540 abstracts** for UEG Week 2024. In total, **2,208 abstracts** were accepted. **236 abstracts** will be delivered as **oral presentations** and **1,972** as **posters**. I am even more pleased to tell you that standards have again reached a very high level and we can expect most interesting research and great presentations. This high volume and high standard confirm that UEG Week remains the most important forum at which to present your best research.

We have received **90 video cases** and **416 clinical cases** which were formally evaluated by the Scientific Committee and invited experts for presentation. As in previous years, late breaking abstracts have been scored by the Scientific Committee.

The quality of reviewing this year was excellent, but if you have any further (positive or negative) comments, please do let us know! Finally, but most importantly, thanks to all investigators both within and outside Europe who have submitted their research to the meeting, and who are contributing to making UEG Week 2024 a great success!



Julia Mayerle
Chair of the UEG Scientific Committee

Acknowledgements

(As per August 2, 2024; in alphabetical order)

United European Gastroenterology Journal

2024, Vol 12 (S8) | © Author(s) 2024

Reprints and permissions: wiley.com/en-gb/permissions

DOI: 10.1002/ueg2.12611 | onlinelibrary.wiley.com/toc/20506414/2024/12/S8

ueg journal
WILEY

UEG gratefully acknowledges the support of the following companies:

Premier Supporter

AbbVie

abbvie

Pfizer Inc.



Bristol Myers Squibb



Sanofi

sanofi

REGENERON

Eli Lilly and Company



Takeda



Main Supporter

Amgen



Johnson and Johnson

Johnson&Johnson

Celltrion Healthcare



Novo Nordisk A/S



FUJIFILM Europe



Olympus



Innovation Hub

MAIA LABS s.r.o.

Satisfai Health

Shanghai Endoangel Medical
Technology Co.,Ltd

PathAI

General Supporter

Abivax

EMED SP. Z O. O. SP. K.

La Lettre de l'Hépatogastroentérologue

Alfasigma S.p.A.

Endo Tools Therapeutics

Leinzett Medical

Alimentiv Inc.

EndoFresh

Leo Medical Co, Ltd

Alton (Shanghai) Medical Instruments Co.,Ltd

EndoRobotics

M.I.Tech Co., Ltd.

AMW Health

Endoscopic Ultrasound Journal

Madrigal Pharmaceuticals

Anrei Medical (HZ) Co.,Ltd

Endostart srl

mdd Company GmbH

AnX Robotica GmbH

ENTEROSGEL®

Meditalia

AOHUA

Erbe Elektromedizin GmbH

Mednova Medical

Augere Medical AS

Eurospital

MICRO-TECH Europe GmbH

BCM Co Ltd

F. Hoffmann-La Roche Ltd

MSD

Beijing ZKSK Technology Co Ltd

Fameco

Ovesco Endoscopy AG

BGI Genomics Co Ltd

FINEMEDIX Co Ltd

Pentax

BioCer Entwicklungs-GmbH

Fischer Analysen Instrumente GmbH

PrecisionBiotics

BioGaia

FORESIGHT TECHNOLOGY CO., LTD.

Promisemed Medical Devices Inc.

Biohit Healthcare Oyj

Fresenius Kabi

Richen Europe S.r.l.

BIOSYNEX Theradiag

GA Health Medical Devices Limited

S. Karger AG

Boditech Med

G-Flex Europe

Shenzhen HugeMed Medical Technical

Boehringer Ingelheim

Guangzhou Red Pine Medical

Development Co., Ltd

Boston Scientific International

Hangzhou AGS MedTech Co.,Ltd.

SonoScape Medical Corp.

BÜHLMANN Laboratories AG

Holdfinger

Sony Europe B.V.

Calpro

Horizons International Corp

STADA Arzneimittel AG

CapsoVision

Immundiagnostik AG

STERIS

Changzhou Intl. Trade & Enterprises

InnerMedical Co., Ltd.

TaeWoong Medical

Cooperative Co., Ltd (CITEC)

IntroMedic Co Ltd

The Standard Co., Ltd.

Choyang Medical Industry Ltd

Jiangsu ATE Medical Technology Co Ltd.

Tillotts Pharma AG

Daewoong Pharmaceuticals

Jiangsu Changmei Medtech Co., Ltd.

Vedkang Medical

Dr. Falk Pharma

Jiangsu Grit Medical Technology Co., Ltd.

VYTIL

Dr. Henke Medical Training + Education

Jiangxi ZhuoRuiHua Medical Instrument

Waldner Technologie Medicali

ECHOSENS

Co.,Ltd

Wisepress Medical Bookshop

ELLA-CS

JINSHAN

ZheJiang Soudon Medical Technology Co.,Ltd

UEG Week 2024 Table of Contents

UEG Week 2024 Oral Presentations

Sunday, October 13, 2024

Opening Plenary	10
Coeliac disease	11
Dyspepsia and <i>H.pylori</i>	13
Pancreatic diseases: From mechanisms to therapy	17
Understanding disease primers of IBD: Part 1	20
IBD: Latest news on a personalised approach	24
Microbiota driven carcinogenesis in GI disease	28
Management of complications and endpoints in cirrhosis and HCC	31
Upper GI endoscopy: From diagnosis to treatment	34
Video Cases	37

Monday, October 14, 2024

Ameliorating acute disease through novel treatment in IBD: Part 1	43
Obesity: Endoscopy and drugs	49
Upper GI basic: Reflux, gastritis and cancer	52
Recent break throughs in treating and monitoring MASH	56
Diagnose and treat to target in GI cancer: Latest news	60
Basic mechanisms of disease in liver, pancreas and intestine	63
AI and reflux	67
IBD: New horizons in medical treatment - Part 1	70
Expanding treatment response in IBD	75
Optimising safety and efficacy of polyp treatment	83
Microbiota, chronic inflammation and cancer	86
Advanced ERCP technology and outcomes	90
Maintaining remission and quality of life in IBD	93
Understanding disease primers of IBD: Part 2	100

Barrett's oesophagus: Treatment and surveillance	103
IBS: Emerging evidence for treatment	107
AI for polyp detection: Advances, pitfalls and challenges	112
Ameliorating acute disease through novel treatment in IBD: Part 2	116
Pancreatic cancer: From bench to bedside	120
<i>H.pylori</i> basics	124
EMR or ESD for colon neoplasia	127

Tuesday, October 15, 2024

Optimising biological treatment in IBD	129
Microbiome: Bench to the future	135
Short bowel syndrome	138
Fit for CRC screening	142
What's new in acute pancreatitis	145
IBD: Diagnosis and monitoring	150
Screening colonoscopy: How to save lives	154
Trends in hepatology: From diagnosis to treatment	157
Finetuning treatment in IBD	161
IBD: New horizons in medical treatment - Part 2	166
Pancreatic diseases: From models to precision medicine	171
AI in diagnostic and therapeutic endoscopy	173
Eosinophilic oesophagitis	176
IBD: A burden for patient and society	182
Upper GI bleeding: Treatment and outcome	187
Local treatment for locally advanced colon cancer: How to improve outcome	191
Pancreatic endoscopy and patient outcome	195

UEG Week 2024 Moderated Poster Presentations

Sunday, October 13, 2024

Risk factors and treatment side effects in IBD	202
Bowel: Preparation is everything	208
Pancreatic endoscopy	215
Challenges in upper GI and small bowel cancer	222
Coeliac disease: Part 1	228
Potpourri of DGBI and motility	234
Marching forward in lower GI endoscopic treatment	240
Advanced chronic liver disease	247
Pancreatic cancer: Basic	254
Diagnosis and treatment of GORD	259
Upper GI bleeding	264
Novel therapeutic approaches in IBD	271
Complications in end stage liver disease	277
Endoscopic techniques	282
Short bowel and nutrition therapies	290
Disease evolution of IBD	297
Mechanisms and treatment of IBS	305
Identification and mechanisms in SLD	312
Medical management of pancreatitis	317
New developments in upper GI endoscopy	322
Gastric mucosa: Basic science	327

Monday, October 14, 2024

IBD management from (non-)pharmaceutical interventions to outcome definitions	333
Leaving CRC behind: Improving endoscopy and surgery	338
Epidemiology in MASLD	343
Pancreatic cancer: Clinical	349
Coeliac disease: Part 2	354

Clinical presentation and impact on treatment in EoE	359
Surgical considerations in IBD	366
Cutting-edge modalities for endoscopic resections	373
Aspects in managing cirrhosis	379
Acute pancreatitis	384
Nutrition and the gut: Mechanisms and therapies	390
Diagnosis and endoscopic treatment of upper GI neoplasms	397
JAK inhibitors in the treatment of IBD	402
IBD in pregnancy and paediatric patients	411
HPB: Autoimmune pancreas and liver	419
Patient outcome: Pancreas	424
Challenges in upper GI oncology	429
AI and beyond	435
Monitoring disease activity in IBD	440
Towards the cure of CRC	447
New clinical aspects in hepatology	453
Outcomes and implications of pancreatic disease	458
<i>H. pylori</i> treatment: Part 1	465
Dysphagia: Diagnostics and therapeutics	474
Identifying drug targets in IBD: Part 1	479
Deciphering cancer	486
Management of hepatobiliary cancer	491
Pancreatic cancer: Clinical and basic science	496
Pharmaceutical treatment of EoE	501
Endoscopic resection for upper GI cancer	510

Tuesday, October 15, 2024

IBD risk factors and outcomes	514
Screening and surveillance of CRC: What's new	522
Advances in MASLD	527
Managing bile duct disease	532
<i>H. pylori</i> treatment: Part 2	538
Endoscopy: Upper GI	545
Identifying drug targets in IBD: Part 2	551
Microbiota as a diagnostic and therapeutic tool	557

Overview of pancreatic diseases	563
Basic science in HPB: Genetic, metabolic and immune	569
The varied spectrum of malnutrition	574
IL-23 inhibitor in UC and Crohn's disease: Part 1	580
Biomarkers and prediction of treatment responses in IBD	592
Clinical features and outcomes in liver disease	598
Chronic pancreatitis	603
Coeliac disease: Part 3	608
Eosinophilic oesophagitis: Mechanisms	614
IL-23 inhibitor in UC and Crohn's disease: Part 2	620
Small molecules in the treatment of IBD	631
Molecular and clinical therapies in HPB	642
Cholangitis and cholecystitis	648
Barrett's oesophagus	653
Upper functional GI disorders: From basic to clinical	659

UEG Week 2024 Poster Presentations

1. Oesophageal, gastric and duodenal disorders	666
2. <i>H. Pylori</i>	794
3. Small Intestinal	822
4. Nutrition	844
5. IBD	856
6. Lower GI	1066
7. Liver	1200
8. Biliary	1246
9. Pancreas	1290
10. Other	1326

Author Index	1361

Downloaded My Connect yet?

Connect with UEG's international digestive health community. **Find Peers**, check out the bustling **Live Feed**, diverse **Interest Groups**, and other opportunities for collaboration.

What makes My Connect great, is **you**.

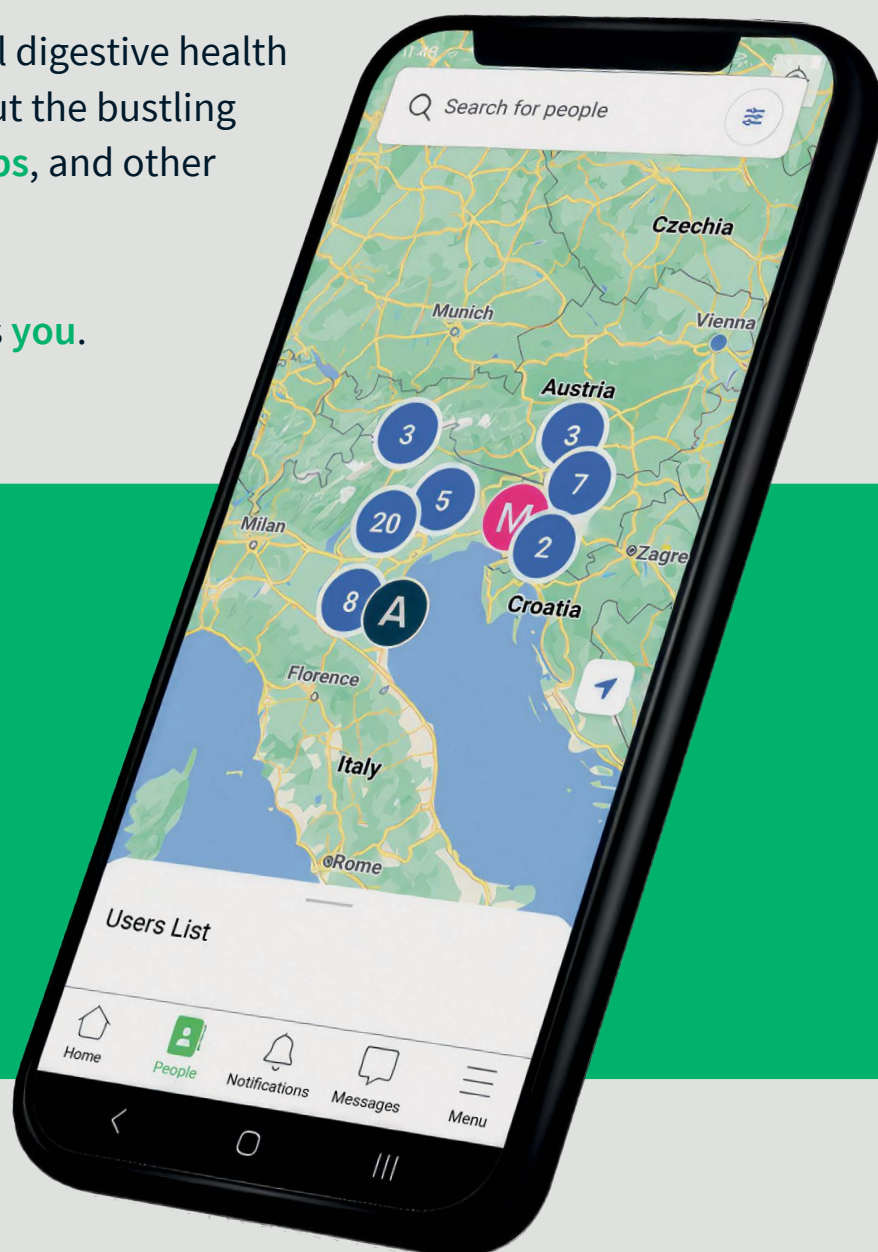
Download
app free of charge



Download on the
App Store



GET IT ON
Google Play



my.ueg.eu/my-connect

Oral presentations

Opening Plenary

13:30-15:00 / C1/4

OP001

CROHN'S DISEASE AND ULCERATIVE COLITIS EXHIBIT PRE-DIAGNOSTIC ANTIBODY SIGNATURES WITH SHARED AND DIVERGENT CHANGES TOWARDS DISEASE ONSET

A.R. Bourgonje^{1,2}, S. Andreu-Sánchez³, R. Gacesa¹, G. Innocenti⁴, I.N. Kalka⁵, S. Klompus⁵, S. Leviatan⁵, A. Weinberger⁵, B. van der Vegt⁶, J. Fu³, E. Segal⁵, A.P. Zhernakova³, T. Vogl⁴, R.K. Weersma¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America, ³University Medical Center Groningen, Genetics, Groningen, Netherlands, ⁴Medical University of Vienna, Center for Cancer Research, Vienna, Austria, ⁵Weizmann Institute of Science, Computer Science and Applied Mathematics, Rehovot, Israel, ⁶University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Inflammatory bowel diseases (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic debilitating. Current clinical practice is focused on managing disease flares and complications, requiring lifelong medical treatment and/or surgery. However, a paradigm shift in IBD care is needed, moving from treatment of established disease towards creating opportunities for prevention of disease development. Such strategies recently proved successful in rheumatoid arthritis and type 1 diabetes. Before being able to achieve this, however, preclinical disease biomarkers are urgently needed. IBD is characterized by unique immunological changes early in development.

Although >300 IBD-specific antibody responses have been identified¹, systemic antibody epitope repertoires of preclinical IBD remain elusive. This study aimed to profile systemic antibody responses at unprecedented depth in individuals before and after the onset of IBD, aiming to identify preclinical disease biomarkers.

Aims & Methods: This study included individuals participating in the Life-lines Cohort Study, a large prospective population-based cohort study in the Netherlands including 167,000 individuals with longitudinal follow-up. Participants without IBD at baseline were screened for any reported IBD diagnosis during follow-up (2006-2021). Individuals who reported IBD during follow-up and with available serum samples were included. Samples at baseline (pre-diagnosis) and during follow-up (post-diagnosis) were used to profile antibody repertoires against 344,000 rationally selected microbial-, food-, and immune antigens using phage-display immunoprecipitation sequencing (PhIP-Seq).

Results: A total of 178 new-onset cases with IBD were identified. Median follow-up time until diagnosis was 3.9 (IQR: 3.4-4.3) years. Most individuals newly developed UC ($n=123$, 69.1%), followed by CD ($n=44$, 24.7%), and undetermined IBD (IBD-U, $n=11$, 6.2%). A total of 5,174 antibody responses were observed in 5-95% of participants. Fifty-nine antibodies were differentially abundant (FDR<0.05) pre-diagnosis vs. post-diagnosis, 14 of which (24%) were previously reported in established IBD¹. Thirteen were more (22%) and 46 less (78%) frequently observed post-diagnosis. Individuals developing IBD exhibited reduced frequencies of antibody

responses against EBV-associated peptides post-diagnosis, e.g. Epstein-Barr nuclear antigen-1 (EBNA-1) and capsid protein V26, and other herpesviruses including varicella-zoster virus (VZV), herpes simplex virus type 1 (HSV-1), and noroviruses. Conversely, significantly increased antibody responses were observed against bacterial flagellins (notably from *Lachnospiraceae* and pathogenic (e.g. *Legionella*) bacteria) in individuals developing CD, already before disease onset. Individuals developing UC showed elevated antibody responses mainly against viruses (e.g. human adenovirus C, enteroviruses B/C) and particular pathogenic bacterial species (e.g. pneumococcal histidine triad proteins) post-diagnosis compared to pre-diagnosis.

Conclusion: This study represents the first comprehensive and high-resolution analysis of the exact antigenic nature of systemic antibody responses changing during the transition from preclinical to established IBD. Distinct antibody responses appear years before IBD diagnosis, indicating potential involvement in pre-clinical disease development. Furthermore, post-diagnosis, lower frequencies of antibody responses against EBV may suggest reduced immunogenicity against this virus in early disease pathogenesis.

References: 1. Bourgonje et al. *Immunity*. 2023.

Disclosure: Nothing to disclose.

Coeliac disease

15:30-16:30 / Strauss 3

OP002

TG2 INHIBITOR (ZED1227) SHOWS DOSE-DEPENDENT PROTECTION FROM GLUTEN-INDUCED INTESTINAL DAMAGE IN CELIAC DISEASE: TRANSCRIPTOMIC ANALYSIS FROM A PHASE 2A STUDY

V. Dotsenko¹, D. Schuppan^{2,3}, S. Yalcin⁴, J. Zhang⁵, J. Tang⁵, D.A. Leffler⁴, T. Zimmerman⁶, R. Mohrbacher⁶, B. Tewes⁶, M. Hils⁷, J. Isola^{1,8}, M. Mäki¹, K. Viiri¹,
on behalf of the CEC-3/CEL Trial Group

¹Tampere University, and Tampere University Hospital, Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere, Finland, ²University Medical Center of the Johannes Gutenberg University Mainz, Institute of Translational Immunology, Mainz, Germany, ³Beth Israel Deaconess Medical Center, Harvard Medical School, Division of Gastroenterology, Boston, United States of America, ⁴Takeda Development Center Americas, Inc., Cambridge, United States of America, ⁵Takeda Development Center Americas, Inc., San Diego, United States of America, ⁶Dr. Falk Pharma GmbH, Freiburg, Germany, ⁷Zedira GmbH, Darmstadt, Germany, ⁸Jilab Inc., Tampere, Finland

Contact E-Mail Address: keijo.viiri@tuni.fi

Introduction: Enzymatic modification of gliadin peptides by human transglutaminase 2 (TG2) is pivotal in celiac disease (CeD) pathogenesis. ZED1227, an oral TG2 inhibitor, shows promise in preventing gluten-induced mucosal damage and symptoms. This study aims to further elucidate the molecular mechanisms underlying the therapeutic efficacy of ZED1227 in CeD.

Aims & Methods: Duodenal biopsy samples were collected from 125 patients with CeD in a phase 2a clinical trial with ZED1227 (CEC-3/CEL; EudraCT-2017-002241-30). Samples were obtained before and after a 6-week gluten challenge (3g/day). Participants received ZED1227 (10mg/day, 50 mg/day, or 100 mg/day) or placebo. RNA extracted from the biopsies underwent next-generation RNA sequencing (RNA-seq) analysis.

Results: Our analysis revealed that after a 6-week gluten challenge, 377 genes exhibited differential expression in the placebo group. Under low-dose ZED1227 (10 mg) treatment, 150 genes remained differentially expressed, primarily affecting metabolism-related pathways but not the interferon- γ (IFN- γ) response. However, higher doses of ZED1227 (50 mg and 100 mg) completely eliminated gluten-induced gene expression changes, including those associated with the IFN- γ response, showing a dose-dependent effect on gene regulation.

Notably, almost half of the gluten induced genes that were suppressed by ZED1227 were related to the IFN- γ response. Initial analysis of human leukocyte antigen (HLA) genotypes suggested that the impact of ZED1227 on mucosal architecture and the IFN- γ response may be modulated by an individual's HLA-DQ2 or -DQ8 genetic background, providing valuable insights into its therapeutic potential in CeD.

Conclusion: ZED1227 effectively prevents gluten-induced mucosal damage in patients with CeD and beneficially modulates gene expression associated with mucosal integrity and the immune response, particularly of the IFN- γ pathway that is central to CD4 T cell mediated CeD pathogenesis. These data corroborate and further elucidate key pathways of intestinal damage in CeD and may suggest new biomarkers of mucosal injury.

Disclosure: SY, JZ, JT and DAL are employees and shareholders of Takeda. DS received study related management/advisory fees from Dr. Falk Pharma. VD has nothing to disclose. TZ, RM and BT are employees of Dr Falk Pharma GmbH. MH is an employee and shareholder of Zedira GmbH.

JJ is the founder and owner of Jilab, Inc.; is a Full Professor at Tampere University, Medical Faculty; and has a consulting agreement with Takeda. MM is the Founder and Chair of Board at Maki HealthTech Ltd (MHT). MHT receives Management/Advisory Affiliation fees from Dr. Falk Pharma, ImmunogenX, Immunic Therapeutics, Topas Therapeutics, and Calypso Biotech; holds patent licensed to Labsystems Diagnostics from where MHT receives royalties via Tampere University Hospital. KV has nothing to disclose.

OP003

ANTI-TRANSGLUTAMINASE 2 IMMUNOGLOBULIN G IN POPULATION-BASED SCREENING FOR COELIAC DISEASE, THE TRØNDELAG HEALTH STUDY, NORWAY

O.T. Dyrli¹, I.L. Andersen^{1,2}, P. Lukina^{1,2}, R.A. Klaasen³, N. Bolstad³, D.J. Warren³, L.M. Sollid^{4,5}, K.E. Lundin^{4,6}, E. Ness-Jensen^{1,2,7,8}

¹NTNU, Norwegian University of Science and Technology, HUNT Research Centre, Department of Public Health and Nursing, Levanger, Norway, ²Nord-Trøndelag Hospital Trust, Department of Medicine, Levanger Hospital, Levanger, Norway, ³Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway, ⁴University of Oslo, Norwegian Coeliac Disease Research Centre, Institute of Clinical Medicine, Oslo, Norway, ⁵Oslo University Hospital, Department of Immunology, Oslo, Norway, ⁶Oslo University Hospital, Department of Gastroenterology, Rikshospitalet, Oslo, Norway, ⁷NTNU, Norwegian University of Science and Technology, HUNT Centre for Molecular and Clinical Epidemiology, Department of Public Health and Nursing, Trondheim, Norway, ⁸Karolinska Institutet & Karolinska University Hospital, Department of Molecular Medicine and Surgery, Stockholm, Sweden

Contact E-Mail Address: eivind.ness-jensen@ntnu.no

Introduction: Coeliac disease (CD) is an immune-mediated disorder of the small intestine triggered by dietary gluten. The diagnosis is based on serological testing and histological examination. Selective immunoglobulin (Ig) A deficiency is a more common condition amongst CD patients than in the general population, complicating the use of IgA antibodies to diagnose CD. Current guidelines suggest testing for the level of total immunoglobulin A (IgA) and the level of specific anti-transglutaminase 2 (TG2) IgA in the search for CD. Only when severe IgA deficiency is found, immunoglobulin G (IgG) based testing is recommended.

In a pilot study for validating a dual TG2 IgA/IgG screening assay, we found CD patients primarily responding with TG2 IgG antibodies and not TG2 IgA, despite IgA sufficiency (1). Thus, these patients risk never being diagnosed.

Aims & Methods: The aim of this study was to assess the additional benefit of testing for TG2 IgG alongside TG2 IgA in screening for CD in adults. The study was based on the fourth Trøndelag Health Study (HUNT4), a population-based study of 56,000 adult (>20 years of age) Norwegians (2). Serum samples were analysed using a combined TG2 IgA and IgG assay and the seropositives were invited to endoscopy with duodenal biopsies for histological confirmation (Marsh grade 3).

The prevalence of primary TG2 IgG responders and the positive predictive value (PPV) of TG2 IgG among TG2 IgA negative participants were calculated.

Results: Serum from 54,505 participants were analysed and 1107 were seropositive. The present study included 593 participants with histological examination and CD was confirmed in 403 participants. Primary TG2 IgG response was found in 75 participants, of whom four got CD confirmed.

None of these four participants had total IgA deficiency. The PPV of TG2 IgG for CD among TG2 IgA negative participants was 5.3% (95% confidence interval 3.5-7.1). In comparison, the PPV of TG2 IgA was 77.0% (73.6-80.4).

Conclusion: This population-based screening for CD among adults found a small group of individuals with CD that risk not being diagnosed using the current diagnostic guidelines, due to primary TG2 IgG response in the absence of IgA deficiency. However, TG2 IgG is still too unspecific to be used in the screening of CD in the general population.

References:

1. Klaasen RA, Warren DJ, Iversen R, Bolstad N, Andersen IL, Mjones P, et al. The development and validation of a high-capacity serological assay for celiac disease. *Clin Biochem.* 2022;107:13-8.
2. Lukina P, Andersen IL, Eggen PT, Mjones PG, Ronne E, Bolstad N, et al. Coeliac disease in the Trondelag Health Study (HUNT), Norway, a population-based cohort of coeliac disease patients. *BMJ Open.* 2024;14(1):e077131.

Disclosure: Nothing to disclose.

OP004

IMPACT OF TRANSGLUTAMINASE 2 INHIBITOR ZED1227 ON SYSTEMIC LIPIDOMIC RESPONSES IN CELIAC DISEASE: A GLUTEN CHALLENGE STUDY

V. Dotsenko¹, A. Dickens², T. Hyötyläinen³, B. Tewes⁴, T. Zimmermann⁴, R. Mohrbacher⁴, M. Oresic^{2,5}, M. Mäki¹, K. Viiri¹

¹Tampere University and Tampere University hospital, Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere, Finland, ²University of Turku and Åbo Akademi University, Turku Bioscience Centre, Turku, Finland, ³Örebro University, School of Science and Technology, Örebro, Sweden, ⁴Dr. Falk Pharma GmbH, Freiburg, Germany, ⁵Örebro University, School of Medical Sciences, Faculty of Medicine and Health, Örebro, Sweden

Contact E-Mail Address: valeriia.dotsenko@tuni.fi

Introduction: Celiac disease (CeD) is an autoimmune disease triggered by dietary gluten in genetically predisposed individuals. This study aimed to explore the systemic plasma lipidomic biomarkers in treated CeD patients undergoing a gluten challenge and to assess the effect of the transglutaminase 2 inhibitor, ZED1227.

Aims & Methods: Mass spectrometry-based lipidomic profiling was applied to plasma samples obtained from 47 CeD patients. The samples were collected at baseline (gluten-free diet, GFD) and post-gluten challenge (PGC). Patients underwent a 6-week gluten challenge and were randomly divided into 2 groups: the placebo drug group (PGCp, $n = 19$) and the group with a daily oral administration of 100mg ZED1227 (PGCd, $n = 28$). Comparative analyses were performed between the groups, with adjustments for BMI, age, sex, and country of origin.

Results: Significantly different gluten-induced serum lipid profiles between GFD vs. PGCp and between GFD vs. PGCd were detected, as 46 lipids were differentially expressed in the first and six in the latter comparison. Additionally, kidney function, measured as glomerular filtration rate and plasma creatinine, decreased significantly in gluten challenge. This correlated with alterations in medium-chain fatty acylcarnitines (CARs), and the function was restored by ZED1227. This suggests that specific carnitines could be early biomarkers for the systemic effects of gluten ingestion in CeD patients.

Conclusion: This study highlights the potential of lipidomic analysis as a tool for early detection of systemic responses to gluten in CeD. The differential lipidomic profiles between the drug and placebo groups suggest that ZED1227 attenuates gluten-induced lipidomic alterations.

Disclosure: B.T., T.Z. and R.M. are employees of Dr. Falk Pharma GmbH. M.M. is the founder, owner and Chair of Board at Maki HealthTech Ltd (MHT). MHT receives Management/Advisory Affiliation fees from Dr. Falk Pharma, Topas Therapeutics, Calypso Biotech, Vaccitech, ImmunogenX, Equillium, and Immunic; holds patent licensed to Labsystems Diagnostics from where MHT receives royalties via Tampere University Hospital.

OP005

INTESTINAL INFLAMMATION AND ASSOCIATED CHANGES OF CYTOKINE AND TRANSMITTER TRANSCRIPTS IN THE BRAIN DURING ACTIVE CELIAC DISEASE IN THE HUMANIZED NOD DQ8 MOUSE MODEL

A. Pesi¹, M. Wiegel¹, P. Frankenbach¹, E. Verdu², P. Bercik², D. Schuppan^{1,3}

¹Medical University Mainz - Institute of Translational Immunology, Medical University Mainz; Mainz/D, Institute of Translational Immunology, Mainz, Germany, ²McMaster University, Hamilton, Canada, ³Beth Israel Deaconess Medical Center, Division of Gastroenterology, Boston, United States of America

Contact E-Mail Address: alinpesi@uni-mainz.de

Introduction: Celiac disease (CeD) is triggered by gluten peptides that bind to HLA-DQ2 or -DQ8 in the small intestinal lamina propria which leads to gluten specific TH1 T cell activation and expansion, small intestinal inflammation, villous atrophy and intraepithelial lymphocytosis (IEL) (1, 2).

With emphasis on the gut-brain axis we analyzed the consequences of active CeD inflammation on immune cell activation in the brain.

Aims & Methods: CeD is associated with symptoms of foggy mind, chronic fatigue and depression (3, 4). The immunological communication between the gut and brain axis has not been studied in-depth in CeD, including the relation of behavior and mental functioning with intestinal immune activation and resultant inflammatory changes in the blood and the brain.

NOD-DQ8 mice were sensitized to gliadin and fed a gluten-containing or gluten-free diet for 2 weeks. Key transcripts in the small intestine and brain were analyzed using qPCR and compared to FACS data of both organs.

Results: The brain is an active site of induced inflammation subsequent to CeD induction of the gut, with a highly significant upregulation of cerebral IL17a, IL23a, IL22b, IL6, IL33, Nlrp3 and COX2. Moreover, the brain dopamine/noradrenaline and neuroactive tryptophan metabolism was upregulated by enhanced production of dopamine beta hydroxylase, kynurenine-3-monooxygenase (KMO) and quinolinate phosphoribosyl transferase (Qprt).

Conclusion: The significant proinflammatory cytokine production in the brain of humanized NOD DQ8 mice with active CeD confirms a gut-brain immune communication in CeD. This is accompanied by elevated transcript levels of inflammation-induced mediators.

Importantly, enzymes encoding neurotransmitter synthesis are upregulated, which may explain fatigue and mental dysfunction in patients with active CeD.

References:

- (1) Lindfors, K., Ciacci, C., Kurppa, K., Lundin, K. E. A., Makharia, G. K., Mearin, M. L., Murray, J. A., Verdu, E. F., & Kaukinen, K. (2019). Coeliac disease. *Nature reviews. Disease primers*, 5(1), 3. <https://doi.org/10.1038/s41572-018-0054-z>
- (2) Verdu, E. F., & Schuppan, D. (2021). Co-factors, Microbes, and Immunogenetics in Celiac Disease to Guide Novel Approaches for Diagnosis and Treatment. *Gastroenterology*, 161(5), 1395–1411.e4. <https://doi.org/10.1053/j.gastro.2021.08.016>

(3) Belpinar, A., Dağ, Y. S., Arıcıoğlu Sülün, A., Yayan, E. H., & Varol, F. İ. (2023). The effect of anxiety and depression levels of children with celiac disease on quality of life. *Journal of pediatric nursing*, 73, e260–e265. <https://doi.org/10.1016/j.pedn.2023.09.019>

(4) Sharma, N., Singh, K., & Senapati, S. (2021). Celiac disease poses significant risk in developing depression, anxiety, headache, epilepsy, panic disorder, dysthymia: A meta-analysis. *Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology*, 40(5), 453–462. <https://doi.org/10.1007/s12664-021-01215-2>

Disclosure: Nothing to disclose.

OP006

WITHDRAWN

Dyspepsia and *H.pylori*

15:30-16:30 / Lehar 1

OP007

EFFICACY AND SAFETY OF TEGOPRAZAN IN FUNCTIONAL DYSPEPSIA: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL STUDY

T. He¹, J. Zhang¹, R. Feng², L. Zhong³, M. Lin⁴, Q. Xiang⁵, X. Chen⁵, H. Chen², L. Liu¹

¹Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China, ²The First Veterans Hospital of Sichuan Province, Chengdu, China, ³Sichuan Tianfu New Area People's Hospital, Chengdu, China, ⁴West China (Airport) hospital Sichuan University, Chengdu, China, ⁵The Sixth People's Hospital of Chengdu, Chengdu, China

Contact E-Mail Address: ht3711@163.com

Introduction: Functional dyspepsia (FD) is one of the most common diseases of the digestive system, which comprises two subtypes, postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). Acid suppression therapy has been recognized as the first-line treatment for *H.pylori*-negative FD patients. Potassium-competitive acid blocker (PCAB), a novel acid suppressant, has the characteristics of faster onset of effect and more stable acid suppression compared with traditional proton pump inhibitor (PPI). However, there has been no prospective study of PCAB for FD treatment.

Aims & Methods: This study was therefore conducted to investigate the efficacy and safety of PCAB in FD patients, and initially explore the effects of PCAB on gut microbiota. Patients diagnosed with FD were included prospectively. Eligible subjects were randomly assigned to the trial group and placebo group by 2:1, respectively, to receive Tegoprazan or placebo treatment with 50mg once a day for 2 weeks. 7-point global overall symptom scale (GOSS) was used to evaluate the relief of dyspepsia symptoms (primary endpoint) before the trial and at 1 and 2 weeks after randomization. Quality of life was assessed using the short form Nepean dyspepsia index (SFNDI). The generalized anxiety disorder-7 (GAD-7) and patient health questionnaire -9 (PHQ-9) were used to evaluate anxiety and depression, respectively. Stool samples were collected for 16SrRNA sequencing to evaluate gut microbiota alterations. Blood samples were collected to detect blood routine and blood biochemistry, and drug-related adverse events reported by subjects were collected to evaluate the safety of Tegoprazan.

Results: A total of 84 subjects were randomized, including 55 in the trial group and 29 in the placebo group. Among the subjects, 58.3% (49/84) were females, the median age was 51.00 (38.75, 55.00) years, and the mean BMI was 21.21 ± 3.06kg/m². For FD subtypes, EPS accounted for 44.0% (37/84), and no significant difference between the two groups was evident. In addition, there were no significant differences in the GOSS score, GAD-7 score and PHQ-9 score between the two groups at baseline. In the ITT analysis, the overall response rate was 25.5% (14/55) in the trial group and 17.2% (5/29) in the placebo group at 1 week, with no significant difference between the two groups (*P*=0.392). The 2-week response rate was 38.2% (21/55) in the trial group and 27.6% (8/29) in the placebo group, with no significant difference between the two groups (*P*=0.331). The results of PP analysis were consistent with ITT analysis. In the analysis of FD subtype, the response rate of EPS receiving Tegoprazan for 1 week was 45.8% (11/24), and that of the placebo group was 7.7% (1/13), with significant difference between the two groups (*P*=0.027). The response rate at 2 weeks of treatment with Tegoprazan was 50.0% (12/24), and the response rate after 2 weeks of placebo treatment was 15.4% (2/13), with no significant difference between the two groups (*P*=0.074).

No significant difference was found between Tegoprazan and placebo on PDS ($P > 0.05$). In terms of gut microbiota, after 2 weeks of Tegoprazan treatment, the abundance of fecal genus *streptococcus* increased significantly ($P < 0.001$), especially *streptococcus salivarius*.

There were no significant differences in the incidence of adverse events between the trial group and the placebo group ($P > 0.05$). No severe adverse events occurred in this study.

Conclusion: Tegoprazan is suitable for short course treatment of EPS. For patients requiring long-term treatment with Tegoprazan, the benefits of acid suppression should be weighed against the risk of intestinal microbiota dysbiosis. Tegoprazan had a similar safety profile to placebo.

Disclosure: Nothing to disclose.

OP008

CHARACTERISING THE DUODENAL IMMUNOLOGICAL ENVIRONMENT AND IMMUNOMODULATORY EFFECTS OF HIGH-DOSE PROTON PUMP INHIBITOR THERAPY IN FUNCTIONAL DYSPESIA

M. Ceulemans¹, P. Huyghe¹, J. Toth¹, I. Jacobs², J. Cremer², L. Wauters¹, J. Tack¹, T. Vanuytsel¹

¹KU Leuven, Translational Research Center for Gastrointestinal Disorders, Leuven, Belgium, ²KU Leuven, Allergy and Clinical Immunology, Leuven, Belgium

Contact E-Mail Address: matthias.ceulemans@kuleuven.be

Introduction: The pathophysiology of functional dyspepsia (FD) is still incompletely understood, although duodenal immune activation with increased eosinophil and mast cell numbers have been reported¹. However, advanced characterisation of the duodenal immune infiltrate beyond routine histology is largely lacking.

Acid suppression with proton pump inhibitors (PPI) is the first line therapy for FD. A routine PPI course was shown to have additional anti-inflammatory effects in the duodenum², although the underlying mechanisms remain to be studied.

Aims & Methods: We aimed to perform the most extensive characterisation of the duodenal immunological environment in FD so far, and assess the immunomodulatory effects of high-dose PPI therapy. Gastroduodenoscopy with duodenal biopsies was performed in Rome IV FD patients before and after 4 weeks PPI (pantoprazole 40mg bid) and healthy controls (HC). Eosinophils and mast cells were quantified via histology and in fresh single cell suspensions by flow cytometry on an LSR Fortessa flow cytometer (BD). Similarly, T cell subsets were characterised by flow cytometry. Gastrointestinal (GI) symptoms were recorded through questionnaires (PAGI-SYM). Cortisol awakening response (CAR), as well as mast cell tryptase and eosinophil derived neurotoxin (EDN) in duodenal biopsy supernatants were measured using ELISA. Data were analysed with Mann-Whitney *U* tests and paired *t* tests, or by linear or mixed models in SAS software.

Results: Data from 30 FD patients (25 F, mean $\pm$ SD age 32 ± 13 yr.) before and after PPI, and 30 HC (23 F, 30 ± 10 yr.) at baseline were obtained. GI-specific symptoms were higher in FD vs controls and decreased after PPI, while CAR was reduced after PPI (Table).

Duodenal tryptase but not EDN release was higher in FD vs. HC. Mast cell numbers were similar at baseline via histology and flow cytometry, but increased after PPI with an increased side scatter profile ($P = 0.06$) reflecting less degranulation.

Eosinophil numbers were not different, although PPI altered their surface marker expression with decreased IL5R α ($P = 0.02$) and CD63 ($P = 0.08$) but increased CD69 ($P = 0.03$) expression. Cytotoxic T cell maturation was elevated in FD with higher CD45RA- but lower CD45RA+ CD8+ T cells, driven

by higher effector memory CD8+ T cells ($P = 0.02$) and lower TEMRA CD8+ T cells ($P = 0.01$). CD45RA- and CD45RA+ CD8+ T cell levels tended to normalise after PPI, while naive Tregs increased after therapy.

Variable (mean $\pm$ SD)	HC	FD	FD vs. HC (p-value)	FD + PPI	FD vs. FD + PPI (p-value)
PAGI-SYM score	0.37 $\pm$ 0.41	2.42 $\pm$ 0.84	<0.0001	1.76 $\pm$ 0.96	0.0002
Cortisol awakening response (ng/mL)	3.94 $\pm$ 1.73	3.95 $\pm$ 2.58	0.33	2.87 $\pm$ 1.97	0.05
Duodenal tryptase (μ g/g biopsy)	0.38 $\pm$ 0.17	0.60 $\pm$ 0.32	0.004	0.53 $\pm$ 0.31	0.33
Duodenal EDN (μ g/g biopsy)	4.69 $\pm$ 2.48	4.81 $\pm$ 2.88	0.62	5.28 $\pm$ 4.32	0.78
Mast cells (% leukocytes)	2.97 $\pm$ 1.38	2.49 $\pm$ 1.12	0.16	3.02 $\pm$ 1.51	0.04
Eosinophils (% leukocytes)	2.69 $\pm$ 1.40	2.39 $\pm$ 1.14	0.47	2.33 $\pm$ 1.54	0.26
CD45RA+ CD8+ T cells (% CD8+ T cells)	21.37 $\pm$ 9.28	15.84 $\pm$ 11.77	0.009	18.86 $\pm$ 12.62	0.08
CD45RA- CD8+ T cells (% CD8+ T cells)	78.62 $\pm$ 9.29	84.16 $\pm$ 11.76	0.008	81.14 $\pm$ 12.63	0.07
Naïve Treg cells (% CD4+ T cells)	1.23 $\pm$ 1.62	1.15 $\pm$ 1.40	0.92	1.78 $\pm$ 1.55	0.04

Conclusion: High-dose proton pump inhibitors improved symptoms in FD and reduced an objective marker of stress. Interestingly, duodenal tryptase release was increased in FD, although not supported by differences in duodenal mast cells or eosinophils, measured via flow cytometric evaluation. Our data suggest that advanced techniques should complement routine histological evaluation in FD to confirm previously reported immune alterations, which may have overestimated the extent of duodenal immune activation in FD. Lastly, subtle alterations in cytotoxic T cell maturation status were normalised after high-dose PPI therapy, which warrants further investigation.

References: 1. Ceulemans *et al.* Frontiers in Neuroscience 2022

2. Wauters *et al.* Gastroenterology 2021

Disclosure: Nothing to disclose.

OP009

EXPERIENCE WITH SINGLE-CAPSULE BISMUTH QUADRUPLE THERAPY IN 11,000 PATIENTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, Á. Pérez-Aísa², L. Rodrigo³, S.J. Martínez-Domínguez⁴, A.J. Lucendo⁵, J. Tejedor-Tejada⁶, B.J. Gómez Rodríguez⁷, Ó. Núñez⁸, M. Perona⁹, A. Moreno Loro¹⁰, J.M. Huguet¹¹, M. Pabón-Carrasco¹², M. Romano¹³, M. Castro-Fernández¹², M. Pavoni¹⁴, A. Gasbarrini¹⁵, I. Ortiz-Polo¹⁶, F. Bermejo¹⁷, M. Planella¹⁸, J. Barrio¹⁹, M. Areia²⁰, G. Losurdo²¹, E. Alfaro⁴, M. Soledad Marcos²², G. Kamto²³, E. Iyo²⁴, R. Pajares Villarroja²⁵, B. Velayos²⁶, A.B. Pozo Blanco²⁷, R. Rosania²⁸, M. Fernandez-Bermejo²⁹, A. G. Gravina¹³, N. Alcaide²⁶, A. Keco-Huerga¹², C. Ramirez¹⁸, L. Fernández-Salazar²⁶, A. Cuadrado³⁰, V. Milivojevic³¹, D. Compare³², L. Hernández³³, R. Marcos-Pinto³⁴, W. Marlicz³⁵, M. Venerito²⁸, M. Doulberis³⁶, A. Cano-Català³⁷, P. Parra¹, L. Moreira³⁸, F. Megraud³⁹, C. O'Morain⁴⁰, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Department of Gastroenterology, Hospital Universitario

Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ³Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ⁴Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁵Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ⁶Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ⁷Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ⁸Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ⁹Department of Gastroenterology, Hospital Quirón Marbella, Marbella, Spain, ¹⁰Department of Gastroenterology, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ¹¹Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ¹²Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ¹³Department of Gastroenterology and Endoscopy, Department of Precision Medicine, Università Vanvitelli, Napoli, Italy, ¹⁴Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ¹⁵Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ¹⁶Department of Gastroenterology, Hospital Universitario y Politécnico la Fe, Valencia, Spain, ¹⁷Department of Gastroenterology, Hospital Universitario de Fuenlabrada, Fuenlabrada, Spain, ¹⁸Department of Gastroenterology, Hospital Universitari Arnau de Vilanova, Institut de Recerca Biomèdica de Lleida (IRBL), Lleida, Spain, ¹⁹Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ²⁰Department of Gastroenterology, Portuguese Oncology Institute of Coimbra, Faculty of Medicine of the University of Porto (FMUP), Center for Health Technology and Services Research (CINTESIS), Coimbra, Portugal, ²¹Department of Gastroenterology, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari, Bari, Italy, ²²Department of Gastroenterology, Hospital 12 de Octubre, Madrid, Spain, ²³Hepatic Medical, Private Medical Center, Krakow, Poland, ²⁴Department of Gastroenterology, Hospital Comarcal de Inca, Inca, Spain, ²⁵Department of Gastroenterology, Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain, ²⁶Department of Gastroenterology, Hospital Clínico de Valladolid, Valladolid, Spain, ²⁷Department of Gastroenterology, Hospital Arnau Vilanova-Llíria, Valencia, Spain, ²⁸Department of Gastroenterology, Hepatology and Infectious Diseases, Otto von Guericke University Hospital, Magdeburg, Germany, ²⁹Hospital Parque San Francisco, Cáceres, Spain, ³⁰Gastroenterology and Hepatology Department, Marqués de Valdecilla University Hospital, Clinical and Translational Research in Digestive Diseases, Valdecilla Research Institute (IDIVAL), Santander, Spain, ³¹Clinical Center of Serbia and School of Medicine, University of Belgrade, Belgrade, Serbia, ³²Department of Gastroenterology, "Federico II" University, Napoli, Italy, ³³Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁴Gastroenterology Department, Centro Hospitalar do Porto, Universidade do Porto, Instituto De Ciências Biomédicas de Abel Salazar, Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal, ³⁵Department of Gastroenterology, Pomeranian Medical University in Szczecin, The Centre for Digestive Diseases, Endoklinika, Szczecin, Poland, ³⁶Department

of Gastroenterology, Kantonsspital Aarau, Aarau, Switzerland, ³⁷Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ³⁸Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ³⁹INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴⁰School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: There has been a resurgence in the use of bismuth quadruple therapy (PPI, bismuth, tetracycline and metronidazole) in Europe with the commercialisation of a three-in-one single-capsule formulation, but the experience with this regimen is still limited.

Aims & Methods: To evaluate the effectiveness and safety of the three-in-one single-capsule in the European Registry on *Helicobacter pylori* Management (Hp-EuReg).

International, multicenter, prospective, non-interventional registry aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists (Hp-EuReg). All infected adult patients treated with 10-day single-capsule according to data sheet (3 capsules/6h) or alternative three times a day (4 capsules/8h) prescriptions were systematically registered at AEG-REDCap e-CRF until December 2023. Variables included: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed, and data were subject to quality review.

Results: Of the 70,683 patients included in the Hp-EuReg, 11,130 (16%) received single-capsule bismuth quadruple therapy. The majority of these patients were naïve (77%), with an average age of 51 years, 61% female and 14% with peptic ulcer. Overall, the single-capsule achieved a high eradication rate based on the mITT (92%) and PP (93%) analyses. Effectiveness (mITT) was higher when using the single-capsule as a first-line treatment (94%), but it had also high effectiveness as a rescue therapy, both in second-line (88%) or subsequent lines of therapy (3rd-6th lines: 84%) (Table 1).

Compliance with treatment (>90% of drug intake) was reported in 97% of cases and was the factor most closely associated with the effectiveness of treatment. Adverse events (26%) were generally mild and transient; only 0.1% of patients reported serious adverse events, leading to the discontinuation of treatment in 1.7% of patients.

	Use, N (%)	mITT, N (%)	95% CI	PP, N (%)	95% CI
Overall	11,130 (16*)	10,441 (92)	(91-93)	10,248 (93)	(92-93)
1 st line (naïve)	8,551 (77)	8,041 (94)	(93-94)	7,909 (94)	(94-95)
2 nd line	1,783 (16)	1,659 (88)**	(86-89)	1,621 (89)	(87-90)
3 rd to 6 th line	796 (7.2)	741 (84)	(81-87)	718 (85)	(83-88)

*Of the total of treatments included in the Hp-EuReg up to December 2023 (i.e., N= 70,683); **achieved over 90% effectiveness when therapy was optimised (i.e., using standard-dose PPIs, that is 40 mg omeprazole equivalent twice a day); mITT: modified intention-to-treat; PP: per-protocol; N: total number of patients analysed, 95% CI –confidence interval.

Table 1. Three-in-one single-capsule effectiveness in first-line and consecutive rescue treatment lines.

Conclusion: The 10-day treatment with single-capsule bismuth quadruple therapy achieves *H. pylori* eradication in approximately 90% of patients by mITT in real-world clinical practice, both as a first-line and rescue treatment, with a favourable safety profile.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

OP010

VONOPRAZAN-DUAL AND TRIPLE THERAPIES WERE NON-INFERIOR TO BISMUTH-BASED QUADRUPLE THERAPY AS FIRST-LINE THERAPY FOR *HELICOBACTER PYLORI* INFECTION IN CHINA: A THREE-ARM, RANDOMIZED CLINICAL TRIAL

K.S. Cheung^{1,2}, T. Lyu¹, Z. Deng¹, S. Han¹, L. Ni¹, J. Wu¹, J.T. Tan², H.Y. Ng³, W.K. Leung², W.-K. Seto^{1,2}

¹The University of Hong Kong-Shenzhen Hospital, Department of Medicine, Shenzhen, China, ²The University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong, ³The University of Hong Kong, School of Clinical Medicine, Hong Kong, Hong Kong

Contact E-Mail Address: mongolhorse2002@gmail.com

Introduction: There are currently no studies comparing vonoprazan-dual, vonoprazan-triple therapies and classic bismuth quadruple therapy.

Aims & Methods: We aimed to compare efficacy of vonoprazan-dual or triple therapies and bismuth-quadruple therapy for treatment-naïve *Helicobacter pylori* (HP) infection in Southern China, where primary resistance rates of clarithromycin and levofloxacin are >30%.

Between March 2022 and August 2023, treatment-naïve HP-infected adults were randomly assigned to receive one of the three 14-day regimens (1:1:1 ratio): vonoprazan-dual (VA-dual; vonoprazan 20mg twice daily and amoxicillin 1g thrice daily), vonoprazan-triple (VAC-triple; vonoprazan 20mg/amoxicillin 1g/clarithromycin 500mg twice daily), or bismuth-quadruple therapy containing bismuth, esomeprazole, tetracycline and metronidazole.

Primary outcome was noninferiority in HP eradication, evaluated by UBT 4-6 weeks post-treatment by intention-to-treat (ITT) (based on all recruited subjects who took at least one dose of treatment regimen, and those lost to follow-up were considered as treatment failure cases), modified intention-to-treat (mITT) (based on patients who took at least one dose of the treatment and completed follow-up) and per-protocol (PP) analysis (based on subjects who completed 14-day treatment and rechecked UBT). Bonferroni-adjusted p-value of <0.017 was used to determine statistical significance. Primary outcome was noninferiority in HP eradication, evaluated by UBT 4-6 weeks post-treatment by intention-to-treat (ITT) and per-protocol (PP) analysis (based on subjects who completed 14-day treatment and rechecked UBT).

Comparative non-inferiority between bismuth-quadruple and VA-dual or VAC-triple was assessed by one-sided μ test and derivation of a two-sided 95% confidence interval (CI), with noninferiority being determined by a lower 95% CI end more than -10% with a Bonferroni-adjusted p-value of <0.017. A two-sided p-value of 0.05 was used to define statistical significance for other analyses.

Results: 298 subjects (mean age:35.7±8.4 years; male:134 [45.0%]; body mass index:23.2±3.5 kg/m²; VC-dual:100, VAC-triple:98, bismuth-quadruple:100) were enrolled, and 292 (98.0%) had UBT rechecked. ITT analysis showed both VA-dual (eradication rate of 96.0%) and VAC-triple therapies (95.9%) were non-inferior to bismuth-quadruple therapy (92.0%) (difference:4.0%, 95% CI:-2.9% to 11.5%, p<0.001; and 3.9%, 95% CI:-3.1% to 11.5%, p<0.001, respectively). mITT analysis also showed non-inferiority of VA-dual and VAC-triple therapies to bismuth-quadruple therapy (97.0% and 96.9% vs 95.8%, with difference:1.1% and 1.1%, p=0.002 and 0.002, respectively).

Similar observation was noted for PP analysis (96.7% and 96.7% vs 97.4%, with difference:-0.7% and -0.7%, p=0.009 and 0.010, respectively) (Table 1). The frequency of adverse events was 39.0%, 56.1% and 71.0% in VA-dual, VAC-triple and bismuth-quadruple therapies, respectively.

	VA-dual vs bismuth-quadruple therapy			VAC-triple vs bismuth-quadruple therapy			VA-dual vs VAC-triple therapy		
	VA-dual therapy	VAC-triple therapy	Bismuth-quadruple therapy	Difference (95% CI)	Non-inferiority p-value	Difference (95% CI)	Non-inferiority p-value	Difference (95% CI)	Non-inferiority p-value
ITT	96.0% (96/100)	95.9% (94/98)	92.0% (92/100)	4.0% (-2.9% to 11.5%)	<0.001	3.9% (-3.1% to 11.5%)	<0.001	0.08% (-6.3% to 6.5%)	0.005
mITT	97.0% (96/99)	96.9% (94/97)	95.8% (92/96)	1.1% (-4.9% to 7.6%)	0.002	1.1% (-5.1% to 7.5%)	0.002	0.01% (-5.8% to 6.1%)	0.004
PP	96.7% (89/92)	96.7% (87/90)	97.4% (75/77)	-0.7% (-6.9% to 6.1%)	0.009	-0.7% (-7.1% to 6.0%)	0.010	0.01% (-6.3% to 6.5%)	0.006

Abbreviation: VA-dual, vonoprazan dual; VAC-triple, vonoprazan triple; CI, confidence interval; ITT, intention-to-treat analysis; mITT, modified intention-to-treat analysis; PP, per protocol analysis
The p-values were adjusted for multiple comparisons using Bonferroni's correction. The significance level was set at 0.05/3 = 0.017 for each comparison.

Table 1. *Helicobacter pylori* eradication rates of vonoprazan-dual, vonoprazan-triple and bismuth-quadruple therapies

Conclusion: VA-dual and VA-triple therapies were non-inferior to bismuth-quadruple therapy in Southern China. Given the lower adverse effects and fewer antibiotic use, VA-dual therapy is the preferred first-line treatment for HP infection.

Disclosure: This study was supported by the National Natural Science Foundation of China (Grant No. 81903581), the Shenzhen Science and Technology Program (Grant Nos. JCYJ20190807150005699 and RCBS20200714115000009), the Shenzhen Key Medical Discipline Construction Fund (Grant No. SZXK059), the Shenzhen Key Laboratory of Prevention and Treatment of Severe Infections (Grant No. ZDSYS20200811142804014), and the Health Commission Grant of Guangdong Province, China (ref. no. B2021239).

OP011

PHARMACOKINETICS AND PHARMACODYNAMICS OF LINAPRAZAN GLURATE AFTER MULTIPLE ORAL DOSES UP TO 14 DAYS IN HEALTHY SUBJECTS

M. Fležar^{1,2}, K. Larsson³, K. Andersson³, G. Huledal³, K. Katkits³, E. Yektaei³, P. Unge³

¹University of Ljubljana, Ljubljana, Slovenia, ²University Clinic Golnik, Golnik, Slovenia, ³Cinclus Pharma Holding AB (publ), Stockholm, Sweden

Contact E-Mail Address: kajsa.larsson@cincluspharma.com

Introduction: Linaprazan glurate (LG) is a next generation P-CAB, a prodrug to linaprazan, with an excellent clinical efficacy in erosive esophagitis (1-2).

The acid control properties of LG were assessed by the holding time ratio (HTR) i.e., percentage of time with intragastric pH>4, during Day 1 and 14 of LG administered once daily (QD) or twice daily (BID) at 3 dose levels. Pharmacokinetic (PK) profiles for LG and Linaprazan were determined and PK parameters, area under the plasma concentration time profile (AUC) and peak plasma concentration (C_{max}) derived.

Aims & Methods: 73 healthy subjects randomized into six dosing groups and received LG, a total of 67 subjects completed the study and had at least one evaluable pH measurement (Table 1).

Measurement of intragastric pH was performed during 24 hours on Day 1 and on Day 14, by means of a pH-measuring electrode in the stomach inserted by the nasogastric route. Intragastric pH was measured every sec-

ond. The pH>4 HTR is presented as the mean of the 10 min median per dose group and day. Blood samples for PK parameters were also collected.

Results: There was a rapid onset of intragastric acid control achieved already within 90 min after the intake of the first dose of LG, irrespective of dose level, with a clear dose response. The HTRs presented in Table 1 show a dose response with pH>4 HTR similar at Day 1 and Day 14. Already on Day 1, the pH>4 HTR reached approximately 90% in the two highest dosing groups (50 mg and 75 mg BID), with a minor difference in acid control between these doses, particularly at steady state (Table 1).

Linaprazan AUC and C_{max} increased approximately in proportion to dose and were comparable on Day 1 and Day 14. AUC and C_{max} for LG was approximately 10-fold lower than for linaprazan.

A *post-hoc* analysis of the pH>4 HTR excluding the initial 90 min after first dosing (pH>4 HTR 1.5-24h) showed that the pH>4 HTR 1.5-24h was close to the Day 14 pH>4 HTR in all dosing cohorts, suggesting a pH-control near steady state already 1.5 hours after the first dosing. It is noteworthy that a pH>4 HTR 1.5-24h above 90% is seen, not only in the 75 mg BID group as noted in the primary endpoint, but also in the 50 mg BID group (Table 1). Comparing 50 mg QD and 25 mg BID, a more sustained pH>4 HTR was seen with BID dosing, with more than 10-15 percentage points higher pH>4 HTR already from the start, indicating a better pharmacodynamic yield when dividing the dose.

There was one serious adverse event in the study, a concussion that occurred before the first dose of LG. The most observed treatment emergent adverse event (TEAE) was headache. There was no dose related increase in TEAEs or other findings as assessed by physical examinations, vital signs, ECG, and laboratory parameters.

Day	Statistics	25 mg LG	50 mg LG	75 mg LG	25 mg LG	50 mg LG	75 mg LG
		QD (N=12)	QD (N=12)	QD (N=13)	BID (N=9)	BID (N=11)	BID (N=10)
Day 1 pH >4 HTR	n	12	12	12	9	11	9
	Mean (SD)	48.0 (23.23)	64.6 (13.33)	68.1 (23.48)	76.0 (13.52)	87.4 (8.62)	94.5 (4.18)
Day 1 (1.5-24h) pH >4 HTR	n	12	12	12	9	11	9
	Mean (SD)	51.0 (24.91)	68.9 (14.02)	73.7 (24.78)	80.5 (14.12)	91.5 (8.98)	98.1 (3.10)
Day 14 pH >4 HTR	n	12	12	11	9	11	8
	Mean (SD)	48.5 (30.62)	63.9 (20.09)	87.2 (11.44)	76.9 (20.13)	95.7 (5.55)	99.0 (1.54)

Table 1: Descriptive statistics of percentage of time within intragastric pH categories- based on 10-minute medians of pH.

Conclusion: A rapid onset of pH>4 HTR was seen with LG with a clear dose response. The two highest dosing groups achieved above 90% pH>4 HTR excluding the initial 90 min after the first dose.

Repeated oral doses of LG 25, 50 and 75 mg QD and BID for 14 days were safe and well tolerated.

References:

1. LINAPRAZAN GLURATE IS HIGHLY EFFECTIVE IN TREATING MODERATE TO SEVERE EROSIIVE ESOPHAGITIS: A DOUBLE-BLIND, RANDOMIZED, DOSE FINDING STUDY. Sharma P *et al*, United European Gastroenterology Journal 2023; 11 (Supplement 8).
2. LINAPRAZAN GLURATE IS WELL TOLERATED IN THE TREATMENT OF PATIENTS WITH EROSIIVE ESOPHAGITIS: A DOUBLE-BLIND, RANDOMIZED, DOSE FINDING STUDY, Sharma P *et al*, United European Gastroenterology Journal 2023; 11 (Supplement 8)

Disclosure: Kajsa Larsson, Kjell Andersson, Gunilla Huledal, Elham Yektaei and Kristofer Katkits are employees of Cinclus Pharma. Peter Unge is a consultant and senior advisor at Cinclus Pharma.

**Pancreatic diseases:
From mechanisms to therapy**

15:30-16:30 / Lehar 2

OP012

**TIME COURSE DEVELOPMENT OF CHRONIC PANCREATITIS
FOLLOWING ACUTE PANCREATITIS. INTERIM ANALYSIS OF THE
GOULASH PLUS TRIAL**

M. Lipp^{1,2}, A. Mikó^{3,4}, A. Szentesi^{2,4}, Z. Abonyi-Tóth², V. Vass⁴, K. Márta^{1,2}, F. Izbéki⁵, L. Gajdán⁵, B. Erőss^{1,2,4}, M. Verbói⁴, Á. Vincze⁶, P.J. Hegyi^{1,2}, P. Sarlós⁶, J. Bajor⁶, V. Lillik^{2,5}, P. Hegyi^{1,2,4,7}, Hungarian Pancreatic Study Group

¹Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary, ²Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ³Department of Medical Genetics, Medical School, University of Pécs, Pécs, Hungary, ⁴Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁵Szent György Teaching Hospital of Fejér County, Szekesfehérvár, Hungary, ⁶Division of Gastroenterology, First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁷Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, University of Szeged, Szeged, Hungary

Contact E-Mail Address: lipp.monika@gmail.com

Introduction: 96-98% of patients survive acute pancreatitis (AP), but in the post-AP phase, patients are at high risk of morbidity and mortality. The primary objective of the GOULASH PLUS (ISRCTN63396106) longitudinal, observational multicentre study is to investigate the development of chronic pancreatitis (CP) following AP. The GOULASH PLUS trial reached 50% of the planned patient enrolment. This interim data analysis aims to understand the time course evolution of CP after AP.

Aims & Methods: 360 patients were yearly followed after AP. We formed four groups according to the baseline morphology status of the pancreas: 1) AP with one episode, 2) RAP with two episodes, 3) ECP with characteristic signs on imaging or three or more episodes of AP 4) CP: Ultrasound or CT were used in the first and third year, whereas, endoscopic ultrasound or magnetic-resonance-cholangiopancreatography in the second and fourth year of follow-up.

Results: Among the 360 patients followed after AP, 269 (74.7%) had AP, 42 (11.7%) RAP, 27 (7.5%) ECP, and 22 (6.1%) had CP at the time of the baseline AP episode. The following data represent the results at 1, 2, 3, and 4 years after AP. In the AP group, ECP was developed in 3%, 12%, 14%, and 18%, whereas, CP was diagnosed in 1%, 6%, 6%, and 11%, respectively. In the RAP population, ECP was developed in 17%, 19%, 21%, and 42% while CP developed in 0%, 0%, 4%, and 8%. In the ECP patient group, CP was developed in 12%, 25%, 35%, and 36%. 15% of patients had exocrine pancreatic insufficiency (EPI) at the first year visit, while this increased to 21% by the fourth annual visit.

Conclusion: RAP and ECP accelerate CP development. Due to the fast progression, it is important to find risk factors and biomarkers associated with recurrence and early morphology changes and to define possible early interventions to avoid or delay the progression to CP.

Disclosure: Nothing to disclose.

OP013

MODELLING JOHANSON-BLIZZARD SYNDROME IN A DISH – MOLECULAR INSIGHTS INTO UBR1 DEFICIENCY USING PLURIPOTENT STEM CELL-DERIVED PANCREATIC ORGANOIDS

L. Reichardt¹, M. Zenker², B. Küster³, M. Breunig¹, A. Kleger¹

¹Ulm University Hospital, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Otto-von Guericke University Magdeburg, Institute of Human Genetics, Magdeburg, Germany,

³Technical University of Munich, Chair of Proteomics and Bioanalytics, München, Germany

Contact E-Mail Address: leon.reichardt@uni-ulm.de

Introduction: Johanson-Blizzard syndrome (JBS) is a rare autosomal recessive genetic disorder characterized by congenital exocrine pancreatic insufficiency, nasal wing aplasia, and various symptoms of varying severity. Although we have previously identified bi-allelic loss-of-function mutations in the *UBR1* gene as the genetic cause of JBS, the precise molecular pathomechanism remains unknown. Since loss of *UBR1* can be partly compensated in mice, no model system has existed to fully recapitulate the phenotype of JBS patients.

Aims & Methods: We have employed *in vitro* differentiation of human pluripotent stem cells (PSCs) to unravel the molecular mechanism of pancreatic insufficiency in JBS. Our collection includes JBS-specific PSCs derived from patient's iPSCs, isogenic controls, and CRISPR/Cas9-engineered hESCs, enabling advanced disease modeling.

Results: *UBR1*-deficient and proficient PSCs exhibited comparable growth and differentiation patterns until the pancreatic progenitor (PP) stage, consistent with a normal pancreatic primordium in JBS patients. To explore later stages of pancreatic development, we employed xenograft and *ex vivo* culture models. Remarkably, grafts from *UBR1*-deficient PPs showed a significant absence of acinar pancreatic tissue after 8 weeks. Our immune cell-free model highlights a potential cell-intrinsic cause of pancreatic tissue degeneration in JBS.

Currently, we are conducting time-resolved *ex vivo* and xenograft analyses alongside our *in vitro* differentiation into ductal, acinar, and endocrine organoids, to intricately dissect the degeneration processes. *UBR1* functions as an E3 ubiquitin ligase in the N-end rule pathway, playing a crucial role in regulating protein degradation. Consistent with its function, global quantitative proteomics revealed a stage-specific upregulation of multiple proteins in *UBR1*-ablated cells starting from the PSC and PP stages. To pinpoint potential disease-causing substrates of JBS, we are currently establishing an E3-ligase substrate trapping strategy.

Conclusion: In summary, our sophisticated JBS model enables us to recapitulate the disease mechanism of this rare and severe syndrome not only in the pancreas but also beyond, offering valuable insights into its pathophysiology.

Disclosure: Nothing to disclose.

OP014

INTRADUCTAL CANCER EXTENSION AND PANCREATIC PARENCHYMAL ATROPHY IN EARLY-STAGE PANCREATIC DUCTAL ADENOCARCINOMA: A MULTICENTER RETROSPECTIVE STUDY

M. Miki¹, A. Masuda¹, M. Takenaka², H. Shiomi³, T. Iemoto⁴, H. Tsumura⁵, M. Tsujimae¹, H. Toyama⁶, K. Sofue⁷, E. Ueshima⁷, S. Omoto², A. Yoshida², T. Fukunaga², H. Tanaka², R. Nakano³, S. Ota¹, T. Kobayashi¹, A. Sakai¹, M. Kanzawa⁸, T. Itoh⁸, Y. Kodama¹
¹Kobe University Graduate School of Medicine, Division of Gastroenterology, Department of Internal Medicine, Kobe, Japan, ²Kindai University Faculty of Medicine, Department of Gastroenterology and Hepatology, Osaka-Sayama, Japan, ³Hyogo College of Medicine, Division of Gastroenterology and Hepatobiliary and Pancreatic Diseases, Nishinomiya, Japan, ⁴Kita-Harima Medical Center, Department of Internal Medicine, Ono, Japan, ⁵Hyogo Cancer Center, Department of Gastroenterological Oncology, Akashi, Japan, ⁶Kobe University Graduate School of Medicine, Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe, Japan, ⁷Kobe University Graduate School of Medicine, Department of Radiology, Kobe, Japan, ⁸Kobe University Graduate School of Medicine, Division of Diagnostic Pathology, Kobe, Japan

Contact E-Mail Address: mk2128@med.kobe-u.ac.jp

Introduction: While advanced pancreatic cancer is a malignant tumor with a high mortality rate and poor prognosis, early-stage pancreatic cancer, including carcinoma in situ (CIS), has a favorable prognosis and may be treatable with curative resection. However, several recent reports have shown that even in some cases of early-stage pancreatic cancer, recurrence in the remnant pancreas can occur. Pathologically, the tumor occasionally spreads laterally along the main pancreatic duct, presenting challenges in determining the extent of surgical resection.

Recently, two types of changes in pancreatic parenchymal volume, called focal pancreatic parenchymal atrophy (FPPA) and upstream pancreatic atrophy (UPA), have been reported to indicate the presence of early-stage pancreatic cancer.

It has been reported that in cases of advanced pancreatic cancer with FPPA in previous imaging studies, greater extension along the pancreatic duct has been found. However, in early-stage pancreatic cancer, a comprehensive pathological evaluation of the correlation between cancer location and pancreatic atrophy has not been adequately explored.

Aims & Methods: In early-stage pancreatic cancer without mass, preoperative assessment of intraductal cancer extension along the main pancreatic duct is necessary to determine the extent of surgical resection.

This study aimed to investigate the association between the pattern of pancreatic parenchymal atrophy and intraductal cancer extension using a substantial number of resected specimens of early-stage pancreatic cancer.

Thirty-two patients with early-stage pancreatic cancer who underwent surgery at five participating centers were enrolled. Of the patients, twenty-seven had CIS, and five had microinvasive carcinoma. Pancreatic atrophy was defined as narrowing of the parenchyma compared to the surrounding parenchyma and was classified as either FPPA (partial atrophy surrounding the pancreatic duct stenosis) or UPA (global atrophy caudal to the site of duct stenosis).

We evaluated the correspondence between atrophy on preoperative computed tomography (CT) images and pathologic cancer extension in detail. The length of cancer extension along the main pancreatic duct was calculated as 5 mm per section of a surgically resected pathology specimen (5 mm wide) in which cancer was present. Intraductal cancer extension was defined as an extension exceeding 10 mm.

Results: Preoperative CT revealed FPPA, UPA, and no parenchymal atrophy in 13, 13, and 6 patients. The lateral distance of cancer extension was significantly longer in cases with FPPA than in those without atrophy (median: 20.0 mm vs. 5.0 mm, $P = 0.005$). Furthermore, a significant difference was observed in the distance of cancer extension between the UPA group and the group without atrophy (median: 20.0 mm vs. 5.0 mm, $P = 0.03$). Intraductal cancer extension was present in all but one case of FPPA. 69% (9/13) of the cases with UPA showed intraductal cancer extension, whereas cases without atrophy showed no intraductal cancer extension. Importantly, two patients with FPPA or UPA showed positive resection margins during surgery, and three patients with FPPA or UPA showed recurrence in the remnant pancreas.

Conclusion: The presence of FPPA and UPA indicates lateral cancer extension in early-stage pancreatic cancer. In cases presenting with FPPA and UPA, caution should be exercised while determining the extent of surgical resection. Preoperative assessment of the pancreatic parenchyma may provide valuable insights for determining the extent of surgical resection.

Disclosure: Nothing to disclose.

OP015

INHIBITION OF PLASMINOGEN ACTIVATOR INHIBITOR-1: A PROMISING NEW APPROACH FOR THE TREATMENT OF CHRONIC PANCREATITIS

T. Molnár^{1,2,3}, V. Szabó^{1,2,3}, B. Jójárt^{1,2,3}, N. Csákány-Papp^{1,2,3}, P. Pallagi^{1,2,3}, J. Maléth^{1,2,3}

¹University of Szeged, Albert Szent-Györgyi Medical School, Department of Internal Medicine, Szeged, Hungary, ²ELKH-USz Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ³University of Szeged, HCEMM-USz Molecular Gastroenterology Research Group, Szeged, Hungary

Contact E-Mail Address: moltunde93@gmail.com

Introduction: Chronic pancreatitis (CP) is a complex inflammatory disorder characterized by progressive destruction of the pancreatic tissue, with fibrotic transformation of the tissue as a major morphological feature. The incidence of the disease is steadily increasing, but no specific therapy is currently available, making the identification of new therapeutic targets a priority.

Plasminogen activator inhibitor-1 (SERPINE1/PAI-1) has been implicated in various pathological processes, including fibrosis and inflammation. However, its specific involvement in the pathogenesis of CP is not yet fully understood.

Aims & Methods: We therefore aimed to explore the role of PAI-1 in the development of CP and assess the therapeutic potential of PAI-1 inhibitors as antifibrotic agents to prevent the progression of CP.

The PAI-1 expression of the pancreatic tissue was determined in mouse and human pancreatic tissue samples with immunohistochemistry. CP was induced in FVB/N mice with 8X50 µg/kgbw i.p. cerulein injection, given every hour, every 3 days for a total of 5 times. PAI-1 activity was inhibited with a specific inhibitor, which was administered per os at a dose of 10 mg/kgbw for 6 consecutive days after the 3rd cerulein treatment. To assess the extent of inflammation and fibrosis hematoxylin-eosin and Crossman's trichrome staining were performed, and biochemical assays were used to determine amylase activity and hydroxyproline concentration. PAI-1 expression and location in the pancreas was examined by RT-qPCR and immunofluorescence co-staining.

Results: PAI-1 expression was significantly higher in pancreatic tissue samples obtained from CP patients. After induction of CP in mice, the body weight and the pancreatic weight/body weight ratio significantly reduced, whereas histopathology showed significant pancreatic atrophy

and fibrosis. This was also confirmed by the increased hydroxyproline concentration and decreased amylase activity of the pancreatic tissue. The gene expression of SERPINE1 increased in pancreas tissue and fibroblast cell culture in CP group, moreover the elevated PAI-1 signal localization suggests a possible expression role for activated stellate cells. Administration of PAI-1 inhibitor resulted in a decrease in both body weight and pancreatic weight loss rates, additionally the atrophy, tissue fibrosis, hydroxyproline concentrations and SERPINE1 gene expression were significantly decreased compared to the CP group.

Conclusion: Our results indicate an elevation in PAI-1 expression in CP, with the potential for fibrosis and tissue atrophy reduction by the inhibition of PAI-1. These findings propose PAI-1 as a promising therapeutic target for the treatment of chronic pancreatitis.

Disclosure: Nothing to disclose.

OP016

OPTIMAL DOSE OF PANCREATIC ENZYME REPLACEMENT THERAPY (PERT) FOR PANCREATIC EXOCRINE INSUFFICIENCY (PEI) IN DIFFERENT PANCREATIC DISEASES: RESULTS OF THE EUROPEAN PEI REGISTRY

J.E. Domínguez Muñoz^{1,2}, X. Martinez-Seara³, P. Hegyi⁴, S. Rollet⁵, M. Phillips⁶, F. Bolado Concejo⁷, G. Capurso⁸, G. De Marchi⁹, S. Powell-Brett¹⁰, Y. Dominguez-Novoa^{1,2}, O. Eperjesi⁴, V. Rebours⁵, R. Thompson¹¹, D. Ruiz-Clavijo⁷, G. Lauri¹², A. Brillo⁹, K.J. Roberts¹⁰, J. Iglesias-Garcia^{13,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain, ⁴Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁵AP-HP, Hôpital Beaujon, Gastroenterology and Pancreatic Diseases, Clichy, France, ⁶Royal Surrey County Hospital, School of Biosciences and Medicine, Guildford, United Kingdom, ⁷Hospital de Navarra, Gastroenterology, Pamplona, Spain, ⁸IRCCS Ospedale San Raffaele, Pancreatobiliary Endoscopy and Endosonography Division, Rome, Italy, ⁹Hospital Trust, Gastroenterology B Unit, Verona, Italy, ¹⁰Queen Elizabeth Hospital, Hepatobiliary and Pancreatic Surgery Unit, Birmingham, United Kingdom, ¹¹University of Surrey, School of Biosciences and Medicine, Guildford, United Kingdom, ¹²IRCCS Ospedale San Raffaele, Pancreatobiliary Endoscopy and Endosonography Division, Pescara, Italy, ¹³University Hospital of Santiago de Compostela, Gastroenterology Department. Foundation for Research in Digestive Diseases, Santiago de Compostela, Spain

Contact E-Mail Address: web.icedig@gmail.com

Introduction: PERT aims to alleviate nutrient malabsorption symptoms and restore the nutritional status of patients with PEI. To achieve this, the PERT dose must be optimized for each patient. It is unknown whether the optimal PERT dose varies depending on the underlying cause of PEI.

Aims & Methods: A prospective, multicenter, European registry of PEI was designed involving expert pancreatic centers. Patients diagnosed with PEI of any cause, confirmed by an expert clinician from January 2021, were included. The initial enzyme dose was determined by the clinician and adjusted as necessary during follow-up. The optimal dose in each patient is defined as the dose that achieves the therapeutic goal. A proton pump

inhibitor (PPI) could be added to the enzyme therapy if needed. Results are expressed as median and IQR and analyzed using the U-Mann-Whitney and Kruskal Wallis tests.

Results: 678 patients with PEI who achieved the therapeutic goal are analyzed (mean age 61.2±13.8 years, 63.6% male). The cause of PEI was chronic pancreatitis (CP) in 340 patients (50.1%), pancreaticoduodenectomy (PD) in 116 (17.1%), pancreatic cancer (PC) in 99 (14.6%), acute pancreatitis (AP) in 68 (10.0%) and other in 56 patients (8.2%). The table shows the optimal dose of PERT for the main meal and the daily dose. Patients with PEI secondary to PD and PC required a significantly higher enzyme dose to achieve the therapeutic goal than patients with CP or AP ($p<0.001$). Similarly, patients with PC (78.8%) and PD (74.1%) required a PPI more often than patients with CP (37.2%) or AP (44.1%) ($p<0.001$).

Cause of PEI	Optimal enzyme dose (Ph.U.) with the main meal	Optimal daily enzyme dose (Ph.U.)
Pancreatic cancer	70,000 (50,000-100,000)	210,000 (150,000-325,000)
Pancreatoduodenectomy	75,000 (55,000-100,000)	225,000 (175,000-350,000)
Chronic pancreatitis	50,000 (40,000-70,000)	150,000 (120,000-210,000)
Acute pancreatitis	40,000 (25,000-50,000)	100,000 (75,000-200,000)

Conclusion: The optimal dose of PERT and the need for a PPI are different for different conditions causing PEI. This study demonstrates, for the first time, that patients with PEI following PD and PC require a significantly higher enzyme dosage than those with PEI resulting from CP or AP to alleviate symptoms and restore nutritional status.

Disclosure: Julio Iglesias-García: Advisor Fujifilm

Understanding disease primers of IBD: Part 1

15:30-16:30 / Lehar 3

OP017

GENETIC SUSCEPTIBILITY AND SEVERITY – A FALSE DICHOTOMY? POLYGENIC SCORES OF INFLAMMATORY BOWEL DISEASE SUSCEPTIBILITY ARE PREDICTIVE OF DISEASE SEVERITY COURSE

M.V. Vestergaard^{*1}, K. Allin^{*1,2}, A.K. Nøhr^{*1}, J.V. Torresano Lominchar¹, H.S. Christensen¹, R.F. Brøndum¹, M. Bøgsted¹, H.B. Krarup³, K.R. Nielsen⁴, H. Albæk Jacobsen¹, L. Larsen^{**1,5}, A. Sazonovs^{**1}, T. Jess^{**1,6}, *co-first authors
**co-last authors

¹Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Aalborg University Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ²Aalborg University Hospital, Department of Gastroenterology & Hepatology, Aalborg, Denmark, ³Aalborg University Hospital, Molecular Diagnostics, Aalborg, Denmark, ⁴Zealand University Hospital, Department of Clinical Immunology, Roskilde, Denmark, ⁵Aalborg Universitetshospital, Gastroenterology And Hepatology, Aalborg, Denmark, ⁶Aalborg University Copenhagen, Center for Molecular Prediction of Inflammatory Bowel Disease, PREDICT; Department Of Clinical Medicine, Hellerup, Denmark

Contact E-Mail Address: alesaz@dcm.aau.dk

Introduction: Polygenic scores (PGS) use the results of genome-association studies (GWAS) to calculate the aggregate effect of trait-associated variants carried by the individual. To date, PGS have primarily been used to model the individual risk of disease onset using summary statistics from susceptibility GWAS, typically with modest clinical relevance. For example, we can identify 1.5% of the population with a threefold increased risk of IBD onset (Khera et al.).

Much less is known about the impact of this onset PGS burden on the presentation and progression of patients with diagnosed IBD. Previous studies have failed to identify an effect of onset PGS on early onset vs late onset presentation (Serra et al.) and CD severity (Lee et al.).

Aims & Methods: We hypothesised that an increased genetic susceptibility burden for IBD has a direct impact on the severity of an individual's IBD disease course.

We genotyped 8179 patients with IBD (3688 CD; 4491 UC), linking them with registry data that captures medical interactions throughout patients' lifetimes. Patients who required 2+ IBD-related hospitalizations, 2+ IBD-related major surgeries, 1 IBD-related hospitalization and 1 IBD-related major surgery or use of systemic corticosteroids (≥ 5000 mg) in the first 3 years of diagnosis were defined as severe. We conducted a GWAS comparing severe patients (N=1203 UC; N=1165 CD) to those who had a less severe disease course (N=3288 UC; N=2523 CD).

We calculated individual PGS for UC and CD among individuals using the PSG scores from Middha et al. (based on De Lange et al. summary statistics) and association tests controlling for age of onset, year of onset, sex and diagnostic cohorts.

Results: We identified a significant difference in PGS between individuals with less severe and severe disease course for both CD ($\beta=0.23$, $p=2.17 \times 10^{-9}$) and UC ($\beta=0.3$, $p<1 \times 10^{-16}$).

Next, we split the cohort into quintiles by PGS and generated a stratified Kaplan-Meier curve for time to hospitalisation and surgery. Remarkably, for both outcomes and in both CD and UC the curves were ranked according to their PGS quintiles with lower ones consistently having a lower risk of adverse outcomes compared to the higher quintiles, suggesting an additive effect of genetic susceptibility on IBD severity.

In a time to event proportional hazards analysis, compared to the 20% of patients with lowest PGS, the top 20% had a much quicker time to hospitalization (CD: HR=1.79 (1.55-2.07), $p=1.82\times10^{-15}$; UC: 1.68 (1.46-1.94), $p=7.92\times10^{-13}$) and surgery (CD: 2.76 (2.19-3.47), $p=4.69\times10^{-18}$; UC: 2.03 (1.54-2.68), $p=5.57\times10^{-7}$).

Conclusion: To our knowledge, this work is the first systematic evidence of a link between IBD disease susceptibility genetics and the severity of the phenotype – patients with a higher genetic burden suffer from a more severe IBD presentation and quicker progression, suggesting that the etiology of the disease susceptibility and severity is not orthogonal.

PGS will not become the singular tool for predicting patient severity, however these are useful to add to the prognostic toolkit. Genotyping required to calculate the PGS can be done for less than €100 and can be combined with known clinically actionable pharmacogenomic variant tests and, in the future, additional targeted PGS of severity, drug response and comorbidity risk.

References: Khera, Amit V., et al. “Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations.” *Nature Genetics* 50.9 (2018): 1219-1224.

Serra, Eva Gonçalves, et al. “Somatic mosaicism and common genetic variation contribute to the risk of very-early-onset inflammatory bowel disease.” *Nature Communications* 11.1 (2020): 995.

Lee, James C., et al. “Genome-wide association study identifies distinct genetic contributions to prognosis and susceptibility in Crohn’s disease.” *Nature Genetics* 49.2 (2017): 262-268.

Middha, Pooja, et al. “Polygenic risk score for ulcerative colitis predicts immune checkpoint inhibitor-mediated colitis.” *Nature Communications* 15.1 (2024): 2568.

De Lange, Katrina M., et al. “Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease.” *Nature Genetics* 49.2 (2017): 256-261.

Disclosure: Nothing to disclose.

OP018

S100A8 AND S100A9 HOMODIMERS DRIVE CHRONICITY OF GUT INFLAMMATION AND TRIGGER CD8⁺ T CELL PATHOGENICITY

A. Jukic¹, R. Hilbe², L. Zundel¹, A. Zollner¹, M. Meyer¹, K. Faserl³, K. Siegmund⁴, V. Klepsch⁴, J. Schwärzler¹, F. Grabherr¹, L. Mayr¹, A. Pfister¹, H. Tilg¹, T. Adolph¹

¹Medical University of Innsbruck, Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology & Metabolism, Innsbruck, Austria, ²Medical University of Innsbruck, Department of Internal Medicine II, Infectious Diseases, Immunology, Rheumatology, Pneumology, Innsbruck, Austria, ³Medical University of Innsbruck, Biocenter, Division of Clinical Biochemistry, Innsbruck, Austria, ⁴Medical University of Innsbruck, Institute of Cell Genetics, Innsbruck, Austria

Contact E-Mail Address: Almina.Jukic@i-med.ac.at

Introduction: For the diagnosis of Inflammatory bowel diseases (IBD) the full spectrum of available tools should be considered. Besides non-invasive and invasive imaging, clinicians increasingly employ fecal Calprotectin as biomarker. Quantification of Calprotectin in stool is used for the diagnosis and assessment of gastrointestinal diseases, mainly for the evaluation of IBD, as calprotectin levels significantly correlate with endoscopic disease activity.

By contrast, the biological function of calprotectin within the human gut lumen remains enigmatic and experimental studies demonstrated conflicting results. Calprotectin is believed to be present as a tetrameric pro-

tein complex (S100A8/S100A9)₂, but the quaternary protein structure of S100A8 and S100A9 in the human gut lumen is still unknown and might explain divergent biologic actions observed for calprotectin.¹

Aims & Methods: We analysed stool samples obtained from patients with IBD by size-exclusion chromatography and subsequent LC-MS/MS analysis to resolve the quaternary protein structure of S100A8 and S100A9. Next, Calprotectin ELISAs used in clinical routine diagnostics were incubated with different S100A8 and S100A9 configurations to assess binding specificity. To define biological functions of S100A8 and S100A9 during gut inflammation, we orally exposed mice in enteritis and colitis models to recombinant human S100A8 and S100A9 proteins. Further, we genetically inactivated S100a9 in murine models and treated mice with an oral S100A9 inhibitor. Finally, we identified molecular mechanism controlled by human S100A8 and S100A9 homodimers using untargeted phenotyping.

Results: We frequently detected S100A8 and S100A9 dimers in stool from IBD patients, while S100A8 and S100A9 dimers were absent in healthy individuals. Moreover, we observed in three independent IBD cohorts that S100A8 and S100A9 homodimers are mainly present in the human gut during inflammation. More specifically, levels of S100A9 homodimer significantly correlated with active IBD compared to patients in remission. Importantly, S100A8 and S100A9 homodimers were not detectable by four fecal calprotectin assays in clinical use. Genetic deletion of S100a9 ameliorated experimental enteritis and colitis in numerous models. In accordance, pharmacologic inhibition of S100A9 protected against acute and chronic colitis. Moreover, oral administration of human recombinant S100A8 and S100A9 homodimers aggravated experimental enteritis and colitis, while the tetrameric calprotectin complex had no effect on gut inflammation. We demonstrate that human S100A8 and S100A9 homodimers trigger CD4⁺ and CD8⁺ T cell pathogenicity and drive chronicity of gut inflammation, as S100A8 and S100A9 homodimers required adaptive immunity in experimental colitis.

Conclusion: Collectively, we identified the quaternary protein structure of calprotectin in the human gut lumen during inflammation and reveal a diagnostic gap for fecal Calprotectin assays used in clinical routine diagnostics. Moreover, we demonstrate that human S100A8 and S100A9 homodimers drive chronicity of gut inflammation by directly activating CD4⁺ and CD8⁺ T cells, which might resemble the underlying cause of chronic unresolved gut inflammation in IBD. Taken together, our findings suggest novel diagnostic and therapeutic approaches in inflammatory diseases of the gut.

References: 1 Jukic, A., Bakiri, L., Wagner, E. F., Tilg, H. & Adolph, T. E. Calprotectin: from biomarker to biological function. *Gut* **70**, 1978-1988 (2021). <https://doi.org/10.1136/gutjnl-2021-324855>

Disclosure: Nothing to disclose.

OP019

THE IMMUNE CIS- REGULOME: WHOLE BLOOD CELL CULTURE - DERIVED RESPONSE EQTLS REVEALS POTENTIAL CAUSATIVE GENES IN RISK LOCI ASSOCIATED WITH INFLAMMATORY BOWEL DISEASES

C. Liefferinckx^{1,2}, D. Stern³, H. Perée⁴, A. Mayer³, C. Dubussy⁴, E. Quertinmont², V. Tafci², C. Minsart^{1,2}, V. Petrov⁴, L. Karim⁵, W. Coppieters⁵, S. Rahmouni⁴, M. Georges^{4,6}, D. Franchimont^{1,2}

¹HUB Hôpital Erasme, Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, Brussels, Belgium,

²University of Brussels, Center for the study of IBD, Laboratory of Experimental Gastroenterology, Brussels, Belgium, ³GIGA Institute, University of Liege, GIGA Bioinformatics Platform, Liège, Belgium,

⁴GIGA Institute, University of Liege, Unit of Animal Genomics, Liège, Belgium, ⁵GIGA Institute, University of Liege, GIGA Genomics Platform, Liège, Belgium, ⁶WEL Research Institute & Faculty of Veterinary Medicine, Liège, Belgium

Contact E-Mail Address: claire2301@gmail.com

Introduction: Genome-wide association studies (GWAS) have successfully identified many genetic regions linked to inflammatory bowel diseases (IBD) but since these often involve non-coding variants, the causative genes remain largely unknown (1).

Matching cis-expression Quantitative Trait Loci (cis-eQTLs) in relevant tissues may help pinpoint candidate genes (2).

Yet matching cis-eQTL can be found for 50% of risk loci with the available eQTL datasets (3). An explanation is that these cis-eQTLs only appear under inflammatory conditions, known as response-QTLs (reQTLs)

Aims & Methods: Toll-like receptor (TLR) and T cell receptor (TCR)-stimulated whole-blood cell cultures were carried out in a cohort of 406 healthy individuals (EC P2015/425). All individuals were genotyped using Illumina's OmniExpress BeadChips. RNA sequencing was performed using QuantSeq 3' mRNA-Seq Library Prep Kit FWD. The cis-regulome of the immune system was examined using QTL-tools and colocalization (4) was performed with summary statistics from the last IBD meta-GWAS (5)

Results: The cohort included 248 females and 159 males without any past medical history, use of medications or smoking habits. We identified 13679 cis-eQTLs (FDR ≤ 0.05) corresponding to 6496 eGenes. Cis-eQTLs that influence the same gene across resting and stimulated conditions were merged into "cis-regulatory modules" (cRM) if they exhibited similar "eQTL association patterns" (EAPs). This yielded 8401 monogenic cRM with 4.695 of them not operating in resting condition, requiring stimulation to be detected.

Next, we colocalized EAPs generated from our cohort with disease associated pattern (DAP) identifying IBD risk loci. This colocalization assumes that if a risk locus influences disease risk by altering gene expression, the DAP for this locus and the EAP should show similar patterns of variant associations, as quantified by the θ metric. We found 187 correlations ($|\theta| > 0.6$) spanning 39 risk loci and encompassing 68 genes. Of note, 19.2% of these correlations were associated with reQTLs, facilitating the colocalization of EAPs with 11 risk loci that would have been overlooked without stimulation. The long non-coding gene *AJ009632.2* is a remarkable example illustrating the relevance of immune stimulation. A positive correlation was observed by colocalizing eQTL captured in resting condition which suggested that the eQTL linked to *AJ009632.2* may increase disease risk. Contrarily, after stimulation, EAP linked to *AJ009632.2* displays an inverse trend. This striking example stresses the need to have a deep knowledge about a regulatory variant before considering it as positively or negatively associated with disease.

Another example is illustrated by *CTSS*, a gene which encodes cathepsin S protein, a lysosomal enzyme expressed by immune and epithelial cells in response to inflammation, regulating antigen presentation and taking

part in degradation of extracellular matrix. The reQTL linked to *CTSS* in our dataset matched the DAP related to the rs4845604. Table 1 shows DAP-EAP correlations which highlight potentially relevant candidate genes

Coordinates	Diseases	Gene	Resting condition θ (p-val)	TCR stimulation θ (p-val)	TLR 4 stimulation θ (p-val)	TLR7/8 stimulation θ (p-val)	True reQTL
Chr1: 150,100,000-151,120,000 (rs4845604-a)	IBD, CD, UC	HORMAD1	-0.02 (0.1)	-0.58 (0.01)	-0.82 (0.0004)	-0.82 (0.0009)	1
	UC	CTSS	-0.05 (0.1)	- (-)	-0.72 (0.004)	-0.45 (0.03)	1
	CD	ZBTB38	0.39 (0.03)	- (-)	0.73 (0.0007)	0.45 (0.03)	1
	UC	TPPP	0.01 (0.1)	- (-)	0.8 (0.0005)	0.45 (0.03)	1
Chr5: 390,000-810,000 (rs4957048)	IBD, CD, UC	AJ009632.2	0.91 (0.0004)	- (-)	-0.9 (0.0009)	-0.66 (0.01)	0
	UC						

Table 1.

Conclusion: In a unique healthy cohort, the identification of specifically stimulated whole- blood cell cultures derived cis-re QTLs expanded our ability to colocalize risk loci, and pinpoint relevant candidate genes in IBD

References:

1. Claussnitzer M, Cho JH, Collins R, Cox NJ, Dermitzakis ET, Hurles ME, et al. A brief history of human disease genetics. *Nature*. 2020;577(7789):179-89.
2. Consortium GT. The GTEx Consortium atlas of genetic regulatory effects across human tissues. *Science*. 2020;369(6509):1318-30.
3. Umans BD, Battle A, Gilad Y. Where Are the Disease-Associated eQTLs? *Trends Genet*. 2021;37(2):109-24.
4. Momozawa Y, Dmitrieva J, Theatre E, Deffontaine V, Rahmouni S, Charlotteaux B, et al. IBD risk loci are enriched in multigenic regulatory modules encompassing putative causative genes. *Nat Commun*. 2018;9(1):2427.
5. de Lange KM, Moutsianas L, Lee JC, Lamb CA, Luo Y, Kennedy NA, et al. Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease. *Nat Genet*. 2017;49(2):256-61.

Disclosure: Nothing to disclose.

OP020

THE ROLE OF SOMATIC MUTATIONS IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE

I.J. Hidding¹, A. Vich Villa², S. Hu³, A.R. Bourgonje¹, M. V D Geijn⁴, R.A.A. Ruigrok¹, S. Andreu-Sánchez⁵, BH Jansen¹, H Van Dullemen¹, M.C. Visschedijk¹, G. Dijkstra¹, EAM Festen¹, R.K. Weersma¹, F. Imhann⁵

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Rega Institute for Medical Research, Microbiology and Immunology, Leuven, Belgium,

³Institute of Precision Medicine, The First Affiliated Hospital of Sun Yat-Sen University, Department of Gastroenterology and Hepatology, Guangzhou, China, ⁴Amsterdam UMC, Amsterdam, Netherlands, ⁵University Medical Centre Groningen, Genetics, Groningen, Netherlands

Contact E-Mail Address: i.j.hidding@umcg.nl

Introduction: Inflammatory bowel disease (IBD) - characterized by chronic inflammation of the gastrointestinal tract - is believed to be caused by an interplay of host genetics, environment and gut microbiome. Recent studies have started investigating the role of somatic DNA mutations in immune-mediated disorders (1, 2). Somatic mutations are mutations that are not present in the germline, but are acquired later in life. We hypothesize that somatic mutations in gut tissue in inflammation-related genes could contribute to the pathogenesis of IBD.

Aims & Methods: Therefore, we investigated somatic mutation patterns in 589 intestinal biopsies of 268 IBD patients and 17 non-IBD controls. We performed whole exome sequencing (WES) on DNA isolated from blood and bulk RNA sequencing (RNAseq) on RNA isolated from intestinal biopsies. Somatic mutations were called using the mutect2 software which compares RNAseq data to the reference genome and the WES data. Somatic mutations were subsequently filtered to reduce the chance of sequencing errors (somatic mutation presence >25% of the RNAseq reads, coverage of at least 10 RNAseq reads). We used 4 gene sets of interest, monogenic very-early-onset IBD (VEO-IBD) genes (n=103), monogenic primary immunodeficiency genes (n=475), the most recent IBD GWAS candidate genes (n=318) and all genes in the IBD GWAS loci (n=3504) and tested whether somatic mutations were more often present in these gene sets compared to the rest of the genome. Finally, we used the MOLGENIS Variant Interpretation Pipeline which uses the CAPICE pathogenicity prediction score and the Clinvar variant database to annotate the called and filtered somatic mutations as benign, likely benign, VUS, likely pathogenic, or pathogenic (3).

Results: We identified 400544 somatic mutations (average 745 per biopsy). We observed a significantly higher accumulation of somatic mutations in the gut biopsies of IBD patients compared to non-IBD controls (p=2e-04). This difference was bigger when only likely pathogenic and pathogenic (LP/P) somatic mutations were considered (p=3e-14). We observed a significant enrichment of somatic mutations in the genes of all 4 gene panels in the biopsies of IBD patients compared to controls (VEO-IBD p=0.0006, PID p=0.0001, GWAS candidate p=0.0015, GWAS loci p=0.0003). Biopsies taken from inflamed tissue contained statistically significantly more LP/P somatic mutations in PID, GWAS candidate and GWAS loci genes. 273 somatic mutations identified in IBD biopsies have been previously reported to the Clinvar database, including stop-gain point mutations in HPS1 c.517C>T and HPS4 c.1132C>T, pathogenic missense mutation IL10RA c.301C>T and pathogenic missense mutation in STAT1 c.884C>A. In-depth analysis of a subset of key genes in the IBD pathogenesis revealed multiple LP/P mutations in several patients in both JAK1 (n=35 LP/P) and JAK2 (n=31 LP/P), primarily in the FERM and protein kinase domains. Additionally, we observed 21 LP/P mutations in PLCG2, a gene in which missense mutations can cause immune dysregulation. (4)

Conclusion: Here, in the largest somatic mutation study in IBD patients to date, we show that there is an increased accumulation of likely pathogenic and pathogenic somatic mutations in gut tissue, particularly in genes in which mutations can cause monogenic very-early-onset IBD and/or primary immune deficiencies. Thus, we show that that somatic mutations in the gut could contribute to the pathogenesis of IBD.

References:

- 1) Nanki, Kosaku, Masayuki Fujii, Mariko Shimokawa, Mami Matano, Shingo Nishikori, Shoichi Date, Ai Takano, et al. 2020. "Somatic Inflammatory Gene Mutations in Human Ulcerative Colitis Epithelium." *Nature* 577 (7789): 254–59. <https://doi.org/10.1038/s41586-019-1844-5>.
- 2) Olafsson, Sigurgeir, Rebecca E. McIntyre, Tim Coorens, Timothy Butler, Hyunchul Jung, Philip S. Robinson, Henry Lee-Six, et al. 2020. "Somatic Evolution in Non-Neoplastic IBD-Affected Colon." *Cell* 182 (3): 672–684. e11. <https://doi.org/10.1016/j.cell.2020.06.036>.
- 3) Maassen, W. T. K., L. F. Johansson, B. Charbon, D. Hendriksen, S. van den Hoek, M. K. Slofstra, R. Mulder, et al. 2024. "MOLGENIS VIP: An Open-Source and Modular Pipeline for High-Throughput and Integrated DNA Variant Analysis." *medRxiv*. <https://doi.org/10.1101/2024.04.11.24305656>.
- 4) Lange, Katrina M. de, Loukas Moutsianas, James C. Lee, Christopher A. Lamb, Yang Luo, Nicholas A. Kennedy, Luke Jostins, et al. 2017. "Genome-Wide Association Study Implicates Immune Activation of Multiple Integrin Genes in Inflammatory Bowel Disease." *Nature Genetics* 49 (2): 256–61. <https://doi.org/10.1038/ng.3760>.

Disclosure: Nothing to disclose.

OP021

ANTI- $\alpha\beta 6$ INTEGRIN ANTIBODIES ASSOCIATE WITH A DISTINCT SERUM INFLAMMATORY PROFILE AT DIAGNOSIS OF ULCERATIVE COLITIS AND DEFINE A SEVERE PHENOTYPE OF THE DISEASE

E. Pertsinidou^{1,2}, B. Salomon³, D. Bergemalm⁴, R. Movérare^{2,5}, N. Rydell², J. Rönnelid¹, C. Eriksson⁴, C.RH Hedin^{6,7}, M. Carlson⁸, Å.V. Keita⁹, M.K. Magnusson¹⁰, M.B. Bengtson¹¹, T.B. Aabrekk^{11,12}, T.E. Detlie^{12,13}, G. Huppertz-Hauss¹⁴, R. Opheim^{15,14}, P. Ricanek^{13,16}, V.A. Kristensen^{15,17}, L. Öhman¹⁰, J.D. Söderholm⁹, R. Kruse³, C.M. Lindqvist³, D. Repsilber³, M.L. Høivik^{12,15}, J. Halfvarson⁴
¹Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden, ²Thermo Fisher Scientific, Uppsala, Sweden, ³Örebro University, School of Medical Sciences, Örebro, Sweden, ⁴Örebro University, Department of Gastroenterology, Faculty of Medicine and Health, Örebro, Sweden, ⁵Uppsala University, Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala, Sweden, ⁶Karolinska Institute, Department of Medicine Solna, Stockholm, Sweden, ⁷Karolinska University Hospital, Centre for Digestive Health, Department of Gastroenterology, Dermatovenereology and Rheumatology, Stockholm, Sweden, ⁸Uppsala University, Department of Medical Sciences, Uppsala, Sweden, ⁹Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden, ¹⁰University of Gothenburg, Sahlgrenska Academy, Department of Microbiology and Immunology, Institute of Biomedicine, Göteborg, Sweden, ¹¹Vestfold Hospital Trust, Department of Gastroenterology, Tønsberg, Norway, ¹²University of Oslo, Institute of Clinical Medicine, Oslo, Norway, ¹³Akershus University Hospital, Department of Gastroenterology, Lørenskog, Norway, ¹⁴University of Oslo, Institute of Health and Society, Oslo, Norway, ¹⁵Oslo University Hospital, Department of Gastroenterology, Oslo, Norway, ¹⁶Lovisenberg Diaconal Hospital, Department of Gastroenterology, Oslo, Norway, ¹⁷Lovisenberg Diaconal Hospital, Unger-Vetlesen Institute, Oslo, Norway

Contact E-Mail Address: eleftheria.pertsinidou@igp.uu.se

Introduction: Autoantibodies against integrin $\alpha\beta 6$ have recently been associated with ulcerative colitis (UC), its preclinical phase, and UC outcomes. However, data on the diagnostic utility of the autoantibody and its dynamics are scarce.

Therefore, we aimed to examine the diagnostic capacity of the anti- $\alpha\beta 6$ autoantibody. Moreover, we assessed its utility in defining a specific phenotype of UC and ascertained its temporal dynamics in relation to the disease course.

Aims & Methods: Using an in-house assay based on the ELIA technology (Thermo Fisher Scientific, Uppsala, Sweden), anti- $\alpha\beta 6$ IgG autoantibodies were measured in serum from adult patients with suspected IBD in the Swedish inception cohort SIC IBD (discovery cohort, n=473) and the Norwegian population-based inception cohort IBSEN III (validation cohort, n=570). A cut-off of 400 $\mu\text{g/L}$ was applied, corresponding to the lower calibrator for IgG (4 $\mu\text{g/L}$) and the 96th percentile of healthy individuals. The course of UC was categorized as indolent or aggressive at 12 months, based on a composite outcome of colectomy, hospital admission for active disease, treatment refractoriness towards ≥ 2 biological agents, or >2 courses of corticosteroids/cumulative dose of >2.5 g. Inflammatory proteins (n=92) were measured (Olink Proteomics, Uppsala). Welch's t-test was used with Benjamini-Hochberg correction, applying a 5% false discovery rate (FDR). Linear-mixed models were applied to investigate differences in autoantibody expression between diagnosis and three months follow-up.

Results: The discovery cohort comprised 327 IBD patients and 146 symptomatic controls without any discernible evidence of IBD, and the validation cohort included 366 IBD patients and 204 symptomatic controls. Patients with UC and those with colonic Crohn's disease in the discovery cohort had higher median anti- $\alpha\beta6$ levels compared to symptomatic controls. The anti- $\alpha\beta6$ autoantibody demonstrated a sensitivity of 73% and a specificity of 84% for distinguishing UC from CD and symptomatic controls in the discovery cohort and 79% and 91%, respectively, in the validation cohort.

Anti- $\alpha\beta6$ positivity was associated with a severe UC phenotype, characterized by more extensive colitis ($p=0.008$), severe Mayo endoscopic activity ($p=0.005$), and pronounced systemic inflammation, defined as higher hsCRP ($p=0.04$) and lower albumin concentrations ($p=0.01$), in the discovery cohort. However, no association of f-Calprotectin was observed. Higher endoscopic activity in anti- $\alpha\beta6$ positive UC patients was confirmed in the validation cohort. In both cohorts, an increasing extent of inflammation and endoscopic activity was observed with higher median levels of anti-integrin $\alpha\beta6$.

Five proteins (SYND1, IL-17A, GZMB, MMP1, CXCL13) were significantly up-regulated in anti- $\alpha\beta6$ positive UC patients in the SIC-IBD, and two of them (IL-17A and GZMB) were validated in the IBSEN III cohort. Compared to patients with indolent UC, patients with an aggressive course presented with higher anti- $\alpha\beta6$ levels at diagnosis in the discovery cohort ($p=0.02$) and potentially also in the validation cohort ($p=0.13$). A significant interaction of disease course was observed in autoantibody levels between diagnosis and 3 months in the SIC cohort ($p<0.0001$), as the levels decreased in patients with indolent UC but not in those with an aggressive course.

Conclusion: Anti- $\alpha\beta6$ autoantibodies demonstrate a diagnostic capacity for UC and define a severe phenotype of the disease. Its temporal dynamics differ between patients with an aggressive and an indolent disease course.

Disclosure: EP, RM and NR are employed by Thermo Fisher Scientific.

IBD: Latest news on a personalised approach

17:00-18:00 / A1

OP022

PERSONALIZED INTESTINAL ORGANOID AND IMMUNE CELL CO-CULTURE MODEL FOR EVALUATION OF BIOLOGICAL THERAPY EFFICACY IN ULCERATIVE COLITIS PATIENTS

D. Tilindė¹, R. Inciuraite¹, U. Kulokiene¹, I. Aleknaviciene¹, V. Kiudelis², L.V. Jonaitis², J. Kupcinskas², J. Skieceviciene¹

¹Lithuanian University of Health Sciences/Institute for Digestive Research, Institute for Digestive Research, Kaunas, Lithuania,

²Lithuanian University of Health Sciences, Gastroenterology, Kaunas, Lithuania

Contact E-Mail Address: valentelyte.deimante@gmail.com

Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease affecting 5 million people worldwide, characterized by mucosal inflammation that can extend throughout the colon [1].

Current treatments often have limited efficacy or severe side effects [2].

As, there are no established criteria for selecting the most effective treatment for IBD, innovative preclinical drug testing systems are of major importance.

Aims & Methods: The aim of this study was to evaluate the effects of biological therapy using ulcerative colitis patient-derived personalized co-culture models of colonic epithelial and immune cells under inflammatory conditions.

The effects of upadacitinib (UPA) and ozanimod (OZA) were tested in personalized co-cultures of colonic epithelial cells and macrophages derived from UC patients ($n=12$) and control (Con) individuals ($n=11$). Inflammation was induced with inflammatory cytokines TNF- α (10 ng/mL) and IFN- γ (10 ng/mL). Barrier integrity was measured by transepithelial electrical resistance (TEER). Expression of *TNF- α* , *CCL5*, and *CXCL9* genes was evaluated using qRT-PCR. Secretion of cytokines in the epithelial cells and macrophages culture media was investigated using a flow cytometry-based target protein assay. Data comparison was conducted using the Shapiro-Wilk test and the Wilcoxon rank-sum test. A difference between the values was considered significant when $p \leq 0.05$ or $p_{adj.} \leq 0.05$.

Results: In cell cultures stimulated with inflammatory cytokines, barrier permeability increased (TEER decreased – Con: by 452.03 $\Omega \cdot \text{cm}^2$, UC: 39.3 $\Omega \cdot \text{cm}^2$), which partially recovered after removal of inflammatory factors (TEER increased – Con: by 65.91 $\Omega \cdot \text{cm}^2$, UC – only 47.31 $\Omega \cdot \text{cm}^2$). Epithelial integrity was restored after incubation with UPA and OZA (TEER increased – Con: by 116.82 $\Omega \cdot \text{cm}^2$ (UPA), by 193.77 $\Omega \cdot \text{cm}^2$ (OZA); UC: by 226.64 $\Omega \cdot \text{cm}^2$ (UPA), by 188.5 $\Omega \cdot \text{cm}^2$ (OZA)). At the molecular level, overnight stimulation with TNF- α and IFN- γ increased expression of *CXCL9* gene in epithelial cells (UC: fold change (FC) = 3064.49 $p_{adj.} = 2.07 \times 10^{-5}$; Con: FC = 664.44, $p_{adj.} = 2.00 \times 10^{-2}$) and macrophages (UC: FC = 140.47 $p_{adj.} = 0.01$; Con: FC = 314.43, $p_{adj.} = 0.01$) in both groups. Co-culture treatment with UPA and OZA showed important trend of patient-specific responses to each therapeutic agent, which probably was the most important factor of non-significant values for observed changes in *CCL5*, *CXCL9*, *TNF- α* expression analysing summarized data. The flow cytometry-based target protein assay revealed that TNF- α and IFN- γ can influence inflammatory cytokine secretion in both epithelial cells and macrophages of UC patients and Control individuals, which can be further modified by novel biological therapy agents – UPA and OZA.

Conclusion: In conclusion, treatment with TNF- α and IFN- γ reduced epithelial barrier integrity and induced increased expression of inflammatory cytokines in epithelial cells and macrophages. Biological therapy (UPA or OZA) tended to restore disrupted barrier integrity. However, the response to novel biological therapy agents (UPA and OZA) on gene expression in

both cell types and inflammatory cytokine levels in the cell culture media showed varying impacts and effectiveness, thereby revealing individualized responses of subjects to different biological preparations.

References: 1. Le Berre C, Honap S, Peyrin-Biroulet L. Ulcerative colitis. *Lancet*. 2023 Aug 12;402(10401):571-584. doi: 10.1016/S0140-6736(23)00966-2. PMID: 37573077.
2. Singh S, Allegretti JR, Siddique SM, Terdiman JP. AGA Technical Review on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020 Apr;158(5):1465-1496.e17. doi: 10.1053/j.gastro.2020.01.007. Epub 2020 Jan 13. PMID: 31945351; PMCID: PMC7117094.

Disclosure: No conflict of interest to declare.

OP023

PREDICTIVE BIOMARKERS OF THERAPEUTIC RESPONSE IN INFLAMMATORY BOWEL DISEASE: A STEP TOWARDS PERSONALIZED MEDICINE

M. Baldan Martín¹, M. Azkargorta², A.M. Aransay³, R. Gil-Redondo⁴, I. Moreno-Indias⁵, I. Iloro², P.J. Martínez¹, I. Soletó¹, M. Orejudo del Río¹, C. Ramírez¹, A.J. Lucendo⁶, C. Rodríguez Gutiérrez⁷, A. Gutiérrez-Casbas⁸, E. Martín-Arranz⁹, L. Bujanda Fernández de Piérola¹⁰, I. Rodríguez-Lago¹¹, R.M. de Francisco García¹², E. Iglesias-Flores¹³, F. Bermejo¹⁴, M. Van Domselaar¹⁵, M.J. García¹⁶, L. Fernández Salazar¹⁷, F.J. García-Alonso¹⁸, X. Calvet¹⁹, L. Torrealba Medina²⁰, I. Bastón-Rey²¹, H. Pallares Manrique²², Y. Ber Nieto²³, E. Leo-Carnerero²⁴, M.J. Casanova¹, O. Millet⁴, F. Elortza², J. Mato⁴, F.J. Tinahones⁵, M. Chaparro^{*1}, J.P. Gisbert^{*1}, *co-last authors

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Proteomics Platform, CIC bioGUNE, BRTA (Basque Research & Technology Alliance), CIBERehd, Derio, Spain, ³Genome Analysis Platform, CIC bioGUNE, Basque Research and Technology Alliance (BRTA), CIBERehd, Derio, Spain, ⁴Precision Medicine and Metabolism Lab, CIC bioGUNE, Derio, Spain, ⁵Virgen de la Victoria University Hospital, Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y la Nutrición (CIBEROBN), Instituto de Salud Carlos III, Department of Endocrinology and Nutrition, Madrid, Spain, ⁶Hospital General de Tomelloso, Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), CIBERehd, Ciudad Real, Spain, ⁷Hospital Universitario de Navarra, Pamplona, Spain, ⁸Hospital General Universitario Alicante, CIBERehd and Instituto de Investigación Sanitaria y Biomédica de Alicante, Gastroenterology, Alicante, Spain, ⁹Hospital Universitario La Paz and Instituto de Investigación Sanitaria La Paz (IdiPaz) and UAM, Madrid, Spain, ¹⁰Hospital Universitario Donostia and Instituto Biodonostia. Universidad del País Vasco (UPV/EHU), San Sebastián, Spain, ¹¹Hospital Universitario de Galdakao, Biocruces Bizkaia HRI, Vizcaya, Spain, ¹²Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ¹³Hospital Universitario Reina Sofía, Cordoba, Spain, ¹⁴Hospital Universitario de Fuenlabrada, Madrid, Spain, ¹⁵Hospital Universitario de Torrejón and Universidad Francisco de Vitoria, Madrid, Spain, ¹⁶Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology and Hepatology Unit, Santander, Spain, ¹⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ¹⁸Hospital Universitario Río Hortega, Valladolid, Spain, ¹⁹Consorci Corporació Sanitaria Parc Taulí, CIBERehd, Sabadell, Spain, ²⁰Hospital Universitario Dr. Josep

Trueta, Girona, Spain, ²¹Hospital Clínico Universitario de Santiago, Gastroenterology and Hepatology, Santiago de Compostela, Spain, ²²Hospital Juan Ramón Jiménez, Huelva, Spain, ²³Hospital San Jorge, Huesca, Spain, ²⁴Hospital Universitario Virgen del Rocío, Sevilla, Spain

Contact E-Mail Address: mbaldanm@gmail.com

Introduction: Inflammatory bowel diseases are complex conditions characterized by heterogeneity at clinical, immunological, molecular, genetic, and microbial levels. The most effective approaches to induce clinical remission and control inflammation in these diseases are biologic and JAK-inhibitor therapies. However, a significant proportion of patients do not respond to treatment.

Consequently, the identification of predictive biomarkers of clinical response to the different available therapies could improve the selection of patients who may benefit from the most appropriate treatment.

Aims & Methods: A multiomic study (transcriptomic, proteomic, metabolomic and metagenomic) was performed in 53 patients with active Crohn's disease (CD) and 50 patients with active ulcerative colitis (UC) before and after 14 weeks of treatment (anti-TNF, ustekinumab, vedolizumab or tofacitinib). Responders and non-responders patients were categorized based on endoscopic findings. Samples (serum, urine, stool and intestinal biopsies) were used for RNA-seq analysis, liquid chromatography-mass spectrometry, nuclear magnetic resonance, and 16S rRNA gene sequencing.

Results: Our findings revealed multiple mRNAs, proteins and metabolites associated with the response to different treatments. Differential gene expression analyses in intestinal tissue showed that the main differences were detected between responders versus non-responders UC patients to anti-TNF, vedolizumab and tofacitinib. Proteomic analysis found numerous differentially expressed proteins between the study groups. Additionally, ROC curves revealed two proteins with good predictive value to discriminate between CD and UC patients responders versus non-responders to anti-TNF treatment (AUC=0.81 and AUC=0.96, respectively). Metabolomics showed up-regulation of 21 lipoproteins in serum from CD patients responders to ustekinumab compared to non-responders. Metabolic analysis pathways identified enrichment in ketone and butyrate metabolism, mitochondrial electron transport chain, carnitine synthesis, and oxidation of chain fatty acids. Regarding metagenomic results, only differences were found in microbial composition in responders versus non-responders UC patients treated with anti-TNF.

Conclusion: This study provides early insights into shifts in gene and protein expression in intestinal tissue, alterations in serum and urine metabolites, and changes in gut microbiota as potential predictors of response to biologics and JAK-inhibitor treatment.

Further research is needed to validate these results and assess their clinical significance in identifying patients most likely to benefit from each therapeutic approach.

Disclosure: Nothing to disclose.

IMMUNE-CELL SPECIFIC BIOMARKER OF EARLY INTESTINAL INFLAMMATION: NEUTROPHIL ELASTASE DEGRADED FRAGMENT OF TYPE III COLLAGEN IS ELEVATED IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

T. Tsapanou Katranara¹, M. Pehrsson¹, M. Sorokina Alexdóttir¹, V. Domislovic², Z. Krznaric², M.A. Ainsworth³, T.L. Boye⁴, C.S. Steenholdt⁴, A.-C. Bay-Jensen¹, M. Asser Karsdal¹, J.H. Mortensen¹
¹Nordic Bioscience A/S, Biomarkers and Research, Herlev, Denmark, ²Clinical Hospital Centre Zagreb, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ³Odense University Hospital, Department of Medical Gastroenterology, Odense, Denmark, ⁴Herlev Hospital, Department of Gastroenterology, Herlev, Denmark

Contact E-Mail Address: tka@nordicbio.com

Introduction: Inflammatory Bowel Disease (IBD) is characterized by epithelial barrier injury of the gastrointestinal (GI) tract. The disease course encompasses abnormal immune responses and excessive secretion of proteases from immune cells. Neutrophils are the first to migrate into the inflamed interstitial matrix, where type III collagen is significantly deposited. Detection of mucosal inflammation in early stages is crucial to prevent cumulative clinical damage, as a delayed diagnosis can hinder effective treatment.

Thus, we aimed to develop a biomarker that reflects early intestinal inflammation prior to it becoming medically evident; allowing us to distinguish patients that would respond to an anti-inflammatory treatment.

Aims & Methods: A competitive enzyme-linked immunosorbent assay targeting a human neutrophil elastase derived fragment of type III collagen was developed (C3-HNE). The validation was conducted by assessing its dilution recovery, matrix spiking, interference, and inter- and intra-assay variation.

The biological relevance was evaluated in commercial samples, one pre-clinical, and two clinical studies. In the preclinical study, C3-HNE was measured in serum samples from a dextran sodium sulfate (DSS)-induced colitis rat model. In the commercial samples and clinical cohorts, C3-HNE was measured in serum from patients with IBD and healthy donors (HD). To compare the biomarker levels between groups, two-way ANOVA with an uncorrected Fisher's LSD, and Mann-Whitney U-tests or Kruskal-Wallis (Dunn's corrected) were conducted.

Results: The novel biomarker C3-HNE was successfully validated, resulting in a technically robust assay with acceptable technical parameters (Table 1). In both clinical cohorts and commercial samples, C3-HNE levels were significantly higher in patients with Crohn's disease (CD), ulcerative colitis (UC) and IBD than in HD ($p<0.01$, $p<0.05$ and $p<0.05$) (Table 1). In the preclinical study, the analysis revealed significant difference in the C3-HNE levels between the control and DSS groups on day 4 ($p=0.02$). Additionally, C3-HNE was released earlier (day 1) in the timeline than the elevation of the current disease activity (DAI) score (day 7) (Table 1).

Conclusion: C3-HNE is elevated in patients with CD, UC and IBD compared with HD. Furthermore, C3-HNE reflects early stages of clinically apparent mucosal damage during experimental colitis. This biomarker holds the potential to identify early mucosal damage or acute inflammation in the GI tract; nevertheless, additional studies are needed to evaluate its clinical validity.

Disclosure: Morten Asser Karsdal, Anne-Christine Bay-Jensen, Joachim H. Mortensen are full-time employed and stock owners at Nordic Bioscience. Marta S. Alexdottir and Martin Pehrsson are full-time employed at Nordic Bioscience.

C3-HNE levels	Healthy vs CD vs UC	HD	CD	UC	p-value	Healthy vs IBD	HD	IBD	p-value
	Commercial	30.85 [25.10, 34.93]	38.2 [32.94, 44.30]	35.86 [29.80, 47.16]	0.001	Cohort II	31.2 [24.48, 36.54]	36.64 [25.17, 50.71]	0.003
	Cohort I	31.2 [24.48, 36.54]	37.44 [27.07, 57.44]	39.8 [25.45, 57.25]	0.006	Cohort I	31.2 [24.48, 36.54]	37.51 [26.90, 57.06]	0.001
Technical Performance characteristics									
	Assay Parameter	Result	Assay Parameter	Recovery	Assay Parameter	Recovery	Assay Parameter	Recovery	
	Measurement range (LLOQ-ULOQ)	15.62 – 965.59 ng/ml	Intra-assay variation (CV%)	4 – 9%	Dilution recovery in serum (1+3)	91 – 108%	Kit Stability 24 hours at 20°C	99 – 119%	
	Mean IC50	58.11 ng/ml	Inter-assay variation (CV%)	3 – 12%	Freeze-thaw stability (5 cycles)	87 – 107%	Interference hemoglobin, low/high	94 – 96% / 87 – 98%	
DSS-induced colitis model	Two-way ANOVA	Source of Variation	% of total variation	p-value	Uncorrected Fisher's LSD	Control - 5% DSS	Predicted (LS) mean diff.	95.00% CI of diff.	p-value
		Control vs. 5% DSS	6.495	0.018		Day 4	-18.57	-34.72 to -2.418	0.0248

Table 1. Technical performance characteristics of the assay C3-HNE and C3-HNE levels in a DSS-induced colitis model, commercial samples and two cohorts. For the validation the acceptance criteria were $100 \pm 20\%$ and $<15\%$ for inter-intra variation. For the biological relevance that was assessed in healthy and diseased (CD, UC and IBD) donors of commercial samples and cohorts I and II, data is presented as medians with IQR. For the DSS-induced colitis model, two-way anova test and uncorrected Fisher's LSD results are presented. The bold values are meant to highlight the significant difference.

LARGE SCALE CLINICAL TRANSCRIPTOMICS ELUCIDATES MOLECULAR PREDICTORS AND CELLULAR DYNAMICS OF VEDOLIZUMAB RESPONSE

M.D. Paraskevopoulou¹, S. Farahmand¹, R. Hou¹, J. Cheng¹, D. Ostanin², G. Xia¹, R. Kamath¹
¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²Takeda Development Center Americas, Inc. (Affiliation at the Time Analysis was Conducted and Abstract Developed), Cambridge, United States of America

Contact E-Mail Address: maria.paraskevopoulou@takeda.com

Introduction: Patients with ulcerative colitis (UC) often have unpredictable response over time. Using clinical parameters has proven useful, however, deeper understanding of the molecular and cellular mechanisms that influence therapeutic outcomes in head-to-head trials is lacking.

Here we performed a large-scale transcriptomics analysis of tissue biopsies derived from moderate-to-severe UC patients treated with vedolizumab (VDZ) or adalimumab (ADA) in the VARSITY trial (Sands, 2019).

Aims & Methods: The aim of this study was to identify biomarkers of response to VDZ and ADA treatment. We performed bulk RNA sequencing of 954 biopsies collected using the flexible sigmoidoscopy from pre-treatment/baseline, week (w)14 and w52. Our dataset comprised complete longitudinal tissue sampling of n=151 non-responders, n=117 responders based on clinical remission at w52. We employed comparative analysis to pinpoint differentially expressed genes (DEG) and differential pathways for ADA and VDZ treated patients. We then employed systems network strategies to identify gene modules (Choobdar, 2019) associated with clinical parameters.

Finally, we utilized multivariate trajectory model (Nagin, 2018) to characterise longitudinal patient trajectories based on study endpoints and integrated transcriptomics signatures to patient variable response (Schreiber, 2023).

Results: Variable baseline gene expression profile was associated with prior exposure to anti-TNF α , corticosteroid or immunomodulator treatment. DEG and gene-modules linked to VDZ response in tissue biopsies revealed inflammatory, fibrotic, epithelial, and neuronal pathways, including but not limited to JAK/STAT, G-Protein Coupled Receptor signalling, ECM interactions, oxidative phosphorylation, and neuroglial signatures. Importantly, these consistent gene and gene-module predictors of clinical remission were detected at pre- and post-treatment (w14 and w52) to VDZ. For ADA treated patients, no DEG and gene-modules were significantly associated with treatment-response at baseline after FDR correction. Upon relaxing stringency, we were able to find pathways such as neutrophil degranulation, MAPK signalling, and Fc-mediated immune regulation linked to ADA response.

Cell type contributions were in silico inferred with deconvolution analysis of bulk gene expression data. In agreement with the pathway analysis, we identified epithelial, plasma, stromal populations as baseline biomarkers of response to VDZ, while specific CD4⁺, CD8⁺ T cell subsets, follicular B cells and inflammation-associated fibroblasts were significantly elevated in non-responders compared to the responders to VDZ from baseline to post-treatment. In ADA non-responding patients, CD4⁺ T cells were significantly increased compared to responders at baseline and post-treatment. Gene-module predictors were linked to distinct patients' trajectories based on symptoms; the greatest correlations with transcriptomics findings were observed between our extreme responding groups from trajectory analyses.

Conclusion: We present first-of-a-kind analysis using large-scale clinical trial integrating longitudinal bulk RNA-seq analysis with clinical outcomes in response to two different therapies. For VDZ, as opposed to ADA, we were able to find strong baseline predictors also preserved after treatment. We hope that similar approaches could support clinical precision medicine applications to help patients achieve faster and lasting disease control.

References: Sands, BE, et al. *N Engl J Med* 2019;381(13):1215-1226.

Choobdar, S, et al. *Nat Methods* 2019;16(9):843-852.

Nagin DS, et al. *Statistical Methods in Medical Research* 2018;27(7):2015-2023

Schreiber, et al., *United European Gastroenterology Journal* 2023; 11 (Supplement 8)

Disclosure: All authors are employees and shareholders of Takeda.

OP026

UNRAVELING THE MECHANISMS UNDERLYING RESISTANCE TO JANUS KINASE INHIBITION IN ULCERATIVE COLITIS PATIENTS

E. Melón-Ardanaz^{1,2}, M. Veny^{1,2}, A.M. Corraliza^{1,2}, A. Garrido-Trigo^{1,2}, V. Gudiño^{1,2}, Á. Sanzo-Machuca^{1,2}, M. Buendia^{1,2}, M. Esteller^{1,2}, M. Rodrigo³, M. Masamunt^{4,2}, Á. Giner^{4,2}, I. Ordás^{4,2}, A. Fernández-Clotet^{4,2}, B. Caballol^{1,2}, Á. Corbí⁵, B. Verstockt⁶, S. Vermeire⁷, J. Panés^{1,2}, E. Ricart^{1,2}, A. Salas^{1,2}

¹Hospital Clínic - IDIBAPS, Gastroenterology. Inflammatory Bowel Disease, Barcelona, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Barcelona, Spain, ³Hospital Clínic, Department of Pathology, Barcelona, Spain, ⁴Hospital Clínic - IDIBAPS, Gastroenterology. Inflammatory bowel disease, Barcelona, Spain, ⁵Centro de Investigaciones Biológicas, CSIC, Centro de Investigaciones Biológicas, CSIC, Madrid, Spain, Myeloid cell Laboratory, Madrid, Spain, ⁶University Hospitals Leuven and KU Leuven, Translational Research in Gastrointestinal Disorders - IB, Department of Gastroenterology and Hepatology and Department of Chronic Diseases, Metabolism and Aging, Leuven, Belgium, ⁷University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: asalas1@clinic.cat

Introduction: Tofacitinib is an oral JAK1 and JAK3 inhibitor approved for the treatment of ulcerative colitis (UC). Despite its proven efficacy, about 40-60% of patients fail to respond to it due to mechanisms not understood. Our aim is to identify the cellular subsets and genes involved in the response and/or resistance to tofacitinib using single-cell RNA sequencing (scRNA-seq) and *in vitro* functional experiments.

Aims & Methods: Colon biopsies from patients with active moderate to severe UC starting tofacitinib 10 mg bid for 8 weeks and 5 or 10 mg bid thereafter were collected at baseline and during follow-up and processed by single-cell RNA sequencing. Patients were classified as responders (R) or non-responders (NR) based in clinical, endoscopic, and histological criteria. Tofacitinib's impact on macrophages and fibroblasts was assessed using M-CSF monocyte-derived blood macrophages and primary colonic fibroblasts under various inflammatory stimuli (LPS, TNF, and IFN γ).

Results: Thirteen out of thirty-one patients enrolled in this study responded to tofacitinib treatment. ScRNA-seq analysis demonstrated partial recovery of the epithelium and a decrease of plasma cells, inflammatory fibroblasts, and neutrophils in R.

Importantly, the proportion of T cells remained unaltered. These findings were transcriptionally and histologically validated. Contrary to R, tofacitinib did not drive any of these changes, instead ongoing inflammation induced an increase in the proportions of neutrophils, inflammatory INHBA⁺ macrophages and inflammatory monocytes in NR after treatment. ScRNA-seq analysis also revealed changes in the transcriptional signature of certain resident populations, including the anti-inflammatory FOLR2⁺ macrophages and the lamina propria fibroblasts. In R, tofacitinib induced a more tolerogenic profile in both populations whereas in NR, both populations upregulated the expression of inflammatory genes during follow-up. In *in vitro* monocyte-derived macrophages tofacitinib was able to block the inflammation induced by IFN γ and TNF.

However, the response to LPS was intensified by tofacitinib as seen by the increased expression of genes normally associated with an inflammatory phenotype (INHBA, CLEC5A) and cytokines (CXCL1, IL6).

In contrast to macrophages, fibroblasts showed an overall down regulation of inflammatory genes in response to tofacitinib regardless of the stimuli. Nonetheless, when fibroblasts were exposed to supernatants from LPS/tofacitinib-treated macrophages, they adopted a more inflam-

matory profile. In response to LPS stimulation monocyte-derived macrophages secrete high levels of the anti-inflammatory IL-10. The transcriptional profile of LPS-stimulated macrophages treated with a blocking anti-IL-10 antibody (Cuevas, Víctor D *et al*, 2022) highly correlated with the genes upregulated in FOLR2+ macrophages from tofacitinib NR patients. Cytosig analysis from scRNA-seq data confirmed significantly increased IL-10 signaling in macrophages from NR patients compared to R before starting treatment with tofacitinib.

Conclusion: Our data underscores the pivotal role of macrophages in orchestrating responses to tofacitinib and strongly suggests that IL-10 blockade in these cells in the context of ongoing inflammation may explain the exacerbated disease in those patients who become refractory. Understanding the mechanisms underlying “drug escape” may aid in ensure efficacy, limit drug failure, and potentially guide follow-up therapeutic decisions.

References: Cuevas VD, Simon-Fuentes M, Orta-Zavalza E, et al. The Gene Signature of Activated M-CSF-Primed Human Monocyte-Derived Macrophages Is IL-10-Dependent. *J Innate Immun* 2022;14:243-256.

Disclosure: This work was funded by Pfizer

Microbiota driven carcinogenesis in GI disease

17:00-18:00 / Strauss 1

OP027

MICROBIAL METABOLITE INDOLE-3-PROPIONIC ACID AMELIORATES INTESTINAL INFLAMMATION THROUGH CD4+ T CELL METABOLIC REPROGRAMMING

Q. Li^{1,2}, R. de Oliveira Formiga^{1,2}, V. Puchois^{1,2}, S. Amouyal^{1,2}, L. Creusot^{1,2}, L. Chollet^{2,3}, Y. Zhao⁴, M. Campos Ribeiro⁴, Y. Hu^{1,2}, Z. Huang^{1,2}, F. Da Silva Lima^{1,2}, A. Haidar Ahmad^{1,2}, T. Ledent¹, R. Jose Arguello⁵, G. Chevreux⁶, M.-L. Michel^{2,3}, C. Danne^{1,2}, N. Rolhion^{1,2}, T. Wai⁴, H. Sokol^{1,2,3,7,8}

¹Sorbonne Université, INSERM UMR5-938, Centre de Recherche Saint-Antoine, CRSA, AP-HP., Paris, France, ²Paris Center for Microbiome Medicine (PaCeMM) FHU, Paris, France, ³Université Paris-Saclay, INRAE, AgroParisTech, Micalis institute, Jouy-en-Josas, France, ⁴Institut Pasteur, Mitochondrial Biology Group, CNRS UMR 3691, Université Paris Cité, Paris, France, ⁵Aix Marseille Univ, CNRS, INSERM, CIML, Centre d'Immunologie de Marseille-Luminy., Marseille, France, ⁶ProteoSeine Core Facility, Institut Jacques Monod UMR 7592, CNRS-Université Paris Cité, Paris, France, ⁷Saint-Antoine Hospital, Gastroenterology Department, Paris, France, ⁸Lead Contact, Paris, France

Contact E-Mail Address: Cyaner_Li@hotmail.com

Introduction: The phenotype and behavior of immune cells have been linked to cellular energy metabolisms, leading to the emergence of a new field of immunometabolism. The crucial role of the gut microbiota in immune system maturation and functions and the relatedness of mitochondria and bacteria suggest a role for the gut microbiota in intestinal epithelial and immune cell energy metabolism. The gut microbiota and its metabolites have a critical role in establishing and maintaining health and in the pathogenesis of diseases, including inflammatory bowel disease (IBD). Following an *in vitro* screening, we showed that indole-3-propionic acid (IPA) stimulates mitochondrial respiration of CD4+ T cells. IPA is a microbiota-derived tryptophan metabolite shown to be decreased in the feces of patients with IBD and which plays a crucial part in regulating intestinal immune tolerance, improving mucus barrier function and suppressing intestinal inflammation.

Aims & Methods: We aim at exploring the mechanisms involved in the anti-inflammatory effects of IPA. SCENITH technology (Single-cell energetic metabolism by profiling translation inhibition) was used to screen and identify the effect of metabolites on energy metabolism of specific subpopulations in mixed immune cell systems in both *in vitro* and *in vivo*. Seahorse, Mitotracker, metabolomics, proteomics experiments were used to explore the role of identified metabolites on energy metabolism in purified cells *in vitro*. Antibiotic-depleted gut microbiota, dextran sodium sulfate-induced colitis and adoptive reinfusion experiments in mice were used to evaluate the effects of metabolites on cellular energy metabolism and their anti-inflammation function *in vivo*.

Results: Using SCENITH technology on human blood mononuclear cells (PBMCs), we showed that IPA stimulates mitochondrial respiration of CD4+ T cells, by promoting fatty acid/amino acid oxidation rather than traditional glucose metabolism in the CD3/CD28 activation setting. Similar results were observed in mouse CD4+ T cells. In parallel with cellular energy reprogramming, IPA impacts CD4+ T cell behavior by favoring Treg over the Th17 phenotype *in vitro*. Blocking mitochondrial respiration with oligomycin or long-chain fatty acid metabolism with etomoxir inhibit IPA effects on T cells phenotype. IPA is a relatively weak Aryl hydrocarbon receptor (AhR) agonist. Using an AhR inhibitor (CH-223191) or AhR KO T cells, we showed that the effect of IPA on CD4+ T cell energy metabolism

was not dependent on AhR. In microbiota-depleted mice, the alteration in mitochondrial respiration of small intestine and colon CD4⁺ T cells was rescued by IPA administration. In DSS-induced colitis, IPA administration increases mitochondrial respiration of CD4⁺ T cells by enhancing the oxidation of fatty acids and amino acids in the colon. Adoptive reinfusion of CD4⁺ T cells from IPA-treated mice into Rag2 KO mice induced protection against intestinal inflammation, confirming that IPA protective effects are mediated by CD4⁺ T cells.

Conclusion: Collectively, our study reveals from a whole new perspective that the anti-inflammatory effects of IPA are mediated by metabolic reprogramming of CD4⁺ T cells toward the enhancement of mitochondrial respiration, thereby leading to an anti-inflammatory phenotype and eventually protection in colitis context in mice. This study paves the way for the development of new therapeutic strategies in IBD.

Disclosure: Competing interests: HS report lecture fee, board membership, or consultancy from Carenity, AbbVie, Astellas, Danone, Ferring, Mayoly Spindler, MSD, Novartis, Roche, Tillots, Enterome, BiomX, Biose, Novartis, Takeda, Biocodex and is cofounder of Exeliom Biosciences.

OP028

ASSOCIATION OF INTRATUMORAL MICROBIOME WITH TUMOR IMMUNITY AND PROGNOSIS IN HUMAN PANCREATIC CANCER

Y. Irie¹, A. Masuda¹, S. Abe¹, T. Matsumoto², J. Inoue¹, M. Tsujimae¹, T. Tanaka¹, A. Sakai¹, T. Kobayashi¹, T. Imai¹, E. Hara³, Y. Kodama¹

¹Kobe graduate school of medicine, Division of gastroenterology, Department of internal medicine, Kobe, Japan, ²Osaka University, graduate school of frontier biosciences, Suita, Japan, ³Osaka University, Research Institute for Microbial Diseases, Osaka, Japan

Contact E-Mail Address: youschi@med.kobe-u.ac.jp

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive and lethal human cancers. In recent years, bacteria resembling gut microbiota have been found within pancreatic cancer tissues, suggesting their potential influence on tumor growth and prognosis. However, the details remain insufficiently elucidated. Therefore, we clarified the characteristics of the tumor microbiota using resected pancreatic cancer specimens from our institution and to analyze their relationship with the tumor microenvironment and prognosis.

Aims & Methods: We analyzed formalin-fixed paraffin-embedded (FFPE) sections from 162 PDAC patients who underwent surgery between April 2008 and March 2017 in our institution.

DNA were extracted from FFPE using Quantitative polymerase chain reaction (qPCR) and in situ hybridization (ISH) targeting 16S rRNA. Microbial community was explored by using 16S metagenomics from FFPE. The profile of intratumoral bacteria was compared with clinical information, pathological findings including tumor-infiltrating T cells, tumor-associated macrophage, fibrosis, and alterations in four main driver genes (KRAS, TP53, CDKN2A/p16, SMAD4) in tumor genomes.

Results: Among 162 cases, 52 showed amplification in qPCR targeting 16S rRNA and positive ISH reactions targeting 16S rRNA within tumor tissues. The presence of bacteria commonly found in gut microbiota such as Proteobacteria and Firmicutes was observed within tumor tissues of these 52 cases. Comparison with paired normal tissues (N=26) revealed differences in α diversity ($P<0.01$) and β diversity ($P<0.01$), suggesting the presence of a unique tumor microbiota. Subsequently, we divided the 52 cases into two groups based on the median survival period.

We identified one bacterial species was dominant in the long-term survival group and ten were in the long-term survival group using Linear Discriminant Analysis Effect Size. Comparison of bacterial profiles between

cases with good and poor prognosis revealed a significant positive correlation between a shorter survival time and the presence of anaerobic bacteria such as *Bacteroides*, *Lactobacillus*, and *Peptoniphilus*. 24 cases which were positive for at least one of the three prognostic bacteria were compared with 28 cases negative for all of them, there were not significant correlation with tumor size, pathological stage, fibrosis, and alterations in four main driver genes, but significant correlation with the lower degree of tumor-infiltrating T cells positive for CD4, CD8, and CD45RO ($P<0.01$, $P<0.01$, $P<0.01$, respectively).

Conclusion: We identified multiple bacterial species within pancreatic cancer tumors associated with prognosis. Increased abundance of *Bacteroides*, *Lactobacillus* and *Peptoniphilus* along with the progression of pancreatic cancer suggests their involvement in worsening prognosis through tumor immunity.

Disclosure: Nothing to disclose.

OP029

CHRONIC STRESS ACCELERATED COLORECTAL CANCER PROGRESSION BY DISTURBING THE BALANCE OF GUT MICROBIOTA

Q. Li¹, J. Yang²

¹Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, Frontiers Science Center for Disease-Related Molecular Network, West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China, ²West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: 2375435621@qq.com

Introduction: Chronic stress has been well-documented to exacerbate the progression of colorectal cancer (CRC), yet the role of the gut microbiota in this process remains elusive.

Aims & Methods: Subcutaneous MC38 tumor models and AOM/DSS-induced murine CRC models were utilized to evaluate the tumor-promoting effects of chronic restraint stress. Antibiotic cocktail (ABXs) administration and Fecal microbiota transplantation (FMT) were employed to determine whether the gut microbiota shaped by chronic stress could potentiate CRC progression. 16S rRNA gene sequencing was conducted to analyze microbiota alterations induced by chronic stress.

Results: Chronic stress significantly accelerated CRC progression in both subcutaneous and AOM/DSS-induced models (all $P < 0.05$), while ABX administration in AOM/DSS-induced models attenuated this effect ($P = 0.9897$). Notably, Mice receiving FMT from the chronic stress group exhibited a higher tumor burden compared to FMT from controls ($P < 0.01$), indicating that the gut microbiota may be involved in the progression of CRC induced by chronic stress.

Further analysis of the disturbed gut microbiota revealed a significant depletion of *Lactobacillus* in CRC models with chronic stress. Specifically, *Lactobacillus johnsonii*, *Lactobacillus gasseri* and *Lactobacillus plantarum* were reduced and inversely correlated with tumor numbers in AOM/DSS induced mouse models, respectively (all P value < 0.05). Interestingly, chronically stressed mice harbored fewer CD8⁺ T cells and IFN- γ ⁺ CD8⁺ T cells within colon tumors compared to controls, however, this disparity was abrogated upon ABX administration.

Furthermore, mice receiving FMT from the chronic stress group exhibited a paucity of CD8⁺ T cells and IFN- γ ⁺ CD8⁺ T cells in tumors relative to FMT from control group, suggesting that the chronic stress-shaped gut microbiota may dampen the anti-tumor effects of CD8⁺ T cells.

Additionally, we found that CD8⁺ T cells in tumor were positively associated with relative abundance of *Lactobacillus johnsonii*, *Lactobacillus gasseri* and *Lactobacillus plantarum*, respectively (all $P < 0.05$). Collectively,

these results suggest that the reduction of *Lactobacillus* species under chronic stress conditions may dampen CD8⁺ T cell anti-tumor immunity, thereby promoting CRC progression.

Conclusion: Our study indicates that chronic stress may promote the progression of CRC by reducing intestinal *Lactobacillus* bacteria, and the possible mechanism is to weaken *Lactobacillus*-mediated CD8⁺ T cell anti-tumor immunity. Future investigations should focus on elucidating the mechanisms by which specific *Lactobacillus* species modulate CD8⁺ T cell function and tumor immunity, as well as exploring the therapeutic potential of *Lactobacillus*-based interventions in managing stress-related CRC exacerbation.

Disclosure: Nothing to disclose.

OP030

MICROBIAL PRODUCTION OF DEOXYCHOLIC ACID PROMOTES COLONIC TUMORIGENESIS IN AN GNONOBIOTIC MOUSE MODEL

A. Oßwald^{1,2}, F. Schumacher³, A. Sander^{2,1}, F. Garcia Carrizo⁴, D. Mahdi-Joest¹, T. Schulz⁴, S. Ocirk^{1,2}

¹German Institute of Human Nutrition, Intestinal Microbiology, Potsdam, Germany, ²Technical University of Munich, WESTGUT Collaborative Lab, ZIEL – Institute for Food and Health, Freising, Germany, ³Free University of Berlin, Department of Pharmacology and Toxicology, Institute for Pharmacy, Berlin, Germany, ⁴German Institute of Human Nutrition, Adipocyte Development and Nutrition, Potsdam, Germany

Contact E-Mail Address: annika.osswald@dife.de

Introduction: Intestinal bacteria with 7 α -dehydroxylating (7 α DH) activity are able to produce the secondary bile acids, such as deoxycholic acid (DCA). Higher concentrations of DCA are linked to a higher risk of colorectal cancer (CRC) risk, yet underlying molecular mechanisms demonstrating a causal role of DCA are still unclear. This includes a recently demonstrated immunomodulatory effect of secondary bile acids, which may contribute to CRC pathogenesis.

Here, we aim to investigate the tumor-promoting and immunomodulatory role of DCA in a gnotobiotic CRC mouse model.

Aims & Methods: Germ-free wildtype mice were colonized with a simplified bacterial consortium, the bile acid converting microbiota (BACOMI). BACOMI is able to produce DCA due to the 7 α DH activity of *Clostridium scindens* (+7 α DH). Control mice were colonized with BACOMI without *C. scindens*, lacking 7 α DH activity (-7 α DH) and DCA. A sub-group of mice was treated with AOM/DSS to induce colonic tumors. Bacterial abundances were measured in colonic content via qPCR, cecal bile acid composition was analyzed using LC-MS/MS and colonic tissue was analyzed using qPCR and immunofluorescence-staining. Primary T-cells and macrophages were isolated from the colon as well as mesenteric and iliac lymph nodes and analyzed by flow cytometry.

Results: DCA was exclusively present in mice colonized with the BACOMI consortium and led to higher colonic tumor numbers compared to mice colonized with BACOMI without *C. scindens* (+7 α DH = 20.5 tumors $\pm$ 7.5 SD vs. -7 α DH = 7.9 tumors $\pm$ 2.0 SD), in particular for small- and medium-sized tumors. Presence of DCA also resulted in shorter colon lengths and lower levels of butyrate in cecal content. In BACOMI colonized mice, the treatment with AOM/DSS promoted colonic colonization by *C. scindens* compared to mice without AOM/DSS treatment.

Even without AOM/DSS treatment, the presence of *C. scindens* and DCA resulted in significantly higher numbers of Ki67⁺ epithelial cells in colonic crypts and more pronounced hypoxia in the colonic epithelium. Colonic expression of genes involved in CRC pathogenesis (e.g., *Axin2*, *Ccnd1*, *Myc*), bile acid metabolism (e.g., *Nr1h4*, *Nr0b2*, *Slc51b*) as well as immune

responses (e.g., *Nfkb1*, *Rorc*, *Ilgam*) was upregulated in mice with DCA. Sub-types of Foxp3⁺ regulatory T-cells were more abundant in mesenteric and iliac lymph nodes whereas numbers of Ly6C high macrophages were lower in the colon and mesenteric lymph nodes of mice with DCA compared to mice lacking DCA.

Conclusion: In a gnotobiotic mouse model for CRC, the presence of microbially-derived DCA promotes colonic tumorigenesis *in vivo*. Even in the absence of chemically-induced tumorigenesis, DCA stimulates the expression of markers closely associated with CRC and promotes colonic epithelial proliferation.

These findings strongly imply a causal role of DCA in the development of CRC. Additionally, DCA shows immunomodulatory effects, which may demonstrate another mechanistic link of how DCA affects intestinal health.

Disclosure: Nothing to disclose.

OP031

SPATIAL TRANSCRIPTOMIC PROFILING REVEALS CHRONIC INFLAMMATION-INDUCED EPITHELIAL AND IMMUNE CELL ADAPTATIONS THAT MAY PROMOTE DYSPLASIA- AND CANCER DEVELOPMENT IN IBD

S. Frigerio^{1,2,3,4,5}, H.N. Khan^{1,2,3,4,5}, A. Neeffjes-Borst⁶, B. Mol^{1,4}, C. Ponsioen^{1,4}, G. D'Haens^{1,4}, J. Grootjans^{1,2,3,4,5}

¹Department of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, Netherlands, ²Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, Amsterdam, Netherlands, ³Oncode Institute, Amsterdam, Netherlands, ⁴Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ⁵Cancer Center Amsterdam, Amsterdam, Netherlands, ⁶Department of Pathology, Amsterdam UMC, Amsterdam, Netherlands

Contact E-Mail Address: s.n.frigerio@amsterdamumc.nl

Introduction: Chronic inflammation in patients with inflammatory bowel disease (IBD) increases the risk of colorectal cancer (CRC). Both sporadic CRC (SCRC) and colitis-associated CRC (CAC) bear similar mutational patterns, including *APC*, *KRAS*, and *TP53* mutations.

However, the dysplasia to carcinoma sequence in CAC is different in that adenomatous transformation often starts with *TP53* and not with *APC* mutations (characteristic of SCRC).

This illustrates that to understand epithelial- and immune cell changes involved in CAC etiology, it is critical to study pre-cancerous tissues instead of end stage disease.

Aims & Methods: We aimed to provide a detailed characterization of the epithelial and immune cell transcriptome in cancers, dysplastic lesions and adjacent normal tissue of both CAC and SCRC patients, using GeoMx Digital Spatial Profiling, to identify chronic inflammation-induced transcriptional changes that predispose for dysplasia and cancer development in IBD. We collected FFPE tissue of 13 IBD patients with either dysplasia (colitis-associated dysplasia (CAD)), CAC, or both. 6 patients without IBD with sporadic dysplasia (SD) or SCRC were used as a control. An expert IBD pathologist scored the tissues to define 3 regions: histologically non-inflamed non-dysplastic mucosa (adjacent normal mucosa: ANM), dysplasia (SD/CAD) or cancer SCRC/CAC). GeoMx Digital Spatial Profiling was used for spatial transcriptomic analysis of both the epithelial and immune cell compartment.

Immunohistochemistry was performed to study immune cell composition. Data analyses were performed using R. Multivariate linear modelling was used for gene and pathway differential expression analyses (significance $p < 0.01$).

Results: Differential gene expression analysis in the epithelial compartment showed that the region with most differentially expressed genes (n=408) was the ANM. Interestingly, transcriptional pathways related to T cell immune responses were downregulated (“Cytotoxicity” and “Lymphocyte Trafficking”) in ANM of CAC patients, as compared to SCRC patients.

Furthermore, we observed decreased intraepithelial T lymphocytes (IELs) abundance in CAC by deconvolution of transcriptional data, which was confirmed by immunohistochemistry (83.71 vs 50.79 IELs cell density/mm², p<0.05). Reduction in IELs in ANM of CAC patients was accompanied by decreased *IL15* expression in epithelial cells, a cytokine critical for IEL recruitment. In the immune compartment, most transcriptional differences were observed in dysplastic tissue (415 differentially expressed genes), with the “T cells” pathway being the most differentially expressed in CAD regions versus SD. Genes encoding for T cell activation were upregulated in CAD, including *CD69*, *ICOS* and *GZMB*, while at the same time, increased gene expression of T-cell checkpoint molecules such as *LAG3*, *CTLA4* and *TIGIT* was observed.

Conclusion: In conclusion, we demonstrated altered cytokine gene expression patterns in ANM of CAC patients versus SCRC patients, including decreased *IL15* expression, a cytokine critical for IEL attraction. This was accompanied by decreased IELs numbers, potentially compromising immunosurveillance and clearance of pre-malignant cells. In contrast, dysplastic tissues in IBD patients were more infiltrated with immune cells, amongst which T cells, as compared to SD patients. Increased expression of T cell checkpoints in the CAD compartment however suggests an immunosuppressed state in CAD.

Together, this study may add a novel concept to how chronic inflammation-induced cell adaptations may favour dysplasia development and progression to cancer.

Disclosure: Nothing to disclose.

Management of complications and endpoints in cirrhosis and HCC

17:00-18:00 / Lehar 1

OP032

REBLEEDING AND MORTALITY IN ACUTE UPPER GASTROINTESTINAL BLEEDING WITH VARICES: INSIGHTS FROM A PROSPECTIVE MULTI-CENTER STUDY IN UK HOSPITALS

G. Nigam¹, J. Grant-Casey², K. Oakland³, S. Hearnshaw⁴, V. Jairath⁵, L. Estcourt², M.F. Murphy², S. Travis⁶, A. Douds⁷, J. Leithead⁸, A. Stanley⁹, UK upper GI bleed group
¹Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ²NHS Blood and Transplant, Oxford, United Kingdom, ³HCA Healthcare UK, Clinical, Oxford, United Kingdom, ⁴Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom, ⁵Alimentiv Inc., Gastroenterology, London, Canada, ⁶John Radcliffe Hospital, Gastroenterology Department, Oxford, United Kingdom, ⁷Queen Elizabeth Hospital, Gastroenterology, Fakenham, United Kingdom, ⁸Forth Valley Royal Hospital, Larbert, United Kingdom, ⁹Glasgow Royal Infirmary, Department of Gastroenterology, Glasgow, United Kingdom

Contact E-Mail Address: gaurav.nigam@nhs.net

Introduction: Acute upper gastrointestinal bleeding (AUGIB) is a common emergency, with 10% linked to varices¹, requiring swift evaluation.

Aims & Methods: We conducted a prospective multi-center study from 3 May to 2 July 2022, involving adults (>16 years old) presenting with AUG-IB in 152 UK hospitals. We evaluated the patient characteristics of those identified to have varices on index endoscopy as the cause of bleeding and used regression analysis to identify predictors of rebleeding and mortality.

Results: Of 4278 AUGIB cases undergoing endoscopy, 10% (418/4278) were noted to have varices (91% oesophageal, 16% gastric, and 2% duodenal). Median age was 58 yrs and 80% (338) were new admissions. At presentation, 76% (330) had known chronic liver disease (Child-Pugh categories: A:3%, B: 85%, C: 12%)., 13% (54) were on antiplatelets and 15% (61) on anticoagulants.

At presentation, 35% (145) had a history of previous AUGIB, 45% (189) were on non-selective beta-blocker prophylaxis and 23% (98) were on a variceal band ligation programme. Glasgow-Blatchford score (GBS) stratified patients into 13% medium-risk (GBS 2-6), 44% higher-risk (7-11), and 29% very high-risk (≥12).

For pre-endoscopy management: 66% (278) received PPI, 65% (269) vasopressors (98% terlipressin, 2% octreotide) and 56% (235) antibiotics. Endotracheal intubation for endoscopy was required for 33% (137) and admission under critical care for 20% (82). Time to endoscopy from presentation: 0-12 hrs:36%, 12-24 hrs:24%, and >24 hrs:32%. Stigmata of recent bleeding observed in 72% (300) – 41% blood in the upper GI tract and 64% high risk markings on varices. Variceal therapy applied in 67% (281 – 91% banding, 10% injection therapy), Danis stent 2% (7) and Sengstaken tube 3% (14). 17% (69) had evidence of further in-patient bleeding after index endoscopy. 26% (109) needed >1 endoscopy during inpatient stay, and 2% (8) underwent transjugular intrahepatic portosystemic shunt. 67% (281) were transfused ≥1 packed red blood cells, 15% (66) platelets, and 20% (86) fresh frozen plasma.

Median length of stay was 7 days (IQR 4-11) and in-hospital mortality was 13% (54). In a multi-variable logistic model assessing predictors of rebleeding and mortality, significant factors for rebleeding included use of pre-endoscopic vasopressors (OR=2.49, 95%CI:1.59-3.88), pre-endoscopic antibiotics (OR=0.4, 95%CI:0.28-0.59) and presence of endoscopic

stigmata (OR=6.89,95%CI:5.11-9.30). For mortality, the significant factors were very high-risk GBS (OR=4.83,95%CI:2.71-24.09), presence of endoscopic stigmata (OR=3.8,95%CI:2.82-138.72) and the use of endotherapy (OR=0.04,95%CI:0.001-0.53).

Conclusion: Pre-endoscopic vasopressors were associated with increased risk of rebleeding, while pre-endoscopic antibiotics with decreased risk. Endoscopic stigmata was significantly associated with both rebleeding and mortality, with endotherapy a crucial influencer for reducing mortality. These findings offer valuable insights for risk stratification and guide appropriate therapeutic interventions in managing AUGIB with varices as per international guidelines.

References: 1. Hearnshaw et al *Gut* 2011

Disclosure: Nothing to disclose.

OP033

EFFECT OF TIME TO TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT ON OUTCOMES IN PATIENTS WITH VARICEAL BLEEDING

X. Wang¹, K. Ba¹, X. Luo¹

¹*Sichuan University West China Hospital, Department of Gastroenterology and Hepatology, Chengdu, China*

Contact E-Mail Address: xiaoze.wang@foxmail.com

Introduction: The pre-emptive transjugular intrahepatic portosystemic shunt (TIPS) within 72 hours is recommended. Nevertheless, recent research emphasizes the challenges associated with timely provision of TIPS within this limited timeframe.

Aims & Methods: The objective of this study was to assess the impact of time for performing TIPS on patient outcomes and identify a more appropriate timeframe. This study enrolled patients referred to our hospital for TIPS procedure between January 2012 and December 2021. The duration between the recent variceal bleeding episode and TIPS procedure was documented. Predetermined outcomes were assessed in relation to various groups at four distinct time intervals: 72 hours, 5 days, 14 days, and 28 days. The primary outcome was the long-term survival rate.

Results: A total of 1180 patients were included in the study. There were no significant differences in patient outcomes between the early and late TIPS groups when patients grouped by 72 hours, 14 days, and 28 days. However, when comparing the late TIPS (>5 days) group to the early TIPS (≤5 days) group, a significantly lower 5-year survival rate was observed in the late TIPS group (71.0% vs 80.4%; HR, 1.88; 95% CIs, 1.14-3.12; P = 0.014). The variceal rebleeding rate did not show a significant difference between the two groups (P = 0.91).

Conclusion: Early TIPS within a 5-day window may confer a survival benefit in contrast to TIPS procedures performed beyond this timeframe. It may be advisable to expand the timeframe for pre-emptive TIPS to align with current clinical practices.

Disclosure: Nothing to disclose.

OP034

LIVER DECOMPENSATION AS A NEW OUTCOME AND PROGNOSTIC INDICATOR IN CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA TREATED WITH ATEZOLIZUMAB PLUS BEVACIZUMAB: A REAL-LIFE MULTICENTER STUDY

L. Stella¹, A. Gasbarrini¹, F. Santopaolo¹, L. Cerrito¹, C. Campani², F. Marra³, F. Trevisani⁴, F. Tovoli⁴, F. Piscaglia⁴, E.G. Giannini⁵, S. Sidali⁶, C. Hollande⁶, E. Pellegrini⁷, B. Stefanini⁴, M. Bouattour⁶, F.R. Ponzi¹

¹Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Roma, Italy, ²Università degli studi di Firenze / Université de Paris, Dipartimento di Medicina Sperimentale e Clinica, Firenze, Italy, ³University of Florence, Dipartimento di medicina Interna, Florence, Italy, ⁴University and General Hospital S. Orsola-Malpighi, Bologna, Italy, ⁵University of Genoa, Department of Internal Medicine, Genova, Italy, ⁶Beaujon Hospital, Hepatology, Clichy, France, ⁷Azienda Ospedaliero Universitaria Careggi, Dipartimento di Oncologia, Florence, Italy

Contact E-Mail Address: leonardo.dr.stella@gmail.com

Introduction: The combination of Atezolizumab plus Bevacizumab (atezobeva) has changed the treatment landscape of advanced hepatocellular carcinoma (HCC), but its efficacy and safety in patients with impaired liver function or portal hypertension is still debated.

Aims & Methods: In this multicenter, real-life, study we compared 247 patients with unresectable HCC treated with atezobeva, matched to 494 patients treated with tyrosine kinase inhibitors (TKIs). We evaluated the impact of liver function and decompensation on treatment outcomes.

Results: Patients in the atezobeva group showed longer median overall survival (OS; 18-30 vs 10-20 months, p<0.0001), longer time to progression (TTP; 13-60 vs 10-10 months, p=0.0002) and increased progression-free survival (PFS; 10-50 vs 6-10 months, p<0.0001) compared with the TKIs group. Although survival was better in Child Pugh A patients than in Child Pugh B patients (20-20 vs 9-83 months, p=0.0008), no clear differences in TTP and overall treatment safety were observed. Liver decompensation occurred in 63 (25-51%) patients, specifically 41 (27-89%) Child Pugh A and 22 (51-16%) Child Pugh B and was associated with worse survival (10-50 vs 20-20 months; p=0.006).

Among decompensated patients, 26 patients (41-26%) were able to resume atezobeva after decompensation, achieving an OS comparable to those who never decompensated (20-87 vs 20-2 months; p=0.77), and significantly better than those who permanently stopped treatment (8-07 months; p=0.02).

Treatment interruption following decompensation was an independent predictor of survival (HR 2.04, 95% CI 1.25-3.33, p=0.004), while ALBI score 2-3 (HR 2.21, 95%CI 1.07-4.55; p=0.03), Child Pugh class B (HR 1.81, 95% CI 1.03-3.18; p=0.04), portal hypertension (HR 2.54, 95%CI 1.37-4.72; p=0.003) and sAEs (HR 1.71, 95%CI 1.04-2.82; p=0.04) emerged as predictors of decompensation. Time to decompensation was similar for patients with ALBI 2, regardless of Child Pugh class, and the probability of recovery from decompensation was similar for Child A and B patients.

Conclusion: In this real-life multicentric study atezobeva was effective in both Child Pugh A and B patients. Child Pugh B patients despite their higher risk of decompensation have an equal chance of recovery.

The possibility to resume treatment after an episode of decompensation highlights the necessity of integrated hepato-oncological management, optimizing the therapeutic efficacy of atezobeva.

References: -Finn R.S. et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med* 2020.

-Cabibbo G, et al. Optimizing systemic therapy for advanced hepatocellular carcinoma: the key role of liver function. *Dig Liver Dis* 2022.

-D'Alessio A, et al. Preliminary evidence of safety and tolerability of atezolizumab plus bevacizumab in patients with hepatocellular carcinoma and Child-Pugh A and B cirrhosis: A real-world study. *Hepatology* 2022.

-Pinato DJ et al. Immunotherapy in hepatocellular cancer patients with mild to severe liver dysfunction: adjunctive role of the ALBI grade. *Cancers Basel* 2020.

-Kudo M, et al. Albumin-Bilirubin Grade Analyses of Atezolizumab plus Bevacizumab versus Sorafenib in Patients with Unresectable Hepatocellular Carcinoma: A Post Hoc Analysis of the Phase III IMbrave150 Study. *Liver Cancer* 2023.

-Tanaka T, et al. Therapeutic efficacy of atezolizumab plus bevacizumab treatment for unresectable hepatocellular carcinoma in patients with Child-Pugh class A or B liver function in real-world clinical practice. *Hepatology Res* 2022.

-Vitale A, et al. Personalised management of patients with hepatocellular carcinoma: a multiparametric therapeutic hierarchy concept. *Lancet Oncol* 2023.

-Thabut D, et al Treatment of portal hypertension in patients with HCC in the era of Baveno VII. *J Hepatol* 2023.

Disclosure: Nothing to disclose.

OP035

COMPARISON OF TREATMENT OUTCOMES BETWEEN CARBON ION RADIOTHERAPY AND HEPATIC RESECTION FOR PRIMARY HEPATOCELLULAR CARCINOMA

S. Kakizaki¹, T. Hatanaka², K. Shibuya^{3,4}, Y. Miyasaka^{3,4}, A. Hiraoka⁵, T. Tada⁶, K. Kariyama⁷, H. Toyoda⁸, T. Ishikawa⁹, E. Itobayashi¹⁰, F. Tada⁵, A. Naganuma¹¹, K. Nouso⁷, T. Kumada¹², T. Ohno^{3,4}, Real-life Practice Experts for HCC (RELPEC) Study Group

¹NHO Taksaki General Medical Center, Department of Clinical Research, Takasaki, Japan, ²Gunma Saiseikai Maebashi Hospital, Department of Gastroenterology, Maebashi, Japan, ³Gunma University Heavy Ion Medical Center, Maebashi, Japan, ⁴Gunma University Graduate School of Medicine, Department of Radiation Oncology, Maebashi, Japan, ⁵Ehime Prefectural Central Hospital, Gastroenterology Center, Matsuyama, Japan, ⁶Japanese Red Cross Himeji Hospital, Department of Internal Medicine, Himeji, Japan, ⁷Okayama City Hospital, Department of Hepatology, Okayama, Japan, ⁸Ogaki Municipal Hospital, Department of Gastroenterology and Hepatology, Ogaki, Japan, ⁹Saiseikai Niigata Hospital, Department of Gastroenterology, Niigata, Japan, ¹⁰Asahi General Hospital, Department of Gastroenterology, Asahi, Japan, ¹¹NHO Taksaki General Medical Center, Department of Gastroenterology, Takasaki, Japan, ¹²Gifu Kyoritsu University, Department of Nursing, Ogaki, Japan

Contact E-Mail Address: kakizaki@gunma-u.ac.jp

Introduction: Hepatic resection is recommended as a curative treatment for hepatocellular carcinoma (HCC), but it may not always be feasible due to tumor localization, liver function, and comorbidities. On the other hand, carbon ion radiotherapy (CIRT) has recently become covered by health insurance in Japan, offering low invasiveness and promising local control. In this study, we compared the treatment outcomes of primary HCC between hepatic resection and CIRT.

Aims & Methods: We compared the treatment outcomes of CIRT (CIRT group, n=111) and hepatic resection (HR group, n=947) for primary HCC from September 2010 to June 2022. Patient backgrounds were adjusted using inverse probability of treatment weighting (IPTW), and we compared the recurrence-free survival (RFS) and overall survival (OS).

Results: CIRT group: HR group, median age 74 (IQR 67-82) years: 71 (65-77) years (p<0.001), male 81 cases (73.0%): 748 cases (79.0%) (p=0.1), PS 0/1=71 cases (64.0%)/40 cases (36.0%): 890 cases (94.0%)/57 cases (6.0%) (p<0.001), Child-Pugh classification A/B=102 cases (91.9%)/9 cases (8.1%): 899 cases (94.9%)/48 cases (5.1%) (p=0.2), solitary/multiple tumors=104 cases (93.7%)/7 cases (6.3%): 729 cases (77.0%)/218 cases (23.0%) (p<0.001), tumor size 3.7 (2.6-5.5) cm: 3.3 (2.2-5.3) cm (p=0.07). The CIRT group had a higher median age, poorer PS, and more solitary cases. The median RFS before IPTW adjustment was 2.3 years in the CIRT group and 2.8 years in the HR group with no significant difference (p=0.1), and there was no significant difference after IPTW adjustment (p=0.5). The median OS was 7.4 years in the CIRT group and 10.1 years in the HR group with a significant difference before IPTW adjustment (p=0.01), but the difference disappeared after IPTW adjustment (9.6 years vs. 10.1 years, p=0.6). In cases with a maximum tumor diameter of 4 cm or more, which is covered by insurance, there was no significant difference in RFS and OS before and after IPTW adjustment (RFS: p=0.8, 0.4; OS: p=0.4, 0.5). Multivariate analysis for RFS and OS showed that treatment modality (CIRT/HR) was not a significant factor (p=0.06, 0.2).

Conclusion: Carbon ion radiotherapy demonstrated comparable local control and prognosis to hepatic resection, suggesting its potential as one of the options for curative treatment.

Disclosure: Nothing to disclose.

OP036

IMPACT OF PRE-EMPTIVE TIPS PLACEMENT FOR VARICEAL BLEEDING IN CIRRHOTIC PATIENTS: A REAL-LIFE STUDY IN A TERTIARY REFERRAL CENTER

D. Feijó¹, A. Silva¹, D. Perdigoto¹, T. Oliveira², P. Donato², P. Figueiredo¹

¹ULS Coimbra, Gastroenterology, Coimbra, Portugal, ²ULS Coimbra, Radiology, Coimbra, Portugal

Contact E-Mail Address: diogofeijo96@gmail.com

Introduction: Variceal bleeding (VB) is a severe and life-threatening complication in patients with cirrhosis, often leading to significant morbidity and mortality. The Baveno VII consensus recommends early transjugular intrahepatic portosystemic shunt (pre-emptive TIPS, or pTIPS) placement within 72 hours of acute VB in select cirrhotic patients to reduce the risk of re-bleeding and improve survival rates. However, the comparative effectiveness of pTIPS with delayed TIPS or no intervention remains unclear.

Aims & Methods: This study aimed to evaluate the benefits of pTIPS in reducing early relapse of VB, compared to delayed TIPS or no intervention, in a referral center setting. Cirrhotic patients with VB and Child-Pugh Class C<14, or B>7 with active bleeding were retrospectively selected between 2016 and 2022 for two control groups: those who underwent TIPS placement after 7 days (Group A) and those who did not undergo TIPS placement (Group B). Additionally, patients who received pre-emptive TIPS placement between August 2022 and January 2024 were prospectively included.

Results: A total of 47 patients were included (pTIPS group=19, Group A=11, and Group B=17). There were no statistically significant differences between the groups regarding age, gender, aetiology of cirrhosis or Child-Pugh and MELD scores (p>0.05). Early relapse rates (under week 6) were significantly lower in the pTIPS-group (5.3%) versus Groups A (63.6%) and B (35.3%) (p<0.001 and p=0.030, respectively).

There were no significant differences in 30-day mortality and length of stay between the pTIPS-group and the whole control group (A+B) (p=0.683 and p=0.269, respectively). Hepatic encephalopathy was significantly lower in the pTIPS-group (after pTIPS placement) compared to Group B (31.6% vs.

81.8%, $p=0.008$). Readmission rates because of VB were significantly lower in the pTIPS group compared to the whole control group (A+B) (0% vs. 39.3%, $p<0.001$).

Conclusion: This real-life study demonstrates that pre-emptive TIPS placement significantly reduces the early relapse rates of variceal bleeding in cirrhotic patients compared to delayed TIPS or no intervention. The lower rates of early relapse, decreased readmissions due to VB, and reduced occurrence of hepatic encephalopathy suggest that pTIPS could play a crucial role in lowering morbidity and complications in these patients. While 30-day mortality rates showed no significant differences between the pTIPS group and the control groups, the decreased need for subsequent interventions and hospital readmissions may translate into improved long-term outcomes and reduced healthcare costs. These results support the proactive use of pTIPS in clinical practice for selected patients with acute VB to optimize patient care and outcomes. Further studies with larger sample sizes and longer follow-up periods are needed to validate these findings and further refine the guidelines for pTIPS placement in this context.

Disclosure: Nothing to disclose.

Upper GI Endoscopy: From diagnosis to treatment

17:00-18:00 / Lehar 2

OP037

THE CAUSES OF POST ENDOSCOPY UPPER GASTROINTESTINAL CANCER IN SURVEILLANCE ENDOSCOPY: PILOT RESULTS FROM THE NATIONAL ROOT CAUSE ANALYSIS PROJECT

A. Srinivasa¹, R. Fiadeiro², S. Goel², T. Rahman², T. Gentry², N.E Burr³, M. Banks⁴, R. Tighe⁵, M. McCord⁶, M. Fullard⁷, C. Healey⁸, A. Moore⁹, A. Dhar¹⁰, D. Mukherjee¹¹, G. Longcroft-Wheaton¹², B. Colley¹³, R. Valori¹⁴, N. Trudgill¹⁵

¹Sandwell and West Birmingham NHS Trust, Gastroenterology, West Bromwich, United Kingdom, ²Health Data Insight CIC, Cambridge, United Kingdom, ³Leeds Institute for Biomedical and Clinical Sciences, Gastroenterology, Leeds, United Kingdom, ⁴University College London Hospital NHS Trust (UCLH), Endoscopy Unit, Gastrointestinal services, London, United Kingdom, ⁵Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom, ⁶Heartburn Cancer UK, Basingstoke, United Kingdom, ⁷WEST HERTFORDSHIRE HOSPITALS NHS TRUST, Watford, United Kingdom, ⁸Airedale Nhs foundation trust, Gastroenterologist, Keighley, United Kingdom, ⁹Royal Liverpool and Broadgreen University Hospital NHS Trust, Gastroenterology, Liverpool, United Kingdom, ¹⁰Darlington Memorial & Bishop Auckland Hospitals, Gastroenterology, Darlington, United Kingdom, ¹¹BARKING, HAVERING AND REDBRIDGE UNIVERSITY HOSPITALS NHS TRUST, Romford, United Kingdom, ¹²Portsmouth Hospitals NHS trust, Gastroenterology, Hampshire, United Kingdom, ¹³Royal United Hospital, Bath, United Kingdom, ¹⁴Gloucestershire NHS Foundation Trust - Medicine, Gloucestershire NHS Foundation Trust; Cheltenham/GB, Medicine, Cheltenham, United Kingdom, ¹⁵Sandwell and West Birmingham NHS Trust, West Bromwich, United Kingdom

Contact E-Mail Address: amarsrinivasa@nhs.net

Introduction: Post endoscopy upper gastrointestinal cancers (PEUGIC) can be missed opportunities to diagnose earlier or even prevent cancer. PEUGIC in patients undergoing endoscopic surveillance for pre-malignant conditions (e.g. Barrett's oesophagus) are an important quality metric. A process for identifying PEUGIC and performing root cause analysis was piloted and the results are described.

Aims & Methods: The aims of the project were to develop a system to identify all PEUGIC in the English NHS and to allow endoscopy providers to conduct standardised root causes analysis of their PEUGIC via an online platform. This study allows local learning from PEUGIC and quantifies the reasons why PEUGIC occur at a national level.

PEUGIC occurring 3-36 months after a non-diagnostic (index) endoscopy between 2017 and 2023 were identified from final or provisional registrations in the National Cancer Registration and Hospital Episode Statistics Datasets held by the National Cancer Registration and Analysis Service. Data for root cause analysis were uploaded onto a secure root cause analysis portal following local hospital review. Only PEUGIC following surveillance endoscopy were included in this analysis.

Results: 305 PEUGIC were examined by local reviewers in 13 hospitals in England. 40 were excluded, due to errors in provisional cancer data. Data were available for 220 PEUGIC (83%). 54 PEUGIC (26%) were undergoing surveillance for either Barrett's oesophagus (87%) or chronic atrophic gastritis (13%).

Table 1 shows the PEUGIC root cause analysis based on World Endoscopy Organisation categorisation (Kamran Endoscopy 2023). Inadequate assessment or decision making was found in 11% of PEUGIC. Findings in addition to the pre-malignant lesion: oesophageal PEUGIC focal lesion 17%; gastric PEUGIC focal lesion 29%. For oesophageal PEUGIC, 40% were diagnosed 3 months after the recommended surveillance date and 10% were interval cancers. In gastric PEUGIC, 29% were diagnosed 3 months after the recommended surveillance date and 29% were interval cancers.

Gastric PEUGIC tended to present more advanced stage 2 cancer or greater (43% vs 22.5% oesophageal). 2% of oesophageal and 14.3% of gastric PEUGIC were considered potentially avoidable by reviewers. Treatment appeared adversely affected with more invasive or palliative not curative treatment in 17% of oesophageal and 43% of gastric PEUGIC. Reviewers considered that 4% of PEUGIC led directly to a premature death.

PEUGIC categorisation	Number of cases
1. Lesion detected, adequate assessment and decision making but PEUGIC occurred	34 (63%)
2. Lesion detected, inadequate assessment and decision making	6 (11%)
3. Possible missed lesion, endoscopy and decision making adequate	14 (25%)
4. Possible missed lesion, endoscopy or decision making inadequate	0

Table 1 Root causes of surveillance endoscopy PEUGIC.

Conclusion: Inadequate assessment or decision making was noted in 11% of surveillance PEUGIC. Focal lesions were noted at non-diagnostic endoscopy in 19%. 43% of gastric surveillance patients presented with stage 2 cancer or greater and adverse treatment outcomes occurred in 22% of surveillance PEUGIC.

References: Kamran U, King D, Abbasi A, Coupland B, Umar N, Chapman WC, Hebbar S, Trudgill NJ. A root cause analysis system to establish the most plausible explanation for post-endoscopy upper gastrointestinal cancer. *Endoscopy*. 2023 Feb;55(2):109-118. doi: 10.1055/a-1917-0192. Epub 2022 Aug 31. PMID: 36044914.

Disclosure: Nothing to disclose.

OP038

ENDOSCOPIC RECOGNITION OF PREMALIGNANT GASTRIC CONDITIONS IN GENERAL ENDOSCOPY PRACTICE IS LOW: DATA FROM A PROSPECTIVE MULTICENTRE COHORT STUDY (PROSPERO)

A.V.Hadjinicolaou^{1,2}, I. Modolell², S. Vishwanathan¹, W.K. Tan¹, J. Ortiz Fernández-Sordo³, K. Patel⁴, D. Morris⁵, L. Chibambo⁶, M. Banks⁷, A. Bagewadi⁸, L. Alexandre⁹, I. Beales⁹, M. Johnson¹⁰, N. Trudgill¹¹, Y. Ang¹², J. Honing¹, M. Di Pietro¹

¹Early Cancer Institute, Department of Oncology, University Of Cambridge, Cambridge, United Kingdom, ²Department of Gastroenterology, Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom, ³Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom, ⁴West Suffolk NHS Trust, Suffolk, United Kingdom, ⁵East and North Herts NHS Trust, Stevenage, United Kingdom, ⁶Maidstone and Tunbridge Wells NHS Trust, Kent, United Kingdom, ⁷University College London Hospitals NHS Trust, London, United Kingdom, ⁸Queen Elizabeth Hospital NHS Trust, Kings Lynn, United Kingdom, ⁹Norfolk and Norwich University Hospitals NHS Trust, Norwich, United Kingdom, ¹⁰The Luton & Dunstable University Hospital, Luton, United Kingdom, ¹¹Sandwell & West Birmingham Hospitals NHS Trust, West Bromwich, United Kingdom, ¹²Salford Royal NHS Trust, Salford, United Kingdom

Contact E-Mail Address: andreas.hadjinicolaou@gmail.com

Introduction: Endoscopic recognition of premalignant conditions, such as Barrett’s oesophagus (BO), gastric atrophy (GA) or gastric intestinal metaplasia (GIM) offers an opportunity to prevent advanced upper gastrointestinal (UGI) cancer. However, since their prevalence in the general population is poorly defined, there are no diagnostic key performance indicators (KPIs) in UGI endoscopy.

We hypothesised that the prevalence of premalignant UGI lesions is underestimated due to poor endoscopic recognition.

Aims & Methods: The aims of this study are to determine the prevalence of premalignant UGI conditions among patients referred for an UGI endoscopy and estimate the rate of missed diagnosis. PROSPERO is a prospective, multicentre study recruiting patients across 11 hospitals in the UK referred for UGI endoscopy (NCT04843397). Patients with previous endoscopy in the last 3 years or undergoing surveillance of known premalignant disease were excluded. All patients underwent 10-picture standard photodocumentation and a standardised biopsy protocol including a minimum of 4 gastric biopsies (2 antrum and 2 body) and 4 oesophageal biopsies (2 proximal and 2 distal) in addition to targeted biopsies of endoscopic lesions. The prevalence of premalignant conditions in our prospective cohort was compared to an equal-sized, matched, historic cohort of consecutive patients at a single institution. The missed rate of premalignant lesions was calculated by comparing endoscopic detection to gold-standard histopathological diagnosis.

Results: To date, 600 patients have been recruited, of which 455 (mean age 58yrs, 42% male and 52% referred on cancer or urgent pathways) had histological data available. Premalignant UGI pathologies were diagnosed in 60 patients (13.2%), including 25 cases of BO (5.5%; mean length 2.2cm), of which three harbouring dysplasia, 36 cases of GA/GIM (7.9%) and one case of duodenal adenoma with dysplasia (0.2%). There were 7 cases of UGI cancer (1.5%). Strikingly, only 9 GA/GIM cases (25%) were suspected endoscopically and 68% of GA/GIM cases actionable for surveillance based on the MAPS guidelines were not reported by the endoscopist. The rate of histological diagnoses of GA/GIM in the historic cohort was significantly lower (1.3% vs 7.9%; p<0.0001). There was no significant difference in the duration of endoscopy between cases where premalignant gastric pathology was recognised compared to those

where it was not (12.0 vs 15.4 mins; $p>0.05$). Premalignant stomach was more likely to be recognised endoscopically by gastroenterologists than surgeons or nurse endoscopists. ($p=0.03$).

Conclusion: In this prospective cohort study, the overall prevalence of any premalignant UGI condition in the UGI endoscopy population is 13%. We found that the rate of endoscopic recognition of premalignant stomach is inadequate, with up to 75% of cases potentially missed. Rigorous training and diagnostic KPIs are warranted to improve quality in UGI endoscopy.

Disclosure: Nothing to disclose.

OP039

HOT VERSUS COLD-SNARE ENDOSCOPIC MUCOSAL RESECTION FOR NON-AMPULLARY DUODENAL LESIONS: CONSOLIDATING THE COLD REVOLUTION INTO CLINICAL PRACTICE

A. Beany^{1,2}, E.J. Aguila^{2,3}, A.A. Wawer^{2,4}, D. Bawa², J. Tan^{2,4}, R. Singh^{4,2}

¹Rambam Health Care Campus, Faculty of Medicine, Technion - Israel Institute of Technology, Department of Gastroenterology, Haifa, Israel, ²Lyell McEwin Hospital, Department of Gastroenterology, Elizabeth Vale, Australia, ³St. Luke's Medical Center Global City, Institute of Digestive and Liver Diseases, Pasig City, Philippines, ⁴University of Adelaide, School of Medical Sciences, Medicine, Adelaide, Australia

Contact E-Mail Address: andrewbeany@gmail.com

Introduction: Endoscopic mucosal resection (EMR) has increasingly gained acceptance as a minimally invasive intervention for the treatment of duodenal lesions. Despite the overall good results, there can be significant morbidity associated with performing EMR in the duodenum. Data comparing hot- and cold-snare approaches in the duodenum are currently scarce.

Aims & Methods: Our aim was to assess the efficacy and safety of hot-snare EMR (H-EMR) versus cold-snare EMR (C-EMR) for the resection of non-ampullary duodenal lesions. A prospectively collected database of duodenal lesions treated using EMR at a single tertiary medical center between 2010 and 2023 was performed. Patient demographics, lesion and procedure characteristics, outcomes, and adverse events were analyzed using R statistical software. The lesion size and procedural time were analyzed using the Mann-Whitney U test while clinical outcomes were analyzed using the Fisher's exact test. Cost savings were calculated from the averted use of clips.

Results: Seventy-one cases of non-ampullary duodenal lesions resected using the EMR technique were included (46 H-EMR; 25 C-EMR). Fifty-one lesions were resected en-bloc (31 H-EMR vs 20 C-EMR) while 20 lesions were resected in a piecemeal fashion (15 H-EMR vs 5 C-EMR). Similar demographics, lesion, and procedure characteristics were observed in both cohorts. Technical success was 100%, and no delayed perforations occurred in either cohort. Lesions resected via H-EMR had higher rates of immediate perforation (2.2% vs 0%; $p=1.0$) and delayed bleeding (9.1% vs 0%; $p=0.28$) compared to C-EMR. Interestingly, recurrence rates were higher in the H-EMR arm (15.2% vs 8%; $p=0.70$). C-EMR technique achieved a crude cost saving from clips alone of USD \$135 per patient compared to the H-EMR technique.

Conclusion: While both cohorts demonstrated excellent technical success, there was a trend towards lower adverse events and recurrence rates, as well as cost savings, when C-EMR technique was used for non-ampullary duodenal lesions. Larger prospective comparative trials are warranted to bolster the present evidence and shape the approach of tackling these rarely encountered but clinically significant lesions safely and effectively.

Disclosure: Nothing to disclose.

	Hot-snare EMR (n=46)	Cold-snare EMR (n=25)	P-value
Age , mean $\pm$ SD, y	66.72 $\pm$ 11.49	63.12 $\pm$ 11.61	0.12
Male gender , n (%)	20 (43.5)	17 (68.0)	0.08
ASA classification			0.56
Class 1, n (%)	2 (4.4)	0 (0.0)	
Class 2, n (%)	29 (63.0)	17 (68.0)	
Class 3, n (%)	15 (32.6)	8 (32.0)	
Antithrombotic use , n (%)			0.50
Antiplatelet other than aspirin	4 (9.1)	0 (0.0)	
Anticoagulation	3 (6.8)	1 (4.3)	
Both	0 (0.0)	0 (0.0)	
Size (mm)	25.93 $\pm$ 15.53	21.68 $\pm$ 38.40	0.003
Adenomatous lesions , n (%)	34 (73.9)	22 (88.0)	0.28
Cancer in final histology	1 (2.2)	0 (0.0)	0.20
Procedural time , min	62.21 $\pm$ 37.00	50.24 $\pm$ 35.50	0.12
Technique			
En-bloc resection	31 (67.4)	20 (80.0)	0.29
Submucosal lifting	44 (95.7)	23 (92.0)	0.61
APC or CAST or STSC	16 (34.8)	5 (20.0)	0.28
Adjunctive			0.002
Hemoclips	25 (54.4)	4 (16.0)	
Hemostatic agent (e.g., Purastat or Hemospray)	3 (6.5)	3 (12.0)	
Clinical outcomes , n (%)			
Technical success	46 (100.0)	25 (100.0)	1.00
Immediate perforation	1 (2.2)	0 (0.0)	1.00
Delayed perforation	0 (0.0)	0 (0.0)	1.00
Delayed bleeding	4 (9.1)	0 (0.0)	0.29
Stricture formation	0 (0.0)	0 (0.0)	1.00
Recurrence	7 (22.6)	2 (15.4)	0.70

APC: Argon Plasma Coagulation

ASA: American Society of Anesthesiologists

CAST: Cold-forceps Avulsion with adjuvant Snare-Tip soft coagulation

STSC: Snare-Tip Soft Coagulation

OP040

WITHDRAWN

OP041

EFFICACY ANALYSIS OF ENDOSCOPIC INJECTION COMBINED WITH ORAL CORTICOSTEROIDS FOR PREVENTING ESOPHAGEAL STRICTURE FOLLOWING CIRCUMFERENTIAL ENDOSCOPIC SUBMUCOSAL DISSECTION

Y. Liu¹, X. Luo¹, B. Xia¹, J. Yang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: liuyuzhi121@foxmail.com

Introduction: Endoscopic submucosal dissection (ESD) is the standard treatment for superficial esophageal cancer. Previous studies have indicated that patients with a circumferential mucosal defect of $\geq 3/4$ post-ESD are at a significantly increased risk of developing postoperative esophageal stricture. Previous research suggests that the incidence of esophageal stricture can be reduced by either endoscopic injection or oral administration of corticosteroids. However, the effectiveness of combined endoscopic injection and oral corticosteroids in preventing post-circumferential ESD esophageal stricture has not been fully analyzed.

Aims & Methods: This retrospective study included patients who underwent circumferential esophageal ESD with a mucosal defect of $\geq 3/4$ at West China Hospital, Sichuan University, from January 2014 to August 2023. Patients were divided into two groups based on whether they received corticosteroids to prevent esophageal stricture: the steroid group and the non-steroid group. The steroid group received multiple uniform injections of 80 mg triamcinolone acetonide directly into the esophageal

lesion immediately after ESD and started oral prednisolone on the third day post-operation, continuing for eight weeks; the non-steroid group did not receive corticosteroid prevention. The main outcomes measured were the incidence and timing of stricture formation.

Results: A total of 221 patients were included in the study, with 150 in the steroid group and 71 in the non-steroid group. The incidence of post-ESD esophageal stricture was 43.33% (65/150) in the steroid group and 47.89% (34/71) in the non-steroid group, with no significant difference ($P=0.564$). However, in patients with a full circumferential mucosal defect (100%), the incidence of stricture was 100% (16/16) in the non-steroid group and 76.67% (46/60) in the steroid group, a difference that was statistically significant ($P=0.032$). For patients with a defect of 3/4 to 1, the incidence was 32.73% (18/55) in the non-steroid group and 21.11% (19/90) in the steroid group, with no significant difference ($P=0.120$).

In follow-up analysis, the median time to stricture occurrence was 9 weeks (range 1.29-82.43 weeks), with median times of 9.86 weeks (range 3.71-82.43 weeks) in the steroid group and 5.27 weeks (range 1.29-49 weeks) in the non-steroid group, a statistically significant difference ($P<0.001$). For patients with a full circumferential mucosal defect, the median time to stricture occurrence was 8.5 weeks (range 1.29-49 weeks), while for patients with a defect of 3/4 to <1, the median time was 9.14 weeks (range 4.57-82.43 weeks), with no significant difference between these groups ($P=0.390$).

Conclusion: Overall, while endoscopic injection combined with oral corticosteroids does not significantly reduce the overall risk of post-circumferential ESD esophageal stricture, it can effectively extend the time to stricture occurrence. Particularly, patients with a full circumferential ESD benefit significantly from this treatment strategy, showing a reduced incidence of postoperative esophageal stricture, suggesting that such patients may benefit more from the combined use of endoscopic injection and oral corticosteroids.

References: 1. Libânio D, Pimentel-Nunes P, Bastiaansen B, et al. Endoscopic submucosal dissection techniques and technology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review. *Endoscopy*. 2023;55(4):361-389. doi:10.1055/a-2031-0874

2. Sami SS, Haboubi HN, Ang Y, et al. UK guidelines on oesophageal dilatation in clinical practice. *Gut*. 2018;67(6):1000-1023. doi:10.1136/gutjnl-2017-315414

3. Ishihara R, Arima M, Iizuka T, et al. Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. *Dig Endosc*. 2020;32(4):452-493. doi:10.1111/den.13654

Disclosure: Nothing to disclose.

Video Cases

17:00-18:00 / Lehar 3

VC01

ENDOSCOPIC CLOSURE OF A CONGENITAL TRACHEO-ESOPHAGEAL FISTULA USING A NEW ENDOSCOPIC, THROUGH-THE SCOPE, SUTURING DEVICE IN A YOUNG BOY – A CASE REPORT

M. Ellrichmann¹, G. Ivanov², I.D. Ellrichmann³, M. Mumm³, A. Meinzer², C.C. Conrad¹, R. Bergholz²

¹University Hospital Schleswig-Holstein, Interdisciplinary Endoscopy, Medical Department 1, Kiel, Germany, ²University Hospital Schleswig-Holstein, Department of General-, Visceral-, Thoracic- and Pediatric Surgery, Kiel, Germany, ³University Hospital Schleswig-Holstein, Department of Pediatric Gastroenterology, Kiel, Germany

Contact E-Mail Address: mark.ellrichmann@uksh.de

Introduction: Tracheoesophageal fistula (TEF) is a congenital or acquired pathology characterized by communication between the posterior tracheal and the anterior esophageal wall. Congenital TEF type E, “H” fistula without esophageal atresia, accounts for only 4% of cases. So far, minimal-invasive surgical techniques are accepted as first line therapy. Endoscopic interventions have been described to be safe and effective in the management of TEF, with lower morbidity and mortality compared to surgical interventions.

Aims & Methods: We present a case of a successful endoscopic closure of a TEF using a new endoscopic, through-the-scope suture device (TTS-SD, X-Tack, Boston Scientific).

Results: A 37-month-old boy presented at our clinic in early 2023 with recurrent postprandial coughing, choking and bronchopulmonary infections. At index endoscopy only a small pore was detected without evidence of a relevant TEF. Patient was rescheduled after 6 months. Over this period, symptoms significantly worsened with non-percentile-appropriate growth/weight gain.

At follow-up (FU) endoscopy a significant H-fistula was noted at 13 cm from the dental arch. After freshening the fistula pore with argon plasma coagulation (APC), a fully covered, self-expanding metal stent (fcSEMS) of 10x80 mm was inserted. This stent dislodged into the stomach after a few days and was replaced by a larger fcSEMS (20 mm diameter), which was only tolerated for another few days.

Immediately after removal, the TEF was closed endoscopically using three TTS clips. The boy was symptom-free for 3 weeks post-intervention, but then experienced a sudden recurrence of the known symptoms. Endoscopically, the clips were completely dislodged, the TEF was detectable again. Another attempt with TTS clips yielded identical results. In March 2024, an endoscopic closure was performed using the novel TTS-SD, which can be applied through the working channel of a regular gastroscope.

After freshening the scarred fistula with APC and brushes, four helices were screwed into the submucosa, the defect was continuously sutured in a cross-cross pattern. Immediately after the intervention the patient was free of symptoms. Endoscopic FU after 2 and 6 weeks showed persistent closure of the TEF with complete resolution of symptoms.

Conclusion: Congenital TEFs can be effectively managed using endoscopic techniques. In young children, fcSEMS appear to be less efficacious when compared to direct closure of the fistula. The introduction of the novel TTS-SD, has enabled successful treatment of the TEF in the present case.

The utilization of the TTS-SD represents a significant advancement in our therapeutic armamentarium for managing these complex cases especially in a small working space. However, there is need for long-term follow-up data.

Disclosure: Prof. Dr. Mark Ellrichmann received lecture honorarium, consultation fees and study support from Boston Scientific.
All other authors have nothing to declare.

VC02

ENDOSCOPIC FULL THICKNESS DISSECTION OF LOCALLY ADVANCED OESOPHAGEAL ADENOCARCINOMA IN PATIENTS UNFIT FOR SURGERY: A CASE SERIES (WITH VIDEO)

P.J. Poortmans^{1,2,3}, M.E. Argenziano^{2,3}, L. Debels^{1,2,3}, S. Smeets^{2,3}, A. Sorge², T. Tornai², L. Desomer^{4,2,3}, D.J. Tate^{2,3}

¹University Hospital Brussels (UZ Brussel), Gastroenterology and Hepatology, Jette, Belgium, ²University Hospital Ghent, Gastroenterology and Hepatology, Ghent, Belgium, ³University of Ghent, Faculty of Medicine, Ghent, Belgium, ⁴AZ Delta, Gastroenterology, Roeselare, Belgium

Contact E-Mail Address: pjpoortmans@hotmail.com

Introduction: The incidence of oesophageal adenocarcinoma (OAC) has increased worldwide and is associated with high mortality.[1] Surgery is considered the backbone of curative intent treatment for locally advanced disease but is associated with a high procedure-related morbidity and mortality [2-4].

Aims & Methods: We present 3 cases of suspected deep submucosal (T1b sm2-3) or muscular invasive (T2) OAC who had no distant or nodal disease, were unfit for surgery, declined chemoradiotherapy and consented to endoscopic full thickness dissection (EFTD) of their tumour. Disease staging was with a combination of endoscopic imaging, endoscopic ultrasound and positron emission tomography and computed tomography.

Prior to resection the lesion was delineated and marked using soft coagulation. A submucosal tunnel was dissected (Spray coag. effect 4.2) towards the suspected area of deep invasion. Once invasion was detected a muscularis propria (MP) incision (EndoCut Q) was made 10mm away (oral-side) until the peri-oesophageal space was reached.

To minimise the area of excised MP the submucosal plane was entered distal from the lesion in retroflexion (via a second tunnel) and an incision into the MP was made 10mm caudal to the invasive component.

Saline-immersion with use of a water exchange device was used to increase visualisation in the peri-oesophageal space and connect both muscular incisions. The margins of the tunnel and MP were then dissected. Subsequently a fully covered self-expanding metal stent was placed to cover the entire defect.

On post-operative day (POD) 2 all patients were restarted with fluids. Oral intake was increased over several days to semi-solid. Broad-spectrum antibiotics were started during the procedure and continued for a total of 5 days. Mean time to discharge was POD 5 (range 3–7 days).

Results: In 2 cases the OAC was poorly differentiated with deep submucosal invasion (pT1b sm3). The third case was a moderately differentiated OAC with MP-invasion (pT2). In each case EFTD provided local clearance of tumour. Initial 30-day follow-up showed no evidence of complications. Patients were followed up from the date of resection to present (range 1–16 months) without evidence of local recurrence or metastatic disease.

Conclusion: Three patients with locally advanced OAC who declined alternative treatments underwent successful endoscopic full thickness resection. No evidence of disease recurrence was found on endoscopy, imaging and pathology during follow-up to date.

These results suggest local endoscopic therapy should be considered in selected patients with locally advanced OAC, especially if ineligible for conventional treatment.

Patient details	Reason for deviating from guidelines	Histopathology	Follow-up (endoscopy, biopsies and PET-CT at 3mo, 6mo, 12mo)
84 y.o. male	Frailty, synchronous colorectal cancer for which surgery is needed.	- Type: Moderately differentiated adenocarcinoma - Depth: pT2 - Lymphovascular invasion: absent - Perineural invasion: absent - Margins: R0 resection	Time since resection: 16 months. Follow-up: ● 3 months: No local recurrence, no evidence for lymphatic or distant metastases (NO M0) ● 6 months: No local recurrence, no evidence for lymphatic or distant metastases (NO M0) ● 12 months: No local recurrence, no evidence for lymphatic or distant metastases (NO M0)
64 y.o. male	Multimorbid (cardiac disease, COPD, morbidly obese) with high peri-operative risk.	- Type: Poorly differentiated mucinous adenocarcinoma - Depth: pT1b sm3 - Lymphovascular invasion: present - Perineural invasion: present - Margins: R0 resection	Time since resection: 6 months. Follow-up: ● 3 months: No local recurrence, no evidence for lymphatic or distant metastases (NO M0) ● 6 months: No local recurrence, no evidence for lymphatic or distant metastases (NO M0)
82 y.o. female	Frailty, multimorbid (cardiovascular disease, cirrhosis) with high peri-operative risk.	- Type: Poorly differentiated adenocarcinoma - Depth: pT1b sm3 - Lymphovascular invasion: absent - Perineural invasion: absent - Margins: R0 resection	Time since resection: 1 month. Follow-up: -

Table 1: overview of cases with cT2N0M0 treated by EFTD, including patient details, reasons for deviating from guidelines, histopathological results of the resection-specimen, and details on follow-up. COPD, chronic obstructive pulmonary disease. EFTD, endoscopic full thickness dissection. PET-CT, positron emission tomography and computed tomography. R0, free deep and lateral margins.

References:

- Bray, F., et al., *Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries*. CA Cancer J Clin, 2024.
- Obermannova, R., et al., *Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up*. Ann Oncol, 2022. 33(10): p. 992-1004.
- Ajani, J.A., et al., *Esophageal and Esophagogastric Junction Cancers, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology*. J Natl Compr Canc Netw, 2019. 17(7): p. 855-883.
- Mota, F.C., et al., *Neoadjuvant therapy or upfront surgery? A systematic review and meta-analysis of T2N0 esophageal cancer treatment options*. Int J Surg, 2018. 54(Pt A): p. 176-181.

Disclosure: Nothing to disclose.

VC03

WHEN A MISFORTUNE DOES NOT COME ALONE: CHALLENGES AND COMPLICATIONS OF BILIARY AND DIGESTIVE TRACT ANASTOMOSIS BY ENDOSCOPIC ULTRASOUND

D. Abrantes¹, J. Cortez Pinto¹, B. Morão¹, R. Loureiro¹, E. Barjas¹, L. Glória¹

¹Unidade Local de Saúde de Loures-Odivelas, Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal

Contact E-Mail Address: dani-abrantes@hotmail.com

Introduction: Malignancies involving the duodenum, major papilla, head of the pancreas and distal common bile duct can lead to malignant biliary and gastric outlet obstruction. When clinical presentation of biliary and duodenal obstruction is simultaneous, these tumors are usually at the late stage of the disease and the only option is palliative treatment to improve the quality of life of these patients.

Aims & Methods: We describe a dual biliary and digestive tract drainage by endoscopic ultrasound (EUS) in a patient with metastatic squamous cell carcinoma (SCC) of the cervix causing dilation of the bile duct, bulb and stomach with sleeve infiltration at the level of the hepatic hilum and duodenal arch.

Results: A 67-year-old woman, performance status 0, diagnosed with SCC of the cervix in 2022 underwent curative treatment. In February 2024 was admitted due to jaundice and vomiting progressing for 2 months. Computed tomography revealed dilatation of the bile duct, bulb and stomach with sleeve infiltration of the duodenal arch. Endoscopic ultrasound (EUS) identified a heterogeneous lesion causing obstruction of the middle third of the bile duct, confirming the diagnosis of metastatic SCC of the cervix. After discussion with multidisciplinary team, the patient was proposed for palliative treatment.

Subsequently, she underwent EUS-guided gastrojejunostomy with placement of a 20x10mm lumen-apposing metal stent (LAMS). Bile duct drainage wasn't done due to absence of bile duct dilatation over 12mm as the total bilirubin levels frankly decreased with corticotherapy.

However, a week later, the total bilirubin levels increased and a biliary drainage was proposed, attempting access to the papilla through gastrojejunostomy, a procedure complicated by migration of the gastric end of the LAMS into the peritoneal cavity. The guidewire was immediately placed, the LAMS was mobilized into the stomach, concurrently initiating broad-spectrum antibiotic therapy.

Despite this initial event, it was decided to proceed with EUS-guided choledocoduodenostomy after identifying the bile duct, placing a 6x8mm LAMS with the distal end released outside the bile duct and positioning a fully covered 40x10mm metal biliary stent coaxially to the LAMS as a rescue, with the end below the confluence and no evidence of contrast extravasation on fluoroscopy. The procedure was complicated by respiratory distress with symptomatic relief after pneumoperitoneum drainage. Recovery was uneventful and the patient was discharged 5 days after biliary drainage and is well after 30 days of follow up.

Conclusion: EUS guided procedures such as biliary drainage and gastrojejunostomy are likely to spread quickly in clinical practice for the treatment of concomitant malignant biliary and gastric outlet obstruction. The following case is presented due to the importance of recognizing and managing intraprocedural complications associated with LAMS.

References: Rizzo GEM, Carrozza L, Quintini D, Ligresti D, Traina M, Tarantino I. A Systematic Review of Endoscopic Treatments for Concomitant Malignant Biliary Obstruction and Malignant Gastric Outlet Obstruction and the Outstanding Role of Endoscopic Ultrasound-Guided Therapies. *Cancers (Basel)*. 2023 Apr 30;15(9):2585.

Disclosure: Nothing to disclose.

VC04

ENDOSCOPIC INTERMUSCULAR DISSECTION FOR EARLY GASTRIC CANCER WITH SEVERE SUBMUCOSAL FIBROSIS

D. Parekh¹, N. Takeuchi², S. Takayanagi², Y. Kimoto², Y. Minato², H. Chiba³, K. Ohata²

¹Mumbai Institute of Gastroenterology, Department of Endoscopy, Mumbai, India, ²NTT Medical Center Tokyo, Department of Endoscopy, Tokyo, Japan, ³Omori Red Cross Hospital, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: dparekh2108@gmail.com

Introduction: Severe submucosal fibrosis (SSF) in early gastric cancer (EGC) is known to cause technical difficulty for endoscopic resection.^{1,2} Various methods have been reported to tackle this problem. However, there is no established consensus on the management of this situation.

Endoscopic intermuscular dissection (EID) has been successfully used in the rectum to overcome SSF.³

The procedure involves the dissection between the circular and longitudinal layers of the muscularis propriae. Recently, the procedure has been used in the stomach for en bloc resection of a neuroendocrine tumor.⁴ We report a case endoscopic resection of early gastric cancer with severe submucosal fibrosis where EID was used to attain a negative vertical margin.

Aims & Methods: We aim to demonstrate the use of EID in the stomach to overcome the challenge of SSF in endoscopic resection of early cancer. An 81 year male underwent an upper endoscopy for heaviness and discomfort in the epigastrium for few months. It revealed an approximately 25mm lesion around a healed ulcer scar at the gastric angle on the lesser curvature side with irregular surface and vascular pattern and a clear demarcation line. Biopsy showed high grade dysplasia and endoscopic resection was planned. Since the lesion was over a healed ulcer scar, and endoscopy showed convergence of gastric folds towards the lesion, SSF was expected. The resection was started by conventional endoscopic submucosal dissection in retroflexion and a tunnel was created under the distal side of the tumor. However, after the incision and initial submucosal dissection, we encountered SSF. We decided to carefully dissect in the intermuscular plane underneath the fibrotic area by identifying and separating the circular and longitudinal muscle layer. Similar method was used on the oral side where EID was performed after initial ESD and tunnel was completed. Resection was accomplished and the circular muscle defect in the middle of the ulcer was closed with multiple endoclips.

Results: Total procedure time was 60 minutes. En bloc specimen measured 56mm x 40mm. There were no immediate or early complications. Patient was started on soft diet on post procedure day 1 and discharged on day 5. Pathology was tubular adenoma with high grade dysplasia. Horizontal and vertical margins were negative and specimen contained the muscle layer.

Conclusion: This case demonstrates the feasibility of EID in the stomach without any special accessories or equipment. EID can be used to overcome severe submucosal fibrosis in early gastric cancer. Further studies on wider applicability of gastric EID in clinical practice would be worthwhile.

References:

1. Jeong JY, Oh YH, Yu YH et al. Does submucosal fibrosis affect the results of endoscopic submucosal dissection of early gastric tumors?. *Gastrointestinal endoscopy*. 2012 Jul 1;76(1):59-66.
2. Higashimaya M, Oka S, Tanaka S et al. Outcome of endoscopic submucosal dissection for gastric neoplasm in relationship to endoscopic classification of submucosal fibrosis. *Gastric Cancer*. 2013 Jul;16:404-10.
3. Toyonaga T, Ohara Y, Baba S et al. Peranal endoscopic myectomy (PAEM) for rectal lesions with severe fibrosis and exhibiting the muscle-retracting sign. *Endoscopy*. 2018 Aug;50(08):813-7.
4. Despott EJ, Lucaci LA, Murino A et al. First report of gastric endoscopic intermuscular dissection. *Endoscopy*. 2024 Dec;56(S 01):E132-3.

Disclosure: Nothing to disclose.

VC05

ANTI-REFLUX MUCOSAL ABLATION -MUCOPLASTY (ARMA-P) AS A MODIFICATION OF ARMA FOR THE MANAGEMENT OF PROTON PUMP DEPENDENT OR REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE (GERD). A PILOT STUDY IN A HIGH PREVALENCE REGION OF THE WORLD

A.H. Raina¹

¹Burjeel Hospital, Gastroenterology and Hepatology, Abu Dhabi, United Arab Emirates

Contact E-Mail Address: hameedraina49@gmail.com

Introduction: Gastroesophageal reflux disease (GERD) is common and found in 8.7 to 33.1% of the population in the middle east(1).

Proton Pump Inhibitor (PPI) is the most common modality of treatment used. Anti reflux Mucosal Ablation (ARMA) is a novel simple minimally invasive endoscopic therapy for PPI dependent or refractory GERD(2).

However, it takes about 4-6 weeks to see its effects and long-term response is not guaranteed.

Further, there is a risk of immediate and delayed bleeding and ulcer formation. Certain modifications like in ARMS(3) can shorten the time of its response, enhance its effectiveness, and make it safer and long lasting.

Aims & Methods: The study aimed to modify the ARMA technique to shorten its response time and enhance its effectiveness and safety in United Arab Emirates which is a high prevalence region for GERD in the world. All adult patients with proven severely symptomatic GERD for more than five years with Hill's grade I to III were recruited.

All patients underwent ARMA in endoscopy suit under general anaesthesia. The standard technique of ARMA was applied. Deep ablation was done till the appearance of the muscle layer. About 1 cms of gap was kept unablated between the esophageal mucosa and the gastric mucosa and along the greater curvature side to prevent stricture. The ablated area spread on about 1.5 to 2cms. The setting used were 1.6 to 1.8 l/min flow rate and 80-100-watt voltage. About 5-8 normal endoclips were used for mucoplasty. The endoclips were applied across the ablated area closing the edges to prevent any bleeding, shorten the scarring time and enhance its effectiveness. All the procedures were performed as out patients. Check EGD was performed after one and three months.

Clinical follow up was done at 2 weeks, four, 12, 24 and 48 weeks. pH metry tests were repeated at three, six and twelve months to confirm or rule out recurrent GERD.

Results: Six patients who consented were included in the study. Four were females and two were males. Mean Age was 43 years (IQR 31-55 years). The average time for ARMA-P was 47 ± 8 minutes. All the procedures were uneventful. Two patients complained of moderate retrosternal pain which responded well to analgesics and PPI during first three days of the procedure.

No immediate or delayed bleeding, perforation, any other adverse events were noted in any patient. PPI were stopped two weeks of the procedure in all the patients.

All the patients did well off PPI only after two weeks of the procedure. Check EGD showed proper healing and adequate scarring, forming a tight flap valve of the cardia around the GE junction as early as four weeks post procedure. All the six patients are asymptomatic and off PPI at 12 months of follow up.

Conclusion: Mucoplasty after ARMA using endoclips makes the results of ARMA faster, safer, more effective, and long lasting. However, large randomized studies are required to validate these findings

References:

1. Li, N., Yang, WL., Cai, MH. et al. Burden of gastroesophageal reflux disease in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of disease study 2019. BMC Public Health 23, 582 (2023).

2. Rodríguez de Santiago E, Sanchez-Vegazo CT, Peñas B, Shimamura Y, Tanabe M, Álvarez-Díaz N, Parejo S, Kazuya S, Marcos-Carrasco N, Vazquez-Sequeiros E, Inoue H, Albillos A. Antireflux mucosectomy (ARMS) and antireflux mucosal ablation (ARMA) for gastroesophageal reflux disease: a systematic review and meta-analysis. Endosc Int Open. 2021 Nov 12;9(11):E1740-E1751.

3. Haruhiro Inoue, Kazuki Yamamoto, Marc Julius Navarro, Kei Ushikubo, et al. Antireflux mucoplasty, an evolution of endoscopic antireflux therapy for refractory GERD. Video GIE, VOLUME 8, ISSUE 11, P435-440, NOVEMBER 2023.

Disclosure: Nothing to disclose.

VC06

MANAGEMENT OF LUMEN APPOSING METAL STENT DISLOCATION DURING ENDOSCOPIC ULTRASOUND-DIRECTED TRANSGASTRIC ERCP WITH A DEDICATED ENDOSCOPIC SUTURING DEVICE

E. Palmeri¹, P. Hindryckx¹

¹Ghent University Hospital Dept. of Gastroenterology, Dept. of Gastroenterology, Ghent, Belgium

Contact E-Mail Address: epalmeri94@gmail.com

Introduction: A 37-year-old woman was referred to our unit because of typical biliary colics with transient cholestasis. Her relevant medical history included a cholecystectomy and a sleeve gastrectomy, later on converted to a gastric bypass.

After multidisciplinary discussion, we opted for an endoscopic ultrasound-directed transgastric ERCP (EDGE) using a 20/10 lumen-apposing metal stent (LAMS).

Due to the previous sleeve gastrectomy, the LAMS had to be placed between the jejunum and the excluded antrum. According to international expert recommendations, the ERCP was scheduled two weeks post-LAMS placement to allow for tract maturation [1].

Nevertheless, the proximal flange of the LAMS dislocated during duodenoscope introduction and ended up in the peritoneal cavity. A decompressing needle was placed and the proximal flange was retrieved in the peritoneal cavity under fluoroscopic guidance, using a therapeutic gastroscope.

After a non-successful attempt to reposition the proximal flange through the fistula tract in the jejunum, a guidewire was placed through the LAMS lumen in the excluded antrum. A bridging attempt with a 22mm x 10 cm fully covered enteral stent through the LAMS lumen failed.

Subsequently, intraperitoneal endoscopic closure of the fistula towards the excluded antrum was performed with the X-tack system.

Next, we removed the LAMS and the enteral stent from the peritoneal cavity and completely sealed the fistula tract from the jejunal side with x-tack endosutures and clips.

The patient was put on antibiotics and could start oral feeding the day after the procedure. Besides moderate abdominal pain the first 2 days after the procedure and a transient elevation of the CRP, the further clinical course was uneventful.

Aims & Methods: The rescue intervention was conducted with a gastroscope with 3,8 mm working channel. A 22 x 10 cm fully covered enteral SEMS was used in the attempt of bridging the excluded antrum. X-tack endosuture system was chosen to achieve the closure of the fistula.

Results: The X-tack system proved to be an effective tool in addressing not only the intraluminal perforation but also in the intraperitoneal endoscopic closure of the fistula extending towards the excluded antrum.

Conclusion: This case illustrates the potential of endoscopic suturing devices as minimally invasive alternatives to surgery for management of large iatrogenic perforations.

References: [1] S. Stefanovic et al., “International Consensus Recommendations for Safe Use of LAMS for On- and Off-Label Indications Using a Modified Delphi Process,” *Am. J. Gastroenterol.*, Dec. 2023, doi: 10.14309/ajg.0000000000002571.

Disclosure: Nothing to disclose.

VC07

CYSTO-GASTRIC BYPASS OS POST-TRAUMATIC HEPATIC SUBCAPSULAR COLLETION USING LUMINAL APPPOSITION STENT

C. Solak¹, E.L.A. Artifon², M. Facanali³, F. Martins Acras¹, R. Maziero¹

¹*Santa Casa de Misericórdia de Ponta Grossa, Endoscopy, Ponta Grossa, Brazil,* ²*Universtiy of Sao Paulo., Endoscopy, Sao Paulo, Brazil,* ³*University of São Paulo, Endoscopy, São Paulo, Brazil*

Contact E-Mail Address: claudiosolak@yahoo.com

Introduction: Ultrasound-guided drainage is already a consolidated and advantageous option in relation to percutaneous drainage, as it promotes greater comfort and safety in addition to shorter hospital stays. The luminal apposition stent (LAMS) has further increased the effectiveness and safety of ultrasound-guided drainage, as it has a larger diameter lumen, improving drainage efficiency and enabling intraluminal access with a standard endoscope. Proximal and distal flanges promote a lower stent migration rate. Its main indications are for the drainage of intra-abdominal liquid collections, decompression of obstructed bile ducts, creation of anastomoses or creation of fistulous tracts between organs that can facilitate other specific endoscopic interventions.

Aims & Methods: We report the case of a 43-year-old male patient, victim of a motorcycle x truck collision, initially diagnosed with a clavicle fracture. Opting for conservative treatment, he was discharged from hospital. Thirty days after the accident, he sought medical attention due to pain and increased abdominal volume. Abdominal computed tomography (CT) showed grade III liver laceration, with hepatic subcapsular collections, the largest measuring 21x18x12cm, in addition to a collection next to the hepatocolledocus suggestive of biliary fistula.

Results: We opted for endoscopic retrograde cholangiopancreatography (ERCP) and ultrasound-guided drainage of the collections. During ERCP, papillotomy was performed to correct the proximal biliary fistula. During ultrasound endoscopy, a subcapsular lesion was assessed in close contact with the gastric wall, followed by ultrasound-guided drainage using LAMS. There was drainage of 3,000mL of hematic-purulent content. Endoscopic control after 7 days revealed improvement in the capsular pattern. On the 14th day of evolution, the LAMS was removed, followed using 2 double-pigtail stents to maintain residual drainage. Two CT scans were performed 30 and 60 days after the procedure, with complete resolution of the collection observed on the last CT scan.

Conclusion: Several cases are reported in the literature of the use of LAMS for drainage of intra-abdominal collections, however, for subcapsular lesions, only one reported case was found and, like ours, there was a satisfactory result. The use of LAMS for this type of intervention is uncommon, but it suggests that it is an effective alternative. Prospective studies are needed to better evaluate the efficacy of LAMS in hepatic subcapsular lesions.

Disclosure: Nothing to disclose.

VC08

ENDOSCOPIC KNIFE-ASSISTED FULL-THICKNESS RESECTION OF A DEEPLY INVASIVE RECTAL CANCER USING A COMBINATION OF POCKET-CREATION AND SALINE-IMMERSION TECHNIQUES

M.E. Argenziano^{1,2}, A. Sorge^{1,3}, P.J. Poortmans^{1,4}, S. Smeets¹, M. Montori^{1,2}, L. Ferdinande⁵, A. Hoorens⁵, L. Debels⁴, T. Tornai¹, L. Desomer⁶, D.J. Tate¹

¹*University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium,* ²*Clinic of Gastroenterology, Hepatology, and Emergency Digestive Endoscopy, Ancona, Italy,* ³*University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy,* ⁴*Vrije Universiteit Brussel, Gastro-enterology & Hepatology, Jette, Belgium,* ⁵*University Hospital Gent, Dept. of Pathology, Gent, Belgium,* ⁶*AZ Delta campus Rumbeke, Gastroenterology and Hepatology, Roeselare, Belgium*

Contact E-Mail Address: mariaeva.argenziano@gmail.com

Introduction: In patients with rectal cancer, deep submucosal invasion is not an independent risk factor for lymph node metastasis (absolute risk: 2.6%). [1] Total mesorectal excision is associated with high rates of morbidity (12.1%-13.4%) mortality (1%-1.5%) and recurrence (3%-6%).[2,3] Valuable options include Transanal minimally invasive surgery (TAMIS) [4], endoscopic full-thickness resection (FTR) using a dedicated device for rectal lesions up to 20 mm[5] and endoscopic intermuscular dissection (EID) for distal rectal lesions. [6] We describe a case of endoscopic knife-assisted FTR for a deeply invasive T1 proximal rectal cancer.

Aims & Methods: A 61-year-old patient with concomitant esophageal (cT2N0M0) and pharyngeal (cT3N2M0) squamous cell cancers in treatment with chemo-radiotherapy was referred with a incidentally detected rectal lesion. Endoscopy showed a sessile 25-mm proximal rectal lesion with a demarcated and slightly depressed central area (Paris 0-Is+IIC, JNET-3). MRI raised suspicion of muscularis propria involvement.

Following a multidisciplinary team discussion, endoscopic resection was chosen considering the patient's active oncologic comorbidities. Due to the lesion size, using a FTR device was not feasible, and EID was unsuitable for the proximal rectum.

Therefore, endoscopic submucosal dissection (ESD) with knife-assisted FTR was performed. Initially, a pocket-creation method was used to reach and assess the point of deepest invasion at the center of the lesion. Loss of the dissection plane due to the lesion adhering to the muscularis propria at its center (revealed by saline-immersion in the pocket) necessitated FTR. Thus, a circular mucosal incision was made, followed by trimming and submucosal dissection to isolate the central deep invasion. Clips, rubber bands, and surgical wires were used to apply traction and enhance access to the resection plane. A full-thickness resection of the muscularis propria with the electrosurgical knife around the center of the lesion was performed. The resection defect was carefully washed with sterile saline and closed with clips. Antibiotic peri-procedural prophylaxis was administered.

Results: The post-procedural course was uneventful, and the patient was discharged home 24 hours after the resection. Histopathology revealed R0 resection of a low-grade intestinal-type adenocarcinoma with a central deep submucosal invasion in contact with the muscular layer without muscularis propria involvement, tumor budding, or perineural invasion (pT1, Kikuchi level sm3). Focal lymphovascular invasion was observed. Given the patient's clinical status endoscopic and radiologic follow-up was advised by a multi-disciplinary team.

Conclusion: The staged approach of pocket creation, assessment of deep SMI and planned endoscopic knife-assisted FTR for a deeply invasive T1 proximal rectal cancer was safe and effective, allowing for R0 deep resection margins.

References: [1] Zwager LW, et al. Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis. *Gastroenterology*. 2022

[2] van Oostendorp SE, et al. Local recurrence after local excision of early rectal cancer: a meta-analysis of completion TME, adjuvant (chemo)radiation, or no additional treatment. *Br J Surg*. 2020

[3] Liu H, et al.; Chinese Transanal Endoscopic Surgery Collaborative (CTE-SC) Group. Morbidity, Mortality, and Pathologic Outcomes of Transanal Versus Laparoscopic Total Mesorectal Excision for Rectal Cancer Short-term Outcomes From a Multicenter Randomized Controlled Trial. *Ann Surg*. 2023

[4] Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. *Surg Endosc*. 2010

[5] Dolan RD, et al. Endoscopic full-thickness resection of colorectal lesions: a systematic review and meta-analysis. *Gastrointest Endosc*. 2022

[6] Moons LMG, et al. Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum: a new endoscopic approach. *Endoscopy*. 2022

Disclosure: DJT Consulting and research founding Olympus, Fujifilm, Pentax.

Ameliorating acute disease through novel treatment in IBD: Part 1

08:30-09:30 / A3

OP042

EFFICACY OF GUSELKUMAB VERSUS PLACEBO IN CROHN'S DISEASE
BASED ON PRIOR RESPONSE/EXPOSURE TO BIOLOGIC THERAPY:
RESULTS OF THE GALAXI 2 & 3 PHASE 3 STUDIES

B.E. Sands¹, G. D'Haens², S. Danese³, T. Hisamatsu⁴, W. Reinisch⁵, N.A. Terry⁶, L. Salese⁶, R. Van Rampelbergh⁷, Z. Yang⁶, J. Johanss⁶, G. DuVall⁸, N. Abu Farsakh⁹, R. Panaccione¹⁰

¹Dr. Henry D Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America,

²Department of Gastroenterology, Amsterdam University Medical Centers, Amsterdam, Netherlands, ³Gastroenterology and Endoscopy, IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Milan, Italy, ⁴Department of Gastroenterology and Hepatology, Kyorin University, Tokyo, Japan, ⁵Division of Gastroenterology & Hepatology, Medical University of Vienna, Vienna, Austria, ⁶Janssen Research & Development, LLC, Spring House, United States of America, ⁷Janssen Research & Development, Antwerp, Belgium, ⁸Tyler Research Institute, LLC, Tyler, United States of America, ⁹King Abdullah University Hospital, Irbid, Jordan, ¹⁰Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Canada

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: GALAXI 2 & 3 are identically designed 48-week, randomized, double-blind, double-dummy, placebo (PBO)- and active-comparator, treat-through registrational trials assessing the efficacy and safety of IV induction and SC maintenance therapy with guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor, in participants (pts) with moderately to severely active Crohn's disease (CD).

Primary results of each study were previously reported; here we explore the impact of biologic therapy exposure on efficacy outcomes with GUS compared to PBO in the pooled GALAXI 2 & 3 dataset.

Aims & Methods: Pts with inadequate response or intolerance to conventional therapy or biologic therapy (BIO-ir), active CD (CDAI 220–450 + mean daily SF>3 or AP>1), and SES-CD≥6 (≥4 for isolated ileal disease) were randomly assigned 2:2:2:1 at week (Wk) 0 to GUS 200mg IV q4w (x3)→100mg SC q8w, GUS 200mg IV q4w (x3)→200mg SC q4w, UST IV→SC, or PBO. In each trial, the composite co-primary endpoints were:

1. Clinical response at Wk12 + clinical remission at Wk48, and;
2. Clinical response at Wk12 + endoscopic response at Wk48, comparing each GUS regimen to PBO. Major secondary endpoints included clinical remission at Wk12 and endoscopic response at Wk12. Analyses of BIO-ir and BIO-naïve subgroups in the individual trials were prespecified; pooled analyses were performed post hoc.

Results: In the pooled dataset, 52% (378/730) of pts randomized to PBO or GUS had a prior history of BIO-ir and 42% (305/730) were BIO-naïve (6% [47/730] had prior exposure to biologics but no documented failure). At Wk12, GUS achieved higher rates of clinical remission and endoscopic response compared to PBO in the overall population and BIO-ir and BIO-naïve subgroups (Table). For the composite co-primary endpoints, both GUS regimens also achieved higher rates of 1) clinical response at Wk12 +

clinical remission at Wk48 and 2) clinical response at Wk12 + endoscopic response at Wk48 compared to PBO in the overall population and BIO-ir and BIO-naïve subgroups.

Overall population			Participants with a history of inadequate response or intolerance to at least 1 prior biologic* (BIO-ir)			Participants with no history of exposure to biologics* (BIO-naïve)			
	PBO N=148	GUS 200mg IV combined ^b N=582		PBO N=78	GUS 200mg IV combined ^b N=300		PBO N=61	GUS 200mg IV combined ^b N=244	
Clinical remission at Wk12	28 (18.9%)	274 (47.1%) Δ 28.0% P<.001*		15 (19.2%)	138 (46.0%) Δ 26.9% P<.001*		10 (16.4%)	121 (49.6%) Δ 32.1% P<.001*	
Endoscopic response at Wk12	18 (12.2%)	215 (36.9%) Δ 25.2% P<.001*		5 (6.4%)	87 (29.0%) Δ 22.6% P<.001*		11 (18.0%)	113 (46.3%) Δ 27.7% P<.001*	
	PBO N=148	GUS 100mg ^c N=286	GUS 200mg ^d N=296	PBO N=78	GUS 100mg ^c N=153	GUS 200mg ^d N=147	PBO N=61	GUS 100mg ^c N=116	GUS 200mg ^d N=128
Clinical response at Wk12 + clinical remission at Wk48 (composite co-primary endpoint)	18 (12.2%)	137 (47.9%) Δ 35.8% P<.001*	152 (51.4%) Δ 39.0% P<.001*	10 (12.8%)	70 (45.8%) Δ 33.2% P<.001*	73 (49.7%) Δ 37.4% P<.001*	7 (11.5%)	60 (51.7%) Δ 40.4% P<.001*	70 (54.7%) Δ 41.8% P<.001*
Clinical response at Wk12 + endoscopic response at Wk48 (composite co-primary endpoint)	8 (5.4%)	104 (36.4%) Δ 30.7% P<.001*	110 (37.2%) Δ 31.8% P<.001*	4 (5.1%)	55 (35.9%) Δ 30.9% P<.001*	46 (31.3%) Δ 26.7% P<.001*	4 (6.6%)	47 (40.5%) Δ 33.0% P<.001*	56 (43.8%) Δ 36.5% P<.001*

Data are presented as n (%); Δ% (adjusted treatment difference) vs PBO; p-value vs PBO. Adjusted treatment differences and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used are baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-ir status (Yes or No; this variable used only in analyses of the overall population), and baseline corticosteroid use (Yes or No). Population N values reflect the primary analysis set, defined as all randomized participants who received at least 1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for participants with isolated ileal disease). PBO pts not in clinical response at week (Wk) 12 switched to UST.

Endpoint definitions: clinical remission, CDAI < 150; endoscopic response, ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2; clinical response, ≥100-point reduction from baseline in CDAI or CDAI < 150. Participants with treatment failure or missing data were considered to not have met the endpoint.

- a. Anti-TNF agents or vedolizumab
b. Participants assigned to either GUS 200mg IV every 4 weeks (q4w) (x3)→100mg SC q8w or GUS 200mg IV q4w (x3)→200mg SC q4w. At the Wk 12 assessment, GUS participants had only received GUS IV.
c. Participants assigned to GUS 200mg IV q4w (x3)→100mg SC q8w
d. Participants assigned to GUS 200mg IV q4w (x3)→200mg SC q4w
* Nominal p-value

Table. Efficacy of guselkumab (GUS) and placebo (PBO) for short- and long-term clinical and endoscopic endpoints in all participants and BIO-ir and BIO-naïve subgroups in the pooled GALAXI 2 & 3 dataset.

Conclusion: In pooled analyses of the double-blind GALAXI 2 & 3 trials, GUS was efficacious versus PBO in pts with CD regardless of prior biologic therapy exposure in both short-term (Wk12) endpoints and long-term (Wk12 + Wk48) composite endpoints.

Disclosure: Bruce E. Sands reports potential conflicts of interest with AbbVie, Abivax, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, AstraZeneca, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evomune, Ferring, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Janssen, Kaleido, Kallyope, Lilly, Merck, Microbiotica, Mobius Care, Morphe Therapeutics, MRM Health, Pfizer,

Nexus Therapeutics, Nimbus Discovery, Odyssey, Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biotherapeutics, Sun Pharma, Surrozen, Target RWE, Takeda, Teva, Theravance Biopharma, TLL Pharmaceutical, TR1X, Union Therapeutics and Ventyx Biosciences.

Geert D'Haens reports potential conflicts of interest with AbbVie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom, Galapagos, GlaxoSmithKline, Gosamerbio, Immunicon, Index, Johnson & Johnson, Kaleido, Origo, Pfizer, Polpharma, Proclis Diagnostics, Prometheus Laboratories, Prometheus Biosciences, Progenity, and Protagonist Therapeutics Inc., Seres Health, and Takeda.

Silvio Danese reports potential conflicts of interest with AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity, Takeda, TiGenix, UCB, and Vifor.

Tadakazu Hisamatsu reports potential conflicts of interest with AbbVie, Bristol Myers Squibb, Daiichi-Sankyo, EA Pharma Co, Ltd., Eli Lilly, Gilead Sciences, Janssen Research & Development, LLC., JIMRO, Kissei Pharmaceutical Co, Ltd., Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., and Takeda Pharmaceutical Co., Ltd.

Walter Reinisch reports potential conflicts of interest with AbbVie, Aesca, Agomab, Algernon, AltruBio, Amgen, AM, AMT, AOP Orphan, Aptalis, Arena, Astellas, AstraZeneca, Avaxia, Roland Berger, Bioclinica, Biogen, Boehringer-Ingelheim, Bristol Myers Squibb, Calyx, Cellerix, Chemocentryx, Celgene, Celltrion, Covance, Danone Austria, DSM, Elan, Eli Lilly, Ernest & Young, Falk, Ferring, Fresenius, Galapagos, Gatehouse, Genentech, Gilead, Grünenthal, ICON, Immundiagnostik, Index, Inova, Intrinsic Imaging, Janssen, Johnson & Johnson, Kyowa Hakko Kirin, Landos, Lipid, LivaNova, Mallinckrodt, Medahead, Medice, MedImmune, Millenium, Mitsubishi Tanabe, MSD, Nash, Nestle, Nippon Kayaku, Novartis, Ocera, OMass, Otsuka, Parexel, PDL, Periconsulting, Pfizer, Pharmacosmos, PLS Education, Procter & Gamble, Prometheus, Protagonist, Provention, Quell, Roberts Clinical Trial, Sandoz, Schering-Plough, Second Genome, Seres, Setpoint-medical, Sigmoid, Sublimity, Takeda, Teva, Therakos, Theravance, Tigeneix, UCB, Vifor, Yakult, Zealand, Zyngenia, and 4SC.

Natalie A. Terry, Leonardo Salese, Rian Van Rampelbergh, Zijiang Yang, and **Jewel Johanns** are employees of Janssen Research & Development (a Johnson & Johnson Company) and may own company stock/stock options.

George DuVall reports potential conflicts of interest with Janssen.

Niazy Abu Farsakh reports potential conflicts of interest with Abbott, Amgen, Antanea medical services, Ferring, Hikma, Janssen, and Pfizer.

Remo Panaccione reports potential conflicts of interest with AbbVie, Abbott, AbbVie, Alimentiv (formerly Roberts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatrix, Ventyx, and UCB.

REAL-WORLD SHORT-TERM EFFECTIVENESS OF RISANKIZUMAB IN REFRACTORY CROHN'S DISEASE: RISANCROHN STUDY FROM THE ENEIDA REGISTRY

M. Barreiro-de Acosta^{1,2}, L. Nieto-García², M. Poncela³, C.J. Gargallo-Puyuelo⁴, F. Rodríguez-Moranta⁵, D. Ceballos⁶, M.I. Calvo Moya⁷, S. García-López⁸, M. Aguas⁹, L. Zabalza¹⁰, C. Martínez Cuevas¹¹, R. de Francisco¹², I. Bastón-Rey^{1,13}, F. Bermejo¹⁴, L. Madero¹⁵, M.D. Martín-Arranz¹⁶, M. Rivero¹⁷, I. Alonso-Abreu¹⁸, P. Varela Trastoy¹⁹, M.L. De Castro Parga²⁰, B. Camps²¹, C. Martínez Pascual²², B. Sicilia²³, J.P. Gisbert²⁴, M. Piqueras²⁵, C. Abril²⁶, E. Brunet²⁷, A. Hernández Camba²⁸, P. Fradejas²⁹, Á. Ponferrada-Díaz³⁰, M. Mañosa Ciria³¹, M. Algara San Nicolas³², J. Castro Poceiro³³, J.A. Ferrer³⁴, E. Ricart³⁵, A. Elorza³⁶, M.F. García Sepulcre³⁷, P. Robledo³⁸, M. Teller³⁹, E. Sesé⁴⁰, D. Busquets Casals⁴¹, F. Mesonero Gismero⁴², R. Pajares⁴³, L. Bujanda Fernández de Piñola⁴⁴, C. González-Muñoz⁴⁵, D. Martín Rodríguez⁴⁶, M.T. Diz-Lois Palomares⁴⁷, I. Nicolas⁴⁸, E. Domenech³¹, R. Ferreira-Iglesias^{1,2}, ENEIDA project of GETECCU

¹Complejo Hospitalario Universitario de Santiago, Gastroenterology, Santiago, Spain, ²Fundación Instituto de Investigación Sanitaria de Santiago de Compostela (FIDIS), Santiago de Compostela, Spain, ³Hospital General Universitario Gregorio Marañón. Instituto de Investigación Biomédica Gregorio Marañón (IISGM), Madrid, Spain, ⁴Hospital Clínico Universitario "Lozano Blesa", IIS Aragón and CIBERehd, Zaragoza, Spain, ⁵Hospital Universitario de Bellvitge, IDIBELL, Gastroenterology, Barcelona, Spain, ⁶Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas, Spain, ⁷Hospital Universitario Puerta de Hierro Majadahonda, Gastroenterology, Madrid, Spain, ⁸Hospital Universitario Miguel Servet, Gastroenterology, Zaragoza, Spain, ⁹La Fe University And Politecnical Hospital, Gastroenterology Unit, Valencia, Spain, ¹⁰Hospital Universitario de Navarra, Gastroenterology, Pamplona, Spain, ¹¹Hospital Universitario Río Hortega, Valladolid, Spain, ¹²Hospital Universitario Central de Asturias and ISPA, Gastroenterology, Oviedo, Spain, ¹³Fundación Instituto de Investigación Sanitaria de Santiago de Compostela (FIDIS), Santiago de Compostela Sps, Spain, ¹⁴H Fuenlabrada, Gastroenterology, Fuenlabrada, Spain, ¹⁵Hospital General Universitario de Alicante and CIBERehd, Gastroenterology, Alicante, Spain, ¹⁶Hospital La Paz, Gastroenterology, Madrid, Spain, ¹⁷Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain, ¹⁸Hospital Universitario de Canarias (H.U.C.), Santa Cruz de Tenerife, Spain, ¹⁹Hospital de Cabueñes, Gijón, Spain, ²⁰Hospital Álvaro Cunqueiro, Estrutura Organizativa de Xestión Integrada de Vigo, Gastroenterology, Vigo, Spain, ²¹Hospital del Mar, IMIM (Hospital del Mar Medical Research Institute), Gastroenterology, Barcelona, Spain, ²²H.C.U. Virgen de la Arrixaca, Gastroenterology, Murcia, Spain, ²³Hospital Universitario de Burgos, Gastroenterology, Burgos, Spain, ²⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology, Madrid, Spain, ²⁵Consorci Sanitari Terrassa, Gastroenterology, Barcelona, Spain, ²⁶Hospital Clínico Universitario de Valencia, Gastroenterology, Valencia, Spain, ²⁷Parc Tauli, Digestive, Sabadell, Spain, ²⁸Complejo Hospitalario Universitario Ntra. Sra. de Candelaria, Gastroenterology, Santa Cruz de Tenerife, Spain, ²⁹Complejo Asistencial de Zamora, Gastroenterology, Zamora, Spain, ³⁰Hospital Infanta Leonor,

Madrid, Spain, ³¹Hospital Universitari Germans Trias I Pujol and CIBEREHD, Gastroenterology, Badalona, Spain, ³²H.12 Octubre, Madrid, Spain, ³³Hospital de Sant Joan Despí Moisès Broggi, Gastroenterology, Barcelona, Spain, ³⁴Hospital Fundacion Alcorcon, Gastroenterology, Alcorcon, Spain, ³⁵Hospital Clínic i Provincial, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Gastroenterology, Barcelona, Spain, ³⁶Hospital de Galdakao-Usansolo, Gastroenterology, Galdakao, Spain, ³⁷Hospital General Universitario de Elche, Gastroenterology, Elche, Spain, ³⁸Hospital Universitario de Cáceres, Cáceres, Spain, ³⁹Althaia Xarxa Assistencial universitària de Manresa, Gastroenterology, Manresa, Spain, ⁴⁰Hospital Universitario Arnau de Vilanova, Gastroenterology, Lleida, Spain, ⁴¹H. DE GIRONA DR. J. TRUETA/ICO GERONA, Gastroenterology, Girona, Spain, ⁴²Hospital Ramon y Cajal, Gastroenterology, Madrid, Spain, ⁴³Hospital Universitario Infanta Sofía, Gastroenterology, Madrid, Spain, ⁴⁴Hospital Universitario Donostia and Biodonostia, San Sebastián, Spain, ⁴⁵Hospital Santa Creu i Sant Pau, Gastroenterology, Barcelona, Spain, ⁴⁶Hospital Infanta Cristina, Madrid, Spain, ⁴⁷Hospital Universitario A Coruña, Gastroenterology, A Coruña, Spain, ⁴⁸Hospital General Universitario Reina Sofía, Gastroenterology, Murcia, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Phase III trials have demonstrated the efficacy of risankizumab (RZB), this being the first humanised monoclonal IgG1 antibody which targets the interleukin 23 p19 subunit, in moderate-to-severe Crohn's disease (CD). However, real-world data in induction with this drug is scarce. The aim of the study was to assess the real-world short-term effectiveness and safety of RZB in multi-refractory patients with CD.

Aims & Methods: Adult CD patients that had received induction doses with RZB in the ENEIDA registry—a large prospectively maintained Spanish database promoted by the Spanish Working Group in Crohn's and Colitis (GETECCU)—were included. Clinical and demographical data including number of previous biologics and advanced therapies were included. The primary endpoint was steroid-free clinical remission evaluated at any point between weeks 8 and 12 (Harvey-Bradshaw [HB] score <5). Secondary endpoints included steroid free clinical remission at the end of follow-up, clinical, biochemical improvement (C-reactive protein (CRP) and/or faecal calprotectin (FC)), need for CD-related surgery and adverse events related with the drug. The data are presented as median (range), and frequencies and percentages. Statistical analysis was performed using the Chi-square or Fisher's test, and the Student-*t* test or U-Mann-Whitney test as appropriate.

Results: 417 CD patients (52% male) were included: median age was 50 (18-84) years, median disease duration 14 years, 27% were smokers. Regarding Montreal classification, 49% were L1, 10% L2, and 38% L3. Most of the patients presented inflammatory pattern (47%), 32% presented structuring, 21% penetrating behavior and perianal disease was present in 24%. 48% had abdominal CD surgery and 41% presented extraintestinal manifestations. Only 8% received concomitant immunosuppressives with RZB. Regarding previous exposure to biologics or JAK inhibitors, only 3% were naïve, 49% had been exposed to 1-2 advanced therapies and 48% to 3 or more biologics or JAKs. After induction 58% of the patients achieved steroid-free clinical remission and at the end of the follow-up steroid-free clinical remission was observed in 62% of the patients. Median FC decreased from week 530 µg/g (week 0) to 333 µg/g after induction ($p < 0.001$). Regarding CRP, this decreased from median 7 mg/L at week 0 to 4.7 mg/L after induction ($p = 0.002$). 15 patients (3.5%) underwent intestinal resection. 23 patients (5.5%) presented adverse events including 6 infections.

Conclusion: This is the largest cohort study of real-world data with RZB,

and it includes highly refractory patients with CD and multiple prior drug failures. RZB induction provided a steroid-free clinical remission in nearly 60% of patients and a significative improvement in biomarkers. Safety was consistent with the known profile of RZB in previous trials.

Disclosure: MBA has served as a speaker, consultant and advisory member for or has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, GALAPAGOS, Pfizer, Sandoz, Biogen, Fresenius, Lilly, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, Adaclyte and Tillots-Pharma.

OP044

EXTENDED INDUCTION RESPONSE OVER TIME IN PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH MIRIKIZUMAB IN THE LUCENT-1 AND -2 TRIALS

D.T. Rubin¹, A. Charabaty², V. Jairath³, J. Walter⁴, K. McGinnis⁵, R. Moses⁵, S. Maier⁵, R. Escobar⁵, S.K. Baygani⁵, L. Zaremba-Pechmann⁵, T. Kobayashi⁶

¹University of Chicago Medicine, Chicago, United States of America,

²John Hopkins University, Baltimore, United States of America,

³Alimentiv Inc., Gastroenterology, London, Canada, ⁴Thomas Jefferson University Hospitals, Philadelphia, United States of America, ⁵Eli Lilly and Company, Indianapolis, United States of America, ⁶Kitasato University Kitasato Institute Hospital, Tokyo, Japan

Contact E-Mail Address: drubin@uchicago.edu

Introduction: The safety and efficacy of mirikizumab (miri), an anti-IL-23p19 antibody, for moderately-to-severely active ulcerative colitis (UC) have been shown in Phase 3 trials (LUCENT-1 and -2; NCT03518086, NCT03524092). Extended induction with 3 additional intravenous (IV) doses of miri induced clinical response at Week (W)24 in more than 50% of patients who did not initially achieve clinical response to induction with miri at W12. Among the clinical non-responders, some had achieved partial response at W12 (Table 1).

We assessed response over time in clinical non-responders at the end of induction who received extended induction with miri for an additional 12W.

Aims & Methods: In LUCENT-1, patients (N=1281) were randomly assigned 3:1 to receive miri 300mg or placebo IV at W0, W4, and W8. Patients not achieving clinical response with miri 300mg IV at W12 of LUCENT-1 (n=272) received extended induction treatment with open-label miri 300mg IV at W12, W16, and W20 (LUCENT-2). Symptomatic remission, symptomatic response, bowel urgency (BU) remission, and BU change from baseline at W16 and W20 are reported (definitions in Table 1) in addition to the previously disclosed outcomes at W24.

For categorical variables, number and percentage of patients who are responders/remitters were presented. For continuous variables, mean change from baseline with standard deviation (SD) was used. Missing data were imputed as non-response.

Results: Among patients who were clinical non-responders to 12W of initial induction treatment (n=272), 53 (19.5%); 73 (26.8%); 101 (37.1%) achieved symptomatic remission and 144 (52.9%); 169 (62.1%); 197 (72.4%) patients achieved symptomatic response at W16, W20, and W24, respectively.

Among miri induction non-responders with Urgency Numeric Rating Scale (NRS) score ≥ 3 at induction baseline (n=256), 10.9% achieved BU remission at W16, 14.8% at W20, and 19.9% at W24. There was a 1.8 ± 2.4 (mean $\pm$ SD) point reduction in Urgency NRS scores at W16, 2.1 ± 2.5 reduction at W20, and 2.5 ± 2.7 reduction at W24 (Table 1).

Outcomes for miri IV extended induction	W12 (W0 extended induction)	W16 (W4 extended induction)	W20 (W8 extended induction)	W24 (W12 extended induction)
	Miri induction non-responders* 300 miri IV, Q4W N= 272	Miri induction non-responders* 300 miri IV, Q4W N= 272	Miri induction non-responders* 300 miri IV, Q4W N= 272	Miri induction non-responders* 300 miri IV, Q4W N= 272
Clinical response ^b	0	n/a	n/a	146 (53.7)
Symptomatic remission ^c	13 (4.8)	53 (19.5)	73 (26.8)	101 (37.1)
Symptomatic response ^d	83 (30.5)	144 (52.9)	169 (62.1)	197 (72.4)
BU remission ^e (Nx= 256)	18 (7.0)	28 (10.9)	38 (14.8)	51 (19.9)
BU change from baseline ^f [mBOCF; mean (SD)]	-1.2 (2.2)	-1.8 (2.4)	-2.1 (2.5)	-2.5 (2.7)

Data reported as n (%) unless otherwise indicated.
Abbreviations: BU=bowel urgency; IV=intravenous; mBOCF=modified baseline observation carried forward; miri=mirikizumab; N=patient population; n=patient subpopulation; Nx=number of patients with Urgency Numeric Rating Scale ≥3 at induction baseline; Q4W= every four weeks; SD=standard deviation; W=week
*The miri induction non-responder population only included patients who continued to the maintenance trial (LUCENT-2)
^bDefined as ≥2-point and ≥30% decrease in Modified Mayo Score from baseline; rectal bleeding =0 or 1 or ≥1-point decrease from baseline
^cDefined as stool frequency =0 or stool frequency =1 with ≥1-point decrease in Modified Mayo Score from baseline; rectal bleeding=0
^dDefined as at least a 30% decrease from baseline in the composite clinical endpoint of the sum of stool frequency and rectal bleeding subscores
^eDefined as Urgency Numeric Rating Scale score=0 or 1
^fChange from baseline in Urgency Numeric Rating Scale score; range 0 to 10; a lower score indicates less severe bowel urgency

Table 1. Clinical outcomes for the mirikizumab induction non-responder patient population.

Conclusion: Among patients who were clinical non-responders to induction at W12, more than 50% achieved clinical response after 3 additional induction doses with miri. A proportion of patients benefited earlier from extended induction at W16 and W20, respectively, regarding symptomatic response and remission, and BU outcomes. The results demonstrate continued symptomatic improvement and further support the potential benefit of extended induction treatment.

Disclosure: DR receives grants or contracts from Takeda, and discloses consultancy fees with Abbvie, Altrubio, Allergan, Inc., American College of Gastroenterology, Arena Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Ltd., Bristol-Myers Squibb, Celgene Corp/Syneos, Cornerstones Health, Inc. (non-profit), GalenPharma/Atlantica, Genentech/Roche, Gilead Sciences, GoDuRn, LLC, InDex Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Eli Lilly and Company, Materia Prima, Pfizer, Prometheus Biosciences, Reistone, Takeda and Techlab, Inc.

AC is on the advisory board of and/or a consultant for and/or receives educational grants from Abbvie, Eli Lilly and Company, Janssen, Pfizer, and Takeda.

VJ has received consulting/advisory board fees from AbbVie, Alimentiv Inc. (formerly Robarts Clinical Trials), Arena Pharmaceuticals, Asieris, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, GlaxoSmithKline, Genentech, Gilead, Janssen, Merck, Mylan, Pandion, Pendopharm, Pfizer, Reistone Biopharma, Roche, Sandoz, Takeda and TopiVert, and speaker's fees from AbbVie, Ferring, Galapagos, Janssen, Pfizer, Shire and Takeda.

JW has received consultancy or advisory board fees from Medtronic and Eli Lilly and Company.

KM, RM, SM, RE, SB are employees and minor shareholders of Eli Lilly and Company

LZ-P is an employee of HaaPACS GmbH and contractor for Eli Lilly and Company

TK has received lecture fees from Abbvie GK, Activaid, Alfresa Pharma, Janssen Pharmaceutical, JIMRO, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Nippon Kayaku, Pfizer Japan, Takeda Pharmaceutical,

Thermo Fisher Diagnostics and Zeria Pharmaceutical; research grants from Abbvie GK, Activaid, Alfresa Pharma, Bristol Myers Squibb, Eli Lilly Japan, Ferring Pharmaceuticals, Gilead Sciences, Janssen Pharmaceutical, JMDC, Mochida Pharmaceutical, Nippon Kayaku, Pfizer Japan and Takeda Pharmaceutical; scholarship contributions from Mitsubishi Tanabe Pharma, Nippon Kayaku and Zeria Pharmaceutical; study group sponsorship by Abbvie GK, EA Pharma, JIMRO, Kyorin Pharmaceutical, Mochida Pharmaceutical, Otsuka Holdings and Zeria Pharmaceutical; and advisory or consultancy fees from Abbvie GK, Activaid, Alfresa Pharma, EA Pharma, Janssen Pharmaceutical, KISSEI Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer Japan and Takeda Pharmaceutical.

OP045
EFFICACY AND SAFETY OF GUSELKUMAB MAINTENANCE THERAPY AMONG GUSELKUMAB INDUCTION WEEK 24 CLINICAL RESPONDERS: RESULTS FROM THE PHASE 3 QUASAR MAINTENANCE STUDY

D.T. Rubin¹, A. Dignass², J. Allegretti³, S. Yarandi⁴, K.-H. Huang⁴, M. Germinaro⁴, J. Zhan⁴, H. Zhang⁴, Y. Rayyan⁵, M. Saruta⁶, D. Balderramo⁷, B. Bressler⁸, L. Peyrin-Biroulet⁹, T. Hisamatsu¹⁰
¹University of Chicago Medicine, Inflammatory Bowel Disease Center, Chicago, United States of America, ²Agaplesion Markus Hospital, Goethe University, Frankfurt, Germany, ³Brigham and Women's Hospital Crohn's and Colitis Center, Boston, United States of America, ⁴Janssen Research & Development, LLC, Spring House, United States of America, ⁵The University of Jordan, School of Medicine, Amman, Jordan, ⁶The Jikei University School of Medicine, Tokyo, Japan, ⁷Hospital Privado Universitario de Córdoba, Instituto Universitario de Ciencias Biomédicas de Córdoba, Córdoba, Argentina, ⁸University of British Columbia, Vancouver, Canada, ⁹Nancy University Hospital, Université de Lorraine, Nancy, France, ¹⁰Kyorin University School of Medicine, Tokyo, Japan

Contact E-Mail Address: thisamatsu@ks.kyorin-u.ac.jp
Introduction: The QUASAR program (NCT04033445) evaluated guselkumab (GUS), a dual-acting interleukin (IL)-23p19 subunit inhibitor that potentially neutralizes IL-23 and binds to CD64 (a receptor on cells that produce IL-23), in patients (pts) with moderately to severely active ulcerative colitis (UC). Induction Week 12 (Week I-12) nonresponders to intravenous (IV) GUS received subcutaneous (SC) GUS through Week I-24.¹ Week I-24 responders were eligible for maintenance therapy. Here, we present the efficacy and safety of maintenance SC GUS among GUS Week I-24 responders.

Aims & Methods: Pts who were not in clinical response (see Table for definition) at Week I-12 after IV GUS 200 mg or 400 mg received SC GUS 200 mg at Weeks I-12, I-16, and I-20. Those who were in clinical response at Week I-24 (GUS Week I-24 responders) received SC GUS 200 mg every 4 weeks during the maintenance study in a blinded fashion and were evaluated as part of the nonrandomized study population. Clinical, symptomatic, endoscopic, histologic, and patient-reported outcome measures at maintenance Week 44 (Week M-44) and safety throughout the maintenance study are reported for GUS Week I-24 responders.

Results: Overall, 123 of 203 (60.6%) Week I-12 nonresponders to IV GUS achieved clinical response at Week I-24 and entered the maintenance study phase. Induction baseline characteristics of GUS Week I-24 responders were: 74.8% had severe disease (modified Mayo score 7-9), 77.2% had a Mayo endoscopy subscore of 3, median C-reactive protein was 5.0 mg/L (upper limit of normal, 3 mg/L), and 59.3% had a history of inadequate response or intolerance to biologic or Janus kinase inhibitor therapy for

UC. At Week M-44, 67.5% of the pts maintained clinical response and 30.1% were in clinical remission. Additional efficacy outcomes are shown in the Table. The proportion of GUS Week I-24 responders in symptomatic remission (defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0) at maintenance baseline (58.5%) was sustained through Week M-44 (56.9%). Adverse events (AEs) were reported for 78.0% of GUS Week I-24 responders, serious AEs for 5.7%, and serious infections for 1.6%. No opportunistic infections or deaths occurred. No new safety concerns were identified.

	GUS 200 mg SC q4w N=123 n (%)
Clinical remission ^b	37 (30.1)
Endoscopic improvement ^c / Endoscopic normalization (remission) ^d	44 (35.8) / 21 (17.1)
Corticosteroid-free clinical remission ^e	37 (30.1)
Maintenance of clinical response ^f	83 (67.5)
Histologic-endoscopic mucosal improvement ^g	34 (27.6)
Fatigue response ^h	49 (39.8)
Maintenance of clinical remission ⁱ , N=20	10 (50.0)

GUS=guselkumab; PROMIS=Patient-Reported Outcomes Measurement Information System; pts=patients; q4w=every 4 weeks; SC=subcutaneous; Week M-44=maintenance Week 44.

Note: Includes only pts with modified Mayo score 5-9 at induction baseline.

^a Clinical response was defined as a decrease from induction baseline in the modified Mayo score by $\geq 30\%$ and ≥ 2 points, with either a ≥ 1 -point decrease from induction baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.

^b Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy.

^c Endoscopic improvement was defined as an endoscopy subscore of 0 or 1 with no friability present on the endoscopy.

^d Endoscopic normalization (remission) was defined as an endoscopy subscore of 0.

^e Corticosteroid-free clinical remission was defined as clinical remission at Week M-44 without any use of corticosteroids for ≥ 8 weeks prior to Week M-44.

^f Maintenance of clinical response was defined as clinical response at Week M-44 among pts in clinical response at maintenance baseline.

^g Histologic-endoscopic mucosal improvement was defined as achieving a combination of histologic improvement (defined as neutrophil infiltration in $<5\%$ of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system [i.e., Geboes score ≤ 3.1]) and endoscopic improvement.

^h Fatigue response was defined as a ≥ 7 -point improvement from induction baseline in the PROMIS Fatigue Short Form 7a.

ⁱ Maintenance of clinical remission was defined as clinical remission at Week M-44 among pts in clinical remission at maintenance baseline.

Table. Efficacy Outcomes at Maintenance Week 44 for GUS Induction Week 12 Nonresponders Who Achieved Clinical Response^a at Induction Week 24.

Conclusion: In this refractory population of GUS Week I-24 responders, maintenance treatment with GUS provided clinical benefit across a range of clinically relevant efficacy endpoints. Safety results were consistent with the overall population and safety profile of GUS in its approved indications.

References:

1. Bressler B, et al. *Am J Gastroenterol*. 2023;118(10S):806-807.

Disclosure: **D. T. Rubin:** research funding from Takeda; consultant to AbbVie, Altrubio, Allergan, Arena, Aslan, Athos, Bellatrix, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corp/Syneos, Connect, Galen-Pharma/Atlantica, Genentech/Roche, InDex, Ironwood, Iterative Scopes, Janssen, Lilly, Pfizer, Prometheus, Reistone, Takeda, and Techlab; and co-founder of Cornerstones Health.

A. Dignass: fees for participation in clinical trials, review activities (data monitoring boards, statistical analysis, endpoint committees) from Abivax, AbbVie, Bristol Myers Squibb, Dr Falk Foundation, Galapagos, Gilead, Janssen, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb,

Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada, Takeda, Tillotts, and Vifor Pharma; payment for lectures/speaker's bureaus from AbbVie, Biogen, CED Service GmbH, Celltrion, Falk Foundation, Ferring, Galapagos, Gilead, High5MD, Janssen, Materia Prima, Med-Today, MSD, Pfizer, Sandoz, Takeda, Tillotts, and Vifor Pharma; payment for manuscript preparation from Abbvie, Falk Foundation, Janssen, Takeda, Thieme, and UniMed Verlag.

J. R. Allegretti: consultant for AbbVie, Adiso, Ferring, Finch, Iterative Scopes, Janssen, Merck, Pfizer, Roivant, and Seres Therapeutics; speaker for AbbVie, Bristol Myer Squibb, and Janssen; and research support from Janssen, Merck, and Pfizer.

Y. Rayyan: fees for participating in clinical trials for Janssen as principal investigator and payment from lectures including service on speaker's bureaus from Janssen, AbbVie, and Amgen.

M. Saruta: grants or contracts from Mochida, Zeria Pharma, EA Pharma, Kissei, and EPS Corporation; and payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from AbbVie GK, Janssen, Mitsubishi Tanabe Pharma, Takeda, EA Pharma, Gilead Sciences, and Kissei.

D. Balderramo: advisor/speaker fees from AbbVie, Janssen, Pfizer, Takeda, and Amgen; and travel/congress support from AbbVie, Janssen, Takeda, and Ferring.

B. Bressler: advisor/speaker for AbbVie, Bristol Myers Squibb, Ferring, Janssen, Merck, Novartis, Organon, Pfizer, Sandoz, and Takeda; advisor for Alimentiv, Allergan, Amgen, AMT, Bausch Health, Bristol Myers Squibb, Celgene, Celltrion, Eupraxia Fresenius Kabi, Genentech/Roche, Gilead, Iterative Scopes, Jamp, Merck, Microbiome Insights, Mylan, Pendopharm, Protagonist, and Viatrix; research support from AbbVie, Amgen, Business Intelligence, Bristol Myers Squibb, Genentech/Roche, GlaxoSmithKline, Janssen, Merck, and Qu Biologic; and holds stock options in Qu Biologic.

L. Peyrin-Biroulet: consultant for AbbVie, Abivax, Alimentiv, Alma, Amgen, Applied Molecular Transport, Arena, Biogen, Bristol Myers Squibb, Celltrion, Connect, Cytoki, Lilly, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech/Roche, Gilead, Gossamer Bio, GlaxoSmithKline, HAC-Pharma, IAG, InDex, Inotrem, Janssen, Medac, Mopac, Morpich, MSD, Norgine, Novartis, OM, ONO, OSE, Pandion, Par'Immune, Pfizer, Prometheus, Protagonist, Roche, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, Viatrix, Vifor, and Ysopia; grants from Celltrion, Fresenius Kabi, and Takeda; honorarium for lectures from AbbVie, Amgen, Arena, Biogen, Celltrion, Lilly, Ferring, Galapagos, Genentech/Roche, Gilead, Janssen, Medac, MSD, Pfizer, Sandoz, Takeda, Tillots, Viatrix, and Vifor; and fees from AbbVie, Adacyte, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytoki Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morpich, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par'Immune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, Viatrix, Vifor, Ysopia, Abivax, Samsung, Ventyx, Roivant, and Vectivbio.

T. Hisamatsu: grant support from AbbVie, Daiichi-Sankyo, EA Pharma, JIMRO, Mitsubishi Tanabe Pharma, Mochida, Nippon Kayaku, Pfizer, and Takeda; consulting fees from EA Pharma, Janssen Research & Development, Gilead Sciences, Lilly, and Bristol Myers Squibb; and lecture fees from AbbVie, EA Pharma, Mitsubishi Tanabe Pharma, Takeda, Mochida, and Kissei.

S. Yarandi, K.-H. G. Huang, M. Germinaro, J. Zhan, and H. Zhang: employees of Johnson & Johnson and own company stock/stock options.

CORTICOSTEROID-SPARING EFFECT OF MIRIKIZUMAB FOR THE TREATMENT OF MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: EXTENDED INDUCTION SUBGROUP ANALYSIS FROM PHASE 3 TRIAL

D. Laharie¹, C.A Siegel², P.S. Dulai³, M. Katsuyoshi⁴, J. P. Gisbert⁵, K. Samaan⁶, I. Redondo⁶, S.K. Baygani⁶, J. Paulissen⁷, V. Jairath⁸
¹CHU de Bordeaux Hopital Haut-Leveque Dept. de Gastroenterologie, Bordeaux, France, ²Dartmouth-Hitchcock Medical Center, Lebanon, United States of America, ³Northwestern Medicine Digestive Health Center, Chicago, United States of America, ⁴Tokyo Medical and Dental University, Gastroenterology and Hepatology, Tokyo, Japan, ⁵Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa [IIS-Princesa], Universidad Autónoma de Madrid, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas [CIBEREHD], Madrid, Spain, ⁶Eli Lilly and Company, Indianapolis, United States of America, ⁷Syneos Health, Morrisville, United States of America, ⁸University of Western Ontario, London, Canada

Contact E-Mail Address: david.laharie@chu-bordeaux.fr

Introduction: Mirikizumab, an anti-IL-23p19 antibody, has demonstrated efficacy and safety in moderately-to-severely active ulcerative colitis (UC) Phase 3 trials (LUCENT-1 and -2; NCT03518086, NCT03524092). A treatment goal for patients with UC is corticosteroid (CS)-free remission. We assessed the CS-sparing effect of mirikizumab among the extended induction patient population receiving CS at induction baseline.

Aims & Methods: In LUCENT-1, patients in the modified intention to treat mirikizumab group (n=868) received mirikizumab 300 mg intravenously (IV) at Week (W)0, W4, and W8. Patients receiving mirikizumab on CS at baseline (n=351) remained on their stable baseline dose (prednisone ≤20 mg/day or equivalent, budesonide MMX 9 mg/day, or beclomethasone 5 mg/day) during induction (W0 to W12).

Patients not achieving clinical response (≥2-point and ≥30% decrease in Modified Mayo Score from baseline; and rectal bleeding=0 or 1, or ≥1-point decrease from baseline) at W12 (n=272) entered LUCENT-2 open label (OL) extended induction and received 300 mg mirikizumab IV at W12, W16, and W20.

Extended induction responders at W24 (n=144) entered OL maintenance and received 200mg mirikizumab subcutaneously (SC) Q4W until W52. CS taper was initiated if clinical response was achieved at W24 or earlier based on investigator discretion if symptomatic improvement was evident.

Patients who discontinued CS and remained off throughout the study were considered "discontinued." Descriptive statistics for efficacy outcomes were summarized. Missing data were imputed as non-response.

Results: Of the 272 mirikizumab patients in the extended induction population, 118 received CS at induction baseline.

The mean prednisone equivalent dose was 15mg. At W24, among the 62/118 (52.5%) who achieved clinical response and continued with maintenance, 8 (12.9%) discontinued CS, 2 (3.2%) achieved clinical remission off CS, and 8 (12.9%) achieved symptomatic remission off CS.

At W52, 43/62 (69.4%) of the extended induction responders discontinued CS, 18 (29.0%) achieved clinical remission off CS, and 37 (59.7%) achieved symptomatic remission off CS. Among patients with non-missing data who completed W52 of mirikizumab treatment, 89.6% had discontinued CS (Table).

		Mirikizumab Extended Induction Responders ^a (N=62)	
		Observed n/Nx (%)	NRI n (%)
Week 24	Clinical remission ^b and off CS	2/62 (3.2)	2 (3.2)
	Symptomatic remission ^c and off CS	8/62 (12.9)	8 (12.9)
	Discontinued CS ^d	8/53 (15.1)	8 (12.9)
Week 52	Clinical remission ^b and off CS	18/50 (36.0)	18 (29.0)
	Symptomatic remission ^c and off CS	37/52 (71.2)	37 (59.7)
	CS-free remission ^e	16/49 (32.7)	16 (25.8)
	Discontinued CS ^d	43/48 (89.6)	43 (69.4)

Abbreviations: CS=corticosteroid; N =number of patients in analysis population; n=number of patients in the specified category; NRI=non-responder imputation; Nx=number of patients with non-missing values

^a Patients without response at week 12 treated with mirikizumab extended induction and responded at week 24. Clinical response defined as ≥2-point and ≥30% decrease in Modified Mayo Score from baseline; and rectal bleeding=0 or 1, or ≥1-point decrease from baseline

^b Defined as stool frequency subscore=0 or 1 with ≥1-point decrease from induction baseline, a rectal bleeding subscore=0, and an endoscopic subscore=0 or 1 (excluding friability)

^c Defined as stool frequency subscore=0 or 1 with ≥1-point decrease from induction baseline, a rectal bleeding subscore=0

^d Patients discontinued CS and remained off through Week 52

^e Clinical remission at Week 52 + symptomatic remission at Week 40 + off CS for ≥12 weeks

Table. Corticosteroid-Sparing Effect of Mirikizumab in Extended Induction Population Receiving Corticosteroids at Induction Baseline

Conclusion: Nearly 70% of extended induction responders discontinued CS by W52. CS-sparing effect of mirikizumab in patients with moderately-to-severely active UC is clinically meaningful and aligns with the treatment goal of CS discontinuation.

Disclosure: DL declares counseling, boards, transports or fees from Abbvie, Biogaran, Biogen, Ferring, HAC-pharma, Janssen, MSD, Novartis, Pfizer, Prometheus, Roche, Takeda, Theradiag, Tillots.

CS reports advisory board and consultant fees for Abbvie, BMS, Lilly, Janssen, Pfizer, Prometheus, Takeda and Trellus Health; speaker for CME activities for Abbvie, Janssen, Pfizer and Takeda; received grant support from Abbvie, Janssen, Pfizer and Takeda; intellectual property for a "System and Method of Communicating Predicted Medical Outcomes"; co-founder of MiTest Health, LLC (software company) that has technology (PROSPECT/CDPATH) that has been licensed to Takeda.

PD reports consulting fees from Johnson and Johnson, Gilead, Lilly, BMS, Novartis, Pfizer, and Takeda; financial support for research from Takeda and Pfizer; stock options for DigbiHealth; and licensing royalties from PreciDiag.

KM has received speaker fees and research grants from AbbVie, EA Pharma, Mochida, Mitsubishi-Tanabe, ZERIA, Nippon Kayaku, and JIMRO; speaker fees from Takeda, Janssen, Pfizer, Kyorin, Kissei, Gilead, Eli Lilly, and Celltrion Healthcare.

JPG has served as speaker, consultant, and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene/Bristol Myers, Gilead/Galapagos, Lilly, Ferring, Faes Farma, Shire Pharmaceuticals, Dr Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Norgine and Vifor Pharma.

KHS, IR, SB are employees and minor shareholders of Eli Lilly and Company

JP is an employee of Syneos Health and contractor for Eli Lilly and Company

VJ has received consulting/advisory board fees from AbbVie, Alimentiv Inc. (formerly Robarts Clinical Trials), Arena Pharmaceuticals, Asieris, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, GlaxoSmithKline, Genentech, Gilead, Janssen, Merck, Mylan, Pandion, Pendopharm, Pfizer, Reistone Biopharma, Roche, Sandoz, Takeda and TopiVert, and speaker's fees from AbbVie, Ferring, Galapagos, Janssen, Pfizer, Shire and Takeda.

OP047

SI-RNA/CS-PLGA NANOPARTICLE SYSTEM TARGETING KNOCKOUT OF INTESTINAL SOAT2 REDUCED INTESTINAL LIPID UPTAKE AND ALLEVIATE OBESITY

W. Shao^{1,2}, J. Liang^{3,4,5}, P. Ni^{5,4,5}, Q. Liu^{4,5}, W. Kong^{3,4,5}, W. Shen¹, Q. Wang¹, A. Huang¹, A. Gu³, Z. Jiang¹

¹Tongji University, Center of Gallstone Disease, Shanghai East Hospital, School of Medicine, Shanghai, China, ²Southeast University, School of Instrument Science and Engineering, Nanjing, China, ³Nanjing Medical University, State Key Laboratory of Reproductive Medicine and Offspring Health, School of Public Health, Nanjing, China, ⁴Nanjing Medical University, Key Laboratory of Modern Toxicology of Ministry of Education, Center for Global Health, Nanjing, China, ⁵Nanjing Medical University, Collaborative Innovation Center for Cardiovascular Disease Translational Medicine, Center for Global Health, Nanjing, China

Contact E-Mail Address: wtaoshao@163.com

Introduction: Limiting exogenous fat intake is proposed as a preventive measure against obesity^[1]. Despite the elucidation of the molecular process of fatty acid uptake in enterocytes, there is no specific inhibitor that has been proven to effectively prevent obesity by inhibiting fatty acid absorption. Sterol O-acyltransferase 2 (SOAT2) is an enzyme responsible for esterifying free cholesterol and fatty acids into cholesteryl esters^[2,3]. Evidence suggests the importance of intestinal SOAT2 in controlling dietary fatty acid absorption, hinting that targeting intestinal SOAT2 could be a promising approach to modulating the incidence of diet-induced obesity. Nanoparticles are vehicles that augment the efficacy of drug delivery and therapy^[4-7]. A novel nanoparticle system specifically designed to deliver SOAT2 siRNAs into the small intestine would be a promising therapeutic option to modulate intestinal fatty acid uptake and prevent obesity.

Aims & Methods: The role of intestinal SOAT2 in obesity was evaluated using intestine-specific SOAT2 knockout (*Soat2*^{-/-KO}) mice through biochemical analyses, isotopic tracer methods, fluorescent palmitic acid assays, and western blot. Subsequently, a novel nanoparticle system composed of poly (D, L-lactic-co-glycolic acid)-block-polyethylene glycol (PLGA-b-PEG) polymer as the core and chitosan (CS) shell, which serves as a protective layer against stomach acid, was developed to facilitate intestinal delivery and *Soat2* inhibition. Mice were orally administered SOAT2 siRNA/CS-PLGA nanoparticles to evaluate their therapeutic efficacy against obesity. To elucidate the underlying mechanisms of how intestinal SOAT2 regulates fatty acid uptake, a SOAT2 knockdown Caco-2 (shSOAT2) cell model was established. Fatty acid uptake, immunofluorescence, mRNA expression profiling, siRNA library screening, subcellular distributions, and ubiquitination of CD36 protein were employed in shSOAT2 cells to assess the ubiquitination and degradation of CD36. Co-immunoprecipitation, immunofluorescence, and western blot were carried out to explore the underlying mechanism by which SOAT2 knockdown regulates CD36 ubiquitination.

Results: *Soat2*^{-/-KO} mice were capable of preventing the development of dietary-induced obesity due to reduced intestinal lipid absorption. Then, the *Soat2* siRNA/CS-PLGA nanoparticle system can specifically deliver SOAT2 siRNAs into the small intestines of mice and effectively inhibit intestinal lipid uptake, thus resolving obesity. In revealing the underlying mechanism by which intestinal SOAT2 regulates fatty acid uptake, we found enhanced CD36 ubiquitination and degradation in enterocytes upon SOAT2 inhibition. Insufficient free cholesterol esterification promotes endoplasmic reticulum stress and the recruitment of E3 ligase RNF5, which activates CD36 ubiquitination in SOAT2 knockdown enterocytes.

Conclusion: The SOAT siRNA/CS-PLGA nanoparticle system offers advantages such as being non-invasive, having low systemic toxicity, and ensuring higher compliance. Our work shows the promising translational relevance of intestinal-specific SOAT2 siRNA-based therapy to prevent obesity. Although SOAT2 is known as a regulator of cholesterol homeostasis, our data provide additional evidence for the role and mechanism of SOAT2 in regulating intestinal fatty acid absorption, suggesting that inhibition of this enzyme might serve as 'a stone to hit two birds'.

References: [1] S. B. Heymsfield, T. A. Wadden, *The New England journal of medicine*. **2017**, 376, 254-266

[2] Y. Azuma, T. Kawasaki, K. Ikemoto, K. Obata, K. Ohno, N. Sajiki, T. Yamada, M. Yamasaki, Y. Nobuhara, *Japanese journal of pharmacology*. **1998**, 78, 355-64.

[3] C. A. Marzetta, Y. E. Savoy, A. M. Freeman, C. A. Long, J. L. Pettini, R. E. Hagar, P. B. Inskeep, K. Davis, A. F. Stucchi, R. J. Nicolosi, et al., *Journal of lipid research*. **1994**, 35, 1829-38.

[4] X. Zhang, V. Goel, G. J. Robbie, *Journal of clinical pharmacology*. **2020**, 60, 573-585.

[5] K. K. Ray, R. S. Wright, D. Kallend, W. Koenig, L. A. Leiter, F. J. Raal, J. A. Bisch, T. Richardson, M. Jaros, P. L. J. Wijngaard, J. J. P. Kastelein, *The New England journal of medicine*. **2020**, 382, 1507-1519.

[6] A. R. Sousa, A. V. Oliveira, M. J. Oliveira, B. Sarmento, *International journal of pharmaceutics*. **2019**, 568, 118530.

[7] M. Song, S. Zhang, Z. Tao, J. Li, Y. Shi, Y. Xiong, W. Zhang, C. Liu, S. Chen, *Biomaterials*. **2021**, 278, 121183.

Disclosure: Nothing to disclose.

OP048

EFFECTS OF ORAL XYLITOL ON SUBSEQUENT ENERGY INTAKE, GASTROINTESTINAL HORMONES AND GLYCEMIC CONTROL IN HEALTHY ADULTS

E. Flad^{1,2}, A. Altstaedt^{1,2}, J.F. Rehfeld³, C. Beglinger⁴, L. Van Oudenhove⁵, B.K. Wölnerhanssen^{1,2}, A.C. Meyer-Gerspach^{1,2}

¹St. Clara Research Ltd, Basel, Switzerland, ²University of Basel, Basel, Switzerland, ³Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, ⁴University Hospital Basel, Division of Gastroenterology, Arlesheim, Switzerland, ⁵Katholieke Universiteit Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium

Contact E-Mail Address: emilie.flad@unibas.ch

Introduction: As sugar consumption contributes to the development of metabolic disease including obesity and type 2 diabetes, a reduction in daily sugar consumption has been proposed as preventive and therapeutic strategy by the World Health Organization [1].

Artificial low-caloric high-intensity sweetener, e.g. acesulfame potassium (ace-K), are often used to replace sugar as they provide sweetness without calories. However, they do not stimulate the secretion of gastrointestinal (GI) satiation hormones and thus lack a satiating effect. Xylitol, a natural low-caloric bulk sweetener, has gained popularity as sugar alternative by offering beneficial properties such as being low-glycemic and low-insulinemic while preserving sweet taste and stimulating the secretion of GI satiation hormones [2].

The effect of orally administered xylitol on subsequent energy intake is not yet known.

Aims & Methods: Therefore, the objective of this study was to investigate the effect of an oral administration of xylitol compared to sucrose, ace-K and tap water on total energy intake during an *ad libitum* test meal, the secretion of GI satiation hormones and glycemic control.

In this randomized, controlled, double-blind crossover trial, 20 healthy adults with normal weight [age: 27.45 ± 7.86 years, BMI: 23.04 ± 1.41 kg/m² (mean $\pm$ SD)] received oral preloads containing either 33.5 g xylitol, 33.5 g sucrose, 0.1675 g ace-K dissolved in 300 mL water or 300 mL pure water in four different study visits. Fifteen minutes later, participants were served an *ad libitum* test meal where they were allowed to consume as much as they want for 20 minutes. Total energy intake was assessed by calculating the calories of the preloads and weighing food and drinks before and after the test meal.

Additionally, blood samples were collected at fixed time points to measure plasma cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), glucose and insulin concentrations.

Results: The results show that total energy intake was significantly lower after xylitol and ace-K compared to sucrose ($p_{\text{Tukey}} = 0.03$ and $p_{\text{Tukey}} < 0.01$, respectively), with no differences between xylitol and ace-K or water ($p_{\text{Tukey}} = 0.93$ and $p_{\text{Tukey}} = 1.00$, respectively). Plasma CCK concentrations increased significantly after xylitol and sucrose (for both, $p_{\text{Tukey}} < 0.01$), but not after water ($p_{\text{Tukey}} = 0.35$), with a significantly higher increase after xylitol compared to sucrose, ace-K or water (for all comparisons, $p_{\text{Holm}} < 0.01$). Plasma GLP-1 concentrations increased significantly after xylitol and sucrose ($p_{\text{Tukey}} = 0.02$ and $p_{\text{Tukey}} = 0.03$, respectively), but not after ace-K or water ($p_{\text{Tukey}} = 0.19$ and $p_{\text{Tukey}} = 0.39$, respectively), with no significant differences between xylitol and sucrose, ace-K or water (for all comparisons, $p_{\text{Holm}} = 0.66$). Plasma glucose concentrations increased significantly after sucrose ($p_{\text{Tukey}} < 0.01$), but not after xylitol, ace-K or water (for all, $p_{\text{Tukey}} = 0.34$, $p_{\text{Tukey}} = 0.86$ and $p_{\text{Tukey}} = 0.75$, respectively), with no significant differences between xylitol and ace-K or water (for both comparisons, $p_{\text{Holm}} = 0.46$). Plasma insulin concentrations increased significantly after sucrose ($p_{\text{Tukey}} = 0.01$), but not after xylitol, ace-K or water ($p_{\text{Tukey}} = 0.08$, $p_{\text{Tukey}} = 0.89$ and $p_{\text{Tukey}} = 1.00$, respectively), with no significant differences between xylitol and sucrose, ace-K or water (for all comparisons, $p_{\text{Holm}} = 0.27$).

Conclusion: An oral preload with xylitol prior to an *ad libitum* test meal induces the release of CCK and results in reduced total energy intake compared to an oral preload with sucrose.

References: 1. World Health Organization. *Guideline: Sugars intake for adults and children*. 2015.

2. Wölnerhanssen, B.K., et al., *Gut hormone secretion, gastric emptying, and glycemic responses to erythritol and xylitol in lean and obese subjects*. Am J Physiol Endocrinol Metab, 2016. **310**(11): p. E1053-61.

Disclosure: Nothing to disclose.

OP049

DURABLE EFFECTS OF DUODENAL ABLATION USING ELECTROPORATION COMBINED WITH SEMAGLUTIDE TO ELIMINATE INSULIN THERAPY IN PATIENTS WITH TYPE 2 DIABETES; THE 24-MONTH RESULTS

C.B.E. Busch¹, K. van den Hoek¹, A. van Baar¹, S. Meiring¹, F. Holleman², M. Nieuwdorp³, J.J. Bergman¹

¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Internal Medicine, Amsterdam, Netherlands, ³Amsterdam UMC, Vascular Medicine, Amsterdam, Netherlands

Contact E-Mail Address: c.b.busch@amsterdamumc.nl

Introduction: Progressive hyperglycemia in type 2 diabetes (T2D) leads to the need for exogenous insulin therapy in many patients, which is associated with weight gain and hypoglycemia. Studies have shown that hydrothermal duodenal mucosal ablation improves glycemic control by improving insulin resistance. Re-Cellularization via Electroporation Therapy (ReCET) is a novel endoscopic procedure that uses electroporation to

induce duodenal mucosal renewal. This technology uses pulsed electric fields to induce natural cell death through an apoptosis-like process without generating heat, thereby eliminating the risk of thermal damage to deeper layers of the duodenum.

In this study, we aimed to eliminate insulin treatment in T2D patients with a single ReCET procedure combined with a GLP-1 receptor agonist (GLP-1RA, semaglutide). Here, we present our 24-month results.

Aims & Methods: Single-arm, single-center, first-in-human study in 14 patients with T2D (28-75 years, body mass index (BMI) 24-40 kg/m², glycosylated hemoglobin (HbA1c) $\leq 8.0\%$, basal insulin dose $< 1\text{U/kg/day}$, C-peptide ≥ 0.2 nmol/L). All patients underwent the ReCET procedure under deep sedation followed by a 2-week isocaloric liquid diet. Thereafter, semaglutide was titrated up to 1 mg/week. Primary feasibility endpoints were procedure time (catheter in-out), technical success, and % of patients tolerating GLP-1RA. Primary safety endpoints were (serious) adverse events ([S]AEs) and hypoglycemic events. Efficacy endpoint was the percentage of patients off exogenous insulin at 6 months while maintaining HbA1c $\leq 7.5\%$. Baseline and follow-up glycemic and metabolic data and treatment satisfaction scores were assessed.

Results: The technical success rate of the ReCET procedure was 100% (14/14 patients) with a median axial treatment length of 12cm. The median procedure time was 58 minutes (IQR 49–79). No device-related SAEs or severe hypoglycemic events were observed. The maximum dose of semaglutide was tolerated by 13 (93%) patients. At 6 and 12 months, 12 (86%) patients were still not using insulin, yet showed significant improvements in glycemic control (HbA1c) and metabolic parameters (Table 1). Eleven patients completed the 24-month follow-up; one patient withdrew consent after 18 months while in good glycemic control. All eleven remained off insulin with adequate glycemic control.

	Baseline	6 months	p-value	12 months*	p-value	18 months	p-value	24 months	p-value
Number of patients	14	14	NA	13	NA	12	NA	11	NA
Hemoglobin A1c, %	7.2 (7.0 - 7.4)	6.6 (5.8 - 6.9)	0.003	6.5 (6.1 - 7.0)	0.011	6.7 (5.9 - 7.1)	0.012	6.7 (6.0 - 7.4)	0.126
Fasting plasma glucose, mmol/L	8.8 (7.6 - 10.6)	6.8 (6.1 - 8.7)	0.004	6.6 (5.8 - 7.2)	0.003	7.6 (6.6 - 8.8)	0.060	7.5 (6.8 - 8.1)	0.286
Homeostatic model assessment for insulin resistance	5.84 (3.92 - 7.50)	2.47 (1.50 - 3.25)	0.013	1.78 (1.05 - 2.71)	0.002	2.70 (1.44 - 4.81)	0.041	3.16 (1.64 - 3.78)	0.008
Time in range, %	72 (46 - 85)	92 (79 - 96)	0.019	89 (76 - 97)	0.011	91 (81 - 93)**	0.248	86 (78 - 98)	0.062
Weight, kg	90.7 (82.3 - 104.2)	77.6 (75.4 - 93.4)	<0.001	74.0 (67.2 - 98.6)	0.002	74.5 (65.8 - 90.4)	0.002	73.0 (64.4 - 89.5)	0.003
Body mass index, kg/m ²	28.8 (25.1 - 31.2)	24.9 (23.0 - 27.0)	<0.001	22.6 (22.1 - 27.1)	0.002	22.9 (21.8 - 27.0)	0.002	23.6 (22.2 - 26.8)	0.003
Waist circumference, cm	107 (97 - 111)	95 (85 - 99)	0.002	91 (79 - 101)	0.002	89 (81 - 98)	0.003	93 (79 - 100)	0.010
Liver fat fraction, %	9.2 (6.0 - 15.4)	6.3 (4.3 - 10.5)	0.030	4.2 (3.0 - 10.0)	0.016	NA	NA	3.9 (1.8 - 9.8)	0.006

Table 1. Glycaemic and metabolic secondary endpoints. Values are presented as median (interquartile range). Differences between the baseline, 6, 12, 18 and 24 months data were assessed using the Wilcoxon signed-rank paired test. *One patient was excluded due to steroid use.

**One patient was excluded since GLP1-RA was discontinued once sensor was placed.

Conclusion: These results suggest that duodenal ReCET is feasible and safe. Combined with semaglutide, ReCET eliminated the need for insulin therapy in 86% of patients until 12 months post-treatment while improving glycaemia and metabolic health. Patients who were off exogenous insulin at 12 months had a durable glycaemic response and remained insulin-free at 24 months.

Disclosure: Unrestricted research grant from Endogenex.

OP050

A PILOT INVESTIGATION OF THE SAFETY, TOLERABILITY AND EFFECTIVENESS OF RADIOFREQUENCY VAPOR (RFV) ABLATION FOR DUODENAL MUCOSAL ABLATION (DA) FOR THE MANAGEMENT OF TYPE-2 DIABETES MELLITUS (STEAN T-2DM PILOT)

B. Norton¹, A. Papaefthymiou¹, A. Telese¹, A. Nieponice², L. Rodriguez Grunert³, P. Becerra Hoebel³, C. Murray¹, K. Chang⁴, C.R. Simons-Linares⁵, R. Haidry¹

¹Cleveland Clinic London, Digestive Disease & Surgery Institute, London, United Kingdom, ²Hospital Universitario, Fundacion Favaloro, Buenos Aires, Argentina, ³Clinica Colonial, Santiago, Chile, ⁴University of California Irvine, Dr., Orange, United States of America, ⁵Cleveland Clinic Ohio, Digestive disease & Surgery Institute, Ohio, United States of America

Contact E-Mail Address: benjamin.norton@nhs.net

Introduction: DA is a promising disease-modifying endoscopic treatment for type 2 diabetes (T2D), which targets hypertrophied duodenal mucosa. The FDA-cleared RFVA system (Aqua Medical Inc., Pleasanton, CA) is an emerging technique for DA. This is a single-use, through-the-scope (10.5 FR), circumferential ablation catheter, and an electrosurgical generator that uses RF energy to convert saline into heated vapor at the catheter tip which is released into the duodenum creating a 2 cm treatment zone. The ablation is performed under direct visualization without fluoroscopy. We investigated the RFVA system in a first-in-human pilot dose-escalation study,

Aims & Methods: We aimed to assess the safety, tolerability, and efficacy of RFVA for DA in patients with T2D (NCT05887635). This was a prospective single-centre study enrolling 27 patients with uncontrolled T2D (glycated hemoglobin (HbA1c) 7.5-10%) despite ≥1 oral antidiabetic drug (OAD). DA was performed under general anaesthesia after a 4-week run-in period to ensure stable glycaemic control.

Patients were admitted overnight and given a modified post-procedure diet for 14 days. The ablation targeted ≥9 cm of the post-ampullary duodenal mucosa. The initial RFVA dose was 180 J single application (n=2). Once acute safety was established the next patients received 180 J double application (n=11).

After establishing chronic safety over four weeks, the final patients received 200 J double application (n=14). The primary outcomes were change in HbA1c at 12- and 24-weeks, and the number of serious adverse events (SAE).

Results: Twenty-seven patients with a mean (SD) T2D duration of 6 years (2.6) underwent DA. The mean age was 54 years (6.6), 48.2% were male, and the mean baseline BMI was 30.3 kg/m² (4.2). The baseline HbA1c was 8.5% (0.7) and fasting glucose was 8.9 mmol/L (2.6). The technical success of DA was 100%.

The mean number of ablations delivered per patient was 5 (180 J single), 14 (180 J double), and 18 (200 J double). In the second half of the cohort, the mean endoscopy time was 43.6 minutes (9.2), catheter time was 30.6 minutes (7), and ablation length was 14.3 cm (1.8).

The change in HbA1c at 4 weeks and 12 weeks was -0.9% (0.9; p<0.001) and -1.2% (1.1; p<0.0001), respectively without change in OADs (Table 1). At 12 weeks, 80% (n=20) undergoing double application had a >0.5% reduction in HbA1c. All patients were discharged the next day with no SAE or unanticipated device-related events. There were no episodes of severe hypoglycaemia.

Abdominal pain was the most common, self-limiting adverse event with five deemed mild and two moderate (requiring temporary oral antispasmodics). A 4-week follow-up endoscopy and duodenal biopsy (n=27) showed no stricture and normal mucosal histology.

Change at 12 weeks (double application)	Mean change (SD)*	P value†
HbA1c - %	-1.2 (1.1)	<0.001
Fasting fingerstick glucose - mmol/L	-1.8 (1.9)	<0.001
Post-prandial fingerstick glucose - mmol/L	-3.5 (2.4)	<0.001
Fasting blood glucose - mmol/L	-1.5 (2.3)	=0.003
HOMA-IR	-1.1 (2.0)	=0.016
Weight - kg	-2.4 (5.0)	=0.024
Body mass index - kg/m ²	-0.9 (1.9)	=0.024

*Compared to baseline values

†Data analysed using t-test

Table 1 – Clinical outcomes for patients undergoing duodenal ablation.

Conclusion: DA using RFVA is a safe, well-tolerated, and relatively quick endoscopic procedure for the management of poorly controlled T2D. Early efficacy data shows a clinically significant reduction in HbA1c at 4- and 12-weeks.

Disclosure: RH declares educational grants to support research infrastructure from Cook Medical, Odin Vision, Pentax Medical, Endogastric Solutions, Apollo Endosurgery, Medtronic, and Aqua Medical. LRG, PBH, AN, KC, and RSL all declare educational grants for research support and/or travel costs from Aqua Medical.

OP051

EFFICACY AND SAFETY OF ORAL SEMAGLUTIDE IN COMBINATION WITH DIETARY AND LIFESTYLE MODIFICATIONS FOR OVERWEIGHT OR OBESITY: A RANDOMIZED CONTROLLED TRIAL (OSO STUDY – ORAL SEMAGLUTIDE FOR OBESITY)

V.A. Katrevula¹, R. Kalapala¹, S. Agrawal¹, C. Merugu², N. Jagtap¹, A.V Kulkarni³, G.R. Katukuri¹, H. Rughwani¹, P. Inavolu¹, N.R. Duvvur¹

¹Asian Institute of Gastroenterology, Medical Gastroenterology, Hyderabad, Telangana, India, ²Asian Institute of Gastroenterology, Endocrinology, Hyderabad, Telangana, India, ³Asian Institute of Gastroenterology, Hepatology, Hyderabad, India

Contact E-Mail Address: anudeep.k65@gmail.com

Introduction: Obesity, characterised by excessive body fat accumulation, not only undermines physical health but also poses significant risks to mental well-being. Recent evidence has demonstrated the substantial benefits of Semaglutide in promoting weight loss among individuals with diabetes. Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, not only aids in glycaemic control but has also shown remarkable efficacy in reducing body weight.

Therefore, in this study, we investigated the effect of oral Semaglutide on weight loss in individuals with overweight or obesity but without diabetes mellitus.

Aims & Methods: The aim of the study was to evaluate the effectiveness and safety of oral Semaglutide when combined with dietary and lifestyle modifications, compared to dietary and lifestyle modifications alone, for the treatment of overweight or obesity in adults without type 2 diabetes. This randomized controlled trial was conducted in the department of Gastroenterology, Asian Institute of Gastroenterology, Hyderabad from June 2022 to December 2023. Consecutive consenting patients of both genders aged 18 years or older with either a BMI of 30 or greater or a BMI of 27 or greater with one or more treated or untreated weight-related coexisting conditions (i.e., prediabetes, hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease).

All the eligible participants after screening were randomized into two groups (Group 1 and 2) by block randomization (block size of 4 and 6) using computer generated random number. Participants in both groups received individual counselling sessions to help them adhere to a re-

duced-calorie diet (500- kcal deficit per day relative to the energy expenditure estimated at the time) and increased physical activity (with 150 minutes per week of physical activity, such as walking). Participants in group 1 also received oral Semaglutide along with diet and exercise. Treatment was initiated with the 3 mg once-daily dose.

The dose was increased to 7 mg and then maximum of 14mg per day in 2-4 weeks interval based on patient tolerance. Participants were assessed for gastrointestinal complaints (nausea, vomiting) during escalation and follow-up. (ClinicalTrials.gov ID: NCT05442450)

Results: A total of 116 (58 per each group) individuals were recruited into the study. Mean percentage(SD) change in body weight from baseline to week 28 was - 10.47% (SD 5.3) with Oral Semaglutide versus 2.4 (SD 4.5) with dietary and lifestyle changes alone ($p < 0.001$). The mean weightloss noted with Semaglutide was 9.19kg (SD 4.7) compared to 2.3kg (SD 4.5) with dietary and lifestyle measures alone. Subjects who received oral Semaglutide have reported >5%, >10%, >15% and >20% weightloss in 51/58 (87%), 28/58 (48%), 13/58 (22.4%) and 4/58 (6.9%) respectively. Subjects received only dietary and lifestyle changes have lost >5% of baseline weight in 14/58 (24%), >10% in 6/58 (10.34%) and none lost more than 15% of baseline weight.

Similarly, body mass index, waist circumference, HbA1C, fasting insulin and CRP were significantly improved with combination of Semaglutide with lifestyle measures. ($p < 0.001$). Body composition analysis revealed a significant change in body fat mass of -7.3 kg (4.8%) with maintained muscle mass in patients who received oral Semaglutide compared to those who underwent diet alone. Adverse events include severe nausea and vomiting noted in the three patients receiving the oral Semaglutide requiring discontinuation of the drug.

Conclusion: In adults with overweight or obesity but without type 2 diabetes, oral Semaglutide combined with dietary and lifestyle modifications resulted in a significant and clinically meaningful reduction in body weight compared to dietary and lifestyle modifications alone.

Disclosure: Nothing to disclose.

Upper GI basic: Reflux, gastritis and cancer

08:30-09:30 / Lehar 2

OP052

ELUCIDATING THE NON-CANONICAL ROLES OF STK3 IN THE CROSSTALK BETWEEN HIPPO AND WNT SIGNALING PATHWAY

F. Xie¹, W. Kang¹, B. Chen¹, Y. Lyu¹, D. Leung¹, K.F. To¹

¹The Chinese University of Hong Kong, Department of Anatomical and Cellular Pathology, State Key Laboratory of Translational Oncology, Li Ka Shing Institute of Health Science, Sir Y.K. Pao Cancer Center, Hong Kong, Hong Kong

Contact E-Mail Address: xiefuda@link.cuhk.edu.hk

Introduction: Serine/Threonine Kinase 3 (STK3) is conventionally recognized as a key regulator in the Hippo pathway. Activation of STK3/4 initiates the phosphorylation of Lats1/2 and subsequently YAP1, leading to its degradation. While STK3 has traditionally been acknowledged as a tumor suppressor in various cancer types, recent studies have revealed its oncogenic role in the development of gastric cancer (GC). Intriguingly, the intricate mechanisms underlying the non-canonical functions of STK3 remain largely uncharted.

Aims & Methods: In this study, our objective is to elucidate the upregulation pattern and the specific mechanisms of STK3 in advancing gastric tumorigenesis. The regulatory influence of YAP1 on STK3 was assessed through a combination of RNA-sequencing (RNA-seq), western blot, and ChIP-qPCR assays. This relationship was subsequently validated using gene knockout mouse models and rescue assays involving colony formation and invasion activity testing. The clinical correlation between YAP1 and STK3 was validated by both online datasets and immuno-histochemistry (IHC) of tissue microarrays.

Furthermore, RNA-seq and TCGA-based functional enrichment analysis were employed to predict the oncogenic roles of STK3, supported by single-cell RNA-seq GSVA analysis. These predicted outcomes were confirmed through siRNA-mediated functional assay including spheroid formation and organoid growth assays.

The downstream target of STK3 was identified via RNA-seq and western blot analysis, with further validation carried out through co-immunoprecipitation and immunofluorescence. The *in vivo* functions of STK3 were demonstrated by subcutaneous xenograft formation and peritoneal metastasis models.

Results: STK3 expression was reduced by siRNA-mediated YAP1 deletion at both mRNA and protein levels. Treatment with YAP1 inhibitors led to a dose-dependent inhibition of STK3 expression.

Notably, MNNG-induced tumors in *Yap^{-/-}/Taz^{-/-}* mice showed no STK3 expression. The deletion of STK3 resulted in a partial attenuation of the oncogenic activity of YAP1. Concurrent elevation of YAP1 and STK3 was detected across multiple online datasets and our in-house cohort.

Bioinformatic analysis revealed that STK3 would participate in DNA damage response and stemness acquisition processes. Knockdown of STK3 led to reduced sphere formation ability, xenograft size, and expression levels of stemness markers.

Deletion of STK3 increased the sensitivity of GC organoids and xenografts to 5-fluorouracil treatment, resulting in decreased organoid sizes, limited metastasis, and downregulation of tumor malignancy markers. Activation of the Wnt pathway and the downstream stemness regulators were strongly associated with the upregulation of STK3.

Deletion of STK3 reduced the levels of phosphorylated GSK-3 β and prevented the nuclear accumulation of β -catenin. Co-IP assays revealed the directly interaction between STK3 and GSK-3 β . IHC staining of mouse xenografts confirmed the *in vivo* inhibition of Wnt signaling following STK3 deletion.

Conclusion: Our study investigated the upregulation mechanism and non-canonical oncogenic roles of STK3 in the progression of GC. YAP1, a typical downstream component in the Hippo pathway, was demonstrated to transcriptionally activate STK3 expression.

Meanwhile, this work also identified STK3 as a promoter of DNA repair and stemness acquisition through activation of the GSK-3 β / β -catenin axis, shedding light on the diverse functional patterns of Hippo signaling in GC progression.

Disclosure: Nothing to disclose.

OP053

OXIDATIVE STRESS –INDUCED HIGH MOBILITY GROUP BOX 1 (HMGB1) RELEASE IN GASTRO-OESOPHAGEAL REFLUX DISEASE: A NOVEL THERAPEUTIC TARGET

T. Leech¹, A. Ustaoglu¹, P. Woodland¹, D. Kellsell², D. Blaydon², M. Peiris¹

¹Queen Mary University of London, Wingate Institute of Neurogastroenterology, London, United Kingdom, ²Queen Mary University of London, Blizard Institute, London, United Kingdom

Contact E-Mail Address: t.leech@qmul.ac.uk

Introduction: In up to 40% of gastro-oesophageal reflux disease (GERD) patients, heartburn symptoms persist despite PPI treatment. This may be due to exposure of the oesophageal mucosa to other refluxate components such as weakly acidic (pH5) bile salts, leading to oxidative stress in epithelial cells and micro-inflammation, potentially resulting in release of mediators which activate sensory nerve fibres. High mobility group box 1 (HMGB1) is a nuclear protein found in oesophageal epithelial cells, which is actively secreted during cellular oxidative stress. Once released, HMGB1 binds to receptors including TLR2, TLR4, and RAGE to induce NF- κ B-mediated inflammatory signalling. We aimed to determine the mechanism of release and potential downstream impacts of HMGB1 in GERD.

Aims & Methods: Oesophageal biopsies were obtained from consented healthy volunteers (n=10) and GERD patients categorised as functional heartburn (FH; n=7), non-erosive reflux disease (NERD; n=13), and erosive reflux disease (ERD; n=13) based on clinical assessment. Biopsies were analysed by bulk RNA-sequencing to determine commonly up-regulated genes between NERD and ERD patients compared to HC. Protein expression of TLR2, TLR4, and RAGE was assessed with immunohistochemistry. NE-1 cells were challenged with pH5 media and/or 500 μ M deoxycholate (DCA), and pre-treated with 50 μ M curcumin, for 2 hours. Cellular translocation of HMGB1 over 10 minutes was measured with immunofluorescence and release of HMGB1 over 20 minutes was measured with ELISA.

Results: Bulk RNA-seq revealed that HMGB1 is one of 11 commonly over-expressed genes in NERD and ERD compared to HC (adjusted $p < 0.01$). Compared to pH7, incubating NE-1 cells at pH5 or DCA alone did not induce HMGB1 release or nuclear translocation, however, the combination of pH5 and DCA caused HMGB1 translocation, represented as increased cytosolic:nuclear fluorescence ratio ($p < 0.0001$). Similarly, HMGB1 release from cells was induced only in response to pH5 + DCA ($p < 0.01$). Pre-treatment with the antioxidant curcumin ameliorated increase in HMGB1 cytosolic:nuclear ratio ($p < 0.001$) and ablated HMGB1 release ($p < 0.05$) caused by weakly acidic bile salts. TLR2 and TLR4 were expressed on oesophageal epithelial cells. Expression of TLR2 was not altered between GERD phenotypes and HCs. Whereas, the percentage of DAPI+ cells which were TLR4+ ($P < 0.05$), as well as fluorescence intensity of TLR4 ($p < 0.05$) in the oesophageal mucosa was higher in ERD compared to HC. RAGE was rarely but exclusively expressed on CD45+ cells located both intra-epithelially and in mucosal papillae.

The number of RAGE+CD45+ cells/field of view was higher in ERD oesophageal mucosa compared to HC ($p < 0.05$). In NERD and ERD patients, a proportion of RAGE+ cells were in close apposition to CGRP+ nerve fibres in papillae of the oesophageal mucosa.

Conclusion: The induction of HMGB1 release from oesophageal epithelial cells by weak acid (pH5) and bile salts –which is inhibited by the antioxidant curcumin describes a novel molecular pathway and new treatment target for GERD. Indeed, increased expression of the HMGB1 receptor, TLR4, in the oesophageal mucosa of ERD patients provides further evidence that this pathway is highly relevant to GERD pathophysiology. The expression of HMGB1 receptor RAGE in CD45+ cells and association with sensory nerve fibres further supports HMGB1 as a potential molecular target for future development.

Disclosure: Nothing to disclose.

OP054

THE EXTRACELLULAR MATRIX PROTEIN EMILIN-1 IMPACTS ON THE MICROENVIRONMENT BY HAMPERING THE DEVELOPMENT AND PROGRESSION OF GASTRIC CANCER

A. Capuano¹, M. Vescovo¹, E. Scanziani², S. Muzzin¹, S. Nomura³, S. Canesi², S. Realdon⁴, S. Maiero⁴, M.G. Nadin⁴, I.V. Albergati⁵, A. Piruzza⁵, L.S. Crocè⁵, R. Cannizzaro^{5,4}, P. Spessotto¹

¹Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Molecular Oncology Unit, Aviano, Italy, ²University of Milan, Department of Veterinary Medicine and Animal Science, Milan, Italy, ³University of Tokyo, Department of Gastrointestinal Surgery, Graduate School of Medicine, Tokyo, Japan, ⁴Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Oncological Gastroenterology Unit, Aviano, Italy, ⁵University of Trieste, Dipartimento universitario clinico di scienze mediche, chirurgiche e della salute, Trieste, Italy

Contact E-Mail Address: acapuano@cro.it

Introduction: The contribution of the tumor microenvironment and extracellular matrix to the aggressive biology of Gastric Cancer (GC) has been recently characterized (1).

During GC progression striking changes in the lymphatic vessels (LVs) occur and lymphatic metastasis is the commonest feature of GC spread, representing the most significant prognostic factor determining the clinical outcomes (2).

Recent evidence supporting a functional link among EMILIN-1, an Extra Cellular Matrix component (ECM), tumour growth and lymph-angiogenesis has been provided. EMILIN-1 represents a key structural element in the maintenance and function of LVs and displays anti-proliferative effects through the interaction with $\alpha 4 \beta 1$ integrin, as demonstrated in skin and colon cancer (3,4,5). Interestingly, $\alpha 4$ integrin is transcriptionally repressed in GC, but not in the normal gastric epithelium (7), suggesting a crucial mechanism exerted by the integrin/EMILIN1 recognition also in this context.

Aims & Methods: The aim of this study is to analyze the possible role of EMILIN-1 as a molecular regulator in the context of GC development and progression.

We performed Immunofluorescence staining of human gastric biopsy samples from normal and neoplastic tissues collected during the endoscopy procedures. Biopsies from pre-malignant lesions were also included. For *in vivo* experiments, we used the syngeneic YTN16 gastric cancer cell line (7) which was injected subcutaneously and intraperitoneally in genetically modified EMILIN-1 mice. In alternative, carcinogenesis was induced in mice using N-methyl-N-nitrosourea (MNU). GES-1 (normal stomach mu-

cosa), and several GC cell lines representative of different GC stages and histotypes (i.e. AGS, Hs746.T, NCI-N87 and KATO-III) were employed for *in vitro* experiments.

Results: EMILIN-1 is diffusely deposited in normal gastric mucosa and is significantly decreased in malignant and pre-neoplastic samples; this finding correlates with the presence of aberrant LVs. EMILIN-1 mutant mice (knock out and E955A knock in) developed tumors earlier compared to WT animals: 20 days post-injection of YTN16 cells, tumors developed in EMILIN-1 mutant mice were larger and displayed a significant increase of lymphangiogenesis. Treatment of transgenic mice with MNU associated with an increased number of tumors, exacerbated aggressive lesions and higher levels of LV abnormalities.

To unveil the main mechanisms responsible for EMILIN-1 reduction we treated *in vitro* fibroblasts and LECs (the major cellular sources of EMILIN1 in the gastric microenvironment) with conditioned media derived from GC cells lines; dramatic effects on EMILIN1 expression were observed, both at the mRNA and protein levels. Small-RNAseq analysis on culture media allowed us to identify miR125a-5p as a possible molecular regulator of EMILIN-1 levels in this context.

Conclusion: This study demonstrates for the first time that loss of EMILIN-1 in GC leads to lymphatic dysfunction and proliferative advantages that sustain tumorigenesis, and assess the use of our animal model as a valuable tool to verify the fate of GC upon loss of EMILIN-1.

References: 1. Rojas A, Araya P, Gonzalez I, Morales E. Gastric Tumor Microenvironment. *Adv Exp Med Biol.* 2020;1226:23–35.8
2. Deng J-Y, Liang H. Clinical significance of lymph node metastasis in gastric cancer. *World J Gastroenterol.* 2014;20:3967–75.
3. Capuano A, Pivetta E, Sartori G, Bosisio G, Favero A, Cover E, et al. Abrogation of EMILIN1- β 1 integrin interaction promotes experimental colitis and colon carcinogenesis. *Matrix Biol J Int Soc Matrix Biol.* 2019;83:97–115.
4. Capuano A, Pivetta E, Baldissera F, Bosisio G, Wassermann B, Buccioti F, et al. Integrin binding site within the gC1q domain orchestrates EMILIN-1-induced lymphangiogenesis. *Matrix Biol J Int Soc Matrix Biol.* 2019;81:34–49.
5. Danussi C, Petrucco A, Wassermann B, Pivetta E, Modica TM, Del Bel Bel-luz L, et al. EMILIN1- α 4/ α 9 integrin interaction inhibits dermal fibroblast and keratinocyte proliferation. *J Cell Biol.* 2011;195:131–45.
6. Park J, Song S-H, Kim TY, Choi M-C, Jong H-S, Kim T-Y, et al. Aberrant methylation of integrin α 4 gene in human gastric cancer cells. *Oncogene.* 2004;23:3474–80.
7. Yamamoto M, Nomura S, Hosoi A, Nagaoka K, Iino T, Yasuda T et al. Established gastric cancer cell lines transplantable into C57BL/6 mice show fibroblast growth factor receptor 4 promotion of tumor growth. *Cancer Sci.* 2018 May;109(5):1480-1492.

Disclosure: Nothing to disclose.

OP055

CYTOPROTECTIVE CARBON MONOXIDE SIGNALING IS MITOCHONDRIA-ORIENTED AND ENHANCES GASTRIC MUCOSAL ABILITY TO COUNTERACT PATHOLOGY-DRIVEN DISINTEGRATION EVOKED BY NON-STEROIDAL ANTI-INFLAMMATORY DRUG

A. Danielak¹, U. Głowacka¹, M. Szetela¹, M. Pinkas¹, K. Krukowska¹, M. Suski^{2,3}, B. Gryzłó⁴, M. Marcinkowska⁴, M. Magierowski¹

¹Jagiellonian University Medical College, Cellular Engineering and Isotope Diagnostics Lab, Department of Physiology, Cracow, Poland, ²Jagiellonian University Medical College, Department of Pharmacology, Cracow, Poland, ³Jagiellonian University Medical College, Proteomics Laboratory, Centre for the Development of Therapies for Civilization and Age-Related Diseases, Cracow, Poland, ⁴Jagiellonian University Medical College, Department of Medicinal Chemistry, Faculty of Pharmacy, Cracow, Poland

Contact E-Mail Address: aleksandra.danielak@uj.edu.pl

Introduction: Carbon monoxide (CO) is an endogenous gaseous messenger produced by the enzymatic activity of heme oxygenase with anti-inflammatory and anti-oxidative properties [1].

Pharmacological CO donors with ability to release small amounts of CO exerted gastroprotective effects against injuries induced by ethanol, ischemia/reperfusion or non-steroidal anti-inflammatory drugs (NSAIDs) [2,3]. Interestingly, further studies revealed that low concentrations of CO influence mitochondrial bioenergetics and respiration by binding to heme proteins in electron transport chain (ETC), resulting in cytoprotective action [4].

Therefore, novel and unique strategy based on “click chemistry” has been invented by the Binghe Wang Lab (Georgia State University, USA) to deliver CO directly to the mitochondria [5].

However, this approach is yet to be implemented in GI pharmacology. Moreover, mitochondria as a fundamental target of endogenous CO-signaling in pathogenesis and prevention of GI pathologies has been ignored.

Aims & Methods: Therefore, we aimed to prove for the first time that mitochondrial rather than stochastic CO-signaling contributes in gastric mucosal integrity maintenance under pathogenic conditions.

We also evaluated if targeted mitochondrial delivery of novel CO-prodrug described by Zheng et al. (Nature Chemistry 2018) [5] (working name: BW-mito-CO) protects gastric mucosa against acute injury evoked by NSAIDs representative, acetylsalicylic acid (ASA).

Thus, male Wistar rats were pretreated intragastrically (i.g.) with:

- 1) DMSO/H₂O as vehicle,
- 2) BW-mito-CO (0.2, 1, 5 mg/kg) and CO-release activating “click”-moiety,
- 3) selected, the most effective dose of BW-mito-CO (5 mg/kg) + rotenone, a mitochondrial complex I inhibitor (5 mg/kg). Subsequently, gastric mucosal injury was induced by i.g. administration of ASA (125 mg/kg).

Gastric mucosal damage and gastric mucosal blood flow (GBF) have been assessed by planimetry and laser flowmetry, respectively. Proteome profiling and molecular targets screening in gastric mucosal biopsies was performed using mass spectrometry-based proteomics. BW-mito-CO platform was synthesized in house according to Zheng et al. (Nature Chemistry 2018) [5].

Results: BW-mito-CO dose-dependently reduced the area of ASA-induced gastric mucosal damage, with the most notable effect observed at the dose of 5 mg/kg, while GBF remained without significant changes. Rotenone did not alter the protective effect of BW-mito-CO.

Proteomic analysis revealed that BW-mito-CO (5 mg/kg) significantly up-regulated proteins related to the tricarboxylic acid cycle and cytoprotective agents associated with gastric mucosal defense, including calpains

and treofil factor that were mostly altered in opposite manner by ASA. Pretreatment with BW-mito-CO upregulated mitochondrial complex I hemoproteins that were not affected by ASA.

Conclusion: We conclude that gastric mucosal CO-signaling mostly relies on its impact on mitochondrial compartments. Increased mitochondrial bioavailability of CO counteracts pathology-driven proteomic shifts in gastric mucosa. Implementation of mito-targeted CO delivery platforms appeared here as a novel and promising approach to GI pharmacology vs NSAIDs-induced gastric mucosal injuries. Mitochondrial CO signaling seems to mechanistically depend on its capacity to activate mitochondrial complex I and to enhance gastric mucosal ability to maintain its integrity under pathological conditions [Founding source: National Science Centre (Poland): 2019/33/B/NZ4/00616; Ministry of Science and Higher Education (Poland): Perty Nauki PN/01/0279/2022].

References: 1. Yang X, Mao Q, Wang B. On the Question of CO's Ability to Induce HO-1 Expression in Cell Culture: A Comparative Study Using Different CO Sources. *ACS Chem Biol.* 2024 Mar 15; 19(3): 725–735. doi:10.1021/acscchembio.3c00750.

2. Danielak A, Wallace JL, Brzozowski T, et al. Gaseous Mediators as a Key Molecular Targets for the Development of Gastrointestinal-Safe Anti-Inflammatory Pharmacology. *Front Pharmacol.* 2021;12: 657457. doi:10.3389/fphar.2021.657457.

3. Bakalarz D, Surmiak M, Yang X, et al. Organic carbon monoxide prodrug, BW-CO-111, in protection against chemically-induced gastric mucosal damage. *Acta Pharm Sin B.* 2021;11(2). doi:10.1016/j.apsb.2020.08.005.

4. Iacono LL, Boczkowski J, Zini R, et al. A carbon monoxide-releasing molecule (CORM-3) uncouples mitochondrial respiration and modulates the production of reactive oxygen species. *Free Radic Biol Med.* 2011; 1;50(11):1556–64. doi: 10.1016/j.freeradbiomed.2011.02.033.

5. Zheng Y, Ji X, Yu B, et al. Enrichment-triggered prodrug activation demonstrated through mitochondria-targeted delivery of doxorubicin and carbon monoxide. *Nat Chem.* 2018;10(7). doi:10.1038/s41557-018-0055-2.

Disclosure: Nothing to disclose.

OP056

MICROBIOTA IN GASTRIC PRECANCEROUS CONDITIONS PROSPECTIVE MÜNCHEN-PADOVA STUDY

L. Bricca¹, M. Rugge², P. Malfertheiner³, R. Vasapolli⁴

¹University of Padua, DIMED - Department of Medicine, Padua, Italy, ²University of Padua, DIMED - Department of Medicine, Padua, Italy, ³LMU Munich, Department of Internal Medicine II, Munich, Germany, ⁴University Hospital LMU Munich, Department of Internal Medicine II, Munich, Germany

Contact E-Mail Address: ludovica.bricca@studenti.unipd.it

Introduction: Gastric microbiota (GMI) plays a significant role in metabolome shaping and it is also potentially involved in gastric oncogenesis.^{1,2} This international prospective cohort study investigates bacterial communities in stomachs with clinically, histologically, and serologically profiled precancerous conditions.

Aims & Methods: The aim of the study was to evaluate whether a certain GMI composition could be related to a specific gastric pathological condition, in order to investigate its oncogenic potential. 112 biopsies from oxyntic and antral mucosa (healthy stomachs [HS] 36; Hp+ Gastritis (G): 21 atrophic [AG] and 22 non-atrophic [NAG]; Autoimmune G. [AIG] 33) were endoscopically obtained from 53 subjects (GE= 27; IT= 26). Serology was tested by Gastropanel. Histology assessment applied validated criteria, as the OLGA-staging system. GMI-communities were profiled by gastric biopsies 16S rRNA sequencing, calculating bacterial genus abundances

across the tested conditions. a- (Faith PD, Observed Features, Shannon Entropy) and b- (PCoA) diversity were valued. The correlation of GMI with clinicopathological variables was tested by Spearman-test. P<0.05 was considered significant.

Results: Multivariate testing revealed significant correlation only for diagnostic categories (p=.0001) in the study of the correlation between GMI-profile (all biopsy samples) and sex, age, country (GE vs IT), alcohol intake, smoking habit, PPI assumption, samples compartment (antrum vs corpus), and diagnostic category.

HS samples featured the highest a-diversity and, compared to each category, b-diversity was sensibly higher, with elective abundance of *Solobacterium*, and *Eubacterium Sulci* genera (p<.05). In oxyntic and antral mucosa of NAG and AG samples, *Helicobacter* genus harmed the microbial community, leading to extremely low a-diversity and is significantly b-diverse from HS. Opposite to Hp+, AIG-GMI featured the microbial community similar to HS, with a prevalence of genus *Granulicatella*, *Pauljensenia*, *Rothia*, *Parvimonas*, and *Veillonella* (p<.05).

This finding was further supported by the clustering of AIG and HS on the same side of the PCoA graph. By applying Spearman test, GMI profile showed significant correlation with patients' clinicopathological profile:

- Normal histology positively correlated with *Solobacterium* and *Eubacterium* and inversely with inflammatory score (polymorphs and lymphocytes) and with G17 and Pg2 (p<.05)

- Hp+ NAG and AG positively correlated with inflammatory score (p<.05), with Pg1, Pg2 and Pg1/Pg2, and inversely correlated with APCA values (p<.05)

- In oxyntic AIG samples, pseudopyloric atrophy positively correlated with *Gemella*, *Granulicatella*, and *Veillonella*, while *Leptotrichia* and *Rothia* with IM atrophy (p<.05)

- *Gemella*, *Granulicatella*, *Haemophilus parainfluenzae*, *Pauljensenia*, *Rothia* and *Veillonella* positively correlated with APCA (p<.05), and inversely correlated with Pg1 (as marker of oxyntic atrophy).

Conclusion: This study explored microbiota composition in gastric precancerous conditions. The present study provides evidence of clinico-biological correlation between GMI and precancerous atrophy and inflammation.

The present results significantly link microbes others than Hp as promoters of the gastric inflammation and, ultimately, in gastric oncogenesis. The overlaps of GMI composition between HS and AIG may provide a biological rationale for the lower cancer risk of AIG compared to Hp+ atrophic patients.³

These results support the potential use of GMI profiling as add-on information in ranking the cancer risk in patients harboring gastric precancerous conditions.

References: 1. Mendes-Rocha M, Pereira-Marques J, Ferreira RM, Figueiredo C. Gastric Cancer: The Microbiome Beyond *Helicobacter pylori*. *Curr Top Microbiol Immunol.* 2023;444:157–84.

2. Liu Z, Zhang D, Chen S. Unveiling the gastric microbiota: implications for gastric carcinogenesis, immune responses, and clinical prospects. *J Exp Clin Cancer Res CR.* 2024;43:118.

3. Rugge M, Bricca L, Guzzinati S, Sacchi D, Pizzi M, Savarino E, Farinati F, Zorzi M, Fassan M, Dei Tos AP, Malfertheiner P, Genta RM, Graham DY. Autoimmune gastritis: long-term natural history in naïve *Helicobacter pylori*-negative patients. *Gut.* 2023;72:30–38.

Disclosure: The authors of this study do not have any conflict of interest into the text field above.

Recent break throughs in treating and monitoring MASH

08:30-09:30 / Lehar 3

OP057

ANALYSES OF FIBROSIS BIOMARKERS PRO-C3 AND ELF IN RESMETIROM TREATED PATIENTS FROM MAESTRO-NASH, A 52 WEEK NASH/MASH SERIAL LIVER BIOPSY STUDY

Q. Anstee¹, N. Alkhoury², J. Schattenberg³, R. Taub⁴, D. Labriola⁴, H. Zang⁴, J. Hennen⁴

¹Newcastle University, Institute of Cellular Medicine, Newcastle, United Kingdom, ²Arizona Liver Health, Tucson, United States of America, ³Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Medizinische Klinik für Innere Medizin II, Homburg, Germany, ⁴Madrigal Pharmaceuticals, Inc., West Conshohocken, United States of America

Contact E-Mail Address: Joern.schattenberg@uks.eu

Introduction: MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating the efficacy of resmetirom in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH/MASH) and fibrosis. 966 patients with biopsy confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo administered once daily.

Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or ≥ 1 -stage improvement in fibrosis with no worsening of NAS (FI). We evaluated the baseline and effect of resmetirom compared with placebo on fibrosis biomarkers PRO-C3 and P3NP/ELF.

Aims & Methods: Pearson's correlation was used to examine the association between 2 PRO-C3 ELISA assay methods (ELISA GEN1 and ELISA GEN2, NORDIC BIOSCIENCE) using PRO-C3 baseline data (N=919). The rest of the analyses used the ELISA GEN2 assay. Mean SD or SE and median [Q1, Q3] were calculated to summarize PRO-C3 data. ANCOVA was used for comparisons between resmetirom 80 or 100 mg vs. placebo in PRO-C3 change from baseline at week 52 (wk52CHG), while controlling for baseline PRO-C3 level.

Mean difference with 95% CI and nominal P-values were obtained from the ANCOVA. Scatterplots and Spearman's correlations with 95% CIs were used to assess the associations between P3NP/ELF and PRO-C3 both at baseline and wk52CHG.

Results: The two PRO-C3 assays ELISA GEN1 and ELISA GEN2 data were positively associated with a Pearson's correlation of 0.78 (P-value <0.0001). At baseline, PRO-C3 was mean (SD)=137 (71.7) ng/ml. At week 52, PRO-C3 wk52CHG for 100 mg resmetirom=-23.05 (4.76), 80 mg=-17.93 (4.61) and placebo=-0.19, 4.07 with mean difference (95% CI) in PRO-C3 wk52CHG between 80 mg and placebo=-16.9 (-27.0, -6.76; p=0.0011); 100 mg and placebo=-22.1 (-32.3, -11.84; p<0.0001).

Larger reductions in PRO-C3 mean (SD) on the resmetirom arms were observed in F3 patients: 80 mg=-22.42 (6.38) and 100 mg=-27.42 (6.72) compared with placebo=-0.50 (5.46). Baseline P3NP and ELF were correlated with PRO-C3 (0.563 and 0.458, respectively).

The wk52CHG in P3NP was positively associated with wk52CHG in PRO-C3 (0.557, 0.548 and 0.524 for 100 mg, 80 mg and placebo; respectively). A weaker positive correlation between wk52CHG for ELF and PRO-C3 (0.483, 0.484 and 0.487 for 100 mg, 80 mg and placebo, respectively) were also observed.

Conclusion: Two Pro-C3 assays (ELISA GEN1 and ELISA GEN2, NORDIC BIOSCIENCE) were correlated at baseline, indicating ELISA GEN2 assay was reasonable for measuring PRO-C3 levels. For PRO-C3 ELISA GEN2,

drug effects were statistically significant for both doses of resmetirom vs. placebo. The assay was more sensitive in detecting resmetirom effect in F3 patients. ELF and PRO-C3 was less strongly correlated than P3NP and PRO-C3.

Disclosure: Authors are investigators in the MAESTRO-NASH trial or employees of Madrigal Pharmaceuticals.

OP058

SEMAGLUTIDE ACHIEVES RESOLUTION OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS VIA MODULATION OF MULTIPLE PATHOGENIC PATHWAYS: INSIGHTS FROM HUMAN AND ANIMAL OMICS STUDIES

M Jara¹, J Norlin², MS Kjær¹, K Almholts², KM Bendtsen², E Bugianesi³, K Cusi⁴, ED Galsgaard², M Geybels⁵, LL Gluud⁶, LM Harder², R Loomba⁷, G Mazzoni², PN Newsome^{8,9}, LM Nitze¹, MS Palles⁵, V Ratzu¹⁰, A-S Sejlting¹, VW Wong¹¹, QM Anstee^{12,13}, LB Knudsen²

¹Novo Nordisk, Clinical Development, Søborg, Denmark, ²Novo Nordisk, Research & Early Development, Måløv, Denmark, ³Division of Gastroenterology, Department of Medical Sciences, University of Torino, Torino, Italy, ⁴Division of Endocrinology, Diabetes, and Metabolism, University of Florida, Gainesville, FL, United States of America, ⁵Novo Nordisk, Data Science, Søborg, Denmark, ⁶Gastro Unit, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark and Department of Medicine, University of Copenhagen, Hvidovre, Denmark, ⁷Radcliffe Department of Medicine, Oxford University, Oxford, United Kingdom, ⁸National Institute for Health Research Birmingham Biomedical Research Centre and Liver Unit at University Hospitals Birmingham NHS Foundation Trust and Centre for Liver & Gastrointestinal Research, Birmingham, United Kingdom, ⁹Institute of Hepatology, Faculty of Life Sciences & Medicine, King's College London and King's College Hospital, London, United Kingdom, ¹⁰Sorbonne University, ICAN - Institute for Cardiometabolism and Nutrition, Hôpital Pitié Salpêtrière, Paris, France, ¹¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China, ¹²Translational & Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom, ¹³Newcastle NIHR Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, United Kingdom

Contact E-Mail Address: elisabetta.bugianesi@unito.it

Introduction: Metabolic dysfunction-associated steatohepatitis (MASH) increases the risk of cardiovascular (CV) events and liver fibrosis. Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, reduces CV risk associated with overweight and obesity in the absence of diabetes and has a profound effect on weight reduction and MASH resolution. Management of MASH may benefit from a deeper understanding of the mechanistic basis of semaglutide-induced MASH resolution.

Aims & Methods: This study used a multi-omics approach to investigate the effects of semaglutide on the hepatic microenvironment and fibrosis development in the context of semaglutide-induced MASH resolution. GLP-1 receptor expression was assessed using RNA *in situ* hybridization and immunohistochemistry in human liver tissue and immunohistochemistry in liver tissue from DIO-NASH and CDA-HFD mice. The effect of semaglutide treatment on liver fibrosis was also assessed using liver transcriptome analysis in both of these mouse models of MASH. Proteomic analyses of 4,979 proteins using the SomaScan Platform were conducted

on serum samples from 293 patients with MASH who received semaglutide or placebo in a phase 2b study (NCT02970942), and an independent cohort of 141 patients with MASH and 89 healthy volunteers.

Results: GLP-1 receptor mRNA or protein expression were not detected in human or mouse liver tissue. However, semaglutide improved histological markers of fibrosis and expression of genes involved in collagen turnover in two distinct mouse models of MASH; one that phenocopies the metabolic-associated features of human disease and another that exhibits non-abdominal obesity-induced advanced steatohepatitis and rapid fibrosis. In semaglutide-treated patients with MASH, proteomics identified 72 proteins significantly associated with MASH resolution after 72 weeks of treatment. These 72 proteins were also identified as differentially expressed in patients with MASH who were not treated for MASH, relative to healthy individuals.

In semaglutide-treated patients with MASH, the abundance of the 72 proteins was similarly altered; however, semaglutide reverted the altered disease profile to that seen in non-pharmacologically treated healthy individuals. In contrast, changes in the levels of the 72 proteins in patients who received placebo were negligible.

Notably, changes in the abundance of 26 of the 72 proteins were significant even after correction for weight loss. Although most of these 26 proteins are associated with metabolic functions, several are implicated in fibrosis-related pathways and CV disease (e.g. ADAMTSL2 and ACY1), and hepatocellular carcinoma (e.g. SERPINC1).

Conclusion: Based on circulating proteomic profiling, semaglutide-induced MASH resolution is associated with changes in multiple pathogenic pathways even after correction for weight loss. Semaglutide appears to re-balance the expression levels of disease-associated proteins in MASH to levels found in healthy individuals.

Disclosure: MJ is an employee of Novo Nordisk A/S. JN is an employee of Novo Nordisk A/S. MSK is an employee of Novo Nordisk A/S. KA is an employee of Novo Nordisk A/S. KMB is an employee of Novo Nordisk A/S. EB served as a consultant or advisory board member for Boehringer Ingelheim, Gilead Sciences, Intercept, Merck, Novo Nordisk, Pfizer, Prosciento. Grants from Gilead Sciences for fatty liver research, Speaker for Gilead Sciences, Intercept, Merck, Novo Nordisk, and Pfizer. KC served as a consultant for Aligos Therapeutics, Arrowhead, AstraZeneca, 89Bio, BMS, Eli Lilly & Co., Merck, Novo Nordisk, Prosciento, Sagimet Biosciences, Siemens, and Terns Pharma. Received research support (University of Florida; Principal Investigator) from Boehringer Ingelheim, Echosens, Inventiva, Labcorp, and Perspectum. EDG is an employee of Novo Nordisk A/S. MG is an employee of Novo Nordisk A/S. LLG is an employee of Novo Nordisk A/S. LMH is an employee of Novo Nordisk A/S. RL is a consultant to Aardvark Therapeutics, Altimmune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol-Myer Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympse bio, Hightide, Inipharma, Intercept, Inventiva, Ionis, Janssen Inc., Madrigal, Metacrine, Inc., NGM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Sagimet, Theratechnologies, 89 bio, Terns Pharmaceuticals and Viking Therapeutics. His institutions received research grants from Arrowhead Pharmaceuticals, Astrazeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galectin Therapeutics, Galmed Pharmaceuticals, Gilead, Hanmi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, Merck, NGM Biopharmaceuticals, Novo Nordisk, Pfizer, Sonic Incytes and Terns Pharmaceuticals. Co-founder of LipoNexus Inc. GM is an employee of Novo Nordisk A/S. PNN is a consultant for Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, Bristol Myers Squibb (BMS), Pfizer, Sun Pharma, Madrigal and GSK. He also reports honoraria as a speaker for Novo Nordisk and AiCME; support for attending meetings from for Novo Nordisk; and participation on an advisory board for Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, BMS, Pfizer, Sun Pharma, Madrigal, and GSK. LMN is an employee of Novo Nordisk A/S. MSP is an employ-

ee of Novo Nordisk A/S. VR received consulting fees from Novo-Nordisk, Sagimet, Madrigal, Enyo, Poxel, Northsea, Intercept Pharmaceuticals, Prosciento. Research grants (to institution) from Gilead Sciences and Intercept Pharmaceuticals. A-SS is an employee of Novo Nordisk A/S. VWW served as a consultant or advisory board member for AbbVie, Boehringer Ingelheim, Echosens, Gilead Sciences, Intercept, Inventiva, Novo Nordisk, Pfizer, Sagimet Biosciences, and TARGET PharmaSolutions. Has received a research grant from Gilead Sciences. Speaker for Abbott, AbbVie, Gilead Sciences, Novo Nordisk, and Unilab. Co-founder of Illuminatio Medical Technology Limited. Has received travel support from AbbVie and Gilead Sciences. QMA is coordinator of the IMI2 Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS) consortium, which is funded by the European Union Horizon 2020 programme and the European Federation of Pharmaceutical Industries and Associations (EFPIA). This multi-stakeholder consortium includes industry partners. He reports research grant funding from AstraZeneca, Boehringer Ingelheim, and Intercept; consultancy on behalf of Newcastle University for Alimentiv, Akero, AstraZeneca, Axcella, 89Bio, Boehringer Ingelheim, Bristol Myers Squibb, Galmed, Genfit, Genentech, Gilead, GlaxoSmithKline, Hanmi, HistoIndex, Intercept, Inventiva, Ionis, IQVIA, Janssen, Madrigal, Medpace, Merck, NGMBio, Novartis, Novo Nordisk, PathAI, Pfizer, Prosciento, Poxel, Resolution Therapeutics, Roche, Ridgeline Therapeutics, RTI, Shionogi, and Terns; speaker fees/honoraria from Fishawack, Integrity Communications, Kenes, Novo Nordisk, Madrigal, Medscape, and Springer Healthcare; and royalties from Elsevier. LBK is an employee of Novo Nordisk A/S.

OP059

NON-INVASIVE PREDICTIVE MARKERS OF RESMETIROM BIOPSY RESPONSE

R. Loomba¹, J. Schattenberg², R. Taub³, D. Labriola³, M. Nouredin⁴, V. Ratzliff⁵, S.A. Harrison⁶

¹University of California, MASLD Research Center, Division of Gastroenterology and Hepatology, San Diego, United States of America, ²Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Medizinische Klinik für Innere Medizin II, Homburg, Germany, ³Madrigal Pharmaceuticals, Inc., West Conshohocken, United States of America, ⁴Houston Methodist Hospital, Research Institute, Houston, United States of America, ⁵Hôpital Pitié Salpêtrière, Hepatology and Gastroenterology, Paris, France, ⁶Pinnacle Clinical Research, San Antonio, United States of America

Contact E-Mail Address: Joern.schattenberg@uks.eu

Introduction: MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo controlled Phase 3 trial evaluating the efficacy of resmetirom in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH) and fibrosis. 966 patients with biopsy-confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo administered once daily.

Histologic endpoints were assessed after 52 weeks. Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or ≥ 1 -stage reduction in fibrosis with no worsening of NAS (FR).

Aims & Methods: Adults with ≥ 3 metabolic risk factors, liver stiffness ≥ 8.5 kPa, hepatic fat $\geq 8\%$, biopsy-confirmed NASH with F1B-F3 fibrosis, and NAS ≥ 4 were eligible to participate in MAESTRO-NASH. In this analysis, the relationship of changes in (1) FibroScan CAP, (2) Fibroscan VCTE, and (3) alanine aminotransferase (ALT) to histological response (NR and/or FR) in the resmetirom 80 mg, resmetirom 100 mg, and placebo groups was assessed.

Results: Patients with biopsy-confirmed NASH with fibrosis had high metabolic risk including obesity (mean BMI=36), type 2 diabetes (70%), hypertension (78%), and 10-year ASCVD risk score>14. Baseline mean (SD) FibroScan VCTE was 13.3 (6.8), 13.6 (7.1), and 12.9 (5.6) kPa for the resmetirom 80 mg, resmetirom 100 mg, and placebo groups. Baseline ELF across all fibrosis groups was 9.8 (0.87). FIB-4 across all dose groups was 1.3. CAP improved with resmetirom treatment. CAP improvement in individual resmetirom patients predicted both NR and FI responses; however, even no change in CAP predicted biopsy responses higher than the mean for placebo. A CAP improvement in placebo patients did not predict an FI on biopsy. VCTE was improved over time (1-3 years) relative to placebo in resmetirom treated patients. Resmetirom treated patients, even those with no VCTE improvement, had higher NASH resolution and fibrosis improvement responses than the mean placebo response rates. VCTE improvement was poorly predictive of a placebo FI or NR response; worsening of VCTE in placebo patients predicted a lower-than-average NASH resolution and fibrosis improvement. Both doses of resmetirom significantly reduced ALT approximately 30% relative to placebo. In resmetirom treated patients, higher % reductions in ALT were associated with higher NR and FI on biopsy. For resmetirom treated patients without a reduction in ALT, the NASH resolution and fibrosis improvement responses were predicted to be higher than the mean placebo biopsy responses.

Conclusion: ALT was reduced and CAP and VCTE improved was by resmetirom relative to placebo. However, biopsy responses were not always associated with changes in these markers. Additional analyses, including artificial intelligence (AI)-based assessments of histological response, are ongoing.

Disclosure: Authors are investigators in the MAESTRO-NASH trial or employees of Madrigal Pharmaceuticals.

OP060

TREATMENT MONITORING WITH THE AGILE 3+ SCORE IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS: ANALYSIS OF DATA FROM A RANDOMISED PLACEBO-CONTROLLED TRIAL OF SEMAGLUTIDE

L. Castéra¹, C. Fournier-Poizat², J. Fouquier², M. Skalskøi Kjær³, N. Krarup³, V. Miette², S. Boris Nygård³, A. Shueb Patel³, L. Sandrin², J.M. Schattenberg⁴

¹Department of Hepatology, Beaujon Hospital, Université Paris Cité, Clichy, France, ²Echosens, Paris, France, ³Novo Nordisk A/S, Søborg, Denmark, ⁴Metabolic Liver Research Program, University Medical Center Mainz, Mainz, Germany

Contact E-Mail Address: Joern.Schattenberg@unimedizin-mainz.de

Introduction: There is an unmet need to evaluate non-invasive biomarkers for monitoring and predicting change in fibrosis in patients with metabolic dysfunction-associated steatohepatitis (MASH) who are receiving treatment. Several biomarkers have been validated for grading and staging in MASH, including the Agile 3+ score, which can identify advanced fibrosis in non-alcoholic fatty liver disease. Agile 3+ was applied to patients enrolled in a clinical trial of semaglutide to investigate the score's ability to monitor treatment effect and to predict change in fibrosis stage.

Aims & Methods: Data were from a phase 2b study in which patients with MASH and fibrosis stage 1-3 were randomised to 72 weeks' treatment with subcutaneous semaglutide 0.1, 0.2 or 0.4 mg, or placebo, once daily (NCT02970942).

For this analysis, Agile 3+ scores were calculated at baseline and weeks 28, 52 and 72 using liver stiffness measurements (LSM) from vibration-controlled transient elastography (VCTE) (where available), alanine- and aspartate aminotransferase levels, platelet count, age, sex and diabetes

status. A mixed model for repeated measures was used to assess treatment effect on Agile 3+ (missing values were not imputed) during the on-treatment period. Change from baseline in Agile 3+ at weeks 28, 52 and 72 and its association with histological fibrosis improvement at week 72 in the 0.4 mg semaglutide and placebo arms was examined using logistic regression with an interaction effect between relative change in Agile 3+ and treatment. Odds ratios (OR) for improvement in fibrosis of ≥1 stage at week 72 associated with a 0.5-fold change in Agile 3+ at each time point were calculated.

Results: The numbers of patients with Agile 3+ data at baseline and weeks 28, 52 and 72 were 208, 210, 209 and 203, respectively. Mean baseline Agile 3+ (standard deviation) was 0.50 (0.28), 0.61 (0.27) and 0.55 (0.30) for semaglutide 0.1, 0.2 and 0.4 mg, respectively, and 0.46 (0.30) for placebo. Agile 3+ was significantly reduced with semaglutide 0.4 mg vs placebo at weeks 28 (estimated treatment ratio 0.64 [95% confidence interval (CI) 0.48; 0.87]; p=0.004), 52 (0.63 [0.48; 0.83]; p=0.001) and 72 (0.59 [0.41; 0.85]; p=0.005). In the placebo group, associations between a decrease in Agile 3+ at weeks 28 and 52 and improvement in fibrosis at week 72 were significant (OR [95% CI] 4.10 [1.50; 11.19]; p=0.006 and 3.71 [1.28; 10.75]; p=0.016, respectively). A similar trend was seen in the semaglutide 0.4 mg group, but this did not reach significance. For changes in Agile 3+ at week 72, the trend did not reach significance for either the placebo or semaglutide groups. Although this analysis is limited by patient drop-out during the study, the results indicate that changes in Agile 3+ as early as week 28 may be predictive of histological changes at week 72.

Conclusion: Semaglutide demonstrated a significant treatment effect on Agile 3+, with change in Agile 3+ partially predicting histological outcomes, irrespective of treatment allocation. A decrease in Agile 3+ was associated with an improvement in histological fibrosis.

Disclosure: Funding: Novo Nordisk A/S.

Medical writing: The authors acknowledge the medical writing assistance of Stephen Purver MChem and Sophie Bruce of OPEN Health Communications, and funded by Novo Nordisk A/S, in accordance with Good Publication Practice (GPP) guidelines (www.ismpp.org/gpp-2022).

Laurent Castéra has received consulting fees from Echosens, Novo Nordisk, Madrigal, MSD, Pfizer, Sagimet and speaker honorarium from Echosens and Novo Nordisk.

Jörn M. Schattenberg has received consulting fees from Apollo Endosurgery, Aged diagnostics, Bayer, Boehringer Ingelheim, Gilead Sciences, GSK, Intercept Pharmaceuticals, Inventiva Pharma, Ipsen, Madrigal, MSD, Northsea Therapeutics, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, Siemens Healthineers; research funding from Boehringer Ingelheim, Gilead Sciences, Siemens Healthcare GmbH; and speaker honorarium from Boehringer Ingelheim, Echosens, Histoindex, Madrigal Pharmaceuticals, MedPublico GmbH, Novo Nordisk.

Céline Fournier-Poizat, Julie Fouquier, Véronique Miette and Laurent Sandrin are employees of Echosens. Echosens received research funding for this study from Novo Nordisk.

Mette Skalskøi Kjær, Niels Krarup, Sune Boris Nygård and Ahsan Shueb Patel are employees of Novo Nordisk A/S. MSK is also a shareholder of Novo Nordisk A/S.

Encore statement: This abstract was also presented at the European Association for the Study of the Liver (EASL) Congress, 21-24 June 2023 in Vienna, Austria.

OP061

RESMETIROM TREATMENT OF A SUBGROUP OF PATIENTS WITH POSSIBLE METALD ENROLLED IN MAESTRO NASH, A PHASE 3 NASH/MASH SERIAL LIVER BIOPSY STUDY

N. Alkhour¹, V. Ratz², J. Schattenberg³, R. Taub⁴, D. Labriola⁴, B. Hill⁴, S.A. Harrison⁵

¹Arizona Liver Health, Tucson, United States of America, ²Hôpital Pitié Salpêtrière, Department of Hepatology and Gastroenterology, Paris, France, ³Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Medizinische Klinik für Innere Medizin II, Homburg, Germany, ⁴Madrigal Pharmaceuticals, Inc., West Conshohocken, United States of America, ⁵Pinnacle Clinical Research, San Antonio, United States of America

Contact E-Mail Address: nalkhour¹@azliver.com

Introduction: MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating efficacy of resmetirom in patients with biopsy-confirmed non-alcoholic steatohepatitis (NASH/MASH) and fibrosis. 966 patients with biopsy confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo once daily. Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or ≥ 1 -stage improvement in fibrosis with no worsening of NAS (FI). The benefit of resmetirom in patients with and without indicators of increased alcohol consumption above protocol-allowed limits for NASH/MASH was assessed on biopsy endpoints and MRI-PDFF (liver fat reduction).

Aims & Methods: Carbohydrate Deficient Transferrin (CDT) was collected longitudinally in all patients over 52 weeks. Post-randomization, a PEth test was performed in patients suspected of increased alcohol consumption. Patients with baseline or post-baseline CDT $>2.5\%$ (ULN 2.47) and/or a PEth $>20\text{ng/ml}$ (ULN 20ng/ml) were assigned to a possible "MetALD" subgroup. Analyses were performed on 782 patients who had both a baseline and Week 52 biopsy.

Results: Of the 782 patients, 75 patients (9.6%) were included in the MetALD subgroup and 707 were not. Baseline characteristics, mean (SD), for the MetALD and non-alcohol subgroups included Age=57.7 (10.5), 60.1 (10.7); percent male=59%, 42%; Presence of diabetes=50.7%, 67.9%; CDT%=2.2 (1.0), 1.6 (0.3); BMI 33.0 (5.5), 35.8 (6.6); MRI-PDFF=21.7% (7.4), 17.4 (6.5); Fibroscan VCTE=13.4 (6.7), 13.2 (6.6); Fibroscan CAP=348.5 (38.5), 347.0 (38.7); FIB-4=1.67 (0.69), 1.37 (0.66); AST=45.6 (21.8), 40.3 (22.9); ALT=55.2 (24.8), 55.5 (32.2); GGT=117.9 (170.8), 75.3 (85.6); Bilirubin=0.69 (0.31), 0.65 (0.29); MCV=92.3 (5.8), 90.3 (5.6); Platelets=200, 229; NAS (median)=5 (5,6), 5 (5,6); and %F3=66.7, 62.5.

For the group of patients with low or no alcoholic consumption: Patients treated with 80 mg and 100 mg resmetirom doses (n=224 and 228, respectively): 29.9% and 36% had NR, 29% and 33.3% had FI, 59.2% and 71.2% showed a $\geq 30\%$ reduction from baseline in MRI-PDFF. For patients treated with placebo (n=255), the corresponding results were 10.3%, 13.7%, and 24.5%.

For the possible MetALD group: Patients treated with 80 mg and 100 mg resmetirom doses (n=34 and 20, respectively): 29% and 35% had NR, 35% and 30% had FI, and 88% and 81% showed a $\geq 30\%$ reduction from baseline in MRI-PDFF. For patients treated with placebo (n=21), the corresponding results were 10%, 19%, and 14%.

Conclusion: A total of 75 (9.6%) of patients had possible MetALD during the first 52 weeks of MAESTRO-NASH. Baseline characteristics showed a higher mean GGT and FIB-4 in the MetALD versus low alcohol group. Response rates to resmetirom in patients with suspected MetALD were similar to those without MetALD.

Disclosure: Authors are investigators in the MAESTRO-NASH trial or employees of Madrigal Pharmaceuticals.

Sunday, October 13, 2024

Monday, October 14, 2024

Tuesday, October 15, 2024

Diagnose and treat to target in GI cancer: Latest news

10:00-11:00 / Strauss 1

OP062

PANCREATIC CANCER PATIENT-DERIVED ORGANOIDS, PRECLINICAL TOOLS FOR PATIENT RESPONSE PREDICTION AND TUMOR EVOLUTION

M. Ekizce¹, J. Gout¹, Y.J. Resheq², J. Lindenmayer³, J. Schwab⁴, J. Kraus⁴, D. Srinivasan¹, E. Roger⁵, M. Hänle², T.J. Ettrich², L. Perkhofer^{1,6}, H.A Kestler⁴, T. Seufferlein², A. Kleger^{1,3,6}

¹Institute of Molecular Oncology and Stem Cell Biology, Ulm University Hospital, Ulm, Germany, ²Universitätsklinikum Ulm - Klinik für Innere Medizin I, Ulm, Germany, ³Core Facility Organoids, Ulm University, Ulm, Germany, ⁴Institute of Medical Systems Biology, Ulm University, Ulm, Germany, ⁵University Ulm Hospital/ Institute of Molecular Oncology and Stem Cell Biology, Department of Internal Medicine 1, Ulm, Germany, ⁶Division of Interdisciplinary Pancreatology, Department of Internal Medicine I, Ulm University Hospital, Ulm, Germany

Contact E-Mail Address: menar.ekizce@uni-ulm.de

Introduction: Pancreatic cancer (PC) is characterized by an aggressive biology and high tumor heterogeneity causing considerable variations in therapy response. Patient-derived organoids (PDOs) reflect parental tumor features and may represent a powerful preclinical tool to predict drug response and advance personalized treatment.

Aims & Methods: We have generated a living organoid biobank with >100 PDO lines derived from treatment-naïve and pretreated PC patient primary tumor and metastases with a reliable efficacy, and previously developed a pharmacotyping-guided prediction model to prognosticate patient therapy response.

Following up our initial feasibility trial (Beutel, 2021), we now validated the model accuracy in real-life in a higher number of PC patients (41 cases). Additionally, a limited set of 6 PDO pairs were derived from the same patients at two distinct timepoints, followed by pharmacotyping and whole exome sequencing (WES).

Results: Real-life chemotherapy responses in 41 patients matched to pharmacotyping-guided predictions with overall 80.0% accuracy, 89.3% sensitivity, and 64.7% specificity. Particularly, successful response prediction for first and second-line regimens culminated with an accuracy of 85.7% in naïve patients.

Prediction power was nevertheless lower in pretreated patients with a precision of 58.3% for subsequent chemotherapy lines. Retrospective analysis of patient clinical data finally showed that the administration of a therapy prognosticated to be efficient ultimately translated into a longer progression-free survival.

Moreover, the implementation of an automated pipetting system and the subsequent miniaturization of screenings enhanced our process capacity, conferring the possibility to extend our drug panel to a second list of approved targeted agents and significantly reducing the time before pharmacotyping.

The access to longitudinal biopsies allowed to conduct WES on 12 PDOs to capture a comprehensive genetic profiling over the time of treatment, notably revealing a CHEK2-mutated patient responding over time upon PARP inhibitor maintenance therapy, in line with our PDO-based prediction, highlighting the robustness of our method and algorithm. Tracking clonal evolution in longitudinal biopsies by WES revealed lower mutational burden and therapy-driven genetic alterations upon progression.

Finally, to decipher molecular mechanisms driving PC chemoresistance with an unprecedented accuracy level, we took advantage of our phenotypically and therapeutically-profiled PDO living biobank and employed sin-

gle-nucleus multiomic approaches, capturing simultaneously the transcriptome as well as the chromatin landscape, of chemoresponsive and non-responsive PC PDOs and of a unique longitudinally-collected case study.

This allowed us to identify transcriptomic and epigenetic variabilities in a longitudinal setting across several sequential therapeutic lines.

Conclusion: We report a robust and clinically-relevant companion tool for therapy-response prediction, one more step towards a PDO therapeutic profiling-guided personalized medicine in clinical routine.

Additionally, uncovering expression signatures driving chemoresistance may strikingly enhance patient stratification and therefore advance precision oncology in PC.

Disclosure: Nothing to disclose.

OP063

A NOVEL LIQUID BIOMARKER GASTRIC ADEQUACY TEST FOR THE CAPSULE SPONGE

A. Bartram¹, S. Pavagada¹, A. Ustaoglu¹, M. di Pietro¹, R.C. Fitzgerald¹

¹University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom

Contact E-Mail Address: alexander.bartram1@nhs.net

Introduction: The offer of a non-endoscopic capsule sponge in individuals on anti-reflux medication has been demonstrated to increase the detection of Barrett's Esophagus compared with GP usual care¹. To determine whether the sponge has reached the stomach, the cellular component of the capsule sponge sample is fixed and undergoes histopathological examination to identify gastric gland groups. In around 8% of cases the sponge is deemed inadequate on histopathological examination².

The current process of gastric quality control testing is a time intensive process at the laboratory level, results in patients being recalled to clinic when samples are inadequate and increases cost - all of which may have impact on potential future wider scale use of the capsule sponge.

We hypothesised that secreted proteins and glycoproteins that are released into the preservative fluid could be used as an adequacy marker and that lectins might provide a cost-effective biomarker.

Aims & Methods: We aimed to identify and validate a novel lectin biomarker using the cell-free liquid fraction of the capsule sponge sample to classify samples which have reached the stomach (adequate) compared to those which did not reach the stomach (inadequate). Triplet endoscopic biopsy samples from n=5 patients, of Normal Esophagus (NE), Barrett's Esophagus (BE) and Gastric Cardia (GC) were screened with 20 distinct fluorescein isothiocyanate conjugated lectins, each with a specific carbohydrate binding preference, using immunofluorescence staining. Lectins which demonstrated differential binding in favour of GC were selected for further testing to determine whether biomarkers could be detected in the liquid fraction of the capsule sponge sample.

We developed a direct Enzyme Linked Lectin Assay (ELLA) using HRP conjugated lectin to enable retrospective validation of 126 liquid based patient samples (18 histopathologically inadequate and 108 adequate samples). Data underwent statistical analysis using the Mann-Whitney U test and AUROC analysis.

Results: Immunofluorescence staining demonstrated that *Cytisus scoparius* (CSA) lectin and Peanut Agglutinin (PNA) lectin showed preferential binding to GC tissue samples, primarily in the apical mucin caps and foveolar cells of the columnar epithelium. After ELLA optimisation, horseradish peroxidase conjugated CSA lectin was shown to successfully bind to the liquid fraction of the capsule sponge sample. Using the n=126 patient sample cohort, lectin CSA demonstrated excellent classification between inadequate and adequate samples, AUROC 0.94 (0.88-1.0 95%

CI, $p < 0.0001$) with sensitivity of 87.96 (80.49 – 92.83 95% CI) and specificity of 94.44 (74.24 – 99.72 95% CI) at the selected threshold, Mann Whitney U test ($p < 0.0001$).

Conclusion: We successfully demonstrate on a large retrospective cohort that lectin CSA can accurately classify the adequacy of capsule sponge samples, using the cell-free liquid based portion of the sample alone. This could reduce overall recall rate, optimise laboratory processing and reduce costs.

References:

1. Fitzgerald RC, di Pietro M, O'Donovan M, Maroni R, Muldrew B, Debi-ram-Beecham I, Gehrung M, Offman J, Tripathi M, Smith SG, Aigret B, Walter FM, Rubin G; BEST3 Trial team; Sasieni P. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. *Lancet*. 2020 Aug 1;396(10247):333-344. doi: 10.1016/S0140-6736(20)31099-0. PMID: 32738955; PMCID: PMC7408501.
2. R Landy, S Killcoyne, C Tang, S Juniat, M O'Donovan, N Goel, M Gehrung, R C Fitzgerald, Real-world implementation of non-endoscopic triage testing for Barrett's oesophagus during COVID-19, *QJM: An International Journal of Medicine*, Volume 116, Issue 8, August 2023, Pages 659–666, <https://doi.org/10.1093/qjmed/hcad093>

Disclosure: RCF is named on patents related to the Cytosponge-trefoil factor 3 test. Covidien GI Solutions (now Medtronic) licensed the Cytosponge from the Medical Research Council, and the device has now received the CE mark and is cleared by the US Food and Drug Administration. RCF is a shareholder in Cyted, a company working on early detection technology. MDP reports personal consultant fees from Medtronic, outside of the submitted work. The remaining authors have no conflicts of interest to declare.

OP064

DISSECTING THE HINDRANCE OF HEDGEHOG PATHWAY IN INTRAHEPATIC CHOLANGIOCARCINOMA: A STEP TOWARDS TARGETED THERAPY

S. Paradiso¹, G. Carpino¹, P. Infante², L. Di Marcotullio², D. Quaglio³, C. Di Meo³, M. Franchitto⁴, T. De Luca⁵, B. Botta³, E. Gaudio¹, D. Alvaro⁵, V. Cardinale⁵

¹Sapienza - University of Rome, Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Rome, Italy, ²Sapienza - University of Rome, Department of Molecular Medicine, Rome, Italy, ³Sapienza - University of Rome, Department of Chemistry and Technologies of Drugs, Rome, Italy, ⁴Sapienza - University of Rome, Department of Medico-Surgical Sciences and Biotechnologies, Rome, Italy, ⁵Sapienza - University of Rome, Department of Translational and Precision Medicine, Rome, Italy

Contact E-Mail Address: savino.paradiso@uniroma1.it

Introduction: Cholangiocarcinoma (CCA) comprises a heterogeneous group of cancers affecting the biliary tree and is considered one of the deadliest cancers. CCA incidence and mortality are increasing dramatically worldwide in the last decades. CCA prognosis is dismal (5-year survival rate <20%) due to various aspects including late diagnosis, poor response to chemotherapy and lack of well-established targeted therapeutic options.

One of the foremost patho-biological features of CCA is the high inter- and intra-tumoral heterogeneity, which has limited the discovery of biomarkers and novel therapeutic alternatives, hampering the development of tools for early diagnosis and effective treatment, with unfavorable implications on patient outcome.

From an anatomical outlook, CCA is classified into intrahepatic (iCCA), perihilar (pCCA) and distal (dCCA). Furthermore, iCCA shows distinct histological subtypes which led the World Health Organization (ICD-O-3.2) to categorize it into *small* and *large* bile duct-type. Noteworthy, thus far no data exist concerning the correlation of molecular traits and specific iCCA subtypes. Indeed, this marked heterogeneity strikingly restricts the possibility of translational research and represents an utmost aspect to be scrutinized.

The Hedgehog (Hh) pathway is one of the molecular networks involved in the pathogenesis of iCCA. As a matter of fact, it is fundamental in various hallmarks of iCCA, including tumor growth, survival, migration, cancer stem cells activation and epithelial-mesenchymal transition. In the light of these observations, targeting this cascade for therapeutic purposes in iCCA is possible owing to evidence of Hh's pathogenetic role in the disease.

Aims & Methods: This study aims to evaluate, *in vitro*, in primary and established cell lines, a novel natural chemical compound called Glabrescione B (GlaB) that specifically inhibits Gli1, a transcriptional factor downstream of Hh pathway.

Using Trypan Blue Exclusion test, the dose- and time-dependent response of free GlaB and hyaluronic acid (HA)-encapsulated GlaB (HA-GlaB) has been evaluated. MTS assay has been performed to determine the IC₅₀. Western blot has been used to analyze the target protein expression levels. Wound-healing assay has been achieved to assess the cell migration. Colony formation assay has been performed to rate the colony-forming ability of cancer cells. Flow cytometry analysis has been accomplished to investigate cell death. The results were confirmed in at least three independent experiments and the quantitative data were reported as the mean ± SEM. Student's t-tests for paired samples were used to assess differences among two groups. A p-value of <0.05 was considered statistically significant (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).

Results: Our findings demonstrate that both free GlaB and HA-GlaB treatments significantly reduce iCCA cell rate viability, migration, colony-forming ability, and Gli1 levels in a dose- and time-dependent manner ($0.05 < p < 0.001$), leading to a decisive decrease in cancer cells invasiveness. Ultimately, compared to controls, early evidence from flow cytometry reveals an induction of necrosis and apoptosis as a result of drug administration.

Conclusion: Hedgehog pathway dysregulation is well known to be correlated with the development and progression of various cancers, including iCCA. A novel natural compound, named Glabrescione B, is able to inhibit cancer cells growth, survival, invasiveness and to induce cancer cell death. Taken together, these data provide insight into a new and potentially beneficial natural compound for the management of iCCA *in vivo*.

- References:** 1. Banales JM. et al., *Nat Rev Gastroenterol Hepatol*. 2020 Sep;17(9):557-588. Epub 2020 Jun 30. PMID: 32606456.
2. Bertuccio P. et al., *J Hepatol*. 2019 Jul;71(1):104-114. Epub 2019 Mar 23. PMID: 30910538.
3. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver. EASL-ILCA Clinical Practice Guidelines on Intrahepatic Cholangiocarcinoma. *J Hepatol*. 2023 Mar 22:S0168-8278(23)00185-X. Epub ahead of print. PMID: 37084797.
4. Riedlinger D. et al., *J Hepatobiliary Pancreat Sci*. 2014 Aug;21(8):607-15. Epub 2014 Apr 15. PMID: 24733827.
5. Cigliano A. et al., *Expert Opin Ther Targets*. 2017 May;21(5):471-483.1310842. Epub 2017 Mar 30. PMID: 28326864.
6. Razumilava N. et al., *J Hepatol*. 2014 Mar;60(3):599-605. Epub 2013 Nov 14. Erratum in: *J Hepatol*. 2014 Jul;61(1):185. PMID: 24239776.
7. Infante P. et al., *Cancer Lett*. 2021 Feb 28;499:220-231. Epub 2020 Nov 26. PMID: 33249196.

Disclosure: Nothing to disclose.

OP065

OPTICAL PD-L1 IMAGING USING ULTRASOUND-GUIDED QUANTITATIVE FLUORESCENCE MOLECULAR ENDOSCOPY COMBINED WITH DURVALUMAB-680LT IN LOCALLY ADVANCED ESOPHAGEAL CANCER PATIENTS

A.M. van der Waaij¹, Y.J. van Ginkel¹, S. Hone-Lopez¹, R. Bijlsma², S.J. van Asselt², L.A. van der Waaij², M.N. Lub-de Hooij³, D.J. Robinson⁴, G. Kats-Ugurlu⁵, M. di Pietro⁶, W.B. Nagengast¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Martini Hospital, Gastroenterology and Hepatology, Groningen, Netherlands, ³University Medical Center Groningen, Clinical Pharmacy and Pharmacology, Groningen, Netherlands, ⁴Center for Optic Diagnostics and Therapy, Otolaryngology, Rotterdam, Netherlands, ⁵University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands, ⁶University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom

Contact E-Mail Address: a.m.van.der.waaij@umcg.nl

Introduction: Locally advanced esophageal cancer (EC) is treated with neoadjuvant chemo(radio)therapy (nCRT) followed by surgery, but only a modest percentage of patients (16-43%) achieves a pathological complete response post-nCRT.

The addition of immune checkpoint inhibition (ICI) targeting programmed death-1 or its ligand (PD-1/PD-L1) is explored to increase response rates, yet adequate patient selection methods are lacking. PD-L1 expression's predictive value in biopsies is inconsistent due to intra- and intertumoral heterogeneity, and the influence of nCRT on ICI response is unclear. Novel imaging methods are crucial to understand PD-L1 heterogeneity in order to ultimately select patients for ICI.

Aims & Methods: This ongoing study aims to assess the safety and feasibility of the innovative technique ultrasound guided quantitative fluorescence molecular endoscopy (US-qFME) using the fluorescently labelled ICI drug durvalumab-680LT before and after nCRT in EC patients to visualize, for the first time, PD-L1 drug distribution from the macroscopic to the cellular level. A durvalumab-680LT dose-optimization was performed in which up to now fifteen EC patients scheduled for nCRT were included in either the control (not receiving durvalumab-680LT), 4.5 mg, or 15 mg cohort. The next five patients will receive 25 mg durvalumab-680LT, after which the most optimal dose group will be expanded with 16 patients. US-qFME procedures were performed both before and after nCRT, consisting of *in vivo* fluorescence signal visualization, quantification by mucosal and ultrasound-guided spectroscopy measurements of healthy esophageal tissue, tumor and/or lymph nodes, and collection of biopsies.

Subsequently, *ex vivo* analyses were performed for quantification of fluorescence signals, correlation to histology and visualization of tissue drug distribution and drug target cells.

Results: Higher fluorescence signals were visualized *in vivo* in tumor compared to healthy tissue. *Ex vivo* quantification of the fluorescence signals revealed higher median fluorescence signal intensities in tumor biopsies compared to healthy esophageal tissue pre-nCRT in both the 4.5 mg and 15 mg dose cohorts with a broad range in signals in the tumor (94.8 a.u. [41.0-131.7] vs. 31.0 a.u. [24.6-38.1] ($p=0.125$), and 103.9 a.u. [40.7-197.6] vs. 27.1 a.u. [25.8-40.8] ($p=0.0625$), respectively).

Similar results were found during both mucosal and ultrasound-guided spectroscopy with higher signals in tumor tissue both *in vivo* and *ex vivo* compared to healthy tissue. The signals in healthy tissues of patients receiving the tracer were comparable to both tumor and healthy tissue in the control cohort (26.2 a.u. [21.5-37.6] and 11.7 a.u. [11.3-19.0]). An SDS-PAGE experiment confirmed the tracer's integrity and stability in the mucosa. During fluorescence microscopy, only a dose of 15 mg durvalum-

ab-680LT was sufficient to visualize membrane-bound durvalumab. Analyses post-nCRT are still ongoing. No (serious) adverse events occurred.

Conclusion: Durvalumab-680LT administration was safe and specifically targeted the tumor tissue as higher signals were found in tumor than in healthy tissue. In addition, the broad range in signals in the tumor tissue indicates, as expected, an inter- and intra-patient difference in PD-L1 expression.

These preliminary findings show the potential of the novel combination of durvalumab-680LT and US-qFME to guide future patient selection for ICI therapy. Further analyses are ongoing, including correlation to PD-L1 staining and fluorescence microscopy to visualize drug distribution and potential drug-target interactions.

Disclosure: Nothing to disclose.

OP066

CRISPR/CAS9 RIBONUCLEOPROTEINS AS A POWERFUL HIGH-THROUGHPUT SCREENING TOOL TO UNCOVER PATHWAY INTERACTIONS IN COLORECTAL CANCER

C.P. Schilling^{1,2,3,4}, K.E. Boonekamp^{1,2,3}, M. Boutros^{1,2,3}

¹German Cancer Research Center (DKFZ), Division of Signaling and Functional Genomics, Heidelberg, Germany, ²Heidelberg University, Medical Faculty Heidelberg, Institute of Human Genetics, Department of Molecular Human Genetics, Heidelberg, Germany, ³DKFZ-Hector Cancer Institute at the University Medical Center Mannheim, Heidelberg, Germany, ⁴Freiburg University Medical Center, Department of Medicine II, Freiburg im Breisgau, Germany

Contact E-Mail Address: cps@schilling-mueller.de

Introduction: The Wnt signaling pathway and the p53 signaling pathway are key regulators in colorectal cancer (CRC) biology. For the development of new potential therapeutic approaches, a deeper understanding of the interactions between these pathways is required. We have developed a high-throughput arrayed phenotypic screening platform that combines multiplexed CRISPR/Cas9 ribonucleoprotein (RNP) knockouts with fluorophore pathway reporters, nuclear immunohistochemistry staining and fluorescence imaging. This allowed us to perform phenotypic analysis of knockout and pathway activation effects on a single-cell level to uncover new connections between Wnt and p53 signaling.

Aims & Methods: We established CRISPR/Cas9 RNP-based multiplexed knockouts both in colorectal cancer cell lines and patient-derived colorectal cancer organoids. We produce single guide RNA (sgRNA) by *in vitro* transcription. Utilizing RNPs for genome editing and mutating specific target genes allows for fast and precise editing and fewer off-target effects when compared with traditional plasmid or lentivirus-based CRISPR delivery methods. Furthermore, the small molecular size of an RNP editing complex provides the opportunity to easily multiplex several target gene knockouts or increase individual knockout efficiency by targeting the same gene with several sgRNAs simultaneously. We experimentally determined the ideal amount of individual sgRNAs to use in order to maximize knockout efficiency of a single target gene.

Using our optimized RNP knockout platform, we then conducted an arrayed phenotypic screen with 180 CRC-relevant target genes in 6 HCT116-derived adherent cell lines with different mutational backgrounds in the Wnt & p53 signaling pathways. After cell fixation and staining of nucleus and cell body, we used fluorescence microscopy images for cell segmentation *in silico*. This allowed us to monitor the transcriptional activity in p53 and Wnt/ β -catenin signaling as well as the cell morphology on a single cell basis.

Results: We were able to show that gene knockout efficiency is highly dependent on the individual sgRNA used. Furthermore, we demonstrated that combining up to four sgRNAs that target the same gene in one knockout experiment significantly increases overall efficiency while not significantly affecting cell growth and viability when compared to using a single sgRNA. Using four target guides per gene, we succeeded in establishing high-efficiency CIRPSR/Cas9 RNP knockout protocols with >90% pooled knockout efficiency in adherent colorectal cancer cell lines using lipofection for complex delivery and >40% pooled knockout efficiency in patient-derived colorectal cancer organoids using electroporation.

In the arrayed phenotypic screen, we were able to detect pathway activation and deactivation using a fluorophore-based reporter system coupled to DNA transcription factor binding sites of Transcription Factor 7 Like 2 (TCF7L2) for Wnt signaling and a fluorescent immunohistochemistry staining for p53.

Conclusion: Our innovative approach combining CRISPR/Cas9 RNP technology with detailed imaging and phenotypic analysis has proven to be a powerful tool in dissecting the roles of the Wnt and p53 signaling pathways in colorectal cancer. This approach can be easily scaled to any other set of genes or signaling pathway of interest. Moving forward, we intend to verify target genes of interest discovered in our arrayed phenotypic screen in patient-derived colorectal cancer organoids.

Disclosure: Nothing to disclose.

Basic mechanisms of disease in liver, pancreas and intestine

10:00-11:00 / Lehar 1

OP067

PIGR-DEPENDENT INCREASE OF CIRCULATORY IGA TITRES EXACERBATES MURINE STEATOHEPATITIS

D. Rajčić¹, C. Hoebinger¹, S. Lang², M. Demir³, T. Hendrikx¹

¹Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria, ²University Hospital Cologne, Department of Gastroenterology and Hepatology, Cologne, Germany, ³Charité Universitätsmedizin Berlin, Department of Hepatology and Gastroenterology, Campus Virchow-Klinikum and Campus Charité Mitte, Berlin, Germany

Contact E-Mail Address: dragana.rajcic@meduniwien.ac.at

Introduction: As the most abundant antibody in the gastrointestinal tract, IgA is an essential component of mucosal immunity due to generation of immune protection against invading pathogens. Interestingly, elevated systemic IgA titres are associated with steatotic liver diseases (SLD). Yet, the underlying mechanism responsible for systemic IgA accumulation is still not fully understood. Due to its control of IgA transport into the gut lumen, either from the liver via bile as well as across intestinal epithelium, the polymeric immunoglobulin receptor (pIgR) is one of the key regulators of IgA localization.

Aims & Methods: Here, our aim was to determine the contribution of pIgR-dependent IgA secretion to the development of steatohepatitis. First, we assessed systemic and faecal IgA titres in a cohort of biopsy-proven metabolic dysfunction-associated steatotic liver disease (MASLD) patients.

Additionally, pIgR expression and IgA levels were assessed in different parts of the gut-liver axis in wild-type (*Wt*) mice fed chow or methionine- and choline-deficient (MCD) diet for 4 weeks to induce murine SLD. To study alterations in hepatic injury resulting from shifts in IgA titres, *Wt* and pIgR-deficient (*pIgR*^{-/-}) mice were fed MCD diet for 4 weeks.

Moreover, IgA-deficient bone marrow was transplanted into *Wt* and pIgR^{-/-} mice which were then fed MCD diet, allowing us to further elucidate the specific effect of circulatory and intestinal IgA disturbances on murine steatohepatitis.

Results: MASLD patients had higher IgA titres in serum and stool in comparison to healthy individuals, which positively correlated with hepatic fibrosis. Similar changes in IgA concentrations were found in various murine MASLD models.

Importantly, while increased faecal IgA levels associated with the induction of pIgR in murine colon epithelium, pIgR expression in the liver as well as in the distal small intestine was reduced during hepatic fibrosis in MCD-fed mice. Hence, altered site-specific pIgR regulation and aberrant hepatic IgA secretion might result in elevated systemic IgA deposition, thereby promoting SLD. In line, pIgR^{-/-} mice, which lack intestinal IgA and accumulate IgA in circulation, developed more hepatic inflammation and injury associated with increased neutrophil and macrophage infiltration compared to their *Wt* littermates after MCD diet. IgA-deficient bone marrow transplantation prevented aggravated hepatic injury and steatohepatitis in pIgR^{-/-} mice, indicating that pIgR-mediated systemic IgA accumulation exacerbates SLD.

Conclusion: Our research identified pIgR-dependent regulation of IgA secretion as an important mechanism contributing to the severity of murine steatohepatitis.

Disclosure: Nothing to disclose.

OP068

SINGLE-CELL SEQUENCING REVEALS THE HETEROGENEITY OF IMMUNE MICROENVIRONMENT OF TYPE 1 AND TYPE 2 AUTOIMMUNE PANCREATITIS WITH ACTIVATION OF HIF-1A INDUCED FIBROSIS RESPONSE THROUGH VISFATIN

J. Li¹, W. Li¹, D. Zhang¹, Z. Jin¹, H. Huang¹

¹Changhai Hospital Department of Gastroenterology, Shanghai, China

Contact E-Mail Address: 850992887@qq.com

Introduction: Autoimmune pancreatitis (AIP) is a chronic inflammatory condition of the pancreas that is characterized by immune-mediated tissue damage and fibrosis and has been categorized into two distinct subtypes^[1].

Notably, storiform fibrosis is an important characteristic among the two types of AIP, especially in type 1^[2].

Although interest in AIP is growing, its pathophysiological mechanisms remain poorly understood. The immune microenvironment is crucial in the inflammatory and fibrotic processes of AIP, but the complexity and diversity of involved immune cells have not been fully characterized. In both subtypes of AIP, various immune cells coexist and interact, potentially leading to pathogenic and fibrotic responses.

The hypoxia-inducible factor 1- α (HIF-1 α) pathway is a key molecular pathway in AIP-related fibrosis. HIF-1 α is a transcription factor that responds to hypoxic conditions and regulates the expression of various genes involved in angiogenesis, metabolism, and fibrosis^[3].

Activation of HIF-1 α can lead to the induction of fibrogenic responses, which are central to the pathology of AIP.

Recent studies suggest that VISFATIN, an adipocytokine associated with inflammation and fibrosis, may act as a downstream effector of HIF-1 α ^[4], but the details of this interaction and its impact on the fibrosis in AIP have yet to be elucidated^[5].

Aims & Methods: In our study, we performed single-cell RNA sequencing in pancreatic lesion of type 1 AIP and type 2 AIP acquired by endoscopic ultrasound-guided fine-needle aspiration, and peripheral blood mononuclear cells from these patients before and after glucocorticoid therapy, integrated with previous published normal pancreas tissue.

We also conducted immunofluorescence staining and functional experiments to examine the mechanism. We aimed to unravel the immune microenvironment complexity in AIP and explore immune cell heterogeneity, activation states, and the potential involvement of HIF-1 α and VISFATIN in fibrosis development.

Results: Based on our single-cell data analysis, we summarized the expansion of B cell and plasma cell that existed in pancreatic lesion of type 1 AIP with various cell subgroup, as well as identify a significant pathogenic differentiated trajectory in B cell subgroup. Additionally, we also observed the expansion of Tfh, T helper CD4+ T cell and a novel NAMPT related CD4 T cell in pancreatic lesion of type 1 AIP. Importantly, our analysis reveals HIF1A+ classical monocytes are enriched in peripheral blood and pancreatic lesion of both two types of AIP. Through cell-cell interaction estimation, we also identified HIF1A+ classical monocytes is the key effective cell group which interacts with pancreatic stellate cells in high level, and Visfatin plays key roles in this biological procedure in both type 1 and type 2 AIP. We further identified and verified the HIF-1 α is involved in transcriptional activation of NAMPT by directly binding to the promoter, and the secretory visfatin could promote the fibrosis of pancreatic stellate cells through activation of TLR4 and ROS. Exogenous visfatin injection could exacerbate the pancreatic fibrosis in AIP mice model and the phenotype could be reversed through treatment of visfatin inhibitor. Moreover, the unregulated serum levels of visfatin in type 1 AIP and type 2 AIP patients comparing to healthy people are also initially verified.

Conclusion: In conclusion, our study depicted the dynamic change of peripheral blood and pancreatic lesion in type 1 and type 2 AIP patients. Additionally, we uncover a mechanism for visfatin induced AIP related pancreatic fibrosis.

References: 1. Masood, M., *Autoimmune pancreatitis: What we know so far*. JGH Open, 2022. **6**(1): p. 3-10.

2. Nista, E.C., et al., *Autoimmune Pancreatitis: From Pathogenesis to Treatment*. Int J Mol Sci, 2022. **23**(20).

3. Tang, Y.Y., et al., *Emerging role of hypoxia-inducible factor-1 α in inflammatory autoimmune diseases: A comprehensive review*. Front Immunol, 2022. **13**: p. 1073971.

4. Luczak, M.W., C. Krawiec, and A. Zhitkovich, *NAD(+) metabolism controls growth inhibition by HIF1 in normoxia and determines differential sensitivity of normal and cancer cells*. Cell Cycle, 2021. **20**(18): p. 1812-1827.

5. Liu, D., et al., *HIF-1 α : A potential therapeutic opportunity in renal fibrosis*. Chem Biol Interact, 2024. **387**: p. 110808.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

OP069

MODELING EARLY ONCOGENIC EVENTS IN PANCREATIC CYSTIC NEOPLASIA IN A GNAS AND KRAS DRIVEN STEM CELL DERIVED ORGANOID MODEL

P. Lopatta¹, M.K. Melzer^{1,2}, M. Breunig¹, M. Hohwieler¹, A. Kleger^{1,3}

¹Ulm University Hospital, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Ulm University Hospital, Clinic of Urology, Ulm, Germany, ³Ulm University Hospital, Division of Interdisciplinary Pancreatology, Department of Internal Medicine I, Ulm, Germany

Contact E-Mail Address: paul.lopatta@uni-ulm.de

Introduction: Intraductal Papillary Mucinous Neoplasias (IPMN) are cystic neoplasias of the ducts of the pancreas. They usually occur at advanced age and can progress to invasive adenocarcinomas.

While there are morphological and spatial features to assess the progression risk, a mutational footprint defining the progression risk remains to be identified. IPMNs often harbor an activating mutation of either GNAS or KRAS or both, but neither interaction nor signaling crosstalk is well understood.

Aims & Methods: Here, we use a patient-derived induced pluripotent stem cell (iPSC) model system, that endogenously harbors either the wildtype GNAS gene or a GNAS R201C mutation and is equipped with an inducible oncogenic KRAS^{G12D} cassette. The various iPSC genotypes were differentiated towards the pancreatic lineage to ultimately form pancreatic duct-like organoids (PDLO)[1,2], followed by transplantation onto the porcine urinary bladder (PUB) – our ex vivo scaffold for long-term culture[3]. Dysplasia, mucin expression and cyst size were subsequently analyzed. Furthermore, we performed transcriptomic bulk RNA-sequencing and proteomic profiling of the PDLOs.

Results: Already two weeks post transplantation onto the PUB a substantial amount of KRT19 positive ductal structures were observed independent of the genotype. Classification of dysplasia over a time of up to 8 weeks showed that high grade-like dysplasia was only present in grafts with a GNAS^{R201C} background. This effect was further enhanced by additional oncogenic KRAS^{G12D}. In ductal structures an expression progression over time of Mucin 1, 2, 5AC and CA19-9 was observed.

Expression of Mucin 2 was only observed in GNAS^{R201C} -harboring grafts, while Mucin 5AC and CA19-9 was the strongest in double mutant grafts. In double mutant ductal structures, the highest amount of Ki67 positive

nuclei was observed. In a GNAS^{WT} background, induction of KRAS^{G12D} led to a strong increase of P21 positive senescent cells, which was again lower when GNAS was also mutated. *In vitro* GNAS^{R201C} led to a higher proliferation of PDLOs and a higher proliferative capacity was maintained upon KRAS^{G12D} induction. On transcriptomic and proteomic level, a decreased oncogene induced senescence signature was observed when comparing KRAS^{G12D} induced GNAS^{R201C} organoids to KRAS^{G12D} GNAS^{WT} organoids. Additionally, double mutant organoids showed a significantly decreased control of genomic stability and an increased angiogenesis and inflammation. Preliminary *in vitro* data indicate that double mutant PDLOs have a 1.9 fold increased amount of cells with double strand breaks compared to WT PDLOs.

Conclusion: These results show an effect of GNAS^{R201C} on early dysplasia formation and progression which was further enhanced by KRAS^{G12D}. Additionally, the increased proliferative and decreased senescent phenotype hints at a GNAS^{R201C}-driven bypass of oncogene induced senescence, which was further supported by transcriptomic and proteomic analysis. The expression pattern of PDLOs indicate early alterations of genomic stability and signaling interaction with adjacent microenvironment. The decreased genomic stability and increased proliferation may explain the increased progression towards low and high grade-like dysplasia in our *ex vivo* model system. Our genuine patient-derived iPSC model featuring an endogenous GNAS^{R201C} will allow us to closely investigate the early formation of IPMNs and timewise resolve their transition towards an invasive phenotype to further unravel the mechanisms of IPMN formation and the collaborative pro-oncogenic signaling of KRAS^{G12D} with GNAS^{R201C}.

References: [1]Breunig, M., Merkle, J., Wagner, M., Melzer, M. K., Barth, T. F. E., Engleitner, T., Krumm, J., Wiedenmann, S., Cohrs, C. M., Perkhof, L., Jain, G., Krüger, J., Hermann, P. C., Schmid, M., Madácsy, T., Varga, Á., Griger, J., Azoitei, N., Müller, M., Wessely, O., ... Kleger, A. (2021). Modeling plasticity and dysplasia of pancreatic ductal organoids derived from human pluripotent stem cells. *Cell stem cell*, 28(6), 1105–1124.e19. <https://doi.org/10.1016/j.stem.2021.03.005>

[2]Merz, S., Breunig, M., Melzer, M.K., Heller, S., Wiedenmann, S., Seufferlein, T., Meier, M., Krüger, J., Mulaw, M.A., Hohwieler, M., Kleger, A. (2023). Single-cell profiling of GP2-enriched pancreatic progenitors to simultaneously create acinar, ductal, and endocrine organoids. *Theranostics*, 13(6), 1949–1973. <https://doi.org/10.7150/thno.78323>.

[3]Melzer, M. K., Breunig, M., Arnold, F., Wezel, F., Azoitei, A., Roger, E., Krüger, J., Merkle, J., Schütte, L., Resheq, Y., Hänle, M., Zehe, V., Zengerling, F., Azoitei, N., Klein, L., Penz, F., Singh, S. K., Seufferlein, T., Hohwieler, M., Bolenz, C., ... Kleger, A. (2022). Organoids at the PUB: The Porcine Urinary Bladder Serves as a Pancreatic Niche for Advanced Cancer Modeling. *Advanced healthcare materials*, 11(11), e2102345. <https://doi.org/10.1002/adhm.202102345>

Disclosure: Nothing to disclose.

OP070

BORTEZOMIB IMPROVES CIRRHOSIS THROUGH INDUCING THE APOPTOSIS OF ACTIVATED HEPATIC STELLATE CELLS

L. Wu^{1,2}, F. Li^{1,3}, X. Huang³, D. Schuppan^{4,2}, S. Chen^{3,1}

¹Zhongshan Hospital, Fudan University, Department of Gastroenterology and Hepatology, Shanghai, China,

²University Medical Center, Johannes Gutenberg University, Institute of Translational Immunology and Research Center for Immunotherapy, Mainz, Germany, ³Minhang Hospital, Fudan University, Department of Gastroenterology, Shanghai, China,

⁴Beth Israel Deaconess Medical Center, Harvard Medical School, Division of Gastroenterology, Boston, United States of America

Contact E-Mail Address: 20111210043@fudan.edu.cn

Introduction: Cirrhosis is a world-widely prevalent disease with a high global burden: approximately one million deaths worldwide are attributed to cirrhosis each year, and cirrhosis is the 11th leading cause of death¹. Fibrosis and cirrhosis develop after a long period of persistent inflammation, which can be caused by a variety of factors such as hepatitis B or C virus, obesity, high alcohol consumption, autoimmune diseases, cholestatic diseases, and so on². However, current clinical treatments for cirrhosis are mainly focused on improving complications such as portal hypertension. Although some patients with early-stage fibrosis may benefit from treatment to remove the cause of fibrosis, there is currently no effective treatment for advanced fibrosis or cirrhosis itself. Bortezomib (B) is a reversible inhibitor of the chymotrypsin-like site of the 20S proteolytic core within the 26S proteasome and is currently mainly used to treat multiple myeloma³. B has been shown to improve fibrosis of the skin, lungs and kidneys^{4,5}.

Aims & Methods: We aimed to evaluate the efficacy of B to improve advanced parenchymal and biliary liver fibrosis in rats and potential underlying mechanisms. Advanced liver fibrosis was induced in 8-week-old rats by intraperitoneal injection of thioacetamide (TAA) for 12 weeks or bile duct ligation (BDL) for 3 weeks. Rats with advanced fibrosis were divided into 2 groups: intravenous injection of B at 0.1 mg/kg in PBS (B) or injection of PBS alone three times a week for 3 weeks (fibrotic controls, FC). Age matched rats with no intervention served as normal controls (NC). Portal vein pressure was measured after anesthesia before sacrifice. Liver and renal function parameters were determined to evaluate liver inflammation and potential toxicity of B. HE and Masson staining were used to evaluate liver inflammation and fibrosis. Liver collagen was quantified via hydroxyproline content. Fibrosis-related gene and protein expression were determined by RT-qPCR and Western blot. Liver samples were subjected to NGS analysis. LX-2 human hepatic stellate cells and LO2 human hepatocytes were cultured with different concentrations of B for 24 h. Cell apoptosis was quantified via flow cytometry.

Results: B treatment induced a decreased portal vein pressure (mmHg), though the p-values did not yet reach statistical significance in the two fibrosis models (B vs FC: TAA, 6.86 ± 0.76 vs 11.42 ± 2.37; BDL, 9.49 ± 2.92 vs 18.57 ± 16.83). On the other hand, B treatment decreased ALT and AST in both fibrosis models, while serum creatinine and bilirubin levels remained unchanged, indicating a beneficial effect of B on liver function with no apparent liver or renal toxicity. Morphometry and biochemical quantification showed a significant amelioration of fibrosis, as evidenced by liver hydroxyproline content and Masson-positive area.

Gene set enrichment analysis indicated the upregulation of pro-inflammation-related Ugt2b7 and anti-proliferation-related gene Marvled1; while the key regulator in ubiquitin-mediated proteolysis and cell cycle pathways Cdc20 decreased after treatment with B, so did the Cdc20 protein. B-treated hepatic stellate cells but not hepatocytes showed prominent apoptosis.

Conclusion: Bortezomib induces activated hepatic stellate cell apoptosis and has a prominent antifibrotic potential in parenchymal and biliary fibrosis.

References: 1. Gines P, Krag A, Abraldes JG, Sola E, Fabrellas N, Kamath PS. Liver cirrhosis. *Lancet*. 2021;398(10308):1359-76.
2. Pellicoro A, Ramachandran P, Iredale JP, Fallowfield JA. Liver fibrosis and repair: immune regulation of wound healing in a solid organ. *Nat Rev Immunol*. 2014;14(3):181-94.
3. Tan CRC, Abdul-Majeed S, Cael B, Barta SK. Clinical Pharmacokinetics and Pharmacodynamics of Bortezomib. *Clin Pharmacokinet*. 2019;58(2):157-68.
4. Fineschi S, Bongiovanni M, Donati Y, Djaafar S, Naso F, Goffin L, et al. In vivo investigations on anti-fibrotic potential of proteasome inhibition in lung and skin fibrosis. *Am J Respir Cell Mol Biol*. 2008;39(4):458-65.
5. Zeniya M, Mori T, Yui N, Nomura N, Mandai S, Isobe K, et al. The proteasome inhibitor bortezomib attenuates renal fibrosis in mice via the suppression of TGF-beta1. *Sci Rep*. 2017;7(1):13086.

Disclosure: Nothing to disclose.

OP071

SINGLE-CELL RNA SEQUENCING IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS AND INFLAMMATORY BOWEL DISEASE: A DISTINCT FORM OF COLITIS

P. Pibiri¹, A. Bangma¹, S. Sun¹, E. Bigaeva¹, S. de Jong¹, J.R. Björk¹, G.M. Verstappen², G. Kats-Ugurlu³, M.A. Hermoso^{1,4}, A. Vich Vila⁵, M.G. Van der Wijk⁶, K.N. Faber¹, R.K. Weersma¹, W.T. Van Nieuwenhoven¹, E.A.M. Festen¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands, ³University Medical Center Groningen, Pathology, Groningen, Netherlands, ⁴Universidad de Chile, Immunology, Santiago, Chile, ⁵KU Leuven, Leuven, Belgium, ⁶University Medical Center Groningen, Genetics, Groningen, Netherlands

Contact E-Mail Address: pibiripaola57@gmail.com

Introduction: Primary sclerosing cholangitis (PSC) is an inflammatory disorder of the bile ducts, in which Inflammatory bowel disease (IBD) concomitantly occurs (PSC-IBD). Substantial differences in clinical presentation are observed between PSC-IBD and ulcerative colitis (UC).

Aims & Methods: In this study we aim to find distinct pathomechanisms for PSC-IBD using single-cell RNA sequencing. Forty-seven colonic samples of PSC-IBD (n=24), UC (n=18) and non-IBD subjects (n=5) were collected. Whole biopsies were dissociated into single cells using one-step collagenase digestion. Library preparation was done with 10x Genomics and sequencing was performed on an MGI2000 sequencer. Then, differential abundance, differential expression, cell-cell interaction analyses, and heritability analyses were performed. Stainings for DUOX2 and HLA-DR were performed on paraffin embedded colon mucosal slides

Results: In total, 71,798 high quality cells identified 54 distinct cell types, including a new type of epithelial cells: DUOX2+ enterocytes. DUOX2+ enterocytes are almost exclusively present in inflamed colon and can act as antigen presenting cells through the expression of MHC2 on its surface. A general shift in cell type composition upon inflammation was observed, comparable between PSC and UC samples. However, an increased abundance was seen for stem cells in non-inflamed (NI) PSC, and not in UC-NI nor non-IBD controls.

Additionally, we found distinct gene expression patterns between PSC and UC inflammation: while activation of inflammatory monocytes was observed in PSC inflammation, several types of fibroblasts were activated

upon UC inflammation. Through heritability analysis, we also highlighted how mucosal follicular B and CD4+ activated Fos-Hi cells carry the heaviest burden of PSC risk genes.

Conclusion: We describe DUOX2+ enterocytes, which may play a role in both PSC and UC colitis inflammation through antigen presentation. Furthermore, we show that intestinal inflammation in PSC-IBD, as compared to UC, is characterized by distinct mucosal cell composition and cell-specific gene expression patterns. PSC colitis, and not UC, is driven by activation of inflammatory monocytes, with antigen presentation through HLA-DRB1, and activation of specific CD4+ T cell subsets. Additionally, an increased abundance of stem cells in PSC-NI could be related with the increased colorectal cancer risk in PSC-IBD.

Disclosure:

S.S. received a grant from China, J.B. received a grant from Searave Foundation, R.K.W., E.A.M.F. and K.N.F. received unrestricted research grants from Takeda, R.K.W. received an unrestricted grant from Tramedico and Ferring and is supported by a Diagnostics Grant from the Dutch Digestive Foundation (D16-14). W.T.C.U.V. and E.A.M.F. received a Gastrostart Grant from the Dutch Society of Gastroenterology. E.A.M.F. received a personalized medicine grant from the University of Groningen a personalized grant a Clinical Fellowship from the ZonMw, and is supported by a MLDS Career Development grant (CDG 14-04).

A.B., P.P., S.d.J., E.B., G.M.P.J.V., F.G.M.K., G.K., M.A.H., A.V.V. and M.G.P.v.d.W. disclose no conflicts of interest.

OP072

PREDICTING LYMPH NODE METASTASIS IN EARLY GASTRIC CANCER THROUGH TWO-STEP MACHINE LEARNING USING WHOLE SLIDE PATHOLOGY IMAGES

B. Lee¹, B. Keum¹, Y. Jeon¹, H. Chun¹¹Korea University, Seoul, South Korea**Contact E-Mail Address:** bomee26288@gmail.com

Introduction: In Early Gastric Cancer (EGC), if the risk of lymph node metastasis (LNM) is negligible, endoscopic curative resection is performed preferentially. If LNM is suspicious, additional gastrectomy with lymphadenectomy should be performed.

Recently, as artificial intelligence has revolutionized medical field, several studies have been conducted to predict LNM applying machine learning in stomach.

The risk of LNM is determined by primary tumor. It is necessary to pick up on fine and diverse morphologic patterns within H&E stained tissue slide. Therefore, the aim of this study is to develop machine learning algorithm for predicting LNM status in patients with EGC using H&E stained WSI.

Aims & Methods: This multicenter study involved five cohorts, including Hanyang University Guri Hospital (HGH), Kangbuk Samsung Medical Center (KBSMC), Seoul St. Mary's Hospital (SS), International St. Mary's Hospital (ISH), and Korea University Medical Center (KUMC). The cohorts were randomly divided into training, validation, and test sets.

Whole slide pathology images were annotated and divided into 512 * 512-pixel patches using ASAP software. Expert pathologists used spline on the rectangle region of interest (ROI) to annotate areas of tumor tissue.

In the first step, Deep Lab V and SE-ResNext101 were trained on 7029 patches from three early gastric cancer (EGC) datasets to segment differentiated and undifferentiated gastric cancer.

In the second step, morphological features inferred by the trained segmentation network from whole slide images (WSI) of primary EGC were used to predict lymph node metastasis (LNM) status.

Results: The data consisted of 243 cases from 5 cohorts. The number of cases in each cohort was 61, 84, 59, 14, and 25, respectively.

The classification results of differentiated/undifferentiated tumor and normal tissue are described.

We represented differentiated tumors as orange, undifferentiated as brown, and normal cells as light orange (apricot color). When visualizing patch images, ground truth, and predictions from both internal and external datasets, we observed significant similarity.

And the performance of the classifier at the patch and slide level, as well as internal and external cohorts.

A mean AUROC of 0.7487 and a mean accuracy of 0.7 were achieved in predicting LNM status in the test set using XGBoost.

Conclusion: Our study is the first proof of concept that machine learning trained with deep learning of whole slide images may be able to predict LNM in early gastric cancer.

The clinical feasibility of this machine learning algorithm could empower clinicians to make informed decisions regarding the appropriate treatment for early gastric cancer patients immediately following biopsy.

Disclosure: No conflict.

OP073

A MACHINE LEARNING PREDICTIVE MODEL FOR POST-ENDOSCOPIC SUBMUCOSAL DISSECTION BLEEDING IN PATIENTS WITH EARLY-STAGE GASTRIC CANCER: INSIGHTS FROM A MULTICENTER STUDY

K. Takahashi¹, H. Maruyama^{1,2}, K. Kojima¹, N. Nakajima¹, H. Sato¹, K.-I. Mizuno¹, S. Sugitani², S. Terai¹

¹Graduate School of Medical and Dental Sciences, Niigata University, Division of Gastroenterology and Hepatology, Niigata, Japan, ²Murakami General Hospital, Department of Internal Medicine, Murakami, Japan

Contact E-Mail Address: kazuya911@hotmail.co.jp

Introduction: Endoscopic submucosal dissection (ESD) is a widely used minimally invasive treatment for early gastric cancer (EGC). Post-ESD bleeding, which occurs in 3.1–6.5% of cases, is the most common complication^{1,2}. With Japan's aging population, more patients with EGC are receiving antithrombotic agents, increasing the risk of bleeding. Accurate prediction of post-ESD bleeding facilitates the implementation of effective preventive measures.

Machine learning (ML) models can predict clinical outcomes and aid in identifying crucial factors³. Thus, a predictive model based on pre- and intra-operative data may prove useful for predicting post-ESD bleeding and elucidating its key contributing factors.

Aims & Methods: This study aimed to develop an ML predictive model for post-ESD bleeding in patients with EGC, using a large sample dataset obtained from a multicenter study, and to investigate the key factors associated with post-ESD bleeding.

This multicenter study included patients who underwent ESD for EGC at Niigata University Hospital and Murakami General Hospital between 2012–2023. Patient data such as age, sex, development of post-ESD bleeding, comorbidities, and intake of antithrombotic agents (i.e., direct oral anticoagulants [DOACs], warfarin, or antiplatelets) were pulled from medical records. The lesion locations and specimen sizes were also recorded. Clinical characteristics were compared between the patients without post-ESD bleeding (control group) and those with bleeding (bleeding group). The factors associated with post-ESD bleeding were investigated using a logistic regression model. A predictive ML model was then constructed using pre- and intra-operative data. An extreme gradient-boosted tree classifier, a commonly used ML algorithm, was used to construct the model. To train it, the data were randomly partitioned so that 80% were used for training and 20% for testing. The area under the curve (AUC) was calculated for each model using the test dataset. Shapley additive explanations values, a quantitative method to evaluate the contribution of each variable to the model, were calculated to determine the key variables related to post-ESD bleeding.

Results: A total of 1,084 consecutive patients who underwent ESD for EGC were included, of whom 63 (5.8%) developed post-ESD bleeding. The median age [interquartile range] was significantly higher in the bleeding group than in the control one (77.0 [71.0–81.0] vs. 75.0 [70.0–79.0], $p=0.040$), although the female ratio was similar (22.2% vs. 25.0%, $p=0.623$). The frequencies of DOACs (39.7% vs. 9.0%, $p<0.001$), warfarin (27.0% vs. 4.8%, $p<0.001$), and P2Y12 receptor antagonist use (12.7% vs. 2.8%, $p<0.001$) were significantly higher in the bleeding group.

Multivariate logistic regression analysis showed significant associations between post-ESD bleeding and DOACs (odds ratio [OR]: 10.50, 95% confidence interval [CI]: 5.48–20.00, $p<0.001$), warfarin (OR: 10.70, 95% CI: 4.57–24.80, $p<0.001$), and P2Y12 receptor antagonist use (OR: 4.09, 95% CI: 1.55–10.80, $p<0.001$). Our ML model with all variables was able to predict post-ESD bleeding with an accuracy of 93.3% and exhibited an AUC of 0.83 (95% CI: 0.76–0.91). The use of DOACs and warfarin were the top two contributing factors in the ML model.

Conclusion: Post-ESD bleeding was predicted with high accuracy using an ML model, revealing that DOACs and warfarin represent key factors related to post-ESD bleeding. For patients predicted to experience bleeding, meticulous hemostasis measures such as post-ESD ulcer closures may be necessary.

References:

1. Yoshio, T. *et al.* Effect of direct oral anticoagulants on the risk of delayed bleeding after gastric endoscopic submucosal dissection. *Dig. Endosc.* **29**, 686–694 (2017).
2. Nagami, Y. *et al.* Antithrombotics increase bleeding after endoscopic submucosal dissection for gastric cancer: Nationwide propensity score analysis. *Dig. Endosc.* **34**, 974–983 (2022).
3. Takahashi, K. *et al.* Achalasia phenotypes and prediction of per-oral endoscopic myotomy outcomes using machine learning. *Dig. Endosc.* (2023) doi:10.1111/den.14714.

Disclosure: Nothing to disclose.

OP074

WITHDRAWN

OP075

THE HIGH-RESOLUTION MANOMETRY MILAN SCORE IS NON-INFERIOR TO ACID EXPOSURE TIME TO PREDICT RESPONSE TO ESCALATED MEDICAL AND SURGICAL TREATMENT FOR PERSISTENT REFLUX DISEASE

S. Siboni¹, M. Sozzi¹, P. Visaggi², B. Rogers³, N. De Bortoli², E. Marabotto⁴, A.R. Hobson⁵, B.E. Louie⁶, Y.Y. Lee⁷, S. Tolone⁸, J. Haworth⁵, M.I. Ivy⁶, E. Vico¹, D. Theodorou⁹, T. Triantafyllou⁹, C. Facchini⁴, V. Tee⁷, D. Bernardi¹, L. Cusmai¹, E. Campioli¹, S. Boveri¹⁰, E. Asti^{1,11}, E.V. Savarino¹², CP. Gyawali¹³

¹IRCCS Policlinico San Donato, General and Emergency Surgery, San Donato Milanese, Italy, ²Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ³Washington University in St. Louis, Gastroenterology, Louisville, United States of America, ⁴POLICLINICO SAN MARTINO, Genova, Italy, ⁵The Functional Gut Clinic, GI Physiology, London, United Kingdom, ⁶Swedish Medical Center, Digestive Health Institute, Division of Thoracic Surgery, Seattle, United States of America, ⁷Universiti Sains Malaysia, Kota Bharu, Malaysia, ⁸Università degli Studi della Campania "Luigi Vanvitelli", Surgery, Naples, Italy, ⁹University of Athens School of Medicine, Athens, Greece, ¹⁰IRCCS Policlinico San Donato, Laboratory of Biostatistics and Data Management, San Donato Milanese, Italy, ¹¹Università degli Studi di Milano, Milan, Italy, ¹²University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ¹³Washington University School Of Medicine, St Louis, Mo, Division Of Gastroenterology, St Louis, United States of America

Contact E-Mail Address: stesibo@gmail.com

Introduction: According to Lyon 2.0 consensus¹, a definitive diagnosis of gastro-esophageal reflux disease (GERD) requires endoscopic and/or pH-metry criteria. The recently developed and validated high-resolution manometry (HRM) metric termed the Milan Score² integrates four HRM variables related to GERD (ineffective esophageal motility (IEM), esophago-gastric junction (EGJ) contractile integral, EGJ morphology and straight leg raise (SLR) maneuver response) to quantify risk for definitive reflux. However, prediction of response to medical and surgical

GERD treatment using the Milan Score has not been studied. The aim of this study is to evaluate the ability of the Milan Score to predict treatment outcome in patients with persistent GERD symptoms.

Aims & Methods: Data from patients who underwent HRM and pH-metry for persistent GERD symptoms were prospectively collected. Demographic, clinical and pathophysiological (HRM and pH-metry) data were extracted from the database, including the GERDQ questionnaire, Milan Score and acid exposure time (AET). A Milan Score ≥ 137 (risk rate 50%) and AET $> 6\%$ were considered positive for GERD. Change in GERDQ was measured in patients with both pathologic and non-pathologic AET and Milan Score. The two methods were compared using the McNemar test to determine the non-inferiority of the Milan Score in comparison with the AET and Choen's k coefficient was calculated to quantify the level of agreement. Receiver operating characteristics (ROC) analysis was performed using Milan Score and AET in determining improvement in GERDQ.

Results: Among 157 patients enrolled (median age 48 years, median body mass index (BMI) 24.6 Kg/m², 47% males), 67 (42.7%) had a positive Milan Score, 59 of which (88.1%) had a pathologic AET. Patients with a positive Milan Score had higher BMI and worse GERD-related metrics on HRM and pH-metry. Medical treatment was offered to 99 patients, and anti-reflux surgery to 45 subjects, therefore statistical analysis was performed in 144 patients. Overall, clinical improvement favored surgical over medical treatment (53% vs. 33%, $p=0.027$), and both treatments were more effective in patients with pathologic AET compared to patients with non-pathologic AET (medical: 52.9% vs. 22.2%, $p=0.002$; surgical: 69.6% vs. 36.4%, $p=0.038$). Similarly, patients with a pathologic Milan Score had better outcomes compared to patients with a non-pathologic Milan Score (medical: 61.5% vs. 13.8%, $p<0.001$; surgical: 76.9% vs. 21.1% surgical, $p<0.001$). A non-pathologic Milan Score failed to predict good treatment response in 16.7% of the patients, while a negative AET in 24.4%. The AET failed to demonstrate its superiority in predicting treatment response when compared with the Milan Score ($p=0.130$) and the Choen's k coefficient was 0.62 (good agreement). ROC analysis showed an area under the curve of 0.790 for Milan Score and 0.715 for AET in predicting improvement in GERDQ.

Conclusion: The Milan Score is non-inferior to the AET in predicting response to medical and surgical GERD management. The Milan Score could therefore help identify patients who could benefit from an escalation of medical or surgical management.

References: 1. Gyawali CP, Yadlapati R, Fass R *et al.* Updates to the modern diagnosis of GERD: Lyon consensus 2.0. *Gut.* 2024 Jan 5;73(2):361-371. doi: 10.1136/gutjnl-2023-330616. PMID: 37734911; PMCID: PMC10846564. 2. Siboni S, Sozzi M, Kristo I *et al.* The Milan score: A novel manometric tool for a more efficient diagnosis of gastro-esophageal reflux disease. *United European Gastroenterol J.* 2024 Mar 27. doi: 10.1002/ueg2.12565. Epub ahead of print. PMID: 38536701.

Disclosure: Nothing to disclose.

OP076

THE OPTIMAL DURATION OF PH-MONITORING: TESTING THE VALIDITY OF LYON 2.0 RECOMMENDATIONS FOR PROLONGED WIRELESS PH MEASUREMENT

R.-L. Rusu¹, M. Fox², R. Sweis³, S.S. Zeki¹, J.M. Dunn¹, A. Anggiansah¹, J. Jafari¹, A. Learoyd⁴, T. Wong¹
¹Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, ²Klinik Arlesheim & Zürich University, Center for integrative Gastroenterology, Arlesheim, Switzerland, ³University College Hospital, London, United Kingdom, ⁴Faculty of Life Sciences & Medicine, King's College London, Department of Population Health Sciences, London, United Kingdom

Contact E-Mail Address: radu75ro@yahoo.com

Introduction: The Lyon 2.0 Consensus accepts that wireless pH monitoring provides equivalent information to catheter-based studies and recommends 96-hr wireless pH studies for gastroesophageal reflux disease (GERD) diagnosis.¹ However, the pH sensor may detach early, and 24-hr and 48-hr studies are routine (and cost-efficient) in many centers. Published studies have used different analyses to summarize prolonged pH data, including “average acid exposure time (AET),” “worst-day AET,” and “dominant pattern analysis.”

Aims & Methods: This study aimed to determine (i) when a shorter recording time is sufficient for conclusive diagnosis of GERD; (ii) the impact of prolonged pH studies on patients with an inconclusive diagnosis of GERD based on 24- and 48-hr measurements; (iii) the replicability and diagnostic yield of 24-hr, 48-hr, and 72-hr studies compared with the 96-hr reference standard; (iv) the performance of different analyses of prolonged pH data. We analyzed endoscopy and pH data from 944/2045 (46%) consecutive patients (age 46.5 ± 14.6 years, 65% F) referred for investigation of typical reflux symptoms off medication that had at least 92-hr measurement. Patients were classified at 24, 48, and 72-hr against the 96-hr reference standard. AET <4% was considered conclusively negative, and AET >6% conclusively positive for GERD. Los Angeles (LA) esophagitis was an independent marker of disease.

The effect of prolonging pH measurement on GERD diagnosis was evaluated using average day, worst-day, and dominant pattern analysis (≥2 negative or positive days). Receiver operating curve (ROC) analysis was performed on the 24- and 48-hr pH data in patients with normal endoscopy, LA A and B esophagitis. Groups defined by 24-hr AET thresholds from 1% to 7% were followed up to 96 hr to assess when 24-hr data were sufficient for conclusive diagnosis.

Results: The proportion of patients with inconclusive results (average AET 4-6%) reduced from 113 at 24 hours to 40 at 96 hours (35% of the subgroup; p=0.02), with similar results for dominant pattern analysis, but not for worst-day analysis (p=0.2). When 24- and 48-hr test periods were assessed, prolonging average day studies to 72 and 96 hr increased conclusive GERD diagnosis to 71% and 65%, respectively.

On dominant pattern analysis, prolonging pH studies up to 96-hr in the subgroup of patients with inconclusive diagnoses at 48-hr showed a decrease in inconclusive diagnoses from 100% to 59% (p < 0.05).

A stepwise improvement in diagnostic accuracy and yield was observed from 24, 48, and 72-hr measurements compared to the 96-hr reference standard (p<0.00001 for trend).

On ROC analysis, 24-hr AET > 6.4% and 48-hr AET > 6.1% predicted GERD based on 96-hr measurements in all patients with normal endoscopy (table). 93% of patients with LA grade B esophagitis had AET >6%.

Only 2.6% of patients with a 24-hr AET ≤ 2.0% had GERD at 96 hr. Over 93% of these had physiologic acid exposure (AET <4%) on reference standard 96-hr studies. When the analysis was repeated for 48-hr data, there was a <1% probability of GERD at 96 hr.

Negative and inconclusive vs conclusive GERD	Endoscopy	Cut-off AET %	Sensitivity %	Specificity %	AUC	PPV %	NPV %
24 hr	Normal (n = 808)	6.4	100	99.6	1	98.9	100
	LA A (n = 61)	6	100	100	1	100	100
	LA B (n = 60)	8.7	73.8	94.4	0.89	96.8	60.7
48 hr	Normal (n = 808)	6.1	100	100	1	99.9	100
	LA A (n = 61)	6	100	100	1	100	100
	LA B (n = 60)	6.4	94.4	94.4	0.9	97.4	84.8

Conclusion: This study confirms that prolonging studies from 24-hr catheter-based or 48-hr wireless pH measurements to ≥72-hr is sufficient for conclusive GERD diagnosis; however, clearly negative (< 2% AET) or positive results (> 6% AET) from 24-hr studies are sufficient to exclude or confirm GERD. Prolonged pH studies of up to 96-hr duration improve the diagnostic yield for conclusive GERD. Analysis methods that utilize average day AET or dominant pattern are preferred.

References: 1. Gyawali CP, Yadlapati R, Fass R, et al. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut 2024;73(2):361-371.

Disclosure: Nothing to disclose.

IBD: New horizons in medical treatment - Part 1

10:00-11:00 / Lehar 3

OP077

RXC008: FIRST-IN-CLASS GASTROINTESTINAL-TARGETED POTENT PAN-ROCK INHIBITOR FOR TREATMENT OF FIBROSTENOTIC CROHN'S DISEASE

E. Kilgour¹, K. Houslay¹, A. Marshall¹, M. La Montagna¹, K. Anderson¹, S. Bos², S. van Welden², J. Celis², K. Eckersley¹, C.D. Jones¹, A. Belfield¹, H. Mckeever¹, H. Timmis¹, R. Armer¹, D. Laukens², C. Philips¹

¹Redx Pharma, Macclesfield, United Kingdom, ²Ghent University, Ghent, Belgium

Contact E-Mail Address: e.kilgour@redxpharma.com

Introduction: Redx Pharma is developing RXC008, a gastrointestinal (GI)-restricted highly potent and selective 'pan-ROCK' inhibitor (inhibits rho-associated coiled-coil kinase ROCK1 and ROCK2) to treat fibrostenosis due to Crohn's disease. ROCK1/2 are key signalling kinases in fibrosis and suppression of ROCK activity is highly efficacious in multiple rodent models of fibrotic disease. Systemic inhibition of both ROCK1/2 leads to hypotension limiting its therapeutic use; RXC008 is therefore designed to be restricted to the GI tract with minimal systemic exposure.

Aims & Methods: RXC008 potency was determined against ROCK1 and ROCK2 isolated enzymes in a biochemistry assay, by surface plasmon resonance (SPR) against ROCK2 and in a T853-pMYPT1 (Thr853 phospho-Myosin Phosphatase Target Subunit 1) cell assay. Anti-fibrotic efficacy was determined *in vivo* using the 9-week chronic dextran sulphate sodium (DSS) and the 45-day adoptive T-cell transfer (AT) murine models of colitis, by staining with Masson's Trichrome and by Magnetic Resonance Imaging (MRI). Gene expression changes were assessed by RNAseq. T853-pMYPT1 was measured in tissue and cells by ELISA. RXC008 concentrations were measured by Liquid Chromatography with Tandem Mass Spectrometry in colon tissue and plasma.

Results: RXC008 inhibited ROCK1 and ROCK2 with 1.19/1.3nM potencies respectively in biochemical assays, displayed picomolar affinity for ROCK2 binding in SPR, and suppressed T853-pMYPT1 levels in HAP1 cells expressing ROCK1 and ROCK2 with a potency of 4.6nM. Blood pressure provides a sensitive biomarker for peripheral pan-ROCK inhibition. Minimal plasma exposure of RXC008 and no clinical signs associated with hypotension were detected in rats administered oral doses up to 1000 mg/kg/day for 28-days.

In a dog telemetry study, minimal plasma exposure of RXC008 and no effect on blood pressure were detected at oral doses up to 1000mg/kg, while an intra-venous dose of 1mg/kg gave plasma compound concentrations ten-fold above the HAP1 cell IC50 together with a significant reduction in blood pressure.

In the DSS model, oral dosing (po) of 10mg/kg RXC008 once daily (QD) attenuated the disease activity index (diarrhea, body weight, hematochezia) and significantly ($p<0.0001$) suppressed colon fibrosis measured by Trichrome staining and MRI. In this model, RXC008 modulated the expression of >2000 genes ($p\leq 0.01$, log2 fold change) in the colon, including fibrotic genes Col1a1 and TGF β , the extra-cellular matrix gene Wisp2 and tissue repair genes AhR and IL-22R α .

Monotherapy RXC008 (10, 30 or 100 mg/kg po QD) reduced the fibrosis score in the AT model ($P<0.05$), in contrast the anti-inflammatory agents anti-p40 or anti-TNF α alone had no effect on fibrosis. RXC008 (3, 10 and 30 mg/kg po QD) also significantly ($p<0.05$) reduced fibrosis in combination with anti-TNF α . Minimal to no plasma exposure of RXC008 was detected in the AT model despite efficacious GI tissue exposure. RXC008 significantly reduced T853-pMYPT1 levels in colon tissue in healthy and AT mice. Ex-vi-

vo, RXC008 suppressed T853-pMYPT1 in fibroblasts (pIC50s: 7.83, 9.55, 9.02) isolated from fibrostenotic resection tissue from three Crohn's Disease patients.

Conclusion: RXC008 suppresses fibrosis in animal models of colitis and is being developed as a novel first-in-class therapy to inhibit fibrotic stricture formation in patients with Crohn's Disease. A first-in-human clinical trial (IS-RCTN82038982) commenced in February 2024 and will include assessment of T853-pMYPT1 in tissue biopsy samples for target engagement.

Disclosure: Kirsty Houslay, Amy Marshall, Manuela La Montagna, Katie Anderson, Kay Eckersley, Clifford D. Jones, Andrew Belfield, Helen Mckeever, Helen Timmis, Richard Armer, Caroline Phillips, Elaine Kilgour are employees of Redx Pharma. Debby Laukens has received research funding from Redx Pharma.

OP078

LONG-TERM EFFICACY AND SAFETY OF TULISOKIBART IN PATIENTS WITH CROHN'S DISEASE (CD): RESULTS FROM THE OPEN-LABEL EXTENSION PERIOD OF THE PHASE 2 APOLLO-CD STUDY

C. Siegel¹, R.W Leong², J.K. Anderson³, M. Yen³, B. Dong³, B.E. Sands⁴, S. Danese⁵, B.G. Feagan⁶

¹Dartmouth-Hitchcock Inflammatory Bowel Disease Center, Section of Gastroenterology and Hepatology, Lebanon, United States of America, ²Concord Hospital and Macquarie University Hospital, Sydney, Australia, ³Merck & Co., Inc., Rahway, United States of America, ⁴Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁵Humanitas Clinical and Research Center - IRCCS, Rozzano and Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Milan, Italy, ⁶Department of Medicine, Division of Gastroenterology, Western University, London, Canada

Contact E-Mail Address: brian.feagan@alimentiv.com

Introduction: Tumor necrosis factor-like cytokine 1A (TL1A) is a mediator of inflammation and fibrosis in CD. Tulisokibart, an anti-TL1A monoclonal antibody, demonstrated robust efficacy without adverse safety signals during the 12-week induction period in adults with moderately to severely active CD in the multicenter, open-label, phase 2a APOLLO-CD study.¹ We report long-term efficacy and safety data for tulisokibart from the APOLLO-CD open-label extension (OLE).

Aims & Methods: Responders to tulisokibart induction at 12-weeks (defined as a decrease from baseline in CD activity index [CDAI] of ≥ 100 points or CDAI < 150 at week 12) were given the opportunity to enter the OLE study, whereas 12-week non-responders discontinued the study. At week 14, responders were randomized to receive intravenous tulisokibart 100 mg or 250 mg every 4 weeks until week 170. Reported here are the endoscopic, clinical, and biomarker endpoints through week 50 in the intention-to-treat population. Safety was evaluated in all patients who received ≥ 1 dose of tulisokibart. Descriptive statistics were used to summarize observed data.

Results: 53 of 55 patients completed the 12-week induction period, 37 were considered induction responders and were randomized to receive tulisokibart 100 mg (n=19) or 250 mg (n=18). A greater proportion of patients who were biologic-naïve entered the OLE in the tulisokibart 250 mg vs 100 mg group (44% vs 21%). Improvements in clinical, endoscopic, and biomarker outcomes observed were generally maintained through week 50 in both dose groups. At week 50, a greater proportion of patients achieved clinical and endoscopic outcomes with tulisokibart 250 mg vs 100 mg (Table).

In addition, normalization of high-sensitivity C-reactive protein (hsCRP) favored the 250 mg dose vs the 100 mg dose. During the 12-week induction period, 78% of patients reported AEs. At week 50, AEs were reported in 83% and 84% of patients receiving tulsokibart 250 mg and 100 mg, respectively, and were mostly mild-to-moderate in severity. Serious AEs occurred in 6% of patients receiving tulsokibart 250 mg and 11% of patients receiving tulsokibart 100 mg.

The most frequently occurring AEs of special interest (>10% of patients in either dose group) were urinary tract infection (11% vs 16%), COVID-19 (11% vs 11%), upper respiratory tract infection (6% vs 16%), bronchitis (11% vs 0%), clostridium difficile infection (11% vs 0%), and influenza (0% vs 11%).

Conclusion: At week 50, maintenance of treatment efficacy was generally observed in 12-week induction responders. A trend for higher maintenance efficacy with tulsokibart 250 mg vs 100 mg maintenance treatment was observed at week 50. Tulsokibart was well tolerated with no safety signals identified through 50 weeks of treatment. Larger trials are needed to confirm these findings.

	Week 12 Tulsokibart ^a (n = 55)	Week 50 Tulsokibart 100 mg (n = 19)	Week 50 Tulsokibart 250 mg (n = 18)
Endoscopic response ^b	13 (24)	3 (16)	5 (28)
Clinical remission ^c	27 (49)	8 (42)	10 (56)
Clinical response ^d	37 (67)	11 (58)	12 (67)
Composite endoscopic and clinical response ^e	9 (16)	3 (16)	4 (22)
Composite biomarker and clinical response ^f	n = 49 17 (35)	n = 16 4 (25)	n = 17 6 (35)
Normalization of hsCRP ^g	n = 36 5 (14)	n = 9 0	n = 16 5 (31)
Normalization of fecal calprotectin ^h	n = 44 6 (14)	n = 14 2 (14)	n = 16 2 (13)

All data are n (%).

^aDuring the 12-week induction period, patients received intravenous tulsokibart 100 mg on day 1 and 500 mg at weeks 2, 6, and 10. All patients treated with tulsokibart with baseline CDAI and SES-CD scores were included in the full analysis set population.

^bEndoscopic response was defined as a decrease in SES-CD total score $\geq 50\%$ from baseline.

^cClinical remission was defined as CDAI score <150.

^dClinical response was defined as either a decrease of ≥ 100 points in CDAI from baseline or CDAI score <150.

^eComposite endoscopic and clinical response was defined as a decrease in SES-CD score $\geq 50\%$ from baseline and either a decrease of ≥ 100 points in CDAI from baseline or CDAI score <150.

^fComposite biomarker and clinical response was defined as a decrease in hsCRP or fecal calprotectin $\geq 50\%$ from baseline and either a decrease of ≥ 100 points in CDAI from baseline or CDAI score <150 (evaluated in patients with ≥ 1 elevated biomarker at baseline).

^gNormalization of hsCRP was defined as a concentration of <5 mg/L among patients with elevated levels at baseline.

^hNormalization of fecal calprotectin was defined as a concentration of <250 $\mu\text{g/g}$ among patients with elevated levels at baseline.

Table. Clinical, endoscopic and biomarker outcomes at week 12 and among 12-week induction responders at week 50.

References: 1. Feagan BG, et al. *J Crohns Colitis*. 2023;17(Supplement_1):i162-i164.

Disclosure: CAS is a consultant/advisory board for AbbVie, BMS, Boomerang, Buhlmann, Janssen, Lilly, Napo Pharmaceuticals, Pfizer, Prometheus Biosciences, Prometheus Labs, Roivant, Takeda, Trellus Health; speaker for CME activities for AbbVie, Janssen, Pfizer, Takeda; grant support from AbbVie, Janssen, Pfizer, Takeda.

RWL reports advisory board membership for AbbVie, Aspen, BMS, Celgene, Celltrion, Chiesi, Ferring, Glutagen, Hospira, Janssen, Lilly, MSD, Novartis, Pfizer, Prometheus Biosciences, Takeda; research grant recipient: Celltrion, Shire, Janssen, Takeda, Gastroenterological Society of Australia, NHMRC, Gutsy Group, Pfizer, Joanna Tiddy grant, McKusker Charitable Foundation.

JKA, BD, and MY are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

BES reports consulting fees from AbbVie, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biologic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck & Co., Inc., Rahway, NJ, USA, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma.

SD has received consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr. Falk Pharma, Eli Lilly and Company, Entera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, and Vifor and lecture fees from AbbVie, Amgen, Ferring, Gilead, Janssen, Mylan, Pfizer, and Takeda.

BGF is a consultant for AbbVie, AbolierS, AgomAB Therapeutics, Alliantera, Amgen, AnaptysBio, Applied Molecular Transport Inc., Arena Pharma, Atomwise, Avoro Capital Advisors, BioJamp, Biora Therapeutics, Boehringer Ingelheim, Boxer, Bristol Myers Squibb/Celgene, Celsius Therapeutics, Connect BioPharma, Cytoki, Disc Medicine, Duality, EcoR1 Capital, Equillum, Ermium, First Wave, First Word Group, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, GlaxoSmithKline, Gossamer Pharma, Hinge Bio, Hot Spot Therapeutics, Imhotex, Immunic Therapeutics, InDex Pharmaceuticals, JAKAcademy, Janssen, Japan Tobacco Inc., Kaleido Biosciences, Landos Biopharma, Leadiant, L.E.K. Consulting, Lenczner Slaght, LifeSci Capital, Lilly, Lument AB, Millennium, MiroBio, Morgan Lewis, Morphic Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Play to Know AG, Prometheus Therapeutics and Diagnostics, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared Ltd., Viatrix, Ysios, Ysopia, and Zealand Pharma; on the Speakers' Bureau for AbbVie, Janssen, and Takeda; and on advisory boards for AbbVie, Amgen, AMT, AnaptysBio, Axio Research, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, EcoR1 Capital, Genentech/Roche, GlaxoSmithKline, InDex Pharmaceuticals, Janssen, Lilly, MiroBio, Morphic, Origo BioPharma, Pfizer, Progenity, Prometheus, REDX Pharma, Sanofi, Takeda, Teva, and Tillotts Pharma.

OP079

EFFICACY AND SAFETY OF RO7790121, A FULLY HUMAN MONOCLONAL ANTIBODY BLOCKING TUMOUR NECROSIS FACTOR-LIKE LIGAND 1A IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING PHASE 2B TUSCANY-2 STUDY

S. Danese¹, J.R. Allegretti², S. Schreiber³, L. Peyrin-Biroulet^{4,5}, V. Jairath⁶, G. D'Haens⁷, J. Kierkus⁸, R.W. Leong^{9,10}, A. Yarur¹¹, J. McBride¹², D. Bojic¹³, K. Lasch¹², C. Schiffman¹², K.E. Hung¹⁴, B. Feagan^{15,16}

¹Department of Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milan, Italy, ²Division of Gastroenterology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America, ³University Hospital Schleswig-Holstein, Department Internal Medicine I, Kiel University, Kiel, Germany, ⁴Department of Gastroenterology, INFINY Institute, FHU-CURE, INSERM NGERE, Nancy University Hospital, Vandœuvre-lès-Nancy, France, ⁵Division of Gastroenterology and Hepatology, McGill University Health Centre, Montreal, Canada, ⁶Departments of Medicine, Epidemiology and Biostatistics, Western University, London, Canada, ⁷Department of Gastroenterology and Hepatology, Amsterdam University Medical Centers, Amsterdam, Netherlands, ⁸Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, The Children's Memorial Health Institute, Warsaw, Poland, ⁹Gastroenterology and Liver Services, Concord Hospital, Sydney, Australia, ¹⁰Department of Gastroenterology, Macquarie University Hospital, Sydney, Australia, ¹¹Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, United States of America, ¹²Genentech, Inc., a member of the Roche Group, South San Francisco, United States of America, ¹³F. Hoffmann-La Roche Ltd, Basel, Switzerland, ¹⁴Pfizer Inc., Cambridge, United States of America, ¹⁵Department of Medicine, University of Western Ontario, London, Canada, ¹⁶Alimentiv Inc., London, Canada

Contact E-Mail Address: sdanese@hotmail.com

Introduction: Tumour necrosis factor-like ligand 1A (TL1A) is a novel therapeutic target for inflammatory bowel disease. Patients (pts) with moderately to severely active ulcerative colitis (UC) treated with the anti-TL1A antibody, RO7790121 (formerly PF-06480605 and RVT-3101), showed significant endoscopic improvement and adequate safety in the phase 2a TUSCANY trial.¹

Here, we report data from the global, randomised, double-blind, placebo-controlled, dose-ranging phase 2b TUSCANY-2 (NCT04090411) trial evaluating the efficacy and safety of subcutaneous (SQ) doses of RO7790121 in adult pts with moderately to severely active UC (total Mayo Score [tMS] ≥ 6 , endoscopic subscore ≥ 2) who had previously failed conventional/advanced therapy.

Aims & Methods: Pts were randomised to receive RO7790121 SQ 50mg, 150mg, 450mg or placebo (PBO) monthly during the 12-week induction period and RO7790121 SQ 50mg, 150mg or 450mg monthly during the treat-through 40-week maintenance period. Efficacy endpoints were assessed at weeks 14 and 56 in the induction and maintenance intent-to-treat analysis sets, respectively.

The primary efficacy endpoint was clinical remission at week 14 by tMS. Safety was assessed throughout the induction and maintenance periods. The secondary endpoint of clinical remission using modified Mayo Score (mMS) is aligned to updated FDA guidance. Other secondary endpoints included clinical remission (by tMS and mMS) at week 56 and endoscopic improvement at weeks 14 and 56. Efficacy analysis by pre-defined biomarker subgroups was also performed.

Results: Overall, 245 pts were randomised and treated; 228 completed the induction and 224 entered the maintenance period of the study. At week 14, 25.5%, 23.3% and 23.9% of pts in the RO7790121 50mg, 150mg, 450mg arms, respectively vs 11.6% in PBO experienced clinical remission by tMS ($p > 0.05$ [Table]). The proportion of pts achieving clinical remission using mMS at week 14 was 29.8%, 35.0% and 31.8% in the RO7790121 50mg, 150mg, 450mg arms, respectively vs 11.6% in PBO (nominal $p < 0.05$). Improvements in clinical remission were sustained throughout the maintenance period (Table). A greater proportion of pts demonstrated endoscopic improvement across all doses of RO7790121 vs PBO at week 14 and week 56. Numerically greater treatment effects were observed in biomarker-positive pts relative to all-comer pts. During the induction period, 47.8% (117/245) of pts reported ≥ 1 treatment-emergent adverse event (TEAE). The most common TEAEs (occurring in $\geq 5\%$ pts overall) were anaemia (5.3%) and headache (5.3%). In the induction period, 10 pts experienced serious TEAEs (PBO=4; 50mg=3; 450mg=3); 2 treatment-related (PBO=1; 450mg=1). No pts discontinued the study due to TEAEs. A generally similar safety profile was observed during the maintenance period.

Conclusion: Data from the phase 2b TUSCANY-2 dose-ranging study suggests that RO7790121 has a favourable benefit/risk profile with clinically meaningful improvements in pts with moderately to severely active UC. A phase 3 study will be conducted to confirm these results.

	PBO (n=43)	50mg (n=47)	150mg (n=60)	450mg (n=88)
Induction, week 14				
Clinical remission by tMS, * % (90% CI)	11.6 (5.8–22.9)	25.5 (15.4–37.2)	23.3 (15.0–34.0)	23.9 (16.6–32.1)
Clinical remission by mMS,† % (90% CI)	11.6 (5.8–22.9)	29.8 (19.9–42.3)	35.0 (25.1–45.2)	31.8 (23.7–40.8)
Endoscopic improvement,‡ % (90% CI)	18.6 (9.6–30.2)	40.4 (28.3–53.5)	38.3 (27.8–48.6)	40.9 (32.1–50.0)
Maintenance, week 56§	N/A**	50mg (n=42)	150mg (n=26)	450mg (n=28)
Clinical remission by tMS, * % (90% CI)		31.0 (19.4–43.3)	34.6 (20.9–52.6)	39.3 (23.8–56.5)
Clinical remission by mMS,† % (90% CI)		31.0 (19.4–43.3)	38.5 (23.3–56.4)	35.7 (20.9–52.7)
Endoscopic improvement,‡ % (90% CI)		38.1 (25.6–52.0)	39.3† (23.8–56.5)	50.0 (33.3–66.7)

Data cut-off: 3 March, 2023.

n=number of participants in the analysis set with observed data or NRI, excluding a total of seven participants with missing data due to medical or operational complications resulting from COVID-19.

*Primary endpoint: defined as tMS ≤ 2 with no individual sub score > 1 .

†Secondary endpoint: defined per FDA definition with an mMS 0–2 (endoscopic subscore=0 or 1, ≥ 1 point decrease from baseline to achieve a stool frequency subscore=0 or 1, and rectal bleeding subscore=0).

‡Defined as endoscopic subscore=0 or 1.

§Analyses were conducted for all dose groups; however, maintenance efficacy results are presented only for pts receiving the same dose during the induction and maintenance periods.

Efficacy data from pts who received a lower dose in maintenance vs induction demonstrated sustained efficacy (data not shown).

**As PBO was not administered during the maintenance period, no data for week 56 are shown.

†For the endoscopic improvement endpoint at week 56 with the 150mg dose, data were available for n=28 pts.

CI, confidence interval; COVID-19, coronavirus disease 2019; FDA, Food and Drug Administration; mMS, modified Mayo Score; N/A, non-applicable; NRI, non-responder imputation; PBO, placebo; pts, patient; tMS, total Mayo Score.

Table. Summary of efficacy outcomes at week 14 and week 56

References: 1. Danese S, et al. *Clin Gastroenterol Hepatol* 2021;19:2324–32.e6.

Disclosure: This study was sponsored by Pfizer Inc and Roivant Sciences Ltd. Medical writing support, under the direction of the authors, was provided by Margarita Gkrava, MSc, of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

SD, consultancy/advisory role/board: AbbVie, Alimentiv, Allergan, Amgen, AMT, AstraZeneca, Athos Therapeutics, Biogen, Boehringer, BMS, Celgene, Celltrion, Dr Falk Pharma, Entera, Ferring, Gilead, Hospira, Inotrem,

Janssen, J&J, Lilly, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc, TiGenix, UCB, Vial, Vifor. Lecture fees: Abbvie, Amgen, Ferring, Gilead, Janssen, Mylan, Pfizer, Takeda.

JRA, consulting/advisory role/board: Abbvie, Adiso, BMS, Ferring, Finch Therapeutics, GSK, Janssen, Merck, Pfizer, Roivant, Seres Therapeutics. Speakers' bureau: Abbvie, BMS, Janssen. Research funding: Janssen, Merck, Pfizer.

SS, consulting/advisory role/board: AbbVie, Amgen, Arena Pharmaceuticals, Biogen, BMS, Celgene, Celltrion, Dr Falk Pharma, Ferring, Fresenius Kabi, Galapagos/Gilead Sciences, Hikma Pharmaceuticals, I-Mab, Janssen, Lilly, Morphic Therapeutic, MSD, Mylan, Pfizer, Protagonist Therapeutics, Provention Bio, Sandoz/Hexal, Takeda, Theravance Biopharma, and Ventyx Biosciences.

LP-B, consulting/advisory role/board : Abbvie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, AMT, Arena, Biogen, BMS, Celltrion, Connect Biopharm, Cytoki Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer, GSK, Hac Pharma, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par Immune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance, Thermo Fischer, Tigenix, Tillots, Viatrix, Vifor, Vectivbio, Ventyx, Ysopia. Speakers' Bureau: Abbvie, Amgen, Arena, Biogen, Celltrion, Ferring, Galapagos, Genentech, Gilead, Janssen, Lilly, Medac, MSD, Pfizer, Sandoz, Takeda, Tillots, Viatrix, Vifor. Research funding: Celltrion, Fresenius Kabi, Takeda. Support travel: Abbvie, Amgen, Celltrion, Connect Biopharm, Ferring, Galapagos, Genentech, Gilead, Gossamer, Janssen, Lilly, Medac, Morphic, MSD, Pfizer, Sandoz, Takeda, Thermo Fischer, Tillots.

VJ, employment: Western University, London Health Sciences Centre, Alimentiv. Consulting or advisory role/board : AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei, Asieris, AstraZeneca, Avoro Capital, BMS, Celltrion, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GSK, Genentech, Gilead, Innomax, JAMP, Janssen, Lilly, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion. Speakers' bureau: AbbVie, Ferring, BMS, Galapagos, Janssen, Pfizer, Shire, Takeda, Fresenius Kabi.

GRD, consulting/advisory role/board: Alimentiv, Abbvie, BMS, Boehringer, Celltrion, GSK, Immunic, Index, J&J, Lilly, Polpharm, Takeda, Tillotts, Ventyx, Pfizer. Speakers' bureau: Lilly, Pfizer, Takeda. Research funding: Celltrion, Lilly, Pfizer, Takeda.

JK, no COI.

RWL, consulting/advisory role/board: AbbVie, Aspen, BMS, Celgene, Celltrion, Chiesi, Ferring, Glutagen, Hospira, Janssen, Lilly, MSD, Novartis, Pfizer, Prometheus, Takeda. Research funding: Celltrion, Shire, Janssen, Takeda, Gastroenterological Society of Australia, NHMRC, Gutsy Group, Pfizer, Joanna Tiddy grant, McKusker Charitable Foundation.

AJY, consulting/advisory role/board: Abbvie, Takeda, Celltrion, BMS, J&J, Abivax.

JMM, employment/stock/other ownership interests: Roche/Genentech.

DB, employment: F. Hoffmann-La Roche.

KL, employment: Roche/Genentech.

CS, employment/stock/other ownership interests: Roche/Genentech.

KEH, employment/stock/other ownership: Pfizer.

BGF, stock/other ownership interests: Connect Biopharm, EnGene. Honoraria/consulting/advisory role/board: AbbVie, Abivax, Adiso, Agomab, Alliantera, Amgen, AnaptysBio, Arena Pharma, Avoro Capital, Atomwise, BioJamp, Biora Therapeutics, Blackbird Laboratories, Boehringer, Boxer Capital, Celsius Therapeutics, Celgene/BMS, Connect BioPharma, Cytoki, Disc Medicine, Duality, EcoR1, Equillum, Ermium, First Wave,

Forbion, Galapagos, Galen Atlantica, Roche/Genentech, Gilead, Gossamer, GSK, Hinge Bio, Index Pharma, Imhotex, Immunic Therapeutics, Intercept, JAKAcademy, Janssen, Japan Tobacco, Kaleido, Klick Health, Landos Biopharma, Lenczner Slaght, LifeSci Capital, Lilly, Lument, Mage Biologics, Mestag, Millennium, MiroBio, Monte Rosa, Morgan Lewis, Morphic Therapeutics, Mylan, Nexys Therapeutics, Nimbus Therapeutics, OM Pharma, OrbiMed, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Roivant/Televant, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Sobi, Spyre Therapeutics, Surrozen, Synedgen, Takeda, Teva, Thelium, Tigenix, Tillotts, Triastek, Ventyx Biosciences, Zagnbio, Zealand Pharma. Speakers' Bureau: Takeda, Janssen, Abbvie.

OP080

FIRST IN HUMAN STUDY OF SOR102, A NOVEL, ORALLY DELIVERED BISPECIFIC ANTI-TNF/ANTI-IL-23 DOMAIN ANTIBODY IN CLINICAL DEVELOPMENT FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

C. Sattler¹, E. Wahab², P. Wedel¹, C. Garasi², V. Jairath³

¹Sorriso Pharmaceuticals, Sandy, United States of America,

²MAC Clinical Research, Manchester, United Kingdom, ³Western University, Department of Medicine, Division of Gastroenterology, London, Canada

Contact E-Mail Address: vjairath@uwo.ca

Introduction: SOR102 is a novel, orally delivered, bispecific antibody construct that neutralizes TNF α and IL-23 activity within GI tissue, targeting the site of inflammation and potentially limiting systemic exposure and immunosuppression¹.

Systemic TNF α /IL-23 inhibition recently demonstrated encouraging clinical efficacy in patients with ulcerative colitis² suggesting additive benefit of dual TNF α /IL-23 inhibition, observed as early as 4 weeks of dosing³, although safety and efficacy of long-term systemic combination therapy is unknown. SOR102 contains two humanized single domain antibodies (SDA) targeting TNF α and IL-23p19 connected by a trypsin-labile linker, enabling monomer separation within the small intestine. SOR102 inhibits TNF α and IL-23 activity pre- and post-trypsin cleavage. SOR102 SDAs were engineered for high stability among intestinal and inflammatory proteases to enable oral dosing.

This Phase 1, first-in-human study (SOR102-101; NCT06080048) consists of 3 parts. Parts 1 and 2 enrolled healthy subjects (HS) and evaluated single ascending (SAD) and multiple doses (MD) of SOR102, respectively.

Aims & Methods: SOR102-101, Parts 1 and 2, was a randomized, double-blind, placebo-controlled, SAD and MD study in HS aged 18 to 55 years that evaluated the safety and tolerability of SAD (Part 1) and MD (Part 2) of SOR102, the concentration of intact SOR102 and its monomers (SOR102-TNF α and SOR102-IL-23) in serum and faeces (Parts 1 and 2) and urine (Part 2), and the incidence of anti-drug antibodies (ADA) (Part 2).

In Part 1, HS were randomized 6:2 to active and placebo treatment into one of 4 ascending dose cohorts. HS were administered a single oral (PO) SOR102 dose ranging approximately between 100mg and 4000mg, or placebo.

In Part 2, HS were randomized 8:2 to active (approximately 1200mg PO BID) or placebo (PO BID) administered for 7 days. Safety and tolerability, faecal, serum and urine concentrations of SOR102 and its monomers, and ADA levels were assessed at predetermined times.

Results: All 42 enrolled participants completed the study. Seven adverse events (AE) were observed, all occurring in Part 1. AE severity was mild or moderate. There was one treatment-related AE (loose stools) of mild intensity and 17 hours duration occurring in the lowest dose cohort.

SOR102 and its monomers were not detected in serum. In Part 1, faecal concentrations of active (via antigen-binding ELISA) monomers were detected at all dose levels, peaking on Day 2 and 3 post-dose, with generally higher concentrations observed in higher-dose cohorts.

The highest faecal concentrations were observed in the third dose cohort on Day 2 post-dose (SOR102-TNF α $\approx$ 260 mcg/mL; SOR102-IL-23 $\approx$ 130 mcg/mL). In Part 2, active monomer faecal concentrations were observed during all dosing days; the highest faecal concentrations observed were SOR102-TNF α $\approx$ 1,700 mcg/mL and SOR102-IL-23 $\approx$ 5,400 mcg/mL. In Parts 1 and 2, intact SOR102 faecal concentrations were on average $\geq$ 800-fold lower than monomer concentrations.

Conclusion: SOR102 was well tolerated at all tested doses. Systemic exposure of SOR102 and its monomers was not observed, supporting its gut selectivity. Low levels of intact SOR102 and high levels of SOR102 monomers in faeces confirm that SOR102 is efficiently cleaved after oral dosing, as designed. Monomer faecal concentrations were observed at all doses in Part 1 and generally increased with each ascending dose, peaking on Day 2 and 3 after administration. In Part 2, monomer faecal concentrations were observed across all dosing days, peaking at >1700 mcg/mL.

References:

1. Roberts KJ et al. Preclinical development of a bispecific TNF α /IL-23 neutralising domain antibody as a novel oral treatment for inflammatory bowel disease. *Sci Rep* 2021;11:19422.
2. Feagan BG et al. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. *Lancet Gastroenterol Hepatol* 2023;8:307-320.
3. Richards D et al. Guselkumab and golimumab combination induction therapy in ulcerative colitis results in early local tissue healing that is sustained through guselkumab maintenance therapy. *J Crohns Colitis* 2024;18(Supplement_1):i171-i172.

Disclosure: VJ has received consulting/advisory board fees from AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avaro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, MRM Health, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; speaker's fees from, Abbvie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi

CS and **PW** are employees of Sorriso Pharmaceuticals

EW and **CG** are employees of MAC Clinical Research

OP081

MH002, AN OPTIMIZED LIVE BIOTHERAPEUTIC PRODUCT, PROVIDES EFFICACY IN ACUTE POUCHITIS: RESULTS FROM A PILOT STUDY

S. Vermeire¹, P. Dewint², T. Lobaton Ortega³, M. Allocca⁴, F. Scaldaferri^{5,6}, S. Possemiers⁷, L. Haazen⁷, S. Bolca⁷

¹University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ²AZ Maria Middelaers, Department of Gastroenterology & Hepatology, Ghent, Belgium, ³GHENT UNIVERSITY HOSPITAL, Department of Gastroenterology & Hepatology, IBD Unit, Gent, Belgium, ⁴IRCCS Hospital San Raffaele and University Vita-Salute San Raffaele, IBD Center, Milano, Italy, ⁵Catholic University of Rome Dept. of Internal Medicine Dept. of Gastroenterology, Internal Medicine, Gastroenterology Division, IBD Unit, Roma, Italy, ⁶Fondazione Policlinico A. Gemelli IRCCS, Italy, entro malattie apparato digerente (CEMAD), UOS Malattie infiammatorie croniche intestinali, Medicina Interna e Gastroenterologia, Rome, Italy, ⁷MRM Health, Ghent, Belgium

Contact E-Mail Address: severine.vermeire@uzleuven.be

Introduction: Pouchitis is an inflammatory disease of the pouch in patients with ulcerative colitis who underwent total colectomy with ileoanal pouch anastomosis. There is no approved treatment for acute pouchitis at present.

First-line treatment consists of antibiotics or probiotics. MH002 is an optimized consortium of 6 non-pathogenic, well characterized commensal bacteria with immune modulating, wound healing and gut barrier protective effects, and is in clinical development for ulcerative colitis.

Aims & Methods: This multi-center, open-label pilot study (EudraCT 2021-006656-14) explored the efficacy and mechanistic effects of MH002 in acute pouchitis. Eligible subjects with a modified pouchitis disease activity index (mPDAI) ≥ 5 and mPDAI endoscopic score ≥ 2 and with symptoms lasting ≤ 4 wks, received 400mg MH002 once daily for 8 wks.

Clinical, biochemical, endoscopic, and histologic disease activity was assessed at baseline and wk8. Pouch biopsies were assessed by an IBD pathologist who was blinded to the time points and clinical outcomes.

Exploratory efficacy endpoints (N=13) included mPDAI remission (mPDAI < 5 and a reduction of ≥ 2 points from baseline), symptomatic response (a reduction of clinical PDAI ≥ 2 points), endoscopic response (a reduction of endoscopic score of ≥ 2 points), and histologic response (a reduction of histologic PDAI ≥ 2) at wk8.

Changes from baseline in severity of urgency (NURS), Robart's histopathologic index (RHI), and faecal calprotectin (FCP) concentrations, were also evaluated.

Results: MH002 was safe and well tolerated with no evidence of adverse reactions when administered for 8 wks (Abstract Vermeire et al.). At wk8, 6/13 (46%) subjects achieved mPDAI remission. Symptomatic, endoscopic, and histologic response rates were 5/13 (39%), 5/13 (39%), and 2/13 (15%), respectively.

Clinical, endoscopic, and histologic PDAI scores were improved at wk8 in 11/13 (85%), 7/13 (54%), and 3/13 (23%) subjects, respectively. In total, 8/13 (62%), 9/13 (69%), and 8/13 (62%) subjects reported an improvement in severity of urgency at wk2, wk4, and wk8, respectively.

Over 8 wks, the number of ulcerations observed endoscopically decreased in 7/13 (54%) subjects, and the RHI improved in 9/13 (69%) subjects. Decreases in FCP were observed as early as wk2 in the subgroup achieving clinical remission (N=6), with a reduction of 68%, 71%, and 80% in median FCP at wk2, wk4, and wk8, respectively (Table 1).

	Full Analysis Set (N=13)			mPDAI remission (N=6)			No mPDAI remission (N=7)		
ΔmPDAI, mean	13	-2.02	(-4.30; -0.30)	6	-4.10	(-4.68; -3.85)	7	-0.24	(-0.70; 0.15)
ΔClinical PDAI, mean	13	-1.10	(-1.70; -0.30)	6	-1.60	(-1.93; -0.85)	7	-0.67	(-1.20; -0.15)
ΔEndoscopic PDAI, mean	13	-0.9	(-2.0; 0.0)	6	-2.5	(-3.0; -2.0)	7	0.4	(0.0; 1.0)
ΔHistologic PDAI, mean	13	-0.5	(0.0; 0.0)	6	-1.0	(-2.3; 0.0)	7	-0.1	(0.0; 0.0)
ΔSeverity of urgency, mean	13	-1.31	(-2.00; 0.00)	6	-1.72	(-2.65; -0.25)	7	-0.96	(-1.70; 0.00)
FCP at baseline (mg/kg), median	13	391.0	(187.0; 864.0)	6	439.0	(218.5; 606.3)	7	391.0	(194.0; 1337.0)
FCP at wk2 (mg/kg), median	12	392.0	(124.0; 1407.5)	5	142.0	(32.0; 231.0)	7	653.0	(348.5; 1407.5)
FCP at wk4 (mg/kg), median	12	251.0	(45.5; 884.0)	6	129.0	(19.3; 259.0)	6	884.0	(310.3; 1140.5)
FCP at wk8 (mg/kg), median	12	354.5	(111.0; 483.5)	5	89.0	(22.0; 479.0)	7	355.0	(327.0; 429.0)

Table 1. Changes (n, mean or median, IQR) in clinical, endoscopic, histologic, and biochemical disease activity observed upon treatment with MH002 in subjects achieving vs. not achieving mPDAI remission at wk8.

Conclusion: In this exploratory study in patients with acute pouchitis, 8-wk treatment with MH002 resulted in consistent and clinically meaningful improvements with a remission rate of 46% according to the mPDAI. These results warrant further development of MH002 in a phase 2/3 study.

Disclosure: SV: financial support for research from AbbVie, J&J, Pfizer, Takeda and Galapagos; speakers' and/or consultancy fees from AbbVie, Abivax, AbolerISPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MRM Health, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Surrozen, Takeda, Theravance, Tillots Pharma AG, VectivBio, Ventyx, Zealand Pharma.

PD: research support for from Biogen and Mundipharma; speakers' fees from Biogen, Janssen, Dentsply and Dr Falk Pharma; congress support from Roche, Amgen, Ferring, Onis and Norgine; advisory board fees from Janssen, Sandoz, Samsung Bioepis, Galapagos and BMS.

TL: financial support for research from Abbvie, Ferring, Viatrix, MSD, EG, Mundipharma, Biogen, Janssen, Pfizer, Takeda, Sandoz and Galapagos; speakers' fees from MSD, Abbvie, Janssen, Amgen, Fresenius Kabi, Galapagos, Viatrix, Ferring and Takeda; consultancy fees from Janssen, Galapagos, Amgen, Bristol Myers Squibb Fresenius Kabi, Takeda and Abbvie.

MA: consulting fees from Nikkiso Europe, Mundipharma, Janssen, Abbvie, Ferring, Galapagos and Pfizer.

ES: consulting fees from Janssen, Abbvie, Takeda, Celltrion, Ferring, Galapagos, Alfa Sigma, Sandoz and Pfizer.

SP, LH & SB: employee, paid consultant and/or shareholder of MRM Health.

Expanding treatment response in IBD

11:30-12:30 / A3

OP082

THE EFFICACY OF MAINTENANCE TREATMENT WITH GUSELKUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: PHASE 3 QUASAR MAINTENANCE STUDY RESULTS AT WEEK 44 BY BIOLOGIC/JANUS KINASE INHIBITOR HISTORY

J. Allegretti¹, J. Panés², L. Peyrin-Biroulet³, B.E. Sands⁴, S. Yarandi⁵, K.-H. Huang⁵, M. Germinaro⁵, J. Zhan⁵, H. Zhang⁵, J. Begun⁶, J. Kierkus⁷, T. Kravchenko⁸, T. Hisamatsu⁹, D.T. Rubin¹⁰, B. Bressler¹¹, A. Dignass¹²

¹Brigham and Women's Hospital Crohn's and Colitis Center, Dept. of Gastroenterology, Boston, United States of America,

²Hospital Clínic Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain, ³Nancy University Hospital, Université de Lorraine, Nancy, France, ⁴Icahn School of Medicine at Mount Sinai,

Division Of Gastroenterology, New York, United States of America, ⁵Janssen Research & Development, LLC, Spring House, United States of America, ⁶Mater Hospital Brisbane,

Gastroenterology, South Brisbane, Australia, ⁷Children's Memorial Health Institute, Warsaw, Poland, ⁸National Medical University, Kyiv, Ukraine, ⁹Kyorin University School of Medicine,

Tokyo, Japan, ¹⁰University of Chicago Medicine, Inflammatory Bowel Disease Center, Chicago, United States of America, ¹¹University of British Columbia, Vancouver, Canada, ¹²Agaplesion Markus Krankenhaus, Medizinische Klinik I, Frankfurt/ Main, Germany

Contact E-Mail Address: axel.dignass@agaplesion.de

Introduction: The Phase 3 QUASAR Maintenance Study evaluated the efficacy of maintenance treatment with subcutaneous (SC) guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor, in patients (pts) with ulcerative colitis (UC) who achieved clinical response following IV GUS induction treatment.

Here, we report Week(Wk) 44 efficacy and safety results for GUS treatment compared with withdrawal (placebo) and by history of treatment with biologics/Janus kinase (JAK) inhibitors.

Aims & Methods: At maintenance baseline, clinical responders to 12 weeks of GUS IV induction from QUASAR Phase 2b and Phase 3 induction studies (NCT04033445) were randomized 1:1:1 to GUS 200 mg SC q4w, GUS 100 mg SC q8w, or PBO (GUS withdrawal).

The primary analysis population included randomized and treated pts in the Maintenance Study with a modified Mayo score of 5-9 at induction baseline. Key clinical, symptomatic, histologic, and endoscopic efficacy endpoints and safety events were evaluated through Wk 44.

Results: Of the 568 pts included, 240 (42.3%) had a history of inadequate response or intolerance to biologics/JAK inhibitors, 309 (54.4%) were biologic/JAK inhibitor naïve, and 19 (3.3%) were biologic/JAK inhibitor experienced without documented inadequate response or intolerance. Among pts with inadequate response or intolerance to biologics/JAK inhibitors (anti-TNFs [87.9%], vedolizumab [49.2%], or tofacitinib [20.0%]), 48.3% had inadequate response or intolerance to two or more biologic/JAK inhibitor therapies.

At induction baseline, pts with a history of inadequate response or intolerance to biologics/JAK inhibitors had longer disease duration (mean 9.94 vs 6.25 yrs) and more severe endoscopic disease (Mayo endoscopy subscore=3, 79.6% vs 56.7%) compared with pts with no such history.

Results for key efficacy endpoints are included in Table 1. At Wk 44, clinical remission was achieved by 40.0% of GUS-treated pts (vs 8.0% of withdrawal pts, nominal p<0.001) who had inadequate response or intolerance to biologics/JAK inhibitors, and 54.2% of biologic/JAK inhibitor

naïve pts who were treated with GUS (vs 25.9% of withdrawal pts, nominal $p < 0.001$). The proportions of pts who met the key endpoints were generally higher in the biologic/JAK inhibitor naïve subpopulation compared with the subpopulation of pts with prior inadequate response or intolerance to biologics/JAK inhibitors across treatment groups, however, the treatment differences were generally greater in pts with prior inadequate response or intolerance to biologics/JAK inhibitors. Through Wk 44, adverse events for these subpopulations were consistent with the overall population, and no new safety concerns were identified.

	History of Inadequate Response/ Intolerance to Biologics/JAK Inhibitors			Biologic/JAK Inhibitor Naïve		
	GUS Withdrawal (Placebo) (N=75)	GUS 100mg SC q8w (N=77)	GUS 200 mg SC q4w (N=88)	GUS Withdrawal (Placebo) (N=108)	GUS 100mg SC q8w (N=105)	GUS 200mg SC q4w (N=96)
Clinical remission, ^{a1,b} n (%)	6 (8.0%)	31 (40.3%)	35 (39.8%)	28 (25.9%)	53 (50.5%)	56
Adjusted treatment difference (95%CI)		30.4% (18.7%, 42.1%) $P < 0.001$	32.4% (21.1%, 43.7%) $P < 0.001$		24.3% (12.0%, 36.5%) $P < 0.001$	(58.3%) 28.8% (16.5%, 41.1%) $P < 0.001$
Maintenance of clinical remission, ^{a2,b} n/N (%)	4/15 (26.7%)	12/20 (60.0%)	10/18 (55.6%)	14/41 (34.1%)	28/43 (65.1%)	38/48 (79.2%)
Treatment difference (95%CI)		33.3% (-0.9%, 62.1%) $P = 0.087$	28.9% (-5.9%, 59.0%) $P = 0.158$		31.0% (9.3%, 50.6%) $P = 0.008$	45.0% (24.9%, 62.2%) $P < 0.001$
Maintenance of clinical response, ^{a3,b} n (%)	21 (28.0%)	54 (70.1%)	59 (67.0%)	58 (53.7%)	87 (82.9%)	78
Adjusted treatment difference (95%CI)		40.8% (27.4%, 54.2%) $P < 0.001$	39.4% (25.8%, 53.0%) $P < 0.001$		29.0% (17.2%, 40.8%) $P < 0.001$	(81.3%) 26.3% (14.0%, 38.6%) $P < 0.001$
Symptomatic remission, ^{a4,b} n (%)	18 (24.0%)	50 (64.9%)	53 (60.2%)	50 (46.3%)	78 (74.3%)	73
Adjusted treatment difference (95%CI)		39.1% (25.9%, 52.2%) $P < 0.001$	36.8% (23.4%, 50.2%) $P < 0.001$		27.6% (15.1%, 40.1%) $P < 0.001$	(76.0%) 28.2% (15.4%, 41.0%) $P < 0.001$
Endoscopic improvement, ^{a5,b} n (%)	6 (8.0%)	35 (45.5%)	37 (42.0%)	28 (25.9%)	56 (53.3%)	57
Adjusted treatment difference (95%CI)		35.8% (23.8%, 47.8%) $P < 0.001$	34.6% (23.1%, 46.0%) $P < 0.001$		27.2% (15.0%, 39.5%) $P < 0.001$	(59.4%) 30.0% (17.6%, 42.4%) $P < 0.001$
Histo-endoscopic mucosal improvement, ^{a6,b} n (%)	6 (8.0%)	29 (37.7%)	34 (38.6%)	25 (23.1%)	52 (49.5%)	54
Adjusted treatment difference (95%CI)		27.7% (16.0%, 39.5%) $P < 0.001$	31.2% (19.8%, 42.5%) $P < 0.001$		26.1% (14.0%, 38.2%) $P < 0.001$	(56.3%) 29.5% (17.3%, 41.7%) $P < 0.001$
Endoscopic normalization (remission) ^{a7,b} n (%)	6 (8.0%)	24 (31.2%)	21 (23.9%)	22 (20.4%)	40 (38.1%)	40
Adjusted treatment difference (95%CI)		21.4% (10.0%, 32.7%) $P < 0.001$	16.3% (6.4%, 26.1%) $P = 0.005$		17.3% (5.6%, 29.1%) $P = 0.005$	(41.7%) 17.5% (6.0%, 29.0%) $P = 0.004$

Biologic/JAK inhibitor experienced without documented inadequate response or intolerance to biologics/JAK inhibitors: placebo, n=7; GUS 100 mg, n=6; GUS 200 mg, n=6. All p-values were nominal. P-values were based on the CMH test, stratified by clinical remission status at maintenance baseline and induction treatment, except for the maintenance of clinical remission, which was based on the Fisher's exact test. Adjusted treatment difference was based on the Wald statistic with CMH weight.

^{a1} Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability.

^{a2} Maintenance of clinical remission: Clinical remission at Wk 44 among pts in clinical remission at maintenance baseline.

^{a3} Maintenance of clinical response: Clinical response at Wk 44 among pts in clinical response at maintenance baseline.

^{a4} Symptomatic remission: A stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0.

^{a5} Endoscopic improvement: An endoscopy subscore of 0 or 1 with no friability present on the endoscopy.

^{a6} Histo-endoscopic mucosal improvement: Achieving a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue per Geboes grading system) and endoscopic improvement.

^{a7} Endoscopic normalization: An endoscopy subscore of 0. ^b Pts who had a prohibited change in UC medication, an ostomy or colectomy, a dose adjustment (including a sham dose adjustment), or discontinued study agent due to lack of efficacy or an adverse event of worsening of UC or other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to the Wk 44 visit were considered not to have achieved the endpoint. Pts who were missing one or more components pertaining to a specified endpoint at Wk 44 were considered not to have achieved the endpoint.

Table 1. Endpoints at maintenance Week 44 by history of biologic/JAK inhibitor therapy: Primary analysis population.

Conclusion: Maintenance treatment with both GUS dosing regimens resulted in greater improvements compared with placebo withdrawal across key clinical, symptomatic, endoscopic, and histologic endpoints at Wk 44 regardless of prior history with biologics/JAK inhibitors. Safety results for both GUS maintenance dose regimens were comparable across subpopulations by treatment history and consistent with the known safety profile of GUS.

Disclosure: JRA: consultant for Finch Therapeutics, Artugen, Pfizer, Takeda, Janssen, and Iterative Scopes; research support from Merck; consultant and speaker for BMS.

JP: received consultancy fees/honorarium from AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman, and has served on a data safety monitoring board for Alimentiv, Mirum, Sorriso, Sanofi, and Surrozen.

LPB: personal fees from AbbVie, Allergan, Alma, Amgen, Applied Molecular Transport, Arena, Biogen, Boehringer Ingelheim, BMS, Celgene, Celltrion, Enterome, Entera, Ferring, Fresenius, Genentech, Gilead, Hikma, Index Pharmaceuticals, Janssen, Lilly, MSD, Mylan, Nestlé, Norgine, Opiphan Pharma, OSE Immunotherapeutics, Pfizer, Pharmacosmos, Roche, Samsung Bioepis, Sandoz, Sterna, Sublimity Therapeutics, Takeda, Tillots and Vifor; grants from AbbVie, MSD and Takeda; stock options from CTMA.

BES: consulting fees from AbbVie, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evomune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphe Therapeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock options from Ventyx Biopharma.

SY, KGH, MG, JZ and HZ: employees of Johnson & Johnson and own company stock/stock options.

JB received grant support from AbbVie, Janssen, Pfizer and Ferring. Consulting fees from Janssen, Pfizer, AbbVie, Takeda, Ferring, Microba, Anata, DrFalk, Bristol Meyers Squibb, Glaxo Smith Klein and Chieisi, and lecture fees from AbbVie, Janssen, Pfizer, Takeda, and Ferring.

JK reports personal fees from Bristol-Myers Squibb, Celltrion, Ferring, Fresenius, Janssen, Lilly, Nestlé.

TK served as an investigator for Janssen.

TH: grant support from AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd. JIM-RO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., Takeda Pharmaceutical Co., Ltd., consulting fees from EA Pharma Co, Ltd., Janssen Research & Development, LLC., and lecture fees from AbbVie, EA Pharma Co, Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Co., Ltd.

DTR: research funding from Takeda, and has served as a consultant to AbbVie, Altrubio, Allergan, Inc., Arena Pharmaceuticals, Aslan Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Ltd., Bristol Myers Squibb, Celgene Corp/Syneos, Connect BioPharma, GalenPharma/Atlantica, Genentech/Roche, Index Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Eli Lilly, Materia Prima, Pfizer, Prometheus Biosciences, Reistone, Takeda, Techlab, Inc and is a co-founder of Cornerstones Health, Inc.

BB: advisor/speaker for AbbVie, BMS, Ferring, Janssen, Merck, Novartis, Organon, Pfizer, Sandoz, Takeda; advisor for Alimentiv, Allergan, AMT,

Bausch Health, BMS, Celgene, Celltrion Healthcare, Eupraxia, Fresenius Kabi, Genentech, Gilead, Iterative Scopes, Jamp Pharma, Merck Amgen, Microbiome Insights, Mylan, Pendopharm, Protagonist, Viatrix; received research support from Abbvie, Amgen, BI, BMS, Genentech, GSK, Janssen, Merck, Qu Biologic; and reports stock options for Qu Biologic.

AD: fees for clinical trials, data monitoring boards, statistical analysis and end point committees from Abivax, AbbVie, BMS, Dr Falk Foundation, Galapagos, Gilead, Janssen, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, BMS, Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz; Stada, Takeda, Tillotts, and Vifor Pharma; payment for lectures from AbbVie, Biogen, CED Service GmbH, Celltrion, Falk Foundation, Ferring, Galapagos, Gilead, High5MD, Janssen, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Takeda, Tillotts, and Vifor Pharma; payment for manuscript preparation from Abbvie, Falk Foundation, Janssen, Takeda, Thieme, and UniMed Verlag.

OP083

SUSTAINED CLINICAL AND ENDOSCOPIC IMPROVEMENTS WITH UP TO 3 YEARS OF RISANKIZUMAB TREATMENT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN’S DISEASE REGARDLESS OF NUMBER OF PRIOR BIOLOGIC FAILURES

M. Ferrante¹, L. Peyrin-Biroulet², A. Dignass³, D.T. Rubin⁴, S. Danese⁵, G.R. D’Haens⁶, K. Kligys⁷, S. Van Haaren⁸, A. Song⁷, J. Zambrano⁷, Y. Zhang⁷, T. Fujii⁹, R. Panaccione¹⁰
¹University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ²Inserm U1256, Nancy University Hospital, Department of Gastroenterology and INSERM U1256, NGERE, Faculty of Medicine, Vandoeuvre-les-Nancy, France, ³Agaplesion Markus Hospital, Medizinische Klinik I, Frankfurt/Main, Germany, ⁴University of Chicago Medicine, Chicago, United States of America, ⁵Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁶AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands, ⁷AbbVie, North Chicago, United States of America, ⁸Abbvie, Wavre, Belgium, ⁹Tokyo Medical and Dental University, Gastroenterology and Hepatology, Tokyo, Japan, ¹⁰University of Calgary, Medicine, Calgary, Canada

Contact E-Mail Address: rpanacci@ucalgary.ca

Introduction: Risankizumab (RZB), a monoclonal antibody targeting the interleukin-23 p19 subunit, has previously demonstrated the ability to improve clinical and endoscopic outcomes during induction (ADVANCE, MOTIVATE) and maintenance (FORTIFY) in patients with moderately to severely active Crohn’s disease (CD) regardless of the number of prior biologic failures.¹⁻³ As sustained clinical and endoscopic improvements are important goals in CD, we evaluated the long-term outcomes of RZB by the number of prior biologic failures in patients who received long-term RZB maintenance treatment in the ongoing FORTIFY open-label extension (OLE) substudy.⁴

Aims & Methods: The FORTIFY OLE enrolled patients who completed 52 wks of maintenance therapy with subcutaneous RZB 180 mg, RZB 360 mg, or placebo (withdrawal) in the FORTIFY substudies or RZB phase 2 OLE. All patients received RZB 180 mg every 8 wks (q8w) starting at wk 56, except for those who received prior rescue therapy (single dose of RZB 1200 mg followed by RZB 360 mg q8w) as they continued RZB 360 mg q8w in the OLE. Patients who demonstrated an inadequate response (increased symptoms plus an objective marker of inflammation) during the OLE could also receive rescue therapy (single dose of RZB 1200 mg followed

by RZB 360 mg q8w). This analysis included all patients who completed 2 years of RZB treatment in the FORTIFY OLE (following 1 additional year of randomized maintenance-see footnotes for complete patient population); herein referred to as 152-wk maintenance completers. We assessed clinical and endoscopic outcomes by the number of prior biologic failures (0, 1, ≥2) in each dose group as well as in a pooled dose group. Outcomes assessed at wk 12 (induction) and wk 52 (maintenance) are shown in the Table for reference.

Results: Among the 710 patients who were 152-wk maintenance completers, approximately 1/3 of patients failed 0 (n=210, 30%), 1 (n=227, 32%), ≥2 prior biologics (n=273, 38%), respectively. Baseline demographics and characteristics were similar across subgroups, although patients who failed ≥2 prior biologics generally had more severe disease, as defined by disease duration, SES-CD, FCP, and CRP. Across the subgroups of patients who failed 0, 1, and ≥2 prior biologics, rates of clinical remission (per CDAI and SF/APS), endoscopic response, endoscopic remission, and ulcer-free endoscopy were sustained through wk 152 with RZB maintenance therapy in the pooled RZB 180 mg and RZB 360 mg maintenance groups (Table). Results for the RZB 180 mg and RZB 360 mg groups are also shown in the Table. For almost all endpoints, patients who failed 0 prior biologics demonstrated numerically higher responses, followed by patients who failed 1, and then ≥2 prior biologics (Table).

Endpoint Number of Prior Failed Biologics, n/N (%)	Week 12 of Induction ^a		Week 52 of Maintenance ^b			Week 152 Completers of Open-Label Extension ^c		
	PBO IV	RZB 600 mg IV	PBO SC (Withdrawal)	RZB 180 mg SC	RZB 360 mg SC	Pooled RZB 180+ 360 mg SC	RZB 180 mg SC	RZB 360 mg SC
CDAI								
Clinical Remission ^d								
0	16/78 (23.1)	69/141 (48.9)	24/41 (58.5)	32/44 (72.7)	25/39 (64.1)	121/210 (57.6)	110/182 (60.4)	11/28 (39.3)
1	31/129 (24.0)	81/192 (42.0)	27/60 (45.0)	24/42 (57.1)	26/51 (50.1)	105/227 (46.3)	85/172 (49.4)	20/55 (36.4)
≥2	31/155 (20.0)	82/194 (42.3)	16/63 (25.4)	31/71 (43.7)	23/51 (45.1)	107/273 (39.2)	80/179 (44.7)	27/94 (28.7)
SF/APS								
Clinical Remission ^d								
0	16/78 (20.5)	67/141 (47.5)	23/41 (56.1)	27/44 (61.4)	24/39 (61.5)	121/210 (57.6)	112/182 (61.5)	9/28 (32.1)
1	31/129 (24.0)	76/192 (39.6)	26/60 (43.3)	23/42 (54.8)	23/51 (45.2)	100/227 (44.1)	87/172 (50.6)	13/55 (23.6)
≥2	27/155 (17.4)	69/194 (35.6)	16/63 (25.4)	23/71 (32.4)	26/51 (51.0)	105/273 (38.5)	79/179 (41.9)	30/94 (31.9)
Endoscopic Response ^e								
0	10/78 (12.8)	71/141 (50.4)	11/41 (26.8)	28/44 (63.6)	21/39 (53.8)	125/210 (59.5)	115/182 (63.2)	10/28 (35.7)
1	19/129 (14.7)	69/192 (35.7)	17/60 (28.3)	20/42 (47.6)	22/51 (42.4)	117/227 (51.5)	95/172 (55.2)	22/55 (40.0)
≥2	13/155 (8.4)	51/194 (26.1)	8/63 (12.7)	26/71 (36.6)	23/51 (45.1)	128/273 (46.9)	86/179 (48.0)	42/94 (44.7)
Endoscopic Remission ^d								
0	11/78 (14.1)	45/141 (31.9)	9/41 (22.0)	23/44 (52.3)	19/39 (48.7)	120/210 (57.1)	109/182 (59.9)	11/28 (39.3)
1	7/129 (5.4)	49/192 (25.6)	8/60 (13.3)	14/42 (33.3)	17/51 (33.5)	88/227 (38.8)	75/172 (43.6)	13/55 (23.6)
≥2	6/155 (3.9)	24/194 (12.4)	4/63 (6.3)	10/71 (14.1)	19/51 (37.3)	88/273 (32.2)	63/179 (35.2)	25/94 (26.6)
Ulcer-free Endoscopy ^f								
0	9/77 (11.7)	42/141 (30.0)	9/41 (22.0)	17/44 (38.6)	16/39 (41.0)	102/210 (48.6)	94/182 (51.6)	8/28 (28.6)
1	8/128 (6.3)	36/191 (18.6)	6/58 (10.3)	13/42 (31.0)	15/51 (29.5)	85/226 (37.6)	74/171 (43.3)	11/55 (20.0)
≥2	4/154 (2.6)	19/194 (9.9)	2/63 (3.2)	8/71 (11.3)	12/51 (23.5)	68/273 (24.9)	42/179 (23.5)	26/94 (27.7)

Table. Clinical and Endoscopic Outcomes at Week 12 (Induction), Week 52 (Maintenance), and Week 152 (in Open-Label Extension). APS, abdominal pain score; CDAI, Crohn’s Disease Activity Index; COVID-19, coronavirus disease 2019; IV, intravenous; NRI-MI, nonresponder imputation-multiple imputation; OLE, open-label extension; PBO, placebo; q8w, every 8 weeks; RZB, risankizumab; SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn’s Disease; SF, stool frequency. NRI-MI was used to handle missing data due to COVID-19 or NRI only if no missing data was due to COVID-19. ^aIncludes randomized patients who received at least one dose of study drug during the 12-week induction period in ADVANCE or MOTIVATE and had baseline eligible SES-CD of ≥ 6 (≥ 4 for isolated ileal disease). ^bIncludes randomized patients who responded to 12 weeks of IV RZB induction therapy in ADVANCE or MOTIVATE and received at least one dose of study drug in FORTIFY substudy 1. ^cIncludes all patients who received at least one dose of study drug in the FORTIFY OLE (substudy 3) and 2-year of data matured. The FORTIFY OLE enrolled patients who completed 52 weeks of maintenance dosing in the FORTIFY substudy 1 or 2 or RZB phase 2 OLE. All patients received SC RZB 180 mg every 8 weeks, starting at week 56, except for patients who had prior rescue therapy (single IV RZB 1200 mg, followed by SC RZB 360 mg every 8 weeks) who continued the 360 mg dose every 8 weeks in the OLE. Patients who demonstrated an inadequate response (increased symptoms plus objective marker of inflammation) during the OLE could also receive rescue therapy (single dose of RZB 1200 mg followed by RZB 360 mg q8w). Clinical and endoscopic outcomes were assessed in 152 wks completers in OLE. ^dCDAI clinical remission: CDAI <150. ^eSF/APS clinical remission: Average daily SF ≤2.8 and not worse than baseline of the induction study and average daily AP score ≤1 and not worse than baseline of the induction study. ^fEndoscopic response: Decrease in SES-CD >50% from baseline of the induction study (or for patients with isolated ileal disease and a baseline SES-CD of 4, at least a 2-point reduction from baseline of the induction study). ^gEndoscopic remission: SES-CD ≤4 and at least a 2-point reduction versus baseline of the induction study and no subscore >1 in any individual variable, as scored by a central reviewer. ^hUlcer-free endoscopy: SES-CD ulcerated surface subscore of 0 in patients with SES-CD ulcerated surface subscore ≥1 at baseline, as scored by a central reviewer.

Conclusion: Patients who completed 2 years of RZB treatment in the FORTIFY OLE demonstrated sustained clinical and endoscopic improvements regardless of the number of prior biologic failures. Biologic naïve

patients demonstrated the most improvement, followed by those who failed 1, and then ≥ 2 prior biologics, suggesting the benefits of RZB in early treatment.

References: D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. *Lancet*. 2022;399(10340):2015-2030. doi:10.1016/s0140-6736(22)00467-6

2. Ferrante M, Panaccione R, Baert F, et al. Risankizumab as maintenance therapy for moderately to severely active Crohn's disease: results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 FORTIFY maintenance trial. *Lancet*. 2022;399(10340):2031-2046.

3. Ferrante M. Clinical and Endoscopic Improvements with Risankizumab Induction and Maintenance Dosing Versus Placebo are Observed Irrespective of Number of Prior Failed Biologics (Abstract OP128). *UEG Journal*. 2022:101.

4. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology*. 2021;160:1570-1583. doi:10.1053/j.gastro.2020.12.031

Disclosure: **AbbVie Disclosure:** AbbVie funded these studies and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, writing of manuscript, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.

Disclosures: **Marc Ferrante** has received speaker and/or consultant fees from AbbVie, AgomAb Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Dr Falk, Eli Lilly, Ferring, Janssen-Cilag, MRM Health, MSD, Pfizer, Regeneron, Takeda, Thermo Fisher, Truvion Healthcare and Viatris; Research Grants: AbbVie, Biogen, EG, Janssen, Pfizer, Takeda and Viatris.

Laurent Peyrin-Biroulet has received consulting and/or lecture fees from AbbVie, Adacety, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytokine Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, Viatris, Vifor, Ysopia, Abivax, Samsung, Ventyx, Roivant, and Vectivbio.

Axel Dignass reports received fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis and end point committees from Abivax, AbbVie, Bristol Myers Squibb, Dr Falk Foundation, Galapagos, Gilead, Janssen, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada, Takeda, Tillotts, and Vifor Pharma; payment for lectures including service on speakers bureaus from AbbVie, Biogen, CED Service GmbH, Celltrion, Falk Foundation, Ferring, Galapagos, Gilead, High5MD, Janssen, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Takeda, Tillotts, and Vifor Pharma; payment for manuscript preparation from AbbVie, Falk Foundation, Janssen, Takeda, Thieme, and UniMed Verlag.

David T. Rubin has served as a consultant for AbbVie, Altrubio, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dizal Pharmaceuticals, Galapagos, Ichnos Sciences S.A., Index Pharmaceuticals, Iterative Health, Janssen, Lilly, Pfizer, Prometheus Biosciences, Reistone, Syneos, and Takeda. He has received grant support from Takeda.

Silvio Danese has received consultancy fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli

Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB Inc., and Vifor.

Geert D'Haens has served as an adviser for AbbVie, Alimentiv, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Galapagos, Pfizer, Immunic, Johnson & Johnson, Takeda, Tillotts, Ventyx, and Vifor Pharma; and has received speaker fees from AbbVie, Johnson & Johnson, Pfizer, Takeda, and Tillotts.

Kristina Kligys, Stijn van Haaren, Alexandra Song, Javier Zambrano, and Yafei Zhang are AbbVie employees and may own AbbVie stock and/or stock options.

Toshimitsu Fujii receives AbbVie GK, Alfresa Corporation, Boehringer Ingelheim GmbH, Bristol Myers Squibb, Celgene, Celltrion, EA Pharma, Eisai, Gilead Sciences, Janssen, Kissei, Lilly, and Takeda. and speaker fees from AbbVie GK, Ajinomoto Pharma, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, EA Pharma, Janssen, Kissei, Kyorin, Kyowa Hakko Kirin, Mitsubishi-Tanabe, Mochida, Nichiiko, Nippon Kayaku, Takeda, and Zeria Pharma.

Remo Panaccione has received consulting fees, speaker fees, and research support from

Abbott, AbbVie, Abbivax, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatris, Ventyx, and UCB.

OP084

CORTICOSTEROID SPARING EFFECTS OF TREATMENT WITH GUSELKUMAB IN PATIENTS WITH MODERATE TO SEVERELY ACTIVE ULCERATIVE COLITIS: PHASE 3 QUASAR MAINTENANCE STUDY RESULTS THROUGH WEEK 44

B. Bressler¹, J. Allegretti², D.T. Rubin³, N. Shipitofsky⁴, K.-H. Huang⁴, M. Germinaro⁴, R. Wilson⁴, H. Zhang⁴, A. Armuzzi⁵, S. Fishman⁶, Y. Wang⁷, J. Panés⁸, G. Lichtenstein⁹, L. Peyrin-Biroulet¹⁰

¹University of British Columbia, Vancouver, Canada, ²Brigham and Women's Hospital, Dept. of Gastroenterology, Boston, United States of America, ³University of Chicago Medicine, Inflammatory Bowel Disease Center, Chicago, United States of America, ⁴Janssen Research & Development, LLC, Spring House, United States of America, ⁵Humanitas Research Hospital, Gastroenterology, Milan, Italy, ⁶Tel Aviv Sourasky Medical Center Tel Aviv University, Tel Aviv, Israel, ⁷West China Hospital, Sichuan University, Chengdu, China, ⁸Hospital Clínic Barcelona, Dept. of Gastroenterology, Barcelona, Spain, ⁹University of Pennsylvania School of Medicine, Medicine, Gastroenterology, Merion Station, United States of America, ¹⁰Nancy University Hospital, Université de Lorraine, Nancy, France

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: The Phase 3 QUASAR Maintenance Study (NCT04033445) evaluated the efficacy of maintenance treatment with SC guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor that binds to CD64 (a receptor on cells that produce IL-23), in patients with ulcerative colitis (UC). Here we report the corticosteroid sparing effects of maintenance treatment with GUS compared with GUS withdrawal (placebo [PBO]) through Week (Wk) 44.

Aims & Methods: At maintenance baseline, clinical responders to 12 weeks of GUS IV induction were randomized 1:1:1 to GUS 200 mg SC q4w, GUS 100 mg SC q8w, or GUS withdrawal (PBO). Patients who were receiving oral corticosteroids upon entry into the maintenance study were required to begin tapering their daily corticosteroid dose at Wk0, unless medically not feasible. Corticosteroid use and corticosteroid-free clinical remission at Wk44 were assessed.

Results: The primary analysis population included 568 patients (induction baseline: mean age, 40.7yr; mean UC duration, 7.8yr; mean modified Mayo score, 6.9 [63.9% with severe disease]; Mayo endoscopy subscore of 3, 66.4%). At maintenance baseline, 38.9% (221/568) of patients were receiving oral corticosteroids and the mean daily prednisone-equivalent corticosteroid dose (excluding budesonide and beclomethasone dipropionate) was similar across all treatment groups (17.3, 15.0, and 14.9mg/day, respectively, for GUS withdrawal, GUS 100mg, and GUS 200mg groups).

	GUS Withdrawal (Placebo)	GUS 100mg SC q8w	GUS 200mg SC q4w
Primary analysis population, N	190	188	190
Clinical remission at Wk44 (multiplicity-controlled), ^{a1,b} n (%)	36 (18.9%)	85 (45.2%)	95 (50.0%)
Adjusted treatment difference (95% CI) ^c		25.2 (16.4, 33.9)	29.5 (20.9, 38.1)
P-value ^d		P<0.001	P<0.001
Clinical remission at Wk44 and not receiving corticosteroids for ≥8 wks prior to Wk44 (multiplicity-controlled) ^{a1,b}	35 (18.4%)	85 (45.2%)	93 (48.9%)
Adjusted treatment difference (95% CI) ^c		25.7% (17.0%, 34.5%)	29.0% (20.5%, 37.6%)
P-value ^d		<0.001	<0.001
Clinical remission at Wk44 and not receiving corticosteroids for ≥12 wks prior to Wk44 ^{a1,b}	35 (18.4%)	85 (45.2%)	93 (48.9%)
Adjusted treatment difference (95% CI) ^c		25.7% (17.0%, 34.5%)	29.0% (20.5%, 37.6%)
Nominal P-value ^d		<0.001	<0.001
Patients receiving oral corticosteroids at maintenance baseline, n (%)	75 (39.5%)	73 (38.8%)	73 (38.4%)
Eliminating oral corticosteroids ≥12 wks prior to Wk44, ^{a2,b} n (%)	27 (36.0%)	51 (69.9%)	48 (65.8%)
Adjusted treatment difference (95% CI) ^c		33.5% (19.0%, 48.0%)	29.2% (14.4%, 44.0%)
Nominal P-value ^d		<0.001	<0.001
Eliminating oral corticosteroids ≥8 wks prior to Wk44 and in clinical remission at Wk44, ^{a2,b} n (%)	10 (13.3%)	35 (47.9%)	29 (39.7%)
Adjusted treatment difference (95% CI) ^c		34.2% (21.4%, 47.1%)	25.8% (13.1%, 38.6%)
Nominal P-value ^d		<0.001	<0.001
Primary analysis population: Randomized and treated patients with a modified Mayo score 5-9 at induction baseline.			

^{a1} Clinical remission is defined as a stool frequency subscore of 0 or 1 that has not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability present. ^{a2} Eliminating oral corticosteroids by a designated time point is defined as not requiring any oral corticosteroid treatment from that time point until maintenance Wk44. ^b Patients who had an ostomy or colectomy, a dose adjustment, a prohibited change in UC medications, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to Wk44 were considered not to have achieved the endpoint. ^c The adjusted treatment difference and confidence intervals were based on the Wald statistic with Cochran-Mantel-Haenszel (CMH) weight. ^d The p-values were based on the CMH test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Table 1. Corticosteroid use and corticosteroid-free clinical remission at Week 44: Primary analysis population.

Among patients who were receiving oral corticosteroids (excluding budesonide and beclomethasone dipropionate) at maintenance baseline, the mean decreases from baseline in the average daily prednisone-equivalent corticosteroid dose at Wk44 were greater in the GUS 100mg and 200mg groups compared with the withdrawal group (-10.22 and -10.25 vs -7.35mg/day, respectively, both nominal p<0.001).

As early as Wk8, higher proportions of patients in both GUS treatment groups had eliminated oral corticosteroid use through Wk44 compared with the withdrawal group (65.8% [48/73] and 64.4% [47/73] for GUS 100mg and GUS 200mg groups, respectively, vs 32.0% [24/75] for withdrawal group, both nominal p<0.001). At Wk44, higher proportions of patients in the GUS treatment groups vs withdrawal group had eliminated oral corticosteroid use (Table 1).

Higher proportions of patients in the GUS treatment groups were in clinical remission at Wk44 and had eliminated oral corticosteroid use for at least 8 weeks prior to Wk44, compared with patients in the withdrawal group (Table 1).

Among GUS-treated patients, 180 achieved clinical remission at Wk44 and 178 (98.9%) of them had eliminated oral corticosteroids at least 8 weeks prior to Wk44.

Conclusion: In patients with UC, maintenance treatment with GUS 100mg SC q8w and GUS 200mg SC q4w sustained clinically meaningful efficacy through Wk44 and allowed successful elimination of concomitant corticosteroids.

Disclosure: BB is an advisor/speaker for Abbvie, BMS, Ferring, Janssen, Merck, Novartis, Organon, Pfizer, Sandoz, Takeda; advisor for Alimentiv, Allergan, AMT, Bausch Health, BMS, Celgene, Celltrion Healthcare, Eupraxia, Fresenius Kabi, Genentech, Gilead, Iterative Scopes, Jamp Pharma, Merck Amgen, Microbiome Insights, Mylan, Pendopharm, Protagonist, Viartis; received research support from Abbvie, Amgen, BI, BMS, Genentech, GSK, Janssen, Merck, Qu Biologic; and reports stock options for Qu Biologic.

JA is a consultant for Finch Therapeutics, Artugen, Pfizer, Takeda, Janssen, and Iterative Scopes and receives research support from Merck. Consultant and speaker for BMS.

DTR reports research funding from Takeda, and has served as a consultant to AbbVie, Altrubio, Allergan, Inc., Arena Pharmaceuticals, Aslan Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Ltd., Bristol Myers Squibb, Celgene Corp/Syneos, Connect BioPharma, GalenPharma/Atlantica, Genentech/Roche, InDex Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Eli Lilly, Materia Prima, Pfizer, Prometheus Biosciences, Reistone, Takeda, Techlab, Inc and is a co-founder of Cornerstones Health, Inc.

NS is an employee of Johnson & Johnson and owns company stock/stock options.

KGH is an employee of Johnson & Johnson and owns company stock/stock options.

MG is an employee of Johnson & Johnson and owns company stock/stock options.

RW is an employee of Johnson & Johnson and owns company stock/stock options.

HZ is an employee of Johnson & Johnson and owns company stock/stock options.

AA reports consulting/advisory board fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, Lionhealth, MSD, Mylan, Nestlé, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda, Tillots Pharma; speaker's fees from AbbVie, AG Pharma, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda, Teva Pharmaceuticals; research grants from MSD, Takeda, Pfizer, Biogen

SF clinical investigator for Janssen

YW clinical investigator for Janssen

JP received consultancy fees/honorarium from AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman, and has served on a data safety monitoring board for Alimentiv, Mirum, Sorriso, Sanofi, and Surrozen.

GRL discloses relationships with Abbvie (Consultant), Allergan (Consultant), American College of Gastroenterology (Honorarium for Associate Editor of American Journal of Gastroenterology), American Gastroenterological Association (CME), American Regent (Consultant, Honorarium [CME Program]), Celgene (Research, Consultant), Chemed (CME), Eli Lilly (Consultant, Data Safety Monitoring Board), Endo Pharmaceuticals

(Consultant), Ferring (Consultant), Gastroenterology and Hepatology (Gastro-Hep Communication, Editor-Honorarium), Gilead (Consultant), IMEDEX (CME), Ironwood (CME), Janssen/ Janssen Orthobiotech (Consultant, Research, Funding to University of PA [IBD Fellow Education]), MedEd Consultants (Consultant), Merck (Consulting, Honorarium [CME Program]), Morphic Therapeutics (Consultant), Pfizer Pharmaceuticals (Consultant, Funding to University of PA [IBD Fellow Education]), Professional Communications, Inc. (Royalty for writing Textbook), Prometheus Laboratories, Inc (Consultant), Romark (Consultant, Honorarium for CME), Sandoz (Consultant), Salix Pharmaceuticals/Valeant (Consultant), Shire Pharmaceuticals (Consultant), SLACK, Inc (Book Royalty), Springer Science and Business Media (Editor [Honorarium]), Takeda (Consultant, Funding to University of PA [IBD Fellow Education], Research), University of Kentucky (CME), UCB (Consultant, Research), Up-To-Date (Author [Honorarium]), Vindico (CME), and Virgo (Consultant [Stock options]).

LPB reports personal fees from AbbVie, Allergan, Alma, Amgen, Applied Molecular Transport, Arena, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Enterome, Entera, Ferring, Fresenius, Genentech, Gilead, Hikma, Index Pharmaceuticals, Janssen, Lilly, MSD, Mylan, Nestlé, Norgine, Oppilan Pharma, OSE Immunotherapeutics, Pfizer, Pharmacosmos, Roche, Samsung Bioepis, Sandoz, Sterna, Sublimity Therapeutics, Takeda, Tillots and Vifor; grants from AbbVie, MSD and Takeda; stock options from CTMA.

OP085

SAFETY OF LONG-TERM OZANIMOD TREATMENT UP TO 5 YEARS IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: AN INTERIM ANALYSIS OF THE TRUE NORTH OPEN-LABEL EXTENSION

J. Torres¹, R. Longman², K. Katsanos³, S. Lee⁴, T. Kobayashi⁵, D. Bettenworth⁶, L. Korman⁷, D. Mehra⁸, N.R. Santiago⁸, A. Petersen⁸, M. Desai⁸, H. Wu⁸, D. Wang⁹, M.T. Osterman⁸, A. Jain⁸, B.P. Abraham¹⁰

¹Division of Gastroenterology, Hospital da Luz, Lisbon, Portugal; ²Division of Gastroenterology, Hospital Beatriz Angelo, Lisbon, Portugal; and ³Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, ⁴Weill Cornell Medicine, New York, United States of America, ⁵Division of Gastroenterology, University of Ioannina, Ioannina, Greece, ⁶Digestive Health Center, University of Washington Medical Center, Seattle, United States of America, ⁷Kitasato University, Kitasato Institute Hospital, Tokyo, Japan, ⁸University of Münster, Münster, Germany; and ⁹CED Schwerpunktpraxis, Munster, Germany, ¹⁰Capital Digestive Care, Washington, United States of America, ⁸Bristol Myers Squibb, Princeton, United States of America, ⁹Bristol Myers Squibb K. K., Tokyo, Japan, ¹⁰Houston Methodist Weill Cornell, Houston, United States of America

Contact E-Mail Address: joanatorres00@gmail.com

Introduction: The 52-week, phase 3 True North (TN) study (NCT02435992) demonstrated the efficacy and safety of ozanimod (OZA), a highly selective sphingosine 1-phosphate receptor 1 and 5 modulator, in patients (pts) with moderately to severely active ulcerative colitis (UC). A prior analysis reported the long-term safety of OZA up to ~4 y from TN baseline through Week (W) 142 of the ongoing TN open-label extension (OLE; NCT02531126).

Aims & Methods: This analysis assessed the cumulative long-term safety of OZA with an additional year of exposure (pt disposition available until OLE W190 [up to ~5 y of OZA]). All pts who entered the OLE from TN (ie, clinical nonresponders at W10 and those who lost response during main-

tenance or completed maintenance at W52) were included in this analysis. Treatment-emergent adverse events (TEAEs) were monitored from the first dose of OZA in TN or the OLE through data cutoff; exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY) are presented. Lab abnormalities, including absolute lymphocyte count (ALC) reductions, were assessed during the OLE through data cutoff.

Results: A total of 823 pts entered the TN OLE. At data cutoff, 43.0% of pts had completed OLE W190 and total OZA exposure was 2681 PY. Overall, the cumulative safety assessments did not meaningfully change with an additional year of OZA exposure (Table). EAIRs of TEAEs, serious TEAEs, and TEAEs leading to treatment discontinuation remained consistent, and there were no new cases of malignancy, bradycardia, third-degree atrioventricular (AV) block, myocardial ischemia, ischemic stroke, pulmonary embolism, deep vein thrombosis, or macular edema with an additional year of OZA exposure. Three pts newly developed infections; however, only 1 pt had a serious infection (keratouveitis), which was not related to treatment. Two additional pts experienced mild hypertension. Reductions in ALC <500 cells/μl were common in the OLE (57.2%), but few pts had ALC <200 cells/μl (6.6%). Occurrence of ALC <200 cells/μl was not temporally associated with serious or opportunistic infections. Most alanine aminotransferase and aspartate aminotransferase elevations were transient and resolved without treatment interruption, and no serious hepatic events occurred.

	Up to ~4 y of OZA exposure ^a (n=823) Total PY ^c = 2536		Up to ~5 y of OZA exposure ^b (n=823) Total PY ^c = 2681			Up to ~4 y of OZA exposure ^a (n=823) Total PY ^c = 2536		Up to ~5 y of OZA exposure ^b (n=823) Total PY ^c = 2681	
	n (%) EAIR ^d		n (%) EAIR ^d			n (%) EAIR ^d		n (%) EAIR ^d	
TEAEs	685 (83.2)	85.5	687 (83.5)	85.1	Third-degree AV block	1 (0.1)	0.04	1 (0.1)	0.04
Serious TEAEs	158 (19.2)	7.0	163 (19.8)	6.8	Hypertension	55 (6.7)	2.3	56 (6.8)	2.2
TEAEs leading to treatment discontinuation	64 (7.8)	2.5	66 (8.0)	2.5	Myocardial ischemia	3 (0.4)	0.12	3 (0.4)	0.11
Infection	378 (45.9)	22.7	381 (46.3)	22.1	Ischemic stroke	3 (0.4)	0.12	3 (0.4)	0.11
Herpes zoster	30 (3.6)	1.2	31 (3.8)	1.2	Pulmonary embolism	3 (0.4)	0.12	3 (0.4)	0.11
COVID-19	103 (12.5)	4.3	103 (12.5)	4.1	Deep vein thrombosis	3 (0.4)	0.12	3 (0.4)	0.11
Serious infection	44 (5.3)	1.8	45 (5.5)	1.7	Macular edema	3 (0.4)	0.12	3 (0.4)	0.11
Malignancy	18 (2.2)	0.71	17 (2.1)	0.63	Cystoid macular edema	3 (0.4)	0.12	3 (0.4)	0.11
Bradycardia	3 (0.4)	0.12	3 (0.4)	0.11					

Table. Cumulative safety assessments during TN and the TN OLE in all pts who entered the OLE.

^aData cutoff of June 30, 2023. ^bData cutoff of January 10, 2024. ^cTotal PY was calculated as the sum of the number of years on study contributed by each pt from time of first dose to last date on study. ^dEAIRs were calculated as number of pts/PY × 100. ^eTN OLE is an ongoing study. Individual TEAE terms may not add up as harmonization of final data is pending. ^fFor the 5 pts who newly reported a serious TEAE, events included 1 pt each with UC exacerbation, colitis, pancreatitis, and umbilical hernia, and 1 pt with ulcerative keratitis and keratouveitis.

Conclusion: The ongoing safety profile of OZA is consistent with previous analyses, with no new safety concerns identified. Long-term OZA use representing 2681 PY of exposure continues to be well tolerated in pts with moderately to severely active UC.

Disclosure:

Acknowledgment: This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Traci Stuve, MA, and Alexandra Stafford, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

JT: received grants from AbbVie and Janssen; received advisory board or speaker fees from AbbVie, Bristol Myers Squibb, Janssen, Pfizer, and Sandoz.

RL: consulted for Bristol Myers Squibb and Pfizer.

KK: received lecture honoraria from Gore.

SL: consulted for AbbVie, Bristol Myers Squibb, Eli Lilly, and Janssen.

TK: served as an advisory board member, consultant, or speaker for AbbVie, Alfresa Pharma, Alimentiv, Astellas, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eli Lilly, Ferring, Galapagos, Gilead Sciences, Janssen, JIMRO, JMDC, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, ThermoFisher Scientific, and Zeria Pharmaceutical; received research funding from AbbVie, Alfresa Pharma, EA Pharma, Gilead, Kyorin Pharmaceutical, Mochida Pharmaceutical, Nippon Kayaku, Otsuka Holdings, Pfizer, Sekisui Medical, Takeda, ThermoFisher Scientific, and Zeria Pharmaceutical.

DB: served as advisory board member or consultant for AbbVie, Amgen, Arena, Atheneum, BNG Service GmbH, Bristol Myers Squibb, CED Service GmbH, Celltrion, DGVS, Diaplan, Doctorflox, Eli Lilly, Else Kröner-Fresenius-Stiftung, Falk Foundation, Ferring, Galapagos, *Gastroenterology Today*, GlaxoSmithKline, Guidepoint, Impulze, Janssen-Cilag, Medical Tribune, MedTriX, MSD, Mylan, Onkowsen, Pfizer, Pharmacosmos, Roche, Sandoz, Streamed Up, Takeda, Tetrameros, Thieme, Tillotts, UCB, Viatrix, and Vifor Pharma.

LK: reported no conflicts of interest.

DM, NRS, AP, MD, HW, DW, MTO, and AJ: employees and/or shareholders of Bristol Myers Squibb.

BPA: consulted for AbbVie, Bristol Myers Squibb, Celltrion, Eli Lilly, Janssen, Medtronic, Pfizer, Prometheus, Samsung Bioepis, and Takeda; lectured for AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Pfizer, and Takeda.

OP086

LONG-TERM EFFECTIVENESS AND SAFETY OF USTEKINUMAB IN PATIENTS WITH ULCERATIVE COLITIS: REAL-WORLD DATA FROM THE IBDREAM AND INITIATIVE ON CROHN AND COLITIS REGISTRIES

K.M Totté¹, L.M.M Verleye^{1,2,3}, R. West⁴, P.B Mensink⁵, A.C. de Vries⁶, A.E van der Meulen-de Jong⁷, M. Löwenberg⁸, F.DM van Schaik⁹, S. van der Marel¹⁰, M. Pierik^{2,3}, Z. Mujagic^{2,3}, T.E. Römkens¹¹, M. Duijvestein¹, on behalf of the IBDREAM registry and the Dutch Initiative on Crohn and Colitis (ICC)

¹Radboudumc, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands, ²Maastricht University Medical Center+, Department of Gastroenterology and Hepatology, Maastricht, Netherlands, ³Maastricht University Medical Center+, School for Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht, Netherlands, ⁴Sint Franciscus Gasthuis, Department of Gastroenterology, Rotterdam, Netherlands, ⁵Medisch Spectrum Twente, Department of Gastroenterology and Hepatology, Enschede, Netherlands, ⁶Erasmus MC, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁷Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ⁸Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁹University Medical Center Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands, ¹⁰Medisch Centrum Haaglanden, Department of Gastroenterology and Hepatology, Den Haag, Netherlands, ¹¹Jeroen Bosch Hospital, Department of Gastroenterology and Hepatology, Den Bosch, Netherlands

Contact E-Mail Address: loriane.verleye@maastrichtuniversity.nl

Introduction: Ustekinumab (UST), a monoclonal antibody targeting the p40 subunit of interleukins IL-12 and IL-23, has been approved by the European Medicines Agency for the treatment of ulcerative colitis (UC) in 2019. Although clinical effectiveness and safety of UST in UC have been shown in clinical trials, long-term real-world data are limited, especially beyond one year of follow-up.

Aims & Methods: We collected data from the IBDREAM registry¹, a telemedicine platform for IBD patients, and the Initiative on Crohn and Colitis (ICC) registry². Both Dutch multicentre registries collect prospective observational data from IBD patients. Adult patients with UC who received at least one intravenous and two subcutaneous doses of UST with no prior history of colectomy were included. The two primary outcomes were corticosteroid-free clinical remission, defined as Simple Clinical Colitis Activity Index (SCCAI) ≤ 2 , and corticosteroid-free biochemical remission, as defined by fecal calprotectin $\leq 250\mu\text{g/g}$, at week 52 and week 104. Furthermore, data on effectiveness up to week 156, drug persistence rate, dose escalations, concomitant medication use and adverse events were collected.

Results: A total of 127 patients were included, 53 (41.7%) of which were female. Median age at baseline was 49 (IQR: 26). Seven patients (5.5%) had not previously been treated with at least one biological and/or small molecule agent, while 35.4%, 30.7%, and 28.3% of patients had previously been treated with one, two or at least three different advanced therapies, respectively.

Effectiveness results are summarised in Table 1. At week 52 and week 104, 39.4% and 39.2% of patients were in corticosteroid-free clinical remission and 36.8% and 33.9% of patients were in corticosteroid-free biochemical remission, respectively. At these timepoints, 39.2% and 37.1% of patients who had clinically active disease at baseline (n=75) achieved corticosteroid-free clinical remission. In the subgroup of patients with biochemically active disease at baseline (n=56), 47.2% and 40.6% achieved corticoste-

roid-free biochemical remission. Similar rates were observed at week 156, although less patients reached this follow-up time. Drug persistence rate was 77.2% after one year, and 65.6% after two years. A total of 39 patients discontinued UST before completing two years of follow-up; 27 of these patients stopped during the first year. Seventeen patients discontinued UST because of primary non-response, sixteen due to secondary loss of response and nine because of other reasons (including colorectal carcinoma (n=1), sustained remission and side effects). Sixty-two adverse drug reactions were recorded in 36 patients and eight patients required hospitalisation during follow-up.

	Corticosteroid-free clinical remission	Corticosteroid-free clinical remission, subgroup with clinically active disease at baseline (n=75)	Corticosteroid-free biochemical remission	Corticosteroid-free biochemical remission, subgroup with biochemically active disease at baseline (n=56)
Baseline	22/101 (21.8%)		22/86 (25.6%)	
Week 12	44/87 (50.6%)	27/60 (45.0%)	29/88 (33.0%)	14/44 (31.8%)
Week 24	43/80 (53.8%)	29/53 (54.7%)	29/75 (38.7%)	17/38 (44.7%)
Week 52	28/71 (39.4%)	20/51 (39.2%)	25/68 (36.8%)	17/36 (47.2%)
Week 104	20/51 (39.2%)	13/35 (37.1%)	19/56 (33.9%)	13/32 (40.6%)
Week 156	8/23 (34.8%)	5/15 (33.3%)	11/28 (39.3%)	10/19 (52.6%)

* total number of patients differs per group due to missing data or not yet reaching follow-up time at time of data analysis

† patients were considered corticosteroid-free if they were not using systemic corticosteroids at the respective timepoints

Table 1. Clinical and biochemical effectiveness of ustekinumab over time*†

Conclusion: In this real-world study, over one third of patients with UC were in corticosteroid-free clinical and/or biochemical remission two years after starting UST. The medication was relatively effective, despite the partly treatment-refractory study population. UST was well-tolerated and no new safety signals were identified. The study results indicate that UST is an effective and safe long-term therapy for patients with UC.

References: 1. de Jong ME, Smits LJT, van Ruijven B, den Broeder N, Russel M, Romkens TEH, et al. Increased Discontinuation Rates of Anti-TNF Therapy in Elderly Inflammatory Bowel Disease Patients. *J Crohns Colitis*. 2020;14(7):888-95.

2. Biemans VBC, van der Meulen-de Jong AE, van der Woude CJ, Lowenberg M, Dijkstra G, Oldenburg B, et al. Ustekinumab for Crohn's Disease: Results of the ICC Registry, a Nationwide Prospective Observational Cohort Study. *J Crohns Colitis*. 2020;14(1):33-45.

Disclosure: **RW** served as a speaker and/or an advisory board member for Ferring, Galapagos, Janssen and Pfizer; **ACdV** served as an advisory board member for AbbVie, Bristol Meyers Squibb, Janssen and Takeda; **AEvdM** served as a speaker and/or an advisory board member for AbbVie, Dear Health, Ferring, Galapagos, Janssen, Takeda, Tramedico, and Vedanta, and has received research grants from Cablon, Galapagos, Nestle, Norgine, and ZonMW; **ML** served as a speaker and/or principal investigator for Abbvie, Celgene, Covidien, Dr. Falk, Ferring, Gilead, GlaxoSmithKline, Janssen-Cilag, Merck Sharp & Dohme, Pfizer, Protagonist therapeutics, Receptos, Takeda, Tillotts, Tramedico; and has received research grants from AbbVie, Merck Sharp & Dohme, Achmea healthcare and ZonMw; **FvS** served as an advisory board member for Galapagos and Takeda; **SvdM** served as an advisory board member for AbbVie, Janssen and Pfizer; **MP** served as a speaker for Bristol Meyers Squibb, Janssen-Cilag and Takeda, has received non-restricted research grants from AbbVie, Galapagos, Horizon 2020, Johnson and Johnson, Maag Lever Darm Stichting, Takeda and ZonMw, and non-financial support from Immunodiagnostics; **ZM** served as a speaker and/or adviser for Abbvie, Galapagos, Johnson and Johnson, Lilly and Pfizer, and has received grants from Galapagos, Maag Lever Darm Stichting, Niels Stensen Fellowship and ZonMw; **TER** served as a speaker and/or an advisory board member for Abbvie, Bristol Meyers Squibb and Janssen

MD served as a speaker and/or an advisory board member for AbbVie, Bristol Meyers Squibb, Celltrion, Galapagos, Janssen and Takeda, and has received grants/research support from Bristol Meyers Squibb, Galapagos Janssen and Pfizer.

Optimising safety and efficacy of polyp treatment

11:30-12:30 / Lehar 1

OP087

EFFICACY OF PROPHYLACTIC CLIP CLOSURE FOLLOWING COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DELAYED BLEEDING: A PHASE III MULTICENTER RANDOMIZED CONTROLLED TRIAL (EPOC TRIAL)

Y. Tamaru¹, T. Kuwai^{2,3}, A. Miyakawa⁴, N. Kanazawa⁵, Y. Sumida⁶, H. Kamada¹, S. Semba¹, N. Kato¹, S. Sugata², Y. Okuda², Y. Teraoka², T. Mizumoto¹, R. Kusunoki², T. Hatakeyama¹, A. Yamaguchi², H. Kouno², S. Yoshida¹
¹National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Endoscopy, Kure, Japan, ²National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Gastroenterology, Kure, Japan, ³Hiroshima University Hospital, Gastrointestinal Endoscopy and Medicine, Hiroshima, Japan, ⁴Asahi General Hospital, Gastroenterology, Asahi, Japan, ⁵Japan Organization of Occupational Health and Safety, Yokohama Rosai Hospital, Gastroenterology, Yokohama, Japan, ⁶Kitakyushu Municipal Medical Center, Gastroenterology, Kitakyushu, Japan

Contact E-Mail Address: tamaru.yuzuru.vh@mail.hosp.go.jp

Introduction: Delayed bleeding is a common adverse event following endoscopic resection of colorectal tumors. Although prophylactic clip closure following endoscopic mucosal resection is reported decreased delayed bleeding rate, the evidence is lacking with regard to colorectal endoscopic submucosal dissection (ESD).

Aims & Methods: This multicenter randomized controlled trial was conducted at 4 Japanese institutions (Kure Medical Center and Chugoku Cancer Center, Asahi General Hospital, Yokohama Rosai Hospital, and Kitakyushu Municipal Medical Center), and aimed to evaluate the efficacy of prophylactic clip closure following colorectal ESD to prevent delayed bleeding. Patients undergoing ESD for 20-50 mm colorectal tumor were enrolled and randomly assigned to closure or non-closure groups. The primary endpoint was delayed bleeding rate, defined as overt bleeding that required endoscopic hemostasis and/or reception of blood transfusions.

Results: The closure and non-closure groups comprised 150 and 149 cases in the intention-to-treat (ITT) analysis, while 142 and 141 cases in the per-protocol (PP) analysis. Patient characteristics, lesion factors, and clinicopathological characteristics of resected lesions were well balanced between the groups. In the ITT analysis, delayed bleeding was 1.3% (2/150) in the closure group, and 8.7% (13/149) in the non-closure group (odds ratio [OR] 0.14; 95% confidence interval [CI] 0.03-0.64; $p = 0.003$). While in the PP analysis, delayed bleeding was 0.7% (1/142) in the closure group, and 8.5% (12/141) in the non-closure group (OR 0.08; 95%CI 0.01-0.59; $p = 0.001$). Delayed perforation was not occurred and post-ESD coagulation syndrome rate (20.0% vs. 20.1%) was not significantly different between the groups.

The multivariate logistic regression analyses revealed prophylactic clip closure was identified as a significant independent preventive factor of delayed bleeding (OR 0.22; 95%CI 0.05-0.76; $p = 0.015$).

Conclusion: The prophylactic clip closure following colorectal ESD is recommended as it reduces delayed bleeding rate (Clinical trial registration number: UMIN000043675).

Disclosure: Nothing to disclose.

OP088

RANDOMIZED CONTROLLED TRIAL OF A CLOUD-BASED ARTIFICIAL INTELLIGENCE (AI) COMPUTER-AIDED DIAGNOSIS (CADX) SYSTEM IN NON-EXPERT ENDOSCOPISTS

R. Kader¹, P. Bassett², Y. Kabir¹, S. Cheung¹, L. Macabodbod¹, A. Jayanthi¹, M. Chand¹, L.B. Lovat¹, CADDIE Investigators Team
¹University College London, Wellcome/EPSCRC Centre for Interventional and Surgical Sciences (WEISS), London, United Kingdom, ²Statsconsultancy Ltd, London, United Kingdom

Contact E-Mail Address: rawen158@hotmail.com

Introduction: Non-expert endoscopists' optical diagnosis (OD) of colorectal polyps falls short of 'resect and discard' and 'diagnose and leave' thresholds. Previous CADx studies are limited to locally deployed hardware AI systems and are mainly evaluated in expert endoscopists. CADDIE is a cloud-based CADx system that receives the live image stream from the endoscopy screen via the hospital's internet network, where the AI algorithm processes the images and outputs its diagnosis (adenoma, non-adenoma or uncertain) on the endoscopy screen.

We aimed to assess the performance of the real-time cloud-based CADDIE system when colonoscopy is undertaken by non-expert endoscopists (adenoma detection rate below 30%).

Aims & Methods: We enrolled 739 patients between April 2021 - Dec 2022, scoped by 32 endoscopists in 9 UK hospitals. Each endoscopist was limited to a maximum of 60 procedures and required to perform more than 20% of this target. Patients were block randomised in a 1:1 ratio to standard of care (SOC) or intervention (CADDIE), stratified by endoscopist and indication. OD accuracy of humans alone (SOC arm) and humans aided by CADDIE (CADDIE arm) were compared to the CADDIE system's stand-alone performance in the CADDIE arm.

High Confidence Optical Diagnosis	Study Arm	Accuracy		Adjusted Analysis	
		n / N	% (95% CI)	% difference (95% CI) (+)	p-value
Small/diminutive (≤10mm)	Human (SOC)	145 / 185	78.4 (71.7, 84.1)	8.1 (0.4, 15.7)	0.04
	Human (CADDIE)	155 / 186	83.3 (77.2, 88.4)	4.5 (-2.0, 11.0)	0.18
	CADDIE	160 / 182	87.9 (82.2, 92.3)	-	-
Diminutive (≤5mm)	Human (SOC)	110 / 133	82.7 (75.2, 88.7)	3.4 (-5.6, 12.4)	0.46
	Human (CADDIE)	105 / 129	81.4 (73.6, 87.7)	4.7 (-3.8, 13.2)	0.28
	CADDIE	103 / 119	86.6 (79.1, 92.1)	-	-

n = Total polyps correctly diagnosed
N = Total number of polyps optically diagnosed
(+) = Percentage difference of CADDIE stand-alone performance in CADDIE arm minus human alone OD in SOC arm (Human SOC) or human OD aided by CADDIE in CADDIE arm (Human (CADDIE))

Results: There were 615 evaluable patients after exclusions as pre-defined in the study protocol. There were 523 eligible polyps (270 SOC arm, 253 CADDIE arm). The CADDIE system diagnosed 17.8% of polyps (45/253) as "uncertain".

Human alone (SOC) OD accuracy was 75.9%, human OD aided by CADDIE was 80.2%, whilst the stand-alone CADDIE system was significantly higher than both at 87.5% ($p=0.005$ and $p=0.04$, respectively). Similarly, in the sub-analysis of small/diminutive polyps (≤10mm), human alone OD accuracy was 73.8%, human OD aided by CADDIE was 79.0%, whilst the CADDIE system was significantly higher than both at 87.9% ($p=0.001$ and $p=0.02$). Although results were not significant for diminutive polyps (≤5mm), the

trend was towards higher accuracy in the CADDIE system (86.6%) compared to humans alone and human OD aided by CADDIE (77.3%; $p=0.05$). In sub-analyses of high-confidence (HC) OD, the CADDIE system's accuracy for ≤ 10 mm polyps was significantly higher (87.9%) than humans alone (78.4%; $p=0.04$), with no difference to humans aided by CADDIE (83.3%; $p=0.18$). For HC OD of ≤ 5 mm polyps, where the sample size is smaller, the CADDIE system's accuracy was higher (86.6%) but not significant compared to humans alone (82.7%; $p=0.46$) and humans aided by CADDIE (81.4%; $p=0.28$).

The OD-derived colonoscopy surveillance interval accuracy was 87.2% in humans alone (SOC), 86.8% in humans aided by CADDIE and 90.9% for the CADDIE system.

Conclusion: We demonstrate proof of concept and robust results for a cloud-based CADx system. Further research is warranted in the human-computer interaction to optimise non-expert endoscopists' OD performance to that of CADx systems.

Disclosure: Dr Rawen Kader and Professor Laurence Lovat have received medical consultancy fees from Odin Vision

OP089

COMPARISON OF THE EFFICACY AND TOLERABILITY OF ELOBIXIBAT PLUS SODIUM PICOSULFATE WITH MAGNESIUM CITRATE AND SPLIT-DOSE 2-L POLYETHYLENE GLYCOL WITH ASCORBIC ACID FOR BOWEL PREPARATION BEFORE OUTPATIENT COLONOSCOPY: RESULTS OF MULTICENTER, RANDOMIZED, CONTROLLED TRIAL

H. Takamaru¹, K. Hotta², Y. Otake³, D. Yamaguchi⁴, Y. Shimodate⁵, N. Hanabata⁶, H. Ikematsu⁷, Y. Yabuuchi⁸, Y. Sano⁹, R. Shimoda¹⁰, S. Sugimoto¹¹, M. Oba¹², T. Kanata¹², K. Kimura³, Y. Kishida², K. Takada², S. Ito², K. Imai², K. Hosotani⁸, T. Murano⁷, M. Yamada¹, K. Shinmura⁷, R. Takezawa⁵, M. Tomonaga¹⁰, Y. Saito¹,

The E-PLUS trial working group

¹National Cancer Center Hospital, Endoscopy Division, Tokyo, Japan, ²Shizuoka Cancer Center, Division of Endoscopy, Sunto, Japan, ³Subaru Health Insurance Society Ota Memorial Hospital, Department of Gastroenterology, Ota, Japan, ⁴National Hospital Organization Ureshino Medical Center, Department of Gastroenterology, Ureshino, Japan, ⁵Kurashiki Central Hospital, Department of Gastroenterology and Hepatology, Kurashiki, Japan, ⁶Aomori Prefectural Central Hospital, Department of Gastroenterology, Aomori, Japan, ⁷National Cancer Center Hospital East, Department of Gastroenterology and Endoscopy, Kashiwa, Japan, ⁸Kobe City Medical Center General Hospital, Department of Gastroenterology, Kobe, Japan, ⁹Sano Hospital, Gastrointestinal Center, Kobe, Japan, ¹⁰Saga University Hospital, Department of Endoscopic Diagnostics and Therapeutics, Saga, Japan, ¹¹Japanese Red Cross Ise Hospital, Department of Gastroenterology, Ise, Japan, ¹²National Center of Neurology and Psychiatry, Department of Clinical Data Science, Clinical Research & Education Promotion Division, Tokyo, Japan

Contact E-Mail Address: htakamar@ncc.go.jp

Introduction: Sodium picosulfate (SP)/magnesium citrate (MC) and polyethylene glycol (PEG) plus ascorbic acid are recommended by Western guidelines as laxative solutions for bowel preparation. The standard formulation for bowel preparation is PEG; however, it requires a large dose and has a distinctive taste that is considered unpleasant. SP/MC requires a small dose and ensures fluid intake because it is administered in another beverage. Therefore, clinical studies have shown that SP/MC is superior to PEG in terms of acceptability.

Aims & Methods: Our aim was to compare the novel bowel cleansing method (test group) consisting of SP/MC with elobixibat hydrate and the standard bowel cleansing method consisting of PEG plus ascorbic acid (standard group) in patients preparing for outpatient colonoscopy. This was a multicenter, single-blind, non-inferiority, randomized controlled trial. Patients 40-69 years of age scheduled for outpatient colonoscopy were enrolled. Patients with a history of abdominal or pelvic surgery, constipation, inflammatory bowel disease, or severe organ dysfunction were excluded. The target number of study participants was 540 (standard group, 270 cases; test group, 270 cases). The primary endpoint was bowel cleansing (Boston Bowel Preparation Scale [BBPS] score ≥ 6). Secondary endpoints were patient acceptability, adverse events, polyp/adenoma detection rate, number of polyps/adenomas detected, degree of bowel cleansing according to BBPS (BBPS score ≥ 8), degree of bowel cleansing according to Aronchik scale, and bowel cleansing time. The non-inferiority margin for the primary endpoint was 10%. A study protocol of the present study has already been published in a peer-reviewed journal.

Results: Of 540 participants enrolled, efficacy was analyzed in 524 participants (test group, $n=263$; standard group, $n=261$) in the full analysis set. Non-inferiority of the test group was demonstrated for the primary endpoint (BBPS ≥ 6): 96.2% vs. 97.7% for test and standard group, respectively difference was -1.5%, [95%confidence interval (CI), -4.8 to 1.6%] with $P<0.001$ for non-inferiority. For the secondary endpoint BBPS ≥ 8 was lower in test group (79.5% vs 91.2%: difference -11.7% [95% CI, -17.8 to -5.8%]). Patient acceptability was superior in the test group in the key questions (1. Was the bowel preparation medication easy to use? 2. Were all bowel preparation medications administered internally? 3. What is your overall impression of the bowel preparation? 4. How did the bowel preparation medicine taste? 5. Would you like to use the same bowel preparation medicine for your next colonoscopy?) Adverse events were similar in both groups.

Conclusion: A new regimen of elobixibat plus sodium picosulfate with magnesium citrate was non-inferior in bowel cleansing and superior in patient's acceptability compared to split-dose 2-L polyethylene glycol with ascorbic acid.

References: 1) Hotta K, Otake Y, Yamaguchi D, et al. Comparison of the efficacy and tolerability of elobixibat plus sodium picosulfate with magnesium citrate and split-dose 2-L polyethylene glycol with ascorbic acid for bowel preparation before outpatient colonoscopy: a study protocol for the multicentre, randomised, controlled E-PLUS trial. BMC Gastroenterol 2024 Feb 3;24(1):61.doi: 10.1186/s12876-024-03146-6.

Disclosure: The primary investigator (Kinichi Hotta) had received research funding from Nippon Chemiphar Co. Ltd.

OP090

ACCURACY OF COMPUTER-AIDED DIAGNOSIS IN COLONOSCOPY VARIES ACCORDING TO POLYP LOCATION. A SYSTEMATIC REVIEW AND META-ANALYSIS

T. Rizkala¹, C. Hassan², M. Spadaccini¹, Y. Mori³, P. Sharma⁴, D.K. Rex⁵, A. Repici¹, CADx study group
¹Humanitas Clinical and Research Center –IRCCS–, Endoscopy Unit, Rozzano, Italy, Milano, Italy, ²Humanitas Clinical and Research Center –IRCCS–, Endoscopy Unit, Rozzano, Italy, Gastroenterology, Rome, Italy, ³University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway, ⁴University of Kansas School of Medicine Dept. of Gastroenterology, Gastroenterology, Leawood, United States of America, ⁵Indiana University School of Medicine, Division of Gastroenterology, Indianapolis, Indiana, USA, Gastroenterology, Indiana, United States of America

Contact E-Mail Address: tommyrizkala@outlook.com

Introduction: Computer-Aided Diagnosis (CADx) is emerging as a tool to assist endoscopists in differentiating neoplastic from non-neoplastic small polyps during colonoscopy. In clinical practice, the application of optical diagnosis strategies, such as “the resect and discard” and the “leave-in-situ”, vary according to the polyp location. This study aimed to evaluate the impact of polyp location (proximal colon vs. distal colon) on the diagnostic performance of CADx systems for small polyps (<5mm) identified during colonoscopy.

Aims & Methods: A comprehensive literature search was conducted in MEDLINE, Scopus, and Embase databases, with the last search performed on March 12, 2024. Studies evaluating the stand-alone performance of real-time CADx for predicting the histology of colorectal polyps ≤5mm in size were included. Studies without pathological confirmation or with fewer than 50 patients were excluded. The primary endpoints were the sensitivity and specificity of the CADx in the proximal and distal colon. Secondary outcomes were the negative predictive value (NPV), positive predictive value (PPV) and accuracy of the CADx alone in the proximal and distal colon. The distal colon comprised the rectum and sigmoid, while the proximal colon comprised the portion extending from the descending colon to the cecum.

Results: We included 11 studies for analysis with a total of 7,782 polyps (≤5mm). CADx accuracy was significantly lower in the proximal colon compared to the rectosigmoid in terms of specificity (62% versus 84%; risk ratio (RR): 0.78 [95% confidence interval (CI): 0.72-0.84], I²=47.08%), NPV (64% versus 93%; RR: 0.71 [95% CI: 0.64-0.79], I²=74.69%), and accuracy (81% vs 86%; RR: 0.95 [95% CI: 0.91-0.99], I²=72.50%). On the other hand, sensitivity (87% vs 87%; RR: 1.00 [95% CI: 0.98-1.02], I²=0%) and PPV (87% vs 76%; RR: 1.11 [95% CI: 1.06-1.17], I²=53.85%) were comparable.

Conclusion: The diagnostic performance of CADx appears to depend on the location of the polyp, being substantially lower for proximal than distal lesions, mainly due to a lower specificity in the proximal colon.

Disclosure: Cesare Hassan: Fujifilm Co. (consultancy); Medtronic Co. (consultancy), Yuichi Mori: Olympus Corp (consultancy, speaking honorarium, equipment loan); Cybernet System (ownership interest), Alessandro Repici: Fujifilm Co. (consultancy); Olympus Corp (consultancy); Medtronic Co. (consultancy).

OP091

A PROSPECTIVE MULTICENTER RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE EFFICACY OF TEXTURE AND COLOR ENHANCEMENT IMAGING (TXI) OBSERVATION IN THE DETECTION OF COLORECTAL LESIONS

K. Shinmura¹, H. Ikematsu^{1,2}, N. Toyoshima³, Y. Mizuguchi³, M. Shiroyama⁴, T. Sakamoto⁴, S. Tomaru⁵, N. Tamai⁶, A. Fujimoto⁷, M. Misawa⁸, T. Okumura⁹, K. Hotta⁹, T. Shibata¹⁰, Y. Saito³

¹National Cancer Center Hospital East, Gastroenterology and Endoscopy, Kashiwa, Japan, ²IMSUT Hospital, The Institute of Medical Science, The University of Tokyo, Gastroenterology, Tokyo, Japan, ³National Cancer Center Hospital, Endoscopy, Tokyo, Japan, ⁴University of Tsukuba Hospital, Gastroenterology, Tsukuba, Japan, ⁵Gunma University Graduate School of Medicine, Gastroenterology and Hepatology, Maebashi, Japan, ⁶Jikei University School of Medicine, Endoscopy, Tokyo, Japan, ⁷Toho University Omori Medical Center, Gastroenterology and Hepatology, Tokyo, Japan, ⁸Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ⁹Shizuoka Cancer Center, Endoscopy, Shizuoka, Japan, ¹⁰National Cancer Center, Biostatistics Division, Center for Research Administration and Support, Tokyo, Japan

Contact E-Mail Address: keshinmu@east.ncc.go.jp

Introduction: Early detection and removal of colorectal adenomatous lesions is effective in reducing the incidence and mortality of colorectal cancer. To achieve this, it is important to improve the detection of colorectal lesions. Newly endoscopy technology, texture and color enhancement imaging (TXI) is expected to enhance visibility of lesion by adjusting the color, structure, and brightness of images taken with white-light imaging (WLI) using EVIS X1 system (Olympus Medical Systems Co., Tokyo, Japan). Our previous retrospective study indicated that TXI improve the detection of colorectal neoplastic lesions. However, it is unclear that ability of detection in TXI is superior to that of WLI.

Aims & Methods: We conducted a prospective multicenter randomized controlled trial to verify the efficacy of TXI in the detection of colorectal neoplastic lesions, when compared with WLI (jRCT1032230089). This trial was conducted at 8 institutions in Japan between May and November 2023. The eligibility criteria included patients aged 20–80 years who were scheduled for screening, post-endoscopic surveillance, or work-up for a positive fecal immunochemical test or abdominal symptoms. Patients were randomly assigned (1:1) to TXI or WLI (control group).

In all colonoscopies, EVIS X1 system and CF-EZ1500DI were used. The primary endpoint was mean adenoma per procedure (MAP) in per protocol set (PPS). Other endpoints included adenoma detection rate (ADR), advanced ADR (advanced adenoma: more than 10 mm in diameter, villous or tubulovillous in histology, or high-grade dysplasia), polyp detection rate (PDR), and flat polyp detection rate (FDR).

We assumed the TXI mode observations to have an improvement effect of MAP with a difference of $\delta=0.3$ on WLI and the standard deviations of MAP in TXI and WLI were expected to be 1.8 and 1.3, respectively. The required number of subjects for analysis was calculated to be 960, considering an expected dropout rate of 10%, when the two-sided significance level was set at 0.05 and power at 0.8.

Results: A total of 960 patients were enrolled. In PPS, 896 patients were analyzed (451 in TXI and 445 in WLI). In MAP, there was no statistically significant difference between the groups (TXI: 1.4 [95% CI: 1.2-1.6] vs. WLI: 1.5 [1.3-1.7]). ADR was similar in the groups (57.21% [52.49-61.82] vs. 55.96 [51.20-60.63]). Advanced ADR tend to be higher in TXI than WLI (11.09% [8.34-14.35] vs. 8.54[6.11-11.53]).

PDR was significantly higher in TXI than WLI (82.48% [78.65-85.88] vs. 74.38 [70.06-78.38]. FDR was significantly higher in TXI than WLI (76.50% [72.31-80.34] vs. 70.34 [65.86-74.55]).

Conclusion: This trial could not show the superiority of TXI over WLI in MAP and ADR. However, it showed that of TXI over WLI in PDR and FDR, indicating that TXI may have ability to detect more flat colorectal lesions which have malignant potential or are difficult to detect.

Disclosure: Nothing to disclose.

Microbiota, chronic inflammation and cancer

11:30-12:30 / Lehar 2

OP092

MULTI-COHORT CROSS-DISEASE METAGENOMIC ANALYSIS OF IMMUNE-MEDIATED INFLAMMATORY DISEASES IDENTIFIES SHARED OR UNIQUE GUT MICROBIAL SIGNATURES AND THEIR POTENTIAL CLINICAL IMPLICATIONS IN INFLAMMATORY BOWEL DISEASE

Y. Jung¹, H.-S. Oh¹, M. Chalita¹, J. Moon¹, J. Yang¹, K. Lee¹, S. Park¹, Y.O. Kim¹, J. Chun¹

¹CJ Bioscience, Inc., Seoul, South Korea

Contact E-Mail Address: jenny.yeonjae.jung@gmail.com

Introduction: Immune-mediated inflammatory diseases (IMID) involve immune dysregulation, potentially damaging various organs [1]. Gut microbiome regulates immune homeostasis, and abnormality of it is associated with various inflammatory diseases [2,3]. However, previously reported biomarkers have considerable limitations.

Findings are often specific or inconsistent across studies, and while some studies assess common microbial patterns across diverse diseases, they often overlook disease pathobiology. To address this, we conducted a consensus-based approach to identify and dissect robust biomarkers common or unique to different IMIDs.

Aims & Methods: We collected and uniformly profiled public human gut metagenome data of IMIDs, using universal bacterial core gene-based taxonomic profiling [4] and pangenome-based functional profiling. A total of 2,252 samples from 18 studies of 28 case-control sub-cohorts of IMIDs (10 for Crohn's disease;CD, 9 for ulcerative colitis;UC, 4 for ankylosing spondylitis;AS, 2 for chronic obstructive pulmonary disease;COPD, 2 for multiple sclerosis;MS, and 1 for psoriasis;PsO) were included as discovery set, and 253 samples from 3 studies for 7 case-control sub-cohort sets of CD or UC were included as external validation set. Cross-cohort and one-study-leave out validations were performed for the discovery set, and the external validation set was evaluated using the trained model from the IMID discovery set. For the individual marker analysis, significance scores were combined for each criteria, including disease diagnosis, and inflammatory bowel disease (IBD) and nonGI-IMIDs (MS, AS, COPD, and PsO). Additionally, multi cohort-based networks of IBD studies were assessed. Furthermore, to explore potential interpretation of the signatures in other clinical settings, we examined the IBD studies with disease activity as well as FMT study.

Results: Cross-cohort validation of IMID case-control sub-cohorts of the discovery set at species-level showed that intra-cohort performance had significantly higher area under curve (AUC) compared to inter-cohort (W=3701, p-value<0.001), and among the inter-cohort, intra-disease had significantly higher AUC than inter-disease (W=23278, p-value<0.001). When the external IBD sub-cohorts were tested, the trained model of the IMID set showed the average AUC 0.818 (SD=0.089).

In individual signatures, there were several features commonly found to be highly scored in at least 5 IMIDs, including *Enterocloster bolteae* and probable pyridine nucleotide-disulfide oxidoreductase (K21739) in the case-side and *Faecalibacterium* sp. (CLG_10009380_s) and *Oscillibacter* sp. (MSSCM00948369_s) in the control-side. There were also disease or disease category-specific patterns such as *Gemmiger formicilis* and *Alistipes shahii* consistently found to be enriched in control-side in IBD but not in nonGI-IMIDs.

Furthermore, we checked the signatures obtained from our analysis in the other clinical settings such as IBD samples with disease activity scores as well as FMT study. For example, *Dysosmobacter welbionis* was negatively correlated with Harvey Bradshaw Index in 2 CD sub-cohorts (Spearman's rho=-0.5 and -0.26, p-value=0.009 and 0.039, respectively).

Conclusion: Our study analyzed multi-cohort gut metagenome data to identify consistent signatures across various IMIDs. Cross-cohort validation showed better intra-disease prediction compared to inter-disease, yet the performance of predictions between diseases was still comparable. Several microbial signatures were either shared or unique across IMIDs, with some showing potential clinical relevance in IBD.

References:

1. McInnes IB, Gravalles EM. Immune-mediated inflammatory disease therapeutics: past, present and future. *Nat Rev Immunol*. 2021 Oct;21(10):680-686. doi: 10.1038/s41577-021-00603-1. Epub 2021 Sep 13. PMID: 34518662; PMCID: PMC8436867.
2. Forbes JD, Van Domselaar G, Bernstein CN. The Gut Microbiota in Immune-Mediated Inflammatory Diseases. *Front Microbiol*. 2016 Jul 11;7:1081. doi: 10.3389/fmicb.2016.01081. PMID: 27462309; PMCID: PMC4939298.
3. Forbes JD, Chen CY, Knox NC, Marrie RA, El-Gabalawy H, de Kievit T, Alfa M, Bernstein CN, Van Domselaar G. A comparative study of the gut microbiota in immune-mediated inflammatory diseases-does a common dysbiosis exist? *Microbiome*. 2018 Dec 13;6(1):221. doi: 10.1186/s40168-018-0603-4. PMID: 30545401; PMCID: PMC6292067.
4. Chalita M, Ha SM, Kim YO, Oh HS, Yoon SH, Chun J. Improved Metagenomic Taxonomic Profiling Using a Curated Core Gene-Based Bacterial Database Reveals Unrecognized Species in the Genus *Streptococcus*. *Pathogens*. 2020 Mar 10;9(3):204. doi: 10.3390/pathogens9030204. PMID: 32164338; PMCID: PMC7157611.

Disclosure: Y Jung, HS Oh, M Chalita, J Moon, J Yang, K Lee, S Park, YO Kim and J Chun are employees of CJ Bioscience, Inc.

OP093

SHIFT IN MICROBIAL COMPOSITION OVER ONE-YEAR AMONG PATIENTS WITH NEWLY DIAGNOSED CROHN'S DISEASE REFLECTS CLINICAL DYNAMICS AND TREATMENT WITH ANTI-TNF: DATA FROM A PROSPECTIVE REAL-WORLD STUDY

T. Sharar Fischler^{1,2}, L. Reshef³, L. Godny^{1,2}, A. Freidenberg^{1,2}, M. Pauker^{1,2}, K.M Rabinowitz⁴, I. Avni-Biron^{1,2}, U. Gophna³, I. Dotan^{1,2}, H. Yanai^{1,2}

¹Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ²Tel Aviv University, Faculty of Medical & Health Sciences, Tel Aviv, Israel, ³Tel Aviv University, The George S. Wise Faculty of Life Sciences, Tel Aviv, Israel, ⁴Rabin Medical Center, The Felsenstein Research Center, Petah Tikva, Israel

Contact E-Mail Address: talifis@yahoo.com

Introduction: Gut microbiota in Crohn's disease (CD) exhibits considerable variability, with conflicting associations with disease severity and response to therapeutic intervention. We aimed to longitudinally investigate the dynamics of microbial composition in a cohort of patients with newly diagnosed, treatment-naïve Crohn's disease (ndCD) over a one-year period.

Aims & Methods: A prospective real-world study was conducted, enrolling patients with ndCD who were treatment-naïve. Treatment decisions were made by physicians with expertise in CD management. Key one-year clinical outcomes included corticosteroid-free clinical remission (CSFR) and biochemical remission (BR), defined as C-reactive protein levels <1mg/dL and fecal calprotectin levels <150ug/g. Paired stool samples were subjected to 16S rRNA gene sequencing (V4 region) at diagnosis and after one year, followed by analysis for microbial diversity and dysbiosis indices. A linear mixed-effect model was constructed to identify factors associated with microbial alterations and specific taxa driving these alterations, while controlling for confounding variables.

Results: Seventy-five patients completed the one-year follow-up (49.3% female, median age 27 years [IQR 22-38.5]); 45 (60%) received biologics (95.5% anti-tumor necrosis factor [TNF]). Rates of CSFR, BR, and combined CSFR-BR at one-year post-diagnosis were 64%, 56%, and 45.3%, respectively. Analysis of microbial composition revealed significant improvements in microbial indices among patients achieving all desired clinical outcomes, characterized by increased microbial diversity (Shannon index, $p=0.004$, $p=0.002$, $p=0.004$, respectively) and decreased dysbiosis (microbial dysbiosis index [MDI], $p=0.003$, $p=0.04$, $p=0.01$, respectively). Such improvements were not observed in patients failing to achieve CSFR, BR or combined CSFR-BR. Notably, patients treated with biologics, irrespective of outcome achievement, exhibited prominent shifts (improvement) in microbial composition (both indices $p<0.001$), whereas non-treated patients did not demonstrate significant changes (Shannon index, $p=0.53$; MDI, $p=0.81$).

Furthermore, microbial composition at baseline was more disrupted among patients treated with biologics compared to non-treated patients (Shannon index, $p=0.04$; MDI, $p=0.03$). The linear mixed model analysis confirmed a positive association between biologics and favorable changes in microbial indices (Shannon index, $p=0.02$; MDI, $p=0.04$), identifying an increase in 20 gut commensal taxa (considered beneficial) and a decrease in *Escherichia coli* among the biologics-treated subgroup. Conversely, no taxa exhibited significant alterations in the non-biologics treated subgroup.

Conclusion: In a real-world cohort of patients with treatment-naïve ndCD, clinical improvement over one year was associated with improvement in microbial composition. Treatment with anti-TNF agents was associated with improvement in microbial composition irrespective of clinical outcomes. These findings suggest that microbial composition reflects inflammatory activity and may be positively and independently modified by anti-TNF treatment.

Disclosure: Nothing to disclose.

OP094

HYPERBILIRUBINEMIA ALTERS LIVER-GUT INTERACTIONS AND GUT MICROBIOTA COMPOSITION

A. Sander^{1,2}, A. Oßwald^{2,1}, J. Unger¹, H. Schmerbach², K. Neuhaus¹, R. Tukey³, D. Haller⁴, T. Grune⁵, S. Ocvirk^{1,2}

¹Technical University Munich, ZIEL - Institute for Food and Health, Freising-Weihenstephan, Germany, ²German Institute for Human Nutrition, Intestinal Microbiology, Potsdam-Rehbrücke, Germany, ³University of California San Diego, Pharmacology, San Diego, United States of America, ⁴Technical University of Munich, School of Life Sciences co-affiliated with School of Medicine, Freising, Germany, ⁵German Institute for Human Nutrition, Molecular Toxicology, Potsdam-Rehbrücke, Germany

Contact E-Mail Address: anika.sander@tum.de

Introduction: Gilbert's Syndrome (GS) is a benign polymorphism of the *UGT1A1* gene, leading to decreased enzyme activity in the liver and increased levels of unconjugated bilirubin in the blood, defined as mild hyperbilirubinemia (HBIL) with serum levels between 20 and 100 µM. Mild HBIL is associated with reduced inflammation, lower levels/numbers of reactive oxygen species (ROS), a lean phenotype, reduced risk for metabolic diseases, and lower cancer risk.

Despite the high prevalence of GS in healthy individuals (~5-12% worldwide) and its well-known clinical features, the effects of HBIL on the intestine, the primary site of bilirubin excretion, and its interactions with the gut microbiota remain unclear. We propose that an altered bilirubin metabolism in the liver affects microbe-host interactions in the colon.

Aims & Methods: Germ-free (GF) and specific-pathogen-free (SPF) C57BL/6N wildtype mice with induced HBIL and transgenic mice with the human *UGT1A1**28 polymorphism (TG) were investigated. Mice with induced HBIL received intraperitoneal bilirubin injections for 14 days. Bilirubin levels were analyzed in mouse serum and colon as well as *in-vitro* using the fluorescent protein UnaG, which specifically binds to unconjugated bilirubin. ROS and inducible nitric oxide (iNOS)-derivates were analyzed using Griess assay and gene expression analysis. Colonic microbiota was studied in TG and SPF mice using 16S rRNA gene sequencing. Colonic adenoma cell lines (ptk-6, Ht-29-mtx E12, and CaCo2) were stimulated with unconjugated bilirubin for 24 or 96 hours.

Results: The colonic mucosa of mice with induced HBIL exhibited higher levels of bilirubin than the control group, indicating the presence of 'intestinal HBIL' (HBIL = 12.34 nM/mg), Control = 0.5951 nM/mg; $p < 0.0001$). This was confirmed when colonic epithelial cells were treated with bilirubin *in vitro*, showing intracellular uptake of bilirubin, which could be led by organic anion transporting protein 1a1 (*Oatp1a1*), a potential candidate transporter for bilirubin that was upregulated in ptk-6 cells stimulated with bilirubin for 96 hours. HBIL mice showed an altered microbiota composition characterized by lower richness, distinct compositional clustering, and increased abundance of operational taxonomic units (OTUs) associated with gram-positive taxa (e.g., *Lachnospiraceae*) compared to wildtype mice. HBIL led to lower expression of iNOS and reduced levels of ROS-associated markers in the colon of mice. This was accompanied by higher expression of the aryl hydrogen receptor (*Ahr*), a bilirubin agonist, in the colon of HBIL and lower hepatic expression of *Ugt1a1*, reflecting GS conditions in HBIL mice.

Conclusion: The analysis of different murine models demonstrates that altered bilirubin metabolism along the liver-gut axis regulates the gut microbiota composition. These effects of intestinal HBIL may provide a new mechanistic explanation for the inverse association of GS with chronic disease risk.

Disclosure: Nothing to disclose.

OP095

GUT MICROBIOTA INFLUENCES COLORECTAL CANCER (CRC) PATIENTS' OUTCOME THROUGH THE METHYLATION OF PHLPP1 GENE

I. Sobhani¹, N. Brito^{2,3}, A. Amiot⁴, E. Bergsten¹, C. Charpy⁴, M. Chamailard³, D. Mestivier⁴, K. Khazaie⁵

¹UPEC-APHP-Hopital Henri Mondor-APHP, Gastroenterology, Creteil, France, ²Institut Pasteur Lille-INSERM, Cancer, Lille, France, ³Institut Pasteur INSERM, Cancer, LilleFrance, France, ⁴Henri Mondor Hospital, APHP Dept. of Gastroenterology, Dept. of Gastroenterology, Creteil, France, ⁵Mayo Clinic, Immunology of tumours, Phenix, United States of America

Contact E-Mail Address: iradj.sobhani@aphp.fr

Introduction: CRC is driven by changes in DNA such as genetic mutations or epigenetic modifications in the epithelium (colonocyte). Gut dysbiosis is a contributor to the alteration of gene function. However, the link between microbiota driven gene-specific alterations and its impact on clinical outcomes is yet unexplored. The Pleckstrin homology domain and leucine-rich repeat protein phosphatase 1 (PHLPP1) is a tumor suppressor gene that regulates signaling pathways in cell growth and survival, inhibits phosphorylation/kinase in PKC/Akt pathway, limits proliferation, inflammation, and trigger histone modification, and cell-activity mediated autophagy.

Aims & Methods: To understand the impact of microbiota on host DNA changes and outcomes, 96 CRC patients presenting with sporadic (n=64), Inflammatory bowel disease (IBD; n=20)- or the hereditary Lynch Syndrome (LS; n=13) were studied and surveyed. Human fresh stool (9 sporadic-

ic-CRC, 9 healthy controls) were orally transferred to germ-free mice. DNA mutation/methylation, cell proliferation, myeloid cell and lymphocyte infiltrates including CD8, Treg cells in the mice colonic epithelium were evaluated three months after human stool transfer and differences screened. Specimens from 96 CRC patients (n=13 LS, n=20 IBD and n=64 sporadic) were analyzed by human RNAseq and WES, and 16r sRNAseq; *in situ* metabolomic analysis and immunohistochemistry (IHC) were performed in human tumour tissues.

Inflammatory/immune cells were estimated using circumvolution approach based on RNAseq and quantified using IHC. Methylation of PHLPP1 gene promotor was determined in either mice colonic mucosa and human tissues by using bisulfite modified qPCR. For associated genes and pathways to the PHLPP1 gene expression, Gene Set Over-representation Analysis (ORA) and Gene Set Enrichment Analysis²⁴ (GSEA) were used according to t statistics and genes involved.

Bionformatics tools in link with patient's outcome up to 3 years follow from the baseline, were used. In a subset of 50 patients undergoing chemotherapy, abundances of bacteria candidates as suggested by 16sRNA analyses were measured using qPCR and associated to the related pathways.

Results: Stool transfer from CRC patients (vs controls) to mice resulted in the hypermethylation (not mutation) of PHLPP1, coinciding with the augmentation of aberrant crypt foci, inflammatory/immune cell infiltrate including FoxP3/RORgt+ cells within mice colonic mucosa and lower SCFA in the lumen. In patients' tumour tissues, intra-tumor Low (vs High, according to the median cutoff in the present series) PHLPP1 expression was significantly associated with a shorter survival, and a higher recurrence rate ($P = .01$). PHLPP1 hypermethylation of the promotor was more observed in CRC patients with Low PHLPP1 expression.

These patients, showed elevated levels of adherent virulent and reduced commensal bacteria taxa, a higher *in situ* metabolic activity in close to bacteria adherence and were more of IBD-CRC phenotype. Higher *E. Coli* and lower *Faecalibacterium Prautsnizii* (FP) as quantified by qPCR were observed in subset of patients who showed lower response to chemotherapy and in whome genes co-associated with PHLPP1 were involved in autophagy pathway.

Conclusion: Higher virulent/lower symbiotic bacteria unbalance influences CRC outcome through epigenetic down regulation of PHLPP1 an antioncogene and immunotolerance within tumour tissues. This bacteria unbalance enhances resistance to chemotherapy through alteration of autophagy. These suggest microbiota-associated failure of therapy is an epigenetic process that might be reversible.

Disclosure: Nothing to disclose.

OP096

THERAPEUTIC MODULATION OF GUT MICROBIOME TO TREAT IMMUNE-CHECKPOINT INHIBITORS-RELATED DIARRHEA AND COLITIS: EXPERIENCE OF A MICROBIOME CLINIC

S. Porcari¹, W. Fusco¹, M. Fiorani¹, A.S. Occhionero¹, T. Rozera¹, A. Severino¹, D. Rondinella¹, I. Venturini¹, A. Di Sabatino², M.V. Lenti², A. Gasbarrini¹, G. Cammarota¹, G. Ianaro¹

¹Digestive Disease Center, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, Dipartimento Universitario di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Gastroenterology, Rome, Italy, Rome, Italy, ²Fondazione IRCCS Policlinico San Matteo, University of Pavia, I Department of Internal Medicine, Pavia, Italy

Contact E-Mail Address: william7134@gmail.com

Introduction: Diarrhea is one of the most common adverse events of cancer therapies and, when severe, it may even cause the temporary suspension or the interruption of these drugs, limiting the treatment chances and potentially the survival of patients¹.

Moreover, immune-checkpoint inhibitors (ICI) are often associated to a more severe clinical picture of inflammatory condition (ICI-related colitis), which may require immunosuppressive treatments and hospitalization.²

An increasing body of evidence suggests that the manipulation of gut microbiome, mainly fecal microbiota transplantation (FMT), but also antibiotics and pre-probiotics, may represent a promising therapeutic strategy for diarrhea and colitis associated with cancer therapies, but these options are rarely applied into clinical practice.

Aims & Methods: Our aim is to evaluate whether an approach based on the modulation of gut microbiome can be an effective strategy for the treatment of diarrhea and colitis related to ICI treatment in cancer patients.

In this study, carried out from January 2023 to January 2024, we evaluated the efficacy of microbiome-modulating therapeutics (antibiotics, probiotics, FMT) in cancer patients referred to our Microbiome Clinic, under indication of their oncologists, for diarrhea and colitis related to ICI.

All patients underwent first a clinical evaluation to establish the severity of the symptoms and the oncological history, and then received a microbiome-modulating therapy.

All patients were followed up to at least 4 weeks after the prescription of the therapy. We collected the following data of patients: age, gender, type of cancer, oncological therapy and its suspension, severity of diarrhea (graded via CTCAE) and its onset since the start of the oncological therapy.

Results: Overall nineteen patients were enrolled in the study period (6 males, 13 females, mean age 54 years-old). Of them, 10 (53%) had Breast cancer, 3 (16%) Lung cancer, 2 (10%) Non-Melanoma Skin Cancer, 2 (10%) Kidney cancer, 1 (5%) Melanoma and 1 (5%) Cervix cancer. All the patients were treated with ICI (12 Pembrolizumab, 2 Atezolizumab, 1 Trastuzumab, 1 Nivolumab, 1 Mogamulizumab, 1 Cemiplimab, 1 Ipilimumab). Four patients had a G1 diarrhea (21%), seven (37%) G2, and eight (42%) G3. Twelve (63%) patients had to interrupt their immunotherapy due to diarrhea.

Multi-species probiotics were given in 10 (59%) patients, rifaximin in 6 (35%). Systemic steroids were necessary only in 10 patients (59%). At 4-week follow-up, 16 patients (94%) had a resolution of the diarrhea (G0), and 50% of the patients who had to interrupt their oncological therapy because of the diarrhea severity were then able to continue the treatment. Moreover, two patients, referred from another Centre (Pavia University) for ICI-related colitis refractory to steroids and biologics, were successfully treated with FMT, and were able to continue ICI.

Conclusion: An approach based on gut microbiome modulation can be an effective strategy to treat ICI-related diarrhea and colitis, and may potentially reduce the need for steroids. Our preliminary findings should be confirmed by more consolidated and well designed studies.

References: 1. He, Y., Zheng, J., Ye, B., Dai, Y. & Nie, K. Chemotherapy-induced gastrointestinal toxicity: Pathogenesis and current management. *Biochem Pharmacol* 216, 115787 (2023).

2. Adiwinata, R. et al. Immune Checkpoint Inhibitor Colitis, a Rising Issue in Targeted Cancer Therapy Era: A Literature Review. *Rom J Intern Med* (2024) doi:10.2478/rjim-2024-0015.

3. Hoang, J. et al. Preliminary Analysis of Gut Microbiome and Gastrointestinal Symptom Burden in Breast Cancer Patients Receiving Chemotherapy Compared to Healthy Controls. *Biol Res Nurs* 26, 219–230 (2024).

Disclosure: G.I. has received personal fees for acting as speaker for Biocodex, Danone, Sofar, Malesci, Metagenics and Tillotts Pharma, and for acting as consultant and/or advisor for Ferring Therapeutics, Giuliani, Malesci and Tillotts Pharma. A.G. reports personal fees for consultancy from Eisai Srl, 3PSolutions, Real Time Meeting, Fondazione Istituto Danone, SinergieSrl, Board MRGE and Sanofi SpA personal fees for acting as a speaker for Takeda SpA, AbbVie and Sandoz SpA and personal fees for acting on advisory boards for VSL3 and Eisai. G.C. has received personal fees for acting as advisor for Ferring Therapeutics. All other authors have no conflicts of interest to disclose.

Advanced ERCP technology and outcomes

11:30-12:30 / Lehar 3

OP097

COMPARISON OF LONG-TERM OUTCOMES OF TRANSLUMINAL EUS- GUIDED BILIARY DRAINAGE VIA HEPATICOGASTROSTOMY VS. CHOLEDOCHODUODENOSTOMY FOR DISTAL MALIGNANT BILIARY OBSTRUCTION: A PROSPECTIVE STUDY

K. Amalou¹, M. Medkour¹, F. Bouaouina², H. Chetroub¹, K. Saidani¹, N. Benboudiaf¹

¹HCA, Gastroenterology, Algiers, Algeria, ²HCA, Anesthesiology, Algiers, Algeria

Contact E-Mail Address: amalou_kh@yahoo.fr

Introduction: Endoscopic ultrasound-guided biliary drainage (EUS-BD) can be performed entirely transgastrically (hepatogastrostomy/EUS-HG) or transduodenally (choledochoduodenostomy/EUS-CDS). It is a feasible and effective alternative for distal malignant biliary obstruction (MBO) in failed endoscopic retrograde cholangiopancreatography. However, the preferred technique for better outcomes is less evaluated.

Aims & Methods: The aims of this study were to compare efficacy and safety of both techniques and identify predictors of adverse events.

Consecutive jaundiced patients with distal malignant biliary obstruction who underwent EUS-BD were included. The primary outcome was the stent patency. The secondary outcomes were technical and clinical success, adverse events (AEs) of each technique, and independent risk factors for stent dysfunction.

Results: A total of 57 patients were divided into EUS-CDS ($n = 30$) and EUS-HGS ($n = 27$) groups. Among them, technical success was achieved in 89.32% of patients (EUS-CDS 93.3 %, EUS-HG 88.2%, $P=0.09$). Clinical success was attained in 84.5% of patients who underwent EUS-CDS group as compared to 80.1% of patients who underwent EUS-HG ($P=0.14$). The mean duration of stent patency for EUS-CDS was 230.3 days while that for EUS-HGS was 143.9 days ($p = 0.01$).

Adverse events occurred more commonly in the EUS-HG group (19.67% vs. 13.3%, $P=0.37$).

In addition, the only independent risk factor for stent dysfunction was systematic treatment after EUS-BD [hazard ratio and 95% confidence interval 0.238 (0.066–0.863), $p = 0.029$]. Length of hospital stay was significantly shorter in the CDS group (5.6 days vs. 12.7 days, $P<0.001$). The incidence of stent dysfunction of EUS-HGS was higher than EUS-CDS (35.1% versus 18.2%, 0.04), despite no significant differences even in late AEs.

Conclusion: In distal MBO, oth EUS-CDS and EUS-HG are effective and safe techniques for the treatment of distal biliary obstruction after failed ERCP. EUS-CDS may be better than EUS-HGS with longer stent patency, shorter hospital stay and fewer AEs. Furthermore, systematic treatment after EUS-BD is recommended for the improvement of stent patency.

Disclosure: Nothing to disclose.

OP098

FEASIBILITY AND SAFETY OF A DEDICATED CAUTERY ENHANCED TUBULAR STENT FOR ENDOSCOPIC ULTRASOUND-GUIDED HEPATICOGASTROSTOMY

J. Vargas¹, S. Chan², J. Dhar³, J. Samanta³, S. Lakhtakia⁴, A. Teoh², M. Giovannini⁵

¹Caja Costarricense del Seguro Social, Hospital San Juan De Dios, San Jose, Costa Rica, ²Chinese University of Hong Kong, Surgery, Hong Kong, Hong Kong, ³Post Graduate Institute of Medical Education and Research, Chandigarh, Gastroenterology, Kolkata, India, ⁴Asian Institute of Gastroenterology, Gastroenterology, Hyderabad, India, ⁵Paoli-Calmettes, Dept. of Endoscopy, Marseille Cedex 9, France

Contact E-Mail Address: jorgevargasr@gmail.com

Introduction: Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) has emerged as a viable alternative for biliary drainage in patients with obstructive pancreatobiliary pathology in whom endoscopic retrograde cholangiography (ERCP) is not feasible.

Despite its effectiveness, however, this procedure is associated with a significant risk of complications. To carry out this procedure, the initial step is the puncture of the intrahepatic bile duct and the positioning of a guide wire; subsequently, the fistulous tract is dilated, and finally, a stent is placed, creating a bridge between the bile duct and the stomach.

Although this sequence is followed in most reported procedures, its technique has not yet been standardized. Therefore, this technique should be homogenized using dedicated devices with the aim of simplifying it as much as possible to reduce the risk of complications.

Aims & Methods: This study aimed to evaluate the feasibility and safety of a newly developed, dedicated, cautery-enhanced tubular stent for EUS-HGS created to simplify this procedure.

This multicenter, prospective study included 20 consecutive patients with malignant biliary obstruction who had failed ERCP due to tumor infiltration or altered anatomy.

A novel dedicated nitinol stent designed for EUS-HGS was used, featuring a cautery tip for tract creation, a 3 cm uncovered distal portion to prevent migration and a 7 cm silicone covered proximal portion with an anti-migratory distal cup to prevent bile leakage. (video 1 Hot Giobor v3.mp4) The technical and clinical success rates, procedure times, and adverse events were evaluated.

Results: Twenty patients underwent EUS-HGS using the dedicated stent, achieving 100% technical and clinical success rates. The mean procedure time was 16 min. Significant reductions in bilirubin levels were observed in all patients, with no reported severe adverse events or mortality.

Conclusion: Dedicated cautery-enhanced tubular stents for EUS-HGS could simplify the procedure and enhance its safety and efficacy, although further studies are required to validate these findings across broader patient populations and settings.

References:

1. Yamazaki H, Yamashita Y, Shimokawa T, Minaga K, Ogura T, Kitano M. Endoscopic ultrasound-guided hepaticogastrostomy versus choledochoduodenostomy for malignant biliary obstruction: A meta-analysis. *DEN Open*. 2024 Apr;4(1):e274.
2. Miyano A, Ogura T, Yamamoto K, Okuda A, Nishioka N, Higuchi K. Clinical Impact of the Intra-scope Channel Stent Release Technique in Preventing Stent Migration During EUS-Guided Hepaticogastrostomy. *J Gastrointest Surg Off J Soc Surg Aliment Tract*. 2018 Jul;22(7):1312–8.
3. Khashab MA, Messallam AA, Penas I, Nakai Y, Modayil RJ, De la Serna C, et al. International multicenter comparative trial of transluminal EUS-guided biliary drainage via hepatogastrostomy vs. choledochoduodenostomy approaches. *Endosc Int Open*. 2016 Feb;04(02):E175–81.

4. Park DH, Jang JW, Lee SS, Seo DW, Lee SK, Kim MH. EUS-guided biliary drainage with transluminal stenting after failed ERCP: predictors of adverse events and long-term results. *Gastrointest Endosc*. 2011 Dec;74(6):1276–84.

5. Honjo M, Itoi T, Tsuchiya T, Tanaka R, Tonoza R, Mukai S, et al. Safety and efficacy of ultra-tapered mechanical dilator for EUS-guided hepaticogastrostomy and pancreatic duct drainage compared with electrocautery dilator (with video). *Endosc Ultrasound*. 2018 Dec;7(6):376–82.

Disclosure: Nothing to disclose.

OP099

ARTIFICIAL INTELLIGENCE FOR AUTOMATIC DIAGNOSIS AND PLEOMORPHIC MORPHOLOGIC CHARACTERIZATION OF MALIGNANT BILIARY STRICTURES USING DIGITAL CHOLANGIOSCOPY: A MULTICENTRIC TRANSATLANTIC STUDY

M. Gonzalez Haba¹, M.J. Mascarenhas Saraiva², J. Widmer³, B. Agudo Castillo¹, T. Ribeiro², M. Martins², P. Cardoso², J. Ferreira², F. Mendes², A.M. Martins Pinto da Costa¹, G. Macedo²
¹Hospital Universitario Puerta De Hierro Majadahonda, Madrid, Spain, ²Centro Hospitalar São João, Gastroenterology, Porto, Portugal, ³NYU Langhorne, New York, United States of America

Contact E-Mail Address: marianoghr@gmail.com

Introduction: Despite the advances of recent years, the diagnosis and characterization of biliary strictures is challenging. Artificial intelligence applied to digital single-operator cholangioscopy (D-SOC) is expected to provide a significant increase in the diagnostic yield of indeterminate biliary strictures. Pilot studies using artificial intelligence (AI) algorithms applied to D-SOC have shown promising results.

This multicentric study aimed to validate a CNN model on a large dataset of D-SOC images, providing automatic detection of malignant biliary strictures, as well as their morphological characterization

Aims & Methods: Our group conducted an international study including D-SOC exams from 3 centers in Portugal (Centro Hospitalar Universitário de São João, Porto, Portugal, n=123), Spain (Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, n=18), and the United States of America (New York University Langone Hospital, New York, USA, n=23). Each frame was labelled as normal/benign findings or as a malignant lesion if histopathological evidence of biliary malignancy was available. Also, we evaluated the network's performance for detecting morphologic features, namely tumor vessels, papillary projections, nodules and masses. The image dataset was split for the constitution of training and validation datasets, with a ratio of 90% and 10%, respectively. The performance of the CNN was measured by calculating the area under the curve (AUC), sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively).

Results: A total of 103,082 images from 164 D-SOC exams from the three centers were included (53,678 of malignant strictures and 49,404 of benign findings). The model had an overall accuracy of 94.1%, a sensitivity of 93.5%, a specificity of 94.8%, a positive predictive value of 95.1%, a negative predictive value of 93.1% and an AUROC of 0.96.

Our group evaluated the performance of the CNN for the detection of morphological characteristics associated with malignancy, including papillary projections, nodules, masses and tumor vessels. The accuracy for the detection of these features was 90.8%, 93.6%, 93.2% and 78.1%, respectively. The AUC values for each morphologic characteristic were determined to be 0.80 for tumor vessels, 0.91 for nodules, 0.95 for masses and papillary projections.

Conclusion: The potential of deep learning algorithms to impact the care

of patients with suspected biliary malignancy is vast. The authors have expanded this line of research with a multicentre study including patients from two continents, thus increasing the variability of the dataset.

This study assessed the performance of a CNN for detecting and differentiating malignant and benign biliary disorders using a large pool of D-SOC images. The excellent performance of this model lays the foundations for future exploration of AI technologies in this subset of patients, aiming to improve the clinical outcome of patients with suspected biliary malignancy.

References: The potential of deep learning algorithms to impact the care of patients with suspected biliary malignancy is vast. The authors have expanded this line of research with a multicentre study including patients from two continents, thus increasing the variability of the dataset.

This study assessed the performance of a CNN for detecting and differentiating malignant and benign biliary disorders using a large pool of D-SOC images. The excellent performance of this model lays the foundations for future exploration of AI technologies in this subset of patients, aiming to improve the clinical outcome of patients with suspected biliary malignancy.

Disclosure: Consultan fees from BSCI.

OP100

ROBOTIC-ASSISTED BILE DUCT CANNULATION IN ERCP - A RANDOMIZED CONTROLLED ANIMAL STUDY

B. Yan¹, Y. Yang¹, H. Liu², Y. Yang², L. Peng¹, J. Yan¹

¹The First Medical Center, Chinese PLA General Hospital, Beijing, China, ²Shenyang Institute of Automation, Shenyang, China

Contact E-Mail Address: sunny301ddc@126.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is the most technically challenging procedure in endoscopic operations. Selective bile duct cannulation is the critical difficulty, which requires a combination of multiple endoscopic operations to align the knife, duodenal papilla and bile duct in vector direction. Poor endoscopic control, improper coordination of the endoscopists, and exposure to radiation are the challenges that ERCP is currently facing. The development of robotic-assisted ERCP can effectively solve a variety of clinical problems, which has important clinical significance for promoting robotic medicine and remote endoscopy.

Aims & Methods: We aim to develop a prototype robot (YunSRobot-ERCP system) that can integrate multiple endoscopic instruments in a single platform to achieve single-person operation. A randomized controlled animal study was conducted to explore the feasibility and efficacy of robotic-assisted ERCP when compared with conventional manual procedure. The robot system adopts master-slave and two-arm design, including an operating platform, duodenoscope manipulator arm and accessory manipulator arm. The endoscopist control the robot through the operating platform to complete the biliary intubation of beagle. A total of three ERCP physicians and 4 beagles participate in the animal experiment. Each ERCP physician performed one robotic-assisted and one manual ERCP bile duct cannulation on each beagle, totaling 24 procedures, which were randomized using a random number table.

We compared the location of duodenal papilla cannulation, time taken to successfully cannulate the bile ducts, cannulation success rate, and incidence of associated complications between manually and robotic-assisted group.

Results: The manual and robotic-assisted groups each involved 12 ERCP procedures. The percentages of time when the major duodenal papilla was in the desired position during cannulation in the manual and robotic-assisted groups were 77.25% and 95.74%, respectively. The robot-

ic-assisted group had significantly better performance in keeping the duodenal papilla in the desired position compared to the manual group ($p < 0.01$). In the manual and robotic-assisted groups, the time taken to successfully cannulate into the bile duct was 169.50 (106.25–207.25) s and 163.5 (126.50–210.75) s, respectively, with no significant difference ($P = 0.862$). The success rate of bile duct cannulation in the manual and robotic-assisted groups was 83.3%.

The number of attempts required to complete bile duct cannulation was 3.5 (2.00–4.00) in the manual group and 2.0 (1.25–3.00) in the robotic-assisted group per ERCP procedure. The robotic-assisted group required fewer attempts than the manual group, albeit with no significance ($P = 0.154$). Five duodenoscope dislocations occurred in the manual group and 0 in the robotic-assisted group, with no significant difference ($P = 0.07$). The manual and robotic-assisted groups showed no significant differences in the incidence of ERCP-associated adverse events, such as upper gastrointestinal mucosal edema and bleeding.

Conclusion: The animal study demonstrated that YunSRobot-ERCP robotic system can perform ERCP successfully, with a success rate of bile duct cannulation similar to that of the manual procedure. The robot performed superior in maintaining the stability of the duodenoscope. This study provides the possibility and research direction for robotic ERCP and remote operation.

Disclosure: Nothing to disclose.

OP101

OPTIMIZING DIAGNOSIS: ISOLATED HILAR/EXTRAHEPATIC IGG4-RELATED SCLEROSING CHOLANGITIS WITH REVISED CLINICAL DIAGNOSTIC CRITERIA 2020: A JAPANESE MULTICENTER STUDY

E. Iwasaki¹, K. Kubota², T. Ishikawa³, M. Kuwatani⁴, M. Takenaka⁵, T. Iwashita⁶, A. Masuda⁷, T. Ikeura⁸, A. Nakamura⁹, A. Tanaka¹⁰, H. Isayama¹¹, Y. Hirooka¹², K. Hirano¹³, S. Ryozaawa¹⁴, T. Ogura¹⁵, T. Fujisawa¹⁶, Y. Kurita², K. Kikuta¹⁷, N. Hayashi¹⁸, A. Masamune¹⁷, I. Yasuda¹⁸

¹Keio University School of Medicine, Tokyo, Japan, ²Yokohama City University Hospital, Yokohama, Japan, ³Nagoya University Graduate School of Medicine, Nagoya, Japan, ⁴Hokkaido University Hospital, Sapporo, Japan, ⁵Kindai University, Osaka, Japan, ⁶Gifu University Hospital, Gifu, Japan, ⁷Kobe graduate school of medicine, Kobe, Japan, ⁸Kansai Medical University, Hirakata, Japan, ⁹Shinshu university, Matsumoto, Japan, ¹⁰Teikyo University School of Medicine, Tokyo, Japan, ¹¹Juntendo University, Tokyo, Japan, ¹²Fujita Health University, Toyoake, Japan, ¹³Tokyo Takanawa Hospital, Tokyo, Japan, ¹⁴Saitama Medical University International Medical Center, Saitama, Japan, ¹⁵Osaka Medical and Pharmaceutical University, Osaka, Japan, ¹⁶Juntendo University Graduate School of Medicine, Tokyo, Japan, ¹⁷Tohoku University Graduate School of Medicine, Sendai, Japan, ¹⁸University of Toyama, Toyama, Japan

Contact E-Mail Address: iwaiwa2007@gmail.com

Introduction: In more than 90% of cases, IgG4-related sclerosing cholangitis (IgG4-SC) is linked with autoimmune pancreatitis (AIP)¹, facilitating its diagnosis. Without AIP, differentiating IgG4-SC from malignant biliary obstruction is challenging, leading to unnecessary resections². Although diagnostic criteria for IgG4-SC were established in 2012³ and revised in 2020⁴, validation is lacking.

Aims & Methods: We retrospectively collected data from 17 Japanese high-volume centers on patients with isolated IgG4-SC. We excluded distal-type isolated IgG4-SC, previously characterized by Nakazawa, due to challenges in identifying distal intra-pancreatic biliary strictures without

pancreatic involvement. Diagnosis of isolated IgG4-SC was based on the 2012 and 2020 criteria, with evaluation of symptoms, serum markers, imaging, and prognosis.

Results: A total of 53 patients with isolated IgG4-SC were included in the study, categorized into two groups based on the primary location of the lesion: hilar type ($n = 40$) and extrahepatic type ($n = 13$). Ten patients with hilar-type lesions underwent unnecessary resection due to a lack of awareness regarding the possibility of IgG4-SC. Common findings of endoscopic ultrasound/intraductal ultrasound, such as symmetric mucosal lesions of the bile duct, were observed in both types. The revised 2020 criteria demonstrated utility in diagnosing extrahepatic lesions, not covered by the 2012 criteria.

While endoscopic biopsy could not reveal characteristic findings of isolated IgG4-SC, such as storiform fibrosis and obliterative phlebitis, it was useful in detecting infiltration of affected surfaces by IgG4-positive plasma cells.

The percentage of patients requiring a steroid trial decreased from 37.7% with the 2012 criteria to 7.6% with the revised 2020 criteria. The revised criteria improved diagnostic specificity from 58.5% to 88.7%.

Conclusion: Our validation of the revised 2020 criteria for diagnosing IgG4-SC holds the potential to mitigate unnecessary surgical interventions in patients with isolated IgG4-SC, classified into hilar and extrahepatic subtypes. These updated criteria can enhance the diagnostic accuracy of isolated IgG4-SC and facilitate the identification of this challenging-to-diagnose condition based on including the imaging findings without sufficient proof by endoscopic biliary forceps biopsy and dependence on a steroid trial.

References: 1)Hart PA, Kamisawa T, Brugge WR, Chung JB, Culver EA, Czako L, et al. Long-term outcomes of autoimmune pancreatitis: a multicenter, international analysis. *Gut*. 2013; 62:1771-76.

2)Takagi Y, Kubota K, Takayanagi T, et al. Clinical features of isolated proximal-type immunoglobulin G4-related sclerosing cholangitis. *Digestive endoscopy* 2019; 31:422-30.

3) Ohara H, Okazaki K, Tsubouchi H, et al. Clinical diagnostic criteria of IgG4-related sclerosing cholangitis 2012. *J Hepatobiliary Pancreat Sci*. 2012; 19: 536-42

4) Nakazawa T, Kamisawa T, Okazaki K, et al. Clinical diagnostic criteria for IgG4-related sclerosing cholangitis 2020. *J Hepatobiliary Pancreat Sci*. 2021 28: 235-42.

Disclosure: Nothing to disclose.

OP102

IMPACT OF GUSELKUMAB MAINTENANCE THERAPY ON HISTOLOGIC AND COMBINED HISTOLOGIC AND ENDOSCOPIC OUTCOMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: WEEK 44 RESULTS FROM THE PHASE 3 QUASAR MAINTENANCE STUDY

J. Panés¹, A. Dignass², T. Hisamatsu³, S. Yarandi⁴, K.-H. Huang⁴, M. Germinaro⁴, S. Sridhar⁴, P. Branigan⁴, R. Wilson⁴, H. Zhang⁴, F. Magro⁵, V. Jairath⁶, B.G. Feagan⁷, G.R. Lichtenstein⁸, D.T. Rubin⁹, B.E. Sands¹⁰

¹Hospital Clínic Barcelona, Dept. of Gastroenterology, Barcelona, Spain, ²Agaplesion Markus Krankenhaus, Medizinische Klinik I, Frankfurt/Main, Germany, ³Kyorin University School of Medicine, Tokyo, Japan, ⁴Janssen Research & Development, LLC, Spring House, United States of America, ⁵University of Porto, Porto, Portugal, ⁶Schulich School of Medicine & Dentistry I, Western University, London, Canada, ⁷Alimentiv Inc, London, Canada, ⁸University of Pennsylvania, Philadelphia, United States of America, ⁹University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States of America, ¹⁰Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America

Contact E-Mail Address: julian.panes@gmail.com

Introduction: The phase 3 QUASAR maintenance study (NCT04033445) evaluated the efficacy and safety of guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64 (a receptor on cells that produce IL-23), in patients (pts) who achieved clinical response to 12 weeks of IV GUS. Here we present results for effects of GUS maintenance on histologic and combined histologic and endoscopic outcomes at Week 44.

Aims & Methods: At maintenance baseline, clinical responders following 12 weeks of GUS IV induction from the QUASAR Phase 2b and 3 induction studies were randomized 1:1:1 to GUS 200 mg SC q4w, GUS 100 mg SC q8w, or GUS withdrawal (PBO SC). Colonic biopsies were collected during endoscopy at maintenance baseline and Week 44 to evaluate treatment effect on histology measured using Geboes, Robarts, and Nancy Histological Index. Histologic improvement, histologic remission, the combination of histologic improvement and endoscopic improvement (histo-endoscopic mucosal improvement; HEMI), the combination of histologic remission and endoscopic improvement, and the combination of histologic remission and endoscopic normalization (remission) were evaluated at Week 44 (see Table for definitions).

Results: Of the 568 pts randomized (at induction baseline: mean age, 40.7yrs; mean UC disease duration, 7.8yrs; mean modified Mayo score, 6.9 [63.9% with severe disease]; Mayo endoscopy subscore of 3, 66.4%), 190 were receiving GUS 200 mg q4w, 188 receiving GUS 100 mg q8w, and 190 receiving PBO. Baseline characteristics were similar across treatment groups. Histologic activity at maintenance baseline was similar for the GUS 200 mg q4w, GUS 100 mg q8w, and PBO treatment groups (mean continuous Geboes total score: 6.7, 6.8, and 6.9, respectively). Improvements in histologic activity at Week 44 were observed in pts treated with GUS 200 mg q4w and GUS 100 mg q8w, while pts assigned to PBO worsened (mean change from maintenance baseline in continuous Geboes total score at Week 44: -1.0, -1.2, and 2.2, respectively [both nominal P<0.001]). At Week 44, a significantly greater proportion of pts treated with GUS 200 mg q4w and GUS 100 mg q8w achieved HEMI compared to PBO (47.9% and 43.6% vs 16.8%, respectively; both P<0.001). Greater proportions of pts in

both GUS treatment groups achieved other relevant endpoints at Week 44 compared to PBO-treated pts as presented in Table. Across biologic/JAK-inhibitor therapy history subpopulations, greater proportions of GUS-treated pts achieved the assessed endpoints compared to PBO.

	GUS Withdrawal (Placebo)	GUS 100 mg SC q8w	GUS 200 mg SC q4w
Primary analysis population, N	190	188	190
Histologic improvement, n (%) (Neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system [ie, Geboes histologic score ≤3.1])	58 (30.5)	122 (64.9)	122 (64.2)
Adjusted treatment difference (95% CI)	-	33.6 (24.3, 42.9)	32.6 (23.3, 41.9)
Nominal p-value		P<0.001	P<0.001
Histologic remission, n (%) (Absence of neutrophils from the mucosa [both lamina propria and epithelium], no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system [ie, Geboes histologic score ≤2 B.0]) ^a	51 (26.8)	111 (59.0)	115 (60.5)
Adjusted treatment difference (95% CI)	-	31.2 (21.9, 40.5)	32.6 (23.5, 41.8)
Nominal p-value		P<0.001	P<0.001
Histo-endoscopic mucosal improvement (HEMI), n (%) (Achieving a combination of histologic improvement and endoscopic improvement [Mayo endoscopy subscore of 0 or 1 with no friability])	32 (16.8)	82 (43.6)	91 (47.9)
Adjusted treatment difference (95% CI)	-	25.7 (17.1, 34.3)	29.6 (21.1, 38.0)
Multiplicity-controlled p-value		P<0.001	P<0.001
Histologic remission and endoscopic improvement, n (%) (Geboes histologic score ≤2 B.0 and endoscopic improvement)	30 (15.8)	78 (41.5)	89 (46.8)
Adjusted treatment difference (95% CI)	-	24.7 (16.2, 33.2)	29.6 (21.3, 38.0)
Nominal p-value		P<0.001	P<0.001
Histologic remission and endoscopic normalization (remission), n (%) (Geboes histologic score ≤2 B.0 and Mayo endoscopy subscore of 0)	27 (14.2)	59 (31.4)	62 (32.6)
Adjusted treatment difference (95% CI)	-	16.2 (8.2, 24.3)	16.9 (9.2, 24.7)
Nominal p-value		P<0.001	P<0.001

^a Results for histologic remission by alternative definitions using Robarts Histopathology Index (RHI ≤ 3, with subscores of 0 for lamina propria neutrophils and neutrophils in the epithelium and without ulcers or erosion) and Nancy Histological Index (NHI ≤ 1) were identical. Note: Patients who had a prohibited change in UC medication, an ostomy or colectomy, a dose adjustment (including sham dose adjustment), discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC, or due to other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to Week 44 were considered not to have achieved the endpoint. Patients who had an unevaluable biopsy (ie, a biopsy that was collected, but could not be assessed due to sample preparation or technical errors) or were missing the endoscopy subscore (if applicable) or any of the histology components pertaining to an endpoint at Week 44 were considered not to have achieved the endpoint. The adjusted treatment difference and confidence intervals were based on the Wald statistic with Cochran-Mantel-Haenszel (CMH) weight. The p-values were based on the CMH chi-square test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Table. Summary of Histologic and Combined Histologic and Endoscopic Outcomes at Week 44.

Conclusion: In this phase 3 maintenance study, pts with UC treated with GUS 200 mg SC q4w or GUS 100 mg SC q8w experienced clinically meaningful improvements in histologic and combined histologic and endoscopic outcomes at Week 44 compared to PBO-treated pts.

Disclosure: JP: AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman.

AD: Abivax, AbbVie, Bristol Myers Squibb, Dr Falk Foundation, Galapagos, Gilead, Janssen, Pfizer, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Celltrion, Ferring Pharmaceuticals, Fresenius Kabi, Lilly, MSD, Pharmacosmos, Roche, Sandoz, Stada, Takeda, Tillotts, Vifor Pharma, CED Service GmbH, High5MD, Materia Prima, MedToday, Thieme, and UniMed Verlag.

TH: AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd. JIMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., Takeda Pharmaceutical Co., Ltd., and Janssen Research & Development, LLC.

SY, KGH, MG, SS, PB, RW, and HZ: Johnson & Johnson.

FM: AbbVie, Arena, Celltrion, Eli Lilly and Company, Ferring, Fresenius, Galapagos, GlaxoSmithKline, Janssen, Merck, Pfizer, Prometheus Biosciences, Roche, Sandoz, Tillotts, Takeda, and Teva.

VJ: AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion, and Shire.

BGF: AbbVie, Abolera, AgomAB Therapeutics, Alliantera, Amgen, AnaptyBio, Applied Molecular Transport Inc, Arena Pharma, Avoro Capital Advisors, Atomwise, BioJamp, Biora Therapeutics, Boehringer-Ingelheim, Boxer, Celsius Therapeutics, Celgene/BMS, Connect BioPharma, Cytokine, Disc Medicine, Duality, EcoR1, Eli Lilly, Equillium, Ermium, First Wave, First Word Group, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, Gossamer Pharma, GSK, Hinge Bio, Hot Spot Therapeutics, Index Pharma, Imhotex, Immunic Therapeutics, JAKAcademy, Janssen, Japan Tobacco Inc., Kaleido Biosciences, Landos Biopharma, Leadiant, L.E.K. Consulting, LifeSci Capital, Lument AB, Millennium, MiroBio, Morphee Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Play to Know AG, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared Ltd., Viatrix, Ysios, Ysopia, Zealand Pharma, Morgan Lewis and Lenczner Slaght, Ecor1Capital, and Axio Research.

GRL: Abbvie, Allergan, American College of Gastroenterology, American Gastroenterological Association, American Regent, Celgene, Chemed, Eli Lilly, Endo Pharmaceuticals, Ferring, Gastroenterology and Hepatology, Gilead, IMEDEX, Ironwood, Janssen/ Janssen Orthobiotech, MedEd Consultants, Merck, Morphee Therapeutics, Pfizer Pharmaceuticals, Professional Communications, Inc., Prometheus Laboratories, Inc, Romark, Sandoz, Salix Pharmaceuticals/Valeant, Shire Pharmaceuticals, SLACK, Inc, Springer Science and Business Media, Takeda, University of Kentucky, UCB, Up-To-Date, Vindico, and Virgo.

DTR: Takeda, AbbVie, Altrubio, Allergan, Inc., Arena Pharmaceuticals, Aslan Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Ltd., Bristol Myers Squibb, Celgene Corp/Syneos, Connect BioPharma, GalenPharma/Atlantica, Genentech/Roche, InDex Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Eli Lilly, Materia Prima, Pfizer, Prometheus Biosciences, Reistone, Takeda, Techlab, Inc, and Cornerstones Health, Inc

BES: Abbvie, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptyBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biologic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Entera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kally-

ope, Merck, Microba, Mobius Care, Morphee Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, Ventyx Biosciences, Abivax, Lilly, Bristol Myers Squibb, Janssen, Pfizer, Takeda, Theravance Biopharma, and Ventyx Biopharma.

OP103

NORMALISATION OF HEALTH-RELATED QUALITY OF LIFE OUTCOMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH UPADACITINIB: A POST-HOC ANALYSIS OF PHASE 3 U-ACHIEVE & U-ACCOMPLISH STUDIES

J. Torres¹, C. Siegel², J. Panés³, E.V. Loftus⁴, R. Panaccione⁵, Y. Sanchez Gonzalez⁶, S. Xuan⁶, J. Klaff⁶, C.T.J. Holweg⁶, V. Remple⁶, D. Sharma⁶, G. Parkes⁷

¹Gastroenterology Division, Hospital Beatriz Angelo;

²Gastroenterology Division, Hospital da Luz, Lisbon, Portugal,

³Dartmouth Hitchcock Medical Center, Lebanon, United States of

America, ⁴Hospital Clínic Barcelona, Dept. of Gastroenterology,

Barcelona, Spain, ⁵Mayo Clinic College of Medicine, Division of

Gastroenterology and Hepatology, Rochester, United States of

America, ⁶University of Calgary, Department of Gastroenterology

and Hepatology, Calgary, Canada, ⁷AbbVie Inc., North Chicago,

United States of America, ⁸Barts Health NHS Trust; Barts and the

London School of Medicine and Dentistry, London, United Kingdom

Contact E-Mail Address: joanatorres00@gmail.com

Introduction: Patients with moderately to severely active ulcerative colitis (UC) have debilitating symptoms that may incur substantial negative effects on health-related quality of life (HRQoL). According to the STRIDE-II consensus, restoration of HRQoL is a desirable long-term treatment goal for patients with active UC.¹

In this post-hoc analysis, we evaluated the extent to which patients treated with upadacitinib (UPA) achieved normalisation of HRQoL after induction and maintenance treatment.

Aims & Methods: Data from the multicentre, double-blind, Phase 3 trials, U-ACHIEVE (NCT02819635) and U-ACCOMPLISH (NCT03653026), were analysed. During induction, patients were randomised 1:2 to oral placebo (PBO) or UPA 45 mg once daily (QD) for 8 weeks. Patients achieving a clinical response to UPA per Adapted Mayo score at Week 8 were re-randomised 1:1:1 to PBO, UPA 15 mg, or UPA 30 mg QD for 52 weeks of maintenance.

The proportion of patients achieving normalisation of each individual HRQoL outcome, per literature-based normative value thresholds, was assessed at Weeks 8 and 52: FACIT-Fatigue score; IBDQ score; WPAl-UC (overall work impairment, work time missed, impairment while working, activity impairment); SF-36 PCS; SF-36 MCS; EQ-5D-5L VAS; and EQ-5D-5L index.

A stringent composite score including these outcomes was also calculated to determine the proportion of patients who achieved normalisation of all individual HRQoL-related scores. Point estimates were calculated for all outcomes and treatment differences between UPA and PBO were compared using the Cochran-Mantel-Haenszel test.

Results: During induction, 660 patients were randomised to UPA 45 mg and 328 patients to PBO. In patients receiving UPA 45 mg vs PBO, more patients achieved normalisation of each individual HRQoL outcome at Week 8 of induction ($p < 0.001$; Table 1). Improvements were also observed at Week 52 of maintenance in patients receiving UPA 15 mg ($n = 148$) and 30 mg ($n = 154$), with more patients achieving normalisation of each HRQoL

outcome with both doses of UPA vs PBO ($p < 0.01$). More patients achieved normalisation of composite HRQoL scores at Weeks 8 (UPA 45 mg: 18.9%; PBO: 5.5%) and 52 (UPA 30 mg: 24.0%; UPA 15 mg: 22.3%; PBO: 8.7%) with all doses of UPA compared to PBO ($p < 0.001$).

HRQoL end-points at Weeks 8 and 52, n (%)	Induction (Week 8) PBO N=328	Induction (Week 8) UPA 45 mg QD N=660	Between group diff. (UPA 45 mg vs PBO) % [95% CI]	Maintenance (Week 52) PBO N=149	Maintenance (Week 52) UPA 15 mg QD N=148	Maintenance (Week 52) UPA 30 mg QD N=154	Between group diff. (UPA 15 mg vs PBO) % [95% CI]	Between group diff. (UPA 30 mg vs PBO) % [95% CI]
FACIT-F score ≥ 40.1	109 (33.2)	357 (54.1)	20.8 *** [14.6, 27.1]	53 (35.7)	77 (52.0)	86 (55.7)	15.7 ** [5.1, 26.3]	19.1 *** [8.3, 29.8]
IBDQ score ≥ 170	85 (25.9)	407 (61.6)	35.6 *** [29.6, 41.5]	42 (28.5)	91 (61.5)	111 (72.3)	32.2 *** [22.1, 42.6]	42.8 *** [32.7, 52.8]
WPAI-UC 0%								
Overall work imp. ^{a,b}	24 (11.9)	112 (26.2)	13.7 *** [7.7, 19.7]	14 (13.9)	37 (33.9)	33 (32.7)	21.1 *** [10.6, 31.6]	19.0 *** [7.9, 30.1]
Work time missed ^{a,b}	92 (45.8)	261 (61.0)	14.7 *** [6.5, 22.9]	41 (40.6)	72 (66.1)	62 (61.4)	24.3 *** [11.4, 37.2]	19.7 ** [6.5, 33.0]
Imp. while working ^{a,b}	27 (13.4)	126 (29.5)	15.3 *** [9.1, 21.6]	14 (13.9)	39 (35.8)	35 (34.7)	23.1 *** [12.5, 33.7]	21.0 *** [9.8, 32.2]
Daily activity imp.	37 (11.3)	199 (30.2)	18.8 *** [14.0, 23.6]	28 (18.8)	55 (37.2)	62 (40.3)	18.8 *** [9.2, 28.5]	21.0 *** [11.2, 30.8]
SF-36 PCS ≥ 50	106 (32.3)	369 (55.9)	23.4 *** [17.2, 29.7]	44 (29.7)	89 (60.1)	102 (66.3)	29.5 ** [19.2, 39.8]	35.4 *** [25.1, 45.6]
SF-36 MCS ≥ 50	98 (29.9)	316 (48.0)	17.9 *** [11.7, 24.1]	38 (25.2)	70 (47.3)	82 (53.0)	22.1 *** [12.0, 32.2]	27.4 *** [17.2, 37.7]
EQ-5D-5L VAS ≥ 80	68 (20.7)	298 (45.1)	24.3 *** [18.6, 30.1]	40 (26.9)	65 (43.9)	88 (57.1)	15.6 ** [5.1, 26.0]	29.0 *** [18.5, 39.6]
EQ-5D-5L Index ≥ 0.825	89 (27.1)	339 (51.4)	24.3 *** [18.2, 30.4]	49 (33.0)	79 (53.4)	90 (58.5)	18.7 *** [8.3, 29.1]	24.1 *** [13.7, 34.6]
Composite HRQoL endpoint ^c	18 (5.5)	125 (18.9)	13.2 *** [9.4, 17.1]	13 (8.7)	33 (22.3)	37 (24.0)	13.6 *** [6.0, 21.6]	14.8 *** [6.9, 22.7]

** $p < 0.01$. *** $p < 0.001$. ^aInduction: PBO, N=201; UPA 45 mg, N=428. ^bMaintenance: PBO, N=101; UPA 15 mg, N=109; UPA 30 mg, N=101. ^cProportion of patients achieving FACIT-F score ≥ 40.1 , IBDQ score ≥ 170 , 0% for WPAI-UC Daily Activity Impairment, SF-36 PCS ≥ 50 and MCS ≥ 50 , EQ-5D-5L VAS ≥ 80.0 and EQ-5D-5L Index ≥ 0.825 ; employment-related scores were excluded.

For induction data, the Cochran-Mantel-Haenszel test was used to calculate the 95% CI for differences between treatment groups and was adjusted for strata: baseline corticosteroid use (yes or no), baseline Adapted Mayo score (≤ 7 or > 7) and bio-IR status (bio-IR or non-bio-IR).

For maintenance data, the Cochran-Mantel-Haenszel test was used to calculate the 95% CI for differences between treatment groups and was adjusted for strata: bio-IR status (bio-IR or non-bio-IR) at the baseline of the induction study, clinical remission status at Week 0 (yes or no), and corticosteroid use at Week 0 (yes or no).

Bio-IR, biologics inadequate response; CI, confidence interval; diff., difference; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Levels; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HRQoL, health-related quality of life; IBDQ, Inflammatory Bowel Disease Questionnaire; imp., impairment; MCS, Mental Component Summary; PBO, placebo; PCS, Physical Component Summary; QD, once daily; SF-36, Short Form 36; UC, ulcerative colitis; UPA, upadacitinib; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment Questionnaire.

Table 1. Proportion of patients with UC achieving normalisation of HRQoL outcomes after treatment.

Conclusion: UPA is more efficacious than PBO at achieving normalisation of patients' HRQoL, at induction and through Week 52 of maintenance. These results suggest that UPA may help patients with moderately to severely active UC achieve the long-term treatment goal of normalisation of HRQoL.

References:

1. Turner D, et al. *Gastroenterology*. 2021;160:1570–83.

Disclosure: Joana Torres has received grant funding/speaker fees from and/or has participated in advisory boards for AbbVie, Galapagos, Janssen, and Pfizer.

Gareth Parkes received personal payments/honoraria/speaker fees and/or accepted travel grants or fellowships from AbbVie, Allergan, BMS, Celltrion, Ferring, Galapagos, Janssen, Napp, Takeda, and Tillotts; and is a Director and Shareholder in Ampersand Health.

Corey Siegel has served as a consultant, advisor, speaker for CME activities, and/or received grant funding from AbbVie, BMS, Celltrion, Fresenius, Janssen, Lilly, Napo, Pfizer, Prometheus, Prometheus Labs, Roivant, and Takeda.

Julian Panés received consultancy fees/honorarium from AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman; and has served on a data safety monitoring board for Alimentiv, Mirum, Sorriso, Sanofi, and Surrozen.

Edward V. Loftus Jr: served as a consultant for AbbVie, Alvotech, Amgen, Arena, Avalo, Boehringer Ingelheim, Bristol-Myers Squibb, Calibr, Celgene, Celltrion Healthcare, Eli Lilly, Fresenius Kabi, Genentech, Gilead,

GlaxoSmithKline, Gossamer Bio, Iota, Iterative Scopes, Janssen, Morphic Therapeutics, Ono Pharma, Pfizer, Protagonist, Scipher Medicine, Surrozen, Sun Pharma, Takeda, and UCB; and received research grants from AbbVie, Bristol-Myers Squibb, Celgene, Genentech, Gilead, Gossamer Bio, Janssen, Pfizer, Receptos, Roberts Clinical Trials, Takeda, Theravance, and UCB.

Remo Panaccione served as a consultant for Abbott, AbbVie, Abbivax, Alimentiv (formerly Roberts), Amgen, AnaptysBio, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatrix, Ventyx, UCB; and received speaker's fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, and Takeda Pharmaceuticals; and was an advisory board member for AbbVie, Alimentiv (formerly Roberts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, and Ventyx.

Yuri Sanchez Gonzalez, Si Xuan, Valencia Remple, Justin Klaff, Cecile Holweg, and Dolly Sharma are full-time employees of AbbVie and may hold AbbVie stock and/or stock options.

Funding statement: Financial support for the study was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. No honoraria or payments were made for authorship. Medical writing services provided by Kay Hallam, MSc, of Fishawack Facilitate, Ltd, part of Avalere Health and funded by AbbVie.

OP104

EFFICACY AND SAFETY OF UPADACITINIB AFTER 3 YEARS OF TREATMENT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: INTERIM LONG-TERM DATA FROM THE PHASE 3 OPEN-LABEL EXTENSION STUDY (U-ACTIVATE)

R. Panaccione¹, P.D. Higgins², H. Nakase³, S. Glover⁴, S. Danese⁵, J.-F. Colombel⁶, J. Eccleston⁷, M. Kujawski⁷, V. Remple⁷, X. Yao⁷, S. Suravaram⁷, S. Schreiber⁸

¹University of Calgary, Medicine, Calgary, Canada, ²University of Michigan Health System School of Public Health, Dept. of Internal Medicine, Ann Arbor, United States of America, ³Sapporo Medical University School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ⁴University of Mississippi Medical Center, Department of Internal Medicine, Jackson, United States of America, ⁵Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal Immunopathology, Milan, Italy, ⁶Icahn School of Medicine at Mount Sinai, Henry Janowitz Division of Gastroenterology, New York, United States of America, ⁷AbbVie Inc, North Chicago, Illinois, United States of America, ⁸University Hospital Schleswig-Holstein, Christian-Albrechts-University, Department of Internal Medicine I, Kiel, Germany

Contact E-Mail Address: rpanacci@ucalgary.ca

Introduction: Upadacitinib (UPA), an oral, reversible JAK inhibitor approved for the treatment of moderately to severely active ulcerative colitis (UC),^{1,2} has shown sustained efficacy and an acceptable safety profile in long-term studies of multiple autoimmune conditions.³⁻⁵

Aims & Methods: We report efficacy and safety of UPA after almost 3 years (yrs) of therapy in patients (pts) with moderately to severely active UC from the U-ACTIVATE (NCT03006068) study, consisting of 1 yr maintenance and around 2 yrs long-term extension (LTE). Pts aged 16–75 yrs with UC for ≥90 days prior to study entry, an Adapted Mayo score (AMS) of 5–9 and an endoscopic subscore of 2 or 3, were eligible for induction studies (U-ACCOMPLISH [NCT03653026]; U-ACHIEVE Induction [NCT02819635]) and randomised to placebo (PBO) or UPA 45 mg once daily (QD) for 8 weeks (wks).

Clinical responders were re-randomised to PBO, UPA 15 mg QD (UPA15) or UPA 30 mg QD (UPA30) for 52 wks (U-ACHIEVE Maintenance). Pts who completed 52-wks of maintenance were eligible to enter this LTE on their maintenance dose. Efficacy was evaluated by clinical remission (per AMS and Partial Mayo score), maintenance of clinical remission (per AMS), clinical response, endoscopic remission, endoscopic improvement and maintenance of endoscopic remission during the LTE at Wk 96 (endpoints are defined in the Table).

Safety was assessed by treatment-emergent adverse events (TEAEs), presented as exposure-adjusted event rates (EAERs; events per 100 pt yrs [E/100 PY]). Efficacy and safety analyses were based on data up to June 30, 2023 and analysed as observed without imputation for missing values.

Results: At Wk 96, approximately three-quarters of pts with UC treated with either UPA15 or UPA30 achieved clinical remission (per AMS) (Table). Of pts in clinical remission at Wk 0 of the LTE (per AMS), a similar proportion maintained this response with UPA15 and a slightly higher response rate was observed with UPA30 at Wk 96 of the LTE. Clinical outcomes and endoscopic improvement were observed in the majority of patients in both UPA groups.

Endoscopic remission was achieved by almost half of pts treated with UPA. Of endoscopic remitters at Wk 0 of the LTE study, more than half maintained remission status at Wk 96 of the LTE, with a slightly higher response rate observed with UPA30. For safety, 369 pts (UPA15, n=142; UPA30, n=227) with 789.4 PY (UPA15, 302.5 PY; UPA30, 486.9 PY) of expo-

sure were analysed. Rates of serious TEAEs and TEAEs leading to treatment discontinuation were similar across treatment groups. No deaths were reported in the UPA15 group; there was 1 TEAE leading to death (EAER: 0.2 E/100 PY) in a pt requiring prolonged hospitalisation for worsening COVID-19 infection in the UPA30 group (Table).

Efficacy endpoints at Week 96 n/N (%) [95% CI]	UPA 15 mg QD	UPA 30 mg QD
Clinical remission per Adapted Mayo score ^a	69/91 (75.8) [67.0, 84.6]	104/141 (73.8) [66.5, 81.0]
Clinical remission per Partial Mayo score ^a	83/92 (90.2) [84.1, 96.3]	123/143 (86.0) [80.3, 91.7]
Maintenance of clinical remission ^a	50/64 (78.1) [68.0, 88.3]	69/82 (84.1) [76.2, 92.1]
Clinical response per Adapted Mayo score ^a	89/91 (97.8) [94.8, 100.0]	136/141 (96.5) [93.4, 99.5]
Endoscopic improvement ^f	78/95 (82.1) [74.4, 89.8]	126/153 (82.4) [76.3, 88.4]
Endoscopic remission ^g	45/95 (47.4) [37.3, 57.4]	69/153 (45.1) [37.2, 53.0]
Maintenance of endoscopic remission ^h	20/31 (64.5) [47.7, 81.4]	37/51 (72.5) [60.3, 84.8]
TEAEs E (E/100 PY)	UPA 15 mg QD (n=142; PY=302.5)	UPA 30 mg QD (n=227; PY=486.9)
Any TEAEs ⁱ	699 (231.1)	1097 (225.3)
Serious TEAEs	32 (10.6)	60 (12.3)
TEAEs leading to discontinuation of study drug	15 (5.0)	17 (3.5)
TEAEs leading to death	0	1 ^j (0.2)

^aEfficacy and safety populations included induction responders (UPA 45 mg for 8 weeks) who completed 52 weeks of maintenance treatment and enrolled in this LTE analysis. Patients who were not in clinical remission could escalate their dose upon entry to this LTE.

^bAdapted Mayo score ≤2 with stool frequency subscore ≤1 and not greater than baseline of induction studies, RBS=0 and ES ≤1 without friability.

^cPartial Mayo score ≤2 with no subscore >1.

^dClinical remission per Adapted Mayo score at Week 96 in those who achieved clinical remission at Week 0 of the LTE study.

^eDecrease in Adapted Mayo score ≥2 points and ≥30% from baseline of induction studies, plus a decrease in RBS ≥1 or an absolute RBS ≤1.

^fES ≤1 without friability.

^gES=0.

^hPatients who achieved endoscopic remission at Week 96 among those who achieved endoscopic remission at Week 0 of the LTE study.

ⁱTEAEs are defined as events that begin either on or after the first dose of study drug in the LTE study, and within the earlier of the first dose change in the LTE study and the last dose of study drug in the LTE study plus 30 days.

^jFifty-seven-year-old male who experienced a suspected pulmonary thromboembolism event while hospitalised for worsening of COVID-19 infection and acute renal failure. Primary cause of death was pulmonary embolism. Risk factors included medical history of arterial hypertension, former cigarette smoker, concurrent COVID-19 infection and prolonged hospitalisation.

CI, confidence interval; E, events; ES, endoscopic subscore; LTE, long-term extension; PY, patient years; QD, once daily; RBS, rectal bleeding subscore; TEAE, treatment-emergent adverse event; UPA, upadacitinib.

Table. Summary of efficacy and safety^a (as observed)

Conclusion: Achievement of clinical and endoscopic endpoints at LTE Wk 96 demonstrates the continued benefit of almost 3 yrs of therapy with UPA. The long-term safety profile for UPA in pts with UC was consistent with previous analyses,^{1,2} with no new safety concerns identified in this ongoing LTE study.

References:

1. Danese S, et al. Lancet 2022;399:2113–28
2. Vermeire S, et al. Lancet Gastroenterol Hepatol 2023;8:976–89
3. Baraliakos X, et al. Arthritis Res & Ther 2023;25:172
4. Fleischmann R, et al. RMD Open 2022;8:e002012
5. Simpson EL, et al. JAMA Dermatol 2022;158:404–13

Disclosure: RP has received consulting fees, speaker fees and research support from Abbott, AbbVie, Alimentiv, Amgen, Arena Pharmaceuticals, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Élan, Ferring, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Mylan, Oppilan Pharma, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Schering-Plough, Shire, Sublimity Therapeutics, Takeda, Theravance and UCB.

PDRH has received grants from AbbVie, Connectome Coordination Facility, National Institute of Health and Takeda; and has served as a consultant for GI Health Foundation, Immedex, Lilly, Pfizer, Takeda and Vindico Medical Education.

HN has received research support from AbbVie, Celgene, Daiichi Sankyo Company, EA Pharma, Janssen, JIMRO, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Mochida Phar-

maceutical, Nippon Kayaku, Pfizer, Takeda and Zeria; and has received grants from Boehringer Ingelheim, Bristol Myers Squibb and Hoya Group Pentax Medical.

SG has no conflicts of interest to disclose.

SD has received consultancy fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Entera, Ferring, Gilead, Hospira, Janssen, Johnson & Johnson, Lilly, Merck Sharp and Dohme, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB and Vifor.

J-FC reports personal fees from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Celltrion, Enterome, Ferring, Genentech, Janssen/Johnson & Johnson, MedImmune, Merck, Pfizer, PPM Services, Protagonist, Second Genome, Seres, Shire, Takeda and Theradiag; has received grant support from AbbVie, Janssen, Johnson & Johnson and Takeda; and holds stock options in Genfit and Intestinal Biotech Development.

JE, MK, VR, XY and **SSuravam** are employees of AbbVie and may own stock and/or options.

SSchreiber has received speaker/consultancy fees from AbbVie, Advanced Molecular Transport, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Falk, Ferring, Galapagos/Gilead, Genentech/Roche, Janssen, Merck/Merck Sharp and Dohme, Pfizer, Prometheus and Takeda.

Acknowledgments:

AbbVie and the authors thank the participants, study sites and investigators who participated in this study. AbbVie funded this study and contributed to its design, research, analysis, data collection, interpretation of data, and the review and approval of this abstract. All authors had access to relevant data and participated in the drafting, review and approval of this abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Helena Patsos, PhD, of 2 the Nth (Cheshire, UK) and was funded by AbbVie.

OP105

LONG-TERM EFFICACY AND SAFETY OF FILGOTINIB 200 MG IN ULCERATIVE COLITIS: 5-YEAR INTERIM DATA FROM SELECTIONLTE

B.G. Feagan^{1,2}, **K. Matsuoka**³, **G. Rogler**⁴, **D. Laharie**⁵, **S. Vermeire**⁶, **S. Danese**^{7,8}, **E.V. Loftus**⁹, **I. Beales**^{10,11}, **S. Schreiber**¹², **H.J. Kim**¹³, **M. Faes**¹⁴, **A. Mangili**¹⁵, **C. Rudolph**¹⁶, **L. Peyrin-Biroulet**^{17,18,19,20,21,22}

¹Alimentiv Inc., London, Canada, ²Western University, London, Canada, ³Toho University Sakura Medical Center, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chiba, Japan, ⁴University of Zurich, Department of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland, ⁵University of Bordeaux, INSERM, Gastroenterology Department, Hospital Center University de Bordeaux, Magellan Medico-Surgical Center, Haut-Lévêque Hospital, Bordeaux, France, ⁶University Hospital Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁷IRCCS Hospital San Raffaele, Department of Gastroenterology and Endoscopy, Milan, Italy, ⁸Vita-Salute San Raffaele University, Milan, Italy, ⁹Mayo Clinic College of Medicine and Science, Division of Gastroenterology and Hepatology, Rochester, United States of America, ¹⁰Norfolk and Norwich University Hospitals NHS Foundation Trust, Department of Gastroenterology, Norwich, United Kingdom, ¹¹University of East Anglia, Norwich Medical School, Norwich, United Kingdom, ¹²University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel University, Kiel, Germany, ¹³Kyung Hee University, Department of Gastroenterology, Center for Crohn's and Colitis, Seoul, South Korea, ¹⁴Galapagos NV, Mechelen, Belgium, ¹⁵Galapagos NV, Basel, Switzerland, ¹⁶Galapagos NV, Leiden, Netherlands, ¹⁷Nancy University Hospital, Department of Gastroenterology, Vandœuvre-lès-Nancy, France, ¹⁸University of Lorraine, INSERM, NGERE, Nancy, France, ¹⁹Nancy University Hospital, INFINY Institute, Vandœuvre-lès-Nancy, France, ²⁰Nancy University Hospital, FHU-CURE, Vandœuvre-lès-Nancy, France, ²¹Paris IBD Center, Private Hospital Group Ambroise Paré – Hartmann, Neuilly-sur-Seine, France, ²²McGill University Health Centre, Division of Gastroenterology and Hepatology, Montreal, Canada

Contact E-Mail Address: brian.feagan@alimentiv.com

Introduction: Filgotinib (FIL), a once-daily, oral, Janus kinase 1 preferential inhibitor, is approved for the treatment of ulcerative colitis (UC). FIL was effective in inducing and maintaining clinical remission and was well tolerated in the placebo-controlled phase 2b/3 SELECTION trial (NCT02914522).¹

Aims & Methods: The efficacy and safety of continued treatment with FIL 200 mg (FIL200) are being assessed in the long-term extension (LTE) study (SELECTIONLTE: NCT02914535). The study design of SELECTION has been published previously.¹ We now report the efficacy and safety of open-label FIL200 through up to 5 years of treatment: LTE week 192 in completers and LTE week 240 in induction non-responders. Completers were defined as patients who completed the SELECTION induction and maintenance studies, and non-responders were those without response at SELECTION week 10; all of whom entered the LTE study. A data cut-off of 23 March 2023 was used for this interim analysis. Proportions of patients who were in partial Mayo Clinic Score (pMCS) remission (pMCS ≤1) and Inflammatory Bowel Disease Questionnaire (IBDQ) remission (score ≥170) were reported both as observed cases and using non-responder imputation (NRI). Adverse events (AEs) and AEs of special interest (AESIs) were evaluated using exposure-adjusted incidence rates per 100 patient-years of exposure (PYE).

Results: This interim analysis included 148 completers and 372 non-responders. AEs and AESIs in patients treated with open-label FIL200 (2464.7 PYE) showed no new safety signals, and safety events were comparable to those seen in previous analyses. The proportions of patients who were in pMCS and IBDQ remission are shown in the *Table*. The proportions of patients who were in pMCS remission increased during SELECTION to reach 72.4% (FIL200, as observed) at week 58/LTE baseline and increased further during SELECTIONLTE (85.0% at LTE week 192) in completers. Proportions in pMCS remission increased more gradually over SELECTIONLTE, reaching 66.7% (FIL200–FIL200, as observed) at LTE week 240 in non-responders. Similar patterns were seen for IBDQ remission; 78.5% (FIL200, as observed) of completers were in IBDQ remission at week 58/LTE baseline, increasing to 84.8% by LTE week 192. In non-responders, increases in the proportions of patients who were in IBDQ remission were gradual, reaching 77.8% (FIL200–FIL200, as observed) at LTE week 240. NRI analyses showed similar but much more conservative results than the as observed analyses for both groups for both endpoints.

Conclusion: Filgotinib 200 mg was effective in maintaining symptomatic remission and health-related quality of life for up to 5 years. No new safety signals were identified, and rates of AEs under long-term exposure were comparable to those previously reported.^{1–4} Prolonged treatment with filgotinib is efficacious for the long-term management of UC, and together with its proven safety profile, results in an acceptable benefit–risk profile.

	Proportion of patients in pMCS remission % (n/N)			Proportion of patients in IBDQ remission % (n/N)		
	Completers IND FIL200 → MNT FIL200 → LTE FIL200 (n = 148)	Non-responders IND FIL100 → LTE FIL200 (n = 212)	Non-responders IND FIL200 → LTE FIL200 (n = 160)	Completers IND FIL200 → MNT FIL200 → LTE FIL200 (n = 148)	Non-responders IND FIL100 → LTE FIL200 (n = 212)	Non-responders IND FIL200 → LTE FIL200 (n = 160)
Week 10						
Observed	45.6% (67/147)	–	–	68.0% (100/147)	–	–
NRI	45.3% (67/148)	–	–	67.6% (100/148)	–	–
Week 58/LTE baseline						
Observed	72.4% (105/145)	0.5% (1/212)	1.3% (2/160)	78.5% (113/144)	16.0% (30/188)	26.8% (37/138)
NRI	70.9% (105/148)	0.5% (1/212)	1.3% (2/160)	76.4% (113/148)	14.2% (30/212)	23.1% (37/160)
LTE week 48						
Observed	75.4% (98/130)	41.9% (62/148)	44.4% (48/108)	82.0% (109/133)	63.3% (100/158)	61.9% (70/113)
NRI	66.2% (98/148)	29.2% (62/212)	30.0% (48/160)	73.6% (109/148)	47.2% (100/212)	43.8% (70/160)
LTE week 96						
Observed	83.3% (95/114)	58.2% (71/122)	64.0% (57/89)	81.5% (97/119)	71.2% (89/125)	66.3% (59/89)
NRI	64.2% (95/148)	33.5% (71/212)	35.6% (57/160)	66.0% (97/147)	42.0% (89/212)	36.9% (59/160)
LTE week 144						
Observed	81.1% (73/90)	58.3% (63/108)	63.3% (50/79)	82.5% (85/103)	78.1% (82/105)	70.9% (56/79)
NRI	51.0% (73/143)	29.7% (63/212)	31.3% (50/160)	60.3% (85/141)	38.7% (82/212)	35.0% (56/160)
LTE week 192						
Observed	85.0% (34/40)	66.7% (50/75)	65.4% (34/52)	84.8% (39/46)	77.3% (68/88)	76.7% (46/60)
NRI	46.6% (34/73)	24.8% (50/202)	22.4% (34/152)	44.8% (39/87)	33.5% (68/203)	30.5% (46/151)
LTE week 240						
Observed	–	62.2% (23/37)	66.7% (14/21)	–	79.5% (31/39)	77.8% (21/27)
NRI	–	18.4% (23/125)	14.9% (14/94)	–	21.1% (31/147)	19.3% (21/109)

Table. Proportions of patients in pMCS or IBDQ remission in SELECTION and SELECTIONLTE (observed case and NRI).

References:

1. Feagan BG *et al.* *Lancet* 2021;397:2372–84.
2. Feagan BG *et al.* *J Crohns Colitis* 2022;16(Suppl1):i456–7.
3. Feagan BG *et al.* *J Crohns Colitis* 2023;17(Suppl1):i47–50.
4. Feagan BG *et al.* *UEG Journal* 2023;11(Suppl 8).

Disclosure: The SELECTION trial was sponsored by Gilead Sciences, Inc. (Foster City, CA, USA), for which Galapagos NV (Mechelen, Belgium) was a collaborator. The SELECTIONLTE trial was sponsored by Galapagos NV (Mechelen, Belgium), who funded these analyses.

Medical writing support for the development of this abstract was provided by Katie Pillidge, PhD, of PharmaGenesis London, London, UK, and was funded by Alfasigma S.p.A.

The authors thank Alessandra Oortwijn for her contributions to this study.

AM and **CR** are employees of Alfasigma S.p.A at the time of abstract submission.

BGF reports grants and personal fees from AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Janssen Biotech/Centocor, Johnson & Johnson/Janssen, Pfizer, Receptos and Takeda; and personal fees from Ablynx, ActoGenix, Admira, Akebia Therapeutics, Allergan, Atlantic Pharmaceuticals, Avaxia Biologics, Avir Pharma... Disclosures truncated – see poster for full details.

KM reports personal fees from AbbVie, Bristol Myers Squibb, Celltrion, EA Pharma, Eli Lilly, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, Takeda... Disclosures truncated – see poster for full details.

GR reports personal fees and/or speaker fees from AbbVie, AstraZeneca, Augurix Diagnostics, Boehringer Ingelheim, Bristol Myers Squibb, Calypso Biotech, Celgene, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Fisher, Genentech, Gilead Sciences, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Phadia, Pierre Fabre, Roche, Takeda, Tillotts Pharma, UCB, Vifor Pharma... Disclosures truncated – see poster for full details.

DL reports consulting, advisory board and transport fees from AbbVie, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Prometheus, Roche and Takeda.

SV reports financial support for research from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; speaker and/or consultancy fees from AbbVie, Abivax, Aboleris Pharma, AgomAb Therapeutics, Alimentiv, Arena Pharmaceuticals... Disclosures truncated – see poster for full details.

SD reports personal fees from AbbVie, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring Pharmaceuticals, Gilead Sciences, Hospira, Inotrem, Janssen Pharmaceuticals, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB and Vifor Pharma.

EVL has consulted for AbbVie, Alvotect, Amgen, Arena Pharmaceuticals, Astellas, Avalo Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Fresenius Kabi, Genentech, Gilead Sciences, Gossamer Bio, GSK, Iterative Health, Iota Biosciences, Janssen Pharmaceuticals, KSL Diagnostics... Disclosures truncated – see poster for full details.

IB reports personal fees from Galapagos, Gilead Sciences, Janssen Pharmaceuticals, Pfizer, Pharmacosmos, Takeda and Vifor Pharma.

SS reports personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos/Gilead Sciences, Hikma Pharmaceuticals, I-Mab, Janssen Pharmaceuticals, Morphic Therapeutic, MSD, Mylan, Pfizer, Protagonist Therapeutics, Provention Bio, Sandoz/Hexal, Takeda, Theravance Biopharma and Ventyx Biosciences

HJK has received consultancy fees from AbbVie, Johnson & Johnson, Celltrion and Takeda.

MF is an employee and shareholder of Galapagos NV.

AM is a former employee and shareholder of Galapagos NV, and an employee of Alfasigma S.p.A.

CR is a former employee and shareholder of Galapagos NV, and an employee of Alfasigma S.p.A.

LPB has received consulting fees from Abivax, AbbVie, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celltrion, CONNECT Biopharma, Cytoki Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, Gossamer Bio, GSK, HAC Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen Pharmaceuticals, Medac, Mopac, Morphic, MSD, Norgine... Disclosures truncated – see poster for full details.

OP106

REAL-WORLD EFFECTIVENESS OF TOFACITINIB ON ULCERATIVE COLITIS ASSOCIATED SPONDYLOARTHROPATHY (RETUCAS): A MULTICENTRE PROSPECTIVE STUDY FROM THE ITALIAN GROUP FOR THE STUDY OF INFLAMMATORY BOWEL DISEASES (IG-IBD)

F.S. Macaluso¹, M. Grova², F. Bossa³, S. Carparelli³, D. Pugliese⁴, G. Cuccia⁴, M. Cappello⁵, S. Muscarella⁵, S. Saibeni⁶, C. Bezzio^{7,8}, A. Armuzzi^{7,8}, A.G. Gravina⁹, F. Caprioli^{10,11}, A. Sorge^{10,11}, A. Soriano¹², D.G. Ribaldone¹³, S. Festa¹⁴, A. Variola¹⁵, C. Ferracane¹⁶, S. Onali^{17,18}, M.C. Fantini^{17,18}, A. Orlando¹, Italian Group for the Study of Inflammatory Bowel Diseases (IG-IBD)
¹"Villa Sofia-Cervello" Hospital, IBD Unit, Palermo, Italy, ²"Villa Sofia-Cervello" Hospital, Digestive Endoscopy Unit, Palermo, Italy, ³Fondazione Casa Sollievo della Sofferenza, Gastroenterology, San Giovanni Rotondo, Italy, ⁴Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD – IBD Unit - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ⁵University of Palermo, Gastroenterology & Hepatology Section, PROMISE, Palermo, Italy, ⁶ASST Rhodense, Gastroenterology Unit, Rho, Italy, ⁷IRCCS Humanitas Research Hospital, IBD Center, Rozzano, Milan, Italy, ⁸Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Milan, Italy, ⁹Division of Hepatogastroenterology, University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy, ¹⁰University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ¹¹Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy Unit, Milan, Italy, ¹²Arcispedale S.Maria Nuova, IBD Unit, Reggio Emilia, Italy, ¹³University of Turin, Department of Medical Sciences, Turin, Italy, ¹⁴S. Filippo Neri Hospital, IBD Unit, Rome, Italy, ¹⁵IRCCS Ospedale Sacro Cuore Don Calabria Negrar, IBD Unit, Negrar, Italy, ¹⁶"Vittorio Emanuele" Hospital, Gastroenterology Unit, Catania, Italy, ¹⁷University of Cagliari, Department of Medical Science and Public Health, Cagliari, Italy, ¹⁸Azienda Ospedaliero-Universitaria di Cagliari, Cagliari, Italy

Contact E-Mail Address: fsmacaluso@gmail.com

Introduction: Tofacitinib (TOFA) is a JAK inhibitor used for the treatment of rheumatologic diseases including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. The efficacy of TOFA in rheumatology led to big expectations on a potential benefit on ulcerative colitis (UC)-associated spondyloarthropathy (SpA), but very few data are currently available.

Aims & Methods: Real-world Effectiveness of Tofacitinib on Ulcerative Colitis Associated Spondyloarthropathy (RETUCAS) is a prospective, multicentre, observational study designed to assess the effectiveness of TOFA on UC associated SpA and promoted by the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD). Patients with UC and an established diagnosis of active axial or peripheral SpA at baseline were included. Active SpA at baseline was defined with an Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP ≥ 1.3 in case of axial SpA, and with a disease activity score (DAS)28-CRP ≥ 2.6 in case of peripheral SpA.

The primary endpoint was the rate of patients achieving a steroid-free joint response (SFJR - defined by a decrease of ≥ 1.1 units of ASDAS-CRP for axial SpA, and a decrease of > 0.6 units of DAS28-CRP for peripheral SpA compared with baseline with no steroids use) at week 8 and 52.

Secondary endpoints were the clinical intestinal response (CIR) and the steroid-free clinical intestinal remission (SFCIR) assessed with the partial Mayo score.

Results: 44 patients were included (mean age: 43.8 ± 12.6 years; mean duration of disease: 14.2 ± 8.9 years; all but two were bio-experienced). Active axial SpA was reported in 4 patients (9.1%), active peripheral SpA

in 31 cases (70.5%), and mixed (axial + peripheral) SpA in 9 cases (20.5%). At baseline, mean ASDAS-CRP was 2.4 ± 0.7 , and DAS28-CRP was 3.5 ± 0.6 . At 8 weeks, SFJR was reported in 52.3% of patients, with a significant difference between patients with peripheral SpA only compared with the subgroup of patients with axial and mixed SpA (67.7% vs. 15.4%; $p=0.001$). At 52 weeks, SFJR was reported in 59.4% of patients (peripheral SpA only: 66.7% vs. axial and mixed SpA: 37.5%; $p=0.3$). CIR was reported in 59.1% of patients at 8 weeks, and in 75.0% of patients at 52 weeks, with SFCIR achieved by 34.1% at 8 weeks, and 56.2% at 52 weeks.

Three adverse events were reported: one case mild hypercholesterolemia, one case of mild elevation of transaminase levels, and one case of fever and malaise causing the withdrawal of TOFA after 3 days of administration.

Conclusion: This is the first prospective study designed specifically for the assessment of IBD-associated SpA and based on rheumatological scores. TOFA showed to be effective on UC-associated peripheral SpA, while more data are needed on axial SpA

Disclosure: The study was promoted by IG-IBD and received no funding.

Understanding disease primers of IBD: Part 2

14:30-15:30 / Strauss 2

OP107

IMPLICATION OF COMMENSAL FAECAL BACTERIA IN REGULATING THE COLONIC EPITHELIAL BARRIER DURING ULCERATIVE COLITIS

R. Inciuraite¹, S. Juzenas^{1,2}, R. Gedgaudas^{1,3}, D. Tilindė¹, R. Lukosevicius¹, G. Kiudelis^{1,3}, L.V. Jonaitis^{1,3}, J. Kupcinskas^{1,3}, J. Skieceviciene¹

¹Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ²Vilnius University, Institute of Biotechnology, Vilnius, Lithuania, ³Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Department of Gastroenterology, Kaunas, Lithuania

Contact E-Mail Address: ruta.inciuraite@ismuni.lt

Introduction: In the gut, intestinal epithelial cells form a structural barrier, delineating the intestinal lumen from the lamina propria¹. Within the lumen, microbes exert essential functions in maintaining gastrointestinal homeostasis and functionality². Regardless of commensal or pathogenic nature of the bacteria, their interaction with gut epithelium is inevitable. During ulcerative colitis (UC), both mucosal barrier and microbial composition are disturbed³. However, it is still unclear whether naturally occurring gut bacteria might influence the control or management of the protective lining of cells in the colon.

Aims & Methods: The aim of the study was to identify which faecal microbiota components remain unaltered during UC and assess the interplay of these bacteria with colonic epithelial cells.

The study was approved by the Kaunas Regional Biomedical Research Ethics Committee (protocol no. BE-2-31). Faecal microbiota was analysed by employing 16S rRNA-gene v1-v2 region sequencing on stool samples of active and quiescent UC patients (n=47) and non-IBD controls (n=25). Functional analysis was performed using colonic epithelial organoid-derived monolayers of UC patients (n=9) and non-IBD controls (n=8). Monolayers were co-cultured with *Escherichia coli* (ATCC 25922) and *Phocaeicola vulgatus* (ATCC 8482) bacteria type strains. The interplay between bacteria and colonic epithelial cells was assessed by analysing the expression of gene markers for epithelial barrier integrity (ZO1), pathogen recognition (TLR4) and stress induction (HSPA1A, HSPB1).

Results: First, 16S rRNA-gene sequencing revealed a persistent bacterial imbalance in both active and quiescent UC patients compared to non-IBD controls. Specifically, Chao1, Shannon, and Simpson α -diversity indices were significantly lower ($p_{\text{Wilcoxon}} < 0.05$) in both active and quiescent UC patient groups when compared to non-IBD controls. Microbial community clusters, assessed by Bray-Curtis dissimilarity index, also differed significantly between UC patients and non-IBD controls ($p_{\text{PERMANOVA}} < 0.05$). Subsequent co-occurrence and differential abundance analyses identified that in contrast to healthy individuals, UC patients exhibited statistical significance ($p_{\text{adj. Wilcoxon}} < 0.05$) in the relative abundance of 5 genera, including *Alistipes*, *Mediterraneibacter*, *Paraprevotella*, etc., while 35 genera were found to be present at comparable levels ($p_{\text{adj. Wilcoxon}} \geq 0.05$). Of them, the most abundant ones were *Phocaeicola*, *Collinsella*, *Roseburia*, *Holdemanella*, and *Bacteroides*.

Functional analysis, utilizing co-cultures of commensal bacteria and colonic epithelial cells of active UC patients and non-IBD controls, showed that both *E. coli* and *P. vulgatus* did not induce pathogen-pattern recognition and stress responses.

Interestingly, both species demonstrated potential to provoke diverse tight junction-related cellular reactivity (however, due to high variation in patient-to-patient responses, results did not reach statistical significance ($p_{\text{adj. Wilcoxon}} \geq 0.05$)).

More precisely, a contact with *E. coli* and *P. vulgatus* tended to increase the expression of ZO1 in non-IBD epithelial cells (FC=3.59 and FC=2.27, respectively) compared to untreated cells, while an opposite trend was observed in epithelial cells of UC patients (FC = 0.67 and FC = 0.75, respectively).

Conclusion: Diverse colonic epithelial cell responses to distinct commensal bacteria species imply the contribution of stably abundant gut microbiota to the impairment of mucosal barrier integrity during UC.

References:

1. Horowitz, A., Chanez-Paredes, S.D., Haest, X. *et al.* Paracellular permeability and tight junction regulation in gut health and disease. *Nat Rev Gastroenterol Hepatol* **20**, 417–432 (2023)
2. Fan, Y., Pedersen, O. Gut microbiota in human metabolic health and disease. *Nat Rev Microbiol* **19**, 55–71 (2021)
3. Kobayashi, T., Siegmund, B., Le Berre, C. *et al.* Ulcerative colitis. *Nat Rev Dis Primers* **6**, 74 (2020)

Disclosure: Nothing to disclose.

OP108

CHARACTERISING THE COLONIC AND UPPER INTESTINAL VIROME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

R.A.A.A. Ruigrok^{1,2}, S. Garmaeva², A. Fernández-Pato², I.J. Hidding¹, R. Gacesa^{1,2}, A.P. Zhernakova², R.K. Weersma^{1,2}, A. Vich Vila^{3,4}

¹University of Groningen & University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ²University of Groningen & University Medical Center Groningen, Department of Genetics, Groningen, Netherlands, ³VIB, Center for Microbiology, Leuven, Belgium, ⁴Rega Institute, KU Leuven, Department of Microbiology and Immunology, Leuven, Belgium

Contact E-Mail Address: r.a.a.ruigrok@umcg.nl

Introduction: The role of the gut microbiota in inflammatory bowel disease (IBD) pathogenesis is widely acknowledged, with numerous bacteria identified as contributing factors. Little however is known about the part viruses play – a likely major component in the structuring and functioning of the gut microbiota. Understanding how viruses interact with the gut microbiota and host cells in the context of IBD could facilitate innovative treatment approaches and personalized interventions.

Aims & Methods: We explore the colonic and upper intestinal virome in patients with IBD compared with general population (GP) controls. Faecal (colonic) and effluent (upper intestinal) derived shotgun metaviromes of 100 IBD individuals (UC = 50, CD = 50) and 50 IBD individuals with an ileostomy, respectively were compared to faecal derived metaviromes of 50 GP individuals. Metaviromes were generated using a combination of shotgun methods and viral particle enrichment, allowing for identification of both eukaryotic and prokaryotic, dsDNA, ssDNA and RNA viruses. Viral diversity, composition and prevalence were compared by calculating Shannon diversity, Bray-Curtis distances and performing logistic regression analyses. P-values were adjusted using false discovery rate (FDR) to correct for multiple testing, where relevant; FDR<0.05 was considered significant.

Results: Similar to bacterial diversity in IBD versus GP samples, we see a significantly lower viral diversity in CD and UC colonic samples compared with the GP, and an even lower diversity when comparing upper intestinal samples to colonic samples (FDR<0.05). Comparing viral populations between groups, we observe that, whilst there is evident interindividual variability within groups, distinct clustering between colonic and upper intestinal samples can be seen, with colonic IBD samples clustering slightly more towards upper intestinal samples.

When comparing viral group prevalences between GP and IBD colonic samples, 83 out of 260 viral groups present in IBD-UC samples are absent in the GP samples and 125 out of 302 viral groups present in the GP were absent in IBD-UC. For IBD-CD samples these numbers are 79 out of 248 and 133 out of 302, respectively. The top 3 viral groups that positively associated with IBD-UC samples are: one unknown phage group (predicted bacterial host: *Parasutterella* spp.), a group containing *Lactobacillus* phages (bacterial host: *Lactobacillus* spp.) and a group containing *Lactococcus* phages (bacterial host: primarily *Lactococcus* spp.). The top 3 viral groups that positively associated with IBD-CD samples are: the same unknown phage group as for IBD-UC, and two other unknown phage groups (predicted bacterial hosts: primarily *Enterocloster* & *Bacteroides* spp, respectively).

Conclusion: This first comprehensive description of the gut virome across multiple gastrointestinal sites shows specific alterations in IBD. Many viral groups differentially present in the IBD intestine infect bacteria often associated with gut health and significantly reduced in IBD patients. Dysregulated bile acid signaling has also been implicated in the pathogenesis of IBD, with bacterial dysbiosis being linked to its cause. In IBD populations, we observe phages with the host *E. boltea* – a bacteria increased in dysbiosis due to their potential to metabolise bile acids.

We speculate that alterations in the gut virome composition are key events that disrupt the equilibrium between gut microbiota and host, promoting a pro-inflammatory state and driving IBD pathogenesis. The next steps will be to investigate the mechanisms underlying these complex interactions.

Disclosure: Nothing to disclose.

OP109

MULTI-DIMENSIONAL IMMUNOPROFILING OF UNCONVENTIONAL T CELLS OF INFLAMMATORY BOWEL DISEASE PATIENTS: ASSOCIATION WITH CLINICAL PHENOTYPES, DISEASE ACTIVITY AND PROGNOSIS

I. Catalan-Serra¹, W. Xu², T. Bruland^{3,4}, A.K. Sandvik^{4,3}, A. Larbi²

¹Levanger Hospital. Norwegian University of Science and Technology. Centre for Molecular Inflammation, Gastroenterology, Levanger, Norway, ²Singapore Immunology Network (SigN), Agency for Science Technology and Research, Singapore, ³Department of Clinical and Molecular Medicine (IKOM), NTNU - Norwegian University of Science and Technology, Trondheim, Norway., ⁴Department of Gastroenterology and Hepatology, Clinic of Medicine, St. Olav's University Hospital, Trondheim, Norway, Trondheim, Norway

Contact E-Mail Address: ignaciocatalan76@hotmail.com

Introduction: Inflammatory bowel disease (IBD) is a chronic systemic condition of unknown etiology. Dysregulated T-cell responses play a fundamental role in perpetuating intestinal inflammation in IBD. Unconventional T cells are a diverse subset of T cells with innate and adaptive characteristics including: Gamma Delta T cells (GDT), mucosa-associated invariant T (MAIT) cells, and invariant natural killer T (iNKT) cells. As new studies emerge, unconventional T cells' role in IBD pathogenesis has been increasingly recognized, but their role in the pathogenesis and possible clinical application remains to be elucidated.

Aims & Methods: The aim of the study is to characterize the immune profile of IBD patients and controls in a large well-characterized cohort with focus on Unconventional T cells. We performed an in-depth, multidimensional flow cytometry analysis of unconventional T cells and plasma proteins from patients' samples collected from the IBD biobank in Norway. We used immunophenotyping from isolated PBMC to study both conventional T cells and unconventional T cells and evaluated their gut-homing

-a4 and b7 expression-, activation and senescence markers. A 65-plex Luminex assay was used to quantify soluble plasma proteins. We studied the variations of T cell profiles within the different disease phenotypes and their correlation with disease activity. A subset of patients was followed-up clinically for 6 (+/-2) years to evaluate the association with disease outcomes.

Statistical analysis was performed using GraphPad Prism (San Diego, CA). Two-tailed Mann-Whitney U test was used to compare two independent groups and ROC analysis was used for diagnostic accuracy; $p \leq 0.05$ was considered statistically significant. Ethical approvals were obtained and all patients gave written informed consent.

Results: A total of 184 individuals (106 F) were included: 149 IBD (84 UC and 65 CD) and 25 healthy controls. We found important quantitative and phenotypical differences in unconventional T cells and plasma protein in IBD and between UC and CD patients. Patients with IBD had a significant reduction in MAIT cells, and increase in GDT VD3+ and CD8+ cells ($p < 0.05$). MAIT cells from IBD patients had lower a4+ and b7+ expression than controls. ($p < 0.05$, $p < 0.001$). Interestingly, Macrophage Migration Inhibitor Factor (MIF) was significantly reduced in patients with UC but not in CD ($p < 0.0001$).

Patients with total colitis presented a significant increase in platelet count, MIG, IL-2R, and CD30 ($p < 0.001$, $p < 0.01$ and $p < 0.05$, respectively). CD patients with colonic affection (L2) had a significant increase in TNF-b, FGF-2, G-CSF compared with patients with ileal (L1) or ileocolonic (L3) CD ($p < 0.01$). Interestingly, MAIT cells were the only immune cells significantly reduced in patients with extraintestinal manifestations. The combination of 6 parameters: IL-4, IL-5, IL-8, MIG, CD30 and Eotaxin-3 showed a good diagnostic accuracy in ROC curves (CI:0.759-1.000; $p = 0.0005$) to distinguish patients with mucosal healing vs those with biochemical and clinical remission alone. A decrease in GDT VD2 cells was found in UC patients with worse outcomes ($p < 0.01$). CD patients with bad prognosis showed a significant increase in platelet counts and a decrease in: FABP2, CXCL10 and APRIL ($p < 0.05$).

Conclusion: These results demonstrate the potential of the characterization of Unconventional T cells and soluble plasma proteins as biomarkers in IBD and as markers of disease progression. Further investigation is warranted to elucidate the use of Unconventional T cells in precision medicine and as potential therapeutic targets in IBD.

References: 1. Catalan-Serra I, Sandvik AK, Bruland T et al. Gammadelta T Cells in Crohn's Disease: A New Player in the Disease Pathogenesis? J Crohns Colitis. 2017;11:1135-1145.

2. Hinks TSC, Zhang XW. MAIT Cell Activation and Functions. Front Immunol. 2020 May 27;11:1014. doi: 10.3389/fimmu.2020.01014.

Disclosure: No

OP110

CADAVERINE, A GUT MICROBIOTA-DERIVED POLYAMINE, TRIGGERS METABOLIC REPROGRAMMING TOWARDS OXPHOS IN MONOCYTES/MACROPHAGES IN VITRO AND DURING INTESTINAL INFLAMMATION

R. De Oliveira Formiga¹, Q. Li¹, V. Pisano Puchois¹, I. Alonso Salgueiro¹, L. Creusot¹, S. Amouyal¹, M. Bredon¹, Y. Zhao², T. Ledent¹, C. Danne¹, M.-L. Michel³, P. Emond⁴, G. Chevreux⁵, H. Phuong Pham⁶, R.J. Argüello⁷, N. Rolhion¹, T. Wai², H. Sokol^{1,8}

¹Sorbonne University, Saint-Antoine Research Center, INSERM UMRS-938, AP-HP, Paris, France, ²Pasteur Institute, Paris, France, ³Paris-Saclay University, INRAE, AgroParisTech, Micalis institute, Jouy-en-Josas, France, ⁴Tours University, INSERM UMRS-1253, Scientific and Technical Platform Analysis of Biological Systems, Metabolomics Department, Tours, France, ⁵Paris Cité University, CNRS, UMRS-7592, ProteoSeine Core Facility, Jacques Monod Institute, Paris, France, ⁶Parean Biotechnologies, Saint Malo, France, ⁷Aix Marseille University, CNRS, INSERM UMRS-1104, CIML, Marseille-Luminy Immunology Center, Marseille, France, ⁸Paris Cité University, CNRS, UMRS-7592, ProteoSeine Core Facility, Institut Jacques Monod, Paris, France

Contact E-Mail Address: rodrigo.formigadc@gmail.com

Introduction:

The gut microbiome exerts a significant influence on the host's cellular energy metabolism during homeostasis and disease, notably due to the production of metabolites (1), such as polyamines (2).

Gut dysbiosis and bioenergetic alterations leading to metabolic shifts have been associated with altered cellular responses and are involved in intestinal disorders, such as inflammatory bowel disease (IBD) (3,4).

Cadaverine, a gut polyamine derived from L-lysine decarboxylation, has been previously proposed to be transported into mitochondrial inner compartments in basal and induced conditions (5).

On the other hand, it seems to be positively regulated in the gut of IBD patients (6). However, the biological significance in both contexts remains still unexplored.

Aims & Methods:

This study uncovers the potential immunometabolic role of cadaverine in vitro and during intestinal inflammation. For that, single-cell energetic metabolism by profiling translation inhibition (SCENITH), luminescence and flow cytometry-based assays, Seahorse real-time cell metabolic analysis, metabolomics, RNAseq, and proteomics were applied to explore the role of cadaverine on energy metabolism in purified cells. Antibiotic-induced gut microbiota perturbations and dextran sodium sulfate (DSS)-induced colitis were carried out to further investigate its effect in vivo.

Results: Here we demonstrate that cadaverine enhances adenosine triphosphate (ATP) levels in THP-1 monocytic cell line as well as in human monocytes and macrophages obtained from healthy donors. Those results were associated with increased glucose uptake and utilization as a metabolic fuel and with higher mitochondrial dependence as a metabolic pathway, particularly elevating basal and maximal oxidative phosphorylation (OXPHOS) rates. The effects of cadaverine on mitochondrial functions persisted even in the presence of lipopolysaccharide (LPS) that triggers aerobic glycolysis in monocytes/macrophages.

Interestingly, cadaverine presented immunomodulatory activity by increasing interleukin (IL)-10 levels and decreasing tumor necrosis factor (TNF)- α production in classical monocytes while triggering the polarization of macrophages to the M2 anti-inflammatory phenotype. Such immunomodulatory potential appears intricately dependent on mitochondrial respiration since this effect was blocked when OXPHOS was pharmaco-

logically inhibited. Omics analysis reveals that itaconate metabolism and Krebs cycle modulation may be associated with cadaverine immunometabolic activity. Oral administration of cadaverine in antibiotics-induced gut microbiota-depleted mice rescued from both small intestine and colon macrophage energy deficiency.

Furthermore, cadaverine also sustained OXPHOS and mitochondrial health features in those cells. As L-lysine decarboxylase genes are mostly expressed by gut Enterobacteriaceae, which in turn are augmented and suggested to be related to IBD, we specifically depleted this bacterial family with colistin in mice and induced colitis with DSS.

In this setting cadaverine administration ameliorates disease severity by polarizing colon macrophages towards the M2 phenotype and preserving the overall mitochondrial features, such as mass, mitochondrial membrane potential, and reactive oxygen species, to sustain ATP production by OXPHOS.

Conclusion: Such discoveries at the metabolic level hold promise for identifying novel therapeutic strategies that target cellular energy metabolism and the gut microbiota to modulate monocyte and macrophage responses in IBD.

References: 1. Michaudel C, Sokol H. The Gut Microbiota at the Service of Immunometabolism. *Cell Metab.* 2020 Oct 6;32(4):514-523.

2. Puleston DJ et al. Polyamines and eIF5A Hypusination Modulate Mitochondrial Respiration and Macrophage Activation. *Cell Metab.* 2019 Aug 6;30(2):352-363.e8.

3. Zeng Z et al. Glycolytic Activation of CD14+ Intestinal Macrophages Contributes to the Inflammatory Responses via Exosomal Membrane Tumor Necrosis Factor in Crohn's Disease. *Inflamm Bowel Dis.* 2024 Jan 5;30(1):90-102.

4. Lloyd-Price et al. Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases. *Nature.* 2019 May;569(7758):655-662.

5. Toninello A, Dalla Via L, Testa S, Siliprandi D. Electrophoretic polyamine transport in rat liver mitochondria. *Amino Acids.* 1992 Feb;2(1-2):69-76.

6. Li M, Yang L, Mu C, Sun Y, Gu Y, Chen D, Liu T, Cao H. Gut microbial metabolome in inflammatory bowel disease: From association to therapeutic perspectives. *Comput Struct Biotechnol J.* 2022 Apr 4;20:2402-2414.

Disclosure: Harry Sokol reports lecture fees, board membership, or consultancy from Carenity, AbbVie, Astellas, Danone, Ferring, Mayoly Spindler, MSD, Novartis, Roche, Tillots, Enterome, BiomX, Biose, Novartis, Takeda, Biocodex and is cofounder of Exelium Biosciences.

OP111

SYSTEMIC ANTIBODY RESPONSES AGAINST GUT MICROBIOTA FLAGELLINS IMPLICATE SHARED AND DIVERGENT IMMUNE REACTIVITY IN CROHN'S DISEASE AND CHRONIC FATIGUE SYNDROME

A.R. Bourgonje^{1,2}, N. Hörstke³, M. Fehrer³, G. Innocenti³, T. Vogl³

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America, ³Medical University of Vienna, Center for Cancer Research, Vienna, Austria

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Patients with Crohn's disease (CD) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) exhibit elevated antibody responses against gut microbiota flagellins. However, flagellin-specific antibody repertoires and functional roles in the diseases remain incompletely understood. Bacterial flagellins can be categorized into three types depending on their interaction with toll-like receptor 5 (TLR5): (1) "stimulator" and (2) "silent" flagellins, binding TLR5 through a conserved

N-terminal motif, with only stimulators activating TLR5 due to a specific C-terminal domain; (3) “evader” flagellins of pathogens, which circumvent TLR5 activation via mutated N-terminal TLR5 binding motifs.

Here we studied the characteristics, epitope binding, and sequence (dis) similarity of anti-flagellin antibody responses in CD and ME/CFS.

Aims & Methods: Since conventional antibody profiling methods like enzyme-linked immunosorbent assays [ELISAs] do not allow for large-scale measurements of antibody repertoires, we leveraged phage-display immunoprecipitation sequencing (PhIP-Seq) to characterize 344,000 rationally selected peptide antigens in 256 patients with CD, 40 patients with ME/CFS and in two equally sized groups of age- and sex-matched healthy controls from population-based cohorts in the Netherlands and U.K., respectively. Different sequence alignment strategies were employed to compare flagellin peptide structures with observed antibody-bound flagellin peptide reactivity.

Results: Both patients with CD and ME/CFS exhibited elevated antibody responses against distinct regions of flagellin peptides compared to healthy individuals ($P < 0.001$). N-terminal binding to *Lachnospiraceae* flagellins was comparable in both diseases, while C-terminal binding was more prevalent in CD. N-terminal antibody-bound flagellin sequences were similar across CD and ME/CFS, resembling ‘stimulator’ and ‘silent’ flagellins more than evaders.

However, C-terminal antibody-bound flagellins showed higher resemblance to stimulator than to silent flagellins in CD, but not in ME/CFS. This group of antibody-bound flagellins was exclusively identified in a subset (10-20%) of patients with CD and characterized by its strong overrepresentation (exceeding 20-fold), underscoring its potential significance in distinguishing pathophysiological subtypes of CD.

Conclusion: Antibody binding to the N-terminal domain of stimulator and silent flagellins may impact TLR5 activation in both CD and ME/CFS patients. Furthermore, elevated antibody binding to the C-terminal domain of stimulator flagellins in CD may explain pathophysiological differences between diseases. Our results highlight the diagnostic potential of these antibody responses and their impact on innate/adaptive immunity balance.

Disclosure: Nothing to disclose.

Barrett’s oesophagus: Treatment and surveillance

14:30-15:30 / Lehar 1

OP112

LOW RECURRENCE RATES AFTER ENDOSCOPIC RESECTION (R0) OF HIGH-RISK T1 ADENOCARCINOMA IN BARRETT’S ESOPHAGUS SUPPORT A STRICT ENDOSCOPIC SURVEILLANCE STRATEGY: PRELIMINARY RESULTS OF A PROSPECTIVE, INTERNATIONAL, MULTICENTER COHORT STUDY (PREFER)

V. Bos¹, M.W. Chan¹, W.B. Nagengast², M.J. Bourke³, T. Beyna⁴, R. Bisschops⁵, A.D. Koch⁶, B.L. Weusten^{7,8}, A. Alkhalaf⁹, O. Pech¹⁰, S. Seewald¹¹, R.J. Haidry^{12,13}, D. De Wulf¹⁴, C. Schlag¹⁵, E.J. Schoon¹⁶, M. Houben¹⁷, J. Ortiz Fernández-Sordo¹⁸, H. Messmann¹⁹, P. Dewint²⁰, J. Westerhof², M.C. Spaander⁶, G. De Hertogh²¹, E.A. Nieuwenhuis¹, M. Jansen²², H. Neuhaus⁴, S.L. Meijer²³, J.J. Bergman¹, R.E. Pouw¹

¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²University Medical Center Groningen, Groningen University, Gastroenterology and Hepatology, Groningen, Netherlands, ³Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia, ⁴Evangelisches Krankenhaus Düsseldorf, Internal Medicine and Gastroenterology, Düsseldorf, Germany, ⁵University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ⁶Erasmus MC Cancer Institute, University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁷Sint Antonius Hospital, Gastroenterology and Hepatology, Nieuwegein, Netherlands, ⁸University Medical Center, Utrecht University, Gastroenterology and Hepatology, Utrecht, Netherlands, ⁹Isala Clinics, Gastroenterology and Hepatology, Zwolle, Netherlands, ¹⁰St. John of God Hospital, Gastroenterology, Regensburg, Germany, ¹¹GastroZentrum Hirslanden, Gastroenterology, Zurich, Switzerland, ¹²University College Hospital NHS Trust, Gastroenterology and Hepatology, London, United Kingdom, ¹³Cleveland Clinic London, Digestive Diseases and Surgery Institute, London, United Kingdom, ¹⁴AZ Delta Roeselare, Gastroenterology, Roeselare, Belgium, ¹⁵Technical University of Munich, Klinikum rechts der Isar der, München, Germany, ¹⁶Catharina Hospital, Gastroenterology and Hepatology, Eindhoven, Netherlands, ¹⁷HagaTeaching Hospital, Gastroenterology and Hepatology, The Hague, Netherlands, ¹⁸Nottingham University Hospitals NHS Trust, Nottingham Digestive Diseases Centre, NIHR Biomedical Research Unit, Nottingham, United Kingdom, ¹⁹University Hospital Augsburg, Gastroenterology, Augsburg, Germany, ²⁰AZ Maria Middelaers, Gastroenterology, Ghent, Belgium, ²¹University Hospitals Leuven, Pathology, Leuven, Belgium, ²²University College London Hospital NHS Trust, Histopathology, London, United Kingdom, ²³Amsterdam UMC, Histopathology, Amsterdam, Netherlands

Contact E-Mail Address: v.bos@amsterdamumc.nl

Introduction: Optimal management after radical endoscopic resection (R0 ER) of high-risk (HR) T1 esophageal adenocarcinoma (EAC) is still a matter of debate due to conflicting reports on the risk of lymph node metastasis (LNM). In case of submucosal (sm) invasion, a/o poor differentiation, a/o lympho-vascular invasion (LVI), additional treatment is often still recommended. In this prospective international multicenter cohort study (PREFER, NCT03222635), we aim to evaluate the safety of a strict endoscopic follow-up (FU) strategy following R0 ER for T1b and HR-T1a EAC.

Aims & Methods: Patients treated with R0 ER of T1b EAC were included from July 2017 - July 2023, in 19 hospitals in Europe and Australia. Pa-

tients were defined as HR-T1b EAC in case of sm invasion $\geq 500\mu\text{m}$, a/o poor differentiation, a/o LVI. From July 2020 we also included HR-T1a EAC, with HR defined as presence of poor differentiation a/o LVI, as part of an ongoing prospective registry. To allow for appropriate FU we assessed outcomes for patients included up to July 2023, at which time inclusion for the prospective PREFER study was complete.

After R0 ER, patients underwent re-staging with endoscopic ultrasound (EUS) and CT/PET. If there were no signs of metastasis (cNOM0), patients were consented for strict endoscopic FU, with gastroscopy and EUS 3-monthly the first 2 years, 6-monthly during years 3 and 4, and at year 5. CT/PET was repeated after 1 year. Primary outcomes were 5-year disease-specific and overall survival; secondary outcomes were rates of distant metastasis, LNM, and local recurrence ineligible for endoscopic treatment.

Results: Per July 2023, 200 patients (166 male, median age 70 (IQR 63 - 76) years) were included, 157 T1b patients (n = 54 low-risk (LR) T1b and n = 103 HR-T1b) and 43 HR-T1a patients.

For the T1b group, median FU was 21 (IQR 12-38) months. Thus far, 11/157 patients (7%) have successfully completed the 5-year FU without signs of metastatic disease or intra-luminal tumor recurrence ineligible for endoscopic re-treatment. Distant metastases were diagnosed in 3/157 (2%, 95%CI 0 - 4) patients, all without signs of local recurrence or LNM: 1/3 underwent resection of a lung metastasis, with no signs of recurrence after 9 months; 1/3 had liver metastasis and started palliative systemic therapy 4 months ago; 1/3 had liver metastasis, declined further treatment and died. Locoregional LNM were diagnosed in 9/157 (6%, 95% CI 2 - 9). All were detected at a curable stage, but 1/9 declined further treatment and died from EAC; the other patients received appropriate treatment and are disease-free after median 26 (IQR 12 - 27) months post additional treatment. In total, 8/157 patients (5%, 95%CI 2 - 9) developed intra-luminal tumor recurrence ineligible for endoscopic re-treatment, 3/8 declined additional treatment and eventually died from EAC. Furthermore, 10/157 patients (6%) died during FU due to unrelated causes.

In the HR-T1a group, no recurrent disease was diagnosed after a median FU of 16 (IQR 12 - 23) months.

Total N=200	FU (months), Median (IQR)	Distant metastasis, N (% [95%CI])	FU until distant metastasis (months), Median (IQR)	Lymph node metastasis, N (% [95%CI])	FU until LNM (months), Median (IQR)	Intra-luminal tumor recurrence ineligible for ER*, N (% [95%CI])	FU until recurrence ineligible for ER*, (months), Median (IQR)	EAC- related death, N (% [95%CI])	Non-EAC- related death, N (% [95%CI])
High-risk T1b (n=103)	21 (12 - 36)	3 (3%[0 - 6])	29 (N/A)	7 (7%[2 - 12])	10 (3 - 13)	6 (6%[1 - 10])	6 (4 - 15)	4 (4%[0 - 8])	7 (7%[2 - 12])
Low-risk T1b (n=54)	22 (11 - 42)	0	-	2 (4%[0 - 9])	15 (N/A)	2 (4%[0 - 9])	8 (N/A)	0	3 (6%[0 - 12])
High-risk T1a (n=43)	16 (12 - 23)	0	-	0	-	0	-	0	0

*1 patient both had LNM and intra-luminal tumor recurrence

Conclusion: The preliminary findings of this first prospective study on HR-T1 EAC support a strict endoscopic FU strategy in select patients who underwent R0 ER with no signs of metastatic disease (cNOM0) at baseline.

Disclosure: Nothing to disclose.

OP113

IDENTIFYING PUTATIVE GENOMIC BIOMARKERS FOR RISK STRATIFICATION IN BARRETT'S ESOPHAGUS PATIENTS WITH NORMAL HISTOLOGICAL FEATURES

P. Stougie¹, N. Frei¹, V. Pappalardo², A. Khoshiwal¹, H. Yu³, R. de Menezes², L. Duits¹, J.J. Bergman¹, M. Stachler³
¹Amsterdam UMC,, Dept. of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Netherlands Cancer Institute, Biostatistics Centre and Department of Psychosocial and Epidemiological Research, Amsterdam, Netherlands, ³University of California, Department of Pathology, San Francisco, United States of America

Contact E-Mail Address: p.stougie@amsterdamumc.nl

Introduction: Current surveillance for low-risk Barrett's Esophagus (BE) patients is burdensome, cost-ineffective and dependent on subjective histological assessment of dysplasia with high inter-observer variability. This study aims to identify genomic features that can be identified in a clinically translatable targeted sequencing panel, enhancing the stratification of low-risk BE patients and enabling personalized surveillance strategies.

Aims & Methods: BE patients identified as progressors to early esophageal adenocarcinoma or non-progressors from a large community-based cohort, were matched for age, sex and BE segment length. DNA from baseline and prior non-dysplastic biopsies was sequenced using a targeted capture-based panel designed to detect mutations and copy number changes (CNV).

Detected mutations, homozygous deletions, and high-level amplifications were filtered for likely pathogenic events. We performed logistic regression, covariate analysis, and penalized mixed-effect models. A joint model for survival and mixed effects was implemented to analyze the data distributed over space and time.

Results: 331 baseline samples and 214 temporal samples, accounting for 105 progressors who progressed after a median 4 (IQR 2.4-7.2) years, and 115 non-progressors who had a median progression-free follow-up of 6 (IQR 4.3-7.3) years, were analyzed. *TP53* mutations strongly predict risk ($p < 0.0001$, Hazard Ratio (HR) = 3.84, 95% confidence interval (CI) 2.89-5.67) as does CNV 17p loss ($p < 0.0001$, HR = 4.41, 95% CI 2.29-8.52).

While there is significant overlap between *TP53* mutations and 17p loss, patients with both trended to progress faster. Chromosomal arm CNVs ($p = 0.0012$, HR = 1.32, 95% CI 1.14-1.52), amplifications ($p < 0.001$, HR = 2.89, 95% CI 1.57-5.31) and mutational burden ($p < 0.0001$, HR = 1.30, 95% CI 1.21-1.40) were also associated with progression risk. A combined model incorporating: —*TP53* mutations, 17p loss, and mutational burden—demonstrated a 57% sensitivity and 84% specificity and an AUC of 0.758. This model identified 60 of 105 progressors in non-dysplastic BE patients.

	Predicted non-Progressive	Predicted Progressive
True Non- Progressors	96	18
True Progressors	45	60

Table.

Conclusion: As expected, *TP53* was a pivotal risk factor in this spatial and time-dependent cohort, even in the absence of dysplasia. Two hits in *TP53* (mutation with 17p loss) suggested a trend toward near term progression, suggesting the possibility of more refined stratification. Prior studies focused on either mutations or CNVs for risk stratification.

We show the combination of both, detected in a clinically translatable assay, improves prognostic value, effectively identifying the majority of pro-

gressors among non-dysplastic BE patients while maintaining an acceptable false-positive rate. This approach has the potential to dramatically impact risk stratification and surveillance strategies in non-dysplastic BE patients.

Disclosure: Nothing to disclose.

OP114

BEHAVIOURAL FACTORS IN ACHIEVING QUALITY BARRETT’S SURVEILLANCE ENDOSCOPY: A QUALITATIVE INTERVIEW STUDY OF UK ENDOSCOPISTS USING THE THEORETICAL DOMAINS FRAMEWORK

E. Ratcliffe¹, M. Horne², J. Britton³, S. Hamdy⁴, J. McLaughlin⁵, Y. Ang⁶

¹University of Manchester, Division of Diabetes, Endocrinology and Gastroenterology Faculty of Biology, Medicine and Health School of Medical Sciences, Manchester, United Kingdom,

²University of Leeds, School of Healthcare, Faculty of Medicine and Health, Leeds, United Kingdom, ³Salford Royal Hospital, Northern Care Alliance NHS Trust, Gastroenterology, Salford, United Kingdom, ⁴Salford Royal Hospital, GI Science, Salford, United Kingdom, ⁵University of Manchester Salford Royal Hospital Gastrointestinal Centre, GI Centre, Manchester, United Kingdom, ⁶Salford Royal NHS Foundation, Gastroenterology, Salford, United Kingdom

Contact E-Mail Address: Elizabeth.ratcliffe@nca.nhs.uk

Introduction: Barrett’s oesophagus endoscopic surveillance pathways exist to aid detection of early progression at the dysplastic phase. Performance in accordance with guidelines can be mixed, and rates of missed dysplasia are high(1). Barrett’s surveillance endoscopy is a complex skill and requires a broad outlook when considering behaviour change interventions. Behavioural theory can be used to target aspects which influence behaviour which are most likely to affect change when used in implementation studies and has been used in prior studies of colonic polyp detection(2).

Aims & Methods: In this study we aimed to explore using qualitative methodology and behavioural theory, factors which influence endoscopists behaviours to identify barriers and facilitators to the adherence of Barrett’s surveillance endoscopy guidelines which could be utilised in future implementation research to improve practice.

Semi-structured interviews were performed over video conferencing software between August 2021 and July 2022 with purposively sampled clinicians who perform endoscopic Barrett’s surveillance from across the UK who work in a range of hospital types. Framework qualitative analysis was used to identify modifiable factors in line with the Theoretical Domains Framework (TDF) and Capability, Opportunity Motivation - Behaviour (COM-B) model of behaviour change(3,4).

Results: Thematic saturation was achieved at 22 interviews consisting of 3 consultant surgeons, 9 consultant gastroenterologists, 6 clinical (nurse) endoscopists, 2 trainee gastroenterologists and 2 trainee surgeons. Themes were mapped into key themes of intrapersonal, interpersonal and organisational factors.

Key intrapersonal factors included the endoscopists’ knowledge of and recall of Barrett’s surveillance guidelines, their technical skills required to perform quality Barrett’s surveillance, the influence of a competing workload and their motivation to perform Barrett’s surveillance well. Interpersonal factors included having a motivated endoscopy team who are skilled in assisting endoscopic surveillance and who understand the importance of surveillance, endoscopists’ training both pre-certification and post certification and facilitating continued professional development for those in later career years.

Organisational factors included departments allowing adequate scheduling of procedure to allow time for lesion detection, the completing burden of other procedures and waiting lists and availability of equipment e.g. acetic acid.

From these themes, 21 barriers and facilitators were identified and mapped to behavioural interventions for use in future intervention studies - some examples are outlined in Table 1.

Barriers	Facilitators	TDF Domains	COM-B domains	Action	Level	Behaviour change wheel Intervention function
- Knowledge and recall of Barrett’s surveillance guidelines	- Barrett’s surveillance performed by those with an interest in the condition	Knowledge	Capability	- Local education sessions on guidelines	Intrapersonal	Training and education
		Skills	Reflective motivation	- Demonstrations of good practice by local experts/ UGI lead	Interpersonal	Restrictions
		Goals and intentions	Psychological capability	- Streamline Barrett’s surveillance procedures to those with an interest in UGI disease on dedicated endoscopy lists	Organisational	Enablement
- Motivation to perform Barrett’s surveillance well to find early lesions	- Motivation to perform Barrett’s surveillance well to find early lesions	Motivation	Social opportunity	- Departments engage in Barrett’s related research		Modelling
		Social and professional role		- Training in Barrett’s surveillance should include focus on tip control and lesion recognition in UGI endoscopy	Interpersonal	Persuasion
				-Improve access to UGI specialist trainers		
- Technical skills required to perform quality Barrett’s surveillance	- Increasing frequency of performing Barrett’s surveillance improves skills	Skills	Physical capability	-Credentialling in Barrett’s surveillance like Bowel cancer screening	Interpersonal	Training and education
		Knowledge	Automatic motivation			Modelling
				-Continue to maintain regular updates on Barrett’s surveillance guidelines to support endoscopists’ behaviour	Organisational	
- Lack of standardisation of Barrett’s audit and credentialling	- Guidelines providing a framework for behaviour and reassurance of quality of care being provided	Motivation	Reflective motivation	-Key performance indicators e.g. oesophageal withdrawal times, completion of Seattle protocol	Interpersonal	Education
		Behaviour regulation	Automatic motivation	-Audit Barrett’s practice, dysplasia detection and post endoscopy cancers	Organisational	Incentivisation
		Reinforcement	Psychological capability			Restrictions
- Negative emotion regarding completion of Barrett’s surveillance endoscopy		Emotions	Reflective motivation	-Reduce the burdensome aspects of surveillance – e.g. AI-assisted lesion recognition	Intrapersonal	Enablement
		Behaviour regulation	Automatic motivation	-Adequate scheduled time for procedures		Incentivisation
		Environmental context	Psychological capability	-Dedicated Barrett’s endoscopy lists ring-fenced away from other tasks	Organisational	Environmental restructuring
- Workload burden for endoscopists			Physical capability	-Wider issues of workload in the health service		Restrictions

Table 1: Outlining examples of barriers and facilitators to performing quality Barrett’s surveillance mapped to the Theoretical domains framework(TDF).

Conclusion: The findings of this study provide potential targets for intervention studies which may improve Barrett’s surveillance practice through facilitating behaviour change. Intra and interpersonal factors such as training and education are vital, but the real challenge may be the organisational shift from high turnover to a quality-centred approach for Barrett’s endoscopy. As a complex care intervention, clinician behaviour is one aspect in a multifaceted care pathway which can be improved.

References: 1) van Putten M, Johnston BT, Murray LJ, et al. ‘Missed’ oesophageal adenocarcinoma and high-grade dysplasia in Barrett’s oesophagus patients: A large population-based study. *United Eur Gastroenterol J*. Published online 2018. doi:10.1177/2050640617737466

2) Atkins L, Hunkeler EM, Jensen CD, et al. Factors influencing variation in physician adenoma detection rates: A theory-based approach for performance improvement. *Gastrointest Endosc*. Published online 2016. doi:10.1016/j.gie.2015.08.075

3) Michie S. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care*. 2005;14(1):26-33. doi:10.1136/qshc.2004.011155

4) Michie S, Atkins L, West R. *The Behaviour Change Wheel: A Guide to Designing interventions* Susan Michie; Lou Atkins; Robert West. Silverback Publishing; 2014

Disclosure: Funding for this study was obtained from Medtronic Ltd ref number ERP-2019-11987. Medtronic Ltd had no input to the study design or undertaking of the study itself.

OP115

ENDOSCOPIC BIOPSY TECHNIQUES IN BARRETT ESOPHAGUS PATIENTS: A MULTIDESIGN STUDY

I.N. Beaufort^{1,2}, S.G. Elias³, A.N. Milne⁴, L.A.A. Brosens⁵, M.A.M.T. Verhagen⁶, L. Alvarez Herrero¹, B.L.A.M. Weusten^{1,2}
¹Sint Antonius Hospital, Gastroenterology and Hepatology, Nieuwegein, Netherlands, ²University Medical Center Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands, ³Julius Center for Health Sciences and Primary Care, Epidemiology and Health Economics, Utrecht, Netherlands, ⁴Sint Antonius Hospital, Pathology, Nieuwegein, Netherlands, ⁵University Medical Center Utrecht, Pathology, Utrecht, Netherlands, ⁶Diakonessenhuis, Gastroenterology and Hepatology, Utrecht, Netherlands

Contact E-Mail Address: i.beaufort@antoniusziekenhuis.nl

Introduction: Different random biopsy techniques exist for Barrett Esophagus (BE) surveillance, of which the impact on histopathological quality is unclear. Therefore, we compared the double-biopsy (DB) versus single-biopsy (SB) method, and advance-and-close (A&C) versus turn-and-suction (T&S) technique in a multidesign study.

Aims & Methods: In a multicenter, factorial design trial, BE patients were randomly assigned to one of two biopsy methods (DB or SB) and techniques (A&C or T&S) in a 1:1:1:1 approach, stratified by BE length and hospital. Endpoints were biopsy size, defined as surface area in mm², and time required to obtain biopsies. Assessment of biopsy size was done in a blinded fashion. Data was analyzed with mixed effects regression analyses with a random intercept per patient including stratification factors as fixed effects.

We assumed no interaction between the co-primary comparisons. In a subsequent before-after study, the optimal biopsy method and technique found in the factorial trial was implemented in routine clinical practice. Biopsies before and after implementation were analyzed on biopsy size, using mixed effects regression analyses with a random intercept per patient including BE length as fixed effect.

Results: In the factorial trial, 107 patients were randomized and 1024 biopsies were assessed. Mean biopsy size for each randomization arm, that is, DB+A&C, DB+T&S, SB+A&C, SB+T&C was 2.77mm² (95%CI 2.44-3.09), 2.61 mm² (95%CI 2.29-2.93), 3.14 mm² (95%CI 2.81-3.46) and 3.54 mm² (95%CI 3.22-3.86), respectively (Table 1).

	Double-biopsy (DB)	Single-biopsy (SB)
Advance-and-close (A&C)	2.77 (2.44-3.09)	3.14 (2.81-3.46)
Turn-and-suction (T&S)	2.61 (2.29-2.93)	3.54 (3.22-3.86)

Table 1: Biopsy size in mm² per biopsy method and technique (95% CI).

Biopsy size increased with 25% from 2.68mm² (95%CI 2.45-2.92) with the DB method to 3.34mm² (95%CI 3.10-3.57) with the SB method (mean difference 0.65mm², [95% CI 0.34-0.97]; p<0.001). In contrast, average biopsy sizes were 2.95mm² (95% CI 2.72-3.19) and 3.08mm² (95%CI 2.85-3.31) using the A&C and T&S, respectively, translating into an increase of 4% using the T&S technique (mean difference 0.13mm², [95%CI -0.19-0.44]; p=0.44). The interaction term between the co-primary comparisons was not statistically significant (p=0.08).

Time required to obtain biopsies was comparable for biopsies obtained with the DB method and SB method (mean difference 2 seconds per biopsy, [95%CI -1-4]; p=0.26), while biopsy time was significantly longer when biopsies were taken with the T&S technique compared to the A&C technique (mean difference 7 seconds per biopsy, [95%CI 4-10]; p<0.001). A total of 46 patients (288 biopsies) and 44 patients (256 biopsies) were included before and after implementation of the SB method and the T&S technique, respectively.

Before implementation, 93/288 biopsies (32%) were obtained with the A&C technique and 163/288 biopsies (57%) were taken with the DB method. Mean biopsy size increased with 18% from 3.31mm² (95%CI 2.95-3.68) to 3.90mm² (95%CI 3.50-4.29) after implementation of the SB method and T&S technique (mean difference 0.58mm² (95%CI 0.07-1.09); p=0.03).

Mean biopsy size did not significantly increase when comparing biopsies before and after implementation (n=117 versus n=97) which were obtained by endoscopists already using the SB method and T&S technique before implementation (3.72mm² [95%CI 2.95-4.48] versus 3.79mm² [95%CI 2.97-4.62], mean difference 0.08mm² [95%CI -0.93-1.08]; p=0.88).

Conclusion: Biopsies in BE patients should be taken with the SB method to increase biopsy size. Implementation of SB-T&S in routine clinical practice resulted in significantly larger biopsies.

Disclosure: B.L.A.M. Weusten is a consultant for Pentax Medical, has received speaker's fee from Pentax Medical and has received research funding from Aqua Medical and Pentax Medical. The remaining authors declare that there is no conflict of interest.

OP116

EFFICACY AND SAFETY OF CRYOBALLOON¹⁸⁰ ABLATION FOR THE TREATMENT OF DYSPLASTIC BARRETT ESOPHAGUS: PRELIMINARY RESULTS FROM A PROSPECTIVE MULTICENTER STUDY

K. Munters^{1,2}, C.N. Frederiks^{2,1}, A. Overwater^{2,1}, R.E. Pouw³, J.J. Bergman⁴, S. van Munster^{1,4}, B.L. Weusten^{2,5}
¹St. Antonius Hospital, Nieuwegein, Netherlands, ²UMC Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands, ³Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁴Academic Medical Centre, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁵St. Antonius Hospital, Gastroenterology and Hepatology, Nieuwegein, Netherlands

Contact E-Mail Address: k.munters-3@umcutrecht.nl

Introduction: Cryoballoon ablation is a relatively novel method which can be used for the eradication of dysplastic Barrett esophagus (BE). While the focal cryoballoon ablation system has shown to be efficacious for BE of limited extent, the cryoballoon¹⁸⁰ ablation system (CBAS¹⁸⁰) is developed to treat longer BE segments by semi-circumferential ablation over 3cm in a single step.

A prior first-in-human study demonstrated the feasibility of CBAS¹⁸⁰ treatment¹, yet the optimal dose needs to be determined. Therefore, in the current prospective multicenter study, we investigate CBAS¹⁸⁰ at lower dosages for patients with dysplastic BE. In addition, we report on the results of CBAS¹⁸⁰ followed by focal cryoballoon ablation (fCBA).

Aims & Methods: A total of 50 patients with ablation naïve BE (C≤3 and M≥1) will be enrolled in six Dutch Barrett expert centers. Treatment consists of a full circumferential ablation over 3 cm of length, using two semi-circumferential ablations at a dose of 1.2 mm/sec. Follow-up consisted of follow-up phone calls at days 1, 7 and 30, a symptom diary during 14 days, and a follow-up endoscopy after 3 months. Outcomes included:

- (1) technical success rate,
- (2) BE regression percentage at follow-up scored by an independent adjudication committee and the treating endoscopist,
- (3) incidence of adverse events,
- (4) post-procedural pain (on a scale of 0-10), and
- (5) post-procedural dysphagia (on a scale of 0-4).

Follow-up treatment consisted of fCBA treatments until complete eradication of visible BE was achieved, confirmed by biopsies from the neo-Z-line.

Results: So far, 25 patients (80% male; mean age 67) with a median BE length of C0M2 (p25-p75 C0-1M2-4) were included. Technical success rate was 92% (23/25). In two patients, treatment was technically unsuccessful due to unstable positioning of the balloon (n=1) or a device malfunction (n=1). Median procedure time was 14 (p25-p75 11-16) 4 minutes and median ablation time was 5 (p25-p75 3-5) minutes. All 23 successfully treated patients completed follow-up endoscopy at 3 months. Median BE regression was 90% (p25-p75 75%-100%) and 95% (p25-p75 75%-99%) as evaluated by the independent adjudication committee and the treating endoscopist, respectively.

Overall, CBAS¹⁸⁰ adverse event rate was 8% (2/23), with one patient developing an esophageal stricture (1/23; 4%) resolved after a single endoscopic dilation. Another patient (1/23; 4%) experienced post-procedural bleeding, resulting in re-endoscopy without intervention. The CBAS¹⁸⁰ procedure was well tolerated with low post-procedural pain (median 2 [p25-p75 1-4] at day 1 and 0 [p25-p75 0-1] at day 7) and dysphagia (44% and 30% of patients with score ≥1 at day 1 and 7) scores.

So far, 22/23 patients were treated with fCBA in the follow-up phase, of whom 4 are still under treatment. The remaining 18 patients achieved complete eradication of all visible BE after median 1 (p25-p75 1-3) fCBA treatments. Based on the histological assessment, a complete eradication of dysplasia and intestinal-metaplasia was achieved in all 18 patients. Two patients developed strictures requiring dilation (2 and 1 dilations, respectively) during the follow-up phase.

Conclusion: Based on these preliminary results, circumferential ablation with CBAS¹⁸⁰ at 1.2 mm/sec, followed by fCBA, emerges as an effective and safe procedure for dysplastic BE eradication in the hands of expert endoscopists. Further avenues for exploration should encompass the assessment of multiple CBAS¹⁸⁰ ablations stacked on top of each other in larger segments and the validation of outcomes in a larger patient cohort.

References:

1. Overwater A, van Munster SN, Nagengast WB, et al. Novel cryoballoon 180° ablation system for treatment of Barrett's esophagus-related neoplasia: a first-in-human study. *Endoscopy*. 2022;54(1):64-70. doi:10.1055/a-1381-7562

Disclosure: PENTAX medical consultancy services & spakker's fee

IBS: Emerging evidence for treatment

14:30-15:30 / Lehar 2

OP117

INCREASED DISEASE BURDEN IN IRRITABLE BOWEL SYNDROME WITH COMORBIDITIES

L. Midenfjord¹, E. Sundelin¹, I.A. Trindade¹, M. Khadija¹, H. Törnblom¹, J. Santos², D. Mulder³, A. Arias-Vasquez³, G. Ruesing⁴, A. Reif⁴, M. Aichholzer⁴, M. Van den Houte⁵, L. Van Oudenhove⁵, M.C. Matteucci⁶, G. Barbara⁶, M. Bosman⁷, D. Jonkers⁷, J.A. Ramos-Quiroga⁸, É. Jekkel⁹, I. Bitter⁹, A.-V. Pop¹⁰, D.L. Dumitrascu¹⁰, C. Alonso-Cotoner², A. Rodríguez-Urrutia⁸, M. Simrén¹

¹University of Gothenburg, Gothenburg, Sweden, ²Vall d'Hebron Hospital Universitari, CIBEREHD, Barcelona, Spain, ³Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands, ⁴Johann Wolfgang Goethe- Universität Frankfurt Am Main, Frankfurt, Germany, ⁵Katholieke Universiteit Leuven, Laboratory for Brain-Gut Axis Studies (LABGAS), Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism, Leuven, Belgium, ⁶University of Bologna and IRCCS Azienda Ospedaliero Universitaria di Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁷Maastricht University Medical Center, Department of Gastroenterology-Hepatology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht, Netherlands, ⁸Vall d'Hebron Hospital Universitari, CIBERSAM, Barcelona, Spain, ⁹Semmelweis University, Department of Psychiatry and Psychotherapy, Budapest, Hungary, ¹⁰Iuliu Hatieganu' University of Medicine and Pharmacy, Second Medical Department, Cluj-Napoca, Romania

Contact E-Mail Address: irina.midenfjord@gu.se

Introduction: Irritable bowel syndrome patients frequently suffer from comorbid mental (anxiety or depression) or somatic (fibromyalgia or chronic fatigue) conditions. In this pan-European project (the DISCOVERIE project), IBS patients with and without comorbidities were compared with disease controls and healthy controls, to further elucidate the effect of comorbid conditions in IBS on the disease burden.

Aims & Methods: We included participants from nine different European centers – IBS patients according to Rome IV criteria, disease controls (patients with comorbid conditions; i.e. fulfilling diagnostic criteria for anxiety, depression, fibromyalgia and/or chronic fatigue, but no IBS) and healthy controls. The participants were further divided into eight groups based on presence or absence of comorbidities: IBS with no/ mental/ somatic/ mental and somatic comorbidity, disease controls with mental/ somatic/ mental and somatic comorbidity, and healthy controls. The severity of IBS symptoms (IBS-SSS), depression (PHQ-9), anxiety (GAD-7), somatic symptoms (PHQ-15), fibromyalgia symptoms (FIQ) and general and mental fatigue (MFI) were compared between these groups.

Results: In total, 849 participants (median age 44 years) were included. A majority were females (76%), with the most pronounced female predominance (83%-86%) in the IBS groups with comorbidities. The most severe IBS symptoms were noted among IBS with both mental and somatic comorbidity and IBS with somatic comorbidity (Table 1).

In IBS, the severity of IBS symptoms increased gradually with increasing number of comorbidities (partial eta squared: 0.053, p<0.001), as did severity of anxiety, depression, somatic symptoms and general fatigue (partial eta squared: 0.214, 0.247, 0.240, 0.239, respectively, all p<0.001). The groups with both mental and somatic comorbidity had the highest levels of anxiety, depression and mental fatigue.

Somatic symptoms and general fatigue were most severe among IBS and disease controls with somatic comorbidity or both somatic and mental comorbidity. Fibromyalgia symptoms were most severe in IBS and disease controls with somatic comorbidity.

	IBS alone (N=268)	IBS comor- bid mental (N=173)	IBS somatic (N=48)	IBS multi- comorbid (N=124)	Disease control mental (N=58)	Disease control somatic (N=51)	Disease control mental + somatic (N=52)	Healthy controls (N=75)	P-value between all groups	p-value between IBS groups
IBS-SSS	226 [170-298]	259 [184-320]	296 [200-358]	300 [239-375]	100 [59-160]	119 [80-188]	114 [82-213]	4 [0-33]	<0.001	<0.001
PHQ-9	4 [1-7]	8 [4-13]	8 [6-10]	12 [8-18]	11 [6-16]	9 [5-11]	12 [8-17]	1 [0-3]	<0.001	<0.001
GAD-7	3 [1-7]	7 [4-11]	4 [2-8]	11 [7-15]	8 [6-9]	6 [3-10]	12 [7-14]	1 [0-3]	<0.001	<0.001
PHQ-15	10 [7-13]	12 [9-15]	16 [13-19]	17 [14-23]	11 [7-14]	15 [11-17]	16 [12-20]	3 [1-4]	<0.001	<0.001
FIQ	23 [9-44]	20 [7-38]	39 [14-56]	24 [10-48]	38 [23-47]	48 [28-67]	41 [20-57]	22 [7-48]	<0.001	0.004
MFI	11 [7-15]	15 [11-17]	18 [15-19]	18 [16-20]	14 [12-17]	17 [16-19]	18 [15-20]	8 [6-10]	<0.001	<0.001
general fatigue										
MFI	9 [6-12]	13 [9-16]	13 [10-18]	16 [13-18]	13 [10-16]	13 [10-16]	15 [13-17]	8 [5-11]	<0.001	<0.001
mental fatigue										

Table 1: Symptom severity of the study groups. Numbers presented as medians with interquartile range. Groups compared through Kruskal-Wallis tests with Holm's correction.

Conclusion: This large European multicenter study strengthens the importance of the impact of mental and somatic comorbid conditions and symptoms in IBS, and their influence on outcomes and disease burden.

Disclosure: Hans Törnblom: Consultant or advisory board member for Allergan, Cinclus Pharma, Medifactia, and VIPUN and as a speaker for Tillyotts, Takeda, and Shire.

Daisy Jonkers: Part of the work of DJ, outside the submitted work has been financed by public-private partnership grants of Top Knowledge Institute (TKI) Agri&Food and Health Holland, by the Carbokinetics program as part of the NWO-CCC Partnership Program, by Organic A2BV/Mothersfinest BV.

OP118

EFFICACY OF BERBERINE IN THE TREATMENT OF PATIENTS WITH IRRITABLE BOWEL SYNDROME COMORBID ANXIETY AND/OR DEPRESSION: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

S. Lu¹, L. Sun², H. Guo³, L. Zhu¹, J. Gao¹, L. Xia⁴, L. Duan¹
¹Peking University Third Hospital, Department of Gastroenterology, Beijing, China, ²Capital Medical University, School of Biomedical Engineering, Beijing Key Laboratory of Fundamental Research on Biomechanics in Clinical Application, Beijing, China, ³Beijing Chaoyang Hospital, Beijing, Department of Gastroenterology, Beijing, China, ⁴Department of Nuclear Medicine, Peking University Cancer Hospital & Institute, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), NMPA Key Laboratory for Research and Evaluation of Radiopharmaceuticals (National Medical Products Administration), Department of Nuclear Medicine, Beijing, China

Contact E-Mail Address: 602458052@qq.com

Introduction: Irritable bowel syndrome (IBS) is defined as a disorders of gut–brain interaction, which shows a high comorbidity tendency with anxiety and depression. Berberine has been suggested in previous studies to alleviate IBS-like symptoms, however, there is currently a lack of research investigating the clinical efficacy of berberine, its modulation of gut microbiota, and its influence on brain functional regulation in IBS patients with comorbid anxiety and depression.

Aims & Methods: We conducted a double-blind, randomized, placebo-controlled clinical trial to evaluate the therapeutic efficacy of berberine on clinical symptoms in patients with IBS comorbid depression and

(or) anxiety. Eligible participants with IBS based on Rome IV criteria and comorbid anxiety/depression based on HAMA/HAMD criteria were recruited. Participants were randomly assigned to receive berberine (300mg tid) or placebo for 8 weeks. Follow-up assessments occurred at 4 and 8 weeks. We collected stool samples from patients and performed resting-state functional magnetic resonance imaging (rs-fMRI) for patients and healthy controls (HCs) recruited at the same period at baseline and after 8 weeks of treatment. Fractional amplitude of low-frequency fluctuations (fALFF) was used to assess brain activation.

Results: 78 patients (40 berberine, 38 placebo) showed no significant baseline differences. Berberine had higher drug response rates at 4 weeks (61.86% vs. 32.26%, $p=0.027$) and 8 weeks (73.53% vs. 32.26%, $p=0.003$). Berberine also had higher drug efficacy rates for anxiety at 8 weeks (79.4% vs. 29.0%, $p<0.001$). Adverse reactions (constipation, nausea) were higher with berberine (35.00% vs. 13.16%, $p=0.025$) but not severe. Metagenomic sequencing revealed that, berberine decreased pathogenic bacteria (*Eubacterium*, *Faecalibacterium*, *Collinsella*, *Streptococcus*, *Lachnospira*) and increased beneficial bacteria (*Bacteroides uniformis* etc.). Correlations indicated associations between *Streptococcus*, *Eubacterium* and diarrhea and abdominal pain. Berberine suppressed flagella assembly and bacterial chemotaxis, accordingly reduced invasiveness by decreasing the abundance of *Eubacterium* and *Streptococcus*, and improved gastrointestinal symptoms. Also berberine may reduce the function of pyrimidine metabolism, one-carbon pool folate, and glycerophospholipid metabolism by suppressing the abundance of *Collinsella*, *Faecalibacterium* and enriching *Bacteroides uniformis*. Patients exhibited decreased activity in several brain regions compared to HC, while increasing activity in brain regions (cingulate gyrus, supplementary motor area, superior frontal gyrus, etc.) after berberine intake was shown. Placebo group showed limited activity increase. Activity in different brain regions negatively correlated with abdominal pain, anxiety scores.

Conclusion: Berberine significantly improves gastrointestinal symptoms and psychometric scale score in IBS patients comorbid depression and (or) anxiety. Berberine reduces the abundance of pathogenetic bacteria, suppresses bacterial chemotaxis, flagella assembly and accordingly decreases bacteria invasiveness, which correlate with symptom improvement. Berberine may affect metabolic pathways linked to anxiety and depression improvement. Following berberine intervention, the activity in these hypoactive brain regions significantly recovers. Moreover, berberine enhances the activity in brain regions related to the functionality of the whole-body action-cognition network and control network, which may serve as important neurobiological foundations for berberine's treatment of the gut-brain comorbidity.

Disclosure: There are no financial conflicts of interest to disclose.

PREVALENCE OF RED FLAGS IN THE GLOBAL GENERAL POPULATION AND IN DISORDERS OF GUT-BRAIN INTERACTION- RESULTS FROM THE ROME FOUNDATION GLOBAL EPIDEMIOLOGY STUDY

J. Sjölund¹, J. Hreinsson¹, B.E Lacy², H. Törnblom¹, M. Simrén^{1,3}, S.I. Bangdiwala⁴, O.S. Palsson³, A.D. Sperber⁵
¹University of Gothenburg, Sahlgrenska Academy, Institute of Medicine, Department of Molecular and Clinical Medicine, Gothenburg, Sweden, ²Mayo Clinic, Division of Gastroenterology and Hepatology, Jacksonville, United States of America, ³University of North Carolina-Chapel Hill, Center for Functional GI & Motility Disorders, Chapel Hill, United States of America, ⁴McMaster University, Department of Health Research Methods, Evidence and Impact, Hamilton, Canada, ⁵Ben-Gurion University of the Negev, Faculty of Health Sciences, Farod, Israel

Contact E-Mail Address: Jessica.sjolund@gu.se

Introduction: Studies on the prevalence of gastrointestinal (GI) red flags (RF) in the general population and among individuals with Rome IV disorders of gut-brain interaction (DGBI) in globally representative samples are scarce.

Aims & Methods: We aimed to describe the global prevalence of GI RF in the general population and in individuals meeting Rome IV criteria for DGBI. We analyzed data on participants across 26 countries who completed the Rome Foundation Global Epidemiology Study online survey, which included the Rome IV diagnostic questionnaire along with inquiries about 14 RF (hematemesis, hoarseness of voice, neck/throat pain, chest pain on exertion/related to heart problems, difficulty swallowing, hematochezia, melena, a major change in bowel movements, fever, unintentional weight loss, anemia/iron deficiency, first degree relative with GI cancer/inflammatory bowel disease/celiac disease). We assessed the global prevalence of RF and compared the prevalence in DGBI-positive (any DGBI [all RF] and anatomical DGBI groups [relevant RF for that anatomical region]) vs DGBI-negative participants without a history of organic GI disease using univariate logistic regression models. All analyses were stratified by age with cutoff at 50 years (y).

Results: Of 54,127 participants completing the internet survey, 58.9% reported at least one RF. A major change in bowel movements (frequency or consistency) was the most prevalent RF (16.5%), while hematemesis was the least prevalent (0.6%). Participants <50 y had a higher prevalence of RF compared to participants ≥50 y for any RF (63.1% vs 51.8%) and for all individual RF, except for a family history of GI cancer (more prevalent ≥50 y). Among 20,668 DGBI-positive participants, 72.8% reported any RF, with a higher prevalence in younger participants (Table). The prevalence of RF was highest in the anorectal DGBI group in participants <50 y, and in the esophageal DGBI group in participants ≥50 y (Table). The most prevalent RF was difficulty swallowing (30.1% <50 y; 30.5% ≥50 y) in esophageal DGBI, anemia/iron deficiency (22.8%) in gastroduodenal DGBI <50 y, a family history of GI cancer (17.2%) in gastroduodenal DGBI ≥50 y, and a major change in bowel movements in bowel (27.9% <50 y; 21.5% ≥50 y) and anorectal (38.4% <50 y; 29.5% ≥50 y) DGBI. In DGBI-positive vs DGBI-negative participants without organic GI disease, reporting any RF was positively associated with any DGBI and all anatomical DGBI groups (Table). Hematemesis was the RF most strongly associated with esophageal (OR 13, 95% CI 8.6-18 <50 y; OR 11, 95% CI 4.4-29 ≥50 y) and gastroduodenal (OR 12, 95% CI 8.4-16 <50 y; OR 11, 95% CI 4.5-26 ≥50 y) DGBI, although rare (0.8-3.2% in DGBI-positive participants). A major change in bowel movements was the RF most strongly associated with bowel DGBI (OR 3.3, 95% CI 3.1-3.5 <50 y; OR 3.5, 95% CI 3.1-3.8 ≥50y) and anorectal DGBI <50 y (OR 5.3, 95% CI 4.8-5.8), while hematochezia was the RF most strongly associated with anorectal DGBI ≥50 y (OR 6.1, 95% CI 5.2-7.3).

	Age <50 years			Age ≥50 years		
	Without DGBI n=17,995	DGBI ^a	OR 95% CI	Without DGBI n=11,370	DGBI ^b	OR 95% CI
Any RF ^c	50.7% (50.0, 51.5)	75.3% (74.5, 76.0)	3.0 (2.8, 3.1)	38.8% (37.9, 39.7)	67.5% (66.4, 68.7)	3.3 (3.1, 3.5)
Any esophageal RF ^d	36.9% (36.2, 37.6)	71.1% (69.1, 73.1)	4.2 (3.8, 4.7)	29.2% (28.4, 30.1)	65.6% (62.6, 68.5)	4.6 (4.0, 5.3)
Any gastroduodenal RF ^e	26.2% (25.5, 26.8)	53.4% (51.9, 55.0)	3.2 (3.0, 3.5)	20.6% (19.8, 21.3)	44.4% (41.8, 47.0)	3.1 (2.8, 3.5)
Any bowel RF ^f	38.3% (37.6, 39.0)	64.3% (63.4, 65.1)	2.9 (2.8, 3.0)	29.3% (28.5, 30.1)	54.9% (53.6, 56.3)	2.9 (2.8, 3.1)
Any anorectal RF ^f	34.1% (33.4, 34.8)	74.3% (72.6, 76.0)	5.6 (5.1, 6.1)	26.5% (25.7, 27.3)	61.6% (58.9, 64.2)	4.4 (4.0, 5.0)

^a Any DGBI, n=14174; esophageal DGBI, n=2066; gastroduodenal DGBI, n=4072; bowel DGBI, n=11803; anorectal DGBI, n=2622.

^b Any DGBI, n=6494; esophageal DGBI, n=1021; gastroduodenal DGBI, n=1438; bowel DGBI, n=5452; anorectal DGBI, n=1327.

^c Includes all RF listed in d-f.

^d Includes hematemesis, hoarseness of voice, neck/throat pain, chest pain on exertion/related to heart problems, difficulty swallowing, fever >38° C, unintentional weight loss >4.5 kg, anemia/iron deficiency, first degree relative with GI cancer.

^e Includes hematemesis, melena, fever >38° C, unintentional weight loss >4.5 kg, anemia/iron deficiency, first degree relative with GI cancer/celiac disease.

^f Includes hematochezia, melena, a major change in bowel movements (frequency or consistency), fever >38° C, unintentional weight loss >4.5 kg, anemia/iron deficiency, first degree relative with GI cancer/inflammatory bowel disease/celiac disease.

Table. Prevalence of red flags (RFs) in DGBI-positive participants vs DGBI-negative participants without organic GI disease.

Conclusion: GI RF are highly prevalent in the global general population with an even higher prevalence in individuals positive for a Rome IV DGBI. Given the substantial prevalence of RF observed in our study, especially among younger individuals, RF in general may not be as valuable at predicting serious underlying pathology as once thought. Further research is needed to validate the predictive utility of RF in the diagnostic approach to gastrointestinal symptoms and suspected DGBI in unselected population samples.

Disclosure: Nothing to disclose.

OP120

EFFICACY AND SAFETY OF PLECANATIDE IN CHINESE PATIENTS WITH FUNCTIONAL CONSTIPATION: A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER TRIAL

T. Bai¹, Z. Xu¹, Y. Jiang², H. Zhao³, P. Yan⁴, N. Dai⁵, X. Chen⁶, K. Huang⁷, J. Cui⁸, M. Xu⁹, S. Jia¹⁰, J. Zhang¹⁰, S. Liu¹¹, X. Li¹², Y. Ai¹³, M. Zhang¹⁴, Y. Wu¹⁵, W. Zhou¹⁶, R. Zhao¹⁷, J. Wu¹⁸, B. Wang¹⁹, B. Xu²⁰, X. Ding²¹, X. Fang²², S. Yang²³, Y. Ma²⁴, Z. Zhou²⁵, L. Lin²⁶, H. Chen²⁷, H. Zhang²⁸, Y. Zhu²⁹, B. Jiang^{30,6}, X. Zhang³¹, X. Wang³², D. Zou³³, B. Ye³⁴, L. Zhang³⁵, R. Shi³⁶, Y. Zhen³⁷, J. Wang³⁸, Y. Liu³⁹, A. Liao⁴⁰, X. Hou⁴¹

¹Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, ²Qingdao University Affiliated Hospital, Qingdao, China, ³Qingdao Central Hospital, Qingdao, China, ⁴Liaocheng People's Hospital, Liaocheng, China, ⁵Sir Run Run Shaw Hospital, affiliated with the Zhejiang University School of Medicine, Hangzhou, China, ⁶Anhui Medical University First Affiliated Hospital, Hefei, China, ⁷Zibo Central Hospital, Zibo, China, ⁸Yantai Yuhuangding Hospital, Yantai, China, ⁹Wuxi People's Hospital, Wuxi, China, ¹⁰Peking University Shougang Hospital, Beijing, China, ¹¹Nanfang Hospital, Guangzhou, China, ¹²Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, ¹³Yichang First People's Hospital, Yichang, China, ¹⁴The First Affiliated Hospital of Xi'an Medical University, Department of Gastroenterology, Xi'an, China, ¹⁵Beijing Friendship Hospital, Capital Medical University, Digestive, Beijing, China, ¹⁶Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing, China, ¹⁷Tianjin People's Hospital, Tianjin, China, ¹⁸Inner Mongolia Autonomous Region People's Hospital, Huhehaote, China, ¹⁹Tianjin Medical University General Hospital, Tianjin, China, ²⁰Beijing Tongzhou District Luhe Hospital, Gastroenterology, Beijing, China, ²¹Wuhan Fourth Hospital, Wuhan, China, ²²Wuhan Puren Hospital, Wuhan, China, ²³General Hospital Of Ningxia Medical University, Gastroesophageal, Yinchuan, China, ²⁴Qinghai Provincial People's Hospital, Xining City, Qinghai Province, China, ²⁵Wuhan University People's Hospital, Department, Wuhan, China, ²⁶Jiangsu Provincial People's Hospital, Nanjing, China, ²⁷Huizhou Central People's Hospital, Huizhou, China, ²⁸Wuhan Central Hospital, Wuhan, China, ²⁹The First Affiliated Hospital of Nanchang University, Nanchang, China, ³⁰Beijing Tsinghua Changgeng Hospital, Beijing, China, ³¹Hebei Medical University Second Hospital, Shijiazhuang, China, ³²Xiangya Third Hospital of Central South University, Changsha, China, ³³Ruijin Hospital, Shanghai JiaoTong University School of Medicine, Shanghai, China, ³⁴Lishui Central Hospital, Lishui, China, ³⁵Baotou Central Hospital, Baotou, China, ³⁶ZhongDa Hospital Southeast University, Gastroenterology, Nanjing, China, ³⁷Jinan Central Hospital, Jinan, China, ³⁸Shanxi Provincial People's Hospital, Taiyuan, China, ³⁹Xuancheng People's Hospital, Xuancheng, China, ⁴⁰The First Affiliated Hospital of South China University, Hengyang, China, ⁴¹Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Gastroenterology, Wuhan, China

Contact E-Mail Address: drbaitao@126.com

Introduction: Functional constipation (FC) occurs in 8.5% Chinese people, seriously affecting their quality of life and mental health. However, there is currently a lack of long-term effective treatment options.

As an oral guanylate cyclase-C (GC-C) agonist, plecanatide has been approved by the US FDA for the treatment of adult chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C), but

it has not yet been approved for use in constipated populations in China. Considering the potential differences in drug responses between races, and the higher proportion of FC than IBS-C in Chinese with constipation, the efficacy of plecanatide in the Chinese FC population is worth studying.

Aims & Methods: This study aimed to comprehensively assess the efficacy, safety, and pharmacokinetics of plecanatide during the treatment of Chinese FC patients. This phase III, randomized, double-blind, placebo-controlled, multicenter trial was performed in 40 hospitals of China. 648 patients with FC were assigned to the plecanatide or placebo group randomly with a ratio of 1:1 for a 12-week treatment and a 2-week follow-up. The primary efficacy endpoint was the durable overall complete spontaneous bowel movement (CSBM) response rate.

Treatment-emergent adverse event (TEAE) and treatment-related emergent adverse event (TRAEE) were collected. Concentration of plecanatide and its metabolite SP-338 were detected.

Results: After 12-week continuous administration, the durable overall complete CSBM response rate of the plecanatide and the placebo were 23.5% and 10.5% respectively ($p < 0.001$). Besides, all secondary efficacy endpoints showed statistically significant improvements compared with placebo. The incidence of TEAE and TRAEE was 55.7% vs 48.6%, and 13.9% vs 8.7% respectively, in the plecanatide group and placebo group.

The most common TRAEE was diarrhea, which occurred in 0.6% (placebo) and 4.3% (plecanatide) of patients. The concentrations of plecanatide and its metabolite SP-338 were below the lower limit of quantification (0.500 ng/ml) at all time points.

	Plecanatide	Placebo	P value
ITT population ^a	N=324	N=324	
Responders (%)	76 (23.5)	33 (10.2)	< 0.001
Non responders (%)	248 (76.5)	291 (89.8)	
PPS ^a	N=286	N=297	
Responders (%)	74 (25.9)	33 (11.1)	< 0.001
Non responders (%)	212 (74.1)	264 (88.9)	

Table 1: Comparison of durable overall CSBM response rate

^a: CMH Test

ITT: Intention-to-treat; PPS: per protocol set

Conclusion: Plecanatide had a significant efficacy for the treatment of Chinese FC patients, with a low rate of AEs and no systemic absorption. Plecanatide will be a good option in the management of Chinese FC patients.

References: ClinicalTrials.gov: NCT0515132.

Disclosure: No Conflict of Interests.

OP121

EXPLORING DYNAMIC TRIGGERS OF ABDOMINAL PAIN IN IRRITABLE BOWEL SYNDROME USING THE EXPERIENCE SAMPLING METHOD - PRELIMINARY RESULTS FROM THE MULTICENTER DISCOVERIE STUDY

M. Bosman¹, L. Vork¹, M. Van Den Houte², I. Midenfjord³, S. Muñoz⁴, M.R. Barbaro⁵, D.L. Dumitrascu⁶, D.M. Jonkers¹, D. Keszthelyi¹, ESM DISCOVERIE group

¹Department of Gastroenterology-Hepatology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center, Maastricht, Netherlands, ²Laboratory for Brain-Gut Axis Studies, Translational Research in Gastrointestinal Disorders (TARGID), Department of Chronic Diseases & Metabolism, KU Leuven, Leuven, Belgium, ³Department of Internal Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ⁴Psychiatry, Mental Health and Addictions Research Group, Vall d'Hebron Institute of Research (VHIR), Barcelona, Spain, ⁵IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ⁶Second Department of Internal Medicine, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania

Contact E-Mail Address: m.bosman@maastrichtuniversity.nl

Introduction: Real-time symptom assessment provides a detailed understanding of the dynamic interplay between gastrointestinal symptoms in irritable bowel syndrome (IBS) and potential triggers, including affect and environmental factors.

This study evaluates the association between abdominal pain and potential triggers over time in IBS patients with and without comorbidities, using the Experience Sampling Method (ESM) as a real-time, ecologically valid measurement method.

Aims & Methods: In this prospective, observational multicenter study, as part of the DISCOVERIE project, we included 215 Rome IV IBS patients (80% female; mean age 42.1) from six European countries, categorized into 103 IBS-alone, 67 IBS-mental (anxiety/depression), 16 IBS-somatic (fibromyalgia/chronic fatigue syndrome), and 29 IBS-multicomorbid patient subgroups. Participants scored abdominal pain and affect using an 11-point Numeric Rating Scale and environmental factors using ESM at up to ten random moments each day over seven consecutive days.

Linear mixed-effects models analyzed the associations between abdominal pain and these potential triggers, both concurrently and predictively (trigger scores lagged by one time point, maximum of 90 minutes), in each subgroup.

Results: ESM assessment completion rate was 63%. Regarding affect triggers, abdominal pain was significantly correlated with concurrent positive and negative affect in all IBS groups ($p < 0.02$), while significant lagged associations were only found within IBS-mental for positive affect ($p = 0.02$) and within IBS-alone and IBS-multicomorbid for negative affect ($p < 0.001$).

Regarding environmental triggers, abdominal pain was significantly associated with concurrent 'feeling comfortable in situation' within IBS-alone, IBS-mental and IBS-multicomorbid ($p < 0.001$), concurrent 'feeling of pleasantness of company' ($p = 0.01$) and being alone (versus with somebody, $p = 0.01$) within IBS-alone, and eating since the last ESM-assessment within IBS-alone ($p = 0.04$) and IBS-multicomorbid ($p = 0.002$).

No significant lagged associations or correlations with location, activity, alcohol consumption, and nicotine use were found.

Conclusion: Our results demonstrate that in IBS patients, real-time abdominal pain is significantly associated with environmental and affect triggers, with both positive and negative affect correlating with abdominal pain irrespective of mental comorbidities.

Moreover, fewer triggers predict abdominal pain over time, underscoring the importance of in-the-moment assessments. This study highlights the value of ESM in accurately identifying symptom triggers, thereby enhancing personalized healthcare in IBS.

Disclosure: MB, LV, MH, IM, SM, MRB, and DD declare no conflicts of interests. DJ has received research funding from public-private partnership grants of Top Knowledge Institute (TKI) Agri&Food and Health Holland, by the Carbokinetics program as part of the NWO-CCC Partnership Program, and by Organic A2BV/Mothersfinest BV. DK has received research funding from ZonMw, MLDS, UEG, Rome Foundation, Horizon Europe, Horizon 2020, Grunenthal, Allergan and speaker's fee from Dr Falk (paid to host institute).

AI for polyp detection: Advances, pitfalls and challenges

14:30-15:30 / Lehar 3

OP122

IMPROVING COLORECTAL POLYP OPTICAL DIAGNOSIS WITH COMPUTER AIDED CHARACTERIZATION: A REAL TIME COMPARISON WITH ENDOSCOPISTS AND ITS IMPACT AS A TRAINING TOOL

E. Hossain^{1,2}, M. Stefanovic³, B. Hayee⁴, E.J. Schoon⁵, P.R. Aepli⁶, S. Subramaniam⁷, Q.E.W. van der Zander⁸, P. Bhandari⁹

¹Queen Elizabeth Hospital, Gastroenterology, London, United Kingdom, ²Portsmouth University Hospitals NHS Trust, Gastroenterology, Portsmouth, United Kingdom, ³Diagnosticni Center Bled, Gastroenteroloski Oddelek, Bled, Slovenia, ⁴Kings College Hospital, Gastroenterology, London, United Kingdom, ⁵Catharina Hospital Gastroenterology and Hepatology, Dept. of Gastroenterology, Eindhoven, Netherlands, ⁶Luzerner Kantonsspital, Gastroenterologie, Luzern, Switzerland, ⁷Queen Alexandra Hospital, Gastroenterology, Portsmouth, United Kingdom, ⁸Maastricht University Medical Center+, Internal Medicine - Gastroenterology and Hepatology, Maastricht, Netherlands, ⁹Portsmouth University Hospital, Dept. of Gastroenterology, Portsmouth, United Kingdom

Contact E-Mail Address: ejaz.hossain@gmail.com

Introduction: Several studies have shown that image enhancement technologies like NBI and BLI in expert hands can meet the PIVI criteria [1-6]. This has led to various calls for implementation of this technique in clinical practice. However, attempts at more widespread generalisation of optical diagnosis have failed due to the inability of general endoscopists to meet the established standards.

CAD-EYE (Fujifilm, Japan) is a novel AI driven optical diagnosis system (CADx) which has shown encouraging preliminary results in expert hands or in single centre studies.

Aims & Methods: To evaluate the diagnostic performance of AI (CAD-EYE) based optical diagnosis of colorectal polyps in the hands of both experts and non-experts and to explore the impact of AI based prediction on the learning curve of non-expert endoscopists.

A multicenter prospective observational study which compares the performance of CAD-EYE with that of the endoscopists, combined with monthly review meetings by all endoscopists involved in the study with the aim of group learning and improving the skills of optical diagnosis for non-expert endoscopists.

Results: Optical diagnosis (OD) was performed with high confidence by the endoscopists in 674/782 (86.2%) of polyps. High confidence OD was achieved in 91.5% polyps by expert endoscopists compared to 85.1% by non-expert endoscopists [$p < 0.05$].

The overall sensitivity, NPV and accuracy by all endoscopists were 84.4%, 74.1% and 86.2% respectively. CAD-EYE diagnosis was recorded in 672/782 (85.9%) of polyps. The overall sensitivity, NPV and accuracy were 83.0%, 72.8% and 85.9% respectively [$p > 0.05$].

Optical diagnosis was performed with high confidence by the endoscopist in 416/590 (84.9%) of diminutive polyps (≤ 5 mm). The overall sensitivity, NPV and accuracy were 84.6%, 74.5% and 84.9% respectively. CAD-EYE diagnosis was recorded in 413/590 (84.2%) of diminutive polyps. The overall sensitivity, NPV and accuracy was 83.4%, 73.2% and 84.2% respectively [$p > 0.05$].

273/590 diminutive polyps were located in the rectosigmoid. Endoscopist's sensitivity, NPV and accuracy was 93.1%, 92.6% and 91.9% respectively, compared to CAD-EYE whose sensitivity, NPV and accuracy were 93.7%, 92.4% and 92.9% respectively [$p > 0.05$].

The endoscopist's optical diagnosis-based post-polypectomy surveillance interval was calculated in all patients and compared with histology based surveillance and it achieved a 90.7% [CI 84.6-93.8] and 92.9% [CI 89.4-95.0] concordance with BSG and ESGE guidelines respectively; achieving the ASGE PIVI criterion. The post-polypectomy surveillance interval based on CAD-EYE diagnosis was calculated and compared with histology based surveillance and it achieved 91.9% [CI 88.7%-93.2 %] and 93.4 % [CI 90.2 %-96.8%] concordance with the BSG & ESGE guidelines; also achieving the ASGE PIVI criterion.

An improvement in the performance of non-experts during the study was noted with an improvement in accuracy from 63% for the first 50 polyps to 85% for the last 50 polyps, with an associated increase in sensitivity (65% and 82%), specificity (50% and 91%), NPV (55% and 79%) and also degree of confidence (65% and 90%) [$p < 0.05$ for all KPIs]

Conclusion: Our data proves that CAD-EYE based diagnosis can meet both PIVI criterion and help introduce both resect & discard and leave in-situ strategies even in the hands of non-experts.

Real time Optical diagnosis of polyps has the potential to transform clinical practice by reducing pathology & polypectomy costs, setting up surveillance intervals without waiting for histology, reducing morbidity and procedure time.

We have also demonstrated an improvement in performance of non-expert endoscopists over the course of the study. This is a novel finding and has not been shown in any study before and we feel that this is an important finding which can help inform the policy makers to invest in CADx.

References:

1. Abu Dayyeh BK, Thosani N, Konda V et al. ASGE technology committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. Vol. 81, Gastrointestinal Endoscopy. 2015. p. 502-16.
2. Rees C, Rajashekar P, Wilson A et al: Narrow band imaging optical diagnosis of small colorectal polyps in routine clinical practice: the Detect Inspect Characterise Resect and Discard 2 (DISCARD 2) study. Gut 2017;66:887-895.
3. Neumann H, Vieth M, Bisschops R et al. Leaving colorectal polyps in place can be achieved with high accuracy using blue light imaging (BLI) United European Gastroenterol J. 2018 Aug
4. Rondonotti E, Paggi S, Amato A et al. Blue-light imaging compared with high-definition white light for real-time histology prediction of colorectal polyps less than 1 centimeter: a prospective randomized study.
5. Vleugels JLA, Hazewinkel Y, Dijkgraaf MGW. Optical diagnosis expanded to small polyps: post-hoc analysis of diagnostic performance in a prospective multicenter study. Endoscopy 2019; 51: 244-252)
6. Rondonotti E, Hassan C, Andrealli A et al. Clinical validation of BASIC classification for the resect and discard strategy for diminutive colorectal polyps. Clin Gastroenterol Hepatol 2020; 18: 2357-2365

Disclosure: Nothing to disclose.

OP123

DESKILLING OF ENDOSCOPISTS CAUSED BY IMPLEMENTATION OF ARTIFICIAL INTELLIGENCE IN COLONOSCOPY: A MULTICENTER OBSERVATIONAL STUDY

K. Budzyn^{1,2}, M. Romanczyk^{1,2}, D. Kitala³, P. Kołodziej⁴, M. Bugajski⁵, H.O. Adami^{6,7}, J. Blom⁸, M. Buszkiewicz⁹, N. Halvorsen⁶, C. Hassan^{10,11}, O. Holme^{12,13}, K. Jarus¹⁴, M. Pellisé Urquiza¹⁵, N. Pilonis^{6,16,17}, P. Sharma¹⁸, M.F. Kaminski^{6,19,20}, M. Bretthauer⁶, Y. Mori^{6,21}

¹Faculty of Medicine, Academy of Silesia, Department of Gastroenterology, Katowice, Poland, ²Endoterapia, H-T. Centrum Medyczne, Tychy, Poland, ³Agency of Medical Research, Warsaw, Poland, ⁴Endomed, Radom, Poland, ⁵Polish Foundation of Gastroenterology, Warsaw, Poland, ⁶Clinical Effectiveness Research Group, University of Oslo and Oslo University Hospital, Oslo, Norway, ⁷Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, ⁸Department of Surgery, Södersjukhuset, Stockholm and Department of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden, ⁹Buszkiewicz Medical Center, Gorzów Wielkopolski, Poland, ¹⁰Humanitas University, Department of Biomedical Sciences, Pieve Emanuele MI, Italy, ¹¹IRCCS Humanitas Research Hospital, Endoscopy Unit, Milan, Italy, ¹²University of Oslo, Institute of Health and Society, Oslo, Norway, ¹³Sorlandet Hospital Kristiansand, Gastrointestinal Endoscopy, Kristiansand, Norway, ¹⁴Centre of Gastroenterology, Wodzisław Śląski, Poland, Gastroenterology, Wodzisław sŚlaski, Poland, ¹⁵Hospital Clinic, Gastroenterology, Barcelona, Spain, ¹⁶The Maria Skłodowska-Curie Institute - Oncology Institute Warsaw, Poland, Department of Oncological Gastroenterology, Warsaw, Poland, ¹⁷Medical University of Gdańsk, Division of General, Endocrine and Transplant Surgery, Gdansk, Poland, ¹⁸University of Kansas School of Medicine Dept. of Gastroenterology, Gastroenterology, Leawood, United States of America, ¹⁹Centre of Postgraduate Medical Education, Department of Gastroenterology, Hepatology and Clinical Oncology, Warsaw, Poland, ²⁰Maria Skłodowska-Curie Memorial Center and Institute of Oncology, Department of Gastroenterology, Warsaw, Poland, ²¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan

Contact E-Mail Address: krzysztof.budzyn96@gmail.com

Introduction: Although randomized controlled trials have shown that artificial intelligence (AI) for polyp detection improve adenoma detection rate (ADR) in colonoscopy, it is unknown how implementation of AI changes endoscopists' behavior on standard colonoscopy (colonoscopy without AI assistance). We aimed at answering this important clinical question.

Aims & Methods: We conducted a multicenter, observational study at four Polish endoscopy centers. These centers implemented AI tools for polyp detection in the end of 2021, after which colonoscopies were done either with or without AI assistance at endoscopists' discretion. We evaluated the change in the quality of all the diagnostic colonoscopies between September of 2021 and February of 2022, by comparing two different phases: 3 months before and after the AI implementation in clinical practice. The primary outcome measure was ADR of standard colonoscopy. To investigate the independent factors that affected ADR, multivariable logistic regression analysis was also done.

Results: A total of 1,460 patients underwent standard colonoscopy before and after the AI implementation (795 and 665, respectively; mean age 57.1±15.5 with female accounting for 58.6%). ADR of standard colonoscopy significantly decreased from 28.4% (226/795; 95% confidence interval [CI] 25.29- 31.56) to 22.1% (147/665; 95% CI 18.95 - 25.26; P=.006)

after the AI implementation, corresponding to a 6.3% absolute reduction (95%CI 6.2 - 6.5) and a 22.2% relative reduction (95% CI 21.8 - 22.7). In multivariable regression analysis showed that AI implementation in clinical practice (risk ratio 0.774; 95% CI 0.64-0.93), sex (risk ratio 1.33; 95% CI 1.14-1.54) and age (risk ratio 1.535; 95% CI 1.29-1.79) were the only independent factors that affected ADR.

Conclusion: Implementation of AI in clinical practice negatively affected the ADR during standard colonoscopy, raising a question of deskilling effect brought about by an advanced AI technology.

Disclosure: Prateek Sharma: Consultant: Boston Scientific, Olympus Inc; Grant support: US Endoscopy, Medtronic, Fujifilm, Ironwood, Cosmo pharmaceuticals, Erbe
Michał Filip Kamiński: Consultant: Olympus, Erbe speaker: Boston Scientific, Ipsen,
Recordati; Grant support: Olympus
Yuichi Mori - Olympus: consultation, speaking fees, device loan
Cessare Hassan is a consultant for Alpha-Sigma, Fujifilm, Medtronic, Norgine, Olympus and Pentax.
Rest of authors: Nothing to declare.

OP124

COMPUTER-ASSISTED OPTICAL DIAGNOSIS OF COLORECTAL POLYPS 1-10MM IN SIZE WHEN USING AUTONOMOUS ARTIFICIAL INTELLIGENCE VERSUS AI-ASSISTED HUMAN DECISION-MAKING: A RANDOMIZED CONTROLLED TRIAL

M. Oleksiw¹, M. Taghiakbari^{1,2}, R. Djinbachian^{2,1}, H. Pohl^{3,4}, A.N. Barkun⁵, S. Sidani², J. Liu Chen Kiow², B. Panzini², S. Bouchard², É. Deslandres², D. von Renteln^{2,1}

¹Montreal University Hospital Research Center, Montreal, Canada, ²Montreal University Hospital Center (CHUM), Division of Gastroenterology, Montreal, Canada, ³Dartmouth-Hitchcock Medical Center, Section of Gastroenterology, Lebanon, United States of America, ⁴White River Junction VA Medical Center, Vermont, United States of America, ⁵McGill University and McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: megan.oleksiw@umontreal.ca

Introduction: Artificial Intelligence (AI) -based optical polyp diagnosis (CADx) allows for pathology prediction during colonoscopies to support resecting and discarding polyps. However, it is unclear if clinical use of such CADx modules should be as an autonomous decision-making device or rather to assist endoscopists in their decision-making. We therefore evaluated outcomes for CADx optical diagnosis when used autonomously versus as an assistive device for polyps up to 10mm.

Aims & Methods: We conducted a secondary analysis of a randomized non-inferiority trial in which 1-10mm polyps found in patients undergoing diagnostic, screening, and surveillance colonoscopies were randomized to undergo optical diagnosis using: 1) an Autonomous AI-based CADx diagnosis or 2) an AI-assisted endoscopist diagnosis (AI-H). Primary outcome was the accuracy of optical diagnosis in both arms with reference standard being the histological evaluation of the polyps. Secondary outcomes included the surveillance interval agreement based on USMSTF guidelines when using CADx (with pathology as a reference standard) as well as the proportion of misclassified polyps with advanced histology.

Results: A total of 223 and 227 polyps 1-10mm in size were found amongst 268 patients randomized to the autonomous AI group versus 229 patients to the AI-H group, respectively. Accuracy for optical diagnosis for cases with high-confidence diagnoses was 77.6% (95% confidence interval [CI], 71.5-82.9) in the autonomous AI group versus 74.0% (95%

CI, 67.8-79.6) in the AI-H group. When comparing surveillance interval agreement, autonomous AI-A did not exhibit superior agreement with USMSTF pathology-based recommendations compared to AI-H (88.5% [95% CI, 82.0-93.3] vs 83.4% [95% CI, 77.0-88.6]; $P = 0.213$), but did nearly reach the 90% PIVI recommendation benchmark to implement optical diagnosis. Prevalence of polyps with advanced histology (adenomas with villous component, high-grade dysplasia) and sessile serrated lesions was 11.2% (25/223 polyps) and 7.9% (18/227 polyps) in the autonomous AI and AI-H groups. The inability of CADx and endoscopists to specifically recognize these higher-risk lesions led to mismanagement of 3 out of 16 patients (18.8%) and 2 out of 16 patients (12.5%) with such lesions in the autonomous AI and AI-H groups, respectively.

Characteristics	Autonomous AI			AI-H		
	1-5mm	6-10mm	1-10mm	1-5mm	6-10mm	1-10mm
Polyps, N	158	65	223	155	72	227
Index Advanced Histology*, n (%)	11 (7.0)	14 (21.5)	25 (11.2)	7 (4.5)	11 (15.3)	18 (7.9)
Accuracy, % (95% CI)	77.8 (70.6-84.1)	76.9 (64.8-86.5)	77.6 (71.5-82.9)	75.5 (67.9-82.0)	70.8 (58.9-81.0)	74.0 (67.8-79.6)
Adenoma, %						
Sensitivity	85.0	100.0	89.1	91.7	91.3	91.5
Specificity	64.4	45.5	41.8	59.3	73.1	63.5

* Adenoma with villous component, high-grade dysplasia or sessile serrated lesion

Table. Diagnostic characteristics for high confidence polyp optical diagnosis.

Conclusion: In this study, autonomous use of CADx for optical diagnosis of polyps up to 10mm exhibited similar accuracy compared to its use as an assistive device. Autonomous AI did not achieve statistically significant different agreement with USMSTF guidelines-based surveillance interval assignment. Development of CADx advanced histology recognition and further evaluation of its use as an autonomous versus assistive device within multi-center studies is needed.

Disclosure: Daniel von Renteln has received research funding from ERBE Elektromedizin GmbH, Ventage, Pendopharm, Fujifilm, and Pentax and has received consultant or speaker fees from Boston Scientific Inc, ERBE Elektromedizin GmbH, and Pendopharm. The remaining authors disclose no conflicts.

OP125

THE ARTIFICIAL INTELLIGENCE IMPLEMENTATION IN THE TRAINING OF YOUNG ENDOSCOPISTS - DOES IT INFLUENCE THE QUALITY OF FUTURE COLONOSCOPIES?

Z. Orzeszko¹, T. Gach¹, M. Szura¹

¹Jagiellonian University, Cracow, Poland

Contact E-Mail Address: zosia.orzeszko@icloud.com

Introduction: Colonoscopy is a widely accepted screening test for detecting colorectal cancer. Computer-aided detection (CADE) based on artificial intelligence (AI) may be the way forward to improve its quality. As AI becomes a common upgrade in endoscopic equipment, an increasing number of young endoscopists are trained in an AI environment. However, how AI will impact trainees' future endoscopy outcomes remains unclear.

Aims & Methods: The study aimed to evaluate quality indicators in the first 1000 colonoscopies performed by newly trained endoscopists, comparing those trained in an AI environment to those trained in a non-AI environment. A study included 6,000 patients over 18 years old who underwent a colonoscopy for various reasons. The procedures were carried out by six young endoscopists, of which three were trained without AI and three with the assistance of the AI-powered Olympus Endo-Aid CADE system. The study retrospectively evaluated the first 1,000 procedures

performed by each endoscopist after completing training. These procedures were performed without AI enhancement and relied entirely on the endoscopists' detection skills. Quality indicators were assessed in non-AI-training and AI-training groups. The morphology of detected polyps was assessed to determine the influence of AI during training on laterally spreading tumors (LST) detection.

Results: A total of 6,000 participants were included in the analysis. Withdrawal time (WT) was longer in the AI-training group (8 vs 9 min, $p < 0.05$). Adenoma detection rate (ADR; 30.3 vs. 35.5%, $p < 0.05$), advanced adenoma detection rate (AADR; 4.6 vs. 5.1%, $p < 0.05$), and adenoma per colonoscopy score (APC; 0.73 vs. 0.75, $p < 0.05$) were higher in the AI-training group. AI-assisted endoscopy training significantly improved LST-NG detection ($p < 0.05$) for lesions smaller than 20mm.

	non-AI-training	AI-training	p-value
WT, min	8 (5-15)	9 (6-16)	<0.05
ADR, %	30.3	35.5	<0.05
AADR, %	4.6	5.1	<0.05
APC	0.73	0.75	<0.05

Conclusion: Implementing CADE during endoscopy training can positively impact quality indicators in the first 1,000 cases. After AI-enhanced training, the detection of LST-NG may improve. The potential of artificial intelligence in endoscopy training requires further investigation through prospective randomized controlled trials.

References: 1. Kaminski MF et al. N Engl J Med. 2010 May 13;362(19):1795-803. doi: 10.1056/NEJMoa0907667. PMID: 20463339.

2. Repici A et al. Efficacy of Real-Time Computer-Aided Detection of Colorectal Neoplasia in a Randomized Trial. Gastroenterology. 2020 Aug;159(2):512-520.e7. doi: 10.1053/j.gastro.2020.04.062. Epub 2020 May 1. PMID: 32371116.

3. Vilmann AS et al. Computerized feedback during colonoscopy training leads to improved performance: a randomized trial. Gastrointest Endosc. 2018 Nov;88(5):869-876. doi: 10.1016/j.gie.2018.07.008. Epub 2018 Jul 19. PMID: 30031803.

4. Kaminski MF et al. Leadership training to improve adenoma detection rate in screening colonoscopy: a randomised trial. Gut. 2016 Apr;65(4):616-24. doi: 10.1136/gutjnl-2014-307503. Epub 2015 Feb 10. PMID: 25670810; PMCID: PMC4819605.

5. Forbes N et al. Association Between Endoscopist Annual Procedure Volume and Colonoscopy Quality: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2020 Sep;18(10):2192-2208.e12. doi: 10.1016/j.cgh.2020.03.046. Epub 2020 Mar 30. PMID: 32240836.

Disclosure: Nothing to disclose.

OP126

CLINICAL IMPACT OF THE MISMATCH BETWEEN OPTICAL DIAGNOSIS AND HISTOLOGY: A RETROSPECTIVE EVALUATION OF THE CAD-ARTIPOD TRIAL

P. Sinonquel¹, T. Eelbode², O. Pech³, D. De Wulf⁴, P. Dewint⁵, H. Neumann⁶, G. Antonelli⁷, F. Iacopini⁸, D.J. Tate⁹, A. Lemmers¹⁰, N. Pilonis¹¹, M.F. Kaminski¹², P. Roelandt¹, C. Hassan¹³, I. Demedts¹, F. Maes², R. Bisschops¹

¹KU Leuven/UZ Leuven, Gastro-enterology and Hepatology, Leuven, Belgium, ²KU Leuven, MIRC, Leuven, Belgium,

³Krankenhaus Barmherzige Brüder Klinik für Gastroenterologie und Interventionelle Endoskopie - Klinik, Klinik für Gastroenterologie und, Regensburg, Germany,

⁴AZ Delta, Gastroenterology and Hepatology, Roeselare, Belgium, ⁵AZ Maria Middelaes, Gastroenterology and Hepatology, Gent, Belgium, ⁶Gastrozentrum Lippe,

Interventional Endoscopy Center, Bad Salzungen, Germany, ⁷Ospedale dei Castelli Hospital, Gastroenterology and Digestive Endoscopy Unit, Roma, Italy, ⁸Ospedale dei Castelli

Hospital, Gastroenterology and Digestive Endoscopy Unit, Rome, Italy, ⁹University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium, ¹⁰Hôpital Univ. Erasme (Gastro), Professor, Gastroenterology Department, Bruxelles, Belgium,

¹¹The Maria Skłodowska-Curie Institute - Oncology Institute Warsaw, Poland, Department of Oncological Gastroenterology, Warsaw, Poland, ¹²Maria Skłodowska-Curie Memorial Center and Institute of Oncology, Department of Gastroenterology, Warsaw, Poland, ¹³Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy

Contact E-Mail Address: pieter.sinonquel@uzleuven.be

Introduction: Guidelines indicate that optical diagnosis can be employed during endoscopy for a leave-in-situ or resect-and-discard strategy of diminutive polyps. Additionally, it aids in determining the appropriate techniques for polyp resection.

Aims & Methods: Our objective was to assess the accuracy and the clinical impact of real-life optical diagnosis during real-time colonoscopy conducted in the context of a CAdE trial.

We retrospectively compared optical diagnosis with histology results of 1608 polyps that were prospectively included in the CAD-ARTIPOD trial (NCT04442607). During CAD-ARTIPOD endoscopists (ADR 20-50%) provided optical diagnosis, polyps were resected, and histological examination was performed by two independent GI histopathologists.

Mismatch was defined as a difference in polyp type (hyperplastic (HP) vs tubular adenoma (TA) vs tubulovillous adenoma (TVA) vs sessile serrated lesion (SSL) vs pseudopolyp vs carcinoma vs no polyp) or a difference in grade of dysplasia (high grade vs low grade vs no dysplasia). Clinical impact on surveillance interval per patient was consecutively evaluated according to ESGE standards.

Results: On a total of 1608 resected and histologically assessed specimens of 946 patients, 1026 (63.8%) showed a match and 582 (36.2%) a mismatch between optical diagnosis and histology. The optical diagnosis was 552 (34.3%) HP, 904 (56.2%) TA, 3 (0.2%) TVA, 119 (7.4%) SSL, 11 (0.7%) carcinoma, 6 (0.4%) inflammatory pseudopolyp and 13 (0.8%) unknown histology. Mismatch was present in 254 (43.6%) HP, 225 (24.9%) TA, 77 (64.7%) SSL, 7 (63.6%) carcinoma and 5 (83.3%) pseudopolyps. Clinical consequences occurred for 48 (8.5%) polyps in as many patients (5.3%), with 12 polyps leading to a prolongation of the surveillance interval and 7 polyps overestimated as carcinomas not truly requiring further treatment. Twenty-nine (4.9%) of the optically misdiagnosed polyps led to a shortened surveillance interval (12 polyps with HGD and 17 as fifth TA)

and two (0.3%) required further surgical therapy. Of the 115 misdiagnosed hyperplastic polyps, 74 (64.4%) were left-sided and may have been left in situ when applying SODA criteria with correct optical diagnosis applied.

Conclusion: Even in the setting of a clinical trial with high detectors, where the focus was detection, rather than optical diagnosis, discordance between optical diagnosis and histology occurred in approximately one out of three polyps. The clinical impact was significant with alterations in clinical management for 8.5% of affected polyps, in 5.3% of patients. This underscores the importance of training in optical diagnoses and the potential role of artificial intelligence to assist in a resect and discard strategy.

Disclosure: Nothing to disclose.

Ameliorating acute disease through novel treatment in IBD: Part 2

16:00-17:00 / A3

OP127

COMPARISON OF OUTCOMES WITH EXCLUSIVE ENTERAL NUTRITION AND STEROIDS INDUCTION THERAPY IN NEWLY-DIAGNOSED CHILDREN WITH ISOLATED ILEAL CROHN'S DISEASE: REAL-WORLD DATA FROM TWO PROSPECTIVE COHORT STUDIES

R. Klomberg¹, A. Griffiths², F. Ruemmele³, N.M. Croft⁴, L. de Ridder¹, T.D Walters⁵, CIDsCaNN & PIBD-SETQuality study group
¹Sophia Children's Hospital, Erasmus Medical Center, Pediatric Gastroenterology, Rotterdam, Netherlands, ²Hospital for Sick Children, Dept. of Paed. Gastroenterology, Toronto, Canada, ³Universite Sorbonne, Paris-Cite Hospital, Paris, France, ⁴Queen Mary University of London, Barts and the London School of Medicine, London, United Kingdom, ⁵Hospital for Sick Children, Dept. of Paed. Gastroenterolgy, Toronto, Canada

Contact E-Mail Address: r.klomberg@erasmusmc.nl

Introduction: Both exclusive enteral nutrition (EEN) and steroids are effective therapies to induce remission in children with Crohn's disease (CD), but comparative data accounting for disease location are scarce.

Aims & Methods: We aimed to compare the effectiveness of EEN and steroids induction treatment in isolated ileal pediatric CD using data from two large real-world data cohorts. Children (age 2-18 years) with newly-diagnosed CD with an isolated ileal disease phenotype prospectively enrolled in the multicenter Canadian CIDsCaNN or predominantly European PIBD-SETQuality inception cohorts, who received either EEN or systemic steroids induction treatment, were eligible for this study. Demographics and extensive clinical data were collected prior to treatment and longitudinally until the last follow-up.

Outcomes, including [sustained] steroid free remission ([S]SFR), normal CRP remission (NCR; defined as remission with CRP <0.5 mg/dl), and (delta) height and BMI z-scores were compared at 3 months and 1 year. Time-to-first-biologic and time-to-luminal-resection were determined by Kaplan Meier curves and compared between groups using the log-rank test.

Results: A total of 221 children (n=134 [61%] CIDsCaNN, n=87 [39%] PIBD-SETQuality) with Crohn's disease with an isolated ileal phenotype receiving EEN (n=158 [72%]) or steroids (n=63 [28%]) as induction treatment were eligible for analysis (median follow-up 868 days [IQR 539 – 1443]). Disease phenotype, clinical and biochemical disease activity indices as well as demographics and anthropometrics, were similar between treatment groups (Table 1) and between cohorts. At 1 year, rates of SSFR (33% vs. 38%; p=0.56) and NCR (53% vs. 44%; p=0.27) were comparable between EEN and steroids-treated patients. Linear growth was borderline reduced in the steroids treated group (median height Z-score -0.42 [IQR -1.21 - 0.12]) compared to the EEN treated group (0.02 [IQR -0.94 - 0.59; p=0.050]. Type of induction treatment did not affect time-to-first-biologic (p=0.84) or time-to-luminal-resection (p=0.11).

At 3 months, combined rates of SFR + NCR were higher in patients who received EEN (38/111 [34%]) compared to those who received steroids (9/47 [19%]; p=0.058), largely because of differences in steroid exposure (14/121 [12%] with EEN, 19/39 [48%] with steroids; p<0.001), and normal CRP (68/108 [57%] and 18/43 [42%] respectively, p=0.084). Only in 20/220 (9%) of patients (15/157 [10%] with EEN, 5/63 [8%] with steroids; p=0.71), an additional induction therapy agent (EEN, steroids, biological, surgery) was started within 30 days after the start of induction treatment.

Characteristics	EEN (N = 158)	CS (N = 63)	Total (N = 221)	p-value
Age in years, median (IQR)	13.6 (11.5 - 15.2)	13.8 (11.9 - 15.6)	13.8 (11.7 - 15.3)	0.47
Male sex, n (%)	90 (57)	41 (65)	131 (59)	0.27
Height z-score, median (IQR)	-0.06 (-0.84 - 0.62)	-0.11 (-1.10 - 0.65)	-0.07 (-0.93 - 0.61)	0.49
BMI z-score, median (IQR)	-0.81 (-1.60 - 0.23)	-0.60 (-1.46 - 0.36)	-0.69 (-1.58 - 0.26)	0.55
Upper gastrointestinal tract involvement, n (%)	N = 149	N = 57	N = 206	
L4a	45 (30)	17 (30)	62 (30)	0.63
L4b	14 (9)	5 (9)	19 (9)	
L4ab	12 (8)	8 (14)	20 (10)	
No upper GI tract disease	78 (52)	27 (47)	105 (51)	
Perianal disease, n (%)	15 (10)	8 (13)	23 (11)	0.44
Disease behavior, n (%)				
B1	135 (85)	55 (87)	190 (86)	0.55
B2	16 (10)	7 (11)	23 (10)	
B3	2 (1)	1 (2)	3 (1)	
B2B3	5 (3)	0 (0)	5 (2)	
Disease activity, n (%)	N = 154	N = 61	N = 215	
Mild/inactive	54 (35)	21 (34)	75 (35)	1.0
Moderate	55 (36)	22 (36)	77 (36)	
Severe	45 (29)	18 (30)	63 (29)	
SES-CD ileal subscore, median (IQR)	N = 120 6 (3 – 8)	N = 48 5.5 (3 – 8)	N = 168 6 (3 – 8)	0.81

Table 1. Patient and disease characteristics at diagnosis of children with Crohn's disease with isolated ileal disease (L1), stratified by induction therapy.

Conclusion: EEN and steroids induction therapy show comparable short- and long-term clinical effectiveness in children with isolated ileal CD, but EEN trended towards better linear growth outcomes at one year.

Disclosure: Nothing to disclose.

OP128

IMPROVEMENT IN FATIGUE WITH MIRIKIZUMAB THERAPY AND ASSOCIATIONS WITH CLINICAL OUTCOMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM THE PHASE 3 VIVID-1 STUDY

P. Bossuyt¹, M. Regueiro², M. Fischer³, K. Traxler⁴, G. Yu⁴, M. Protic⁴, K. Tsilkos⁴, A. Vadhariya⁴, T. Hisamatsu⁵, P. Juillerat⁶
¹Imelda General Hospital, Bonheiden, Belgium, ²Cleveland Clinic, Cleveland, United States of America, ³IUPUI, Gastroenterology, Indianapolis, United States of America, ⁴Eli Lilly and Company, Indianapolis, United States of America, ⁵Kyorin University School of Medicine, Tokyo, Japan, ⁶Intesto Crohn's and Colitis Center, Bern and Fribourg, Switzerland

Contact E-Mail Address: peter.bossuyt@imelda.be

Introduction: Fatigue is a debilitating, multifactorial symptom experienced by many patients with Crohn's disease (CD).¹ Mirikizumab (MIRI), an anti-interleukin-23p19 antibody, demonstrated significant improvement in fatigue in patients with moderately to severely active CD in the Phase 2 AMAG² and Phase 3 VIVID-1³ studies.

Aims & Methods: This analysis examines the association of changes in clinical, endoscopic (endo) and selected patient-reported outcomes with changes in fatigue in MIRI-treated patients in the VIVID-1 study. Co primary and gated secondary outcomes, including comparisons with ustekinumab, have been presented elsewhere^{4,5} Adult patients (N=1065) with moderately to severely active CD were randomized 6:3:2 to MIRI, ustekinumab or placebo. MIRI was given every 4 weeks (W) as 900 mg intravenous at W0, W4, and W8, then 300 mg subcutaneous from W12 to W52. Fatigue was assessed via the validated Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire (scale from 0-52, higher scores indicating less fatigue⁶ and at least 6-point increase identified as a clinically meaningful within-patient change). Achievement of ≥6-point increase in FACIT-F at W52 was reported among those with and without

clinical remission by Crohn's Disease Activity Index (CDAI), endo response, endo remission, and Urgency Numeric Rating Scale (NRS) ≤ 2 at W52. For stool frequency (SF), abdominal pain (AP), fecal calprotectin (FCP), and C-reactive protein (CRP), the association of the change from baseline (CFB) at W52 vs. the CFB in FACIT-F at W52 was assessed by the Pearson correlation coefficient.

Results: At W52, 50.9% (268/527) of MIRI-treated patients achieved FACIT-F ≥ 6 -point increase from baseline. Greater proportions of patients who achieved clinical and endo outcomes had ≥ 6 -point increase in FACIT-F ($p < 0.05$) vs. those who did not achieve the outcome (Table). There was weak/moderate correlation between CFB at W52 in AP, SF and log-transformed FCP and CRP, and the CFB in FACIT-F at W52 (Table).

A. W52 FACIT-F ≥ 6 -point Increase From BL by Outcome at W52 ^a , NRI	Outcome Achieved n/N (%) (95% CI) ^b	Outcome NOT Achieved n/N (%) (95% CI) ^b	Risk Difference (95% CI) ^b	p-Value ^c
Clinical remission by CDAI ^d	185/280 (66.1) (60.5-71.6)	83/247 (33.6) (27.7-39.5)	32.5 (24.4-40.6)	<0.0001
Endo response ^e	154/256 (60.2) (54.2-66.2)	114/271 (42.1) (36.2-47.9)	18.1 (9.7-26.5)	<0.0001
Endo remission ^f	59/96 (61.5) (51.7-71.2)	209/431 (48.5) (43.8-53.2)	13.0 (2.1-23.8)	0.0216
Urgency NRS ≤ 2 ^g	127/188 (67.6) (60.9-74.2)	127/311 (40.8) (35.4-46.3)	26.7 (18.1-35.4)	<0.0001
B. CFB in FACIT-F vs. CFB in Outcomes at W52	N	Pearson Correlation Coefficient	95% CI ^h	p-Value
CFB in AP score	574	-0.379	-0.447 to -0.306	<0.0001
CFB in SF score	572	-0.306	-0.378 to -0.230	<0.0001
CFB in log-transformed FCP	461	-0.112	-0.201 to -0.020	0.0166
CFB in log-transformed CRP	576	-0.208	-0.285 to -0.128	<0.0001

Table: W52 FACIT-F, A: ≥ 6 -pt Increase From BL by Outcomes at W52 and B: CFB Correlation With CFB at W52 in Outcomes.

^aMIRI-treated patients with baseline (BL) FACIT-F score ≤ 46 points; ^bConfidence interval (CI) constructed using asymptotic method without continuity correction; ^cChi Square test; ^dCDAI < 150 ; ^eSimple Endoscopic Score for CD (SES-CD) Total Score $\geq 50\%$ improvement from BL; ^fSES-CD Total Score ≤ 4 , ≥ 2 -point reduction from BL and no subscore > 1 ; ^gIn those with BL Urgency NRS ≥ 3 ; ^hPearson correlation with Fisher's z-transformation. A negative correlation indicates an improvement in outcome is associated with an improvement in FACIT-F. Correlation strength defined as: > 0.5 =strong, 0.3 to ≤ 0.5 =moderate, 0.1 to < 0.3 =weak, < 0.1 =insubstantialⁱ NRI=nonresponder imputation.

Conclusion: In patients with moderately to severely active CD treated with MIRI, improvements in clinical, endoscopic, and selected patient-reported outcomes were associated with clinically meaningful improvements in fatigue at W52.

References:

1. D'Silva A, et al. *Clin Gastroenterol Hepatol.* 2022;20:995-1009.
2. Regueiro MD, et al. *Am J Gastroenterol.* 2023;118:S816.
3. Travis S, et al. *J Crohn's Colitis.* 2024;18:i21-i23.
4. Ferrante M, et al. *J Crohn's Colitis.* 2024;18:S1 i7-i9.
5. Jairath V, et al. *J Crohn's Colitis.* 2024;18:i62-i64.
6. Tinsley A, et al. *Aliment Pharmacol Ther.* 2011;34:1328-36.
7. Cohen J. *Statistical Power Analysis for the Behavioural Sciences*, 1988, Routledge.

Disclosure: **P. Bossuyt** has received financial support for research from: AbbVie, Amgen, Janssen, Pfizer, and Viartis; lecture fees from: AbbVie, Bristol Myers Squibb, CAG, Celltrion, Eli Lilly and Company, EPGs, Galapagos NV, Globalport, Janssen, Materia Prima, Pentax, Scope, and Takeda; and advisory board fees from: AbbVie, Bristol Myers Squibb, Celltrion, CIRC, Dr. Falk Pharma Benelux, Eli Lilly and Company, Galapagos NV, Janssen, Pentax, PSI-CRO, Roche, Takeda, and Tetrameros; **M. Regueiro** has served as an advisor and/or consultant for: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Genentech, Gilead Sciences, Janssen, Organon, Pfizer, Prometheus Therapeutics and Diagnostics, Salix Pharmaceuticals, Takeda, and UCB Pharma; **M. Fischer** has

received consulting fees from: AbbVie, Bristol Myers Squibb, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Pfizer, Rebiotix, Scioto Biosciences, and Seres Therapeutics; **K. Traxler**, **G. Yu**, **M. Protic**, **K. Tsilkos**, and **A. Vadhariya** are employees and shareholders of: Eli Lilly and Company; **T. Hisamatsu** has received lecture fees from: AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceutical K.K., JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; has received honoraria as an advisory board member or consultant for: AbbVie, Bristol Myers Squibb, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Pfizer, and Takeda; and has received pharmaceutical/research grants from: AbbVie, Boston Scientific, Daiichi Sankyo, EA Pharma, Kissei Pharmaceutical, JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nichi-Iko Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical; **P. Juillerat** has received fees for lectures and consulting/advisory board from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly and Company, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Merck Sharp & Dohme, Pfizer, Pierre Fabre, Sandoz, Takeda, Tillotts Pharma AG, and UCB Pharma

OP129

RISANKIZUMAB, BUT NOT USTEKINUMAB OR VEDOLIZUMAB, DOWNREGULATES IL-23-INDUCED MUCOSAL PATHOGENIC TH17 CELLS IN PATIENTS WITH CROHN'S DISEASE

D. Noviello¹, **I. Dusetti**², **V. Pivorunas**³, **A.E. Lovati**⁴, **C. Ciafardini**⁴, **C. Amoroso**⁴, **F. Conforti**⁴, **N. Piazza O Sed**⁴, **M. Vecchi**¹, **F. Facciotti**⁵, **M. Paroni**², **F. Caprioli**¹

¹University of Milan, Department of Pathophysiology and Transplantation, Milano, Italy, ²University of Milan, Department of Medical Sciences, Milano, Italy, ³AbbVie, Chicago, United States of America, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁵University Of Milano Bicocca, Milan, Italy

Contact E-Mail Address: noviellodaniele@gmail.com

Introduction: We recently described an interleukin(IL)-23-inducible pathogenic subset of CCR6⁺CXCR3⁺CCR5⁺ mucosal T helper (Th)17 cells (pTh17) infiltrating Crohn's disease (CD) inflamed mucosa and specifically activated in response to Adherent-Invasive Escherichia Coli. pTh17 cells are functionally and phenotypically distinct from CCR6⁺CXCR3⁺CCR5⁺ Th17 cells (cTh17) and from IL-12-induced CCR6⁺CXCR3⁺ Th1/17 subset. Here, we investigated pTh17 cells' recirculation into the bloodstream, localization into the intraepithelial lymphocyte (IEL) compartment, and in-vivo modulation by different biological therapies.

Aims & Methods: Adult patients with active CD initiating either vedolizumab as per clinical practice or ustekinumab and risankizumab during the SEQUENCE trial were prospectively recruited at Fondazione IRCCS Cà Granda, Ospedale Policlinico di Milano. In vedolizumab-treated patients, peripheral blood and intestinal biopsies were collected at baseline and at the end of induction. In ustekinumab- and risankizumab-treated patients, intestinal biopsies were collected outside study protocol assessments at baseline and week 24. Endoscopic response was defined as a greater than 50% decrease in the Simple Endoscopic Score from baseline. Peripheral blood mononuclear cells, lamina propria mononuclear cells (LPMC), and IEL were isolated and analyzed through flow cytometry.

Results: Overall, 34 CD patients were assessed. Demographic and baseline disease characteristics are summarized in Table 1. At baseline, as compared with cTh17, pTh17 cells: 1. are rarely found in the peripheral blood and express low levels of CCR9 and $\alpha 4\beta 7$, 2. express high levels of tissue-resident markers CD69⁺CD103⁺ in the mucosa, and 3. infiltrate the IEL layer upon binding of CD103 with E-cadherin. Baseline pTh17 cells

were upregulated in patients not achieving vedolizumab-induced endoscopic response. Upon vedolizumab treatment, a selective downregulation of mucosal cTh17 cells but not pTh17 was observed. Remarkably, risankizumab induced a specific downregulation of pTh17 cells, but not cTh17, in both LPMC and IEL layers. Conversely, ustekinumab reduced Th1/17 mucosal subsets, but not pTh17 cells (Figure 1).

Conclusion: pTh17 cells are largely unable to recirculate through the bloodstream, express markers of gut-tissue residency, and infiltrate the IEL compartment. IL-23 neutralization by risankizumab specifically downregulates mucosal pTh17 cells, as compared with vedolizumab and ustekinumab. Our immunologic results might provide mechanistic clues to vedolizumab latency effect in CD, and potentially explain early signs of risankizumab superiority over ustekinumab in the SEQUENCE study in terms of endoscopic response at 24 weeks.

Disclosure: DN received research grant from Pfizer, consulting fees from Dr. Falk, lecturer fees from Ferring. VP is employee of AbbVie. MV served as a consultant for Abbvie, MSD, Takeda, Janssen-Cilag, and Celgene. He received lecturer fees from Abbvie, Ferring, Takeda, MSD, Janssen-Cilag, and Zambon. FCa has served as consultant for Mundipharma, AbbVie, MSD, Takeda, Janssen, Roche, and Celgene; received lecture fees from AbbVie, Ferring, Takeda, Allergy Therapeutics, and Janssen; and received unrestricted research grants from Giuliani, SOFAR, MS&D, Takeda, Pfizer, and AbbVie.

OP130

UPADACITINIB IMPROVES CLINICAL, BIOCHEMICAL, AND SONOGRAPHIC PARAMETERS IN A MULTINATIONAL REAL-WORLD COHORT OF PATIENTS WITH ULCERATIVE COLITIS – WEEK 16 RESULTS FROM THE IBD-DACH STUDY EUROPE

S. Zeissig¹, R. Schmelz¹, U. Helwig^{2,3}, A.R. Moschen⁴, T. Greuter⁵, I. Fischer⁶, L. Hammer⁷, S. Rath⁷, T. Kucharzik⁸, C. Maaser⁹

¹Technical university of Dresden, Germany, Department of Medicine I and Center for Regenerative Therapies Dresden, Dresden, Germany, ²Gastroenterology Practice, Oldenburg, Germany, Oldenburg, Germany, ³University of Kiel, Kiel, Germany, ⁴Johannes Kepler University of Linz; Austria, Department of Internal Medicine 2, Linz, Austria, ⁵GZO AG Spital Wetzikon; Switzerland, Department of Gastroenterology, Wetzikon, Switzerland, ⁶Biostatistik Tübingen, Tübingen, Germany, ⁷AbbVie Germany GmbH & Co. KG, Wiesbaden, Germany, Medical Department, Wiesbaden, Germany, ⁸University Teaching Hospital Lueneburg, Lueneburg, Germany, Department of Internal Medicine and Gastroenterology, Lüneburg, Germany, ⁹University Teaching Hospital Lueneburg, Lueneburg, Germany, Outpatients Department Gastroenterology,, Lüneburg, Germany

Contact E-Mail Address: Sebastian.Zeissig@ukdd.de

Introduction: Upadacitinib (UPA), an oral, reversible and selective Januskinase-inhibitor (JAKi), was licensed for the treatment of seven immune-mediated inflammatory diseases, including moderate to severe ulcerative colitis (UC) (1). Real-word (RW) evidence on the effectiveness and safety of UPA in UC remains sparse (2). Here, we present clinical, biochemical, and sonographic data after 8 and 16 weeks of UPA induction in a large, multinational RW cohort of UC patients.

Aims & Methods: EUROPE is an ongoing, prospective, non-interventional, international multicentric study in patients with active UC selected for therapy with UPA. The study aims to analyse the predictive value of early disease improvements including sonographic parameters for the long-term outcome after 52 and 104 weeks. For this interim analysis, we report clinical, biochemical and sonographic results at baseline (BL), week 8 (8W), and 16W of 139 UC patients enrolled until January 2024. W2 results have been previously presented by Zeissig et al. at ECCO 2024 (P905). For 92 patients, sonographic BL data for the most affected bowel segment was available. The safety population included all 211 patients enrolled until data base lock. Because of lacking data on w52 no predictive value could be shown.

Results: Overall, 139 patients had a documented W16 visit until January 2024. Of these, 59.7% (n = 83) were male and .7%, n = 83) 54.0% (n = 75) had pancolitis. The median disease duration was 6.9 years (2.6–12.7) and a minority was fully vaccinated against herpes zoster at baseline (30.9%, n = 43). The majority of patients was bio-experienced (85.6%, n = 119) and about one third had been exposed to ≥ 3 biologicals (36.1%, n = 43/119). At BL, patients had a median bowel wall thickness (BWT) of 5.0 mm (4.0–6.2) in the sigmoid colon. It was the most affected segment in 70.7% of patients (n = 65/92). At BL, disease activity was high, reflected by a median partial Mayo score (incl. rectal bleeding (RB), stool frequency (SF), physician's global assessment (PGA) of 5.0 (4.0–7.0). After UPA induction, patients demonstrated high rates of symptomatic remission (SF≤1, RB=0) at 8W and 16W (65.5% (n = 91) and 69.1% (n = 96) vs. 26.5% (n = 23) at BL; both p < 0.001 vs. BL). BWT was ≤ 3mm (considered normalisation) in 63.0% (n = 58) and 60.9% (n = 56) at 8W and 16W (both p < 0.001 vs. BL with 10.9%, n = 10). Remission of biomarkers fecal calprotectin (fCal ≤ 250 µg/g) and CRP (< 5 mg/L) was observed in 59.0% (n = 82) and 60.4% (n = 84) at 8W and 16W (both p < 0.001 vs BL with 28.1%, n = 39). After 8W induction, 38.1% (n = 53) were still on 45mg UPA, while 37.4% (n = 52) had

switched to 30mg and 10.8% (n = 15) to 15mg maintenance dosing. This could potentially be confounded by visit time points. In total, 104 adverse events (AE), of which most were non-serious (7.1%, (n = 15) SAEs), were documented.

Conclusion: In this interim analysis of the EUROPE study, UPA induction treatment in UC provided relief of clinical symptoms and was associated with early sonographic and biochemical improvement.

References:

1. Current SmPC Upadacitinib
2. Danese and Vermeire et al. *Lancet*. 2022 Jun 4;399(10341):2113-2128. doi: 10.1016/S0140-6736(22)00581-5. Epub 2022 May 26

Disclosure: S. Zeissig, R. Schmelz, A. Moschen, T. Greuter, T. Kucharzik, U. Helwig, C. Maaser have received lecture and consulting fees from AbbVie. I. Fischer has received consulting fees from AbbVie. L. Hammer and S. Rath are AbbVie employees and may own AbbVie stock or options.

AbbVie sponsored the study; contributed to the design; participated in the collection, analysis, and interpretation of data; in writing, reviewing, and approval of the final version. Statistical analysis support was provided by Dr. Imma Fischer, Biostatistik Tübingen, which was funded by AbbVie. No honoraria or payments were made for authorship. This abstract was previously submitted to DGVS 2024, where is currently under consideration.

OP131

EFFECTS OF MIRIKIZUMAB AND USTEKINUMAB ON HISTOLOGIC INFLAMMATION EVALUATED BY COMPREHENSIVE ASSESSMENT IN 5 INTESTINAL SEGMENTS IN A RANDOMIZED CONTROLLED PHASE 3 TRIAL OF PARTICIPANTS WITH CROHN'S DISEASE

V. Jairath¹, F. Magro², G. De Hertogh³, B. Feagan⁴, N. Harpaz⁵, T. Hisamatsu⁶, G. D'Haens⁷, R. Pai⁸, Z. Lin⁹, N. Morris⁹, M. Protic⁹, E. Hon⁹, C. Owen⁹, R. Escobar⁹, W. Reinisch¹⁰

¹Western University, London, Canada, ²Faculty of Medicine, University of Porto, Porto, Portugal, ³Laboratory of Translational Cell and Tissue Research, Department of Imaging and Pathology, Faculty of Medicine, KU, Leuven, Belgium, ⁴Alimentiv Inc., London, Canada, ⁵Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁶Kyorin University, Tokyo, Japan, ⁷Inflammatory Bowel Disease Centre, Amsterdam University Medical Centers, Amsterdam, Netherlands, ⁸Department of Laboratory Medicine and Pathology, Mayo Clinic, Scottsdale, United States of America, ⁹Eli Lilly and Company, Indianapolis, United States of America, ¹⁰Medical University of Vienna, Vienna, Austria

Contact E-Mail Address: vjairath@uwo.ca

Introduction: Histologic inflammation persists in up to 1/4 of patients (pts) with Crohn's Disease (CD) despite endoscopic mucosal healing. Responsiveness of histologic inflammation and of combined endoscopic-histologic endpoints to treatment are evolving measures of disease activity in CD. Mirikizumab (MIRI) increased histologic response (H-Res) and remission (H-Rem) relative to placebo (PBO) in the Phase 2 SERENITY trial.¹

Aims & Methods: To evaluate the impact of MIRI and ustekinumab (UST) on H-Res and H-Rem and combined endoscopic-histologic response (EH-Res) and remission (EH-Rem) in all pts, pts with prior biologic failure (BF), pts without prior BF in moderately to severely active CD, in the randomized, double-blind, double-dummy, treat-through Phase 3 VIVID-1 trial (NCT03926130). Two biopsy specimens from each of 5 intestinal segments (1 ileal and 4 colonic) were obtained from the edge of the ulcers, or the most inflamed mucosa from randomized pts at screening, and weeks (W)12, and 52. Criteria for H-Res were the absence of epithelial neutrophils and epithelial damage, erosions and ulceration or ≥50% decrease in

either the active Robarts Histopathology Index or the active Global Histologic Disease Activity Score. H-Rem was defined as complete absence of mucosal neutrophils (in epithelium and lamina propria), and no epithelial damage, erosions and ulcers; these criteria had to be met in all biopsy specimens. Endoscopic response was defined as ≥50% improvement from baseline in Simple Endoscopic Score for CD (SES-CD). Endoscopic remission was defined as SES-CD total score ≤4 and ≥2-point reduction from baseline and no subscore >1 in any individual variable.

Results: At W52, nominally significant differences between MIRI and UST were observed in achieving H-Res in all pts (58.2% vs 48.8%; p=.007 and in BF pts (56.5% vs 41.3%; p=.006). For EH-Res, differences of MIRI vs UST were numerically greater but not statistically significant in all pts (41.1% vs 34.4%; p=.063) but were nominally significant among BF pts (39.6% vs 27.8%; p=.023). While numerical differences between MIRI and UST were observed in H-Rem and EH-Rem in all pts (H-Rem: 30.2% vs 28.9%; p=.685; EH-Rem: 17.2% vs 14.8%; p=.363) and in BF pts (H-Rem: 24.3% vs 19.8%; p=.365; EH-Rem: 13.3% vs 8.7%; p=.237), no significant differences were observed in these endpoints (Table).

		MIRI	USTE	P	Difference (95%CI)
Histologic Response (%)	All patients	58.2	48.8	0.007	9.6 (2.6, 16.6)
	Without prior biologic failure	61.9	56.9	0.383	5.0 (-5.3, 15.3)
	With prior biologic failure	56.5	41.3	0.006	15.2 (4.7, 25.7)
Endoscopic-Histologic Response (%)	All active patients	41.1	34.4	0.063	6.8 (-0.3, 14.0)
	Without prior biologic failure	42.5	40.8	0.829	1.7 (-8.6, 12.0)
	With prior biologic failure	39.6	27.8	0.023	11.8 (2.0, 21.7)
Histologic Remission (%)	All patients	30.2	28.9	0.685	1.3 (-5.0, 7.7)
	Without prior biologic failure	33.3	34.6	0.822	-1.3 (-11.2, 8.6)
	With prior biologic failure	24.3	19.8	0.365	4.5 (-4.3, 13.2)
Endoscopic-Histologic Remission (% 95%CI)	All active patients	17.2	14.8	0.363	2.6 (-2.8, 7.9)
	Without prior biologic failure	20.9	20.8	>0.999	0.1 (-8.4, 8.6)
	With prior biologic failure	13.3	8.7	0.237	4.6 (-1.9, 11.1)

All active patients are patients with active histologic disease at baseline. Histologic response and histologic remission in all patients were prespecified, non-multiplicity-controlled endpoints. All analyses in patients without prior biologic failure, patients with biologic failure and combined endoscopic-histologic response and remission were analyzed post hoc. For achieving histologic response, the sum of five segments active RHI or active GHAS needed to be reduced by ≥50% from baseline.

CI=confidence interval; GHAS=Global Histologic Disease Activity Score; MIRI=mirikizumab; PBO=placebo; RHO=Robarts Histopathology Index; USTE=ustekinumab

Conclusion: Using strict definitions, all histology-based endpoints were achieved by MIRI versus PBO. For comparison versus UST, MIRI also showed nominal statistical difference for H-Res, which was prespecified and is considered the most sensitive to change, particularly driven by BF pts. The implication of these results on clinical endpoints and long-term outcomes, including hospitalization rates and surgeries, requires further evaluation.

References:

1. Magro F, et al. *Clin Gastroenterol Hepatol*. 2023;S1542-3565(23)00948-5.

Disclosure:

V. Jairath received consulting/advisory board fees: AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris Pharmaceuticals, Astra-Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Endpoint Health, Enthera, Ferring Pharmaceuticals, Flagship Pioneering, Fresenius Kabi, Galapagos NV, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead Sciences, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Biosciences, Protagonist Therapeutics, Reistone Biopharma, Roche, Roivant Sciences, Sandoz, SCOPE, Second Genome, Sorriso Pharmaceuticals, Takeda, TD Securities, Teva, Topivert, Ventyx Biosciences, and Vividion Therapeutics;

and speaker's fees: AbbVie, Bristol Myers Squibb, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos NV, Janssen, Pfizer, Shire, and Takeda

F. Magro speaker: AbbVie, Arena, Biogen, Bristol Myers Squibb, Eli Lilly and Company, Falk, Ferring Pharmaceuticals, Hospira, Janssen, Laboratórios Vitoria, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, UCB, and Vifor

G. De Hertogh received fees for clinical trial activities with Centocor Inc; and received consultancy fees: Eli Lilly and Company and MRM Health

B. Feagan was a consultant: AbbVie, AbolentS Pharma, Agomab Therapeutics, Alliantera, Amgen, AnaptysBio, Applied Molecular Transport, Arena Pharmaceuticals, Avoro Capital Advisors, Atomwise, BioJamp, Biora Therapeutics, Boehringer Ingelheim, Boxer, Celgene/BMS, Celsius Therapeutics, Connect BioPharma, Cytokine Pharma, Disc Medicine, Duality, EcoR1, Eli Lilly and Company, Equillium, Ermiu Therapeutics, First Wave BioPharma, First Word Group, Galapagos NV, Galen Atlantica, Genentech/Roche, Gilead Sciences, Gossamer Pharma, GlaxoSmithKline, Hinge Bio, Hot Spot Therapeutics, InDex Pharma, Imhotex, Immunic Therapeutics, JAKAcademy, Janssen, Japan Tobacco, Kaleido Biosciences, Landos Biopharma, Leadiant, L.E.K. Consulting, Lenczner Slaght, LifeSci Capital, Lument AB, Millennium Pharmaceuticals, MiroBio, Morgan Lewis, Morphic Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Play to Know AG, Progenity, Protagonist Therapeutics, PTM Therapeutics, Q32 Bio, Rebiotix, Redx Pharma, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared, Viatrix, Ysios, YSOPIA Bioscience, and Zealand Pharma; was on the speaker's bureau: AbbVie, Janssen, and Takeda; member of the Scientific Advisory Board, DSMB for: AbbVie, Amgen, AMT, AnaptysBio, Axio Research, Boehringer Ingelheim, Celgene/BMS, Ecor1Capital, Eli Lilly and Company, Genentech/Roche, GlaxoSmithKline, InDex Pharma, Janssen, MiroBio, Morphic, Origo BioPharma, Pfizer, Progenity, Prometheus, Redx Pharma, Sanofi, Takeda, Tillotts Pharma, and Teva; stock shareholder of: Gossamer Pharma; and employee as Senior Scientific Director of: Western University and Alimentiv

N. Harpaz advisory board member and/or consultant: AbbVie, Bristol Myers Squibb, Eli Lilly and Company, and PathAI Inc

T. Hisamatsu received lecture fees: AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceutical K.K., JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; received honoraria as an advisory board member or consultant: AbbVie, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Pfizer, and Takeda; and received pharmaceutical/research grants from: AbbVie, Alfresa Pharma, Daiichi Sankyo, EA Pharma, JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nichi-Iko Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical

G. D'Haens advisor: AbbVie, Agomab Therapeutics, Alimentiv, AstraZeneca, Biora, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Exeliom Biosciences, Galapagos NV, Genentech/Hoffmann-La Roche, GlaxoSmithKline, Immunic Therapeutics, Johnson & Johnson, Merck Sharp & Dohme, Pfizer, Protagonist Therapeutics, Samsung Bioepis, Sandoz, Seres Therapeutics/Nestec/Nestlé, Takeda, Tillotts Pharma AG, Ventyx; received speaker fees: AbbVie, Johnson & Johnson, Takeda, Pfizer, Tillotts Pharma AG

R. Pai received consulting fees: Alimentiv Inc, Allergan, and BRACCO

Z. Lin, N. Morris, M. Protic, E. Hon, C. Owen, R. Escobar are employees and shareholders: Eli Lilly and Company

W. Reinisch received lecture and consulting fees from and/or served as an advisory board member: AbbVie, Actelion, Alpha Wasserman, AstraZeneca, Cellerix, Cosmo Pharmaceuticals, Ferring Pharmaceuticals, Genentech, Grunenthal, Johnson & Johnson, Millennium, Merck, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos, Schering-Plough, Salix Pharmaceuticals, Takeda, UCB Pharma, and Vifor Pharma

Pancreatic cancer: From bench to bedside

16:00-17:00 / Lehar 1

OP132

SINGLE-NUCLEUS RNA SEQUENCING REVEALS THE CRUCIAL ROLE OF TERTIARY LYMPHOID STRUCTURES IN DRIVING B CELL MATURATION INTO PLASMA CELLS IN PDAC

C. Mota Reyes¹, C. van Eijck², J.E. Friedrich³, L. Rupp⁴, M. Kiessler¹, I. Dietsche⁴, J. Martinez Villareal⁵, A. Muckenhuber⁶, K. Steiger⁶, L. Alonso⁵, L. Estudillo⁵, B. Kong⁷, C. Michalski⁸, F.X. Real⁹, H. Friess¹⁰, G.O. Ceyhan¹¹, R. Istvanffy¹⁰, M. Schmitz⁴, N. Malats¹², C.H. van Eijck², I.E. Demir¹³, PanGenEU Study Investigators

¹Technical University of Munich, Chirurgische Klinik und Poliklinik, München, Germany, ²Erasmus Medical Center, Rotterdam, Netherlands, ³Technical University of Munich, Institute of Experimental Oncology and Therapy Research, Munich, Germany, ⁴Technical University of Dresden, Institute of Immunology, Dresden, Germany, ⁵Spanish National Cancer Research Centre, Madrid, Spain, ⁶Technical University of Munich, Institute of Pathology, Munich, Germany, ⁷Heidelberg University Hospital, Department of General, Visceral and Transplantation Surgery, Heidelberg, Germany, ⁸Heidelberg University Hospital, Heidelberg, Germany, ⁹Spanish National Cancer Research Center-CNIO, Cancer, Madrid, Spain, ¹⁰Klinikum rechts der Isar, Department of Surgery, Munich, Germany, ¹¹Acibadem Mehmet Ali Aydinlar University, Department of General Surgery, Istanbul, Turkey, ¹²Spanish Cancer Research Cancer Center, Madrid - Genetic and Molecular Epidemiology Group, Spanish Ca, Genetic and Molecular Epidemiology Group, Madrid, Spain, ¹³Klinikum Rechts Der Isar, Technical University of Munich, Department of Surgery, Muenchen, Germany

Contact E-Mail Address: carmen.mota@tum.de

Introduction: In pancreatic ductal adenocarcinoma (PDAC), the prognostic relevance of B cells remains controversial, and only when aggregated within tertiary lymphoid structures (TLS) have they been unanimously associated with extended survival. Our aim is to provide the first transcriptomic characterization of B cell subtypes and gain new insights into the immune-promoting role of TLS in PDAC.

Aims & Methods: We generated a comprehensive transcriptomic atlas of tumor-associated B cells in PDAC by integrating single cell technology with spatial transcriptomic approaches. Histological characterization of the B cell immune landscape was performed using a novel multiplexed immunohistochemistry panel in treatment-naïve PDAC patients. In addition, TLS assessment on routine H&E slides from two independent PDAC cohorts, comprising participants from the randomized controlled PREOPANC trial (n=44) and the PanGenEU study (n=66), were subjected to uni- and multivariate prognostic analyses, with associated bulk-RNAseq data utilized for additional validation.

Results: The presence of TLS was linked with an expansion of the B cell compartment and their differentiation into antibody-producing plasma cells. Using single nucleus (sn)RNAseq and spatial mapping, we uncovered that certain differentiated B cell subtypes including germinal center (GC) B cells and plasma cells, were exclusively identified in patients with late-stage TLS harbouring GCs. In addition, CD38+ CD138+ plasma cells were predominantly located forming clusters in stromal regions situated in close proximity to TLS.

Accordingly, the expression of antibody production and plasma cell markers was significantly heightened in patients with late-stage TLS, indicative of augmented adaptive immune responses. We further validated the prog-

nostic significance of GC formation within TLS in two independent PDAC cohorts (HR=0.45, 95%CI 0.27-0.77, P.adj.=0.034). Notably, in the PREOPANC cohort a positive TLS status was also associated with a favorable immune milieu enriched with antibody-presenting cells and B cell subsets, including plasma cells.

Conclusion: Our multiomic analysis unveils compelling evidence of selective B cell maturation and active adaptive immunity in PDAC patients harboring late-stage TLS. From a clinical perspective, TLSs emerge as robust prognosticators of survival in PDAC.

Overall, our findings provide novel insights into B cell biology and hold potential to refine immunotherapeutic strategies in this challenging tumor context.

Disclosure: Nothing to disclose.

OP133

CANCER SUSCEPTIBILITY GENE TESTING IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA: IMPLEMENTATION IN AN ACADEMIC TERTIARY REFERRAL CANCER CENTER ONCOLOGY CLINIC

H. Sinan¹, D. Cunningham², T. McPhaul³, J. He³, R. Burkhardt³, L. Zheng², N.S. Azad², D. Laheru², M. Goggins^{1,2,4}
¹Johns Hopkins University, Department of Pathology, Baltimore, United States of America, ²Johns Hopkins University, Department of Oncology, Baltimore, United States of America, ³Johns Hopkins University, Department of Surgery, Baltimore, United States of America, ⁴Johns Hopkins University, Medicine, Baltimore, United States of America

Contact E-Mail Address: hsinan1@jh.edu

Introduction: Approximately 10% of patients diagnosed with pancreatic ductal adenocarcinoma (PDAC) carry a pathogenic variant in a PDAC susceptibility gene. Current guidelines recommend offering germline cancer susceptibility testing for all individuals with PDAC regardless of family history.

Previous studies have shown moderate rates of uptake of gene testing, highlighting the need for efficient and accessible clinical pathways for delivering gene testing education and counseling.

We evaluated the uptake of gene testing when offered at the point-of-care by an oncology nurse specialist in an outpatient setting.

Aims & Methods: We undertook a retrospective chart review of PDAC patients treated at the Johns Hopkins Hospital between January 2021 and December 2023. Patients were educated about germline testing by an oncology nurse specialist during their initial clinic visit, and provided with instructional handouts, links to videos, instructions on kit ordering and given time to consider testing. “MyChart” reminders are sent as needed. Patients who desired testing were sent a saliva kit to their home that they had to send back to the testing lab.

Results were communicated by the oncology nurse to the patients, and those with pathogenic variants or variants of uncertain significance (VUS) are referred to formal genetic counseling.

Results: Of 1022 patients seen by the oncology and surgery teams, all but 2 were seen by oncology, 377 underwent surgery, 52% were male, 74.9% were White, 15.8% African American (AA), 6% were Asian, 3% were Hispanic, and 17.5% had a family history of pancreatic cancer. At diagnosis, median age was 67.1 +/- 10.6 years; 51.9% of cases had resectable-stage disease.

Among the 87.5% of patients offered gene testing, 77.6% completed testing. Completion rates among those offered testing increased from 72.4% (2021) to 78.5% (2022) and 82.2% (2023).

Factors significantly associated with reduced gene testing uptake includ-

ed African American patients, those that were single, had advanced-stage disease, did not receive chemotherapy and of older age at diagnosis (Table 1).

Among tested individuals, 55 (7.9%) involving PDAC susceptibility genes, with BRCA2, ATM and PALB2 being the most common. 50 out of these 55 patients (91%) were referred to genetic counseling, with 76% completing their counseling visit to date. Germline testing results led to a change in the treatment regimen in 23 of the 55 patients.

		Coefficient	Odds Ratio	95% Confidence Interval	P Value
Sex	Male vs Female	0.215	1.240	0.872-1.763	0.231
	White vs AA	-1.065	0.345	0.224- 0.531	<0.001
Race	White vs Asian	0.440	1.553	0.671- 3.596	0.304
	White vs Other	-1.508	0.221	0.083- 0.590	0.003
Ethnicity	Non-Hispanic Vs Hispanic	1.038	2.822	0.733- 10.863	0.131
Marital Status	Married vs Single	-0.755	0.471	0.295- 0.750	0.002
Stage at diagnosis	Resectable vs Metastatic	-0.5738	0.564	0.379-0.839	0.005
	Resectable vs Locally advanced	0.170	1.185	0.767-1.830	0.444
Age at diagnosis		-0.022	0.978	0.961- 0.996	0.015
Family History of PDAC	Yes vs No	-0.354	0.702	0.434- 1.136	0.149
Personal history of other cancers	Yes vs No	-0.036	0.965	0.629- 1.480	0.869
Received Chemotherapy	Yes vs No	-1.162	0.313	0.107- 0.910	0.033

Table 1: Multivariate analysis results for completion of germline genetic testing among offered patients.

Conclusion: The implementation of point-of-care encounters for cancer susceptibility gene testing by an oncology nurse specialist in the outpatient setting yielded a high uptake of testing. African American, older-age, single and advanced-stage disease individuals had lower rates of completing gene testing.

Disclosure: Nothing to disclose.

OP134

INHIBITION OF EXOSOMES SUPPRESSES THE PROGRESSION OF PANCREATIC DUCTAL ADENOCARCINOMA: A STUDY USING MOUSE MODELS AND HUMAN ORGANOIDS

C.M. Zhao^{1,2}, H.-L. Rabben¹, M. Resell¹, M.K. Svensson¹, A. Ianevski¹, A. Sharma^{1,3,2}, L. Hagen^{1,3,2}, A. Diez-Sanchez¹, M. Martin-Alonso¹, G. Qvigstad⁴, D. Kainov¹, S.K. Batra⁵, T. Wang⁶, D. Chen¹
¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²Central Norway Regional Health Authority Norway, Trondheim, Norway, ³Norwegian University of Science and Technology, PROMEC Core Facility for Proteomics and Modomics, Trondheim, Norway, ⁴St. Olavs Hospital, Department of Gastroenterology, Trondheim, Norway, ⁵University of Nebraska College of Medicine, Department Biochemistry and Molecular Biology, Nebraska, United States of America, ⁶Columbia University, Digestive & Liver Diseases, New York, United States of America

Contact E-Mail Address: chun-mei.zhao@ntnu.no

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a systemic disease that resists almost any available therapies and is strikingly associated with thrombosis. We hypothesize that cell membrane of PDAC exhib-

its a high level of plasticity through exocytosis/endocytosis coupling-associated exosomes (or “extracellular vesicles”), leading to the cancer-related systemic effects, and reducing the biogenesis, release, and/or function of exosomes could offer a new therapeutic approach for PDAC.

Aims & Methods: We aimed to test whether pharmacological inhibition of exosomes might suppress the progression of PDAC. We first predicted the protein-protein interactions in our proteomics datasets with the focus on botulinum toxin A (BTX-A) and/or ivermectin (IVM) targets. We obtained PDAC cells from a genetically engineered C57BL/6 mouse model with KrasG12D/Pdx1-Cre for in vitro and in vivo tests.

We implanted the cells in 521 mice (C57BL/6) orthotopically (in the pancreas), subcutaneously, through hemi-spleen injection or tail vein injection, and treated the mice with BTX-A, IVM, gemcitabine plus paclitaxel (Gem/Pac) or their combinations.

Of note, BTX-A was given before the cell transplantation. In addition, we used PDAC mouse and human organoids. Measurements included survival rate, tumor size, growth of organoids, proteomics, exosomes, immunohistochemistry, electron microscopy, and bioinformatics.

Results: In response to orthotopical injection of PDAC cells, all 18 mice died within 12 days after receiving 1.0×10^5 cells and all 13 mice died within 18 days after receiving 2.25×10^5 cells due to thrombosis. Treatments with BTX-A and/or IVM in vitro suppressed the plasma membrane plasticity of PDAC cells (e.g., neurite-like outgrowth and expression of plasticity protein GAP43) in response to nerve growth factor or conditioned media of PDAC cells.

BTX-A in vitro exerted no effect on PDAC cell proliferation, but inhibited the SNARE protein complex signaling pathway, whereas IVM eliminated the formation of membrane microvilli (volume density 0.5% vs 10% saline) and inhibited cell proliferation, clathrin-mediated endocytic signaling and particularly Rab27a. BTX-A+IVM treated PDAC cells showed impaired formation and release of exosomes and down-regulation of proteins involved in exocytosis/endocytosis coupling and biogenesis of exosomes.

The exosomes of PDAC cells contained 301 proteins involved in axonal guidance signaling, clathrin-mediated endocytosis signaling, neuroinflammation signaling pathway, epithelial adherents junction signaling, EIF2 signaling and integrin signaling, and toxicities in neuro-immune, kidney, liver, and heart.

In vivo, treatment with IVM showed down-regulation of serum exosome proteins. Treatments with BTX-A, IVM or combination had no effects on the tumor size and the cell proliferation rate (Ki67 and DCLK1), but enhanced the inhibitory effects of Gem/Pac on tumors implanted in the pancreas, liver, lung or under the skin. Importantly, BTX-A and/or IVM increased median survivals of PDAC mice, i.e., 26 days without treatment vs. 21 days with Gem/Pac, 40 days with BTX-A, 89.5 days with IVM, and 90.5 days with BTX-A+IVM+Gem/Pac, and of mice with PDAC liver or lung metastasis (>135 days). IVM inhibited the growths of PDAC mouse organoids and human organoids which were derived from a PDAC patient at T2N2MO stage III without neoadjuvant therapy.

Conclusion: Inhibition of exosomes with IVM and/or BTX-A increased the survival rate in PDAC mice (probably by retardation of thrombosis) and the growth of human PDAC organoids, suggesting a translational potential.

Disclosure: Nothing to disclose.

OP135

SPATIALLY RESOLVED DYNAMICS OF HETEROGENEOUS CANCER SUBCLUSTERS AND CANCER-ASSOCIATED NICHE IN HUMAN PANCREATIC CANCER

G. Leem¹, S. Bang¹

¹Yonsei University College of Medicine, Division of Gastroenterology, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: huntguy22@yuhs.ac

Introduction: Recent studies using single-cell transcriptomic analysis have reported several distinct clusters of neoplastic epithelial cells and cancer-associated fibroblasts in the pancreatic cancer tumor microenvironment.

However, their molecular characteristics and biological significance have not been clearly elucidated due to intra- and inter-tumoral heterogeneity.

Aims & Methods: We performed single cell RNA sequencing using enriched epithelial cells and fibroblasts from 17 pancreatic cancer tissues. Then, to resolve the spatial information of heterogeneous cancer subclusters and cancer-associated niches in human pancreatic cancer tissues, we performed RNA in situ hybridization and spatial transcriptome analysis using 10X Visium technique in paired tumor tissues.

Results: We identified five distinct functional subclusters of pancreatic cancer cells and six distinct cancer-associated fibroblast subclusters. We deeply profiled their characteristics, and we found that these subclusters successfully deconvoluted most of the features suggested in bulk transcriptome analysis of pancreatic cancer.

Among those subclusters, we identified a novel cancer cell subcluster, Ep_VGLL1, showing intermediate characteristics between the extremities of basal-like and classical dichotomy, despite its prognostic value. Molecular features of Ep_VGLL1 suggest its transitional properties between basal-like and classical subtypes.

In the spatial transcriptome analysis, we constructed an adjacency network graph reflecting the neighborhood enrichment relationships across diverse cell types and draw a putative cancer progression axis from Ep_FXYD2, ADM population, to Ep_TRIM54, Ep_VGLL1, and Ep_KRT6A, supporting our model of pancreatic cancer cell dynamics.

In addition, we also discovered that the spatial distributions of Fb_LRRC15, representing the myCAF population, were highly correlated with pancreatic cancer cell distributions, whereas Fb_SFRP1, representing the iCAF population, were located distal to the cancer-associated niche.

Conclusion: This integrative analysis not only provides a comprehensive landscape of pancreatic cancer and fibroblast population, but also suggests a novel insight to the dynamic states of pancreatic cancer cells and unveils potential therapeutic targets.

References:

- Collisson, E. A. et al. Subtypes of pancreatic ductal adenocarcinoma and their differing responses to therapy. *Nat. Med.* 17, 500-503, (2011).
- Moffitt, R. A. et al. Virtual microdissection identifies distinct tumor- and stroma-specific subtypes of pancreatic ductal adenocarcinoma. *Nat Genet* 47, 1168-1178, (2015).
- Collisson, E. A. et al. Molecular subtypes of pancreatic cancer. *Nat. Rev. Gastroenterol. Hepatol.* 16, 207-220, doi:10.1038/s41575-019-0109-y (2019).
- Chan-Seng-Yue, M. et al. Transcription phenotypes of pancreatic cancer are driven by genomic events during tumor evolution. *Nat Genet* 52, 231-240, (2020).
- Porter, R. L. et al. Epithelial to mesenchymal plasticity and differential response to therapies in pancreatic ductal adenocarcinoma. *Proc. Natl. Acad. Sci. U. S. A.*, doi:10.1073/pnas.1914915116 (2019).

Guo, J. A. et al. Refining the Molecular Framework for Pancreatic Cancer with Single-cell and Spatial Technologies. Clin Cancer Res 27, 3825-3833, doi:10.1158/1078-0432.CCR-20-4712 (2021).

Hannah L. W, et al. Spatially Resolved Single-Cell Assessment of Pancreatic Cancer Expression Subtypes Reveals Co-expressor Phenotypes and Extensive Intratumoral Heterogeneity. Cancer Res 83, 441-455 (2023).

Liu, X. et al. Conditional reprogramming and long-term expansion of normal and tumor cells from human biospecimens. Nat Protoc 12, 439-451, doi:10.1038/nprot.2016.174 (2017).

Disclosure: Nothing to disclose.

OP136

PRELIMINARY RESULTS OF THE PROPH-ITA STUDY: GENETIC BACKGROUND OF FAMILIAL PANCREATIC CANCER (FPC) PATIENTS ENROLLED IN THE ITALIAN REGISTRY OF FAMILIES AT RISK FOR PANCREATIC CANCER (IRFARPC)

L. Archibugi¹, F. Casciani², S. Carrara³, E. Secchettin², M. Falconi⁴, S. Paiella⁵, G. Capurso⁶

¹Hospital San Raffaele, Pancreato-biliary Endoscopy And Endosonography Division, Milan, Italy, ²University of Verona Hospital Trust, Verona, Italy, ³Istituto Clinico Humanitas, Gastrointestinal Endoscopy, Milano, Italy, ⁴Università Vita-Salute San Raffaele, San Raffaele, Italy, ⁵Pancreas Institute, University of Verona, General and Pancreatic Surgery Unit, Verona, Italy, ⁶San Raffaele Scientific Institute Irccs, Pancreas Translational & Clinical Research Center, Rome, Italy

Contact E-Mail Address: livia.archibugi@hotmail.it

Introduction: The Italian Registry of Families at Risk for Pancreatic Cancer (IRFARPC) is a surveillance program that enrolls individuals at increased risk (HRIs) as either mutation carriers (MC) of a pathogenic variant (PV) of a susceptibility gene or familial pancreatic cancer (FPC) individuals based on family history. It has been reported that FPC patients carry a lower risk of PC compared to MC, but their genetic background is often poorly evaluated.

Nonetheless FPC represent the larger part of subjects enrolled in surveillance protocols. In addition, PC predisposing genetic backgrounds can be shared with other malignant tumors that require a tailored surveillance program.

Aims & Methods: Our aim was to evaluate the prevalence of PV or variants of uncertain significance (VUS), in patients enrolled in IRFARPC. FPC patients enrolled in the IRFARPC registry at three forerunner centers (Verona, Milano, Rozzano) underwent buccal swabs in the context of the "PROPH-ITA" study funded by Italian Patients' Advocacy Groups ("Fondazione Nadia Valsecchi", "Associazione Oltre la Ricerca" and other individual initiatives), with germline evaluation of a panel of 41 genes. Genomic DNA was isolated from the biological samples for Whole Exon Sequencing. Considering scientific literature data and the main mutation databases, mutations defined as PV or VUS were reported in the genetic report, and subjects with a positive test were offered a genetic consultation.

Results: From December 2022 up to February 2024, a total of 270 FPC candidates participating to the IRFARPC were recruited and underwent buccal swab and genetic testing, of whom eighteen (6.6%) found carrying one or multiple PV: 6 CFTR, 5 ATM, 3 MUTYH, 1 CTSC, 1 TET2, 1 BRCA2, 1 PALB2. Ninety (33.3%) patients carried one or multiple VUS, mostly in the CFTR, APC, and ATM genes. All these one-hundred-eight patients (40%) accepted genetic counselling.

Conclusion: Genetic profiling of FPC patients in the context of the IRFARPC screening protocol retrieved a relatively small, yet not negligible, number of patients carrying a previously unknown PV and a large rate of

VUS. Further studies are needed to elucidate the relevance of VUS in this context and the association between mutational status and pancreatic and extrapancreatic findings during surveillance. In 2024, the PROPH-ITA study will be open to all IRFARPC centers.

Disclosure: Nothing to disclose.

OP137

INNOVATIVE PROCEDURE FOR GENOTYPIC ANTIBIOTIC SUSCEPTIBILITY TESTING IN GASTRIC ASPIRATES FOLLOWING THE INTRAPROCEDURAL DETECTION OF H. PYLORI BY THE COMBINED ENDOSCOPY/ENDOFASTER METHOD

R. Vasapolli^{1,2}, F. Ailloud^{3,4}, B. Spiessberger^{3,4}, P. Malfertheiner¹, S. Suerbaum^{3,4,2}, C. Schulz^{1,2}

¹University Hospital LMU Munich, Department of Medicine II, Munich, Germany, ²DZIF Deutsches Zentrum für Infektionsforschung, Partner Site Munich, Munich, Germany, ³Max von Pettenkofer Institute, Ludwig Maximilians University of Munich, Munich, Germany, ⁴National Reference Center for Helicobacter pylori, Munich, Germany

Contact E-Mail Address: riccardo.vasapolli@med.uni-muenchen.de

Introduction: Antibiotic resistance in *Helicobacter pylori* (*H. pylori*) poses an increasing challenge for infection management. Genotypic antibiotic susceptibility testing (GAST) is proposed as cost-effective approach for successful treatment.

Aims & Methods: Aim of our study was to evaluate GAST for detecting clarithromycin and levofloxacin resistance in gastric aspirates from *H. pylori*-positive patients compared to conventional phenotypic AST (PAST). Patients undergoing upper GI endoscopy (UGE) between February 2022 and April 2023 were prospectively recruited. Real-time diagnosis of *H. pylori* was pursued during UGE through gastric juice analysis by Endofaster¹. In case of intraprocedural *H. pylori* detection, two types of gastric aspirates were collected: a) undiluted gastric juice (GJ) and b) water rinse aspirate (WR). The WR was obtained after complete removal of the GJ and instillation of 30 mL sterile saline solution against the wall of the stomach corpus. Furthermore, gastric biopsies were collected for histology and culture-based PAST by E-test. Sanger sequencing of the 23S rRNA and *gyrA* genes from *H. pylori* was performed using gastric aspirates to detect polymorphisms associated with resistance to macrolides and fluoroquinolones, respectively. The test accuracy of GJ-GAST and WR-GAST was determined using PAST as the gold standard. The McNemar test was used to compare sensitivities and specificities between GJ- and WR-GAST. The level of agreement among different AST was assessed by Cohen's κ -value.

Results: Seventy-two consecutive patients (29/43 male/female; mean age, 47.0 $\pm$ 13.5 years) tested *H. pylori*-positive during the UGE were included in the study. According to PAST the resistance rates were 15.3% (11/72) for clarithromycin and 18.1% (13/72) for levofloxacin. The diagnostic measures of GJ-GAST and WR-GAST for resistance detection, as well as their agreement with PAST are shown in Table 1. Overall, GAST and PAST results showed substantial agreement (κ -value ranging from 0.67 to 0.77) and a very high level of concordance (>93%) for detecting clarithromycin and levofloxacin resistance using both GJ and WR.

There were no significant differences in diagnostic performances between GJ- and WR-GAST ($p > 0.05$), as confirmed by an almost perfect agreement with a κ -value of 0.93 for both clarithromycin and levofloxacin. Additionally, molecular analysis, involving the inspection of Sanger chromatograms, enabled an increase in the detection of heteroresistance cases by 33% for clarithromycin and up to 50% for levofloxacin, compared to PAST.

	GJ-GAST		WR-GAST	
	Clarithromycin	Levofloxacin	Clarithromycin	Levofloxacin
Sensitivity	63.6% (30.8% - 89.1%)	69.2% (38.6% - 90.9%)	54.6% (23.4% - 83.3%)	66.7% (34.9% - 90.1%)
Specificity	100 % (94.0% - 100%)	98.3% (90.8% - 100%)	100% (94.1% - 100%)	100% (93.7% - 100%)
Accuracy	94.4% (86.2%-98.4%)	93.0% (84.3% - 97.7%)	93.1% (84.5% - 97.7%)	94.2% (85.8% - 98.4%)
Positive predictive value	100% (59.0% - 100%)	90.0% (56.0% - 98.5%)	100% (54.1% - 100%)	100% (63.1% - 100%)
Negative predictive value	93.8% (87.3% - 97.0%)	93.4% (86.3% - 97.0%)	92.4% (86.5% - 95.9%)	93.4% (86.5% - 96.9%)
Pairwise concordance	67/71 (93.1%)	66/71 (93.0%)	67/72 (93.0%)	66/70 (94.3%)
κ -value	0.75 (0.51 - 0.98)	0.74 (0.53 - 0.95)	0.67 (0.41 - 0.93)	0.77 (0.55 - 0.98)

Table 1. Diagnostic performances of GJ-GAST and WR-GAST for detection of clarithromycin and levofloxacin resistances, as compared to PAST. 95% confidence intervals are indicated in brackets.

Conclusion: Genotypic AST from gastric aspirates, following intraprocedural diagnosis of *H. pylori*, provides highly accurate results for detecting clarithromycin and levofloxacin resistances, comparable to conventional phenotypic AST. This novel method of GAST, performed using water rinse aspirates collected during UGE, is a valid and practical tool for tailoring eradication regimens.

References: 1. Vasapolli R, Ailloud F, Suerbaum S, et al. Intraprocedural gastric juice analysis as compared to rapid urease test for real-time detection of *Helicobacter pylori*. World J Gastroenterol 2023;29:1638-1647.

Disclosure: Nothing to disclose.

OP138

WITHDRAWN

OP139

RNA-BINDING PROTEIN AUF1 ACTIVATES THE NLRP3 INFLAMMASOME BY UPREGULATING THE EXPRESSION OF NLRP3 TO PROMOTE THE DEVELOPMENT OF H. PYLORI-ASSOCIATED GASTRITIS

H. Zheng¹, S. Ding¹, W. Fu¹, J. Zhang¹, Y. Wang¹, J. Ning¹

¹Peking University Third Hospital, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: 2781829818@qq.com

Introduction: The NLRP3 inflammasome induced by *Helicobacter pylori* (*H. pylori*) infection serves as a crucial platform for the maturation and secretion of IL-1 β and IL-18, leading to pyroptosis, which thus exacerbates *H. pylori*-associated gastritis and accelerates its progression to gastric cancer. Inhibiting NLRP3 expression can attenuate the intensity of the inflammatory response and impede the progression of *H. pylori*-induced gastric mucosal lesions.

However, the post-transcriptional regulatory mechanisms governing NLRP3 in *H. pylori* infection remain unclear. Therefore, elucidating the molecular mechanisms underlying post-transcriptional regulation of NLRP3 could offer potential intervention strategies for *H. pylori*-related gastric mucosal diseases.

Aims & Methods: In the co-culture experiment of human gastric epithelial cells or mouse mononuclear macrophage and *H. pylori* in vitro, knock-down or overexpression of AUF1 was performed, and the effect of AUF1 on the activation of NLRP3 inflammasome was detected by Western blot assay and ELISA. Scanning or transmission electron microscopy, immunofluorescence (IF) assay, lactate dehydrogenase (LDH) release assays were used to detect the effect of AUF1 on pyroptosis.

Transcriptome analysis was used to explore the changes of inflammatory cytokine genes in gastric epithelial cells with *H. pylori* by AUF1 knockdown. RNA immunoprecipitation and RNA-pulldown assay were used to detect the interaction of AUF1 and NLRP3 mRNA. Immunohistochemical staining was used to detect the expression of AUF1, NLRP3, Caspase1 and GSDMD in gastric mucosa of *H. pylori*-infected patients. Exosomes from gastric juice of *H. pylori*-related gastric mucosal diseases were collected by ultracentrifugation and AUF1 expression was detected.

Results: The expression of AUF1 in gastric mucosa and gastric juice exosomes of *H. pylori*-infected patients with chronic superficial gastritis was significantly up-regulated, and gradually increased with the aggravation of inflammation. Transcriptome analysis of *H. pylori* infected gastric epithelial cells showed that inflammatory pathways were significantly inhibited and NLRP3 was the most significantly altered inflammatory gene after AUF1 knockdown.

After *H. pylori* infection, AUF1 knockdown can inhibit NLRP3 expression, NLRP3 inflammasome activation and the secretion of IL-1 β and IL18 both in gastric epithelial cells and macrophages.

On the contrary, overexpression of AUF1 promoted NLRP3 expression and inflammasome activation, while NLRP3 inhibitor MCC950 can counteract the activating effect of AUF1 overexpression on NLRP3 inflammasome.

Also, we confirmed that AUF1 promoted pyroptosis in *H. pylori*-infected gastric epithelial cells, and the treatment of MCC950 could relieve pyroptosis. Mechanically, we found that AUF1 can bind to the 3'UTR region of NLRP3 mRNA, thereby enhancing the stability of NLRP3 mRNA and upregulating the expression of NLRP3. In gastric mucosa tissues of *H. pylori*-infected patients, AUF1 expression was positively correlated with NLRP3, Caspase1 and GSDMD expression.

In addition, *H. pylori* CagA promotes the interaction between AUF1 and exportin CRM1, thus promoting the cytoplasmic redistribution of AUF1.

Conclusion: *H. pylori* infection promotes the cytoplasmic redistribution of AUF1 through CRM1 and AUF1 promotes NLRP3 inflammasomes activation by upregulating the expression of NLRP3.

Our findings identify AUF1 as a novel positive regulator of NLRP3 inflammasomes and suggest that dysregulation of AUF1 expression leads to an increased risk of *H. pylori*-gastritis.

References: 1. Ng GZ, Menheniott TR, Every AL, et al. The MUC1 mucin protects against *Helicobacter pylori* pathogenesis in mice by regulation of the NLRP3 inflammasome. *Gut*. 2016;65(7):1087-1099.

2. Li S, Liang X, Ma L, et al. MiR-22 sustains NLRP3 expression and attenuates *H. pylori*-induced gastric carcinogenesis. *Oncogene*. 2018;37(7):884-896.

3. Yu Q, Shi H, Ding Z, Wang Z, Yao H, Lin R. The E3 ubiquitin ligase TRIM31 attenuates NLRP3 inflammasome activation in *Helicobacter pylori*-associated gastritis by regulating ROS and autophagy. *Cell Commun Signal*. 2023;21(1):1

Disclosure: Nothing to disclose.

OP140

HELICOBACTER PYLORI-RELATED GENES ARE NOT DETECTABLE IN GASTRIC MUCOSA OF PATIENTS WITH HISTOLOGICALLY HP NEGATIVE AUTOIMMUNE ATROPHIC GASTRITIS COMPLICATED WITH GASTRIC CANCER

G. Cozza¹, L. Belloni¹, S. Cingolani¹, M. Vavallo¹, L. Dottori¹, F.P. Schiavone¹, B. Annibale¹, E. Lahner¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea University Hospital, Gastroenterology Unit, Rome, Italy

Contact E-Mail Address: giulio.cozza@uniroma1.it

Introduction: Chronic atrophic gastritis (CAG) is primarily caused by *Helicobacter pylori* (Hp) infection but also by autoimmune phenomena giving rise to autoimmune atrophic gastritis (AAG), whose hallmark is corpus-restricted atrophy sparing the antrum (unlike Hp infection causing extensive CAG). AAG triggered by Hp has been proposed, but diagnosis of Hp in this condition is difficult. Hp infection is one of the main risk factors for gastric cancer (GC), while the role of AAG in the onset of GC is still debated.

Assessing the association of GC with AAG is thus challenging, as it requires the exclusion of Hp infection. Hence, investigating the presence of Hp-related genes in the gastric mucosa of histologically Hp negative AAG patients complicated by GC could be useful for accurately assessing the role of Hp in GC associated with AAG.

Aims & Methods: The aim was to assess the presence of Hp-related genes in corpus mucosa biopsies using Real-time and Digital PCR in AAG patients with GC and negative Hp at histology, along with Hp-positive and -negative controls.

Single-centre, experimental molecular biology study derived from 713 pts with histological diagnosis of CAG (2009-2022). Pts without corpus-restricted CAG (n=118) and with histological positivity for Hp (n=57) were excluded, resulting a source population of 538 AAG pts with negative Hp at histology. Out of these, 10 pts (80%F, age 69.5 (range 50-83) yrs) were diagnosed with gastric neoplastic lesions (GNL), including gastric cancer (GC) and high-grade intraepithelial neoplasia (HG-IEN). Real-time and Digital PCR were used to assess the presence of Hp-related genes in corpus mucosa biopsies of the 10 GNL-AAG pts and 2 Hp-positive non-atrophic gastritis pts (positive controls: 1 F, 1 M, age 39, 68 yrs) and 2 subjects with a healthy stomach (negative controls: 1 F, 1 M, age 22, 34 yrs).

DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) tissue sections of corpus mucosa biopsies and Real-time and Digital PCR were performed using specific probes for UreA, UreC, and CagA Hp-related genes. 16sRNA and Beta2 microglobulin specific probes were used as amplification ctr of bacterial and human DNA. Real-Time PCR gives a semi-quantitative analysis, whereas Digital PCR measures the accurate copy numbers of Hp DNA.

Results: GNL were diagnosed in 3/10 pts at AAG diagnosis, while in 7 at follow-up (median 96, range 12-156 mos). GNL were frequently in the corpus (50%), less commonly at *incisura angularis* (30%) or antrum (20%), and consisted of 8 GC and 2 HG-IEN. None had family history of GC, all pts were parietal cell autoantibodies positive. ELISA Hp serology was negative in all 5/10 available sera. Hp-related genes were not detected in any of the GNL-AAG pts nor in negative controls, but UreA and UreC were found in both positive controls and CagA in one. 16sRNA gene was detected in GNL-AAG by Real-time(CT mean 26.0, SD 0.3) and Digital PCR (copies μ l mean 1397, SD 348) in similar amounts as in positive controls (mean CT 25.7, SD 0.9, mean copies/ μ l 4977.5, SD 2185.7), indicating the detectability of bacterial genes in the extracted DNA.

Conclusion: In FFPE corpus mucosa biopsies of pts with histologically Hp negative AAG and GC, specific Hp-related genes are detectable by nor Real-time neither Digital PCR. This result supports the idea that GC develop-

ment cannot be excluded *a priori* in primary, Hp negative AAG, suggesting that Hp-unrelated cancerogenetic mechanisms may be involved and regular surveillance should be considered in primary AAG.

References:

- Lenti MV et al. Autoimmune gastritis. Nat Rev Dis Primers. 2020.
- Lahner E et al. Chronic atrophic gastritis: Natural history, diagnosis and therapeutic management. A position paper. Dig Liver Dis. 2019.
- Rugge M et al; RE.GA.IN; RE GA IN. RE.GA.IN.: the Real-world Gastritis Initiative-updating the updates. Gut. 2024.
- Neumann WL et al. Autoimmune atrophic gastritis--pathogenesis, pathology and management. Nat Rev Gastroenterol Hepatol. 2013.

Disclosure: Nothing to disclose.

OP141

A NOVEL *TLR4* MUTATION DEREGULATES INFLAMMATION DURING *HELICOBACTER PYLORI* INFECTION AND RELATED GASTRIC CARCINOGENESIS

E. Otaegui-Campos¹, I. Simovic¹, K. Vinasco Pacheco¹, L.D.W. Luu², N. Kaakoush³, N. Castaño Rodríguez¹

¹School of Biotechnology and Biomolecular Sciences, UNSW, Sydney, Australia, ²School of Life Sciences, UTS, Sydney, Australia,

³School of Biomedical Sciences, UNSW, Sydney, Australia

Contact E-Mail Address: ezekiel.otaegui-campos@hotmail.com

Introduction: While *Helicobacter pylori* infection is largely recognised in gastric cancer (GC) aetiology, only 1-3% of infected individuals will develop this inflammatory disease. Inheritable mutations in Toll-like receptor 4 (TLR4) deregulate responsiveness to *H. pylori* and may influence clinical outcomes. To date, *TLR4* mutations are often understudied in ethnically diverse populations with a high-risk of GC, yielding inconclusive findings and a limited understanding of their true biological relevance.

This study delineates the effect of the novel *TLR4* rs11536889 (G>C) mutation in the host response during *H. pylori*-related gastric carcinogenesis.

Aims & Methods: The relationship between the *TLR4* rs11536889 mutation, *H. pylori* infection and GC aetiology was evaluated in a multiethnic (Australian Caucasian, Colombian Mestizo, Han Chinese and Iranian) case-control study encompassing 315 GC cases, 372 gastric precancerous lesion cases and 1043 controls.

Local host transcriptomics of gastric biopsies and systemic inflammation of sera were interrogated and correlated with carriage of rs11536889. Inflammation and bacterial clearance were further examined in *H. pylori*-challenged *in vitro* models of CRISPR/Cas9-edited mutant gastric epithelial (AGS) and macrophage (THP-1) cell lines.

Results: Carriage of rs11536889 confers reduced susceptibility to *H. pylori* infection, meanwhile, it independently increases the risk of GC in high-risk populations but not the low-risk population. Transcriptomics of gastric tissue revealed rs11536889 carriage in high-risk patients modulated tumour suppression (*CPA6*, *KDM5D*, *TCL1A*), mucosal inflammation (*DEFB1*, *CXCL10*, *FAS*, *NLRP6*) and metabolism (*GLUT4*). In parallel, a systemic pro-inflammatory signature was consistent in high-risk individuals harbouring rs11536889, but was inversed in low-risk individuals. Interestingly, while both rs11536889-carrying human gastric epithelial and macrophage cell lines demonstrating augmented IL-8 and TNF- α expression, *H. pylori* clearance was ameliorated in mutant epithelial cells but impeded in macrophages.

Conclusion: This study offers appreciable insight into the genetic underlining of the host immune responses to *H. pylori* and related GC. These findings hint at a possible race-specific trend with carriage of rs11536889, which could confer the opposite phenotype outcomes between high- and low-risk populations worldwide.

Uncovering the clinical relevance of rs11536889 advances our efforts to establish effective and non-invasive biomarkers for global-scale GC screening programs, and posits TLR4 signalling as a potential target for immunotherapies to benefit high-risk patients.

Disclosure: Nothing to disclose.

EMR or ESD for colon neoplasia

16:00-17:00 / Lehar 3

OP142

SAFETY AND EFFICACY OF ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL POLYPS WITH MARGIN, COMPLETE BASE AND VESSEL ABLATION: A PROSPECTIVE MULTI-CENTER STUDY

M. Taghiakbari¹, E. Medawar², R. Djinbachian¹, N. Shahidi³, J. Levenick⁴, J.D. Mosko⁵, E. Lam³, C. Teshima⁵, M. Moyer⁴, S. Bouchard¹, É. Deslandres¹, D. von Renteln¹

¹University of Montreal, Montreal, Canada, ²University of Ottawa, Ottawa, Canada, ³University of British Columbia, Vancouver, Canada, ⁴Penn State College of Medicine, Hershey, United States of America, ⁵University of Toronto, Toronto, Canada

Contact E-Mail Address: edgard.medawar@mail.mcgill.ca

Introduction: Endoscopic mucosal resection (EMR) is the mainstay of therapy for large colorectal polyps. A previous study has shown low complication and recurrence rates after EMR when performing margin and selective base ablation using hybrid argon plasma coagulation (h-APC). We were interested in evaluating the safety and efficacy of EMR with systematic complete margin, base and vessel ablation in a multicenter study.

Aims & Methods: Adults (18–89 years) undergoing EMR of large nonpedunculated colorectal polyps ≥ 20 mm were enrolled in a multicenter prospective study. After EMR completion and removal of all visible adenoma, patients received systematic h-APC ablation of the post-resection margin, the resection base, and of any visible vessels as the only prophylactic therapy for bleeding. Patients were contacted at 4 weeks to assess any adverse events. First surveillance colonoscopies were scheduled at 4–6 months.

The primary outcome was the rate of severe delayed bleeding within 4 weeks, defined as the need for hospitalization, transfusion, repeat endoscopy, embolization, or surgery.

Secondary outcomes were the rate of recurrence, defined as pathology confirmed adenoma or serrated recurrence at the EMR site at first surveillance, and other adverse events within 4 weeks, including abdominal pain, deep mural injury (using the Sydney Classification), perforation and post-polypectomy syndrome.

Continuous variables were compared using t-tests, and categorical variables were compared using chi-squared tests, with a $p < 0.05$ considered statistically significant.

Results: A total of 178 patients (mean age 67.3 y, 44.4% female) undergoing 190 EMRs were included. h-APC margin ablation was done in all cases, partial base ablation in 43/190 and complete base ablation in 127/190. 127 post-resection defects had visible base vessels, of which 122/127 underwent h-APC as prophylactic therapy to prevent delayed bleeding. The mean polyp size was 36.7 mm, with 77.1% being proximal to the splenic flexure, and 81.8% being adenomas.

The primary outcome, severe delayed bleeding, occurred in 1.7% ($n=3$). With regards to recurrence, 46.1% of patients ($n=83$) underwent a first surveillance colonoscopy at the time of writing, at a median of 4.0 months post-EMR, of which 1.2% (1/83) developed a local recurrence at the EMR resection site. Severe intraprocedural bleeding occurred in 0.6% ($n=1$). Post-procedural non-severe abdominal pain occurred in 3.4% ($n=6$), while no patients developed severe post-procedural abdominal pain. Perforation occurred in 0.6% ($n=1$). This was identified immediately after the procedure in a patient who received partial base ablation, and the defect was clipped. There was no deep mural injury seen during the procedure.

Post-polypectomy syndrome occurred in 1.6% of patients who underwent complete base ablation (2/122). Intraprocedural type 2 deep mural injury

occurred in 5.1% ($n=9$), with six out of nine being in the context of complete base ablation. Eight out of nine were clipped, and no patient with type 2 deep mural injury developed a perforation. There were no cases of deep mural injury type 3 to 5 identified intraprocedurally.

Conclusion: EMR with systematic h-APC ablation of the post-resection margin, base and visible vessels demonstrated to be safe and highly effective to treat large nonpedunculated colorectal polyps.

References: 1. Motchum L, Levenick JM, Djinbachian R, et al. EMR combined with hybrid argon plasma coagulation to prevent recurrence of large nonpedunculated colorectal polyps (with videos). *Gastrointest Endosc.* 2022;96(5):840-848.e2. doi:10.1016/j.gie.2022.06.018

Disclosure: Daniel von Renteln has received research funding from ERBE Elektromedizin GmbH, Ventage, Pendopharm, Fujifilm and Pentax, and has received consultant or speaker fees from Boston Scientific Inc., ERBE Elektromedizin GmbH, and Pendopharm. The remaining authors have no conflict of interest relevant to this abstract to declare.

OP143

ADVANCES IN COLORECTAL ENDOSCOPIC RESECTION HAVE ALTERED INCIDENCE AND RISK FACTORS FOR RECURRENCE: A COMPARATIVE STUDY OVER TWO TIME PERIODS

H. Ayubi¹, O. Olabintan¹, A. Egbal², M.-A. Noreillie², J. Bhoday², A. Adeyeye², M. Anand¹, B.H. Hayee², S. Gulati¹, S. Thrumurthy², A. Haji³, A. Emmanuel³

¹King's College Hospital, Endoscopy and Gastroenterology, London, United Kingdom, ²King's College Hospital, London, United Kingdom, ³King's College Hospital, Colorectal Surgery, London, United Kingdom

Contact E-Mail Address: homira.ayubi@gmail.com

Introduction: EMR remains the primary therapeutic option for LNCP in western practice, but new procedures and techniques are increasingly employed. Large published series previously defined expected rates of, and risk factors for, residual/recurrent adenoma after endoscopic resection (ER). However, these may no longer be relevant.

Aims & Methods: We aimed to identify independent risk factors for recurrent/residual adenoma in a contemporary cohort of LNCP treated by ER compared to a historical cohort. Patients with LNCP treated by ER at a tertiary referral centre between January 2011 and September 2023 who had completed 6 month surveillance (SC1) were included.

Patients were divided into contemporary (January 2018 – September 2023) and historical (January 2011 – December 2017) cohorts. Post-ER scars were examined using with magnification chromoendoscopy and NBI/BLI.

Clinicopathological features significantly associated with recurrent/residual adenoma on univariate analysis were subjected to multiple logistic regression to identify independent risk factors.

Results: 1517 ER were performed over the study period of which 946 met the inclusion criteria and had undergone SC1: 483 in the contemporary cohort and 463 in the historical cohort. In the contemporary cohort 313 (65%) were treated using ESD compared to 117 (25%) in the historical cohort ($p < 0.001$).

En bloc resection was more frequently achieved in the contemporary cohort compared to the historical cohort (70% versus 33%, $p < 0.001$). Recurrent/residual adenoma at SC1 was detected in 2.5% in the contemporary cohort compared to 8.9% in the historical cohort ($p < 0.001$).

For the historical cohort, multivariate analysis revealed that previous failed attempt at resection (OR 2.80, 95% CI 1.14–6.88, $p = 0.02$); piecemeal resection (OR 5.21, 95% CI 1.18–23.02, $p = 0.03$) and involvement of $> 75\%$ of the circumference of the lumen (OR 5.80, 95% CI 2.07–16.25, $p < 0.001$) were

independently associated with recurrent/residual adenoma: However, for the contemporary cohort, only difficult access to the lesion (OR 4.24, 95% CI 1.21-14.78) was independently associated with recurrent residual adenoma at SC1.

Conclusion: Significant changes have taken place in ER practice over the last decade. This study demonstrates this has led to a marked alteration in previously established expected outcomes and risk factors for recurrence.

Furthermore, the increasing use of adjunctive measures and techniques such as ESD throughout the colorectum may help drive down recurrence rates with the advantage of producing high quality histopathological specimens and accurate diagnosis, leading to a reduction in surveillance requirements. These data should help define performance standards for advanced resection units as well as guide informed consent and decision making for patients.

Disclosure: Nothing to disclose.

OP144

WITHDRAWN

OP145

RISK FACTORS FOR POSITIVE VERTICAL MARGINS IN ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL PT1 CANCER

Y. Ebisawa¹, H. Chiba¹, M. Koga¹, A. Hayashi¹, M. Kobayashi¹, J. Arimoto¹, H. Kuwabara¹, M. Nakaoka¹

¹Omori Red Cross Hospital, Gastroenterology, Ota-ku, Japan

Contact E-Mail Address: you.ebisawa603@gmail.com

Introduction: For colorectal T1 cancers, factors such as invasion depth and vascular involvement vary the risk of recurrence and metastasis, often making diagnosis challenging based solely on endoscopic findings. The utility of ESD as a diagnostic treatment is being discussed to avoid excessive surgical procedures. In cases of positive vertical margins of T1 cancer, additional surgery is recommended regardless of risk factors. Accurate diagnosis and avoidance of overtreatment require negative vertical margins.

We retrospectively examined ESD for colorectal T1 cancers at our hospital and identify risk factors associated with positive vertical margins and safety of ESD for T1 cancer.

Aims & Methods: From April 2012 to December 2023, among the 1560 colorectal lesions treated with ESD at our hospital, those diagnosed with pT1 cancer were selected. These cases were divided into two groups: VM positive and VM negative, and their endoscopic findings and treatment outcomes were compared.

Results: Of the 708 early-stage colorectal cancer cases treated with ESD, 112 cases (15.8%) were diagnosed with pT1. Dividing these by VM status, there were 11 cases in the VM positive group and 101 cases in the VM negative group. The median age was 76 years (range 40-87) in the VM positive group and 73 years (range 44-92) in the VM negative group, with a male/female ratio of 8/3 in the VM positive group and 56/45 in the VM negative group.

The tumor locations were colon/rectum in 8/3 cases in the VM positive group and 66/35 cases in the VM negative group. The median tumor size was 22 mm (range 17-60 mm) in the VM positive group and 35 mm (range 15-141 mm) in the VM negative group. The macroscopic types were elevated/flat in 5/6 cases in the VM positive group and 46/55 cases in the VM negative group, and the invasion depths were pT1a/pT1b in 2/9 cases in the VM positive group and 45/59 cases in the VM negative group. The median operation time was 49 minutes (range 10-333) in the VM positive group

and 42 minutes (range 8-250) in the VM negative group.

An analysis of the endoscopic features associated with T1b or deeper, such as depression, expansion, and fold convergence, showed the following: indentation present/absent was 7/4 in the VM positive group and 19/82 in the VM negative group; fullness present/absent was 0/11 in the VM positive group and 17/84 in the VM negative group; fold convergence was not observed in any case.

In the univariate analysis of risk factor for VM positive, significant differences were observed for tumor size greater than 3 cm, vascular invasion, depression, and severe fibrosis.

However, in the multivariate analysis, severe fibrosis (OR 5.792, 95% CI: 1.364-24.589, p=0.017) and depression (OR 9.95, 95% CI: 2.335-42.403, p=0.02) were independent risk factors for VM positive. All cases in the VM positive group underwent additional surgical resection, with one case of local residual disease and two cases with N1 or higher metastases observed.

Conclusion: ESD for T1 cancer was performed safely. Colorectal cancer with depression or severe fibrosis is risk factors for VM positive in ESD. When depression is observed in preoperative findings, it is necessary to select an experienced physician and the treatment strategy. In cases of intraoperative findings of severe fibrosis, identification of the dissection line can be difficult, potentially leading to incomplete resection or an increased risk of complications. It is desirable to develop treatment strategies (traction/tunneling method, PAEM, LECS, etc.) that allow for safe en bloc resection of these difficult cases.

Disclosure: Nothing to disclose.

OP146

WITHDRAWN

Optimising biological treatment in IBD

08:30-09:30 / A1

OP147

VEDOLIZUMAB TREATMENT IS MORE EFFECTIVE AND SAFER IN EARLY VERSUS LATE CROHN'S DISEASE: FINAL RESULTS OF THE LOVE-CD TRIAL

G.R. D'Haens¹, M. Lowenberg¹, F. Baert², P. Bossuyt³, F. Hoentjen⁴, E. Clasquin¹, L. Oldenburg¹, M. Hulshoff¹, T. Molnár⁵, S. Vermeire⁶

¹Amsterdam University Medical Centers, Gastroenterology, Amsterdam, Netherlands, ²Az Delta, Dept of Gastroenterology, Roeselare, Belgium, ³Imelda General Hospital, Dr, Bonheiden, Belgium, ⁴Radboud University Medical Center, Dept of Gastroenterology and Hepatology, Nijmegen, Netherlands, ⁵University Of Szeged, Department of Internal Medicine, Szeged, Hungary, ⁶University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Vedolizumab (VDZ) is efficacious to induce and maintain clinical remission in Crohn's disease (CD). However, prospective data about its efficacy including endoscopy in early CD are lacking.

Aims & Methods: We conducted a prospective multi-centre international (Belgium, the Netherlands and Hungary) open label trial comparing the efficacy and safety of VDZ therapy in patients with early or late moderate-severe active CD (Crohn's Disease Activity Index [CDAI] 220-450 and presence of ulcers at endoscopy).

Early CD was defined as diagnosis <2 years and treatment naïve or only treated with corticosteroids and/or immunomodulators; late CD was defined as diagnosis >2 years and previously treated with corticosteroids, immunomodulators and anti-tumor necrosis factor agents.

Patients received intravenous VDZ (300 mg) at weeks 0-2-6 and q8 weeks thereafter for a total of 52 weeks, with an extra infusion at w10 in the absence of a CDAI drop <70. Ileocolonoscopy was performed at baseline, w26 and w52 and all procedures were centrally read. The sample size was calculated for 1/3 early and 2/3 late CD.

An extremely strict primary composite endpoint was used: proportion of patients with clinical and endoscopic remission (CDAI≤150 and Simple Endoscopic Score for CD [SES-CD]≤4) at both w26 and w52.

Key secondary endpoints included the proportion of patients with absence of ulcers, proportion of patients with endoscopic response (SES-CD reduction ≥50%) at w26 and w52 and safety.

Results: We recruited 86 early and 174 late CD patients, of whom 52 early and 104 late CD patients completed w52 (insufficient clinical response and adverse events were the main reasons for early withdrawal). Baseline characteristics including disease activity parameters were similar across both groups (median total SES-CD 9 [6-17] and 12 [7-17], median CDAI 254.7 [235.7-287.2] and 259 [235.2-314.5] for early and late CD, respectively), apart from disease duration and age (median disease duration 0 [0-1] and 11 [5.5-15.5], median age 29.5 [23.8-45.3] and 36 [28-48] for early and late CD, respectively). The primary endpoint was reached in 31.4% vs. 8.6% (p=0.001; ITT) and 45.0% vs. 16.0% (p<0.001; per protocol [PP]) of patients with early vs. late CD (Table 1). All key secondary endpoints were also met in favour of patients with early CD (Table 1). Serious adverse events (SAEs) occurred in 4.7% of patients with early vs. 27% of pa-

tients with late CD (p<0.0001) and included infection (1.2 vs 7.5%) bowel obstruction (0 vs 2.3%), exacerbation of CD (2.3 vs 4%), abdominal pain (0 vs 1.7%) and malignancy (0 vs 1.7%).

		Early vs late CD (ITT)	Early vs late CD (PP)	P values (ITT/PP)
Primary composite endpoint				
Clinical and endoscopic remission ^A	w26 and w52	31.4% vs 8.6%	45.0 vs 16.0%	0.001*; <0.001*
Separate primary outcome measures				
Clinical remission	w26 w52	62.8% vs 37.4% 59.3% vs 43.7%	77.1% vs 57.0% 67.1% vs 54.7%	<0.001*; 0.006* 0.018*; 0.076
Endoscopic remission	w26 w52	55.8% vs 27.6% 51.2% vs 27.0%	67.6% vs 39.7% 62.0% vs 37.3%	<0.001*; <0.001* <0.001*; <0.001*
Key secondary endpoints				
Absence of ulcers	w26 w52	52.3% vs 24.1% 47.7% vs 23.0%	63.4% vs 34.7% 57.7% vs 31.7%	<0.001*; <0.001* <0.001*; <0.001*
Endoscopic response	w26 w52	64.0% vs 34.5% 57.0% vs 35.6%	82.1% vs 49.6% 71.0% vs 49.2%	<0.001*; <0.001* 0.001*; 0.003*

Table 1. Primary composite endpoint and key secondary endpoints (ITT and PP analysis)

^ADefined as CDAI≤150 and SES-CD <4; ~Defined as SES-CD reduction by ≥50%.

Conclusion: VDZ treatment is more effective and safer in early than in late CD (IIS Funded by Takeda Nederland B.V. [IISR-2014-100757]; LOVE-CD EudraCT number 2014-005376-29).

Disclosure: GD: served as advisor and/or speaker for Abbvie, Alimentiv, Astrazeneca, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Glaxo Smith Kline, Immunic, Index Pharmaceuticals, Johnson and Johnson, Polpharm, Prometheus biosciences, Prometheus laboratories, Procise diagnostics, Protagonist, Sandoz, Setpoint, Spyre, Takeda, Tillotts and Ventyx.

ML: consultancy/ lecture fees from Abbvie, Bristol Myers Squibb, Eli Lilly, Galapagos, Janssen-Cilag, Johnson & Johnson, Medtronic, Pfizer, Takeda, Tillotts. Central reader for Alimentiv. Grant received from Galapagos and NFU.

FB: reports grants/research supports from AbbVie, Amgen, Takeda, Janssen, honoraria or consultation fees from AbbVie, Amgen, Arena, MSD, Celgene, Kabi-Fresenius, Takeda, Ferring, Pfizer, Norgine, Janssen and participation in a company sponsored speaker's bureau for AbbVie, MSD, Takeda, Ferring, Pfizer, Janssen.

PB: has received research grants from AbbVie, Amgen, Celltrion, Mylan, Pfizer, and Takeda; lecture fees from AbbVie, Celltrion, Janssen, Lilly, and Takeda; and consulting fees from AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Celltrion, Dr Falk Pharma, Galapagos, Janssen, Lilly, Pentax, PSI-CRO, Roche, Takeda, and Tetrameros.

FH: has served on advisory boards or as speaker for Abbvie, Janssen, MSD, Takeda, Pfizer, Celltrion, Teva, Sandoz, Amgen and Pendopharm, and has received independent research funding from Janssen, Abbvie, Pfizer and Takeda.

EC: has no conflicts of interest.

LO: has no conflicts of interest.

MH: has no conflicts of interest.

TM: has received speaker's honoraria from MSD, AbbVie, Egis, Goodwill Pharma, Takeda, Pfizer, Janssen, Sandoz, MundiPharma, Phytotec, Roche, Fresenius and Teva.

SV: financial support for research from: AbbVie, J&J, Pfizer, Takeda and

Galapagos and receives speakers' and/or consultancy fees from: AbbVie, Abivax, AbolersPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, Astrazeneca, BioraTherapeutics, BMS, Boehringer Ingelheim, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, Mestag Therapeutics, Microbiotica, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Surrozen, Takeda, Theravance, Tillots Pharma AG, VectivBio, Ventyx, Zealand Pharma.

OP148

POTENTIAL FOR THERAPY MODIFICATION IN IBD PATIENTS WITH SUBOPTIMAL DISEASE CONTROL TREATED WITH BIOLOGICS: AN IBD-PODCAST STUDY SUBANALYSIS

F. D'Amico¹, F. Gomollón², G. Bamias³, L. Gemignani⁴, T. Heatta-Speicher⁴, C. Leitner⁴, R. Prata⁴, V. Tornatore⁴, A. Dignass⁵

¹IRCCS Ospedale San Raffaele and Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ²Hospital Clínico Universitario Lozano Blesa, IIS Aragón CIBEREHD, Servicio de Aparato Digestivo, Zaragoza, Spain, ³National and Kapodistrian University of Athens, GI-Unit, 3rd Academic Dpt. of Internal Medicine, Athens, Greece, ⁴AbbVie Inc., North Chicago, United States of America, ⁵Agaplesion Markus Krankenhaus, Medizinische Klinik I, Frankfurt/ Main, Germany

Contact E-Mail Address: damico.ferdinando@hsr.it

Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are chronic and progressive inflammatory bowel diseases (IBD), frequently associated with bowel damage and extraintestinal manifestations, and present a significant burden for patients.

Aims & Methods: The IBD-PODCAST was a descriptive non-interventional, cross-sectional study, which aimed to estimate the proportion of patients with CD and UC with Suboptimal Disease Control (SDC) in a real-world setting, across 103 sites in 10 countries. Criteria for SDC were largely based on STRIDE-II¹ and modified by an expert panel. The original cohort consisted of 2185 IBD patients. We previously reported that treatment modification opportunities were possible in 49% of CD and 61% of UC patients on advanced therapy².

The aim of this analysis was to evaluate treatment patterns and potential treatment modifications in patients on standard or escalated maintenance therapy with biologics according to summary of product characteristics (SmPC), at index date. Patients who were receiving induction phase regimen or concomitant multiple advanced therapies or were treated with lower dosages according to the label were excluded from this analysis. Patients whose therapy was escalated beyond SmPC indications (i.e., with shorter intervals of administration) were classified as "further escalated".

Results: A total of 796 CD and 549 UC patients treated with biologics (infliximab, adalimumab, ustekinumab and vedolizumab) were analyzed. Results are summarized in Table 1. Overall, 52% CD and 47% UC patients were in SDC. Among patients treated with adalimumab standard biweekly dose, 50% CD and 37% UC patients had the potential to modify therapy, while 70% CD and 50% UC patients were still in SDC despite dose escalation; concerning patients further escalated with adalimumab, 60% CD and 75% UC were in SDC.

Nearly half of the infliximab-treated-patients were still in SDC. In ustekinumab-treated group, 58% of CD patients treated every 12 weeks had SDC and were eligible for treatment modifications, while SDC was observed in 57% CD and 49% UC patients treated every 8 weeks and in 56% of CD and 82% of UC patients furtherly escalated.

Among vedolizumab-treated patients, 42% CD and 39% UC patients with intravenous (IV) maintenance every 8 weeks were in SDC and candidates for treatment modification; SDC was observed also in 65% CD and 35% UC patients treated every 4 weeks with IV Vedolizumab.

		Adalimumab		Infliximab**		Ustekinumab			Vedolizumab					
Treatment group and dosage at index date	80mg 40mg SC SC EOW	SC EOW or 40mg SC EOW	Further SC escalation*	5-10 mg/kg IV q8W**	Further IV escalation*	120mg SC q2W	90mg SC q12W	90mg SC q8W	Further SC escalation*	300mg IV q8W	300mg IV q6W	300mg IV q4W	108mg SC EOW	Further SC escalation*
Crohn's Disease (n= 796)	Sub-optimal Disease Control (n=412, 52%)	66 (50%)	37 (70%)	6 (60%)	106 (46%)	33 (54%)	7 (54%)	11 (58%)	67 (57%)	18 (56%)	35 (42%)	1 (17%)	22 (65%)	4 (57%)
	Optimal Disease Control (n=384, 48%)	65 (50%)	16 (30%)	4 (40%)	124 (54%)	28 (46%)	6 (46%)	8 (42%)	51 (43%)	14 (44%)	48 (58%)	5 (83%)	12 (35%)	3 (43%)
Ulcerative Colitis (n= 549)	Sub-optimal Disease Control (n=257, 47%)	18 (37%)	5 (50%)	3 (75%)	99 (55%)	14 (52%)	6 (46%)	3 (60%)	17 (49%)	9 (82%)	60 (39%)	3 (33%)	13 (35%)	6 (35%)
	Optimal Disease Control (n=292, 53%)	31 (63%)	5 (50%)	1 (25%)	80 (45%)	13 (48%)	7 (54%)	2 (40%)	18 (51%)	2 (18%)	92 (61%)	6 (67%)	24 (65%)	11 (65%)

*Further escalation = Patients whose therapy was escalated beyond SmPC indications (i.e., with shorter intervals of administration); ** The maintenance dose of IV IFX 5mg/kg q8W and IFX 10mg/kg q8W were not collected separately in the study and put together in this analysis;

TNF, Tumor Necrosis Factor; ADA, Adalimumab; IFX, Infliximab; qnW, very n Weeks; EOW, Every other Week, IV, Intravenous administration; SC, Subcutaneous administration

Table 1: treatment patterns in patients affected by UC and CD (total n = 1345).

Conclusion: This descriptive analysis showed suboptimally-controlled disease in nearly half of 1345 IBD patients treated with biologics. Moreover, almost half of patients whose therapy had already been escalated may still require treatment modification. These results further enhance the need for a targeted management strategy and additional therapeutic alternatives in IBD.

References:

- Turner D, et al.; International Organization for the Study of IBD. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology*. 2021 Apr;160(5):1570-1583
- D'Amico F, et al. Proportion of IBD patients with suboptimal control in daily clinical practice – Real-world evidence from the IBD-Podcast study. *United European Gastroenterol J*. 2024 (article in press).

Disclosure: This study was funded by AbbVie. No honoraria or payments were made for authorship. Fortrea, funded by AbbVie, oversaw data management, biostatistics, clinical study report, and medical writing. AbbVie reviewed and approved the publication. All authors had access to all relevant data and participated in data interpretation, writing, review, and approval of this abstract.

Ferdinando D'Amico served as a speaker for Sandoz, Takeda, Janssen, Omega Pharma, and Galapagos and served as an advisory board member for Abbvie, Ferring, Galapagos, Janssen, and Nestlé.

Fernando Gomollón has received honoraria as speaker from Janssen, AbbVie, Takeda, and MSD; and participated in advisory panels for Faes-Farma and AbbVie

Giorgos Bamias has received honoraria as an Advisor/Lecturer and/or research grants and/or clinical trial participant from Janssen, Pfizer, Takeda, Abbvie, MSD, Mylan, Genesis Pharma, Adaclyte Therapeutics, Amgen, Ferring, Cooper, BMS, and Aenorasis.

Tobias Heatta-Speicher, Valentina Tornatore, Ricardo Prata and Lorenzo Gemignani are employees of AbbVie and may own stock/options.

Axel Dignass reports received fees for participation in clinical trials, review activities such as data monitoring boards, statistical analysis and end point committees from Abivax, AbbVie, Bristol Myers Squibb, Dr Falk Foundation, Galapagos, Gilead, Janssen, and Pfizer; consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada, Takeda, Tillotts, and Vifor Pharma; payment for lectures including service on speakers bureaus from AbbVie, Biogen, CED Service GmbH, Celltrion, Falk Foundation, Ferring, Galapagos, Gilead, High5MD, Janssen, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Takeda, Tillotts, and Vifor Pharma; payment for manuscript preparation from Abbvie, Falk Foundation, Janssen, Takeda, Thieme, and UniMed Verlag

OP149

TWO YEAR RESULTS OF SUBCUTANEOUS INFLIXIMAB (CT-P13 SC) DOSE ESCALATION THERAPY AS AN OPTION FOR MANAGING LOSS OF RESPONSE IN INFLAMMATORY BOWEL DISEASE – FROM LIBERTY-UC AND LIBERTY-CD STUDY

S. Schreiber¹, J.-F. Colombel², S. Hanauer³, W. Sandborn⁴, B.E. Sands⁵, S. Danese⁶, S. Lee⁷, S. Kim⁷, Y. Bae⁷, S. Lee⁷, S. Lee⁷, J. Lee⁷, J. Kim⁷, G. Park⁷, J. Lee⁷, J. Lee⁷
¹University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ²Icahn School of Medicine at Mount Sinai, Gastroenterology, New York, United States of America, ³Northwestern University/ Feinberg School of Medicine, Gastroenterology and Hepatology, Chicago, United States of America, ⁴University of California San Diego, Gastroenterology, San Diego, United States of America, ⁵Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ⁶Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastroenterology, Milan, Italy, ⁷Celltrion, Inc, Incheon, South Korea

Contact E-Mail Address: s.schreiber@mucosa.de
Introduction: Dose escalation (DE) of intravenous infliximab is an option for inflammatory bowel disease (IBD) patients who lose response after induction therapy^{1,2}. DE of subcutaneous (SC) infliximab from 120 mg to 240 mg every 2 weeks (Q2W) showed restoring efficacy in the 54-week LIBERTY-UC and LIBERTY-CD studies, and safety profiles were generally comparable between patients with or without DE³. Both two studies included an extension phase through Week (W) 102, and we present post-hoc long-term efficacy and safety results of DE in patients who treated in extension phase in two studies.
Aims & Methods: Patients with moderately to severely active UC and CD were treated with 3 doses of infliximab IV 5mg/kg as induction therapy (Weeks 0, 2 and 6). Clinical responders at W10 were randomized (2:1) to receive either CT-P13 SC 120 mg or placebo Q2W as maintenance therapy up to W54. Patients who, in the opinion of the investigator, would benefit from continued treatment entered open-label extension study from W56 to W102 and received CT-P13 SC 120 mg regardless of previously assigned arm. From W22, the patients who met loss of response criteria were permitted to escalate the dose to CT-P13 SC 240 mg Q2W through W102 for both arms. The results from CT-P13 SC arm are analyzed.
Results: A total of 237 and 180 patients who were randomly assigned to CT-P13 SC 120 mg arm and treated in extension phase in UC and CD study, each. Among them, DE from CT-P13 SC 120 mg to CT-P13 SC 240 mg prior to W102 was more common in UC than CD (30.0% [71/237] vs 20.6% [37/180]). Patients showed improvement in terms of clinical remission at W102 (both CD and UC) or endoscopic response at W102 (CD) after DE.

Also, patients showed improvement in other efficacy endpoints after DE (Table 1). Compared to the first DE visit, patients who escalated the dose had a statistically significant reduction of more than half in mean modified Mayo score in UC (5.9 vs 2.1, P<0.0001) and mean CDAI score in CD (270.58 vs 76.31, P<0.0001) at W102.
The incidence rate of treatment-emergent adverse events (TEAEs) in the maintenance and extension phase of both studies was comparable between patients with and without DE (In UC, 84.7% [61/72] vs 78.1% [132/169], In CD, 86.8% [33/38] vs 79.7% [118/148]). Among these, TEAEs of infection were as follows; In UC, 40.3% (29/72) vs 43.2% (73/169), In CD, 55.3% (21/38) vs 42.6% (63/148).
The incidence rate of treatment-emergent serious adverse events in the maintenance and extension phase of both studies was also comparable between patients with and without DE (In UC, 12.5% [9/72] vs 10.1% [17/169], In CD, 13.2% [5/38] vs 10.8% [16/148]).

	CT-P13 SC in LIBERTY-CD		CT-P13 SC in LIBERTY-UC	
	Proportion of patients achieving efficacy outcomes at W102 regardless of dose escalation, n/N* (%)	Proportion of patients with dose escalation achieving efficacy outcomes at W102, n/N** (%)	Proportion of patients achieving efficacy outcomes at W102 regardless of dose escalation, n/N (%)	Proportion of patients with dose escalation achieving efficacy outcomes at W102, n/N' (%)
Clinical remission ¹	142/180 (78.9%)	26/37 (70.3%)	Clinical remission ⁷	132/237 (55.7%) 25/71 (35.2%)
Endoscopic response ²	102/180 (56.7%)	15/37 (40.5%)	Endoscopic-histologic mucosal improvement ⁸	119/237 (50.2%) 21/71 (29.6%)
Clinical response ³	148/180 (82.2%)	25/37 (67.6%)	Clinical response ⁹	167/237 (70.5%) 43/71 (60.6%)
Corticosteroid-free remission ⁴	44/74 (59.5%)	13/19 (68.4%)	Corticosteroid-free remission ¹⁰	49/96 (51.0%) 14/41 (34.1%)
Clinical remission (alternative definition) ⁵	131/180 (72.8%)	24/37 (64.9%)	-	- -
Endoscopic remission ⁶	71/180 (39.4%)	8/37 (21.6%)	-	- -

n = Number of patients achieving efficacy endpoints at Week 102 regardless of dose escalation; N* = Number of patients who were randomly assigned to CT-P13 SC 120 mg arm and treated in extension phase and have a SES-CD score of at least 6 (or at least 4 if isolated ileal disease) at Screening; n' = Number of patients achieving efficacy endpoints at Week 102 among dose-escalated patients; N** = Number of patients with dose escalation to CT-P13 SC 240 mg prior to Week 102 in CT-P13 SC 120 mg arm and treated in extension phase and have a SES-CD score of at least 6 (or at least 4 if isolated ileal disease) at Screening; N = Number of patients who were randomly assigned to CT-P13 SC 120 mg arm and treated in extension phase; N' = Number of patients with dose escalation to CT-P13 SC 240 mg prior to Week 102 in CT-P13 SC 120 mg arm and treated in extension phase.

- Clinical remission, defined as an absolute Crohn's disease activity index (CDAI) score of <150 points
- Endoscopic response at Week 102, defined as > 50% decrease in Simplified endoscopic activity score for Crohn's disease (SES-CD) score from the baseline value
- Clinical response, defined as a decrease in CDAI score of 100 points or more from the baseline value
- Corticosteroid-free remission, defined as being in clinical remission (by an absolute CDAI score of <150) in addition to not receiving any corticosteroids for at least 8 weeks prior to Week 102, among the patients who used oral corticosteroids at baseline
- Clinical remission, defined as an average worst daily abdominal pain (AP) score of ≤1 (using 4-point scale) and an average daily loose/watery stool frequency (SF) score of ≤3 (of Type 6 or Type 7 on BSFS) with no worsening in either average score compared with the baseline value.
- Endoscopic remission, defined as an absolute SES-CD score of ≤4 with no sub-score of >1
- Clinical remission, defined as modified Mayo score with stool frequency subscore of 0 or 1 point, rectal bleeding subscore 0 point, and endoscopic subscore 0 or 1 point
- Endoscopic-histologic mucosal improvement, defined as absolute endoscopic subscore of 0 or 1 point from modified Mayo score and an absolute Robarts Histopathology Index (RHI) score of 3 points or less with an accompanying lamina propria neutrophils and neutrophils in epithelium subscore of 0 point
- Clinical response, defined as decrease in modified Mayo score from baseline of at least 2 points and at least 30%, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point
- Corticosteroid-free remission, defined as being in clinical remission (by modified Mayo score) in addition to not requiring any treatment with corticosteroid for at least 8 weeks at Week 102, among the patients who used oral corticosteroids at baseline

Table 1. Summary of efficacy outcome in CT-P13 SC treated patients at Week 102.

Conclusion: DE of CT-P13 SC from 120 mg to 240 mg Q2W following IV induction in patients who initially respond but subsequently lose response, shows clinical efficacy over an extended observation period of 102 weeks.

Safety profiles were generally comparable between patients with or without DE, and no new safety concerns were found after DE as well in long term treatment.

References:

1 Taxonera C et al. Infliximab dose escalation as an effective strategy for managing secondary loss of response in ulcerative colitis. *Digestive Diseases and Sciences* 2015; 60 (10): 3075-3084

2 Cesarini M et al. Dose optimization is effective in ulcerative colitis patients losing response to infliximab: A collaborative multicentre retrospective study. *Dig Liver Dis*.2014; 46(2): 135-139

3 S. Danese et al. MP362 Subcutaneous infliximab (CT-P13 SC) dose escalation as an option for managing the loss of response in inflammatory bowel disease: post hoc analysis of LIBERTY-UC study and LIBERTY-CD study. *Gastroenterology*. Volume 166, Issue 3, Supplement, 2024, Page S13

Disclosure: • S. Schreiber: Consultancy and personal fees from AbbVie, Arena, BMS, Biogen, Celltrion, Celgene, Falk, Ferring, Fresenius, Gilead, HIKMA, IMAB, Janssen, MSD, Morphic, Pfizer, Protagonist, Provention Bio, Sandoz, Takeda, and Theravance.

• J.F. Colombel: Receiving payment for lectures from AbbVie, Amgen, Allergan, Inc. Ferring Pharmaceuticals, Shire, and Takeda; Receiving consulting fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, BMS, Celgene Corporation, Eli Lilly, Ferring Pharmaceuticals, Galmed Research, Genentech, Glaxo Smith Kline, Janssen Pharmaceuticals, Kaleido Biosciences, Imedex, Immunicon, Iterative Scopes, Merck, Microbia, Novartis, PBM Capital, Pfizer, Protagonist Therapeutics, Sanofi, Takeda, TiGenix, Vifor; Hold stock options in Intestinal Biotech Development.

• S.B. Hanauer: Consultancy from AbbVie, Allergan, Amgen, Arena, Astra Zeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cosmos, Catalys Pacific, Covance, Genentech, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Progenity, Prometheus, Receptos, Salix, Samsung Bioepis, Seres Therapeutics, Sorriso, Takeda, TLL, UCB, Vhsquared; Clinical Research for AbbVie, Allergan, Amgen, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Prometheus, Receptos, Takeda, UCB; Speaker for AbbVie, Bristol Myers Squibb, Janssen, Pfizer, Takeda; Independent Data Monitoring Conference for Arena, Boehringer Ingelheim, Bristol Myers Squibb, Gossamer, Prometheus, Protagonist.

• W. Sandborn: Consulting fees from Alimentiv, Shoreline Biosciences; Stock or stock options from Prometheus Biosciences, Prometheus Laboratories, Ventyx Biosciences, Mirador Therapeutics; Employee at Ventyx Biosciences, Mirador Therapeutics; Board of Directors at Prometheus Laboratories.

• B.E. Sands: Consultant or received speaker's fees from AbbVie, Abivax, Adiso Therapeutics, AgomAb, Alimentiv, Amgen, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytokine Pharma, Eli Lilly and Company, Entera, Evomune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunicon, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morphic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio.

• S. Danese: Consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma,

Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, Vifor. Reports lecture fees from Abbvie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, Takeda. • S.J. Lee, S.H. Kim, Y.J. Bae, S.H. Lee, S.G. Lee, J.H. Lee, J.M. Kim, G.H. Park, J.M. Lee, J.H. Lee are Employee of Celltrion, Inc.

OP150

THE PODIUM STUDY: A THREE-ARM COMPARISON OF TARGET THERAPIES AFTER ANTI-TNFA IN ULCERATIVE COLITIS – AN INTERIM ANALYSIS

G. Privitera¹, C. Bezzio², E.V. Savarino³, D. Pugliese⁴, D. Noviello⁵, I. Rodríguez-Lago⁶, M. Barreiro de Acosta⁷, S. Onali⁸, M.C. Fantini⁸, K. Karmiris⁹, H. Yanai¹⁰, A. Gutiérrez-Casbas¹¹, L. Pastorelli¹², M. Chaparro¹³, Y. Zabana¹⁴, A. Armuzzi²

¹Università degli Studi di Milano, Milan, Italy, ²IBD Center, IRCCS Humanitas Research Hospital, Gastroenterology, Rozzano, Milan, Italy, ³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁴Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ⁵University of Milan, Gastroenterology and Endoscopy, Milano, Italy, ⁶Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ⁷University Hospital of Santiago, Gastroenterology, Santiago de Compostela, Spain, ⁸University of Cagliari, Department of Medical Science and Public Health, Gastroenterology Unit, Cagliari, Italy, ⁹Venizeleio General Hospital, Gastroenterology, Heraklion, Greece, ¹⁰RABIN Medical Center, Dr., Tel Aviv, Israel, ¹¹Hospital General Universitario Alicante, Gastroenterology, Alicante, Spain, ¹²Università degli Studi di Milano, Department of Health Sciences, Milan, Italy, ¹³Hospital Universitario de La Princesa, Gastroenterology Unit, Madrid, Spain, ¹⁴Hospital Universitari Mútua Terrassa, Department of Gastroenterology, IBD Unit, Terrassa, Spain

Contact E-Mail Address: gpp.privitera@icloud.com

Introduction: Anti-tumor necrosis factor (TNF)- α are the first target therapies approved for the treatment of steroid-dependent or -refractory ulcerative colitis (UC). Drugs with different mechanisms of action have recently entered the market, but data on the optimal management of UC after failure of first-line anti-TNF- α are lacking.

Aims & Methods: The PODIUM study is a multicentre, retrospective, observational study that aims to compare the real-life effectiveness and safety of second-line vedolizumab (VDZ), ustekinumab (UST) and tofacitinib (TOF) in patients with UC. Consecutive patients with UC who had failed at least one anti-TNF- α and were never exposed to other target therapies were enrolled from 12 centres across Europe.

Sociodemographic data, data on clinical activity and adverse events of interest (AEIs, defined as AE requiring temporary/permanent drug discontinuation or medical intervention) were retrospectively extracted from medical records, from the initiation of second-line therapy until one year of observation/drug discontinuation/last available follow-up.

The primary outcome was the cumulative probability of achieving steroid-free clinical remission (SFCR), defined as stool frequency=0-1 and rectal bleeding=0 and no concomitant steroids, over the first year of treatment; inverse probability of treatment weighting (IPTW), calculated as the inverse of the probability of receiving each drug (IPTW=1/Propensity Score), was applied to the primary outcome to account for imbalances in

cohorts' characteristics. We performed an interim analysis including all data collected up to March 15th 2024; data collection is still ongoing at the submission of this Abstract.

Results: Data on 303 patients (172 VDZ, 63 UST, 68 TOF) were included in the analysis. The main baseline characteristics are presented in Table 1. After IPTW, the cumulative probability of achieving SFCR during the first year was 51.0%, 59.1% and 64.1% for VDZ, UST and TOF, respectively; both UST and TOF were superior to VDZ at Log-rank test ($p<0.001$), with no differences between the two. At weighted logistic regression, female sex (adjusted Odds Ratio, aOR, 0.06, Confidence Interval, CI, 95% 0.41-0.73, $p<0.001$) and higher Charlson Comorbidity Index calculated without considering age (aOR 0.73, 95% CI 95% 0.60-0.88, $p=0.001$) were independently associated with a lower probability of achieving SFCR during the first year. Recorded AEs were 16 (4 infections) in the VDZ group (9.3% of VDZ-treated patients), 6 (1 infection) in the UST group (9.5% of UST-treated patients), and 15 (5 infections, including 1 Zoster reactivation) in the TOF group (22.1% of TOF-treated patients).

	VDZ	UST	TOF	p
N	172	63	68	
Sex (F), n (%)	66 (38.4)	31 (49.2)	34 (50.0)	$p<0.05$ (VDZ vs both)
Age, mean (SD)	45.2 (16.0)	48.43 (16.5)	38.7 (12.9)	$p<0.05$ (TOF vs both)
Disease duration, mean (SD)	8.16 (11.1)	11.1 (11.8)	7.4 (7.4)	$p<0.05$ (UST vs TOF)
Extent (E3), n (%)	107 (62.2)	35 (60.4)	38 (55.9)	$p=ns$
CCI without age, mean (SD)	0.4 (1.0)	0.8 (1.8)	0.2 (0.5)	$p<0.05$ (UST vs both)
Baseline steroids, n (%)	74 (43.0)	26 (41.2)	38 (55.8)	$p<0.05$ (TOF vs both)
Baseline clinical activity				
SF, mean (SD)	1.9 (1.0)	2.0 (1.0)	2.2 (0.8)	$p=ns$
RB, mean (SD)	1.0 (0.9)	0.9 (0.9)	1.0 (0.8)	$p=ns$
Baseline biochemical activity				
CRP (mg/dL), mean (SD)	15.4 (29.3)	21.2 (43.1)	15.7 (33.0)	$p=ns$
FCP (ug/g), mean (SD)	1611 (2627)	1111 (1466)	1331 (1684)	$p=ns$

Table 1.

Conclusion: This preliminary analysis suggests that both UST and TOF might have superior effectiveness, compared to VDZ, as second-line agents in patients with UC after anti-TNF- α . Confirmatory analysis with a larger sample size will be performed. A slightly higher rate of AEs was observed in the TOF group.

Disclosure: Giuseppe Privitera received consultancy fees from Alphasigma and Janssen. Cristina Bezzio received lecture fees and served as a consultant for Takeda, MSD, Ferring, Abbvie, Galapagos and Janssen. Edoardo Vincenzo Savarino has served as speaker for Abbvie, Agave, AGPharma, Alfasigma, Aurora Pharma, CaDiGroup, Celltrion, Dr. Falk, EG Stada Group, Fenix Pharma, Fresenius Kabi, Galapagos, Janssen, JB Pharmaceuticals, Innovamedica/Adacyte, Malesci, MayolyBiohealth, Omega Pharma, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda, Tillots, and Unifarco; has served as a consultant for Abbvie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, DiademaFarmaceutici, Dr. Falk, Fenix Pharma, Fresenius Kabi, Janssen, JB Pharmaceuticals, Merck & Co, Nestlè, Reckitt Benckiser, Regeneron, Sanofi, SILA, Sofar, Synformulas GmbH, Takeda, and Unifarco; he has received research support from Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, Zeta Farmaceutici. Daniela Pugliese received speaker fees and/or advisory board from AbbVie, Galapagos, MSD, Takeda and Janssen, Pfizer. Iago Rodriguez-Lago has received financial support for traveling and educational activities from or has served as an advisory board member for Abbvie, Adacyte, Celltrion, Chiesi, Danone, Ferring, Faes Farma, Janssen, Galapagos, MSD, Pfizer, Roche, Takeda, and Tillotts Pharma. Financial support for research: Tillotts Pharma. Manuel Barreiro-de Acosta has served as a speaker, consultant and advisory member for and has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, Gilead, Celgene, Pfizer, Sandoz, Biogen, Fresenius, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, Gebro Pharma, Adacyte and Vifor Pharma. Sara Onali has received speaker fees from Ab-

bVie, Takeda, Janssen, Amgen, Galapagos and Norgine. Massimo Claudio Fantini has received speaker and consultancy fees from AbbVie, Takeda, Janssen-Cilag, Pfizer, Sandoz, Biogen, Galapagos, Bristol-Myers Squibb, and MSD; and research grants from Pfizer and Janssen-Cilag. Karmiris K has served as speaker, consultant, and advisory member for Abbvie, Amgen, Enorasis, Ferring, Galenica, Genesis, Janssen, MSD, Pfizer, Takeda and Vianex. Henit Yanai has received consulting fees Abbvie, Ferring, Janssen, Neopharm Ltd., Pfizer, Takeda; Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events Abbvie, Janssen, Pfizer, Takeda, Neopharm Ltd.; Participation on a Data Safety Monitoring Board or Advisory Board Abbvie, Neopharm Ltd., Pfizer, Takeda. Ana Gutierrez has served as speaker, consultant and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Takeda, Janssen, Ferring, Faes Farma, Shire Pharmaceuticals, Tillotts Pharma, Chiesi and Otsuka Pharmaceutical. Luca Pastorelli has received consultant and/or speaker fees from Giuliani, Ferring, Janssen, Takeda. Maria Chaparro has served as a speaker and consultant for and has received research or education funding from MSD, AbbVie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Biogen, Gilead and Lilly. Yamile Zabana has received speaker and/or consultant fees from AbbVie, Adacyte, Almirall, Amgen, Dr Falk Pharma, FAES Pharma, Ferring, Janssen, MSD, Otsuka, Pfizer, Shire, Takeda, Galapagos, Boehringer Ingelheim and Tillots. Alessandro Armuzzi: consulting and/or advisory board fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Arena, Biogen, Bristol-Myers Squibb, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mitsubishi-Tanabe, Novartis, Pfizer, Roche, Sandoz, Samsung Bioepis, Takeda; and research grants from MSD, Pfizer, Takeda and Biogen. The remaining authors declare no competing interests. The remaining Authors declare no competing interests.

NEED FOR A SECOND INTESTINAL RESECTION IN PATIENTS WITH CROHN'S DISEASE BEFORE AND AFTER ANTI-TNF AVAILABILITY. LONG-TERM DATA FROM THE ENEIDA REGISTRY

G. Piñero¹, V. Pérez Torrado¹, P. Nos Mateu², E. Ricart³, M. Calafat Sard¹, S. Riestra⁴, F. Mesonero Gismero⁵, E. Iglesias-Flores⁶, I. Pascual-Moreno⁷, M.I. Vera Mendoza⁸, M.D. Martín-Arranz⁹, L. de Castro¹⁰, C. Taxonera Samso¹¹, M. Rivero¹², J. Guardiola¹³, J. Gisbert¹⁴, L. Arranz Hernández¹⁵, A. Giordano¹⁶, P. Varela Trastoy¹⁷, L. Arias García¹⁸, J. Barrio¹⁹, A. Gutiérrez²⁰, S. García-López²¹, X. Calvet Calvo²², C.J. Gargallo-Puyuelo²³, J.M. Huguet²⁴, L. Bujanda²⁵, J.L. Pérez-Calle²⁶, I. Moraleja²⁷, L. Ramos Lopez²⁸, Y. Zabana²⁹, D. Carpio³⁰, M. Sierra³¹, M. Barreiro de Acosta³², F. Bermejo³³, R. Lorente Poyatos³⁴, Y. González Lama³⁵, M. Navarro-Llavat³⁶, L. Márquez Mosquera³⁷, R. Camargo Camero³⁸, M.F. García-Sepulcre³⁹, N. Rull Murillo⁴⁰, L. Zabalza San Martín⁴¹, P. Vega⁴², D.S. Ceballos Santos⁴³, E. Sese⁴⁴, Á. Ponferrada-Díaz⁴⁵, D. Monfort⁴⁶, M. Mañosa Ciria¹, E. Domenech Morral¹, on behalf of the ENEIDA project of GETECCU.

¹Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ²Hospital Universitario y Politécnico La Fe, Valencia, Spain, ³Hospital Clinic Barcelona, Gastroenterology, Barcelona, Spain, ⁴Hospital Universitario Central de Asturias, Oviedo, Spain, ⁵Hospital Universitario Ramón y Cajal, Gastroenterology, Los Santos de la Humosa, Spain, ⁶Hospital Universitario Reina Sofía de Córdoba, Digestive, Córdoba, Spain, ⁷Hospital Clínico Universitario de Valencia, Valencia, Spain, ⁸Hospital Universitario Puerta de Hierro Majadahonda, Digestive, Madrid, Spain, ⁹Hospital Universitario La Paz, Madrid, Spain, ¹⁰Hospital Álvaro Cunqueiro, Vigo, Spain, ¹¹Hospital Clínico San Carlos, Madrid, Spain, ¹²Hospital Universitario Marques de Valdecilla, Gastroenterology, Santander, Spain, ¹³Hospital Universitari de Bellvitge, Gastroenterology, L'Hospitalet de Llobregat (Barcelona), Spain, ¹⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa, Digestive Services, Madrid, Spain, ¹⁵Hospital Universitario Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Spain, ¹⁶Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, ¹⁷Hospital Universitario de Cabueñes, Gijón, Spain, ¹⁸Hospital Universitario de Burgos, Burgos, Spain, ¹⁹Hospital Universitario Río Hortega, Valladolid, Spain, ²⁰Hospital General Universitario de Alicante, Alicante, Spain, ²¹Hospital Universitario Miguel Servet, Zaragoza, Spain, ²²Consorci Corporació Sanitària Parc Taulí de Sabadell, Unitat de Malalties Digestives, Barcelona, Spain, ²³Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ²⁴Consorcio Hospital General Universitario de Valencia, Valencia, Spain, ²⁵Hospital Universitario Donostia, Donostia-San Sebastián, Spain, ²⁶Hospital Universitario Fundación de Alcorcón, Alcorcon, Spain, ²⁷Hospital Universitario de Galdakao, Galdakao, Vizcaya, Spain, ²⁸Hospital Universitario de Canarias, Tenerife, Spain, ²⁹Hospital Universitari Mútua Terrassa, Department of Gastroenterology, IBD Unit, Terrassa, Spain, ³⁰Complejo Hospitalaria de Pontevedra, Pontevedra, Spain, ³¹Complejo Asistencial Universitario de León, Gastroenterology, León, Spain, ³²Hospital Clínico Universitario de Santiago, Gastroenterology, Santiago de Compostela, Spain, ³³Hospital Universitario Fuenlabrada, Madrid, Spain, ³⁴Hospital General Universitario de Ciudad Real, Ciudad real, Spain, ³⁵Hospital Universitario 12 de Octubre, Madrid, Spain, ³⁶Hospital de Sant Joan Despí Moisès Broggi, Barcelona, Spain, ³⁷Hospital del Mar de Barcelona,

Gastroenterology, Barcelona, Spain, ³⁸Hospital Universitario Virgen de la Victoria, Málaga, Spain, ³⁹Hospital General Universitario de Elche, Elche, Spain, ⁴⁰Hospital Universitario Son Llàtzer, Palma de Mallorca, Spain, ⁴¹Hospital Universitario de Navarra, Pamplona, Spain, ⁴²Complejo Hospitalario Universitario de Ourense, Gastroenterology Department, Ourense, Spain, ⁴³Hospital Universitario de Gran Canaria Dr Negrín, Las Palmas de Gran Canaria, Spain, ⁴⁴Hospital Universitario Arnau de Vilanova de Lleida, Lleida, Spain, ⁴⁵Hospital Universitario Infanta Leonor, Madrid, Spain, ⁴⁶Consorci Sanitari de Terrassa, Barcelona, Spain

Contact E-Mail Address: gipinero@gmail.com

Introduction: Anti-TNF availability has been associated with a decrease or delay of the first intestinal resection in patients with Crohn's disease (CD). However, few studies have evaluated the impact of availability of biological therapies on the change in postoperative recurrence (POR) preventive strategies and the need for second intestinal resection.

Aims & Methods: Aims: To assess time trends in the management strategies in the postoperative setting after a first intestinal resection for CD and the rate of second surgeries through the last three decades.

Methods: Adult patients with CD who underwent a first ileocolic resection with ileocolic anastomosis between 1990 and 2020 and at least one year of clinical follow-up, were identified from the Spanish ENEIDA registry. Patients in whom ileocolic resection was due to cancer were excluded. Patients were grouped by date of surgery (before biologicals -BB- 1990-2000; early biological era -EB- 2000-2010; widespread biological era -WB- 2011-2020). Medical prevention of POR was defined as any immunomodulator or biological agent started within the first 6 months after the ileocolic resection and maintained for at least 3 months.

Medical treatment of POR was defined as any immunomodulator or biological agent started at least 6 months after the index surgery. Surgical POR was defined as the need for a second intestinal resection at least 6 months after the index surgery.

Results: A total of 5,084 patients were included (24% BB, 38% EB and 38% WB). Main characteristics of the whole cohort were as follows: 51% men, 39% active smokers at the first surgery, 40% penetrating and 40% stricturing behaviour and 25% perianal disease. 34% exposed to immunomodulators and 25% to biologicals before the first surgery.

Median disease duration at first surgery of 3 years (range, 0-46), median age at index surgery was 35 years (range, 9-89), median follow-up until second resection or last visit of 125 months (range 6-408). 55% followed medical prophylaxis (33% thiopurines, 10% biological monotherapy, 12% combotherapy). Surgical POR occurred in 17%.

A significant increase in medical prevention of POR with both thiopurines (BB 13%, EB 45%, WB 32%) and biological agents (BB 0%, EB 12%, WB 46%) was observed; moreover, an increasing proportion of patients started medical treatment with biologicals for POR (BB 35%, EB 48%, WB 43%) (P<0.001 for all comparisons).

The cumulative surgical POR-free survival was significantly higher in both EB and WB cohorts as compared to BB cohort at 3, 5 and 10 years (BB 96%, 91%, 82%; EB 97%, 95%, 89%; WB 97%, 96%, 90%; P=<0.001).

Conclusion: A significant increase in the use of medical prevention for POR after a first intestinal resection for CD was observed in the last two decades.

Moreover, almost half of the patients started biologicals to treat POR. These changes resulted in a significant decrease in the cumulative probability of a second intestinal resection in the long-term.

Disclosure: Nothing to disclose.

Microbiome: Bench to the future

08:30-09:30 / Strauss 1

OP152

THE FUNGAL COMMUNITY IN THE LOWER GASTROINTESTINAL TRACT OF MONOZYGOTIC AND DIZYGOTIC TWINS

K. Lehr¹, R. Vilchez-Vargas¹, J. Skieceviciene², N. Hipler¹, C. Thon¹, A. Gecioniene², D. Schanze³, M. Zenker³, J. Kupcinskas^{4,2}, A. Link¹
¹Otto-von-Guericke University, Department of Gastroenterology, Hepatology and Infectious Diseases, Magdeburg, Germany, ²University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³Otto-von-Guericke University, Institute of Human Genetics, Magdeburg, Germany, ⁴University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania

Contact E-Mail Address: konrad.lehr@med.ovgu.de
Introduction: A wide range of relationships between the microbial community and various environmental or individual factors have been proposed. Monozygotic and dizygotic twins provide a unique model for assessing host-microbial interactions. The mycobiome has been increasingly implicated in the development of several diseases, but knowledge of the dynamics of the fungal community, particularly in twins, has not been addressed.
Aims & Methods: In this work, we investigated the fungal community in a twin cohort and explored its relationship with associated genetic and environmental factors through in-depth analysis. The twin cohort consisted of 106 well-characterised and systematically studied monozygotic and dizygotic pairs (212 stool samples). DNA was extracted and PCR reactions were performed to sequence the lower gastrointestinal microbiome and the mycobiome community. The bacterial community was characterised using the V1-V2 region of the 16 rRNA gene and the fungal community was analysed using the ITS1-ITS2 region.
Results: The fungal community, represented by the sum of all fungal sequences, showed a significantly higher heterogeneity than the bacterial community. Several individual and genetic factors, such as the zygotic status of the twins (monozygotic vs. dizygotic), as well as sex, mode of birth, breast-feeding as newborns or living in the same household, were independent of the total number of fungal sequences. The bacterial community was significantly more abundant than the fungal community, the most common representatives of which were *Candida* and *Geotrichum* with sometimes very high abundances. *Saccharomyces* was also common in the cohort, but only in low abundance, other fungi with a wider distribution were *Cladosporium* or *Penicillium*. The environmental and individual factors mentioned above were also correlated with the individual fungal genera, but there were no significant correlations found here either. The next step was to correlate the bacterial and fungal communities with each other, and strong negative correlations were found with certain bacteria such as *Prevotella*.
Conclusion: Genetic factors in twins are not associated with dynamics in the faecal fungal community and were the subject of high inter-individual variability. However, there is a strong association between bacterial and mycobial interaction, which requires further in-depth understanding of microbial interactions.
Disclosure: Nothing to disclose.

OP153

SIMBA CAPSULE CAPTURES SMALL INTESTINAL LUMINAL CONTENT FOR METAGENOMICS ANALYSIS AND MAPS SPATIAL DIFFERENCES ALONG THE GI TRACT AS VALIDATED BY MATCHED SALIVA, DUODENAL ENDOSCOPY AND FECES

G. Wang¹, C. Bundalovic-Torma¹, S. Bruehlmann¹, Y. Nasser², M. Woo³, C.N. Andrews²
¹Nimble Science, Calgary, Canada, ²University of Calgary, Calgary, Canada, ³University Of Calgary, Calgary, Canada

Contact E-Mail Address: joseph@nimblesci.com
Introduction: The small intestine (SI) microbiome plays a crucial role in nutrient absorption and emerging evidence indicates that fecal microbiome is insufficient to represent SI microbiome. Ingestible sampling capsule technologies are emerging. However, potential contamination becomes a major limitation of these devices [1].
Aims & Methods: We previously reported the Small Intestinal MicroBiome Aspiration (SIMBA) capsules as effective means for sampling, sealing and preserving SI luminal contents for 16s rRNA sequencing analysis [2,3]. A subset of the DNA samples, including SI samples collected by SIMBA capsules (CAP) and the matched saliva (SAL), fecal (FEC) and duodenal endoscopic aspirate (ASP) and brush (BRU) samples, from 16 participants recruited for an observational clinical validation study [3] were sent for shotgun metagenomic sequencing. The aims are:
1) to compare the sampling performance of the capsule (CAP) compared to endoscopic aspirates (ASP) and 850 small intestine, large intestine and fecal samples from the Clinical Microbiomics data warehouse (PR-JEB28097), and;
2) to characterize samples from the 4 different sampling sites in terms of species composition and functional potential.
Results: 4/80 samples (1/16 SAL, 2/16 ASP, 0/16 BRU, 1/16 CAP and 0/16 FEC) failed library preparation and 76 samples were shotgun sequenced (average of 38.5 M read pairs / sample). Quality assessment showed that despite the low raw DNA yield of CAP samples, they retained a minimal level of host contamination, in comparison to ASP and BRU (mean 5.27 % vs. 93.09 - 96.44% of average total reads per sample). 3/14 ASP and all BRU samples have too few reads per sample mapping to genes, failed the rarefaction procedure and were excluded from analysis.

Site	Total (read pairs)	Host %	High Quality Non-Human (HQNH, %)	HQNH	Mapped to Gene Catalog
SAL	37.59 M	70.30	26.07	9.58 M	7.22 M
BRU	34.80 M	96.44	0.13	0.04 M	0.03 M
ASP	39.81 M	93.09	5.43	1.98 M	1.48 M
CAP	36.53 M	5.27	88.01	32.06 M	24.98 M
FEC	43.74 M	2.71	85.26	37.35 M	29.54 M

CAP samples shared majority of the species with ASP samples and a big fraction of CAP species detected in the terminal ileum samples. ASP and CAP sample composition was more similar to duodenum, jejunum and saliva and very different from large intestine and stool samples. Functional genomics further revealed GI regional-specific differences: In both ASP and CAP samples we detect a number of Gut Metabolic Modules for carbohydrate digestion and short-chain fatty acids. However, probiotic species, and species and genes involved in the bile acid metabolism were mainly prevalent in CAP and FEC samples and could not be detected in ASP samples.
Conclusion: CAP and ASP microbiome are compositionally similar despite of the high level of host contamination of ASP samples. CAP appears to be of better quality to reveal GI regional-specific functional potentials

than ASP. This analysis demonstrates the great potential for the SIMBA capsule for unveiling the SI microbiome.

References:

- [1] Yersin S and Vonaesch P. Small intestinal microbiota: from taxonomic composition to metabolism. *Trends in Microbiology*, 2024, <https://doi.org/10.1016/j.tim.2024.02.013>
- [2] Wang G, Menon S, Wilsack L, Rehak R, Lou L, Turbide C, et al. Spatially and Temporally Precise Microbiome Profiling in the Small Intestine using the SIMBA Capsule with X-ray tracking. *MedRxiv* 2024:2024.04.02.24305212. <https://doi.org/10.1101/2024.04.02.24305212>.
- [3] Wang G, Bundalovic-Torma C, Menon S, Bruehlmann S, et al. Clinical Sampling of Small Intestine Luminal Content for Microbiome Multi-Omics Analysis: A Performance Analysis of The Small Intestine Microbiome Aspiration (SIMBA) Capsule and Benchmarking Against Endoscopy. *MedRxiv* 2024:04.07.24305299. <https://doi.org/10.1101/2024.04.04.24305299>.

Disclosure: G.W, C.BT and S.B are employees of Nimble Science. G.W, C.BT, S.B. and C.N.A. are shareholders and hold stock options of Nimble Science.

OP154

FAECAL MICROBIOTA TRANSPLANTATION FOR PATIENTS WITH DIABETES TYPE 1 AND SEVERE GASTROINTESTINAL NEUROPATHY (FADIGAS): A RANDOMISED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL

K. Hoyer^{1,2}, S.M.D. Baunwall^{1,2}, D. Smed Kornum^{1,2}, M. Klinge¹, A.M. Drewes³, K. Bonnet Yderstræde⁴, S. Mikkelsen⁵, C. Erikstrup⁵, C.L. Hvas^{1,2}, K. Krogh^{1,2,6}

¹Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ²Aarhus University Hospital, Department of Clinical Medicine, Aarhus, Denmark, ³Aalborg University Hospital, Mech-Sense and Centre for Pancreatic Diseases, Department of Gastroenterology and Hepatology, Clinical Institute, Aalborg, Denmark, ⁴Odense University Hospital, Steno Diabetes Center Odense, Odense, Denmark, ⁵Aarhus University Hospital, Department of Clinical Immunology, Aarhus, Denmark, ⁶Aarhus University Hospital, Steno Diabetes Center Aarhus, Aarhus, Denmark

Contact E-Mail Address: katrine_hoyer@hotmail.dk

Introduction: Diabetic gastroenteropathy is a condition that can cause debilitation symptoms such as vomiting, intense nausea, bloating, abdominal pain, constipation, diarrhea and faecal incontinence. These symptoms not only impact the patient's morbidity but also significantly reduce their quality of life.

The condition occurs due to damage to the nerves of the sympathetic, parasympathetic and enteric nerve systems. Treating the condition can be difficult since many available therapies have limited effectiveness or pose long-term safety concerns.

Consequently, this leaves the patients with few alternatives beyond general dietary advice, broad-spectrum antibiotics, or prokinetic laxatives. Faecal microbiota transplantation (FMT) involves transferring minimally processed faeces from a healthy donor to a recipient. This leads to the establishment of a donor-like microbiota in the recipient. By restoring the intestinal microbiota, FMT holds the potential for a safe and effective means to alleviate gastrointestinal symptoms and enhance the quality of life in patients with type 1 diabetes.

Aims & Methods: We conducted a pilot trial that was randomised, double-blinded and placebo-controlled. We enrolled adults who had type 1 diabetes and moderate to severe gastrointestinal symptoms. The patients

were randomly assigned to receive either encapsulated FMT or placebo in a 1:1 ratio. After six weeks, all patients received encapsulated FMT as a second intervention. Our primary endpoint was the occurrence of adverse events of severity grade 2 or higher, assessed by the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v5) during the initial intervention.

Secondary endpoints included assessing gastrointestinal symptoms and quality of life. The trial is registered with ClinicalTrials.gov, NCT04749030.

Results: From June 2021 to May 2023, we conducted a screening of 23 patients, out of which ten were randomly selected for FMT and ten for placebo. During the first intervention, we registered 26 adverse events of severity grade 2 or above. Out of these, four patients who received FMT reported seven adverse events, while five patients who received placebo group reported 19 adverse events. None of the adverse events related to the treatment were serious. The most commonly reported adverse events were diarrhea, bloating, and abdominal pain. Patients who received FMT experienced a significant reduction in their median Gastrointestinal Symptom Rating Scale – Irritable Bowel Syndrome (GSRS-IBS) score from 58 at baseline to 35, while patients receiving placebo had only a slight increase in the median score from 64 to 56 ($p=0.01$). The Irritable Bowel Syndrome Impact Scale (IBS-IS) score also improved from 108 to 140 points in the FMT group compared with an increase from 77 to 92 points in the group of patients receiving placebo ($p=0.02$). The Patient Assessment of Gastrointestinal Symptom Severity Index (PAGI-SYM) also showed improvement with patients who received FMT reducing their median score from 42 points at baseline to 25, while the score of patients receiving placebo was reduced from 47 to 41 ($p=0.03$).

Conclusion: This study is the first randomised trial of FMT for patients with type 1 diabetes and symptoms of severe diabetic gastroenteropathy. As far as we know, this study shows the most promising clinical effect of FMT beyond *C. difficile* infection.

This study demonstrates that FMT is safe and markedly improves clinical outcomes for patients with type 1 diabetes who suffer from debilitating bowel symptoms.

Disclosure: The study was funded by a Steno Diabetes Collaborative Grant. They had no influence on the design, analysis, or reporting of the study.

OP155

EFFECTS OF LYOPHILIZED FECAL FILTRATE COMPARED TO LYOPHILIZED DONOR STOOL IN THE TREATMENT OF RECURRENT CLOSTRIDIODES DIFFICILE INFECTION: A MULTI-CENTER RANDOMIZED TRIAL

D. Kao¹, K. Wong¹, C. Lee², T. Steiner³, R. Franz¹, C. McDougall¹, M. Silva⁴, K.V MacDonald⁴, D. Marshall⁴, H. Xu⁵, T. Monaghan⁶, J. Walter⁷, R. Loebenberg⁸, M. Yaskina⁹, T. Louie⁴

¹University of Alberta, Medicine, Edmonton, Canada, ²University of British Columbia, Victoria, Canada, ³University of British Columbia, Vancouver, Canada, ⁴University of Calgary, Calgary, Canada, ⁵Indiana University, Bloomington, United States of America, ⁶University Of Nottingham, Nddc, Nottingham, United Kingdom, ⁷University College Cork, Cork, Ireland, ⁸University of Alberta, Pharmacy and Pharmaceutical Sciences, Edmonton, Canada, ⁹University of Alberta, Women and Children's Health Research Institute, Edmonton, Canada

Contact E-Mail Address: dkao@ualberta.ca

Introduction: Fecal microbiota transplantation (FMT) is the most effective therapy in the treatment of recurrent *Clostridioides difficile* infection (rCDI), and can be offered in fresh, frozen or lyophilized formulation with similar efficacy. Microbial engraftment is thought to be one of the mech-

anisms mediating its efficacy. However, the importance of microbes has been questioned by two small preliminary clinical studies that showed sterile fecal filtrate could prevent *C. difficile* recurrence.

Aims & Methods: Aims: 1) determine if lyophilized sterile fecal filtrate (LSFF) is non-inferior to lyophilized FMT (LFMT) in efficacy; 2) evaluate changes in patient reported health related quality of life (HRQOL); 3) understand patient preferences for different attributes of FMT.

Methods: This double-blind, non-inferiority (margin= 10%) study in 4 academic centers in Canada randomized rCDI patients with ≥ 3 CDI episodes to either LSFF or LFMT (1:1) between 2019 and 2023. Each treatment consisted of 15 oral capsules. Primary outcome was proportion of participants without CDI recurrence at 8 week. Secondary outcomes included 1) proportion of participants without CDI recurrence at week 24 weeks, 2) serious adverse events (mortality, hospitalization and infections related to treatments), and 3) minor adverse events (nausea, vomiting, abdominal pain and fever). Exploratory outcomes included changes in HRQOL and relative importance of different attributes of FMT.

Results: 137 participants were randomized (mean [SD] age, 61.2 [18.6] years; 89 women [65.4%]; mean CDI episodes 3.8) to LFMT group (66 participants) and LSFF (71 participants) group. In per-protocol analysis, prevention of rCDI 8 weeks after assigned treatment was achieved in 63.8% of participants in LSFF group and 86.9% in LFMT group (difference, -23.1%), resulting in trial termination. Serious adverse events were infrequent: 4 hospitalizations deemed not related and 1 hospitalization possibly related, and 1 death from COVID deemed not related to assigned treatment. Minor adverse events were self-limited and infrequent: nausea (6), vomiting (2), abdominal discomfort (15) and fever (2). Following treatment, participants had significant increases in EQ-5D-5L (n=99) VAS (median change: 10; p<0.001) and index value (median change: 0.04; p<0.001), and Cdiff32 (n=94) physical domain (median change: 16.07; p<0.001), mental domain (median change: 29.46; p<0.001), and social relationships domain (median change: 7.37; p<0.001). Work impairment decreased (n=21; median change: -10%; p<0.001) and activity impairment decreased (n=101; median change: -20%; p<0.001). Participants (n=103) indicated the 3 most important attributes of FMT were: treatment effectiveness, unknown risks of treatment and known risks of treatment.

		LFMT N (%)	LSFF N (%)
Total randomized		66 (48.2%)	71 (51.8%)
Sex	Female	42 (64.6%)	47 (66.2%)
Ethnicity	Caucasian	59 (89.4%)	69 (97.2%)
	Asian	5 (7.6%)	1 (1.4%)
History of inflammatory bowel disease (IBD)	Yes	6 (9.2%)	2 (2.8%)
Chronic Proton pump inhibitor use	Yes	12 (18.5%)	11 (15.5%)
Total # of episodes of RCDI prior to enrollment	Mean (SD)	3.6 (0.8)	3.9 (1.0)
# of ED visits or hospitalization prior to enrollment	Mean (SD)	1.5 (1.5)	1.4 (1.5)
Duration of rCDI prior to enrollment (interval between first CDI directed Rx till enrollment), in months	Mean (SD)	5.0 (2.9)	6.3 (2.6)

Table 1. Participant baseline characteristics.

Conclusion: Among adults with rCDI, LSFF was inferior to LFMT by oral capsules in preventing recurrent infection over 8 weeks. The result emphasizes the importance of microbes in mediating FMT efficacy. Preserving microbial viability in future development of microbial therapeutics is paramount.

Disclosure: None.

OP156

SAFETY AND TOLERABILITY OF MH002, A LIVE BIOTHERAPEUTIC PRODUCT, IN INFLAMMATORY BOWEL DISEASE: SUMMARY OF DATA FROM TWO PHASE 2 CLINICAL TRIALS

S. Vermeire¹, S. Danese², F. Magro³, S. Possemiers⁴, S. Bolca⁴, L. Haazen⁴
¹University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ²Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ³Faculty of Medicine of the University of Porto, Porto, Portugal, ⁴MRM Health, Ghent, Belgium

Contact E-Mail Address: severine.vermeire@uzleuven.be

Introduction: Inflammatory bowel diseases (IBD) have an ongoing, unmet medical need for new medicinal products with a different mode of action and a favourable safety profile. MH002 is a live biotherapeutic product (LBP) consisting of 6 commensal bacteria and is entering phase 3 clinical development as a therapeutic treatment developed to restore dysbiosis and depletion of butyric acid producing-bacteria that are associated with IBD. The non-pathogenic nature of the MH002 strains and absence of systemic bioavailability are expected to result in a particularly favourable safety profile.

Aims & Methods: To assess the safety of MH002 in ulcerative colitis (UC) and pouchitis (PC).

Safety data from 45 UC patients randomized (2:1) to double-blind treatment with 400mg MH002 or placebo daily for up to 16 weeks (MH002-UC-201), and from 14 PC patients treated open label with 400mg MH002 daily for 8 weeks (MH002-PC-201) were collected prospectively, the primary endpoint being occurrence of treatment emergent adverse events (AEs). UC patients were on stable 5-ASA treatment with or without low-dose corticosteroid throughout the study. Concomitant and recent antibiotic use was prohibited in all, as was treatment with advanced therapies. Placebo-treated UC patients who did not have a clinical response after 8 weeks were switched to MH002 treatment for 8 weeks.

Results: A total of 52 patients were exposed to MH002 with a total of about 136 patient-months of exposure. At baseline, the mean (range) modified Mayo score in UC patients was 5.76 (4.0-8.0) and the modified mean (range) Pouchitis Disease Activity Index score in PC patients was 6.91 (5.3-9.3). In UC patients, 20% were on stable, low dose corticosteroid, none was in the PC study. In both studies, no deaths, no severe AEs, no related serious AEs were reported in MH002-treated subjects, and no discontinuation occurred for an AE in MH002-treated participants. In particular, no bacteremia or sepsis was reported. Most AEs were mild and unrelated. Numerically less patients experienced an AE with MH002 than with placebo in UC.

	MH002-UC-201		MH002-PC-201	Total
Nr (%) of subjects	MH002 (n=31)	Placebo (n=14)	MH002 (n=14)	MH002 (n=45)
with a severe Adverse Event (AE)	0	0	0	0
discontinuing for an AE	0	1 (7%)	0	0
with at least 1 AE	11 (35%)	8 (57%)	11 (79%)	22 (49%)
with a Serious AE (not related)	1 (3%)	1 (7%)	1 (7%)	2 (4%)
with a possibly related AE	1 (3%)	1 (7%)	3 (21%)	4 (9%)
with an AE of gastro-intestinal disorders	2 (6%)	4 (29%)	4 (29%)	6 (13%)

Possibly related AEs reported with MH002 included rash (UC) and abdominal pain, diarrhoea, flatulence and nausea (PC), while abdominal distension was reported with placebo (UC). Type 2 diabetes, arterial hypertension (MH002) and Clostridioides difficile infection (placebo) were the unrelated serious AEs that were reported. No clinically significant changes

were observed during physical examination, vital signs assessment and in routine laboratory safety analyses (biochemistry, hematology and urinalysis) with MH002 or placebo. Efficacy data showed positive trends for clinical and endoscopic improvement and have been reported previously.

Conclusion: MH002 was well tolerated and safe in the first-in-disease phase 2 clinical trials conducted in UC and PC. MH002 may exhibit a particularly favourable safety profile if these results are confirmed in larger, late-stage clinical studies.

Disclosure: **SV:** financial support for research from AbbVie, J&J, Pfizer, Takeda and Galapagos; speakers' and/or consultancy fees from AbbVie, Abivax, AbolierS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MRM Health, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Surrozen, Takeda, Theravance, Tillots Pharma AG, VectivBio, Ventyx, Zealand Pharma.

SD: consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, Vifor; reports lecture fees from Abbvie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, Takeda.

FM: served as speaker and received honoraria from: Abbvie, Arena, Biogen, Bristol-Myers Squibb, Falk, Ferring, Hospira, Janssen, Laboratórios Vitoria, Pfizer, Lilly, Merck Sharp & Dohme, Sandoz, Takeda, UCB, Vifor.

SP, SB & LH: employee, paid consultant and/or shareholder of MRM Health.

Short bowel syndrome

08:30-09:30 / Lehar 1

OP157

INTESTINAL ADAPTATION IMPROVES SARCOPENIA IN SHORT BOWEL SYNDROME: RESULTS FROM A PROSPECTIVE STUDY (SARCO-SBS)

L. Wauters¹, A. Mohamed², L. De Meyere¹, S. Dermine², J. Bettolo², C. Hutinet², C. Chollet³, N. Rohmer³, F. Castelli³, A. Nuzzo², L. Billiauws², O. Corcos², T. Vanuytsel¹, F. Joly²

¹University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ²APHP Beaujon Hospital, Department of Gastroenterology and Nutrition Support, Clichy, France, ³Université Paris Saclay, CEA, INRAE, MetaboHUB, Gif-sur-Yvette, France

Contact E-Mail Address: lucas.wauters@kuleuven.be

Introduction: Sarcopenia is highly prevalent in chronic gastrointestinal diseases, including short bowel syndrome (SBS, <2m of small bowel). While restoration of colonic continuity (RC) improves intestinal adaptation, the link with sarcopenia and underlying mechanisms are unknown.

Aims & Methods: We prospectively studied the presence of sarcopenia and the link with intestinal adaptation in SBS (1). Patients were prospectively included at 2 tertiary care centers (Belgium and France) from 2022 onwards. Sarcopenia and malnutrition were assessed before and 1 year after RC, using age- and gender-specific cut-offs (2,3). The primary outcome was the evolution of sarcopenia, defined as a reduced handgrip strength (HGS) and fat free mass index (FFMI, using bioimpedance analysis). Secondary outcomes were changes in body weight (BW) or composition, serum albumin levels and urinary metabolites. Subgroup analyses were performed based on gender, weaning off home-parenteral nutrition (HPN) and anatomy, i.e. presence of a jejuno-colonic (JC) or jejuno-ileocolonic (JIC) anastomosis. Untargeted urinary metabolomics was performed using liquid chromatography coupled with high-resolution mass spectrometry with metabolite identification as previously described (4). Comparisons were done using Wilcoxon tests with Benjamini-Hochberg (BH) correction for multiple testing and multivariate linear regression using Partial Least Squares-Discriminant Analysis (PLS-DA).

Results: In total, 112 patients (68 female, mean age 57 ±15.5 years, 74 SBS-JC and 38 SBS-JIC) were included. Proportions of sarcopenia were lower 1 year after RC (5% vs. 16%, p<0.05), with a significant increase in HGS (δ = 4.7kg, p=0.001) and albumin (δ = 5.6g/L, p<0.0001) in all patients. In contrast, proportions of malnutrition were similar 1 year after RC, with no significant change in BW, BMI or FFMI in all patients. Sarcopenia was more common in females vs. males at baseline (46% vs. 21%, p<0.01) but not at 1 year. Complete weaning off HPN was seen in 57 (51%) patients after 1 year and similar according to gender, but less frequent in SBS-JC vs. SBS-JIC patients (36% vs. 79%, p<0.0001). Despite these (baseline) differences, the decrease in sarcopenia after RC was significant in females (9% vs. 29%, p<0.05), in those without weaning (3% vs. 28%) and in SBS-JC patients (5% vs. 21%, both p=0.04). Urinary metabolites significantly associated with weaning off HPN (n= 31) and SBS-anatomy (n= 22) were mainly related to amino acid metabolism (top metabolites with adj. p-value <0.001 in the table).

Subgroup	Pathway	Metabolite	Fold change	Adj. p-value (BH)
Weaning vs. no-weaning	Proline	L-proline	3.55	0.0002
	Other	α -Hydroxyhippuric acid	8.06	0.0006
	Arginine	Methylhydantoin	2.67	0.0007
		Guanidineacetic acid	2.19	0.0008
	Alanine	N-Acetyl-alanine	1.94	0.0009
SBS-JIC vs. SBS-JC	Other	α -Hydroxyhippuric acid	8.13	0.0001
	Glycine	N,N-Dimethylglycine	2.2	0.0003

PLS models were built with significant separation based on weaning off HPN (Q2cum= 0.6, pQ2= 0.005) and SBS-anatomy (Q2cum= 0.5, pQ2= 0.005).

Conclusion: Intestinal adaptation after restoration of colonic continuity improves sarcopenia in SBS patients, even in those without weaning off HPN or unfavorable anatomy (no ileum). Differences in amino acid metabolism were found based on weaning or SBS-anatomy. The potential benefits of additional nutritional and/or physical interventions need to be studied as malnutrition was not yet reversed.

References:

- 1) Clinicaltrials.gov NCT05441345
- 2) Cederholm T et al. Clin Nutr. 2017;36(1):49-64.
- 3) Cruz-Jentof A et al. Age and Ageing 2019;48:16–31.
- 4) Boudah et al. J Chromatogr B Analyt Technol Biomed Life Sci 2014;966:34-47.

Disclosure: Nothing to disclose.

OP158

MAGNETIC RESONANCE IMAGING (MRI) SHOWS CHANGES IN BOWEL MORPHOLOGY AND MOTILITY IN SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE (SBS-IF) AND COLON-IN-CONTINUITY (CIC) AFTER TREATMENT WITH THE LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 (GLP-2) ANALOG APRAGLUTIDE

A. Verbiest^{1,2}, A. Menys³, R. Vanslambrouck⁴, R. Peeters⁴, R. Sartoris⁵, M.K. Hvistendahl⁶, F. Bolognani⁷, C. Li⁸, N.N. Youssef⁹, P.B. Jeppesen⁶, F. Joly¹⁰, T. Vanuytsel^{1,2}

¹University of Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium,

²University Hospitals Leuven, Leuven Intestinal Failure and Transplantation Center (LIFT), Leuven, Belgium, ³Motilent, London, United Kingdom, ⁴University Hospitals Leuven, Medical Imaging Research Center, Leuven, Belgium, ⁵Hôpital Beaujon, Medical Imaging Service, Clichy, France, ⁶Rigshospitalet, Copenhagen University Hospital, Department of Intestinal Failure and Liver Diseases, Copenhagen, Denmark, ⁷VectivBio/Ironwood, Clinical Development, Basel, Switzerland, ⁸VectivBio/Ironwood, Data Science, Basel, Switzerland, ⁹VectivBio/Ironwood, Medical Affairs, Basel, Switzerland, ¹⁰Hôpital Beaujon, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support, Clichy, France

Contact E-Mail Address: astrid.verbiest@kuleuven.be

Introduction: SBS-IF is a severe organ failure with long-term parenteral support (PS) dependence. In the first years after extensive surgery, spontaneous structural (elongation of intestinal villi and crypts) and functional (incl. motility) intestinal changes occur, stimulating a more efficient nutrient and fluid absorption in the remnant bowel. GLP-2 analogs are hypothesized to boost intestinal adaptation resulting in increased intestinal absorption and reduced PS needs. Apraglutide (APRA) is a long-acting GLP-2 analog in development for SBS-IF. We investigated the effect of APRA at 52 weeks (W) on bowel morphology and motility based on magnetic resonance imaging (MRI).

Aims & Methods: STARS Nutrition is a 52-W multicenter, open-label, phase 2 study in adult SBS-IF-CiC pts receiving weekly subcutaneous APRA injections (5mg). We hypothesized that APRA treatment would lead to thickening of the intestinal mucosa, intestinal lengthening, reduced bowel dilatation and reduced intestinal motility. Therefore, MRI scans of the abdomen, incl. cine sequences, after oral intake of a manitol solution (600mL) were performed at baseline and at 4W, 24W and 48W of treatment. Morphology parameters were measured on static MRI

sequences; GI Quant software was used to quantify motility on cine MRI sequences. Data are presented as median (IQR). Nominal p-values are calculated using Wilcoxon matched-pairs signed rank tests with significance set at 0.05.

Results: Nine pts were included and comprise the full study population. While the numerically increased colon length failed to reach significance, small bowel length increased significantly from 29.7 to 40.7 cm (p=0.012) at 48W. Duodenal wall thickness increased by 0.8 (0.2;1.2) mm (p=0.020). There were no diameter changes in the small bowel nor colon. Changes in motility were evaluated using data from 7 pts, due to missing data. Over time, small bowel motility gradually reduced, albeit not significant. Motility in the proximal colon was significantly reduced at 48W. In the distal colon, decreased motility was observed at 4W and 24W, but returned to baseline level at 48W.

Conclusion: Using static and cine MRI sequences in pts with SBS-IF-CIC, STARS Nutrition shows that APRA treatment was associated with small bowel lengthening and increased duodenal wall thickness suggesting an intestinotrophic effect. Both effects may contribute to an increased surface area for absorption. The reduced motility, especially in the proximal colon may reduce transit time, allowing more time for absorption of nutrients, fluids and electrolytes; and reduced fecal output. Whether bowel lengthening results from a direct effect of APRA vs. changes in motility with passive elongation is subject of further investigation.

Disclosure: Astrid Verbiest, Mark Krogh Hvistendahl, Ragna Vanslambrouck, Ronald Peeters, Riccardo Sartoris – nothing to declare.

Palle Bekker Jeppesen – received grants/research support/honoraria or consultation fees from Agomab, Albumedix A/S, ArTara Therapeutics, Bainan Biotech, Baxter, Coloplast, Ferring, Fresenius Kabi, GLyPharma, Naia Pharma, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, The Novo Nordisk Foundation, Therachon, VectivBio and Zealand Pharma.

Francisca Joly – has received grants/research support/honoraria or consultation fees from Agomab, Baxter, Fresenius Kabi, Nestlé Health Sciences, BBraun, Theradial, Mayoli, Biocodex, mobile3e Consulting, Carembouche, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, Therachon, VectivBio and Zealand Pharma.

Tim Vanuytsel – has served on the speaker bureau for Abbott, Agomab, Baxter, Biocodex, Dr. Falk Pharma, Fresenius Kabi, Ipsen, Menarini, Microbiotica, MyHealth, Remedus, Takeda, Truvion, VectivBio and Zealand Pharma. TV has provided clinical advice to Baxter, Danone, Dr. Falk Pharma, MyHealth, NorthSea Therapeutics, Shire, Therachon, Takeda, VectivBio, Zealand Pharma. TV has received research grants from Danone, MyHealth, Takeda and VectivBio.

Federico Bolognani, Carrie Li and Nader N. Youssef – employees of VectivBio/Ironwood.

This research was supported by VectivBio AG/Ironwood.

OP159

EFFICACY AND SAFETY OF APRAGLUTIDE ONCE-WEEKLY IN PATIENTS WITH SHORT BOWEL SYNDROME AND INTESTINAL FAILURE (SBS-IF): RESULTS FROM THE STARS STUDY – A GLOBAL PHASE 3 DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

F. Joly¹, T. Vanuytsel², D. Kirby³, S. Lal⁴, K. Tappenden⁵, P.B. Jeppesen⁶, N.N. Youssef⁷, C. Li⁷, R. Sheik⁷, I. Statovci⁷, S. Huh⁸, F. Bolognani⁷, K. Iyer⁹

¹Beaujon Hospital Service de Gastroenterologie, Gastroenterology, Clichy, France, ²KU Leuven, Department of Gastroenterology, Leuven, Belgium, ³Cleveland Clinic, Digestive Disease and Surgery Institute, Cleveland, United States of America, ⁴University of Manchester, Division of Diabetes, Endocrinology and Gastroenterology, Manchester, United Kingdom, ⁵The University of Utah, Salt Lake City, United States of America, ⁶Rigshospitalet, Department Of Gastroenterology Ca-2121, Copenhagen, Denmark, ⁷Ironwood Pharmaceuticals, Basel, Switzerland, ⁸Ironwood Pharmaceuticals, Boston, United States of America, ⁹Mount Sinai Medical Center, Rehabilitation Program, New York, United States of America

Contact E-Mail Address: francisca.joly@aphp.fr

Introduction: In SBS-IF, patients (pts) depend on parenteral support (PS) to meet nutritional and/or fluid requirements. Apraglutide (APRA) is a long-acting novel GLP-2 analogue dosed once-weekly that stimulates intestinal adaptation, with the potential to reduce PS requirements. This phase 3 trial assessed the efficacy and safety of APRA vs placebo (PBO) in adult pts with SBS-IF.

Aims & Methods: In this phase 3 double-blind, PBO-controlled trial (NCT04627025) conducted in 73 centres and 18 countries, 164 pts were randomized 2:1 to once-weekly subcutaneous APRA (5 mg if pt ≥ 50 kg, 2.5 mg if pt < 50 kg) or PBO, stratified by intestinal anatomy (stoma or colon-in-continuity [CIC]).

The primary endpoint was relative change from baseline (BL) in weekly PS volume at Week (Wk) 24.

Key secondary endpoints at Wk 24 were reduction of additional ≥ 1 day/Wk off PS from BL, and in the stoma subgroup, relative change from BL in weekly PS volume.

Two other key secondary endpoints at Wk 48 in the CIC subgroup were reduction of ≥ 1 day/Wk off PS, and percentage of pts reaching total enteral autonomy. Wk 24 clinical responders were defined as proportion of pts with $\geq 20\%$ PS reduction at Wks 20 and 24. Adverse events (AEs) were collected.

Results: A total of 163 dosed pts (80 stoma; 83 CIC), 155 (95%) completed the study. BL demographics and mean BL weekly PS volume (APRA 13.1 L; PBO 12.9 L) were similar in both arms. At Wk 24, APRA-treated pts had a significantly larger reduction from BL in weekly PS volume vs PBO (APRA -25.5%; PBO -12.5%; $p=0.001$); both stoma and CIC subgroups demonstrated comparable treatment effects. In pts with stoma, the relative reduction from BL to Wk 24 in weekly PS volume in APRA pts vs PBO was statistically significant (-25.6% vs -7.8%; $p<0.001$) (Table 1). In pts with CIC, there was a numerical benefit in APRA that did not reach statistical significance (APRA -25.2%; PBO -17.6%; nominal $p=0.179$).

In the overall population, statistically significant PS reductions from BL were seen from Wk 8 onward. A significantly higher proportion of APRA pts achieved a reduction of ≥ 1 day/Wk off PS at Wk 24 (APRA 43.0%; PBO 27.5%; $p=0.040$). At Wk 48 in the CIC subgroup, 51.8% of APRA vs 44.4% of PBO-treated pts achieved ≥ 1 day/wk off PS ($p=0.348$), and enteral autonomy was reached in 7 of 56 (12.5%) APRA vs 2 of 27 (7.4%). APRA was well tolerated. Of 110 APRA-treated pts, only 4 (3.6%) discontinued APRA due to an AE, vs 1 of 53 (1.9%) PBO-treated pts.

Conclusion: APRA is the first once-weekly GLP-2 analogue to demonstrate efficacy in a phase 3 trial in SBS-IF. At Wk 24, APRA demonstrated significantly greater relative reductions in weekly PS volume from BL and a higher proportion of pts achieved an additional ≥ 1 day off PS, with comparable treatment effects in pts with stoma or CIC. APRA showed a favourable safety profile consistent with prior APRA studies in SBS-IF.

Endpoint	Population	Apraglutide (n=110)	Placebo (n=53)	APRA vs PBO Difference [LSM or % (95% CI)]	p-value
Primary Endpoint					
LSM or n (%)					
Relative % change from BL in actual PS weekly volume at Wk 24, Least Square Mean (LSM)	Overall	-25.5	-12.5	-13.0 (-20.9, -5.0)	0.001
Key Secondary Endpoints					
Percentage of subjects achieving a reduction of ≥ 1 day/wk off PS from BL at Wk 24, n (%) *	Overall	46 (43.0)	14 (27.5)	15.6 (0.7, 30.5)	0.040
Relative % change from BL in actual PS weekly volume at Wk 24, mean	Stoma (n=80)	-25.6	-7.8	-17.8 (-28.4, -7.3)	<0.001
Percentage of subjects achieving a reduction of ≥ 1 day/wk off PS from BL at Wk 48, n (%)	CIC (n=83)	29/56 (51.8)	12/27 (44.4)	7.3 (-16.4, 29.8)	0.348
Subjects reaching enteral autonomy at Wk 48, n (%)	CIC (n=83)	7/56 (12.5)	2/27 (7.4)	5.1 (-12.9, 18.5)	0.387
Other Secondary Endpoint					
Clinical responders at Week 24 ($\geq 20\%$ PS reduction at both Wks 20 and 24), n (%)	Overall	47 (42.7)	11 (20.8)	22.0 (7.7, 36.2)	0.003**

*n for the first key secondary is observed value and the percentage, difference in percentages and its p-value is based on results of multiple imputations. **nominal p-value.

APRA, apraglutide; BL, baseline; CI, confidence interval; LSM, least square mean; PBO, placebo; PS, parenteral support; SBS-IF, short bowel syndrome and intestinal failure.

Disclosure: FJ: Research funding from Takeda Pharma, VectivBio, Zealand, Baxter, Mobile3esolutions, Carembouche Consultant or advisor for Takeda, VectivBio, Ironwood; NorthSea Therapeutics, Hamni, Zealand, Mobile3esolutions, Carembouche. Lecturer for Baxter, BBraun, Fresenius Kabi, Janssen, Theradial; TV: Research Grants for Danone, MyHealth, Takeda, VectivBio. Consultancy for Baxter, BMS, Dr. Falk Pharma, Hanmi Pharm, North Sea Therapeutics, Takeda, Truvion, VectivBio, Zealand Pharma. Lecturer for Abbott, Baxter, Biocodex, Dr. Falk Pharma, Fresenius Kabi, Ipsen, Menarini, MyHealth, Remedus, Takeda, Truvion, VectivBio. DK: Consultant or advisor for Takeda Pharma, VectivBio, OWYN; SL: Investigator-initiated/unrestricted research grants from Fresenius Kabi, Baxter and Takeda. Honoraria and/or educational support from Takeda, Zealand, VectivBio, Fresenius Kabi, B Braun, Baxter, Northsea. KT: Board Member/ Advisory Panel/Speaker for Abbott Nutrition Health Institute, Nutricia North America, Takeda Pharmaceuticals, VectivBio – now part of Ironwood Pharmaceuticals, Inc; PJ: Honoraria, educational and/or grants from Al-bumedix A/S, ArTara Therapeutics, Bainan Biotech, Baxter, Coloplast A/S, Ferring Pharmaceuticals, Fresenius Kabi, GlyPharma Therapeutic, Hanmi Pharmaceuticals, Ironwood, Naia Pharmaceuticals, NPS Pharmaceuticals, Protara Therapeutics, Shire, Takeda, The Novo Nordisk Foundation, Therachon, VectivBio AG, Zealand Pharma A/S; NNY, CL, RS, IS, SH: Ironwood employees; FB: Ironwood consultant; KI: Grant support from Takeda Pharma, VectivBio, NorthSea Therapeutics. Consultant or advisor for Takeda Pharma, VectivBio, Northsea Therapeutics, Hanmi Pharmaceuticals. Speaker or member of speakers bureau for Takeda Pharma.

OP160

DISCOVERY OF AN ORAL, LONG-ACTING GLUCAGON-LIKE PEPTIDE 2 AS BEST-IN-CLASS TREATMENT FOR SHORT BOWEL SYNDROME

H. Zou¹, X. Wu¹, R. Zhu¹, R. Wang¹, Y. Wang¹, J. Zhao¹, S. Jiang¹
¹Hangzhou Sciwind Biosciences, Beijing, China

Contact E-Mail Address: haixia.zou@sciwindbio.com

Introduction: Glucagon-like peptide 2 (GLP-2) is a gut secreted hormone in response to dietary nutrients. GLP-2 derivatives demonstrated therapeutic efficacy for Short Bowel Syndrome (SBS), a malabsorptive disease due to physical or functional loss of parts of the small intestine. However, injection administration may decrease patient compliance. The objective of this study is to discover an oral, long-acting and best-in-class GLP-2.

Aims & Methods: The objective of this study is to discover an oral, long-acting and best-in-class GLP-2. Following methods were applied in the discovery. Fatty acid conjugated peptides were designed and tested in CHO-K1 CRE reporter cells overexpressing human or rat GLP-2 receptor. 1037331 was selected, evaluated for small intestine growth (intestine weight and thickness coefficient as readout) by once daily injection for 5 days in SD rats, and tested in pharmacokinetic (PK) study in SD rats, minipigs and beagle dogs by subcutaneous injection. Finally 1037331 was formulated into pills (7 mg 1037331/pill) and assessed for oral absorption in beagle dogs by once daily dosage for 5 days. Apraglutide (VectiveBio), a GLP-2 analog in Phase 3 studies, was used as a comparator.

Results: Among the peptide tested, 1037331 activated both human and rat GLP-2 receptor more potently than apraglutide (EC₅₀ for 1037331 and apraglutide, respectively, human receptor: 0.68 nM vs 2.11 nM; rat receptor: 0.17 nM vs 1.07 nM). In SD rats, 10 nmol/kg 1037331 increased small intestine weight and thickness comparable to 250 nmol/kg apraglutide. In PK study, 1037331 showed longer half-lives resulting higher exposure by injection in all animal models (T_{1/2} for 1037331 and apraglutide, respectively, SD rat: 10.3 h vs 7.3 h; minipig: 22.4 vs 16.6 h; beagle dog: 54.8 h vs 17.7 h). In oral PK study, daily dosing leads to accumulation of 1037331 in circulation and C_{max} at 62.4 nM was achieved.

Conclusion: Overall, 1037331 demonstrated better in vitro and in vivo potencies, and better PK profiles than apraglutide. Most importantly, 1037331 with fatty acid conjugation showed oral bioavailability, which may improve patient compliance and convenience.

Disclosure: Nothing to disclose.

OP161

GLEPAGLUTIDE REDUCES NEED OF PARENTERAL SUPPORT OF FLUIDS, ELECTROLYTES, ENERGY AND MACRONUTRIENTS IN SHORT BOWEL SYNDROME PATIENTS: RESULTS FROM THE 52-WEEK OPEN-LABEL EASE SBS-4 STUDY

L. Pinar¹, T.SS Nielsen², L. Soldbro², M. Berner-Hansen^{2,3}, P.B. Jeppesen¹
¹Rigshospitalet, Department of Intestinal Failure and Liver Diseases, Copenhagen Ø, Denmark, ²Zealand Pharma, Copenhagen, Denmark, ³Bispebjerg Hospital, Digestive Disease Center, Copenhagen, Denmark

Contact E-Mail Address: ismail.pinar.01@regionh.dk

Introduction: Glepaglutide, a novel long-acting glucagon-like peptide-2 (GLP-2) analog, is currently in development for treatment of patients with short bowel syndrome (SBS) with intestinal failure (SBS-IF). GLP-2 facilitates intestinal adaptation, thereby enhancing intestinal absorptive

capacity in SBS patients. Employing metabolic balance studies including patients with SBS-IF and intestinal insufficiency, 24 weeks of treatment with glepaglutide has recently been reported to numerically increase wet weight absorption by 398 g/day and energy absorption by 1038 kJ/day, as measured by bomb calorimetry¹.

Here, the corresponding sustained effects of glepaglutide on the need for parenteral support (PS) in SBS-IF patients over 52-week treatment period are presented.

Aims & Methods: Patients received a once-weekly 10 mg subcutaneous injection of glepaglutide via a ready-to-use autoinjector. Prior to study visits, a 48-hour collection period at home was completed: Urine volumes were measured while adhering to a fixed drinking menu (individually determined before the first study visit).

Adjustments to PS volume were guided by a prespecified algorithm: PS volume reduction equaled seven times the difference between observed and baseline urine volumes, when observed urine volumes were ≥10% higher than baseline.

For the first 24 weeks, patients adhered to the fixed drinking menu; thereafter, beverage consumption was unrestricted intending to simulate usual living conditions. Changes from baseline to weeks 24 and 52 in PS volume and its content of electrolytes, energy and macronutrients were evaluated by post-hoc one-sample t-tests.

Results: 10 patients were included: mean age 55 years, 5 females, 8 with SBS-IF, 8 without colon-in-continuity (CIC). Mean baseline PS volume was 2.55 L/day (SD=1.72). Mean PS volume was decreased by -0.76 L/day at week 24 (p=0.0285), corresponding to a -25% reduction from baseline (see table). By week 52, mean PS volume reduction amounted to -0.80 L/day, a -30% reduction from baseline (p=0.0106).

PS sodium and potassium decreased at weeks 24 and 52. PS calcium and magnesium showed numerical reductions.

PS energy content decreased by -859 kJ/day (-37% reduction) at week 24 (p=0.0038) and remained stable and low until week 52.

PS carbohydrate content was reduced by -702 kJ/day at week 24 (-42% reduction) and remained consistently low until week 52. Protein content decreased by -151 kJ/day (-36%) at week 24. PS lipid content showed a numerical reduction at weeks 24 and 52. Body weight and urine volume remained constant throughout the study.

		Week 24	95% CI and p-value	Week 52	95% CI and p-value
Volume (L/day)		-0.76	[-1.41 ; -0.11], p=0.0285	-0.80	[-1.33 ; -0.26], p=0.0106
Electrolytes (mmol/day)	Sodium	-68.0	[-128.4 ; -7.5], p=0.0326	-57.2	[-112.2 ; -2.3], p=0.0436
	Potassium	-8.4	[-14.6 ; -2.3], p=0.0145	-8.8	[-17.3 ; -0.3], p=0.0437
	Magnesium	-0.8	[-2.6 ; 0.9], p=0.3084	-1.4	[-2.9 ; 0.1], p=0.0594
	Calcium	-1.0	[-2.1 ; 0.1], p=0.0727	-1.2	[-2.5 ; 0.2], p=0.0800
Energy (kJ/day)		-859	[-1337 ; -382], p=0.0038	-866	[-1441 ; -291], p=0.0103
Macronutrients (kJ/day)	Carbohydrate	-702	[-995 ; -409], p=0.0008	-645	[-1089 ; -201], p=0.0120
	Lipid	-6	[-229 ; 217], p=0.9508	-81	[-264 ; 103], p=0.3244
	Protein	-151	[-269 ; -34], p=0.0188	-140	[-302 ; 22], p=0.0795

Table: Mean changes from baseline in PS volume and its content of electrolytes, energy and macronutrients, with 95 % confidence intervals and p-values.

Conclusion: Glepaglutide induced clinically meaningful, sustained reduction in the PS need, including fluids, electrolytes, energy and macronutrients at 52 weeks in SBS patients with and without CIC.

These data are in alignment with glepaglutide-induced increases in intestinal absorptive capacity as demonstrated in state-of-art metabolic balance studies.

References: 1 Pinar I, Nielsen T SS, Soldbro L, Berner-Hansen M, Jeppesen P B (2024). Changes in intestinal absorption following 24-weeks of treatment with glepaglutide in patients with short bowel syndrome. [Abstract submitted to the ESPEN 2024 Congress on Clinical Nutrition & Metabolism, Milan, Italy].

Disclosure: Nothing to disclose.

Fit for CRC screening

08:30-09:30 / Lehar 2

OP162

IMPACT OF USING THE ESGE GUIDELINE RISK-PROFILES FOR SURVEILLANCE AS OUTCOME PARAMETER IN A FIT-BASED COLORECTAL CANCER SCREENING PROGRAM

E. Rijnders¹, E. Toes-Zoutendijk², S. de Boer³, R. Schauwen⁴, M. Oudkerk Pool⁵, C. Verveer⁶, E. Dekker⁷, M. van Leerdam⁸, I. Nagtegaal⁹, M.C. Spaander¹⁰

¹Erasmus MC University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²University Medical Center Rotterdam, Public Health, Rotterdam, Netherlands, ³Slingeland Hospital, Gastroenterology and Hepatology, Doetinchem, Netherlands, ⁴Bernhoven hospital, Gastroenterology and Hepatology, Uden, Netherlands, ⁵Wilhelmina hospital, Gastroenterology and Hepatology, Assen, Netherlands, ⁶Ikazia Ziekenhuis, MDL, Rotterdam, Netherlands, ⁷AMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁸Netherlands Cancer Institute, Dept. of Gastroenterology, Amstelveen, Netherlands, ⁹Radboud University Nijmegen Medical Center Dept. of Pathology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands, ¹⁰Erasmus Medical Center Rotterdam, Gastroenterology & Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: e.rijnders@erasmusmc.nl

Introduction: Recent guideline from the European Society of Gastrointestinal Endoscopy (ESGE) recommends the use of risk-profiles to determine surveillance colonoscopy after polypectomy.¹

These risk-profiles are potentially a better predictor for the development of colorectal cancer (CRC) incidence after polypectomy. CRC screening programs use advanced neoplasia as primary outcome parameter.² It might be more recognizable for doctors and policy makers to use the same outcome parameter.

However, by changing the outcome parameter from advanced neoplasia to high-/low-risk profiles in a FIT-based CRC screening program, the definition of what is considered a relevant lesions will change. Using risk-profiles as outcome parameter may impact both colonoscopy surveillance capacity and the positive predictive value (PPV) of finding a relevant lesions after a positive FIT.

Aims & Methods: Study aim: assessing the impact of applying the ESGE risk-profiles as outcome parameter of a FIT based CRC screening program on colonoscopy surveillance and PPV after a positive FIT.

Methods: We retrospectively analyzed all persons who had a positive FIT ($\geq 47\mu\text{g Hb/g feces}$) followed by a colonoscopy in the Dutch CRC screening program from 2019-2022. Colonoscopy and pathology reports were used to define the surveillance interval based on the old and new guideline.

The old guideline used a scoring table in which, adenoma count, location, villous type ($\geq 75\%$) or the presence of an adenoma or serrated polyp $\geq 10\text{mm}$ were used to determine a 3 or 5 year surveillance interval.² The new guideline defined a high-risk profile as either a high-risk adenoma or high-risk serrated polyp or ≥ 5 adenomas. A high-risk adenoma is an adenoma $\geq 10\text{mm}$ or with high-grade dysplasia. A high-risk serrated polyp is a serrated polyp $\geq 10\text{mm}$ or with any dysplasia.³ All persons with a high-risk profile receive surveillance in 3 years.

The old definition of the PPV was advanced neoplasia. Advanced neoplasia is defined as CRC or advanced adenoma (adenoma $\geq 10\text{mm}$ or high-grade dysplasia or $\geq 25\%$ villous type).³ The new definition of the PPV was CRC, high-risk adenoma or high-risk serrated polyps. A chi-squared test was used to determine significant differences between the old and new definition.

Results: 218,109 persons with a positive FIT underwent a colonoscopy between 2019-2022. Based on the old surveillance guideline, 51.2% of the persons would require colonoscopy surveillance. When applying high-risk profiles only 32.3% persons required surveillance. However, the number of persons referred for a 3-year surveillance interval was now doubled (Table 1). This is a result of 723 persons who first qualified for 10-year return to screening, and 34,451 persons who previously had a 5-year interval. In contrast, only 32 persons who initially had a 3-year interval will be advised to return to screening in 10 years, when risk-profiles are applied. The corresponding PPV for CRC, high-risk adenoma or high-risk serrated polyps was 34.4%, showing an increase of 1.7% ($p < 0.05$) compared to PPV based on advanced neoplasia.

	Treatment CRC		Surveillance 3- years		Surveillance 5-years		Return to screening in 10 years	
Old surveillance guideline	10,163	(4.7%)	35,004	(16.0%)	76,856	(35.2%)	96,086	(44.1%)
New surveillance guideline	10,163	(4.7%)	70,146	(32.3%)	x	x	137,800	(63.2%)

Table 1: surveillance count based on the old surveillance guideline and the new surveillance guideline.

Conclusion: This study shows that when the new ESGE surveillance guideline risk-profiles are applied as outcome parameter in FIT CRC screening, a total reduction of 18.9% of surveillance colonoscopies can be achieved although the number of persons in the 3-year surveillance interval will be doubled. A minor change in PPV can be expected.

References:

1. Hassan C, Antonelli G, Dumonceau JM, Regula J, Bretthauer M, Chaussade S, et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2020. Vol. 52, Endoscopy. Georg Thieme Verlag; 2020. p. 687–700.

2. Nederlandse Vereniging van maag-darm-leverartsen (NVM DL) Nederlandse coloscopie surveillance richtlijn 2013 [Internet] cited April 2024, https://www.mdl.nl/files/richtlijnen/Richtlijn_Coloscopie_Surveillance_definitief_2013.pdf

3. Federatie Medisch Specialisten (FMS) richtlijn colorectal carcinoom [Internet] cited April 2024, available from https://richtlijndatabase.nl/richtlijn/coloscopie_surveillance/startpagina.html

Disclosure: Nothing to disclose.

OP163

EVALUATION OF CIRCULATING EXOSOMAL MICRORNAS AS BIOMARKERS OF EARLY COLORECTAL CANCER: A PRELIMINARY ANALYSIS

X.-H. Lv¹, Q. Lu¹, J.-L. Yang¹
¹Sichuan University West China Hospital, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: mogaraa2008@126.com

Introduction: The current screening and diagnostic methods for colorectal cancer (CRC) primarily involve tumor markers, imaging examinations, and endoscopic evaluations, which have inherent limitations. Therefore, it is imperative to explore novel diagnostic techniques for early-stage CRC to improve patient prognosis and survival rates. Recent studies have demonstrated the significant potential of circulating exosome-associated microRNAs (miRNAs) as biomarkers in CRC; however, these investigations are limited and predominantly focused on advanced tumors. Consequently, the differences in circulating exosomal miRNAs, among different stages of CRC within the classic developmental model of ‘normal mucosa, adenoma, early adenocarcinoma, advanced adenocarcinoma’, remain unknown.

Aims & Methods: Plasma exosomes were isolated from colorectal adenoma (CRA), early CRC (Tis-T1), advanced CRC (T2-T4), and healthy control (NC) groups (n=5 for each group) using ultracentrifugation. The miRNA expression profiles of plasma exosomes in the four groups were compared using miRNA microarray analysis to identify differentially expressed miRNAs in the three colorectal disease groups compared to the NC group. The results of miRNA microarray detection were validated by qRT-PCR to increase the sample size (n=30 for each group) and confirm the expression of characteristic miRNAs identified. Receiver operating characteristic curves were utilized to assess the diagnostic efficacy through area under curve (AUC).

Results: The extracted exosomes exhibited consistent morphology, size, and expression of protein markers that align with the fundamental characteristics of exosomes. Microarray analysis results revealed that both early and advanced CRC groups shared 31 up-regulated miRNAs and 34 down-regulated miRNAs compared to the CRA and NC groups. By intersecting with the GSE40247 dataset (CRC cell secreted exosome-derived microarray results), we identified five up-regulated miRNAs (miR-150-3p, miR-1224-5p, miR-1246, miR-1268a, and miR-1290). The expression levels of all five miRNAs showed a progressive increase with CRC advancement at different developmental stages. Notably, significant diagnostic potential was observed for miR-1224-5p, miR-1246, and miR 1290 in distinguishing patients with early CRC from NC (AUC 0.638 to 0.719).

All five identified miRNAs demonstrated relatively good diagnostic performance in discriminating patients with advanced CRC from NC (AUC 0.745 to 0.838), while none of them had clear diagnostic value in distinguishing early CRC patients from individuals with CRA (AUC 0.548 to 0.654). Logistic regression analysis was employed to construct a multi-panel diagnosis model based on three specific miRNAs: miR-1224 -5p, miR-1246, and miR-1290. The combined AUCs were found to be as follows: for discrimination between early CRC and NC groups, AUC=0.817 (P=0.0008); for discrimination between advanced CRC and NC groups, AUC=0.907 (P<0.0001); for discrimination between early CRC and CRA groups, AUC=0.754 (P=0.0035).

Conclusion: The miRNA expression profiles of plasma exosomes in early CRC patients exhibit similarities to those observed in advanced CRC patients. Specifically, the presence of miR-150-3p, miR-1224-5p, miR-1246, miR-1268a, and miR-1290 within plasma exosomes can serve as reliable indicators for the diagnosis of CRC. Importantly, a combination of miR-1224-5p, miR-1246, and miR-1290 shows promise for the early detection of CRC.

Disclosure: Nothing to disclose.

OP164

COLONOSCOPY FINDINGS AFTER INCREASING FECAL IMMUNOCHEMICAL TEST (FIT) CUTOFF: CROSS-SECTIONAL ANALYSIS OF THE SCREESCO RANDOMIZED TRIAL

M. Westerberg¹, J. Eriksson², C. Metcalfe³, C. Löwbeer⁴, A. Ekblom⁵, R. Steele⁶, L. Holmberg⁷, A. Forsberg⁸
¹Uppsala University, Department of Surgical Sciences, Uppsala, Sweden, ²Karolinska Institutet, Institution of Medicine Solna, Division of clinical epidemiology, Stockholm, Sweden, ³University of Bristol, Bristol Medical School: Population Health Sciences, Bristol, United Kingdom, ⁴Karolinska Institutet, Department of Laboratory Medicine, Division of Clinical Chemistry, Stockholm, Sweden, ⁵Karolinska Institutet, Department of Medicine Solna, Division of clinical epidemiology, Stockholm, Sweden, ⁶Dundee University, Department of Surgery, Population Health and Genomics, School of Medicine, Dundee, United Kingdom, ⁷King's College London, Translational Oncology & Urology Research (TOUR), School of Cancer and Pharmaceutical Sciences, London, United Kingdom, ⁸Karolinska Institutet, Institution of Medicine Solna, Stockholm, Sweden

Contact E-Mail Address: anna.forsberg@ki.se

Introduction: We determined the impact of an increased two-stool FIT cutoff on colonoscopy positivity and relative sensitivity and specificity in the randomised controlled screening trial SCREESCO conducted in Sweden.

Aims & Methods: We performed a cross-sectional analysis of participants in the FIT arm that performed FIT between March 2014 and March 2020 within the study registered with ClinicalTrials.gov, NCT02078804, who had a fecal hemoglobin concentration of at least 10 µg/g in at least one of two stool samples and who underwent a colonoscopy (n=3841). For each increase in cutoff, we computed the positive predictive value (PPV), numbers needed to scope (NNS), sensitivity and specificity for finding colorectal cancer (CRC) and advanced neoplasia (AN; advanced adenoma or CRC) relative to cutoff 10 µg/g.

Results: The PPV for advanced neoplasia (colorectal cancer, or adenoma with high grade dysplasia or size >10mm or villous component) increased from 23.0% (95% CI: 22.3-23.6%) at cutoff 10 µg/g to 28.8% (95% CI: 27.8-29.7%) and 33.1% (95% CI: 31.9-34.4%) at cutoffs 20 and 40 µg/g respectively while the NNS to find a CRC (not shown in the table) correspondingly decreased from 41 to 27 and 19. The PPV for advanced neoplasia was higher in men than women at each cutoff, e.g. 31.5% (95% CI: 30.1-32.8%) in men and 25.6% (95% CI: 24.3-27.0%) in women at 20 µg/g. The relative sensitivity and relative specificity were similar in men and women at each cutoff.

Cutoff (µg/g)	N colonoscopies (%)	N with advanced neoplasia	PPV	NNS	relative sensitivity	95% CI	relative specificity	95% CI
10	3841 (100)	882	23	4.4	100		0	
20	2319 (60)	667	29	3.5	76	74-77	44	44-46
40	1428 (37)	473	33	3.0	54	52-55	68	67-69
60	1059 (28)	384	36	2.8	44	42-45	77	76-78
80	861 (22)	331	38	2.6	38	36-39	82	81-83
120	653 (17)	272	42	2.4	31	29-32	87	87-88
160	541 (14)	240	44	2.3	27	26-29	90	89-90

Number of colonoscopies, number with finding of advanced neoplasia (AN), positive predictive value (PPV), numbers needed to scope (NNS), relative sensitivity and relative specificity by FIT-cutoff (maximum of two stool samples).

The table shows the results for for advanced neoplasia with the number of colonoscopies and number of findings with AN for each cutoff. Furthermore for each cutoff the positive predictive value (PPV) and numbers needed to scope to find one AN is given. The relative sensitivity and specificity (each with 95% CI given) are calculated relative to the cutoff 10 µg/g.
Conclusion: The risk of advanced adenoma and colorectal cancer increased with increasing fecal hemoglobin concentration in both men and women, and a low cutoff around 20 to 40 µg/g for two-stool FIT allows detection and removal of many advanced adenomas and colorectal cancers. The findings suggest that a higher cutoff in women than in men could lead to comparable colonoscopy positivity for advanced adenomas and cancer.

References: Brenner H, Werner S. Selecting a Cut-off for Colorectal Cancer Screening With a Fecal Immunochemical Test. *Clin Transl Gastroenterol* 2017; **8**: e111.

Brenner H, Haug U, Hundt S. Sex differences in performance of fecal occult blood testing. *Official journal of the American College of Gastroenterology* | ACG 2010; **105**: 2457-64.

Meulen MPV, Kapidzic A, Leerdam MEV, et al. Do Men and Women Need to Be Screened Differently with Fecal Immunochemical Testing? A Cost-Effectiveness Analysis. *Cancer Epidemiol Biomarkers Prev* 2017; **26**: 1328-36.
 Blom J, Löwbeer C, Elfström KM, Sventelius M, Öhman D, Saraste D, Törnberg S. Gender-specific cut-offs in colorectal cancer screening with FIT: Increased compliance and equal positivity rate. *Journal of medical screening* 2019; **26**: 92-7.

Forsberg A, Westerberg M, Metcalfe C, et al. Once-only colonoscopy or two rounds of faecal immunochemical testing 2 years apart for colorectal cancer screening (SCREESCO): preliminary report of a randomised controlled trial. *Lancet Gastroenterol Hepatol* 2022; **7**: 513-21.

Stromberg U, Bonander C, Westerberg M, et al. Colorectal cancer screening with fecal immunochemical testing or primary colonoscopy: An analysis of health equity based on a randomised trial. *EClinicalMedicine* 2022; **47**: 101398.

Disclosure: Nothing to disclose.

OP165

THE EFFICACY OF FECAL M2-PYRUVATE KINASE ANTIGEN RAPID TEST IN DETECTION OF COLORECTAL NEOPLASM: A MULTICENTER STUDY

B.M. Ko¹, W.M. Lee¹, T.I. Kim², J.J. Park³, Y.-T. Jeon⁴, D. Park²
¹SoonChunHyang University School of Medicine, Korea, Digestive Disease Center and Research Institute, Department of Internal Medicine, Bucheon, South Korea, ²Yonsei University College of Medicine, Division of Gastroenterology, Department of Internal Medicine and Institute of Gastroenterology, Seoul, South Korea, ³Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, South Korea, ⁴Institute of Digestive Disease and Nutrition, Korea University College of Medicine, Department Of Internal Medicine, Division Of Gastroenterology And Hepatology, Seoul, South Korea

Contact E-Mail Address: pdy0615@yuhs.ac

Introduction: Tumor cells are known to express a unique isoform of the glycolytic enzyme pyruvate kinase, called pyruvate kinase isoenzyme type M2 (M2-PK). This study aims to evaluate the effectiveness of the M2-PK antigen rapid test, compared to the conventional fecal occult blood test (FOBT), for diagnosing colorectal neoplasms, including colorectal cancer (CRC) and advanced adenoma.

Aims & Methods: Participants screened by endoscopy in three South Korean referral hospitals (December 2020 - June 2023) were classified into three groups: CRC, advanced adenoma, and normal control. This study is parallel-design, [CYY1] comparing the fecal M2-PK antigen test (Sche-

bo® M2-PK Quick™ test, Biotech AG) to the FOBT for detecting CRC and advanced adenoma, using the normal control group as a reference. The study aimed to demonstrate the non-inferiority of the M2-PK antigen test for detecting CRC (non-inferiority margin: -15%) and its superiority in advanced adenoma group compared to FOBT.

Results: A total of 270 patients [CYY1] were analyzed. The sensitivity of CRC by M2-PK test was 0.88 and 0.75 in FOBT with margin difference of 0.13 [95% CI (0.02, 0.25), $p=0.01$]. In advanced adenoma group, sensitivity was 0.43 and 0.17, respectively. The M2-PK test showed a PPV of 0.73 (vs. 0.96 for FOBT) and an NPV of 0.82 (vs. 0.76 for FOBT) in the CRC group. For advanced adenoma, PPV and NPV were 0.51 (vs. 0.82 for FOBT) and 0.53 (vs. 0.55 for FOBT), respectively. The clinical specificity for colorectal neoplasms was 0.62 for the M2-PK test and 0.97 for FOBT.

Conclusion: The M2-PK antigen rapid test is non-inferior to FOBT for detecting CRC. While its sensitivity for advanced adenoma detection is higher than FOBT, further studies are needed to fully evaluate its role.

Disclosure: Nothing to disclose.

OP166

EFFECTIVENESS OF COLONOSCOPY ON EARLY ONSET COLORECTAL CANCER INCIDENCE AMONG PERSONS 40-49 YEARS

H.-S. Kim¹, S.-Y. Kim¹, H. Kim¹

¹Wonju Severance Christian Hospital, Internal Medicine, Wonju, South Korea

Contact E-Mail Address: hyskim@yonsei.ac.kr

Introduction: Recently, some guidelines recommend conducting colorectal cancer (CRC) screening at ages younger than 50 years. However, there are few data on the preventive effect of colonoscopy at ages 40-49 years at the population level.

Aims & Methods: In this study, the risk of CRC according to the presence or absence of CSP in their 40s was evaluated in a retrospective cohort design using a nationwide database. Using the Korean National Health Insurance System data between 2004 and 2006, we constructed 1:5 colonoscopy cohort (CsC) and non-colonoscopy cohort (NCsC) at ages 40-49 years and followed through 2014. A total of 2,940,792 subjects were enrolled and CRC risk was evaluated after propensity score matching between CsC and NCsC based on age, sex, smoking, metabolic syndrome (MetS) and potentially relevant variables related CRC risk.

Results: Among 490,132 CsC subjects and 2,450,660 NCsC subjects at baseline periods in 40-49 ages, 689 (0.14%) and 9,440 (0.39%) cases of CRC were found during 10 years follow up period, respectively. According to age group, cumulative CRC incidences in early 40's (40-44) were 0.10% in CsC and 0.25% in NCsC respectively. For late 40's (45-49), those were 0.17% in CsC group and 0.49% in NCsC group, respectively. Compared with NCsC, the adjusted hazard ratios (aHRs) for CRC development in CsC group were 0.42 (men, 95% CI: 0.35-0.50) and 0.37 (women, 95% CI: 0.30-0.47) in early 40's and 0.33 (men, 95% CI: 0.29-0.37) and 0.39 (women, 95% CI: 0.33-0.45) in late 40's.

Conclusion: Overall, colonoscopy in their 40s significantly lowered the risk of colorectal cancer development by 58-67%. This cancer prevention effect of colonoscopy was different according to age and gender, and it was most effective in men in their late 40s, suggesting the rationales for optimization of age and gender to start colonoscopy.

Disclosure: Korea Health Technology R&D Project through the Korea Health Industry Development Institute, National Research Foundation of Korea grant and the National R&D Program for Cancer Control through the National Cancer Center funded by the Korea Ministry of Health & Welfare, Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education.

What's new in acute pancreatitis

08:30-09:30 / Lehar 3

OP167

THE SPECTRUM OF MICROORGANISMS IS ASSOCIATED WITH THE OUTCOMES OF ENDOSONOGRAPHY-GUIDED THERAPY FOR INFECTED PANCREATIC FLUID COLLECTIONS

M. Razpotnik¹, C. Jürgensen¹, M. Sigal¹, C. Makris¹, F.J. Körner¹, T.M. Holtmann¹, Ö. Celebi¹, A. Adler¹, F. Branchi², J. Buchkremer², F. Tacke¹, A. Wree¹

¹Charité - Universitätsmedizin Berlin, Department of Hepatology and Gastroenterology, Campus Virchow-Klinikum (CVK) and Campus Charité Mitte (CCM), Berlin, Germany, ²Charité - Universitätsmedizin Berlin, Department of Gastroenterology, Infectology and Rheumatology, Campus Benjamin Franklin (CBF), Berlin, Germany

Contact E-Mail Address: marcel.razpotnik@gmail.com

Introduction: Previous studies have demonstrated that infected pancreatic fluid collections are associated with worse clinical outcomes¹.

Aims & Methods: In light of the global rise in antibiotic resistance, this study investigates the impact of the spectrum of infecting microorganisms on the effectiveness of endosonography (EUS)-guided drainage for these conditions. Data on EUS-guided drainage of pancreatic fluid collections performed between 2018 and 2022 at three endoscopy units of Charité Berlin, regardless of the etiology, were reviewed and analyzed. The primary- endpoints were the duration of hospital stay and clinical success of the therapeutic EUS, defined as (1) the resolution of the collection to <50% within 1-3 months as observed in follow-up imaging and (2) clinical improvement. The secondary endpoints were the duration of ICU stay, mortality, and the total number of required interventions to achieve treatment success, including the initial intervention, removal and replacement of stents, and additional procedures, e.g., necrosectomy or therapy of complications during 12 months follow-up. The infection of the fluid collection was diagnosed based on microbiological evidence obtained from EUS-guided fine needle aspiration or positive blood culture, after excluding other sources of infection, along with clinical presentation and elevated inflammatory markers. The microorganisms were categorized based on microscopic appearance, Gram staining, and the number of germs in a collection. Patients with sterile necrotic collections undergoing the same therapeutic modality were used as a control group to compare the outcomes.

Results: A total of 102 patients (71.6% male, mean age 55.9±13.9 years) were included in the final analysis. In 91 of the 102 cases (89.2%), double pigtail plastic stents were utilized (46.1% were multiple), and in 38 (37.3%) patients, a transmural endoscopic necrosectomy was performed. In 29.5% of cases, penicillin; 18.2%, carbapenems; 13.6%, cephalosporins; 6.8%, metronidazole; 6.8%, vancomycin; and 18.2%, other antibiotics were administered. Compared to the control group, Gram-positive germs were associated with a significantly longer hospital stay (32 vs. 21 days, $p < 0.001$) and a greater need for ICU services (49 vs. 2 days, $p < 0.001$). Endoscopic therapy was less successful for *Candida glabrata* infections compared to those caused by *Candida albicans* (45.5% vs. 85.4%). While both were associated with a significantly prolonged hospital stay, infections with *Enterococcus faecium* (including 4 cases of vancomycin-resistant *Enterococcus faecium*, VRE) resulted in significantly higher mortality (29.4% vs. 4.5%, $p < 0.05$), and infections with *Enterococcus faecalis* were associated with significantly worse clinical outcomes as defined by the resolution of the collection in follow-up assessments (33.3% vs. 88%, $p < 0.05$). These correlations remained significant in the multivariate regression analysis, with *Enterococcus faecium* showing an odds ratio (OR) of 8.1 (95% CI: 1.4-47.4) for higher mortality.

	Number (%)	Hospital (days)	ICU (days)	Interventions (n)	Resolution (%)	Outcome (%)	Mortality (%)
Non-infected (control)	44 (43.1)	21 (1-71)	2 (1-60)	3 (1-8)	100 (14.3-100)	88	4.5
Infected	58 (56.9)	23 (1-243)*	15 (1-186)*	5 (2-21)*	81.4 (22.5-100)	75.8	12.1
Gram-positive	42 (41.2)	32 (1-243)**	49 (2-186)**	5 (2-21)*	70.8 (22.5-100)	69.6	14.3
Gram-negative	22 (21.6)	29.5 (7-243)*	49 (1-107)*	5 (2-11)*	100 (32.3-100)	76.9	13.6
Mixed infections	39 (38.2)	27.5 (1-243)*	49 (1-143)*	5 (2-21)*	81.2 (22.5-100)	73.9	12.8
Enterococcus faecium	17 (16.7)	34 (6-210)**	36 (3-186)*	6 (2-21)	83.5 (22.5-100)	62.5	29.4*
Enterococcus faecalis	6 (5.9)	93 (62-210)**	61.5 (7-92)*	8 (3-12)*	60.0 (32.3-69.2)*	33.3*	16.7
Candida albicans	18 (17.6)	20 (4-205)	9 (1-143)	3.5 (2-11)	85.4 (32.3-100)	76.9	5.9
Candida glabrata	7 (6.9)	34 (6-169)	16 (7-74)*	6.5 (2-20)	45.5 (22.5-83.8)*	50	28.6
Streptococcus spp.	13 (12.7)	10 (1-28)*	9	5 (3-5)*	78.9 (63.0-100)	100	0
Klebsiella pneumoniae	8 (7.8)	26 (12-107)	42 (9-92)	3 (2-6)	100 (32.3-100)	80	12.5
Escherichia coli	5 (4.9)	35 (7-107)	59 (1-92)	6	100 (32.3-100)	75	0
Others	22 (21.6)	47.5 (9-243)**	16 (2-143)*	5.5 (2-21)*	79.2 (32.3-100)	76.9	13.6

Compared to non-infected: *p <0.05, **p<0.001

Conclusion: The type of infecting organism significantly impacts clinical outcomes in patients undergoing EUS-guided drainage for infected peri-pancreatic fluid collections. *Enterococcus faecalis* and *faecium* infections were associated with poorer clinical outcomes, highlighting the need for targeted therapeutic strategies.

References: 1. Werge M, Novovic S, Schmidt PN, Gluud LL. Infection increases mortality in necrotizing pancreatitis: A systematic review and meta-analysis. *Pancreatol.* 2016 Sep-Oct;16(5):698-707.

Disclosure: Nothing to disclose.

OP168

THE EFFECT OF A PERIPHERALLY ACTING OPIOID ANTAGONIST ON ACUTE PANCREATITIS: A MULTICENTRE RANDOMISED CONTROLLED TRIAL

C.S. Knoph^{1,2}, M.E. Cook^{1,2}, S. Novovic^{3,4}, M. Berner-Hansen⁵, M.B. Mortensen⁶, L.B.J. Nielsen⁵, I.M. Høgsberg⁶, C. Salomon⁷, S. Pandanaboyana⁸, L.S. Sørensen⁹, O. Thorlacius-Ussing⁹, J.B. Frøkjær¹⁰, S. Schou Olesen^{1,2}, A.M. Drewes^{2,1}

¹Aalborg University Hospital, Centre for Pancreatic Diseases, Department of Gastroenterology & Hepatology, Aalborg, Denmark, ²Aalborg University, Department of Clinical Medicine, Aalborg, Denmark, ³University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ⁴Copenhagen University Hospital Hvidovre, Pancreatitis Centre East, Gastro Unit, Hvidovre, Denmark, ⁵Bispebjerg Hospital, Digestive Disease Center K, Bispebjerg, Denmark, ⁶Department of Surgery, Odense University Hospital, Odense Pancreas Centre, HPB Section, Odense, Denmark, ⁷Odense University Hospital, Department of Surgery A4, Svendborg, Denmark, ⁸Freeman Hospital, HPB and Transplant Unit, Newcastle upon Tyne, United Kingdom, ⁹Aalborg University Hospital, Department of Gastrointestinal Surgery A, Aalborg, Denmark, ¹⁰Aalborg University Hospital, Mech-Sense, Department of Radiology, Aalborg, Denmark

Contact E-Mail Address: c.siggaard@rn.dk

Introduction: Opioids used to manage severe pain in acute pancreatitis might exacerbate the disease through effects on gastrointestinal and immune functions. Methylnaltrexone, a peripherally acting μ -opioid receptor antagonist, may counteract these effects without changing analgesia.

Aims & Methods: This multicentre, double-blind, randomised, placebo-controlled, investigator-initiated trial included adult patients with predicted moderately severe or severe acute pancreatitis at four Danish pancreatitis referral centres. Patients having chronic pancreatitis, contraindications to methylnaltrexone, or renal insufficiency were excluded. Participants were randomised to receive 5 days of continuous intravenous methylnaltrexone (0.15mg/kg/day) or placebo added to the standard of care, including intravenous fluids, analgesics, and nutrition. The primary endpoint was the Pancreatitis Activity Scoring System score after 48 hours of treatment. Main secondary outcomes included pain questionnaire scores, use of opioids and laxatives, admission length, disease severity (revised Atlanta classification), and mortality.

Results: In total, 105 patients (54% males; median age 57 [IQR, 45-69]) were randomised to methylnaltrexone (n=51) or placebo (n=54). After 48 hours, the Pancreatitis Activity Scoring System score was 134.3 points in the methylnaltrexone group and 130.5 points in the placebo group (difference, 3.8 points [95% CI, -40.1 to 47.6]; $P=0.87$). At 48 hours, we found no differences between groups in pain severity (difference, 0.0 [95% CI, -0.8 to 0.9]; $P=0.94$), pain interference (difference, -0.3 [95% CI, -1.4 to 0.8]; $P=0.55$), and morphine equivalent doses (difference, 6.5 mg [95% CI, -2.1 to 15.2]; $P=0.14$). Compared to placebo, methylnaltrexone did not affect the median admission length (difference, -23 hours, [95% CI, -85 to 39]); $P=0.47$). Methylnaltrexone also did not affect the risk of laxative use (risk difference, -15% [95% CI, -34 to 2]; $P=0.10$), moderately severe or severe disease according to the Atlanta classification (risk difference, 8% [95% CI, -11 to 28]; $P=0.38$), 30-day mortality (risk difference, 6% [95% CI, -1 to 12]; $P=0.11$), or adverse events (risk difference, 10% [95% CI, -9 to 29]; $P=0.30$).

Conclusion: Methylnaltrexone treatment did not change the outcome of acute pancreatitis. Indirectly, the study supports that short-term opioid use is safe for pain control in acute pancreatitis.

Disclosure: Nothing to disclose.

M.C. Conti Bellocchi¹, M. Cattani Mottes², A. Bles³, A. Cremer⁴, S. Festa⁵, M. Uzzan⁶, T. Cúrdia Gonçalves⁷, A. Rispo⁸, C. Viganò⁹, I. Koutroubakis¹⁰, A.G. Gravina¹¹, D. Pugliese¹², P. Eder¹³, S. Vieujean¹⁴, M.C. Fantini¹⁵, C. Yzet¹⁶, K. Argyriou¹⁷, L. Pouillon¹⁸, D.G. Ribaldone¹⁹, A. Michielan², N. Swietek²⁰, A. Viola²¹, E.V. Savarino²², P. Ellul²³, M. Chaparro²⁴, S. Vrakas²⁵, M. Campigotto²⁶, R. Oliveira²⁷, A. Variola²⁸, L. Loy²⁹, A.D. Guarino⁸, A. Pukitis³⁰, M. Fragaki³¹, A. Mantaka³², L. Ramos³³, R. Ciccocioppo³⁴, L. Frulloni³⁴, PANDORA STUDY GROUP

¹University of Verona, Gastroenterology- Diagnostic and Interventional Endoscopy of Pancreas, Verona, Italy, ²Santa Chiara Hospital, Gastroenterology, Trento, Italy, ³Medizinische Universität Graz, Graz, Austria, ⁴Erasme, Gastroenterology, Brussels, Belgium, ⁵San Filippo Neri Hospital, IBD Unit, Rome, Italy, ⁶Hôpital Mondor, Gastroenterology, Paris, France, ⁷Hospital da Senhora da Oliveira - Guimarães, Gastroenterology Department, Guimarães, Portugal, ⁸University "Federico II" of Naples, Dept. Clinical Medicine and Surgery, Naples, Italy, ⁹University of Milano-Bicocca School of Medicine, Monza, Italy, ¹⁰University Hospital Heraklion, Heraklion, Greece, ¹¹University of Campania Luigi Vanvitelli, Department of Precision Medicine, Naples, Italy, ¹²Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD - IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ¹³Heliodor Świącicki University Hospital, Poznań, Poland, ¹⁴CHU Liege Hospital, Gastroenterology, Liège, Belgium, ¹⁵University of Cagliari, Presidio Policlinico of Monserrato, Cagliari, Italy, ¹⁶Amiens university hospital, Gastroenterology, Amiens, France, ¹⁷University Hospital Of Thessaly, Gastroenterology, Serres, Greece, ¹⁸Imelda Hospital Bonheiden, Gastroenterology, Bonheiden, Belgium, ¹⁹University of Turin, Department of Medical Sciences, Turin, Italy, ²⁰Universiteit Gent, Gastroenterology, Gent, Belgium, ²¹University of Messina, Messina, Italy, ²²University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ²³Mater Dei Hospital, Mater Dei Hospital, Msida, Malta, ²⁴Hospital Universitario de La Princesa, Gastroenterology Unit, Madrid, Spain, ²⁵Tzaneio Hospital, Gastroenterology Department Than Ein Hospital Piraeus, Athens, Greece, ²⁶Azienda Sanitaria Universitaria Giuliano Isontina, Gastroenterologia ed Endoscopia Digestiva/ Clinica Patologie del Fegato, Trieste, Italy, ²⁷Unidade Local de Saúde do Algarve - Portimão Unit, Gastroenterology Department, Cortegaça OVR, Portugal, ²⁸IRCCS Ospedale Sacro Cuore Don Calabria Negrar, Centro delle malattie rettointestinali (IBD Unit), Negrar, Italy, ²⁹Humanitas Clinical and Research Center, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Gastroenterology, Rozzano, Italy, ³⁰Pauls Stradins Clininic University Hospital Gastroenterology Center, University Hospital, Riga, Latvia, ³¹Venizeleion General Hospital, Department of Gastroenterology, Heraklion, Greece, ³²Chania General Hospital, Chania, Greece, ³³Hospital Universitario de Canarias, Gastroenterology, Santa Cruz de Tenerife, Spain, ³⁴University of Verona, Department of Medicine- Gastroenterology, Verona, Italy

Contact E-Mail Address: Mariacristina.contibellocchi@aovr.veneto.it

Introduction: Although an increased risk of acute pancreatitis (AP) in inflammatory bowel disease (IBD) has been previously described, there are only small series, and data on clinical management are lacking.

We aimed to investigate the prevalence, etiology, and outcome of AP in IBD patients, including management, in a multicenter international study.

Aims & Methods: A two-step retrospective study was conducted involving 34 centers across Europe. The first step consisted of a survey questionnaire examining the number of AP (according to the Atlanta criteria) in adult IBD patients observed during a 10-year study period (2011-2020), and the second one in collecting data on IBD characteristics, onset of AP, etiology, clinical management, and outcome.

The study's primary aim was to estimate the prevalence of AP in IBD patients based on the total number of IBD patients observed in the study period indicated in the survey form.

Secondary aims included investigating the etiology of AP in IBD patients, the relationship between IBD medications and AP, the role of different imaging modalities in improving the diagnosis of pancreatic abnormalities, and the clinical outcome of AP. The study protocol has been disseminated through the ECCO (European Crohn's and Colitis Organization) platform after review and support by Clinical Research Committee.

	Overall N= 398	CD patients N= 225	UC patients N=173	P value
Sex				
Male	191 (48%)	106 (47.1%)	85 (49.1%)	0.688
Female	207 (52%)	119 (52.9%)	88 (50.8%)	
Mean age at AP onset (range)	37.6±15.3 (11-85)	39.2±14.9 (11-71)	35.5±15.6 (12-85)	0.970
EIMs				
No	285 (71.6%)	152 (67.5%)	133 (76.9%)	0.040
Yes	113 (28.4%)	73 (32.5%)	40 (23.1)	
Surgery for IBD				
Yes	100 (25.1%)	78 (34.6%)	22 (12.7%)	< 0.00001
No	298 (74.9%)	147 (65.4%)	151 (87.3%)	
Alcohol assumption at AP onset				
unknown	59 (14.8%)	35 (15.6%)	24 (13.9%)	0.399
none	265 (66.6%)	146 (64.9%)	119 (68.8%)	
< 20 g/day	57 (14.3%)	38 (16.9%)	19 (11%)	
>20 g/day	12 (3%)	4 (1.7%)	8 (4.6%)	
binge drinking	5 (1.3%)	2 (0.9%)	3 (1.7%)	
Smoking habit at AP onset				
unknown	14 (3.5%)	8 (3.6%)	6 (3.4%)	< 0.00001
no smoker	234 (58.8%)	106 (47.1%)	128 (74%)	
ex smoker	44 (11%)	24 (10.7%)	20 (11.6%)	
median time from stop (years)	4.5 [1-9]			
active smoker	106 (26.7%)	87 (38.6%)	19 (11%)	
mean cig/day (range)	13 (5-40)			
Pancreatic enzyme dosage				
unknown	24 (6%)	12 (5.3%)	12 (6.9%)	0.439
normal	2 (0.5%)	1 (0.4%)	1 (0.6)	
≤2 fold unv	30 (7.5%)	16 (7.1%)	14 (8.1%)	
≥3 fold unv	342 (86%)	196 (87.2%)	146 (84.4%)	
Aetiology				
Idiopathic	54 (13.6%)	16 (7.1%)	38 (21.9%)	< 0.00001
Drug-related	220 (55.3%)	150 (66.7%)	70 (40.5%)	
Biliary	59 (14.8%)	40 (17.8%)	19 (11%)	
Autoimmune	31 (7.8%)	7 (3.1%)	24 (13.9%)	
Alcohol-related	14 (3.5%)	4 (1.8%)	10 (5.8%)	
Dislipidemic/metabolic	1 (0.2%)	0	1 (0.6%)	
Post-endoscopic intervention#	4 (1%)	2 (0.9%)	2 (1.2%)	
Others	15 (3.8%)	6 (2.7%)	9 (5.2%)	

Results: The expected prevalence of AP in IBD patients, according to the survey results, was 1.13% (780 out of 68989). However, the number of entered patients in the database was 501 (0.73%), but only 398 (0.58%) fulfilled the inclusion criteria. The mean age was 33.6± 14.3, 52% were female, 225 (56.5%) were CD, and 173 (46.4%) were UC. AP was clinically mild in most (86.9%) and, when imaging was performed (n=347, 86.7%), a normal pancreatic gland was described in 81 (23.3%), whereas edematous AP in 218 (62.8%).

The most frequent etiology was the drug-induced (220, 55.3%), due to azathioprine in 172 (77.8%), with AP occurring at 2 mg/kg dosage, after a median duration of 1 month.

Other causes included gallstones (59, 14.8%) and autoimmune (8.3%). In 54 (13.5%) AP was considered idiopathic. During a median follow-up of 67 months [IQR 34-96] from the index episode, 52 (13%) patients had AP recurrence, and 6 (1.5%) patients progressed to chronic pancreatitis.

According to a subgroup analysis by IBD type, CD patients were more often smokers, had a family history of IBD and/or pancreatic disease, extraintestinal manifestations (arthropathy), and a history of surgery, usually ileocecal resection. Ileal location with or without colonic involvement was present in 90.3%, with non-stricturing non-penetrating behavior in most (56%). Medications (66.7%) and gallstones (17.8%) were CD's most common AP etiologies.

In contrast, no risk factors for AP were found in UC patients, and extensive disease was described in 102 (59%). The etiology differed significantly from the CD group ($p < 0.0001$), since in addition to medication (40.5%), autoimmune pancreatitis was found in 13.9% and idiopathic AP in 22%.

Conclusion: PANDORA study established a 0.58% prevalence of AP in IBD patients, lower than expected. The AP is usually mild both clinically and radiologically. In 14% of cases no imaging is performed, in 23% pancreas is normal, suggesting that the real prevalence might be even lower. An ileal location in CD and extensive colitis in UC are usually reported and azathioprine seems the most common cause of AP in this setting, especially a few weeks after its introduction.

Disclosure: Nothing to disclose.

OP170

LONG TERM OUTCOMES OF A EUROPEAN COHORT OF AUTOIMMUNE PANCREATITIS PATIENTS

M. Lanzillotta¹, K. Overbeek², J. Lykke Poulsen³, P. Macinga⁴, O. Vinge Holmquist⁵, M. Löhr⁶, J. Rosendahl⁷, PrescrAIP Study Group

¹San Raffaele Hospital: IRCCS Ospedale San Raffaele, Internal Medicine, Milan, Italy, ²Erasmus MC University Medical Center, Rotterdam, Gastroenterology & Hepatology, Rotterdam, Netherlands, ³Aalborg, Gastroenterology & Hepatology, Aalborg, Denmark, ⁴Institute For Clinical And Experimental Medicine, Department Of Gastroenterology And Hepatology, Prague, Czech Republic, ⁵Department of Digestive Surgery, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, ⁶Karolinska Institutet, Center for Digestive Diseases, Stockholm, Sweden, ⁷University Clinic Halle (Saale) - Department of Internal Medicine I, University Clinic Halle (Saale), Department of Internal Medicine I, Halle (Saale), Germany

Contact E-Mail Address: lanzillotta.marco@hsr.it

Introduction: Type 1 autoimmune pancreatitis (AIP) represents the most common manifestation of IgG4-related disease. Type 1 AIP responds well to glucocorticoids, but relapses are common requiring multiple treatment courses and ultimately leading to end-organ damage and treatment-related morbidity.

To date, scant reports exist on the long-term outcomes of these patients. Moreover, the role of maintenance treatment in preventing disease relapse is still debated.

Aims & Methods: We aimed to evaluate the long-term outcomes of a large European cohort of patients with type 1 AIP and to assess the role of maintenance treatment in preventing disease relapse. Patients with type 1 AIP fulfilling ICDC criteria were included in this multicentric retrospective study within the PrescrAIP framework involving 40 European university Hospital. Relapses were defined as new onset of either AIP related symptoms or radiological abnormalities after a successful induction of remission. Patients without either complete or partial remission were excluded.

The primary endpoint was time to relapse. Predictors of relapse were identified by multivariable logistic regression. A bootstrapping technique was performed to internally validate the model. Regression coefficients from the multivariable model were employed to develop a score for computing the risk of relapse for each patient. Patients were divided into four categories according to the score, from the lowest to highest risk of relapse.

Results: 477 patients were included in this analysis (325 male, 68%). Mean age at baseline was 59 (IQR 40-68). 60% of the patients presented with jaundice while 7% of the patient with acute pancreatitis. Other organs involvement was present in 238 patients (48%), being biliary involvement the most frequent one (40%). At baseline, diabetes mellitus and pancreatic exocrine insufficiency were present in 30% and 27% of patients, respectively. After a mean follow up of 32 months (IQR 13-68), 150 (31%) AIP relapses occurred. After accounting for confounders, biliary tree involvement (OR 1.62 95%CI 1.1-2.2), acute pancreatitis at baseline (OR 2.1 95%CI 1.1-4.2), narrowing of the main pancreatic duct (OR 1.6, 95%CI 1.1-2.1) were independently associated with relapse, while AIP presenting as a focal mass resulted in a protective factor (OR 0.65 95%CI 0.46-0.92). Increased serum IgG4 level (OR 1.2 95%CI 0.9-1.7) pointed to higher relapse rate without reaching statistical significance.

Notably, any maintenance treatment reduced the relapse rate after correcting for the above-mentioned risk factors (OR 0.51, 95%CI 0.37-0.72). There was no difference in term of relapse free survival between maintenance treatment with any anti-rheumatic drugs (azathioprine, methotrexate, mycophenolate) and low-dose GCs. Maintenance treatment reduced relapse rate only in patients with higher relapse risk. At the longest follow up, DM and PEI were recorded in 33% and 29% of the patients, respectively. Only one pancreatic cancer was detected.

Conclusion: Several disease features increase the risk of relapse in type 1 AIP. Any of the maintenance treatment reduce relapse rate in type 1 AIP. Patients showing multiple risk factors for relapse benefit the most from maintenance treatment. The development of a score predicting disease relapse enhances a personalized approach toward AIP treatment. In European AIP patients the development of pancreatic cancer during follow up appears rare.

Disclosure: Nothing to disclose.

IMPACT OF FLUID RESUSCITATION IN THE EMERGENCY DEPARTMENT ON CLINICAL OUTCOMES AND SAFETY IN ACUTE PANCREATITIS. A POST-HOC ANALYSIS OF THE WATERFALL CLINICAL TRIAL

L. Guilabert¹, J.L. Buxbaum², P. Maisonneuve³, A. Garcia Garcia de Paredes⁴, P. Zapater⁵, A. Vaillo-Rocamora¹, M.Á. Rodríguez Gandía⁶, É.E. Lozada Hernández⁷, A.J.R. Collazo Moreno⁷, A. Lira-Aguilar⁸, L.P. Llovet Soto⁹, R. Mehta¹⁰, R. Tandel¹⁰, P. Navarro-Cortés¹¹, A.M. Sánchez Pardo¹¹, C. Sánchez-Marin¹², M. Marina Cobreros del Caz¹², I. Fernández Cabrera¹³, F. Casals-Seoane¹⁴, D. Casas-Deza¹⁵, E. Lauret-Braña¹⁶, E. Martí-Marqués¹⁷, L.M. Camacho-Montaño¹⁸, J. Donate Ortega⁴, V. Ubieto¹⁹, M. Ganuza¹⁹, C. Fabbri²⁰, A. Anderloni²¹, F. Bolado Concejo¹⁹, E. de-Madaria¹

¹Hospital General Universitario Dr. Balmis, Gastroenterology, Alicante, Spain, ²University of Southern California, Los Angeles, United States of America, ³IRCSS European Institute of Oncology, Division of Epidemiology and Biostatistics, Milan, Italy, ⁴Hospital Universitario Ramon y Cajal, Gastroenterology and Hepatology, Madrid, Spain, ⁵Hospital General Universitario Dr. Balmis, Clinical Pharmacology, Alicante, Spain, ⁶Hospital Universitario Ramón y Cajal, Madrid, Spain, ⁷Regional Hospital of High Specialty of Bajío, General Surgery Department of Diseases of the Digestive Tract, León, Mexico, ⁸Hospital Parc Taulí, Gastroenterology, Barcelona, Spain, ⁹Hospital Parc Taulí, Gastroenterology, Barcelona, Spain, ¹⁰Surat Institute of Digestive Sciences Hospital and Research Center, Gastroenterology, Surat, India, ¹¹Hospital Clínico Universitario de Valencia, Gastroenterology, Valencia, Spain, ¹²Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain, ¹³Hospital Dr. Negrín, Gastroenterology, Las Palmas, Spain, ¹⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa, Madrid, Spain, ¹⁵Miguel Servet University Hospital and Health Research Institute of Aragón, Gastroenterology, Zaragoza, Spain, ¹⁶Central de Asturias University Hospital, Instituto de Investigación Sanitaria del Principado de Asturias, Gastroenterology, Oviedo, Spain, ¹⁷Lucas Augusti University Hospital, Gastroenterology, Lugo, Spain, ¹⁸Puerta del Mar University Hospital, Gastroenterology, Cadiz, Spain, ¹⁹University Hospital of Navarre, Pamplona, Gastroenterology, Pamplona, Spain, ²⁰AUSL Romagna, Forlì-Cesena gastroenterology, Gastroenterology, Bologna, Italy, ²¹Humanitas Research Hospital, Gastroenterology, Milan, Italy

Contact E-Mail Address: lucia.guilabert@gmail.com

Introduction: The WATERFALL randomized controlled trial¹ demonstrated that aggressive fluid resuscitation is associated with fluid overload without improving clinical outcomes compared to moderate fluid resuscitation. However, these fluid resuscitation regimens were administered up to 8 hours after disease diagnosis, and the effect of fluid resuscitation administered before recruitment in the emergency department (FRED) was not analyzed. We aimed to assess the effect of FRED on clinical and safety parameters among patients with acute pancreatitis who participated in the WATERFALL trial.

Aims & Methods: We conducted a post-hoc analysis of the WATERFALL clinical trial¹. FRED was the volume received until recruitment (up till 8 hours from diagnosis) and it was not determined by protocol in the trial but it was registered. Patients were categorized into two groups according to median FRED administered in the whole cohort: a) low volume group: patients who received $\leq$ median FRED before recruitment b) high volume group: patients who received $>$ median FRED before recruitment.

The primary efficacy outcome was the development of moderately severe or severe AP during admission. The main safety outcome was the development of fluid overload.

As secondary endpoints, we evaluated the influence of FRED in the development of severe AP, local complications, pancreatic or peripancreatic necrosis and its infection, systemic inflammatory syndrome (SIRS) at 24 hours, persistent SIRS (> 48 h), fluid overload symptoms, signs or imaging, intensive care unit (ICU) admission, death during admission and symptom intensity. Prediction of severity was calculated with the Bedside Index Severity in Acute Pancreatitis (BISAP) score, comorbidity with Charlson comorbidity score, and symptom intensity by Patient-Reported Outcome Scale in Acute Pancreatitis (PAN-PROMISE score).

We performed a univariate and multivariate analysis adjusted by possible confounding factors. Age, center, sex, BISAP ≥ 3 , gallstone etiology, urea and arm of treatment of the WATERFALL trial were included in the model (those which could potentially influence the administration of different volume rates of FRED and the ones with a p-value $< 0,1$ between both groups in the baseline characteristics bivariate analysis).

Results: 186 out of 249 patients of the WATERFALL trial were included for whom data on FRED was available. 93 of the patients were in the aggressive fluid resuscitation arm of treatment and 93 in the moderate fluid resuscitation arm of treatment. There were statistically significant differences amongst both groups in gallstone etiology and urea ($p < 0.05$). Median FRED was 700 mL. 94 (50,5%) of the cohort received low volume FRED (FRED ≤ 700 ml) and 92 patients (49,5%) received high volume FRED (FRED > 700 ml). There were no statistically significant differences in the main efficacy outcome with 20 patients (21,3%) with moderately severe to severe AP in low volume group and 18 (19,6%) in high volume group in the univariate or multivariate analysis with an adjusted Odds Ratio (IC 95%) of 0,85 (0,39-1,86) and $p = 0.68$.

No statistically significant differences were found regarding fluid overload, with 15 patients (16%) in low volume group and 9 patients (9.8%) in high volume group in the univariate or multivariate analysis with an adjusted Odds Ratio of 0.75 (0.27-2.10) and $p = 0.58$. Regarding secondary outcomes, we did not find statistically significant differences except for symptom intensity at recruitment. Higher intensity symptoms were associated to high volume FRED at recruitment with an adjusted Odds Ratio of 2.12 (1.12-4.01) and $p = 0.02$.

Conclusion: To conclude, high volume FRED is not linked to improved clinical outcomes in AP nor does it pose a higher risk of fluid overload.

References: 1.- de-Madaria E, Buxbaum JL, Maisonneuve P, et al. Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis. N Engl J Med 2022;387:989-1000.

Disclosure: Nothing to disclose.

IBD: Diagnosis and monitoring

10:00-11:00 / Strauss 3

OP172

PRO-C11 AND PRO-C16 ARE MARKERS OF INTESTINAL FIBROSIS AND ARE ASSOCIATED WITH MRE-CONFIRMED INTESTINAL STRICTURES – RESULTS FROM THE IMAGEKIDS STUDY

J.H. Mortensen¹, G. Focht², M. Pehrsson¹, A. Griffiths³, M. Sorokina Alexdóttir¹, A. Quteineh², P. Church⁴, R. Baldassano⁵, A.-C. Bay-Jensen¹, J. Silverstein⁶, M.A. Karsdal¹, D. Turner⁷

¹Nordic Bioscience A/S, Herlev, Denmark, ²Shaare Zedek Medical Center, The Juliet Keidan Institute Of Paediatric Gastroenterology And Nutrition, Jerusalem, Israel,

³Hospital for Sick Children, Dept. of Paed. Gastroenterology, Toronto, Canada, ⁴SickKids Hospital, Division Of Gastroenterology, Toronto, Canada, ⁵The Children's Hospital of Philadelphia, Division of Gastroenterology, Hepatology, and Nutrition, Philadelphia, United States of America, ⁶Harvard Medical School, Division of Gastroenterology, Hepatology and Nutrition Instructor of Pediatrics, Boston, United States of America, ⁷Shaare Zedek Medical Center, Pediatric GI, Jerusalem, Israel

Contact E-Mail Address: jhm@nordicbio.com

Introduction: Intestinal fibrosis and strictures is one of the most challenging complications in patients with Crohn's disease (CD). There is an urgent medical need for non-invasive serological biomarkers for intestinal fibrosis, as magnetic resonance enterography (MRE) is not a feasible tool for repeated monitoring.

Here we wanted to investigate the role of the minor collagens; fibrillar type XI collagen and the Fibril-Associated Collagens with Interrupted Triple Helices (FACIT) type XVI collagen in relation to intestinal fibrosis. Therefore, we quantified the biomarkers PRO-C11 (formation of type XI collagen) and PRO-C16 (formation of type XVI collagen) in serum from pediatric CD (pCD).

Aims & Methods: We enrolled children with CD who underwent MRE in the ImageKids study. (ImageKids study: NCT01881490). Serum samples were collected at enrolment (n=203), and from healthy age- and gender-matched healthy subjects (HS) (n=82). The Nordic PFA biomarkers of tissue fibrosis PRO-C11 and PRO-C16 were measured. Intestinal fibrosis and stenosis were determined by MRE, and VAS score was applied to assess severity of intestinal fibrosis. Pearson-r correlation, students t-test and one-way-ANOVA with false discovery rate correction were applied for statistical analysis.

Results: The sample size of the different groups were as follows, no fibrosis [n=138]: VAS=0, mild fibrosis [n=55]: VAS=1-44, moderate/severe [n=17]: VAS>44). PRO-C11 (r=0.20, p=0.01) and PRO-C16 (r=0.20, p=0.01) correlated with the MRE VAS score. Both PRO-C11 (with fibrosis: median 26.4 ng/mL [IQR: 13.25-39.53 ng/mL]) and without fibrosis: median 20.6 ng/mL IQR 11.3-28.8 ng/mL) and PRO-C16 (with fibrosis: median 2990 ng/mL IQR: 2093-3884 ng/mL, and without fibrosis: median 2548 ng/mL [IQR: 1579-3286 ng/mL]) were significantly elevated in those with fibrosis compared to without fibrosis MRE-confirmed stenosis[AG1] [JHM2] (p<0.01). Serum PRO-C11 levels were significantly elevated in patients with moderate/severe intestinal fibrosis (median 32.2 ng/mL [IQR: 19.5-46.7 ng/mL]) as judged by VAS compared to patients with mild intestinal fibrosis (p<0.05, median 28.8 ng/mL [IQR: 12.6-37.3 ng/mL]), with no intestinal fibrosis (p<0.01) and HS (p<0.0001, median 8.3 ng/mL [IQR: 7.0-12.5 ng/mL]). PRO-C16 was significantly elevated in patients with moderate/severe intestinal fibrosis (median 3567 ng/mL [IQR: 2287-4608 ng/mL]) com-

pared to patients with mild intestinal fibrosis (p<0.05, (median 2791 ng/mL [IQR: 1970-3670 ng/mL]), with no intestinal fibrosis (p<0.001, (median 2548 ng/mL [IQR: 1579-3286 ng/mL]) and HS (p<0.0001, (median 1456 ng/mL [IQR: 1072-1804 ng/mL])).

Conclusion: Based on these biomarker data from the ImageKids study, PRO-C11 and PRO-C16 demonstrate potential as important non-invasive biomarkers reflecting intestinal fibrosis and stenosis.

Disclosure: Full time employee at Nordic Bioscience A/S.

OP173

BIOLOGIC DRUG AND ANTI-DRUG ANTIBODY MONITORING: TNF INHIBITORS, INFLIXIMAB, ADALIMUMAB, AND CERTOLIZUMAB PEGOL, IN 128,537 PATIENT SAMPLES

K.Y. Chun¹, J. Yang¹

¹Labcorp, Specialty Medicine, Calabasas, United States of America

Contact E-Mail Address: chunk@labcorp.com

Introduction: Serum assays to measure biologic drugs, especially TNF inhibitors, and their anti-drug antibodies (ADAb) are utilized to manage sub-optimal response and to proactively titrate doses and dosing intervals. Sensitive, drug-tolerant and high-resolution anti-drug antibody assays are an increasingly important tool necessary for detection and management of immunogenicity, especially when low-intermediate in titer and potentially reversible.¹

Aims & Methods: Serum samples from 72,819, 53,131, and 2587 patients were analyzed for infliximab (IFX), adalimumab (ADL), and certolizumab pegol (CTZ) drug (in µg/mL) and corresponding anti-drug antibodies (in ng/mL) as measured by drug-specific lab developed chemiluminescent immunoassays. Drug assays measure the free ADAb-unbound fraction of drug when serum ADAb are present. All ADAb assays detect total antibodies (including IgM & IgG subtypes), and their drug tolerance has been validated. Drug-specificity of ADABs is verified by a confirmatory test step. An extensive blinded method comparison of our IFX and Anti-IFX assays has been published.²

	IFX	ADL	CTZ
Therapeutic Target Drug Concentration (ug/mL) ³	5.0	7.5	20.0
Range of Drug Concentrations in ADAb-Negative Samples	n=50,325 0.4 to 593 µg/mL	n=37,653 0.6 to 74 µg/mL	n=837 1.0 to 138 µg/mL
Distribution of Drug Concentrations in Anti-Drug Ab-negative samples	25%: <5.0 µg/mL 27%: 5-10 µg/mL 21%: >20 µg/mL	45%: <7.5 µg/mL 37%: 7.5-12 µg/mL 14%: 13-20 µg/mL 4%: >20 µg/mL	40%: <20 µg/mL 32%: 20-39 µg/mL 28%: >40 µg/mL
Immunogenicity	n=22,494 31%	n=15,478 29%	n=1750 68%
Range of ADAb Titers	22 to 582,749 ng/mL	25 to 863,115 ng/mL	40 to 236,148 ng/mL
Anti-Drug Ab Titer Designation Cut-points (ng/mL)	Low: <200 High: >1000	Low: <100 High: >800	Low: <1000 High: >5000
Inverse Relationship Between Drug and Anti-Drug Ab Levels?	yes	yes	yes
Interpretive Comments for Anti-Drug Ab	Anti-drug antibody levels should be interpreted in the context of the concomitant free drug concentration at trough. Low titer anti-drug antibodies may be transient while high titers are likely to be more consequential. Some immunogenicity is reversible. Elimination of intermediate titer and some high titer anti-drug antibodies has been achieved with dose escalation and/or methotrexate or thiopurine. Non-neutralizing anti-pegol antibodies cannot be ruled out.		

Table 1. Analysis of Patient Samples for IFX, ADL, CTZ and Respective Anti-Drug Antibodies.

Results: Drug and ADAb results are summarized in Table 1. Immunogenicity rates were 31%, 29%, and 68% for IFX, ADL, and CTZ, respectively. ADAb-free samples were used to evaluate distribution of drug levels. Even in the absence of immunogenicity, many patients are subtherapeutic, 25%, 45% and 40%, for IFX, ADL, and CTZ, respectively, when using proposed therapeutic targets of 5 µg/mL for IFX, 7.5 for ADL, and 20 for CTZ.³ Therapeutic levels were observed in 27% for IFX, 37% for ADL and 32% for CTZ. Higher drug concentrations in the remaining samples may represent non-tough collected samples.

A wide range of immunogenicity titers was observed. Analyses of the inverse relationship between ADAb and drug led to determination of cut-points for low/high titer designations where in the setting of high ADAb, almost invariably, concomitant free drug is very low or nil. As a good rule, anti-drug antibodies should be interpreted in the context of the concomitant free drug trough concentration.

Conclusion: Here, we report concentrations of TNF-inhibitors used to treat IBD and their anti-drug antibodies in >128,000 patient samples. Though clinical histories and blood collection timing are not known, we observed that many patients may have insufficient drug levels. Immunogenicity to TNF inhibitors was frequent where a wide numeric range of ADAb was observed. Numeric ADAb antibody results should be interpreted with the help of titer designations by the laboratory because low to intermediate titers may be transient or reversible whereas high titers with nil or very low drug indicate refractory immunogenicity. High resolution ADAb assays have enabled the early detection and successful reversal of intermediate titers of Anti-IFX and Anti-ADL with dose escalation +/- co-immunomodulator.¹ Thus, biologic TDM aims to optimize drug efficacy and longevity by informing and expediting adjustments to medication.

References: 1. Colman RJ et al. Antibodies-to-infliximab accelerate clearance while dose intensification reverses immunogenicity and recaptures clinical response in paediatric Crohn's disease. *Aliment Pharmacol Ther*. 2022;55:593–603.

2. Marini J et al. Comparisons of Serum Infliximab and Antibodies-to-Infliximab Tests Used in Inflammatory Bowel Disease Clinical Trials of Remicade. *American Association of Pharmaceutical Scientists Journal* 2016 DOI: 10.1208/s12248-016-9981-3.

3. Feuerstein JD et al. American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. *Gastroenterology* 2017;153:827–834.

Disclosure: Nothing to disclose.

OP174

SYSTEMATIC ASSESSMENT OF PRIMARY SCLEROSING CHOLANGITIS USING MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE – A PROSPECTIVE POPULATION-BASED INCEPTION COHORT STUDY

M. Attauabi^{1,2,3}, G. Madsen^{2,3}, J. M. Møller⁴, Y. J.W. Nielsen⁴, A. B. Jensen⁵, F. K. Jensen⁵, H. R. Siebner^{6,7,8}, E. Fallentin⁹, F. Bendtsen^{2,3,7}, J.B. Seidelin^{1,7}, J. Burisch^{2,3,7}

¹Copenhagen University Hospital, Herlev Hospital, Department of Gastroenterology and Hepatology, Herlev, Denmark, ²Copenhagen University Hospital - Hvidovre Hospital, Gastroint, Medical Section, Hvidovre, Denmark, ³Hvidovre Hospital, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents, and Adults, Hvidovre, Denmark, ⁴Copenhagen University Hospital - Herlev hospital, Department of Radiology, Herlev, Denmark, ⁵Copenhagen University Hospital - Hvidovre Hospital, Department of Radiology, Centre for Functional and Diagnostic Imaging and Research, Hvidovre, Denmark, ⁶Copenhagen University Hospital - Hvidovre Hospital, Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Hvidovre, Denmark, ⁷Faculty of Health and Medical Sciences, University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ⁸Copenhagen University Hospital - Bispebjerg and Frederiksberg, Department of Neurology, Copenhagen, Denmark, ⁹Copenhagen University Hospital - Rigshospitalet, Department of Radiology, Copenhagen, Denmark

Contact E-Mail Address: mohamed.attauabi.02@regionh.dk

Introduction: Inflammatory bowel diseases (IBD), encompassing ulcerative colitis (UC) and Crohn's disease (CD), are associated with increased risk of primary sclerosing cholangitis (PSC). However, population-level data for optimal screening strategies in incident IBD are lacking.

Aims & Methods: We aimed to determine the occurrence and predictors of PSC in patients with newly diagnosed IBD. Since May 1st, 2021, all adult and pediatric patients with incident IBD within a catchment area encompassing 20% of Denmark were enrolled in the prospective population-based Copenhagen IBD Inception Cohort.¹

All adult patients were invited for MRCP and blood tests (albumin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin, and INR) at IBD diagnosis. PSC-like lesions on MRCPs were evaluated by two experienced radiologists.

Multivariate Cox proportional hazard analyses adjusting for age, gender, smoking, and disease phenotype were performed (adjusted HR, aHR, 95% confidence interval).

Results: Between May 2021 and May 2023, 527 patients (UC: 326; CD: 201) were included, with 242 (74.2%) and 147 (73.1%) undergoing MRCP, respectively, within a median of 2.4 months (interquartile range (IQR) 1.3–4.9) of IBD diagnosis. No clinical differences were observed between patients who underwent MRCP and those who did not.

PSC-like lesions on MRCP were detected in 33 patients (8.5%), including 17 (7.0%) and 16 (10.9%) with UC and CD, respectively. Of those, 19 patients (4.9%), including 11 (4.5%) with UC and 8 (5.4%) with CD, had definite PSC. No difference was observed in the occurrence of PSC (p=0.37) or PSC-like lesions (p=0.08) in UC vs. CD, nor according to the phenotype of CD; however, PSC lesions in both intra- and extrahepatic bile ducts were more common in UC than in CD (46.2% vs. 6.3%, p=0.02). In addition, a larger proportion with PSC had extensive UC (62.5% vs. 27.1%, p=0.04) or were males (87.5% vs. 44.9%, p=0.03) compared to those without PSC.

Abnormal hepatobiliary biochemistry was found in 34 (14.0%) and 39 (26.5%, p<0.01) patients with UC and CD, respectively, with a higher prevalence observed in patients with definite PSC (9/19 (47.4%)) or PSC-like

lesions (8/14 (57.1%)) compared to those with normal MRCP (56/356 (15.7%), $p < 0.01$). Receiver operating characteristic analysis identified ALT ≥ 25 U/L and ALP ≥ 117 U/L to predict PSC best (accuracy and sensitivity: 0.65, specificity: 0.63, positive predictive value (PV): 0.96, and negative PV: 0.09).

During a follow-up of 2.1 years (IQR 1.6-2.6), PSC and PSC-like lesions were both independently associated with increased risk of intestinal resections (aHR 5.69, 1.13-28.54), biologics (aHR 2.00, 1.04-3.86), hospitalization (aHR 2.70, 1.02-7.12), and systemic steroids (aHR 2.45, 1.02-5.89) in CD but not in UC. Abnormal hepatobiliary biochemistry was associated with hospitalization (aHR 2.11, 1.12-4.00) and flare-up of CD (aHR 1.13, 1.02-1.96) as well as biologics in UC (aHR 2.49, 1.15-5.38). None of the PSC cases died, developed cancers, varices, or required liver transplantation within the follow-up period.

Conclusion: In this prospective population-based cohort, we found a considerable proportion (8.5%) to have undetected PSC or PSC-like lesions, despite normal hepatobiliary biochemistry in half of these cases. Notably, both definite PSC, PSC-like lesions, and abnormal hepatobiliary biochemistry had a negative impact on IBD prognosis. The results underscore the importance of systematic screening to mitigate the risk of overlooking PSC, thereby improving the management and outcomes of IBD.

References: 1. Attauabi M, Madsen GR, Bendtsen F, et al. Influence of Genetics, Immunity and the Microbiome on the Prognosis of Inflammatory Bowel Disease (IBD Prognosis Study): the protocol for a Copenhagen IBD Inception Cohort Study. *BMJ Open*. 2022;12(6):e055779. doi:10.1136/bmjopen-2021-055779

Disclosure: Mohamed Attauabi: None

Gorm Roager Madsen: Personal fees from Tillotts

Jakob M Møller: None

Yousef Jesper Wirenfeldt Nielsen: None

Annette Bøjer Jensen: None

Frank Krieger Jensen: None

Hartwig Roman Siebner: has received honoraria as speaker from Sanofi Genzyme, Denmark and Novartis, Denmark, as consultant from Sanofi Genzyme, Denmark, Lophora, Denmark, and Lundbeck AS, Denmark, and as editor-in-chief (Neuroimage Clinical) and senior editor (Neuroimage) from Elsevier Publishers, Amsterdam, The Netherlands. He has received royalties as book editor from Springer Publishers, Stuttgart, Germany and from Gylndendal Publishers, Copenhagen, Denmark.

Eva Fallentin: None

Flemming Bendtsen: Tillotts, Ferring

Jakob Benedict Seidelin: has received research grants from Takeda, Janssen, the Danish Research Council, and the Capital Region Denmark, and is national coordinator of studies from AbbVie, Arena Pharmaceuticals, Ely Lilly, and Boehringer Ingelheim.

Johan Burisch: reports grants and personal fees from AbbVie, grants and personal fees from Janssen-Cilag, personal fees from Celgene, grants and personal fees from MSD, personal fees from Pfizer, grants and personal fees from Takeda, grants and personal fees from Tillotts Pharma, personal fees from Samsung Bioepis, grants and personal fees from Bristol Myers Squibb, grants from Novo Nordisk, personal fees from Pharmacosmos, personal fees from Ferring, personal fees from Galapagos, outside the submitted work.

OP175

APPLICABILITY OF THE INTERNATIONAL BOWEL ULTRASOUND SEGMENTAL ACTIVITY SCORE (IBUS-SAS) TO ULCERATIVE COLITIS: A PROSPECTIVE STUDY

T. Innocenti^{1,2}, C. Rocco^{1,2}, E.N. Lynch², M. Gatti^{1,2}, S. Bagnoli¹, G. Macri¹, F. Rogai¹, B. Orlandini¹, A.G. Bonanomi¹, M. Milla¹, S. Milani², A. Galli², M.R. Biagini², G. Dragoni^{1,2}

¹Careggi University Hospital, Clinical Gastroenterology Unit, IBD Referral Centre, Florence, Italy, ²University of Florence, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", Florence, Italy

Contact E-Mail Address: tommaso.innocenti@unifi.it

Introduction: Intestinal ultrasound (IUS) is gaining increasing acceptance as a reliable tool for tight monitoring of ulcerative colitis (UC). Although several IUS scores have been proposed, none has been formally implemented into official recommendations of international scientific societies.

Aims & Methods: We aimed to compare an IUS score validated for Crohn's disease (CD), the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS)¹, with other IUS scores specifically developed for UC, in terms of correlation with endoscopic activity.

Patients with UC ≥ 18 years old undergoing partial or full colonoscopy between April 2023 and January 2024 were prospectively included. Endoscopic evaluation of at least the sigmoid colon was mandatory for inclusion, and patients with proctitis (Montreal E1) were excluded. Endoscopic activity was scored with both the Mayo Endoscopic Subscore (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS), and defined by MES ≥ 1 and UCEIS ≥ 2 .

Moderate endoscopic activity was determined by a MES = 2 or an UCEIS = 5-6, while severe activity was defined by a MES = 3 or an UCEIS ≥ 7 . IUS was performed within 4 weeks of endoscopy. The IBUS-SAS, the Milan Ultrasound Criteria (MUC)², the UC-IUS score³, the US Score from Parente et al.⁴, and the Hata index⁵ were included in the analysis.

Applicability of the Civitelli index⁶, an IUS score developed for pediatric patients, was also evaluated. The Spearman's rank coefficient [ρ] was used to perform correlations, while receiver operating characteristic (ROC) curves were compared with the Hanley & McNeil method.

Results: Collectively, 104 patients were included in the study. The majority of patients (61.5%) had extensive colitis (Montreal E3), with half of them having an active disease at endoscopy (54.8% using MES and 48.1% using UCEIS). IUS examination was performed at a median time of 8 days (IQR 2-15) after endoscopy.

All the investigated scores were significantly able to distinguish between the 3 grades of severity of colonic inflammation, using both MES and UCEIS as a reference, with the exception of the Parente's US Score for the severe endoscopic activity assessed with UCEIS [0 (IQR 0-1) for UCEIS < 7 vs 1 (IQR 0-1) for UCEIS ≥ 7 , $p = 0.09$]. The IBUS-SAS showed a strong correlation with endoscopic activity, both with MES ($\rho = 0.71$, $p < 0.01$) and UCEIS ($\rho = 0.73$, $p < 0.01$) assessments.

The Area Under the Curve (AUC) of IBUS-SAS to detect an endoscopic activity of at least moderate severity (MES ≥ 2 and UCEIS ≥ 5) was 0.85 and 0.90, respectively. The optimal cutoff to detect a MES ≥ 2 and UCEIS ≥ 5 was > 11 (sensitivity 75% and specificity 82%) and > 22 (sensitivity 92% and specificity 80%), respectively.

Both cut-offs showed progressive increase from mild to severe activity, with IBUS-SAS maintaining a consistently high AUC at different thresholds. Consistent with IBUS-SAS results, all the investigated UC-developed IUS scores correlated with both the MES and the UCEIS ($p < 0.01$). AUC values and relative comparisons between the AUC are detailed in Table 1.

A) AUC for MES ≥ 2	IBUS-SAS 0.85 (0.77-0.91)	Civitelli index 0.85 (0.76-0.91)	Hata index 0.77 (0.67-0.84)	US Score 0.74 (0.64-0.82)	UC-IUS 0.86 (0.78-0.92)	
MUC 0.85 (0.77-0.91)	0.99	0.92	0.03	< 0.01	0.55	
UC-IUS 0.86 (0.78-0.92)	0.45	0.55	0.02	< 0.01	0.62	Civitelli index 0.92 (0.83-0.95)
US Score 0.74 (0.64-0.82)	0.02	0.01	0.48		0.18	0.48 Hata index 0.87 (0.79-0.93)
Hata index 0.77 (0.67-0.84)	0.06	0.02		0.45	0.09	0.20 US Score 0.83 (0.75-0.90)
Civitelli index 0.85 (0.76-0.91)	0.93		0.09	0.30	0.95	0.50 UC-IUS 0.92 (0.85-0.96)
		0.92	0.05	0.24	0.98	0.59 MUC 0.92 (0.85-0.96)
		UC-IUS 0.92 (0.85-0.96)	US Score 0.83 (0.75-0.90)	Hata index 0.87 (0.79-0.93)	Civitelli index 0.92 (0.83-0.95)	IBUS-SAS 0.90 (0.83-0.95)
						B) AUC for UCEIs ≥ 5

Table 1. Relative comparisons between the AUC of each score to detect a MES ≥ 2 (A, top-right) and an UCEIS ≥ 5 (B, bottom-left) are reported.

Grey rows and columns: AUC values (with 95%CI).

White cells: *p*-values obtained via the Hanley and McNeil method (significant *p*-values are shown in bold).

Conclusion: In this study we provide a successful validation of 6 IUS scores for UC. The IBUS-SAS has an optimal performance in predicting endoscopic activity also in patients with UC, despite having been developed initially for CD.

References: 1. Novak KL, Nylund K, Maaser C, et al. Expert Consensus on Optimal Acquisition and Development of the International Bowel Ultrasound Segmental Activity Score [IBUS-SAS]: A Reliability and Inter-rater Variability Study on Intestinal Ultrasonography in Crohn's Disease. *J Crohns Colitis* 2021;15:609-616

2. Allocca M, Fiorino G, Bonovas S, et al. Accuracy of Humanitas Ultrasound Criteria in Assessing Disease Activity and Severity in Ulcerative Colitis: A Prospective Study. *J Crohns Colitis* 2018;12:1385-1391
3. Bots S, Nylund K, Löwenberg M, et al. Intestinal Ultrasound to Assess Disease Activity in Ulcerative Colitis: Development of a novel UC-Ultrasound Index. *J Crohns Colitis* 2021;15:1264-1271
4. Parente F, Molteni M, Marino B, et al. Are colonoscopy and bowel ultrasound useful for assessing response to short-term therapy and predicting disease outcome of moderate-to-severe forms of ulcerative colitis?: a prospective study. *Am J Gastroenterol* 2010;105:1150-7
5. Kinoshita K, Katsurada T, Nishida M, et al. Usefulness of transabdominal ultrasonography for assessing ulcerative colitis: a prospective, multi-center study. *J Gastroenterol* 2019;54:521-529
6. Civitelli F, Di Nardo G, Oliva S, et al. Ultrasonography of the colon in pediatric ulcerative colitis: a prospective, blind, comparative study with colonoscopy. *J Pediatr* 2014;165:78-84.e2

Disclosure: GD reports speaker fees from Alfasigma, Johnson & Johnson, Novartis, Pfizer, Takeda, and has served in advisory board for Celltrion Healthcare and Pfizer. The other authors have no conflict of interests to declare.

OP176

A COHORT STUDY OF INFLAMMATORY BOWEL DISEASE CARE IN PREGNANCY IN A LARGE TERTIARY CENTRE

H. Mackenzie¹, S. McCartney¹, D. Nzelu², D. Williams², P. Harrow¹

¹University College London Hospitals NHS Foundation Trust, Department of Gastroenterology, London, United Kingdom,

²University College London Hospitals NHS Foundation Trust, Department of Obstetric Medicine, London, United Kingdom

Contact E-Mail Address: harry.mackenzie@nhs.net

Introduction: Treatment of IBD during pregnancy poses a clinical challenge. Myths and misconceptions abound. Numerous studies have shown active IBD is associated with adverse maternal and fetal outcomes. A growing field of new medication also creates challenges. We conducted a retrospective cohort study to report pregnancy outcomes and clinical practice in a large tertiary centre in the UK in 2023.

Aims & Methods: Tertiary care for pregnant patients with IBD is provided through a specialist joint gastroenterology-obstetrics service. Data was retrospectively extracted from the electronic health records of 50 women looked after between January 1st and July 1st 2023. We describe the patient population including IBD characteristics, treatments and disease activity during pregnancy and report obstetric outcomes.

Results: 50 unique pregnant women were included; 30 (60.0%) had Crohn's disease (CD) and 20 (60.0%) had Ulcerative Colitis (CD) with a median age of 34. Within the CD cohort, 4 (13.3%) had prior or active perianal disease. Vaginal delivery is relatively contraindicated in this cohort and all patients underwent C-section.

Overall, 22/50 (44.0%) patients were taking biologics, 6/50 (12.0%) on thiopurines, 14/50 (28.0%) on mesalazine only and 14/50 (28%) were on no IBD medication at the time of conception. Of those taking biologics, 3/22 (13.6%) discontinued in the third trimester while 19/22 (86.4%) continued biologics throughout pregnancy. This reflects a recent change in practice; only patients in remission with low risk of flare stopped biologic medication during pregnancy.¹

50% experienced an IBD flare during pregnancy. A flare was defined as a faecal calprotectin >250µg/g or exacerbation of symptoms requiring change in medical management.

A significant proportion (20/50, 40.0%) developed anaemia during pregnancy (Hb <116g/L). 6 (12%) developed anaemia according to pregnancy parameters (Hb <106g/L. 21 (42.0%) received iron supplementation. 11 (52.4%) received it exclusively orally, 3 (14.3%) exclusively intravenously and 5 (23.8%) received both. Oral iron was tolerated poorly.

Regarding obstetric outcomes; 48 (96.0%) had live singleton births, with 1 (2.00%) miscarriage and 1 (2.00%) elective termination following an abnormal anomaly scan; found at post-mortem to have Turner's syndrome. 35/48 (72.9%) women delivered in our hospital while 13/48 (18.1%) delivered in a local hospital.

1/48 (3.9%) baby was born prematurely (<37 weeks). Median birthweight was 3235g (2410g – 4280g). 2/48 (4.2%) were born with low birth weight (<2.5Kg), and 4/48 (8.3%) had fetal macrosomia (>4.0Kg). Median birthweight was lower in mothers who experienced flare (3210g) compared to those with no flare (3310g).

Incidence of gestational diabetes mellitus (GDM) (25.7%) was higher compared with the national average of 5%. Antenatal steroid use is associated with hyperglycaemia and GDM. Steroids were required to control disease flares in 6/48 (12.5%) women; 3 had prednisolone, 2 had budesonide and 1 buccal hydrocortisone. Only 1/6 (16.7%) exposed to steroids developed GDM.

Conclusion: IBD flares were common in pregnancy, which may reflect the complexity of patients referred to the tertiary service. Most patients continued biologic medication during pregnancy including the third

trimester. Obstetric and neonatal outcomes were similar to the general population. Anaemia was similar to and GDM was more common than the local population. Awareness and proactive management of these issues including continuing IBD medication is important to reduce the risk of associated complications.

References: 1. Torres J, Chaparro M, Mette Julsgaard, Katsanos K, Zuzana Zelinkova, Agrawal M, et al. European Crohn's and Colitis Guidelines on Sexuality, Fertility, Pregnancy, and Lactation. *Journal of Crohn's and Colitis* [Internet]. 2022 Aug 25;17(1):1–27. Available from: <https://academic.oup.com/ecco-jcc/article/17/1/1/6675338>

Disclosure: Nothing to disclose.

Screening colonoscopy: How to save lives

10:00-11:00 / Lehar 1

OP177

THE IMPACT OF SCREENING COLONOSCOPY KEY PERFORMANCE INDICATORS ON THE RISK OF FUTURE COLORECTAL CANCER AND ADVANCED POLYPS

J. Parker¹, G. Greene², J. Torkington¹, S. Dolwani³

¹Cardiff and Vale University Health Board, Cardiff, United Kingdom, ²Welsh Cancer Intelligence and Surveillance Unit, Cardiff, United Kingdom, ³Cardiff University, Population Medicine, Cardiff, United Kingdom

Contact E-Mail Address: dolwanis@cardiff.ac.uk

Introduction: Polyp detection rates are considered surrogate indicators of colonoscopy quality. Current evidence suggests that improving these in low detectors may reduce the risk of post colonoscopy colorectal cancer (PCCRC). It is unclear whether an upper threshold exists above which this becomes less clinically meaningful.

The aim of this study was to assess the impact of KPIs in a high polyp detector group on the future risk of advanced polyps and colorectal cancer diagnoses within 3 years of screening colonoscopy. The PCCRC rate and number of interval cancers and advanced polyps detected were also described.

Aims & Methods: This was a retrospective cohort study of patients undergoing screening colonoscopy. Endpoints of advanced polyps or colorectal cancer and were identified by analysis of routine linked healthcare data through the Secure Anonymised Information Linkage (SAIL) databank. A multivariate cox regression analysis assessed the impact of colonoscopist performance indicators on outcomes of future diagnoses of advanced polyps or colorectal cancer.

Results: 5807 patients were included with a median follow-up of 60.1 months. There were 1.5% interval advanced polyps and 0.9% colorectal cancers identified with a median time to diagnosis of 19.8 and 39.2 months respectively. PCCRC rate was 3.8%. The median polyp detection rates were 62.2% with an adenoma detection rate of 50.9% amongst the colonoscopists. There was minimal variation in outcomes of advanced polyp or colorectal cancer diagnoses in these high detectors with no impact demonstrated of higher thresholds of the assessed key performance indicators on this.

Conclusion: It appears a threshold exists above which increasing performance indicators may not translate to better clinical outcomes. This is the first evidence assessing this in a group of high polyp detectors. The thresholds suggested may be utilised in endoscopy training, guiding surveillance recommendations, new technology and screening programmes.

Disclosure: N/A

OP178

ADENOMA DETECTION RATE LEVELS AND COLORECTAL CANCER RISK AFTER COLONOSCOPY

N. Pilonis¹, M. Bretthauer², M.F. Kaminski³, M. Kalager⁴, J. Regula⁵

¹The Maria Skłodowska-Curie Institute - Oncology Institute Warsaw, Poland, Department of Oncological Gastroenterology, Warsaw, Poland, ²University of Oslo, Department of Medicine, Gastrointestinal Endoscopy, Oslo, Norway, ³Maria Skłodowska-Curie Memorial Center and Institute of Oncology, Department of Gastroenterology, Warsaw, Poland, ⁴Oslo University Hospital, Oslo, Norway, ⁵Maria Skłodowska-Curie National Research Institute of Oncology and Centre of Postgraduate Medical Ed, Department of Gastroenterology, Warsaw, Poland

Contact E-Mail Address: nastazja@gmail.com

Introduction: Physician adenoma detection rate (ADR) is associated with colorectal cancer risk after screening colonoscopy (post-colonoscopy CRC). Quality assurance e.g., using computer-aided detection, are increasingly used to improve ADR. It is unknown if increasing ADR for physicians with already adequate performance is beneficial for CRC prevention.

Aims & Methods: To determine whether increasing ADR for physicians with already adequate performance reduces the risk of CRC incidence and mortality after screening colonoscopy. We analyzed 485,615 screening colonoscopies performed by 789 physicians in the Polish CRC screening program between 2000 and 2017 and used joinpoint regression analyses to identify trends between ADR levels and post-colonoscopy CRC incidence and mortality with follow-up until December 2022. We also compared CRC risk for individuals examined by physicians who did or did not improve performance by ADR levels

Results: During median follow-up of 10.2 years, we observed 1,873 CRCs and 474 CRC-related deaths. Median ADR was 21.8% (IQR 15.9-28.2%), maximum ADR was 63.0%. Joinpoint regression analyses showed strongest associations between ADR and CRC incidence for physicians with ADR's ≤26%, and weaker associations for physicians with ADR's >26%. Increasing ADR from the lowest level to a 26% threshold reduced post-colonoscopy CRC incidence by 42.7 per 100,000 person-years compared to 10.0 per 100,000 person-years for ADR increases from 26% to the maximum. For physicians with ADR of below 26% who increased ADR, post-colonoscopy CRC incidence was 31.8 (95%CI 29.5 to 34.3) per 100,000 person-years as compared to 40.7 (95%CI 37.8 to 43.8) for those who did not improve (Difference 8.9 per 100,000).

For physicians with ADR of above 26% who increased ADR, post-colonoscopy CRC incidence was 23.4 (95%CI 18.4 to 29.8) per 100,000 person-years as compared to 22.5 (95%CI 18.3 to 27.6) for those who did not improve (Difference 0.9 per 100,000). CRC mortality yielded similar results.

Conclusion: Higher ADRs are significantly associated with lower CRC risk, but associations are weak and may not be clinically relevant for patients examined by physicians with already adequate detection rates

Disclosure: None

OP179

WHICH PATIENTS REMAIN AT INCREASED RISK OF COLORECTAL CANCER AFTER FIRST SURVEILLANCE COLONOSCOPY AND NEED ONGOING SURVEILLANCE? A RETROSPECTIVE, COHORT ANALYSIS

E.C. Robbins¹, K. Wooldrage¹, A.J Cross¹

¹Imperial College London, Department of Surgery and Cancer, Cancer Screening and Prevention Research Group (CSPRG), London, United Kingdom

Contact E-Mail Address: e.robbs@imperial.ac.uk

Introduction: Patients deemed to remain at increased risk of colorectal cancer (CRC) following detection and removal of colorectal polyps are recommended to undergo surveillance by colonoscopy. Risk stratification to inform recommendations for the first surveillance colonoscopy, according to characteristics of baseline polyps, is well established.

However, the UK, European, and US post-polypectomy surveillance guidelines highlight the paucity of data to inform ongoing surveillance beyond the first surveillance colonoscopy.

Aims & Methods: Our aim was to identify which patient groups, defined by combinations of polyp findings at baseline and first surveillance, need ongoing surveillance and how many surveillance colonoscopies they might need. We performed a retrospective analysis of patients who underwent baseline colonoscopy with polypectomy at 17 UK hospitals, mostly from 2000 to 2010, and had ≥1 surveillance examinations. Cancer registration and death certificate data were collected through 2017. We examined patients in four groups defined by combinations of polyp findings at baseline and first surveillance: group 1 (low-risk findings at both baseline and first surveillance), group 2 (low-risk findings at baseline and high-risk findings at first surveillance), group 3 (high-risk findings at baseline and low-risk findings at first surveillance), and group 4 (high-risk findings at both baseline and first surveillance). High-risk findings included 2 premalignant polyps (PMPs: adenomas or serrated polyps) of which ≥1 was 'advanced' (adenoma ≥10mm or with high-grade dysplasia, or serrated polyp ≥10mm or with any dysplasia), ≥5 PMPs, or ≥1 non-pedunculated polyp ≥20mm, while all other findings were included as low-risk findings, as per the UK post-polypectomy surveillance guidelines. We examined CRC incidence after first surveillance, in the presence of a single surveillance examination, and after second surveillance, in the presence of ≥2 examinations. We compared incidence to that in the general population of England in 2007 using standardised incidence ratios (SIRs).

Results: After exclusions, 10,832 patients were available for analysis, of whom 6,746 (62%), 248 (2%), 3,437 (32%), and 401 (4%) were classified into group 1, 2, 3, and 4, respectively. Among each respective group, 3,581 (53%), 84 (34%), 1,478 (43%), and 119 (30%) had a single surveillance examination; remaining patients had ≥2 surveillance examinations. The median time from first surveillance to end of follow-up was 10.9 years, during which 158 patients were diagnosed with CRC. Compared to the general population, CRC incidence after first surveillance, with a single surveillance examination, was lower in group 1 (SIR 0.51, 95%CI 0.36-0.71), non-significantly different in group 2 (SIR 2.51, 95%CI 0.81-5.85) and group 3 (SIR 1.22, 95%CI 0.90-1.63), but higher in group 4 (SIR 2.84, 95%CI 1.30-5.39). After second surveillance, CRC incidence in group 4 was no longer higher than that in the general population (SIR 1.86, 95%CI 0.89-3.42).

Conclusion: In our cohort of patients undergoing post-polypectomy surveillance, high-risk polyp findings were uncommon at first surveillance, even among those with high-risk findings at baseline. Only those with high-risk findings at both baseline and first surveillance appear to have needed ongoing surveillance, with the second surveillance examination appearing sufficient to eliminate the excess CRC risk in these patients.

Disclosure: Nothing to disclose.

OP180

RETHINKING POST-COLONOSCOPY COLORECTAL CANCER RISK: ENDOSCOPIST PERFORMANCE VERSUS PRESENCE OF HIGH-RISK POLYPS

N.S. van Roermund^{1,2,3}, E. Dekker^{1,2,3}, M.E. van Leerdam^{4,5}, M.C. Spaander⁶, V.M.H. Coupé⁷, J.E. Ijspeert⁴

¹Amsterdam University Medical Center (AUMC), University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam Gastroenterology, Endocrinology & Metabolism, Amsterdam, Netherlands, ³Cancer Center Amsterdam, Amsterdam University Medical Center, Amsterdam, Netherlands, ⁴Netherlands Cancer Institute-Antoni van Leeuwenhoek, Gastrointestinal Oncology, Amsterdam, Netherlands, ⁵Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ⁶Erasmus MC University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁷Amsterdam University Medical Center (AUMC), Epidemiology and Data-science, Amsterdam, Netherlands

Contact E-Mail Address: n.vanroermund@amsterdamumc.nl

Introduction: At present, for the average risk population, colonoscopy surveillance intervals are based on previous detected and resected polyps in an individual. Although an inverse association between the endoscopist's adenoma detection rate (ADR) and the risk of developing post colonoscopy colorectal cancer (PCCRC) is widely recognized, performance measures of endoscopists are not taken into account when deciding on surveillance intervals.

This study aims to evaluate how the individual endoscopist's ADR compares to the presence of high-risk polyps when evaluating the risk of PC-CRC in the 3 years following a complete screening colonoscopy.

Aims & Methods: Data of all complete colonoscopies in which no CRC was found, performed within the Dutch fecal immunochemical test (FIT) based CRC population screening program between 2014 and 2020, were used for this study. Data were linked to the Dutch cancer registry. Individuals were categorized into having high-risk polyps or no/low risk polyps based on the 2020 ESGE post-polypectomy colonoscopy surveillance guideline. ADR was calculated per endoscopist. Risk of PCCRC, defined as any CRC diagnosed 6 months after the index colonoscopy, within 3 years was evaluated with shared frailty cox proportional hazard regression analysis in which ADR and presence of high-risk polyps were utilized as independent variables.

Secondary, endoscopists were categorized into three equal groups based on ADR (low/medium/high) to enable stratified analysis.

Results: In total 239.217 individuals were included of which 74.289 (31.1%) had high-risk polyps at baseline and 202 had PCCRC in the subsequent 3 years. Median ADR of the 441 endoscopists involved was 66.3% (IQR 61.4-69.9). Cumulative incidence of PCCRC was 2.66 (95%CI 2.21-3.11, table 1) per 10.000 person-years of follow-up in individuals with no or low-risk polyps and 2.54 (95%CI 1.92-3.15) in individuals with high-risk polyps. Presence of high-risk polyps was not associated with risk of PCCRC (HR 1.00; 95%CI 0.75-1.35), while ADR was associated (HR 0.94 per point increase in ADR; 95%CI 0.92-0.96).

The cumulative incidence of PCCRC was 3.68 (95%CI 2.74-4.62, table 1) per 10.000 person-years of follow-up for individuals with no or low-risk polyps that were treated by an endoscopist with low ADR, as compared to 1.69 (95%CI 0.89-2.50) for individuals with high-risk polyps treated by an endoscopist with high ADR (HR 2.11; 95%CI 1.21-3.65).

Individuals with high-risk polyps treated by an endoscopist with low ADR had the highest risk of PCCRC, while individuals with no or low-risk polyps treated by an endoscopist with high ADR had the lowest risk (HR 3.30; 95%CI 1.79-6.10).

	Overall	ADR Low	ADR high	
	PCCRC risk per 10.000 prs-y (95% CI)	PCCRC risk per 10.000 prs-y (95% CI)	PCCRC risk per 10.000 prs-y (95% CI)	HR* (95% CI)
No/low-risk polyp	2.66 (2.21-3.11)	3.68 (2.74-4.62)	1.16 (0.66-1.66)	3.17 (1.92-5.21)
High-risk polyp	2.54 (1.92-3.15)	4.18 (2.66-5.71)	1.69 (0.89-2.50)	2.11 (1.07-4.17)
	HR** (95% CI)	HR** (95% CI)	HR** (95% CI)	
	1.00 (0.75-1.35)	1.13 (0.73-1.77)	1.52 (0.80-2.89)	

Table 1: Cumulative incidence and stratified risk of ADR/presence of high-risk polyps on post colonoscopy colorectal cancer.

*= ADR high = reference, **= No or low-risk polyp = reference

Conclusion: We demonstrated that in the Dutch FIT-based CRC population screening program, the ADR of the endoscopist has a major impact on relative risk of PCCRC within 3 years after a complete colonoscopy, while the presence of high-risk polyps does not. This underscores the significant impact of quality of colonoscopy on the short-term development of PC-CRC and undermines the current surveillance guidelines that rely solely on polyp features.

Disclosure: Nothing to disclose.

OP181

PATIENT'S PER-PROCEDURAL COLONOSCOPY EXPERIENCE: HOW ACCURATE IS THE CLINICIAN'S ASSESSMENT?

Q.N. van Bokhorst¹, C.V. Geerlings¹, M. van der Vlugt^{1,2}, K.J. Nass³, P. Fockens^{1,2}, L.J. Neilson^{4,5}, C.J. Rees^{4,5}, E. Dekker^{1,2}

¹Amsterdam UMC, location VU Medical Center, Dept. of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Bergman Clinics, Dept. of Gastroenterology and Hepatology, Amsterdam, Netherlands, ³Rijnstate Hospital, Dept. of Internal Medicine, Arnhem, Netherlands, ⁴South Tyneside and Sunderland NHS Foundation Trust, Dept. of Gastroenterology, South Shields, United Kingdom, ⁵Population Health Sciences Institute Newcastle University, Newcastle Upon Tyne, United Kingdom

Contact E-Mail Address: q.vanbokhorst@amsterdamumc.nl

Introduction: Per-procedural patient comfort is one of the key performance measures for colonoscopy [1]. In daily practice, patient comfort is generally reported by clinicians using rating scales such as the Gloucester Comfort Scale (GCS) [2]. However, despite the widespread use of the GCS, insights regarding the extent to which clinician-reported GCS scores really represent the patient's experience are lacking. Therefore, we aimed to assess the level of agreement between clinician-reported GCS scores and the level of patient-reported discomfort and pain.

Aims & Methods: Consecutive patients undergoing colonoscopy for any indication at two Dutch endoscopy clinics were invited to complete the Newcastle ENDOPREM™, a validated measure of patient experience of gastrointestinal endoscopy [3], within 48 hours after colonoscopy. Colonoscopies were performed by gastroenterologists or supervised gastroenterologists in training. Per-procedural comfort from the clinician's perspective is routinely reported by either the endoscopy nurse or endoscopist using the GCS (1 to 5 scale). Per-procedural experience from the patient's perspective was reported in terms of both the level of discomfort and pain on a 1 (no discomfort/pain) to 5 (worst discomfort/pain imaginable) scale. Moderate to high discomfort scores were defined as scores ≥ 3 . Levels of agreement between clinician- and patient-reported scores were assessed using Cohen's kappa statistic. Regression analyses were used to identify factors associated with moderate to high discomfort and pain scores.

Results: Of 579 invited patients, 243 (42%) returned a completed questionnaire and fulfilled the inclusion criteria (signed informed consent, no

deep sedation [4]). Percentual agreement between GCS and patient-reported scores is displayed in Table 1. A GCS score ≥ 3 was reported for 18 (7%) patients. Discomfort and pain scores ≥ 3 were reported by 53 (22%) and 60 (25%) patients respectively. For these patients, GCS underestimated discomfort and pain levels as reported by patients in almost all cases (discomfort: 49/53 [92%], pain: 54/60 [90%]). The level of agreement between GCS and discomfort scores was minimal (Cohen's κ : 0.34), agreement between GCS and pain scores was weak (Cohen's κ : 0.47). Levels of agreement were better for sedated patients (asleep but with response to verbal or tactile stimulation, n = 125) compared to patients who were awake or slightly drowsy (n = 116) for both discomfort (Cohen's κ : 0.45 vs. 0.20) and pain (Cohen's κ : 0.45 vs. 0.38). Based on multivariable regression analyses, female gender, age <55 years and high procedural difficulty (as defined by the endoscopist) were associated with moderate to high patient-reported discomfort and pain scores.

Moreover, where patients reported that they were anxious about discomfort and pain, anxious about procedure results, had a negative bowel preparation experience, felt unsafe, felt embarrassed or where procedures were longer than expected, moderate to high discomfort and pain scores were more common (all p<0.05).

	Matching GCS score and patient-reported score, n (%)	GCS score lower than patient-reported score, n (%)	GCS score higher than patient-reported score
Discomfort	119 (49%)	72 (30%)	52 (21%)
Pain	133 (55%)	71 (29%)	39 (16%)

Conclusion: Clinician-reported GCS scores, used to indicate per-procedural patient comfort, underreport discomfort and pain as reported by patients. A validated experience tool also allows the definition of patient factors that may be associated with greater patient reported discomfort and pain at colonoscopy. These findings support the use of patient-reported comfort scores for accurate monitoring of patients' experience.

References: [1] Kaminski MF, Thomas-Gibson S, Bugajski M et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. *Endoscopy* 2017; 49: 378-397. DOI: 10.1055/s-0043-103411

[2] Ekkelenkamp VE, Dowler K, Valori RM et al. Patient comfort and quality in colonoscopy. *World J Gastroenterol* 2013; 19: 2355-2361. DOI: 10.3748/wjg.v19.i15.2355

[3] Neilson LJ, Sharp L, Patterson JM et al. The Newcastle ENDOPREM: a validated patient reported experience measure for gastrointestinal endoscopy. *BMJ Open Gastroenterol* 2021; 8. DOI: 10.1136/bmjgast-2021-000653

[4] Lee JK, Lee YJ, Cho JH et al. Updates on the Sedation for Gastrointestinal Endoscopy. *Clin Endosc* 2019; 52: 451-457. DOI: 10.5946/ce.2019.172

Disclosure: PF received research support from Boston Scientific and a consulting fee from Olympus and Cook Endoscopy. CR has received grant funding from ARC medical, Norgine, 3-D Matrix, Medtronic and Olympus medical. He was an expert witness for ARC medical and for Olympus medical. ED received a research grant from Fujifilm, a consulting fee for medical advice from Olympus, Fujifilm, GI Supply, PAION, Ambu and CPP-FAP and a speakers fee from Olympus, Roche, GI Supply, Norgine, Fujifilm and IPSEN.

Trends in hepatology: From diagnosis to treatment

10:00-11:00 / Lehar 2

OP182

LIPOFUSCINOSIS AS A NOVEL DISCRIMINATING FEATURE FOR DRUG-INDUCED LIVER INJURY VS. AUTOIMMUNE HEPATITIS

S. Weber¹, F. Erhardt¹, J. Neumann², J. Allgeier¹, D. Saka¹, N. Donga¹, C. Lange¹, A.L. Gerbes¹
¹LMU Klinikum, Department of Medicine II, Munich, Germany,
²LMU Klinikum, Institute of Pathology, Munich, Germany

Contact E-Mail Address: Julian.Allgeier@med.uni-muenchen.de

Introduction: Differentiating drug-induced liver injury (DILI) from autoimmune hepatitis (AIH) is a challenge in clinical practice¹⁻³. Liver biopsy is recommended in unclear cases¹, however available studies comparing histopathological patterns between DILI and AIH have major limitations due to lack of control groups or limited sample sizes^{4,5}.

Aims & Methods: We aimed to further identify typical histopathological features of DILI in comparison to AIH. Clinical and histopathological data of well-characterized 136 DILI and 43 AIH patients from our prospective cohort on patients with acute liver injury and potential drug-related cause were analysed. Logistic regression was performed to identify models that could differentiate both entities and predict adverse outcome.

Results: We identified high overlaps regarding histological patterns between DILI and AIH, leading to a low overall agreement between clinical and histopathological diagnosis of only 48.9%. Interface hepatitis, plasma cell infiltration and portal-intralobular infiltration was favouring AIH over DILI, however relevant proportions of DILI patients also presented with those features (interface hepatitis: 69.8% vs. 44.1%, p=0.003, plasma cells: 72.1% vs. 46.3%, p=0.003, portal-intralobular infiltration 51.2% vs. 29.2%, p=0.005). Interestingly, lipofuscinosis showed the strongest association with DILI diagnosis on univariate analysis (odds ratio [OR] 1.33, 95% confidence interval [CI] 1.17-1.50). A model comprised of interface hepatitis, cholestasis, lipofuscinosis, portal-intralobular inflammation and steatosis could differentiate DILI from AIH with an accuracy of 77.7% and a sensitivity as high as 94.1% (specificity 25.6%). Multivariate analysis also identified lipofuscinosis as a highly discriminatory feature (OR 8.05, Table 1). Prediction of adverse outcome (defined as death or need for liver transplantation [LT]) in DILI and AIH patients using only histopathological patterns was possible with an accuracy of 88.7% (specificity 97.0%, sensitivity 48.1%). Severe necrosis and ductular proliferation were associated with poor outcome (OR 5.48 and OR 5.00, respectively) while presence of eosinophilic cells and lipofuscinosis (OR 0.36 and OR 0.163, respectively) lowered the risk for death or LT significantly.

Logistic regression models including histopathological parameters discriminating DILI vs. AIH.			
	OR	95 % CI	p
Interface hepatitis	0.453	0.209-0.982	0.045*
Cholestasis	1.986	0.925-4.267	0.079
Lipofuscinosis	8.050	1.019-63.617	0.048*
Portal-intralobular inflammation	0.471	0.222-1.000	0.050*
Steatosis	2.784	0.881-8.801	0.081

Logistic regression models including histopathological parameters discriminating DILI vs. AIH.

Conclusion: We here present the largest prospectively collected cohort of DILI and AIH patients for whom histopathological analysis was performed. Interestingly, DILI and AIH showed highly similar histological patterns, neither interface hepatitis nor plasma cell infiltration could specifically differentiate AIH from DILI patients.

However, lipofuscinosis was identified as a novel distinctive feature for DILI with a high discriminatory power. Moreover, a model combining histological features could differentiate both entities with high sensitivity. Histological analysis was especially helpful for predicting severe outcome in DILI and AIH patients showing higher specificity when compared to traditional risk scores predicting acute liver failure in DILI⁶.

References:

- 1 European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Autoimmune hepatitis. *J Hepatol*. 2015; 63(4): 971-1004. doi:10.1016/j.jhep.2015.06.030.
- 2 Kullak-Ublick GA, Andrade RJ, Merz M, et al. Drug-induced liver injury: recent advances in diagnosis and risk assessment. *Gut*. 2017; 66(6): 1154-64. doi:10.1136/gutjnl-2016-313369.
- 3 Weber S, Benesic A, Rotter I, Gerbes AL. Early ALT response to corticosteroid treatment distinguishes idiosyncratic drug-induced liver injury from autoimmune hepatitis. *Liver Int*. 2019; 39(10): 1906-17. doi:10.1111/liv.14195.
- 4 Kleiner DE, Chalasani NP, Lee WM, et al. Hepatic histological findings in suspected drug-induced liver injury: systematic evaluation and clinical associations. *Hepatology*. 2014; 59(2): 661-70. doi:10.1002/hep.26709.
- 5 Suzuki A, Brunt EM, Kleiner DE, et al. The use of liver biopsy evaluation in discrimination of idiopathic autoimmune hepatitis versus drug-induced liver injury. *Hepatology*. 2011; 54(3): 931-9. doi:10.1002/hep.24481.
- 6 Andrade RJ, Robles-Diaz M. Diagnostic and prognostic assessment of suspected drug-induced liver injury in clinical practice. *Liver Int*. 2020; 40(1): 6-17. doi:10.1111/liv.14271.

Disclosure: Sabine Weber, Didem Saka, Nirali Donga and Alexander L. Gerbes received funding from TransBioLine (Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease; Grant Agreement ID: 821283). The TransBioLine project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 821283. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

OP183

INSIGHT FROM THE AUSTRIAN HEPATITIS D REGISTRY: INCREASING RESPONSE RATES TO BULEVIRTIDE-BASED REGIMENS DESPITE HIGH BURDEN OF CIRRHOSIS AND PORTAL HYPERTENSION

M. Schwarz¹, C. Schwarz^{1,2}, D.J.M. Bauer^{1,2}, M. Panzer³, M. Strasser⁴, S. Reiter⁵, L. Dorn⁶, A. Maieron⁶, A.R. Moschen⁵, E. Aigner⁴, M. Trauner¹, A.F. Stättermayer¹, M. Mandorfer¹, H. Zoller³, M. Gschwantler², T. Reiberger¹, M. Jachs¹

¹Medical University of Vienna, Department of Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria,

²Klinik Ottakring, Department of Internal Medicine IV, Vienna, Austria, ³Medical University of Innsbruck, Department of Internal Medicine I, Innsbruck, Austria, ⁴Paracelsus Medical University, First Department of Medicine, Salzburg, Austria, ⁵Johannes Kepler University, Department of Internal Medicine 2, Linz, Austria, ⁶Karl Landsteiner University of Health Sciences, University Hospital of St. Pölten, Internal Medicine II, Gastroenterology and Hepatology and Rheumatology, Sankt Pölten, Austria

Contact E-Mail Address: schwarz.medizin@gmail.com

Introduction: Chronic infection with the hepatitis D virus (HDV) may lead to rapid progression towards liver cirrhosis and portal hypertension. For this study, we characterized the cohort of Austrian HDV patients and their response to bulevirtide (BLV) treatment.

Aims & Methods: We included anti-HDV positive patients who visited one of six participating Austrian hepatology centers from 2020 onwards. At baseline (BL), demographic, clinical and laboratory data, endoscopy and imaging reports, liver stiffness measurement (LSM) and liver steatosis assessment (using controlled attenuation parameter, CAP) were recorded. If available, hepatic venous pressure gradient (HVPG) and histologic assessment of liver biopsies were included. In a subset of patients, single nucleotide polymorphisms (SNPs) in IL28B, PNPLA3, SERPINA1 and NTCP were assessed. Patients without BLV treatment were characterized at last contact. Patients who received treatment with BLV were evaluated for biochemical response (BR, defined by normalization of ALT), virological response (VR, negative HDV RNA PCR or ≥ 2 log decline in viral load), or combined response (CR, meeting both BR+VR) every 24 weeks (W24, W48, W72, W96).

Results: Overall, 84 anti-HDV positive patients were included (median age 45.5 years [IQR 37-56], 58.3% male, median BMI 25.0 [IQR 21.4-29.0]), of which 59 (70.2%) had detectable HDV RNA. Nine (10.7%) patients reported daily alcohol intake. Eleven (13.1%) patients were coinfecting with HIV and 17 (20.2%) had anti-HCV antibodies. A LSM ≥ 10 kPa was found in 36 (54.4% of 66) of patients and ≥ 25 kPa in 9 (13.6%).

Liver biopsy showed F4 fibrosis in 19 (52.8% of 36) of patients. Esophageal varices were found in 15/61 (15.4%) in endoscopy and 12/50 (19.4%) had signs of portal hypertension on imaging reports.

Median HVPG was 10 mmHg (IQR 6.75-15.5, n=28) and eleven (13.1%) patients were decompensated at baseline. Median MELD was 8 points (IQR 6-10). No polymorphisms were found regarding SERPINA1 or NTCP, while for PNPLA3 we found C/C n=15 (37.5%), C/G n=22 (55.0%) and G/G n=3 (7.5%); and for IL28B we found C/C n=17 [49.9%], C/T n=16 (43.2%) and T/T n=4 (10.8%).

Of 59 viremic patients, 50 were started on treatment with BLV (median treatment duration 17 [7.5-24] months). BR rates at W24, W48, and W96 were 27/46 (58.7%), 28/38 (73.7%), and 16/22 (72.7%). VR rates at M6, M12, and M24 were 15/46 (32.6%), 24/38 (63.2%), and 15/22 (68.2%). CR rates at M6, 12, and M24 were 10/46 (21.7%), 18/38 (47.4%), and 11/22 (50.0%). At W48 BLV treatment led to a decline of ALT ($p < 0.001$), HDV RNA ($p < 0.001$), and LSM ($p < 0.006$).

SNPs in either PNPLA3 or IL28B did not affect treatment outcomes. Ten patients who achieved clearance of HDV discontinued BLV, of which 4 relapsed and were restarted on BLV. Pegylated interferon alfa-2a was added to BLV treatment in 13 (26%) patients after a median of 10 (7-18) months. During follow-up, three (3.6%) patients – all without BLV treatment – were diagnosed with hepatocellular carcinoma and overall, five (6.0%) patients died, of which four deaths were liver-related.

Conclusion: Our Austrian HDV patient cohort showed a substantial burden of cirrhosis and signs of portal hypertension – still we observed high and steadily increasing rates of virologic and biochemical response to BLV treatment. Liver stiffness – as a surrogate of the risk for liver-related events – decreased significantly at W48.

Disclosure: M.P., M.Str., A.F.S., S.R., A.M., L.D., E.A. have nothing to disclose.

M.S. received travel support from MSD, Sandoz, BMS, AbbVie and Gilead; and speaking honoraria from BMS and Gilead.

C.S. received travel support from Gilead, AbbVie, Galápagos, and Gebro; speaking honoraria from AbbVie and Gilead; and payments for consulting from Gilead.

D.B. received travel support from Gilead and AbbVie; speaking honoraria from AbbVie and Siemens and grant support from Gilead and AbbVie.

A.M. received grant support from AbbVie and Gilead; speaking honoraria from AbbVie, Gilead, Janssen, Roche, Intercept, and MSD; consulting/advisory board fees from AbbVie, Gilead, Janssen, Roche, Intercept, Norgine, and MSD; and travel support from AbbVie, Gilead and Roche.

M.T. served as a speaker and/or consultant and/or advisory board mem-

ber for Albireo, BiomX, Falk, Boehringer Ingelheim, Bristol-Myers Squibb, Falk, Genfit, Gilead, Intercept, Janssen, MSD, Madrigal, Novartis, Phenex, Pliant, Regulus, and Shire, and received travel support from AbbVie, Falk, Gilead, and Intercept, as well as grants/research support from Albireo, Alnylam, Cymabay, Falk, Gilead, Intercept, MSD, Takeda, and UltraGenyx. He is also co-inventor of patents on the medical use of 24-norursodeoxycholic acid filed by the Medical Universities of Graz and Vienna.

M.M. served as a speaker and/or consultant and/or advisory board member for AbbVie, Collective Acumen, Echosens, Gilead, Takeda, and W. L. Gore & Associates and received travel support from AbbVie and Gilead.

H.Z. has received grant support and honoraria for lecturing and consulting fees from Vifor, the manufacturer of ferric carboxymaltose.

M.G. received grant support from Abbvie, Gilead, and MSD; speaking honoraria from Abbvie, Gilead, Janssen, Roche, Intercept, and MSD; consulting/advisory board fees from Abbvie, Gilead, Janssen, Roche, Intercept, Norgine, AstraZeneca, Falk, Shionogi, and MSD; and travel support from Abbvie and Gilead.

T.R. served as a speaker and/or consultant and/or advisory board member speaking honoraria from AbbVie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Roche, Siemens, and W. L. Gore & Associates and received travel support from AbbVie, Boehringer-Ingelheim, Gilead, and Roche as well as grants/research support from AbbVie, Boehringer-Ingelheim, Gilead, Intercept, MSD, Myr Pharmaceuticals, Philips Healthcare, Pliant, Siemens, and W. L. Gore & Associates.

M.J. served as a speaker and/or consultant for Gilead.

OP184

ASSOCIATION BETWEEN POSITIVE ANTI-MITOCHONDRIAL ANTIBODIES AND PRIMARY BILIARY CHOLANGITIS IN PATIENTS WITH NORMAL ALKALINE PHOSPHATASE LEVELS

E. Larrea¹, R. Gómez Rioja², M. Sanz de Pedro², L. Sancho San Martín¹, P. Castillo Grau¹, M. Romero Portales¹, A. García Sánchez¹, M. Abadía Barno¹, C. Amiama Roig¹, J. García-Samaniego Rey¹, J.C. Erdozain Sosa¹, P. Torrijos García¹, R. Gayoso Gayo¹, M. Serrés Gómez², A. Buño Soto², A. Oliveira Martín¹

¹La Paz University Hospital, Gastroenterology and Hepatology, Madrid, Spain, ²La Paz University Hospital, Clinical Analysis Department, Madrid, Spain

Contact E-Mail Address: larreaemily@gmail.com

Introduction: The current EASL and AASLD guidelines establish a risk of primary biliary cholangitis (PBC) development in patients with antimitochondrial antibodies (AMA) >1:40 and normal baseline alkaline phosphatase (ALP) of 16% after 5 years. However, this important data is based on a single retrospective study using questionnaires sent to responsible physicians, with only 66 patients.

Aims & Methods: Retrospective study of patients in our prospectively followed database with AMA >1:40 and normal baseline ALP. Analysis of the incidence of PBC development (elevated ALP on at least two occasions during follow-up along with elevated GGT) and associated risk factors. The date of the first AMA >1:40 was considered as the baseline. Patients with possible alternative causes of cholestasis, follow-up <2 years, and incomplete data were excluded.

Results: Since 2005, 559 patients were identified. 315 were excluded, mainly due to follow-up or incomplete data. In the 244 valid cases: mean age 64 years, 88.5% female, 10 visits, ALP 75.8 U/L, GGT 44.5 U/L, AMA titer 1:640, IgM 178 mg/dL. After a mean follow-up of 10.5 years, 84/244 developed PBC (34.4%; 95% CI: 28.8-40.6). Among them, 64/84 (76.2%) developed it in the first 3 years of follow-up. In the multivariate analysis using

Cox regression, baseline ALP values (>80 vs. ≤80 U/L; ULN 116), AST (≥34 vs. <34 U/L; ULN 34), and GGT (>40 vs. ≤40 U/L; ULN 40) were independently associated with the risk of PBC development, with an adjusted HR (95% CI) for age and gender of 2.45 (1.49-4.02, p<0.001), 1.97 (1.17-3.31, p=0.011), and 2.4 (1.28-4.51, p=0.006), respectively.

Conclusion: One-third of patients with AMA >1:40 and normal baseline ALP are susceptible to developing PBC after a 10-year follow-up. Baseline values of ALP, AST, and GGT are associated with this risk.

References:

1. Dahlqvist G, Gaouar F, Carrat F, Meurisse S, Chazouilleres O, Poupon R, et al. Large-scale characterization study of patients with antimitochondrial antibodies but non established primary biliary cholangitis. *Hepatology* 2017;65:152-63.
2. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019;69:394-19.
3. Sun C, Xiao X, Yan L, et al. Histologically proven AMA positive primary biliary cholangitis but normal serum alkaline phosphatase: Is alkaline phosphatase truly a surrogate marker?. *J Autoimmun*. 2019;99:33-8

Disclosure: Nothing to disclose.

OP185

SERUM AUTOTAXIN AND FIBROBLAST GROWTH FACTOR-19 ARE BIOMARKERS OF LINERIXIBAT TREATMENT RESPONSE IN PATIENTS WITH CHOLESTATIC PRURITUS ASSOCIATED WITH PRIMARY BILIARY CHOLANGITIS

S. Mukherjee¹, L. Casillas¹, B. Swift², J. Fettiplace³, S. Das⁴, M.M. McLaughlin¹, A.E. Kremer⁵

¹GSK, Collegeville, PA, United States of America, ²GSK, Durham, NC, United States of America, ³GSK, London, United Kingdom, ⁴GSK, Hyderabad, India, ⁵University of Zurich, Zurich, Switzerland

Contact E-Mail Address: andreas.kremer@usz.ch

Introduction: Cholestatic pruritus (itch) is common in primary biliary cholangitis (PBC) and is associated with significantly impaired quality of life. Lysophosphatidic acid (LPA) and bile acids may have a pathophysiological role in pruritus. Autotaxin (ATX) is the primary enzyme that produces LPA and is a surrogate for LPA levels. ATX activity correlates with itch intensity in PBC. Linerixibat is a minimally absorbed, small-molecule ileal bile acid transporter inhibitor that improves pruritus and reduces systemic bile acid levels, ATX, and fibroblast growth factor-19 (FGF-19), a downstream effector of farnesoid X receptor activation and regulator of bile acid biosynthesis.¹

Here, we analyze the association between itch response and changes in ATX and FGF-19 biomarker levels following linerixibat treatment.

Aims & Methods: The Phase 2b, placebo-controlled, dose-ranging GLIMMER study (NCT02966834) enrolled 147 adult patients with PBC and pruritus.¹ Patients were randomized to receive linerixibat or placebo for 12 weeks (Weeks 4-16).

Patients reported itch on a 0-10 numerical rating scale. As patient numbers were too low to analyze biomarkers in individual dose groups, the two twice daily (BID) dose groups, 40 and 90 mg BID, which showed a greater response in pharmacodynamic biomarkers compared to once daily dosing, were combined. Serum ATX and FGF-19 levels were compared post hoc in patients receiving linerixibat 40/90 mg BID or placebo, at baseline versus Week 16, in itch responders and non-responders.

Responder analysis from individual dose groups is not shown. Itch responders were defined as patients with a monthly itch score improvement of ≥2 at Week 16 compared with baseline.

Results: Patients treated with linerixibat 40/90 mg BID (n=45), or placebo (n=36) were included; baseline demographics have been reported previously.¹ Itch responders in the 40/90 mg BID group, but not in the placebo group, had greater reductions in serum ATX at Week 16 compared with baseline. In linerixibat-treated patients, ATX levels at Week 16 were reduced in itch responders compared to non-responders, and in comparison with placebo. Similarly, FGF-19 reduction was associated with itch response in patients receiving linerixibat 40/90mg BID compared with placebo.

Conclusion: Serum ATX and FGF-19 may function as biomarkers of itch response to linerixibat treatment. Reductions in these biomarkers are associated with clinical response in patients with PBC and pruritus.

Funding: GSK (201000).

Encore statement: This abstract was originally presented as poster 4574-C at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting on November 13, 2023; this encore is presented on behalf of the original authors with their permission.

Disclosure: SM, LC, BS and MMM are employees of, and hold stocks/shares in, GSK. JF is a former employee of, and holds stocks/shares in, GSK. SD is an employee of GSK. AEK reports grant/research support from Intercept Pharmaceuticals and Gilead, and speaker/consultancy fees from AbbVie, Bristol Myers Squibb, CymaBay Therapeutics, Eisai, Escient, Falk, Gilead, GSK, Intercept Pharmaceuticals, Janssen, Lilly, Mirum, MSD, Vifor, and Zambon.

OP186

ULTRASOUND DERIVED FAT FRACTION (UDFF) AND AUTOMATED POINT SHEAR WAVE ELASTOGRAPHY (AUTO PSWE) ACCURATELY ASSESS LIVER STEATOSIS AND FIBROSIS RISK - A PROSPECTIVE COMPARATIVE STUDY

N. Dominik¹, L. Nixdorf², M. Schwarz¹, B. Hofer¹, L. Hartl¹, L. Balcar¹, G. Semmler¹, L. Fritz¹, L. Hauptmann³, M. Jachs¹, J. Jedamzik², B. Mozayani⁴, L. Gensthaler², D.M. Felsenreich², M. Trauner¹, F. Langer², M. Mandorfer¹, T. Reiberger¹, D. Bauer^{1,5}, G. Prager²

¹Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ²Medical University of Vienna, Division of General Surgery and Metabolic- and Bariatric Surgery, Department of Surgery, Vienna, Austria, ³Medical University of Vienna, Division of Cardiology, Department of Medicine II, Vienna, Austria, ⁴Medical University of Vienna, Clinical Institute of Pathology, Vienna, Austria, ⁵Klinik Ottakring, Department of Internal Medicine IV, Vienna, Austria

Contact E-Mail Address: nina.dominik@meduniwien.ac.at

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) can lead to fibrosis and cirrhosis. Assessment of fibrosis and steatosis via vibration-controlled transient elastography (VCTE) and controlled attenuation parameter (CAP) requires a dedicated device and time to obtain ≥ 10 reliable measurements.

Automated point shear wave elastography (Auto pSWE) allows for the collection of 15 ARFI based liver stiffness measurements (LSM) together with ultrasound derived fat fraction (UDFF) based steatosis assessment in a single acquisition.

Aims & Methods: This prospective study included patients who underwent liver biopsy - mostly during bariatric surgery - at the Vienna General hospital between 11/2021 and 12/2023. Paired Auto pSWE/UDFF and VCTE/CAP assessments of LSM and hepatic steatosis were performed within ± 90 days of liver biopsy.

Results: Among 134 patients (65% women, mean age: 42.6 $\pm$ 13.3 years) with a high prevalence of obesity (mean BMI: 42.7 $\pm$ 10.4), MASLD was the most common aetiology (88%). Median histologic fibrosis and steatosis

stages were F0 and S2. 68 (51%) and 36 (27%) patients had moderate steatosis ($\geq$ S2) and significant fibrosis ($\geq$ F2) on biopsy, respectively.

With Auto pSWE, 1x15 acquisitions were as accurate as using 5x15 acquisitions. Similarly, one UDFF measurement was as accurate as 5 UDFF measurements. Auto pSWE ($\geq$ F2, AUC=0.58; $\geq$ F3, AUC=0.96; F4, AUC=0.97) and VCTE ($\geq$ F2, AUC=0.60; F3, AUC=0.92; F4, AUC=0.93) showed moderate diagnostic accuracy for lower fibrosis stages and high diagnostic accuracy for higher fibrosis stages. There was no statistical difference between the diagnostic accuracy of UDFF ($\geq$ S1, AUC=0.79; $\geq$ S2, AUC=0.78; S3, AUC=0.67) and CAP ($\geq$ S1, AUC=0.80; $\geq$ S2, AUC=0.78; S3, AUC=0.66). The median time for a single VCTE measurement was 2.47 minutes (IQR 1.44-5.38), while a single composite acquisition of Auto pSWE/UDFF takes eight seconds and is integrated into standard ultrasound devices.

Conclusion: Auto pSWE and UDFF represent accurate non-invasive tests for liver fibrosis and steatosis assessment in MASLD patients, including those with severe obesity. Importantly, 15 individual LSM can be acquired using Auto pSWE simultaneously with UDFF in a single acquisition, saving valuable time without the need for a dedicated device.

Disclosure: N.D. none to declare.

L.N. none declared.

M.S. none declared.

B.H. none declared.

L.H. none to declare.

L.F. none to declare.

M.J. has served as a speaker and consultant for Gilead Sciences and has received travel support from Gilead Sciences.

G.S. received travel support from Gilead.

Lo.H. none to declare.

L.F. none to declare.

L.B. none to declare

D.M.F. has no conflict of interest.

M.T. received speaker fees from BMS, Falk Foundation, Gilead, Intercept, Janssen, Madrigal, MSD, and Roche; he advised for AbbVie, Albireo, BiomX, Boehringer Ingelheim, Cymabay, Falk Pharma GmbH, Genfit, Gilead, Hightide, Intercept, Janssen, MSD, Novartis, Phenex, Pliant, Rectify, Regulus, Siemens, and Shire. He further received travel support from AbbVie, Falk, Gilead, Intercept, and Janssen and research grants from Albireo, Alnylam, Cymabay, Falk, Gilead, Intercept, MSD, Takeda and UltraGenyx. He is also a co-inventor of patents on the medical use of norUDCA filed by the Medical Universities of Graz and Vienna.

J.J. none declared.

B.M. received a speaker fee from Astellas Pharma

L.G. none declared.

F.B.L. none declared.

M.M. none declared.

G.P. none declared.

T.R. received grant support from AbbVie, Boehringer-Ingelheim, Gilead, Gore, Intercept, MSD, Myr Pharmaceuticals, Philips Healthcare, Pliant, and Siemens; speaking honoraria from AbbVie, Gilead, Gore, Intercept, Roche, MSD; consulting/advisory board fee from AbbVie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from AbbVie, Boehringer-Ingelheim, Gilead and Roche.

D.B. received grant support from Gilead; travel support from Siemens, AbbVie, and Gilead; and speaking honoraria from AbbVie, Röntgen Eisenstadt and Siemens.

OP187

WITHDRAWAL OF BIOLOGICAL TREATMENT AND SMALL MOLECULES IN IBD PATIENTS DIAGNOSED WITH CANCER: REAL WORLD EVIDENCE FROM ENEIDA REGISTRY OF GETECCU

M. Calvo^{1,2,3,4}, I. Ordás^{5,6,4}, J. Llaó⁷, I. Pérez-Martínez⁸, F. Mesonero Gismero⁹, M.L. De Castro Parga^{10,11}, N. Marcos Carrasco¹², M. Vela¹³, C.J. Gargallo-Puyuelo¹⁴, L. Miguel García¹, C. Roig Ramos¹⁵, M.D. Martín-Arranz¹⁶, C. Rivas¹⁷, J. Guardiola¹⁸, L. Arias-García¹⁹, L. Bernal²⁰, F. Bermejo²¹, S. González Padilla²², L. Márquez-Mosquera²³, A. Elorza^{24,25}, M.F. García Sepulcre²⁶, S. Izquierdo²⁷, A. Minguez Sabater²⁸, M. Quñones²⁹, M. Barreiro de Acosta³⁰, C. Taxonera Samso³¹, Á. Ponferrada-Díaz³², E. Iglesias-Flores³³, M. Piqueras Cano³⁴, E. Sesé³⁵, D. Busquets Casals³⁶, F. Bas-Cutrina^{37,38}, E. Betoré Glaria³⁹, A.Z. Gómez Moreno⁴⁰, L. Ramos Lopez⁴¹, P. Pérez-Galindo⁴², A. López-García⁴³, A. Royo⁴⁴, J. Castro-Poceiro⁴⁵, A.J. Lucendo⁴⁶, P. Robledo Andrés⁴⁷, L. Bujanda Fernández de Piérola^{48,4,49}, J.M. Huguet⁵⁰, C. Cepero⁵¹, L. Hernández⁵², M. Van Domselaar^{53,54}, M.T. Diz-Lois Palomares⁵⁵, E. Domenech Morral^{56,4}, J. P. Gisbert^{*1,2,3,4}, M. Chaparro^{*1,2,3,4}, On behalf of CRABS IBD study Group, *co-last authors

¹Hospital Universitario de la Princesa, Madrid, Spain, ²Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain,

³Universidad Autónoma de Madrid, Madrid, Spain, ⁴Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain, ⁵Hospital Clinic of Barcelona, Gastroenterology, Barcelona, Spain, ⁶IDIBAPS, Barcelona, Spain, ⁷Gastroenterology Department, Hospital Universitari Germans Trias i Pujol, Badalona, Badalona, Spain,

⁸Hospital Universitario Central de Asturias, Oviedo, Spain, ⁹Hospital Ramon y Cajal, Gastroenterology, Madrid, Spain, ¹⁰Hospital Alvaro cunqueiro. CHUVI., Vigo, Spain, ¹¹Fundación biomédica Galicia Sur, Galicia, Spain, ¹²Hospital Universitario Nuestra Señora de Candelaria, Tenerife, Spain, ¹³H. Universitario Ntra. Señora Candelaria, Tenerife, Spain, ¹⁴Hospital Lozano Blesa, Zaragoza, Spain, ¹⁵Hospital de la Santa Creu i Sant Pau, IBD Unit, Department of Gastroenterology, Barcelona, Spain, ¹⁶Hospital La Paz, Gastroenterology, Madrid, Spain, ¹⁷Hospital Universitario Marqués de Valdecilla e IDIVAL, Gastroenterology, Santander, Spain, ¹⁸Hospital Universitario de Bellvitge, Gastroenterology, L'Hospitalet de Llobregat (Barcelona), Spain, ¹⁹Hospital de Burgos, Burgos, Spain, ²⁰Hospital General Universitario Dr Balmis, Alicante, Spain, ²¹H Fuenlabrada, Gastroenterology, Fuenlabrada, Spain, ²²Hospital Clínico Universitario, Valencia, Spain, ²³Servei de Digestiu, Hospital del Mar, Barcelona.IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain, ²⁴Hospital Universitario Galdakao-Usansolo, Galdakao, Spain, ²⁵Instituto De Investigación Sanitario Biobizkaia, Vicaya, Spain, ²⁶Hospital General Universitario, Elche, Spain, ²⁷Servicio de Aparato Digestivo. Hospital Clínico Universitario de Valladolid., Valladolid, Spain, ²⁸Hospital Universitario Politécnico la Fe, Valencia, Spain, ²⁹Hospital Universitario Fundación Alcorcón, Madrid, Spain, ³⁰University Hospital of Santiago, Gastroenterology, Santiago de Compostela, Spain, ³¹Hospital Clinico, Madrid, Spain, ³²Hospital Infanta Leonor, Madrid, Spain, ³³Hospital Universitario Reina Sofía, Córdoba, Spain. Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Digestive, Córdoba, Spain, ³⁴Hospital Consorci Terrassa, Terrassa, Spain, ³⁵Hospital

Universitario Arnau de Vilanova, Lleida, Spain, ³⁶Hospital de Girona Dr. J. Trueta, ICO GERONA, Gastroenterology, Girona, Spain, ³⁷Hospital Universitari de Bellvitge - IDIBELL, Endoscopy Unit. Digestive Diseases Department., L'Hospitalet de Llobregat, Barcelona, Catalonia., Spain, ³⁸Universitat de Barcelona, Barcelona, Spain, ³⁹Hospital Universitario San Jorge de Huesca, Huesca, Spain, ⁴⁰Hospital General Universitario de Ciudad Real., Ciudad Real, Spain, ⁴¹Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, ⁴²Complejo Hospitalario Universitario de Pontevedra, Pontevedra, Spain, ⁴³Hospital Universitario Infanta Sofía, Madrid, Spain, ⁴⁴Hospital Universitario Miguel Servet, Zaragoza, Spain, ⁴⁵Hospital Sant Joan Despí Moisès Broggi, Barcelona, Spain, ⁴⁶Hospital General de Tomelloso, Dept. de Gastroenterology, Madrid, Spain, ⁴⁷Hospital Universitario de Cáceres, Cáceres, Spain, ⁴⁸Biogipuzkoa Health Research Institute, Department of Gastroenterology, San Sebastián, Spain, ⁴⁹Universidad del País Vasco (UPV/EHU), Bilbao, Spain, ⁵⁰Hospital General Universitario de Valencia, Valencia, Spain, ⁵¹Hospital Joan XXIII de Tarragona, Tarragona, Spain, ⁵²Hospital Santos Reyes, Aranda de Duero, Spain, ⁵³Hospital Universitario de Torrejón, Madrid, Spain, ⁵⁴Universidad Francisco de Vitoria, Madrid, Spain, ⁵⁵Hospital Universitario A Coruña, A Coruña, Spain, ⁵⁶Gastroenterology Department, Hospital Universitari Germans Trias i Pujol, Badalona. CIBEREHD. Universitat Autònoma de Barcelona, Barcelona, Spain

Contact E-Mail Address: mariocsoto@gmail.com

Introduction: While biologic agents and small molecules have revolutionized inflammatory bowel disease (IBD) treatment, concerns persist regarding their usage in patients with a history of malignancy due to potential impact on cancer development or recurrence.

There remains a notable gap in understanding their utilization in this setting, especially concerning newer agents like ustekinumab, vedolizumab, and small molecules.

Aims & Methods: We aimed to study clinicians' views on using biologic therapy in IBD patients with extracolonic cancer, focusing on whether to continue or stop treatment and analysing factors influencing their decisions. We also aimed to describe clinical characteristics of this group of patients.

IBD patients under biologics or small molecules at the time of cancer diagnosis in ENEIDA registry, a prospectively maintained database from GETECCU, were included. Variables included demographic and clinical data, biologic drugs received, and start/discontinuation dates.

Additional information on oncologic history and IBD treatment changes after cancer diagnosis were collected directly from investigators. Main variable was the discontinuation of biologics/small molecules due to the diagnosis of cancer. Logistic regression analysis was used to identify factors associated with biologics/small molecules discontinuation due to cancer diagnosis.

Results: 1,386 patients with extra-colonic malignancies receiving biologics or small molecules were identified from ENEIDA registry. From this cohort, we identified 467 patients that were under biological treatment at the time of cancer diagnosis. Demographic and clinical characteristics revealed a median age at IBD diagnosis of 38 years, with 61% males. Crohn's disease accounted for 71% of cases. The most common cancer types were non-melanoma skin cancer (26%) and haematological neoplasms (14%), followed by nefrourotelial cancers, breast cancer, prostate cancer and melanoma. Vedolizumab, ustekinumab and small molecules represented 15% of the patient cohort, while anti-TNF were the most prevalent biologics at cancer diagnosis. Before cancer diagnosis, 40% patients had received previous biological drugs, while 60% were receiving their first biologic therapy.

Clinical decisions post-cancer diagnosis included discontinuing biological treatment (56%) and no changes in treatment (44%) as described in table 1. Multivariate analysis showed significant differences in discontinuing biologic therapy depending on neoplasm origin and type of biologic treatment. While patients with non-melanoma skin cancer were more likely to continue with biologic therapy after having an extracolonic cancer diagnosis, other types of cancer led clinicians to discontinue treatment more frequently (Table 2). We also observed that the probability of maintaining biological treatment was significantly higher in patients receiving ustekinumab and vedolizumab compared with anti-TNF agents. No significant differences were found based on the type of IBD, number of biologic treatments received before cancer diagnosis, sex and age at cancer diagnosis.

Biological treatment when diagnosed with cancer	No changes in biological treatment	Discontinuation of biological treatment
Anti-TNF agents	158 (39.8%)	239 (60.2%)
Ustekinumab	20 (66.7%)	10 (33.3%)
Vedolizumab	24 (68.6%)	11 (31.4%)
Type of extracolonic cancer		
Non melanoma skin cancer	105 (86.8%)	16 (13.2%)
Hematologic neoplasms	8 (12.3%)	57 (87.7%)
Nefro-urologic neoplasms	20 (43.5%)	26 (56.5%)
Breast cancer	7 (15.9%)	37 (84.1%)
Prostate cancer	9 (28.1%)	23 (71.9%)
Melanoma	4 (23.5%)	13 (76.5%)
Other cancers	51 (35.9%)	91 (56.3%)
Probability of discontinuation biological treatment	OR (95% CI)	
Depending on biological treatment		
Ustekinumab vs Anti-TNF	0.24 (0.10-0.60)	
Vedolizumab vs Anti-TNF	0.18 (0.08-0.41)	
Depending on cancer origin		
Hematologic neoplasms vs. non-melanoma skin cancer	59.9 (23.2-154.9)	
Breast cancer vs. non-melanoma skin cancer	33.1 (12.4-88.2)	
Melanoma vs. non-melanoma skin cancer	22.2 (6.1-80.8)	
Prostate cancer vs. non-melanoma skin cancer	18.7 (7.1-48.9)	
Other cancers vs. non-melanoma skin cancer	13.3 (7.0-25.3)	
Nefro-urologic neoplasms vs. non-melanoma skin cancer	11.1 (4.9-25.2)	

Table 1.

Conclusion: In real life, over 50% of IBD patients discontinue biologics/ small molecules when extracolonic cancer is diagnosed. The likelihood of treatment discontinuation is higher with anti-TNF agents than with more recently approved drugs (such as vedolizumab or ustekinumab). The type of cancer has great impact on the decision of treatment discontinuation. Management of IBD in patients diagnosed with cancer remains a challenge.

Disclosure: Nothing to disclose.

OP188

HISTOPATHOLOGICAL FEATURES IN THE RESECTION MARGINS FOR PREDICTION OF EARLY POSTOPERATIVE ENDOSCOPIC RECURRENCE IN CROHN'S DISEASE: A PROSPECTIVE, MULTICENTER COHORT STUDY

M.T. Bak¹, A.H.A.G. Ooms², L. Oudijk³, E.M. Beelen¹, J. van der Bilt^{4,5}, M. Romberg-Camps⁶, G. Dijkstra⁷, M. Duijvestein⁸, S. van der Marel⁹, L. Stassen¹⁰, J.P. Maljaars¹¹, C.J. Buskens⁵, J.F. Lange¹², S. Jansen¹³, B. Jharap¹⁴, C. Horjus Talabur Horje¹⁵, F. Van Schaik¹⁶, R. West¹⁷, N.K. de Boer¹⁸, C.J. van der Woude¹, O. van Ruler^{19,20}, M. Doukas³, A.C. de Vries¹,
On behalf of the RAP-CD Study Group, the Dutch Initiative on Crohn and Colitis (ICC) & Dutch Initiative on Crohn and Colitis–Surgery (ICC-S)

¹Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Pathan BV, Pathology, Rotterdam, Netherlands, ³Erasmus University Medical Center, Pathology, Rotterdam, Netherlands, ⁴Flevoziekenhuis, Surgery, Almere, Netherlands, ⁵Academic University Medical Center, Surgery, Amsterdam, Netherlands, ⁶Zuyderland Medical Center, CO-MIK, Sittard-Geleen, Netherlands, ⁷University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ⁸Radboudumc, Gastroenterology and Hepatology, Nijmegen, Netherlands, ⁹Haaglanden Medical Center, Gastroenterology and Hepatology, Den Haag, Netherlands, ¹⁰Maastricht University Medical Center, Surgery, Maastricht, Netherlands, ¹¹Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ¹²University Medical Center Groningen, Surgery, Groningen, Netherlands, ¹³Reinier de Graaf Group, Gastroenterology and Hepatology, Delft, Netherlands, ¹⁴Meander Medical Center, Gastroenterology and Hepatology, Amersfoort, Netherlands, ¹⁵Rijnstate Hospital, Gastroenterology and Hepatology, Arnhem, Netherlands, ¹⁶University Medical Centre Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands, ¹⁷Sint Franciscus Gasthuis, Gastroenterology and Hepatology, Rotterdam, Netherlands, ¹⁸Academic University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁹IJsselland Hospital, Surgery, Capell a/d IJssel, Netherlands, ²⁰Erasmus University Medical Center, Surgery, Rotterdam, Netherlands

Contact E-Mail Address: m.bak@erasmusmc.nl

Introduction: Several histopathological features have been identified as risk factors for postoperative recurrence (POR) in Crohn's disease (CD) including active inflammation, submucosal plexitis and transmural inflammation.

Furthermore, granulomas and myenteric plexitis have been included as risk factor for POR in the current international guidelines. However, these factors have been identified in predominantly retrospective and older studies without adjustment for clinical risk factors.

Aims & Methods: This study aimed to assess the association between these histopathological features and early postoperative endoscopic recurrence in a large prospective, multicenter cohort study.

CD patients (≥16 years) scheduled for ileocolic (re-)resection (ICR) and those who underwent an ileocolonoscopy at 6 months following ICR were included. Primary outcome of the study was early postoperative endoscopic recurrence (ePOR)(modified Rutgeerts' score ≥ i2b at 6 months).

Proposed histopathological risk factors for postoperative recurrence were assessed in the ileal and colonic resection margins by expert pathologists blinded for clinical risk factors and outcome. Uni- and multivariable logistic regression was performed to explore the association of the histopathological features.

Results: In total, 293 patients (60% female; median age 33.3 years; primary resection 79%) underwent an ICR after a median disease duration of 5.2 (IQR 0.9–12.4). ePOR was observed in 37% of patients. At ICR, active smoking at surgery was reported in 22%. Isolated ileal location (64%) and stricturing disease (53%) were the most common disease location and behaviour at surgery. Postoperative prophylactic medication was initiated in 30% of patients (immunomodulator [IMM] 25%, anti-TNF agent with or without IMM 56%, vedolizumab 5% and ustekinumab 15%).

Active inflammation, transmural inflammation, myenteric plexitis, submucosal plexitis and granulomas were reported at the ileal resection margin in 29%, 9%, 14%, 16% and 4%.

At the colonic resection margin, the above mentioned parameters were reported in 9%, 2%, 7%, 8% and 3%. Univariate analyses identified associations for moderate to severe inflammation at the ileal (OR 2.3; 95%CI 1.3-4.0) and colonic resection margin (OR 3.7; 95%CI 1.3-10.3), submucosal plexitis at the ileal resection margin (OR 1.9; 95%CI 1.0-3.5) and transmural inflammation at the colonic resection margin (OR 10.7; 95%CI 1.3-90.5) (Table 1).

	Univariable analysis OR (95% CI; p-value)	Multivariable analysis* aOR (95% CI; p-value)
<u>Ileal resection margin</u>		
Active inflammation		
None	REF (-; -)	REF (-; -)
Mild	1.8 (0.7 - 4.5; 0.23)	1.7 (0.5 - 5.9; 0.38)
Moderate to severe	2.3 (1.3 - 4.0; <0.01)	1.7 (0.9 - 4.1; 0.27)
Transmural inflammation	1.6 (0.7 - 3.7; 0.21)	1.0 (0.3 - 3.4; 0.96)
Plexitis	1.3 (0.8 - 2.2; 0.26)	-
Myenteric plexitis	1.3 (0.7 - 2.6; 0.38)	-
Submucosal plexitis	1.9 (1.0 - 3.5; 0.05)	1.1 (0.4 - 3.0; 0.81)
Granulomas	0.7 (0.2 - 2.5; 0.63)	-
<u>Colonic resection margin</u>		
Active inflammation		
None	REF (-; -)	REF (-; -)
Mild	0.9 (0.2 - 3.8; 0.92)	-
Moderate to severe	3.7 (1.3 - 10.3; 0.01)	4.6 (1.1 - 19.5; 0.04)
Transmural inflammation	10.7 (1.3 - 90.5; 0.03)	2.4 (0.2 - 32.5; 0.51)
Plexitis	0.9 (0.7 - 1.2; 0.47)	-
Myenteric plexitis	1.3 (0.5 - 3.3; 0.59)	-
Submucosal plexitis	2.2 (0.9 - 5.1; 0.07)	1.4 (0.4 - 4.4; 0.61)
Granulomas	0.7 (0.4 - 1.3; 0.33)	-
<u>Clinical variables</u>		
Male sex	1.3 (0.8 - 2.1; 0.33)	-
Age at surgery (in years)	1.0 (0.9 - 1.0; 0.76)	-
Disease duration (in years)	1.0 (0.9 - 1.0; 0.17)	1.0 (1.0 - 1.0; 0.76)
Preoperative exposure to biologicals	1.1 (0.7 - 1.8; 0.69)	-
Active smoking	2.3 (1.3 - 4.1; <0.01)	2.8 (1.4 - 5.6; <0.01)
Prior ileocolic resection	0.9 (0.5 - 1.6; 0.63)	-
<u>Disease localization at surgery</u>		
Ileal disease	REF (-; -)	REF (-; -)
Ileocolic disease	0.3 (0.2 - 0.6; <0.01)	0.3 (0.2 - 0.7; <0.01)
<u>Penetrating disease behaviour at surgery</u>		
Perianal fistula at surgery	1.1 (0.7 - 1.8; 0.70)	-
Length of resection specimen (in cm)	1.0 (0.4 - 2.7; 0.98)	-
Length of resection specimen (in cm)	1.0 (1.0 - 1.0; 0.05)	1.0 (1.0 - 1.0; 0.41)
Postoperative prophylactic medication	0.4 (0.2 - 0.6; <0.01)	0.3 (0.2 - 0.7; <0.01)

Table 1.

Abbreviations. OR = odds ratio; aOR = adjusted odds ratio; REF = reference. * variables with a p-value <0.25 in univariable analysis were entered in multivariable analysis

In multivariable analysis, moderate to severe inflammation (aOR 4.6; 95%CI 1.1-19.5) at the colonic resection margin was associated with ePOR. No other histopathological features were significantly associated with ePOR in multivariable analysis. Active smoking was identified as risk

factor (aOR 2.8; 95%CI 1.4-5.6), whereas postoperative prophylactic medication (aOR 0.3; 95%CI 0.2-0.7) and ileocolic disease at time of surgery (aOR 0.3; 95%CI 0.2-0.7) were identified as protective factors.

Conclusion: In this study, a predictive value of histopathological features in ICR specimens of CD patients for early POR has not been confirmed, with the exception of moderate to severe inflammation at the colonic resection margin.

Therefore, there is a strong need for new biomarkers to adequately predict POR in patients with Crohn's disease.

Disclosure: Nothing to disclose.

OP189

COMPARISON OF NORMAL VS INTENSIFIED VACCINE REGIMENS AGAINST PNEUMOCOCCUS IN CD PATIENTS UNDER BIOTHERAPY: A PROSPECTIVE, MULTICENTER, RANDOMIZED, OPEN-LABEL PNEUMOMICI STUDY

X. Roblin¹, S. Nancey², X. Hebuterne³, N. Arab³, G. Savoye⁴, S. Vienne⁵, G. Bouguen⁶, M. Fumery⁷, A.-E. Berger⁸, M. Barrau⁹, S. Paul¹⁰

¹University of St. Etienne Dept. de Gastroenterologie, Saint Etienne, France, ²University Hospital, Dept. de Gastroenterologie, Pierre Benite, France, ³Hospital Archet 2, Nice, Department of gastroenterology and clinical nutrition, Nice, France, ⁴Hopiaux de Rouen, Hépatogastro-Entérologie, Rouen, France, ⁵CHRU de Caen HGE 19^e étage, Caen Cedex, France, ⁶CHU Pontchaillou, Service des Maladies de l'Appareil Digestif, Rennes, France, ⁷Amiens University Hospital, Gastroenterology department, Amiens, France, ⁸University Hospital Of Saint Etienne, Immunology, Saint Etienne, France, ⁹Centre Hospitalo-universitaire De Saint Etienne, Saint Etienne, France, ¹⁰Hôpital Nord, Immunology, Saint Etienne, France

Contact E-Mail Address: xavier.robilin@chu-st-etienne.fr

Introduction: Pneumococcal vaccination is essential in IBD patients. However, its efficacy in patients on immunosuppressive or anti-TNF therapy is much lower than in the normal population (45% vs 80%). Vaccine regimen recommendations vary according to the degree of immunodepression.

The aim of our study was to identify an optimal vaccination strategy for immunocompromised IBD patients treated with anti-TNF, vedolizumab and/or IS.

Aims & Methods: This is a prospective, multicenter, randomized study comparing two vaccine regimens: intensified vaccine strategy (Prevenar13®/Prevenar13®/PSV-23® (or Pneumovax as a replacement for PSV-23) vs. normal strategy (Prevenar13®/PSV-23® (or Pneumovax as a replacement for PSV-23), (randomization 1: 1) on vaccine immunogenicity measured by antibody titer against at least 9 of the 13 pneumococcal serotypes contained in Prevenar13®.

Any patient with confirmed IBD under biotherapy (anti TNF with or without immunosuppressive drugs or Vedolizumab) and in clinical remission (HBI <4 for CD and partial Mayo Score <3 for UC) was included. Vaccination and vaccine monitoring were carried out by the vaccination center of each center, with adverse events reported at each visit (8 for 36 months of follow-up), and ELISA and OPA serotype assays systematically collected and clinical activity was reported by the gastroenterologist at the same time. Correlate of protection in adults using serology testing was classically defined as at least 9 out of 13. Serotypes > 1 µg/mL. For functional testing of antibodies using the Opsonophagocytic assays, we apply the well-defined 4 times increase of titer between pre and post-vaccination against at least 70% of serotypes. *ClinicalTrials.gov Identifier: NCT02255227*

Results: 51 patients in the normal vaccination arm and 53 in the intensified vaccination arm were included (mean age: 42.9 years, male: 63%, CD: 68%, active smoking: 21%, duration of IBD: 10.2 years, 98% IBD inactive). Around 88% of patients were under anti-TNF monotherapy (28% on combotherapy) and 12% under vedolizumab. Serology criteria for good responders at M5 were 57.5% for the intensified regimen vs 25.6% for the standard regimen (RR: 2.25 (1.26;4.00), $p = 0.003$). For OPA correlate of protection, vaccine response was significantly greater in the intensified arm at all-time points: M5 (96% vs. 89%), M12 (76 vs. 58%) and M36 (68% vs. 36.8%). In multivariate analysis, two factors reduced vaccine response: anti-TNF use (RR: 6.84; CI95: 1.01-46.1; $p=0.048$) and CD type (RR: 9.48; CI95: 2.74-32.8; $p:0.0004$).

The tolerability of the vaccine regimens was comparable throughout follow-up. In terms of IBD activity, percentage of clinical relapse was similar during follow-up (16.8% under the intensified regimen versus 25% under the normal regimen ($p:NS$)).

Conclusion: In IBD on biotherapy and/or IS, the intensified pneumococcal vaccine regimen (2 injections of Prevenar followed by one of Pneumo 23) is significantly more immunogenic than a standard regimen, especially when using functional correlate of protection. The duration of the response is also greater in this intensified arm.

Disclosure: Nothing to disclose.

OP190

DISEASE BURDEN CATEGORIZATION AND MEDICATION USE IN POST-OPERATIVE CROHN'S DISEASE: A POPULATION-BASED COHORT STUDY

A. Poulsen^{1,2}, M.D. Wewer³, J. Rasmussen⁴, H. Søre Riis Jespersen¹, E. Surnacheva¹, D. Christiansen⁴, E. Holm Hansen⁵, R. Nordestgaard³, V. Lin⁶, K. Anne Verlo³, N. Aydemir⁴, F. Pachler², P.D. Ovesen², K. Fuglsang⁷, C. Filtenborg Brandt⁷, L.T. Sørensen¹, P.-M. Krarup¹, I. Gogenur⁶, J. Burisch³, J. Seidelin²

¹Copenhagen University Hospital, Bispebjerg, Digestive Disease Center, København N, Denmark, ²Copenhagen University Hospital, Herlev and Gentofte, Gastroenterology and Hepatology, Herlev, Denmark, ³Copenhagen University Hospital - Amager and Hvidovre, Gastroint-Medical Section, Hvidovre, Denmark, ⁴Zealand University Hospital, Medical Gastroenterology, Koege, Denmark, ⁵North Zealand University Hospital, Gastroenterology, Hilleroed, Denmark, ⁶Zealand University Hospital, Center for Surgical Science, Koege, Denmark, ⁷University Hospital of Copenhagen, Rigshospitalet, Intestinal Failure and Liver Diseases, Copenhagen, Denmark

Contact E-Mail Address: anjapoulsen@live.dk

Introduction: Resection rates for Crohn's disease (CD) have decreased over time, while re-resection rates have remained stable at about one-third in historic cohorts. Medical treatment has been shown to influence the course of the disease.

Aims & Methods: We aimed to assess the impact of disease burden categorization on medication use and risk factors. This cohort study encompassed all CD patients undergoing primary intestinal resection in Eastern Denmark from 2010 to 2020 (46% of the Danish population, $n=2,730,000$).

We isolated all patients with five years follow up and divided them into three groups based on post-operative disease burden: high (one or more resections after the initial resection), intermediate (recurrence without need for resection), and low (no recurrence within five years). Disease recurrence was defined based on colonoscopy (SES-CD ≥ 3 , Rutgeerts score

≥ 2), inflammation or stenosis on imaging (MRI, CTA, IUS), fecal calprotectin ≥ 250 mg/kg, starting corticosteroids or re-resection due to disease activity. Medication was classified by potency, with each patient assigned to only one category (no therapy<corticosteroids<immunomodulators<biologics). We used nonparametric statistics and the Kruskal-Wallis test to compare outcomes across groups.

Results: Primary resection was performed on 631 patients due to disease activity. Patients were categorized into burden groups: high burden ($n=59$), intermediate ($n=287$), and low ($n=170$). The median age at diagnosis was 28.2 years (range: 21.6-43.9), with no significant differences between the three disease burden groups ($p=0.069$). Age at primary resection differed across groups: 38 years (25-53) for high burden, 32 (24-45) for intermediate, and 36 (27-47) for low burden ($p=0.019$). Smoking rates were highest in the high burden group (47%) versus intermediate (37%) and low (27%) ($p=0.010$).

Pre-resection medical consumption was similar across the three burden groups ($p=0.2$). Postoperatively, the high burden group used more biologics (54%) compared to the low burden group (16%). Additionally, 57% of the low burden group remained recurrence-free and unmedicated for five years (Table 1).

In the high burden group, no patients received prophylactic biologics, compared to 8% in the intermediate and low burden groups ($p=0.001$). Disease location varied: colon resections were most common in the high burden group (31%), and small bowel disease, including ileocecal resections, predominated in the low burden group (47%) ($p<0.001$). Strictures were more common in the intermediate and low burden groups, while luminal disease was mostly seen in the high-risk group ($p=0.046$) (Table 1)

	High N = 59	Intermediate N = 287	Low N = 170	p-value
After resection, biological therapy	32 (54%)	108 (38%)	28 (16%)	<0.001
After resection, immunomodulators	8 (14%)	106 (37%)	45 (26%)	
After resection, no therapy	14 (24%)	56 (20%)	97 (57%)	
L1 ileal	20 (34%)	119 (41%)	80 (47%)	<0.001
L2 colonic	18 (31%)	19 (6.6%)	12 (7.1%)	
L3 ileocolonic	21 (36%)	149 (52%)	78 (46%)	
B1 non-stricturing, non-penetrating	19 (32%)	43 (15%)	23 (14%)	0.046
B2 stricturing	32 (54%)	179 (62%)	108 (64%)	
B3 penetrating	8 (14%)	64 (22%)	38 (22%)	

Table 1. Medical characteristics and Montreal classification.

Conclusion: High burden patients relied more on biologics, while half of the low burden patients stayed recurrence-free unmedicated for five years, suggesting tailored treatments could improve post-resection CD management.

Disclosure: Nothing to disclose.

LONG-TERM FOLLOW-UP OF PROTDILAT STUDY; LONG-PROTDILAT. SELF-EXPANDABLE METAL STENTS (SEMS) VERSUS ENDOSCOPIC BALLOON DILATION (EBD) FOR THE TREATMENT OF STRICTURES IN CROHN'S DISEASE: AN OPEN-LABEL, MULTICENTRE, RANDOMISED TRIAL

P. Ruiz-Ramírez^{1,2}, C. Loras Alastruey^{3,4}, J.B. Gornals⁵, M.M. Boscá Watts⁶, E. Brunet⁷, E. Iglesias-Flores⁸, J. Barrio Andrés⁹, B. Sicilia Aladrén¹⁰, C. Dueñas Sadornil¹¹, J.R. Foruny¹², M.D. Martín-Arranz¹³, D. Busquets Casals¹⁴, E. Cerrillo Bataller¹⁵, N. García Morales¹⁶, D. Monfort Miquel¹⁷, F. Pérez-Roldán¹⁸, E. Pijoan Comas¹⁹, B. González-Suárez²⁰, J. Reyes Moreno²¹, G. Torres-Vicente²², E. Maristany Bosch²³, V. Sanchiz²⁴, J. Guardiola²⁵, M. Esteve Comas^{4,26}

¹Hospital Universitari Mútua Terrassa, Gastroenterology department, Terrassa, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, CIBERehd, Madrid, Spain, ³Hospital Universitari Mútua Terrassa, Gastroenterology, Sant Cugat del Vallès, Spain, ⁴Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, CIBERehd, Madrid, Spain, ⁵Hospital Universitari De Bellvitge, Bellvitge Biomedical Research Institute (idibell), Barcelona, Spain, ⁶Hospital Clínico Universitario de Valencia, Valencia, Spain, ⁷Parc Tauli, Digestive, Sabadell, Spain, ⁸Hospital Universitario Reina Sofía, Digestive, Córdoba, Spain, ⁹Rio Hortega University Hospital, Valladolid, Spain, ¹⁰H Universitario de Burgos, Gastroenterology, Burgos, Spain, ¹¹Hospital San Pedro de Alcántara, Gastroenterology department, Cáceres, Spain, ¹²Hospital Universitario Ramón y Cajal, Madrid, Spain, ¹³Hospital Universitario La Paz, Madrid, Spain, ¹⁴H. de Girona Dr. J. Trueta/ICO Gerona, Gastroenterology, Girona, Spain, ¹⁵Hospital Universitario y Politécnico La Fe, Gastroenterology Department, Valencia, Spain, ¹⁶Xerencia Xestion Integrada de Vigo- SERGAS, Gastroenterology, Vigo, Spain, ¹⁷H. Consorci de Terrassa, Terrassa, Spain, ¹⁸Hospital General Mancha Centro, Gastroenterology, Alcazar de San Juan, Spain, ¹⁹Clínica Girona, Girona, Spain, ²⁰Hospital Clinic, Barcelona, Spain, ²¹Hospital Comarcal Inca Dept. de Gastroenterología, Gastroenterology, Palma Mallorca, Spain, ²²Hospital Arnau de Vilanova, Digestive Diseases, Lerida, Spain, ²³Hospital Universitari de Bellvitge, Gastroenterology Department, L'Hospitalet de Llobregat, Spain, ²⁴Hospital Clinico de Valencia, Valencia, Spain, ²⁵Hospital Universitario de Bellvitge, Gastroenterology, L'Hospital de Llobregat (Barcelona), Spain, ²⁶Gastroenterology, Hospital Universitari Mutua Terrassa, Barcelona, Spain

Contact E-Mail Address: pau89rr@gmail.com

Introduction: The PROTDILAT study (Loras et al. Lancet Gastroenterol Hepatol. 2022) at 1-year follow-up showed greater efficacy of EBD vs SEMS for the treatment of short strictures in CD.

However, long term efficacy of endoscopic treatment is still debated, especially for EBD.

Aims & Methods: Aims: To assess the long-term evolution of patients included in PROTDILAT study.

1. Percentage of patients free of surgery;
2. Factors related to surgery;
3. Need for endoscopic retreatments;
4. Effectiveness related to the type of initial endoscopic treatment (EBD vs SEMS);
5. Complications related to endoscopic or surgical treatment.

Methods: Retrospective study based on PROTDILAT trial database (patients with CD, obstructive symptoms, with stenosis <10cm). Data on medical, endoscopic and surgical treatment and smoking habits were collected. The effectiveness of endoscopic treatment is defined by the percentage of patients free of surgery and endoscopic retreatment at the end of follow-up.

Results: Information available on 80/80 patients (39 SEMS, 41 EBD), 39 women, age (median): 45y (IQR: 38-55); median stricture length 3.4cm (IQR: 2-5.5), 42.5% being anastomotic. Thirty-one percent (25/80) of patients required surgical resection [(median time to surgery 30.61 months (6.35-55.24)). Factors associated to surgery: non-intensification of therapy (HR 0.26 (0.10-0.68)), treatment with EBD exclusively (HR 0.22 (0.08-0.58)) (with respect to treatment with EBD + SEMS) and number of stents (HR 2.31 (1.10-4.84)). Of the 55 patients free of surgery, during the entire follow-up (median 84 months (74.7-84.0)), a median of 2 endoscopic procedures (1-3) were performed: EBD in 45 cases (80.0%) and SEMS in 26 cases (46%). Thirty-eight-point seventy-five percent (31/80 patients) did not require neither surgery nor endoscopic retreatment during the follow-up. The long-term effectiveness of endoscopic treatment was 45% for SEMS and 57.6% for EBD (p=0.374). The complications related to endoscopic or surgical treatment were 8.75% (7/80) versus 36% (9/25) respectively (p=0.002). As for the severity of complications (AGREE/CLAVIEN-DINDO ≥ III), it was observed that surgical treatment presented more severe complications than endoscopic treatment (Endoscopic vs surgical treatment: 38% (3/8) vs 84% (10/12), p=0.011).

Conclusion: Endoscopic treatment (predominantly EBD) avoids surgery in most cases, requiring a low number of endoscopic treatments in the long-term. Patients at higher risk for surgery are those with a greater number of endoscopic treatments that include SEMS and EBD. On the contrary, protective factors are non-intensification of therapy and having been treated exclusively with EBD. Although there are no significant differences in the long effectiveness between SEMS and EBD, a trend for a better outcome is observed for EBD. To highlight a significant higher rate of complications observed in surgical treatment compared to endoscopic treatment.

References: Loras et al. Lancet Gastroenterol Hepatol. 2022

Disclosure: No conflict of Interest.

IBD: New horizons in medical treatment - Part 2

11:30-12:30 / Strauss 2

OP192

EFFICACY AND SAFETY OF MIRIKIZUMAB THERAPY IN PEDIATRIC PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 2 SHINE-1 STUDY

J.L. Kaplan¹, A. Bousvaros², D. Turner³, M.C. Dubinsky⁴, W. J. Komocsar⁵, A. Larkin⁵, J. Johns⁵, X. Zhang⁵, W. Crandall⁵, V. Arora⁵, K. Todd⁵, J. Hyams⁶

¹Massachusetts General for Children, Boston, United States of America, ²Boston Children's Hospital, Boston, United States of America, ³Shaare Zedek Medical Center, Pediatric GI, Jerusalem, Israel, ⁴Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ⁵Eli Lilly and Company, Indianapolis, United States of America, ⁶Connecticut Children's Medical Center, GI, Hartford, United States of America

Contact E-Mail Address: marla.dubinsky@mssm.edu

Introduction: Mirikizumab is a humanized immunoglobulin G4 monoclonal antibody against the p19 subunit of interleukin-23, a key inflammatory mediator in ulcerative colitis (UC). Here we report efficacy and safety in pediatric patients with moderate to severe UC from the Phase 2 SHINE-1 study (NCT04004611) following 52 weeks of mirikizumab treatment.

Aims & Methods: Patients aged 2 to <18 years with active UC who had an inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressants, or biologic therapies, or had corticosteroid-dependent colitis, were included in the study. Patients weighing >40 kg received an induction dose of 300 mg via intravenous infusion; patients weighing ≤40 kg received 5 or 10 mg/kg via intravenous infusion at weeks 0, 4, and 8. At week 12, patients were assessed for clinical response using the Modified Mayo Score. Responders entered the maintenance period and received subcutaneous doses of mirikizumab at 200 mg (>40 kg), 100 mg (>20 kg to ≤40 kg), or 50 mg (≤20 kg) once every 4 weeks, with the last patient visit at week 52.

Results: All patients (N=26) completed induction through week 12, and 73.1% (N=19) completed through week 52. At week 12, 69.2% (18/26) were Modified Mayo Score responders; at week 52, 55.6% (10/18) of responders were in clinical and endoscopic remission. Clinical response, remission, and endoscopic remission rates were consistent with LUCENT Phase 3 UC adult studies.

The safety profile of mirikizumab was consistent with the safety profile in LUCENT adults. Three serious adverse events (11.5%) were reported: non-infective appendicitis, UC flare, and pseudarthrosis. The UC flare resulted in study discontinuation.

Conclusion: Mirikizumab demonstrated an acceptable safety profile, and similar clinical response, clinical remission, and endoscopic remission compared to LUCENT adults. These results are the foundation of the pivotal Phase 3 pediatric SHINE-2 study.

Disclosure: **J. L. Kaplan** has nothing to disclose; **D. Turner** received consulting fees from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Pfizer, Prometheus Biosciences, Takeda, Galapagos, and Sorriso Pharmaceuticals; and research funding from: AbbVie, Ferring Pharmaceuticals, Janssen, Pfizer, and Takeda; **A. Bousvaros** has received research support from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, BUHLMANN Diagnostics, Eli Lilly and Company, Janssen, ProCise Diagnostics, and Takeda; was a consultant for: Best Doctors, Eli Lilly and Company, Fresenius Kabi, and Takeda; and has received honoraria and royalties from: Boston University and UptoDate; **M. Dubinsky** has received honoraria as a consultant for: AbbVie, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Com-

pany, F. Hoffmann-La Roche, Genentech, Gilead Sciences, Janssen, Pfizer, Prometheus Therapeutics and Diagnostics, Takeda, and UCB Pharma; has been contracted for research by: AbbVie, Janssen, Pfizer, and Prometheus Biosciences; has stock interest in: Trellus Health; and has received licensing fees from: Takeda; **W. J. Komocsar**, **A. Larkin**, **J. Johns**, **X. Zhang**, **W. Crandall**, **V. Arora**, and **K. Todd** are employees and shareholders of: Eli Lilly and Company; **J. S. Hyams** is on an advisory board for: AbbVie, Eli Lilly and Company, Janssen, and Pfizer; and has been a consultant to: Boehringer Ingelheim, Bristol Myers Squibb, and Takeda.

OP193

GUSELKUMAB BINDING TO CD64⁺ IL-23-PRODUCING MYELOID CELLS ENHANCES POTENCY FOR NEUTRALIZING IL-23 SIGNALING

R. Atreya¹, J. Allegretti², M.T. Abreu³, A. Hart⁴, H. Li⁴, T. Freeman⁴, E. Lacy⁴, M. DuPrie⁴, P. Bao⁵, T. Smets⁶, J. Wertheimer⁴, I. Sarabia⁵, K. Kohler⁵, A. Fourie⁵, K. Sachen⁵

¹Erlangen University Hospital, Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Medicine 1, Erlangen, Germany, ²Brigham and Women's Hospital, Harvard Medical School, Division of Gastroenterology, Hepatology and Endoscopy, Department of Medicine, Boston, United States of America, ³University of Miami, Leonard M. Miller School of Medicine, Miami, United States of America, ⁴Janssen Research & Development, LLC, Spring House, United States of America, ⁵Janssen Research & Development, LLC, San Diego, United States of America, ⁶Janssen Research & Development, LLC, Beerse, Belgium

Contact E-Mail Address: ksachen@its.jnj.com

Introduction: The efficacy of IL-23 blockade has implicated IL-23 in the pathogenesis of inflammatory bowel disease (IBD) and myeloid cells that express FcγRI (CD64) have been identified as the primary cellular source of IL-23 in inflamed IBD gut tissue [1, 2]. Guselkumab (GUS), risankizumab (RZB), and mirikizumab (MIRI) are monoclonal antibodies (mAbs) specifically directed against the IL-23p19 subunit. GUS is a fully human IgG1 mAb, RZB is a humanized IgG1 mAb, and MIRI is a humanized IgG4 mAb. Guselkumab has a native Fc domain while RZB and MIRI contain mutations in the Fc domain that diminish binding to FcγRs.

Aims & Methods: Here, we evaluated CD64 and IL-23 transcript expression in IBD patient gut biopsies, binding of GUS, RZB, and MIRI to IL-23 and CD64, and their potency for neutralization of recombinant or endogenous, locally produced, IL-23 in *in vitro* assays. *IL23A*, *IL12B*, and *FCGR1A* (CD64) expression was analyzed from bulk and single-cell RNA sequencing datasets. IL-23 binding affinity was evaluated using a kinetic exclusion assay. Binding of GUS, RZB, and MIRI to CD64 was assessed in cells with recombinant expression of CD64. Potency for inhibition of recombinant IL-23 was evaluated by impact on IL-23-induced phosphorylation of signal transducer and activator of transcription 3 (pSTAT3) in human peripheral blood mononuclear cells. Potency for inhibition of endogenous, locally produced IL-23 was determined in a co-culture of THP-1 (a CD64⁺ monocyte cell line activated to produce IL-23) and an IL-23 reporter cell line (measuring biologically active IL-23).

Results: Analysis of bulk and single cell RNA sequencing datasets showed that *FCGR1A*, *IL23A*, and *IL12B* were significantly increased in inflamed versus non-inflamed IBD gut biopsies, and that *IL23A* was predominantly expressed by *FCGR1A*-expressing myeloid cells. GUS, RZB, and MIRI displayed single-digit picomolar binding affinity for IL-23. GUS demonstrated binding to CD64, while no binding was observed for RZB or MIRI. GUS, RZB, and MIRI demonstrated comparable potency for inhibition of signaling by recombinant IL-23 in human PBMCs.

However, in a co-culture of IL-23–producing CD64⁺ THP-1 cells with an IL-23–responsive reporter cell line, GUS demonstrated enhanced potency compared to RZB and MIRI for inhibition of IL-23 signaling.

Conclusion: Our transcriptomic analysis supported previous observations of CD64⁺ myeloid cells as a key source of IL-23 production in inflamed IBD gut tissue. GUS binding to CD64 on IL-23–producing cells likely contributed to the enhanced functional potency of GUS compared to RZB and MIRI for inhibition of IL-23 signaling in the co-culture assay. These *in vitro* data support a hypothesis for optimal localization of GUS in inflamed tissues where CD64⁺ IL-23–producing myeloid cells are increased and in proximity to IL-23–responsive lymphoid cells, enabling GUS to more potentially neutralize IL-23 at its source of production.

References: 1. Chapuy, L., et al., *IL-12 and Mucosal CD14⁺ Monocyte-Like Cells Induce IL-8 in Colonic Memory CD4⁺ T Cells of Patients With Ulcerative Colitis but not Crohn's Disease*. *J Crohns Colitis*, 2020. **14**(1): p. 79-95.
2. Chapuy, L., et al., *Two distinct colonic CD14(+) subsets characterized by single-cell RNA profiling in Crohn's disease*. *Mucosal Immunol*, 2019. **12**(3): p. 703-719.

Disclosure: RA served as a paid or unpaid consultant for or received honoraria from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr. Falk Pharma, Ferring, Fresenius Kabi, Galapagos, Gilead, GSK, InDex Pharmaceuticals, Janssen, Kiniksa Pharmaceuticals, Merk Sharp & Dohme, Novartis, Pfizer, Roche, Samsung Bioepis, Stellic, sterna biologicals, Takeda, and Tillotts.

JRA served as a consultant for Abbvie, Ferring, Finch, Iterative Scopes, Janssen, Merck, Pfizer, Roivant, Seres Therapeutics, and Roivant Adiso; served as a speaker for Abbvie, Bristol Myer Squibb, and Janssen; and received research support from Janssen, Merck, and Pfizer.

MTA is a consultant or served on advisory boards for AbbVie, Arena Pharmaceuticals Inc. (now Pfizer), Bristol Myers Squibb, Celsius Therapeutics, Lilly, Gilead, Janssen Pharmaceuticals, Janssen Global Services, Pfizer, Prometheus Biosciences, and UCB; and received fees for lecturing from Alimentiv, Janssen Pharmaceuticals, Prime, and WebMD Global LLC.

AH, HI, TF, EL, MD, PB, TS, JW, IS, KK, AF and KS are employees of Janssen Research & Development, LLC and may hold stock in Johnson & Johnson.

OP194

LONG-TERM EFFICACY AND SAFETY OF TULISOKIBART IN PATIENTS WITH ULCERATIVE COLITIS (UC): RESULTS FROM THE OPEN-LABEL EXTENSION PERIOD OF THE PHASE 2 ARTEMIS-UC STUDY

C. Ma¹, S. Hoque², M.P. Sparrow³, J.K. Anderson⁴, M. Yen⁴, B. Dong⁴, B.G. Feagan⁵, B.E. Sands⁶
¹University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada, ²Barts Health NHS Trust, Department of Gastroenterology, London, United Kingdom, ³Monash University and Alfred Health, Department of Gastroenterology, Melbourne, Australia, ⁴Merck & Co., Inc., Rahway, United States of America, ⁵Western University, Departments of Medicine, Epidemiology, and Biostatistics, Ontario, Canada, ⁶Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America

Contact E-Mail Address: christopher.ma@ucalgary.ca

Introduction: Tumor necrosis factor–like cytokine 1A (TL1A) is a regulator of inflammation and fibrosis in inflammatory bowel disease. Tulisokibart, an anti-TL1A monoclonal antibody, demonstrated efficacy without clinically meaningful safety findings vs placebo after a 12-week induction

period in adults with moderately to severely active UC in the phase 2 ARTEMIS-UC study.¹ We report long-term efficacy and safety of tulisokibart among cohort 1 induction responders from the open-label extension (OLE) period of ARTEMIS-UC.

Aims & Methods: ARTEMIS-UC was a phase 2, multicenter, double-blind, placebo-controlled study of tulisokibart in patients with moderately to severely active UC. Cohort 1 enrolled patients regardless of genetic-based diagnostic test (Dx) status whereas cohort 2 enrolled only Dx-positive patients. Patients were randomized to receive intravenous (IV) tulisokibart 1000 mg on day 1 and 500 mg at weeks 2, 6, and 10 or placebo; after the 12-week induction period, all participants had the option to continue in the OLE period.

Participants were classified as induction responders (defined as reduction of ≥ 2 points and $\geq 30\%$ in modified Mayo score from baseline, accompanied by a reduction ≥ 1 in rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1 at week 12) or induction nonresponders. Cohort 1 induction responders in the tulisokibart group were randomized (stratified by Dx status) to receive open-label IV tulisokibart 100 mg or 250 mg every 4 weeks at week 14 until week 170.

We report data from cohort 1 through week 50 of the OLE period: clinical and endoscopic efficacy outcomes and biomarkers through week 50 are reported for cohort 1 induction responders from the tulisokibart group whereas safety through week 50 are reported for cohort 1 induction responders from both the tulisokibart group and the placebo group. Descriptive statistics were used to summarize observed data.

Results: 47 of 68 tulisokibart-treated patients in cohort 1 were induction responders and were randomized to receive tulisokibart 250 mg (n = 25) or 100 mg (n = 22). Improvements in clinical, endoscopic, and biomarker outcomes observed with tulisokibart were generally maintained through week 50 in both dose groups (Table).

	Week 12 Tulisokibart Induction (n = 68)	Week 50 Tulisokibart 100 mg (n = 22)	Week 50 Tulisokibart 250 mg (n = 25)
Clinical remission, ^a %	26	32	48
Endoscopic improvement, ^b %	37	36	48
Clinical response, ^c %	66	59	68
Symptomatic remission, ^d %	19	23	32
Histologic-endoscopic mucosal improvement, ^e %	n = 65 31	n = 15 47	n = 20 50
High-sensitivity C-reactive protein fold change from baseline, geometric LS mean (95% CI)	n = 65 0.56 (0.48–0.66)	n = 17 0.51 (0.22–1.19)	n = 24 0.56 (0.26–1.19)
Fecal calprotectin fold change from baseline, geometric LS mean (95% CI)	n = 54 0.21 (0.16–0.27)	n = 13 0.28 (0.09–0.88)	n = 17 0.27 (0.10–0.77)

LS least squares; mMS, 3-component modified Mayo score.
^aClinical remission per mMS was defined as endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than baseline.
^bEndoscopic improvement was defined as endoscopy subscore ≤ 1 with no friability.
^cClinical response per mMS was defined as reduction from baseline ≥ 2 points and $\geq 30\%$ in mMS, accompanied by a reduction ≥ 1 in rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1 .
^dSymptomatic remission was defined as stool frequency subscore of 0 and rectal bleeding subscore of 0.
^eHistologic-endoscopic mucosal improvement was defined as Geboes score ≤ 3.1 and endoscopy subscore ≤ 1 .

Table. Clinical, endoscopic, and biomarker outcomes at week 12 in the cohort 1 tulisokibart group and at week 50 among cohort 1 induction responders in the tulisokibart group.

However, at week 50, a greater proportion of patients achieved clinical and endoscopic outcomes with tulisokibart 250 mg vs 100 mg. In the safety population, (tulisokibart 250 mg, n = 35; 100 mg, n = 30), through week 50, AEs occurred in 63% and 77% of patients receiving tulisokibart 250 mg

and 100 mg, respectively; most were mild to moderate in severity. Serious AEs occurred in 1 patient (3%) and two patients (7%) in the tulisokibart 250 mg and 100 mg groups, respectively.

Conclusion: At week 50, maintenance of treatment effect was generally observed in cohort 1 induction responders in the tulisokibart group. A trend for higher efficacy with tulisokibart 250 mg vs 100 mg maintenance treatment was observed at week 50. Tulisokibart was well tolerated with no identified safety signals. Larger trials are needed to confirm these findings.

References: 1. Sands B, et al. *J Crohns Colitis*. 2023;17 (Supplement_1): i56-i59.

Disclosure: CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Pendopharm, Pfizer, Prometheus Biosciences Inc., Roche, Sanofi, and Takeda; speaker's fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, Bristol Myers Squibb, Ferring, Fresenius Kabi, Janssen, Pendopharm, Pfizer, and Takeda; royalties from Springer Publishing; and research support from Ferring and Pfizer.

SH has received advisory fees from Eli Lilly and Tilotts.

MPS has received educational grants or research support from Gilead and Celltrion, speakers fees from Janssen, AbbVie, Ferring, Takeda, Pfizer, Shire, Celltrion, Eli-Lilly and Dr. Falk Pharma, and has served on advisory boards for Janssen, Takeda, Pfizer, Celgene, AbbVie, MSD, Emerge Health, Gilead, BMS, Celltrion, and Eli-Lilly.

JKA, MY, and BD are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

BGF is a consultant for AbbVie, AbolierIS, AgomAB Therapeutics, Alliantera, Amgen, AnaptysBio, Applied Molecular Transport Inc., Arena Pharma, Atomwise, Avoro Capital Advisors, BioJamp, Biora Therapeutics, Boehringer Ingelheim, Boxer, Bristol Myers Squibb/Celgene, Celsius Therapeutics, Connect BioPharma, Cytokine, Disc Medicine, Duality, EcoR1 Capital, Equillium, Ermius, First Wave, First Word Group, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, GlaxoSmithKline, Gossamer Pharma, Hinge Bio, Hot Spot Therapeutics, Imhotex, Immunic Therapeutics, InDex Pharmaceuticals, JAKAcademy, Janssen, Japan Tobacco Inc., Kaleido Biosciences, Landos Biopharma, Leadiant, L.E.K. Consulting, Lenczner Slaght, LifeSci Capital, Lilly, Lument AB, Millennium, MiroBio, Morgan Lewis, Morphic Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Play to Know AG, Prometheus Therapeutics and Diagnostics, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared Ltd., Viatrix, Ysios, Ysopia, and Zealand Pharma; on the Speakers' Bureau for AbbVie, Janssen, and Takeda; and on advisory boards for AbbVie, Amgen, AMT, AnaptysBio, Axio Research, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, EcoR1 Capital, Genentech/Roche, GlaxoSmithKline, InDex Pharmaceuticals, Janssen, Lilly, MiroBio, Morphic, Origo BioPharma, Pfizer, Progenity, Prometheus, REDX Pharma, Sanofi, Takeda, Teva, and Tillotts Pharma.

BES reports consulting fees from AbbVie, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biologic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceuticals,

cal, Tr1X, Union Therapeutics, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma.

OP195

EFFICACY AND SAFETY OF OBEFAZIMOD IN UC PATIENTS AT WEEK 48 OF AN OPEN-LABEL MAINTENANCE STUDY AMONG CLINICAL NON-RESPONDERS AT WEEK 8 OF THE PHASE 2B INDUCTION TRIAL

B.E. Sands¹, L. Peyrin-Biroulet², S. Danese³, P.S. Dulai⁴, H. Tilg⁵, B. Siegmund⁶, J. Nitchu⁷, S. Sloan⁷, C. Rabbat⁸, S. Vermeire⁹

¹Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America,

²University of Lorraine, Gastroenterology, Vandoeuvre-les-Nancy, France, ³Vita-Salute San Raffaele University - IRCCS

San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁴Feinberg School of Medicine

Northwestern University, Chicago, United States of America,

⁵Innsbruck Medical University - Department of Medicine,

Innsbruck Medical University; Innsbruck/AT, Department of

Medicine, Innsbruck, Austria, ⁶Charité - Universitätsmedizin

Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und

Rheumatologie, Berlin, Germany, ⁷Abivax, Paris, France,

⁸Abivax, Medical Affairs, Paris, France, ⁹University Hospital

Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: Obefazimod is an investigational, oral, once-daily, small molecule which enhances expression of microRNA-124 and is currently in phase 3 clinical trials for the treatment of patients with moderately to severely active ulcerative colitis (UC) [1]. Obefazimod demonstrated efficacy and safety in patients with UC at week-8 in a placebo-controlled, Phase 2b induction trial and in the subsequent open-label maintenance (OLM) study [2]. Here we present efficacy and safety among patients who did and those that did not achieve clinical response at week 8 of the double-blind induction trial.

Aims & Methods: Patients received placebo or obefazimod 25mg, 50mg or 100mg once daily (od) during the Phase 2b, induction trial and, irrespective of their clinical response, could enter the optional 96-week OLM study with obefazimod 50mg od. Patients were followed monthly for safety and efficacy. This analysis evaluates efficacy (at week 48) and safety (through week 96) among patients who achieved and those who did not achieve clinical response (decrease from baseline in the Modified Mayo score (MMS) ≥ 2 points and $\geq 30\%$ from baseline, plus a decrease in rectal bleeding sub-score (RBS) ≥ 1 or an absolute RBS ≤ 1) at week 8 of double-blind induction and continued treatment in the OLM.

Results: Among the 217 patients who participated in the OLM, 57% (124/217) achieved clinical response at week 8 of the induction trial (CR group), and 43% (93/217) did not (NCR group). Proportions of patients achieving efficacy endpoints were numerically higher within the CR group than those observed in NCR group. At week 48, 66% of CR patients and 40% of NCR patients achieved clinical remission; 86% of CR patients and 75% of NCR patients achieved clinical response; endoscopic improvement was achieved by 70% of CR patients and by 50% of NCR patients, and endoscopic remission was achieved by 38% of CR patients and 27% of NCR patients (Table 1). There was no significant difference in the safety profile between these two subpopulations.

Efficacy Endpoint, % (n)	Patients with clinical response at week 8 (N=124)	Patients with no clinical response at week 8 (N=93)
Clinical remission	66.1 (82)	39.8 (37)
Clinical response	86.3 (107)	75.3 (70)
Endoscopic improvement	70.2 (87)	49.5 (46)
Endoscopic remission	37.9 (47)	26.9 (25)

Table 1: Efficacy at week 48 of open-label maintenance study among clinical responders and non responders at week 8 of induction trial

Non-responder imputation (NRI) was used for missing efficacy data; clinical remission: stool frequency sub-score ≤ 1 , RBS = 0 and endoscopic sub-score ≤ 1 ; clinical response: decrease from baseline in the Modified Mayo score (MMS) ≥ 2 points and $\geq 30\%$ from baseline, plus a decrease in rectal bleeding sub-score (RBS) ≥ 1 or an absolute RBS ≤ 1 ; endoscopic improvement: endoscopic sub-score ≤ 1 ; endoscopic remission: endoscopic sub-score = 0

Conclusion: Substantial proportions of patients treated with obefazimod 50 mg od achieved clinical outcomes at week 48 of an open label maintenance study, irrespective of whether they achieved clinical response at week 8 of the prior induction trial. Patients achieving clinical response at week 8 of the induction trial consistently showed higher efficacy rates throughout the 48-week open-label maintenance trial. The safety profile remains consistent over time, regardless of treatment response at week 8.

References:

1. Vermeire S, et al. J Crohns Colitis. 2023; 17: 1689-1697
2. Vermeire S, et al. The Lancet Gastroenterology & Hepatology. 2022; 7: 1024-1035.

Disclosure: Bruce E Sands has served as a consultant or received speaker's fees from AbbVie, Abivax, Adiso Therapeutics, AgomAb, Alimentiv, Amgen, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytoki Pharma, Eli Lilly and Company, Entera, Evommune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morphic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio, and stock options from Ventyx Biosciences.

S  verine Vermeire has received grants from AbbVie, J&J, Pfizer, Takeda and Galapagos; SV has received consulting and/or speaking fees from: AbbVie, Abivax, AbolerIS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance, Tillots Pharma AG, Zealand Pharma.

Laurent Peyrin-Biroulet has received grants from Celltrion, Fresenius Kabi, Takeda; LPB has served as a consultant or received speaker's fees from AbbVie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, Connect Biopharm, Cytoki Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, Hac Pharm, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopa, Morphic, MSD, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandi-

on Therapeutics, Par Immune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance, Thermo Fischer, Tigenix, Tillots, Viatrix, Vifor, Vectivbio, Ventyx, Ysopia.

Silvio Danese has served as consultant or received speaker's fees from AbbVie, Ferring, Hospira, Johnson & Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim.

Parambir Dulai received speaker's fees from AbbVie, Abivax, Adiso, Bristol Meyer Squibb, Geneoscopy, GSK, Janssen, Lilly, Pfizer, Takeda.

Herbert Tilg has served as a consultant or received speaker's fees from AbbVie, Abivax, Dr Falk Pharma, ferring, Galapagos, Microbiotica, MSD, Pfizer, Takeda.

Britta Siegmund has served as consultant for AbbVie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forga Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; Speaker fees: AbbVie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer and grant support by Arena/Pfizer (served as representative of the Charit  ).

OP196

TOWARD A SAFER, NON-SYSTEMIC JAK INHIBITOR FOR IBD:

A PHASE 2A STUDY TO EVALUATE SAFETY, PHARMACOKINETICS AND PRELIMINAR CLINICAL EFFICACY OF ORAL TREATMENT WITH OST-122 IN PATIENTS WITH ULCERATIVE COLITIS

M. Barreiro de Acosta¹, S. Skybalo², C. Rodr  guez³, S. Garc  a-L  pez⁴, M.D. Mart  n-Arranz⁵, L. Torrealba⁶, E. Iglesias-Flores⁷, F. Arg  uelles-Arias⁸, Y. Ber Nieto⁹, V. Shevchuk¹⁰, C. Castro-Fern  ndez¹¹, J.C. Castro-Palomino¹¹, A. Heredia¹¹, G. Kurz¹¹

¹Hospital Cl  nico Universitario de Santiago De Compostela, Gastroenterology Department, Santiago de Compostela, Spain, ²Medical Center "Ok!Clinic" of International Institute of Clinical Research LLC, Gastroenterology and Hepatology Unit of the Inpatient Department, Kyiv, Ukraine, ³Complejo Hospitalario Universitario de Navarra, Gastroenterology Department, Pamplona, Spain, ⁴Hospital Universitario Miguel Servet, Gastroenterology Department, Zaragoza, Spain, ⁵Hospital Universitario La Paz, Gastroenterology Department, Madrid, Spain, ⁶Hospital Universitario Dr. Josep Trueta, Girona, Spain, ⁷Hospital Universitario Reina Sof  a, Gastroenterology Department, UCO, IMIBIC, C  rdoba, Spain, ⁸Universidad de Sevilla, Hospital Universitario Virgen Macarena, Gastroenterology Department, Sevilla, Spain, ⁹Hospital Universitario San Jorge, Gastroenterology Department, Huesca, Spain, ¹⁰Medical and Diagnostic Center PE PMC "Acinus", Kropyvnytskyi, Ukraine, ¹¹Oncostellae S.L., Santiago de Compostela, Spain

Contact E-Mail Address: Manuel.Barreiro.de.Acosta@sergas.es

Introduction: JAK inhibitors have become an efficacious oral treatment option to antibody-based therapies for ulcerative colitis (UC). However, they have received a black box warning by the FDA for causing serious systemic adverse events.

To increase safety, OST-122 is being developed as an orally administered, GI-targeted and non-systemic JAK3/TYK2 inhibitor for the local treatment of UC. In preclinical models and in healthy volunteers, OST-122 has demonstrated excellent safety and tolerability with minimal systemic exposure reducing the risk of causing serious systemic toxicities associated with current JAK inhibitors.

Here, we report the results of a phase 2a study in patients with UC on the safety, tolerability, pharmacokinetics and preliminary efficacy of OST-122.

Aims & Methods: In this randomized, double-blind trial, 37 adult patients with active UC were treated with oral OST-122 400 mg (n=28) or placebo (n=9) for 28 days. Eligibility criteria required a total Mayo Score TMS 5-10, endoscopic Mayo Score EMS ≥ 2 , inadequate/loss of response to conventional therapy (5-ASA, steroids, immunomodulators) or biologics (anti-TN- α , anti-integrin, anti-interleukin 12/23). Stable cotreatment with oral 5ASAs and corticosteroids was permitted.

To evaluate the safety and tolerability of OST-122, the number and severity of AEs, including changes in vital signs, safety laboratory values and ECGs, were analyzed. Plasma, tissue and stool samples were collected at various time points to examine the gut-restricted pharmacokinetic profile of the compound in UC patients. Preliminary efficacy was assessed through Mayo Clinical Scores including rectal bleeding (RB) and stool frequency (SF) along with clinical response and remission.

Results: During the 6-week observation period, no serious AEs nor treatment-related AEs leading to discontinuation were reported. Most AEs were tabulated as mild, followed by moderate, and the number of subjects reporting AEs were distributed equally in the placebo and OST-122 group (78% vs. 71%). There were no clinically relevant changes in vital signs, laboratory values or ECG parameters which raise any safety concerns.

Pharmacokinetic analysis indicated minimal plasma concentrations (C_{max} 0.92 ng/mL) and therapeutically relevant levels in colon tissue (15.5 $\mu\text{g/g}$ tissue) confirming a gut-restricted PK profile of OST-122.

Preliminary efficacy data after 28 days of treatment are summarized in the table below:

Outcome	400 mg OST-122 (n=28)	Placebo (n=9)	Δ
Rectal Bleeding			
Improvement of RB score by ≥ 1	63% (17/27)	33% (3/9)	33%
Stool Frequency			
Improvement of SF score by ≥ 1	52% (14/27)	33% (3/9)	19%
PRO-2 score (RB + SF)			
Improvement of PRO-2 by ≥ 2	48% (13/27)	11% (1/9)	37%
Clinical Response			
Decrease of TMS by ≥ 3 or $\geq 30\%$, plus improvement in RB by ≥ 1 and an absolute RB of 0 or 1	44% (12/27)	11% (1/9)	33%
Clinical Remission			
TMS ≤ 2 and no individual subscore >1 , plus RB of 0	22% (6/27)	0% (0/9)	22%

Table.

63% of patients taking OST-122 showed an improvement in rectal bleeding and 52% in stool frequency (vs 33% in the placebo group), and 48% had an improvement of ≥ 2 in PRO-2 (RB+SF, vs 11% Pbo). Clinical response was achieved by 44% (vs 11% Pbo) and 22% reached clinical remission (vs 0% Pbo). In addition, 16% of patients in the OST-122 group achieved both histological response and remission (vs 0% Pbo). A subgroup analysis showed that OST-122 was able to induce clinical response both in bio-naïve and bioexperienced patients. Confirmatory studies will be designed to determine dose and statistical significance.

Conclusion: GI-restricted OST-122 was well tolerated during the 4-week treatment. Its excellent safety profile, minimal systemic exposure and promising trends of clinical activity may provide a safer therapeutic option for a broad range of ulcerative colitis patients.

Disclosure: M. Barreiro de Acosta has served as a speaker, consultant and advisory member for or has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, Gilead, Celgene, Pfizer, Sandoz, Biogen, Fresenius, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, Gebro Pharma, Adaclyte, Vifor Pharma and Oncostellae.

C. Rodríguez has received consultancy and/or speaking honoraria fees from AbbVie, Ferring, Galapagos, Janssen, Pfizer, Lilly and Takeda.

M.D. Martin-Arranz has received fees as a speaker, consultant and advisory member for or has received funding from MSD, AbbVie, Hospira, Pfizer, Takeda, Janssen, Shire Pharmaceuticals, Tillots Pharma, and Faes Pharma.

L. Torrealba has served as a speaker for Janssen.

E. Iglesias Flores has served as a speaker, consultant and advisory member for or has received research funding from AbbVie, Janssen, Takeda, Gilead, Celgene, Pfizer, Lilly, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, and Adaclyte.

F. Argüelles-Arias has served as a speaker, consultant and advisory member for or has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, Gilead, Celgene, Pfizer, Sandoz, Biogen, Fresenius, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, Gebro Pharma, Adaclyte and Vifor Pharma.

Y. Ber-Nieto has served as a speaker from Abbvie and has received education funding from Abbvie and Pfizer.

Pancreatic diseases: From models to precision medicine

11:30-12:30 / Lehar 1

OP197

MODELLING PIEZO1-MEDIATED PRESSURE-INDUCED INFLAMMATORY PHENOTYPE OF HUMAN PANCREATIC ORGANOIDS

A.K. Kiss^{1,2,3}, A. Varga^{1,2,3}, P. Susánszki^{1,2}, G. Lázár⁴, G. Groma^{5,5}, P. Pallagi^{1,2,3}, J. Maléth^{1,2,3}

¹University of Szeged, Department of Internal Medicine, Szeged, Hungary, ²University of Szeged, ELKH-USz Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ³University of Szeged, HCEMM-USz Molecular Gastroenterology Research Group, Szeged, Hungary, ⁴University of Szeged, Department of Surgery, Szeged, Hungary, ⁵University of Szeged, Department of Dermatology and Allergology, Szeged, Hungary, ⁶University of Szeged, HUN-REN-SZTE Dermatological Research Group, Szeged, Hungary

Contact E-Mail Address: kissalettakata@gmail.com

Introduction: Pancreas inflammation is frequently brought on by sustained intraductal pressure, which is mostly caused by gallstones or ERCP, a minimally invasive diagnostic technique. It has been demonstrated that in mice, this brief pressure reduces tight junction integrity through calcineurin. Another effector protein of intraluminal pressure is the mechanosensitive Ca²⁺ channel PIEZO1, which senses cell elongation, increases Ca²⁺ influx, and hence controls both epithelial cell division and apoptosis.

However, the development of treatment approaches that specifically target post-ERCP and gallstone-induced pancreatitis has been hampered in recent years due to challenges in *in vitro* modeling of pressure-related changes.

Aims & Methods: Therefore, our *aim* was to use apical-out organoids (hPOCs) generated from human pancreas to demonstrate the pressure-related disease processes *ex vivo*.

Pancreatic tissue samples were collected from 3 cadaver donors and used for establishment of hPOCs. Polarity switching of organoids was induced by Matrigel removal. Conventional and apical-out hPOCs were compared by RNA-sequencing and fluorescent live cell imaging. Gene expression changes in response of 1 µM PIEZO1 activator (YODA1) treatment were measured by qRT-PCR in apical-out hPOCs.

Results: Polarity switching reduced PIEZO1 expression, although decreasing intraluminal pressure and therefore cell elongation reduced expression of cytoskeletal and cell cycle related genes such as ACTB, VCL, LPXN, LMNA, and cyclin gene family members. In the same experiment, pro-inflammatory cytokines like CXCL1, CXCL2, CXCL3, and CXCL8 were found to be downregulated. We demonstrated that polarity switching resulted in enhanced Cl⁻ efflux via CFTR and ANO1 due to the absence of sustained intraluminal pressure maintained by basal secretion in the closed lumen of conventional organoids.

The production of pro-inflammatory cytokines in apical-out hPOCs was reversed upon pharmacological activation of PIEZO1 by YODA1, indicating that PIEZO1 is responsible for the development of the inflammation-like pre-stimulated phenotype of apical-in hPOCs.

Conclusion: Altogether, our results suggest that conventional organoid cultures, previously used as physiologically relevant models, may represent a pressure-induced inflammatory state by overexpressing elements of the epithelial innate immune response, while polarity switching of organoids may overcome the previous limitations and open new perspectives in modelling pressure-induced pancreatitis *in vitro*.

Disclosure: Nothing to disclose.

OP198

EUS-GUIDED DETECTIVE FLOW IMAGING (DFI), A NOVEL ADVANCED IMAGING TECHNIQUE, FOR THE DIFFERENTIAL DIAGNOSIS OF SOLID PANCREATIC TUMORS

J. Iglesias-Garcia^{1,2}, Y. Dominguez-Novoa^{1,2}, J. Lariño-Noia^{2,1}, X. Martinez-Seara³, J.E. Domínguez Muñoz^{2,1}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: joselarnoi@outlook.es

Introduction: The diagnosis of solid pancreatic tumours (SPT) is a clinical challenge and endoscopic ultrasound (EUS) is an essential tool in this setting. A new EUS-guided advanced imaging technique, detective flow imaging (DFI), has been developed to provide information on microvascularisation and low-velocity blood flow without the need for contrast agents.

Aims & Methods: The aim of our study was to evaluate DFI-EUS findings in SPT and compare them with those of contrast-enhanced harmonic EUS with Sonovue® (CEHEUS).

Methods: Prospective and descriptive study including patients with SPT who underwent EUS evaluation. The procedures were performed with a linear echoendoscope (Fujifilm 740UT) attached to the Arietta-850 ultrasound system. Lesions were graded according to the degree of vascularisation using DFI and CEHEUS. The final diagnosis was based on EUS sampling and long-term clinical and radiological follow-up when histology was not available.

Results: 106 patients (mean age 67.9 years [range 24-88 years], 48 males) were finally included. The mean lesion size was 28.4±16.2 mm. 46 (43.4%) tumours were located in the pancreatic head, 35 (33.0%) in the body, 1 (0.9%) in the neck, 19 (17.9%) in the tail and 5 (4.7%) in the uncinate process. 63 (59.4%) patients were diagnosed with adenocarcinoma, 30 (28.4%) with neuroendocrine tumour, 6 (5.6%) with inflammatory mass, 2 (1.9%) with pancreatic squamous cell carcinoma and lipoma, and 1 (1.2%) each with pancreatic necrosis, acinar carcinoma and accessory spleen. The vascular pattern of SPT evaluated by CEHEUS and EUS-DFI was concordant in 98.1% of cases.

All adenocarcinomas, pancreatic necrosis and pancreatic squamous cell carcinoma were hypovascular. Inflammatory masses were isovascular. Lipomas, accessory spleen and acinar carcinoma were hypervascular on both CEHEUS and EUS-FI. All 30 neuroendocrine tumours were hypervascular on CEHEUS and 28 (93.3%) on EUS-DFI.

Conclusion: DFI-EUS allows evaluation of the vascularisation pattern of pancreatic tumours with comparable accuracy to CEHEUS but without the need for contrast.

Disclosure: Julio Iglesias-Garcia: Advisor Fujifilm.

OP199

RISK STRATIFICATION FOR BD-IPMN MALIGNANT TRANSFORMATION. THE ROLE OF OPERATIVE DIMENSIONAL GROUPING IN THE COST-EFFECTIVENESS OPTIMIZATION OF SURVEILLANCE GUIDELINES. THE PACMANS STUDY

S. Kayali¹, E. Marabotto², S. Dibitetto³, F. Gaiani¹, A. Busatto⁴, S. Caprioli², A.P. Luzzi², E.V. Savarino⁴, L.A. Laghi¹, C.G. De Angelis⁵, E.G. Giannini²

¹University of Parma, Department of Medicine and Surgery, Parma, Italy, ²University of Genoa, Department of Internal Medicine, Genova, Italy, ³University of Turin, Division of Gastroenterology, Turin, Italy, ⁴University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ⁵'San Giovanni Battista' Hospital, University of Turin, Turin, Italy

Contact E-Mail Address: jstefanok@gmail.com

Introduction: In recent years, the detection of Branch Duct Intraductal Papillary Mucinous Neoplasms (BD-IPMN) has increased. The Association of Pancreatology (IAP) approved specific guidelines for their management in Fukuoka in 2017. The rates of malignant degeneration of these lesions remain unclear, raising concerns about the cost-effectiveness of the suggested surveillance strategies.

Aims & Methods: This study aimed to identify the rates of BD-IPMN malignant degeneration and their associated risk factors to propose a new, more cost-effective surveillance strategy. In this multicentric retrospective observational study, clinical and histopathological data of patients with IPMN were collected by four tertiary centers in Northern Italy. Multivariate Cox regression identified factors associated with a higher risk of malignant degeneration.

A segmentation analysis aimed to define new dimensional cut-offs for better risk stratification. Demographic and anamnestic data relating to the patient (age, gender, comorbidities based on the Age-Adjusted Charlson Comorbidity-Index (ACCI), imaging, endoscopic examinations, and surgical interventions), to IPMN (presence of Worrisome Features (WF) and High-Risk Stigmata (HRS) as defined by IAP), and surveillance costs were collected. Malignant degeneration was defined as the presence of high-grade dysplasia or invasive neoplasia.

Results: The study enrolled 333 patients, with a total of 1400 visits and a median follow-up of 4 years. IPMN developed malignant degeneration in 3.3% of cases. Cancer risk factors included the presence of HRS (HR 4.4, 95%CI 1.1-17.8, $p = 0.04$), of at least two WFs (HR 5.8, 95%CI 1.5-22.4, $p = 0.01$), and cyst size (HR 2.0, 95%CI 1.3-3.0, $p < 0.001$). The latter discriminated this risk (AUC 0.91, 95%CI 0.84-0.97), and two new cut-offs of 1.5 and 3.0 cm identified three dimensional categories with significantly different neoplastic potential (OR 6.6, 95%CI 1.7-25.4, $p = 0.007$, OR 9.8, 95%CI 1.1-89.7, $p = 0.04$).

Based on this, we proposed a new surveillance strategy that maintained diagnostic accuracy while reducing the cost per patient for a 3-year follow-up from 670.01 (407.33-1130.32) to 587.01 (347.10-930.28) euro, resulting in a total savings of 11% ($p = 0.001$).

Conclusion: IPMN malignant degeneration was infrequent. The presence of at least one WF, currently a cornerstone of guideline recommendations, did not independently associate with neoplastic risk, unlike HRS and the presence of at least two WFs. Implementing a follow-up strategy based on operatively identified dimensions (1.5 and 3 cm) could potentially enhance the cost-effectiveness of the 2017 Fukuoka IAP guidelines.

Disclosure: Nothing to disclose.

OP200

REFINED TARGETING OF DNA DAMAGE RESPONSE AS AN EFFECTIVE THERAPEUTIC STRATEGY FOR HOMOLOGOUS REPAIR-DEFICIENT PANCREATIC CANCER

A.K. Beutel^{1,2}, M. Ekizce³, C.J. Halbrook^{2,4}, E. Roger³, S. Calderon², J. Lindenmayer⁵, T. Seufferlein¹, A. Kleger^{3,5}, J. Gout³, L. Perkhof^{1,3}

¹University Hospital Ulm, Internal Medicine 1, Ulm, Germany,

²University of California Irvine, Molecular Biology and Biochemistry, Irvine, United States of America, ³University Hospital Ulm, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ⁴University of California Irvine, Chao Family Comprehensive Cancer Center, Orange, United States of America, ⁵University Hospital Ulm, Core Facility Organoids Ulm, Ulm, Germany

Contact E-Mail Address: alicabeutel@hotmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a devastating malignancy with a high mortality rate. While up to 25% of PDAC patients harbor mutations in genes involved in homologous recombination (HR) repair, targeted treatment with the PARP inhibitor (PARPi) olaparib is currently only approved in less than 5% of germline (g) *BRCA1/2* mutation carriers. Characterizing HR-deficient genotypes beyond g*BRCA1/2* that are susceptible to PARPi has potential to substantially broaden the eligible patient population, and defining the optimal inhibitor may further optimize treatment strategies to advance personalized medicine in PDAC.

Aims & Methods: Our previous preclinical work showed synthetic lethality of a multi-pronged DNA repair inhibition strategy using the PARPi olaparib, ATR inhibitor VE-822, and DNA-PK inhibitor CC-115 (termed PAD) in ATM deficiency¹. In the present study, we aimed to challenge the role of olaparib in our PAD combination and assess the regimen's efficacy across various HR-defective genotypes.

We assessed a spectrum of DNA-damaging agents and PARPi to identify the most potent inhibitor in HR-deficiency. Using *ATM*, *BRCA1*, *BRCA2* and *PALB2*-defective vs. HR-proficient murine PDAC cells, we systematically investigated the feasibility of expanding an optimized PAD regimen within defined HR-defective genotypes *in vitro* and *in vivo*.

Results: Here, we demonstrate a remarkable potency of the PARPi talazoparib in HR-deficient PDAC. Substituting olaparib, currently the only approved inhibitor in PDAC, with talazoparib in our PAD regimen enhanced its efficacy while maintaining comparable tolerability *in vivo*. Importantly, we demonstrate that PAD is an effective therapeutic regimen that can be extended to the most prevalent HR-defective genotypes in PDAC including *ATM*, *BRCA1*, *BRCA2* and *PALB2*.

Conclusion: Collectively, these data provide a strong rationale to implement the optimized regimen, talazoparib-based PAD, as a therapeutic concept tailored for the broad subgroup of HR-deficient PDAC patients.

References: 1 Gout J, Perkhof L, Morawe M, Arnold F, Ihle M, Biber S, et al. Synergistic targeting and resistance to PARP inhibition in DNA damage repair-deficient pancreatic cancer. *Gut*. 2021;70(4):743-60.

Disclosure: Nothing to disclose.

OP201

CANCER-ASSOCIATED FIBROBLASTS REGULATE THE FORMATION OF MACROPHAGE EXTRACELLULAR TRAPS VIA CCL11/CCR5 AXIS TO RESIST IMMUNOTHERAPY IN PANCREATIC DUCTAL ADENOCARCINOMA

Z. Shi¹, Q. Zhou², K. Liu², Y. Jiang², S. Nie², Y. Yu², L. Wang², X. Zou², S. Shen², H. Li²

¹Clinical College of Nanjing Medical University, Nanjing, China,

²The Affiliated Hospital of Nanjing University Medical School, Nanjing, China

Contact E-Mail Address: cathyshizhao@163.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the most lethal malignancy with limited effective treatments options. PDAC remains resistant to immunotherapy due to its immunosuppressive tumor micro-environment and dense desmoplastic stroma, which are attributed to an abundance of cancer associated fibroblasts (CAFs) and infiltrating immunocytes. Macrophages release extracellular traps which are composed of a backbone of extracellular DNA fibers containing histones and cytotoxic proteases such as myeloperoxidase, elastase, and matrix metalloproteinase in order to exert local immunoregulation. However, the role of macrophages extracellular traps (METs) in PDAC is at present unclear.

Aims & Methods: METs expression was evaluated in human PDAC tissues using Immunofluorescence co-localization of citrullinated histone H3 (H3cit) and CD68. Patients cohorts were classified into METs-High and METs-Low groups based on their numbers of positive cells. The collagen deposition and infiltrating immune cell populations were detected by Immunohistochemistry in both human and mice PDAC tissues. Cytokine production in human serum was assayed using the Olink proteomic platform. The level of C-C motif chemokine ligand 11 (CCL11) and double-stranded DNA (dsDNA) in serum and conditioned medium were determined by ELISA. Pancreatic orthotopic transplantation tumors were constructed using panc02 cell line and organoids derived from KrasG12D/+; Trp53R172H/+; Pdx1Cre (KPC) mouse PDAC tissue. Western blot and q-PCR were utilized to validate the expression levels of CAFs and METs markers across different groups. T cell activation, macrophage phenotype and programmed death-ligand 1 (PD-L1) level in mouse pancreatic tumors were evaluated by flow cytometry.

Results: The METs level was elevated in PDAC compared to paracancerous tissues and it was significantly linked to poor patient survival, advanced tumor grade and stage, fewer infiltrating CD8+ T-cells, increased CD86+ macrophages, and increased α -SMA+ CAFs. CCL11, secreted by CAFs, was a key upstream signaling molecule for METs formation. Mechanistically, CCL11 binded to chemokine receptor 5 (CCR5) on the surface of macrophages and promoted PAD2 expression, facilitating MET formation. Maraviroc, a CCR5 inhibitor, effectively suppressed this process and increased the expression of PD-L1 and the infiltration of CD8+ T cells in PDAC tissue. In vivo, maraviroc effectively enhanced the anti-tumor effects of immunotherapy.

Conclusion: CAFs promoted the formation of METs via CCL11/CCR5 axis and further contributed to the formation of an immunosuppressive microenvironment in PDAC. Through the inhibition of METs formation by antagonizing CCR5 reshaped the immune microenvironment of PDAC and enhanced the sensitivity of immunotherapy.

Disclosure: Nothing to disclose.

AI in diagnostic and therapeutic endoscopy

11:30-12:30 / Lehar 2

OP202

ARTIFICIAL INTELLIGENCE-ASSISTED “ENDO-VASCULAR HEALING” PREDICTS LONG-TERM SUSTAINED REMISSION IN PATIENTS WITH ULCERATIVE COLITIS: A POST-HOC ANALYSIS OF A PROSPECTIVE COHORT STUDY

T. Kuroki¹, S. Kudo¹, Y. Maeda¹, N. Ogata¹, K. Takenaka², K. Takabayashi³, J. Kawashima¹, K. Takishima¹, Y. Ogawa¹, K. Ichimasa¹, T. Hayashi¹, K. Wakamura¹, H. Miyachi¹, T. Baba¹, K. Ohtsuka^{2,4}, H. Ogata⁵, Y. Mori^{6,1}, M. Misawa¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Kanagawa, Japan, ²Tokyo Medical and Dental University, Department of Gastroenterology and Hepatology, Tokyo, Japan, ³Keio University School of Medicine, Center for Diagnostic and Therapeutic Endoscopy, Tokyo, Japan, ⁴Tokyo Medical and Dental University Hospital, Endoscopic Unit, Tokyo, Japan, ⁵Fujita Medical Innovation Center Tokyo, Tokyo, Japan, ⁶University of Oslo, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway

Contact E-Mail Address: kuroki65black@gmail.com

Introduction: The integration of artificial intelligence (AI) during colonoscopy in patients with ulcerative colitis (UC) has garnered attention as an objective tool for predicting disease activity. Recently, we developed two types of AI-assisted software for assessing the inflammatory severity of UC: an AI-based white light endoscopy (WLE) system (EB-UC2 prototype; Cybernet Systems, Tokyo, Japan) and an AI-based Narrow-Band Imaging (NBI) system (EB-UC3). The AI-based WLE system is a fully automated video-based system that provides a three-class Mayo endoscopic subscore (MES) output (0, 1, and 2 or 3). The AI-based NBI system is a fully automated system that delivers a two-class predictive output (“Vascular active” or “Vascular healing”) of disease activity based on intramucosal vascular findings¹.

We are targeting the clinical implementation of these two systems and envisage their integration in real-world clinical practice, although the utility of integrating the two systems has not yet been investigated.

Aims & Methods: The aim of this study was to assess the usefulness of integrating the two AI systems in identifying patients with future clinical relapse among those with UC in clinical remission. This post hoc analysis included patients who achieved sustained corticosteroid-free remission (for 6 months) with a partial Mayo score ≤ 1 and underwent endoscopy using both AI systems between December 2021 and June 2022 at our institution. Patients were monitored in the outpatient clinic every 8 or 12 weeks for 12 months or until clinical relapse occurred. Clinical relapse was defined as a partial Mayo score > 2 .

Results: A total of 98 patients were enrolled in this analysis. Fifteen patients experienced a flare-up during the follow-up period. Patient background factors include gender: male 52.0%(51), median age 54 (IQR:64-44)years, disease type: pancolitis 51.2%(60), left-sided colitis 24.5%(24), and proctitis 14.3%(14).

The clinical relapse rate was significantly lower in patients achieving both AI-based MES=0-1 and “Vascular-healing” [3.2% (1/31)] compared to others [3.2% (1/31)] ($P < 0.01$). The AI-based NBI system was able to stratify the risk of relapse for patients assigned each MES by the AI-based WLE system: in patients with AI-based MES=2-3, the relapse rate was 0% (0/2) in AI-based vascular-healing and 53.8% (7/13) in AI-based vascular-active. In patients with AI-based MES=1, the relapse rate was 6.7% (1/15) and 18.6% (6/32) in AI-based vascular-healing and AI-based vascular-active, respectively. In patients with AI-based MES=0, the relapse rate was 0% (0/16) and 5% (1/20) in AI-based vascular-healing and AI-based vascular-active, respectively.

AI-based WLE output	AI-based NBI output		
	Vascular healing	Vascular active	Over all
MES=0	0% (0/16)	5.0% (1/20)	2.8% (1/36)
MES=1	6.7% (1/15)	18.6% (6/32)	14.9% (7/47)
MES=2-3	0% (0/2)	53.8% (7/13)	46.7% (7/15)
Over all	3.0% (1/33)	21.5% (14/65)	15.3% (15/98)

Table 1: The 12-month relapse rates following colonoscopy, according to the outputs from the AI-based white light endoscopy (WLE) system and the AI-based narrow band imaging (NBI) system.

Conclusion: The integrated use of AI-based WLE system for assessing MES and AI-based NBI system for diagnosing “vascular-healing” during colonoscopy effectively identifies patients with UC at high risk of relapse and thereby aiding in future disease management.

References: 1. Kuroki T, Maeda Y, Kudo SE, et al. A novel artificial intelligence-assisted “vascular-healing” diagnosis for prediction of future clinical relapse in patients with ulcerative colitis: a prospective cohort study. *Gastrointest Endosc* 2024.

Disclosure: Nothing to disclose.

OP203

THE ADDED VALUE OF A NOVEL COMPUTER AIDED DETECTION ALGORITHM FOR NEOPLASIA DETECTION IN INFLAMMATORY BOWEL DISEASE (CADE-IBD): A MULTI-CENTRE VIDEO-BASED VALIDATION STUDY

K. Siggins¹, H. Htet¹, N. Maeda², S. Namiki³, P. Aslam⁴, W. Siu⁴, A.A. Alkandari⁵, A. Repici⁶, P. Bhandari⁷

¹Portsmouth Hospitals University NHS Trust, Portsmouth, United Kingdom, ²Medical AI Research Department, NEC Corporation, Japan, Tokyo, Japan, ³Biometrics Research Laboratories, NEC Corporation, Japan, Kawasaki, Japan, ⁴Canberra Hospital, Gastroenterology, Georges Hall, Australia, ⁵Queen Alexandra Hospital, Gastroenterology, London, Kuwait, ⁶Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy, ⁷Portsmouth University Hospital, Dept. of Gastroenterology, Portsmouth, United Kingdom

Contact E-Mail Address: katie.siggins@nhs.net

Introduction: Neoplasia detection in inflammatory bowel disease (IBD) poses a clinical challenge. We have previously reported the efficacy of a novel computer aided detection (CADE) algorithm for use in IBD (CADE-IBD) in images and videos. CADE-IBD is designed for use in high-definition white light endoscopy which may reduce operator variability which comes with chromoendoscopy. The added value of CADE-IBD is yet to be explored which this study aims to address.

Aims & Methods: Based on pilot data this study was powered as a superiority test, with 90% power for increased sensitivity of non-expert endoscopists with CADE-IBD compared to without CADE-IBD. 10 experienced and 11 less experienced endoscopists were asked to review short video clips of high definition white-light IBD endoscopy on a bespoke computer software designed by NEC Japan. The videos were watched once without CADE-IBD and then again with CADE-IBD when the videos were randomly redistributed to reduce recall bias. After each video the endoscopist was asked to select ‘polyp’, ‘no polyp’ or ‘uncertain’. If the endoscopist selected ‘polyp’ for a video they were asked to annotate the suspected abnormality.

Results: The study included 285 videos from IBD colon. 131 videos had lesions which showed a diverse range of size, morphology, histology and background mucosal inflammation. Videos were from all 3 major endoscopy processors (Pentax, Olympus and Fuji).

The standalone CADE-IBD sensitivity and specificity were 94.7% and 70.8% respectively. In comparison, experienced endoscopist sensitivity and specificity were 90.5% and 80.2% and less experienced endoscopists sensitivity and specificity of 73.7% and 82.1%. CADE-IBD sensitivity was significantly better than both experts and non-experts ($p < 0.05$).

With the addition of CADE-IBD, less experienced endoscopists sensitivity increased significantly to 89.2% ($p < 0.01$) and specificity remained similar at 81.0%. Experienced endoscopist sensitivity also improved with CADE-IBD to 93.4% which was again statistically significant ($p < 0.05$).

Sub-analysis was performed based on neoplastic or non-neoplastic histology, polypoid (Paris Is, Isp, Ip) and non-polypoid (Paris IIa/IIb/IIc) morphology and Mayo endoscopic sub-score for mucosal inflammation (Table 1).

	CADE-IBD sensitivity	Less experienced endoscopist sensitivity	Less experienced + CADE-IBD sensitivity	Experienced endoscopist sensitivity	Experienced + CADE-IBD sensitivity
Overall (n=131)	94.7%	73.7%	89.2%	90.5%	93.4%
Histology					
Neoplastic (n=62)	96.8%	72.6%	90.2%	92.1%	95.0%
Non-neoplastic (n=69)	92.8%	74.7%	88.4%	89.0%	92.0%
Morphology					
Polypoid (n=29)	100%	93.7%	98.1%	99.3%	99.7%
Non-polypoid (n=102)	93.1%	68.0%	86.7%	87.9%	91.7%
Mayo score					
0 (n=105)	95.2%	74.1%	90.9%	90.7%	93.7%
1 (n=21)	90.5%	68.4%	80.1%	89.5%	92.9%
2 (n=5)	100%	87.3%	92.7%	90.0%	90.0%

Table 1.

Conclusion: CADE-IBD has a standalone performance which is superior to both less experienced and experienced endoscopists. The addition of CADE-IBD significantly improved lesion detection regardless of experience. This superior performance was observed in neoplastic lesions, non-polypoid lesions and in the presence of mild background mucosal inflammation which is of high clinical importance. This calls for a head to head comparison of CADE-IBD with conventional surveillance techniques.

References: Abdelrahim M, Siggins K, Iwade Y, et al New AI model for neoplasia detection and characterisation in inflammatory bowel disease *Gut* 2024;73:725-728.

Disclosure: Professor Bhandari has received research grants or is the advisory board for Fujifilm, Boston, Olympus, Pentax, 3-D matrix, NEC (Japan) and Medtronic.

OP204

DEVELOPMENT AND VALIDATION OF AN ARTIFICIAL INTELLIGENCE MODEL SCORING THE ULCERATIVE COLITIS ENDOSCOPIC INDEX OF SEVERITY: A POTENTIAL IMPROVEMENT OVER EXPERT EVALUATIONS

B. Lo^{1,2}, B.L. Møller³, A. Poulsen⁴, M.F. Kristiansen⁴, I.B. Gottschalck⁴, M.W. Brandt⁴, S. Rashid⁴, E.E. Dahl⁴, I. Vind^{1,2}, F. Bendtsen^{1,2}, C. Igel³, B. Ibragimov³, J. Burisch^{1,2}

¹Copenhagen University Hospital – Amager and Hvidovre, Hvidovre, Gastro Unit, Medical Section, Hvidovre, Denmark, ²Copenhagen University Hospital – Amager and Hvidovre, Hvidovre, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre, Denmark, ³University of Copenhagen, Department of Computer Science, Copenhagen, Denmark, ⁴Copenhagen University Hospital – Bispebjerg and Frederiksberg, Bispebjerg, Digestive Disease Center, København N, Denmark

Contact E-Mail Address: bobby.lo@regionh.dk

Introduction: Endoscopic evaluation of disease severity remains the cornerstone of disease assessment in ulcerative colitis (UC). Endoscopic evaluation using scoring systems such as the Mayo Endoscopic Subscore (MES) is, however, subjective with interrater agreements typically ranging from a kappa of 0.4 to 0.7. Post-hoc analysis from clinical trials indicates that up to 30% of patients were incorrectly included due to misclassification of disease severity. Recent studies including our own using artificial intelligence (AI) to assess the MES have shown enhanced classification accuracy using only white light procedures¹.

Aims & Methods: In this study, we aimed to refine our AI model to assess disease severity using the Ulcerative Colitis Endoscopic Index of Severity (UCEIS).

We extracted 2000 images from recorded sigmoidoscopy/colonoscopy performed on UC patients at the Gastrounit, Copenhagen University Hospital Hvidovre, Denmark. Six IBD experts from The Digestive Disease Center, Copenhagen University Hospital Bispebjerg, scored each image according to the UCEIS and MES. The majority score from the six experts for each subscore (Bleeding, Erosions and Ulcers, Vascular Pattern) was considered the gold standard. In cases of tied scores, the higher score was selected, preferring a model that overestimates rather than underestimates disease severity. The final UCEIS score was the sum of the gold standards for each subscore.

A convolutional neural network was trained on 80% of the images, and then validated on the remaining 20%. The network performance was evaluated against gold standard and individual experts' scores.

Results: All six experts evaluated all 2000 images; the results are summarized in Table 1.

(linear) Kappa	Expert Mean	Min	Max	AI Model
Bleeding	0.62	0.44	0.73	0.78
Erosion and Ulcers	0.65	0.46	0.71	0.82
Vascular pattern	0.73	0.41	0.88	0.88
Total UCEIS	0.69	0.44	0.80	0.84
Total MES	0.68	0.50	0.77	0.87

Table 1: Comparative kappa scores from the leave-one-out analysis of experts and the model versus gold standard (majority score from all six experts) for each subscore and the total of the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and Mayo Endoscopic Subscore (MES).

The model surpassed the interrater reliability of expert IBD endoscopists in all subscores, showing particularly strong performance in the erosion and ulcers and vascular patterns subscores. The model's moderate performance in the "bleeding" subscore reflects the lower kappa scores among

experts, underscoring the challenges of visual assessments in this area. Notably, the model's performance on the MES was high, indicating significant overlap in the visual cues used for both UCEIS and MES scoring.

Conclusion: This study demonstrates the potential of using an AI model to enhance the accuracy of UC severity assessments with the UCEIS with results surpassing experts. The overlapping visual cues for MES and UCEIS suggest that the AI model can streamline training and application across different scoring systems, enhancing clinical practice efficiency.

We plan to validate the model on a new test set from another hospital to further evaluate its generalizability and effectiveness across various settings. This is essential for confirming its potential to significantly improve the consistency and precision of UC severity assessments.

References: 1. Lo, B. *et al.* High accuracy in classifying endoscopic severity in ulcerative colitis using convolutional neural network. *American Journal of Gastroenterology* Publish Ah, (2022).

Disclosure: Nothing to disclose.

OP205

DEEP LEARNING AND CAPSULE ENDOSCOPY: AUTOMATIC PANENDOSCOPIC DETECTION OF VASCULAR LESIONS

M. Martins¹, M.J. Mascarenhas Saraiva¹, J. Afonso¹, T. Ribeiro¹, P. Cardoso¹, F. Mendes¹, M.J. Almeida¹, J. Mota¹, A.P. Andrade¹, H. Cardoso¹, J. Ferreira², G. Macedo¹

¹São João University Hospital, Gastroenterology, Porto, Portugal, ²Faculty of Engineering of University Porto, Department of Mechanical Engineering, Porto, Portugal

Contact E-Mail Address: miguel.pedro96@gmail.com

Introduction: Capsule endoscopy (CE) is frequently employed as the first exam when mid-gastrointestinal bleeding is suspected, following normal upper and lower endoscopies. While its primary focus is on evaluating the small bowel, detection of vascular lesions both upstream and downstream could also hold clinical importance.

Aims & Methods: The aim of this study is to develop and test a Convolutional Neural Network (CNN)-based model for panendoscopic automatic detection of vascular lesions during CE. A retrospective study involving 2 centers was conducted, involving 1188 CE exams. A total of 152,312 frames were utilized, obtained from seven distinct types of CE devices, with 14,942 frames being classified as vascular lesions (angiectasias or varices) after triple validation. The data was divided in training/validation (90%) and test (10%) sets, using an exam-split design. A 5-fold cross-validation was conducted during training/validation set. The all process was iterated five times. The primary outcome measures were sensitivity, specificity, accuracy, area under the conventional receiver operating characteristic curve (AUC-ROC) and the precision-recall curve (AUC-PR), from the training/validation set.

Results: The model demonstrated a mean sensitivity and specificity of 87.5% (IC95% 81.5 – 93.6%) and 99.5% (IC95% 99.3 – 99.7%), respectively. Mean accuracy was 98.4% (IC95% 97.7 – 99.1%). Mean AUC-ROC value was 0.987 (IC95% 0.980 – 0.995), while AUC-PR value was 0.998 (IC95% 0.997 – 1.000).

Conclusion: This represents the first proof-of concept AI deep learning model developed for panendoscopic automatic detection of vascular lesions during CE. The CCN's high diagnostic performance in multibrand devices addresses a critical issue of technological interoperability, allowing it to be replicated in multiple technological settings.

Disclosure: Nothing to disclose.

OP206

FRAME BY FRAME INTRAPROCEDURAL PHASE RECOGNITION DURING ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) USING ARTIFICIAL INTELLIGENCE

M. Scheppach¹, D. Weber Nunes², X. Arizi¹, D. Rauber², A. Probst¹, S. Nagl¹, C. Römmele¹, C. Palm², H. Messmann¹, A. Ebigo¹

¹University Hospital of Augsburg, Internal Medicine III - Gastroenterology, Augsburg, Germany, ²Ostbayerische Technische Hochschule Regensburg, Regensburg Medical Image Computing (ReMIC), Regensburg, Germany

Contact E-Mail Address: markus.scheppach@uk-augsburg.de

Introduction: Recent evidence suggests a possible role of artificial intelligence in procedural quality measurement for endoscopic submucosal dissection by artificial intelligence¹. Precise frame by frame differentiation of operational phases may allow for a deeper understanding of the procedure and open a wide range of possibilities from automated documentation to concise training support.

Aims & Methods: In this study, we aimed to develop an algorithm for frame by frame procedural phase recognition during ESD. To this end, a dataset (27 ESDs, 2071546 single frames) was annotated for the operational supra-phases diagnostics, marking, needle injection, dissection and bleeding. Furthermore, the subphases scope manipulation, injection and application of electrical current were annotated where appropriate. A training-subset (17 ESDs, 898440 single frames) was used to train a video swin transformer with uniform frame sampling to detect the classes. The trained algorithm was evaluated internally (6 ESDs, 769523 single frames) and on a separate dataset (4 ESDs, 403583 single frames).

Results: Overall F1 Scores for internal validation and validation on the separate dataset were 83% and 90%, respectively. True positive rates for diagnostics, marking, needle-injection, dissection and bleeding were 100%, 100%, 96%, 97% and 93%, respectively. Overall F1 score over all supra-phases was 94%, overall accuracy was 93%. True positive rates for scope manipulation, injection and application of electrical current were 92%, 98% and 91%, respectively. Overall F1 score for subphases was 91%, overall accuracy was 97%.

Conclusion: The trained algorithm classified full length ESD videos on a frame by frame basis for concise surgical phases with high accuracy. Future research will focus on the development of intraprocedural quality measures, as well as automated reporting.

References: 1. Cao J, Yip HC, Chen Y, et al. Intelligent surgical workflow recognition for endoscopic submucosal dissection with real-time animal study. *Nat Commun* 2023;14:6676.

Disclosure: All authors declare no conflict of interest concerning this study.

Eosinophilic oesophagitis

11:30-12:30 / Lehar 3

OP207

EFFICACY AND SAFETY OF THE SELECTIVE SPHINGOSINE 1-PHOSPHATE RECEPTOR MODULATOR, ETASIMOD, IN ADULT PATIENTS WITH EOSINOPHILIC OESOPHAGITIS OVER 52 WEEKS IN THE PHASE 2 VOYAGE STUDY

E.S. Dellon¹, M.H. Collins², A.J. Bredenoord³, H. Philpott⁴, L. Biedermann⁵, M. Dulcine⁶, T. Nguyen-Cleary⁷, C. Su⁷, J. Yu⁷, H. Tan⁸, F. Cataldi⁷, H. Zheng⁹, W. Wang⁷, P. Clax⁷, J.C. Woolcott⁷, I. Hirano¹⁰

¹University of North Carolina School of Medicine, Center for Esophageal Diseases and Swallowing, and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, Chapel Hill, United States of America, ²Cincinnati Children's Hospital Medical Center, Division of Pathology and Laboratory Medicine, Cincinnati, United States of America, ³Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁴University of Adelaide, Northern Adelaide Local Health Network (NALHN), Department of Gastroenterology Lyell McEwin and Modbury Hospitals, Adelaide, Australia, ⁵University Hospital Zürich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ⁶Pfizer Brazil, São Paulo, Brazil, ⁷Pfizer Inc, Collegeville, United States of America, ⁸Pfizer Inc, Groton, United States of America, ⁹Pfizer Inc, New York, United States of America, ¹⁰Northwestern University, Kenneth C. Griffin Esophageal Center, Division of Gastroenterology and Hepatology, Feinberg School of Medicine, Chicago, United States of America

Contact E-Mail Address: luc.biedermann@usz.ch

Introduction: Etrasimod is an investigational, oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator in development to treat immune-mediated inflammatory disorders.

Aims & Methods: This analysis aimed to report the 52-week (wk) efficacy and safety data from the phase 2 VOYAGE study in adults with active eosinophilic oesophagitis (EoE). VOYAGE (NCT04682639) included a 24-wk randomised, double-blind, placebo (PBO)-controlled treatment period, followed by a 28-wk extension.

At Wk 24, patients (pts) continued on etrasimod 1 or 2 mg QD or were randomised from PBO to etrasimod 1 or 2 mg QD (data not shown) for 28 wks (investigator and pts remained blinded). The efficacy analyses presented include data from PBO-controlled and extension treatment period outcomes at Wk 52, with a focus on pts who received etrasimod in both periods (etrasimod 2 mg–2 mg and 1 mg–1 mg).

Efficacy endpoints included percentage change from baseline (BL) (%CFB) in oesophageal peak eosinophil count (PEC) at Wk 16 (primary endpoint), proportion of pts who achieved PEC <15 and ≤6 eosinophils/high power field (eos/HPF), and CFB in EoE-Histology Scoring System (EoE-HSS) grade and stage scores, EoE Endoscopic Reference Score (EREFS), Patient Global Impression of Severity (PGIS) and Dysphagia Symptom Questionnaire (DSQ; overall and by BL dilation history) at Wks 16, 24 and 52. Safety data are presented to Wk 52.

Results: 108 pts were randomised in the PBO-controlled period; 85 pts entered the extension period, with 30 and 31 pts maintaining etrasimod 2 and 1 mg QD, respectively. Treatment with etrasimod 2 mg resulted in a 46.1% decrease from BL in PEC (PBO-adjusted) at Wk 16 ($p=0.0103$) with the improvement maintained at Wk 24; improvements vs BL were seen at Wk 52 (Table). Other histological and endoscopic endpoints, including oe-

Time point								
Endpoint	BL		Wk 16 ^a		Wk 24 ^a		Wk 52 ^b	
Dose; PBO-controlled period/ extension treatment period	Mean (SD) [median]	Observed value, mean (SD) [median]	Mean CFB (SD or SE) ^c [median]	Mean difference from PBO [median]	Observed value, mean (SD) [median]	Mean CFB (SD or SE) ^c [median]	Mean difference from PBO [median]	Observed value, mean (SD) [median]
PEC ^{c,d}								
Etrasimod								
2 mg QD (N=41)	116.5 (82.59)	66.3 (91.73)	-38.3 (77.91)	-46.1 [-36.9]	57.8 (111.23)	-52.4 (59.66)	-113.7 [-103.9]	71.4 (81.20)
/Etrasimod	[88.0]	[27.0]	[-58.4]	p=0.0103	[16.0]	[-76.2]	p<0.0001	[40.5]
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	106.3 (83.31)	101.7 (110.45) [67.0]	40.3 (269.93)	32.5 [-17.9]	72.2 (80.81)	-27.4 (78.00)	-88.7 [-78.0]	119.2 (176.04) [56.0]
1 mg–1 mg QD (N1=30)	[87.0]		[-39.4]	p=0.2861	[32.5]	[-50.3]	p=0.0022	
EoE-HSS grade ^{e,d,e}								
Etrasimod								
2 mg QD (N=41)	0.4 (0.18)	0.3 (0.19)	-0.1 (0.02)	-0.11	0.2 (0.18)	-0.2 (0.03)	-0.21	0.3 (0.17)
/Etrasimod		[0.2]		p=0.0040	[0.2]		p<0.0001	[0.3]
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	0.4 (0.19)	0.3 (0.19)	-0.1 (0.02)	-0.07	0.2 (0.20)	-0.1 (0.03)	-0.19	0.3 (0.17)
1 mg–1 mg QD (N1=30)		[0.3]		p=0.0712	[0.2]		p<0.0001	[0.3]
EoE-HSS stage ^{e,d,e}								
Etrasimod								
2 mg QD (N=41)	0.4 (0.20)	0.2 (0.20)	-0.2 (0.03)	-0.13	0.2 (0.20)	-0.2 (0.03)	-0.23	0.2 (0.17)
/Etrasimod		[0.2]		p=0.0038	[0.1]		p<0.0001	[0.3]
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	0.4 (0.24)	0.3 (0.24)	-0.1 (0.03)	-0.06	0.2 (0.24)	-0.2 (0.03)	-0.20	0.2 (0.18)
1 mg–1 mg QD (N1=30)		[0.3]		p=0.1790	[0.2]		p=0.0001	[0.2]
EREFs ^{c,f,g}								
Etrasimod								
2 mg QD (N=41)	3.7 (1.74)	2.4 (1.78)	-1.3 (0.24)	-1.0	2.4 (1.78)	-1.3 (0.26)	-0.91	1.9 (1.77)
/Etrasimod		[2.0]		p=0.0135	[2.0]		p=0.0303	[1.5]
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	3.2 (1.59)	2.7 (1.53)	-0.8 (0.24)	-0.5	2.4 (1.75)	-1.0 (0.26)	-0.61	2.3 (1.71)
1 mg–1 mg QD (N1=30)		[3.0]		p=0.2160	[2.0]		p=0.1473	[2.0]
Proportion with PEC <15 eos/HPF, %								
Etrasimod								
2 mg QD (N=41)	N/A		22.0			31.7		34.6
/Etrasimod								
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	N/A		12.8			30.8		23.3
1 mg–1 mg QD (N1=30)								
Proportion with PEC ≤6 eos/HPF, %								
Etrasimod								
2 mg QD (N=41)	N/A		12.2			24.4		23.1
/Etrasimod								
2 mg–2 mg QD (N1=26)								
Etrasimod								
1 mg QD (N=39)								
/Etrasimod	N/A		7.7			15.4		13.3
1 mg–1 mg QD (N1=30)								

^aFull analysis set; includes all randomised pts who received at least one dose of study treatment.

^bEfficacy evaluable set; includes all randomised pts who received at least one dose of study treatment with an extension BL measurement and a Wk 52 measurement in the extension treatment period. The efficacy evaluable set can vary with endpoints since some pts may have the required data for some endpoints but not others.

^c%CFB (mean [SD] [median]) calculated for PEC, and CFB (least squares mean [SE]) calculated for EoE-HSS grade and stage, EREFS, PGIS and DSQ. All PBO-adjusted differences from PBO are expressed as least squares mean, except %CFB in PEC, which is expressed as the mean and median difference.

^dp values are from an analysis of covariance model for rank score of %CFB, including factors for treatment group, BL history of oesophageal dilation (Yes/No), concurrent PPI therapy (Yes/No), and BL eosinophil PEC (eos/HPF) as a covariate.

^eGrade and stage score range from 0–3 for each individual component of the EoE-HSS. Total scores are reported and are the ratio of observed component scores divided by the maximum possible score depending on the number of individual components that are present/evaluable.

^fp values are from a linear mixed effects model for change from BL, including factors for treatment group, visit, interaction of treatment-by-visit, BL history of oesophageal dilation (Yes/No), concurrent PPI therapy (Yes/No), and BL score as a covariate.

^gScore ranges from 0–9.

^hScore ranges from 0–4.

ⁱScore ranges from 0–84.

%CFB, percentage change from baseline; BL, baseline; DSQ, Dysphagia Symptom Questionnaire; EoE-HSS, Eosinophilic Oesophagitis-Histology Scoring System; eos, eosinophils; EREFS, Eosinophilic Oesophagitis Endoscopic Reference Score; HPF, high power field; N, number of pts in the treatment group; N1, number of pts in the efficacy evaluable set for the extension treatment period; N/A, not available; PBO, placebo; PEC, peak eosinophil count; PGIS, Patient Global Impression of Severity; PPI, proton pump inhibitor; pt, patient; QD, once daily; SD, standard deviation; SE, standard error; Wk, Week.

OP207 Table. Change from BL (CFB) in oesophageal PEC at Wk 16 (primary endpoint) and additional efficacy endpoints at Wks 24 and 52 in the VOYAGE study.

sophageal PEC <15 and ≤ 6 eos/HPF, EREFS and EoE-HSS, also showed statistically significant improvement at Wks 16 and 24, with improvements vs BL at Wk 52 in pts who received etrasimod 2 mg QD for the full study duration (Table, following page).

Statistically significant reductions in PGIS in the overall population and DSQ in pts without BL dilation history who received etrasimod 2 mg QD were observed at Wk 24 (-0.48 and -11.95, respectively; $p < 0.05$ for both parameters). PGIS and DSQ score improvements vs BL (overall population) were seen at Wk 52 in pts who received etrasimod 1 or 2 mg. In total, 16/30 (53.3%) and 19/31 (61.3%) pts reported treatment-emergent adverse events (TEAEs) in the 2 and 1 mg groups, respectively.

No TEAEs were considered serious or resulted in death. In the 2 mg etrasimod QD group, 2 pts discontinued treatment due to TEAEs of Alanine aminotransferase increased and Hypoglossal nerve paralysis; 1 pt in the 1 mg etrasimod QD group discontinued due to Dry eye and Dyspnoea.

Conclusion: PBO-adjusted improvements in histological and endoscopic features of EoE at Wks 16 and 24, and improvements in symptoms (PGIS and DSQ in pts without dilation) at Wk 24 in pts who received etrasimod 2 or 1 mg QD were also seen at 52 wks vs BL. The etrasimod safety profile appears consistent in pts with EoE and those in other indications.

Disclosure: ESD has received grant/research support from Adare/Ello-di, Allakos, Arena/Pfizer, AstraZeneca, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo and Shire/Takeda; has received consulting fees from Abbott, AbbVie, Adare/Ello-di, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, EsoCap, Eupraxia, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, Lilly, LucidDx, Morphee, Nexstone Immunology, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE and Upstream Bio; and has received educational grants from Allakos, Holoclara and Invea. **MHC** has been a consultant for Alimentiv/Robarts, Allakos, Arena, BMS, EsoCap, Pfizer, Regeneron, Sanofi, Shire a Takeda company and AstraZeneca. **AJB** has received grant/research support from Nutricia, Norgine, Dr. Falk Pharma, Thelial, Sanofi/Regeneron and SST; lecture fees from Laborie, Medtronic, Dr. Falk Pharma, Reckitt, Aqilion, Eupraxia, Alimentiv, Sanofi/Regeneron and AstraZeneca; and has received consulting fees from Laborie, Medtronic, Dr. Falk Pharma, Reckitt, Aqilion, Eupraxia, Alimentiv, Sanofi/Regeneron and AstraZeneca. **HP** has received research grants from Hospital Research Foundation South Australia; is a speaker for Falk and GSK; and has received consulting fees from AusEE and Falk. **LB** has received consulting fees from AbbVie, Calypso, Esocap, Ewopharma, Falk, Ferring, Janssen, MSD, Pfizer Inc, Sanofi, Shire, Takeda and Vifor. **MD, CS, JY, HT, WW** and **JCW** are employees and shareholders of Pfizer Inc. **TNC** and **HZ** were employees and shareholders of Pfizer Inc at the time the work was completed. **FC** was an employee of Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, at the time of analysis. **PC** is an employee and shareholder of Pfizer Inc; and is a stockholder of Zoetis Animal Health Co, Merck & Co. and various privately purchased stock. **IH** has received research grants from NIH, Adare/Ello-di, Allakos, Arena, AstraZeneca, Meritage, Celgene/Receptos/BMS, Regeneron and Shire/Takeda; has received consulting fees from Adare/Ello-di, Allakos, Amgen, Arena/Pfizer, Aslan, AstraZeneca, Celgene/Receptos/BMS, Celldex, EsoCap, Gossamer Bio, Nexstone Immunology, Parexel/Calyx, Phathom, Regeneron, Sanofi and Shire/Takeda.

OP208

BUDESONIDE ORAL SUSPENSION IS EFFECTIVE AND SAFE FOR INDUCTION THERAPY OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN AND ADOLESCENTS: RESULTS FROM TWO SEQUENTIAL INDUCTION PHASES OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (PEDEOS-1)

A.J. Lucendo¹, H. Antunes^{2,3}, A. Papadopoulou⁴, M.K.-H. Auth⁵, S. Dutt⁶, J.C. Escher⁷, M.P. van Wijk⁸, G. Dominguez-Ortega⁹, C. Gutiérrez-Junquera¹⁰, N. Zevit¹¹, T. Zangen¹², E. Trindade¹³, M. Fotoulaki¹⁴, B. Dalgic¹⁵, A.I. Lopes¹⁶, S. Feo-Ortega¹, F. Neiva², V.-M. Karagianni⁴, M. Rogalidou⁴, D. Hendriks⁷, C. Mussies⁸, N. Puente Ubierna⁹, M.d.C. Espinheira¹³, H. Loreto¹⁶, M. Vieth¹⁷, S. Burrack¹⁸, R. Mueller¹⁸, R. Greinwald¹⁸, S. Buderus¹⁹, J. Amil-Dias¹³, International PEDEOS-1 Study Group

¹Hospital General de Tomelloso, Dept. de Gastroenterology, Madrid, Spain, ²Hospital de Braga, Pediatric Gastroenterology Unit and Clinical Academic Center 2CA-Braga, Braga, Portugal, ³Life and Health Sciences Research Institute, ICVS/3B's, University of Minho, Associate Laboratory and School of Medicine, Braga, Portugal, ⁴University of Athens, First Department of Pediatrics, Athens, Greece, ⁵Alder Hey Children's NHS Foundation Trust and University of Liverpool, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Liverpool, United Kingdom, ⁶The Children's Hospital at Westmead, Department of Gastroenterology, Westmead, Australia, ⁷Erasmus MC Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands, ⁸Emma Children's Hospital, Amsterdam UMC, VU University, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands, ⁹Niño Jesús University Children's Hospital, Gastroenterology and Nutrition Department, Madrid, Spain, ¹⁰Hospital Puerta de Hierro-Majadahonda, Autonomous University of Madrid, Pediatric Gastroenterology, Madrid, Spain, ¹¹Schneider Children's Medical Center of Israel, Institute of Gastroenterology, Hepatology, and Nutrition, Petah-Tikva, Israel, ¹²Wolfson Medical Center, Pediatric Gastroenterology and Nutrition Unit, Holon, Israel, ¹³Centro Hospitalar Universitário São João, Department of Pediatrics, Porto, Portugal, ¹⁴Aristotle University of Thessaloniki, Dept. Paediatric Gastroenterology, Thessaloniki, Greece, ¹⁵Gazi University Medical School, Departments of Paediatric Gastroenterology, Ankara, Turkey, ¹⁶University Hospital Santa Maria, Medical School, University of Lisbon, Pediatric Gastroenterology Unit, Lisbon, Portugal, ¹⁷Friedrich-Alexander-University Erlangen-Nuremberg, Klinikum Bayreuth, Institute of Pathology, Bayreuth, Germany, ¹⁸Dr. Falk Pharma GmbH, Clinical Research and Development, Freiburg, Germany, ¹⁹GFO-Kliniken Bonn, St. Marien-Hospital, Bonn, Germany

Contact E-Mail Address: henedinaantunes@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus with increasing incidence in all age groups^{1,2} and limited treatment options for pediatric patients. We evaluated the efficacy and safety of two doses of a novel budesonide oral suspension (BOS) for induction therapy of pediatric EoE in a phase 2/3 trial.

Aims & Methods: An initial 12-week randomized, double-blind (DB) induction phase enrolled 76 pediatric patients with active EoE aged 2-11 years (stratum I; n=35) and 12-17 years (stratum II; n=41). Patients were randomized to high-dose BOS (BOS-H: 0.5 mg (stratum I)/1 mg (stratum II) BOS, twice daily; n=26), low-dose BOS (BOS-L: 0.5 mg (stratum I)/1 mg (stratum II) BOS, once daily; n=26) or placebo (n=24). The composite primary endpoint was the proportion of patients with histologic remission plus clin-

ical response at week 12. Secondary endpoints included the proportion of patients with histologic remission, change in peak eosinophil counts, and the proportion of patients with clinical response. Patients who did not achieve the primary endpoint at week 12, who experienced a food impaction requiring endoscopic intervention or dilation, or with a lack of efficacy after week 8 were eligible for a subsequent open-label induction (OLI) phase. In this additional phase, 45 patients all received BOS-H for a further 12 weeks, after which the same endpoints were assessed.

Results: In the DB phase, the proportion of patients achieving the composite endpoint of histologic remission plus clinical response was significantly higher in both BOS treatment groups compared with placebo, with superior and clinically relevant results with high-dose versus low-dose BOS (Table). Both BOS doses demonstrated significantly superior benefits versus placebo on the secondary endpoints of histologic remission and peak eosinophil counts. However, no relevant differences were observed in clinical response between any groups. In the OLI phase, patients who received BOS-L or placebo in the DB phase achieved comparable rates of histologic remission and clinical response as the BOS-H group in the DB phase (Table).

Esophageal candidiasis was observed in 1 patient receiving BOS-H in the DB phase and 4 patients in the OLI phase. Decreased cortisol levels were recorded in 1 BOS-H patient, 1 placebo patient, and 1 OLI patient, with 1 case each of adrenal insufficiency and adrenal suppression in the OLI phase. Adrenal-related events were of mild severity. No bolus impactions requiring emergency endoscopy or serious adverse events related to BOS were reported.

	Double-Blind induction (DB, 12 weeks)			Open-Label Induction (OLI, 12 weeks)		
	BOS-H (n=26)	BOS-L (n=26)	Placebo (n=24)	BOS-H > BOS-H (n=8)	BOS-L > BOS-H (n=14)	Placebo > BOS-H (n=23)
Primary endpoint						
Patients with both histologic remission ¹ and clinical response ² at week 12 (LOCF), n (%)	18 (69.2%)	12 (46.2%)	0 (0%)	4 (50.0%)	11 (78.6%)	13 (56.5%)
	69.2%	46.2%				
Difference in proportions • [98.75% CI]	[46.6; 91.8] p < 0.0001*	[21.7; 70.6] p < 0.0001*				
Secondary endpoints						
Patients in histologic remission ¹ at week 12 (LOCF), n (%)	23 (88.5%) p < 0.0001*	16 (61.5%) p < 0.0001*	0 (0%)	7 (87.5%)	12 (85.7%)	20 (87.0%)
Peak eos/mm ² hpf						
Mean (SD) at baseline ¹	238 (123.1)	246 (108.7)	239 (122.1)	35 (74.0)	140 (188.0)	228 (155.6)
Mean (SD) at week 12 (LOCF)	10 (40.4)	76 (153.1)	228 (155.6)	7 (20.1)	16 (46.7)	24 (83.9)
Mean change from baseline ² to week 12 (LOCF)	-229 [-278.0; -179.5] p < 0.0001*	-170 [-248.2; -92.2] p < 0.0001*	-8 [-77.8; 62.3]	-27 [-102.2; 47.4]	-124 [-232.7; -15.4]	-221 [-294.2; -147.9]
• [95% CI]						
Patients with clinical response ² at week 12 (LOCF), n (%)	20 (76.9%) p = 0.4328*	18 (69.2%) p = 0.6663*	17 (70.8%)	5 (62.5%)	13 (92.9%)	16 (69.6%)

¹Peak eosinophils < 16 eos/mm² hpf (i.e. < 5 eos/hpf); ²≥ 30% decrease on Pediatric EoE Symptom Severity Module, version 2.0 (PEESS v2.0) from baseline (DB baseline or OL baseline, respectively); ³DB baseline or OL baseline, respectively. * p-values shown depict comparison of treatment groups with placebo.
BOS: Budesonide oral suspension; BOS-H: High-dose BOS; BOS-L: Low-dose BOS; CI: Confidence interval; eos: Eosinophils; hpf: High-power field; LOCF: Last observation carried forward; SD: Standard deviation

Table. Efficacy endpoints (full analysis set).

Conclusion: BOS was safe and effective in inducing histologic remission associated with clinical response in pediatric patients with EoE. Superiority of BOS on the primary clinico-histologic endpoint and secondary histologic endpoints was demonstrated over placebo and for high-dose versus low-dose BOS. Clinical response rates were comparable among treatment groups. Treatment with high-dose BOS for a further 12 weeks led to improvement in patients not achieving remission in the DB phase. Adverse events were of mild or moderate severity.

References: 1 Navarro P, Arias Á, Arias-González L, Laserna-Mendieta EJ, Ruiz-Ponce M, Lucendo AJ. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. *Aliment Pharmacol Ther.* 2019;49(9):1116-1125.

2 Roberts SE, Morrison-Rees S, Thapar N, Williams JG. Incidence and prevalence of eosinophilic oesophagitis across Europe: A systematic review and meta-analysis. *United European Gastroenterol J.* 2024;12(1):89-102.

Disclosure: Alfredo J. Lucendo: Consulting fees from Dr. Falk, Escap; research support from Arena, AstraZeneca, Dr. Falk, EsoCap, Regeneron, Sanofi.

Alexandra Papadopoulou: Speaker and consulting fees from Adare, Cross, Dr. Falk, Danone (Nutricia), Nestle, Petsiavas, Sanofi, Specialty Therapeutics, Touch Independent Medical Education, Uni-Pharma Pharmaceutical Laboratories; research support from Abbvie, AstraZeneca, Dr. Falk, Takeda, United Pharmaceuticals.

Marcus Karl-Heinz Auth: Consulting fees from Dr. Falk; research support from GutsUK/BSPGHAN; travel support from Abbott, Danone (Nutricia), and RD.

Johanna C. Escher: Consulting fees from Abbvie, Janssen; education support from Abbvie; research support from MSD.

Michiel van Wijk: Speaker fees from Danone (Nutricia).

Gloria Dominguez-Ortega: Consulting fees from RD (Mead Johnson Nutrition); education support from Nestle Health Service, Danone (Nutricia).

Noam Zevit: Speaker fees from Rafa, Regeneron, Sanofi; consulting fees from AstraZeneca, Rafa, Regeneron, Sanofi.

Vassiliki-Maria Karagianni: Research support from AstraZeneca, Dr. Falk, Takeda.

Maria Rogalidou: Research support from AstraZeneca, Takeda, United Pharmaceuticals; speaker fees and travel support from Danone (Nutricia), Nestle.

Michael Vieth: Speaker fees from Abbvie, Dr. Falk, Eli Lilly, Malesci.

Jorge Amil-Dias: Speaker fees from Capricare, Danone, Ferrer, Takeda; consulting fees from Adacyte.

Sarah Burrack, Ralph Mueller, Roland Greinwald: Employees of Dr. Falk Pharma GmbH.

OP209

A NOVEL DELIVERY-SYSTEM FOR TOPICAL EOSINOPHILIC ESOPHAGITIS TREATMENT WITH MOMETASONE FUROATE: RESULTS OF THE PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED ACESO-TRIAL

A. Lucendo¹, E.S. Dellon², A. Bredenoord³, A. Straumann⁴, I. Racamier⁵, G. Gouya-Lechner⁶

¹Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain, ²University of North Carolina School of Medicine, Chapel Hill, NC, United States of America, ³Amsterdam UMC, Dept. of Gastroenterology, Amsterdam, Netherlands, ⁴Department of Gastroenterology, University Hospital Zurich, Switzerland, ⁵Gastroenterology FMH, Kappel, Switzerland, ⁶Escap AG, Ceo, Basel, Switzerland, ⁶GOUYA INISGHTS GmbH & Co KG, Clinical, Vienna, Austria

Contact E-Mail Address: ajlucendo@hotmail.com

Introduction: Eosinophilic esophagitis (EoE) is an increasingly prevalent esophageal disease resulting in dysphagia and food impaction. ESO-101 targets the esophageal mucosa by significantly increasing topical medication contact time through the slow release of mometasone furoate. This innovative application technology consists of a drug-loaded thin-film rolled up in a capsule that unravels and sticks to the esophageal mucosa when swallowed. The current proof-of-concept phase 2 study evaluated the efficacy and safety of ESO-101.

Aims & Methods: This randomized, double-blind, placebo-controlled trial (NCT04849390) investigated the safety and efficacy of ESO-101 in adult patients with EoE and dysphagia. Patients were randomized 2:1 to once-daily treatment with ESO-101 800 µg or placebo and treated for 4-weeks. The

primary endpoint was the absolute change in peak eosinophil count (eos/hpf) from baseline. Secondary endpoints were the change in EoE Endoscopic Reference Score (EREFS) and dysphagia symptoms measured by the 11-point numeric rating scale (NRS). Safety was also assessed.

Results: 59 patients were screened at 13 European study sites, 43 patients were randomized, and 40 (27 to ESO-101 and 13 to placebo) completed the trial. For all histological and endoscopic endpoints, ESO-101 led to a statistical improvement compared to placebo. The mean decrease in peak eosinophil count was 49.1 (± 88.4) eos/hpf with ESO-101, while counts increased by a mean of 6.6 (± 65.1) eos/hpf in the placebo group ($p=0.0318$). Mean EREFS decreased by 3.9 (± 2.6) with ESO-101 and there was no change with placebo (-0.1 [2.3]) ($p=0.0001$). A higher proportion of patients showed a histological response (<15 eos/hpf) with ESO-101 versus placebo (48% vs 0%; $p=0.0028$). There was also numerical improvement in the dysphagia severity score in the ESO-101 group (median improvement in the dysphagia severity of 4 scores [relative change: -71%]) compared to placebo (improvement in 3 scores [relative change: -57%]). No cases of oropharyngeal or esophageal candidiasis were observed (Table 1).

Outcome parameters ACESO study	ESO-101 (n=28)	Placebo (n=15)	p-value
Absolute change in peak eosinophil count CFB mean (SD)	-49.11 (88.42)	6.63 (65.11)	0.0318
Histological response < 15 eos/hpf (n [%])	13 (48.1)	0 (0.0)	0.0028
Histological response < 15 eos/hpf and improvement in the dysphagia severity score (n [%])	12 (44.4)	0 (0.0)	0.0035
Absolute change in the EREFS CFB mean (SD)	-3.9 (2.6)	-0.1 (2.3)	0.0001
Absolute change in dysphagia severity score CFB mean (SD)	-3.2 (2.0)	-3.0 (2.2)	n.s.
Relative change in dysphagia severity score CFB mean (SD)	-61.46 (37.87)	-47.27 (30.36)	n.s.
Oropharyngeal or esophageal candidiasis (n [%])	0 (0)	0 (0)	-
Treatment compliance defined as proportion of days IMP was taken (n [%])	96.44 (5.52)	92.88 (17.12)	-

Table 1: Main Outcome Parameters ACESO Study.

SD= standard deviation; CFB=change from baseline;

EREFS=endoscopic reference score; IMP=investigational medicinal product

Conclusion: ESO-101 resulted in statistically significant histologic and endoscopic improvements compared with placebo, even with the 4-week treatment duration. ESO-101 was well tolerated. The ACESO study underscores the promise of topical drug delivery to the esophagus using the ESO-101 drug delivery system and provides a robust foundation for future ESO-101 development for EoE therapy.

Disclosure:

- Lucendo AJ: Principal Investigator of the ACESO Study sponsored by EsoCap Biotech AG
- Dellon ES: Consultant to EsoCap Biotech AG
- Bredenoord AJ: Investigator of the ACESO study sponsored by EsoCap Biotech AG
- Straumann A: Consultant to EsoCap Biotech AG
- Racamier I: CEO of EsoCap Biotech AG
- Ghazaleh Gouya-Lechner: Medical Advisor of EsoCap Biotech AG

OP210

DUPILUMAB EFFICACY IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS AND PRIOR USE OF OR PRIOR INADEQUATE RESPONSE, INTOLERANCE, OR CONTRAINDICATION TO SWALLOWED TOPICAL CORTICOSTEROIDS: RESULTS FROM THE PHASE 3 EOE KIDS STUDY

M. Chehade¹, S. Oliva², D. Ashok³, R. Liu⁴, J. Maloney⁴, R.M. Abdulaj⁵, M. Louisias⁵, A. Radin⁴

¹Mount Sinai Center for Eosinophilic Disorders, Icahn School of Medicine at Mount Sinai, Departments of Pediatrics and Medicine, New York, United States of America, ²University Hospital Umberto, Sapienza University of Rome, Pediatric Digestive Endoscopy, Pediatric Gastroenterology and Liver Unit, Maternal and Child Health Department, Rome, Italy, ³Western University, Department of Paediatric Gastroenterology, London, Canada, ⁴Regeneron Pharmaceuticals Inc., Tarrytown, United States of America, ⁵Sanofi, Bridgewater, United States of America

Contact E-Mail Address: mirna.chehade@mssm.edu

Introduction: Eosinophilic esophagitis (EoE) is a chronic, type 2 inflammatory disease of the esophagus. Swallowed topical corticosteroids (STCs) are commonly used to treat EoE, however not all patients respond to STC treatment, and side effects may occur with long-term use. Dupilumab, a fully human monoclonal antibody that blocks drivers of type 2 inflammation, is approved for EoE in patients aged ≥ 1 year, weighing ≥ 15 kg in the US, and for adult and adolescent patients aged ≥ 12 years, weighing ≥ 40 kg in the EU.

We assessed the efficacy of dupilumab in children with EoE by baseline history of prior use of or prior inadequate response, intolerance, or contraindication to STCs in the Phase 3 EoE KIDS study (NCT04394351).

Aims & Methods: Eligible patients were aged 1 to <12 years with EoE unresponsive to proton pump inhibitors. This analysis includes patients randomized at Part A baseline to weight-tiered dupilumab higher-exposure (HE) or pooled placebo up to Week 16 (W16). Part B data were analyzed for patients who continued to receive dupilumab HE, and for patients who switched from exposure-matched placebo to dupilumab HE through to Week 52 (W52).

Patients were required to be withdrawn from STCs at least 8 weeks prior to study baseline. The study primary endpoint was the proportion of patients achieving peak eosinophil count (PEC) ≤ 6 eosinophils/high-power field (eos/hpf) at W16.

Secondary endpoints included the proportion of patients achieving PEC <15 eos/hpf, absolute change in the Endoscopic Reference Score (EREFS), EoE-Histologic Scoring System (EoE-HSS) grade/stage scores, and proportion of days with ≥ 1 EoE sign as assessed by the Pediatric EoE Sign/Symptom Questionnaire – Caregiver version (PESQ-C). Efficacy was assessed by prior use of or prior inadequate response, intolerance, or contraindication to STCs.

Results: Of the 102 patients who entered the study, most (80.4%) had a history of STC therapy, and 57.8% had a prior inadequate response, intolerance, or contraindication to STCs. Regardless of prior STC use, dupilumab HE improved the proportion of patients achieving ≤ 6 and <15 eos/hpf, and improved EREFS and EoE-HSS grade/stage scores at W16 versus placebo (Table). Up to W52, improvements continued or were maintained in patients continuing dupilumab HE, and improved in patients who switched from placebo to dupilumab HE regardless of prior STC use, although patient numbers were small in the subgroup without prior STC use (Table).

Similar improvements in PESQ-C with dupilumab HE were observed regardless of prior STC use (Table). Outcomes were similar in patients with/without prior inadequate response, intolerance, or contraindication to STCs.

		Week 16				Week 52			
		PBO (N = 34)		DUP HE (N = 37)		PBO/DUP HE (N = 18) ^a		DUP HE/DUP HE (N = 37) ^a	
		n/N ^b		n/N ^b		n		n	
Patients with PEC of ≤6 eos/hpf, n (%)	With prior STC	27/0	0	28/0	17 (60.7)	16	8 (50.0)	26	13 (50.0)
	Without prior STC	4/3	1 (14.3)	9/0	8 (88.9)	1	1 (100.0)	9	9 (100.0)
Patients with PEC of <15 eos/hpf, n (%)	With prior STC	27/0	0	28/0	22 (78.6)	16	10 (62.5)	26	21 (80.8)
	Without prior STC	4/3	1 (14.3)	9/0	9 (100.0)	1	1 (100.0)	9	9 (100.0)
EREFS total score ^c	With prior STC	22/0	0.3 (0.50)	24/2	-3.8 (0.46)	13	-3.08 (2.69)	22	-5.14 (3.30)
	Without prior STC	5/2	-0.7 (0.68)	8/0	-2.1 (0.63)	1	-11.00 (NA)	8	-3.75 (2.25)
HSS grade ^c	With prior STC	27/0	0.07 (0.05)	28/0	-0.91 (0.05)	16	-0.87 (0.30)	26	-1.03 (0.42)
	Without prior STC	4/3	-0.14 (0.09)	9/0	-0.74 (0.08)	1	-1.07 (NA)	9	-0.77 (0.23)
HSS stage ^c	With prior STC	27/0	0.06 (0.05)	28/0	-0.87 (0.05)	16	-0.85 (0.36)	26	-0.93 (0.33)
	Without prior STC	4/3	-0.01 (0.10)	9/0	-0.71 (0.09)	1	-1.01 (NA)	9	-0.78 (0.25)
PESQ-C ^c	With prior STC	25/2	-0.13 (0.06)	23/4	-0.27 (0.06)	8	-0.50 (0.41)	19	-0.28 (0.34)
	Without prior STC	5/2	-0.27 (0.10)	8/1	-0.26 (0.09)	1	-0.22 (NA)	8	-0.37 (0.17)

^aNumber of patients who completed the Week 52 visit in Part B were n = 17 for PBO/DUP HE and n = 35 for DUP HE/DUP HE. ^bPatients with missing PEC were considered non-responders if not due to COVID-19, and were imputed by MI if due to COVID-19; patients with missing values for change from Part A baseline in EREFS total score, and HSS grade and stage scores were imputed by WOCF method if not due to COVID-19, and by MI if due to COVID-19; patients with missing values for change from Part A baseline in the proportion of days with ≥1 EoE sign measured by PESQ-C were imputed by WOCF method if due to rescue treatment/adverse events/lack of efficacy, and by MI if due to other reasons. ^cChange from Part A baseline: LS mean (SE) at W16; mean (SD) at W52. DUP, dupilumab; EoE, eosinophilic esophagitis; eos/hpf, eosinophils/high-power field; EREFS, Endoscopic Reference Score; HE, higher-exposure; HSS, Histologic Scoring System; LS, least squares; MI, multiple imputations; NA, not applicable as n=1; NI, number imputed; PBO, placebo; PEC, peak eosinophil count; PESQ-C, Pediatric EoE Sign/Symptom Questionnaire – Caregiver version; SD, standard deviation; SE, standard error; STC, swallowed topical corticosteroid; WOCF, worst observation carried forward.

Table. Efficacy at Week 16 and Week 52 by prior STC use.

Conclusion: In children with EoE in the EoE KIDS study, dupilumab HE showed sustained improvements in histologic, symptomatic, and endoscopic aspects of EoE, regardless of prior use of or prior inadequate response, intolerance, or contraindication to STCs.

Disclosure: M.C.: Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, BMS, Nexstone Immunology, Phathom, Recludix Pharma, Regeneron Pharmaceuticals Inc., Sanofi, and Shire/Takeda – consultant; Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, Celgene/BMS, Danone, Regeneron Pharmaceuticals Inc., and Shire/Takeda – research funding. **S.O.:** Celgene/Receptos/BMS, Medtronic, Ocean Pharma, Sanofi/Regeneron Pharmaceuticals Inc. – consulting/advisory board; Medtronic, Sanofi/Regeneron Pharmaceuticals Inc. – speaker fees. **D.A.:** Alexion Pharma, LaunchitDTx, Mirum Pharma – consultant; Sanofi – speaker fees. **R.L., J.M., A.R.:** Regeneron Pharmaceuticals Inc. – employees and shareholders. **R.M.A., L.G.:** Sanofi – employees, may hold stock and/or stock options in the company.

OP211

ANALYSIS OF SMALL-RNAs FROM PLASMA EXTRACELLULAR VESICLES REVEALS THE DIAGNOSTIC POTENTIAL OF A MICRORNA PANEL FOR EOSINOPHILIC ESOPHAGITIS

E. Grueso-Navarro^{1,2,3}, L. Rodríguez-Alcolado^{2,3,1,4}, L. Arias-González^{2,3,5,1}, MP. Navarro Sánchez^{3,2,5,1}, J. González-Cervera^{2,6}, A.J. Lucendo^{3,7,2,5}, E.J. Laserna-Mendieta^{3,2,5,1}

¹Hospital General de Tomelloso, Gastroenterology Research Unit, Tomelloso, Spain, ²Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain, ³Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ⁴Universidad de Alcalá, Surgery, Medical and Social Sciences, Alcalá de Henares (Madrid), Spain, ⁵Instituto de Investigación Sanitaria de La Princesa, Madrid, Spain, ⁶Hospital General de Tomelloso, Allergy, Tomelloso, Spain, ⁷Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain

Contact E-Mail Address: Leticia3r@gmail.com

Introduction: Current diagnostic reliance on invasive endoscopy for eosinophilic esophagitis (EoE) underscores the urgent need for non-invasive biomarkers. Plasma-derived-extracellular vesicles (pEVs) offer a promising solution (1) as they are known carriers of inflammation-related molecules and are involved in immunity (2).

Particularly, extracellular microRNAs exhibit numerous functions in inflammation (3) and their utilisation as a source of biomarkers in immunity is being exploited.

Aims & Methods: Here we aimed to evaluate the potential of plasma-EVs (pEVs) RNA cargo as biomarker for diagnosing and monitoring EoE. Plasma was withdrawn from EoE-patients (basal and post-treatment samples), and control subjects for isolation of circulating EVs using size exclusion chromatography and ultrafiltration. Plasma EVs were then characterised by electron microscopy and flow cytometry. Profiling small RNA content was performed through high-throughput RNA sequencing across a discovery cohort (26 EoE patients and 16 controls), and biomarker candidates were evaluated by RT-qPCR in a validation cohort (33 EoE-patients and 14 controls). Functional insights were analysed by identifying KEGG and GO terms, and the area under the ROC curve (AUC) was used for assessing the diagnostic potential of selected candidates.

Results: The overall profile of RNA cargo of pEVs was sufficient to discriminate control subjects from EoE patients as shown by principal component analysis. Notably, a shift in pEVs cargo was also observed in EoE patients before and after successful treatment, suggesting an impact of the inflammatory state in the small-RNA cargo of EVs. A total of 575 small RNAs were identified, with 32 displaying significant differential regulation and among which microRNAs and tRNA fragments (tRFs) were the most represented biotypes. Eight microRNAs distinguished controls from basal samples, while 4 served to differentiate basal from post-treatment cases based on diagnostic accuracy (AUC>0.75). Functional analysis of microRNAs upregulated in basal samples indicated that these RNAs target genes are involved in the regulation of inflammatory response, epithelial barrier, and eosinophil activity-related pathways. Then, we explored whether the combination of dysregulated microRNA pairs could improve diagnostic power, and highlighted two sets of microRNAs, miR10b-5p/miR221-3p (AUC=0.86) and miR15a-5p/miR30a-3p (AUC=0.90) as robust diagnostic and monitoring biomarkers, respectively. These combinations were further validated by RT-qPCR in an independent cohort with AUC values of 0.70 (CI 95% 0.54-0.87) for miR10b-5p/miR221-3p and 0.71 for miR15a-5p/miR30a-3p (CI 95% 0.58-0.84). Noteworthy, miR30a-3p appeared strongly upregulated in basal samples across discovery and validation cohorts.

Conclusion: We present, for the first time, the potential of different microRNAs derived from plasma-EVs as non-invasive biomarkers for EoE, which could significantly improve patient management by reducing dependency on invasive procedures. This work establishes a foundation for further research exploring the role of EVs in EoE.

References:

1. Grueso-Navarro E, Navarro P, Laserna-Mendieta EJ, Lucendo AJ, Arias-González L. Blood-Based Biomarkers for Eosinophilic Esophagitis and Concomitant Atopic Diseases: A Look into the Potential of Extracellular Vesicles. *Int J Mol Sci.* 2023 Feb 11;24(4):3669. doi: 10.3390/ijms24043669. PMID: 36835081; PMCID: PMC9967575.
2. Buzas EI. The roles of extracellular vesicles in the immune system. *Nat Rev Immunol.* 2023 Apr;23(4):236-250. doi: 10.1038/s41577-022-00763-8. Epub 2022 Aug 4. PMID: 35927511; PMCID: PMC9361922.
3. Lee S, Ko JH, Kim SN. The Extracellular MicroRNAs on Inflammation: A Literature Review of Rodent Studies. *Biomedicines.* 2022 Jul 5;10(7):1601. doi: 10.3390/biomedicines10071601. PMID: 35884901; PMCID: PMC9312877.

Disclosure: Nothing to disclose.

IBD: A burden for patient and society

14:30-15:30 / Strauss 3

OP212

THE HIDDEN BURDEN OF FATIGUE IN MODERATE-TO-SEVERE CROHN'S DISEASE AND ULCERATIVE COLITIS: RESULTS FROM THE COMMUNICATING NEEDS AND FEATURES OF IBD EXPERIENCES (CONFIDE) SURVEY

S. Schreiber¹, A. Potts Bleakman², T. Hunter Gible², M.C. Dubinsky³, D.T. Rubin⁴, R. Panaccione⁵, T. Hibi⁶, C. Kayhan², T. Panni⁷, A.D. Favia², E.J. Flynn², C. Atkinson⁸, S. Travis⁹

¹University Hospital Schleswig-Holstein, Kiel, Germany, ²Eli Lilly and Company, Indianapolis, United States of America, ³Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁴University of Chicago, Inflammatory Bowel Disease Center, Chicago, United States of America, ⁵University of Calgary, Calgary, Canada, ⁶Kitasato University, Kitasato Institute Hospital, Center for Advanced IBD Research and Treatment, Tokyo, Japan, ⁷Eli Lilly and Company, Bad Homburg, Germany, ⁸Adelphi Real World, Bollington, United Kingdom, ⁹University of Oxford, Oxford, United Kingdom

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: Severe fatigue, which has a large negative impact on quality of life, is often present in Crohn's disease (CD) and ulcerative colitis (UC), even in remission.¹

The Communicating Needs and Features of Inflammatory bowel disease (IBD) Experiences (CONFIDE) study explored patient and healthcare professional perspectives on the experiences and impact of CD/UC-related symptoms on patients in Europe (France, Germany, Italy, Spain, and UK), the United States (US), and Japan. These analyses focus on the experience and impact of fatigue among European and US patients with moderate-to-severe CD/UC.

Aims & Methods: Online, quantitative, cross-sectional surveys were conducted among patients with moderate-to-severe CD/UC, defined using criteria based on previous treatment, steroid use, and/or hospitalization. Fatigue over the past seven days was assessed using the 13-item Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) scale² (range: 0–52, higher scores indicate less fatigue; mean score in general population: 43/52³; scores <30/52 indicate severe fatigue⁴). The Manitoba IBD Index⁵ assesses disease activity based on patient-reported symptom persistence in the last six months (6-level scale:

- 1=constantly active,
- 2=often active,
- 3=sometimes active,
- 4=occasionally active,
- 5=rarely active, and
- 6=remission/absence of symptoms).

Disease was considered active if symptoms were experienced constantly to occasionally (responses 1–4), and inactive when infrequent/absent (responses 5/6). Patient-reported impact of CD/UC on energy levels was reported on a scale of 1–7, where 1=no impact and 7=high impact. Data are presented as descriptive statistics.

Results: A total of 547 European (55.4% male, mean age: 38.0 years) and 215 US (54.9% male, 40.9 years) patients with CD and 556 European (57.4% male, 38.9 years) and 200 US (61.5% male, 40.4 years) patients with UC completed the surveys.

Overall, 34.2% European and 35.8% US patients with CD, and 20.9% European and 27.5% US patients with UC reported currently (in the last month) experiencing fatigue. More than 80% of all patients indicated that CD/UC

negatively impacted their energy levels (scores 4–7): CD, Europe: 80.1%, US: 84.2%; UC, Europe: 81.1%, US: 88.0%. Mean (SD) FACIT-F scores were 27.4 (11.3) and 26.8 (10.8) for European and US patients with CD, and 29.4 (10.0) and 26.2 (11.3) for European and US patients with UC, respectively. Among patients currently experiencing fatigue, FACIT-F scores were 24.3 (10.8) and 26.1 (10.9) for European and US patients with CD, and 26.0 (10.6) and 24.5 (11.5) for European and US patients with UC. Among those currently experiencing fatigue, most patients with CD described their disease as active (Europe: 92.5%, US: 93.5%).

Similar results were observed among patients with UC (Europe: 92.2%, US: 98.1%). Among patients reporting ever experiencing fatigue (CD, Europe: 45.2%, US: 45.6%; UC, Europe: 30.6%, US: 40.0%), most reported experiencing fatigue at least once a week (CD, Europe: 67.5%, US: 79.6%; UC, Europe: 66.4%, US: 70.0%).

Conclusion: European and US patients with CD/UC reported severe fatigue (FACIT-F scores <30)⁴, indicating a major burden of fatigue, which is also clearly associated with patient-reported active disease. Both CD and UC negatively impact energy levels for the majority of patients. The findings of this study underscore the importance of active fatigue management in CD/UC to improve patients' overall quality of life.

References:

- Uhlir, V et al. (2023) BMC Gastroenterol. 23(1):288.
- Yellen et al. (1997) J Pain Symptom Manage. 13(2):63–74.
- Eek, D et al. (2021) J Patient Rep Outcomes. 5(1):27.
- Saraiva, S et al. (2019) Scand J Gastroenterol. 54(4):465–70.
- Clara, I et al. (2009) Am J Gastroenterol. 104(7):1754–63.

Disclosure: **Stefan Schreiber**, Consultancy fees: AbbVie, Arena, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Falk, Fresenius, Gilead Sciences, IMAB, Janssen, Eli Lilly and Company, Hikma, MSD, Mylan, Pfizer Inc, Protagonist, Provention Bio, Takeda, Ventyx, and Theravance.

Marla C. Dubinsky, Consultancy fees: AbbVie, Abivax, AstraZeneca, Boehringer Ingelheim International GmbH, Bristol Myers Squibb, Celgene Corporation, Eli Lilly and Company, F. Hoffman-La Roche Ltd, Genentech Inc., Gilead Sciences, Janssen, LLC, Merck, Pfizer, Prometheus Biosciences, Takeda Pharmaceuticals USA, Inc., and UCB; Stock options: TrellusHealth Inc.; Research support: AbbVie, Janssen, LLC, Pfizer, and Prometheus Lab-sa; and licensing fees: Takeda.

David Rubin, Grant support: Takeda; Consultant: AbbVie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. Board of Trustees: Crohn's & Colitis Foundation; Board of Directors: Cornerstones Health.

Remo Panaccione, Consultant for: Abbott, AbbVie, Abivax, Alimentiv (formerly Robarts), Amgen, AnaptysBio, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatrix, Ventyx, UCB; Speaker's Fees for: AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, Takeda Pharmaceuticals; Advisory Boards for: AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, SandozShire, Sublimity Therapeutics, Takeda Pharmaceuticals, Ventyx.

Toshifumi Hibi, Personal fees: AbbVie GK, EA Pharma, Janssen Pharmaceutical K.K, JIMRO, Mitsubishi-Tanabe, Mochida Pharmaceutical, Pfizer Japan, Sandoz K.K, Takeda Pharmaceutical, Zeria Pharmaceutical, Celltrion Healthcare Japan, Eli Lilly Japan, Gilead Sciences, Miyarisan Pharmaceutical, Alfresa Pharma Corporation, Kyorin Pharmaceutical; Grants: JIMRO, Mochida Pharmaceutical, Zeria Pharmaceutical, Miyarisan Pharmaceutical, Alfresa Pharma Corporation, and Kyorin Pharmaceutical.

Christian Atkinson, Employment: Adelphi Real World.

Simon Travis, Grants: AbbVie, ECCO, Eli Lilly and Company, Helmsley Trust International, International Organization for the Study of Inflammatory Bowel Disease, Norman Collision Foundation, Pfizer, Takeda, UCB Pharma, UKIERI, Vifor Pharma; Honoraria: Ferring Pharmaceuticals, Takeda, Eli Lilly and Company, Bristol Myers Squibb, Janssen, Viacom; Travel grants: AbbVie, Eli Lilly and Company, Janssen, Pfizer, Takeda, Ferring Pharmaceuticals, Amgen, Biogen; Consultancy fees: AbbVie, Allergan, Amgen, Apexian, Bioclinica, Biogen, Bristol Myers Squibb, ChemoCentryx, Cosmo Pharmaceuticals, Endpoint Health, Eli Lilly and Company, Enterome, Equillum, Ferring Pharmaceuticals, Genentech/Roche, GlaxoSmithKline, Immunocore, Immunometabolism, Janssen, Merck, Merck Sharp & Dohme, Mestag Therapeutics, Novartis, Pfizer, Protagonist Therapeutics, Proximagen, Receptos, Roche, Sanofi, Satisfai Health, Sensyne Health, Sorriso Pharmaceuticals, Takeda, UCB Pharma, VHSquared, Vifor Pharma.

Alison Potts Bleakman, Theresa Hunter Gible, Cem Kayhan, Tommaso Panni, Angelo D. Favia, and Eoin J. Flynn are employees and stockholders of Eli Lilly and Company.

OP213

PREVALENCE AND FACTORS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE (IBD) ACTIVITY DURING PREGNANCY: UPDATED DATA FROM THE DUMBO REGISTRY

M. Chaparro¹, **M. García Donday**¹, **A. Nuñez Ortiz**², **C. Calviño Suarez**³, **S. Rubio Iturría**⁴, **M. Sanchez-Azofra**⁵, **M.I. Calvo Moya**⁶, **I. Pérez-Martínez**⁷, **A. Fernández-Clotet**⁸, **E. Alfambra**⁹, **S. Marín Pedrosa**¹⁰, **M.T. Diz-Lois Palomares**¹¹, **M. Figueira**¹², **A. Ruiz-Cerulla**¹³, **M.J. Casanova**¹, **M. Rivero**¹⁴, **J.M. Huguet**¹⁵, **R. Vicente Lidón**¹⁶, **L. Arias García**¹⁷, **I. Guerra**¹⁸, **D. Hervías Cruz**¹⁹, **A. Gutiérrez-Casbas**²⁰, **E. Gómez Delgado**²¹, **R. Camargo Camero**²², **I. Rodríguez-Lago**²³, **M. Aguas**²⁴, **M.Á. De Jorge Turrión**²⁵, **A. Masedo Gonzalez**²⁶, **P. López Serrano**²⁷, **G. Valldosera Gomis**²⁸, **D. Ceballos**²⁹, **L. Bujanda**³⁰, **G. Molina Arriero**³¹, **P. Vega Villamil**³², **M. Van Domselaar**³³, **M.M. Boscá Watts**³⁴, **A.J. Lucendo**³⁵, **B. Zúñiga de Mora-Figueroa**³⁶, **D. Busquets Casals**³⁷, **C. Tardillo Marín**³⁸, **M. Piqueras Cano**³⁹, **V. Robles Alonso**⁴⁰, **E. Bernardos Martín**⁴¹, **E.M. Armesto González**⁴², **P. Sendra Rumbau**⁴³, **L. Márquez-Mosquera**⁴⁴, **P. Ramírez de la Piscina**⁴⁵, **M. Mañosa Ciria**⁴⁶, **R. Rodríguez Insa**⁴⁷, **J.P. Gisbert**¹, on behalf of DUMBO study group

¹Hospital Universitario de La Princesa, IIS-Princesa, UAM, and CIBEREHD, Gastroenterology Unit, Madrid, Spain, ²Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ³Complejo Hospitalario Universitario de Santiago, Gastroenterology Unit, Santiago de Compostela, Spain, ⁴Hospital Universitario de Navarra, Gastroenterology Unit, Pamplona, Spain, ⁵Hospital Universitario La Paz and IdiPAZ, Gastroenterology Unit, Madrid, Spain, ⁶Hospital Universitario Puerta de Hierro Majadahonda, Gastroenterology Unit, Madrid, Spain, ⁷Hospital Universitario Central de Asturias, Diet- Microbiota and Health Group and ISPA, Gastroenterology Unit, Oviedo, Spain, ⁸Hospital

Universitario Clínic i Provincial, CIBERehd and IDIBAPS, Gastroenterology Unit, Barcelona, Spain, ⁹Hospital Clínico Universitario Lozano Blesa and IIS Aragón, Gastroenterology Unit, Zaragoza, Spain, ¹⁰Hospital Universitario Reina Sofía, Gastroenterology Unit, Córdoba, Spain, ¹¹Complejo Hospitalario Universitario de A Coruña, Gastroenterology Unit, A Coruña, Spain, ¹²Hospital Álvaro Cunqueiro, IIS Galicia Sur, SERGAS-UVIGO, Gastroenterology Unit, Vigo, Spain, ¹³Hospital Universitario de Bellvitge, Gastroenterology Unit, L'Hospitalet de Llobregat, Spain, ¹⁴Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology Unit, Santander, Spain, ¹⁵Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ¹⁶Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain, ¹⁷Hospital Universitario de Burgos, Gastroenterology Unit, Burgos, Spain, ¹⁸Hospital Universitario de Fuenlabrada and IdiPAZ, Gastroenterology Unit, Madrid, Spain, ¹⁹Hospital General Universitario de Ciudad Real, Gastroenterology Unit, Ciudad Real, Spain, ²⁰Hospital General Universitario Dr Balmis, ISABIAL and CIBERehd, Gastroenterology Unit, Alicante, Spain, ²¹Hospital Universitario Juan Ramón Giménez, Gastroenterology Unit, Huelva, Spain, ²²Hospital Universitario Virgen de La Victoria, Gastroenterology Unit, Málaga, Spain, ²³Hospital Universitario de Galdakao and Biobizkaia Health Research Institute, Gastroenterology Unit, Galdakao, Spain, ²⁴Hospital Universitario La Fe and IISLaFe, Gastroenterology Unit, Valencia, Spain, ²⁵Hospital Universitario de Cabueñes, Gastroenterology Unit, Gijón, Spain, ²⁶Hospital Universitario 12 de Octubre, Gastroenterology Unit, Madrid, Spain, ²⁷Hospital Universitario Fundación Alcorcón, Gastroenterology Unit, Madrid, Spain, ²⁸Hospital Universitario Joan XXIII, Gastroenterology Unit, Tarragona, Spain, ²⁹Hospital Universitario de Gran Canaria "Dr Negrín", Gastroenterology Unit, Las Palmas de Gran Canaria, Spain, ³⁰Biodonostia Health Research Institute - Donostia University Hospital, UPV/EHU and CIBERehd, Gastroenterology Unit, San Sebastián, Spain, ³¹Complejo Hospitalario Universitario de Ferrol, Gastroenterology Unit, Ferrol, Spain, ³²Complejo Hospitalario Universitario de Ourense, Gastroenterology Unit, Ourense, Spain, ³³Hospital Universitario de Torrejón and Universidad Francisco de Vitoria, Gastroenterology Unit, Madrid, Spain, ³⁴Hospital Clínico Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ³⁵Hospital General de Tomelloso, IIS-Princesa, IDISCAM and CIBERehd, Gastroenterology Unit, Ciudad Real, Spain, ³⁶Hospital Clínico Universitario San Cecilio, Gastroenterology Unit, Granada, Spain, ³⁷Hospital Universitari Dr. Josep Trueta, Gastroenterology Unit, Girona, Spain, ³⁸Hospital Universitario Nuestra Señora de Candelaria, Gastroenterology Unit, Tenerife, Spain, ³⁹Consorci Sanitari de Terrassa (CST), Barcelona, Spain, ⁴⁰Hospital Vall D'Hebron, Barcelona, Spain, ⁴¹Hospital Mancha Centro, Gastroenterology Unit, Alcázar de San Juan, Spain, ⁴²Hospital Universitario San Agustín, Gastroenterology Unit, Avilés, Spain, ⁴³Hospital Universitario Son Espases, Gastroenterology Unit, Palma de Mallorca, Spain, ⁴⁴Hospital del Mar and IMIM, Gastroenterology Unit, Barcelona, Spain, ⁴⁵Hospital Universitario de Álava, Gastroenterology Unit, Álava, Spain, ⁴⁶Hospital Universitari Germans Trias i Pujol and CIBERehd, Gastroenterology Unit, Badalona, Spain, ⁴⁷Hospital General Universitario de Castellón, Gastroenterology Unit, Castellón, Spain

Contact E-Mail Address: mariachs2005@gmail.com

Introduction: IBD remission is key for pregnancy outcomes. Previous studies have suggested a disease recurrence risk of approximately 30%

in patients in remission at conception, but this could be influenced by disease control in the periconceptional period and the discontinuation of treatments for IBD during pregnancy.

Aims & Methods: Aim: To provide updated data on the incidence of disease relapse during pregnancy in IBD patients and to identify predictive factors of relapse.

Methods: Pregnant patients with IBD from DUMBO registry were included. DUMBO is a prospective, observational, and multicentre registry, endorsed by GETECCU which enrolls pregnant women with IBD over 5 years in 70 centres in Spain. Relapse was defined based on the Crohn's Disease Activity Index and the Partial Mayo Score in Crohn's disease (CD) and ulcerative colitis (UC), respectively. Only patients in clinical remission at conception were considered for the relapse risk analysis (Cox-regression analysis). Only serious adverse events (SAE) were recorded.

Results: 1,033 patients were available in DUMBO registry, 56% had CD, 19% had previous surgery, 29% were exposed to thiopurines, 40% to biologics and 5.5% had active disease at conception. 830 patients had given birth (98% singleton), 69 had early termination (48 of them miscarriages), and 134 pregnancies were still ongoing.

The probability of having active disease at each trimester was higher in patients with active disease at conception than in those in remission [41% vs. 2% in the 1st trimester (TM), 18% vs. 2.6% in the 2nd TM, 14% vs. 2.7% in the 3rd TM; all p-values<0.001]. Seven patients underwent surgery due to IBD during pregnancy (3 abdominal and 4 perianal surgery); all of them were in remission at conception.

The proportion of patients with severe infections during pregnancy was higher in patients with active disease during pregnancy (2.8% vs. 0.8%, p<0.05); there were no differences in other SAE based on the activity.

A total of 73 out of 976 patients in remission at conception relapsed throughout pregnancy or puerperium (incidence rate of disease flare=11% per patient-year of follow-up); most cases from the 2nd TM of gestation. To have UC vs. CD (Hazard ratio=3, 95% confidence interval=1.8-5.3) was the only variable associated with the risk of relapse.

The proportion of patients who relapsed was similar among those who withdrew the biological treatment and those who maintained it (4% vs. 8%, p>0.05). Focusing on patients treated with biologics, the proportion of disease relapse based on biologics withdrawal and TM of withdrawal is summarised in Table 1.

Drug	N	Withdrawal	Relapse	p-value	Trimester of gestation	Relapse by trimester of withdrawal
Adalimumab, n (%)	159	Yes: 39 (25) No: 120 (75)	0 (0) 7 (6)	0.1	1TM: 9 (23); 2TM: 9 (23); 3TM: 20 (52)	None
Infliximab, n (%)	120	Yes: 27 (22.5) No: 93 (77.5)	1 (3.7) 7 (7.5)	0.4	1TM: 1(3.7); 2TM: 15 (56); 3TM: 9 (33)	One patient (6.6) discontinued in 2TM)
Certolizumab, n (%)	6	Yes: 1 (17) No: 5 (83)	0 (0) 3 (60)	0.2	2TM: 1 (100) 3TM: 2 (100)	None One patient (50%) discontinued in 3TM)
Golimumab, n (%)	3	Yes: 2 (67) No: 1 (33)	1 (50) 0 (0)	0.3		
Vedolizumab, n (%)	30	Yes: 6 (20) No: 24 (80)	0 (0) 5 (21)	0.2	1TM: 1(17); 2TM: 2 (33); 3TM: 2 (33)	None
Ustekinumab, n (%)	79	Yes: 18 (23) No: 61 (77)	2 (11) 3 (5)	0.3	1TM: 2 (11); 2TM: 13 (72); 3TM: 3 (17)	One patient of those who discontinued 1TM (50%) and one patient (7.7%) of those who discontinued 2TM

TM: trimester

Table 1.

Conclusion: The risk of having active disease during pregnancy was higher in patients with activity at conception. The risk of relapse in patients in remission at conception was lower than previously described. The risk of relapse was 3-fold higher in UC than in CD. Since most relapses occur from the second trimester of gestation onwards, and serious complications (including surgery) can occur also in patients in remission at conception, monitoring IBD during this period should be closely conducted

Disclosure: María Chaparro has served as speaker, consultant or research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Biogen, Gilead and Lilly. Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene/Bristol Myers, Gilead/Galapagos, Lilly, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Norgine and Vifor Pharma. Pilar López Serrano has received grants from MSD, Abbvie, Takeda, Janssen, Faes, Ferring and Dr Falk Pharma. Noemí Manceñido Marcos has served as a speaker and consultant for or received financial support for educational activities from Janssen, Abbvie, Pfizer, Takeda, Ferring, Faes Farma, Dr. Falk Pharma, and Tillots Pharma. Marta Maia Boscá Watts Conflictos de interés: MSD, Ferring, Abbvie, Janssen, Biogen, Pfizer, Galápagos, Otsuka, Kern pharma y Takeda. Agnès Fernández-Clotet has served as a speaker, or has receives education funding from Dr. Falk, Janssen, Takeda, Chiesi and Pfizer. Lara Arias García has served as speaker or has received research or education funding from MSD; Abbvie; Kern Pharma; Ferring; Faes Farma; Shire Pharmaceuticals; Pfizer; Takeda; Janssen; Tillots Pharma and OtsuKa Pharmaceutical. Lucía Marquez-Mosquera has been served as speaker and / or has received research or education funds from Abbvie, Pfizer, Takeda, Janssen. Marta Calvo Moya has served as a speaker, consultant and advisory member for or has received research funding from MSD, Abbvie, Takeda, Janssen, Pfizer, Lilly, Mylan, Kern Pharma, Ferring, Shire Pharmaceuticals, Tillots, Dr. Falk Pharma, Chiesi, and Gebro Pharma. Miriam Mañosa has served as a speaker, consultant and advisory member for or has received research funding from Abbvie, Janssen, MSD, Pfizer, Faes, Takeda, Tillots, Ferring. Vicent Hernandez has served as consultant, has served as speaker, has received travel support or research funding from MSD, Abbvie, Ferring, Dr. Falk Pharma, Tillotts Pharma, Pfizer, Takeda, Janssen, KernPharma Biologics, Adacyte, Sandoz, Biogen, Fresenius-Kabi, FAES Farma and Galapagos. Raquel Camargo Camero, He recibido financiación para diferentes tipos de actividades formativas de Janssen, Ferring, Abbvie, Falk, Pfizer, Galápagos y Takeda. Ivan Guerra has served as speaker or has received education funding from Takeda and Tillots. María Sánchez Azofra has received financial support for traveling and educational activities, or has received fees as a speaker from Janssen, Takeda, Pfizer, Tillotts Pharma, Ferring Pharmaceuticals. David Busquets declares educational activities, research projects and scientific meetings sponsored by Abbvie, Janssen, Ferring, Pfizer, Tillots Pharma and Takeda. Montserrat Rivero has served as a speaker or advisory member from Takeda, Janssen, Galapagos, Ferring and Pfizer. Iago Rodríguez-Lago has received financial support for traveling and educational activities from or has served as an advisory board member for Abbvie, Adacyte, Celltrion, Chiesi, Danone, Ferring, Faes Farma, Janssen, Galapagos, MSD, Pfizer, Roche, Takeda, and Tillotts Pharma. Financial support for research: Tillotts Pharma. Cristina Calvino-Suarez, has served as a speaker for or has received research funding from MSD, Abbvie, Janssen, Takeda and Adacyte. Javier Sola Sanchez, has served as speaker for Takeda. Rest of authors have nothing to declare.

OP214

BIDIRECTIONAL ASSOCIATION BETWEEN INFLAMMATORY BOWEL DISEASE AND TYPE 1 DIABETES: A NATIONWIDE COHORT AND MATCHED CASE-CONTROL STUDY

J. Sun¹, J. Yao¹, O. Olén¹, J. Halfvarsson², D. Bergman¹, F. Ebrahimi¹, S. Carlsson¹, J. Ludvigsson³, J.F Ludvigsson¹
¹Karolinska Institutet, Stockholm, Sweden, ²Örebro University, Örebro, Sweden, ³Crown Princess Victoria's Children's Hospital, Linköping, Sweden

Contact E-Mail Address: jiangwei.sun@ki.se

Introduction: The co-occurrence of inflammatory bowel disease (IBD) and type 1 diabetes (T1D) has been linked to poor clinical outcomes. However, few longitudinal studies have explored their temporal relationships.

Aims & Methods: This study aimed to investigate the bidirectional association between IBD and T1D. In this nationwide cohort and case-control study, patients with biopsy-confirmed IBD were identified between 1987 and 2017. The cohort included 20,314 patients with IBD (≤ 28 years; Crohn's disease [CD, $n=7,277$], ulcerative colitis [UC, $n=10,112$], and IBD-unclassified [IBD-U, $n=2,925$]) and individually matched reference individuals from the general population ($n=99,200$). The case-control study enrolled 87,001 patients with IBD and 431,054 matched controls. We estimated adjusted hazard ratios (aHRs) of incident T1D by IBD status with flexible parametric survival models and adjusted odds ratios (aORs) of IBD by history of T1D with conditional logistic regression, with 95% confidence intervals (CIs). The familial factors from genetics and early environmental factors were additionally accounted for via sibling comparisons.

Results: In the cohort, during a median follow-up of 14 years, 116 patients with IBD and 353 reference individuals developed T1D. Patients with IBD had a higher incidence of T1D than reference individuals (incidence rate: 3.7 vs. 2.3 per 10,000 person-years; $aHR=1.58[95\%CI=1.27 \text{ to } 1.95]$). The HR was increased in patients with UC ($aHR=2.02[1.51 \text{ to } 2.70]$) but not in those with CD ($aHR=1.11[0.76 \text{ to } 1.64]$) or IBD-unclassified ($aHR=1.48[0.82 \text{ to } 2.69]$). In the case-control study, a total of 1,018 IBD patients and 3,496 controls had been diagnosed with T1D.

Compared with controls, patients with IBD tend to have higher odds of having previous T1D ($aOR=1.36[95\%CI=1.26 \text{ to } 1.46]$). Such positive association was observed in all IBD subtypes. Comparisons with siblings showed similar associations ($aHR=1.44 [0.97 \text{ to } 2.15]$ and $aOR=1.32 [1.18 \text{ to } 1.49]$).

Conclusion: Patients with IBD had a moderately increased incidence of developing T1D and higher odds of having a previous diagnosis of T1D. These findings demonstrate a bidirectional association between IBD and T1D independent of shared genetics and early environmental factors.

Disclosure: All authors have completed the ICMJE uniform disclosure form and declare:

OO has been PI on projects at Karolinska Institutet financed by grants from Janssen, Pfizer, Abbvie, Takeda, Bristol Myer Squibb and Ferring, and Karolinska Institutet has received fees for lectures and participation on advisory boards from Janssen, Ferring, Galapagos, Bristol Myer Squibb, Takeda, and Pfizer. OO also reports grants from Pfizer, Janssen, Galapagos, and Abbvie in the context of a national safety monitoring programs. JH served as speaker and/or advisory board member for Abbvie, Aqilion, BMS, Celgene, Celltrion, Dr Falk Pharma and the Falk Foundation, Eli Lilly, Ferring, Galapagos, Gilead, Hospira, Index Pharma, Janssen, MEDA, Medivir, MSD, Novartis, Pfizer, Prometheus Laboratories Inc., Sandoz, Shire, STADA, Takeda, Thermo Fisher Scientific, Tillotts Pharma, Vifor Pharma, UCB and received grant support from Janssen, MSD and Takeda.

FE has served as an advisory board member for Boehringer Ingelheim.

JFL has coordinated a study on behalf of the Swedish IBD quality register (SWIBREG). That study received funding from Janssen Corporation. JFL

has also received financial support from MSD developing a paper reviewing national healthcare registers in China. JFL has a research collaboration on celiac disease with Takeda. The other authors report no disclosures relevant to the manuscript.

OP215

INCREASED RISK OF CROHN'S DISEASE AND ULCERATIVE COLITIS FOLLOWING HOSPITALISATION WITH INFECTIOUS MONONUCLEOSIS

A. Ebert¹, S. Harper², M. Vibeke Verstergaard¹, W. Mitchell², T. Jess^{1,3}, R. Elmahdi^{1,3}

¹Aalborg University, Department of Clinical Medicine, Copenhagen, Denmark, ²Imperial College London, Department of Immunology and Inflammation, London, United Kingdom, ³Aalborg University Hospital, Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: re107@ic.ac.uk

Introduction: Infectious mononucleosis (IM) is a largely self-limiting syndrome mainly affecting adolescents and young adults but can present as a severe disease requiring hospitalisation. The infectious agent most commonly causing IM, Epstein-Barr virus (EBV), has been associated with the development of several immune-mediated and inflammatory diseases¹. Recent epidemiological studies have also identified a potential association with IM and inflammatory bowel disease (IBD)^{2,3}.

Aims & Methods: We therefore aimed to investigate the risk of IBD diagnosis following hospitalisation with IM using Danish nationwide registry data. We identified severe IM patients (those hospitalised with infectious mononucleosis) and matched these by sex-, age- and residence municipality to non-severe IM controls, from 1st January 1977 to 31st December 2021. We undertook Cox regression modelling to assess the hazards (HR) and 95% CI of IBD diagnosis, including Crohn's disease (CD) and ulcerative colitis (UC), following severe IM. Analyses were stratified by sex, age at, and calendar year of IM hospitalisation.

	Severe IM cases (N = 39,684)		Severe IM controls (N = 396,840)		Adjusted HR*	Adjusted HR 95% CI
	IBD events in severe IM (N)	IBD IR (per 1000 person years)	IBD events in controls (N)	IBD IR (per 1000 person years)		
Inflammatory Bowel Disease	496	0.67	3982	0.5	1.35	1.22-1.49
Crohn's Disease	203	0.27	1417	0.18	1.56	1.34-1.83
Ulcerative Colitis	293	0.40	2565	0.32	1.23	1.08-1.40

Abbreviations: IM; infectious mononucleosis, IR; incidence rate, HR; hazard ratio, 95% CI; 95% confidence interval. Severe IM cases include individuals hospitalised with IM between 1st January 1977 and 31st December 2021. Severe IM controls include individuals matched on sex, date of birth (within 6 months), and municipality of residence without an IM hospitalisation to severe IM cases; *adjusted for sex, age and municipality of residence as appropriate.

Table 1. Crude incidence rates and adjusted hazard ratios for IBD, CD and UC diagnosis in severe IM patients compared with severe IM controls.

Results: We identified 39,684 patients with severe IM who were sex-, age-, and municipality-matched to 396,840 non-severe IM controls. Severe IM was significantly associated with the development of IBD (HR: 1.35; 95% CI: 1.22-1.49) and this was seen particularly in CD (HR: 1.56; 95% CI: 1.34-1.83) and to lesser extent in UC (HR: 1.23; 95% CI: 1.08-1.40). Sex at severe IM diagnosis was not found to be a significant modifier to the risk of IBD diagnosis, with risk increased in both females (HR: 1.36; 95% CI: 1.20-1.55) and males (HR: 1.34; 95% CI: 1.17-1.54). Only those receiving a severe IM diagnosis at 10-16 years (HR: 1.42; 95% CI: 1.22-1.64) or 17-29 years (HR: 1.34; 95% CI: 1.15-1.56) had a significantly increased risk of IBD diagnosis. Finally, this increased risk remained present across calendar year of IM diagnosis, from 1977 to 2022.

Conclusion: This study demonstrated an association between IM hospitalisation and later IBD diagnosis, indicating an association between severe EBV disease and IBD development. Further exploration of the potential factors contributing to IBD susceptibility following EBV infection is warranted.

References:

1. Houen G, Trier NH. Epstein-Barr Virus and Systemic Autoimmune Diseases. *Front Immunol* 2021;11.
2. Loosen SH, Kostev K, Schöler D, et al. Infectious mononucleosis is associated with an increased incidence of Crohn's disease: results from a cohort study of 31 862 outpatients in Germany. *Eur J Gastroenterol Hepatol* 2023;35:255-260.
3. Nandy A, Petralia F, Torres J, et al. 463: EPSTEIN BARR VIRUS (EBV) EXPOSURE PRECEDES CROHN'S DISEASE DEVELOPMENT. *Gastroenterology* 2022;162:S-105.

Disclosure: Nothing to disclose.

OP216

HEALTHCARE COSTS AND PRODUCTIVITY LOSSES IN PATIENTS WITH MICROSCOPIC COLITIS: REAL-WORLD EVIDENCE FROM A NATIONWIDE LONGITUDINAL COHORT STUDY

S.R. Bozorg^{1,2}, D. Bergman¹, K. Mårild³, Å.H. Everhov^{4,5}, H. Khalili², J.F. Ludvigsson^{1,6}

¹Karolinska Institute, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, ²Harvard Medical School and Massachusetts General Hospital, Clinical and Translational Epidemiology Unit, Boston, United States of America, ³Sahlgrenska Academy, Institute of Clinical Sciences, Department of Pediatrics, Gothenburg, Sweden, ⁴Karolinska Institute, Department of Medicine, Clinical Epidemiology Division, Stockholm, Sweden, ⁵Karolinska Institute, South General Hospital, Department of Clinical Science and Education, Stockholm, Sweden, ⁶Columbia University College of Physicians and Surgeons, Department of Medicine, New York, United States of America

Contact E-Mail Address: soranbozorg@gmail.com

Introduction: Microscopic colitis (MC) is a chronic disabling inflammatory disease. Yet, the economic impact of MC is still largely unknown. In this nationwide study, we investigated societal costs, comprised of healthcare costs and productivity losses, in relation to MC diagnosis.

Aims & Methods: We identified 8,659 biopsy-verified patients diagnosed with MC between 2008 and 2017. Patients were followed from 4 years before diagnosis until either 4 years after diagnosis, emigration, death, or 2019 (end of follow-up), whichever came first. Each patient was compared to up to 5 general-population comparators matched on birthyear, sex, county of residence, and calendar year.

Using real-world data from Swedish national registers, we determined healthcare costs from prescribed medications, non-primary outpatient visits, and hospitalizations, while costs for productivity losses were derived from lost workdays due to sick leave or disability leave. All costs were adjusted for inflation and converted from Swedish currency, SEK, to USD (1 USD = 10.61 SEK).

Results: Patients with MC had 1.54 times higher societal costs than their general-population comparators already at 4 years before diagnosis, and the excess cost further increased during the years leading up to diagnosis. The excess cost of MC peaked during the year of diagnosis when patients with MC had 2.11 times the cost of comparators, corresponding to a mean annual excess cost of \$6,402 (adj. mean difference [95%CI]: \$6,460 [\$6,099; \$6,820]).

Although the mean cost of MC decreased after diagnosis, it did not return to pre-diagnostic levels. Instead, the cost of MC persisted at 1.85 times the costs of their comparators 4 years after diagnosis. The absolute excess cost of MC was also significantly higher 4 years after diagnosis compared with 4 years before diagnosis (\$4,654 vs \$2,926; P-value <0.05). Stratification by age, sex, and education level showed similar cost trajectories, with cost ratios peaking in the year of diagnosis and persisting at higher levels after diagnosis.

While work loss was the largest contributor to the absolute excess cost of MC both before and after diagnosis, the cost ratio (1.83) was lower than for other cost categories. Compared with the general population, the relative excess cost was highest for outpatient visits with a cost ratio of 3.00 during the year of diagnosis, followed by 2.54 for medications and 2.36 for hospitalizations.

Years in relation to diagnosis	Outpatient visits MC vs Control	Hospitalizations MC vs Control	Medications MC vs Control	Work loss MC vs Control	Total Cost MC vs Control	Crude Mean Difference ^A (95%CI)	Adjusted Mean Difference ^{A,B} (95%CI)	Cost Ratio ^C
-4	\$788 vs \$476	\$1,020 vs \$705	\$753 vs \$400	\$6,137 vs \$4,050	\$8,344 vs \$5,418	\$2,926 (\$2,460; \$3,392)	\$3,010 (\$2,547; \$3,474)	1.54
-3	\$991 vs \$598	\$1,434 vs \$871	\$843 vs \$418	\$6,066 vs \$4,026	\$9,333 vs \$5,914	\$3,412 (\$2,971; \$3,868)	\$3,482 (\$3,036; \$3,928)	1.58
-2	\$1,098 vs \$593	\$1,520 vs \$904	\$900 vs \$438	\$5,941 vs \$3,935	\$9,459 vs \$5,870	\$3,589 (\$3,177; \$4,002)	\$3,640 (\$3,229; \$4,050)	1.61
-1	\$1,232 vs \$622	\$1,933 vs \$956	\$962 vs \$459	\$6,126 vs \$3,739	\$10,253 vs \$5,778	\$4,476 (\$4,089; \$4,862)	\$4,524 (\$4,138; \$4,909)	1.77
0	\$1,965 vs \$656	\$2,426 vs \$1,027	\$1,206 vs \$474	\$6,549 vs \$3,587	\$12,146 vs \$5,744	\$6,402 (\$6,040; \$6,763)	\$6,460 (\$6,099; \$6,820)	2.11
1	\$1,347 vs \$632	\$1,943 vs \$1,136	\$1,267 vs \$483	\$6,058 vs \$3,363	\$10,616 vs \$5,615	\$5,001 (\$4,628; \$5,373)	\$5,036 (\$4,664; \$5,408)	1.89
2	\$1,306 vs \$655	\$2,029 vs \$1,200	\$1,195 vs \$480	\$5,684 vs \$3,229	\$10,214 vs \$5,564	\$4,650 (\$4,259; \$5,040)	\$4,705 (\$4,315; \$5,096)	1.84
3	\$1,293 vs \$684	\$2,030 vs \$1,187	\$1,174 vs \$498	\$5,499 vs \$3,120	\$9,997 vs \$5,488	\$4,508 (\$4,139; \$4,878)	\$4,552 (\$4,183; \$4,920)	1.82
4	\$1,307 vs \$692	\$2,055 vs \$1,211	\$1,191 vs \$520	\$5,549 vs \$3,025	\$10,102 vs \$5,448	\$4,654 (\$4,268; \$5,040)	\$4,678 (\$4,293; \$5,063)	1.85

Table 1. Mean societal costs of patients with microscopic colitis (MC) and general-population comparators (control) in relation to year of diagnosis.

A: All mean differences had P-values <0.001.
B: Adjusted for age, sex, education level, and calendar year.
C: Cost of microscopic colitis as numerator and cost of general-population comparators as denominator (MC/Control).

Conclusion: Patients with MC have higher societal costs than the general population before diagnosis, and the excess costs increase and persist for several years after diagnosis. While excess costs may be multifactorial, improved disease control could provide opportunities to reduce the post-diagnostic cost of MC.

Disclosure: Nothing to disclose.

Upper GI bleeding: Treatment and outcome

14:30-15:30 / Lehar 1

OP217

A PROSPECTIVE, SINGLE-CENTER, RANDOMIZED, OPEN-LABEL STUDY TO INVESTIGATE EFFICACY AND LONG-TERM OUTCOME OF CYANOACRYLATE GLUE FOR ALL GASTRIC VARICES (GOV1, GOV2, IGV1, IGV2) VERSUS ITS USE ONLY GOV 2 AND IGV 1 GASTRIC VARICES WITH STIGMA OF RECENT HAEMORRHAGE IN CIRRHOTIC PATIENTS AT INDEX BLEED

P. Desai¹, C. Patel¹, M.V Kabrawala¹, R. Prajapati¹, R. Kakadiya¹, M. Sethia¹, N. Patel¹
¹SIDS Hospital & Research Centre, Endoscopy, Surat, India

Contact E-Mail Address: riteshprajapati87@gmail.com

Introduction: There is significant interpersonal variation in management of gastric varices. In real life scenario both large esophageal and gastric varices coexist in a significant number of cases.

In patients presenting with variceal bleed, source of bleed whether esophageal or gastric varices is not clear in most patients. How aggressively to manage the large gastric varices in patients who had variceal bleed is not defined.

The aim of this study was to compare aggressive management of gastric varices with conservative management of gastric varices in patient with variceal bleed.

Aims & Methods: Consecutive patients with cirrhosis presenting with 1st episode of variceal bleed and having large gastric varices (Gastroesophageal varices (GOV)1, GOV2, Isolated gastric varices (IGV) 1) were randomized to receive aggressive (Group A, n=66) or conservative therapy (Group B, n=68) for gastric varices.

Aggressive group received glue injection for all types of gastric varies followed by band ligation of the oesophageal varies.

While group B patients were treated primarily with band ligation for oesophageal and GOV 1 varies and glue was used only those IGV or GOV 2 varies which revealed stigma of recent haemorrhage (SRH) (Table 1). Primary outcomes were variceal rebleed, rate of obliteration of varices or death at 1 year follow up.

Group A	Group B
Index endoscopy procedure	
Endoscopic cyanoacrylate (CYA) injection for all visible GOV1, GOV2 and IGV1, and EVL for esophageal varices	EVL for esophageal varices, GOV1 with SRH Endoscopic cyanoacrylate injection for: GOV2, IGV1 with SRH or; High risk* GOV 2, IGV1 with no SRH
Follow up endoscopy procedure	
Endoscopic cyanoacrylate (CYA) injection for all visible GOV1, GOV2 and IGV1, and EVL for esophageal varices	EVL for esophageal varices, GOV1 with SRH Endoscopic cyanoacrylate injection for: GOV2, IGV1 with SRH

Table 1: Endoscopic management on index and follow up endoscopy.
*High risk: size of varix (> 10mm) & red wale marks
Abbreviations: SRH, stigmata of recent haemorrhage;
EVL, Endoscopic variceal ligation; GOV, gastroesophageal varices;
IGV, Isolated gastric varices.

Results: There was no difference in the number of rebleed events among groups at 1 year (p=0.639).

Mortality due to variceal rebleed was comparable in both groups at 1 year (p=0.261), 6 months and 1 month. 1-year all-cause mortality was comparable in both groups.

The mean number of sessions required for obliteration of varices was lower in Group A than in Group B (1.24 ± 0.69 and 2.49 ± 1.38 respectively, p=0.01).

There was no significant difference between the two groups regarding the adverse events.

Conclusion: Aggressive approach to management of gastric varices using cyanoacrylate glue leads to early obliteration of varices but has similar rebleeding rates and survival benefit as compared to a more conservative approach.

Disclosure: Nothing to disclose.

OP218

BLOOD TRANSFUSION FOR ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH ISCHEMIC HEART DISEASE: A MULTICENTER, PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL

X. Xing^{1,2}, L. Ma^{1,2}, J. Zhang^{1,2}, H. Yan^{1,2}, X. Xiao^{1,2}, J. Yang^{1,2}

¹West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China, ²Sichuan University-Oxford University Huaxi Gastrointestinal Cancer, Chengdu, China

Contact E-Mail Address: ariannaxing@foxmail.com

Introduction: Patients with ischemic heart disease have a high risk to develop gastrointestinal bleeding because of antiplatelet therapy. It is argued that these patients might need a higher hemoglobin level for the oxygen demand when bleeding occurs [1-3].

There is little data about blood transfusion strategy for patients with ischemic heart disease complicated with acute upper gastrointestinal bleeding.

Aims & Methods: We designed a multicenter, prospective, randomized controlled trial to compare the outcomes of restrictive blood transfusion strategy with liberal blood transfusion strategy.

From 2019 June, we prospectively recruited 126 ischemic heart disease patients complicated with acute upper gastrointestinal bleeding. All of them were randomly assigned to restrictive blood transfusion group (blood transfusion when hemoglobin $\leq$ 80g/L) or liberal blood transfusion group (blood transfusion when hemoglobin $\leq$ 100g/L). The primary endpoint was 30 days rebleeding rate after randomization.

Results: There were 64 patients received restrictive blood transfusion, and 62 had liberal blood transfusion. The baseline characteristics, including sex, age, hemoglobin concentration, Glasgow-Blatchford score, endoscopic findings, types of ischemic heart disease, history of coronary angiography, use of proton pump inhibitor and hemostatic drugs were similar in the two groups. In an intention-to-treat (ITT) analysis, 13 (19.7%) of the restrictive blood transfusion group and 9 (14.3%) of the liberal blood transfusion group reached the primary endpoint (HR: 0.84, 95% CI: 0.56-1.25, $p=0.414$) (Table 1).

Treatment outcomes	Restrictive blood transfusion group n= 64	Liberal blood transfusion group n= 62	HR (95%CI)	p
30 days rebleeding, n (%)				
ITT analysis	13 (19.7%)	9 (14.3%)	0.84 (0.56- 1.25)	0.414
PP analysis	10 (20.8%)	5 (22.7%)	1.04 (0.70- 1.55)	0.858
30 days death, n (%)				
ITT analysis	2 (3.0%)	1 (1.6%)	0.76 (0.34- 1.73)	0.587
PP analysis	1 (2.1%)	1 (4.5%)	1.38 (0.34-5.58)	0.566
Major cardiovascular events, n (%)				
ITT analysis	12 (18.2%)	3 (4.8%)	0.52 (0.43- 0.81)	0.017
PP analysis	6 (12.5%)	2 (9.1%)	0.90 (0.58-1.40)	0.677

Table 1. Outcomes of both groups.

ITT, intention-to-treat; PP, per-protocol; HR, hazard ratio; CI, confidence interval

In a per-protocol (PP) analysis, 10 of 48 (20.8%) in the restrictive blood transfusion group compared 5 of 22 (22.7%) in the liberal blood transfusion group occurred rebleeding in 30 days after randomization (HR: 1.04, 95% CI: 0.70-1.55, $p=0.858$). The 30 days all-cause death were similar in the two groups (HR: 0.76, 95% CI: 0.34-1.73, $p=0.587$ in ITT analysis; HR: 1.38, 95% CI: 0.34-5.58, $p=0.566$ in PP analysis). The hospital stay length (8.95 $\pm$ 4.99 vs. 8.52 $\pm$ 4.68, days, in ITT analysis) were reduced in liberal blood transfusion group.

There was a reduction in 30-day major cardiovascular events in liberal blood transfusion group (HR: 0.52, 95% CI: 0.43-0.81, $p=0.017$ in ITT analysis; HR: 0.90, 95% CI: 0.58-1.40, $p=0.677$ in PP analysis). Of these, 6 (9.4%) patients in restrictive blood transfusion group had heart failure, 4 (6.3%) had myocardial infarction and 2 (3.1%) had both heart failure and myocardial infarction, while 2 (3.2%) patients in liberal blood transfusion group had heart failure and 1 (1.6%) had myocardial infarction.

Conclusion: In ischemic heart disease patients who occurred acute upper gastrointestinal bleeding, liberal blood transfusion reduced the hospital stay length, and the events of major cardiovascular events after bleeding. There was no significant difference in the 30-day rebleeding and 30-days all-cause death found between the restrictive and liberal blood transfusion groups.

References: 1. Docherty AB, Walsh TS. Anemia and blood transfusion in the critically ill patient with cardiovascular disease. Crit Care.2017,21(1): 61.

2. Gralnek IM, Dumonceau JM. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015 Oct;47(10):a1-46.

3. Sung JJ, Chiu PW. Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018. Gut. 2018 Oct;67(10):1757-1768.

The study is funded by 1-3-5 Project for Disciplines of Excellence-Clinical Research Incubation Project 2020HXFH039, West China Hospital, Sichuan University.

Disclosure: Nothing to disclose.

FACTOR XA INHIBITOR–ASSOCIATED GASTROINTESTINAL BLEEDING INCIDENCE AND OUTCOMES IN THE MULTICOUNTRY OBSERVATIONAL AXIOM STUDY

A. Cohen¹, J. Leentjens², R.C. Welsh³, J. Arenillas⁴, C.I. Coleman⁵, D.C. Dover⁶, E. Houben⁷, R. Zhang⁸, J.B. Mamza⁸, G. Godfrey⁹, E. Lang¹⁰, A. Canbay¹¹, On behalf of AXIOM Research Group
¹Department of Haematological Medicine, Guys and St. Thomas' Hospitals NHS Foundation Trust, King's College, London, United Kingdom, ²Radboud UMC, Nijmegen, Netherlands, ³University of Alberta and Mazankowski Alberta Heart Institute, Edmonton, Canada, ⁴Hospital Clinico Universitario, Valladolid, Spain, ⁵Department of Pharmacy Practice, University of Connecticut, Storrs, United States of America, ⁶Canadian VIGOUR Centre, University of Alberta, Alberta, Canada, ⁷PHARMO Institute for Drug Outcomes Research, Utrecht, Netherlands, ⁸AstraZeneca, Medical and Scientific Affairs, Biopharmaceuticals Medical, London, United Kingdom, ⁹AstraZeneca, Biopharmaceuticals Medical, Europe and Canada, Gothenburg, Sweden, ¹⁰Cumming School of Medicine, University of Calgary, Calgary, Canada, ¹¹Universitätsklinikum Knappschafts Krankenhaus Bochum, Bochum, Germany

Contact E-Mail Address: ali.canbay@kk-bochum.de

Introduction: Gastrointestinal bleeds (GIBs) are associated with use of anticoagulants, such as Factor Xa inhibitors (FXai), and may result in significant morbidity and mortality.

The goal of this multicountry study was to explore the incidence and burden of GIBs following initial FXai use.

Aims & Methods: This retrospective observational cohort study involved analysis of electronic health records from new users of direct-acting oral anticoagulants (DOACs), specifically FXai, in Germany, the Netherlands, and the UK. Patients with a FXai prescription for a therapeutic indication (eg, venous thromboembolism, atrial fibrillation, non-mechanical cardiac-valve replacement) were included. Incidence rates of GIBs associated with FXai use and mortality after GIB were assessed and reported per 100 person years (PYR) with 95% confidence intervals.

Results: Among new FXai users (Germany, n=78,086; Netherlands, n=17,356; UK, n=212,378), 1583 GIBs were reported in Germany, 205 in the Netherlands, and 4683 in the UK (Table 1). Mean age across countries for patients experiencing a GIB ranged from 75 to 77 years and the proportion of female patients ranged from 42% to 62%. The most common FXai indication among patients with a GIB was atrial fibrillation (85% to 90%). The incidence of GIB at 1 year following FXai initiation was generally consistent across Germany (1.92 per 100 PYR), the Netherlands (1.27 per 100 PYR), and the UK (1.84 per 100 PYR; Table 1). Rates of upper GIBs were higher compared with rates of lower GIBs or unspecified location GIBs in Germany; in the UK and Netherlands, unspecified GIBs occurred at a higher rate than upper or lower GIBs. Rates of all-cause mortality declined from 3 months to 1 year following a GIB for Germany, the Netherlands, and the UK.

Conclusion: In this observational study, FXai-associated GIB incidence rates were similar across Germany, the Netherlands, and the UK. Rates of all-cause mortality after a GIB varied between countries and decreased over the first year for all countries.

Disclosure: ATC: consultant for AbbVie, ACI Clinical, Alexion, AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Cardinal Health, Centrix, Daiichi-Sankyo, EmstoPA Ltd, Janssen, Johnson & Johnson, Medscape, Sanofi Aventis, and Pfizer.

JL: consulting fees from AstraZeneca, BMS-Pfizer, and Viatrix.

RW: reports grants and fees from AstraZeneca, Bayer, and Novartis.

JA: advisor or consultant for BMS-Pfizer, Medtronic, and Amgen; research funding from Carlos III Research Institute, Ministry of Science, Madrid, Spain, Department of Health, Castilla y León regional government, Spain (GRS-SACYL), Aptatargets, and European Commission; researcher for AstraZeneca; speaker for BMS-Pfizer, Medtronic, Boehringer-Ingelheim, and Bayer; and other fees from Daichii-Sankyo.

CIC: grants and consulting fees from AstraZeneca, Bayer, and Janssen.

DCD: no conflicts of interest to report.

EH: employee of the PHARMO Institute for Drug Outcomes Research, an independent research institute that performs financially supported studies for government and related healthcare authorities and several pharmaceutical companies.

EL: no conflicts of interest to report.

AC: advisor for ADIVO Associates LLC, Alexion Pharma Germany, Allergon GmbH, Biotest AG, Böhringer-Ingelheim International GmbH, CSL-Behring GmbH, CytoSorbents Europe GmbH, Dr. Falk Pharma GmbH, Eisai GmbH, and Elsevie; speaker for Abbvie Deutschland GmbH & Co KG, Academy 2 GmbH & Co. KG, Ardeypharm GmbH, Ärztekammer Nordrhein, Ärztekammer Westfalen-Lippe, BDC e.V., BDI Bundesverband Deutscher Internisten, bng Service GmbH, and CSL.

RZ, JBM, and GG are employees of AstraZeneca.

New FXai users	Germany (N=78,086)	Netherlands (N=17,356)	UK (N=212,378)
1-Year incidence of GIB per 100 PYR (95% CI)			
Overall	1.92 (1.80, 2.04)	1.27 (1.07, 1.50)	1.84 (1.77, 1.91)
Lower GIB	0.30 (0.26, 0.35)	0.38 (0.27, 0.51)	0.67 (0.63, 0.72)
Upper GIB	1.14 (1.05, 1.24)	0.32 (0.23, 0.45)	0.10 (0.08-0.12)
Unspecified GIB	0.65 (0.58, 0.72)	0.75 (0.60, 0.93)	1.06 (1.01, 1.12)
3-Year incidence of GIB per 100 PYR (95% CI)			
Overall	1.51 (1.43, 1.59)	0.98 (0.85, 1.12)	1.55 (1.51, 1.60)
Lower GIB	0.22 (0.20, 0.26)	0.30 (0.23, 0.39)	0.56 (0.53, 0.59)
Upper GIB	0.92 (0.86, 0.98)	0.29 (0.22, 0.37)	0.09 (0.08, 0.10)
Unspecified GIB	0.49 (0.45, 0.54)	0.51 (0.42, 0.62)	0.90 (0.86, 0.94)
GIB events after FXai use	N=1583	N=162 ^a	N=4683
All-cause mortality at 3 months after GIB			
n (%)	409 (25.8)	6 (3.7)	510 (10.9)
Per 100 PYR (95% CI)	131.2 (118.8, 144.6)	16 (6, 35)	47.5 (43.5, 51.8)
All-cause mortality at 1 year after GIB			
n (%)	590 (37.3)	12 (7.4)	914 (19.5)
Per 100 PYR (95% CI)	60.3 (55.5, 65.4)	9.3 (4.8, 16.2)	24.1 (22.6, 25.7)

Table 1. Incidence of FXai-associated (DOAC only) GIB and All-Cause Mortality after GIB^a

CI, confidence intervals; CPRD, Clinical Practice Research Datalink; DOAC, direct oral anticoagulant; HES APC, Hospital Episode Statistics Admitted Patient Care; ONS, Office for National Statistics; PYR, person-years.

^aData sources: Germany, WIG2 Claims Database (2016 – 2021); Netherlands, PHARMO Data Network (2008 – 2021); UK, HES APC and ONS data linked to CPRD primary care (2012 – 2020).

^bOf the 205 observed GIBs in the 3 years after FXai initiation, 162 could be followed after the GIB to assess further outcomes such as all-cause mortality.

OP220

UTILIZATION OF PROTON PUMP INHIBITORS IN PATIENTS WITH OVERT GASTROINTESTINAL BLEEDING: EFFECTS ON SHORT- AND LONG-TERM MORTALITY AND REBLEEDING

K. Barada¹, A.E. Zreik¹, J. Mrad¹, C. Rizk¹, H. Tamim^{2,3}, W. ElSheikh², A. Sharara¹, F. Mourad¹, F. Daniel¹, A. Soweid¹, Y. Shaib¹, N. El Asmar¹, D. Rockey⁴

¹American University of Beirut Medical Center, Internal Medicine, Beirut, Lebanon, ²American University of Beirut, Clinical Research Institute, Biostatistician Support Unit, Beirut, Lebanon, ³Alfaisal University, College of Medicine, Riyadh, Saudi Arabia, ⁴Medical University of South Carolina, Digestive Disease Research Center, Charleston, SC, United States of America

Contact E-Mail Address: jm117@aub.edu.lb

Introduction: Proton pump inhibitors (PPI) may be over or underutilized in patients with acute gastrointestinal bleeding (AGIB). Further, the effects of their use on short- and long-term outcomes are not clear.

Aims & Methods: We examined utilization of PPI in patients with AGIB and its effect on short- and long-term rebleeding and mortality in a prospective study of patients admitted with AGIB to a tertiary referral center between Jan. 2013 and Aug. 2023. We determined intake of PPI on admission and on discharge, and intake of antithrombotics [antiplatelets (AP) only, anti-coagulants (AC) only or both AP and AC] on admission and on discharge. Univariate analysis was done to compare patients using PPI on admission or on discharge to patients not using PPI. Multivariate analysis was done to determine independent predictors of mortality and rebleeding.

Results: 846 patients with AGIB (462 had upper GIB) were admitted and followed-up for a median of 59 (29-88) months. 385 were admitted already taking PPI. 623 patients were discharged on PPI and 150 were discharged off PPI (73 patients died in hospital). 49% of patients admitted on PPI and 27% of patients discharged on PPI did not have a clear indication for their use. The overall PPI overutilization rate was 36%. 25% of patients discharged off PPI had at least one clear indication for their use.

Compared to patients admitted off PPI, those admitted on PPI were older (66 vs 70 years, $p<0.001$), had higher Charlson Comorbidity Index (CCI) (2.4 vs 3.2, $p<0.001$), were more likely to be on antithrombotics (56% vs 70%, $p<0.001$) and to require blood transfusion (54% vs 64%, $p=0.003$). They also had higher 1-month mortality (8% vs 16%, $p<0.001$). However, they had less stigmata of recent hemorrhage (SRH) (39% vs 30%, $p=0.022$) and were less likely to require endoscopic therapy (25% vs 15%, $p=0.002$). Compared to patients discharged off PPI, patients discharged on PPI were more likely to have had in-hospital re-bleeding (1.3% vs 5.3%, $p=0.036$) but had similar short- and long-term mortality (4.7% vs 2.9%, $p=0.301$ and 37% vs 44%, $p=0.122$, respectively).

On multivariate analysis, PPI on admission was not an independent predictor of 1-month mortality or re-bleeding [OR 1.46 (0.83, 2.57), $p=0.187$ and 0.91 (0.51, 1.59), $p=0.730$], respectively. Predictors of 1-month mortality were CCI [OR 1.13 (1.04, 1.22), $p=0.002$], severe bleeding [OR 2.48 (1.21, 5.10), $p=0.013$], blood transfusion [OR 2.72 (1.20, 6.15), $p=0.017$], and SRH [OR 2.53 (1.40, 4.59), $p=0.002$]. Predictors of 1-month re-bleeding were AC only on admission [OR 2.30 (1.20, 4.42), $p=0.012$], severe bleeding [OR 1.96 (1.03, 3.73), $p=0.041$], and SRH [OR 2.03 (1.16, 3.54), $p=0.013$]. PPI on discharge was not a predictor of long-term mortality or re-bleeding (table 1). Being on AC only on discharge was a predictor of long-term mortality, while being on AP only on discharge was protective against long-term re-bleeding (table 1).

	Variables	OR (95% CI)	p-value		Variables	OR (95% CI)	p-value
Long-term Mortality**	PPI on discharge	1.38 (0.85, 2.26)	0.194	Long-term Re-bleeding**	PPI on discharge	1.26 (0.76, 2.07)	0.375
	Age-related CCI	1.53 (1.41, 1.67)	<0.001		AP only on discharge	0.45 (0.28, 0.72)	0.001
	Blood transfusion	1.72 (1.18, 2.51)	0.005		AC only on discharge	0.91 (0.54, 1.56)	0.741
	AP only on discharge	0.85 (0.55, 1.32)	0.479		AP and AC on discharge	0.56 (0.29, 1.10)	0.095
	AC only on discharge	2.51 (1.45, 4.36)	0.001		Severe bleeding*	1.53 (1.03, 2.25)	0.034
	AP and AC on discharge	0.91 (0.50, 1.7)	0.749		SRH	1.78 (1.21, 2.64)	0.004

Table 1: Multivariate analysis showing predictors of long-term mortality and re-bleeding in patients with acute GIB. AP: antiplatelets; AC: anticoagulants; Hb: Hemoglobin level; CCI: Charlson Comorbidity Index; *Severe bleeding is defined as: Hb drop ≥ 2 units, blood transfusions ≥ 2 units, or systolic blood pressure on admission ≤ 100 mmHg. ** long term mortality and re-bleeding are defined as mortality or re-bleeding by the end of follow-up.

Conclusion: There is marked overutilization and underutilization of PPI in patients with GIB, without a significant effect on short- or long-term mortality or rebleeding. A PPI utilization stewardship program is needed to decrease health care costs and potential PPI related side effects.

Disclosure: Nothing to disclose.

OP221

"THE DIAGNOSTIC YIELD OF GASTROSCOPY IN THE EVALUATION OF ASYMPTOMATIC PATIENTS WITH IRON DEFICIENCY ANEMIA"

R. Taher Natour¹, A. Beshara¹, A. Mari², A.-R. Zeina³, F. Younis⁴, D. Nicola⁴, F. Abu Baker⁴

¹Hillel Yaffe Medical Center, Department of Gastroenterology and Hepatology, Hadera Isreal, Israel, ²Nazareth EMMS Hospital., Department of Gastroenterology, Nazareth, Israel, ³Hillel Yaffe Medical Center, Hadera, Israel, Department of Radiology, Hadera Isreal, Israel, ⁴Hillel Yaffe Medical Center, Hadera, Israel, Department of Gastroenterology and Hepatology,, Hadera Isreal, Israel

Contact E-Mail Address: randataher12@gmail.com

Introduction: Asymptomatic patients with iron deficiency anemia (IDA) of indeterminate etiology are usually referred to bidirectional endoscopy evaluation. However, gastroscopy performance is questionable considering the low prevalence of gastric cancer in practice.

Aims & Methods: We conducted a retrospective, large cohort by reviewing electronic files of patients who underwent gastroscopy between 2005 and 2020. None had other active clinical symptoms than IDA. Asymptomatic patients referred routinely for gastroscopy before bariatric procedures served as controls.

Results: 6215 patients with IDA and 2010 controls were included. Female predominance was noted in both groups, IDA patients were significantly older (63.8 $\pm$ 17.3 vs. 40.6 $\pm$ 12.8; $P<0.001$), and significantly associated with severe gastritis (4.8% vs. 1%; $P<0.01$), gastric ulcer (2% vs. 0.5%; $P<0.01$), gastric cancer (1.4% vs. <0.01%; $P<0.01$), and gastric polyps (7% vs. 1.5%; $P<0.01$). The need for endoscopic intervention (1.9% vs. 0.1%; $P<0.01$) and biopsy performance (55% vs. 19%, $P<0.01$) were significantly higher among the IDA group. Overall, gastroscopy evaluation of IDA was significantly and independently associated with clinically significant findings (19.5% vs. 8.3%; OR 1.7, 95%CI=1.44-1.98; $P<0.001$). The highest yield of gastroscopy was documented among males (NNTI=13) and females

(NNTI=11) above 50, while the lowest was among young females in detecting clinically significant findings (NNTI=77), and upper GI malignancy (NNTI=1000).

Conclusion: Gastroscopy evaluation of asymptomatic patients with IDA is associated with an overall high yield of clinically significant findings detection, yet, among younger, colonoscopy performance first, rather than bi-directional endoscopic evaluation may be cost-effective.

References:

1. Yung DE. Earlier use of capsule endoscopy in inpatients with melena or severe iron deficiency anemia reduces need for colonoscopy and shortens hospital stay. *Endosc Int Open*. 2018 Sep;6(9):E1075-E1084. doi: 10.1055/a-0640-2956. Epub 2018 Sep 11.
2. Snook J. British Society of Gastroenterology guidelines for the management of iron deficiency anemia in adults. *Gut*. 2021 Nov;70(11):2030-2051.
3. De Franceschi L. Clinical management of iron deficiency anemia in adults: Systemic review on advances in diagnosis and treatment. *Eur J Intern Med*. 2017 Jul;42:16-23. doi: 10.1016/j.ejim.2017.04.018. Epub 2017 May 18.
4. Ko CW. AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia. *Gastroenterology*. 2020 Sep;159(3):1085-1094.
5. Taghvaei, T. (2017). Role of Upper and Lower Gastrointestinal Endoscopy in Investigating the Etiologies of Iron Deficiency Anemia in Postmenopausal Women. *Iranian Journal of Gastroenterology & Hepatology (GOVARESH)*, 22(2), 119–125.
6. Rockey DC. AGA Technical Review on Gastrointestinal Evaluation of Iron Deficiency Anemia. *Gastroenterology*. 2020 Sep;159(3):1097-1119.
7. Bard V. The Dynamic Changing Incidence of Gastric Cancer in Israel: Time for a National Surgical Management Committee? *Isr Med Assoc J*. 2022 Feb;24(2):112-116.
8. Odhaib SA. Do Gastrointestinal Symptoms Affect the Endoscopic Outcome in Anemic Premenopausal Women Due to Iron Deficiency: A Multicenter Study From Basrah-Iraq. *Cureus*. 2021 Apr 16;13(4):e14524.

Disclosure: Nothing to disclose.

Local treatment for locally advanced colon cancer: How to improve outcome

14:30-15:30 / Lehar 2

OP222

RISK OF LYMPH NODE METASTASIS IN T2 COLON CANCER IN THE NETHERLANDS - A NATIONWIDE POPULATION-BASED COHORT STUDY: PUSHING THE BOUNDARIES OF LOCAL TREATMENT?

J. Hanevelt¹, R.M. Brohet², L.M. Moons³, F.P. Vleggaar³, H.L. van Westreenen⁴, W. De Vos Tot Nederveen Cappel¹
¹Isala, Department of Gastroenterology and Hepatology, Zwolle, Netherlands, ²Isala, Department of Epidemiology & Statistics, Zwolle, Netherlands, ³University Medical Center Utrecht, Department of Gastroenterology & Hepatology, Utrecht, Netherlands, ⁴Isala, Department of Surgery, Zwolle, Netherlands

Contact E-Mail Address: j.hanevelt@isala.nl

Introduction: The implementation of the national bowel-screening program for colorectal cancer has had a significant impact on detecting early colorectal cancer (pT1 & pT2 carcinomas). In recent decades, there has been a shift towards minimally invasive approaches for treating T1 colon carcinomas (CC), favoring local resection techniques over major surgeries. It is unknown whether risk stratification could establish organ preservation in T2 CC.

Aims & Methods: We aimed to evaluate the incidence of lymph node metastases (LNMs) in patients with pT2 CC in the Netherlands and to develop a prediction model to estimate the risk of LNMs which could be helpful to compare the risk of LNMs against the age-specific adverse events associated with segmental surgery.

A retrospective nationwide cohort study was performed including all consecutive patients diagnosed with pT2 CC who underwent (completion) surgery between 2012 and 2020 in the Netherlands. Patients were identified by use of the Dutch ColoRectal Audit (DCRA).

Exclusion criteria were:

- 1) neoadjuvant therapy;
- 2) synchronous CRC;
- 3) hereditary predisposition
- 4) history of IBD; and,
- 5) non-adenocarcinoma.

Data obtained from the DCRA were linked to the Dutch Nationwide Pathology Databank (PALGA). A subgroup analysis was conducted on patients up to 70 years old, who were treated between 2018 and 2020, to examine the association between mismatch repair (MMR) status and the presence of LNMs.

Predictive factors for LNMs were evaluated with univariate- and multivariate logistic regression. Four machine learning (ML) models were developed and validated to predict LNM, including generalized linear modeling (GLM), GLM-Least Absolute Shrinkage and Selection Operator (GLM-LASSO), random forest (RF), and gradient boosting (XGB).

Results: In total 9,803 patients were included. The overall 30-day complication and mortality rates were 25.2% and 2.2%, respectively. In elderly patients (age ≥ 74), the complication and mortality rates increased to 30%, and 3.5%, respectively. LNMs were found in 1877 out of 9803 patients (19.1%). Younger age (OR 0.98, 95% CI 0.979 - 0.990), left-sided CC (OR 1.5, 95% CI 1.4-1.7), poor differentiation (1.7, 95% CI 1.4-2.2), and lymphovascular invasion (LVI) (OR 4.1, 95% CI 3.6-4.7) were independent risk factors for LNMs.

In the subgroup analysis, deficient MMR (dMMR) status was found to be associated with a significantly lower risk of LNMs (OR 0.3, 95% CI 0.2-0.5). GLM demonstrated the highest prediction accuracy, achieving AUCs of 0.67 for the full model and 0.68 for the model focusing on patients up to 70 years old.

The risk of LNMs in the lower-risk group (age ≥ 74 , right-sided CC, LVI absent, good/moderate tumor differentiation) was 10.7%. In the absence of other risk factors, patients with a dMMR carcinoma had a risk of LNMs of 6.1%.

		Right sided CC			Left sided CC			dMMR / pMMR
		Age ≥ 74	66 - < 74	Age < 66	Age ≥ 74	66 - < 74	Age < 66	
Good/ Moderate differentiation (G1-G2)	LVI -	10.7	12.6	14.1	15.6	18.2	20.2	6.1 / 17.2
	LVI +	33.2	37.5	40.6	43.4	48.1	51.4	19.3 / 43.1
Poor differentiation (G3)	LVI -	16.5	19.3	21.4	23.4	26.9	29.6	27.9 / 55.1
	LVI +	45.2	49.9	53.2	56.1	60.6	63.7	58.6 / 81.8
Complication rate		30.1	22.6	18	30.1	22.6	18	19.2
Mortality rate		3.5	1	0.5	3.5	1	0.5	0.7

Table. Predicted probability (%) of LNM in patients with T2 colon cancer.

Conclusion: The predicted probability of LNMs should be balanced against the risks associated with segmental colon surgery. The findings of this study could serve as valuable guidance for clinicians, enabling them to inform patients about these competing risks before making a shared decision.

Disclosure: Nothing to disclose.

OP223

RISK OF OCCULT LYMPH NODE METASTASIS IN PT2 RECTAL CANCER: A NATIONWIDE RETROSPECTIVE ANALYSIS

S.C. Albers¹, R. Geitenbeek², E.GM van Geffen³, T.C Sluckin³, S.-M. Hazen³, M. Kusters³, P.J. Tanis⁴, E.C. Consten⁵, E. Dekker¹, B.A. Bastiaansen¹, J.K. Wiggers³, R. Hompes³, Dutch Snapshot Research Group and MIRECA (Taskforce for Minimally Invasive Rectal Carcinoma surgery)

¹Amsterdam University Medical Centers, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²University Medical Center Groningen, Gastroenterology and Hepatology, Haren, Netherlands, ³Amsterdam University Medical Centers, Department of Surgery, Amsterdam, Netherlands, ⁴Leiden University Medical Center, Dept. of Surgery, Leiden, Netherlands, ⁵Meander Medisch Centrum, Dept. of Surgery, Amersfoort, Netherlands

Contact E-Mail Address: s.c.albers@amsterdamumc.nl

Introduction: Advances in transanal resection techniques have led to the increased use of surgical and endoscopic local excision (LE) as a diagnostic and potentially organ-sparing approach for early-stage (cT1-2N0) rectal cancer (RC). Current international guidelines recommend completion total mesorectal excision (TME) following LE for surgically fit patients with pT2 RC due to the 20-30% overall risk of lymph node metastasis (LNM). However, the risk of LNM is known to vary according to the presence of histological risk factors.

Therefore, omitting completion TME in selected patients with pT2 RC may constitute an oncologically safe alternative, provided there are no additional high-risk histological features other than muscularis propria invasion. The aim of this study was to determine the rate of LNM in patients with pT2 RC without additional histological risk factors.

Aims & Methods: Data from two large Dutch multicentre registries were analysed to evaluate the rate of LNM in patients with pT2 RC who underwent surgery between 2012 and 2020. In accordance with the clinical selection criteria for LE, only patients without suspected LNM on baseline imaging (cN0) were included in the study. Patients who received (neo)ad-

juvant (chemo)radiotherapy were excluded. Treatment strategies included primary TME, surgical LE followed by completion TME, or surgical LE followed by active surveillance with MRI for at least 24 months. Histological risk factors available in both registries were lymphovascular invasion (LVI) and poor tumour differentiation (PD).

Definitive LNM status was determined by histology after TME. Patients on active surveillance after LE were classified as LNM-negative if there was no evidence of LNM (cN0) on MRI during a minimum surveillance period of 24 months.

The primary study outcome was the rate of LNM in pT2 RC patients without LVI and PD. Secondary outcomes included the association between the two histological risk factors and the rate of LNM using univariable and multivariable analyses adjusted for age and sex.

Results: A total of 334 patients with pT2 RC met the inclusion criteria (mean age 69 years, 64% male). The majority of patients (262/334, 78%) underwent primary TME, while initial surgical LE was performed in 72/334 (22%). Within the LE group, subsequent TME surgery was performed in 59/72 (82%) patients, either as completion surgery (n=51) or as salvage surgery during the follow-up period (n=8). The remaining 13/72 (18%) patients underwent active surveillance for at least 24 months without suspicion of LNM on MRI during a median follow-up of 42 months (IQR 32-55).

The overall rate of LNM in the cohort was 17% (55/334). In the 266/334 (80%) patients without LVI and PD, the rate of LNM was 13% (34/266). The presence of either LVI alone or PD alone resulted in LNM rates of 31% (18/58) and 14% (1/7), respectively. When both LVI and PD were present, LNM occurred in 2 out of 3 cases. In our study, only LVI was identified as an independent predictor of LNM in multivariable analysis ($p < 0.001$; OR = 3.1, 95% CI 1.6-5.9).

Conclusion: In this large retrospective surgical cohort of patients with pT2 RC, the absence of LVI and PD was associated with a 13% risk of LNM. However, more detailed histological reassessment including risk factors such as tumour budding and perineural invasion may identify a subgroup of pT2 RC with an even lower risk of LNM. This may allow the omission of completion TME.

Disclosure: Nothing to disclose.

OP224

THREE-YEAR ONCOLOGICAL OUTCOMES OF ENDOSCOPIC INTERMUSCULAR DISSECTION FOR SUSPECTED DEEP SUBMUCOSAL INVASIVE RECTAL CANCER

L. van der Schee¹, S.C. Albers², P. Didden¹, M.M. Lacle³, A. Fariña Sarasqueta⁴, M. Richir⁵, M. Intven⁶, J. Tuynman⁷, R. Hompes⁷, E. Dekker², F.P. Vleggaar¹, B.A. Bastiaansen², L.M. Moons¹

¹University Medical Center Utrecht, Gastroenterology & Hepatology, Utrecht, Netherlands, ²Amsterdam University Medical Centers, Gastroenterology & Hepatology, Amsterdam, Netherlands, ³University Medical Center Utrecht, Pathology, Utrecht, Netherlands, ⁴Amsterdam University Medical Centers, Pathology, Amsterdam, Netherlands, ⁵University Medical Center Utrecht, Surgery, Utrecht, Netherlands, ⁶University Medical Center Utrecht, Radiotherapy, Utrecht, Netherlands, ⁷Amsterdam University Medical Centers, Surgery, Amsterdam, Netherlands

Contact E-Mail Address: l.vanderschee-2@umcutrecht.nl

Introduction: Endoscopic intermuscular dissection (EID) was recently introduced as a novel resection technique for deep submucosal invasive rectal cancer (D-SMIC)¹. While short-term outcomes are promising, inter-

mediate- and long-term oncological safety has not yet been established. Therefore, we aimed to evaluate the 3-year oncological outcomes of EID for suspected rectal D-SMIC.

Aims & Methods: In this prospective cohort study, data of consecutive patients treated with EID for suspected rectal D-SMIC at two academic hospitals in the Netherlands between 2018 and 2022 were analyzed. Superficial submucosal invasive cancer (S-SMIC) was defined as Sm1 and D-SMIC as Sm2-3. Tumors were considered high-risk if they exhibited at least one of the following histological risk factors: high-grade tumor differentiation (G3), lymphovascular invasion, tumor budding grade 2-3, R1/Rx resection margins (<0.1 mm), or $\geq$ pT2 invasion. Patients with D-SMIC or $\geq$ pT2 invasion who did not undergo further treatment after EID, either due to the absence of additional risk factors or based on patient preference, underwent close surveillance. This surveillance involved biannual MRI and endoscopic scar inspection for 2 years, followed by annual MRI and endoscopy for 3 years. A complete colonoscopy was performed after 1 and 4 years. CEA blood levels were measured every six months for 5 years. Study outcomes included the 3-year locoregional recurrence rate (LRR), 3-year distant recurrence rate (DRR), 3-year salvageable recurrence rate (SRR) and 3-year rectal preservation rate. The 3-year estimates were calculated using the Kaplan-Meier method. Locoregional recurrence was defined as intramural cancer recurrence and/or mesorectal lymph node metastasis, while distant recurrences referred to other cancer recurrences. Salvageable recurrence was defined as cancer recurrence that could be treated with curative intent. Rectal preservation was defined as the absence of completion total mesorectal excision (TME) following EID or cancer recurrence.

Results: EID was initiated in 188 patients (median age 67 years, 33% female, 85% ASA I-II, median lesion size 25 mm) and successfully completed in 177 (94%). Histology showed non-invasive histology in 20 (11%), S-SMIC in 9 (5%), D-SMIC in 94 (53%) and $\geq$ pT2 in 53 (30%) cases. R0 resection rates within these groups were 100%, 100%, 93% and 58%, respectively. Among the 94 D-SMIC cases, 35 (37%) had no histological risk factors other than deep submucosal invasion. Out of the D-SMIC cases, 72/94 (77%) followed a rectal preserving strategy (64/72 close surveillance and 8/72 adjuvant chemoradiotherapy), while 22/94 (23%) underwent completion TME. The median follow-up period within the D-SMIC group was 30 months (IQR 18-48). At three years, the LRR was 5.9% (95%CI 0.0-11.5%) and the DRR was 1.1% (95%CI 0.0-3.4%). The 3-year SRR was 100% (95%CI 100-100%). One patient (1.1%) died of a non-CRC-related cause. Among the subgroup of 35 D-SMIC cases without additional histological risk factors, all of whom underwent close surveillance following EID, no recurrences occurred within the first three years of follow-up. Beyond this period, one locoregional recurrence (2.9%) occurred at 37 months and one distant recurrence (2.9%) at 51 months, both salvageable. Overall, the 3-year rectal preservation rate among all 188 patients who underwent EID for suspected rectal D-SMIC, was 64.6% (95%CI 58.0-71.9%).

Conclusion: EID for suspected rectal D-SMIC resulted in favorable 3-year rectal preservation rates and demonstrated excellent 3-year oncological outcomes for rectal D-SMIC without additional risk factors.

References: 1) Moons LMG, Bastiaansen BAJ, Richir MC, Hazen WL, Tuynman J, Elias SG, Schrauwen RWM, Vleggaar FP, Dekker E, Bos P, Fariña Sarasqueta A, Lacle M, Hompes R, Didden P. **Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum: a new endoscopic approach.** *Endoscopy*. 2022 Oct;54(10):993-998.

Disclosure: Nothing to disclose.

OP225

THREE-YEAR ONCOLOGICAL OUTCOMES OF ENDOSCOPIC FULL-THICKNESS RESECTION FOR SCAR EXCISION AFTER INCOMPLETE RESECTION OF LOW-RISK T1 COLORECTAL CANCER: RESULTS FROM THE DUTCH NATIONWIDE PROSPECTIVE EFTR REGISTRY

S.C. Albers¹, L. Zwager², F. Bekkering³, J.J. Boonstra⁴, F. ter Borg⁵, P. Fockens⁶, E. Gielisse⁷, M. Houben⁸, W.R. ten Hove⁹, W.B. Nagengast¹⁰, L. Perk¹¹, F.J. Rando Munoz¹², R.-M. Schreuder¹³, M.P. Schwartz¹⁴, H. van der Sluis¹⁵, B.W. van der Spek¹⁶, J.S. Terhaar Sive Droste¹⁷, M.S. Vlug¹⁸, B.L. Weusten¹⁹, C. Wientjes²⁰, T. de Wijkerslooth²¹, A. Fariña Sarasqueta²², E. Dekker², B.A. Bastiaansen², Dutch eFTR Study Group
¹Amsterdam University Medical Centers, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam University Medical Centers, Gastroenterology & Hepatology, Amsterdam, Netherlands, ³IJsselland Hospital, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁴Leids University Medical Center, Gastroenterology and Hepatology, Oegstgeest, Netherlands, ⁵Deventer Hospital, Gastroenterology & Hepatology, Deventer, Netherlands, ⁶Amsterdam UMC, Department of Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁷Rode Kruis Ziekenhuis, Department of Gastroenterology and Hepatology, Beverwijk, Netherlands, ⁸HagaTeaching Hospital, Gastroenterology, The Hague, Netherlands, ⁹Alrijne Medical Group, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ¹⁰University Medical Center Groningen, Gastroenterology and Hepatology, Haren, Netherlands, ¹¹Medisch Centrum Maaglanden, Department of Gastroenterology and Hepatology, Leidscherdam, Netherlands, ¹²Nij Smellinghe Hospital, Department of Gastroenterology and Hepatology, Drachten, Netherlands, ¹³Catharina Hospital, Gastroenterology, Eindhoven, Netherlands, ¹⁴Meander Medical Center, Amersfoort, Gastroenterology & Hepatology, Amersfoort, Netherlands, ¹⁵Isala Clinics, Department of Gastroenterology and Hepatology, Zwolle, Netherlands, ¹⁶Noordwest Hospital Group, Department of Gastroenterology and Hepatology, Alkmaar, Netherlands, ¹⁷Jeroen Bosch Ziekenhuis, Gastroenterology and Hepatology, 's-Hertogenbosch, Netherlands, ¹⁸Dijklander Hospital, Department of Gastroenterology and Hepatology, Hoorn, Netherlands, ¹⁹St Antonius Hospital, Department of Gastroenterology and Hepatology, Nieuwegein, Netherlands, ²⁰OLVG, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²¹Antoni van Leeuwenhoek, Department of Gastroenterology, Amsterdam, Netherlands, ²²Amsterdam University Medical Centers, Department of Pathology, Amsterdam, Netherlands

Contact E-Mail Address: s.c.albers@amsterdamumc.nl

Introduction: Scar excision with endoscopic full-thickness resection (eFTR) offers a minimally invasive alternative to completion surgery after incomplete resection of low-risk T1 colorectal cancer (CRC). While this strategy has demonstrated promising technical and short-term results, long-term data on oncological safety are lacking.

Aims & Methods: Consecutive patients undergoing eFTR scar excision after incomplete resection of low-risk T1CRC were selected from the Dutch prospective eFTR registry. Incomplete resection was defined as indeterminate (Rx), tumour-positive (R1, <0.1mm) or <1mm tumour-free (R0) resection margins. Lesions were considered low-risk in absence of lymphovascular invasion, poor tumour differentiation and tumour budding grade 2-3 (if assessed). A retrospective analysis was conducted to evaluate the procedural outcomes, subsequent treatment after eFTR, and surveillance

data, including endoscopy, CEA and imaging studies, as outlined by local protocols. Study outcomes included the 3-year locoregional recurrence rate (LRR), distant recurrence rate (DRR), salvageable recurrence rate (SRR), overall survival (OS) and organ preservation rate. The 3-year estimates were calculated using the Kaplan-Meier method. Locoregional recurrence was defined as intramural cancer recurrence and/or locoregional lymph node metastasis. Other cancer recurrence was defined as distant recurrence. Salvageable recurrence was defined as cancer recurrence that could be treated with curative intent.

Results: Out of the 1341 procedures registered in the Dutch prospective eFTR registry between 2015 and 2023, 314 patients met the inclusion criteria (mean age 69 years, 62% male). Initial histology showed Rx/R1 margins in 260/314 (83%) and R0 <1mm in 54/314 (17%). Mean time from initial resection to eFTR was 2 months (SD 2). Macroscopic complete scar excision was achieved in 259/314 (83%) patients. At histology, 36/314 (12%) eFTR specimens had residual cancer (15 low-risk T1CRC, 21 high-risk T1CRC/≥T2CRC). Residual cancer was found in 26/143 (18%) patients after initial piecemeal resection versus 10/171 (6%) after en bloc resection. No residual cancer was found after R0 <1mm (0/54). The R0-resection rate for residual cancer was 25/36 (69%). After eFTR, 30/314 (10%) patients underwent completion surgery, of whom 9/30 (30%) had residual cancer. One patient received adjuvant chemoradiotherapy. Surveillance was initiated in the remaining 283/314 (90%) patients. In the surveillance-only group, 246/283 (87%) had at least one recorded follow-up visit, with a median follow-up time of 36 months (IQR 16-52). Of these, 17/246 (7%) had residual cancer in the eFTR specimen. The 3-year LRR, DRR, SRR and OS for this subgroup (n=17) were 13%, 0%, 100% and 94%, respectively. Of the 229/246 (93%) patients without residual cancer in the scar, 187/229 (82%) had no risk factors at initial histology, while the presence of risk factors could not be reliably assessed in 42/229 (18%). In the low-risk group (n=187), the 3-year LRR, DRR, SRR and OS were 1%, 1%, 99% and 98%, respectively. In the group with indeterminate risk factors (n=42), these were 7%, 3%, 97% and 92%. The overall 3-year organ preservation rate for all 314 eFTR procedures initiated was 87%.

Conclusion: In this analysis of a large Dutch prospective eFTR registry, the use of completion eFTR after incomplete resection of low-risk T1CRC demonstrated excellent 3-year oncological outcomes. However, caution should be exercised if the presence of histological risk factors cannot be adequately assessed. Further prospective studies with strict surveillance are warranted.

Disclosure: Nothing to disclose.

OP226

ADDED VALUE OF ADJUVANT CHEMOTHERAPY IN T1-2 NODE-POSITIVE COLON CANCER PATIENTS

J. Hanevelt¹, J.W.B. De Groot², E. Rademaker³, B. Zamaray³, R.M. Brohet⁴, E.C. Consten^{5,6}, P.J. Tanis⁷, L.M. Moons⁸, F.P. Vleggaar⁹, H.L. Van Westreenen³, W.H. de Vos Tot Nederveen Cappel¹, on behalf of the Dutch Snapshot Research Group (DSRG), Dutch Complex Colon Cancer Initiative (DCCCI)
¹Isala, Department of Gastroenterology and Hepatology, Zwolle, Netherlands, ²Isala, Department of Medical Oncology, Zwolle, Netherlands, ³Isala, Department of Surgery, Zwolle, Netherlands, ⁴Isala, Department of Epidemiology & Statistics, Zwolle, Netherlands, ⁵Meander Medisch Centrum, Department of Surgery, Amersfoort, Netherlands, ⁶University Medical Center Groningen (UMCG), Department of Surgery, Groningen, Netherlands, ⁷Erasmus MC, Department of Surgical Oncology and Gastrointestinal Surgery, Rotterdam, Netherlands, ⁸University Medical Center Utrecht, Department of Gastroenterology & Hepatology, Utrecht, Netherlands, ⁹University Medical Center Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands

Contact E-Mail Address: j.hanevelt@isala.nl

Introduction: According to the current guidelines, all patients with lymph node metastases after curative surgery for colon cancer (CC) are recommended to undergo adjuvant chemotherapy, regardless of the T-stage. However, a limited number of patients with pT1-2 CC were included in the trials that demonstrated a benefit of adjuvant chemotherapy for lymph node positive CC patients.

The aim of this study was to evaluate the value of adjuvant chemotherapy in patients with lymph node-positive pT1-2 CC.

Aims & Methods: A multicenter retrospective cohort study was conducted, including patients who underwent curative surgery for T1 or T2 CC between 2014 and 2015. Patients were originally identified through the Dutch ColoRectal Audit (DCRA), a prospective national registry of all patients undergoing surgery for primary colorectal cancer. Long-term oncological follow-up data from the original patient records were added to the DCRA data by surgical residents affiliated with the Dutch Snapshot Research Group (DSRG) from 61 participating hospitals. Patients were stratified by age (< 75 or ≥75 years).

Survival outcomes were compared with the Kaplan-Meier method and log-rank test. Cox proportional hazard models were used to determine risk factors associated with 5-year metastasis-free and overall survival (MFS/OS).

Results: Among the 2277 surgically treated pT1-2 CC patients, 370 (16.2%) were found to have lymph node metastases, with 262 (70.8%) of them receiving adjuvant chemotherapy (CT+). Patients who did not receive adjuvant chemotherapy (CT-) were significantly older, had a higher ASA score, and experienced more frequently a complicated postoperative course, compared to the CT+ group. Among the total cohort, the vast majority of patients (78.6%) received oxaliplatin-based chemotherapy (CAPOX) and 13% capecitabine monotherapy.

Among those under < 75 years old (n = 272), CAPOX was administered in 86.3% of cases, whereas in patients ≥ 75 (n = 97), capecitabine monotherapy was given in 42.9% and CAPOX in 38.1%. In younger patients (< 75), chemotherapy significantly improved OS (68.2% CT-group versus 91.8% in CT+ group, multivariate HR 0.3, 95% CI 0.1 - 0.6) and also had a favorable effect on MFS (83.7% in CT-group versus 91.6% in CT+ group, multivariate HR 0.5, 95% CI 0.2 - 1.09). In elderly patients (≥75 years old), the administration of adjuvant chemotherapy did not significantly affect the development of distant metastases (MFS of 81.7% in the CT- group versus

84.5% in the CT+ group, log rank p value 0.73, adjusted HR 1.2, 95% CI 0.4 – 3.8)), nor survival after correction for confounders (OS of 52.7% in the CT-group versus 77% in the CT+ group, age adjusted HR 0.6, 95% CI 0.2 – 1.5). The choice of chemotherapy regimen (CAPOX or capecitabine monotherapy) had no influence on MFS (HR 0.6, 95% CI 0.1 – 3.5) or OS (0.6, 95% CI 0.1 – 2.7).

	Age < 75 No CTx n = 53	Age < 75 CTx n = 219	p value	Age ≥ 75 No CTx n = 55	Age ≥ 75 CTx n = 42	p value
Follow-up (months), median [IQR]	53 [28-61]	64 [60-70]	<.001	49 [28-63]	59 [44-63]	0.11
Recurrent disease, n (%)	8 (15.1)	19 (8.7)	0.16	11 (20)	6 (14.3)	0.46
Loco regional recurrence only	1 (1.9)	2 (0.9)		3 (5.5)	0	
Distant metastases only	6 (11.3)	13 (5.9)		7 (12.7)	5 (11.9)	
Loco regional recurrence + distant metastases	1 (1.9)	4 (1.8)		1 (1.8)	1 (2.4)	
Unadjusted 5-Year Overall Survival (%)	68.2	91.8	<.001	52.7	77	0.02
Unadjusted 5-Year Metastasis Free Survival (%)	83.7	91.6	0.07	81.7	84.5	0.73

Conclusion: In the largest cohort of node-positive pT1-2 colon cancer patients currently available, no significant benefit of adjuvant chemotherapy in patients over 75 years of age could be demonstrated, irrespective of the regimen that is chosen.

Disclosure: Nothing to disclose.

Pancreatic endoscopy and patient outcome

14:30-15:30 / Lehar 3

OP227

PERFORMANCE OF A NOVEL ARTIFICIAL INTELLIGENCE SYSTEM FOR DETECTION OF SOLID PANCREATIC MASS LESIONS AT REAL-TIME ENDOSCOPIC ULTRASOUND (EUS)

J.Y. Bang¹, A. Saftoiu², J. Ramesh¹, A. Udristoiu³, L. Gruionu⁴, E. Gheorghe⁵, G. Gruionu⁶, U. Navaneethan¹, R. Hawes¹, S. Varadarajulu¹
¹Orlando Health, Digestive Health Institute, Orlando, United States of America, ²Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ³University of Craiova, Faculty of Automation, Computers and Electronics, Craiova, Romania, ⁴University of Craiova, Faculty of Mechanics, Craiova, Romania, ⁵University of Craiova, Department of Family Medicine, Craiova, Romania, ⁶Indiana University School of Medicine, Indianapolis, United States of America

Contact E-Mail Address: jybang213@gmail.com

Introduction: As outcomes in pancreatic cancer are stage dependent, high technical proficiency in EUS is required for early detection and accurate diagnosis of pancreatic lesions. We evaluated performance of artificial intelligence enhanced EUS (AI-EUS) to detect solid and cystic lesions in the pancreas.

Aims & Methods: An AI-EUS software was developed using convolutional neural network (CNN) model that included 32,713 linear-array EUS frames (training and testing phases) of normal, solid and >10mm cystic pancreatic lesions from 202 patients. A prospective, nonrandomized, comparative study was conducted in patients referred for pancreatic cancer screening and suspected solid or cystic lesions in pancreas. EUS findings were examined concurrently in real-time by two independent expert examiners, one using conventional EUS and another with AI-EUS. EUS procedures were projected to separate monitors with examiners blinded to alternate assessments. Main outcome was detection of solid pancreatic mass lesions. Secondary outcome was detection of pancreatic cysts.

Results: 180 patients were included (mean age 66.5 years [SD 14.5]; male 45.6%) between January to April 2024. There was 100% (95% CI, 94.6-100) concordance between conventional EUS and AI-EUS for detection of solid masses (n=67; mean size 32.7 mm [SD=16.7]) that were biopsy proven to be adenocarcinoma in 46, metastatic lesion 2, neuroendocrine tumor 7, lymphoma 1, solid pseudopapillary neoplasm 1, and benign disease in 10. Likewise, there was 100% (95% CI, 92.7-100) concordance for detection of normal pancreas (n=49). For pancreatic cysts (n=64; median size 22 mm [IQR 13-34.5]), as compared to AI, conventional EUS diagnosed more cysts (100 [95% CI 94.4-100] vs. 84.4% [95% CI 73.1-92.2], p=0.001), particularly those < 15 mm.

Conclusion: In this first human trial, performance of AI-EUS was comparable to conventional EUS for detection of solid pancreatic mass lesions. AI has potential to standardize technical performance at EUS which can further optimize clinical outcomes in pancreatic cancer. Additional refinements to CNN model incorporating Doppler techniques could improve detection of small pancreatic cysts.

Disclosure: JYB: Consultant for Olympus America Inc. and Boston Scientific Corporation.
SV: Consultant for Boston Scientific Corporation, Olympus America Inc. and Medtronic.
RH: Consultant for Olympus America Inc, Fujifilm, GIE Medical
UN: Consultant for Janssen, Pfizer, Takeda, AbbVie, Bristol Myers Squibb and GIE Medical Inc.
Other authors have no disclosures to declare.

OP228

DEEP LEARNING AND AUTOMATIC DIFFERENTIATION OF PANCREATIC LESIONS IN ENDOSCOPIC ULTRASOUND – A TRANSATLANTIC STUDY

B. Agudo Castillo¹, M.J. Mascarenhas Saraiva², M. González-Haba Ruiz¹, J. Widmer³, T. Gonda³, M.E. Lera dos Santos⁴, F. Vilas-Boas², F. Mendes², M.G. Macedo²

¹Hospital Universitario Puerta de Hierro Majadahonda, Department of Gastroenterology, Majadahonda, Spain,

²Centro Hospitalar São João, Gastroenterology, Porto, Portugal,

³New York University Langone Hospital, Gastroenterology, New York, United States of America, ⁴Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Endoscopy, São Paulo, Brazil

Contact E-Mail Address: miguelmascarenhassaraiva@gmail.com

Introduction: Accurate diagnosis of pancreatic lesions poses a considerable challenge due to the involvement of multiple examinations in the diagnostic process. Endoscopic ultrasound (EUS) stands out as a valuable tool enabling characterization and tissue sampling of both cystic and solid lesions, thereby influencing treatment decisions and follow-up strategies significantly. Pancreatic cystic neoplasms (PCNs) encompass mucinous (M-PCN) and non-mucinous lesions (NM-PCN), while pancreatic adenocarcinoma (P-ADC) remains the most prevalent cause of pancreatic solid lesions (PSL), trailed by pancreatic neuroendocrine tumors (P-NET). Despite the potential benefits of artificial intelligence, particularly deep learning algorithms, in EUS, research on the role of convolutional neural networks (CNNs) in pancreatic lesions is scarce.

Aims & Methods: This multicentric study aims to develop a CNN tailored for the detection and differentiation of PCNs (specifically M-PCN and NM-PCN) as well as PSLs (particularly P-ADC and P-NET). Our group developed a retrospective multicenter study based on patients submitted to EUS for pancreatic lesion characterization. A trinary CNN differentiated normal pancreas tissue from M-PCN and NM-PCN. A binary CNN distinguished P-ADC from P-NET. The total dataset was divided into a training and testing dataset (used for model's evaluation) in a 90/10% ratio. The model performance was evaluated through its sensitivity, specificity, positive and negative predictive values and accuracy. The Sci-kit learn v0.22.2 was used for statistical analysis of the model.

Results: A total of 378 videos of EUS performed for evaluation of pancreatic lesions during November 2017 and December 2023 in four reference centers (Hospital Universitario Puerta de Hierro Majadahonda, n=234; Centro Hospitalar Universitário São João, n=33; New York University Langone and Manhattan Hospital, n=60; Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, n=51) were used for development of the model. A total of 126.000 frames were extracted for development of CNN: 64.286 of P-ADC, 29.153 of P-NET, 4.858 of normal pancreas, 19.528 of M-PCN and 8.175 of NM-PCN.

Pancreatic Cystic Neoplasms

The trinary CNN was developed in order to distinguish between normal pancreas images and cystic lesions, differentiating M-PCN from NM-PCN. The deep learning model identified normal pancreas images with 98.6% sensitivity, 99.2% specificity and 99.1% accuracy. M-PCN were detected with 98.9% sensitivity, 99.1% specificity, a PPV of 99.4% and NPV of 98.3%, with a global accuracy of 99%. Finally, the testing dataset of our CNN revealed 99.3% sensitivity, 99.9% specificity, 99.9% PPV, 99.8% NPV and 99.8% accuracy for the diagnosis of NM-PCN.

Pancreatic Solid Lesions

The binary CNN was developed to differentiate between the two commoner PSL, namely P-ADC and P-NET. The testing dataset revealed 94.0% accuracy for the distinction between the lesions, with 98.7% and 83.7% sensitivities for P-ADC and PNET, respectively.

Conclusion: Our group developed a deep learning model capable of differentiating the main types of pancreatic solid lesions, as well as pancreatic cystic lesions, with high performance values. To our knowledge this is the first multicentric approach for the development of an AI algorithm designed to simultaneously characterize cystic and solid pancreatic lesions.. The development of deep learning models may help differentiate pancreatic lesions. Larger multicentric and prospective studies are needed for the validation and future clinical implementation of this technology.

References: Kuwahara T, Hara K, Mizuno N, et al. Current status of artificial intelligence analysis for the treatment of pancreaticobiliary diseases using endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography. *DEN Open*. 2024;4(1):e267.

Disclosure: Nothing to disclose.

OP229

PROTON PUMP INHIBITORS ARE ASSOCIATED WITH INCREASED LAMS OCCLUSION RATE AND A HIGHER NUMBER OF REQUIRED ENDOSCOPIC NECROSECTOMIES IN PATIENTS WITH PANCREATITIS

J. Hamm¹, A. Busana¹, A. Arlt², T. Asendorf³, G. Beyer⁴, S. Carswell⁵, U.W. Denzer⁶, A. Dürr⁷, L. Elsing⁸, F. Frost⁹, P. Falt¹⁰, L. Guilabert¹¹, K. Hamesch¹², A. Hoffmeister¹³, M. Hollenbach¹⁴, P. Hegyi¹⁵, P.J. Hegyi¹⁶, A. Kleger¹⁷, T. Kohlmann¹⁸, J. Krivinka¹⁹, L. Kunovský²⁰, B. Martinez-Moreno¹¹, J. Mayerle²¹, C. Meinhardt²², P. Michl²³, T. Mollnow²⁴, M. Müller-Schilling²⁵, S. Pandanaboyana²⁶, V. Phillip²⁷, J. Rosendahl²⁸, S. Schlosser-Hupf⁷, L. Schulte²⁹, H. Seifert³⁰, S. Sirtl³¹, E. Steiner-Gager³², S. Sulzer¹, L. Welsch²⁴, J.C. von Widdern³³, A. Amanzada¹, R. Knoop¹, G. Petzold¹, V. Ellenrieder¹, A. Neese¹, C. Ammer-Herrmenau¹

¹University Medical Center Goettingen, Department of Gastroenterology, Gastrointestinal Oncology and Endocrinology, Goettingen, Germany, ²Israelitisches Krankenhaus, Department of Gastroenterology, Hamburg, Germany, ³University Medical Center Goettingen, Department of Medical Statistics, Goettingen, Germany, ⁴University Hospital LMU Munich, Department of Medicine II, München, Germany, ⁵Freeman Hospital, HPB and Transplant Unit, Newcastle Upon Tyne, United Kingdom, ⁶University Clinic Marburg, Gastroenterology, Department of Endoscopy, Marburg, Germany, ⁷University Hospital Regensburg, Department of Gastroenterology, Regensburg, Germany, ⁸University Hospital Leipzig, Department of Oncology, Gastroenterology, Hepatology, Pneumology and Infectiology, Leipzig, Germany, ⁹Universität Greifswald, Department of Gastroenterology, Greifswald, Germany, ¹⁰University Hospital Olomouc, 2nd Department of Internal Medicine – Gastroenterology and Geriatrics, Olomouc, Germany, ¹¹Dr. Balmis General University Hospital from Alicante, Gastroenterology, Alicante, Spain, ¹²University Hospital RWTH Aachen, Medical Clinic III, Gastroenterology, Metabolic Diseases and Intensive Care, Aachen, Germany, ¹³University of Leipzig, Department of Oncology, Gastroenterology, Hepatology, Pneumology and Infectiology, Leipzig, Germany, ¹⁴University Hospital Heidelberg, Department of Gastroenterology, Heidelberg, Germany, ¹⁵University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ¹⁶Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, Pécs, Hungary, ¹⁷Institute of Molecular Oncology and Stem Cell Biology, Ulm University Hospital, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ¹⁸University Hospital Greifswald, Institute for Community Medicine, Greifswald, Germany, ¹⁹University Hospital Olomouc, 2nd Department of Internal Medicine – Gastroenterology and

Geriatrics, Olomouc, Czech Republic, ²⁰2nd Department of Internal Medicine – Gastroenterology and Geriatrics, University Hospital Olomouc, Faculty of Medicine, Palacky University Olomouc, University Hospital Brno, Faculty of Medicine, Masaryk University, Olomouc, Czech Republic, ²¹Klinikum der LMU München-Grosshadern, Medizinische Klinik und Poliklinik II, München, Germany, ²²Klinikum Oldenburg AöR, University Clinic of Internal Medicine - Gastroenterology, Oldenburg, Germany, ²³Heidelberg University Hospital, Gastroenterology, Heidelberg, Germany, ²⁴Klinikum Hanau, Department of Gastroenterology, Diabetology and Infectiology, Hanau, Germany, ²⁵University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany, ²⁶Freeman hospital, HPB and Transplant Unit, Newcastle upon tyne, United Kingdom, ²⁷Technische Universität München, Klinik und Poliklinik für Innere Medizin II, München, Germany, ²⁸University Clinic Halle (Saale) - Department of Internal Medicine I, University Clinic Halle (Saale), Department of Internal Medicine I, Halle (Saale), Germany, ²⁹University Hospital Ulm, Department for Internal Medicine 1, Ulm, Germany, ³⁰University of Oldenburg, Univ. Clinics Gastroenterology, Oldenburg, Germany, ³¹LMU University Hospital, Department of Medicine II, Munich, Germany, ³²University Hospital St. Pölten, Department of Internal Medicine II, St. Pölten, Austria, ³³University Hospital Halle, Department of Gastroenterology, Halle, Germany

Contact E-Mail Address: jacob.hamm@med.uni-goettingen.de

Introduction: Patients with necrotizing pancreatitis are at risk of developing numerous complications as a consequence of their more severe disease course. Effective drainage strategies are essential for patients with symptomatic walled off necroses (WON). Here, most patients receive interventional-endoscopic drainage using Lumen apposing metal stents (LAMS)¹. However, LAMS-associated complications such as occlusion are still considered a relevant clinical problem. Occlusion rates ranging from 3,8% to 24,3% of all LAMS applied have been reported in literature^{1,2}. Thus far, few studies have identified factors, which could potentially affect LAMS occlusion rate such as preemptive placement of coaxial double pig-tails through the LAMS³. A recent study suggested a potential influence of Proton Pump Inhibitors (PPI) on LAMS occlusion and the rate of endoscopic necrosectomies⁴. However, the results of this study were contradictory.

Aims & Methods: We performed a European-wide distributed expert survey in combination with a European-wide multicentric retrospective cohort study. Data was acquired using the electronic case record form (eCRF) tool REDCap and analyzed using R Studio (V4.2.3). 75 interventional endoscopists participated in the expert survey and 882 patients with 956 LAMS implanted were included in the retrospective cohort study. The primary aim of the expert survey was to assess the clinical relevance of LAMS occlusion. The primary aim of the retrospective cohort study was to investigate the potential correlation of PPI intake and LAMS occlusion and the numbers of necrosectomies.

Results: We observed that in the majority of cases, patients included received PPIs (746 cases (79.3%) with versus 195 without PPIs (20.7%). Moreover, we observed that a relevant number of experts would discontinue PPIs upon LAMS implantation (n=18; 27%) – even though this is not resembled by the real-world data. By performing a multivariable logistic regression of various factors potentially affecting LAMS occlusion we show that concomitant continuous intake of PPIs significantly increases the LAMS occlusion rate (Odds Ratio (OR): 0.62; p-value 0.045). Moreover, our data reveals that patients who continuously receive PPIs exhibit a significantly higher rate of required endoscopic necrosectomies (mean continuous PPI intake: 4.13; mean no PPI intake: 2.99; p-value 0.006). In addition, we show that this effect is dose-dependent with a significantly higher ne-

crosectomy rate in patients who receive more than double the standard PPI dose in comparison to the standard dose of PPIs (p-value <0.001). For other complications such as relevant gastrointestinal bleeding (defined as with a need for blood transfusions or interventional measures) we did not observe any significant differences between the PPI and the Non-PPI group (bleeding: OR 1.37, p-value 0.3).

Conclusion: Our data suggests that concomitant PPI-intake could be disadvantageous in patients receiving LAMS. However, further studies are needed to investigate the mechanism behind the effects observed and to validate our findings prospectively.

References: 1. Chandrasekhara, V. *et al.* Safety and efficacy of lumen-apposing metal stents versus plastic stents to treat walled-off pancreatic necrosis: systematic review and meta-analysis. *Endosc Int Open* **08**, E1639–E1653 (2020).

2. Giri, S., Harindranath, S., Afzalpurkar, S., Angadi, S. & Sundaram, S. Does a coaxial double pigtail stent reduce adverse events after lumen apposing metal stent placement for pancreatic fluid collections? A systematic review and meta-analysis. *Ther Adv Gastrointest Endosc* **16**, (2023).

3. Gopakumar, H. Endoscopic ultrasound-guided lumen-apposing metal stent with or without coaxial plastic stent for pancreatic fluid collections: a systematic review and meta-analysis comparing safety and efficacy. *Ann Gastroenterol* (2024) doi:10.20524/aog.2024.0858.

4. Powers, P. C. *et al.* Discontinuation of proton pump inhibitor use reduces the number of endoscopic procedures required for resolution of walled-off pancreatic necrosis. *Endosc Ultrasound* **8**, 194–198 (2019).

Disclosure: Nothing to disclose.

OP230

POST-DISCHARGE MORTALITY IN ACUTE PANCREATITIS: A NATIONWIDE POPULATION-BASED MATCHED COHORT STUDY

L. Davidsen^{1,2}, C.S. Knoph^{1,2}, M.E. Cook^{2,1}, A.M. Drewes^{1,2}, S.S. Olesen^{1,2}

¹Clinical Institute, Aalborg University, Aalborg, Denmark,

²Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark

Contact E-Mail Address: l.davidsen@rn.dk

Introduction: Acute pancreatitis (AP) is one of the most common gastrointestinal diseases necessitating acute hospitalisation. It is associated with notable morbidity and mortality, with a growing recognition of post-discharge mortality's importance. Nonetheless, comprehensive population-based studies in this regard are lacking.

Aims & Methods: In a Danish nationwide population-based cohort study, we aimed to investigate the post-discharge mortality risk in AP patients, including cause-specific mortality. We included all adults (>18 years) hospitalised with incident AP from January 1, 2002, through December 31, 2017. For each patient, we matched five individuals from the general population based on age and sex. The date of hospital discharge was used as the index date. Cox regression analysis was used to assess post-discharge mortality risk at 90 days, 1, 2, and 5 years. Models were adjusted for demographics, comorbidities and alcohol and smoking-related diseases. Furthermore, we examined the cause-specific mortality, including cardiovascular death, pancreatic ductal adenocarcinoma (PDAC), mortality from other cancers, and infection-related mortality, using Cox regression analysis.

Results: Among 28,763 adults with incident AP, 956 (3.3%) died in hospital. The 27,807 patients surviving the index AP event were matched with 139,035 comparison individuals (mean age 58.1 years, 51.1% men). The cumulative post-discharge mortality at 90 days was 5.02% for the AP cohort and 0.55% for the comparison cohort. The mortality risk was sig-

nificantly increased in AP patients at 90 days (adjusted hazard ratio [aHR] 7.62; 95% CI 6.86-8.45), 1 year (aHR 3.39; 95% CI 3.19-3.60), 2 years (aHR 2.47; 95% CI 2.36-2.60), and 5 years (aHR 1.85; 95% CI 1.79-1.92) post-discharge. Cause-specific mortality analysis revealed heightened risks of death from cardiovascular disease (90 days aHR 2.94; 95% CI 2.32-3.73), infectious disease (90 days aHR 11.67; 95% CI 6.78-20.07), PDAC (90 days aHR 73.08; 95% CI 22.58-236.54), and other cancers (90 days aHR 3.43; 95% CI 2.75-4.28) among AP patients when compared to the comparison group.

Conclusion: Patients discharged after an incident episode of AP are at increased risk of death compared to the general population. While PDAC presents the highest cause-specific mortality risk, cardiovascular and infectious mortality rates are also notably heightened post-discharge.

Disclosure: Nothing to disclose.

OP231

IMMEDIATE NECROSECTOMY VS. DRAINAGE-ORIENTED STEP-UP APPROACH AFTER ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE OF WALLED-OFF NECROSIS—A MULTICENTRE RANDOMISED CONTROLLED TRIAL (WONDER-01)

T. Saito¹, T. Fujisawa², T. Ogura³, M. Kuwatani⁴, H. Ohyama⁵, M. Takenaka⁶, S. Doi⁷, K. Iwata⁸, S. Hashimoto⁹, H. Kamada¹⁰, T. Iwashita¹¹, H. Shiomi¹², A. Masuda¹³, S. Matsubara¹⁴, N. Hayashi¹⁵, A. Maruta¹⁶, H. Kogure¹⁷, T. Inoue¹⁸, R. Yamada¹⁹, T. Shiratori²⁰, T. Hamada¹, S. Ueno²¹, A. Okuda²¹, S. Takahashi²², R. Sugiura⁴, K. Kawakubo⁴, K. Takahashi⁵, M. Kan⁵, S. Omoto⁶, T. Yamazaki⁶, N. Katsukura⁷, M. Okuno^{8,23}, M. Hinokuchi⁹, D. Namima¹⁰, S. Uemura¹¹, R. Nakano¹², M. Tsujimae¹³, A. Sakai¹³, K. Suda¹⁴, K. Yoshida¹⁶, K. Saito¹⁷, R. Kitano¹⁸, K. Nose¹⁹, S. Nakaji²⁰, T. Mukai²⁴, K. Nakahara²⁵, K. Chinen²⁶, H. Isayama²⁷, I. Yasuda¹⁵, Y. Nakai^{28,29}, the WONDERFUL study group in Japan

¹The University of Tokyo, Department of Gastroenterology, Tokyo, Japan, ²Juntendo University Graduate School of Medicine, Department of Gastroenterology, Tokyo, Japan, ³Osaka Medical and Pharmaceutical University Hospital, Endoscopy Center, Osaka, Japan, ⁴Hokkaido University Hospital, Gastroenterology and Hepatology, Sapporo, Japan, ⁵Chiba University, Department of Gastroenterology, Chiba, Japan, ⁶Kindai University, Department of Gastroenterology and Hepatology, Faculty of Medicine, Osaka, Japan, ⁷Teikyo University Mizonokuchi Hospital, Department of Gastroenterology, Kawasaki, Japan, ⁸Gifu Municipal Hospital, Department of Gastroenterology, Gifu, Japan, ⁹Kagoshima University, Digestive And Lifestyle Diseases, Kagoshima, Japan, ¹⁰Kagawa University, Department of Gastroenterology and Neurology, Kagawa, Japan, ¹¹Gifu University Hospital, First Department of Internal Medicine, Gifu, Japan, ¹²Hyogo Medical University, Division of Hepatobiliary and Pancreatic Diseases, Department of Gastroenterology, Hyogo, Japan, ¹³Kobe University, Division of Gastroenterology, Department of Internal Medicine, Hyogo, Japan, ¹⁴Saitama Medical Center, Saitama Medical University, Department of Gastroenterology and Hepatology, Saitama, Japan, ¹⁵University of Toyama, Third Department of Internal Medicine, Toyama, Japan, ¹⁶Gifu Prefectural General Medical Center, Department of Gastroenterology, Gifu, Japan, ¹⁷Nihon University School of Medicine, Division of Gastroenterology and Hepatology, Department of Medicine, Tokyo, Japan, ¹⁸Aichi Medical University, Department of Gastroenterology, Aichi, Japan, ¹⁹Mie university graduate school of medicine, Gastroenterology and Hepatology, Tsu, Japan, ²⁰Kameda Medical Center, Department of Gastroenterology, Kamogawa, Japan, ²¹Osaka

Medical and Pharmaceutical University Hospital, 2nd Department of Internal Medicine, Osaka, Japan, ²²Juntendo University, Department of Gastroenterology, Tokyo, Japan, ²³Matsunami General Hospital, Department of Gastroenterology, Gifu, Japan, ²⁴Kanazawa Medical University, Department of Gastroenterological Endoscopy, Kanazawa, Japan, ²⁵St. Marianna University School of Medicine, Department of Gastroenterology, Kawasaki, Japan, ²⁶Yuuai Medical Center, Department of Gastroenterology, Okinawa, Japan, ²⁷Juntendo University, Gastroenterology, Tokyo, Japan, ²⁸The University of Tokyo, Endoscopy and Endoscopic Surgery, Tokyo, Japan, ²⁹Tokyo Women's Medical University, Department of Internal Medicine, Institute of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: tomsaito623@gmail.com

Introduction: There has been an ongoing debate over the appropriate timing of direct endoscopic necrosectomy (DEN) following the initial endoscopic ultrasound (EUS)-guided transmural drainage of walled-off necrosis (WON). We aimed to examine the superiority of immediate DEN over the drainage-oriented step-up approach in terms of the time to WON resolution.

Aims & Methods: This multicentre, open-label, superiority, randomised trial (WONDER-01) was implemented including patients who were scheduled to receive EUS-guided treatment of WON at 23 centres in Japan (1). Eligible patients were randomly assigned at a 1:1 ratio to receive either immediate DEN or the step-up approach. In both arms, a lumen-apposing metal stent was used as the first-choice stent for EUS-guided drainage. In the immediate DEN arm, DEN was initiated during (or within 72 hours of) the initial EUS-guided drainage session. In the step-up approach group, drainage-based step-up treatment with on-demand DEN was considered after clinical observation for 72-96 hours. The primary endpoint was time from the randomization to clinical success, which was defined as a decrease in a WON size to ≤ 3 cm and an improvement of inflammatory markers (i.e., body temperature, white blood cell count, and C-reactive protein). The secondary endpoints included technical success, procedure-related adverse events, and mortality. All efficacy and safety endpoints were analysed on an intention-to-treat basis. This study was registered with ClinicalTrials.gov (registration number, NCT05451901), and the recruitment and follow-up for the primary endpoint have been completed.

Results: Between July 2022 and December 2023, a total of 70 patients were enrolled (33 and 37 patients in the immediate DEN and step-up arms, respectively) with baseline characteristics being well-balanced between the arms. In an analysis of the primary endpoint, the immediate DEN was associated with a shorter time to clinical success compared to the step-up approach ($P < 0.001$) with median times of 31 days (95% confidence interval, 19-34 days) and 44 days (95% confidence interval, 38-52 days), respectively. As per the protocol, all patients in the immediate DEN arm received DEN compared to 46% in the step-up approach arm ($P < 0.001$), but the rates of procedure-related adverse events were compatible between the arms (24% vs. 22%, respectively; $P = 0.79$). No differences were noted between the immediate DEN and step-up approach arms in terms of the rates of technical success (100% vs. 98%, respectively; $P = 0.26$) and mortality (12% vs. 5.4%, respectively; $P = 0.31$).

Conclusion: In patients with symptomatic WON, immediate DEN following EUS-guided transmural drainage shortened the time to clinical success compared to the drainage-oriented step-up approach without increase in adverse outcomes. Immediate DEN can be a first-line treatment option for this patient population.

References: (1) Sato T, Saito T, Takenaka M, Iwashita T, Shiomi H, Fujisawa T, et al. WONDER-01: immediate necrosectomy vs. drainage-oriented step-up approach after endoscopic ultrasound-guided drainage of walled-off necrosis-study protocol for a multicentre randomised controlled trial. *Trials*. 2023;24(1):352.

Disclosure: H.I. declares research funding from Boston Scientific Japan, Fujifilm, and Piolax Medical Devices; honoraria from Boston Scientific Japan, Century Medical, Create Medic, Fujifilm, Gadelius Medical, Hitachi Medical, Japan Lifeline, Kaneka, Kawasumi Laboratories, Olympus Medical, Piolax Medical Devices, Sumitomo Bakelite, UMIDAS, and Zeon Medical; and contributions from Boston Scientific Japan, Gadelius Medical, Japan Lifeline, and Zeon Medical. Y.N. declares research funding from Boston Scientific Japan, Century Medical, Fujifilm, Gadelius Medical, HOYA Pentax Medical, Hitachi Medical, Kaneka, and Medico's Hirata; and honoraria from Boston Scientific Japan, Fujifilm, Gadelius Medical, Hitachi Medical, J-MIT, Medico's Hirata, and Olympus Medical. This work was not supported by any of those companies. The other authors declare no conflicts of interest related to this article.

Moderated Posters

Risk factors and treatment side effects in IBD

10:30-11:30 / Poster Stage 1

MP001

LONG-TERM HEALTH OUTCOMES IN OFFSPRING OF WOMEN WITH INFLAMMATORY BOWEL DISEASE: A NATIONWIDE POPULATION BASED STUDY

H. Shin¹, J.-S. Koo²

¹Korea University Ansan Hospital, Department of Internal Medicine, Gyeonggi, South Korea, ²Korea University College of Medicine, Department of Internal Medicine, Division Of Gastroenterology, Seoul, South Korea

Contact E-Mail Address: shg0715@nate.com

Introduction: Long-term health outcomes of children of mother with inflammatory bowel disease (IBD) are poorly understood. Therefore, this study aimed to evaluate the long-term impact of maternal IBD on disease in children, including IBD.

Aims & Methods: This nationwide retrospective study included women who delivered a singleton baby after 37 weeks between 2003 and 2004 in South Korea. Women gave birth to low birth weight babies were excluded from the study. We compared risk of diseases in offspring according to maternal IBD. Multivariate analysis was performed to estimate the hazard ratios (HRs) for the future disease risk.

Results: Among a total 542,780 woman who gave birth during study periods, 1,096 women with IBD and 541,684 non-IBD control were identified. In multivariate analysis, the offspring of IBD women frequently had lower respiratory infections (HR 1.124[1.018-1.242]), asthma (HR 1.209[1.065-1.372]), atopic dermatitis (HR 1.217[1.112-1.332]), allergic urticaria (HR 1.276[1.129-1.443])HRHR, and allergic rhinitis (HR 1.151[1.084-1.222]) than those of women without IBD. And the offspring of IBD mother had a higher risk of developing ulcerative colitis (UC) (HR 6.334[4.391-9.136]) and Crohn's disease (CD) (HR 2.325[1.463-3.694]) than others. Offspring of CD women were significantly associated with asthma (HR 1.244[1.048-1.476]), allergic rhinitis (HR 1.132[1.043-1.229]), and CD (HR 3.44[2.035-5.813]). The offspring of UC women had higher rates of pneumonia (HR 1.332[1.052-1.687]), gastroenteritis (HR 1.469[1.151-1.873]), juvenile arthritis (HR 2.872[1.194-6.909]), atopic dermatitis (HR 1.33[1.174-1.507]), allergic urticaria (HR 1.39[1.174-1.647]), allergic rhinitis (HR 1.158[1.063-1.261]), and UC (HR 11.776[8-17.336]).

Conclusion: Our results show that the offspring of IBD women have higher risk of developing allergic and autoimmune disorders including UC and CD.

Disclosure: Nothing to disclose.

MP002

SARCOIDOSIS-LIKE LESIONS INDUCED BY TUMOR NECROSIS FACTOR INHIBITORS IN INFLAMMATORY BOWEL DISEASES

Z. Chkolnaia¹, B. Lebrun-Vignes², A. Amiot³, M. Uzzan⁴, G. Savoye⁵, M. Charkaoui⁶, G. Le Cosquer⁷, Y. Bouhnik⁸, M. Serrero⁹, L. Plastaras¹⁰, S. Vieujean¹¹, D. Laharie¹², P. Seksik¹³

¹Paris Cité University, Paris, France, ²Pitie Saint-Antoine Pharmacovigilance Centre, Paris, France, ³Bicetre Hospital, Gastroenterology, Kremlin-Bicetre, France, ⁴Henri Mondor Hospital, Gastroenterology, Creteil, France, ⁵Rouen University Hospital, Hepato-Gastroenterology, Rouen, France, ⁶Bocage University Hospital, Hepato-Gastroenterology, Dijon, France, ⁷Toulouse University Hospital, Gastroenterology and Pancreatology, Toulouse, France, ⁸MICI Institute, Neuilly-sur-Seine, France, ⁹North Hospital, Gastroenterology, Marseille, France, ¹⁰Colmar Pasteur Hospital, Gastroenterology, Colmar, France, ¹¹Liege University Hospital, Gastroenterology, Liège, Belgium, ¹²Groupe d'Etude Thérapeutique des Affections Inflammatoires du Tube Digestif, Paris, France, ¹³Saint-Antoine Hospital, Gastroenterology and Nutrition, Paris, France

Contact E-Mail Address: zlata.chkolnaia@gmail.com

Introduction: Tumor necrosis factor inhibitors (anti-TNF) are associated with several adverse effects, including paradoxical reactions like psoriasis-like lesions and less common drug-induced sarcoidosis-like reactions. They present significant diagnostic and therapeutic challenges, as they require careful differential diagnosis and often necessitate the discontinuation of treatment. Initially described in patients with inflammatory rheumatic diseases, sarcoidosis-like lesions induced by anti-TNF therapy have been sparsely documented only through case reports in the context of Inflammatory Bowel Diseases (IBD).

Aims & Methods: This study aimed to comprehensively describe epidemiological, diagnostic and therapeutic features of sarcoidosis-like lesions in IBD patients treated anti-TNF therapy, along with patient outcomes. We conducted a nationwide observational case series across 59 institutions affiliated with the Groupe d'Etude Thérapeutique des Affections Inflammatoires du Tube Digestif (GETAID). The diagnosis of anti-TNF-induced sarcoidosis was based on typical clinical and radiological signs, histological evidence of non-necrotizing granuloma, exclusion of differential diagnoses, and a timeline consistent with drug exposure. Each case was reviewed by a pharmacovigilance expert to confirm drug causality.

Results: We identified 12 cases of sarcoidosis-like lesions during anti-TNF therapy, with an equal distribution of male and female and a median age of 39 years (range 25-55). Underlying conditions were Crohn's Disease (58.3%), Ulcerative Colitis (33.3%) and Inflammatory Bowel Disease Unclassified (8.3%). The median duration of IBD prior to diagnosis was 14 years (range 5-29).

The anti-TNF medications involved were infliximab (58.3%), adalimumab (33.3%) and golimumab (8.3%), with the majority of patients (75%) being first-time users of biotherapy.

6 patients had optimized treatment. The median time from anti-TNF initiation to diagnosis was 22.7 months (range 3-91).

The most commonly observed clinical manifestations were dyspnea (75%) and fever (58.3%). Affected organs included the lungs (100%), liver (16.7%), extrathoracic adenopathy (16.7%), spleen (16.7%), parotid gland (8.3%), and kidneys (8.3%). There was a case of Löfgren syndrome

and one of meningitis. Eight patients discontinued anti-TNF therapy and started oral steroids, resulting in complete resolution of symptoms in five cases and improvement in two. One patient with multivisceral sarcoidosis required azathioprine addition due to renal insufficiency. Anti-TNF discontinuation was the only intervention in 2 cases, giving clinical remission in both. In 2 other cases, resolution of symptoms was observed with addition of steroids without anti-TNF discontinuation. Median time from steroid initiation (daily dose of 30 or 60 mg) to clinical remission was 91 days (range 11-305).

After a median follow-up of 48 months (range 18-175), one case showed persistent sarcoidosis activity, while no relapses were noted in the others. Anti-TNF therapy was resumed in only one patient, without recurrence of granulomatous lesions. Of the 10 patients who discontinued anti-TNF, all needed a new line of treatment, which was mostly vedolizumab. At last follow-up, IBD activity was noted in 4 patients.

Conclusion: Sarcoidosis-like lesions represent a rare but significant adverse reaction to anti-TNF therapy in IBD patients. This diagnosis should be considered when patients present with persistent respiratory or systemic symptoms after ruling out mycobacterial infection. Management involves discontinuation of anti-TNF and introduction of steroids.

Disclosure: Nothing to disclose.

MP003

LOW INCIDENCE OF MACULAR OEDEMA IN PATIENTS IN THE ETASIMOD CLINICAL PROGRAMME

M.C. Dubinsky¹, J. Wu², A. McDonnell³, K. Lazin⁴, M. Goetsch⁴, D. Branquinho⁵, I. Modesto⁵, A. Armuzzi^{6,7}

¹Icahn School of Medicine at Mount Sinai, Susan and Leonard Feinstein IBD Center, New York, United States of America, ²Pfizer Inc, Cambridge, United States of America, ³Pfizer Ltd, Sandwich, United Kingdom, ⁴Pfizer AG, Zürich, Switzerland, ⁵Pfizer Inc, New York, United States of America, ⁶IRCCS Humanitas Research Hospital, IBD Unit, Milan, Italy, ⁷Humanitas University, Pieve Emanuele, Department of Biomedical Sciences, Milan, Italy

Contact E-Mail Address: alearmuzzi@yahoo.com

Introduction: Sphingosine 1-phosphate (S1P) receptor modulators have been associated with an increased risk of macular oedema.¹ Etrasimod is an oral, once-daily, selective S1P_{1,4,5} receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC) and in development for the treatment of other immune-mediated inflammatory diseases.

Aims & Methods: We assessed the proportions and incidence rates (IRs; patients with events per 100 patient-years [PY] of exposure) of Macular oedema and Cystoid macular oedema in a comprehensive analysis of safety data from the etrasimod clinical programme. UC data were analysed in two cohorts: Placebo-controlled UC (completed phase [ph] 2 OASIS, ph 3 ELEVATE UC 52 and ELEVATE UC 12) and All UC (patients treated with etrasimod in the Placebo-controlled UC plus open-label extension [OLE] studies; completed ph 2 OASIS OLE and ongoing ph 3 ELEVATE UC and ES101002 OLE studies, both datacut at 31 Jan 2022). Data from completed ph 2 studies in Crohn's disease (CULTIVATE substudy A), and Placebo-controlled studies in eosinophilic oesophagitis (VOYAGE), alopecia areata and atopic dermatitis (ADVISE) were also analysed.

Results: Across the etrasimod UC clinical programme, 942 patients received ≥ 1 dose of etrasimod 2 mg once daily (QD), with 757.9 PY of exposure. In the Placebo-controlled UC cohort, Macular oedema was reported in two patients (0.3%; IR 0.70) receiving etrasimod 2 mg QD (one patient with long-term corticosteroid use in ELEVATE UC 52 and one patient with prior uveitis in ELEVATE UC 12, which was not considered clinically significant by the investigator) and one patient (0.3%; IR 0.84) receiving placebo

(ELEVATE UC 12). In the All UC cohort, one patient (0.1%; IR 0.13) receiving etrasimod 2 mg QD during the ELEVATE UC OLE reported two events of Cystoid macular oedema (Table). Four of five Macular oedema events began at Days 74–94, all were non-serious and only one event led to treatment discontinuation. No events of Macular oedema were reported in studies of etrasimod in other indications (Table).

Indication	Cohort/study	Treatment	Macular oedema		Cystoid macular oedema	
			n (%)	IR per 100 PY (95% CI)	n (%)	IR per 100 PY (95% CI)
UC	Placebo-controlled UC cohort ^a	Etrasimod 2 mg QD (N=577) ^b	2 (0.3) ^b	0.70 (0.00, 1.66)	0	0
		Placebo (N=314)	1 (0.3) ^c	0.84 (0.00, 2.50)	0	0
	All UC cohort ^c	Etrasimod 2 mg QD (N=942) ^b	2 (0.2) ^b	0.26 (0.00, 0.61)	1 (0.1) ^d	0.13 (0.00, 0.38)
Crohn's disease	CULTIVATE substudy A ^d	Etrasimod 2 or 3 mg QD (N=83)	0	N/A	0	N/A
Eosinophilic oesophagitis	VOYAGE ^e	Etrasimod 1 or 2 mg QD (N=80)	0	N/A	0	N/A
		Placebo (N=28)	0	N/A	0	N/A
Alopecia areata ^f		Etrasimod 2 or 3 mg QD (N=56)	0	N/A	0	N/A
		Placebo (N=23)	0	N/A	0	N/A
Atopic dermatitis	ADVISE ^g	Etrasimod 1 or 2 mg QD (N=94)	0	N/A	0	N/A
		Placebo (N=46)	0	N/A	0	N/A

Adverse events were coded according to the Medical Dictionary for Regulatory Activities, version 24.1, and reported by preferred term.

Reported events of Macular oedema or Cystoid macular oedema occurring before the available datacut (31 Jan 2022) were included.

Severity was classified by the investigators using the CTCAE v5.0. Grade 1 = mild, Grade 2 = moderate.

^aPlacebo-controlled UC cohort included: completed ph 2, 12-week induction OASIS (NCT02447302), ph 3, 52-week (12-week induction followed by 40-week maintenance period with treat-through design) ELEVATE UC 52 (NCT03945188), and ph 3, 12-week induction ELEVATE UC 12 (NCT03996369).

^bData are presented for patients receiving etrasimod 2 mg QD. There were no events of Macular oedema or Cystoid macular oedema reported in the etrasimod 1 mg QD group (N=52) in OASIS.

^cAll UC cohort included: Placebo-controlled UC cohort (patients in the etrasimod group only) plus patients treated with etrasimod in: completed ph 2, 34–40-week OASIS OLE (NCT02536404) and ongoing ELEVATE UC OLE (NCT03950232) and ES101002 OLE (NCT04176588), both datacut at 31 January 2022. IRs (per 100 PY) were calculated based on 2 mg etrasimod exposure only.

^dPh 2, 66-week (14-week induction period followed by 52-week extension period) CULTIVATE substudy A (NCT04173273).

^ePh 2, 24-week induction period VOYAGE study (NCT04682639).

^fPh 2, 24-week induction period study (NCT04556734).

^gPh 2, 12-week treatment period ADVISE study (NCT04162769).

^hOne patient with prior corticosteroid use receiving etrasimod 2 mg in ELEVATE UC 52 experienced non-serious, moderate Macular oedema on Day 74. This was considered by the investigator to be related to the study treatment, led to treatment discontinuation and resolved. One patient with prior uveitis receiving etrasimod 2 mg in ELEVATE UC 12 experienced non-serious, mild Macular oedema on Day 86, which was not resolved at the time of datacut and was not considered by the investigator to be related to the study treatment. One patient receiving placebo in ELEVATE UC 12 experienced non-serious, mild Macular oedema on Day 94. The event was resolving at the time of datacut.

ⁱOne patient receiving placebo in ELEVATE UC 52, then switching to etrasimod 2 mg in the ELEVATE UC OLE experienced two events of Cystoid macular oedema. The first began on Day 85 (first OLE etrasimod dose as Day 1), was not considered by the investigator to be related to the study treatment and resolved; the second began on Day 248, was considered to be related and the outcome was unknown at the time of datacut. Both events were non-serious, moderate and led to dose interruption.

CI, confidence interval; CTCAE, Common Terminology Criteria for Adverse Events; IR, incidence rate (patients with events per 100 PY); n, number of patients with Macular oedema or Cystoid macular oedema event; N, number of patients in treatment group; N/A, not available; OLE, open-label extension; ph, phase; PY, patient-years; QD, once daily; UC, ulcerative colitis.

Table. Incidence of Macular oedema and Cystoid macular oedema events in the etrasimod clinical programme.

Conclusion: The incidence of Macular oedema in patients treated with etrasimod in the clinical programme was low and generally comparable with placebo. These results are consistent with other S1P receptor modulators¹ and provide clinically relevant information on events of Macular oedema.

References:

1. Bencardino S et al. J Clin Med 2023; 12: 5014.

Disclosure: MCD is a consultant for AbbVie, Abivax, AstraZeneca, Bristol Myers Squibb, Janssen, Lilly, Merck, Pfizer Inc, Prometheus Labs, Spyre and Takeda. JW, DB and IM are employees and shareholders of Pfizer Inc. AM is an employee of Pfizer Ltd and shareholder of Pfizer Inc. KL is an employee of Pfizer AG and a shareholder of Pfizer Inc. MG is an employee and shareholder of Pfizer AG. AA is a consultant for AbbVie, Allergan, Amgen, Arena, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene,

Celltrion, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen, Lilly, Lionhealth, MSD, Mylan, Nestlé, Pfizer Inc, Roche, Samsung Bioepis, Sandoz, Takeda and Tillots Pharma; has received grant/research support from Biogen, MSD, Takeda and Pfizer Inc; and lecture/speaker fees from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen, Lilly, Lionhealth, MSD, Novartis, Pfizer Inc, Roche, Samsung Bioepis, Sandoz, Takeda and TiGenix.

MP004

BODY COMPOSITION ANALYSIS AND PREVALENCE OF SARCOPENIA AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE

M. Bhowmick¹, K.K Prasad¹, P. Gupta², H.S Mandavdhare¹, J. Samanta¹, S. Shruti³, S. Roy¹, S.K Sinha¹

¹Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Radio Diagnosis and Imaging, Chandigarh, India, ³Government Medical College, Chandigarh, India

Contact E-Mail Address: bhowmickmithu@gmail.com

Introduction: Inflammatory bowel disease (IBD) that includes Ulcerative colitis (UC) and Crohn's disease (CD) may be associated with considerable changes in body composition, which include alterations in muscle and adipose tissue mass as well as osteopenia and osteoporosis which can have considerable impact on disease course and outcome.

Aims & Methods: Body composition and presence of sarcopenia were assessed in patients with UC and CD and their relationship with disease duration, location and severity was studied. This was a Single-Centre cross-sectional study conducted from January 2022 to June 2023.

Body composition analysis was performed using bioelectrical impedance (BIA) method and sarcopenia assessment was done with hand grip strength (HGS) using digital hand dynamometer and skeletal muscle index (SMI) at 3rd lumbar vertebral (L3) level using computed tomography (CT).

Results: A total of 132 patients (92 UC and 40 CD) were included. Mean age and sex in UC (37.33 ± 12.91 years, 46.7% males) and in CD (39.05 ± 15.05 years, 52.5% males). Mean duration of disease in UC and CD were 5.9 ± 5.28 years and 6.13 ± 4.33 years respectively. In UC group 41.3% patients had pancolitis and 37% had left sided colitis, among CD patients ileal (L1) and colonic disease (L3) was 37.5% each and 55% patients had inflammatory disease behavior.

In UC patients 33.7% had active disease and in CD 40% had active disease. In UC group, mean total body fat percentage was significantly lower with disease duration of 1-5 years compared to those with disease duration > 5 years (23.67 ± 8.52% vs 29.39 ± 7.14%, p=0.003) and mean visceral fat level was lower in those with active disease than in remission (3.26 ± 3.09 vs 6.49 ± 6.77, p=0.013). CD patients did not show any significant change in BMI, total body fat percentage, whole body skeletal muscle percentage with respect to disease duration, location, behavior and severity.

In UC group mean dominant HGS and L3-SMI were lower in active disease than remission (22.27 ± 8.72 kg vs 28.57 ± 9.1 kg, p=0.002 and 36.5 ± 13 cm²/m² vs 42.74 ± 13.92 cm²/m², p=0.02). Among CD patients no significant change in HGS and L3-SMI were observed. As per European consensus definition, prevalence of probable sarcopenia and sarcopenia in UC and CD were (26% and 9.4%) and (32.5% and 15%) respectively.

On comparison between UC and CD, SMI was significantly lower in CD patients (Table 1). When BIA method was used to measure low muscle mass, the prevalence of sarcopenia in UC and CD were 13.4% and 17.5%. Difference observed with the two methods of measurement of sarcopenia prevalence was not significant.

Parameters	UC(92)	CD(40)	P value
Body composition variables(mean)			
BMI (Kg/m ²)	21.91 ± 6.61	21.41 ± 5.55 kg/m	0.680
Body fat (%)	26.26 ± 8.42	24.45 ± 9.37	0.277
Whole body subcutaneous fat (%)	20.84 ± 7.29	19.17 ± 6.87	0.227
Whole Body Skeletal Muscle (%)	28.16 ± 5.62	27.55 ± 7.34	0.608
Visceral fat	5.52 ± 5.99	5.11 ± 5.196	0.679
Sarcopenia variables(mean)			
Dominant HGS (kg)	26.28 ± 9.4	25.96 ± 9	0.856
L3-CSA of muscles (cm ²)	108.08 ± 40.9	99.4 ± 28.08	
SMI (cm ² /m ²)	40.74 ± 15.18	37.11 ± 9.13	0.048
Probable sarcopenia and Sarcopenia	26% and 9.4%	32.5% and 15%	

Table 1- Body composition and sarcopenia variables in UC and CD

*CSA- cross-sectional area, BMI-Body mass index

Conclusion: Point prevalence of probable sarcopenia and sarcopenia was found to be 26% & 9.4% among UC and 32.5% and 15% patients with CD. CD patients had lower muscle mass as compared to UC patients. BIA showed good diagnostic accuracy compared to CT in assessing muscle mass. Both these methods can be considered complementary diagnostic tools in assessment of sarcopenia among patients with UC or CD.

Disclosure: Nothing to disclose.

MP005

COMPARISON BETWEEN THE CARDIO-METABOLIC RISK AND LIVER STEATOSIS AND FIBROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND RHEUMATOID ARTHRITIS – POTENTIAL IMPLICATIONS FOR THERAPEUTIC CHOICE

A. Bargas Bárbara¹, C. Moreira-Barbosa¹, A. Guedes¹, A.C. Bravo¹, J. Revés¹, L.M. Roque Ramos¹, C. Gouveia¹, C. Frias-Gomes¹, M. Canhoto¹, D. Raimundo², N. Gonçalves², S. Falcão², C. Palmela¹, M.L. Gloria¹, J. Torres¹

¹Hospital de Loures, Gastroenterology, Lisboa, Portugal, ²Hospital de Loures, Rheumatology, Lisboa, Portugal

Contact E-Mail Address: bargasandre2@gmail.com

Introduction: Auto-inflammatory conditions like inflammatory bowel disease (IBD) and rheumatoid arthritis (RA) have a higher prevalence of liver fibrosis and cardiovascular risk (CVR), compared to the general population. This is relevant, given the potential metabolic and cardiovascular adverse effects of some drug classes.

Aims & Methods: Cross-sectional study of IBD and RA patients. Pregnancy or known cause of chronic liver disease were excluded. All patients underwent transient elastography, clinical and laboratorial assessment. International Physical Activity Questionnaire (IPAQ) classified activity as low, moderate, or high. Presence of steatosis and fibrosis was defined as Controlled Attenuated Parameter (CAP) measurement of >248 dB/m and Liver Stiffness Measurement (LSM) >8 kPa, respectively. For CVR, SCORE2 was calculated according to European Society of Cardiology (if >40 years).

Results: 130 patients were enrolled (79 with IBD and 51 with RA). Most RA patients (80%) have received treatment with methotrexate. Demographics and CVR factors are presented in table 1. RA patients were significantly older and had higher prevalence of CVR factors. Nonetheless, no differences in the median SCORE2 were found [4 (IQR 3-10) vs 8 (IQR 6-11), p=0.06]. 16% of IBD and 57% of RA patients had liver fibrosis (p<0.01); No differences were found in liver fibrosis between RA patients on methotrexate (70% vs 54%; p=0.35); 46% of IBD and 73% of RA patients had liver steatosis (p=0.006). RA had a higher risk of fibrosis (OR=5.16 (95%CI 1.8-14.7), p=0.004), even after adjustment for age, gender, body mass index, physical activity and CVR factors.

	IBD	RA	p
Male,%	51%	45%	0.54
Age, median,IQR	40, 30-54	64, 54-69	<0.001
Diabetes mellitus,%	5%	17%	0.027
Dyslipidemia,%	11%	39%	<0.001
thromboembolic diseases,%	6%	10%	0.48
Smoker/Previous smoker,%	38%	24%	0.46
Low IPAQ,(%)	87%	71%	0.93

Conclusion: In our cohort, more than half of the RA patients had undiagnosed liver fibrosis and RA appears to be to be an independent risk factor for this condition. Further research is warranted to elucidate the underlying pathophysiology and identify actionable risk factors for the development of these condition.

Disclosure: Nothing to disclose.

MP006

THROMBOEMBOLIC AND CARDIOVASCULAR RISK PROFILES IN ULCERATIVE COLITIS PATIENTS INITIATING ADVANCED THERAPIES: A SINGLE-CENTER STUDY

V. Calvez¹, G. Cuccia¹, A. Del Gaudio¹, I. Capobianco¹, L. Parisio¹, A. Gasbarrini², F. Scaldaferri¹, L. Carbone³, D. Pugliese⁴
¹Fondazione Policlinico Universitario “A. Gemelli” IRCCS, Catholic University of Rome, Department of Translational Medicine and Surgery, Rome, Italy, ²Fondazione Policlinico Universitario Gemelli IRCCS, Università’ Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ³Ospedale Isola Tiberina Gemelli Isola, Medicina d’Urgenza e Medicina Interna, Rome, Italy, ⁴Fondazione Policlinico Universitario “A. Gemelli” IRCCS, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy

Contact E-Mail Address: valentino.calvez@gmail.com

Introduction: Inflammatory bowel disease (IBD) especially during flare periods, seems to be associated with an increased risk of thromboembolic and cardiovascular (CV) events[1]. After the results of the ORAL Surveillance study[2] enrolling patients with rheumatoid arthritis, several concerns have also been raised on the intrinsic risk of Janus kinase inhibitors (JAK-i), but population enrolled was predominantly >50 years old and had several CV risk factors.

Accordingly, regulatory agencies recommend that JAK-i should be used only if no suitable treatment alternatives are available in patients at increased CV risk for all indication[3]. However, the real prevalence of CV risk factors (CVRF) and the risk related to JAK-i seem to be lower for patients with Ulcerative Colitis (UC).

Aims & Methods: The aim of our study is to explore the prevalence of thromboembolic and CV risks factors in a large cohort of UC patients suitable for advanced therapies.

We conducted a single-center study including all consecutive adult patients with UC, who initiated advanced therapies from June 2020 to December 2023. To assess thrombosis and CV risks, an online questionnaire was administered, collecting following variables: BMI, smoking status, varicose vein (presence or previous surgery), personal or family history of (FHx) venous thromboembolism (VTE), presence of known genetic thrombophilic factors, active or previous cancer, admission to hospital in the last 6 months, leg or hip fractures or surgery in the last month, C reactive protein (CRP) serum levels, history of (h/o) abortion, ongoing treatment with estrogen or hormone replacement therapy (HRT), presence of heart failure, chronic kidney disease (CKD), chronic obstructive pulmonary disease, h/o acute myocardial infarction (AMI), hypertension, atrial fibril-

lation (AF), h/o stroke or TIA, diabetes, FHx CV disease and serum lipids levels. The International Physical Activity Questionnaire (IPAQ) was used to assess sedentary lifestyle.

Results: Out of 320 patients surveyed, 305 responded (95.3%): of whom 54% male, with a mean age was 45 years ($\pm$ SD 15.4) and a median disease duration of 7 years (IQR 2.9-16). Elderly patients ($\geq$ 60 years) were 21.3%. The average BMI was 23.9 ($\pm$ SD 14.1), with 34.8% being overweight and 8.5% obese. Active and former smokers accounted for 19.7% and 41.6% of the cohort, respectively; 54.1% were sedentary. Overall, 119 patients (39%) were biologic-naïve; 21.6% of patients started a JAK-i. Overall, 19% were recently hospitalized and in 86% of cases for IBD-related reasons. A genetic predisposition for thrombosis was identified in 4.6% of patients; varicose vein disease in 14.1%. CRP was high in 44.9% of patients. Of the female population 17.9% had h/o abortion, 7.1% were taking estrogen and 2.1% in HRT. Cumulatively only 27 patients (8.8%) had 4 thrombotic risk factors, 11 (3.6%) five, and 6 (2%) had $\geq$ 6.

Regarding CV risks, 15.1% of the population were hypertensive, 4.9% were diabetic, 4.3% had h/o AMI, 1.3% had h/o stroke or TIA, 2.3% had AF and 3.9% had CKD stage III. Total cholesterol values were available for 212 patients (69.5%), and 8% had cholesterol >240 mg/dl. The total cholesterol/HDL ratio was available for 171 patients (56.1%); 10.5% had values > 5 (medium risk). Overall, 92 (30.2%) had 1 CVRF, 17 (5.6%) had 2 CVRF, and 5 patients (1.65%) had more than 3 CVRF.

Conclusion: Our study confirms the prevalence of thrombotic and CV risk factors among patients affected by UC is quite low. Accordingly, the concerns regarding the use of JAK-i observed in rheumatological cohorts, may not be applicable for patients with UC.

References: [1] Fumery M, Xiaocang C, Dauchet L, Gower-Rousseau C, Peyrin-Biroulet L, Colombel J-F. Thromboembolic events and cardiovascular mortality in inflammatory bowel diseases: A meta-analysis of observational studies. *Journal of Crohn’s and Colitis* 2014;8:469–79. <https://doi.org/10.1016/j.crohns.2013.09.021>.

[2] Ytterberg SR, Bhatt DL, Mikuls TR, Koch GG, Fleischmann R, Rivas JL, et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. *N Engl J Med* 2022;386:316–26. <https://doi.org/10.1056/NEJ-Moa2109927>.

[3] EMA confirms measures to minimise risk of serious side effects with Janus kinase inhibitors for chronic inflammatory disorders | European Medicines Agency n.d. <https://www.ema.europa.eu/en/news/ema-confirms-measures-minimise-risk-serious-side-effects-janus-kinase-inhibitors-chronic-inflammatory-disorders> (accessed April 25, 2024).

Disclosure: Nothing to disclose.

MP007

THIOPURINES AND THE RISK OF CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE – A DANISH NATIONWIDE COHORT STUDY (1996-2018)

M.D. Wewer^{1,2}, G. Letnar³, K.K. Andersen³, M. Malham^{4,2}, V. Wewer^{4,2,5}, J.B. Seidelin^{6,7}, F. Bendtsen^{2,1,5}, J. Burisch^{2,1}

¹Amager Hvidovre University Hospital, Gastrounit, Medical Division, Hvidovre, Denmark, ²Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre Hospital, Copenhagen, Denmark, ³Omicron ApS, Copenhagen, Denmark, ⁴Amager Hvidovre University Hospital, Paediatrics and Adolescent Medicine, Copenhagen, Denmark, ⁵University of Copenhagen, Department of Clinical Medicine, Faculty of Health and Medical Sciences, Copenhagen, Denmark, ⁶University of Copenhagen, Clinical Medicine, Faculty of Health and Medical Sciences, Copenhagen, Denmark, ⁷Herlev University Hospital, Gastroenterology, Copenhagen, Denmark

Contact E-Mail Address: madssewer@gmail.com

Introduction: Thiopurine therapy is a cornerstone in the treatment of patients with inflammatory bowel disease (IBD).

Aims & Methods: We aimed to assess the effect of thiopurines on the risk of cancer in IBD according to drug exposure and age. Danish national registers were used to identify incident IBD patients, exposure to drugs and status of cancers, in 1996-2018. Cox regressions were used to:

- compare IBD to non-IBD reference individuals,
- analyse IBD according to drug exposure status, and;
- assess patients' cumulative drug exposure and the association to first reported cancer, excluding non-melanoma skin cancer.

Results: In total, 43,419 IBD patients were followed for a median of 8.2 years (IQR:3.7-14.2) after IBD diagnosis. Cancer was reported in 3,128 (7.2%) IBD patients. Both monotherapy and combination therapy were associated with developing cancer (aHR:1.36 (95%CI:1.17-1.58) and (aHR:2.48 (95%CI:1.64-3.76), respectively) compared to unexposed IBD patients. Among the elderly (>65 years), the risk was especially high in those receiving combination therapy.

In patients who discontinued thiopurines, the aHR returned to the level of unexposed patients (aHR:0.89 (95%CI:0.78-1.01)). The aHR was positively associated with cumulative thiopurine exposure and in patients with more than five years of exposure, reaching aHR of 1.36 (95%CI:1.14-1.61).

Conclusion: Thiopurines were associated with increased risk of cancer, especially when used in combination therapy in the elderly. The risk increased by 36% when patients were exposed to thiopurines for more than five years. Reassuringly, the risk returned to baseline after discontinuation of thiopurines.

This study suggests avoiding combination therapy in the elderly and not treating patients with thiopurines for longer than five years, regardless of age.

Disclosure: This study was funded by an unrestricted grant from Aage og Johanne Louis-Hansens Fond.

MP008

EMERGING ROLE OF IL-33 ACTIVATED CD73-EXPRESSING CELLS IN THE PROMOTION OF TUMORIGENESIS DURING COLITIS-ASSOCIATED COLORECTAL CANCER

L.R. Lopetuso^{1,2}, S. De Santis³, G. Privitera⁴, D. Corridoni³, A. Gasbarrini⁵, F. Cominelli³, C. De Salvo³, T.T. Pizarro⁶

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Surgical and Medical Sciences Department, Roma, Italy, ²Università degli Studi "G. D'Annunzio", Chieti, Italy, ³Case Western Reserve University, Cleveland, United States of America, ⁴Università Cattolica del Sacro Cuore, Rome, Italy, ⁵Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁶Case Western Reserve University School of Medicine, Pathology and Medicine, Cleveland, United States of America

Contact E-Mail Address: lopetusoloris@libero.it

Introduction: Colorectal cancer associated to chronic colitis (CAC) has a different pathogenesis compared to sporadic or familial colorectal cancer (CRC) and represents the major complication of inflammatory bowel disease (IBD). It is now well-established that IL-33 and its receptor, ST2, are important factors in the pathogenesis of IBD.

Emerging evidence also suggests its critical role in epithelial proliferation and the potential contribution to inflammation-driven tumorigenesis that can lead to CRC.

Aims & Methods: The aim of our study was to characterize the precise contribution of IL-33/ST2 axis in the azoxymethane (AOM)/dextran sodium sulfate (DSS) model of colitis-associated CRC.

C57/BL6 wild-type (WT), IL33^{-/-}, T1/St2^{-/-} and Nt5e^{-/-} mice were given a single dose of AOM (10 mg/kg) followed by two cycles of 3% DSS for 7d in drinking water. Vehicle-treated WT mice served as controls and were sacrificed at the same time points. Another group of WT followed the same protocol and received CD73 inhibitor i.p. treatment or vehicle.

Disease Activity Index (DAI), as well as endoscopic, stereomicroscopic and histological evaluations of colons were performed. IHC, immunofluorescence (IF), qPCR, and ELISA were done on full-thickness colons of WT for IL-33 and ST2 localization and identification, as well as mRNA and protein expression, respectively. RNA-Seq was performed on whole tissues from AOM/DSS treated WT, IL33^{-/-} and T1/St2^{-/-}. qPCR analysis was done on isolated polyps from WT, IL33^{-/-} and T1/St2^{-/-} for Nt5e (CD73) and adenosine pathway targets.

Results: IL33, Ilr1(ST2L), and Ilr1(sST2) mRNA transcripts, as well as IL-33 and total ST2 proteins were dramatically elevated in AOM/DSS-treated WT mice vs. controls. IHC and IF of treated WT mice revealed localization of IL-33 to the colonic epithelium and to cells within the polyp LP morphologically consistent with stromal and mast cells. Little to no staining for IL-33 was present in controls.

Using IF, IL-33 co-localized with sub-epithelial myofibroblast markers Actin and Vimentin, or with mast cell markers Tryptase and MCPT1. AOM/DSS treatment in IL33^{-/-} and T1/St2^{-/-} mice resulted in a significant decreased polyp number and size vs. WT, with colonoscopy revealing the development of protruding lesions with abnormal vascular patterns, suggesting tumorous lesions in WT mice, while all deficient mice showed their absence with a more impressive mucosal inflammation, likely due to reduced epithelial proliferation and repair caused by the deficiency of IL-33 signaling. RNA-Seq identified a significant reduction of Nt5e and adenosine pathway targets in IL33^{-/-} and T1/St2^{-/-} vs. WT. qPCR on isolated polyps confirmed this observation. AOM/DSS-treated Nt5e^{-/-} showed a significant decreased polyp number and size vs. controls. Therapeutic inhibition of CD73 produced similar results.

Conclusion: Our results suggest that the IL-33/ST2 axis promotestumor-igenesis in colitis-associated CRC through the activation of CD73. Further studies are underway to determine mechanisms of action that support these findings.

Disclosure: Nothing to disclose.

MP009

KCNQ10T1 IS THE MOST DISCRIMINANT GENE IN THE TRANSCRIPTOMIC SIGNATURE OF THE INFLAMMATION-DYSPLASIA-CANCER SEQUENCE IN INFLAMMATORY BOWEL DISEASE

A. Cremer^{1,2}, N. Rosewick², M. Kelsey³, E. Trepo^{1,2}, F. Libert⁴, M. De Vos⁵, F. Baert⁶, T. Moreels⁷, E. Louis⁸, J.-F. Rahier⁹, P. Demetter², J.M. Sedivy³, S. Vermeire¹⁰, D. Franchimont^{1,2}
¹HUB Erasme University Hospital, Université Libre de Bruxelles, Gastroenterology, Brussels, Belgium, ²Laboratory of Experimental Gastroenterology, Université Libre de Bruxelles, Brussels, Belgium, ³Brown University, Center on the Biology of Aging, and the Department of Molecular Biology, Cell Biology, and Biochemistry, Providence, United States of America, ⁴Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire (IRIBHM), Université Libre de Bruxelles, Brussels, Belgium, ⁵University Hospital Ghent, Ghent University, Gastroenterology, Ghent, Belgium, ⁶Az Delta, Gastroenterology, Roeselare, Belgium, ⁷Cliniques Universitaires Saint-Luc, Gastroenterology, Brussels, Belgium, ⁸CHU Liège, Liège University, Gastroenterology, Liège, Belgium, ⁹CHU UCL Namur site Mont-Godinne, Université Catholique de Louvain, Gastroenterology, Yvoir, Belgium, ¹⁰University Hospital Leuven, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: anneline.cremer@erasme.ulb.ac.be

Introduction: Inflammatory bowel disease (IBD) is associated with a higher risk of developing colorectal cancer, according to the inflammation-dysplasia-cancer (IDC) sequence from inflammation to colitis-associated colorectal cancer (CAC).

Aims & Methods: The objective of this study was to identify and generate a transcriptomic signature and score, related to the IDC sequence, that could ultimately classify dysplasia and cancer in IBD. This is a national cohort study conducted across 7 Belgian tertiary centres within the Belgian Inflammatory Bowel Disease Research and Development (BIRD) Group. We retrospectively evaluated IBD patients diagnosed with low- or high-grade dysplasia (LGD or HGD) and/or CAC between January 1, 1990, and December 31, 2016. An exploratory and a validation cohort of lesions were analysed. RNA-seq was analysed in 134 formalin-fixed paraffin-embedded samples. We followed an ordinal logistic regression (olm) method to screen for significant IDC sequence-associated genes and computed a transcriptomic signature score.

Results: Principal component analysis and unsupervised clustering on 1% of the most variable genes showed an overall good clustering between the 4 lesion groups (Normal Mucosa, Inflamed Mucosa, LGD and HGD, and CAC). A gene signature was identified on 27 genes that correlated with the lesion groups in the exploratory cohort. Among these 27 genes, 23 were downregulated and 4 were upregulated. Based on these 27-genes expression, we built and validated a transcriptomic signature score to classify dysplasia and CAC in IBD patients. The overall accuracy of the transcriptomic signature score was 85.71 % in the exploratory cohort and 90.91% in the validation cohort. The most weighted gene in this transcriptomic signature was the long non-coding regulatory RNA KCNQ10T1, a gate keeper against genomic instability and transposon activation. We found a direct correlation in the expression of KCNQ10T1 and retrotransposable elements (RTEs) across the lesion groups of IDC sequence.

Conclusion: We have identified a transcriptomic 27 gene signature associated with the IDC sequence and uncovered some of the pivotal genes and underlying mechanisms in the progression of the IDC sequence. The tissue-based transcriptomic score generated here helps the classification of the lesions of the IDC sequence in patients with IBD but should be further evaluated for its prognostic value in prospective independent cohorts. The most discriminant top gene in this signature, the non-coding RNA KCNQ10T1, is consistent with the activation of RTEs that may be involved in the progression of the IDC sequence.

Disclosure: Nothing to disclose.

MP010

MICROBIAL-DERIVED METABOLITES PROMOTE NKT22 RESPONSES IN COLITIS ASSOCIATED COLORECTAL CANCER PATIENTS

E. Facciotti¹, F. Perillo², A. Baeri³, F. Strati³, D. Noviello⁴, G. Lopez⁵, L. Boni⁵, E. Sommella⁶, F. Ungaro⁷, E.V. Savarino⁸, M. Vecchi⁹, F. Caprioli¹⁰
¹University Of Milano Bicocca, Milan, Italy, ²IEO, Experimental oncology, Milano, Italy, ³University of Milano-Bicocca, Milan, Italy, ⁴University of Milan, Gastroenterology and Endoscopy, Milano, Italy, ⁵Policlinico Hospital Milan IRCCS, Milano, Italy, ⁶University of Salerno, Salerno, Italy, ⁷HSR Research Institute, Milan, Italy, ⁸University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico University of Milan, Milan, Italy, ¹⁰University of Milan, Fisiopatologia Medico-Chirurgica e dei Trapianti, Milano, Italy

Contact E-Mail Address: federica.facciotti@unimib.it

Introduction: Patients suffering from inflammatory bowel diseases (IBD) manifest an increased risk of developing colitis-associated colon cancer (CAC). Interleukin 22 (IL22) is a cytokine involved in the proliferation and survival of epithelial cells.

However, it also correlates with the development of tumoral lesions. IL22 is secreted by different immune cell types, including iNKT cells, tissue resident cells possessing cytotoxic properties in colorectal cancer (CRC). In IBD patients, though, iNKT cells perform both pro-inflammatory or tolerogenic functions in a microbiota-dependent fashion, opening questions on their functional role in CAC development.

Aims & Methods: Immune cell composition and iNKT cell phenotype of inflamed, non-tumor and cancerous tissue lesions of CAC (n=49), IBD (n=20) and sporadic CRC (n=38) patients were analysed in samples obtained from Policlinico Hospital, Milan, and IOV-IRCCS, Padua. High-dimensional single-cell flow cytometry, metagenomics, RNAseq, spatial immunophenotyping and transcriptomic (Cosmx, Nanostring), ex vivo and in vitro experiments were performed to evaluate the phenotype and function of human iNKT cells. Metabolomics was performed to identify microbial-derived molecules involved in iNKT cells activation. Mechanisms were dissected in CAC murine models, either iNKT proficient or deficient.

Results: An increased expression of IL22 and a higher NKT22 infiltration was observed in CAC tissues, as well as an enrichment of *Odoribacter*, a gram-negative bacteria implicated in tryptophan metabolism. Stimulation of iNKT cells with *Odoribacter*-derived metabolites induced Ahr-dependent IL22 production by iNKT cells. Metabolomic analyses revealed an increased presence of tryptophan metabolites in the *Odoribacter* supernatant, promoting NKT22 differentiation both in vitro and in vivo models.

Moreover, the administration of *Odoribacter* Supernatant or of the single purified metabolites were sufficient to increase tumorigenesis in CAC mouse models, but not in iNKT-deficient mice.

Spatial proteomics and transcriptomic analyses of human CAC tissues confirms the microbiota-dependent functional skewing of iNKT cells residing closely to cancer cells.

Conclusion: iNKT cells in CAC patients are the major IL22 producing cells and are induced by the recognition of microbiota-derived metabolites implicated in tryptophan metabolism and Aryl hydrocarbon receptor (AhR) stimulation. NKT22-microbiota interaction in CAC patients plays a potential crucial role in tumor development.

Disclosure: Nothing to disclose.

Bowel: Preparation is everything

10:30-11:30 / Poster Stage 2

MP011

PRIORITIZE STUDY (PRIORITIZING RESUMPTION OF COLORECTAL SCREENING AFTER COVID PANDEMIC)

S. Pecere¹, L. Frazzoni², C. Hassan³, L.E. Del Vecchio¹, C. Fabbri⁴, F. Iacopini⁵, L. Fuccio⁶, A. Repici³, C. Spada¹, C. Senore⁷, G. Antonelli⁵

¹Catholic University of Rome, Gemelli Hospital, Gastroenterology and Digestive Endoscopy Unit, Roma, Italy, ²S.Orsola-Malpighi Hospital, Department of Medical and Surgical Sciences, Bologna, Italy, ³Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ⁴AUSL Romagna, Forlì-Cesena gastroenterology, Gastroenterology, Bologna, Italy, ⁵Ospedale dei Castelli, Gastroenterology and Digestive Endoscopy Unit, Ospedale dei Castelli, Ariccia, Roma, Italy, ⁶S.Orsola-Malpighi University Hospital, Department of Medical and Surgical Sciences, Bologna, Italy, ⁷University Hospital Città della Salute e della Scienza, Epidemiology and screening unit - CPO, Torino, Italy

Contact E-Mail Address: livioenricodelvecchio@gmail.com

Introduction: FIT-based colorectal cancer screening programs have been severely hampered during COVID-19 pandemic and its aftermath. Both test distribution and post-FIT colonoscopies have seen a manifold decrease in number of performed procedures. It is well known that any delay in post-FIT+ colonoscopy results in an increase in advanced neoplasia and CRC. Since colonoscopy slots are limited, any means to risk-stratify subjects before post-FIT colonoscopy may result in timely diagnosis of CRC and advanced adenomas, but such tools are currently lacking.

Aim of our study was to develop and validate a simple scoring system to effectively sub-stratify CRC/advanced adenomas risks in FIT+ patients, based on the retrospective analysis of a large cohort of patients in a long-standing FIT based CRC screening program.

Aims & Methods: This was a retrospective analysis of prospectively collected data from a regional CRC screening program in Italy, from 2004 to 2019. Men and women aged 58 to 70 years were invited to undergo quantitative FIT (OC-sensor FIT) and subsequent colonoscopy if $\geq 20 \mu\text{g Hb/g}$ of feces (FIT+). Patients who underwent both FIT test with positive results and colonoscopy were included in the study.

A multivariable logistic regression analysis was performed to identify variables independently associated to CRC and advanced adenoma risks in the derivation cohort (2004-2015), and the discriminative performance of the model was tested on the validation cohort (2016-2019).

Results: Overall, 40,640 patients undergoing colonoscopy after a FIT+, were included. Prevalence of first-round FIT+ subjects was 58.5%. Median FIT was 52.4 mcg/g (IQR, 29.8-137.3). CRC was found in 2,164 (5.4%) subjects, high-risk adenomas in 12,218 (30.3%), and low-risk adenomas in 5,990 (14.9%).

Variables independently associated with CRC were age ≥ 70 years (OR 1.20, 95%CI 1.03-1.40), male sex (OR 1.23, 95%CI 1.11-1.37), FIT ≥ 50 mcg/g and < 200 mcg/g (OR 2.84, 95%CI 2.47-3.27), FIT ≥ 200 mcg/g (OR 6.91, 95%CI 5.99-7.98), and first round of FIT (OR 1.53, 95%CI 1.35-1.73). From these variables, a hierarchical approach based on marginal effect predicted probabilities was used to derive a clinically usable risk-stratification flow-chart.

The discriminative ability of the model was fair, as the AUROC was 0.65 (95%CI 0.65-0.66) in the derivation cohort and 0.63 (95%CI 0.62-0.64) in the validation cohort.

Conclusion: We show that the use of readily available clinical variables is effective in identifying FIT+ subjects at increased risk of CRC. This tool

could be integrated in FIT-based screening programs to maximize their effectiveness through the correct prioritization of colonoscopy resources.

Disclosure: The authors declare no conflict of interest

MP012

MORE BENEFIT OF EXCELLENT VERSUS GOOD BOWEL PREPARATION FOR EARLY COLORECTAL CANCER COLONOSCOPY SCREENING: RESULT OF A PROSPECTIVE, MULTICENTER, OBSERVATION STUDY

J. Zhou¹, T. Bai², T. Han³, X. Dong⁴, S. Li⁵, W. Luo⁶, T. Xinxing⁷, Y. Hu⁸, J. Zhang⁹, Y. Guo¹⁰, W. Chen¹¹, W. Wang¹², M. Chen¹³, P. Fu¹⁴, Y. Ye¹⁵, J. Liu¹⁶, R. Lin²

¹Union Hospital, Tongji Medical College, Huazhong University of Science and TechnologyV, Department of Gastroenterology, Wuhan, China, ²Union Hospital, Tongji Medical College, Huazhong University of Science and Technology,, Department of Gastroenterology,, Wuhan, China, ³The Fourth Affiliated Hospital, Zhejiang University School of Medicine, Department of Gastroenterology, Hangzhou, China, ⁴Karamay Central Hospital, Department of Gastroenterology, Xinjiang, China, ⁵Taihe Hospital, Department of Gastroenterology, Shiyao, China, ⁶The Afficated Shangsha Hospital of Xiangya School of Medicine, Central South University, Department of Gastroenterology, Changsha, China, ⁷The Second Affiliated Hospital of Xi'an Jiaotong University, Department of Gastroenterology,, Xi'an, China, ⁸The Affiliated Nanhua Hospital, Hengyang Medical School, University of South China, Department of Gastroenterology, Hengyang, China, ⁹Liping Campus , Second Affiliated Hospital, Zhejiang University School of Medicine, Department of Gastroenterology, Hangzhou, China, ¹⁰Haidian Section of Peking University Third Hospital, Department of Gastroenterology, Beijing, China, ¹¹First Affiliated Hospital of Shihezi University, Department of Gastroenterology, Xingjiang, China, ¹²Shanghai Ruijin Gubei Hospital,, Department of Gastroenterology, Shanghai, China, ¹³The Affiliated Drum Tower Hospital of Nanjing University, Department of Gastroenterology, Nanjing, China, ¹⁴Union Jiangnan Hospital Huazhong University of Science and Technology, Department of Gastroenterology, Wuhan, China, ¹⁵Nangfang Hospital Zengcheng Compus, Southern Medical University, Department of Gastroenterology, Guangzhou, China, ¹⁶Union Hospital Tongji Medical College Huazhong University Of Science And Technology, Wuhan, China

Contact E-Mail Address: 51638593@qq.com

Introduction: Bowel preparation is essential to high quality colonoscopy examination. Whether excellent bowel preparation can increase adenoma detection rate(ADR) comparing with good bowel preparation are still controversial.

Aims & Methods: A prospective, multi-center, observation study was designed to compare ADR between excellent and good bowel preparation based on BBPS in early CRC screening. Subjects aged 40 that received PEG bowel preparation were enrolled. Subject characteristics, bowel preparation quality and colonoscopy data were collected. BBPS score 8-9 was defined as excellent and 6-7 as good.

Primary endpoint was ADR. Secondary endpoints included polyp detection rate (PDR), advanced adenoma detection rate (AADR), and the detection rate of different diameter lesions (≤5mm, 6-9mm, ≥10mm).

Results: 1503 subjects (aged 40-75, ITT population) from 14 hospitals enrolled, 723 (48.1%) got excellent quality of bowel preparation, 707 (47.0%) got good quality of bowel preparation. ADR was significant higher in excellent quality group (35.8% vs 26.9%, P<0.001), especially in trans (13.0% vs 9.6%, P=0.036) and right colon (12.5% vs 8.2%, P=0.008),

numerical higher but no significant difference for left colon (23.5% vs 19.8%, P=0.089) . Excellent quality group had significant higher PDR (57.0% vs 45.1%, P<0.001), especially in left (44.7% vs 35.6%, P<0.001) and trans colon(18.9% vs 14.1%, P=0.015). numerical higher but no significant difference for right colon (16.0% vs 14.0%, P=0.280). AADR was also significant higher in excellent quality group (3.2% vs 1.4%, P=0.026) . ≤5mm lesions detection rate was significant higher in excellent quality group (47.6% vs 35.4%, P<0.001), no significant difference for the lesions of 6-9mm/≥10mm. PP set on analysis supported these result. Sex(female 53.9% vs male 47.1%, RR: 1.1, 95%CI[1.0-1.3], P<0.001), risk factors of inadequate bowel preparation (no 60.9% vs yes 42.8%, RR 1.4, 95%CI[1.3-1.6, P<0.001]), bowel preparation regiment (split dose 53.7% vs one dose 46.3%, RR1.1, 95%CI [1.1-1.2], P<0.001), PEG volume (4L 53.4% vs <4L 46.6%, RR 1.4, 95%CI[1.3-1.6], P<0.001), diet compliance (full compliance 52.2% vs other 44.26%, RR: 1.2, 95%CI[1.0, 1.4], P=0.015) as well as run-away time (2-5hour 53.8% vs other 46.2%, RR: 1.1, 95%CI[1.0, 1.3], P=0.017) were significant associated factors of excellent bowel preparation.

Item	Excellent N=723, n(%)	Good N=707, n(%)	Difference 95%CI,%	P-Value
Adenoma detection rate	259(35.8)	190(26.9)	8.9[4.0-13.8]	<0.001
Polyps detection rate	412(57.0)	319(45.1)	11.9[6.6-17.1]	<0.001
Advanced Adenoma detection rate	23(3.2)	10(1.4)	1.8[0.9-3.5]	0.026
≤5mm lesion detection rate	344(47.6)	250(35.4)	12.2[7.0-17.3]	<0.001
6-9mm lesion detection rate	123(17.0)	108(15.3)	1.7[-2.2-5.7]	0.372
>10mm lesion detection rate	45(6.2)	42(5.9)	0.3[-2.3-2.8]	0.823

Table 1. Lesion Detection Rate Comparing Between Excellent and Good Bowel Preparation (ITT population).

Conclusion: We should seek excellent bowel preparation due to higher ADR, PDR and AADR, especially for ≤5mm lesions. For male and populations with inadequate bowel preparation risk factors, enhance diet education, 4L PEG, split dose and right run-away time could help to get excellent bowel preparation.

Disclosure: Nothing to disclose.

MP013

BOWEL PREPARATION IN INFLAMMATORY BOWEL DISEASE PATIENTS: A MULTICENTRE RETROSPECTIVE STUDY ON COMPARISON BETWEEN 1L-PEG AND 2L-PEG REGIMENS IN OUTPATIENT SETTING

D. Scalvini^{1,2}, C. Bezzi³, S. Maimaris⁴, M.V. Lenti⁵, F. Lusetti⁶, A. Cappellini⁷, C. Cicalini⁸, M. Dota⁹, R. Muscia⁹, D. Brinch⁹, M.I. Parisi¹⁰, M. Devani⁹, M. Schettino⁹, A. Mauro¹¹, S. Mazza¹¹, S. Agazzi¹¹, A. Schieppati⁷, A. Di Sabatino⁵, F. Biagi⁷, G. Manes⁹, A. Anderloni¹¹, S. Saibeni⁹

¹University of Pavia, Experimental Medicine, Pavia, Italy,

²Fondazione IRCCS Policlinico San Matteo, Gastroenterology and Digestive Endoscopy Unit, Pavia, Italy, ³IBD Center, IRCCS Humanitas Research Hospital, Humanitas University Pieve Emanuele, Department of Biomedical Sciences, Rozzano, Italy, ⁴University of Pavia, Pavia, Italy, ⁵Fondazione IRCCS Policlinico San Matteo, University of Pavia, I Department of Internal Medicine, Pavia, Italy, ⁶University of Pavia, Fondazione IRCCS Policlinico San Matteo, Gastroenterology and Digestive Endoscopy Unit, Pavia, Italy, ⁷University of Pavia, Istituti Clinici Scientifici Maugeri IRCCS, Gastroenterology Unit of Pavia Institute, Pavia, Italy, ⁸University of Pavia, Gastroenterology and Digestive Endoscopy Unit, ASST Rhodense, Rho Hospital, Rhodense, Italy, ⁹Gastroenterology and Digestive Endoscopy Unit, ASST Rhodense, Rho Hospital, Rhodense, Italy, ¹⁰University of Pavia, Gastroenterology and Digestive Endoscopy unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, ¹¹Gastroenterology and Digestive Endoscopy Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Contact E-Mail Address: davidescalvini.med@gmail.com

Introduction: Colonoscopy is crucial for diagnosis, disease monitoring and colorectal cancer surveillance in patients with inflammatory bowel disease (IBD), which is a population at increased risk. Perfect bowel preparation (BP) is essential for high-quality monitoring, because an inadequate one lead to incomplete colonoscopy and higher rate of missing precancerous lesions. In contrast to general population, there is limited data on the most effective BP to use in an outpatient setting for IBD patients, especially after the introduction of 1L-PEG.

This study aims to compare the effectiveness of 1L-PEG and 2L-PEG in IBD undergoing outpatient colonoscopy and to identify any risk factors that lead to inadequate BP.

Aims & Methods: This is a cross-sectional, multicentric, retrospective study, including IBD patients aged ≥ 16 years, who underwent outpatient split-dose colonoscopy between Jan-2021 and Dec-2022. Patients at each center received a standard pamphlet with BP instruction, without any specific recommendations, and a list of available laxatives. Only Movi-prep® and Clensia® for 2L-PEG group, and Plenvu® for 1L-PEG group were included as they were recommended by all three centres, to avoid selection bias. Boston Bowel Preparation Scale (BBPS) was used to assess the adequacy of BP. Demographic, clinical and endoscopy data were collected and analyzed. A multivariable logistic regression model was used to compare 1L-PEG and 2L-PEG.

Results: 506 patients (F 42.9%, mean age 48.9 $\pm$ 15.2 years), 306 with ulcerative colitis and 200 with Crohn's disease (CD) were collected; 1L-PEG was used by 265 (52.4%) while the remaining 241 (47.6%) used 2L-PEG. Adequate BP was achieved in 440 (87.0%) and 1L-PEG was associated with a higher rate of adequate BP compared to 2L-PEG (238/265, 89.8% vs 202/241, 83.8%, $p=0.048$) and a higher BBPS score (median 8, IQR 7-9 vs 6, IQR 6-8, $p<0.001$). Male sex ($p=0.03$), previous ileal/colonic surgery ($p=0.01$) and stricturing CD ($p=0.01$) were associated with inadequate BP. No correlation was found between BP and maximum localization/ex-

tension of IBD, the use of advanced therapy, the presence of endoscopic activity, Mayo endoscopic score and the presence of CRC or pseudopolyps. At multivariable analysis, 1L-PEG was a predictor of adequate BP (OR=1.70, 95%CI 1.00-2.90, $p<0.05$); on the contrary, male sex (OR=0.51, 95%CI 0.29-0.90, $p=0.02$) and previous ileal/colonic surgery (OR=0.40, 95%CI 0.21-0.77, $p<0.01$) were confirmed as risk factors for inadequate BP.

Conclusion: These findings, from a large cohort of IBD patients, highlight the superiority of 1L-PEG compared to 2L-PEG in achieving adequate BP and suggests its routine use in an outpatient setting for IBD patients. Male patients, those with a history of ileal/colonic surgery and stricturing CD require careful attention and the implementation of adjuvant strategies.

Disclosure: Nothing to disclose.

MP014

PREFERENCES RESPECT OF ENDOSCOPIC SURVEILLANCE IN PATIENTS WITH ADVANCED COLORECTAL LESIONS. VIGNETTES STUDY

J. Hernández-Camoiras^{1,2}, C. Regueiro^{1,2}, Á. Gómez-Amorín³, C. Tourne-García⁴, S. Castán⁵, R. Almazán³, E. Rodríguez-Camacho³, A. Ono⁶, M. Besó Delgado⁵, M.I. Civera Peris^{7,8}, A. Martínez-Roca⁹, R. Jover⁹, R. Cuesta Cortijo¹⁰, M. Vanaclocha⁸, A. Molina-Barceló¹¹, J. Cubiella^{2,11,12}

¹Research Group in Gastrointestinal Oncology, Ourense, Spain, ²Galicia Sur Health Research Institute, Vigo, Spain, ³Conselleria de Sanidade, Dirección Xeral de Saúde Pública, Santiago de Compostela, Spain, ⁴Health Promotion and Educate Service, General Directorate of Public Health and Addictions, Región de Murcia, Spain, ⁵Screening Service, General Directorate of Public Health, Valencia, Spain, ⁶Department of Gastroenterology, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain, ⁷Cancer and Public Health Research Area, Valencia, Spain, ⁸Foundation for the Promotion of Health and Biomedical Research in the Valencia Region, Valencia, Spain, ⁹Clinical Medicine Service, Digestive Medicine Service, Dr. Balmis University General Hospital, Biomedical Research Institute ISABIAL, Alicante, Spain, ¹⁰Digestive System Section, Internal Medicine Service, Hospital de Sagunto, Sagunto, Spain, ¹¹Public Health Research Center, Valencia, Spain, ¹²Department of Gastroenterology, Hospital Universitario de Ourense, Ourense, Spain

Contact E-Mail Address: joaquin.cubiella.fernandez@sergas.es

Introduction: There are no randomised clinical trials evaluating the effect of endoscopic surveillance on the long-term incidence of colorectal cancer. In this context, it is relevant to know the preferences of the patients. The Polyprev study (NCT04967183) is a randomised clinical trial evaluating the impact of the incidence on colorectal cancer incidence of faecal occult blood surveillance versus endoscopic surveillance after resection of advanced lesions in screening programmes.

Aims & Methods: The aim of our study is to know the preferences of surveillance after resection of advanced lesions. Included patients were presented with a decision support tool using vignettes, presenting 8 scenarios based on estimated incidences of colorectal cancer, number of colonoscopies and associated complications. In each scenario, patient chose one of the following options: endoscopic surveillance, faecal occult blood surveillance or no surveillance. We conducted a descriptive analysis of the responses obtained in the questionnaires. Subsequently, we determined which variables were independently associated with a preference for endoscopic surveillance using a multivariate logistic regression.

Results: Out of the 1023 patients included, 521 subjects answered to the values and preferences questionnaire. The mean age was 57.89 (± 4.87) years, the percentage of women was 39.3% and the mean of resected adenomas was 3.07 (± 2.01) adenomas per patient. In the 8 scenarios, the preferred rate for endoscopic surveillance, faecal occult blood surveillance and no surveillance was 32.8 - 4.5%, 55.7 - 66.2% and 0.6 - 1.4%, respectively. The endoscopic surveillance was significantly associated with the female gender (OR: 1.27 95% CI: 1.11 - 1.44), the age (50 - 54 year OR: 1.25 95% CI: 1.07 - 1.47; 55 - 59 years OR: 1.47 95% CI: 1.26 - 1.72), the assignment to the colonoscopy branch (OR: 1.93 95% CI: 1.69 - 2.20) and the risk of colorectal cancer estimated by faecal occult blood surveillance (2% OR: 1.43 95% CI: 1.04 - 1.97; 2.5% OR 1.67 95% CI: 1.29 - 2.32).

Conclusion: Patients in the Polyprev study prefer to return to the colorectal cancer screening programme. Variables independently associated with endoscopic surveillance were sex, age, assigned study branch and estimated risk of colorectal cancer.

Disclosure: Nothing to disclose.

MP015

EFFECT OF WATER EXCHANGE ON QUALITY OF COLONOSCOPY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

B. Wei¹, X. Bingxin¹, X. Chen¹, Q. Zhan¹, Y. Cheng²

¹The Affiliated Wuxi People's Hospital of Nanjing Medical University, Wuxi People's Hospital, Wuxi Medical Center, Wuxi, China, ²WUXI People's Hospital, Digestive Medicine, Wuxi, China

Contact E-Mail Address: weibingnicherish@163.com

Introduction: Colonoscopy techniques is an independent factor of adenoma detection rate. However, the colonoscope insertion methods and cecal intubation time is often ignored compared with relevant technology or colonoscopy performance indicator in withdrawal stage. The effect of water exchange (WE) method characterized by water infusion with water removal primarily during insertion stage on colonoscopy has remained controversial.

We aimed to carry out a meta-analysis to systematically evaluate the relationship between WE and quality of colonoscopy compared with the conventional methods include air insufflation and carbon dioxide insufflation.

Aims & Methods: Aims: To evaluate the effect of water exchange method versus conventional methods including air insufflation and carbon dioxide insufflation method for the quality of colonoscopy.

Methods: We searched randomized controlled trials published up to October 2022 from PubMed, Web of Science, the Cochrane Library, CNKI, Wanfang, SinoMed databases. Two reviewers independently searched the literatures based on standards to extract the data and evaluate the quality. The primary outcomes were cecal intubation time and adenoma detection rate. The secondary outcomes included cecal intubation rate, quality of bowel preparation, pain score, number of abdominal compression, number of position change. Meta-analysis was conducted by RevMan5.4.1. The study protocol was registered in PROSPERO (CD42022327954).

Results: A total of 23 studies involving 10654 patients were included. Although cecal intubation time was prolonged in WE (MD=1.81, 95%CI: 1.28, 2.35; $P < 0.001$), WE had higher adenoma detection rate (OR=1.40, 95%CI: 1.26, 1.55; $P < 0.001$), cecal intubation rate (OR=1.62; 95%CI: 1.24, 2.10; $P < 0.001$) and quality of bowel preparation (MD=0.61; 95%CI: 0.42, 0.79; $P < 0.001$) compared with conventional colonoscopy. In addition, WE had significantly lower pain scores (MD=-1.07; 95%CI: -1.39, -0.76; $P < 0.001$), number of abdominal compression (OR=0.42; 95%CI: 0.29, 0.60; $P < 0.001$) and number of position change (OR=0.59; 95%CI: 0.42, 0.82; $P = 0.002$) than conventional colonoscopy.

Conclusion: Despite WE colonoscopy prolonged cecal intubation time, it could significantly increase adenoma detection rate, cecal intubation rate and quality of bowel preparation. And beyond that, WE reduced patient pain, the proportion of abdominal compression and position change. WE is a better choice for high-quality colonoscopy.

Disclosure: Nothing to disclose.

MP016

REAL-WORLD EVIDENCE ON THE USE OF CAPNOGRAPHY MONITORING DURING PROCEDURAL SEDATION AND ANALGESIA FOR GASTROENTEROLOGY AND BRONCHOSCOPY

F. Distler¹, R. Bisschops², M. Özçelik³, I. Valbuena Gómez⁴, N. Sfeir⁵, R. Saunders¹

¹Coreva Scientific GmbH & Co. KG, Koenigswinter, Germany,

²Katholieke Universiteit Leuven, Gastroenterology, Leuven,

Belgium, ³Faculty of Medicine, Ankara University, Department

of Anaesthesiology and ICM, Ankara, Turkey, ⁴La Paz University

Hospital, Department of Anaesthesiology and Resuscitation,

Madrid, Spain, ⁵Medtronic, Paris, France

Contact E-Mail Address: ozcelikmenekse@yahoo.com

Introduction: Procedural sedation and analgesia (PSA) can be associated with respiratory depression that must be recognised rapidly and managed appropriately to avoid the risk of hypoxic brain damage, cardiac arrest, and death. Standard of care monitoring (SOCM) during PSA includes electrocardiogram, respiratory rate, blood pressure, and pulse oximetry but these do not reliably identify airway or respiratory compromise. Capnography can be used to measure exhaled carbon dioxide, providing real-time identification of airway obstruction and respiratory depression.

We aimed to measure the real-world impact of using capnography in addition to SOCM on patient safety during PSA for gastroenterology and bronchoscopy procedures.

Aims & Methods: A before-and-after, quality-improvement protocol was followed at four centres in Leuven, Ankara, Madrid, and Toronto using a specialised Microsoft Excel application for data collection. Collected adverse events were death, escalation of care, mild (75–90%; up to 60 seconds (s)) and severe (<75% or <90% for over 60 s) oxygen desaturation, prolonged apnoea (>60 s), bradycardia, tachycardia, airway obstruction, cardiovascular shock or collapse, and cardiac arrest. Data for SOCM were collected first, without modification to the centre's standard practice for PSA.

Then capnography was introduced, including staff training and a 2–4 week wash-in period, after which data collection commenced for capnography. Data were collected between 2017 and 2021 and combined by procedures into those using SOCM and those using SOCM plus capnography (capnography). Patients could have more than one procedure performed.

Results: Data were collected for 6,100 procedures (N=3,100 SOCM and N=3,000 capnography). Procedures were split as follows with 94.7% gastroenterology procedures: colonoscopy (n=2,773), gastroscopy (n=1,868), combined gastroscopy and colonoscopy (n=502), endoscopic ultrasound (n=362), bronchoscopy (n=326), endoscopic retrograde cholangiopancreatography (n=225), and others (n=44).

Total adverse events were decreased by 38.53% from 353 (SOCM) to 217 (capnography) events. The relative risk (RR) of at least one adverse event occurring per procedure with capnography versus (vs) SOCM was 0.68 (95% confidence interval: 0.57–0.81; 9.77% vs 6.63%).

Escalation of care was decreased when using capnography by RR 0.11 (0.01–0.91; 9 vs 1 events). Oxygen desaturation was decreased with RR 0.64 (0.52–0.79; 223 vs 139 events) for mild and RR 0.44 (0.24–0.82; 33 vs

14 events) for severe cases. Bradycardia and tachycardia were also reduced by RR 0.50 (0.28–0.89; 35 vs 17 events) and RR 0.14 (0.05–0.39; 30 vs 4 events), respectively. Prolonged apnoea was increased by RR 4.39 (1.48–13.04; 4 vs 17 events) when using capnography vs SOCM, potentially due to easier detection of apnoea using capnography. Airway obstruction and cardiovascular events were non-significantly different and no patient deaths were recorded.

Conclusion: In this, to date the largest real-world data set on PSA capnography monitoring, patient safety was found to be significantly improved in those procedures using capnography. Additional analyses, such as patient matching, are required to examine the potential influence of confounders on results.

Disclosure: NS is employed by Medtronic, the manufacturer of capnography. FD is employed by and RS is the owner of Coreva Scientific GmbH & Co. KG. They provided data analysis and writing services. RB, MÖ, and IVG declare no conflict of interest.

Funding: This work was funded by Medtronic.

MP017

COLORECTAL ADENOMA DETECTION RATE USING TEXTURE AND COLOR ENHANCEMENT IMAGING (TXI) VS WHITE LIGHT IMAGING WITH CHROMOENDOSCOPY: A PROPENSITY-SCORE MATCHING STUDY

O. Toyoshima¹, T. Nishizawa¹, S. Yoshida¹

¹Toyoshima Endoscopy Clinic, Gastroenterology, Tokyo, Japan

Contact E-Mail Address: t@ichou.com

Introduction: Improving the adenoma detection rate (ADR) can contribute to reducing the incidence and mortality of post-colonoscopy colorectal cancer (PCCRC). Texture and color enhancement imaging (TXI) enhances subtle tissue textures, selectively brightens dark areas, and emphasizes the differences between red and white colors^{1,2}. Several studies have investigated the visibility and color differences of TXI in vitro and reported its superiority over WLI³⁻⁷.

However, A few studies have evaluated the ADR of colonoscopy with TXI, which is a novel image-enhancing technology. This study aims to compare the detection of colorectal polyps using TXI to that using white light imaging (WLI).

Aims & Methods: This study was conducted retrospectively in a single center using propensity-matched scoring based on the patients' baseline characteristics, such as age, sex, indication, bowel preparation, endoscopist, colonoscope type, and withdrawal time. This study compared the effectiveness of WLI and TXI in patients who underwent chromocolonoscopy with indigo carmine spraying.

The study determined the differences in the adenoma, including high-risk adenoma, and sessile serrated lesion (SSL) detection rates and the mean number of detected adenomas and SSLs per colonoscopy between the TXI and WLI groups. High-risk adenomas were defined as three or more adenomas, an adenoma ≥ 10 mm, an adenoma with a villous component, and an adenoma with high-grade dysplasia. The Wald test with logistic regression was used to analyze the *P* values.

Results: After propensity score matching, 1970 patients were enrolled into each imaging modality group. The mean patient age was 57.2 ± 12.5 years, and 44.5% of the cohort were men. The ADR was higher in the TXI group than in the WLI group (55.0% vs. 49.4%, odds ratio: 1.25). High-risk ADR were more common in the TXI group than in the WLI group (17.6% vs. 12.8%; OR: 1.45). The mean number of adenomas per colonoscopy (APC) was higher in the TXI group than in the WLI group (1.187 vs. 0.943, OR: 1.12). APC with a 0-II morphology according to the Paris classification (1.093 vs. 0.848, OR: 1.14) and APC of ≤ 6 mm (0.992 vs. 0.757, OR: 1.16) were higher in the TXI group than in the WLI group. The adenoma plus SSL

detection rate (ASDR) was higher in the TXI group than in the WLI group (58.8% vs. 53.2%, OR: 1.25). The mean number of adenomas plus SSLs per colonoscopy (ASPC) was greater in the TXI group than in the WLI group (1.287 vs. 1.025, OR: 1.13, *Table*).

	WLI	TXI	Odds ratio	95% CI	P value
ADR, %	49.4	55.0	1.25	1.10-1.42	<0.001
High-risk ADR, %	12.8	17.6	1.45	1.22-1.73	<0.001
APC, n	0.94	1.19	1.12	1.07-1.17	<0.001
APC, 0-II type, n	0.85	1.09	1.14	1.09-1.19	<0.001
APC, ≤ 6 mm, n	0.76	0.99	1.16	1.10-1.22	<0.001
ASDR, %	53.2	58.8	1.25	1.11-1.42	<0.001
ASPC, n	1.03	1.287	1.13	1.08-1.18	<0.001

Table. Polyp detection using TXI compared with WLI.

Conclusion: A randomized controlled trial⁸ and a cross-over study⁹ previously showed that the ADR of TXI was higher than that of WLI. In this study, we found that the ADR, high-risk ADR, APC, ASDR, and ASPC of TXI were higher than those of WLI after propensity-score matching of patients who underwent chromoendoscopy. TXI may help prevent PCCRC.

References:

- 1 Sato T. TXI: Texture and Color Enhancement Imaging for Endoscopic Image Enhancement. *J Healthc Eng* 2021; 2021.
- 2 Tani Y, *et al.* Gastrointestinal: Texture and color enhancement imaging is useful for detection of small gastric adenocarcinoma of fundic-gland type. *J Gastroenterol Hepatol* 2024.
- 3 Nishizawa T, *et al.* TXI (Texture and Color Enhancement Imaging) for Serrated Colorectal Lesions. *J Clin Med* 2021.
- 4 Toyoshima O, *et al.* Texture and color enhancement imaging in magnifying endoscopic evaluation of colorectal adenomas. *World J Gastrointest Endosc* 2022.
- 5 Tamai N, *et al.* Visibility evaluation of colorectal lesion using texture and color enhancement imaging with video. *DEN Open* 2022.
- 6 Yoshida N, *et al.* Analysis of Texture and Color Enhancement Imaging for Improving the Visibility of Non-polypoid Colorectal Lesions. *Dig Dis Sci* 2022.
- 7 Hiramatsu T, *et al.* Improved visibility of colorectal tumor by texture and color enhancement imaging with indigo carmine. *World J Gastrointest Endosc* 2023.
- 8 Antonelli G, *et al.* Texture and color enhancement imaging versus high definition white-light endoscopy for detection of colorectal neoplasia: a randomized trial. *Endoscopy* 2023.
- 9 Sakamoto T, *et al.* Detection of colorectal adenomas with texture and color enhancement imaging: Multicenter observational study. *Dig Endosc* 2023.

Disclosure: None.

MP018

FACTORS ASSOCIATED REMNANT TUMOR AFTER INCOMPLETE RESECTION OF RECTAL NEUROENDOCRINE TUMOR

H.-H. Oh¹, C.-M. Im¹, J.G. Lee², J.H. Ji³, K. Lim⁴, D.-H. Kim¹, H.-S. Kim¹, Y.-E. Joo¹

¹Chonnam National University Medical School, Gwangju, South Korea, ²Hallym University College of Medicine, Department of Internal Medicine, Dongtan, South Korea, ³Institute of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea, ⁴Yeungnam University College of Medicine, Daegu, South Korea

Contact E-Mail Address: hyung1125@naver.com

Introduction: Over the past two decades, there has been an increase in the incidence of rectal NET, which has in turn heightened the importance of optimizing its treatment and managing care after treatment. However, many cases of rectal NETs are removed by conventional EMR or even forceps polypectomy methods without being aware that it is NET which results in incomplete resection.

Currently, no strong clinical evidence is supported for the need of salvage treatment in case of incompletely resected rectal NETs.

Aims & Methods: In this study, we aimed to find the factors that can predict the presence of remnant tumor after incomplete resection performed for the treatment of rectal NET in order to appropriately select patients who may require additional resection. We retrospectively reviewed clinical data of patients who underwent salvage treatment for incompletely resected rectal NETs between January 2010 and November 2023 at 5 tertiary hospitals.

Results: A total of 190 patients were enrolled in the study. Of these, 109 patients (57.4%) had a positive resection margin, while 81 patients (42.6%) had an indeterminate resection margin. 128 (67.4%) patients had no remnant tumor and 62 (32.6%) patients had remnant tumor at salvage resection specimen. The presence of remnant tumor varied according to the initial resection method used: 38.1% (16/42) for cold forcep polypectomy, 70.6% (24/34) for cold snare polypectomy, and 29.9% (26/87) for conventional EMR.

Notably, no remnant tumors were found in patients who underwent modified EMR (n=21) or ESD (n=6) methods. Also, initial endoscopic resection performed by tertiary hospital expert showed significantly lower rate of remnant tumor compared to those performed by non-tertiary hospital expert with rate of 8.9% (4/45) and 40.9% (58/145) respectively.

Lastly, patients with endoscopically remnant tumor before salvage treatment showed significantly higher rate of remnant tumor compared to those with endoscopically no remnant tumor with rate of 63.5% (47/74) and 12.9% (15/116) respectively. In multivariate analysis, endoscopic resection performed by non-tertiary expert (OR, 3.887; p=0.045) and endoscopically remnant tumor (OR, 10.891; p<0.001) were significant risk factors for the presence of remnant tumor.

Conclusion: Follow-up rather than resection may be considered for patients with positive resection margin after modified EMR or ESD for rectal NET. Also, endoscopic resection done by non-tertiary hospital expert and endoscopically remnant tumor are significant risk factors for the need of salvage treatment.

Disclosure: Nothing to disclose.

MP019

THE PRESENCE OF SCARRING SIGNIFICANTLY IMPACTS BLINK DECISION MAKING IN LARGE NON-PEDUNCULATED COLORECTAL POLYPS BUT DOES NOT INTERFERE WITH CANCER DETECTION

L. Debels^{1,2}, P.J. Poortmans^{2,1}, S. Smeets¹, M.E. Argenziano¹, M. Montori¹, T. Tornai¹, L. Desomer³, D.J. Tate¹

¹University Hospital of Ghent, Gastroenterology and Hepatology, Ghent, Belgium, ²University Hospital of Brussels, Gastroenterology and Hepatology, Brussel, Belgium, ³AZ Delta, Gastroenterology and Hepatology, Roeselare, Belgium

Contact E-Mail Address: lynn_debels@hotmail.com

Introduction: The detection of cancer within large non-pedunculated colorectal polyps (LNPCPs) is suboptimal in non-expert settings. Identification of 6 macroscopic (Blink) features (6BF) of deep submucosal invasive cancer (SMI) has shown significant improvement in the sensitivity of cancer detection by inexperienced endoscopists at the expense of decreased specificity.

This study investigates the impact of endoscopic resection scars, which can resemble deep SMI, on the accuracy of non-expert endoscopists using the 6BF evaluation system known as Blink Impression.

Aims & Methods: An online survey was disseminated containing 20 overview images of LNPCPs (1 image/polyp). Images (randomized) were shown before, and after a 2-minute educational video (the intervention) introducing the 6BF - fold deformation, extra redness, depression, chicken skin mucosa, ulceration and spontaneous bleeding.

Before and after the intervention participant Blink Impression was elicited (cancer/no cancer) and only after, the presence of the 6BF. Responses were analysed relative to histopathology (no vs superficial vs deep SMI) and expert opinion on the presence of the 6BF and endoscopic resection scars.

Results: 7/20 LNPCPs contained cancer (3 superficial, 4 deep SMI), 3 contained scars. 191 participants from 21 countries completed 3,755 observations. 129/191 (67.5%) participants were inexperienced. Expert-identified scarred LNPCPs contained median 1.0 (IQR 2.0) BF vs 1.0 (IQR 2.0) for no cancer, 2.0 (IQR 2.0) for superficial SMI and 3.0 (IQR 2.0) for deep SMI (all P<.001). Presence of ≥2 BF therefore reliably identifies cancer within LNPCPs but not scars. Fold deformation was the only BF identified more commonly amongst scarred LNPCPs (44.6%) vs no cancer (22.5%, P<.001) and vs superficial SMI (33.0%, P<.001), but similar to deep SMI (44.6%, P=1.000).

Depression, chicken skin mucosa and spontaneous bleeding were less commonly identified in scarred polyps (12.3%, 7.6% and 1.8%) than both no cancer (33.1%, 14.4% and 8.6%, all P<.001), superficially invasive (68.6%, 14.3% and 5.8%, all P<.001) or deeply invasive polyps (45.9%, 19.6% and 40.5%, all P<.001).

Extra redness and ulceration were identified with similar frequency to no cancer in scars (26.4% vs 26.8%, P=0.891 and 10.2% vs 9%, P=0.441 respectively), but less commonly than superficial (64.2%, P<.001 and 15.7%, P<.001) or deep SMI (60.2%, P<.001 and 24.7%, P<.001) (Table 1, next page).

Conclusion: The presence of ≥2BF reliably discriminates LNPCPs with cancer from non-cancer even in the presence of scarred lesions amongst non-expert endoscopists. Scarred LNPCPs exhibit fold deformation at a similar rate to LNPCPs with deep SMI but other BF are not present.

References: Debels LK, Smeets S, Poortmans PJ, Argenziano ME, Desomer L, Anderson J, Valori R, David J Tate. Identification of 6 key features of colorectal polyps increases the sensitivity of cancer detection and ability to discriminate deep submucosal invasion The basis of the Blink (first impression)? United European Gastroenterology Journal 2023; Vol.11

Disclosure: Nothing to disclose.

Blink Feature	No SMI	Scar	Superficial SMI	Deep SMI	Comparison	p
Fold deformation	22.5 (20.6-24.4)	44.6 (40.6-48.7)	33.0 (29.1-36.9)	44.6 (41.2-48.2)	No SMI - Scar	<.001
					No SMI - sSMI	<.001
					No SMI - dSMI	<.001
					Scar - sSMI	<.001
					Scar - dSMI	1.000
Extra redness	26.8 (24.8-28.8)	26.4 (22.7-30.0)	64.2 (60.3-68.1)	60.2 (56.7-63.7)	sSMI - dSMI	<.001
					No SMI - Scar	0.891
					No SMI - sSMI	<.001
					No SMI - dSMI	<.001
					Scar - sSMI	<.001
Depression	33.1 (31.0-35.2)	12.3 (9.6-15.0)	68.6 (64.8-72.4)	45.9 (42.3-49.4)	Scar - dSMI	<.001
					sSMI - dSMI	<.001
					No SMI - Scar	<.001
					No SMI - sSMI	<.001
					No SMI - dSMI	<.001
Chicken skin mucosa	14.4 (12.8-16.0)	7.6 (5.4-9.7)	14.3 (11.4-17.2)	19.6 (16.8-22.4)	Scar - sSMI	<.001
					Scar - dSMI	<.001
					sSMI - dSMI	.014
					No SMI - Scar	0.441
					No SMI - sSMI	<.001
Ulceration	9.0 (7.7-10.3)	10.2 (7.7-12.7)	15.7 (12.7-16.7)	24.7 (21.6-27.8)	No SMI - dSMI	<.001
					Scar - sSMI	<.001
					Scar - dSMI	<.001
					sSMI - dSMI	<.001
					No SMI - Scar	<.001
Spontaneous bleeding	8.6 (7.6-10.1)	1.8 (0.7-2.8)	5.8 (3.9-7.8)	40.5 (37.0-44.0)	No SMI - sSMI	.026
					No SMI - dSMI	<.001
					Scar - sSMI	<.001
					Scar - dSMI	<.001
					sSMI - dSMI	<.001
Number of features (median)	1.0 (2.0)	1.0 (2.0)	2.0 (2.0)	3.0 (2.0)	No SMI - Scar	.651
					No SMI - sSMI	<.001
					No SMI - dSMI	<.001
					Scar - sSMI	<.001
					Scar - dSMI	<.001
					sSMI - dSMI	<.001

Table 1. Comparison of the presence (% [95% confidence interval]) of the 6 different Blink features and the median number of Blink features per histopathological group (No SMI, Superficial SMI, Deep SMI) and resection scars with associated p-values. Submucosal invasive cancer, SMI; Superficial SMI, sSMI; Deep SMI, dSMI.

MP020

INITIAL EXPERIENCES WITH NAVICAM COLON CAPSULE ENDOSCOPY FOCUSING ON THE FEASIBILITY, EFFICACY, AND TRANSIT TIMES

A. Finta¹, M. Szalai¹, R. Liebe¹, L. Oczella¹, L. Madácsy¹
¹Endo-Kapszula Ltd., Endoscopy Unit, Szekesfehervar, Hungary

Contact E-Mail Address: traveler.uni@gmail.com

Introduction: Colon capsule endoscopy (CCE) may be recommended as a screening test for individuals under the age of 50 with low familial risk, diagnosed with irritable bowel syndrome (IBS) but lacking alarming symptoms and showing no fecal immunochemical test (FIT) positivity.

Aims & Methods: In the present study, our aim was to assess the efficacy, feasibility and acceptance of CCE in IBS patients with low risk of CRC, and our secondary aim was to assess polyp detection rates, transit times, cleanliness level and patient satisfaction. From April 2022 to April 2024, we conducted a prospective study at our institution involving 196 patients with IBS under the age of 50 (130 (66%) males, 66 (44%) females). We applied first in the literature, the recently developed colon capsule endoscopy technology of the Anx Robotics (USA) Navicam dual-camera CCE for this comprehensive assessment. The new first generation Navicam CCE measures 31mm in length and 11.6mm in diameter, weighing approximately 3 grams.

The two cameras operate at adaptive frame rate of 0.5 to 16 pic/sec, with adaptive focus of 0-30 mm, providing an image resolution of 480x480 pixels. The minimum battery time is 12h, and this is a fully functional panenteric capsule. Colonoscopy under anaesthesia was offered to all patients, and after detailed information and signing the consent form, they chose CCE as the first examination method.

We identified and addressed the incomplete cases, recorded capsule transit times, and calculated the polyp detection rates. If polyps were detected, patients underwent subsequent colonoscopy with Propofol sedation for polyp removal and histological analysis.

Results: Out of the total cases, 8.7% (n=17) were incomplete. The average colon and total transit time was 201.95 and 360.55 mins, respectively. Our study revealed a remarkable 14.8% (n=29) polyp detection rate (PDR) among the participants. PDR varied across age groups (18-30yo: 12.5%, 31-40yo: 14.04%, 41-50yo: 17.39%). Polyp sizes were categorized as <5mm (n=20), 5-7mm (n=6), and >7mm (n=3).

The majority of polyps were located in the sigmoid colon (n=12), followed by the unspecified left colon (n=10) and the right colon (n=7). Subsequent colonoscopy due to positive CCE performed in all patients and detected an additional 6 small polyps (<3mm). In 4 cases, colonoscopy yielded negative results. However, upon conducting a back-to-back colonoscopy all of the previously undetected polyps were eventually found. Histology results revealed one high-grade dysplastic polyp.

The average cleanliness level of the colon was assessed using the CCE Cleansing Score (CC-CLEAR). For the cecum, the right and left colon, the average scores were 5.5-7-8, respectively. Impressively, 95% of participants reported high tolerance, and 91% of respondents expressed a preference for CCCE as the next screening procedure too and colonoscopy only after a positive CCE result.

Conclusion: Navicam colon capsule endoscopy emerges as a useful and feasible screening tool, demonstrating unparalleled promise in detecting polyps among asymptomatic individuals. Its polyp detection rate, cost-effectiveness, patient-friendly nature, and agreement with colonoscopy findings position it as a potent complementary method for advancing colorectal screening in low CRC risk individuals.

Disclosure: Nothing to disclose.

MP021

COMPLICATIONS OF THE FIRST ENDOSONOGRAPHY-GUIDED DRAINAGE VS. FOLLOWING INTERVENTIONS IN PANCREATIC FLUID COLLECTIONS AND NECROSIS

M. Razpotnik¹, C. Jürgensen¹, M. Sigal¹, C. Makris¹, F.J. Körner¹, Ö. Celebi¹, T.M. Holtmann¹, A. Adler¹, F. Branchi², J. Buchkremer², F. Tacke¹, A. Wree¹

¹Charité - Universitätsmedizin Berlin, Department of Hepatology and Gastroenterology, Campus Virchow-Klinikum (CVK) and Campus Charité Mitte (CCM), Berlin, Germany, ²Charité - Universitätsmedizin Berlin, Department of Gastroenterology, Infectology and Rheumatology, Campus Benjamin Franklin (CBF), Berlin, Germany

Contact E-Mail Address: marcel.razpotnik@gmail.com

Introduction: In general, it is recognized that there is a considerable risk of complications following early endotherapy in the development of pancreatic fluid collections. However, there is still limited information regarding the optimal timing for endosonography (EUS)-guided drainage once a well-defined wall has formed and the relative risk of complications in subsequent interventions.

Aims & Methods: Our study aims to examine the risk of the first EUS-guided drainage compared to the following interventions in pancreatic fluid collections and necrosis. Data on EUS-guided drainage of pancreatic fluid collections performed between 2018 and 2022 at three endoscopy units of Charité- Berlin, regardless of the etiology, were reviewed and analyzed. Adverse events were defined and graded according to the recommendations of the American Society of Gastrointestinal Endoscopy¹.

A severe event following an endoscopic procedure is defined as one that necessitates unplanned admission, prolongs hospital stay by > 10 nights, requires ICU admission for > 1 night, or results in surgery or permanent disability. The Cox proportional hazards regression model was used to examine the relationship between the timing of EUS-guided therapy and the occurrence of complications, adjusting for patient- and procedure-related (age, gender, body-mass index, comorbidities, etiology, size) covariates.

Results: In a cohort of 102 patients (72.5% male, mean age 57.0 ± 14.1 years), 202 procedures were performed, of which 71 (35.1%) were necrosectomies. The predominant etiology was fluid collection complicating pancreatic resection (31.4%), followed by alcohol-induced (22.5%) and biliary (18.6%) pancreatitis. Nearly half of the cases presented with necrotic particles on pre-interventional imaging and 85.3% had a fully definable wall. Adverse events were observed in 24 of the 202 (11.9%) procedures. Six were classified as severe and predominantly occurred during the initial session.

The most frequently reported adverse event was bleeding (4.5%), followed by abdominal pain (1.9%), infection (1.9%), and perforation (0.9%). Three patients died within 30 days after the intervention and were indirectly associated with iatrogenic-induced infection of previously sterile collection. In the Cox proportional hazards regression analysis, which was adjusted for confounding variables, the first intervention emerged as a significant predictor of complications, with a hazard ratio (HR) of 3.5 (95% CI 1.2-10.7). This finding suggests an increased risk of complications during the initial endotherapy session for pancreatic fluid collections.

Conversely, there was an association between the post-pancreatitis fluid collections and complications with an HR of 3.1 (95% CI 0.7- 14.0) compared to post-surgery collections but it did not reach statistical significance. The procedure's duration and the collection size were not associated with the risk of complications.

	1. Intervention	2. Intervention	3. Intervention	4. Intervention
Number	n=102	n=53	n=26	n=21
Time after symptoms (days)	32.1 ± 24.0	44.6 ± 24.7	46.6 ± 26.2	50.3 ± 20.6
Time of the procedure (min)	36.9 ± 16.3	46.9 ± 28.3	60.8 ± 26.7	64.6 ± 30.9
Necrosectomy (%)	5 (4.9%)	32 (60.4%)	18 (69.2%)	16 (76.2%)
Complications (%)	14 (13.7%)	5 (9.4%)	2 (7.7%)	3 (14.3%)
Complication severity				
Mild	7 (6.9%)	3 (5.7%)	2 (7.7%)	1 (4.8%)
Moderate	3 (2.9%)	1 (1.9%)	0	1 (4.8%)
Severe	4 (3.9%)	1 (1.9%)	0	1 (4.8%)

Conclusion: In the EUS-guided therapy of pancreatic fluid collections, the initial intervention emerged as a significant predictor of complications. While post-pancreatitis collections tend toward a higher complication rate compared to post-surgical collections, early intervention strategies require careful consideration to reduce risks.

References: 1. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc.* 2010 Mar;71(3):446-54.

Disclosure: Nothing to disclose.

MP022

LONG-TERM RESULTS OF A PROSPECTIVE STUDY COMPARING LUMEN-APPPOSING METAL STENTS VERSUS DOUBLE-PIGTAIL PLASTIC STENTS FOR INFECTED NECROTIZING PANCREATITIS

A. Beij^{1,2,3}, L. Boxhoorn¹, A. Onnekink⁴, R.C. Verdonk⁵, M.G. Besselink^{6,2}, T.L. Bollen⁷, S.A. Bouwense⁸, V. Cappendijk⁹, W.L. Curvers¹⁰, H. van Dullemen¹¹, C.H. van Eijck¹², M. Hadithi¹³, W.L. Hazen¹⁴, P. Honkoop¹⁵, J. van Hooft⁴, M. Kop¹⁶, E. Kouw¹⁷, S. Kuiken¹⁸, M. Ledebor¹⁹, V.B. Nieuwenhuijs²⁰, L. Perk²¹, J.W. Poley²², R. Quispel²³, R. de Ridder²⁴, H.C. van Santvoort²⁵, M.W. Stommel²⁶, B.J. Witteman²⁷, N.G. Venneman²⁸, F.P. Vleggaar²⁹, R... Van Wanrooij¹, M.J. Bruno²², P. Fockens¹, R.P. Voermans¹, Dutch Pancreatitis Study Group

¹Amsterdam UMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ²Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³St. Antonius Hospital, Research and Development, Nieuwegein, Netherlands, ⁴Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ⁵St. Antonius Hospital, Gastroenterology & Hepatology, Nieuwegein, Netherlands, ⁶Amsterdam UMC, Surgery, Amsterdam, Netherlands, ⁷St. Antonius Hospital, Radiology, Nieuwegein, Netherlands, ⁸Maastricht UMC+, Surgery, Maastricht, Netherlands, ⁹Jeroen Bosch Ziekenhuis, Radiology, 's Hertogenbosch, Netherlands, ¹⁰Catharina Hospital, Gastroenterology and hepatology, Eindhoven, Netherlands, ¹¹University Medical Centre Groningen, Gastroenterology and hepatology, Groningen, Netherlands, ¹²Erasmus University Medical Center, Surgery, Rotterdam, Netherlands, ¹³Maasstad Hospital, Gastroenterology & Hepatology, Rotterdam, Netherlands, ¹⁴Elisabeth TweeSteden Hospital, Gastroenterology & Hepatology, Tilburg, Netherlands, ¹⁵Albert Schweitzer Hospital, Gastroenterology & Hepatology, Dordrecht, Netherlands, ¹⁶Amsterdam Umc, Radiology, Amsterdam, Netherlands, ¹⁷Gelre hospital, Gastroenterology and Hepatology, Apeldoorn, Netherlands, ¹⁸OLVG, Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁹Deventer Hospital, Gastroenterology & Hepatology, Deventer, Netherlands, ²⁰Isala Clinics, Surgery, Zwolle, Netherlands, ²¹Medisch Centrum Haaglanden, Gastroenterology and Hepatology, Den Haag, Netherlands, ²²Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²³Reinier de Graaf Gasthuis, Gastroenterology and Hepatology, Delft, Netherlands, ²⁴Maastricht UMC+, Gastroenterology and Hepatology, Maastricht, Netherlands, ²⁵University Medical Center Utrecht, Surgery, Utrecht, Netherlands, ²⁶Radboud University Medical Center, Surgery, Nijmegen, Netherlands, ²⁷Gelderse Vallei Hospital, Gastroenterology & Hepatology, Ede, Netherlands, ²⁸Medisch Spectrum Twente, Gastroenterology & Hepatology, Enschede, Netherlands, ²⁹University Medisch Centrum Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands

Contact E-Mail Address: a.beij@amsterdamumc.nl

Introduction: In our recent multicentre prospective study (AXIOMA), the effectiveness of lumen-apposing metal stents (LAMS) in endoscopic transluminal drainage of infected necrosis was comparable to that of double-pigtail plastic stents(1). The use of LAMS did not reduce the need for additional drainage procedures and resulted in similar patient outcomes compared to double-pigtails plastic stents. However, long-term follow-up data (>6 months) from prospective studies were still lacking for comparison of the stents.

Aims & Methods: We examined the long-term outcomes of patients with infected necrotizing pancreatitis enrolled in two prospective studies. Patients were treated with endoscopic transluminal drainage with LAMS (n=52) as part of a multicentre prospective cohort in 16 hospitals, or with double-pigtail plastic stents (n=48) as part of the endoscopic step-up arm of a randomized multicentre trial (TENSION) in 19 hospitals(2, 3). The protocol of both studies, including in- and exclusion criteria, were identical except for the type of transluminal stent.

The primary endpoint was the proportion of patients requiring additional endoscopic, percutaneous or surgical drainage procedures due to (recurrence of) symptomatic or infected (peri-)pancreatic collections. Secondary endpoints included the individual components of the primary endpoint, major complications, mortality, number of (pancreatitis-related) readmissions and interventions, length of hospital stay, pancreatic function and quality of life.

Results: The median follow-up period was 4 years. By the end of this period, 77 out of 100 patients were still alive. Among the 47 surviving patients treated with LAMS, 9 were lost to follow-up after the initial 6-month study. An additional percutaneous, endoscopic or surgical drainage or necrosectomy procedure was needed in 37 patients (77%) in the plastic stent group and 40 patients (77%) in the LAMS group (RR 1.002 95% CI 0.809-1.242). The median number of interventions did not differ during overall follow-up (2 [IQR, 1-5] vs 2 [IQR, 1.5-7.5], respectively, P = 0.66). Overall, there was no significant difference in mortality rates (12 patients (25%) vs. 11 (21%) respectively; RR 1.18 95% CI 0.576-2.42), and there was no difference in new mortality after the initial follow-up (3 patients (8%) vs. 6 (13%) respectively; RR 0.603 95% CI 0.16-2.254). No deaths during long-term follow-up were related to pancreatitis. The plastic stents group and LAMS group had a similar rate of pancreatitis-related readmissions (2 [IQR, 0-2] vs 1 [IQR, 0-3], P = 0.67) and associated length of hospital stay (9 [IQR, 0-20.75] vs 6 [IQR, 0-19.75], P = 0.58).

Conclusion: During the long-term follow-up of the AXIOMA study participants, we found no differences in mortality, major complications, readmissions or the need for additional interventions between double-pigtails plastic stents and LAMS. These long-term results are consistent with our prior findings, suggesting that double-pigtail plastic stents and LAMS have comparable clinical outcomes and adverse events in the endoscopic step-up approach for infected necrotizing pancreatitis.

References: 1. Boxhoorn L, Verdonk R, Besselink M, Boermeester M, Bollen T, Bouwense S, et al. Comparison of lumen-apposing metal stents versus double-pigtail plastic stents for infected necrotising pancreatitis. Gut. 2023;72(1):66.

2. van Brunshot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018;391(10115):51-8.

3. Onnekink AM, Boxhoorn L, Timmerhuis HC, Bac ST, Besselink MG, Boermeester MA, et al. Endoscopic Versus Surgical Step-Up Approach for Infected Necrotizing Pancreatitis (ExTENSION): Long-term Follow-up of a Randomized Trial. Gastroenterology. 2022;163(3):712-22.e14.

Disclosure: MGB reports grants from Intuitive, grants from Ethicon Endo-Surgery, grants from Medtronic, outside the submitted work; MBr reports grants and personal fees from Boston Scientific, grants and personal fees from Cook Medical, grants from Pentax Medical, grants from Mylan, grants from 3M, grants from InterScope, outside the submitted work; PF reports personal fees from Cook Medical, personal fees from Olympus, personal fees from Ethicon Endo-Surgery, outside the submitted work; J-WP reports personal fees and other from Cook Endoscopy, personal fees and other from Boston Scientific, personal fees and other from Pentax Medical, outside the submitted work; JEvH reports personal fees from Olympus Endoscopy, grants from Cook Medical, personal fees from Boston Scientific, personal fees from Medtronic, outside the submitted work;

FV reports grants from Boston Scientific, outside the submitted work; RPV reports grants and personal fees from Boston Scientific, grants from Zambon, outside the submitted work.

MP023

HETEROZYGOUS VARIANT OF CYP2C8*3 AS PROTECTIVE FACTOR FOR DEVELOPING POST-ERCP PANCREATITIS

M.J. de Jong¹, R.N. Kuipers¹, C. Serna Weiland², R.C. Verdonk³, T.M. Bisseling¹, D. Dalloyaux¹, N.G. Venneman⁴, M. Hadithi⁵, E.-J.M. Van Geenen¹, J.P. Drenth⁶, R. te Morsche¹, M.J. Bruno⁷, F. van Delft¹, P.D. Siersema^{7,1},

on behalf of the Dutch Pancreatitis Study Group

¹Radboud university medical center, Gastroenterology & Hepatology, Nijmegen, Netherlands, ²Jeroen Bosch Hospital, Gastroenterology and Hepatology, 's Hertogenbosch, Netherlands, ³St. Antonius Ziekenhuis, Gastroenterology & Hepatology, Nieuwegein, Netherlands, ⁴Medisch Spectrum Twente, Gastroenterology & Hepatology, Enschede, Netherlands, ⁵Maasstad Hospital, Gastroenterology & Hepatology, Rotterdam, Netherlands, ⁶Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁷Erasmus University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: mike.dejong@radboudumc.nl

Introduction: Even though numerous risk factors and methods for prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) have been identified, it persists as the most prevalent complication. Administration of 100mg diclofenac prior to ERCP represents the most frequently used prophylaxis. Diclofenac is predominantly metabolized by various cytochrome P450 enzymes. The potential presence of single nucleotide polymorphisms (SNP) in these enzymes could cause interindividual variability in metabolism rates, which could affect serum plasma levels of diclofenac. Given the limited available research on this subject, the aim of this study was to investigate whether differences in presence of SNPs in the CYP-enzymes involved in diclofenac metabolism were associated with PEP.

Aims & Methods: This multicentre cohort study included patients above 18 years who underwent ERCP between 2012 and 2022. Upon inclusion, patients were divided into the PEP or control group. Real-time polymerase chain reactions were performed on buccal smear samples to identify gene variants involved in the diclofenac metabolism (e.g. CYP2C8*3). Secondary endpoints were validation of known and possibly yet unknown risk factors for PEP.

Results: In total, 103 patients were included in the PEP group and 245 in the control group. DNA amplification was possible in 91.5% of the genetic variants and revealed that heterozygous carriers of CYP2C8*3 variant were associated with a lower frequency of PEP (OR 0.2; 95% CI 0.0-0.8). Pancreatic duct cannulation (OR 3.0; 95% CI 1.4-6.6) and pre-cut sphincterotomy (OR 3.1; 95% CI 1.2-8.0) were both found as independent risk factors for PEP.

Conclusion: This study showed that heterozygous carriers of the CYP2C8*3 variant have a lower risk of developing PEP. To investigate gene variants affecting real-time diclofenac plasma levels, we have started a study in which we prospectively collect blood samples to enhance DNA quality and to analyze the existence of a correlation between PEP and reduced diclofenac levels. If this correlation is confirmed, further research is needed to investigate the optimal dosage of diclofenac in wild type CYP2C8 patients.

Disclosure: Nothing to disclose.

MP024

RNA-SEQUENCING ON EUS-ACQUIRED TISSUE OF PANCREATIC CANCER IS FEASIBLE AND ALLOWS IDENTIFICATION OF BIOMARKERS OF PROGNOSIS AND OF RESPONSE TO INTENSIFIED CHEMOTHERAPY

L. Archibugi¹, C. Fortunato¹, P. Lazzano¹, R. Ponz de Leon Pisani¹, M. Tacelli¹, P. Zaccari¹, M.C. Petrone¹, G. Rossi¹, L. Apadula¹, G. Vanella¹, C. Sette², C. Doglioni³, M. Falconi³, M. Reni³, P.G. Arcidiacono¹, G. Capurso¹

¹Hospital San Raffaele, Pancreato-biliary Endoscopy And Endosonography Division, Milan, Italy, ²Cattolica University, Rome, Italy, ³Hospital San Raffaele, Milan, Italy

Contact E-Mail Address: livia.archibugi@hotmail.it

Introduction: There are limited molecular features to allow treatment personalization and outcome prediction of Pancreatic-Ductal-Adenocarcinoma (PDAC) patients. Two transcriptome subtypes have been identified: classical and basal-like. Classical PDACs show better prognosis and response to FOLFIRINOX, while basal-like display an opposite behaviour. This transcriptome-based classification is not straightforward and relies mainly on surgical series, with limited data on EUS-FNA samples. We have recently showed that the splicing factor QKI is a determinant of basal-like signature and that its evaluation together with GATA6 has strong prognostic capacity.

Aims & Methods: Our aim was to investigate transcriptome subtypes and gene expression of specific biomarkers on baseline EUS-FNA samples of PDAC patients and their association with prognosis and response to chemotherapy. 85 PDAC patients who underwent EUS at diagnosis were enrolled in a prospective study and FNA samples investigated by RNA-seq. PURIST score was applied to define subtypes, Differential Gene Expression DGE analysis was performed and the prognostic value of QKI and GATA6 expression was investigated. The outcomes were overall survival (OS) and progression-free survival (PFS) corrected for age and stage.

Results: RNA-seq was successful in 84/85 (98.8%) samples. According with PURIST, 4 patients were classified as basal-like (4.8%), 80 being classical. OS was lower in Basal-like vs classical patients (5.5 vs 13 months; p=0.01), with increased risk of death (HR 5.6; 95%CI: 1.5-20.9; p=0.01). PURIST score also correlated inversely with OS (r=-0.4; p=0.0002).

In 64 patients treated with first-line chemotherapy (FOLFIRINOX n=24; Abraxane-Gemcitabine, AG n=30; PAXG n=10) QKI expression correlated with OS (r=-0.36; p=0.0038). Among patients treated with FOLFIRINOX, median PFS was 7 months (IQR 2-9) in patients with a QKI/Gata6 ratio >1.13 and not reached in patients with ratio ≤1.13 (HR=5.1; 95%CI: 1.2-21.5); QKI/GATA6 ratio was not associated with PFS in patients treated with the other regimens.

At DGE analysis REG4 was the most enriched gene in patients with PFS >6 months; a cut-off for REG4 expression >111 was associated with response to AG (HR=0.2; 95%CI: 0.090-0.59; p=0.002).

Conclusion: Transcriptome analysis of EUS-FNA samples is feasible and allows stratification of PDAC patients in terms of prognosis and chemosensitivity. Few selected classifiers such as QKI, GATA6 and REG4 may be sufficient to predict response to certain treatments.

Disclosure: Nothing to disclose.

MP025

INCREASED NEEDLE PASSES FOR COMPARABLE DIAGNOSTIC YIELD IN ENDOSCOPIC ULTRASOUND-GUIDED TISSUE ACQUISITION FOR PANCREATIC STIFF LESIONS MEASURED BY ELASTOGRAPHY

W.H. Paik¹, T.S. Lee¹, S.H. Lee², J.-K. Ryu¹

¹Seoul National University Hospital, Dept. of Internal Medicine, Seoul, South Korea, ²Seoul National University Hospital, Internal Medicine, Seoul, South Korea

Contact E-Mail Address: iatrus@hanmail.net

Introduction: Pancreatic cancer is characterized by tissue stiffness due to the high concentration of cancer-associated fibroblasts and extracellular matrix. Endoscopic ultrasound-guided tissue acquisition (EUS-TA) is performed to diagnose pancreatic cancer but yields false-negative results attributed to inadequate specimens. EUS-elastography is a real-time assessment method to pancreatic tissue stiffness.

Aims & Methods: This study aims to investigate the correlation between diagnostic yield and the number of needle passes based on the stiffness measured by elastography. Patients who underwent EUS-TA for pancreatic solid mass were enrolled. The number of needle passes during EUS-TA was determined based on macroscopic on-site evaluation. Tissue stiffness measurements were taken using EUS-elastography.

The primary study outcome was the diagnostic yield. The secondary outcome included the number of needle passes required for a diagnosis.

Results: A total of 652 patients were included. The average stiffness differed depending on the location of the tumor, and high-stiffness group had more malignant lesions.

Although the diagnostic yield was not significantly different between groups, the number of needle passes was significantly higher in the high-stiffness group (3.6 ± 1.0 vs. 3.2 ± 0.9 , $p < 0.001$).

Conclusion: The higher the stiffness of the pancreatic mass in EUS-elastography, the more needle passes are required to achieve a comparable diagnostic yield.

Disclosure: Nothing to disclose.

MP026

DRY SUCTION VERSUS WET SUCTION TECHNIQUE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSY FOR DIAGNOSIS OF SOLID PANCREATIC LESIONS: A MULTICENTER RANDOMIZED CONTROLLED NON-INFERIORITY TRIAL

S. Xu¹, J. Wang¹, J. Guo², F. Xie¹, Y. Meng³, P. Peng⁴, H. Hu⁵, Y. Huang⁵, S. Liu¹, M. Qin⁴, J. Yao³, Y. Li¹

¹Nanfang Hospital, Southern Medical University, Guangzhou, China, ²Second Affiliated Hospital, Guangzhou Medical University, Guangzhou, China, ³Shenzhen People's Hospital, Second Clinical Medical Sciences of Jinan University, Shenzhen, China, ⁴The Second Affiliated Hospital of Guangxi Medical University, Nanning, China, ⁵Nanfang Hospital, Southern Medical University, Guangzhou, China

Contact E-Mail Address: xushenglin16@163.com

Introduction: Endoscopic ultrasound-guided fine-needle aspiration/biopsy (EUS-FNA/B) has been widely used for the diagnosis of solid pancreatic lesion.

Studies have shown that the wet suction technique in EUS-FNA generates better histologic diagnostic accuracy and specimen quality than the dry suction technique.

However, conclusions of wet suction on the diagnostic accuracy of EUS-FNB are still controversial. Besides, the optimal number of passes for EUS-FNB has not been determined.

We aimed to design a multicenter randomized trial to compare the diagnostic accuracy of dry suction versus wet suction technique in solid pancreatic lesions using 22G Franseen needles and determine the optimal number of passes required for EUS-FNB without onsite cytopathologist.

Aims & Methods: This is a multi-center, open-label, randomized controlled and non-inferiority trial with two parallel groups. The patients with solid pancreatic lesion will undergo EUS-FNB using 22G Franseen needle in 4 tertiary hospitals in China and will be randomly assigned to the dry suction group and wet suction group in a ratio of 1:1.

The primary endpoint of this study is to compare the diagnostic accuracy of EUS-FNB for solid pancreatic lesions using the dry or wet suction technique.

Secondary endpoints include the optimal number of needle passes, sensitivity, specificity, specimen quality, time of the procedure, and rates of complications.

Results: Of the 195 patients undergoing EUS-FNB enrolled in the final analysis, 96 were randomized to the dry suction group and 99 to the wet suction group. The diagnostic accuracy was 98.95% and 98.98% in the dry and wet groups, respectively, with a 0.05% difference in accuracy between the study groups (two-sided 90% CI, -4.88% to 4.82%, $P=0.989$).

Diagnostic accuracy was shown to be non-inferior because the lower bound of the 90% confidence interval falls to the right of the non-inferiority margin. Compared to the wet group, no significant differences were seen in the sensitivity (98.80 % vs 98.77 %, $P = 1$) and specificity (100 % vs 100 %, $P = 1$) in the dry suction group.

The overall adverse event rate was 0.52 %, with 0 and 1.02 % in the dry and wet groups, respectively ($P = 1$). In terms of specimen quality, no significant differences were also seen in the two groups in sample adequacy (100 % vs 98.3 %, $P = 0.492$) and level of blood contamination ($P = 0.319$). In terms of puncture time in the dry group compared to the wet group, there was no statistically significant (18.82±8.21 min vs. 18.92±8.99 min, $P=0.952$), but the wet suction required more time to prepare the saline and the needle.

No significant improvement in diagnostic accuracy was seen with the 2nd needle compared to the 1st needle of EUS-FNB (97.41% vs 95.34% , $P=0.276$), and no significant improvement in diagnostic accuracy was seen with the 3rd shot compared to the 2nd shot of EUS-FNB (98.96% vs 97.41% , $P=0.446$).

Conclusion: The dry suction technique is non-inferior to the wet suction technique, while saving steps and time. In the absence of rapid on-site evaluation (ROSE), only 1 pass was required to reach the diagnostic accuracy ≥ 95% using EUS-FNB with Franseen needle.

Disclosure: Nothing to disclose.

MP027

PREDICTING THE NEED FOR STEP-UP AFTER EUS-GUIDED DRAINAGE OF PERIPANCREATIC FLUID COLLECTIONS, INCLUDING QNI SCORE VALIDATION: A PROSPECTIVE COHORT STUDY

G. Vanella^{1,2}, R. Leone^{1,2}, F. Frigo^{1,2}, G. Dell'Anna^{1,2}, G. Rossi¹, G. Guazzarotti³, D. Palumbo³, P. Preatoni⁴, L. Aldrighetti^{2,5}, M. Falconi^{2,6}, G. Capurso^{1,2}, P.G. Arcidiacono^{1,2}

¹IRCCS San Raffaele Scientific Institute, Pancreatobiliary Endoscopy and Endosonography Division, Milan, Italy, ²Vita-Salute San Raffaele University, Milan, Italy, ³IRCCS San Raffaele Scientific Institute, Radiology Department, Milan, Italy, ⁴IRCCS San Raffaele Scientific Institute, Gastroenterology and Digestive Endoscopy Unit, Milan, Italy, ⁵IRCCS San Raffaele Scientific Institute, Hepatobiliary Surgery Unit, Milan, Italy, ⁶IRCCS San Raffaele Scientific Institute, Pancreatic Surgery Unit, Milan, Italy

Contact E-Mail Address: g.e.vanella@gmail.com

Introduction: Despite EUS-guided drainage (EUS-FCD) is the preferred modality for management of peripancreatic fluid collections (PFCs), factors predicting the need for step-up to additional procedures (including radiology, surgery or additional endoscopies) are retrospectively explored in studies restricted to Lumen Apposing Metal Stents (LAMS) or excluding pseudocysts and post-surgical collections, which might require a step-up as well.

Aims & Methods: All consecutive candidates to EUS-FCD with either LAMS or Double-pigtail Plastic Stents (DPPS) between 2020-2023 were included in a Prospective Registry of Therapeutic EUS (PROTECT). The role of baseline clinical and morphological factors, including the Quadrant / Necrosis / Infection (QNI) score, in predicting the need for any step-up to additional procedures was evaluated by stepwise logistic regression.

Results: Twenty-three post-surgical PFCs, 19 pseudocysts and 18 walled-off necrosis (WOPN) were included, 42% treated with LAMS and 58% with DPPS based on morphology. Clinical success was 92.9%, but 38% of patients required a step-up to necrosectomy (26.7%) or additional procedures.

Patients requiring step-up versus those sufficing drainage had a higher number of quadrants involved (OR=3.6 [1.5-8.4]), a more frequent paracolic extension (OR=6 [1.4-26]), a higher necrosis content ($\geq 30\%$, OR=7.2 [1.8-28.4]; $\geq 60\%$ OR=25.2 [4.2-153]) and were in the high-risk group according to the QNI score, with no difference in the diameter and rate of superinfection.

At multivariate analysis, being in the high-risk QNI group was the only independent predictor of step-up (OR=9.8 [2.9-32.9]). The score however was not able to stratify in analyses restricted to WOPN only or LAMS only. High-risk QNI patients presented also a longer hospital stay (17.5 [8-45] vs 4 [2-6.5], $p=0.001$), without any difference in ICU stay and nutritional support.

Conclusion: In this prospective series of consecutive non-selective PFCs undergoing EUS-FCD, QNI score was the only independent predictor of any need for step-up to additional procedures, and strongly correlated to the EUS-FCD allocation to LAMS versus DPPS, unravelling a potential additional utility.

Disclosure: GV reports travel grants from Pentax Medical, Boston Scientific and Euromedical, and lecture fees by Boston Scientific. All the other authors declare no conflict of interest.

MP028

NEED OF ENDOSCOPIC NECROSECTOMY IN WALLED-OFF PANCREATIC NECROSIS TREATED WITH LAMS: A PROSPECTIVE VALIDATION OF A PREDICTIVE CLINICAL INDEX

S. Bosso¹, G. Rizzatti¹, G. Tripodi¹, F. Borrelli de Andreis¹, F. Attili¹, A. Milani¹, A. Gasbarrini¹, C. Spada¹, A. Larghi¹

¹Policlinico Universitario A. Gemelli IRCSS, Rome, Italy

Contact E-Mail Address: silvia.bosso01@icatt.it

Introduction: The endoscopic ultrasound-guided drainage by means of Lumen-Apposing Metal Stent (LAMS) represents a minimally invasive treatment of Walled-Off Pancreatic Necrosis (WOPN). In order to achieve a complete healing of the lesion and depending on the amount of the necrosis, a subset of patients may benefit from a further endoscopic necrosectomy (EN).

Aims & Methods: An early identification of the subjects requiring EN may therefore represent a valuable clue in the clinical management of patients with WOPN.

In a first step of the study we retrospectively evaluated 53 patients ("training group") diagnosed with WOPN (16 females and 37 males, aged from 28 to 87) admitted to our Institution over the period 2013-2023. In 24 cases (45.3%) EN was required and then performed after LAMS placement. In this group, we identified a predictive Necrosectomy-index (NI), by means of a discriminant-function statistical analysis, taking into consideration only the individual variables showing a statistical difference (single tail $p < 0.10$, one-way variance analysis) between the patients requiring EN and the remaining subjects. Such a retrospectively-assessed NI is then able to provide an "a priori" identification of the subset of WOPN patients requiring necrosectomy.

Thereafter, NI predictive value and clinical reliability (global accuracy, predictive value and overall statistical significance) were prospectively tested in a separate set of patients with WOPN ("challenge group"), consisting of 53 patients (15 females and 38 males, aged from 23 to 85).

Results: In the "training" group, the retrospective analysis of our data allowed to calculate individual NI by means of the simple function:

$$NI = 336 - (PT\% * 1.26 + Hb \text{ (g/dL)} * 29.54 + PLT \text{ (kU/mm}^3\text{)} * 0.11 - 48.56 * EUS)$$

where EUS stands for the endoscopic US subjective rank of the collection features (0 = fluid; 1 = solid debris; 2 = purulent; 3 = necrosis $< 50\%$; 4 = necrosis $> 50\%$; 5 = completely necrotic).

The proposed NI provides an early discrimination of the subset of WOPN patients requiring EN after LAMS placement (identified by a positive NI) from those not requiring necrosectomy (NI lower than zero), the cut-off between the two groups being therefore represented by a NI = 0.

To increase the predictive ability of the model, the subjects with a NI close to 0 (between 3 and -3) may be considered as "undeterminable", being therefore addressed to EN on the basis of the clinical status, regardless of NI.

In the prospectively evaluated "challenge" group, NI showed a remarkable overall statistical significance ($p < 0.01$). The prospective statistical analysis allowed us to confirm NI clinical value (with a global accuracy of 73.3%, a 68.2% predictive value for positivity and a 78.3% for negativity respectively) in the early identification of WOPN patients requiring EN after LAMS placement. Three patients only (5.7%) showed a NI between 3 and -3, being therefore considered as "undeterminable".

Conclusion: Our data provided a prospective validation of the proposed Necrosectomy Index, confirming its reliable intrinsic predictive value. NI may therefore represent a powerful clinical tool in the patients with WOPN, providing an early identification of those requiring further endoscopic necrosectomy after LAMS placement.

Disclosure: Nothing to disclose.

MP029

VINEGAR INDUCED PANCREATIC JUICE COLLECTION VIA ENDOSCOPIC ULTRASOUND: OPERATING CONDITION EXPLORATION TOWARD MOLECULAR BIOMARKER DISCOVERY AND EARLY DIAGNOSIS OF PANCREATIC CANCER

W. Shi¹, Z. Yan¹, S. Zhang¹, Y. Zhang¹, Q. Jiang¹, Y. Feng¹, Q. Wang¹, X. Wu¹, A. Yang¹

¹Peking Union Medical College Hospital, Gastroenterology, Beijing, China

Contact E-Mail Address: ysfu_2005@126.com

Introduction: Early detection of pancreatic cancer (PDAC) in high-risk patients through molecular biomarkers in pancreatic juice (PJ) is promising but is limited by the lack of safe and effective methods for collecting PJ[1]. Traditional method via ERCP and pancreatic duct cannulation may bring additional risks[2], and intravenous injection of secretin is expensive, may cause complications and is not available in countries including China. Intraduodenal acid infusion can induce secretin release physiologically and is proved to facilitate pancreatic duct cannulation and decrease difficult pancreatic cannulation rate[3].

Thus we aim to investigate the feasibility and safety of PJ collection for molecular biomarker detection via endoscopic ultrasound (EUS) after injection of vinegar into duodenal bulb.

Aims & Methods: 20ml vinegar (5% acetic acid) or 20ml saline was injected into the duodenal bulb and PJ was collected via suction during EUS in patients suspected of having PDAC. The yield of cfDNA concentration, KRAS mutation load and PLA2G1B protein concentration (representing pancreatic source) was compared between vinegar-induced PJ and saline-control-induced PJ, as well as between 3 time periods of vinegar-stimulated PJ (0-5 vs. 5-10 vs. 10-15 minutes). Whole-exome sequencing (WES) was performed on genomic DNA extracts from exfoliated cells from vinegar-stimulated PJ.

Results: PJ from 19 patients diagnosed with PDAC were collected, of which 13 were in the vinegar group and 6 in the saline group. cfDNA concentration, KRAS mutation load and PLA2GB1 level are higher in the vinegar group than in the saline group ($p<0.01$). cfDNA concentration (ng/ μ L) at 5-10min timeframe was higher than 0-5min (82.59 ± 55.44 vs. 5.95 ± 4.60 , $p<0.05$), yet did not differ from 10-15min (75.06 ± 51.65 , $p=0.29$) in the vinegar group. KRAS mutation load (%) showed the same trend. However, PLA2G1B concentrations at 3 timeframes were not significantly different in the vinegar group. WES on genomic DNA extracted from PJ exfoliated cells was performed in 10 patients of the vinegar group, which revealed a large number of driver mutations (*PLEC*, *MUC16*, *BIRC6*, *HERC1*, *SYNE1*, etc.) and the expression of high-frequency mutated genes (*CSMD2*, *EPPK1*, *FSIP2*, *MUC17*, *AGMO*, etc.), some of which were common across different individuals. Furthermore, according to pathological result and clinical follow-up for more than 6 months, 8 patients were finally diagnosed of PDAC while 2 patients were diagnosed of pancreatitis (one with chronic pancreatitis and the other with autoimmune pancreatitis).

Of note, some mutations highly associated with PDAC were only observed in the malignant group, represented by *PTGER1*, *RHEB*, *IER3IP1*, *DLC1*, *GKN1*, *TNS3*, etc.

Conclusion: Vinegar-induced PJ collection via EUS is feasible and safe. We established that the optimal protocol is suction under EUS for 10 minutes after injection of 20ml vinegar into duodenal bulb for 2 minutes.

This resulted in the most favourable detection of molecular biomarkers including PJ cfDNA as well as exfoliated cells based on their yield, concentration and expression, which were helpful for precise diagnosis of PDAC. Further studies are needed to explore the potential of the collected PJ biomarkers in early detection and pathogenesis researches of PDAC and its precursor lesions.

References: [1] Wang J, Raimondo M, Guha S, et al. Circulating microRNAs in pancreatic juice as candidate biomarkers of pancreatic cancer. *J Cancer* 2014;5:696-705.

[2] Hart PA, Topazian M, Raimondo M, et al. Endoscopic pancreas fluid collection: Methods and relevance for clinical care and translational science. *Am J Gastroenterol* 2016;111:1258-66.

[3] Fang J, Wang SL, Zhao SB, et al. Impact of intraduodenal acetic acid infusion on pancreatic duct cannulation during endoscopic retrograde cholangiopancreatography: A double-blind, randomized controlled trial. *JGH* 2018;33: 1804-1810.

Disclosure: None.

MP030

IMPACT OF EUS-GUIDED CHOLEDOCHODUODENOSTOMY VERSUS CONVENTIONAL BILIARY DRAINAGE IN PATIENTS UNDERGOING PANCREATODUODENECTOMY FOR MALIGNANT DISTAL BILIARY OBSTRUCTION: A MULTICENTER PROPENSITY SCORE MATCHED STUDY AND SURVEY

J.A. Fritzsche^{1,2,3}, M.J. de Jong⁴, B. Bonsing⁵, O.R. Busch^{2,3,6}, F. Daams^{2,3,7}, F. van Delft⁴, W.J. Derksen^{8,9}, L.M.J.W. van Driel¹⁰, J.I. Erdmann^{2,3,6}, S. Festen¹¹, P. Fockens^{1,2,3,12}, E.-J.M. Van Geenen⁴, B. Groot Koerkamp¹³, F.J. Hoogwater¹⁴, A. Inderson¹⁵, G. Kazemier^{2,3,7}, S.D. Kuiken¹⁶, M.S. Liem¹⁷, D.J. Lips¹⁷, M. Meerdink¹⁴, M. Nijkamp¹⁴, W.W. te Riele^{8,9}, H.C. van Santvoort^{8,9}, P.D. Siersema^{4,10}, M. Stommel¹⁸, N.G. Venneman¹⁹, R.C. Verdonk²⁰, F.P. Vleggaar²¹, R.F. de Wilde¹³, M.G. Besselink^{2,3,6}, R.L. van Wanrooij^{2,3,12}, R.P. Voermans^{1,2,3}

¹Amsterdam UMC, location University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands,

²Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³Cancer Center Amsterdam, Amsterdam, Netherlands, ⁴Radboud University Medical Center, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands,

⁵Leiden University Medical Center, Department of Surgery, Leiden, Netherlands, ⁶Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands, ⁷Amsterdam UMC, location Vrije Universiteit, Department of Surgery,

Amsterdam, Netherlands, ⁸St Antonius Hospital, Department of Surgery, Nieuwegein, Netherlands, ⁹University Medical Center Utrecht, Department of Surgery, Utrecht, Netherlands, ¹⁰Erasmus University Medical Center, Department of Gastroenterology

and Hepatology, Rotterdam, Netherlands, ¹¹OLVG, Department of Surgery, Amsterdam, Netherlands, ¹²Amsterdam UMC, location Vrije Universiteit, Department of Gastroenterology and

Hepatology, Amsterdam, Netherlands, ¹³Erasmus University Medical Center, Department of Surgery, Rotterdam, Netherlands, ¹⁴Universitair Medisch Centrum Groningen, Department of

Surgery, Groningen, Netherlands, ¹⁵Leiden University Medical Center, Department of Gastroenterology and Hepatology,

Leiden, Netherlands, ¹⁶OLVG, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁷Medisch Spectrum Twente, Department of Surgery, Enschede, Netherlands,

¹⁸Radboud University Medical Center, Department of Surgery, Nijmegen, Netherlands, ¹⁹Medisch Spectrum Twente, Department of Gastroenterology and Hepatology, Enschede, Netherlands,

²⁰St Antonius Hospital, Department of Gastroenterology and Hepatology, Nieuwegein, Netherlands, ²¹University Medical Center Utrecht, Department of Gastroenterology and Hepatology,

Utrecht, Netherlands

Contact E-Mail Address: j.a.fritzsche@amsterdamumc.nl

Introduction: Patients with malignant distal biliary obstruction who are eligible for curative resection face the risk of complications from preoperative biliary drainage, especially pancreatitis. Endoscopic ultrasound guided choledochoduodenostomy (EUS-CDS) using a lumen apposing metal stent (LAMS) is a promising alternative for endoscopic retrograde cholangiopancreatography (ERCP) but data in patients undergoing pancreatoduodenectomy (PD) are limited. Therefore, in daily clinical practice multidisciplinary teams are reluctant to opt for EUS-CDS in patients with potentially resectable tumors.

Aims & Methods: Patients who underwent a PD between January 2020 and December 2022 after preoperative biliary drainage by EUS-CDS were included. Prospectively collected data from patients in the Dutch Pan-

creatic Cancer Audit were retrospectively analyzed. Primary endpoint was major postoperative complications, defined as Clavien-Dindo score ≥ 3 . Secondary endpoints included overall complications, pancreatic surgery specific complications (i.e. postoperative pancreatic fistula, delayed gastric emptying, hemorrhage, and chyle leakage), in-hospital mortality and hospital stay. A propensity score matching (1:3) analysis was performed using patient and tumor characteristics, neoadjuvant therapy, type of stent, and hospital volume. Surgeons who performed a PD in a patient who underwent pre-operative EUS-CDS were requested to fill-out a 5-questions survey directly after the surgical procedure.

Results: Overall, 937 patients after PD were included of which 42 patients underwent EUS-CDS pre-operatively and 895 patients ERCP. Major postoperative complications occurred in 8 patients (19%) in the EUS-CDS group and 292 patients (33%) in the ERCP group (RR 0.50; 95% CI, 0.23-1.07). No significant differences were observed in the secondary endpoints. Time between biliary drainage and surgery in patients without neoadjuvant therapy differed significantly between the EUS-CDS group (median 32 days [IQR 22-39.25]) and the ERCP group (median 41 days [IQR, 28-57]; $p=0.005$). Operative time was shorter in the EUS-CDS group (median 309 min [IQR 245.75-353] vs 349 min [IQR 281-425]; $p=0.002$). Results were similar after propensity-score matching.

The survey was completed on 29 resections after EUS-CDS. In the majority ($n=22$, 76%) there was no direct visualization of the stent during the PD. In most patients, the resection was not ($n=13$, 45%) or slightly ($n=8$, 28%) influenced by the EUS-CDS according to the surgeon. The stent did not hamper the creation of the hepaticojejunostomy.

Conclusion: This nationwide retrospective study found EUS-CDS to be safe without increase in (major) postoperative complications after PD as compared to ERCP. Moreover, surgeons did not encounter evident difficulties during most of the resections.

Disclosure: Freek Daams reports research grants from Medtronic, and received speaker's fees from Medtronic, and proctoring fees from Intuitive. Paul Fockens performed as a consultant for Olympus and Cook Endoscopy. Erwin M. van Geenen reports research grants from Olympus, Boston Scientific, and MTW Endoskopie. Peter D. Siersema reports research grants from Pentax and Fujifilm. Roy L.J. van Wanrooij performed as a consultant for Boston Scientific. Rogier P. Voermans reports research grants from Boston Scientific and Prion Medical, performed as a consultant for Boston Scientific, and received speaker's fees from Mylan and Zambon. All outside the submitted work. The remaining authors have no conflicts of interest or financial ties to disclose.

Challenges in upper GI and small bowel cancer

10:30-11:30 / Poster Stage 5

MP031

GASTRIC CANCER RISK ASSESSMENT OF GASTRITIS IN CLINICAL PRACTICE BY USING THE HISTOLOGICAL INFORMATION RECOMMENDED BY THE UPDATED SYDNEY SYSTEM: THE OLGIMA SYSTEM

P.G. Delgado-Guillena¹, E. Barreiro Alonso², J. Tejedor-Tejada³, A. Huerta Madrigal⁴, S.P. Ortega⁵, O. Patrón⁶, D. Zaffalon⁷, R. Vicente Lidón⁸, N. Felipez Varela⁹, C. Mangas-Sanjuan¹⁰, P. Gonçalves Da Cunha¹¹, L. Hernández Villalba¹², R.M. Saiz Chumillas¹³, S. Montori Pina⁹, J. Llach¹⁴, M. Cuatrecasas¹⁵, M.G. Fernández-Esparrach¹⁶, L. Moreira Ruiz¹⁷, E. Albéniz-Arbizu¹⁸, EDGAR/EPIGASTRIC Consortium
¹Hospital de Mérida, Department of Gastroenterology, Mérida, Spain, ²HOSPITAL DE CABUEÑES, APARATO DIGESTIVO, Gijón, Spain, ³Hospital Universitario Río Hortega, Gastroenterology, Valladolid, Spain, ⁴H. Galdakao-Usansolo, Gastroenterology Service, Galdakao, Spain, ⁵Hospital Comarcal de Inca, Department of Gastroenterology, Mallorca, Spain, ⁶Hospital Llevant, Islas Baleares, Spain, ⁷Hospital Clinic, Institut Clínic de Malalties Digestives i Metabòliques, Barcelona, Spain, ⁸H. U. MIGUEL SERVET, Zaragoza, Spain, ⁹Hospital Universitario de Navarra, Pamplona, Spain, ¹⁰Hospital General Universitario de Alicante, Gastroenterology, Alicante, Spain, ¹¹SERVIDIGEST CLINIC, Advanced Endoscopy, Barcelona, Spain, ¹²Santos Reyes, Gastroenterology, Aranda de Duero, Spain, ¹³Hospital Universitario de Burgos, Gastroenterology, Burgos, Spain, ¹⁴HOSPITAL CLINIC OF BARCELONA, Medicine, Barcelona, Spain, ¹⁵Hospital Clinic de Barcelona, Department of Pathology, Barcelona, Spain, ¹⁶Hospital Clinic de Barcelona, Inst. de Malalties Digestives, Barcelona, Spain, ¹⁷Hospital Clinic de Barcelona, Gastroenterology, Gava, Spain, ¹⁸COMPLEJO HOSPITALARIO DE NAVARRA, Servicio Aparato Digestivo, Pamplona, Spain

Contact E-Mail Address: pgdg20@gmail.com

Introduction: The Updated Sydney System recommends reporting the severity of both glandular atrophy (GA) and intestinal metaplasia (IM) as two independent parameters. However, the OLGA system assesses both GA and IM together as part of the same entity which should be reported as an average severity. The OLGIM system is based on the IM severity recommended by the updated Sydney system.

Thus, the final OLGIM score can be estimated by any clinician. Currently, no system addresses the severity of both GA and IM as they are reported following the updated Sydney recommendation.

Aims & Methods: This study aimed to assess the utility of a new system, OLGIMA (Operative Link on Gastric IM and GA assessment), as a tool to identify patients at higher risk for GC in daily practice.

Consecutive diagnostic UGI endoscopies performed for any indications in patients older than 18 years old were recorded prospectively in 21 Spanish hospitals between April 2021 and July 2023. Protocolized gastric biopsies were taken according to the Updated Sydney consensus.

We excluded patients with dysplasia, any malignancy, suspicion of autoimmune chronic atrophic gastritis, and lack of histological data. The severity of both GA and IM was assessed in the antrum (including incisura) and corpus following the updated Sydney system.

After that, we considered the most advanced severity (none:0; mild:1; moderate:2; marked:3) provided for any of them in each of the two topographical areas.

Then, the OLGIMA staging was done according to the same methodology used by the OLGA and OLGIM systems.

Results: A total of 998 patients were included. The median age was 57 (IQR 46 - 67), and 64% were women. Hp infection was identified in 334 (35%) patients (19% active infection and 16% eradicated). GA was identified in 192 (19.2%) patients which was limited to the antrum in 113 (11.3%) cases and extensive in 79 (7.9%). IM was identified in 159 (15.9%) patients which was limited to the antrum in 114 (11.4%) cases and extensive in 45 (4.5%). According to IM severity, 27 (2.7%) patients were OLGIM III/IV. According to GA severity, 22 (2.2%) patients were significantly extensive. The OLGIM system would have missed 12 (1.2%) patients with GA at higher risk. Considering both criteria, we would have detected 39 (3.9%) patients at higher risk in total (17 OLGIM III-IV, 12 extensive significant GA, and 10 both OLGIM III-IV and extensive significant GA). The new OLGIMA system categorized all 39 (3.9%) patients, OLGIM III-IV and significantly extensive GA, in the high-risk group (OLGIMA III/IV).

Conclusion: The new OLGIMA system (based on the severity of IM and GA recommended by the updated Sydney system) was able to detect patients at higher risk including all cases of OLGIM III/IV and also with advanced GA. The OLGIMA staging is much simpler and it can be estimated by any clinician regardless of whether the biopsy from incisura was taken.

References: Rugge M, Meggio A, Pennelli G et al. Gastritis staging in clinical practice: the OLGA staging system. Gut. 2007;56:631-6

Capelle LG, de Vries AC, Haringsma J et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. Gastrointest Endosc. 2010;71:1150-8

Pimentel-Nunes P, Libânio D, Marcos-Pinto R et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy. 2019;51:365-388.

Disclosure: Nothing to disclose.

MP032

ANTITUMOR[A1] EFFECT[A2] OF TALAPORFIN PHOTO DYNAMIC THERAPY (PDT) COMBINED WITH DUAL IMMUNE CHECKPOINT INHIBITION

M. Tanaka¹, M. Sasaki¹, Y. Kojima¹, H. Nishie¹, H. Kataoka¹

¹Nagoya City University Graduate School of Medical Sciences, Departments of Gastroenterology and Metabolism, Nagoya, Japan

Contact E-Mail Address: mtanaka@med.nagoya-cu.ac.jp

Introduction: Photodynamic therapy (PDT) is a treatment method in which tumor tissues incorporated with a photosensitizer (PS) are irradiated with incident light at an appropriate wavelength, causing a photochemical reaction that releases free radicals, resulting in the necrosis of tumor cells via oxidative stress. The second-generation photosensitizer, talaporfin, is rapidly eliminated from the skin and requires a shorter sunshade period (two weeks). The "abscopal effect," where radiotherapy at one site leads to regression of metastatic tumors not irradiated, has been reported in PDT (1). Studies on the synergistic effect of the abscopal effect in combination with immune checkpoint inhibitors (ICIs) have been reported in radiotherapy and other related fields. PDT induces not only a direct cytotoxic effect but also enhances tumor immunity (2). Therefore, we hypothesized that the addition of ICIs to PDT would regulate the immune system and promote the cancer immunity cycle, leading to the effective inhibition of tumor growth at both irradiated and non-irradiated sites. CTLA-4 and PD-1 inhibit T-cell activation through distinct and potentially synergistic mechanisms (3). In this study, we investigated the therapeutic efficacy of combining talaporfin PDT (TS-PDT) with dual ICIs (targeting PD-L1 and targeting CTLA-4).

Aims & Methods:

1. To analyze the cell death mechanism induced by TS-PDT, we performed an apoptosis/necrosis assay and stained the cells with annexin V-fluorescein isothiocyanate and propidium iodide for flow cytometric analysis.
2. Furthermore, we measured CRT translocation after TS-PDT using immunofluorescence staining. We also measured the supernatant concentration of HMGB1 in the culture medium treated with TS-PDT to evaluate the release of HMGB1.
3. We assessed the in vivo efficacy of Talaporfin PDT, ICIs, and their combination using a xenograft tumor model.
4. For immunohistochemical analysis, we examined the expression of CD4, CD8, and PD-L1.
5. IFN- γ , perforin 1 and granzyme B mRNA expression levels in tumors were measured by qRT-PCR.

Results:

1. The percentage of cells undergoing apoptosis and necrosis was higher in the TS-PDT group than in the untreated group. The mean fluorescence intensity of active caspase-3, a marker of apoptosis, was higher in the TS-PDT-treated cells than in the untreated cells.
2. Translocation of CRT from the nucleus to the cytoplasm was induced by TS-PDT. HMGB1 levels in the supernatant increased after TS-PDT.
3. The combination exhibited significantly greater tumor growth inhibition than either agent alone in a xenograft tumor model.
4. In non-irradiated tumors, the expression levels of CD4, CD8, and PD-L1 were elevated in the TS-PDT group. Combination of TS-PDT and ICIs reduced PD-L1 expression.
5. In the tumors on the non-irradiated side, combination therapy tended to induce IFN- γ , perforin 1, and granzyme B

Conclusion: Our results demonstrate that TS-PDT not only induces a direct cytotoxic effect on tumor cells but also enhances anti-tumor immunity and exhibits synergism with dual ICIs. Therefore, these findings suggest that a combination of TS-PDT and dual ICI antibodies may be a promising approach for the development of anti-tumor therapeutics.

References: (1) Duan X., Chan C., Guo N., Han W., Weichselbaum R.R., Lin W. Photodynamic therapy mediated by nontoxic core-shell nanoparticles synergizes with immune checkpoint blockade to elicit antitumor immunity and antimetastatic effect on breast cancer. *J. Am. Chem. Soc.* 2016;138:16686–16695. doi: 10.1021/jacs.6b09538.

(2) Makiko Sasaki, Mamoru Tanaka, Yuki Kojima, Hirotada Nishie, Takaya Shimura, Eiji Kubota, Hiromi Kataoka. Anti-tumor immunity enhancement by photodynamic therapy with talaporfin sodium and anti-programmed death 1 antibody. *Mol Ther Oncolytics*. 2023 Jan 2;28:118-131. doi: 10.1016/j.omto.2022.12.009. eCollection 2023 Mar 16.

(3) Parry RV, Chemnitz JM, Frauwirth KA, Lanfranco AR, Braunstein I, Kobayashi SV, Linsley PS, Thompson CB, Riley JL. CTLA-4 and PD-1 receptors inhibit T-cell activation by distinct mechanisms. *Mol Cell Biol*. 2005 Nov; 25(21): 9543–9553. doi: 10.1128/MCB.25.21.9543-9553.2005.

Disclosure: Nothing to disclose.

MP033

COMBINED OESOPHAGEAL AND AIRWAY STENTING FOR MALIGNANT OESOPHAGEAL STRICTURES: THE UK'S LARGEST TERTIARY CENTRE EXPERIENCE AND DEVELOPMENT OF A NOVEL ALGORITHM

J. Gertner¹, M. Mullin¹, R. Shea¹, N. Aslam¹, M. Banks¹, O.F Ahmad^{1,2}, R. Sweis¹, D. Graham¹, N. Navani¹, R. Thakrar¹, V. Sehgal¹

¹University College London Hospital, London, United Kingdom,

²Wellcome/EPSC Centre for Interventional & Surgical Sciences, UCL, London, United Kingdom

Contact E-Mail Address: juliangertner@gmail.com

Introduction: Malignant oesophageal strictures can cause airway compromise and fistula formation¹. Combined oesophageal and airway stenting is a potential treatment yet no guidelines exist². This study aims to describe the outcomes of same-session oesophageal and airway endoscopic stenting for malignant strictures and propose an algorithm for intervention.

Aims & Methods: A retrospective study on patients undergoing same-session gastroenterology (GI) and respiratory endoscopy at University College London Hospital, 2019-2023. All procedures were with anaesthetic-led propofol sedation. Endoscopic decision making was based on preprocedure multidisciplinary team meeting (MDM) and intra-procedure clinical assessment. Data collected included malignancy type, luminal narrowing, complications, and mortality.

Results: 26 patients were identified. Mean age was 63 years. Cancer type was oesophageal (81%) or lung (19%). The most common referral indication was dysphagia (42%); airway compromise was often seen on imaging (65%). Stent insertion was oesophageal only (35%), airway only (19%) and dual (27%) (Table 1).

Characteristic	Dual Intervention (N=7)	Oesophageal Intervention alone (N=9)	Airway Intervention alone (N=5)	No Intervention (N=5)
Procedure time, mins	87 (66, 152)	41 (36, 43)	64 (55, 66)	39 (28, 86)
Procedural Airway				
None	6 (86)	8 (89)	3 (60)	3 (60)
Endotracheal tube	0	1 (11)	1 (20)	0
Rigid Bronchoscopy	1 (14)	0	1 (20)	2 (40)
Fistula at endoscopy	4 (57)	3 (33)	3 (60)	2 (40)
Oesophageal narrowing:				
<50%	1 (14)	3 (33)	2 (40)	0
>50%	5 (71)	5 (56)	2 (40)	4 (80)
Not reported	1 (14)	1 (11)	1 (20)	1 (20)
Airway narrowing:				
0-25%	0	7 (78)	0	1 (20)
25-50%	0	2 (22)	0	1 (20)
50-75%	1 (14)	0	0	0
75-100%	6 (86)	0	5 (100)	3 (60) [†]
Location of airway narrowing:				
Not documented	0	3 (33)	0	0
Trachea	3 (43)	4 (44)	0	1 (20)
Left main/lower lobe	3 (43)	1 (11)	3	2 (40)
Right main/lower lobe	0	1 (11)	1	0
Multiple locations	1 (14)	0	1	2 (40)
Type of airway stent:				
Self-expanding metal	6 (86)	0	4 (80)	0
Silicone stent*	1 (14)	0	1 (20)	0
Post Procedure Complications:				
Oesophago-airway fistula	1 (14)	1 (11)	2 (40)	0
Airway stent migration	0	3 (33)	0	0
Airway stent obstruction	1 (14)	0	1 (20)	0
Significant bleeding	0	0	0	0
Respiratory failure	1 (20)	0	1 (20)	0
Repeat procedure	3 (43)	7 (78)	1 (20)	2 (40)

Table 1: Procedure and intervention details for same-session procedures.

Data is presented as N (%) or median (IQR). *Silicone stent includes the placement of one straight bronchial stent and one tracheal Y-stent. [†]two of three patients with no intervention despite significant airway stenosis had multiple locations of airway involvement and stent placement was not feasible.

Airway stenting was common (80%) if airway stenosis was >50%. No airway stenting occurred if stenosis was <50%. After oesophageal stenting, repeat bronchoscopy showed increased airway stenosis in 4 patients (25%). The only intraoperative complication was one oesophageal perforation. New tracheoesophageal fistula was the most common post-intervention complication (15%). Median time from malignancy diagnosis to death was 7.9 weeks.

Conclusion: We present the first algorithm (Figure 1) for endoscopic stenting in patients with malignant oesophageal stricture and airway involvement. We suggest upper GI and respiratory MDM to plan same-session endoscopy with decision-making framed by patient-centred goals given their poor prognosis.

References: 1. Khan A, Hashim Z, Neyaz Z, Agarwal A, Mohindra S, Nath A. Dual Airway and Esophageal Stenting in Advanced Esophageal Cancer With Lesions Near Carina. *J Bronchology Interv Pulmonol.* 2020;27(4):286-293. doi:10.1097/LBR.0000000000000672

2. Bi Y, Ren J, Chen H, Bai L, Han X, Wu G. Combined airway and esophageal stents implantation for malignant tracheobronchial and esophageal disease. *Medicine.* 2019;98(3):e14169. doi:10.1097/MD.00000000000014169

Disclosure: Nothing to disclose.

MP034

PRIMARY GASTRIC SQUAMOUS CELL CARCINOMA : RECENT TRENDS AND SURVIVAL OUTCOME OF DIFFERENT TREATMENT MODALITIES

A. Ellaithy¹, I. Ellaithy¹, M. Ahmed², A.A. El-Sakka³

¹Suez Canal University, Faculty of Medicine, Ismailia, Egypt,

²Cairo University, Faculty of Medicine, Cairo, Egypt, ³Suez Canal University Teaching Hospital, Ismailia, Egypt

Contact E-Mail Address: asmaa.ellithy1@gmail.com

Introduction: Gastric squamous cell carcinoma (GSCC) is an aggressive rare histological subtype accounting for 0.04-0.5% only of all gastric tumors. Due to its scarcity, there are very few case reports in the literature and data are limited to institutional case series with significant variations. Thus, no recommendations for GSCC were published by the European Society of Medical Oncology or the National Comprehensive Cancer Network societies.

Aims & Methods: The aim of this study is to provide the literature with an updated evidence about this rare type for better understanding for its nature and establish a proper management strategy. Data were extracted from the Surveillance, Epidemiology and End Results (SEER) database for 784 patients diagnosed with primary GSCC with sequence 0 or 1 from 2000 to 2020. Patients were selected based on microscopic confirmation for the diagnosis. We used a rate session to calculate the age-adjusted trends as Percent Chance (PC) and Annual Percent Change (APC). We subdivided the patients according to the treatment modality into medical therapy, partial gastrectomy and total gastrectomy group, then followed by smaller subgroups (primary therapy and surgery with systemic therapy). We used a survival session to calculate the relative survival. SPSS version 23 was used for data analysis, Kaplan-Meier and Log-Rank test for survival analysis. The results were considered significant when $P < 0.05$.

Results: GSCC had 2000-2020 PC of -13.3 [APC= -0.5, 95% CI (-1.6: 0.6), $P > 0.05$]. African-Americans had increased rate compared to Caucasians (RR=2.32, 95%CI: 1.96-2.73, $P < 0.0001$). The overall 3-year and 5-year relative survival of GSCC were 21.7% and 17.4%. Out of 502 patients, 341(68.1%) received medical treatment only, 43(8.6%) had partial gastrectomy and 117(23.3%) had total gastrectomy with 5-year relative survival of 10.4%, 38.1% and 44.6% respectively; $P < 0.0001$. Adjuvant chemoradiotherapy had similar 5-year survival compared to surgery with no systemic therapy while both had improved survival compared to surgical

management with systemic chemotherapy only (43.4%, 51.5% and 22.9% respectively; $P = 0.07$). Among the group who received systemic therapy only, primary chemoradiotherapy had improved 5-year relative survival compared to primary chemotherapy and primary radiotherapy (16.3%, 8.1% and 0.0%; $P < 0.0001$).

Conclusion: GSCC is an aggressive malignancy with poor survival outcome. GSCC rates have decreased over the past 20 years. However, the rate in African-Americans is two folds greater to develop GSCC compared to Caucasians. Total gastrectomy had significant improved survival compared to partial gastrectomy and the medical treatment.

These results highlights total gastrectomy as the modality of choice for primary GSCC. As adjuvant chemoradiotherapy had no significant benefit over surgery with no systemic therapy, we discourage the use of systemic therapy to avoid serious systemic side effects related to the systemic treatment for better quality of life after the surgical management.

References: 1. de Lange G, Bouroumeau A, Coron E, Koessler T. Gastric squamous cell carcinoma: A rare malignancy, literature review and management recommendations (Review). *Mol Clin Oncol.* 2023;19(4):2-7.

2. Dong C, Jiang M, Tan Y, Kong Y, Yang Z, Zhong C, et al. The clinicopathological features and prognostic factors of gastric squamous cell carcinoma. *Med (United States).* 2016;95(34):1-7.

3. Akce M, Jiang R, Alese OB, Shaib WL, Wu C, Behera M, et al. Gastric squamous cell carcinoma and gastric adenosquamous carcinoma, clinical features and outcomes of rare clinical entities: A National Cancer Database (NCDB) analysis. *J Gastrointest Oncol.* 2019;10(1):85-94.

Disclosure: Nothing to disclose.

MP035

MULTI-BIOINFORMATICS REVEALED DRUGGABLE PROTEIN NETWORK OF PROGRESSION FROM GASTRIC INTESTINAL METAPLASIA TO GASTRIC ADENOCARCINOMA

G.T. Andersen^{1,2,3}, A. Ianevski¹, M. Resell¹, N. Pojskic⁴, H.-L. Rabben¹, S. Geithus¹, Y. Kodama¹, H. Tomita⁵, D. Kainov¹, J.E. Grønbech^{1,2}, Y. Hayakawa⁶, T.C. Wang⁷, C.-M. Zhao^{1,8}, D. Chen¹

¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²St. Olav's Hospital, Department of Surgery, Trondheim, Norway, ³Namsos Hospital, Department of Surgery, Namsos, Norway, ⁴University of Sarajevo, Institute for Genetic Engineering and Biotechnology, Sarajevo, Bosnia and Herzegovina, ⁵Gifu University Graduate School of Medicine, Department of Tumor Pathology, Gifu, Japan, ⁶Tokyo University Hospital, Department of Gastroenterology, Tokyo, Japan, ⁷Columbia University Medical Center, Division of Digestive and Liver Diseases, New York, United States of America, ⁸Central Norway Regional Health Authority, Trondheim, Norway

Contact E-Mail Address: duan.chen@ntnu.no

Introduction: Biomarkers associated with the progression from gastric intestinal metaplasia (GIM) to gastric adenocarcinoma (GA) could provide valuable insights into identifying patients with increased risk for GA. Currently, the discovery of effective GA biomarkers poses a challenge due to the complexity of predictive and actionable value. Rarely can tumorigenesis be attributed solely to an individual molecule, as GA arises from the complex interplay of various intrinsic and environmental factors and collective interactions among multiple molecules.

Aims & Methods: The aim of this study was to identify potential biomarkers for the GIM-to-GA progression and potential drug repurposing for GIM. Sixty-four surgical biopsies were collected from 16 patients (4 tissue biopsies per patient) at St. Olav's Hospital, Norway. Transcriptome datasets of

GIM, GA, and normal tissues were compared within the same stomachs. Computational platform ScType was used for cell-type identification based on given scRNA-seq data and a comprehensive cell marker database. Ingenuity pathway analysis, Pagerank centrality, GO and MSigDB enrichments, CopyKat, aneuploid analysis, docking analysis, pathology and immunohistochemistry (IHC) were used for data and pathway mining, protein-protein interaction (PPI), and molecular structure-based drug repurposing.

Results: GIM displayed 110 canonical pathways that exhibited a negative correlation with GA. Wnt/ β -catenin, ERK/MAPK, mTOR, neuregulin, and BRCA1 pathways were activated in both GIM and GA. Conversely, pathways such as HIPPO, p53, toll-like receptor, aryl hydrocarbon receptor, LPS/IL-1-mediated inhibition of RXR function, and eIF2 were inactivated in GIM but activated in GA. GIM exhibited elevated gene expression compared to GA in tumor microenvironment-related cells. Particularly, RBP2 expression and goblet cell-related gene expression were found to be restricted in GIM, but not in GA. Chromosome instability occurred mainly in GA cells with high rates of gain or loss of chromosomes 1, 7, 12, 21 (gain), and 5, 7, 8, X (loss). CD44 IHC expression was expanded from the basal part of mucosa in normal and GIM stomachs to the upper part of the mucosa in GA stomachs. PPI analysis of 865 GIM-related proteins showed seven network nodes (i.e., drug targets) including epidermal growth factor receptor (EGFR), SRC (proto-oncogene tyrosine-protein kinase), paxillin (PXN), Jun proto-oncogene (JUN), breast cancer type 1 susceptibility protein (BRCA1), tumor protein P53 (TP53 or p53), mouse double minute 2 homolog (MDM2), and CD44. These network node proteins were also shown in The Human Protein Atlas and IHC, with the exception of SRC in GA. Computational drug repurposing of approved and investigational drugs/compounds (e.g., as found on www.clinicaltrials.gov) identified the following drugs as effective for GIM: dasatinib with or without erlotinib, nilotinib, afatinib on SRC, SM1-71 on SRC, JNJ-26483327 on EGFR, Afatinib on EGFR, ingenol mebutate on protein kinase C (PKC) family, amoxapine, benoxaprofen, avobenzon, amlexanox, alprazolam, praziquantel, ibuprofen piconol, tranilast, and restoril.

Conclusion: The druggable protein network associated with GIM progression toward GA was identified. The distinct phenotypic patterns between GIM and GA might challenge the notion that GIM serves as the primary precancerous lesion in GA tumorigenesis rather than shares a common cause with tissue-resident stem cells. Further validation of the druggable protein network is needed for the development of a cost-effective surveillance program and preventive treatment of the GIM-to-GA progression.

Disclosure: Nothing to disclose.

MP036

CLINICOPATHOLOGICAL SIGNIFICANCE OF LGR5 EXPRESSION IN SMALL BOWEL ADENOCARCINOMA

Y. Shimazu¹, A. Tatsuguchi¹, A. Hoshimoto¹, T. Nishimoto¹, J. Omori¹, N. Akimoto¹, K. Iwakiri¹

¹Department of Gastroenterology, Nippon Medical School, Graduate School of Medicine, Tokyo, Japan

Contact E-Mail Address: Yuge0stripe@gmail.com

Introduction: Small bowel cancers are rare, accounting for less than 5% of gastrointestinal cancers, but their incidence is increasing. Small bowel adenocarcinoma (SBA) accounts for one-third of small bowel cancers, and due to its rarity, scarce data exist on its molecular and clinicopathological features. According to the stem cell hypothesis, only a very small number of cancer cells in a tumor have the ability to promote its growth and development. Lgr5 is known as a Wnt/ β -catenin target gene, marking normal stem cells in various tissues, including the small and large intestine. Lgr5

expression has been shown to correlate with poor prognosis in colorectal cancer. However, the clinicopathological significance of Lgr5 expression in SBA remains unclear.

Aims & Methods: Aims: To explore the localisation of Lgr5 in human SBA tissue and draw comparisons and determine the relationship between their expression and clinicopathological factors and Wnt/ β -catenin signaling pathway-related genomic alterations and proteins.

Methods: We examined 50 surgical resections from patients with primary SBA for immunohistochemical analyses of Lgr5, cyclin D1, c-Myc, and β -catenin expression. DNA mismatch repair (MMR) status was defined by immunostaining for all MMR proteins; MLH1, MSH2, MLH6, and PMS2. A comparative investigation was then performed with the clinicopathological data of patients (sex, age, localisation, histological type, depth of invasion, lymph node metastasis, distant metastasis, and clinical stage) and cancer specific survival. In addition, genomic profiling was performed on 31 patients using targeted next-generation sequencing. Correlation between the positive rate for each protein and prognosis was determined by the Kaplan-Meier method and multivariate analysis using the Cox regression.

Results: The average observation period was 53 months (median, 48; range, 4–110 months), and 18 patients died during the analysis. The primary localisation of the tumor was the duodenum (n=20), jejunum (n=25), and ileum (n=5). Forty-one cases were well differentiated; 5, poorly differentiated; and 4, mucinous adenocarcinoma. In terms of TNM classification, 25 cases were stage I; 16, stage II; 12 stage III; and 16, stage IV. Lgr5 expression was observed in 38% of SBA patients and correlated with lymph node metastasis, distal metastasis, and advancing TNM stage. Lgr5 expression was not associated with DNA mismatch repair status. Lgr5 expression was significantly associated with reduced membranous β -catenin staining, which correspond to an activation of the Wnt/ β -catenin pathway in cancer cells. CTNNB1 mutations (N=3) were found in only Lgr5 positive SBA patients, although the difference was not significant (P=0.090). APC mutations (N=5) were not associated with Lgr5 expression. Lgr5 expression, lymph node metastasis, and distant metastasis were significantly associated with worse cancer specific survival. In multivariate analysis for cancer specific survival, lymph node metastasis and Lgr5 expression retained independent prognostic significance.

Conclusion: Lgr5 expression is associated with an activation of the Wnt/ β -catenin pathway and worse cancer specific survival independent of lymph node metastasis in SBA.

Disclosure: Nothing to disclose.

MP037

SIZE, BUT NOT THE NUMBER OF POSITIVE LYMPH NODES IS ASSOCIATED WITH WORSE OVERALL SURVIVAL IN PATIENTS WITH SMALL BOWEL NEUROENDOCRINE TUMOURS

B. Timmermans^{1,2}, R. Srirajaskanthan¹, C. Mestre – Alagarda³, A. Wasif⁴, M. Abildtrup⁴, S. Brown¹, D. Clement¹

¹Kings College Hospital, Gastroenterology, London, United Kingdom, ²Radboudumc, Nijmegen, Netherlands, ³King's College Hospital, Liver Histopathology, London, United Kingdom, ⁴King's College Hospital, Gastroenterology Histopathology, London, United Kingdom

Contact E-Mail Address: baer.timmersmans@ru.nl

Introduction: Until recently lymph node metastases (LNM) in small bowel neuroendocrine tumours (SB-NETs) were classified as absent (N0) or present (N1). However, the American Joint Committee on Cancer (AJCC) updated the classification to N0, N1 < 12 positive LNM and, N2 as $\geq$ 12 positive LNM and/or a large mesenteric mass (> 2 cm) (1). All patients will

be offered the same surveillance strategy with 6-monthly cross-sectional imaging. This updated N-classification has not been explored in a real-life cohort of patients with SB-NETs.

Aims & Methods: Aim to describe the prevalence of N1 and N2 LMN in a cohort of patients with SB-NETs and to explore its association with recurrence-free survival (RFS) and overall survival (OS).

A retrospective study was performed in a single NET expert centre King's College Hospital. All patients with curative resection of an SB-NET in the absence of metastases between January 2010 and December 2022 and a histology report available were included. All histology reports were reviewed and reclassified according to the new AJCC N-classification. Additional demographic data were collected from patient records. Recurrence-free survival was calculated from the date of the histology report to the date of documentation of disease recurrence in the multidisciplinary tumour board. Overall survival was calculated from the date of the histology report until the date of death due to any cause. Kaplan-Meier curves were plotted, log-rank test and uni- and multivariate Cox regression analysis were performed.

Results: A total of 112 patients, 52% male with a median age 63.5 years (IQR 55 – 72 year) were included. Sixty-seven patients (60%) had N1 disease and 45 patients (40%) had N2 disease. Within the N2 group, 35 patients (79%) had a large mesenteric mass, 7 patients (17%) had ≥ 12 positive LMN and 2 patients met both criteria (4%). The median mesenteric mass size in the N2 group was 30mm (IQR 25 – 40mm). Three quarters of patients had grade 1 disease and 27 patients (24%) had grade 2 disease. Recurrence occurred in 35 patients (31.5%), of which 18 (26.9%) belonged to the N1-group, while 17 (38.6%) were patients with N2. No significant difference (p-value 0.291) was found in the median time to recurrence, which was 83 months in N1-staged patients versus 61 months in N2-staged patients. There was no significant difference (p-value 0.155) in the median overall survival time between the N1-staged patients (134 months), compared to the N2-staged patients (106 months). Patients with a large mesenteric mass had a significantly (p-value 0.006) shorter overall survival of 102 months compared to the patients with a smaller or no mesenteric mass, median not reached. In multivariate analysis a larger mesenteric mass points towards an association with worse overall survival HR 3.71 (0.93 – 14.83), p-value 0.06.

Conclusion: For patients with small bowel NETs, N1 or N2 lymph node metastases do not affect recurrence-free survival or overall survival. However, a larger mesenteric mass is associated with a significantly shorter overall survival. These data could help develop more patient-tailored surveillance strategies, especially for patients with a larger mesenteric mass who could benefit from more frequent surveillance. Future research in a prospective, multi-center setting could help to clarify better the role of N1 and N2 LNM on recurrence-free and overall survival.

References: 1) Woltering E, Bergsland E, Beyer D, O'Dorisio T, Rindi G, Klimstra D, et al. Neuroendocrine Tumors of the Jejunum and Ileum. 2017. p. 375-87.

Disclosure: None.

MP038

CLINICOPATHOLOGICAL SIGNIFICANCE OF CD44 AND CD44 VARIANT ISOFORMS EXPRESSION IN SMALL BOWEL ADENOCARCINOMA

H. Machida¹, A. Tatsuguchi¹, R. Inoue¹, Y. Shimazu¹, R. Hamkubo¹, A. Hoshimoto¹, T. Nishimoto¹, J. Omori¹, N. Akimoto¹, S. Tanaka¹, S. Fujimori¹, K. Iwakiri¹

¹Nippon Medical School, Gastroenterology, Tokyo, Japan

Contact E-Mail Address: s13-089mh@nms.ac.jp

Introduction: The molecular and clinicopathological features of primary small bowel adenocarcinoma (SBA) are not as fully understood as are those of colorectal cancer and gastric cancer because SBA is relatively rare. According to the stem cell hypothesis, only a very small number of cancer cells in a tumor have the ability to promote its growth and development. CD44 and CD44 variant isoforms are known as stem cell markers of colorectal cancer. CD44 upregulation has been shown associated with cancer progression, invasion, and metastasis. In addition, CD44 plays an important role in epithelial-mesenchymal transition. However, the clinicopathological significance of CD44 and CD44 isoforms expression in SBA remains unclear.

Aims & Methods: To explore the localisation and clinicopathological significance of CD44 and CD44 variant isoforms in SBA.

We performed immunohistochemical analysis of CD44, CD44v, CD44v9, β -catenin and E-cadherin using formalin-fixed paraffin-embedded tissue specimens obtained from 50 cases of SBA. For E-cadherin and β -catenin, cases showing membranous staining equivalent to that of normal small intestinal epithelial cells in $> 75\%$ of cancer cells were considered preserved expression and otherwise considered reduced expression. A comparative investigation was then performed with the clinicopathological data of patients (sex, age, localisation, histological type, depth of invasion, lymph node metastasis, distal metastasis and clinical stage) and cancer-specific survival. The average age of the patients was 64 years old (median 68; range, 32–84 years old). Correlation between the positive rate for each protein and prognosis was determined by the Kaplan-Meier method and multivariate analysis using the Cox regression.

Results: The average observation period was 53 months (median, 48; range, 4–110 months), and 18 patients died during the analysis. The primary localisation of the tumor was the duodenum (n=20), jejunum (n=25), and ileum (n=5). Forty-one cases were well differentiated; 5, poorly differentiated; and 4, mucinous adenocarcinoma. In terms of TNM classification, 14 cases were stage I; 13, stage II; 10, stage III; and 13, stage IV. The positive rates for each protein were CD44, 54%; CD44v6, 50%; and CD44v9, 52%. CD44 and CD44 isoforms were significantly associated with lymph node metastasis and distal metastasis. There was a mutual interrelationship between CD44, CD44v6 and CD44v9 expression. CD44 and CD44v6 immunostaining significantly correlated with abnormal reduced membranous β -catenin staining. CD44 and CD44v9 immunostaining significantly correlated with reduced membranous E-cadherin staining. Factors showing a significant correlation with cancer-specific survival in univariate analysis included lymph node metastasis, distant metastasis, CD44, CD44v6, and CD44v9. In multivariate analysis performed by introducing lymph node metastasis and CD44, CD44v6, and CD44v9 expression in the Cox proportional hazards model, both lymph node status (hazard ratio: 18.5) and CD44 expression (hazard ratio: 7.5) retained independent prognostic significance.

Conclusion: These results suggest that CD44 and CD44 variant isoforms expression are associated with epithelial-mesenchymal transition and could be prognostic factors independent of lymph node metastasis in SBA.

Disclosure: Nothing to disclose.

MP039

LONG-TERM RESULTS AFTER TAILORED LYMPHADENECTOMY USING SENTINEL NODE NAVIGATED SURGERY IN HIGH-RISK T1 ESOPHAGEAL ADENOCARCINOMA PATIENTS

C.N. Frederiks^{1,2}, J.J. Bergman³, R.E. Pouw³, B. de Keizer⁴, R. Bennink⁵, L. Brosens⁶, S.L. Meijer⁷, R. Van Hillegersberg⁸, M. van Berge Henegouwen⁹, J.P.H. Ruurda⁸, S.S. Gisbertz⁹, B.L. Weusten^{1,2}

¹UMC Utrecht, Gastroenterology & Hepatology, Utrecht, Netherlands, ²St Antonius Hospital, Gastroenterology & Hepatology, Nieuwegein, Netherlands, ³Amsterdam UMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁴UMC Utrecht, Radiology & Nuclear Medicine, Utrecht, Netherlands, ⁵Amsterdam UMC, Radiology & Nuclear Medicine, Amsterdam, Netherlands, ⁶UMC Utrecht, Pathology, Utrecht, Netherlands, ⁷Amsterdam UMC, Pathology, Amsterdam, Netherlands, ⁸UMC Utrecht, Surgery, Utrecht, Netherlands, ⁹Amsterdam UMC, Surgery, Amsterdam, Netherlands

Contact E-Mail Address: c.n.frederiks-4@umcutrecht.nl

Introduction: A recent prospective, multicenter pilot study demonstrated that a radical endoscopic resection (ER) of a high-risk T1 esophageal adenocarcinoma (EAC) followed by sentinel node navigated surgery (SNNS) might be feasible without impairment of the esophageal and gastric function at three months.¹ In the current study, we present the follow-up data of this new, esophageal preserving treatment strategy.

Aims & Methods: Ten patients underwent SNNS in two tertiary hospitals after radical ER of a high-risk T1 EAC (i.e. deep submucosal invasion [$\geq 500\mu\text{m}$], poor differentiation, and/or lymphovascular invasion) without the clinical presence of lymph node or distant metastases at baseline (i.e. cN0M0). SNNS consisted of endoscopic injection of a hybrid tracer around the ER scar followed by preoperative imaging the day before surgery. The next day, sentinel nodes were identified and subsequently resected during thoracoscopy and laparoscopy.

Follow-up after SNNS involved three-monthly upper endoscopy supplemented with endoscopic ultrasound (EUS) during 24 months. During each procedure, the esophagus was assessed for new visible lesions, while any suspicious lymph nodes were evaluated with fine-needle aspiration (FNA). Additional ablation therapy for any residual Barrett esophagus (BE) could be initiated at the discretion of the treating endoscopist.

Complementary to strict endoscopic surveillance, radiological follow-up (i.e. CT thorax/abdomen or PET/CT) was performed at 12 months after the initial ER to evaluate for distant metastases. Endpoints were the incidence of new visible lesions, metastases, mortality, and gastroesophageal functional disorders during follow-up.

Results: A median of 3 (range 1-6) sentinel nodes were identified and resected in the included patients (10 male, median age 69). Two patients (20%) were found to have a metastasis in one of the resected sentinel nodes. Since none of these patients had signs of residual disease upon restaging directly after SNNS, both patients were kept under endoscopic and radiologic follow-up after discussion in a multidisciplinary meeting, considering patient's older age (n=1) and patient's preference (n=1). After median 23 (range 12-28) months of follow-up, none of the 10 patients (0%) were diagnosed with lymph node or distant metastases related to esophageal cancer.

One patient (10%) however died as a result of a second primary tumor with distant metastases at 12 months after SNNS. In two patients (20%), FNA (median 2 [range 1-2] sessions) was performed during EUS to assess suspicious lymph nodes, without signs of esophageal malignancy. Three patients (30%) developed a new visible lesion in median C1M4 (range C0-9M1-11) residual BE, which were all amenable for ER with histopathology

revealing low-grade dysplasia (n=1), high-grade dysplasia (n=1) and moderately differentiated T1m2 EAC with no lymphovascular invasion (n=1). None of the patients (0%) developed functional gastroesophageal disorders during follow-up.

Four patients (40%) underwent additional radiofrequency ablation (median 3 [range 2-4] sessions) of whom two patients had a new visible lesion prior to the initiation of ablation therapy.

Conclusion: Based on these long-term results demonstrating a low risk of metastasized disease, SNNS appears to be a feasible and safe instrument to tailor the extent of lymphadenectomy in patients with high-risk T1 EAC who underwent a prior radical ER. The exact position of this new strategy in the treatment algorithm for high-risk T1 esophageal cancer needs to be studied in future research.

References: 1) Frederiks CN, Overwater A, Bergman JJGHM, et al. Feasibility and safety of tailored lymphadenectomy using sentinel node navigated surgery in high-risk T1 esophageal adenocarcinoma patients. *Ann Surg Oncol.* 2023 Jul;30(7):4002-4011.

Disclosure: R. van Hillegersberg is a consultant for Intuitive Surgical and Medtronic. J.P. Ruurda is a consultant for Intuitive Surgical. M.I. van Berge Henegouwen is a consultant for Alesi Surgical, BBraun, Johnson & Johnson, Medtronic and Viatrix, and has received research funding from Stryker. The remaining authors declare to have no disclosures relevant to this manuscript.

MP040

CLINICOPATHOLOGICAL SIGNIFICANCE OF WNT/B-CATENIN SIGNALING PATHWAY-RELATED GENES AND PROTEINS IN SPORADIC SMALL BOWEL ADENOCARCINOMA

R. Inoue¹, A. Tatsuguchi¹, T. Yamada², Y. Shimazu¹, H. Machida¹, R. Hamakubo¹, A. Hoshimoto¹, T. Nishimoto¹, J. Omori¹, N. Akimoto¹, S. Tanaka¹, S. Fujimori¹, K. Iwakiri¹

¹Nippon Medical School, Department of Gastroenterology, Tokyo, Japan, ²Nippon Medical School, Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Tokyo, Japan

Contact E-Mail Address: s13-015ir@nms.ac.jp

Introduction: Background: Small bowel cancers are rare, accounting for less than 5% of gastrointestinal cancers, but their incidence is increasing. Small bowel adenocarcinoma (SBA) accounts for one-third of small bowel cancers, and due to its rarity, scarce data exist on its molecular and clinicopathological features. The genomic profiling of SBA has been shown to be distinct from colorectal cancer and gastric cancer through comprehensive analysis of genomic alterations. The low incidence of APC mutations in SBA suggests that the adenoma-carcinoma sequence is not the main carcinogenic mechanism.

However, the extent to which the Wnt β -catenin signaling pathway, which is important in the adenoma-carcinoma sequence, is involved in the process of carcinogenesis in SBA remains controversial.

Aims & Methods: Aims: We examined the clinicopathological significance of gene mutations involved in the Wnt/ β -catenin pathway and their downstream target gene products in SBA.

Methods: Immunostaining for β -catenin, Cyclin D1, c-Myc, E-cadherin and p53 was performed in 69 surgical resections from patients with primary SBA. Genomic alterations were analyzed by targeted next-generation sequencing in 32 cases out of the 69 cases. For cyclin D1 and c-Myc, cases showing nuclear staining in $\geq 10\%$ of cancer cells were considered positive. For E-cadherin and β catenin, cases showing membranous staining equivalent to that of normal small intestinal epithelial cells in $> 75\%$ of cancer cells were considered preserved expression and otherwise considered reduced expression.

Results: Results: Patients included 49 men and 20 women, ranging in age from 32 to 84 years (mean 65 years; median 68 years). At the time of analysis, 21 patients had died. The overall 5-year survival rate was 64%. The median follow-up duration for the entire series was 36 months (mean 51.4 months; range, 5-124 months). The primary localisation of the tumor was the duodenum (n=36), jejunum (n=28), and ileum (n=5). Fifty-five cases were well differentiated; 9, poorly differentiated; and 5, mucinous adenocarcinoma. In terms of TNM classification, 25 cases were stage I; 16, stage II; 12 stage III; and 16, stage IV. Reduced membranous β -catenin staining pattern, which correspond to an activation of the Wnt/ β -catenin pathway in cancer cells was observed in 39% of the cases. Cyclin D1 and c-Myc was positive in cancer cells in 58% and 30% of cases, respectively. A significant positive relationship was observed between aberrant β -catenin and cyclin D1. The Wnt pathway-associated gene mutations in SBA were APC in 18.8% and CTNNB1 in 12.5% of the cases, and no cases exhibited both of them. Concurrent reduced β -catenin immunostaining was observed in 4/4 CTNNB1 and 2/6 APC mutation cases, respectively. Reduced β -catenin immunostaining correlated significantly with lymph node metastasis and distant metastasis, and thereby advanced TNM stage. Furthermore, a combined reduced E-cadherin and β -catenin expression was associated with worse prognosis, independent of lymph node metastasis by Cox regression multivariate analysis.

Conclusion: Conclusion: Wnt-related genomic alterations including APC and CTNNB1 were only found in a third of cases examined. The above results suggest that the Wnt/ β -catenin pathway is involved in carcinogenesis and cancer progression in SBA, although to a lesser extent than in colorectal cancer.

Disclosure: Nothing to disclose.

Coeliac disease: Part 1

10:30-11:30 / Poster Stage 6

MP041

POTENTIAL COELIC DISEASE (PCD) IN ADULTS: CLINICAL PRESENTATION AND OUTCOMES

E. Del Zanna¹, N. Nandi¹, L. Scaramella², M. Topa¹, L. Roncoroni³, A. Scricciolo³, V. Lombardo³, M. Vecchi², L. Elli²

¹Università degli Studi di Milano, Milano, Italy, Department of Pathophysiology and Transplantation, Milano, Italy,

²Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milano, Italy., Milano, Italy, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Contact E-Mail Address: elena.delzanna@unimi.it

Introduction: Potential Coeliac Disease (PCD) is defined by the presence of positive CD serology, anti-endomysial antibodies (EmA) and anti-tissue transglutaminase (anti-tTG), positive genetic predisposition (HLA-DQ2/DQ8), and absence of atrophy (Marsh ≥ 3) at duodenal histology in patients on a gluten containing diet (GCD).

Currently, there is no established consensus on the management of patients with PCD, particularly regarding treatment and follow-up. Literature on PCD remains limited, especially in adults, including mostly retrospective studies with small cohorts and short follow-up often without a second endoscopic sampling.

Aims & Methods: The aim of our study is to describe the presentation and outcome, including the rate of progression to biopsy-proven CD, in a cohort of adult PCD patients.

This is a retrospective single-center study including all adult PCD patients (>16 years old) referred to our Celiac Disease Clinic between January 2006 and March 2024. All patients with positive anti-tTG and at least one esophagogastroduodenoscopy (EGD) with duodenal biopsy were included. Presenting manifestations, serology and HLA-DQ genotyping, endoscopy and histology as well as outcome were recorded.

Results: A total of 34 PCD patients (mean age at presentation 33.1 $\pm$ 14.3 years, 75% female) were included in the study. The median follow-up time from first presentation (T0) was 4 years (IQR 1-6).

Out of the 34 patients, 24 were tested for CD due to the presence of symptoms (most frequently abdominal pain, dyspepsia and diarrhea), while the rest were tested in the context of CD screening for positive family history. At T0, the median anti-tTG IgA titre was 2.5 times higher than the upper limit of normal (ULN) and EMA were positive in 27 out of 34 patients. All patients had Marsh 0-1 at duodenal histology performed within 12 months from the first positive tTG-test. The majority of patients (75%, 24/34) had at least a second EGD with duodenal biopsies. At follow-up, 8 (24%) patients were diagnosed with CD confirmed histologically (Marsh ≥ 3); CD diagnosis occurred after 2.95 $\pm$ 2.84 years from T0. In the remaining PCD patients, 20 patients (59%) kept following a GCD while continuing clinical and endoscopic follow-up. Specifically, 60% of them (followed for 3.79 $\pm$ 2.71 years), had at least another follow-up duodenal biopsy still confirming absence of atrophy with either spontaneous resolution or reduction of presenting symptoms while on a GCD. Conversely, 6 patients decided to start a gluten-free diet (GFD), despite the absence of villous atrophy at duodenal biopsies which was confirmed on a second duodenal histology in 4 out of 6 of them. In these patients, the GFD led to symptoms improvement in 83% of patients.

Conclusion: In our cohort, 24% of PCD patients develop celiac disease within almost 3 years (2.95 $\pm$ 2.84 years) from the first presentation. Most patients (59%) upon PCD diagnosis preferred staying on a GCD while being regularly followed with serology and endoscopy. Among those who

decided to start a GFD despite CD not being histologically confirmed, symptoms improvement occurred in 83% (5/6), confirming that a trial of GFD in symptomatic patients could be proposed.

References: Al-Toma A, Volta U, Auricchio R, et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *United European Gastroenterol J.* 2019;7(5):583-613. doi:10.1177/2050640619844125

Disclosure: Nothing to disclose.

MP042

SYMPTOM BURDEN AMONG PATIENTS WITH CELIAC DISEASE BEFORE AND AFTER DIAGNOSIS: A US HEALTH CLAIMS DATABASE STUDY

F. Zingone¹, M. Arvizu², S. Manne², V. Gandhi², S. Ghura², R. Saad², D.A. Leffler², I. Petrakis², N. Cheinquer², B. Lebowitz³

¹University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ²Takeda Development Center Americas, Inc., Cambridge, United States of America, ³Columbia University Irving Medical Center, Division of Gastroenterology, Department of Medicine, New York, United States of America

Contact E-Mail Address: fabiana.zingone@unipd.it

Introduction: Among patients with celiac disease (CeD), following a gluten-free diet after diagnosis is expected to reduce symptom burden. Using a large US claims database, we compared symptoms in individuals with CeD pre- and post-diagnosis with those in matched individuals without CeD to evaluate the burden of CeD.

Aims & Methods: This case-control study was conducted among individuals of all ages enrolled in MarketScan from 2002 to 2023. CeD diagnosis (index date) was defined as ≥ 1 inpatient or ≥ 2 outpatient International Classification of Diseases (ICD)-9/-10 diagnostic codes; controls were matched (1:5 ratio) for age, sex, region, and diagnosis year. All individuals had continuous medical and pharmacy enrolment for 2 years pre- and post-index. Core CeD symptoms (abdominal pain, diarrhoea, joint pain, bloating, fatigue, and nausea) were defined as ≥ 1 inpatient or ≥ 2 outpatient ICD-9/-10 codes during each 2-year period. Unadjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated by logistic regression comparing CeD cases versus controls.

Results: During the 21 years of data coverage, we identified 39 814 patients with CeD and 198 961 matched individuals without CeD with similar age and sex distribution (mean age 41.6 years [standard deviation 20.1]; 70.5% female). The burden of CeD symptoms pre-diagnosis was significantly higher among patients with CeD versus controls, particularly for diarrhoea, bloating, and abdominal pain. The pre-diagnosis OR (95% CI) for abdominal pain was 5.37 (5.22, 5.52), joint pain 1.87 (1.81, 1.93), diarrhoea 11.64 (11.10, 12.20), bloating 8.64 (7.86, 9.51), fatigue 3.63 (3.48, 3.79), and nausea 5.78 (5.36, 6.24). As expected, symptom burden decreased post-diagnosis, however all symptoms (except joint pain) had an approximately twofold greater burden compared with controls, 2 years post-diagnosis: OR (95% CI) abdominal pain 2.43 (2.57, 2.30), joint pain 1.61 (1.51, 1.71), diarrhoea 2.47 (2.21, 2.76), bloating 2.47 (1.86, 3.27), fatigue 2.17 (1.98, 2.38), and nausea 2.24 (1.83, 2.74). When we evaluated symptoms only among individuals with CeD, on average symptom persistence 2 years after diagnosis occurred in 29.7% of patients while an average of 6.3% had new-onset symptoms (most commonly abdominal pain; 17.0%).

Conclusion: Claims databases were able to capture CeD symptom burden and demonstrated that patients with CeD continue to experience symptoms (including new-onset) post-diagnosis. Although a gluten-free diet might control some symptoms, there is still considerable remaining burden and some unresolved symptoms (e.g. joint pain and fatigue) or new-onset symptoms.

Disclosure: MA, SM, VG, SG, RS, DAL, IP, and NC are employees and shareholders of Takeda. BL has nothing to disclose. FZ served as a speaker for Werfen and a consultant for Takeda.

MP043

CELIAC DISEASE EDUCATIONAL NEEDS IN PATIENT DIAGNOSIS AND MANAGEMENT: RESULTS OF A CASE-BASED SURVEY

N. Cheinquer¹, S. Cazzetta², A. Schwind², M. Arvizu¹, D.A. Leffler¹

¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²Takeda Pharmaceuticals USA, Inc., Boston, United States of America

Contact E-Mail Address: nelson.cheinquer@takeda.com

Introduction: Accurate and timely identification and treatment of celiac disease (CeD) by clinicians is increasingly recognized to be an important issue. This study aimed to identify educational needs of healthcare providers (HCPs) in diagnosing and managing CeD by surveying HCPs across Europe (EU) and the United States (US).

Aims & Methods: A survey focused on practices, knowledge, experience, and attitudes towards CeD was conducted among gastroenterology (GI) physicians (EU and US), nurse practitioners (NPs), and physician associates (PAs); primary care physicians (PCPs), NPs, and PAs; and dietitians (US only) who see patients with CeD. The survey used a simulated patient case for decision-making context and was distributed from August to September 2023.

Results: Respondents included 378 HCPs (75 EU, 303 US); most were physicians in group practices, with significant representation from community settings. After reviewing the case, most GIs (76%-88%) included CeD in their top 3 differential diagnosis versus 65% of PCPs. 83% of PCPs recommended starting a gluten-free diet (GFD) before endoscopy vs 36%-37% for GIs. Most dietitians were comfortable providing dietary guidance for CeD but the majority would also recommend initiation of a GFD prior to endoscopy. 87%-93% of GIs would order an endoscopy to confirm diagnosis, but many are not obtaining a guideline-recommended number of biopsies, particularly from the distal duodenum.

Conclusion: This study highlights a significant need for targeted interventions to enhance the identification and evidence-based diagnosis of CeD across various healthcare specialties. In particular, the practice of initiating a GFD prior to diagnosis should be addressed.

Disclosure: NC, SC, AS, MA and DL are employees and shareholders of Takeda.

MP044

SEROLOGY AND MUCOSAL PATHOLOGY AT DIAGNOSIS, AND MUCOSAL HEALING IN CELIAC DISEASE

J. Ibsen¹, H.M. Reims², N. Warmbrodt³, V. Paulsen⁴, H. Andreassen⁴, S.R. Lund⁴, O. Darre-Ness⁴, K. Garborg⁴, C. Tønnesen⁴, L. Aabakken⁴, K.E. Lundin⁵

¹University of Oslo, Oslo, Norway, ²Oslo University Hospital, Pathology, Oslo, Norway, ³Oslo University Hospital Rikshospitalet, Clinical nutrition, Oslo, Norway, ⁴Oslo University Hospital Rikshospitalet, Gastroenterology, Oslo, Norway, ⁵Norwegian Coeliac Disease Research Centre, University of Oslo and Oslo University Hospital, Gastroenterology, Oslo, Norway

Contact E-Mail Address: jostein.ibsen@gmail.com

Introduction: Diagnosis of coeliac disease (CeD) rests on clinical signs, serology (IgA against transglutaminase 2 (IgA-TG2), alternatively IgG to deamidated gliadin peptides (IgG-DGP)) and mucosal damage in duodenal biopsies [1, 2]. Mucosal pathology is often classified according to the modified Marsh criteria [3].

A gluten free diet leads to clinical, serological and mucosal improvement and rapid immunological improvement as well as mucosal healing after 1 year after rigid follow-up [4].

However, we previously reported that only ½ of treated patients in a community-based setting reached mucosal healing one year after diagnosis [5]. We here report recent results.

Aims & Methods: Patients with suspected CeD were referred from general practice to secondary care endoscopy service at Oslo University Hospital; no tertiary referral patients are reported here. All patients gave written, informed consent. Serology was repeated at the day of endoscopy. Diagnosis of CeD was given for patients with combination of positive serology and definite mucosal damage (Marsh 3a-c). Exceptions to this was agreed in selected cases after careful clinical evaluation. All participants who received the CeD diagnosis were referred to one individual consultation with a clinical dietician and to a follow-up endoscopy after 12 months. Patients with CeD in Norway receives a monthly reimbursement of approximately EUR 66 pr month to cover their additional costs for a gluten-free diet.

Results: In total 138 of the 214 eligible participants were diagnosed with CeD between 2018 and 2021. Among these, 6 patients had negative (<4 U/L) IgA-TG2, 29 a negative (<20 U/L) IgG-DGP and only 2 were seronegative for both markers. Correlation between levels of IgA-TG2 and IgG-DGP were calculated with Pearson (assuming normal distribution) showing a correlation coefficient (r) = 0.4893, p -verdi = 0.0000112, i.e. a significant moderate positive correlation. Spearman's rank correlation coefficient (r_s) = 0.52095, p -verdi = 0.00002301 showed significant strong positive correlation (assuming not normal distribution). Within the CeD group, 63 were diagnosed with a Marsh 3C, 44 with Marsh 3B, 22 with Marsh 3A, and 9 with Marsh 1 or 2. One hundred and four patients came to the 1-year control. Eighty had achieved mucosal healing (Marsh 0 or 1), while 19 showed improvement but still showed mucosal damage (Marsh 3). Nine of the patients who did not achieve mucosal healing were followed up for an additional year where 6 achieved recovery. Thus, only 3 could be classified as non-responsive CeD. No data are available for those who did not return to repeated endoscopy.

Conclusion: Simultaneous testing of both IgA-TG2 and IgG-DGP renders very few patients truly seronegative, as only 2 of 139 new CeD patients were negative for both. Wide ranges were seen for both IgA-TG2 and IgG-DGP. We now investigate factors in serum leading to predominant IgA-TG2 vs IgG-DGP responses using multi-plex inflammation panel analysis. One year after the diagnosis, and with the mentioned follow-up system, the prognosis for mucosal healing is achieved in 77% of patients and better than often anticipated.

- References:** 1. Al-Toma, A., et al., *European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders*. United European Gastroenterol J, 2019. 7(5): p. 583-613.
2. Rubio-Tapia, A., et al., *American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease*. Am J Gastroenterol, 2023. 118(1): p. 59-76.
3. Oberhuber, G., G. Granditsch, and H. Vogelsang, *The histopathology of coeliac disease: time for a standardized report scheme for pathologists*. Eur J Gastroenterol Hepatol, 1999. 11(10): p. 1185-94.
4. Risnes, L.F., et al., *Gluten-free diet induces rapid changes in phenotype and survival properties of gluten-specific T cells in celiac disease*. Gastroenterology, 2024.
5. Haere, P., et al., *Long-term mucosal recovery and healing in celiac disease is the rule - not the exception*. Scand J Gastroenterol, 2016. 51(12): p. 1439-1446.

Disclosure: Nothing to disclose.

MP045

THE COMBINATION OF IGA TISSUE TRANSGLUTAMINASE AND IGG DEAMIDATED GLIADIN PEPTIDE ANTIBODIES AS A STRATEGY FOR CELIAC DISEASE DIAGNOSIS WITHOUT DUODENAL BIOPSY

F. Zingone¹, G.L. Norman², E.G. Smecuol³, D. Maniero¹, A. Carroccio⁴, F. Biagi⁵, J.P. Stefanolo³, S. Niveloni³, G.H. Holmes⁶, V. Villanacci⁷, A. Santonicola⁸, J. Bai³, C. Ciacci⁸

¹University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ²Research and Development, Headquarters & Technology Center Autoimmunity, Werfen, San Diego, United States of America, ³Small Bowel Section, Dr. C. Bonorino Udaondo Gastroenterology Hospital, Buenos Aires, Argentina, ⁴Villa Sofia Cervello United Hospitals - University of Palermo, Unit of Internal Medicine, PROMISE Department, Palermo, Italy, ⁵Gastroenterology Unit of Pavia Institute, Istituti Clinici Scientifici Maugeri IRCCS. University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy, ⁶Royal Derby Hospital, Department of Gastroenterology, Derby, United Kingdom, ⁷SPEDALI CIVILI - UNIVERSITY OF BRESCIA, Brescia, Italy, ⁸University of Salerno, Medicine Surgery Dentistry, Scuola Medica Salernitana, Salerno, Italy

Contact E-Mail Address: fabiana.zingone@unipd.it

Introduction: Several studies have proposed a non-biopsy serological diagnosis of celiac disease (CeD) based on the sequential detection of anti-tissue transglutaminase (tTG) IgA and follow-up with anti-endomysial IgA as a confirmatory test or, more recently, using one test, the tTG IgA at cut-off values ≥ 10 UNL in both children and adults.

However, while the non-biopsy strategy was well received by pediatricians, gastroenterologists still raise concerns about adopting such a strategy for diagnosing CeD in adults, especially in a non-expert setting.

Aims & Methods: The study aimed to assess the performance and clinical utility of the concurrent detection of two autoantibodies targeting two independent antigens, tTG and deamidated gliadin peptides (DGP), as an effective alternative approach for a non-biopsy diagnosis of CeD in adults with high pre-test probability.

This prospective, multicenter, binational study collected consecutive patients with a high pre-test probability for CeD. Between 2018 and 2020, adults were enrolled at four Italian and one Argentinian centers. Patients underwent evaluation for serology and duodenal biopsy at local centers. Serology was also blindly analyzed by a central laboratory (Werfen, San

Diego, USA) for tTG IgA and DGP IgG by Aptiva Particle Multi-Analyte Technology (PMAT) assays. CeD diagnosis required histological confirmation of Marsh 3 damage.

Results: 181 adult patients with suspected CeD were enrolled (134 with histological diagnosis of CeD and 47 not histologically confirmed as CeD). The sensitivities of tTG IgA and DGP IgG were 98.5 and 93.3%, respectively. Patients positive for both tTG IgA and DGP IgG (double positive) were predictive of CeD in 92.5% of patients at >1x upper limit of normal (ULN). Double positivity for tTG IgA and DGP IgG, both at >10x ULN, had a 100% positive predictive value for the presence of Marsh 3 histology.

Conclusion: The presence of both tTG IgA and DGP IgG at concentrations >10x ULN was 100% predictive of CeD. Incorporating DGP IgG alongside tTG IgA in a single-step approach can be considered a valid confirmatory strategy for definitive non-biopsy diagnosis of CeD, particularly for patients with high pretest probability, even in non-expert settings.

References: Ciacci C et al Serum anti-tissue transglutaminase IgA and prediction of duodenal villous atrophy in adults with suspected coeliac disease without IgA deficiency (Bi.A.CeD): a multicentre, prospective cohort study. *Lancet Gastroenterol Hepatol.* 2023 Nov;8(11):1005-1014.

Disclosure: FZ served as a speaker for Werfen and a consultant for Takeda. CC served as a speaker for Werfen and Takeda. GLN was employee of Werfen at time of study. JB JCB was consultant for Takeda. All other authors declared no conflict of interest.

MP046

PERSISTENT VILLOUS ATROPHY IN CELIAC DISEASE: RISK STRATIFICATION AND LONG-TERM OUTCOMES

R. Saidani¹, H. Dabbebi², D. Cherif², H. Yacoub², H. Hassine², H. Kchir², N. Maamouri²

¹La Rabta Hospital, Tunis, Tunisia, ²La Rabta Hospital, Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: raouia.saidani@etudiant-fmt.utm.tn

Introduction: Celiac disease (CD) is an autoimmune disorder triggered by gluten ingestion, leading to intestinal villous atrophy. While a gluten-free diet (GFD) is the mainstay of treatment, some patients exhibit persistent villous atrophy (pVA) on follow-up biopsies.

This raises concerns about the long-term health consequences of pVA in CD patients adhering to GFD.

Aims & Methods: Objectives: To evaluate the association between pVA and long-term outcomes in CD patients.

To assess the performance of a scoring system identifying patients at high risk of pVA.

Methods: We conducted a retrospective analysis including all the patients diagnosed with CD between 2014 and 2020, who underwent follow-up duodenal biopsies. Patients were categorized as having pVA or not based on the Marsh classification ($\geq 3a$).

We considered as complications of CD malignant and premalignant conditions arising in the abdomen, including refractory CD, ulcerative jejuno-ileitis, abdominal lymphomas and small bowel carcinomas.

In particular, persistence of malabsorption symptoms and VA despite a strict GFD for at least 12 months in the absence of lymphoma, malignancies and non-coeliac enteropathies allowed the diagnosis of refractory CD (RCD).

Additionally, we applied the 5-point scoring system to predict pVA risk, incorporating the following factors:

- Age at diagnosis ≥ 45 years
- Classical pattern of celiac disease (CCD)
- Lack of clinical response to GFD
- Poor GFD adherence

Each of the first three factors was assigned a point score and the fourth item was assigned two points score, with higher scores indicating a greater risk of pVA.

Results: We collected 151 patients with CD. Approximately 24.5% of patients had pVA. Patients with pVA exhibited a significantly higher risk of complications (HR 7.61, 95% CI 3.18 to 17.64, $p < 0.001$). Overall, during follow-up, 9 patients (5.96%) developed a complication (three refractory CD, one B-cell lymphoma, three persistence of malabsorption symptoms and two ulcerative jejuno-ileitis). Over these 9, 7 patients had a pVA.

While most patients adhered to GFD, 35.1% still had persistent VA at follow-up.

Up to 29.72% of patients with persistent villous atrophy do not have ongoing symptoms.

The 5-point scoring system stratified patients by risk of pVA into

- Low risk (0-1 points): 4.1% pVA prevalence (3 patients out of 73).
- Intermediate risk (2 points): 20% pVA prevalence (9 patients out of 45).
- High risk (3-5 points): 75.75% pVA prevalence (25 patients out of 33).

Conclusion: This study demonstrates that persistent villous atrophy in CD patients following GFD is associated with increased risk of complications. It also shows the effectiveness of the 5-point scoring system, in stratifying CD patients by risk of pVA. The system accurately identified high-risk patients with a significantly higher prevalence of pVA. It can also help identify these individuals who, despite a lack of current symptoms, may still be at higher risk for future complications so it can be used in clinical practice to personalized follow-up modalities.

References: Rossi A, Lohi J, Mustalahti K, et al. Persistent villous atrophy predicts development of complications and mortality in adult patients with coeliac disease: a multicentre longitudinal cohort study and development of a score to identify high-risk patients [Internet]. *BMJ Gut.* 2023;72(11):2095-2105. Available from: <https://gut.bmj.com/content/72/11/2095>

Disclosure: Nothing to disclose.

MP047

LONG TERM RISK OF CHRONIC LIVER DISEASE IN PATIENTS WITH CED: A NATIONWIDE POPULATION-BASED, SIBLING-CONTROLLED COHORT STUDY

J. Yao¹, J. Sun¹, F. Ebrahimi¹, D. Bergman¹, P.H. Green², B. Lebwohl², D.A. Leffler³, H. Hagström⁴, J.F. Ludvigsson⁵

¹Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, ²Columbia University College of Physicians and Surgeons, Division of Digestive and Liver Diseases, Department of Medicine, New York, United States of America, ³Takeda Pharmaceuticals International Co., Cambridge, United States of America, ⁴Department of Upper GI Diseases, Karolinska university hospital Huddinge, Department of Medicine, Huddinge, Stockholm, Sweden, ⁵Karolinska institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden

Contact E-Mail Address: yao.jialu@outlook.com

Introduction: Little is known about the association of (CeD) with chronic liver diseases (CLD) and major adverse liver outcomes (MALO).

Aims & Methods: To investigate the long-term risk of CLD in patients with CeD. In a Swedish nationwide histopathology cohort, patients with biopsy-confirmed CeD were identified between 1969 and 2017 (n=48,033). Each patient was matched with up to five general population reference individuals (n=231,940) by sex, birth year, calendar year, and county of residence and followed-up until 31 December 2021. We used Cox proportional hazard regression to estimate the adjusted hazard ratio (aHR) of incident overall and specific CLD (i.e., viral hepatitis, metabolic

dysfunction-associated steatotic liver disease [MASLD], alcohol-related liver disease [ALD], and autoimmune liver disease) and major adverse liver outcomes (composite endpoint for compensated or decompensated cirrhosis, hepatocellular carcinoma, liver transplant, and liver-related death), along with 95% confidence intervals (CIs). Outcomes were identified from the National Patient Register using relevant ICD-codes. Familial risk factors were additionally accounted for by comparison with CeD-free full siblings (n=53,003).

Results: During a median follow-up of 16.0 years, there were 646 incident CLD in patients with CeD and 1,567 in reference individuals (incidence rate [IR]: 79.1 vs. 39.4 per 100,000 person-years). Compared with reference individuals, patients with CeD had higher hazards of overall CLD (aHR=1.84, 95%CI=1.67 to 2.02). The hazards of overall CLD remained significantly increased ≥ 15 years after CeD diagnosis, leading to one extra CLD case per 214 patients with CeD until then. The hazards elevation was primarily driven by MASLD (aHR=2.35 [1.90 to 2.91]), ALD (aHR=1.35 [1.08 to 1.68]), and autoimmune liver disease (aHR=4.36 [3.67 to 5.18]), but not by viral hepatitis (Table 1). There were 646 incident MALO cases in patients with CeD and 1567 in reference individuals over the follow-up period. Both absolute and relative risks of MALO were higher in patients with CeD than reference individuals (IR: 65.6 vs. 41.6; aHR=1.44 [1.31 to 1.59]). Our main findings were confirmed in the sibling comparison (aHR=1.81 [1.57 to 2.09] for overall CLD and 1.33 [1.14 to 1.56] for MALO) and were robust in sensitivity analyses.

	Including first three years of follow-up			Excluding first three years of follow-up		
	No. of events (IR, per 100,000 person-years)		HR (95%CI) *	No. of events (IR, per 100,000 person-years)		HR (95%CI) *
	Patients	References		Patients	References	
Any CLD	646 (79.1)	1567 (39.4)	1.84 (1.67 to 2.02)	505 (62.0)	1365 (34.4)	1.65 (1.49 to 1.83)
Viral hepatitis	134 (16.3)	731 (18.3)	0.88 (0.73 to 1.07)	103 (12.6)	606 (15.2)	0.81 (0.66 to 1.00)
MASLD	142 (17.7)	262 (6.7)	2.35 (1.90 to 2.91)	113 (14.2)	239 (6.1)	2.05 (1.63 to 2.59)
ALD	109 (13.3)	364 (9.1)	1.35 (1.08 to 1.68)	88 (10.7)	332 (8.3)	1.21 (0.95 to 1.54)
Autoimmune liver disease	291 (35.5)	266 (6.7)	4.36 (3.67 to 5.18)	221 (27.0)	234 (5.9)	3.75 (3.10 to 4.54)
MALO	538 (65.6)	1660 (41.6)	1.44 (1.31 to 1.59)	426 (52.0)	1472 (37.0)	1.29 (1.15 to 1.44)

ALD: alcohol-related liver disease; CeD: celiac disease; CI: confidence interval; CLD: chronic liver disease; HR: hazard ratio; IR: incidence rate; MALO: major adverse liver outcomes; MASLD: metabolic dysfunction-associated steatotic liver disease;

* Conditioned on matching variables (birth year, sex, county of residence, and calendar year) and further adjusted for country of birth, educational attainment, number of healthcare visits before the index date, and history of autoimmune diseases.

Table 1 Incident CLD and MALO in patients with CeD and their matched reference individuals, including or excluding the first three years of follow-up.

Conclusion: Patients with CeD had higher hazards of overall CLD and MALO for more than 15 years after diagnosis. However, absolute risks were low. The increased hazards of CLD were driven by MASLD, ALD, and autoimmune liver disease. Our findings support diagnostic work-up and regular follow-up for possible CLDs in patients with CeD who had elevated liver enzymes.

Disclosure: All authors have completed the ICMJE uniform disclosure form and declare:

FE has served as an advisory board member for Boehringer Ingelheim.

DAL receives a salary as an employee of Takeda Pharmaceuticals.

HH's institutions have received research funding from Astra Zeneca, Echo-Sens, Gilead, Intercept, MSD, Novo Nordisk and Pfizer. HH has served as consultant or on advisory boards for Astra Zeneca, Bristol Myers-Squibb, MSD and Novo Nordisk and has been part of hepatic events adjudication committees for KOWA and GW Pharma.

JFL has coordinated a study on behalf of the Swedish IBD quality register (SWIBREG). That study received funding from Janssen Corporation. JFL has also received financial support from MSD developing a paper reviewing national healthcare registers in China. JFL also has a research collaboration on celiac disease with Takeda.

The other authors report no disclosures relevant to the manuscript.

MP048

HEPATIC STEATOSIS AND BODY COMPOSITION IN PATIENTS WITH CELIAC DISEASE. PRELIMINARY RESULTS OF A PROSPECTIVE, MULTICENTER, CASE-CONTROL STUDY (ARCTIC STUDY)

J. Bajor¹, M.Z. Peresztegi², Z. Vereczkei³, K. Hagymási⁴, N. Faluhelyi⁵, G. Szekeres⁵, G. Pásztor⁶, B. Szirmay⁷, Z. Sipos³, K. Lemes⁸, V. Papp⁴, Z. Lénárt⁸, G. Pár¹

¹University of Pécs, Medical School, First Department of Medicine, Division of Gastroenterology, Pécs, Hungary, ²University of Pécs, Medical School, Pécs, Hungary, ³University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ⁴Semmelweis University, Faculty of Medicine, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary, ⁵University of Pécs, Medical School, Department of Radiology, Pécs, Hungary, ⁶University of Szeged, Albert Szent-Györgyi Medical School, Department of Radiology, Szeged, Hungary, ⁷University of Pécs, Medical School, Department of Laboratory Medicine, Pécs, Hungary, ⁸University of Szeged, Albert Szent-Györgyi Medical School, Department of Medicine, Szeged, Hungary

Contact E-Mail Address: bajor.judit8@gmail.com

Introduction: According to literature data, the occurrence of hepatic steatosis is more common in patients with celiac disease than in the general population. The reasons behind this include malabsorption, proinflammatory processes, as well as weight gain and unfavorable metabolic changes on a gluten-free diet.

Aims & Methods: In our prospective multicenter, case-control study (ARCTIC study), we examined the occurrence of hepatic steatosis determined by ultrasound (US), body composition parameters, and blood lipid levels in patients with celiac disease who had been on a gluten-free diet for at least 1 year. We investigated the proportion of celiac patients with and without steatosis, and compared the data of celiac patients with and without steatosis.

Patients from three university centers with celiac disease participated in the study. Body composition analysis was performed using an Inbody 770 device, measuring parameters such as BMI, waist-hip ratio, Inbody score, Skeletal muscle mass (SMM), Percent body fat (PBF), and Visceral fat area (VFA). Blood lipids including total cholesterol, LDL, and triglyceride levels were measured. Hepatic steatosis was assessed by US using the Hamaguchi score and the NAFLD-LFS score. If either score was positive, the patient was classified into the steatosis group. Fischer's exact test was used for categorical variables, and Welch Two Sample t-test was used to assess continuous variables. A p-value less than 0.05 was considered statistically significant.

Results: 97 patients with celiac disease and 47 control individuals were included. Hepatic steatosis was described in 13.8% of control subjects and 35% of celiac patients (p=0.012). In celiac patients, steatosis developed in 31% with normal BMI. The occurrence of hepatic steatosis in celiac patients showed a significant association with BMI (p<0.001), waist circumference (p<0.001), hip circumference (p<0.001), percent body fat (p=0.037), visceral fat area (p=0.006), and triglyceride levels (p=0.006). However, there was no significant difference in waist/hip ratio (p=0.56), Skeletal Muscle Mass (p=0.164), Inbody score (p=0.31), LDL (p=0.80), and total cholesterol level (p=0.73). The adherence to a gluten-free diet did not influence hepatic steatosis (p=0.60). Among celiac disease patients with hepatic steatosis, 83% met the Metabolic Dysfunction-Associated Liver Disease (MASLD) criteria.

Conclusion: The occurrence of hepatic steatosis is substantial in celiac patients on a gluten-free diet, even in those with normal BMI. Increased attention should be paid to its examination and monitoring during care, weight control, dietary and lifestyle counseling, as well as timely recogni-

tion and prevention of cardiovascular and metabolic diseases.

Funding: National Research, Development and Innovation Office (grant FK142942), ÚNKP-23-3-II-PTE-1855

References: Reilly, N.R., et al., Increased risk of non-alcoholic fatty liver disease after diagnosis of celiac disease. *J Hepatol*, **2015**. 62(6): p. 1405-11. DOI: 10.1016/j.jhep.2015.01.013.

Valvano, M., et al., Celiac disease, gluten-free diet, and metabolic and liver disorders. *Nutrients*, 2020. 12(4).DOI: 10.3390/nu12040940.

Tovoli, F., et al., Increased risk of nonalcoholic fatty liver disease in patients with coeliac disease on a gluten-free diet: beyond traditional metabolic factors. *Aliment Pharmacol Ther*, 2018. 48(5): p. 538-546.DOI: 10.1111/apt.14910.

Tortora, R., et al., Metabolic syndrome in patients with coeliac disease on a gluten-free diet. *Aliment Pharmacol Ther*, 2015. 41(4): p. 352-9.DOI: 10.1111/apt.13062.

Disclosure: The authors declare that they have no competing interests.

MP049

WITHDRAWN

MP050

PSYCHOMETRIC EVALUATION OF THE CELIAC DISEASE SYMPTOM DIARY 2.1[®]

S. Ghura¹, N. J. Rockwood², D. Adams³, M.G. Geller⁴, D.A. Leffler^{1,5}, E. Liu⁶, L. McLeod², L. M. Meckley⁷, M. J. Tahir¹, M. Arvizu¹, R. Saad¹

¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²RTI Health Solutions, Research Triangle Park, United States of America, ³Vanderbilt University Medical Center, Nashville, United States of America, ⁴Celiac Disease Foundation, Woodland Hills, United States of America, ⁵Celiac Center, Beth Israel Deaconess Medical Center, Harvard Medical School Celiac Research Program, Boston, United States of America, ⁶Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, United States of America, ⁷At the time of this study: Takeda Development Center Americas, Inc., Cambridge, United States of America

Contact E-Mail Address: sonal.ghura@takeda.com

Introduction: There is a need to reliably measure celiac disease (CeD) symptom severity in clinical trials. The Celiac Disease Symptom Diary 2.1[®] (CDSD 2.1[®]) is a daily diary that assesses five core symptoms of CeD (abdominal pain, bloating, diarrhoea, nausea and tiredness) and was developed following FDA guidelines for fit-for-purpose patient-reported outcome measures (PROMs). The objective of this study was to psychometrically validate the CDSD 2.1[®].

Aims & Methods: Psychometric properties of the CDSD 2.1[®] were evaluated using data from a 12-week US observational study (NCT05309330) in patients with CeD maintaining a gluten-free diet. Participants completed the CDSD 2.1[®] daily and other symptom severity PROMs at specified timepoints to evaluate validity, reliability and responsiveness. The average CDSD 2.1[®] weekly severity scores did not include tiredness in order to focus on GI-related symptoms.

Results: Overall, 480 participants (338 adults, 142 adolescents) completed the study. Weekly average gastrointestinal (GI; abdominal pain, bloating, nausea, diarrhoea) CDSD 2.1[®] scores demonstrated high internal consistency reliability (Cronbach's alpha, Week 0 = 0.77). Convergent validity was confirmed by moderate-to-strong correlations between weekly average GI CDSD 2.1[®] scores and Gastrointestinal Symptom Rating Scale

(GSRS) domains at Week 0 and Celiac Symptom Index (CSI) scores at Week 3 ($r = 0.48-0.73$; $p \leq 0.05$). Known-groups validity was supported with significant differences in weekly average GI CDSD 2.1[®] scores observed by Patient Global Impression of Severity (PGIS) groups ($p < 0.001$). Test-retest reliability of GI CDSD 2.1[®] scores was demonstrated among stable patients on the PGIS (intraclass correlation coefficient = 0.89). Responsiveness was established as weekly average GI CDSD 2.1[®] change scores followed the expected pattern among PGIS change groups.

Conclusion: This study demonstrates that CDSD 2.1[®] is a valid, reliable and responsive PROM of CeD GI symptom severity that could be used to construct endpoints in clinical trials for CeD therapies.

Disclosure: SG, DAL, LMM, MJT, MA and RS are employees and shareholders of Takeda. NJR and LMc are employees of RTI Health Solutions, which receives funding from pharmaceutical companies for patient-reported outcome consulting services. They receive no compensation from the pharmaceutical companies and their RTI salary is not related to the projects on which they work. DA has served as a consultant for Takeda Pharmaceuticals and Ironwood Pharmaceuticals. MG is an employee of the Celiac Disease Foundation, which received financial support from Takeda. EL serves as a consultant for Takeda Pharmaceuticals and is an author for UpToDate (celiac section) for which he receives royalties.

Potpourri of DGBI and motility

12:00-13:00 / Poster Stage 1

MP051

INTESTINAL PERMEABILITY IN IRRITABLE BOWEL SYNDROME: RESULTS FROM THE MULTICENTRIC EUROPEAN STUDY DISCOVERIE

A. Rustichelli¹, S. Rinckhout², K. Verbeke³, J. Santos⁴, M. Simrén⁵, G. Barbara⁶, D.L. Dumitrascu⁷, D.M. Jonkers⁸, C. Alonso-Cotoner⁹, R. Farré¹⁰

¹KU Leuven, Chronic Diseases, Metabolism and Ageing (CHROMETA), Leuven, Belgium, ²KU Leuven, Translational Research Centre In Gastrointestinal Disorders (TARGID), Leuven, Belgium, ³UZ Leuven, Leuven, Belgium, ⁴Institut de Recerca Vall d'Hebron, Department of Gastroenterology, Barcelona, Spain, ⁵Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Dept of Internal Medicine, Gothenburg, Sweden, ⁶University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁷Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, 2nd Medical Dept., Cluj-Napoca, Romania, ⁸Maastricht University Medical Center - Department of Internal Medicine, Division of Gastroenterology, Department of Internal Medicine, Division of Gastroenterology-Hepatology, Maastricht, Netherlands, ⁹Hospital Val Hebron, Gastroenterology, Barcelona, Spain, ¹⁰University of Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Chronic Diseases, Metabolism and Ageing (CHROMETA), Leuven, Belgium

Contact E-Mail Address: alice.rustichelli@kuleuven.be

Introduction: Irritable bowel syndrome (IBS) is a disorder of brain-gut interaction often accompanied by psychiatric and/or somatic comorbidities. Intestinal barrier dysfunction has long been hypothesised to be a key player in IBS pathophysiology. However, it is unknown how psychiatric and somatic comorbidities affect intestinal barrier dysfunction. This study aims to assess intestinal barrier function in a large multicentric cohort of adult IBS patients with and without psychiatric/somatic comorbidities.

Aims & Methods: IBS patients (Rome IV) with (N=197) and without (N=171) comorbidities, and healthy volunteers (N=23), were included in six European hospitals. Intestinal permeability (IP) was assessed *in vivo* with the lactulose-mannitol-sucralose test (LMS) and *ex vivo* in colonic biopsies using Ussing chambers. Sugar concentrations in the urine were assessed through HPLC-ELSD and GC-MS. The L/M ratio after 2 hours was used as an estimation of the small intestinal permeability, and the %S excreted and the S/M ratio from 2 to 24 hours, for colonic permeability. Colonic biopsies were collected from 17 controls and 18 IBS patients and mounted in Ussing chambers to measure the paracellular permeability to FITC-dextran (4 kDa).

Results: When compared with healthy controls, L/M ratio did not differ in IBS patients with (p=0.33) or without comorbidities (p=0.44). Moreover, the %S excreted and S/M were not altered in IBS patients with (respectively p=0.3 and p=0.09) and without (p=0.14, p=0.1) comorbidities. Interestingly, when comparing results from IBS patients among recruiting hospitals in different parts of Europe, significant differences were found in L/M ratio (p<0.0001), %S (p<0.0001), and S/M ratio (p<0.0001). Lastly, paracellular permeability assessed *ex vivo* in colonic biopsies was not different between IBS patients and controls (p=0.46).

Conclusion: These results suggest that psychiatric and somatic comorbidities do not alter small intestinal and colonic permeability in IBS patients. Interestingly, our results highlight a strong variability between IBS patients from different countries, which may be explained by lifestyle, environmental, and genetic factors. Further investigations are needed to better understand these findings.

Disclosure: Nothing to disclose.

MP052

CLINICAL CHARACTERISTICS OF PATIENTS WITH DYSSYNERGIC DEFECATION AND THE VALUE OF CURRENT HIGH-RESOLUTION MANOMETRY PARAMETERS IN ITS DIAGNOSIS

C. Rodríguez Carrillo¹, M. Aparicio Cabezudo², R. Sánchez del Hoyo³, C. Ciriza de Los Rios²

¹Hospital Clinico San Carlos, Gastroenterology and Hepathology, Madrid, Spain, ²Hospital Clinico San Carlos, Neurogastroenterology and Motility, Madrid, Spain, ³Hospital Clinico San Carlos, Research Methodological Support Unit and Preventive Department, Madrid, Spain

Contact E-Mail Address: clararc31@gmail.com

Introduction: Functional defecation disorders are causes of obstructive defecation due to alteration in the coordination of abdominal contraction and anal relaxation. Four manometric patterns of dyssynergic defecation (DD) have been described, such that in type I and III there is an alteration of anal relaxation with adequate rectal propulsion, and in types II and IV rectal propulsion fails.

According to the Rome IV criteria, the diagnosis of DD requires confirmation with two tests of anorectal function, with the most commonly used being high-resolution anorectal manometry (HRAM) and the balloon expulsion test (BET). Within the manometric parameters, the rectoanal gradient (RAG) appears to be the most useful.

Aims & Methods: To evaluate the clinical characteristics of patients according to patterns of DD defecation and to establish the cutoff point of the RAG and relaxation percentage (RP) that allows predicting balloon expulsion or not.

A total of 960 high-resolution anorectal manometries (HRAMs) performed from January 2021 to April 2024 were reviewed, including 337 patients with DD (35%). Prior to performing the HRAM, epidemiological and clinical data of the patients were collected. Although retrospectively reviewed, all data were prospectively collected. HRAM was performed with solid-state catheters (Medtronic). For BET a balloon (Matla Systems S.L) was filled with 50 mL of water was used under conditions of privacy while sitting on a toilet. Values of 60 seconds or less were considered normal.

Results: Included were 337 patients with a mean age of 61.7 ± 13.9 years. Among them, 226 (67.1%) were female. The diagnosis of DD was confirmed with an altered BET in 96 (28.5%) of the patients. In the remaining cases, the diagnosis of DD was inconclusive.

	Types I-III (N= 240)	Types II-IV (N=97)	P value
Confirmed DD (HRAM and abnormal BET)	58 (24,2%)	38 (39,2%)	0.006
Gender (female vs male)	148 (61,7%)	78 (80,4%)	0.001
Age (years)	63,85 ± 13,1	56,36 ± 14,6	0.000
BMI (kg/m ²)	26,42 ± 4,4	24,41 ± 4,7	0.000
Anal surgery	54 (22,6%)	11 (11,3%)	0.018
Comorbidities			0.006
No comorbidity	64 (26,7%)	24 (24,7%)	
Neurologic/Psychiatric	42 (17,5%)	32 (33%)	
Others	134 (55,8%)	41 (42,2%)	
Drugs			0.206
No drugs	35 (14,7%)	17 (17,5%)	
Inhibit motility (opioid, anticholinergic, psychotropic)	42 (25,8%)	24 (41,4%)	
Others	121 (74,2%)	34 (58,6%)	
Structural alterations (rectocele, cystocele, prolapse, etc)	102 (42,7%)	52 (53,6%)	0.068
Bristol			0.572
1, 2	61 (26,3%)	26 (27,7%)	
3, 4	103 (44,4%)	36 (38,3%)	
5, 6, 7	68 (29,3%)	32 (34%)	

Table 1.

The epidemiological and clinical characteristics are described in table 1. The presence of associated structural causes was observed in all groups: 102 cases (42.7%) in types I-III; and 52 patients (53.6%) in types II-IV. The frequency for rectal hyposensitivity was 47.5%, and it was similar in both groups: 112 cases (46,6%) in types I-III, and in 48 cases (49,5%) in types II-IV.

The Area Under the Curve (AUC) for RAG was 0.738 (95% CI 0.682 - 0.794), identifying a cut-off value for RAG of -34.1 with an estimated sensitivity of 81.3% and specificity of 57.3% (figure 1). The AUC for RP was 0.544 with a cutoff point of 5.5% (95% CI 0.476 - 0.611), demonstrating low sensitivity (62,5%) and specificity (52,7%) (figure 2).

Conclusion: The frequency of DD diagnosed by HRAM is high (35% in our series), being more common in women. The high coexistence of structural causes, which can give a false manometric pattern of DD, is noteworthy. In types II and IV (rectal propulsion disorders), the diagnosis was confirmed by the failure to expel the balloon more frequently than in types I and III. Rectal hyposensitivity is very frequent in these patients.

So far, the Rectoanal Gradient (RAG) is the best parameter of HRAM to evaluate DD. A value below -34 mmHg allows reasonably discriminating whether patients will expel the balloon or not.

Disclosure: Nothing to disclose.

MP053

HOME BIOFEEDBACK TRAINING WITH LOCAL SPHINCTER STIMULATION FOR FECAL INCONTINENCE: A FEASIBILITY STUDY

P. Liptak¹, M. Vojtko¹, J. Hoferica¹, M. Ďuriček¹, P. Banovcin¹

¹University Hospital in Martin, Clinic of Internal Medicine-Gastroenterology, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia

Contact E-Mail Address: liptak@jfm.uniba.sk

Introduction: Fecal incontinence is a diagnosis represented by recurrent uncontrolled passage of fecal material for at least 3 months. Although there are no sufficient data, based on large-community studies, FI is relatively common, with prevalence up to 7% of population worldwide. The therapy of fecal incontinence should be specifically tailored to each individual symptom presentation of the patients. One of the treatment options for incontinence is biofeedback training.

As office biofeedback is often time consuming and comes with substantially high cost there is an emerging trend of home biofeedback administration. However, only few studies considering this new approach were published so far and without consideration of commercially available biofeedback devices. Also, there are no relevant data published regarding the efficacy of commercially available devices.

Aims & Methods: The aim of this study is to evaluate the feasibility and efficacy of commercially available biofeedback devices. We performed a prospective single center study on patients with fecal incontinence (age>18 years). The duration of the training was 12 weeks, with training twice (2) daily for 5-6 days a week. Two types of biofeedback devices were used, both with the application of local electric stimulation of sphincters during the training.

Parameters for device one were: Frequency: 40 Hz; Impulse Width: 0.2 s; Ramp up time: 1s; Work out time: 6s; Rest: 15s; Training duration: 20min. Parameters for the second device: Continual stimulation with 35 Hz, 0.33 impulse width followed by workout: Frequency: 30 Hz; Impulse Width: 0.25 s; Ramp up time: 0.3s; Work out time: 5s; Ramp down time: 0.3s; Rest 5 s. Training duration: 6+20 min. 3D anorectal manometry was performed according to the IAPWG protocol at the initiation visit and at the control visit. Clinical evaluation was performed by self-reporting Wexner score for fecal incontinence at both visits.

Results: Twenty-seven patients (27) were randomly assigned either to device No. 1 or No.2. Two patients did not attend the control visit for unknown reasons and one patient stop the study because of adverse event (pain in rectum and worsening of the incontinence). Two patients did finish the study but did not attend the planned clinical control in the pre-defined date due to travel reasons and thus were excluded from the evaluation. Thus, twenty-two patients (22) were considered for the final evaluation. Average increase of sphincter rest medium pressure was 11.45% and average increase of maximum sphincter pressure was 26.1%. The absolute pooled average of the cohort for maximum voluntary pressure was significantly higher after the therapy compared to basal values (135.82 mmHg vs. 110.13 mmHg, p<0.05). This was not observed in the case of rest pressure (54.88 mmHg vs. 57.72 mmHg). The average improvement of Wexner score was 1.7 points and was statistically significant (p<0.05).

Conclusion: To our current knowledge this is a first study evaluating commercially available home biofeedback devices for fecal incontinence and one of few for home biofeedback devices in the defecation disorders generally. Here presented data shows the feasibility and safety of the home biofeedback device for the treatment of fecal incontinence as there was only one mild adverse event recorded. Efficacy is shown by significant improvement of the maximum voluntary sphincter pressure. Based on these results a randomized, double-blind study will be performed to further explore and evaluate the efficacy of the different devices.

Disclosure: Nothing to disclose.

MP054

CATEGORIZATION OF SMALL INTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS USING HIGH-RESOLUTION JEJUNAL MANOMETRY

L.G. Alcalá Gonzalez¹, A. Guillen-del-Castillo², A. Aguilar^{1,3}, C. Barber Caselles^{3,1}, F. Yañez¹, J. Serra^{3,1}, C.P. Simeon-Aznar², C. Malagelada^{3,1,4}

¹Vall d'Hebron University Hospital, Digestive System Research Unit, Department of digestive diseases, Barcelona, Spain, ²Vall d'Hebron University Hospital, Systemic Autoimmune Diseases Unit, Barcelona, Spain, ³Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (Ciberehd), Madrid, Spain, ⁴Universitat Autònoma de Barcelona, Barcelona, Department of Medicine, Barcelona, Spain

Contact E-Mail Address: lgalcala1986@gmail.com

Introduction: Gastrointestinal involvement is universal among patients with systemic sclerosis (SSc). Small intestinal dysfunction manifests with non-specific gastrointestinal symptoms (abdominal pain, distension, nausea, or vomiting), along with objective signs such as malnutrition, small intestinal bacterial overgrowth, and, in severe cases, chronic intestinal pseudo-obstruction. The pathogenesis of small intestinal dysmotility in SSc has been proposed to follow a sequential progression, beginning with neuropathy, progressing to myopathic damage, and ultimately culminating in fibrosis. Currently, there are no diagnostic techniques available to differentiate between stages of small intestinal involvement.

Aims & Methods: Aim: To assess the discriminative potential of high-resolution jejunal manometry in categorizing small intestinal dysmotility among patients with SSc.

Prospective study evaluating small intestinal motility in consecutive patients with SSc and digestive symptoms between January 2018 and July 2023 and healthy volunteers as controls. A 35-channel high-resolution manometry catheter was trans-nasally inserted into the jejunum under fluoroscopic radiological guidance. Small intestinal motility was continuously recorded for 5 h; 3 h fasting and 2 hours during continuous nutrient perfusion at 2 kcal/min. Tracings were analyzed by conventional qualitative

tive analysis (identifying neuropathic and myopathic motility patterns) and by quantitative analysis of high-resolution parameters (measuring a motility index (MI) that integrates contractile frequency and amplitude over time, and manually counting the number of propagated contractile fronts)

Results: Twenty patients (52 ± 10 years, 95% women) with SSc and 18 healthy subjects (HS) (27 ± 6 years, 78% women) were included. By conventional visual analysis, 6 (30%) patients exhibited abnormal small intestinal motility patterns indicative of neuropathic involvement (uncoordinated bursts n=3 and postprandial minute-rhythm n=3), and 7 (35%) patients showed diminished contractile activity during fasting and after nutrient infusion (mean amplitude <20mmHg), indicative of myopathic involvement. The remaining 7 (35%) patients had apparently normal small intestinal motility.

Quantitative analysis of high-resolution parameters detected additional abnormalities in patients with SSc compared to healthy controls (table 1). A significant decrease in fasting (phase II) propagated fronts was observed in all subgroups, including those with apparently normal motility by conventional analysis. The postprandial response to nutrient infusion was reduced in 15 of 20 patients with SSc. All patients with myopathic involvement had a null response to nutrient infusion. Patients with neuropathic patterns and those with apparently normal motility by conventional analysis also exhibited a poor postprandial response, which was similarly reduced in both groups.

	Healthy controls (n=18)	Patients with systemic sclerosis		
		Apparently normal motility (n=7)	Neuropathic involvement (n=6)	Myopathic involvement (n=7)
Fasting phase II MI (Log mmHg. contractions)	7.1 ± 0.2	6.9 ± 0.4	7.6 ± 0.7	4.7 ± 0.3*
Phase II propagated contractile fronts (n/3hrs)	24.3 ± 2.7	10.1 ± 3.1*	10.3 ± 5.5*	0.6 ± 0.4*
Postprandial MI (Log mmHg. contractions)	9.8 ± 0.2	8.4 ± 0.8	9.1 ± 0.5	4.4 ± 0.5*
MI increase after nutrient infusion (Log mmHg. contractions)	41% ± 5%	21% ± 8%*	23% ± 11%*	-6% ± 12%*

Table 1: Results from quantitative analysis of high-resolution jejunal manometry

*p<0.05 by Mann-Whitney U test compared to healthy controls.

Conclusion: High-resolution jejunal manometry detects abnormalities in fasting and postprandial small intestinal motility in patients with systemic sclerosis, even at early stages of intestinal involvement, when neuropathic and myopathic patterns are not evident.

References: Alcalá-González LG, Malagelada C, Galán C, Nieto A, Accarino A, Azpiroz F. Propagation patterns of jejunal motor activity measured by high-resolution water-perfused manometry. *Neurogastroenterol Motil.* 2021 Dec;33(12):e14240. doi: 10.1111/nmo.14240. Epub 2021 Aug 11. PMID: 34378830.

Disclosure: Nothing to disclose.

MP055

PREVALENCE OF BOWEL, BLADDER AND SEXUAL DYSFUNCTION SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

C. Dell'Oro¹, L. Hicks^{1,2}, E.V. Carrington^{1,2}

¹Imperial College, Department of Surgery and Cancer, London, United Kingdom, ²Imperial College NHS Trust, Gastroenterology and Hepatology, London, United Kingdom

Contact E-Mail Address: chiara.delloro20@imperial.ac.uk

Introduction: Bowel, bladder and sexual dysfunction symptoms in patients with Inflammatory Bowel Disease (IBD) are common. Treatment with biofeedback, medication, neuromodulation or surgery can improve

quality of life. Unfortunately, few patients proactively report symptoms for reasons including: embarrassment, lack of awareness of associations / treatment options or concerns about consultation time.

Aims & Methods: Between February-April 2024, patients with IBD attending infusion units and outpatient clinics at a tertiary hospital in the United Kingdom were asked to complete the validated ICIQ-IBD (International Consultation on Incontinence Questionnaire for IBD patients), and the ICIQ-MLUTS / ICIQ-FLUTS (Male / Female Lower Urinary Tract Symptoms) questionnaire, which assesses bowel, bladder and sexual dysfunction symptom frequency and impact on quality of life (QoL) using a 5 point scale of never-always. Presence of symptoms was defined as those rated more than 'never'. Regular symptoms were those occurring 'most of the time' or 'always'. Patients were asked to rate QoL, bowel and sexual symptoms during both remission and relapse. Patients with unclassified IBD, microscopic colitis, stomas and J-pouches were excluded.

Results: One hundred and sixteen patients received the questionnaire. Sixteen were excluded on clinical grounds and 30 due to incomplete questionnaire data leaving 70 for analysis. Thirty-three (47%) were female, 38 (54%) had Crohn's disease (CD) and 32 (46%) ulcerative colitis (UC). All patients were on biologics (96%) and/or JAK inhibitors (7%). Median age was 36 (range 20-77). Faecal urgency was the most commonly reported symptom, with 55 (79%) reporting symptoms during relapse and 45 (64%) during remission. Regular symptoms during remission were present in 9 (13%). Faecal incontinence (FI) was reported in 51 (73%) during relapse and 30 (43%) during remission. Regular FI symptoms were present in 6 (9%) during remission. Of those patients reporting to be sexually active (n=57), sexual dysfunction was common, reported in 41 (72%) during relapse and 25 (44%) during remission. Urinary incontinence (UI) was reported in 12 (17%) patients, with 10 (14%) patients reporting the presence of both UI and FI. Even during remission, patients commonly reported a bowel-control related QoL impact, with 31/70 (44%) reporting disruption to family, 36/70 (51%) to social and 38/67 (57%) to working life. Forty-three out of 70 (61%) patients worried about getting to a toilet in time and 24/54 (44%) reported feeling less attractive to their partner.

		Symptoms ^A		Regular symptoms ^B	
		Remission	Relapse	Remission	Relapse
Bowel ^C	Faecal urgency	45 (64%)	55 (79%)	9 (13%)	40 (57%)
	Faecal incontinence	30 (43%)	51 (73%)	6 (9%)	20 (30%)
	Anorectal pain	32 (46%)	43 (61%)	6 (9%)	19 (27%)
	Constipation	41 (59%)	26 (37%)	3 (4%)	3 (4%)
Sexual ^D	Sexual dysfunction ^E	25 (44%)	41 (72%)	4 (7%)	27 (47%)
Bladder ^F	Urinary incontinence	12 (17%)		2 (3%)	

Table 1: Bowel, sexual and bladder symptom frequency

N = 70

^A Symptoms reported more than 'never'

^B Symptoms reported 'most of the time' or 'always'

^{C&D} assessed using the ICIQ-IBD

^E patients reporting 'not applicable' excluded (n = 57)

^F assessed using the ICIQ-M/FLUTS

Conclusion: Bowel, bladder and sexual dysfunction symptoms are common in IBD patients and negatively impact QoL. Even during remission, symptoms are more common than in the background population and interfere with QoL. An appreciation of the prevalence of these symptoms with proactive screening may facilitate triage to pelvic floor services for targeted care.

Disclosure: Nothing to disclose.

MP056

ACUTE MUCOSAL REACTIONS FOLLOWING FOOD ADMINISTRATION IN IRRITABLE BOWEL SYNDROME ARE ASSOCIATED WITH MAST CELL ACTIVATION EX VIVO IN A SUBGROUP OF PATIENTS

L. Balsiger¹, K. Raymenants^{1,2}, C. Van de Bruaene¹, J. Schol¹, L. Juvyns¹, K. Routhiaux¹, J. Toth¹, R. Farré¹, T. Vanuytsel^{1,2}, J. Tack^{1,2}

¹TARGID KU Leuven, Leuven, Belgium, ²University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: lukas.balsiger@proton.me

Introduction: Irritable bowel syndrome (IBS) is a prevalent disorder of gut-brain interaction characterized by abdominal pain and altered bowel movements. While the pathophysiology underlying IBS is incompletely understood, local allergic reactions to foods are a candidate mechanism. Confocal laser endomicroscopy (CLE) has shown acute alterations of the duodenal epithelium in IBS within minutes of local food administration and these findings have been used to identify foods contributing to IBS symptoms. However, the mechanisms and relevance of the observed alterations remain elusive.

Aims & Methods: Aim: To visualize the effect of local food administration on the duodenal mucosa using CLE and assess whether visible changes are associated with altered permeability or markers of mast cell activation ex vivo.

Methods: Non-constipated Rome IV IBS patients with negative serum specific IgE for tested foods underwent baseline gastroscopy (EGD) and CLE performed during a second EGD. Duodenal mucosa was visualized using CLE at baseline and after luminal administration of foods (egg white, soy, milk, wheat, lyophilized fish and shellfish, and nuts solutions sequentially applied in a random order) through the working channel. Altered mucosa was defined as leakage of fluorescein into the lumen and presence of particles (previously termed “cell shedding”). Serum samples were taken at index endoscopy and 30 minutes after acute mucosal alterations. Biopsies were taken at index EGD and after visualized alterations to measure transepithelial electrical resistance (TEER) in Ussing chambers and tryptase levels in biopsy supernatants. Data are reported as mean ± SEM or median and IQR as appropriate.

Results: 45 CLE exams were carried out in 28 patients (age 35±2 y, 93%^f, BMI 24±1 kg/m², mean IBS symptom severity score 320±20).

At baseline, mucosal alterations were present in 9% of exams (n=4), whereas all other exams (n=41) demonstrated alterations after food administration. The highest rate of acute alterations was observed after fish/shellfish mix (50%; 10 altered / 20 exposed). The rate of observed alterations per food is presented in the table. TEER was not altered after observed alterations vs baseline (25±0.8 Ωxcm² vs 25±1 Ωxcm²). Serum tryptase was not altered after food exposure vs baseline (ratio after/before = 0.9, IQR= 0.8-1.1, n=13). Tryptase release from biopsies increased after exposure compared to baseline in 5/9 (56%) of patients after one hour and in 13/19 (68%) patients after 24h. Overall, the average tryptase release of the tissue was 1.48-fold increased after food exposure compared to baseline in the first hour after exposure (IQR = 0.3-2.1, n=9) and 1.29-fold following 24h incubation (IQR = 0.9-2.1, n = 19).

Food	Exposed	Altered n(%)	Food	Exposed	Altered n(%)
Fish/Shellfish mix	20	10 (50%)	Egg	21	6 (29%)
Milk	21	10 (48%)	Wheat	18	5 (28%)
Nuts	19	6 (32%)	Soy	15	4 (27%)

Conclusion: In this group of IBS patients, we found a high rate of acute food-induced mucosal alterations as visualized with CLE. Ex vivo permeability was unaltered after observed alterations vs. baseline. Systemic

tryptase remained unchanged after acute alterations compared to baseline whereas tryptase release from biopsies was increased following food exposure compared to baseline in more than half of patients.

Disclosure: Nothing to disclose.

MP057

SAFETY AND EFFICACY OF VELUSETRAG IN CHRONIC INTESTINAL PSEUDO-OBSTRUCTION: A PHASE II PROOF-OF-CONCEPT STUDY

V. Stanghellini^{1,2}, C. Malagelada^{3,4,5}, R. De Giorgio⁶, R.F. Cogliandro¹, L. Alcala-Gonzalez³, A. Costanzini⁶, M. Grimaldi⁷, R. Giovannini⁷, E. Gentile⁷, V. Scuderi⁷, S. Manzoni⁷, E. Pasquali⁷, C. Costantini⁷, M. Barone⁷, A. Pellacani⁷, J. Tack⁸

¹IRCCS University Hospital S. Orsola, Bologna, Italy, ²University of Bologna, Department of Medical and Surgical Science, Bologna, Italy, ³University Hospital Vall d’Hebron, Digestive System Research Unit, Barcelona, Spain, ⁴Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain, ⁵Universitat Autònoma de Barcelona, Barcelona, Spain, ⁶University of Ferrara, Department of Translational Medicine, Ferrara, Italy, ⁷Alfasigma S.p.A., R&D Department, Bologna, Italy, ⁸Leuven University Hospital, Department of Gastroenterology and Hepatology, Leuven, Belgium

Contact E-Mail Address: cmalagelada@gmail.com

Introduction: Chronic Intestinal Pseudo-Obstruction (CIPO) is a rare disease characterized by a severe impairment of intestinal propulsive activity resulting in a clinical picture mimicking a mechanical intestinal obstruction despite the absence of any physical obstruction. Velusetrag (VEL) is a highly selective oral 5-hydroxytryptamine type 4 receptor (5-HT₄R) agonist that enhances peristalsis, stimulates intestinal secretion and inhibits gastrointestinal visceral sensitivity via acetylcholine and calcitonin gene-related peptide released from motor and sensory neurons, respectively. This phase II, multicenter, double-blind, placebo-controlled, 2 treatments, 4 periods, multi-crossover (N-of-1) trial investigates the efficacy and safety of VEL in CIPO patients.

Aims & Methods: Seventeen patients with idiopathic or secondary (to primary neurodegenerative disorders) CIPO with at least 30% of their daily caloric intake from oral nutrition were treated for 4 periods of 4 weeks each with either VEL 15 mg once daily or placebo (PLA), with a washout period of 2 weeks between treatment periods. Each cycle with two periods assigned to either VEL or PLA is considered as a pair of observations. Analysis was performed on the evaluable pairs (i.e., evaluation available both for VEL and PLA within cycle). Each subject could be evaluated twice, once for each cycle, thus, each subject could contribute to 0, 1 or 2 observations for each treatment. The present analysis was performed on 15 patients, assessed as responders or naïve to 5-HT₄R agonists. The number of pseudo-obstructive episodes and stool type (Bristol stool scale) were assessed during the entire study.

Results: A 50% reduction in the number of pseudo-obstructive episodes in VEL (n=4) vs PLA (n=8) was detected in 30 evaluable pairs of observations. During VEL treatment, pseudo-obstructive episodes occurred once in 2 patients and twice in 1 patient; during PLA treatment 7 patients experienced 1 episode and 1 during wash-out period after PLA. Complete normalization of constipation was observed only with VEL. In 23 evaluable pairs, all 4 observations with constipation on VEL at pre-treatment had normal stools at end of treatment (from Bristol stool type 1-2 to 3-4); additionally, observations with normal stools increased from 3 (pre-treatment) to 6 (end of treatment). In contrast, all 3 observations with constipation on PLA at pre-treatment remained constipated at end of treatment and other 2 observations with diarrhea at pre-treatment shifted to consti-

pation at the end of treatment (Tab. 1). These results did not reach statistical significance due to limited sample size. The number of subjects with treatment emergent adverse events was similar between VEL and PLA. No cardiovascular adverse reactions or serious treatment emergent adverse events were observed in both treatment groups.

Conclusion: A VEL prokinetic effect was confirmed by a decreased number of pseudo-obstructive episodes and a normalization of constipation, two main clinical features of CIPO. VEL was also well-tolerated and safe, with no serious drug-related adverse event reported.

	Velusetrag				Placebo		
	0	1	2		0	1	2
Number of pseudo-obstructive episodes							
During treatment period n (%)	27 (90.00)	2 (6.67)	1 (3.33)		23 (76.67)	7 (23.33)	0
During wash-out period n (%)	30 (100.00)	0	0		29 (96.67)	1 (3.33)	0
Bristol scale class at pre-treatment	Constipation (Total: 4)	Normal (Total: 3)	Diarrhea (Total: 16)	Total (Total: 23)	Constipation (Total: 3)	Normal (Total: 3)	Diarrhea (Total: 17)
Bristol scale class at end of treatment							
Constipation n (%)	0	0	0	0	3 (100.00)	0	2 (11.76)
Normal n (%)	4 (100.00)	1 (33.33)	1 (6.25)	6 (26.09)	0	2 (66.67)	2 (11.76)
Diarrhea n (%)	0	2 (66.67)	15 (93.75)	17 (73.91)	0	1 (33.33)	13 (76.47)

Tab. 1: Number of pseudo-obstructive episodes (30 evaluable pairs) and stool consistency (23 evaluable pairs) by treatment.

Disclosure: Publications management support was provided by Pharma-Genesis London, London, UK, and was funded by Alfasigma S.p.A.

This study was sponsored by Alfasigma S.p.A.

Stanghellini V is a member of advisory boards and/or is a speaker for Alfasigma, Bayer, GE Healthcare and Vibrant Pharma; and receives research support from Alfasigma.

Tack J and Malagelada C have relevant financial relationship(s) to disclose: Alfasigma S.p.A.; consultancy and honoraria.

Grimaldi M, Giovannini R, Gentile E, Scuderi V, Manzoni S, Pasquali E, Costantini C, Barone M and Pellacani A have relevant financial relationship(s) to disclose: Alfasigma S.p.A.; employees.

All other authors declare that they have no relevant conflicts of interest to disclose.

MP058

EFFECT OF INTERMITTENT COLONIC EXOPERISTALSIS ON PEOPLE TAKING CONSTIPATION-INDUCING MEDICATION. MEDICAL DEVICE USE AT HOME WITHOUT PATIENT SUPERVISION

I. Herrero-Fresneda¹, D. McClurg²

¹USMIMA S.L., Scientific & Medical Dpt., Esplugues Llobregat, Barcelona, Spain, ²Glasgow Caledonian University, Glasgow, United Kingdom

Contact E-Mail Address: ihf@mowoot.com

Introduction: Opioids and many other chronic medications are risk factors for constipation [1]. Lifestyle changes and second-line treatment with laxatives are not enough to solve the problem [2]. Indeed, most laxative agents show limited efficacy for chronic use, especially in people under concomitant medication, in addition to potential adverse effects [3]. Intermittent colonic exoperistalsis (ICE) administered with the MOWOOT medical device, is a non-invasive, non-drug solution for chronic constipation. It has been developed to facilitate natural bowel movements and

reduce the burden of laxatives, enemas, and other invasive approaches. ICE has been proven safe and effective in a previous multicentric clinical trial [4].

Aims & Methods: The aim of the present study was to assess the effect of ICE treatment on those people included in the previous clinical trial [4] who were under constipation-inducing medication (CIM).

The patients under CIM were identified by searching the clinical trial data base for concomitant medication. A medication was considered as constipation-inducing (CIM) when its medical leaflet indicated constipation as secondary adverse event occurring with a frequency >10%.

The ICE device was used daily for 20 minutes over 4 weeks at home without the direct supervision of a medical professional.

The difference after ICE-treatment (V2) respect to baseline (V1) was assessed for the number of complete bowel movements/week (CBM/w; primary outcome), the constipation symptoms (KESS score [5]), and the quality of life (PACQoL [6]).

Results: Out of the total 92 participants [4], there were n=42 under CIM, which include opioids (n=6; 14.29%), antidepressants (n= 29; 69.05%), antipsychotics (n=3; 7.14%), anticonvulsants (n=2; 4.76%), antihypertensives (n=13; 30.95%), and other CIM (n=9; 21.43%). Most people were women (78.57%), aged 53'86 (10.16) yr, with BMI: 27,68 (5,25). The rest of the sample not taking CIM were also mostly women (82.61%), aged 49.64 (13.12) yr, with BMI: 24.23 (4.83).

All the constipation-related assessed parameters significantly improved after ICE treatment, both in people taking CIM or not (Table). The number of CMB/w in the CIM sample after 4 weeks of ICE treatment increased to 7.1 (5.4), while participants not taking CIM increased to 5.9(3.3). Although this difference between groups did not reach statistical significance (Table), the clinical impact was notable for people taking CIM who achieved the goal of a daily deposition. The symptoms of chronic constipation and the quality of life were similarly ameliorated in both CIM and no-CIM groups.

	CIM	V2-V1 mean (SD)	*P _{V2-V1}	**P _{Yes vs No}
Compleat Bowel Movements/week	Yes	2.4 (3.1)	<0.0001	0.0517
	No	1.3 (2.1)	0.0002	
KESS score	Yes	-3.6 (5.3)	0.0001	0.6402
	No	-4.2 (4.8)	<0.0001	
PAC-QoL	Yes	-0.6 (0.7)	<0.0001	0.3360
	No	-0.7 (0.8)	<0.0001	

KESS (0 to 39) & PAC-QoL (0 to 4): the lower value, the better result. The Wilcoxon test (*paired, **unpaired) was used. Statistical significance reached at P<0.05.

Conclusion: The results favour the use of intermittent colonic exoperistalsis (ICE) with the MOWOOT medical device to treat constipation at home, without direct supervision of a medical professional, in people under constipation-inducing medication. As a non-invasive and non-drug solution, ICE would offer important advantages over the current standard of care (laxatives, enemas...) to CIM patients and the healthcare system.

References: 1. Camilleri, M., et al., *Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation*. Neurogastroenterol Motil, 2014. **26**(10): p. 1386-95.

2. Holzer, P., *Non-analgesic effects of opioids: management of opioid-induced constipation by peripheral opioid receptor antagonists: prevention or withdrawal?* Curr Pharm Des, 2012. **18**(37): p. 6010-20.

3. Prichard, D.O. and A.E. Bharucha, *Recent advances in understanding and managing chronic constipation*. F1000Res, 2018. **7**.

4. McClurg, D., L. Booth, and I. Herrero-Fresneda, *Safety and Efficacy of Intermittent Colonic Exoperistalsis Device to Treat Chronic Constipation: A Prospective Multicentric Clinical Trial*. Clin Transl Gastroenterol, 2020. **11**(12): p. e00267.

5. Knowles, C.H., et al., *Linear discriminant analysis of symptoms in patients with chronic constipation: validation of a new scoring system (KESS)*. Dis Colon Rectum, 2000. **43**(10): p. 1419-26.

6. Marquis, P., et al., *Development and validation of the Patient Assessment of Constipation Quality of Life questionnaire*. Scand J Gastroenterol, 2005. **40**(5): p. 540-51.

Disclosure: IHF works at USMIMA S.L., the manufacturer of MOWOOT.

MP059

DISORDERS OF GUT-BRAIN INTERACTION IN PATIENTS WITH CELIAC DISEASE ADHERING TO GLUTEN-FREE DIET: A PROSPECTIVE 10-YEAR STUDY

L. Colecchia¹, F. Candia², A. Gobbato¹, A. Di Biase², S. Crestani², G. Cammarata², V. Boarino³, E. Dajti¹, F. Ravaoli¹, M.R. Barbaro¹, C. Cremon⁴, G. Barbara¹, A. Colecchia², L. Iughetti², G. Marasco¹

¹University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ²University of Modena and Reggio Emilia, Modena, Italy, ³Modena Hospital, Gastroenterology and Digestive Endoscopy Unit, Modena, Italy, ⁴IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Contact E-Mail Address: giovannimarasco89@gmail.com

Introduction: Patients with celiac disease (CD) can present persistence or de-novo occurrence of gastrointestinal (GI) symptoms later in life even following a strict gluten-free diet (GFD). Indeed, GFD can alter the gut microbiota inducing dysbiosis that with time may lead to the development of disorders gut-brain interaction (DGBI).

Aims & Methods: In this prospective study, we evaluated the rate of irritable bowel syndrome (IBS), functional dyspepsia (FD), anxiety, and depression over a follow-up period of more than 10 years in a population of patients with CD following GFD.

Patients with CD diagnosed between 2004 to 2014 at the University Hospital in Modena, Italy were re-evaluated to assess the presence of DGBI. Rome-IV (pediatric modules if patients were younger than 17 years old), gastrointestinal symptoms rating scale (GSRS) and hospital anxiety and depression scale (HADS) questionnaires were administered along with the evaluation of the last blood examinations. The rates of IBS, FD, anxiety, and depression were then assessed. Univariate and multivariate analyses were performed to investigate the presence of factors associated with IBS and FD.

	No IBS 130 (85.53%)	IBS 22 (14.47%)	No FD 141 (92.76%)	FD 11 (7.24%)	Multivariate (IBS) OR (95% CI)	P-value	Multivariate (FD) OR (95%CI)	p- value
Age at diagnosis (months)	62 (35-97)	79 (49-116)	62 (35-97)	84 (49-121)				
Follow-up (months)	151 (123- 177)	177 (152- 189)	152 (123- 179)	179 (154-225)	1,142 (1,023 - 1,275)	0,018		
Gender (Male)	41 (32.28%)	3 (13.64%)	42 (30.43%)	2 (18.18%)				
Depression (HADS)	9 (6.92%)	4 (18.18%)	9 (6.92%)	2 (18.18%)				
Anxiety (HADS)	28 (21.54%)	14 (63.64%)	35 (24.82%)	7 (63.64%)	6,595 (2,441 - 17,815)	< 0,001	5.045 (1.322 - 19.248)	0.018
BMI percentile	33 (8-74)	44 (10-71)	33 (8-67)	44 (21-95)				
Diarrhea	6 (4.72%)	2 (9.09%)	8 (5.8%)	0				
Constipation	6 (4.72%)	2 (9.09%)	8 (5.8%)	0				
Abdominal pain	40 (31.5%)	8 (36.36%)	42 (30.43%)	6 (54.55%)				

Results: We contacted 197 patients out of 340 from our original pediatric cohort. Patients who were not strictly adhering to GFD (25 patients) and who did not complete the questionnaires (20 patients) were excluded

from the study. The median follow-up time was 154 months (inter-quartile range 125-180). The rate of IBS was 14.47% (22/152) which increased to 22.3% (21/94) considering only the adult population (Table 1 panel A). Patients were then subclassified in IBS-C (5/22, 22.7%), IBS-M (6/22, 27.3%) and IBS-D (10/22, 45.5%). The overall rate of FD was 7.24% (11/152) (Table 1 panel B) and up to 11.7% (11/94) in the adult population and none in the pediatric one.

We found that postprandial distress syndrome (PDS) was present in 7.89% (12/152) of the population and epigastric pain syndrome (EPS) in 5.26% (8/152). Significantly higher rates of anxiety were found in patients developing IBS and FD (Table 1 and 2).

Univariate and multivariate analyses showed that a longer follow-up time was significantly correlated with a higher rate of IBS and that anxiety was correlated with both IBS and FD diagnosis (Table 1).

Conclusion: Over more than 10 years from the initial diagnosis of CD, we found a higher rate of IBS and FD than the one reported for the general population. In our cohort, DGBIs are correlated with higher levels of anxiety and longer follow-up time.

Disclosure: None.

MP060

ARTIFICIAL INTELLIGENCE AS A TRANSFORMING FACTOR IN MOTILITY DISORDERS – AUTOMATIC DETECTION OF MOTILITY PATTERNS IN HIGH-RESOLUTION ANORECTAL MANOMETRY

F. Mendes¹, M.J. Mascarenhas Saraiva¹, J. Mota¹, T. Ribeiro¹, P. Cardoso¹, M. Martins¹, M.J. Almeida¹, J. Cordeiro², J. Ferreira², G. Macedo¹, C. Santander³

¹Centro Hospitalar Universitário São João, Department of Gastroenterology, Porto, Portugal, ²Faculdade de Engenharia da Universidade do Porto, Porto, Portugal, ³Hospital Universitario de la Princesa, Madrid, Spain

Contact E-Mail Address: francisco.cnm@gmail.com

Introduction: Anorectal functional disorders are common in clinical practice, impacting the life of over 5% of the world population. High-resolution anorectal manometry (HR-ARM) is considered the gold standard for evaluating anorectal functional disorders. However, progress is hindered by the limited accessibility of the procedure, which is not available across all centers, and by the complexity of the data analysis involved. The London Protocol and Classification were developed as a standardized method for anorectal motility patterns classification. Artificial intelligence models have increasingly been developed in medical areas with a strong imaging component and Gastroenterology is not an exception. However, when it comes to functional anorectal disorders it remains uncharted territory, with only a few research articles published.

This study aims to develop and validate an AI model for the identification and differentiation of disorders of anal tone and contractility during HR-ARM, based on the London Classification.

Aims & Methods: A dataset of 701 HR-ARM exams from a tertiary center was used for developing and testing of multiple machine learning (ML) algorithms. All HR-ARM procedures were performed with Solar™ GI High-Resolution Anorectal Manometry HRAM single use Water Perfused Catheters Cathethers (Laborie™, Enschede, The Netherlands). Classification of anorectal motility disorders was based on the London Classification.

The training dataset had 80% of the total exams, with the remaining 20% being used for the testing dataset. The testing dataset was used for the models' evaluation through its accuracy, f1-weight score, sensitivity, specificity, positive and negative predictive values and area under the receiving-operating characteristic curve.

Results: After models' fine tuning, LGBM Classifier had the best performance, with a mean accuracy of 87.0% and a F1 weight score of 85.0% for identifying disorders of anal tone and contractility. Different ML models excelled in distinguishing specific disorders of anal tone and contractility, with mean accuracy over 90.0%. LGBMClassifier identified anal hypotension with normal contractility with a F1 weight score of 91.0%. On the other hand, AdaBoostClassifier had a F1 weight score of 97.0% for combined anal hypotension and hypocontractility. Anal normotension with hypoco- ntractility was detected with 90.0% F1 weight score by LGBM Classifier. Finally, DecisionTreeClassifier excelled in the detection of anal hyperten- sion, with a F1 weight score of 97.0%.

Conclusion: This is the first worldwide study proving the accuracy of ML models for differentiation of motility patterns in HR-ARM, based on London Classification. The evaluation of disorders of anal tone and con- tractility with HR-ARM is an indirect measure of the internal and external anal sphincter function and accurate identification of these disorders is of utmost importance for guiding clinical practice. Artificial intelligence has the potential to enhance accessibility to HR-ARM by facilitating the evaluation of the data and, perhaps, making it more cost-efficient. Finally, interoperability, a key point of interest, can be achieved using AI models.

References:

1. Heitmann PT, Vollebregt PF, Knowles CH, et al. Understanding the phys- iology of human defaecation and disorders of continence and evacua- tion. *Nat Rev Gastroenterol Hepatol* 2021;18:751-769.
2. Drossman DA, Hasler WL. Rome IV-Functional GI Disorders: Disorders of Gut-Brain Interaction. *Gastroenterology* 2016;150:1257-61.
3. Carrington EV, Knowles CH, Grossi U, et al. High-resolution Anorectal Manometry Measures Are More Accurate Than Conventional Measures in Detecting Anal Hypocontractility in Women With Fecal Incontinence. *Clin Gastroenterol Hepatol* 2019;17:477-485.e9.
4. Scott SM, Carrington EV. The London Classification: Improving Char- acterization and Classification of Anorectal Function with Anorectal Ma- nometry. *Curr Gastroenterol Rep* 2020;22:55.
5. Carrington EV, Heinrich H, Knowles CH, et al. The international anorec- tal physiology working group (IAPWG) recommendations: Standardized testing protocol and the London classification for disorders of anorec- tal function. *Neurogastroenterol Motil* 2020;32:e13679.

Disclosure: Nothing to disclose.

Marching forward in lower GI endoscopic treatment

12:00-13:00 / Poster Stage 2

MP061

AFFORDABLE ENDOSCOPIC VACUUM THERAPY FOR COLORECTAL ANASTOMOTIC LEAKS: A COMPREHENSIVE COMPARATIVE ANALYSIS OF MANUAL AND COMMERCIAL KITS

L. Correia Gomes¹, M. Rajão Saraiva¹, A. Bestetti²,
D. Conceição¹, J. Cortez-Pinto³, I. Rosa¹,
D.T. Hourneaux de Moura², E.G. Hourneaux de Moura²

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, Gastroenterology, Lisboa, Portugal, ²Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, Gastrointestinal Endoscopy Unit, Department of Gastroenterology, São Paulo, Brazil, ³Hospital beatriz ângelo, Gastroenterology, Loures, Portugal

Contact E-Mail Address: luisfilipe.gomes@outlook.com

Introduction: Colorectal surgery for oncological diseases has progressed significantly, yet anastomotic leaks (AL) remain a daunting challenge, with an incidence rate of up to 10%. AL not only entails reintervention but also leads to increased costs, discharge delays, and elevated morbidity and mortality risks. Endoscopic vacuum therapy (EVT) has emerged as a preferred minimally invasive approach, offering favorable outcomes. However, despite its recognized effectiveness, widespread EVT adoption remains limited, one of the limitations is cost. Manual EVT kits present a cost-effective alternative, particularly beneficial in resource-limited set- tings, however there's a lack of comparative studies between both kits.

Aims & Methods: Our study aims to address these gaps by comparing the efficacy and safety of manual and commercial EVT kits.

Retrospective multicenter study from October 2017 to December 2023, all patients undergoing EVT for colorectal and ileo-anal AL. The analysis covered patients' demographics, surgery type, number of EVT sessions, their efficacy and safety.

Patients displaying indications of rectal defects after colorectal surgery underwent diagnostic assessment using endoscopic exam and CT scan. EVT initiation depended on identifying leakage or defect as the primary in- fection focus. Two self-manufactured EVT options (polyurethane or open pore) and one commercial (Endo-sponge®) were available, chosen based on leak characteristics. Clinical success was defined as successful sepsis control (clinically and analytical) and closure of the leak, either endo- scopically and radiologic. Technical success involved successful vacuum device positioning.

Results: 35 patients underwent EVT for colorectal and ileo-anal anasto- motic leaks following various surgical procedures. Average age was 53.63 years with 62.9% males. The interval from surgery to EVT placement aver- aged 235.9 days, on average, 6.97 sponge exchanges were performed with treatment duration of 31 days. Leak sizes ranged from 0.5 to 12 cm. Stoma reversal was possible in nearly half of the patients (48.6%), with 65.7% achieving long-term gastrointestinal tract preservation.

Manual EVT: 17 patients were included, average age of 56 years and leaks ranging from 2 to 5cm (mean: 3,55cm). The mean time from surgery to treatment initiation was 343.24 days, with an average of 4.59 EVT ses- sions over 29.65 days to successfully close the defect. Technical success was achieved in all patients, with clinical success rate of 94.1%. 41.7% of patients successfully underwent ostomy reversal, and 70.59% maintained long-term intestinal continuity.

Commercial EVT: 18 patients, average age was 51 years and leaks rang- ing from 2 to 12cm (mean: 6,47cm). The mean duration from surgery to treatment initiation was 134.56 days, with an average of 9.22 EVT sessions over 32.89 days to successfully close the defect. Technical success was

achieved in all patients, with clinical success rate of 83.3%. 61.11% of patients had stoma reversal all maintained long-term intestinal continuity. Statistical analysis showed no significant differences between the two groups in patient demographics, clinical success ($p = 0.603$), stoma reversal ($p = 0.857$) or long-term intestinal preservation ($p = 0.349$). Adverse events were comparable between the groups.

Conclusion: Our data demonstrate that EVT is an extremely safe and highly effective therapy for managing colorectal leaks, whether using commercial or manual kits. EVT can be feasibly implemented in resource-limited settings without compromising treatment outcomes.

References:

1. Ali F, Keshinro A, Weiser MR. Advances in the treatment of locally advanced rectal cancer. *Ann Gastroenterol Surg.* 2020 Aug 30;5(1):32-38. doi: 10.1002/ags3.12389. PMID: 33532678; PMCID: PMC7832958.
2. Yamauchi S, Matsuyama T, Tokunaga M, Kinugasa Y. Minimally Invasive Surgery for Colorectal Cancer. *JMA J.* 2021 Jan 29;4(1):17-23. doi: 10.31662/jmaj.2020-0089. Epub 2021 Jan 14. PMID: 33575499; PMCID: PMC7872784.
3. Degiuli M, Elmore U, De Luca R, De Nardi P, Tomatis M, Biondi A, Persiani R, Solaini L, Rizzo G, Soriero D, Cianflocca D, Milone M, Turri G, Rega D, Delrio P, Pedrazzani C, De Palma GD, Borghi F, Scabini S, Coco C, Cavaliere D, Simone M, Rosati R, Reddavid R; collaborators from the Italian Society of Surgical Oncology Colorectal Cancer Network Collaborative Group. Risk factors for anastomotic leakage after anterior resection for rectal cancer (RALAR study): A nationwide retrospective study of the Italian Society of Surgical Oncology Colorectal Cancer Network Collaborative Group. *Colorectal Dis.* 2022 Mar;24(3):264-276. doi: 10.1111/codi.15997. Epub 2021 Dec 6. PMID: 34816571; PMCID: PMC9300066.

Disclosure: Nothing to disclose.

MP062

ENDOSCOPIC MANAGEMENT OF STRICTURES AND LEAKS FOLLOWING COLORECTAL SURGERY: A SYSTEMATIC REVIEW

G. Chlorakis¹, T.K. Nikolouzakakis², A. Augoustaki¹, V. Valatas¹, E. Kalaitzakakis¹

¹University Hospital of Heraklion, Gastroenterology Clinic, Heraklion, Greece, ²University Hospital of Heraklion, General Surgery, Heraklion, Greece

Contact E-Mail Address: giwrgosw92@hotmail.gr

Introduction: Leaks and strictures on the anastomotic site of the lower gastrointestinal tract increase morbidity and mortality of colorectal surgery. Multiple endoscopic methods have been described to treat anastomotic leaks, namely, endoscopic vacuum-assisted therapy, over-the-scope clips and sealants (fibrin glue and cyanoacrylate). As for anastomotic strictures, lumen apposing metal stents, self-expandable metal stents, balloon dilatation, intralesional steroid injection and endoscopic stricturotomy have all been proposed.

Aims & Methods: We aimed to report the indications and the overall clinical efficacy of endoscopic therapies applied for anastomotic leaks and/or strictures following colorectal surgery. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines were followed and a literature search was performed by two independent reviewers using relevant search terms in the databases PubMed and Scopus. A total of 14 studies were found and 21 additional reports were obtained from their references, overall, containing 992 patients.

Results: The overall clinical success rate of all endoscopic methods to treat leaks and strictures was 78.3%. For the treatment of leaks in 572 patients 83.4% long-term success was achieved. In 68 patients over-the-scope clips reached 67.2% symptom relief, in 473 patients the endoscopic

vacuum therapy had 86.3% success rate and in 31 individuals sealants reached 79.8% efficacy. A sum of 420 cases with strictures were identified. Clinical success was reported at 72.3% for this group. A total of 101 cases with strictures were managed with self-expanding metal stents and 54.7% experienced clinical improvement. The introduction of lumen apposing metal stents for the treatment of strictures in 19 patients produced 92.4% clinical efficacy. Migration rate for fully covered stents was 46.1% and for lumen apposing metal stents 9.1%. Balloon dilatation was applied in 182 patients reporting clinical improvement in 94% of cases and in 71 cases the strictures were treated with endoscopic stricturotomy, leading to symptom relief in 41% of patients. Forty-four patients had anastomotic strictures with concomitant leaks and were managed with self-expanding metal stents reaching clinical success in 82.1% of cases. Major complications, namely bleeding or perforation, were recorded in 2.4% and the highest rate (7.2%) was reported for stricturotomy.

Conclusion: Patients with anastomotic colorectal strictures should be treated with balloon dilation initially. Self-expandable metal stent deployment, either fully-covered or uncovered or lumen-apposing metal stents, can be used in refractory cases, with the latest expressing lower rates of migration. Colorectal anastomotic leaks with concomitant cavity can be treated with endoscopic vacuum therapy and avoid re-surgery. In the case of no cavity, sealants represent an appropriate alternative method. Strictures with leaks should be considered for treatment with fully-covered metal stent deployment. Stricturotomy is associated with high rates of complications and it is not recommended unless the technique is modified appropriately to guarantee safety.

References:

1. Kwon YH, et al. Endoscopic management of refractory benign colorectal strictures. *Clin Endosc* 2013 Sep;46(5):472-5 [DOI: 10.5946/ce.2013.46.5.472 PMCID: PMC3797928 PMID: 24143305]
2. Rahbari NN, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery* 2010 Mar;147(3):339-51 [PMID: 20004450 DOI: 10.1016/j.surg.2009.10.012]
3. Shalaby M, et al. Systematic review of endoluminal vacuum-assisted therapy as salvage treatment for rectal anastomotic leakage. *BJS Open* 2018 Dec 26;3(2):153-160 [PMID: 30957061 PMCID: PMC6433422 DOI: 10.1002/bjs.5.50124]
4. E. Girard, et al. Anastomotic leakage after gastrointestinal surgery: Diagnosis and management. *J Visc Surg.* 2014 Dec;151(6):441-50 [PMID: 25455960 DOI: 10.1016/j.jvisc.2014.10.004]
5. Yuan-Yao Tsai, et al. Management of anastomotic leakage after rectal surgery: a review article. *J Gastrointest Oncol* 2019 Dec;10(6):1229-1237 [PMID: 31949944 PMCID: PMC6955017 DOI: 10.21037/jgo.2019.07.07]
6. Bartell N, et al. Clinical efficacy of the over-the-scope clip device: A systematic review. *World J Gastroenterol* 2020 Jun 28;26(24):3495-3516 [PMID: 32655272 PMCID: PMC7327783 DOI: 10.3748/wjg.v26.i24.3495]

Disclosure: Nothing to disclose.

MP063

COMBINATION OF COMPUTER AIDED DETECTION SYSTEM (CADE) AND G-EYE BALLOON FOR ADENOMA DETECTION IN A FIT-BASED ORGANIZED COLORECTAL CANCER SCREENING PROGRAM: A RANDOMIZED CONTROLLED TRIAL (COMBAT STUDY)

S. Rocchetto^{1,2}, F. Segatta^{1,2}, A. Piagnani³, S. Paggi², N. Bina², D. Di Paolo², G. Scardino², G. Mandelli², T. Natalia², E. Buscarini⁴, S. Romeo⁴, S. Alicante⁴, A. Buda⁵, C. Hassan^{6,7}, A. Repici^{6,7}, E. Rondonotti², F. Radaelli²

¹University of Milan, Department of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ²Gastroenterology Unit, Ospedale Valduce, Como, Italy, ³Gastroenterology, Como, Italy, ⁴Manzoni Hospital, ASST Lecco, Digestive Endoscopy and Gastroenterology Department, Lecco, Italy, ⁵'Maggiore' Hospital, Gastroenterology and Digestive Endoscopy Unit, Crema, Italy, ⁶Department of Gastrointestinal Oncological Surgery, Gastroenterology Unit, GI Oncological Surgery, Feltre, Italy, ⁷Humanitas Clinical and Research Center - IRCCS, Endoscopy Unit, Rozzano, Italy, ⁸Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy

Contact E-Mail Address: simone.rocchetto@gmail.com

Introduction: Recent evidence suggests that Computer-Aided Detection (CADE) systems, when used alongside mucosal-exposure devices, may enhance adenoma detection during colonoscopy. This study evaluates whether the integration of CADe with the GEYE balloon, an endoscope with a reusable on-demand inflatable balloon at the tip, enhances adenoma detection in a fecal immunochemical test (FIT)-based colorectal cancer screening program.

Aims & Methods: Subjects aged 50-74 who tested FIT-positive as part of a national colorectal cancer (CRC) screening program, were randomized to undergo colonoscopy with either CADe alone (CADEYE, Fujifilm Co., Tokyo, Japan) or CADe combined with the GEYE balloon (G-EYE 760R, Fujifilm Co., Tokyo, Japan), performed by accredited endoscopists. The primary outcome measures included the rate of "high-risk" individuals, who need intensive surveillance, as defined by the ESGE criteria (≥ 5 low risk adenoma, at least one adenoma with high-risk features, any serrated polyp ≥ 10 mm or with dysplasia) and the adenoma detection rate (ADR). Based on prior research, the study was intended to include 600 subjects.

Variables	CADE, n (%)	CADE+G-EYE	p-value
Rate of „high risk” subjects	61/229 (26.3%)	45/216 (20.8%)	0.19
ADR	139/229 (60.7%)	117/216 (54.2%)	0.19
PDR	154/229 (67.2%)	136/216 (63.0%)	0.39
SSLDR	6/229 (2.6%)	6/216 (2.7%)	0.91
APC	1.46 $\pm$ 1.86	1.41 $\pm$ 1.99	0.79

Results: From May 2023 to April 2024 (ongoing), 479 subjects were randomized; 34 were subsequently excluded due to incomplete examination (4), inadequate preparation (12), or malfunctioning of the G-EYE balloon or CADe (18). The remaining 445 subjects were enrolled in the study (median (IQR) age 61 y/o (58-66); 216 men). Of them 229 and 216 underwent CADe colonoscopy and CADe+GEYE colonoscopy, respectively. No significant differences were observed between the two groups in terms of patient characteristics, cleansing levels, insertion times, overall withdrawal times, or inspection durations. At interim analysis, the rate of "high-risk" individuals post-colonoscopy was 26.3% (95% CI: 20.9-32.4%) with CADe and 20.8% (95% CI: 15.4-26.3%) with CADe+GEYE. The ADR was 60.7%

(95% CI: 54.4-67%) for CADe and 54.2% (95% CI: 47.5-60.8%) for CADe+GEYE, respectively. Secondary outcomes, including Polyp Detection Rate (PDR), Sessile Serrated Lesion Detection Rate (SSLDR), and Adenoma Per Colonoscopy (APC), showed no significant differences.

Conclusion: Data suggest that adding GEYE to CADe does not significantly increase the adenoma detection. Although the data are still not definitive, we can hypothesize that a "ceiling effect" due to the high detection rate of lesions with CADe have marginalized the impact of mucosal-exposure device.

Disclosure: Nothing to disclose.

MP064

CLINICAL VALIDATION OF POLYDEEP, A COMPUTER-AID DIAGNOSIS SYSTEM: RANDOMISED MULTICENTRE CLINICAL TRIAL WITH TANDEM COLONOSCOPY DESIGN

P. Davila-Piñón^{1,2}, C. Regueiro^{1,2}, A.I. Díez-Martín^{1,2}, J. Hernández-Camoiras^{1,2}, S. Zarraquinos³, L. De Castro Parga⁴, J. Herrero³, N. Fernández⁴, P. Vega³, D. Remedios³, A. Martínez⁴, M. Puga³, S. Alonso⁴, N. Pin³, N. García-Morales⁴, L. Rivas³, A. Ledo⁵, R. Macenlle³, L. Cid⁴, A. Rodríguez⁴, S. Soto³, F. Baiocchi³, I. Miosotis⁵, E. Sánchez³, R. Domínguez-Carbajales⁶, A. Nogueira-Rodríguez^{7,8}, H. López-Fernández^{7,8}, F. Fdez-Riverola^{7,8}, D. Glez-Peña^{7,8}, M. Reboiro-Jato^{7,8}, J. Cubiella^{1,3}

¹Research Group in Gastrointestinal Oncology, Ourense, Spain, ²Galicia Sur Biomedical Foundation, Ourense, Spain, ³Complejo Hospitalario Universitario de Ourense, Department of Gastroenterology, Ourense, Spain, ⁴Hospital Álvaro Cunqueiro de Vigo - CHUVI, Department of Gastroenterology, Vigo, Spain, ⁵Hospital Montecelo - CHUP, Department of Gastroenterology, Pontevedra, Spain, ⁶Complejo Hospitalario Universitario de Ourense, Department of IT, Ourense, Spain, ⁷CINBIO, Universidade de Vigo, ESEI-Escuela Superior de Ingeniería Informática, Department of Computer Science, Ourense, Spain, ⁸SING Research Group., Galicia Sur Health Research Institute (IIS Galicia Sur), SERGAS-UVIGO, Ourense, Spain

Contact E-Mail Address: pedrodavilapinon@gmail.com

Introduction: Computer-Aided polyp Detection (CADE) systems based on artificial intelligence (AI) can increase the detection rate of colonic lesions. PolyDeep is a CADe that has demonstrated its ability to detect lesions.

Aims & Methods: The aim of the study is to evaluate its performance in the context of expert endoscopists in a population-based colorectal cancer screening programme. PolyDeep Advance 2 (NCT05512793) is a multicentric randomised clinical trial with a tandem colonoscopy design. The primary endpoint of this study is to determine and compare whether PolyDeep-assisted colonoscopy reduces the Adenoma Miss Rate (AMR). The secondary outcomes are to determine and compare the serrated lesion miss rate, the polyp miss rate including adenomas and serrated lesions in this category, the advanced lesion miss rate (adenomas and serrated lesions) and the small or diminutive lesion miss rate. We included patients referred for colonoscopy with a positive faecal immunochemical test result, or who required surveillance after resection of advanced adenomas. All baseline, patient, procedure and lesion characteristics were compared using chi-squared and t-Student tests.

Results: Between May 2023 and November 2023 we included 260 patients who were randomised to first colonoscopy with PolyDeep (130) or first colonoscopy without PolyDeep (130). We excluded 16 patients due to lack of double cecal intubation (15) or poor bowel preparation (1). Baseline characteristics of the 244 patients (124 first PolyDeep-assisted colonoscopy, 120 first non-assisted colonoscopy) were equivalent (male: 62.3%,

years of age: 62.3 ± 6.5, FIT positive: 66.0%, mean Boston Bowel Preparation Scale: 7.5 ± 1.3, first withdrawal time: 13:47 ± 08:34 min, second withdrawal time: 07:52 ± 03:39 min, detection rate of colonic lesions: 77.0%, mean number of colorectal lesions per colonoscopy: 3.0 ± 4.3). We detected 727 colonic lesions (66.4% adenomas, 23.8% serrated lesions, 6.1% other histologies, 3.7% non-retrieved lesions). We found no statistically significant differences in the miss rates between groups (Table).

	PolyDeep-assisted colonoscopy	Non-assisted colonoscopy	p
Adenoma Miss Rate	21.6%	17.0%	0.2
Serrated Lesion Miss Rate	23.4%	24.0%	0.9
Polyp Miss Rate	22.0%	19.0%	0.2
Advanced Lesion Miss Rate	10.9%	10.4%	0.9
Small lesion Miss Rate	23.4%	21.0%	0.5
Diminutive lesion Miss Rate	25.5%	21.6%	0.3

Conclusion: In colonoscopies performed by experienced endoscopists, PolyDeep does not reduce the AMR.

Disclosure: Nothing to disclose.

MP065

EFFECT OF ARTIFICIAL INTELLIGENCE ON ADENOMA AND POLYP DETECTION RATE IN A REAL-WORLD, NON-RANDOMIZED SETTING

J. Harki^{1,2,3}, T. O’Sullivan^{1,2}, K. Ryan¹, M. Lamba¹, F. Grimpén¹, E. Gonsalkorala^{1,2}, S. Llewellyn⁴, K. Hanigan^{1,2}, M. Appleyard^{1,2}
¹Royal Brisbane and Women’s Hospital, Gastroenterology and Hepatology, Brisbane, Australia, ²Surgical Treatment and Rehabilitation Service, Gastroenterology, Brisbane, Australia, ³Hagaziekenhuis, Gastroenterology and Hepatology, The Hague, Netherlands, ⁴QIMR Berghofer Medical Research Institute, Biostatistics, Brisbane, Australia

Contact E-Mail Address: j.harki87@gmail.com

Introduction: The benefit of computer-assisted detection systems (CADE) has been evaluated in several randomized controlled trials (RCTs) showing improved adenoma detection rate (ADR) and polyp detection rates (PDR) (1-3). However, the generalizability of these studies is questioned as these studies are performed in highly controlled setting and thus not representing a real-world clinical setting (4). It is also believed that the increase in ADR by CADe-assisted colonoscopy is mainly observed in lower detector endoscopists (5, 6).

We aimed to evaluate the effect of CADe-assisted colonoscopy on ADR in an actual clinical setting in a high-volume, non-tertiary endoscopy centre with high detector endoscopists.

Aims & Methods: A single-centre, observational study was conducted on all patients undergoing colonoscopy due to symptoms of colorectal cancer (CRC), screening colonoscopies for CRC, post-polypectomy surveillance, or colonoscopy due to positive results from a fecal immunochemical test in an Australian hospital between March 2023 to October 2023. Colonoscopies were performed by 19 experienced endoscopists using the validated CADe system that allows for real-time image analysis (GI Genius, Cosmo IMD Ireland). Historical procedural data regarding colonoscopies were obtained up to 10 months before the start of the study and were compared to the CADe-assisted colonoscopies in a 2:1 fashion. The primary outcome of the study was the ADR. Data were analyzed using logistic mixed effects models with random intercepts for patient and endoscopist, expressed as Odds ratio (OR) with a 95% confidence interval (CI).

Results: A total of 7798 colonoscopies were performed for 7460 patients during the timeframe, including 2813 colonoscopies using CADe and 4985 standard colonoscopies. The ADR in the CADe-assisted colonoscopy group

was 52% compared to 46% in the standard colonoscopy group. There was a significant difference in ADR (OR 1.22, 95% CI 1.09 - 1.36, p<0.001) and PDR (OR 1.22, 95% CI 1.09 - 1.37, p<0.001) between CADe-assisted colonoscopy and standard colonoscopy respectively, adjusted for age, bowel preparation quality, withdrawal time and sex.

	Standard colonoscopy n=4985	CADe-assisted colonoscopy n=2813	OR (95% CI)
ADR (%)	2318/4985 (46%)	1455/2813 (52%)	1.22, 1.09 - 1.36
PDR (%)	2865/4985 (57%)	1769/2813 (63%)	1.22, 1.09 - 1.37
Advanced ADR (%)	536/4985 (11%)	343/2813 (12%)	
Serrated lesion detection rate (%)	1107/4985 (22%)	667/2813 (24%)	
Mean number of adenomas per colonoscopy	2.0 (1.0-3.0)	2.0 (1.0-3.0)	
Polyps per colonoscopy	1.0 (0.0-3.0)	2.0 (1.0-4.0)	

Table 1 Adenoma detection and polyp detection rate of the CADe-assisted colonoscopy group compared to the standard colonoscopy group. Data are number (%) and median (IQR).

Conclusion: In this real-time, observational study, CADe-assisted colonoscopy significantly improves the adenoma detection rate and polyp detection rate. Our study shows that the implementation of CADe-assisted colonoscopies in daily practice is useful, even in high-detector endoscopists.

References: 1. Wang P, Liu X, Berzin TM, Glissen Brown JR, Liu P, et al. Effect of a deep-learning computer-aided detection system on adenoma detection during colonoscopy (CADE-DB trial): a double-blind randomised study. *Lancet Gastroenterol Hepatol.* 2020;5(4):343-51.

2. Repici A, Spadaccini M, Antonelli G, Correale L, Maselli R, et al. Artificial intelligence and colonoscopy experience: lessons from two randomised trials. *Gut.* 2022;71(4):757-65.

3. Hassan C, Spadaccini M, Mori Y, Foroutan F, Facciorusso A, et al. Real-Time Computer-Aided Detection of Colorectal Neoplasia During Colonoscopy : A Systematic Review and Meta-analysis. *Ann Intern Med.* 2023;176(9):1209-20.

4. Patel HK, Mori Y, Hassan C, Rizkala T, Radadiya DK, et al. Lack of Effectiveness of Computer Aided Detection for Colorectal Neoplasia: A Systematic Review and Meta-Analysis of Nonrandomized Studies. *Clin Gastroenterol Hepatol.* 2023.

5. Karsenti D, Tharsis G, Perrot B, Cattani P, Percie du Sert A, Venezia F, et al. Effect of real-time computer-aided detection of colorectal adenoma in routine colonoscopy (COLO-GENIUS): a single-centre randomised controlled trial. *Lancet Gastroenterol Hepatol.* 2023;8(8):726-34.

6. Mangas-Sanjuan C, de-Castro L, Cubiella J, Díez-Redondo P, Suarez A, Pellise M, et al. Role of Artificial Intelligence in Colonoscopy Detection of Advanced Neoplasias : A Randomized Trial. *Ann Intern Med.* 2023;176(9):1145-52.

Disclosure: Nothing to disclose.

MP066

EFFECT OF COLON ENDOSCOPIC RESECTION ON ALL-CAUSE MORTALITY AMONG HEALTH CHECK-UP POPULATION OLDER THAN 80 YEARS WITH EARLY COLORECTAL LESIONS IN KOREA : A NATIONWIDE POPULATION-BASED LONG-TERM FOLLOW-UP STUDY IN KOREA

Y.I. Choi¹, C.K. Lee¹, J.W. Choi¹, S.Y. Won¹, Y.S. Cho¹, B.K. Park¹

¹National Health Insurance Service Ilsan Hospital, Department of Gastroenterology and Hepatology, Goyang, South Korea

Contact E-Mail Address: cys7like@hanmail.net

Introduction: Even colon endoscopic resection (ER: endoscopic mucosal resection, endoscopic polypectomy, and endoscopic submucosal dissection) has been an effective tool for treating early colorectal lesions, there is limited data on efficacy (colorectal cancer (CRC) related mortality, and all causes mortality), and safety profiles of ER among extremely elderly patients (≥ 80 years) who have early colorectal lesions which needs ER.

Aims & Methods: This study investigated the efficacy, and safety profiles of colon ER among extremely elderly patients (>80 years) detection of early colorectal lesions after Fecal occult blood test (FOBT) positive results as Korean national Free-CRC screening process. We designed a nested case-control study using data from Korean National health insurance data (NHIS), and National health check-up data from 2009 to 2021. Among patients (≥ 80 year) with FOBT positive, and following confirmative test (colonoscopy) results as with early colorectal lesions >8 mm sized which needs ER, according to whether or not performed ER within 1 year, case ($n =$), and control ($n =$) groups were divided. Efficacy profiles were defined as CRC related, and all causes mortality. After adjusting for confounding variables, multivariable analysis was performed to analyze the effect of colonoscopy guided ER on the risk CRC related, and all-causes mortality. Safety profiles were defined as ER related perforation, bleeding, aspiration pneumonia, and cardiovascular attack events which need admission within 1 month after ER. For comparing the risk of ER among extremely elderly patients (≥ 80 years), 75-79 year of elderly patients who performed ER (with same including criteria except for age) were used as control group.

Results: We identified total of 7000 patients (≥ 80 years) with early colorectal lesions which needs ER. Among them, total of 700 case of patients undergone Colonoscopy guided ER within 1 years, others were not undergone following ER nor operation. During more than 5 year of follow up periods, total of 300 case (incidence rate: 00) and 250 case of CRC and mortality were defined in case, and control group, respectively.

Colonoscopy guided ER was statistically significantly reduced CRC related death (HR, 95%CI;), and all causes of mortality (HR, 95%CI;) even after adjusting for confounding variables.

Safety profiles for colonoscopy guided ER of extremely elderly patients group (≥ 80 years) showed no statistically higher complication risk after ER as compared to those of 75-79 years group.

Conclusion: For extremely elderly patients (≥ 80 year), colon ER after early colorectal lesions detection is associated with reduced CRC related mortality, and all causes mortality with reasonable safety profiles. Therefore, physicians should keep in mind that not refrain from performing colon ER solely based on the patients advanced age. Instead of relying on rigid age cut off, physicians still should be with cautious comparing risk, and benefit of CFS for extremely old patients.

References: 1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians 2021;71:209-249.

2. Morgan E, Arnold M, Gini A, et al. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. Gut 2023;72:338-344.

3. Siegel RL, Wagle NS, Cercek A, et al. Colorectal cancer statistics, 2023. CA: a cancer journal for clinicians 2023;73:233-254.

4. Sidhu R, Turnbull D, Haboubi H, et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut 2024;73:219-245.

5. Davidson KW, Barry MJ, Mangione CM, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. Jama 2021;325:1965-1977.

6. Aparicio T, Pamoukdjian F, Quero L, et al. Colorectal cancer care in elderly patients: unsolved issues. Digestive and Liver Disease 2016;48:1112-1118.

7. Terret C, Castel-Kremer E, Albrand G, et al. Effects of comorbidity on screening and early diagnosis of cancer in elderly people. The lancet oncology 2009;10:80-87.

Disclosure: conflict of interest: none.

MP067

COMPARATIVE RESULTS OF HIGH-RISK T1 COLORECTAL MALIGNANT POLYPS AFTER ENDOSCOPIC RESECTION – A PARADIGM SHIFT IN THERAPEUTIC DECISION-MAKING?

S. Bragança¹, J. Tinoco², M. Cardoso¹, D. Horta¹, M.N. Costa¹, L.C.C. Lourenço¹

¹Hospital Prof. Doutor Fernando Fonseca, E.P.E., Gastroenterology Department, Amadora, Portugal, ²Hospital Prof. Doutor Fernando Fonseca, E.P.E., Pathology Department, Amadora, Portugal

Contact E-Mail Address: sofia_58632@hotmail.com

Introduction: Patients with T1 stage colorectal cancer (CRC) according to TNM classification can undergo endoscopic resection (ER) with curative intent. However, in the presence of high-risk recurrence characteristics, additional surgery may be proposed, which is associated with considerable morbidity, especially those involving rectum. Additionally, it is not yet established that surgery prevents the risk of distant recurrence of CRC.

Aims & Methods: We aim to compare the outcomes of high-risk T1 CRC patients who remained under surveillance versus those who underwent additional surgery. Unicentric, retrospective cohort study, including left colon high-risk T1 CRC patients who underwent to ER, between January 2015 and December 2020. After ER, the patients were included in one of the two groups: surveillance (clinical, laboratory, imaging, endoscopic) versus surgery with lymphadenectomy. The decision regarding follow-up (surveillance vs surgery) was based on the histological characteristics of the malignant polyp, the patient's age, surgical and anesthetic risk (patient's comorbidities), and the patient's willing. Minimum follow-up period was 3 years after the initial colonoscopy for ER (baseline). Primary outcome: recurrence or death at 36 months.

Results: Among the 109 included T1 CRC patients, 70 were deemed high-risk for recurrence and had a median follow-up of 73 months (IQR=55.93), either in the surveillance group (SvG, $n=20$) or the surgery+lymphadenectomy group (SG, $n=50$). Older age or history of cerebrovascular/cardiovascular disease was associated with a higher propensity for surveillance only (propensity score). The endoscopic resection technique used was mostly conventional mucosectomy (97%). The incidence of complications related to ER was 1.4% (1 patient, colonic perforation). In the SG, 51% of the patient were submitted to surgery involving rectum and colorectal anastomosis. The incidence of complications directed related to surgery with lymphadenectomy was 20% (10 patients; 3 Anastomotic dehiscence; 1 lower gastrointestinal haemorrhage related to colorectal anastomotic; 5 wound infection ; 1 colorectal anastomotic stenosis). In SG, 84% ($n=42$) showed no evidence of CRC in the specimen (pT0N0). From baseline to 36 months, no patient in SvG experienced recurrence, while 1 patient in SG

did. During this period, 2 patients in SvG and 2 in SG died, all from causes unrelated to CRC. There was no significant difference in recurrence and mortality between the two groups (p-value >0.05). Additionally, within SG, there was no difference in recurrence and mortality between the subgroup of patients with pT0N0 versus non-pT0N0 disease (p-value > 0.05).

Conclusion: Our study suggests that high-risk T1 CRC patients undergoing ER may not benefit from additional surgery with lymphadenectomy, which, if confirmed in further studies, represents a paradigm shift in therapeutic decision-making based on current evidence.

References: 1 - Corre F, Albouys J, Tran VT, et al. Impact of surgery after endoscopically resected high-risk T1 colorectal cancer: results of an emulated target trial. *Gastrointest Endosc.* 2024;99(3):408-416.e2. doi:10.1016/j.gie.2023.09.027

2 - Bartel MJ, Brahmabhatt BS, Wallace MB. Management of colorectal T1 carcinoma treated by endoscopic resection from the Western perspective. *Dig Endosc.* 2016;28(3):330-341. doi:10.1111/den.12598

3 - Chen Y, Jing W, Chen M, et al. Long-term outcomes of local resection versus surgical resection for high-risk T1 colorectal cancer: a systematic review and meta-analysis. *Gastrointest Endosc.* 2023;97(6):1016-1030.e14. doi:10.1016/j.gie.2023.02.027

4 - Zaffalon D, Daca-Alvarez M, Saez de Gordo K, Pellisé M. Dilemmas in the Clinical Management of pT1 Colorectal Cancer. *Cancers.* 2023; 15(13):3511. <https://doi.org/10.3390/cancers15133511>

Disclosure: Nothing to declare.

MP068

PROPHYLACTIC CLIPPING AFTER COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION DOES NOT REDUCE DELAYED BLEEDING RATES: A MULTICENTER PROPENSITY-SCORE MATCHED ANALYSIS

E. De Cristofaro¹, S. Montori Pina^{2,3}, V. Van der Voort⁴, M. Schaefer⁵, T. Wallenhorst⁶, V. Lepilliez⁷, T. Degand⁸, Y. Le Baieur⁹, P. Leclercq¹⁰, A. Berger¹¹, E. Chabrun¹², B. Brieau¹³, M. Barret¹⁴, E. Albeniz^{3,15}, G. Rahmi¹⁶, R. Legros⁴, J. Rivory¹⁷, S. Leblanc⁷, G. Vanbiervliet¹⁸, L. Alfarone¹⁹, J.-B. Zeevaert¹⁰, J. Albouys⁴, G. Perrod¹⁶, C. Yzet¹⁷, H. Lepetit⁴, A. Belle¹⁴, S. Chaussade¹⁴, F. Rostain¹⁷, M. Dahan¹¹, A. Lupu¹⁷, J.-B. Chevaux⁵, M. Pioche¹⁷, J. Jacques⁴, FECCo Group
¹Gastroenterology Unit, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, Roma, Italy, ²Gastrointestinal Endoscopy Research Unit, Navarrabiomed, Hospital Universitario de Navarra (HUN), Universidad Pública de Navarra (UPNA), Pamplona, Spain, Navarra, Spain, ³IdiSNA, Instituto de Investigación. Universidad de Navarra, Pamplona, Spain, Pamplona, Spain, ⁴Department of Gastroenterology and Endoscopy, Dupuytren University Hospital, Limoges, France, Limoges, France, ⁵Department of Gastroenterology and Hepatology, Nancy Regional University Hospital Center, Nancy, France, Nancy, France, ⁶Department of Gastroenterology and Endoscopy, Pontchaillou University Hospital, Rennes, France, Rennes, France, ⁷Department of Gastroenterology and Endoscopy, Hôpital Privé Jean Mermoz, Lyon, France, Lyon, France, ⁸Department of Gastroenterology and Endoscopy, Dijon University Hospital, Dijon, France, Dijon, France, ⁹Department of Gastroenterology and Endoscopy, Hospital Saint Joseph, Paris, France, Paris, France, ¹⁰Department of Gastroenterology, CHC Groupe Santé, Liège, Belgium, Liège, Belgium, ¹¹Department of Gastroenterology and Endoscopy, Bordeaux University Hospital, Department of Gastroenterology and Endoscopy, Bordeaux University Hospital, Bordeaux, France, Bordeaux, France, ¹²Department of Gastroenterology and Endoscopy, Clinique de l'Anjou, Angers, France, Angers, France, ¹³Department of Gastroenterology and Endoscopy, Cliniques Jules Verne, Nantes, France, Nantes, France, ¹⁴Department of Gastroenterology and Endoscopy, Cochin University Hospital, Paris, France, Paris, France, ¹⁵Gastroenterology Department, Hospital Universitario de Navarra (HUN), Navarrabiomed, Universidad Pública de Navarra (UPMNA), Pamplona, Spain, Pamplona, Spain, ¹⁶Department of Gastroenterology and Endoscopy, Georges Pompidou European Hospital, Paris, France, Paris, France, ¹⁷Department of Gastroenterology and Endoscopy, Hôpital Edouard Herriot, Hospices Civils de Lyon, Lyon, France, Lyon, France, ¹⁸Department of Gastroenterology and Endoscopy, Nice University Hospital, Nice, France., Nice, France, ¹⁹Department of Gastroenterology and Endoscopy, Humanitas Research Hospital, Milan, Italy, Milan, Italy

Contact E-Mail Address: elena_decr@hotmail.it

Introduction: Clinically significant delayed bleeding (CSDB) is the most frequent complication after colorectal endoscopic submucosal dissection (ESD). The Limoges Bleeding Score was recently developed to identify patients at risk of CSDB after colorectal ESD. The efficacy of prophylactic clipping to prevent bleeding has been a topic of ongoing debate.

Aims & Methods: This study aimed to evaluate the real effectiveness of complete clip closure in preventing CSDB after colorectal ESD.

We performed a retrospective analysis of data prospectively collected from ten-centers between 2017 and 2023. Specifically, pre- and periprocedural data were collected prospectively, while post-procedural data,

including the evaluation of CSDB, was retrospectively assessed. All epithelial colorectal lesions treated by ESD were included. The patients were allocated into the closure and non-closure groups which were compared before and after propensity-score matching based on risk factors of the Limoges Bleeding Score (age > 75 yrs, size > 50 mm, ASA III-IV, location in rectum and anticoagulant/antiplatelet). We further analyzed post-ESD CSDB in the subgroups of patients on anticoagulants and with high risk of bleeding (5 to 8 points according to Limoges score).

Results: A total of 3431 patients were included, 1236 in the closure group and 1985 in non-closure group. The propensity score matching based on risk factors of the Limoges Bleeding Score created 1064 matches pairs. The rate of CSDB was not significantly different between the two groups (closure group 7.04% vs non-closure group 6.8%; $p = 0.85$), nor after propensity score matching (closure group 7.47% vs non-closure group 6.11%; $p = 0.38$). The subgroup analysis including patients on anticoagulants (165 patients in closure group vs 251 in non-closure group) and those identified at high-risk by Limoges score (181 in each group), found no significant difference of CSDB between the groups ($p = 0.31$ and $p = 0.16$, respectively).

Conclusion: In our population, prophylactic clipping after colorectal ESD did not significantly reduce the incidence of CSDB. These findings were confirmed even when the analysis was restricted to high-risk patients. Considering the technical challenges of complete clip closure, it could be reserved for selected clinical scenarios.

References: [1] Saito H, Igarashi K, Hirasawa D et al. The risks and characteristics of the delayed bleeding after endoscopic submucosal dissection for early gastric carcinoma in cases with anticoagulants. *Scand J Gastroenterol* 2020; 55: 1253–1260

[2] Boda K, Oka S, Tanaka S et al. Clinical outcomes of endoscopic submucosal dissection for colorectal tumors: a large multicenter retrospective study from the Hiroshima GI Endoscopy Research Group. *Gastrointest Endosc* 2018; 87: 714–722

[3] Bordillon P, Pioche M, Wallenhorst T et al. Double-clip traction for colonic endoscopic submucosal dissection: a multicenter study of 599 consecutive cases (with video). *Gastrointest Endosc* 2021; 94: 333–343

[4] Probst A, Ebigbo A, Märkl B et al. Endoscopic submucosal dissection for early rectal neoplasia: experience from a European center. *Endoscopy* 2017; 49: 222–232

[5] Albouys J, Montori Pina S, Boukechiche S et al. Risk of delayed bleeding after colorectal endoscopic submucosal dissection: the Limoges Bleeding Score. *Endoscopy* 2024; 56(2):110-118

Disclosure: Nothing to disclose.

MP069

IMPACT OF MARGINS ABLATION ON THE EFFICACY OF COLD-FORCEPS AVULSION WITH SNARE-TIP SOFT COAGULATION (CAST) FOR NON-LIFTING LARGE NON-PEDUNCULATED COLORECTAL POLYPS

F.V. Mandarin¹, T. O'Sullivan¹, J. Gauci¹, C. Kerrison¹, A. Whitfield¹, R. Medas¹, B. Lam¹, V. Perananthan¹, S. Gupta¹, O. Cronin¹, S. Williams¹, E. Lee¹, N.G. Burgess¹, M.J. Bourke¹
¹Westmead Hospital, Sydney, Australia

Contact E-Mail Address: mandarinofrancesco@hsr.it

Introduction: Endoscopic Mucosal Resection (EMR) with Margin Thermal Ablation by Snare-tip Soft Coagulation (MTA) is effective to treat Large (>20mm) Non-Pedunculated Colorectal Polyps (LNPCP) with recurrence in large studies at <2%. Non-lifting LNCP (NL-LNPCP) account for approximately 10% of LNCP and are well managed by EMR with adjunctive Cold-forceps Avulsion with adjuvant Snare-Tip soft coagulation (CAST) for non-lifting areas, however recurrence occurs in >10%. We sought to evaluate the effect of MTA on NL-LNPCPs treated by EMR and CAST.

Aims & Methods: Prospective observational data on consecutive patients with NL-LNPCPs treated by EMR and CAST at a single tertiary center was evaluated. Two cohorts were established: the pre-MTA period (January 2012-June 2017) and the MTA period, (July 2017-October 2023). The primary outcome was the comparison of recurrence rates between the two groups at first surveillance colonoscopy at 6 months (SC1).

Results: From January 2012 to October 2023, 298 NL-LNPCPs in 298 patients (median age 69.1 years, interquartile range [IQR] 61.5-76.7 years, 43.4% male) underwent EMR and CAST (median size 36.0mm, IQR 24.7-54.2mm): 72 lesions pre-MTA and 226 with MTA. The MTA cohort had a higher rate of NL-LNPCP in complex locations (ileocecal valve, ano-rectal junction, appendiceal orifice) (18.6% vs 5.6%, $p=0.02$), granular lesions (61.9% vs 41.7%, $p=0.01$), and lesions with submucosal fibrosis (87.2% vs 72.2%, $p=0.05$). No differences were observed in procedural time. At SC1, recurrence was lower in the MTA cohort compared to the pre-MTA cohort (2.7% vs 9.7%, $p<.001$). Deep mural injury type III-V (4.4% vs 4.2%, $p=.93$) and post-procedural bleeding (5.3 vs 4.2%, $p=.94$) was similar between the MTA and pre-MTA cohort respectively. There was one case of delayed perforation in the pre-MTA group.

	EMR + CAST overall cohort n=298	EMR + CAST with no STSC margins n=72	EMR + CAST with STSC margins n=226	P value
Age, median (IQR) (years)	69.1 (61.5-76.7)	68.8 (61.0-76.6)	69.3 (59.5-79.1)	.76
Size of NL-LSL, median (IQR) (mm)	36.0 (24.7-54.2)	35.8 (26.7-44.9)	36.8 (23.5-50.1)	.59
Complex location (ileocecal valve, anorectal junction, appendiceal orifice) (n,%)	46 (15.4)	4 (5.6)	42 (18.6)	.02
Morphology, (n,%)				.01
Granular	170 (57.0)	30 (41.7)	140 (61.9)	
Non-Granular	101 (33.9)	31 (43.0)	70 (31.1)	
Mixed	13 (4.4)	3 (4.2)	10 (4.4)	
Consistent with SSL	4 (1.3)	3 (4.2)	1 (0.4)	
Unable to be classified	10 (3.4)	5 (6.9)	5 (2.2)	
Procedure duration, median (IQR) (min)	44.2 (23.8-64.7)	39.8 (17.8-61.8)	45.6 (21.6-69.6)	.38
Submucosal fibrosis (n,%)	249 (83.6)	52 (72.2)	197 (87.2)	.05
Delayed bleeding (n,%)	15 (5.0)	3 (4.2)	12 (5.3)	.94
Delayed perforation (n,%)	1 (0.3%)	1 (1.4)	0 (0)	.09
Recurrence at first follow-up (n,%)	13/216 (4.4)	7/66 (9.7)	6/150 (2.7)	<.001

Conclusion: The implementation of MTA significantly reduced recurrence at SC1 for NL-LNPCP treated by EMR with CAST. The refinement of CAST and addition of MTA in recent years has enabled the treatment of more complex lesions with greater effectiveness without compromising safety.

Disclosure: Nothing to disclose.

MP070

PREDICTIVE FACTORS AND RISK MODEL FOR POSITIVE CIRCUMFERENTIAL RESECTION MARGIN RATE AFTER ROBOT-ASSISTED TOTAL MESORECTAL EXCISION, AN INTERNATIONAL MULTICENTER RETROSPECTIVE COHORT STUDY

R. Geitenbeek¹, T. Burghgraef¹, R. Duhoky², M. Friebe³, C. Fleming⁴, A. Moussion⁵, N. Bouazza⁵, E. Cotte⁶, A. Dubois⁷, E. Rullier⁸, Q. Denost⁹, P. Rouanet⁵, J. Khan², R. Hompes¹⁰, E. Consten¹, EUREKA

¹University Medical Center Groningen, Groningen, Netherlands,

²Portsmouth Hospitals University NHS Trust and the University of

Portsmouth, Portsmouth, United Kingdom, ³University Hospital Heidelberg, Surgery, Heidelberg, Germany, ⁴Bordeaux Colorectal

Institute, Clinique Tivoli, Bordeaux, France, ⁵Clinical Research

Department, Montpellier Cancer Institute, Montpellier, France,

⁶Department of Digestive and Oncological Surgery, Lyon University

Hospital, Lyon, France, ⁷Department of Colorectal Surgery, Chu

Estaing, Clermont-Ferrand, France, ⁸Department of Digestive

Surgery, Colorectal Unit, Haut-Lévêque Hospital, Bordeaux

University Hospital, Bordeaux, France, ⁹CHU de Bordeaux, Centre

Medico-chirurgical Magellan, Department of Colorectal Surgery,

Pessac, France, ¹⁰Department of Surgery, Academic Medical

Centre, Amsterdam, Netherlands

Contact E-Mail Address: maikiefriebe@gmail.com

Introduction: Positive circumferential resection margin (CRM) after total mesorectal excision (TME) predicts higher local and systemic recurrence rates, affecting overall survival in rectal cancer patients. Although predictive factors for positive CRM have been identified for open, laparoscopic, and transanal TME, these may differ for robot-assisted TME (R-TME).

Aims & Methods: This study aimed to assess the incidence of positive CRM and to identify preoperative risk factors associated with this outcome following R-TME. An international multicenter retrospective study included patients receiving R-TME between January 2013 and January 2022 in participating Dutch, English, and French centers. Endpoints were the incidence of and predictive factors for positive CRM.

Univariate and multivariate logistic regressions were performed, and factors associated with positive CRM were then assessed by formulating a predictive model.

Results: Of 1390 patients undergoing R-TME, the incidence of positive CRM was 6.0% (83 cases). Multivariate analysis revealed significant associations between positive CRM and tumors located up to 1 cm from the anorectal junction, cT4 tumors, cN+ tumors, and non-sphincter-saving surgery (odds ratios of 1.91, 3.04, 1.84, and 2.02, respectively). The predictive model exhibited satisfactory discrimination (area under the receiver-operating characteristic curve 0.71) and predicted a 37% risk of positive CRM when all identified risk factors were present.

Conclusion: Preoperative tumor- and procedure-related factors, rather than patient-related factors, significantly influenced CRM involvement after R-TME. The proposed predictive model allows preoperative calculation of the risk of positive CRM, offering valuable insights for optimizing patient selection and tailoring treatment approaches to enhance oncological outcomes.

Disclosure: Nothing to disclose.

Advanced chronic liver disease

12:00-13:00 / Poster Stage 3

MP071

A SCREENING PROGRAM FOR LIVER DISEASE IN INDIVIDUALS WITH ALCOHOL USE DISORDER ATTENDING AN ADDICTION UNIT ALLOWS EARLY DIAGNOSIS OF ADVANCED FIBROSIS AND IDENTIFIES RISK FACTORS FOR LIVER FIBROSIS

Q. Herms¹, J. Gratacós-Ginés^{1,2,3}, E. Avitabile², M. Moreta^{1,2}, A.B. Rubio^{2,4}, M. Pérez-Guasch^{1,2,4}, M.T. Pons^{5,2}, M. Cervera², P. Bruguera^{5,2}, A. Lligón⁵, A. Lopez Lazcano⁶, L. Ortega⁵, A. Díaz⁷, R. Nadal², M. Carol^{2,4}, A. Arslanow², N. Fabrellas⁴, A. Soria^{1,2,3}, A. Juanola^{1,2,3}, I. Graupera^{1,2,3,4}, R. Bataller^{1,2,3,4}, P. Ginès^{1,2,3,4}, H. López-Pelayo^{2,5,8}, E. Pose^{1,2,3,4}

¹Liver Unit Hospital Clínic, Barcelona, Spain, ²Institut d'Investigacions Biomèdiques August Pi i Sunyer, IDIBAPS, Barcelona, Spain, ³Centro de Investigación en Red de Hepatología y Gastroenterología, CIBERehd, Madrid, Spain, ⁴Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain, ⁵Addictions Unit, Department of Psychiatry, Hospital Clínic de Barcelona, Barcelona, Spain, ⁶Clinical Health Psychology Section, Psychiatry and Clinical Psychology Service, Institute of Neurosciences, Hospital Clínic, Barcelona, Spain, ⁷Pathology Department, Hospital Clínic, IDIBAPS., Barcelona, Spain, ⁸Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Madrid, Spain

Contact E-Mail Address: qherms@clinic.cat

Introduction: Individuals with alcohol use disorder (AUD) are at high risk of liver disease. Despite international clinical practice guidelines recommend screening for liver fibrosis in at risk populations, information regarding fibrosis prevalence, predictive factors and screening strategies in patients with AUD is scarce. Recently, a novel score (LiverRisk score) has been developed to predict liver fibrosis and liver-related outcomes in the general population.

Aims & Methods: We conducted a screening program for liver disease in subjects who attended the Addiction Unit of the Hospital Clínic of Barcelona between 2019 and 2022. Data regarding socio-economic status, medical history and alcohol consumption were recorded. Blood tests and transient elastography (TE) were performed in all patients. The main aim of the study was to analyze the prevalence of significant liver fibrosis in patients with AUD.

The secondary objectives were to analyze the prevalence of advanced chronic liver disease in this population, identify the factors associated with the presence of significant liver fibrosis in patients with AUD and to evaluate the diagnostic accuracy of non-invasive liver fibrosis tests (Fibrosis-4 [FIB-4], NAFLD fibrosis score [NFS], Fatty Liver Index [FLI], AST to Platelet Ratio Index [APRI] and LiverRisk score) using TE as the Gold Standard. Significant liver fibrosis was defined as a liver stiffness (LS) value ≥ 8 kPa measured by TE. Advanced liver fibrosis was defined as a LS ≥ 15 kPa.

Results: Out of 334 total patients, 40 had significant liver fibrosis (prevalence of 12%). Out of the 40 patients with significant liver fibrosis, 19 (48%) had advanced chronic liver disease.

Multiple factors were associated with the presence of significant fibrosis in univariate analysis; however, on multivariate analysis BMI ($p=.04$) and GGT levels ($p=.001$) were confirmed as the only independent predictors. Regarding non-invasive tests, the LiverRisk score was the test with the best diagnostic performance for detecting significant liver fibrosis, with an area under the receiver operating characteristic (AUROC) of 0'854. All other tests had similar diagnostic performance, with AUROC of 0'799 (NFS), 0'798 (FIB-4), 0'797 (FLI) and 0'784 (APRI).

Conclusion: The prevalence of significant liver fibrosis (TE > 8 kPa) in population with at-risk alcohol consumption is high. BMI and GGT are the main factors associated with the presence of liver fibrosis and could be useful for selecting patients with higher risk. The most accurate serological test to assess liver fibrosis in our cohort is the LiverRisk score. These results demonstrate the usefulness of a screening program for early detection of liver disease in patients with AUD and support the implementation of screening programs in this population.

References:

1. Bataller R, Cabezas J, Aller R et al. Alcohol-related liver disease. Clinical practice guidelines. Consensus document sponsored by AEEH. Gastroenterology and Hepatology. 2019 Dec 1;42(10):657–76.
2. Caballeria L, Pera G, Arteaga I et al. High Prevalence of Liver Fibrosis Among European Adults With Unknown Liver Disease: A Population-Based Study. Clinical gastroenterology and hepatology. 2018 Jul 1;16(7):1138–1145.e5.
3. Berzigotti A, Tsochatzis E, Boursier J et al. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2021 update. Journal of Hepatology. 2021 Sep 1;75(3):659–89.
4. Pose E, Pera G, Torán P et al. Interaction between metabolic syndrome and alcohol consumption, risk factors of liver fibrosis: A population-based study. Liver International. 2021 [2021 Jun 16];00:1–9.
5. Ginès P, Castera L, Lammert F et al. Population screening for liver fibrosis: Toward early diagnosis and intervention for chronic liver diseases. Hepatology. 2022 [2023 Oct 17];75:4.
6. Serra-Burriel M, Juanola A, Serra-Burriel F, et al. Development, validation, and prognostic evaluation of a risk score for long-term liver-related outcomes in the general population: a multicohort study [published correction appears in Lancet. 2023 Sep 16;402(10406):964]. *Lancet*. 2023;402(10406):988–996. doi:10.1016/S0140-6736(23)01174-1

Disclosure: Pere Ginès has received research funding from Gilead & Grifols. He has consulted or attended advisory boards for Gilead, RallyBio, SeaBeLife, Merck, Sharp and Dohme (MSD), Ocelot Bio, Behring, Roche Diagnostics International and Boehringer Ingelheim, and received speaking fees from Pfizer. Ramon Bataller consults for GlaxoSmithKline, Novo Nordisk and Boehringer Ingelheim. He is on the speakers' bureau for Abbvie and Gilead. Pol Bruguera is on the speakers' bureau and received grants from Lundbeck. He received grants from Camurus and Pfizer. Maria T. Pons-Cabrera is employed by Lundbeck, Pfizer, and Esteve. Hugo López-Pelayo received grants from Lundbeck. The remaining authors declare that they have no conflicts of interest.

MP072

INCREASED RISK FOR ACLF AND LIVER-RELATED DEATH IN PATIENTS WITH PATHOLOGIC ALCOHOL CONSUMPTION AFTER TIPS IMPLANTATION FOR ALCOHOL-RELATED ACLD

C. Schwarz^{1,2}, A. Kornfehl¹, R. Abid¹, T. Theresa Müllner-Bucsics¹, M. Schwarz¹, B. Hofer¹, N. Dominik¹, B. Simbrunner¹, M. Jachs¹, L. Reider¹, M. Schoder¹, M. Mandorfer¹, M. Trauner¹, T. Reiberger¹, L. Hartl¹

¹Medical University of Vienna, Vienna, Austria, ²Klinik Ottakring, Vienna, Austria

Contact E-Mail Address: schwarz.caroline1990@gmail.com

Introduction: The recommended treatment for severe complications of portal hypertension (PH) is transjugular intrahepatic portosystemic shunt (TIPS) implantation. Despite alcohol-related liver disease (ALD) representing the most frequent cause of advanced chronic liver disease (ACLD) and PH, literature on the effects of ongoing alcohol use (AU) after TIPS placement currently remains scarce.

Aims & Methods: The study population consisted of patients with ALD-related ACLD who had undergone TIPS implantation at two Viennese tertiary care centers (pooled cohort from the prospective AUTIPS study, NCT03409263: 01/2017–11/2022; and a retrospective cohort: 09/2000–09/2019). Through the electronic patient management system, individual demographic, laboratory, and clinical data were retrieved. AU after TIPS placement was investigated according to clinical documentation, serum ethanol quantification if available, and patients' reporting.

Results: Overall, the study population consisted of 276 patients (median follow-up 29 [IQR 54] months), 196 (71.0%) of which had received TIPS for refractory ascites while in 80 (29.0%) the indication for TIPS implantation had been variceal hemorrhage. The median age was 56 (IQR 13) years and 215 (77.9%) of the patients were men. At the time of the TIPS insertion, the median MELD was 11 (IQR 9) and 38 (13.8%) individuals were classified as Child-Pugh C. AU after TIPS placement was documented in 85 (30.8%) study participants. Baseline characteristics at TIPS implantation were similar in patients with and without post-TIPS AU, specifically regarding the prevalence of ascites ($p=0.51$), variceal hemorrhage ($p=0.87$), and hepatic encephalopathy ($p=0.87$).

Bacterial infections were more frequently detected among patients with ongoing AU (log-rank $p=0.002$). Importantly, patients with ongoing AU showed a higher incidence of acute-on-chronic liver failure (ACLF; log-rank $p<0.001$) and higher overall mortality (log-rank $p=0.005$; including liver-related death [log-rank $p<0.001$]).

Furthermore, cumulative incidence of ACLF ($p=0.014$) and liver-related death ($p=0.004$) were significantly higher in patients with ongoing AU. Of note, ongoing AU was independently associated with ACLF (aSHR: 1.66; 95%CI: 1.13–2.44; $p=0.010$) and liver-related death (aSHR: 2.09; 95%CI: 1.32–3.33; $p=0.002$) in multivariable competing risks regression analysis adjusted for age, MELD, and portal pressure gradient after TIPS implantation.

Conclusion: AU represents an independent risk factor for outcome deterioration after TIPS placement. These findings emphasize the paramount role of psychiatric care and harm reduction measures in addition to hepatological optimization after TIPS implantation.

Disclosure: C.S. received travel support from Gilead, Abbvie, Galapagos and Gebro; speaking honoraria from Abbvie and Gilead; and payments for consulting from Gilead.

M.S. received travel support from MSD, Sandoz, BMS, Abbvie and Gilead; and speaking honoraria from BMS.

M.J. received speaking honoraria from Abbvie and Gilead.

T.R. received grant support from Abbvie, Boehringer- Ingelheim, Gilead, MSD, Philips Healthcare, Gore; speaking honoraria from Abbvie, Gilead,

Gore, Intercept, Roche, MSD; consulting/advisory board fee from Abbvie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from Boehringer-Ingelheim, Gilead, and Roche.

M.M. served as a speaker and/or consultant and/or advisory board member for AbbVie, Bristol-Myers Squibb, Collective Acumen, Gilead, and W. L. Gore & Associates and received travel support from AbbVie, Bristol-Myers Squibb, and Gilead.

B.S. received travel support from AbbVie and Gilead.

MP073

THE PREVALENCE OF DYSGEUSIA IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE (ACLD): RELATIONSHIP WITH THE LIVER-DISEASE PROGRESSION STATUS, AND IMPACT ON “MALNUTRITION-SARCOPENIA-FRAILITY TRIANGLE” (THE PREDYCI STUDY)

M. Dallio¹, M. Romeo¹, F. Di Nardo¹, C. Napolitano¹, M. Cipullo¹, A. Coppola¹, G. Iadanza¹, P. Vaia¹, S. Olivieri¹, A. Federico¹

¹University of Campania “Luigi Vanvitelli”, Department of Precision Medicine, Hepatogastroenterology Division, Naples, Italy

Contact E-Mail Address: marcello.dallio@gmail.com

Introduction: Malnutrition, sarcopenia, and frailty constitute the three vertices of a nutrition-status-determined physio-pathological triangle constantly featuring and dramatically burdening the prognosis of advanced chronic liver disease (ACLD) patients.

Dysgeusia is defined by a distortion of the sense of taste whose prevalence, relationship with the progression of the disease, and the direct contribution to malnutrition (and consequently, sarcopenia-frailty) in ACLD have never been systematically explored.

Aims & Methods: This observational study aimed to explore the prevalence of dysgeusia in a cohort of ACLD patients and evaluate the impact of this disorder on appetite levels and nutritional status (malnutrition, sarcopenia, and frailty), as well as to prospectively estimate the repercussions of dysgeusia-induced impaired nutritional status on liver-related events (LREs) occurrence. For this purpose, 40 controls, 50 chronic-liver disease-affected individuals staging initial-mild fibrosis (<F3), and 150 ACLD patients of various etiologies were enrolled. Anthropometrical, biochemical, clinical, and nutritional [European Prospective Investigation into Cancer and Nutrition (EPIC) questionnaire] data were collected. The opportunely modified Chemotherapy-induced Taste Alteration Scale (CITAS) questionnaire was used to assess the dysgeusia. Child-Pugh (CP) and Liver Frailty Index (LFI) calculations, Liver Stiffness Measurement (LSM), and Bioelectrical Impedance Analysis (BIA) were performed. Skeletal Muscle Mass (SMM) index (SMMI) ($\text{SMM}/\text{height}^2 < 7 \text{ kg}/\text{m}^2$ (male) and $< 5.7 \text{ kg}/\text{m}^2$ (female) defined sarcopenia. ACLD patients were 3 years followed up semiannually and LREs (including ascites, hepatic encephalopathy, and bleeding) were collected.

Results: The prevalence of dysgeusia was significantly higher in ACLD (68%) in comparison to <F3 (8%) individuals and controls (5%) and in decompensated ACLD (dACLD) than compensated (cACLD) (54% vs 6%) patients (all $p < 0.0001$). In line, CITAS-dysgeusia severity positively correlated with CP ($R: 0.81$), as well as with the levels of appetite impairment ($R: 0.93$) (both $p < 0.0001$). Logistic regression analysis, appropriately weighted for factors notoriously impacting food intake in ACLD patients (low-sodium diet, drugs/supplements taken, physical activity frequency, occurrence of encephalopathy and ascites episodes in the previous 2 weeks), revealed the level of impairment of the appetite as a factor significantly associated with dysgeusia [$\text{HR}: 2.12$; $p: 0.02$]. Compared to no-dysgeusia-affected dACLD ($p: 0.03$), dysgeusia-affected dACLD patients (dys-dACLD) showed a decreased daily protein intake, reduced Free Fat Mass % ($p < 0.0001$), and SMMI ($p < 0.0001$; $p: 0.04$), in contrast with increased LFI ($p < 0.0001$). Consis-

tently, dys-dACLD patients showed a higher prevalence (59% vs 39%) of sarcopenia ($p: 0.0002$). The Kaplan-Meier Log-Rank Test analysis on LREs occurrence showed $\text{HR}: 3.53$ [95% C.I.: 1.58-4.92] for dys-dACLD individuals.

Conclusion: The prevalence of dysgeusia, increasing in parallel to the worsening of liver disease, promoted sarcopenia-frailty pictures, negatively influencing ACLD patients' outcomes.

References:

1. Jafari A, Alaei A, Ghods K. The etiologies and considerations of dysgeusia: A review of literature. *Journal of oral biosciences*. 2021;63(4):319-26.
2. Sieber CC. Malnutrition and sarcopenia. *Aging clinical and experimental research*. 2019;31(6):793-8.
3. Tandon P, Montano-Loza AJ, Lai JC, Dasarathy S, Merli M. Sarcopenia and frailty in decompensated cirrhosis. *Journal of hepatology*. 2021;75 Suppl 1(Suppl 1):S147-s62.

Disclosure: Nothing to disclose.

MP074

LIVR WELL, A MULTIDISCIPLINARY, HOME-BASED PROGRAM VS. STANDARD AMBULATORY CARE FOR ACUTE-ON-CHRONIC LIVER FAILURE AND HEPATIC DECOMPENSATION. INTERIM ANALYSIS

N. Ngu^{1,2}, T. Worland¹, J. Abasszade¹, E. Flanagan¹, S. Yung¹, P. Anderson¹, J. Hunter³, W. Sievert^{1,2}, A. Irving⁴, S. Bell^{1,2}, S.T.T. Le^{1,2}

¹Monash Health, Gastroenterology and Hepatology, Clayton, Australia, ²Monash University, Melbourne, Australia, ³Monash Health, Pharmacy, Clayton, Australia, ⁴Monash University, Centre for Health Economics, Melbourne, Australia

Contact E-Mail Address: natalielyngu@gmail.com

Introduction: Globally, rates of acute-on-chronic liver failure (ACLF) and hepatic decompensation necessitating hospitalisation are rising¹ and patients frequently have barriers to healthcare engagement including substance abuse, psychosocial stressors, and limited health literacy^{2,3}. Previous chronic disease management (CDM) programs have had variable impact on re-admission rates^{4,5}.

LivR Well is a 28-day, multidisciplinary, ambulatory intervention targeting the critical period after hospitalisation.

Aims & Methods: A randomised controlled study was conducted at an Australian, non-liver transplant hospital from February 2022 to March 2024. Patients with acute hepatic decompensation were recruited from inpatient admissions or outpatient clinic and randomised to LivR Well, or standard care in a 1:1 ratio. The control group received a hepatology consultation within 4 weeks of discharge and then at clinician discretion. The intervention group received a hepatology consultation weekly and allied health consultations as required from physiotherapist, dietitian, pharmacist, social worker, and/or addiction medicine specialist, coordinated by a hepatology clinical nurse consultant.

Follow up was to week 12. Quality of life instruments were performed at baseline, week 6 and week 12. The primary outcome was 30-day re-admission. Secondary outcomes were 28-day mortality, patient reported outcomes, and change in liver disease severity.

Results: Eighty nine patients were recruited with a combined median age of 56 years (IQR: 47-65), a median baseline Model for End-Stage Liver Disease-Sodium (MELD-Na) score 19.5 (IQR: 16-23), median Child-Pugh score 10 (IQR: 8-11), 71.1% were male, and 26.7% had ACLF. The primary liver disease aetiologies were alcohol (74.4%) and metabolic dysfunction-associated fatty liver disease (16.7%). There were no differences in baseline characteristics or median index admission length of stay (LOS) between intervention and control groups.

There was no difference in readmission rates in LivR Well vs. control group at 30 days (Incidence Rate Ratio 1.28, 95%CI 0.50-3.45, $p=0.58$), 90 days (IRR 1.0, 95%CI 0.56-1.81, $p=0.99$), or 6 months (IRR 0.99, 95% CI 0.63-1.55, $p=0.95$). The median MELD-Na improved in both groups. Attrition was similar in control and LivR Well (17.5% vs. 16.3%, $p=0.59$), with half those in LivR Well never commencing the program.

	Total (n=90)	Control (n=40)	Intervention (n=49)	p-value
Total mortality, n(%)	19 (21)	8(20)	11 (22)	0.43
Time to death, median (IQR)	117 (57-245)	115 (50-242)	203 (57-262)	0.30
MELD-Na, median (IQR)	Baseline 19.5 (16-23)	20(16-23)	18 (16-22)	0.30
	28-day 15 (9-21)	14 (11-21)	15(9-20)	0.94
EQ-5D VAS, median (IQR)	Baseline 54 (35-70)	60 (45-67)	50 (35-70)	0.03
	Week 12 77 (40-85)	77 (50-88)	76 (35-85)	0.66

There was no difference in mortality rate with a total 19 deaths over follow up, at a median days post randomisation of 115 (IQR: 50-242) and 203 (IQR: 57-462) respectively ($p=0.30$), and 28-day mortality was 0%. Health-related quality of life measured with the Chronic Liver Disease Questionnaire overall score and a self-reported visual analogue scale improved from baseline in both groups.

Conclusion: A multidisciplinary, ambulatory intervention did not reduce 30-day re-admission rates in patients admitted with hepatic decompensation. In a population with challenging healthcare engagement reflected in dropout rates, improvements in liver disease severity and quality of life were observed but not attributable to the intervention. Additionally, no deaths within 28-days, and a trend towards longer time to death may reflect medium-long term benefits of this unique program not yet captured.

References:

1. Collaborators GC. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol.* 2020;5(3):245-66
2. Haque L, Jakab S, Deng Y, Ciarleglio M, Tetrault J. Substance use disorders in recently hospitalised patients with cirrhosis. *J Addiction Med.* 2020;14(6):e337-e343
3. Volk M, Fisher N, Fontana R. Patient knowledge about disease self-management in cirrhosis. *A J Gastroenterol.* 2013; 108(3):302-305
4. Wigg A, Narayana S, Woodman R, Adams L, Wundke R....Ramachandran J et al. A randomized multicenter trial of a chronic disease management intervention for decompensated cirrhosis. *The Australian Liver Failure (ALFIE) trial. Hepatology.* 2024. | DOI: 10.1097/HEP.0000000000000862
5. Tapper E, Finkelstein D, Mittleman M, Piatkowski G, Chang M, Lai M. A quality improvement initiative reduces 30-day rate of readmission for patients with cirrhosis. *Clin Gastroenterol Hepatol.* 2016;14(5):753-759

Disclosure: Nothing to disclose.

MP075

MAS1 DEFICIENCY PROTECTS AGAINST ACUTE LIVER FAILURE BY SUPPRESSING THE FXR/S1P/RAF-DEPENDENT NETOSIS IN MICE

B. Yang¹, J. Li¹, C. Yang¹

¹Tongji University, School of Medicine, Tongji hospital, Division of Gastroenterology and Hepatology, Shanghai, China

Contact E-Mail Address: cqyang@tongji.edu.cn

Introduction: Mas is a newly discovered G protein-coupled receptor that plays a critical role in inflammatory responses. The gut-liver axis regulated neutrophilic inflammation is crucial in acute liver failure (ALF); however, the underlying mechanisms remain poorly understood.

Aims & Methods: The aim of this study is to investigate Mas signaling and neutrophilic inflammation in ALF, and to elucidate its underlying mechanisms. The 8-10 week-old male *Mas1^{-/-}*, *Vil1^{cre}Mas1^{fl/fl}*, and wild-type control mice were subjected to intraperitoneal challenge with D-galactosamine/lipopolysaccharide (D/L) for *in vivo* analysis of the gut-liver axis-dependent formation of neutrophil extracellular traps (NET), utilizing pharmacological compounds and genetic tools. Age-matched mice received injections of phosphate-buffered saline as vehicle controls.

Results: The hepatic expression of Mas was significantly upregulated in ALF patients and mice models. The knockout of the *Mas1* gene in both systemic and intestinal epithelial cells significantly alleviated D/L-induced NETosis and hepatotoxicity in mice. The involvement of gut microbiota in the attenuated hepatotoxicity of *Mas1^{-/-}*-D/L mice was confirmed through antibiotic experiments. The co-housed experiments between *Mas1^{-/-}* and WT mice have demonstrated that *Mas1^{-/-}* may confer protection by reducing the intestinal abundance of *Eubacterium* sp. and inhibiting deoxycholic acid (DCA) production. This was accompanied by hepatic activation of farnesoid X receptor (FXR) signaling and suppression of downstream sphingosine-1-phosphate (S1P)-dependent NETosis. As revealed by single-cell transcriptomics, the downregulation of NETosis in *Mas1^{-/-}*-D/L mice was found to be dependent on the senescence of *Cldn1⁺CD177⁺* neutrophils and the activation of Raf signaling.

Conclusion: *Mas1^{-/-}* significantly protects mice from D/L-induced hepatotoxicity by suppressing the FXR/S1P/Raf-dependent NETosis, thereby suggesting Mas as a promising therapeutic target for ALF.

Disclosure: Nothing to disclose.

MP076

THE IMPORTANT ROLE OF HYALURONAN SYNTHASE 2 IN HEPATOCYTES IN OXALIPLATIN-INDUCED PORTAL HYPERTENSION

L. Wu^{1,2}, X. Huang², F. Li^{2,3}, D. Schuppan^{4,1}, S. Chen^{3,2}

¹University Medical Center, Johannes Gutenberg University, Institute of Translational Immunology and Research Center for Immunotherapy, Mainz, Germany, ²Zhongshan Hospital, Fudan University, Department of Gastroenterology and Hepatology, Shanghai, China, ³Minhang Hospital, Fudan University, Department of Gastroenterology, Shanghai, China, ⁴Beth Israel Deaconess Medical Center, Harvard Medical School, Division of Gastroenterology, Boston, United States of America

Contact E-Mail Address: 20111210043@fudan.edu.cn

Introduction: Esophageal and gastric variceal bleeding is a life-risk complication of portal hypertension, with a high mortality. Recently, the number of patients with unexplained portal hypertension is gradually increasing¹. Non-cirrhotic portal hypertension caused by pre-hepatic/post-hepatic causes can also cause esophageal and gastric varices, of which the clinical diagnosis and treatment are still difficult². Oxaliplatin (Op) is a first-line drug in chemotherapy regimens for many kinds of cancers³, while the incidence of portal hypertension (PH)-related symptoms during follow-up of Op-treated patients without prior liver disease is increasing⁴. Chronic liver damage and portal hypertension caused by platinum-based drugs have an insidious onset and almost half of them are diagnosed due to the emergency treatment for esophageal and gastric variceal bleeding, which is highly dangerous and affects the long-term survival of patients⁵. To date, oxaliplatin-related PH studies are mainly clinical reports, and the underlying mechanisms are unclear.

Aims & Methods: We aimed to explore the pathology, mechanisms and key molecular players and potential pharmacological prevention of Op-induced PH. Gene expression profiles related to Op treated vs normal human livers were obtained from the GEO database, to identify key mol-

ecules and pathways via differentially expressed genes (DEG). OP-induce PH was induced in rats and liver transcriptome profiles were compared with the human samples, and key signatures confirmed by PCR. Since main Op-induced signatures were due to hepatocytes, human hepatocytes LO2 were treated with Op, and molecular responses measured in these cultures and in cultures of primary human liver sinusoidal endothelial cells (HHSEC) exposed to LO2-conditioned media.

Results: Totally, 19 Op-treated and 5 Op-treated rats were analyzed with 5 and 3 controls, respectively. Liver samples from Op-treated patients showed apparent hepatic sinusoidal dilatation. PH was induced by a 6-week Op treatment in rats, with sinusoidal endothelial activation and perivenous monocyte-macrophage infiltration, while a classical sinusoidal obstructive syndrome was missing. Hyaluronan synthase 2 (HAS2) and prominently the ERK pathway were upregulated after Op treatment in both rats and patients. Op-treated LO2-hepatocytes showed the activation of ERK pathway, and the up-regulation of HAS2; Co-culture of HHSEC and Op-treated LO2-hepatocytes showed that mediators released from LO2 cells induced HHSEC activation: up-regulated von Willebrand and tissue factor, increased migration, and activation of the ERK pathway. Notably, HHSEC migration was also increased after hyaluronic acid (HA) treatment, confirming an important role of HAS2 in Op-induced pathology.

Conclusion: Activation of the MAPK/ERK cascade is central to Op-induced PH. This pathway is implicated in the upregulation of HAS2 in hepatocytes, which releases HA, which activates sinusoidal endothelial cells, resulting in LSEC damage and subsequent portal hypertension.

References:

1. Biecker E. Portal hypertension and gastrointestinal bleeding: diagnosis, prevention and management. *World J Gastroenterol*. 2013;19(31):5035-50.
2. Gioia S, Nardelli S, Ridola L, Riggio O. Causes and Management of Non-cirrhotic Portal Hypertension. *Current Gastroenterology Reports*. 2020;22(12).
3. Zhang, C., et al., Platinum-based drugs for cancer therapy and anti-tumor strategies. *Theranostics*, 2022. 12(5): p. 2115-2132.
4. Gioia S, Di Martino M, Minozzi M, Nardelli S, Cortesi E, Riggio O. Incidence of portal hypertension in patients exposed to oxaliplatin. *Dig Liver Dis*. 2019;51(9):1348-50.
5. Huang, X., et al., Endoscopic treatment of gastroesophageal variceal bleeding after oxaliplatin-based chemotherapy in patients with colorectal cancer. *Endoscopy*, 2020. 52(9): p. 727-735.

Disclosure: Nothing to disclose.

MP077

SERUM COPEPTIN LEVELS PREDICT PORTAL HYPERTENSION-RELATED OUTCOMES IN PATIENTS WITH CIRRHOSIS

M. Hintersteiner¹, L. Hartl^{1,2}, B. Simbrunner^{1,2,3}, M. Jachs^{1,2}, B.S. Hofer^{1,2}, D.J.M. Bauer^{1,2}, N. Dominik^{1,2}, M. Schwarz^{1,2}, L. Balcar^{1,2}, G. Kramer¹, R. Marculescu⁴, M. Trauner¹, M. Mandorfer^{1,2}, T. Reiberger^{1,2,3}

¹Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ²Medical University of Vienna, Vienna Hepatic Hemodynamic Lab, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ³Medical University of Vienna, Christian Doppler Lab for Portal Hypertension and Liver Fibrosis, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ⁴Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria

Contact E-Mail Address: n11718197@students.meduniwien.ac.at

Introduction: Copeptin is a stable surrogate biomarker for the activation of the arginine vasopressin (AVP) system [1] as occurs in patients with cirrhosis and clinically significant portal hypertension (CSPH). Specifically, CSPH-induced haemodynamic alterations characterized by reduced peripheral vascular resistance and splanchnic hyperemia cause subsequent AVP system activation [2]. We aimed to evaluate serum copeptin levels (i) in different stages of cirrhosis and (ii) their prognostic value for clinical events in a cohort of stable outpatients with cirrhosis.

Aims & Methods: Stable outpatients with cirrhosis undergoing hepatic venous pressure gradient (HVPG) measurements and available copeptin levels were included; while patients with liver transplantation, malignancy, vascular liver disease, transjugular intrahepatic portosystemic shunt, heart failure and infection were excluded. Patients were stratified into 6 subgroups (S0-S5) for their clinical stage of cirrhosis, with S0-S2 representing compensated cirrhosis (S0: subclinical portal hypertension (PH) with an HVPG of 6-9 mmHg, S1: CSPH without varices, S2: CSPH with varices) and S3-S5 decompensated cirrhosis (S3: history of variceal bleeding, S4: non-bleeding decompensation, S5: further decompensation). Competing risk regression models were used to evaluate the association between copeptin levels and the risk of acute on chronic liver failure (ACLF) and liver-related death (LRD). Liver transplantation was considered as a competing event. Our previously established serum copeptin cut-off at >11.4 pmol/L [3] was used to stratify the patients into a high vs. low AVP system activation group.

Results: In total, 475 patients (S0: n=49, S1: n=53, S2: n=75, S3: n=22, S4: n=156, S5: n=120) with male predominance (72.6%; median age: 57.1 years) were included. Median follow-up time was 26.4 months. Median copeptin levels significantly increased throughout the substages of ACLD (from S0: 7.5 pmol/L to S5: 14.3 pmol/L; p<0.001). Patients with ascites had significantly higher copeptin levels (11.3 pmol/L vs. 7.2 pmol/L in non-ascites patients; p<0.001).

Serum copeptin correlated significantly with C-reactive protein (p=0.281; p<0.001) and interleukin-6 levels (p=0.416; p<0.001) in patients with decompensated cirrhosis.

AVP system activation (i.e., Copeptin high >11.4 pmol/L) was found in n=194/475 (40.8%) patients. Patients with high-Copeptin had a significantly higher median MELD-Na (15 vs. low-Copeptin: 12; p<0.001) as well as significantly lower median mean arterial pressure (97 mmHg vs. low-Copeptin: 101 mmHg; p=0.027). The cumulative incidence of ACLF and LRD was significantly higher in patients with high-Copeptin at 1 year (ACLF: 24.1% vs. 4.0%; LRD: 21.9% vs. 4.0%), 2 years (ACLF: 32.0% vs. 7.2%; LRD: 26.7% vs. 6.3%) and 3 years (ACLF: 34.4% vs. 11.6%; LRD: 29.9% vs. 11.2%) of follow-up (p<0.001 for ACLF and LRD).

In competing risk regression adjusted for age, Child Turcotte Pugh score, creatinine, sodium and HVPG, higher levels of copeptin were independently predictive of ACLF (adjusted subdistribution hazard ratio [asHR] per pmol/L: 1.01; 95% confidence interval [95%CI]: 1.00-1.01; $p=0.014$), as well as LRD (asHR: 1.01; 95%CI: 1.00-1.01; $p=0.024$).

Conclusion: In ACLD, copeptin levels are upregulated with increasing disease severity suggesting progressive AVP system activation, associated with hemodynamic dysregulation and systemic inflammation. High-Copeptin represents an independent risk factor for ACLF and LRD development.

References: 1. Abudeif A, Hashim MS, Ahmed NM, Ahmed AO. Serum copeptin is associated with major complications of liver cirrhosis and spontaneous bacterial peritonitis. *Clin Exp Hepatol*. 2023;9(1):71-8.

2. Kerbert AJ, Weil D, Verspaget HW, Moréno JP, van Hoek B, Cervoni JP, et al. Copeptin is an independent prognostic factor for transplant-free survival in cirrhosis. *Liver Int*. 2016;36(4):530-7.

3. Hartl L, Jachs M, Desbalmes C, Schaufler D, Simbrunner B, Paternostro R, et al. The differential activation of cardiovascular hormones across distinct stages of portal hypertension predicts clinical outcomes. *Hepatol Int*. 2021;15(5):1160-73.

Disclosure: Nothing to disclose.

MP078

ESOPHAGEAL VARICES SCREENING AND MANAGEMENT IN PATIENTS WITH CHRONIC LIVER DISEASE: A RETROSPECTIVE ANALYSIS OF AN AUSTRALIAN TERTIARY HEALTH SERVICE

T.H. Yiu¹, A. Khalid^{1,2}, H. Mautong^{2,3}, J. Andraos¹, E. Matejin¹, K. Curin¹, N. McGuinn¹, Z. Valaydon^{1,4}

¹Western Health, Department of Gastroenterology, Melbourne, Australia, ²Harvard Medical School, Department of PGME (Post graduate medical education), Boston, United States of America, ³John H. Stroger, Jr. Hospital of Cook County, Department of Medicine, Chicago, United States of America, ⁴University of Melbourne, Department of Medicine, Melbourne, Australia

Contact E-Mail Address: aisha.khalid000@gmail.com

Introduction: The Baveno Consensus Workshops recommend gastroscopy for advanced chronic liver disease (CLD) patients to detect varices, with Grade 2 or 3 varices advised to receive prophylactic treatment using non-selective beta blockers (NSBB) or band ligation [1-2].

Western Health (WH) is a tertiary health service serving a population of 1.2 million, primarily in socioeconomically disadvantaged Melbourne suburbs with a high density of non-English speaking background (NESB) immigrants with low health literacy [3-4]. This demographic presents challenges such as poor health service engagement, impacting guideline adherence and patient management.

Aims & Methods: The objective of this study is to evaluate adherence to the Baveno criteria for variceal management among CLD patients at WH. We retrospectively collected data from the electronic medical records of all CLD patients admitted to WH in 2021. We documented demographics, presenting complaints, underlying liver disease, adherence to varices screening and treatment. Univariate and multivariable logistic regression assessed predictors of liver-related mortality, which is defined as death resulting directly from a CLD complication at a 2-year follow-up.

Results: Our study included 275 CLD patients (mean age 60 years, SD 13; 64% male), 142 (52%) were born in Australia and 116 (42 %) were immigrants from NESB. The leading causes of CLD were alcohol-related (62%, $n=169$), metabolic liver disease (20 %, $n=56$), Hepatitis C (15 %, $n=42$) and B (4 %, $n=10$). Cirrhosis developed in 92 % ($n=253$) of patients, with 30 % ($n=75$) classified as Child-Pugh score A, 40 % ($n=102$) as B, and 30% ($n=76$)

as C. Ascites (23.3%, $n=64$), hepatic encephalopathy (16%, $n=44$), and variceal bleeding (9.5%, $n=27$) were the common presenting complaints. 245 patients met BAVENO criteria for variceal screening, 77.6% ($n=190$) underwent gastroscopy, revealing Grade 1 varices in 33.6% ($n=43$) and Grade 2 or 3 varices in 36.7% ($n=47$). Follow-up gastroscopy was scheduled for 56.7% ($n=21$) without initial varices and 75.6% ($n=31$) with Grade 1 varices. Among those with Grade 2 or 3 varices, 80.9% ($n=38$) underwent variceal banding, with 94.7% ($n=36$) receiving follow-up gastroscopy. However, only 19.1% ($n=9$) were prescribed NSBB. Of the 27 variceal bleeding cases, 21 warranted varices screening, yet only 11 had prior gastroscopy. Within these, 6 patients had Grade 1 and 1 had Grade 2 varices. The Grade 2 varices were ligated but NSBB was not initiated.

Univariate regression showed correlation between reduced liver-related mortality and variceal screening (OR 0.42, 95% CI 0.22-0.81, $p=0.01$) as independent variable, confirmed by multivariate logistic regression, after adjusting for confounders like age and Child-Pugh scores. Intriguingly, among unscreened patients, the most common cause of death is infection ($n=10$, 16.1%), only 4 had variceal bleeding with no resulting deaths. This is possibly due to selection bias as high-risk patients with prior varices bleeding history were more likely to be connected to the service.

Conclusion: Our study shows that variceal screening reduces liver-related mortality, yet it also reveals deficiencies in the current clinical approach to screening and treating varices at WH. These deficiencies may arise from various challenges, including communication barriers such as language constraints or time limitations in outpatient clinics, as well as patient factors such as limited health literacy resulting in poor compliance. Efforts should be directed towards improving the uptake of varices surveillance and enhancing the utilization of NSBB among patients.

References:

1. de Franchis R; Baveno VI Faculty. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. *J Hepatol*. 2015 Sep;63(3):743-52. doi: 10.1016/j.jhep.2015.05.022. Epub 2015 Jun 3.
2. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol*. 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022. Epub 2021 Dec 30. Erratum in: *J Hepatol*. 2022 Apr 14
3. Australian Bureau of Statistics. Regional Population Growth, Australia, 2019-20. [cited 2024 April 25]. Available from: <https://dbr.abs.gov.au/region.html?lyr=sa4&rgn=213>
4. Chiu HT, Tsai HW, Kuo KN, Leung AYM, Chang YM, Lee PH, Hou WH. Exploring the Influencing Factors of Health Literacy among Older Adults: A Cross-Sectional Survey. *Medicina (Kaunas)*. 2020 Jul 2;56(7):330.

Disclosure: Nothing to disclose.

MP079

SPLEEN STIFFNESS BY SHEAR-WAVE ELASTOGRAPHY AS AN INDICATOR OF PORTAL HYPERTENSION AND RESPONSE TO PREEMPTIVE TIPS PLACEMENT: A PROSPECTIVE STUDY

D. Feijó¹, C. Borges Chaves¹, D. Perdigoto¹, B. Rato², P. Donato², P. Narra Figueiredo¹

¹ULS Coimbra, Gastroenterology, Coimbra, Portugal, ²ULS Coimbra, Radiology, Coimbra, Portugal

Contact E-Mail Address: diogofeijo96@gmail.com

Introduction: Portal hypertension (PH) is a significant complication of advanced chronic liver disease (ACLD), often leading to acute variceal bleeding (VB), a life-threatening emergency. Preemptive transjugular intrahepatic portosystemic shunt (pTIPS) has become a critical intervention in managing PH-related complications, specifically in reducing the risk

of re-bleeding. The hepatic venous pressure gradient (HVPG) is the gold standard for assessing PH severity, but its invasive nature necessitates the exploration of non-invasive alternatives.

Aims & Methods: This study aimed to investigate the role of spleen stiffness, measured through shear-wave elastography (SWE), as a non-invasive predictor of PH severity and its correlation with HVPG in ACLD patients undergoing pTIPS after acute VB. We conducted a prospective study correlating spleen stiffness, measured by shear-wave elastography (SWE), with HVPG in ACLD patients (Child-Pugh class C<14 or B>7 with active bleeding) undergoing pTIPS placement following acute VB. Eleven patients with pre- and post-TIPS spleen stiffness measurements were included.

Results: Spleen stiffness was positively correlated with both pre-TIPS HVPG (Spearman's coefficient $r=0.527$; $p=0.145$) and post-TIPS HVPG ($r=0.719$; $p<0.05$). Furthermore, spleen stiffness significantly decreased after p-TIPS placement (pre-pTIPS: 36.42 [IQR 6.06] vs. post-pTIPS: 28.94 [IQR 7.80]; $p<0.05$), while the decrease in liver stiffness measurement was not statistically significant.

Conclusion: The results of this prospective study indicate that spleen stiffness, as measured by SWE, offers a valuable non-invasive method for assessing portal hypertension severity in patients with ACLD. We found a positive correlation between spleen stiffness and both pre- and post-TIPS HVPG. Additionally, significant reductions in spleen stiffness post-TIPS suggest that this metric can serve as a useful tool for monitoring patient response to pTIPS and potentially predicting outcomes. These findings highlight the importance of incorporating spleen stiffness measurement into the clinical management of patients with PH undergoing pTIPS, providing clinicians with an additional tool for assessing treatment efficacy and guiding patient care. Further research with larger cohorts is recommended to confirm these results and establish spleen stiffness as a reliable non-invasive alternative for PH assessment.

Disclosure: Nothing to disclose.

MP080

EARLY PREDICTION OF CORTICOSTEROID RESPONSE AND MORTALITY IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS

H.-O. Minea¹, A.M. Singeap¹, C.M. Muzica¹, S. Zenovia¹, C. Sfarti¹, I. Girleanu¹, S. Chiriac¹, R. Stafie¹, A. Rotaru¹, R. Nastasa¹, S. Ermina¹, S. Juncu¹, C. Stanciu¹, A.-V. Trifan¹

¹University of Medicine and Pharmacy Gr.T.Popa/Institute of Gastroenterology and Hepatology Iasi, Gastroenterology, Iasi, Romania

Contact E-Mail Address: horia.minea@yahoo.com

Introduction: Alcoholic hepatitis (AH) represents a medical challenge, from moderate to life-threatening episodes, with high mortality. This study aimed to compare prognostic scales to evaluate early response to corticosteroids and prediction to 28 days and 90 days mortality in patients with severe AH.

Aims & Methods: We performed a retrospective study that included patients with severe AH (Maddrey/MDF score ≥ 32) admitted to a tertiary center. Clinical and paraclinical data were collected on the response to corticosteroid administration and were assessed based on Lille scores (from days four and seven) and neutrophil to lymphocyte ratio (NLR) calculated on admission. MELD (Model for End-Stage Liver Disease), MELD-Na, MELD 3.0, ABIC (age-bilirubin-INR-creatinine), Maddrey and Glasgow scale scores were used to predict survival at 28 and 90 days, respectively. AH.

Results: Out of 310 patients enrolled with severe AH, 59% received corticosteroids, achieving a response rate of 75.4%. Lille score on day four presents a better performance than NLR in early anticipation of a response to

corticotherapy ($R^2=0.824$ versus $R^2=0.233$, $p<0.001$). Predictive factors for non-response were identified: presence of cirrhosis (OR= 2.11, $p<0.001$), MELD scores exceeding 30 (OR=2.42, $p<0.001$), hypoalbuminemia (<2.8 g/dl) (OR=2.46, $p<0.001$), and increased serum creatinine (OR=1.5, $p<0.001$). Non-responders have a five times higher risk of developing infections compared to responders (OR=6.74, versus OR=1.34, $p<0.001$). Among the prognostic scores, MELD 3.0 score proved superior efficacy for 28 days (AUC=0.734) and 90 days mortality (AUC=0.777) compared to alternative scoring systems.

Conclusion: An improvement in risk stratification based on the implementation of therapeutic response evaluation scores and mortality prediction, represent tools with applicability for adjusting the treatment scheme and prioritizing patients who require liver transplantation.

Disclosure: Nothing to disclose.

Pancreatic cancer: Basic

12:00-13:00 / Poster Stage 4

MP081

DECIPHERING THE REGULATORY ROLE OF LONG NON-CODING RNA IN PANCREATIC DEVELOPMENT AND DIABETES

S. Heller¹, S. Merz¹, C. Julier², A. Kleger¹

¹Ulm University Clinics, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Université de Paris, Institut Cochin, INSERM U1016, CNRS UMR-8104, Paris, France

Contact E-Mail Address: sandra.heller@uni-ulm.de

Introduction: Gene regulatory networks play a vital role in pancreatic development and function. However, pathomechanisms associated with the non-coding genome are just starting to be discovered. Our recent work demonstrated that mutations in the *ONECUT1* gene are responsible for a new neonatal diabetes syndrome in homozygous patients, whereas heterozygous carriers develop early-onset diabetes. Stage-specific characterization of *in vitro* differentiated human embryonic stem cells (hESC) revealed that *ONECUT1* plays an important role in transcriptional regulation during pancreatic progenitor formation and the initiation of the endocrine developmental program.

Nonetheless, the complex regulation is only partly uncovered. While investigating the *ONECUT1* locus, we found a variant most strongly associated with T2D (rs2440374). This variant is located within the lncRNA RP11-209K10.2 (further lncRNA-RP11), 11 kbp distant to *ONECUT1*. GTEx Portal database shows decreased lncRNA-RP11 expression in the pancreas in the presence of the T2D-associated allele.

Also, this SNP disrupts a binding motif for transcription factor NKX2.2 essential for endocrine pancreas development and pancreatic islet-cell fate. Since promoters of lncRNAs can also act as enhancer elements stimulating the regulation of neighboring genes, we hypothesize that the lncRNA-RP11 locus plays an important role in regulating *ONECUT1* and that disturbance of this transcriptional network promotes diabetes onset.

Aims & Methods: After deletion of lncRNA-RP11, hESC were differentiated into the pancreatic endocrine lineage followed by characterization of the developmental stages.

Results: Although differentiation of pancreatic progenitors is not impaired by the loss of the regulatory region, stem cell-derived islets further generated from these progenitors exhibit reduced number and function of beta-cells supporting an involvement during pancreas differentiation. The transcript of lncRNA-RP11 with main localization in the nucleus follows similar stage-specific dynamics as *ONECUT1* allowing for several modes of action.

Conclusion: Next, a comprehensive mechanistic characterization will provide insights into the exact function of lncRNA-RP11 in pancreatic endocrine development and pathophysiology. Thus, identifying novel molecular mechanisms involved in diabetes will improve our understanding of the transcriptional landscape and lay the groundwork for personalized diabetes treatment.

References: Philippi, A., Heller, S., Costa, I.G. *et al.* Mutations and variants of *ONECUT1* in diabetes. *Nat Med* **27**, 1928–1940 (2021). <https://doi.org/10.1038/s41591-021-01502-7>

Disclosure: Nothing to disclose.

MP082

PSYCHOLOGICAL DISTRESS AND QUALITY OF LIFE IN FAMILIES WITH A GERMLINE CDKN2A PATHOGENIC VARIANT

A. Onnekink¹, D. Klatte^{1,2}, J. van Hooft¹, S. van den Berg¹, S. van der Zwaan¹, R. van Doorn³, C. Hinnen^{4,5}, T. Potjer⁶, E. Bleiker^{7,6,8}, M. van Leerdam^{1,9}

¹Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ²Mayo Clinic, Gastroenterology and Hepatology, Jacksonville, Florida, United States of America, ³Leiden University Medical Center, Dermatology, Leiden, Netherlands, ⁴Leiden University Medical Center, Psycho-Oncology, Leiden, Netherlands, ⁵Spaarne Gasthuis, Medical Psychology, Haarlem, Netherlands, ⁶Leiden University Medical Center, Clinical Genetics, Leiden, Netherlands, ⁷Netherlands Cancer Institute, Division of Psychosocial Research and Epidemiology, Amsterdam, Netherlands, ⁸Netherlands Cancer Institute, Clinical Genetics, Amsterdam, Netherlands, ⁹Netherlands Cancer Institute, Gastrointestinal Oncology, Amsterdam, Netherlands

Contact E-Mail Address: a.m.onnekink@lumc.nl

Introduction: Individuals with the Dutch founder *CDKN2A*/p16-Leiden pathogenic variant (PV) have an increased lifetime risk of melanoma (70%) and pancreatic cancer (20%). Consequently, skin surveillance is offered from the age of 12 to those with a confirmed or suspected PV, while pancreatic cancer surveillance is exclusively offered to confirmed carriers from the age of 40. It is unknown whether the *CDKN2A* PV impacts quality of life (QoL). Therefore, we aimed to assess QoL and psychological distress in individuals from affected families.

Aims & Methods: This cross-sectional study included confirmed carriers and those with a 50% risk of the *CDKN2A* PV (at-risk carriers) undergoing cancer surveillance. Individuals ≥ 18 years were identified from the skin and pancreatic cancer surveillance programs at the Leiden University Medical Center and invited for a one-time, validated self-report questionnaire, including the 12-Item Short Form Health Survey (SF-12), Hospital Anxiety and Depression Scale (HADS), and Cancer Worry Scale (CWS).

Scale	Scale range / threshold	Skin surveillance group (N = 59)	Pancreatic surveillance group (N = 188)	General population
		Mean (±SD) % > threshold	Mean (±SD) % > threshold	Mean (±SD) % > threshold
Health-related QoL				
SF-12 PCS	Range 0-100	54.7 (6.6)**	50.4 (8.1)**	51.7 ¹ / 48.1 [‡]
SF-12 MCS	Range 0-100	46.9 (10.1)	51.4 (8.8)	48.0 ¹ / 51.0 [‡]
General and cancer-related distress				
HADS - anxiety	Range 0-21 Abnormal threshold ≥ 11	4.7 (3.7) 6 (10%)	4.0 (3.6)** 11 (6%)	5.1 (3.6) [§] -
HADS - depression	Range 0-21 Abnormal threshold ≥ 11	2.8 (3.1) 2 (3%)	2.7 (2.8)* 3 (2%)	3.4 (3.3) [§] -
CWS - melanoma-related worries	Range 8-32 Abnormal threshold ≥ 14	12.7 (3.2) 26 (44%)	13.4 (3.9) 76 (40%)	-
CWS - pancreatic-related worries	Range 8-32 Abnormal threshold ≥ 14	11.4 (3.0) 10 (17%)	13.6 (3.9) 84 (45%)	-

Table 1. Descriptive statistics and summary of group comparisons for psychological variables

**P<0.01. *P<0.05. SF-12, 12-item Short Form Health Survey; PCS, Physical Component Scale; MCS, Mental Component Scale; HADS, Hospital Anxiety and Depression Scale; cancer worries measured by the adapted Cancer Worry Scale (CWS). Scores of the SF-12 ranged from 0-100, with higher scores indicating better health. The HADS cut-off score was ≥ 11 , indicating a clinically significant anxiety or depressive disorder. The CWS cut-off score was ≥ 14 , indicating increased cancer-related distress. ¹ age-matched QoL norm scores from Dutch general population with skin surveillance group. [‡] age-matched QoL norm scores from Dutch general population with pancreatic surveillance group. [§] HADS scores were compared with 199 individuals from the general Dutch population. ²

Results: A total of 537 individuals were screened for eligibility, of whom 59/249 (24%) individuals under skin surveillance (skin surveillance group) and 188/288 (65%) individuals under combined pancreatic cancer and skin surveillance (pancreatic cancer surveillance group) responded. In both surveillance groups, health-related QoL and general distress levels were within the general population norms (Table 1). However, more than 40% of all study participants reported melanoma-related distress. Pancreatic cancer-related distress was experienced by 45% of the pancreatic surveillance group. Determinants of cancer-related distress were a first-degree relative with melanoma or pancreatic cancer, increased cancer risk perception, and poor general health perception. Over 80% of the participants felt that the benefits of cancer surveillance outweigh the disadvantages.

Conclusion: In conclusion, confirmed and at-risk carriers of the *CDKN2A* PV experienced similar levels of QoL and general distress compared with the general population. However, cancer-related worry was substantial in this population. These findings can help identify individuals who may benefit from psychological support.

References: 1. Netherlands S. Gezondheid en zorggebruik; persoonskenmerken. Accessed 05-01-2024.

2. Spinhoven PH, Ormel J, Sloekers PPA, Kempen GJUM, Speckens AEM, Hemert AMV. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological Medicine*. 1997;27(2):363-370. doi:10.1017/S0033291796004382

Disclosure: Nothing to disclose.

MP083

HIGH AMOUNTS OF STROMAL COLLAGEN IN PANCREATIC CANCER CORRELATE WITH FAVORABLE PROGNOSIS, ENHANCED CHEMOTHERAPEUTIC RESPONSES, AND DISTINCTIVE GENE EXPRESSION PROFILES

N. Juri¹, A. Masuda¹, M. Tsujimae¹, S. Ashina², A. Sakai¹, T. Kobayashi¹, Y. Kodama¹

¹Kobe University, Division of Gastroenterology, Department of Internal Medicine, Kobe, Japan, ²Akashi Medical Association Akashi Medical Center, Division of Gastroenterology, Akashi city, Japan

Contact E-Mail Address: njuri3@med.kobe-u.ac.jp

Introduction: Pancreatic cancer is a highly fatal disease with a 5-year survival rate of approximately 10%. Pancreatic ductal adenocarcinoma (PDAC) is characterized by abundant collagen deposition in the tumor stroma. However, the precise impact of this phenomenon on PDAC remains unclear.

Aims & Methods: This study aimed to clarify the interactive relationship between tumor stromal collagen and its molecular characteristics, immune characteristics, and tumor progression in human PDAC. The goal is to elucidate the mechanism of fibrosis in PDAC. A comprehensive examination was performed using a molecular pathological epidemiology database on 169 cases with resected PDAC.

Among 234 patients who underwent pancreatectomy surgery between April 2008 and March 2017 at Kobe University, 169 conventional PDAC patients were analyzed. Patients with special type pancreatic cancers, with stage IV PDAC, who underwent preoperative radiation, and without available FFPE samples were excluded. The following information was collected retrospectively about these patients: age, gender, body mass index, family history, blood test results, surgical pathology specimen, and treatment course.

We quantified the amount of tumor stromal collagen by digitally processing EVG-stained whole-section slides. Gene alterations (KRAS, TP53, *CDKN2A/p16*, and *SMAD4*), immune parameters (CD4+ tumor-infiltrating

lymphocytes [TILs], CD8+ TILs, FOXP3+ TILs, and tertiary lymphoid structures), and marker of cancer-associated fibroblasts such as α SMA were evaluated by immunohistochemistry, next-generation sequencing, and droplet digital PCR.

Results: Multivariate logistic regression analysis revealed that low stromal collagen levels were linked to poor differentiation ($P=0.008$) and *CDKN2A/p16* alteration ($P=0.03$) of PDAC. Additionally, low stromal collagen levels were found to be an independent poor prognostic factor. The overall survival of such patients was significantly shorter (22.1 months vs. 38.0 months, $P=0.001$).

Regarding those who underwent chemotherapy, low amounts of stromal collagen were linked to poor prognosis in the S-1 ($P=0.005$) and gemcitabine ($P=0.007$) treatment groups. Furthermore, they were linked to low levels of CD4+ tumor-infiltrating lymphocytes (TILs) ($P=0.046$), CD8+ TILs ($P=0.09$), and tertiary lymphoid structures ($P=0.001$).

The mechanism by which fibrosis is associated with prognosis is not well-defined. The components of tumor microenvironment are diverse, including cancer cells, fibroblasts, immunocompetent cells, and extracellular matrix. Thus, we explored comprehensively the factors and mechanisms that define fibrosis with Spatial Transcriptome. Gene expression analysis was performed using two sets of four cases with different amounts of stromal collagen. The gene expression could be classified into 7 clusters. The cancer cells in the low amounts group consisted of one cluster and those in the high amounts group consisted of two clusters on the hand. Enrichment analysis on the distinctive cluster in the high amounts group revealed that it was genes that activated the TGF β pathway.

Conclusion: The amount of tumor stromal collagen varies in tumor characteristics, prognosis, and response to postoperative chemotherapy in PDAC, and may affect the modulation of the tumor immune microenvironment. We found that there is a group of genes that are characteristically expressed in PDAC with high amounts of stromal collagen and a good prognosis. Further studies will be conducted to elucidate the mechanisms that regulate fibrosis.

Disclosure: Nothing to disclose.

MP084

PANCREATIC ORGANIDS ESTABLISHMENT FROM EUS FINE NEEDLE BIOPSY IN PATIENTS AFFECTED BY PANCREATIC CANCER: PRELIMINARY RESULTS FROM THE BILE BIOPSY STUDY

C. Binda¹, P. Giuffrida¹, M. Zanoni², G. Marisi², C. Coluccio¹, B. Perini³, G. Gibiino¹, S. Fabbri¹, F. Limarzi⁴, A. Vizzuso⁵, I.G. Rapposelli⁶, E. Giampalma⁵, M. Cricca⁷, C. Camma⁸, V. Sambri⁷, P. Ulivi², C. Fabbri¹

¹AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena Hospitals, Forlì, Italy, ²IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) 'Dino Amadori', Biosciences Laboratory, Meldola, Italy, ³University of Padua, Department Of Surgery, Oncology And Gastroenterology, Padova, Italy, ⁴AUSL Romagna, Pathology Unit, Morgani-Pierantoni Hospital, Forlì, Italy, ⁵AUSL Romagna, Unit of Radiology, Morgagni-Pierantoni Hospital, Forlì, Italy, ⁶IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) 'Dino Amadori', Department of Medical Oncology, Meldola, Italy, ⁷Alma Mater Studiorum, University of Bologna, Department Medical and Surgical Sciences (DIMEC), Bologna, Italy, ⁸Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Section of Gastroenterology and Hepatology, Department of Health Promotion, Palermo, Italy

Contact E-Mail Address: cecilia.binda@gmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the seventh leading cause of cancer related death worldwide, with a progressive increasing incidence¹ and 5 years overall survival (OS) of 12.5% irrespective of the disease stage². Given the tumor biological aggressiveness and the limited response to chemotherapy, it arises the need to develop preclinical study models able to understand the underlying mechanism of tumor progression and chemoresistance³. These models need to be easily generable, reproducible, representative of the entire population affected by PDAC and to have the ability of mimicking the cancer behavior. Patients derived organoids (PDOs) are models of epithelial cells with self-regeneration and self-organization abilities able to behave and mimic the tumors of origin⁴. Liquid biopsy has also gained importance in tailoring the treatment for oncological patients, although the role of bile as biological fluid in patients affected by biliopancreatic malignancies is still uncertain.

Aims & Methods: We performed a prospective observational study aiming to evaluate the feasibility to create tridimensional PDOs from fine needle biopsy (FNB) samples of patients affected by PDAC and to correlate PDOs with native cancer histology. The secondary endpoint of our study was to assess the feasibility of using bile as biological fluid for cell free DNA (cfDNA) and to investigate the landscape of cfDNA in bile and plasma of patients affected by PDAC.

Patients with strong suspicion or recent diagnosis of PDAC and concomitant jaundice were included. Each patient underwent EUS guided FNB (EUS-FNB) for histological diagnosis and organoid collection was performed. By the time of biliary drainage, bile and plasma were collected for DNA extraction and analysis.

Results: From June 2023 to September 2023, 36 patients with neoplastic jaundice were evaluated. Eighteen patients with final diagnosis of PDAC have been included in the study. Eighteen underwent biliary drainage with collection of bile and plasma. Sixteen underwent EUS-FNB for organoid collection.

Mean tumor size was 33.7±9.6 mm. Tumor was located in the head of pancreas in 94.4% of cases. Nine patients (50%) were metastatic by the time of diagnosis, eight patients (44%) had locally advanced disease and only one patient was considered resectable. Tissue acquisition was performed using FNB needles. Organoids establishment rate was successful in 100% of cases. No EUS-FNB related adverse events were observed.

At a quality concordance pathological analysis between PDAC and PDOs, morphological similarities have been observed in all cases (100%). Cellular morphology and nuclei atypia were the most consistent similarities. Organoids showed a glandular over expression compared to native PDAC. Extracted cfDNA was significantly higher in bile supernatant than in plasma (2.9 ng/ml vs 19.8 ng/ml p=0.0001). No significant differences were found for plasma and bile cfDNA among disease stages. Higher level of bile cfDNA in locally advanced disease and a trend of higher level of plasma cfDNA in metastatic stage. Bile cfDNA showed longer DNA fragment compared to plasma.

Conclusion: Organoids establishment is feasible and safe with a single passage of EUS-FNB. PDOs maintain the morphological architecture of native cancer, although the absence of dense stromal reaction leads to a remarkable organoids ability to create glandular structures. Qualitative and quantitative composition of ctDNA is superior in bile rather than in plasma, making this fluid an important tool for NGS analysis and a better comprehension of tumor mutations.

References:

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249. doi:10.3322/caac.21660
2. Arnold M, Rutherford MJ, Bardot A, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995-2014 (ICBP SURVMARK-2): a population-based study. Lancet Oncol. 2019;20(11):1493-1505. doi:10.1016/S1470-2045(19)30456-5
3. Baker LA, Tiriac H, Clevers H, Tuveson DA. Modeling pancreatic cancer with organoids. Trends Cancer. 2016;2(4):176-190. doi:10.1016/j.trecan.2016.03.004
4. Moreira L, Bakir B, Chatterji P, Dantes Z, Reichert M, Rustgi AK. Pancreas 3D Organoids: Current and Future Aspects as a Research Platform for Personalized Medicine in Pancreatic Cancer. Cell Mol Gastroenterol Hepatol. 2017;5(3):289-298. Published 2017 Dec 16. doi:10.1016/j.jcmgh.2017.12.004

Disclosure: Nothing to disclose.

MP085

PROTEOMICS-BASED SYSTEM MODELING REVEALED POTENTIAL TRANSLATIONAL TARGETS OF PANCREATIC DUCTAL ADENOCARCINOMA

M. Resell¹, H.-L. Rabben¹, M.P. Amrutkar², A. Aarvik¹, A. Sharma^{1,3,4}, L. Hagen^{1,3,4}, L. Hoang¹, N.T. Skogaker¹, C.S. Verbeke⁵, S.K. Batra⁶, G. Qvigstad⁷, T. Wang⁸, D. Chen¹, C.M. Zhao^{1,4}

¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²Institute of clinical medicine, University of Oslo, Department of Hepato-Pancreato-Biliary surgery, Oslo, Norway, ³Norwegian University of Science and Technology, PROMEC Core Facility for Proteomics and Modomics, Trondheim, Norway, ⁴Central Norway Regional Health Authority Norway, Trondheim, Norway, ⁵Oslo University Hospital - Pathology, Oslo University Hospital; Oslo/NO, Pathology, Oslo, Norway, ⁶University of Nebraska College of Medicine, Department Biochemistry and Molecular Biology, Nebraska, United States of America, ⁷St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, ⁸Columbia University, Digestive & Liver Diseases, New York, United States of America

Contact E-Mail Address: mathilde.resell@ntnu.no

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a lethal disease with the lowest 5-year survival rate of all cancers due to late diagnosis and lack of effective treatment. One of the challenges of developing molecular diagnosis and molecular targeted therapy for PDAC is the “mismatch” between research models and patients.

Aims & Methods: This study aimed i) to identify common proteins among different research models and patients and accordingly ii) to identify potential hub proteins and signaling pathways involved in the PDAC pathogenesis by using proteomics-based system modeling of multimodal datasets derived from multiple research models and patients. Mouse PDAC cells (derived from a genetically engineered mouse model with KrasG12D/Pdx1-Cre), PDAC orthotopically tumors in C57B/L6 mice (n=5), mouse PDAC spheroids, mouse pancreatic organoids, mouse PDAC organoids, normal mouse pancreatic tissues (n=5), human PDAC tumor tissue samples from treatment-naïve (n=20), neoadjuvant chemotherapy (n=22), and human PDAC organoids were included. Mass spectrometry-based proteomics, Rstudio, Cytoscape 3.10 and pathway enrichment analysis (using ingenuity pathways analysis, including human PDAC transcriptomic in addition) were used.

Results: In the comparison of PDAC models and patients, shared proteins were identified as follows: 60% between the mouse PDAC cells and the mouse PDAC spheroids, 78% between the mouse PDAC cells and the mouse PDAC tissue, 56% between the mouse PDAC spheroids and the mouse PDAC tissue, 66% between the mouse PDAC cells and the mouse PDAC organoids, 54% between the mouse PDAC spheroids and the mouse PDAC organoids, 38% between the mouse PDAC and the human PDAC tissues, 31% between the human PDAC tumor and the human PDAC organoids, and 60% between the mouse and the human PDAC organoids. A total of 1,367 common proteins were identified within all the PDAC models. Among these proteins ACTB, HSP90AA1, HSPA8, HSP90AB1, HSPA4, EEF2, RPS3, RPS20 and GAPDH were the top 10 hub proteins (with >300 node connections). Upon comparison of all eight models, eight proteins were identified as unique to PDAC, namely FAHD1, ARSA, NEK9, SERPINB9, LAMTOR2, SNRPG, TMED3, and RAB1A. There was a correlation in terms of z-score regarding signaling pathways between the mouse PDAC and human PDAC ($p < 0.001$), particularly in activations of nerve growth factor signaling, integrin signaling, and neuregulin signaling. Central hub proteins commonly found in the mouse models included vinculin (membrane-cytoskeletal protein) as one of the high connectivity nodes and β -catenin

and probable ubiquitin carboxyl-terminal hydrolase FAF-X (involved in axonal growth and neuronal cell migration) as high centrality nodes. In patients, central hub proteins that were dysregulated after chemotherapy included 14-3-3 protein zeta/delta (encoded by YWHAZ gene), β -catenin and SRC. Among the 47 proteins that were associated with altered metabolism after the chemotherapy in patients, CD44, CTNND1, APOA1, PARVA, and SCRBS1 were nodes with low degrees, and desmosomes (DSP, KP3, PPL, PRTN3, thrombospondin-2 (THBS2), and DMBT1 were the most down-regulated proteins without nodes, and APOA1, caveolin-1 (encoded by CAV1), LRP1 were the most up-regulated proteins with nodes.

Conclusion: The system modeling identified the common proteins among the research models and patients and the hub proteins and signaling pathways, suggesting the potential translational targets of PDAC.

Disclosure: Nothing to disclose.

MP086

SINGLE-CELL PROFILING UNLEASHES KRAS-DRIVEN REDRAFTING OF THE TUMOR MICROENVIRONMENT BEFORE CANCER ONSET

C. Allgöwer¹, J. Nagai², M. Breunig¹, M. Hohwieler¹, I. Costa², A. Kleger¹

¹University Hospital Ulm, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²RWTH Aachen University, Institute for Computational Genomics, Aachen, Germany

Contact E-Mail Address: chantal.allgoewer@uni-ulm.de

Introduction: Pancreatic cancer is a highly lethal disease, commonly characterized by aggressiveness and a unique tumor microenvironment, where mutant KRAS signaling stands as a hallmark event in its pathophysiology.

Aims & Methods: To deepen our understanding of KRAS-dependent signaling, stem cell-derived pancreatic ductal-like organoids (PDLOs) were induced by oncogenic KRAS expression, followed by time-resolved single-cell RNA- and bulk ATAC-sequencing. This unique precancerous state model facilitated a comprehensive characterization of early oncogenic events at cellular resolution.

Results: Specifically, mutated KRAS triggers two distinct gene signature programs: extracellular matrix remodeling and inflammation-related signaling. Correlation with published datasets underscored relevance of these distinct gene signatures in advanced cancer states within human patients. Various co-culture systems showed that KRAS^{G12D}-expressing PDLOs could induce cancer-associated fibroblast (CAF) activation while simultaneously shielding KRAS-activated, yet non-cancerous, organoids from T cell infiltration *in vitro*. Furthermore, *in silico* approaches were employed to reconstruct a virtual pancreatic cancer space, demonstrating that our PDLOs transcriptomically bridge healthy and malignant duct, while also unveiling the KRAS driven pathways mediating CAF reprogramming and T cell shielding preceding cancer onset.

Conclusion: In summary, our human PDLO model enables us to explore the transition from normal to cancerous states, overcoming gaps in our understanding of tumor development and tumor niche preparation.

Disclosure: Nothing to disclose.

MP087

ALDH1A3/AP-1 AXIS FOSTERS AN ONCOGENIC ENHANCER NETWORK IN PANCREATIC CANCER

S. Nie¹, H. Li¹, Y. Yu¹, Y. Lv¹, L. Wang¹, X. Zou¹, B. Kong², S. Shen¹
¹Affiliated Drum Tower Hospital of Nanjing University, Department of Gastroenterology, Nanjing, China, ²University Hospital of Heidelberg, Department of General, Visceral and Transplantation Surgery, Heidelberg, Germany

Contact E-Mail Address: skyler1208@163.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a histopathologically defined tumour entity with a devastating prognosis. We previously defined a highly aggressive PDAC subtype labelled by ALDH1A3 (aldehyde dehydrogenase 1 family member A3) expression, partially overlapping with defined molecular subtypes with unfavourable prognosis. ALDH1A3 is a known enzyme catalyzing multiple metabolic processes in nuclear, which could further provide intermediate metabolites (i.e. acetyl coenzyme A and S-adenosyl methionine) for histone modification and affect chromatin accessibility.

Aims & Methods: In this study, we aim to examine the relationship between ALDH1A3 and pancreatic cancer malignancy, focusing to its influence on transcriptional subtype determination. ATAC-seq (assay for transposase-accessible chromatin using sequencing), CUT&Tag (cleavage under targets and tagmentation), RNA-seq, and several other assays were performed to evaluate the impact of ALDH1A3 on enhancer reprogramming and transcriptional subtyping. Pancreas-specific Aldh1a3 inhibition or overexpression was studied in mouse models, and the results were validated using human samples.

Results: A consistent overexpression of ALDH1A3 was observed in aggressive PDAC subtypes. Mechanistically, ALDH1A3 orchestrated the AP-1-dependent enhancer landscape in a dose-dependent manner, potentiating oncogenic MAPK (mitogen-activated protein kinase) signalling. Using an integrative multi-omics approach, we identified the pivotal role of RUNX2 (runt-related transcription factor 2)- a transcription factor downstream of the ALDH1A3/AP-1 axis. RUNX2 formed a functional complex with BRD4 (bromodomain containing 4), enabling the discernment of acetylated chromatin and DNA sequences, and thereby activation of an oncogenic enhancer network, which underpins oncogenic MAPK signalling.

Conclusion: These findings elucidate the integral crosstalk among an ALDH1A3-mediated oncogenic enhancer network and signal transduction pathways in aggressive PDAC subtypes, providing a molecular framework for targeted and personalized therapeutic intervention.

Disclosure: Nothing to disclose.

MP088

THE EZH2 EPIGENETIC FACTOR, A CRITICAL ONCOGENIC PLAYER OF THE ATM-DEFICIENT PANCREATIC CANCER TUMORIGENESIS

E. Roger¹, A. Härle¹, M. Ekizce¹, D. Srinivasan¹, J. Gout¹, E. Hessmann², A. Kleger^{1,3}, L. Perkhofer^{3,1}

¹University Ulm Hospital, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Universitätsmedizin Göttingen, Göttingen, Deutschland, Göttingen, Germany, ³Division of Interdisciplinary Pancreatology, Ulm University Hospital, Department of Internal Medicine I, Ulm, Germany

Contact E-Mail Address: menar.ekizce@uni-ulm.de

Introduction: By 2030, pancreatic ductal adenocarcinoma (PDAC) is predicted to become the second leading cause of cancer-related death. Due to its resistance to conventional therapies and heterogeneous mutational landscape, molecular stratification and the development of targeted

therapeutic options are essential for improving survival of PDAC patients. Previous work from our group investigated loss-of-function mouse models for the ATM serine/threonine kinase causing homologous recombination deficiency (HRD) in PDAC. Specifically, ATM loss was reported to accelerate tumorigenesis, support metastatic burden, and coincide with oncogenic programs, including epithelial-mesenchymal transition (EMT). Interestingly, ATM-deficient tumors accumulated EZH2, suggesting that ATM status contributes to rewiring the epigenetic landscape of pancreatic tumors, subsequently supporting oncogenic features.

Aims & Methods: To investigate whether and how EZH2 impacts ATM-deficient PDAC pathogenesis, we generated conditional double ATM and EZH2 knockouts in *Kras*^{G12D/+}; *Ptf1a*^{Cre/+} mice. *In vitro* approaches were conducted using primary cell lines isolated from murine endpoint tumors. Additionally, CRISPR/Cas9 strategy was implemented on ATM-deficient cell lines to decipher the ATM-EZH2 molecular axis.

Results: Double-null mice showed extended mouse survival and decreased undifferentiated malignant cell features. Strikingly, interrogation of publicly available human datasets (TCGA, PanCancer Atlas) revealed a significant extended progression-free survival of *ATM*^{neg} *EZH2*^{neg} PDAC patients compared to *ATM*^{neg} *EZH2*^{pos} PDAC cases. Furthermore, we identified the histone-methyltransferase EZH2 as a direct ATM substrate impacting the mesenchymal phenotype of ATM-depleted tumors. Interestingly, RNA-seq analysis of ATM-deficient pancreatic cancer cells revealed upregulation of a transcriptomic program associated with cell differentiation upon EZH2 depletion by CRISPR/Cas9 strategy. In line, EZH2 depletion restored differentiated tumor features *ex vivo*. Further *in vitro* investigations revealed that ATM status significantly impacts EZH2 activity via a post-translational regulation axis, leading to a fostered tumor supporting EZH2 activity during pancreatic carcinogenesis. Specifically, the ATM kinase activity results in EZH2 ubiquitination and degradation by promoting Cullin1 E3-ubiquitin ligase recruitment. Finally, we demonstrated that a combinatorial therapy involving a potent EZH2 inhibitor promotes genomic instability and exacerbates the cytotoxic effects of PARP interference in ATM-deficient HRD PDAC.

Conclusion: Overall, we show that ATM deficiency significantly impacts EZH2 epigenetic functions and highlight the molecular stratification according to ATM status prior to pharmacological EZH2 interference in PDAC therapies as a valuable approach to target ATM-deficient HRD tumors.

Disclosure: Nothing to disclose.

MP089

AGR2 ACTS THROUGH MULTIPLE MECHANISMS TO RESTRUCTURE THE IMMUNE MICROENVIRONMENT OF PANCREATIC DUCTAL ADENOCARCINOMA BY IMPACTING THE IGF1 SIGNALING PATHWAY

H. Li¹, S. Zhou¹, S. Shen¹, Z. Shi¹, Q. Zhou¹, X. Wang¹, Y. Yu¹, S. Nie¹, Y. Lv¹, L. Wang¹, X. Zou¹, B. Kong¹

¹Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Gastroenterology, Nanjing, China

Contact E-Mail Address: 13405443939@163.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis, with a five-year survival rate of only about 10%, primarily attributed to the desmoplastic stroma and the immunosuppressive microenvironment. The regulatory mechanism of anterior gradient 2 (AGR2) as an oncogene in the tumor microenvironment remains unclear.

Aims & Methods: The purpose of this study was to investigate the mechanism by which AGR2 regulates the tumor microenvironment and its role in the malignant progression of PDAC. ELISA and immunohistochemistry (IHC) were utilized to assess the expression of AGR2 in the serum and tumor tissues of PDAC patients. Different truncated forms of AGR2 cDNA

were employed to restrict the subcellular distribution of AGR2 to assess its impact on tumor cells and the tumor microenvironment. AGR2 knockout and overexpressing transgenic mice with spontaneous pancreatic cancer were utilized to assess the influence of AGR2 on the tumorigenesis and tumor progression of PDAC. AGR2 monoclonal neutralizing antibody was developed to validate the therapeutic efficacy of targeting AGR2 in PDAC.

Results: We find that AGR2, exclusively produced by neoplastic cells, was highly expressed in both precursor lesions and overt cancer cells, contributing to PDAC tumorigenesis and progression. AGR2 was activated by IGF1 signal from cancer-associated fibroblasts (CAFs) and secrete outside the tumor cells which further induces IGF1 expression, transforming fibroblasts into an inflammatory CAFs (iCAFs) phenotype through a positive feedback loop. At the same time, the intracellular AGR2 promoted the maturation and cell surface transport of IGF1R to provide receptors for IGF1 signaling. Combining a monoclonal neutralizing antibody against AGR2 with an IGF1R inhibitor had a synergistic effect in restructuring the tumour microenvironment and disrupting the immunosuppressive state, exerting an anti-tumour effect.

Conclusion: AGR2 promotes the interaction between tumor cells and CAFs by amplifying the IGF1 signaling pathway, further enhancing the immunosuppressive signals emitted by iCAFs. Targeting AGR2 as a potential PDAC treatment method may improve immune infiltration in the tumor microenvironment and attenuate malignant progression of PDAC.

Disclosure: The authors declare no potential conflicts of interest.

Diagnosis and treatment of GORD

12:00-13:00 / Poster Stage 5

MP090

MEAN BASAL ESOPHAGOGASTRIC JUNCTION PRESSURE IS A BETTER PREDICTOR OF CONCLUSIVE GERD THAN ESOPHAGOGASTRIC JUNCTION CONTRACTILE INTEGRAL DIFFERENTIATING REFLUX PHENOTYPES

E. Vespa^{1,2}, S. Passaretti^{1,2}, A. Barchi^{1,2}, J. Fanizza^{1,2}, E. Fasulo^{1,2}, R. Bara^{1,2}, M.C. Fratto², S. Danese^{1,2}

¹IRCCS Ospedale San Raffaele, Gastroenterology and Digestive Endoscopy, Milano, Italy, ²Università Vita-Salute San Raffaele, Milano, Italy

Contact E-Mail Address: edo.vespa93@gmail.com

Introduction: Esophagogastric junction contractile integral (EGJ-CI) is a metric of EGJ barrier function on high-resolution manometry (HRM), which may be limited by measurement discrepancies and unclear clinical utility. Mean EGJ basal pressure is a novel, simple HRM metric assessing barrier function. We compared their performance to predict conclusive gastroesophageal reflux disease (GERD).

Aims & Methods: Consecutive patients (Nov 2022-Oct 2023) undergoing combined HRM and 24 hour pH-impedance testing OFF antisecretory therapy (except for Barrett's patients) for known or suspected GERD were eligible, all with prior upper endoscopy. Mean (between end-expiration and end-inspiration) basal EGJ pressure, referenced to mean intragastric pressure, was calculated manually using the isobaric contour tool. EGJ-CI was calculated using the smart box tool, with the isobaric contour set 2 mmHg above intragastric pressure, over three respiratory cycles and normalized for its duration. On pH-impedance testing, Lyon classification 2.0 was applied. Conclusive GERD was defined as acid exposure time (AET) >6% or histologically confirmed Barrett's. Mann-Whitney U and Kruskal-Wallis test, with Bonferroni correction, were used. ROC curves were plotted.

Results: 125 patients were included (mean age 51.6 ± 16.5 years, 60% males). Upon applying Lyon 2.0 classification, 45 (36%) patients had conclusive GERD (25 Barrett's), 7 (6%) borderline GERD, 16 (13%) reflux hypersensitivity (RH), while 57 (45%) had functional symptoms. Patients with conclusive GERD, on HRM, had a significantly lower mean basal EGJ pressure (11.0 vs 18.5 mmHg; p<0.001) than patients without conclusive GERD, while EGJ-CI was not statistically different (26.1 vs 35.1 mmHg·cm; p=0.101). Mean basal EGJ pressure was significantly different across Lyon v2.0 subgroups (median values in GERD: 11, borderline GERD: 16, RH: 19, FH: 20 mmHg; p<0.001), while EGJ-CI did not differ (p=0.283). Mean basal EGJ pressure (AUROC: 0.73, 95%CI 0.64-0.82) showed greater predictive performance of conclusive GERD than EGJ-CI (AUROC: 0.59, 95%CI 0.49-0.69). The optimal cut-off of 13 mmHg had 72% sensitivity and 62% specificity; a cut-off of 9.5 mmHg had 86% sensitivity, while a cut-off of 23.5 mmHg had 91% specificity.

	GERD	Borderline GERD	Reflux Hypersensitivity	Functional	p-value
N	45	7	16	57	
Mean EGJ basal pressure, mmHg, median (IQR)	11 (9-17)	16 (11-19)	20 (14-24)	20 (12-30)	<0.001
EGJ-CI, mmHg·cm, median (IQR)	26 (13-51)	25 (12-37)	41 (25-52)	37 (15-67)	0.283
DCI, mmHg·cm·s, median (IQR)	466 (227-959)	723 (401-997)	1270 (504-2074)	1160 (675-2172)	<0.001
LES total length, mm, median (IQR)	2.8 (2.6-3.1)	3.0 (2.9-3.1)	3.3 (2.9-3.6)	3.1 (2.8-3.5)	0.037
EGJ morphology					
Type I (%)	20 (44)	5 (72)	9 (56)	44 (77)	
Type II (%)	8 (18)	1 (14)	6 (38)	8 (14)	
Type III (%)	17 (38)	1 (14)	1 (6)	4 (7)	

p-values for Kruskal-Wallis test

Conclusion: Mean EGJ basal pressure is a simple HRM metric to predict conclusive GERD, well differentiating GERD phenotypes, with greater performance than EGJ-CI. This metric could be preferred over EGJ-CI as a useful adjunctive measure to support GERD diagnosis.

Disclosure: Nothing to disclose.

MP091

A COMPARISON OF TWO WIRELESS PH RECORDING SYSTEMS - AN ANALYSIS OF THE ATTACHMENT DURATION AND PATIENT TOLERABILITY

R.-L. Rusu¹, D.-M. Borrow¹, J. Jafari¹, G.P. Sui¹, S.S. Zeki¹, J.M. Dunn¹, T. Wong¹

¹Guy's and St Thomas' NHS Foundation Trust, Gastroenterology, London, United Kingdom

Contact E-Mail Address: radu75ro@yahoo.com

Introduction: Prolonged wireless pH monitoring is the preferred diagnostic tool in unproven GERD when available.¹ The Bravo system is better tolerated and increases the diagnostic yield compared to 24-hour transnasal catheter studies.^{2, 3} A novel system, Alpha, uses a stitch rather than a pin to attach the capsule to the esophageal wall. It stores data temporarily inside the capsule before transmission to the recorder and has been introduced in the United States and worldwide. We aim to compare the two systems with respect to the duration of attachment and patient tolerability.

Aims & Methods: We aim to compare the two systems with respect to the duration of attachment and patient tolerability. Three hundred and ninety-nine patients who underwent prolonged wireless pH monitoring at a regional esophageal center from November 2020 to October 2022 were prospectively studied. The clinical indications for wireless pH studies were set out in published guidelines, and patients followed the same standard procedures. The total capsule retention time and duration of artifacts were measured in minutes. A complete day was defined as more than 20 hours of attachment. Patients completed a previously validated tolerability questionnaire, which included symptoms graded on a Likert scale.³

Results: Two hundred and two symptomatic patients (mean age 47 (18-82) years, 65% F) underwent wireless Alpha, and 197 patients (mean age 48 (18-81) years, 72% F) underwent wireless Bravo catheter-free pH monitoring. Capsule attachment for 96, 72, and 48 hour studies were obtained in 184 (91%), 11 (5.4%), and 3 (1.5%) patients who received Alpha studies, respectively, and in 149 (75.6%), 22 (11%) and 16 (8%) patients who received Bravo studies. No complications occurred with either method (capsule retention, bleeding, perforation). The total capsule retention time was longer in patients receiving the Alpha system when compared to the Bravo system (mean 5560 minutes vs 5194 minutes, $p < 0.00001$). The Bravo system recordings had more artifacts than Alpha (mean 272 minutes vs 133 minutes, $p < 0.00001$). In patients who achieved a 96-hour study, there were no significant differences in patient tolerability and acceptance between the two systems across all domains (table 1). One hundred and fifteen out of 126 (91%) would recommend Alpha, and 83 out of 91 (91%) patients would recommend Bravo to another patient ($p=0.7$).

Question	n	Alpha 96 hours	n	Bravo 96 hours	p value
Overall experience of the system	127	3.62	89	3.89	0.08
Chest pain	130	3.4	94	3.37	0.7
Swallowing difficulty	130	3.33	94	3.62	0.1
Eating feel different	130	3.27	93	3.36	0.6
Restriction daily activities	128	3.7	93	4.01	0.1
Throat discomfort	130	3.32	94	3.35	0.9

Table 1.

Values are presented as n, number of patients; Alpha and Bravo mean scores.

Conclusion: Both wireless pH monitoring systems had excellent tolerability and low capsule detachment rates before 96 hours. The Alpha system had a lower premature detachment rate, lower artifacts and similar tolerability when compared with the Bravo system.

References: 1. Gyawali CP, Yadlapati R, Fass R, et al. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut 2023.

2. Sweis R, Fox M, Anggiansah A, Wong T. Prolonged, wireless pH-studies have a high diagnostic yield in patients with reflux symptoms and negative 24-h catheter-based pH-studies. Neurogastroenterol Motil 2011;23:419-26.

3. Sweis R, Fox M, Anggiansah R, et al. Patient acceptance and clinical impact of Bravo monitoring in patients with previous failed catheter-based studies. Aliment Pharmacol Ther 2009;29:669-76.

Disclosure: Nothing to disclose.

MP092

EXTERNAL VALIDATION OF THE MANOMETRIC SCORE OF GERD PROBABILITY (MILAN SCORE) IN A HIGH-VOLUME TERTIARY REFERRAL CENTER

G. Adamo¹, P. Visaggi¹, F. Ovidi¹, I. Solinas¹, D. Stefani Donati¹, S. Siboni², E.V. Savarino³, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²Policlinico San Donato, San Donato Milanese, Italy, ³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: nicola.debortoli@unipi.it

Introduction: High resolution manometry (HRM) currently has a marginal role in the diagnosis of gastroesophageal reflux disease (GERD) except for the correct placement of pH-impedance (MII-pH) probes. However, a Manometric Score for Gerd Probability (i.e., the Milan Score) has been recently developed to predict a diagnosis of GERD based on HRM findings prior to pH monitoring studies.

Aims & Methods: In this study, we performed the external validation of the Milan Score in a high-volume tertiary referral center. HRM and MII-pH tracings of consecutive patients reporting GERD symptoms between 2019-2022 were retrospectively reviewed. Clinical, MII-pH, and HRM data were recorded for all patients. Patients with achalasia, body mass index $> 35 \text{ Kg/m}^2$, previous esophageal surgery, paraesophageal hiatal hernia, eosinophilic esophagitis and scleroderma were excluded. To calculate the Milan Score score, data on diagnosis of ineffective esophageal motility (IEM) according to Chicago Classification v4.0, esophagogastric junction contractile integral (EGJ-CI), EGJ morphology (i.e., type I, II or III), intraesophageal pressure (IEP) during reference ID and straight-leg raise (SLR) pressures were collected. A SLR maneuver was considered positive if $> 11 \text{ mmHg}$. The Milan Score was calculated using the nomogram published in the Milan Score paper (United European Gastroenterology Journal 2024 [1]). Wilcoxon rank sum test, Pearson's chi-squared test and Fisher's exact test were used for comparison. ROC curve analysis was used to calculate the diagnostic accuracy (AUC) of the MSGP score.

Results: Of the 86 included patients, 36 (41.8%) had conclusive GERD based on acid exposure time (AET) $> 6\%$, while 50 (58.2%) had AET $< 6\%$. Patients with AET $> 6\%$ and AET $< 6\%$ were comparable in terms of age, weight, regurgitation, chest pain, dysphagia, erosive esophagitis, and HRM diagnosis. Patients with AET $> 6\%$ more frequently had heartburn ($p=0.009$), EGJ type 3, MNBI $< 1500 \text{ Ohms}$ ($p < 0.001$) and positive symptoms index and symptoms association probability ($p=0.007$). The median Milan Score was 78 (IQR, 54-132) in patients with AET $< 6\%$ and 164 (IQR, 125-198) in patients with AET $> 6\%$ group. Based on ROC curve analysis,

a Milan Score higher than 103 was associated with a diagnosis of conclusive GERD (i.e., AET>6%) with AUC of 0.78, with 70% specificity and 80% sensitivity.

Conclusion: The Milan Score has good performance in the diagnosis of GERD upon HRM recording, prior to MII-pH in patients reporting GERD symptoms. The Milan Score proved external validity and can be used as a screening test for GERD in patients undergoing HRM.

Characteristic	AET ≤6%, n = 50 (58%)	AET >6%, n = 36 (42%)	p-value
Ineffective esophageal motility	5 / 50 (10%)	5 / 35 (14%)	0.24
SLR >11mmHg	13/50 (26.0%)	26/36 (72.2%)	<0.001
EGJ-Contractile Index (CI)	42 (28, 55)	27 (13, 42)	0.015
Positive SI/SAP	2 / 50 (4.0%)	9 / 36 (25%)	
EGJ type			0.005
1	26 / 50 (52%)	14 / 36 (39%)	
2	20 / 50 (40%)	9 / 36 (25%)	
3	4 / 50 (8.0%)	13 / 36 (36%)	
Total Milan Score	78 (54, 132)	164 (125, 198)	<0.001

References: [1] Siboni, S., Sozzi, M., Kristo, I., Boveri, S., Rogers, B. D., De Bortoli, N., Hobson, A., Louie, B. E., Lee, Y. Y., Tolone, S., Marabotto, E., Visaggi, P., Haworth, J., Ivy, M. L., Greenan, G., Masuda, T., Penagini, R., Barcella, B., Coletta, M., Theodorou, D., ... Gyawali, C. P. (2024). The Milan score: A novel manometric tool for a more efficient diagnosis of gastro-esophageal reflux disease. *United European gastroenterology journal*, 10.1002/ueg2.12565. Advance online publication. <https://doi.org/10.1002/ueg2.12565>

Disclosure: Nothing to disclose.

MP093

LYON 2.0 OPTIMIZES THE COST-EFFECTIVE EVALUATION AND MANAGEMENT ALGORITHM FOR HEARTBURN ACROSS GENERAL GASTROENTEROLOGY: COST-EFFECTIVENESS ANALYSIS

E. Shah¹, CP. Gyawali², W. Chan³

¹University of Michigan, Division of Gastroenterology, Ann Arbor, United States of America, ²Washington University School Of Medicine, St Louis, Mo, Division Of Gastroenterology, St Louis, United States of America, ³Brigham and Women's Hospital, Boston, United States of America

Contact E-Mail Address: ershah@med.umich.edu

Introduction: Heartburn is the most common symptom leading to gastroenterology referral. The Lyon 2.0 consensus advocates up-front OFF-PPI ambulatory pH testing in unproven GERD when erosive esophagitis is absent, followed by ON-PPI pH-impedance testing when PPI therapy fails in proven GERD. Due to cost concerns with routine diagnostic testing and since wireless pH testing is not widely available in parts of the world, most patients receive rotating, prolonged courses of PPIs for persistent symptoms.

We performed an economic analysis to compare evaluation/management strategies for heartburn in routine practice.

Aims & Methods: We developed a Markov model to compare routine care strategies for patients with heartburn and no alarm features:

- (1) Reassurance alone;
- (2) EGD with PPI optimization;
- (3) EGD with a PPI discontinuation trial when erosive esophagitis is absent; EGD with OFF-PPI
- (4) wireless pH testing or
- (5) pH-impedance testing to phenotype care based on physiology;
- (6) EGD with OFF-PPI wireless pH testing followed by ON-PPI pH-impedance testing when needed following Lyon 2.0.

Definitions to interpret diagnostic tests and treatment recommendations were extracted from practice guidelines. Model inputs were extracted from appropriate US cost databases and from systematic reviews, clinical trials, and national observational studies that considered diagnostics and clinical outcomes. We used a one-year time horizon and a willingness-to-pay threshold of \$100,000/quality-adjusted-life-year (QALY) gained.

Results: Reassurance alone (Strategy 1) cost \$3,936/year to insurers due to repeated diagnostics and visits, and \$2,976/year to patients due to out-of-pocket expenses and impaired work productivity. EGD with a trial of PPI optimization (Strategy 2) or discontinuation (Strategy 3) was more expensive and less effective than strategies that involved up-front pH testing, because EGD-only strategies exclude erosive esophagitis but do not optimize treatment. Up-front wireless pH (Strategy 4) or pH-impedance (Strategy 5) monitoring defining GERD were similarly cost-effective. The most cost-effective strategy was to follow Lyon 2.0 (Strategy 6), resulting in \$2,542 annual savings to patients, \$2,311 annual savings to insurers, and health gains of +0.07 QALY or 23 more healthy days per year. Findings were similar from insurer and patient perspectives.

Strategy	Total cost (\$USD per year)	Total effectiveness (quality-adjusted life years [QALY] gained per year)	Incremental cost	Incremental effectiveness	Incremental cost-effectiveness ratio or ICER (\$/QALY-gained)
Reassurance alone	\$3,936 to insurers \$2,976 to patients	0.89	Reference	Reference	Reference
EGD with PPI optimization trial	\$2,865 to insurers \$1,417 to patients	0.92	\$1,071 saved to insurers \$1,559 saved to patients	+0.03	Dominates reassurance alone
EGD with PPI discontinuation trial for non-erosive findings	\$3,706 to insurers \$1,770 to patients	0.95	\$230 saved to insurers \$1,206 saved to patients	+0.06	Dominates reassurance alone
EGD with up-front OFF-PPI 96hr wireless pH testing	\$1,695 to insurers \$638 to patients	0.95	\$2,241 saved to insurers \$2,338 saved to patients	+0.06	Dominates EGD-only strategies
EGD with up-front OFF-PPI 24hr pH/impedance testing	\$1,652 to insurers \$1,028 to patients	0.95	\$2,284 saved to insurers \$1,948 saved to patients	+0.06	Dominates EGD-only strategies
Lyon 2.0	\$1,625 to insurers \$434 to patients	0.96	\$2,311 saved to insurers \$2,542 saved to patients	+0.07	Dominates all strategies

Table. Cost-effectiveness of routine strategies to manage heartburn in general gastroenterology from insurer and patient perspectives. Strategies 1-5 are updated from our previous report (doi 10.1016/j.cgh.2023.08.026) to reflect availability of Lyon 2.0.

Conclusion: By matching patients to the appropriate therapeutic targets based on diagnostics and PPI response, Lyon 2.0 optimizes the cost-effective care pathway for heartburn in general gastroenterology. Since wireless pH and pH-impedance monitoring are equivalent strategies, availability of technique and local expertise should dictate choice for evaluation of heartburn. Our findings advocate the need for access to, coverage for, and usage of diagnostic testing and broad adoption of the Lyon 2.0 consensus.

Disclosure: EDS consults for Ardelyx, Laborie, Mahana, Mylan, Neuraxis, Salix, Sanofi, and Takeda.

MP094

WITHDRAWN

MP095

WITHDRAWN

MP096

EFFICACY AND SAFETY OF FEXUPRAZAN IN PATIENTS WITH EROSIVE ESOPHAGITIS AND MODERATE SEVERITY OF MAJOR SYMPTOMS: POOLED ANALYSIS OF TWO RANDOMIZED CONTROL TRIALS IN SOUTH KOREA AND CHINA

G.H. Kim¹, Y. Xiao², H. Lee³, M.H. Park³, H. Park³, S. Moon³, D.H. Kim³, S.J. Park³, J.H. Chae³, O.Y. Lee⁴

¹Pusan National University School of Medicine, Busan, South Korea, ²The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, ³Daewoong Pharmaceutical Co., Ltd., Korea, Seoul, South Korea, ⁴Hanyang University Hospital, Seoul, South Korea

Contact E-Mail Address: 2210467@daewoong.co.kr

Introduction: Fexuprazan, a novel potassium-competitive acid blocker (P-CAB), is currently recognized as a successful alternative to proton pump inhibitors (PPIs) for acid-related disorders. However, its experience in the global market remains limited.

Aims & Methods: This study aimed to integrate two randomized phase 3 studies (NCT03736369 in South Korea and NCT05813561 in China) investigating the efficacy and safety of fexuprazan in subjects with erosive esophagitis (EE) across Asian populations, especially those with at least moderate severity of major symptoms (≥ 2 days of heartburn or acid regurgitation at baseline). The Cochran-Mantel-Haenszel method was used to assess the efficacy of fexuprazan 40 mg and esomeprazole 40 mg in treating EE and relieving major symptoms, whereas the Wilcoxon signed-rank test evaluated safety by testing changes in gastrin levels within each treatment group.

Results: Of the 595 randomized subjects, 513 (256 in the fexuprazan group and 257 in the esomeprazole group) were included in the efficacy analysis set (per-protocol set, PPS). In the PPS, the healing rates of EE in the fexuprazan and esomeprazole groups at weeks 4 and 8 were 86.90% and 84.00% (95% confidence interval [CI] = -2.80, 9.23) and 98.05% and 98.44% (95% CI = -2.30, 2.02), respectively. In the subgroup analysis of patients with at least a moderate severity of major symptoms (205 in the fexuprazan group and 197 in the esomeprazole group), the healing rates of EE did not differ between the two groups (week 4, 85.57% vs. 83.33% [95% CI = -4.70, 9.28]; week 8, 97.56% vs. 97.97% [95% CI = -2.84, 2.61]). However, the proportion of subjects without symptoms in the first 3 days in both full day and nighttime in the fexuprazan group was significantly higher than that in the esomeprazole group (20.44% vs. 11.90%, $p = 0.0212$ and 32.04% vs. 22.02%, $p = 0.0387$, respectively). In the safety set, serum gastrin levels at the final visit significantly increased by 87.23 pg/ml and 61.99 pg/ml from baseline serum gastrin levels in both fexuprazan and esomeprazole groups, respectively. However, the mean gastrin levels at the final visit in both groups did not increase to the clinically significant levels (121.89 pg/ml vs. 96.40 pg/ml, respectively). None of the observed increases in gastrin levels resulted in discontinuation of the study, and no significant safety risks were identified in either group.

Conclusion: The efficacy of fexuprazan in treating EE was not inferior to that of esomeprazole in Asian populations. In subjects with at least a moderate severity of major symptoms, symptom relief in the fexuprazan group was higher in the first 3 days, regardless of full-day or nighttime. In terms of safety, serum gastrin level was tolerable in both groups, and no serious adverse events occurred in the fexuprazan group.

Disclosure: Nothing to disclose.

MP097

CLINICAL RESULTS OF 158 PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE TREATED BY A NOVEL IMPLANTABLE DEVICE: TWO-YEAR FOLLOW-UP

M. Elshafei¹, T. Lehmann²

¹Krankenhaus Nordwest, Klinik für Allgemein-, Viszeral- und Minimal Invasive Chirurgie, Frankfurt, Germany, ²Klinikum Friedrichshafen, Department of Visceral Surgery, Friedrichshafen, Germany

Contact E-Mail Address: elshafei.moustafa@gmail.com

Introduction: Standard-of-care treatments for gastroesophageal reflux disease (GERD) include proton pump inhibitor (PPI)-based medical management and conventional antireflux surgery (i.e., Nissen fundoplication). However, these modalities are associated with a significant burden of unmet needs, such as irresponsiveness and postoperative adverse events (AEs), respectively. This study presents the results of 158 patients managed with RefluxStop in Germany.

Aims & Methods: One-hundred fifty-eight reflux patients were treated with RefluxStop between July 2021 and November 2023. Clinical endpoints included GERD Health-Related Quality of Life (GERD-HRQL), postoperative AEs, and change in PPI use.

Results: Baseline characteristics are shown in Table 1. Median GERD-HRQL score improved by 90.9% from a baseline of 22 (IQR 19-31.5) to 2 (IQR 0-2) at 20 $\pm$ 7-month follow-up ($p < .001$). A 96.3% reduction in PPI use was also observed; baseline PPI use in 96.5% of $n = 113$ decreased to 3.6% of $n = 110$ at follow-up. All cases of preoperative dysphagia ($n = 18$) resolved after surgery. New-onset dysphagia occurred in five patients (3.2%) post-operatively but did not require esophageal dilation. Hiatal hernia recurred in 1.3% ($n = 2$) of patients and was managed with device repositioning. Device penetration and migration occurred in 1.3% ($n = 2$) of patients due to excessively tight suturing of the fundic pouch in which the device was invaginated. One of these patients was later treated by Toupet fundoplication.

Characteristic	Observation
Age, mean (SD)	49.3 (13.3) years
Sex	Male 51.3%; female 48.7%
Body mass index, mean (SD)	27.1 (4.5) kg/m ²
Large hiatal hernia (>3 cm)	22.2%
Esophagitis	44.3%
Barrett's esophagus	10.1%

Table 1 Baseline characteristics.

Conclusion: This report demonstrates the promising clinical effectiveness of RefluxStop as a novel treatment principle in management of GERD. Additional evaluation is necessary to enhance the evidence supporting this new antireflux procedure.

Disclosure: The authors disclose travel grants and speaking honoraria from Implantica (Zug, Switzerland).

MP098

OUR ONE YEAR EXPERIENCE OF ANTI-REFLUX MUCOSAL ABLATION AS A MINIMALLY INVASIVE TREATMENT FOR PPI DEPENDENT OR REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE PATIENTS. A RETROSPECTIVE STUDY FROM A HIGH PREVALENCE COUNTRY IN THE MIDDLE EAST

A.H. Raina¹, K. Elsayed¹

¹Burjeel Hospital, Gastroenterology and Hepatology, Abu Dhabi, United Arab Emirates

Contact E-Mail Address: hameedraina49@gmail.com

Introduction: Gastroesophageal reflux disease (GERD) is found in 8.7 to 33.1% of the population in middle east. Proton Pump Inhibitor (PPI) is the most common modality of treatment used. Surgical intervention is less commonly accepted by the patients in this region of the world. Anit reflux Mucosal Ablation (ARMA) is a novel minimally invasive endoscopic therapy for it.

Aims & Methods: The study aimed to find out the safety and efficacy of ARMA in GERD in this part of the world.

Patients and Methods:

All Proton Pump Inhibitor (PPI) dependent or refractory GERD patients who presented to our hospital from April 2022 to August 2023 who consented were recruited. Retrospective analysis of a prospectively maintained data was used. GERDq questionnaire was used for diagnosing and treatment success of the GERD. The same was confirmed with OGD and pH metry tests. Argon Plasma Coagulation (APC) with 1.6-1.8 L/min flow rate and 70-100 watts voltage were used for ablation. Repeat OGD and pH metry tests were performed after 3, 6 and 12 months. Clinical success was defined as a > 50% reduction in a validated GERDq questionnaire or daily stoppage of PPI use. Objective success was defined by normalization of Total Acid Exposure time and DeMeester score and no significant esophagitis on OGD.

Age, median (range), years	35.5 (18-75)	ARMA Performed n(%)	P value
Sex		Technical success n (%)	51/51(100%)
Male n(%)	36		
Female n(%)	24		
Duration of symptoms median Years	1.8	Mean time durations (Minutes)	36.4± 5.8
Major symptoms		Adverse events n (%)	
Heartburn n(%)	56(93.33%)	GE junction stricture	2/51(3.92%)
Dyspepsia n(%)	32(53.33%)	Moderate to Severe pain	1/51(1.96%)
Sorethroat n(%)	13(21.66%)	Esophageal Mucosal Burn	2/51(3.92%)
Cough n(%)	8 (13.33%)	Bleeding	0
Belching n(%)	15(25%)	Perforation	0
Regurgitation n(%)	3(4.99%)		
Esophagitis on OGD		Clinical Success n (%)	
None n(%)	07	At 3 months	42/51(82.35%)
LA grade A n(%)	23		
LA Grade B n(%)	16	AT 6 months	41/51(80.39%)
LA Grade C n(%)	09		
LA grade D n(%)	04	At 12 months	39/51(76.47%)
Peptic Stricture n(%)	01		
Hill's Grade		Median DeMeester Score	21.6
I n(%)	17(28.33%)	Pre- ARMA	
II n(%)	21(35%)	Median DeMeester Score	4.9
III n(%)	09 (15%)	Post -ARMA	P= 0.003
IV n(%)	05 (8.33%)		
Large Hiatal Hernia n(%)	04 (6.66%)		
PPI use n(%)	60	Off PPI use n(%) at 12 months	39/51(76.47%) P=0.0001
		Occasional PPI use n(%)	12/51 (37.25%)
PreARMA Mean GERDq question-naire score	29.3± 3.8	Post ARMA Median GREDq Questionnaire score	13.4± 2.1 P<0.001

Table.

Results: Total of 60 patients with definitive GERD on OGD or pH tests were recruited. Among them 51 patients underwent ARMA. There was 100 % (51/51) technical success rate. Mean procedure time was 36.4± 5.8 minutes. Clinical success rates at 3 and 6 and 12 months post-ARMA were 82.35% (42/51) and 80.39% (41/51), and 76.47 % (39/51), respectively. The mean GERD-health-related quality of life score improved from mean of 29.3± 3.8 to 13.4± 2.1 at 3 -12 months ($P < 0.01$). Median DeMeester score decreased from 21.6 to 4.9 in 88.23% (45/51) ($P = 0.003$) in 3-12 Months. Multivariate analysis showed Hill's grade I to II and PPI depend GERD as predictors of success.

Adverse events in the form of stricture (3.92%), Severe pain requiring three days of analgesics (3.92%) and Esophageal Mucosal burn injury (1.96%) were seen. All were managed endoscopically. 76.47% of the patients were completely off PPI at 12 months compared to 0% pre ARMA procedure($p=0.0.001$).

Conclusion: ARMA was safe and effective endoscopic modality of treatment for GERD. Majority of the patients who underwent ARMA were off PPI at one year. PPI dependent GERD and Hill's grade I to II were predictors of success of ARMA. Large prospective randomized studies are required to further substantiate these findings.

References: Rodríguez de Santiago Enrique et al. Antireflux mucosectomy (ARMS) ... Endosc Int Open 2021; 09: E1740-E1751 | © 2021.

Disclosure: Nothing to disclose.

MP099

RISK OF CLOSTRIDIODES DIFFICILE INFECTION IN PATIENTS RECEIVING PROTON PUMP INHIBITORS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

D.-E. Floria^{1,2}, M. Obeidat², S. Váncsa^{3,2}, S.B. Kávási^{4,2}, L. Földvári-Nagy^{2,5}, P. Hegyi^{2,3,6}, D.S. Veres^{7,2}, V.L. Drug¹, B. Eross^{2,6,3}

¹Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁴Toldy Ferenc Hospital, Department of Surgery, Cegléd, Hungary, ⁵Semmelweis University, Department of Morphology and Physiology, Faculty of Health Sciences, Budapest, Hungary, ⁶Medical School, University of Pécs, Institute for Translational Medicine, Pécs, Hungary, ⁷Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary

Contact E-Mail Address: iovdiana95@gmail.com

Introduction: The safety profile of proton pump inhibitors (PPIs) is considered excellent; however, concerns regarding the potential side effects linked to prolonged usage are emerging.

Aims & Methods: This work focused on assessing the risk of *Clostridioides difficile* infection (CDI) in patients undergoing treatment with PPIs compared to non-users, in the context of randomized controlled trials (RCTs). The study protocol was prospectively registered on PROSPERO (CRD42023403322). The systematic search was conducted on March 2nd, 2023 across three medical databases (PubMed, Embase, and CENTRAL). We included all RCTs that reported the rates of CDI in adults receiving treatment with PPIs compared to non-users (placebo, other medications). Risk ratio (RR) with its corresponding 95% confidence interval (CI) was used as an effect size measure using a random effects model.

Heterogeneity was described using Higgins and Thompson's I² statistics. The risk of bias was estimated using the Revised Cochrane Risk-of-bias Tool for Randomized Trials (RoB 2).

Results: We identified and analysed seven RCTs investigating the rates of CDI in individuals receiving treatment with PPIs compared to placebo, which included 25.118 patients. No significant difference was observed regarding the risk of acquiring CDI between the two study groups (32/12.561 vs. 33/12.557; RR: 0.94, 95% CI: 0.55; 1.59, I²=0%). Four RCTs compared subjects receiving PPIs to H₂-receptor blockers, totalling 27.254 patients. Similarly, the pooled analysis found no significant difference regarding the risk of developing CDI between the two study groups (43/13.658 vs. 59/13.598; RR: 0.72, 95% CI: 0.49; 1.07, I²=0%). We would like to highlight the fact that the overall number of events in the included studies were low. Additional subgroup analyses were intended based on patient population, treatment duration, and follow-up time; however, there was insufficient data available for conducting meta-analytical calculations.

Conclusion: Previous works that reported associations between PPI use and adverse effects have been derived from observational data only. It is known that these types of studies cannot definitely establish causality and are highly susceptible to bias, such as confounding by indication and protopathic bias. Based on data derived from RCTs only, treatment with PPIs does not seem to increase the risk of acquiring CDI, both when compared to placebo and to other acid-suppressive medications.

Disclosure: Nothing to disclose.

Upper GI bleeding

12:00-13:00 / Poster Stage 6

MP100

OPTIMAL TIMING OF ENDOSCOPY IN ACUTE UPPER GASTROINTESTINAL BLEEDING: IMPACT ON REBLEEDING, MORTALITY AND RESOURCE UTILISATION

G. Nigam¹, S.B. Laursen², J. Leithead³, S. Hearnshaw⁴, K. Oakland⁵, V. Jairath⁶, J. Grant-Casey⁷, J. Morris⁸, S. Travis⁹, A. Douds¹⁰, A. Stanley¹¹

¹Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ²Odense University Hospital, Odense, Denmark, ³Forth Valley Royal Hospital, Larbert, United Kingdom, ⁴Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom, ⁵HCA Healthcare UK, Clinical, Oxford, United Kingdom, ⁶Alimentiv Inc., Gastroenterology, London, Canada, ⁷NHS Blood and Transplant, Oxford, United Kingdom, ⁸Glasgow Royal Infirmary, Glasgow, United Kingdom, ⁹John Radcliffe Hospital, Gastroenterology Department, Oxford, United Kingdom, ¹⁰Queen Elizabeth Hospital, Gastroenterology, Fakenham, United Kingdom, ¹¹Glasgow Royal Infirmary, Department of Gastroenterology, Glasgow, United Kingdom

Contact E-Mail Address: gaurav.nigam@nhs.net

Introduction: The optimal timing of endoscopy in acute upper gastrointestinal bleeding (AUGIB) management remains debated. We assessed time to endoscopy's impact on rebleeding and mortality based on patient characteristics and pre-endoscopic factors.

Aims & Methods: Data from 3,001 patients with AUGIB undergoing endoscopy within 48 hrs of referral from the prospective multicentre UK 2022 audit were analysed. Patients were categorised into 0-12 hrs, 12-24 hrs, and 24-48 hrs groups based on the time to endoscopy from referral. Regression analyses, adjusting for age, admission status (inpatient vs new admission), vital signs, symptoms, comorbidities, laboratory parameters, red blood cell transfusion, and pre-endoscopic management, assessed the association between endoscopy timing and rebleeding and mortality.

Results: Patients undergoing endoscopy within 0-12 hrs were younger, more likely to be haemodynamically unstable, and had a higher median Glasgow Blatchford Score (GBS) compared to those undergoing endoscopy in the 12-24 and 24-48 hrs groups. Despite a higher proportion receiving endotherapy (41% for the 0-12 hrs group, 28% for the 12-24 hrs group, and 17% for the 24-48 hrs group; p<0.001), the 0-12 hrs group had the highest rates of rebleeding (16%) and mortality (10%), compared to 9% rebleeding and 6% mortality in the 12-24 hrs group, and 7% rebleeding and 5% mortality in the 24-48 hrs group (p<0.001). The median length of stay was longer for the 0-12 hrs and the 24-48 hrs groups at 5 days, compared to 4 days in the 12-24 hrs group (p < 0.001). (see table)

Characteristic	0-12 hrs, N = 1,366	12-24 hrs, N = 944	24-48 hrs, N = 691	p-value*
Age	67 (52, 79)	69 (55, 80)	71 (56, 81)	0.001
Hemodynamically unstable	653 (50%)	377 (42%)	270 (41%)	<0.001
GBS	10.0 (7.0, 13.0)	9.0 (6.0, 12.0)	8.0 (5.0, 11.0)	<0.001
Pre-endoscopy peak blood lactate	2.20 (1.40, 3.90)	1.80 (1.20, 2.80)	1.80 (1.30, 2.90)	<0.001
Stigmata of recent bleed	642 (47%)	259 (28%)	121 (18%)	<0.001
Endo therapy	563 (41%)	224 (24%)	114 (17%)	<0.001
Death	136 (10%)	60 (6.4%)	35 (5.1%)	<0.001
Rebleeding	196 (16%)	74 (8.9%)	41 (6.7%)	<0.001
Length of stay	5 (3, 10)	4 (2, 8)	5 (3, 10)	<0.001

Table: Patient characteristics in relation to time of endoscopy (n=3001)

*Between the group comparison

Regression analysis indicated that, compared to the 12–24-hrs group, the 0–12 hrs group had higher odds of rebleeding (OR 1.91, 95% CI 1.38–2.69, $p < 0.001$), after adjusting for confounding variables. However, the 24–48 hrs group exhibited comparable odds of rebleeding (OR 0.93, 95% CI 0.60–1.45, $p < 0.001$) compared to the 12–24-hrs group. Regression analysis for mortality showed the 0–12 hrs group had higher odds of mortality compared to the 12–24 hrs group (OR 1.59, 95% CI 1.09–2.34, $p = 0.001$), while the 24–48 hrs group had similar odds of death (OR 0.74, 95% CI 0.43–1.23, $p = 0.001$).

Conclusion: The findings suggest a complex relationship between the timing of endoscopy and clinical outcomes in patients with AUGIB. Earlier endoscopy (0–12 hrs) may be associated with a higher risk of rebleeding, mortality and resource utilisation, while later endoscopy (24–48 hrs) may not be associated with increased adverse outcomes, but may lead to a longer hospital stay. Despite the initial severity of illness, early endoscopy may not translate to improved patient outcomes in AUGIB management. These results highlight the need for individualised management when determining the optimal timing of endoscopy in AUGIB.

Disclosure: Nothing to disclose.

MP101

COMPARISON OF GASTRIC ULCER CASES IN PATIENTS TAKING WARFARIN OR DOACS

Y. Shimada¹, H. Nago¹, M. Yamaguchi¹, Y. Terai¹, R. Om¹, Y. Kita¹, Y. Ikeda¹, S. Sato¹, A. Murata¹, S. Sato¹, A. Nagahara², T. Genda¹
¹Juntendo University Shizuoka Hospital, Gastroenterology and Hepatology, Izunokuni-city, Japan, ²Juntendo University School of Medicine, Gastroenterology, Tokyo, Japan

Contact E-Mail Address: yshimada@juntendo.ac.jp

Introduction: In Japan, more than ten years have passed since direct oral anticoagulants (DOACs) was released in 2011. The differences between DOACs and warfarin (VKA) have gradually become clearer, and many studies have been reported regarding the differences in gastrointestinal bleeding risk⁽¹⁾⁽²⁾⁽³⁾. However, there are few reports that examine the prevalence of gastric mucosal injury or ulcers rather than the risk of bleeding.

Aims & Methods: The aim of this study is to reveal the clinical features about patients with gastric ulcer taking anticoagulants (DOACs or VKA). This study is a retrospective cross-sectional study conducted in a single hospital. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and December 2022. We focused on subjects who took anticoagulants (DOACs or VKA), and compared the prevalence of gastric ulcer between subjects taking DOAC and those taking VKA. Subjects taking anticoagulants were limited to those taking that anticoagulant as the only anti-thrombotic agents. This study was conducted separately for subjects taking antacids (P-CAB or PPI) and those not taking antacids (NO P-CAB, NO PPI and NO H2RA). Statistical analyses were performed by Fisher's exact test.

Results: Of the 8,602 subjects analyzed, 522 subjects were taking anticoagulants, of which 103 were taking VKA (76 men, 27 women, mean age 73.1±12.0 years) and 297 were taking DOACs (205 men, 92 women, mean age 74.9±8.7 years). Among subjects taking DOACs, 33 subjects received Dabigatran, 93 received Edoxaban, 87 received Rivaroxaban, and 84 received Apixaban. The prevalence of gastric ulcer in subjects taking antacids was 6.7% (4/60) on VKA and 2.9% (5/170) on DOACs ($p=0.24$). The prevalence of gastric ulcer in subjects not taking antacids was 23.1% (9/39) on VKA and 5.4% (6/111) on DOACs ($p=0.004$).

Conclusion: Without concomitant use of antacids, subjects taking DOACs had a statistically significantly lower prevalence of gastric ulcers than

those taking warfarin. These results suggest that DOACs are gentler on the gastric mucosa and user friendly than warfarin.

References: (1) Miller CS, et al. Clin Gastroenterol Hepatol. 15(11): 1674–1683, 2017

(2) Ray WA, et al. JAMA. 320(21): 2221–2230, 2018

(3) Ingason AB, et al. Ann Intern Med. 174(11): 1493–1502, 2021

Disclosure: Nothing to disclose.

MP102

IS GLASGOW BLATCHFORD SCORE UNDERESTIMATED IN INFECTED HELICOBACTER PYLORI BLEEDING PEPTIC ULCER?

G. Reis¹, C. Montes², M. V. Sá dos Santos Rondon³, C.R. Pavan³, N. Hifumi Hara³, C. Rodrigues dos Santos³, C. Kibune Nagasako⁴
¹Helena Reis, Gastroenterology, Campinas, Brazil, ²Unicamp (Universidade Estadual de Campinas), Clinical, Campinas, Brazil, ³Campinas University, Campinas, Brazil, ⁴University of Campinas, Gastroenterology, Cerquillo, Brazil

Contact E-Mail Address: glauciaruppert@yahoo.com.br

Introduction: Peptic ulcer is the most common cause of upper gastrointestinal bleeding (UGB), accounting for about 50 percent of cases. Several scoring systems have been developed for the early and accurate assessment of patients with UGB to predict clinical outcomes, assisting in the management of patients. The Glasgow-Blatchford score (GBS) is currently recommended for risk stratification of UGB in the emergency department, helping triage patients to in-hospital or ambulatory management. GBS includes hemoglobin, urea, heart rate, systolic blood pressure, co-morbidity and symptoms like syncope and melena.

Aims & Methods: Aim: To compare GBS in patients with bleeding peptic ulcer (BPU) infected and non-infected by Helicobacter pylori (HP).

Methods: We conducted a prospective observational study from September 2019 to March 2002, 48 patients with BPU were prospectively evaluated in a tertiary hospital. During emergency endoscopy, two gastric mucosal biopsy samples (one from corpus and one from the antrum) were collected for polymerase chain reaction (PCR) and invasive rapid urease test (RUT). Two hours later, all underwent carbon-13 urea breath test (13C-UBT). Patients were considered HP infected when two or more tests were positive. The clinical data were obtained from the patients' records immediately before the endoscopy. The Qui-square test and Fisher were used to compare the groups. Written informed consent was obtained from all patients. The study protocol was approved by the local ethical committee.

Results: Mean age was 61.7±17.3 years, 25 (52.1%) presented with melena. Gastric ulcers were the major cause of acute bleeding in 39 (81.3%) and duodenal in 9 (18.8%) patients. Data about blood transfusion (BT), Rockall Score (RS) and presence of blood in the stomach are represented in table 1. GBS was significantly lower in HP positive patients (n=19) compared to HP negative (n=25): 9.1±3.3 e 11.5±3.1, $p = 0.0441$.

Variable	Total (n=48)	HP negative (n=26)	HP positive (n=22)	p-value
Age	61.7±17.3	64.8±15.	58.9±18.8	0.4624
Melena	25 (52.1%)	13 (50%)	12 (54.5%)	1.000
Gastric ulcer	39 (81.3%)	23 (88.5%)	16 (72.7%)	0.2669
BT.*	16 (33.3%)	10 (38.5%)	6 (27.3%)	0.4126
Associated diseases	27 (56.3%)	15 (57.5%)	12(54.5%)	0.8267
Complete RS*	4.0±2.0	4.4±2.0	3.6±1.8	0.726
Blood in the stomach	4.0 (8.3%)	1 (3.8%)	3(13.6%)	0.3202
GBS*	10.5±3.4 (n=25)	11.5±3.1 (n=19)	9.1±3 (n=44)	0.0441

Table 1. Comparison between H.pylori negative and positive groups

* BT: blood transfusion, RS: Rockall score, GBS: Glasgow Blatchford score.

Conclusion: H pylori positive patients showed less comorbidities and lower GBS in the BPU scenario. HP negative patients need more severe clinical conditions to bleed than those HP positive. HP is a pathogenic factor by itself, suggesting that GBS might be underestimated in this population. A score using HP presence could be better to predict prognostic in the episode of bleeding peptic ulcer.

References:

1. Akhila Arya PV, Thulaseedharan NK, Raj R, Unnikrishnan DC, Jacob A. AIMS65, Glasgow-Blatchford bleeding score and modified Glasgow-Blatchford bleeding score in predicting outcomes of upper gastrointestinal bleeding: An accuracy and calibration study. *Indian J Gastroenterol.* 2023 Aug;42(4):496-504. doi: 10.1007/s12664-023-01387-z. Epub 2023 Jun 29. PMID: 37382854.
2. Jang HJ, Lee D, Kim TH, Kim JS, Lee HJ, Kim JB, Kim JY. Clinical outcomes of gastrointestinal bleeding management during anticoagulation therapy. *PLoS One.* 2022 Jun 3;17(6):e0269262. doi: 10.1371/journal.pone.0269262. PMID: 35658063; PMCID: PMC9165820.
3. Gralnek IM, Stanley AJ, Morris AJ, Camus M, Lau J, Lanas A, Laursen SB, Radaelli F, Papanikolaou IS, Cúrdia Gonçalves T, Dinis-Ribeiro M, Awadie H, Braun G, de Groot N, Udd M, Sanchez-Yague A, Neeman Z, van Hooft JE. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy.* 2021 Mar;53(3):300-332. doi: 10.1055/a-1369-5274. Epub 2021 Feb 10. PMID: 33567467.

Disclosure: Nothing to disclose.

MP103

IN-HOSPITAL AND DELAYED MORTALITY IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING ON ANTITHROMBOTIC TREATMENT. EFFECTS OF WITHDRAWAL AND RESUMING

E. Redondo-Cerezo¹, R. Fernandez-García¹, M. López-Vico¹, E.J. Ortega-Suazo¹, C. Tintero-Peinado¹, J.M. López-Tobaruela¹, A. Lancho Munoz¹, J.G. Martínez-Cara¹, F. Valverde-López¹, R. Jiménez-Rosales¹

¹Hospital Universitario Virgen de las Nieves, Gastroenterology, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: Antithrombotic drugs (AT) pose an increased risk of upper gastrointestinal bleeding (UGIB), and their discontinuation carries the risk of thromboembolic events, presenting a challenge for clinicians (1,2). Clinical practice guidelines advocate for a restrictive approach, recommending non-discontinuation and/or early reintroduction based on the drug and its indication (3).

Despite available literature, controversy persists regarding the outcomes of patients with UGIB on antithrombotic therapy, both in the short and long term, as well as the potential impact of drug discontinuation (4,5).

Aims & Methods: Aim: To determine the impact of ATs on in-hospital and delayed outcomes. Also, to determine whether suspension and resumption influenced delayed outcomes.

Methods: Prospective registry analysis of UGIB patients between 2013-2021. Anticoagulants and antiplatelets were classified as AT drugs. Outcomes examined included in-hospital mortality and delayed-6 months cardiovascular, bleeding and mortality events.

Results: 1345 patients were included, with 21.7% on anticoagulants and 19.1% on antiplatelets. Patients on ATs were older (73 vs. 59 years; p<0.0001) and had a higher rate of comorbidities, has longer delay of endoscopic performance (11±11h vs. 9.6±8h; p=0.027), with gastric erosions being more usual (14.2% vs. 9.1%; p=0.006). Table shows main outcomes.

	Non-AT (n=839)	AT (n=506)	P	Aspirin (n=195)	Thienopyridine (n=29)	Double anti- aggregating (n=24)	VKA (n=179)	NACO (n=49)
Endoscopy therapy	48.3%	38.5%	0.001	75 (38.5%)	12 (41.4%)	7 (29.2%)	62 (34.6%)	20 (40.8%)
Rescue therapy	6.1%	3.8%	0.083	8 (4.1%)	17 (58.6%)	0	4 (2.2%)	1 (2%)
Rebleeding	10.5%	9.7%	0.702	20 (10.3%)	1 (3.4%)	18 (75%)	12 (6.7%)	4 (8.2%)
Transfusion	56.3%	66.2%	0.000	127 (65.1%)	17 (58.6%)	0	115 (64.2%)	41 (83.7%)
In-hospital mortality	12%	8%	0.028	14 (7.2%)	0	1 (4.2%)	13 (7.3%)	1 (2%)
Delayed cardiovascular event	3.4%	13.7%	0.000	18 (9.2%)	5 (17.2%)	1 (4.2%)	31 (17.3%)	12 (24.5%)
Delayed hemorrhagic event	12.9%	22.9%	0.000	43 (22.1%)	5 (17.2%)	6 (25%)	41 (22.9%)	12 (24.5%)
Delayed mortality	6%	9.4%	0.034	17 (8.7%)	2 (6.9%)	2 (8.3%)	19 (10.6%)	4 (8.2%)

AT suspension <72h was associated with increased in-hospital mortality (14.9% vs. 2.3%; p=0.001), especially <24h (20.9% vs. 2.6%; p<0.0001).

Delayed mortality was higher in patients on ATs who suspended them more than 7 days (17% vs. 8.7%; p= 0.033), with no differences when last <72h. Suspension/reintroduction have no effect on other delayed outcomes.

Multivariate analysis identified ASA≥3 (HR 12.20; 95%CI 3.69-56.92; p<0.001), disseminated malignancy (HR 4.73; 95%CI 1.92-11.42; p=0.001) and rebleeding (HR 19.25; 95%CI 9.07-43.04) as independent risk factors for in-hospital mortality, with AT therapy (HR 0.27; 95%CI 0.13-0.55; p<0.001), NSAIDs (HR 0.26; 95%CI 0.07-0.75; p=0.023), endoscopic therapy (HR 0.49; 95%CI 0.24-0.96; p=0.040) and hemoglobin levels being protective factors HR 0.80; 95%CI 0.69-0.93; p=0.004).

Logistic regression analysis for delayed mortality showed that age (HR 1.04; 95%CI 1.02-1.07; p=0.001), disseminated malignancy (HR 3.49; 95%CI 1.81-7.86; p=0.004), esophageal varices HR 3.34; 95%CI 1.62-6.64; p=0.001), ischemic heart disease (HR 2.44; 95%CI 1.10-5.19; p=0.023) and a being an inpatient (HR 1.92; 95%CI 1.00-3.98; p=0.042) were independent risk factors for the outcome.

Conclusion: Despite increased comorbidities and older age, patients with AUGIB on ATs had lower in-hospital mortality, with no differences in other relevant outcomes. In fact, our results suggest that AT treatment provides a survival benefit, possibly related to a higher risk of bleeding in milder lesions.

Regarding delayed mortality, it was higher in patients on AT, determined by the comorbidity leading to their prescription.

Interestingly, early resumption of AT was associated with higher in-hospital mortality, while reintroduction after 7 days increased delayed one.

References:

1. Lanas A, Carrera-Lasfuentes P, Arguedas Y, et al. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clin Gastroenterol Hepatol* 2015;13:906-12 e2.
2. Chan FK, Leung Ki EL, Wong GL, et al. Risks of Bleeding Recurrence and Cardiovascular Events With Continued Aspirin Use After Lower Gastrointestinal Hemorrhage. *Gastroenterology* 2016;151:271-7.
3. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy* 2021;53:300-332.
4. Dunne PDJ, Laursen SB, Laine L, et al. Previous Use of Antithrombotic Agents Reduces Mortality and Length of Hospital Stay in Patients With High-risk Upper Gastrointestinal Bleeding. *Clin Gastroenterol Hepatol* 2019;17:440-447 e2.
5. Marmo R, Occhipinti V, Zullo A, et al. Improved Survival for Patients With Acute Upper Gastrointestinal Bleeding While on Antithrombotic Therapy: A Multicenter Prospective Cohort Study. *J Clin Gastroenterol* 2023;57:278-284.

Disclosure: Nothing to disclose.

MP104

PRE-ENDOSCOPIC ASSESSMENT IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING: AN INTERNATIONAL SURVEY OF 533 CLINICIANS

M. Obeidat^{1,2}, D.-E. Floria^{1,3}, M. Camus⁴, B. Teutsch^{1,5,6}, S. Laursen⁷, K. Siau⁸, V. Drug³, F. Verdonk⁹, Á. Vincze¹⁰, Z. Bognár¹¹, I. Gralnek^{12,13}, P. Hegyi^{1,2,6}, B. Eröss^{1,2,6}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ³Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania, ⁴Sorbonne University, Endoscopic Unit, Saint Antoine Hospital Assistance Publique Hopitaux de Paris, Paris, France, ⁵Semmelweis University, Department of Radiology, Medical Imaging Centre, Budapest, Hungary, ⁶University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ⁷Odense University Hospital, Department of Gastroenterology and Hepatology, Odense, Denmark, ⁸Royal Cornwall Hospitals NHS Trust, Department of Gastroenterology, Truro, United Kingdom, ⁹Sorbonne University, Hôpital Saint-Antoine, Assistance Publique-Hôpitaux de Paris, Department of Anesthesiology and Intensive Care, Paris, France, ¹⁰University of Pécs, Medical School, Division of Gastroenterology, First Department of Medicine, Pécs, Hungary, ¹¹Heim Pal National Paediatric Institute, Department of Paediatric Emergency Medicine, Budapest, Hungary, ¹²Institute of Gastroenterology and Hepatology, Emek Medical Center, Afula, Israel, ¹³Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Contact E-Mail Address: dr.mahmoud.obeidat@gmail.com

Introduction: Upper gastrointestinal bleeding (UGIB) continues to pose a significant threat to patients presenting at the emergency department, especially if the patients present with hemodynamic instability. There are still some uncertainties in the guidelines about the stepwise assessment and management for those patients before undergoing endoscopy.

Aims & Methods: Our study aims to report practice patterns to better understand the pre-endoscopic assessment for patients presenting with acute UGIB. This is an international online survey that included a prospective two-phase data collection. The distribution was conducted from April 2023 to November 2023. The target population was active physicians with clinical practices focusing on the management of patients with UGIB. Study data were collected and managed using Research Electronic Data Capture (REDCap), an electronic data collection tool. The survey included four main sections (demographics and clinical practice, definition of hemodynamic instability, pre-endoscopy assessment, and optimal time for endoscopy) with a total of 33 relevant questions. The survey was endorsed by several national and international gastroenterology societies. The primary analysis was a descriptive assessment of individual survey response items in different domains. Descriptive statistics were reported as proportions. Secondary analysis evaluated differences in survey responses according to the years of clinical experience, type of practice location, and the estimated number of UGIB patients presented annually.

Results: In total, 533 clinicians completed our survey from 50 countries. Over half of the respondents work at university-based hospitals (54.6%) and have over 100 UGIB patients hospitalized annually (67.7%). In terms of clinical experience, 55.7% reported less than 10 years and 44.3% with more than 10 years. In 29.1% of the hospitals, there was no specific protocol or guideline for the initial assessment of patients with suspected UGIB, and in 44.7%, there were no emergency on-call interventional radiology services for such cases. Among the respondents, 39.6% do not use any risk stratification scores at the time of patient presentation. Both 0.9% saline

(40.9%) and balanced crystalloid fluid (39.5%) were almost equally chosen as initial fluid resuscitation. However, the rate of fluid resuscitation was dependent on the hemodynamic status of 40.2% of the answers. In 40.7% of the answers, clinicians do not use any major hemorrhagic protocol for patients with severe ongoing bleeding and at risk of exsanguination. Prokinetics were generally little or never used prior to endoscopy in patients with UGIB (34.3%) or even in those with known gastric emptying problems (27.6%). The most chosen optimal time for endoscopy was within 24 hours for stable patients with non-variceal bleeding and within 12 hours for variceal bleeding. If patients were unstable but responding to resuscitation, the most chosen time was within 6 hours regardless of the source of bleeding and within 2 hours for those with persistent hemodynamic instability.

Conclusion: Adherence to international gastroenterology guidelines is low. There is a significant variability in different assessment approaches among respondents. Based on our data, the optimal time for endoscopy seems to be dependent on the hemodynamic status of patients with acute UGIB in both variceal and non-variceal bleeding. Our study highlights opportunities for improving consistency in reporting data and identifies potential areas for research.

Disclosure: Nothing to disclose.

MP105

MANAGING ACUTE UPPER GASTROINTESTINAL BLEEDING IN ANTICOAGULATED PATIENTS: FINDINGS FROM A LARGE UK MULTICENTER STUDY OF 5000 PATIENTS

G. Nigam¹, J. Grant-Casey², S. Hearnshaw³, K. Oakland⁴, J. Leithead⁵, L. Estcourt², M.F. Murphy², V. Jairath⁶, S. Travis⁷, A. Stanley⁸, A. Douds⁹, UK upper GI bleed group
¹Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ²NHS Blood and Transplant, Oxford, United Kingdom, ³Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom, ⁴HCA Healthcare UK, Clinical, Oxford, United Kingdom, ⁵Forth Valley Royal Hospital, Larbert, United Kingdom, ⁶Alimentiv Inc., Gastroenterology, London, Canada, ⁷John Radcliffe Hospital, Gastroenterology Department, Oxford, United Kingdom, ⁸Glasgow Royal Infirmary, Department of Gastroenterology, Glasgow, United Kingdom, ⁹Queen Elizabeth Hospital, Gastroenterology, Fakenham, United Kingdom

Contact E-Mail Address: gaurav.nigam@nhs.net

Introduction: A global surge in anticoagulant use raises concerns about managing acute upper gastrointestinal bleeding (AUGIB) in affected patients.

Aims & Methods: This study presents findings from a large UK multicenter study of AUGIB in patients on anticoagulants. A prospective multicenter observational study included adults (>16 years) from 152 UK hospitals with AUGIB between 3 May- 2 Jul, 2022.

Results: Of 5101 AUGIB cases enrolled, 31%(1566) were on anticoagulants – 10%(n=159) warfarin, 58%(n=912) direct oral anticoagulants (DOACs), and 34%(n=530) heparin (prophylactic dose – 76%, therapeutic dose – 18%, and bridging therapy – 2%). The median age was 78 yrs (IQR 68-85), with 58% being new admissions. Anticoagulants were discontinued post-AUGIB in 87%. The major hemorrhage protocol activated for 4%. Transfusion rates were: 59% packed red blood cells, 7% prothrombin complex concentrate (PCC), 5% fresh frozen plasma, 3% platelets, 0.8% cryoprecipitate, and 0.3% fibrinogen. For DOACs (n=912) a reversal agent was needed for 6% (46% - andexanet alfa and 54% -PCC). Glasgow-Blatchford score (GBS) categorized patients into: 3% low-risk(GBS 0-1), 16% medi-

um-risk(2-6), 33% higher-risk(7-11), and 34% very high-risk(≥ 12). Inpatient endoscopy was performed in 85%(n=1335). Time to endoscopy from presentation was: 0-6 hrs 5%, 6-24 hrs 32%, 24-48 hrs 25%, and >48 hrs 24%. Bleeding etiologies identified (n=798) included: peptic ulceration (49%), esophagitis (26%), varices (8%), portal hypertensive gastropathy (4%), malignancy (7%), and other (27%). Stigmata of recent bleeding observed in 29% (390/1335) of cases, leading to endotherapy in 25% (328/1335). Anticoagulants resumed while in-patient for 46% (613/1335) – 19% within 24 hrs, 14% 24-48 hrs, 9% 48-72 hrs, and 41% >72 hrs after the index endoscopy. 10% (136/1335) had evidence of further in-patient bleeding after the index endoscopy. Overall, 10%(160/1566) had >1 endoscopy, 1% (16) underwent surgery, and 2.8% (44) had interventional radiology. Median length of stay was 7 days (IQR 4-13), with in-patient mortality at 13%(211). A multivariable logistic regression revealed delayed endoscopy (>48 hrs) was associated with reduced rebleeding odds (OR:0.19,95%CI:0.04-0.99), while early endoscopy (0-6 hrs) was linked to higher rebleeding odds (OR:1.81,95%CI:0.44-7.46). Importantly, stigmata of recent bleeding on endoscopy significantly elevated rebleeding odds (OR:4.88,95%CI:1.75-13.64), emphasizing its prognostic relevance in AUGIB.

Conclusion: A third of AUGIB patients in this multi-center UK study were on anticoagulants at the time of presentation. Real-world evidence underscores the importance of appropriate resuscitation and careful restarting of the anticoagulants based on the indication. Further development of predictive models to guide the time to restart different anticoagulants is needed.

Disclosure: Nothing to disclose.

MP106

CLINICAL PREDICTIVE MODEL FOR PACKED RED BLOOD CELL TRANSFUSION IN GASTROINTESTINAL BLEEDING: THE APICA SCORE

E. Mikhael¹, A. Khoury¹, A. Asmar¹, S. Helou¹, J. Amara¹, K. Honein¹, E. Mahfouz¹, R. Slim Karam¹, C. Yaghi¹

¹Université Saint-Joseph, Beirut, Lebanon

Contact E-Mail Address: eliomikhael7@gmail.com

Introduction: Gastrointestinal bleeding is a common presentation in the emergency department, or a complication of a hospital stay, in which red blood cells (RBC) transfusion is often needed (1).

Aims & Methods: The aim of this paper is to create a clinical score to predict the need of transfusion in a patient presenting for gastrointestinal bleeding. This is a retrospective observational study, including all patients that presented for gastrointestinal bleed or that developed bleeding in-hospital, from January 2018 till December 2023. Patients that were under 18 years old and patients with portal hypertension related bleeding were excluded from analysis. Demographic data (gender, age), past medical history, history of gastrointestinal bleeding, and chronic medication were collected. Data from the hospitalization that were included were vital signs at presentation, initial laboratory results, endoscopic exams or other work-up performed, need of transfusion of packed red blood cells (RBC), platelets, or fresh frozen plasma, length of hospitalization, recurrence, length of follow-up, and mortality.

Results: In total, 279 patients were included for analysis, with a mean age of 67.5 ± 16.7 years old. There were 166 (59.5%) males and 113 (40.5%) females. Mean length of hospitalization was 6.6 days. Recurrence occurred in 33 patients (11.8%) during a mean follow-up of 368.7 days, 7 (21.2%) of which occurred during initial hospitalization. Death occurred in 23 (8.2%) patients, in average 276.7 days after index bleeding. In our population, 153 (54.8%) patients needed transfusion of packed RBC, with an average of 3.4 packed RBCs per patient. Average hemoglobin at presentation is of 10.0g/dL.

A multivariate analysis was performed. Variables that were independently associated with the need of packed RBC transfusion were included in a predictive model. The APICA score was constructed using these variables: Anticoagulation agent (multiplied by 50), antiPlatelet agent (multiplied by 50), In-hospital bleed (multiplied by 500), Coronary artery disease (multiplied by 20), and Age. The score had an AUC of 0.749 with a p-value less than 0.001. In comparison, the Glasgow-Blatchford score had an AUC of 0.805 (p<0.001) and the Oakland bleeding score had an AUC of 0.879 (p<0.001). The table below represents the sensitivity, specificity, negative predictive value, and positive predictive value for different cut-offs of the APICA score.

	APICA Score		
	≥ 108	≥ 118	≥ 129
Sensitivity	76.4%	71.9%	60.1%
Specificity	61.1%	67.4%	76.2%
Negative predictive value	68.1%	66.4%	61.5%
Positive predictive value	70.5%	72.8%	75.6%

Conclusion: The APICA score is a good clinical predictive model for the need of packed RBC transfusion for gastrointestinal bleeding with an AUC of 0.749. Unlike existing scores for gastrointestinal bleeding, it does not require hemoglobin levels, therefore sparing time for transfusion preparation. Prospective studies are required to further assess the benefits of this model and to validate it.

References:

- Costa AP, Pereira CL, Garção A, Rodrigues A. Transfusion Practices in Gastrointestinal Bleeding - a Tertiary Care Single-Centre Analysis. Clin Appl Thromb Hemost. 2022 Jan-Dec;28:10760296221087219. doi: 10.1177/10760296221087219. PMID: 36503291; PMCID: PMC9749046.

Disclosure: Nothing to disclose.

MP107

INFLUENCE OF ENDOSCOPY TIMING ON CLINICAL OUTCOMES IN VARICEAL BLEEDING PATIENTS

R. Jiménez-Rosales¹, R. Fernandez-García¹, E.J. Ortega-Suazo¹, C. Tendaro-Peinado¹, J.M. López-Tobaruela¹, A. Lancho Munoz¹, M. López-Vico¹, J.G. Martínez-Cara¹, E. Redondo-Cerezo¹

¹Hospital Universitario Virgen de las Nieves, Gastroenterology, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: In patients with upper gastrointestinal bleeding (UGIB), the European Society of Gastrointestinal Endoscopy (ESGE) recommends adopting the following definitions regarding the timing of upper GI endoscopy: urgent (6-12h), early (≤ 24 h), and delayed (>24 h) (1). There is no consensus definition of emergent endoscopy, but previous publications use the timeline of <6h (2).

Early endoscopy is associated with better outcomes, and guidelines suggest that it should be performed within this time frame (1).

Last ESGE guideline about variceal bleeding (VB) suggests performing urgent endoscopy in this context (3). This is based on a meta-analysis showing lower overall mortality when endoscopy was performed <12h compared to >12h (4). Surprisingly, ESGE concludes that the optimal timing in this setting is controversial due to a lack of high-level evidence. In fact, except for this study, all the others examining this aspect show that performing endoscopy before 12h does not provide benefits (5,6).

Aims & Methods: We aim to compare whether urgent endoscopy (6-12h) provides benefits to VB and explore predictors for mortality.

Methods: Retrospective analysis of a prospective registry of UGIB patients admitted to 'Virgen de las Nieves University Hospital' (2013-2020). VB was

defined as that coming from gastric or esophageal varices. Endoscopy timings were defined according to ESGE: emergent (<6h), urgent (6-12h), early (≤24h) and delayed (>24h) (1).

Main outcomes were in-hospital (endoscopy therapy, transfusion, re-bleeding, misbalance of chronic condition, hospital stay, and mortality) and delayed-6 months (bleeding, cardiovascular events, mortality). Statistical analysis was performed using SPSS.

Results: 1459 UGIB patients were collected, 216 with VB.

Statistical differences in main outcomes are shown in Table 1 (each letter in the subscript denotes column proportions that do not differ significantly from each other). No differences were found for the other outcomes.

Timing (% patients)	<6h (39.7%)	6-12h (28.8%)	12-24h (17.4%)	24h (2.7%)	p
Endoscopy therapy	85.1% _a	63.5% _b	65.8% _b	66.7% _b	0.014
Misbalance of chronic condition	48.3% _a	30.2% _b	23.7% _b	50% _a	0.026
Rebleeding	22.1% _a	7.9% _b	7.9% _b	16.7% _a	0.037
In-hospital mortality	27.4% _a	13.6% _b	11.1% _b	50% _a	0.025

We also compared basal characteristics and found differences in MAP(ASH) score≥2 (92.3% vs. 66.7% vs. 77.4% vs. 75%; p=0.003) and GBS≥12 (69% vs. 44.4% vs. 52.6% vs. 83.3%; p=0.011).

Independent risk factors for in-hospital mortality were MAP(ASH)≥2 (1.26, 95% CI 1.03-1.54), misbalance of chronic condition (OR 9.92, 95% CI 3.56-27.61, p=0.000), and rebleeding (OR 3.95, 95% CI 1.45-10.79, p=0.007). The timing of endoscopy performing was not an independent prognostic factor for mortality.

We also conducted subgroup analysis to assess whether performing endoscopy before 12h provides benefits in other UGIB patients, without finding differences for patients with non-variceal bleeding or in those at higher risk of poor outcomes (GBS≥12, MAP(ASH)≥2, ASA≥3).

Conclusion: Our study highlights, in line with the majority of available ones (5,6), that endoscopy before 12h does not provide a benefit in patients with VB. This necessitates a reconsideration of the ESGE recommendation. Patients with endoscopy performed before 6 or after 24h have poor outcomes. However, multivariate analysis shows that the timing of endoscopy is not an independent prognostic factor for mortality. On the other hand, the decompensation of basal chronic disease and the severity of bleeding (determined by MAP(ASH) and rebleeding) are the determinants of patient outcomes.

References:

- Gralnek IM, Stanley AJ, Morris AJ, Camus M, Lau J, Lanas A, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy*. 2021 Mar;53(3):300-332.
- Laursen SB, Leontiadis GI, Stanley AJ, Møller MH, Hansen JM, Schaffalitzky de Muckadell OB. Relationship between timing of endoscopy and mortality in patients with peptic ulcer bleeding: a nationwide cohort study. *Gastrointest Endosc*. 2017 May;85(5):936-944.e3.
- Gralnek IM, Camus Duboc M, Garcia-Pagan JC, Fuccio L, Karstensen JG, Hucl T, et al. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2022 Nov;54(11):1094-1120.
- Bai Z, Wang R, Cheng G, Ma D, Ibrahim M, Chawla S, Qi X. Outcomes of early versus delayed endoscopy in cirrhotic patients with acute variceal bleeding: a systematic review with meta-analysis. *Eur J Gastroenterol Hepatol*. 2021 Dec 1;33(1S Suppl 1):e868-e876.
- Zhang W, Huang Y, Xiang H, Zhang L, Yuan L, Wang X, et al. Timing of endoscopy for acute variceal bleeding in patients with cirrhosis (CHESS1905): A nationwide cohort study. *Hepatol Commun*. 2023 May 4;7(5):e0152.

Disclosure: Nothing to disclose.

MP108

URGENT ENDOSCOPY MAY NOT IMPROVE OUTCOME IN ACUTE VARICEAL BLEEDING: A MULTICENTER COHORT STUDY

S.B. Laursen¹, G. Nigam², J. Leithead³, S. Hearnshaw⁴, K. Oakland⁵, J. Grant-Casey⁶, V. Jairath⁷, J. Morris⁸, A. Douds⁹, A. Stanley¹⁰

¹Odense University Hospital, Department of Gastroenterology and Hepatology, Odense, Denmark, ²Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ³Glasgow University, UK, Glasgow, United Kingdom, ⁴Newcastle Hospital, Newcastle, United Kingdom, ⁵HCA Healthcare UK, Clinical, Oxford, United Kingdom, ⁶National Comparative Audit of Blood Transfusion, Bristol, United Kingdom, ⁷Alimentiv Inc., Gastroenterology, London, Canada, ⁸Glasgow Royal Infirmary, Glasgow, United Kingdom, ⁹Queen Elizabeth Hospital, Gastroenterology, Fakenham, United Kingdom, ¹⁰Glasgow Royal Infirmary, Department of Gastroenterology, Glasgow, United Kingdom

Contact E-Mail Address: stig.laursen@rsyd.dk

Introduction: Optimal timing of endoscopy in patients with acute variceal bleeding (AVB) remains unclear. Studies in patients with peptic ulcer bleeding (PUB) have indicated that urgent endoscopy <6 hours from presentation may be associated with worsened patient outcome. We aimed to analyse the association between timing of endoscopy and mortality in AVB.

Aims & Methods: Prospective multicenter cohort study based on data from the 2022UK Audit on Acute upper gastrointestinal bleeding. The association between timing of endoscopy and in-hospital mortality was evaluated using logistic regression analyses with adjustment for differences in patients' characteristics and severity of bleeding.

Results: We included 401 AVB patients. Mean age was 58 years, 65% were males, 75% had known cirrhosis at time of presentation, mean Child-Pugh score was 8.2, 31% had other comorbidities, 13% had ongoing bleeding at time of endoscopy, 78% were treated with terlipressin, 75% were treated with antibiotics, and 12.6% died during hospital admission. Mortality rates were 22%, 17%, 11%, and 11% for patients undergoing endoscopy in the periods <6, <12, 6-24 and >24 hours from presentation. Patients undergoing endoscopy < 6 hours had lower blood pressure, higher heart rate, lower haemoglobin, and higher peak-lactate levels than patients undergoing later endoscopy (see table). However, even haemodynamically stable patients with systolic blood pressure above 100mmHg had high mortality rates (16%) when performing urgent endoscopy < 6 hours. When adjusting for differences in patients' characteristics, and severity of bleeding, we did not find any association between timing of endoscopy and mortality (Odds ratio (95% confidence interval): 1.01 (0.99-1.03); p=0.17).

Characteristics	<6hrs (n=60)	6-24hrs (n=181)	>24hrs (n=160)	P
Age (mean, 95%CI)	56 (34-78)	58 (37-77)	58 (36-83)	NS
Child Pugh score (mean, 95%CI)	8.4 (6-12)	8.2 (5-12)	8.2 (5-11)	NS
SBP (mean, 95%CI)	106 (69-140)	118 (85-160)	120 (90-156)	<0.001
Heart Rate (mean, 95%CI)	101 (66-142)	99 (67-134)	94 (64-131)	0.008
Hemoglobin (mean, 95%CI)	83 (40-122)	87 (52-127)	93 (57-128)	0.014
Peak blood lactate (mean, 95%CI)	5.8 (1.4-14)	5.0 (1.0-13)	3.3 (1.0-9.2)	<0.001
Oesophageal varices	55 (92)	166 (92)	144 (90)	NS
Treatment with EDS, SBT or TIPS	9 (15%)	11 (6%)	11 (7%)	NS
Mortality (overall)	13 (21.7)	20 (11.2)	17 (10.8)	NS

Table: Patient characteristics in relation to time of endoscopy (n=401).

Reported values represent n(%) unless otherwise stated.

CI: Confidence Interval; EDS: Ella Danis Stent; NS: Not Significant; SBP: Systolic Blood Pressure; SBT: Sengstaken-Blakemore Tube; TIPS: Transjugular Intrahepatic Portosystemic Shunt

Conclusion: AVB is associated with significant mortality, in particular in patients undergoing urgent endoscopy <6 hours from presentation, which may be explained by more severe bleeding. When taking differences in patients characteristics and severity of bleeding into consideration, endoscopy within 6-12 hours appears to be associated with similar outcomes to endoscopy undertaken 6-24 hours from presentation, despite less time to patient optimization before endoscopy. Thus, the association between timing of endoscopy and outcome may differ between patients with AVB and patients with PUB.

Disclosure: No conflicts of interest.

MP109

SUCCESSFUL TECHNICAL APPROACH WITH VERY LOW RECURRENCE RATE AFTER ENDOSCOPIC ULTRASOUND-GUIDED COILS DEPLOYMENT AND CYANOACRYLATE EMBOLIZATION OF GASTRIC VARICES: AN EIGHT-YEAR REAL WORLD STUDY

C. Robles-Medranda¹, R. Del Valle Zavala¹, M. Egas-Izquierdo¹, D. Cunto¹, J. Baquerizo-Burgos¹, M. Arevalo-Mora^{1,2}, M. Puga-Tejada¹, F. Ferber-Reyes¹, J. Alcivar-Vasquez¹, D. Tabacelia^{3,1}, H. Pitanga-Lukashok¹

¹Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Cook County Health and Hospitals System, Chicago, United States of America, ³Saint Mary's Hospital, Gastroenterology, Bucharest, Romania

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Even though gastric varices (GV) are less frequently encountered than oesophageal varices, they are associated with severe bleeding¹. Novel endoscopic ultrasound (EUS)-guided therapeutics approaches have emerged from GV recent classification based on afferent and efferent hemodynamics^{2,3}.

Aims & Methods: We aim to target the feeder vessel or afferent component displaying a novel therapeutic approach comprising a combined application of cyanoacrylate (CYA) and coils. This approach is intended to address the vascular pathology of GV with enhanced precision and efficacy. A single-centre, prospective registry was conducted from Jul/2015-Oct/2023. Enrolled patients included adults ≥18 years old considered for primary or secondary prophylaxis of gastro-oesophageal varices (GOV) II and isolated GV (IGV) I. First, the location of the feeder's vessel was determined by angiography using a 10 ml water-soluble contrast. Subsequently, using a FNA needle, coils were EUS-guided deployed (10-20 mm coiled diameter, 14-20 cm straight lengths, 0.035 inches diameter), followed by CYA injection (2-Octyl-CYA). The number of deployed coils and injected CYA was documented. Outcomes were technical success, immediate disappearance, complete obliteration, recurrence rate, recurrence-free survival (RFS) and recurrence management.

Results: Over eight years, 167 patients underwent EUS-guided coils and CYA: 49.7% females, a median age of 63 years, and 19% alcohol-related cirrhosis. Child-Pugh B and C were estimated in 65.9% and 18% of patients, respectively. The most common previous therapies included B-blockers (32.3%), band ligation (26.9%), and CYA (21.0%). GV treatment was intended as secondary prophylaxis in 88.6%. More than one feeder vessel was targeted in 38.9%. In 67.7% of cases up to three coils were required, with a median injection of 3.6 ml of CYA. A 100% technical success was achieved. Among the 167 patients, 15 experienced recurrences (8.9%), with a median RFS of 4.9 months. When comparing non-recurrence vs recurrence patients, immediate disappearance was noticed in 69.7% vs 40.0% with white light endoscopy ($p=0.039$) and complete obliteration in 90.1% vs 73.3% during EUS ($p=0.072$), respectively. Immediate disappearance was a significant predictive factor for non-recurrence (OR 0.29; IC 95% 0.09 –

0.85; $p=.026$), with a 95% positive predictive value. All recurrences were managed with EUS-guided coils and CYA (9/15) and clips and CYA (6/15), with a 12/15 non-recurrence rate (Table 1). On multivariate analysis, a lower recurrence was associated with previous B-blockers therapy (OR 0.18; 95% CI 0.02 to 0.78; $p=.045$), while a previous CYA attempt represented a high-risk factor for recurrence (OR 10.2; 95% CI 1.08 to 110; $p=.044$).

	n=15	
Re-intervention procedure, n (%)	Coils + CYA	9 (60.0)
	Clips + CYA	6 (40.0)
Re-intervention-free survival (months), median (IQR)		4.9 (3.10 - 12.5)
Recurrence post-re-intervention, n (%)	No recurrence	12 (80.0)
	Reappearance	3 (20.0)
	Re-bleeding	-
Post-reintervention procedure, n (%)	Coils alone	-
	Coils + CYA	3/3 (100.0)
	Clips + CYA	-

Table 1. Management and follow-up in patients with recurrence. IQR, interquartile range.

Conclusion: EUS-guided coils and CYA in feeder vessels have shown high technical success and low recurrence rate in treating IGV I and GOV II. CYA attempts should be misadvised in GV. Non-immediate disappearance requires shorter follow-ups to assess for early recurrence.

References:

- Philips, C.A., Ahamed, R., Rajesh, S. et al. Beyond the scope and the glue: update on evaluation and management of gastric varices. *BMC Gastroenterol* 20, 361 (2020). doi: 10.1186/s12876-020-01513-7
- Rana, S.S, Sharma, R, Dhalaria, L, Gupta R. Contrast-Enhanced Endoscopic Ultrasound-guided coil and glue injection for bleeding gastric/ectopic varices. *Techniques and Innovations in Gastrointestinal Endoscopy* 2021. 23 (3): 244-247. doi:10.1016/j.tige.2021.01.001
- Romero-Castro R, Jimenez-Garcia VA, Irisawa A, Carmona-Soria I, Caunedo-Alvarez A, Teoh AYW, Giovannini M. Anatomic and hemodynamic findings during endoscopic ultrasound-guided angiography of gastric varices: a note of caution for endoscopic ultrasound-guided therapy. *Endoscopy*. 2022 Dec;54(S 02):E966-E967. doi: 10.1055/a-1884-9245.

Disclosure: Nothing to disclose.

Novel therapeutic approaches in IBD

15:30-16:30 / Poster Stage 1

MP110

DIALLYL ETHER, A SELECTIVE INHIBITOR OF CYP2E1, PREVENTS
INTESTINAL HYPERPERMEABILITY AND ALLEVIATES INTESTINAL
INFLAMMATION *IN VITRO AND IN VIVO*

A. Makaro¹, M. Swierczynski¹, Z. Kasprzak¹, A. Grochowska¹,
M. Salaga¹

¹Medical University of Lodz, Department of Biochemistry, Lodz,
Poland

Contact E-Mail Address: adammakaro@gmail.com

Introduction: CYP2E1 is one of the main members of cytochromes P450 superfamily, which is expressed in numerous tissues, including intestines. Overactivity of intestinal CYP2E1 leads to the loss of intestinal wall integrity and contributes to the development of the leaky-gut syndrome (LGS) which is observed in inflammatory bowel diseases (IBD). Moreover, activity of CYP2E1 may contribute to the severity of inflammation due to the production of reactive oxygen species.

Aims & Methods: The main aim of the study was to evaluate the therapeutic effects of selective CYP2E1 inhibitors in *in vitro* and *in vivo* models of intestinal hyperpermeability and inflammation. We used 1) Allyl methyl sulfide, 2) Diallyl ether (DE), and 3) Thiophene (T).

First we used MTT test to assess the cytotoxicity of CYP2E1 inhibitors in Caco-2 cells. Then, we measured the permeability of Caco-2 monolayer exposed to fructose; alone or after pretreatment with CYP2E1 inhibitors, with the use of transepithelial electrical resistance (TEER). Finally, we evaluated the effect of CYP2E1 inhibitors on cellular inflammatory response to the cocktail of IFN γ , TNF α , IL-1 β , and LPS.

In the *in vivo* part of the study we used three mouse models of intestinal inflammation and disrupted permeability. Acute colitis was induced by the addition of 3% dextran sulfate sodium (DSS) to drinking water for 5 days. Chronic colitis was induced by treatment with 2% DSS in drinking water followed by 4 days of water without DSS. Fructose-induced intestinal hyperpermeability was induced through free access to water containing 30% fructose solution for 8 weeks. In all models, DE was administered orally (*p.o.*) or rectally (*i.c.*) at a dose of 10 mg/kg body weight.

After each *in vivo* experiment, we performed macroscopic assessment of mouse colon, determination of tissue myeloperoxidase activity, measurement of intestinal permeability with FITC-dextran method, and analysis of mRNA expression of the following genes: occludin, ZO-1, CLDN-1, TNF α , IL-1 β , IL-6, CYP2E1.

Results: We did not see cytotoxicity of CYP2E1 inhibitors in Caco-2 cells. Further research showed that monolayers of cells pretreated with DE and T were significantly resistant to the increase in its permeability induced by fructose. Moreover, DE completely prevented the cellular inflammatory response as indicated by low IL-6 secretion. These results allowed us to choose DE for the *in vivo* phase.

In the first *in vivo* experiment, we assessed the effect of DE administered *p.o.* and *i.c.* on acute intestinal inflammation induced by DSS. DE treatment (*p.o.*) significantly prevented DSS-induced increase in TNF α and CYP2E1 expression. DE administered *i.c.* once daily significantly prevented from the decrease in colon length caused by DSS.

Then, we modeled chronic intestinal inflammation induced by DSS. DE was administered *p.o.* and *i.c.*. DE *p.o.* and *i.c.* significantly prevented DSS-induced increase in macroscopic intestinal damage. Additionally, DE *p.o.* significantly increased ZO-1 expression compared to the DSS group. In the fourth experiment, we assessed the effect of DE administered *p.o.* and *i.c.* on the gut permeability in the model of LGS induced by high doses of fructose. DE *p.o.* significantly reduced intestinal permeability compared to the fructose group.

Conclusion: Our experiments show, that CYP2E1 selective inhibitors display beneficial properties. Further studies on these substances may bring additional opportunities to develop novel therapeutics for IBD and LGS.

Disclosure: Nothing to disclose.

MP111

MELANIN NANOPARTICLES AMELIORATES COLITIS IN MICE BY
REDUCING OXIDATIVE STRESS

吴^{1,2}, J. Sun², S. Chen², Z. Qiang²

¹Affiliated Wuxi Fifth Hospital of Jiangnan University, The Fifth People's Hospital of Wuxi, Gastroenterology department, Wuxi, China, ²Wuxi People's Hospital Affiliated to Nanjing Medical University, Department of Gastroenterology, Wuxi, China

Contact E-Mail Address: wuyihao0313@163.com

Introduction: Oxidative stress disruption are involved in the occurrence and development of inflammatory bowel disease (IBD). Previous reports have shown that melanin nanoparticles (MNPs) have the function of regulating oxidative stress. The aim of this study is to explore the preventive effect of MNPs on DSS-induced colitis in mice and its mechanism.

Aims & Methods: In this study, C57BL/6 wild-type mice were divided into 7 groups according to whether induced colitis by DSS, whether prophylactic application of MNPs or mesalazine, and different administration method. Mice were randomly assigned to control group, DSS group, MNPs gavage (MNPs-ig+DSS), MNPs enema (MNPs-en+DSS), MNPs enema + gavage (MNPs-bo+DSS), MSL gavage (MSL-ig+DSS), and MSL gavage + enema group (MSL-bo+DSS). The effect of MNPs on DSS-mice was evaluated by clinical manifestation, length of colon, pathological scores of colon tissues, and the level of inflammatory cytokines. The distribution and expression of intestinal mucosal junction proteins Occludin (OCC) and ZO-1 were detected to evaluate the effect of MNPs on colon mucosal barrier. In addition, the abundance and species distribution of intestinal microbiota were determined by 16S rRNA sequencing in each group. In the mechanism exploration part, the level of superoxide dismutase (SOD) and malondialdehyde (MDA) were used to evaluate the activity of reactive oxygen species (ROS) in mouse colon tissue, and the expression of ROS-related NLRP3/NF- κ B signaling pathway-related proteins was further detected. In addition, this study verified the effect of MNPs on liver and kidney through the evaluation of organ morphology and function.

Results: C57BL/6 wild-type mice showed weight loss, colon shortening, increase of DAI and intestinal pathological scores, accompanied by increased levels of intestinal inflammatory cytokines TNF- α , IL-1 β and IL-6 and decreased levels of IL-10 in colon tissue, which can be prevented by the application of MNPs to a certain extent. MNPs can help protected the integrity of the intestinal mucosal barrier, which is manifested by the restoration of the distribution and expression of tight junction proteins ZO-1 and Occludin. However, 16S rRNA sequencing failed to show a significant regulatory effect of MNPs on the intestinal microbiota. MNPs can significantly reduce the level of colonic SOD and increase the level of MDA induced by DSS, and this effect was related to the inhibition of the activation of NLRP3 inflammasome and the expression of downstream NF- κ B inflammatory signaling pathway proteins. Finally, MNPs had no effect on the morphology and function of liver and kidney.

Conclusion: MNPs can improve colitis and regulate mucosal barrier function in mice, which may be related to reduced oxidative stress and inhibited activation of NLRP3 inflammasome and downstream NF- κ B inflammatory signaling pathway. Our findings suggest the potential value of MNPs as a treatment for IBD.

Disclosure: Nothing to disclose.

MP112

EXPOSURE OF THE SELECTIVE SIK2/SIK3 INHIBITOR GLPG3970 TO ORGANOIDS DERIVED FROM ULCERATIVE COLITIS PATIENTS INDUCES UPREGULATION OF MUCUS EXPRESSION AND TARGET-SPECIFIC MARKERS

L. Giorio¹, K. Arnauts¹, D. Merciris², B. Verstockt^{1,3}, S. Vermeire^{1,3}, S. De Vos⁴

¹KU Leuven, Department of Chronic Diseases and Metabolism (CHROMETA), Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ²Galapagos SASU, Romainville, France, ³KU Leuven, University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁴Galapagos NV, Mechelen, Belgium

Contact E-Mail Address: kaline.arnauts@kuleuven.be

Introduction: GLPG3970, a potent and selective small molecule salt-inducible kinase (SIK) 2/3 inhibitor, exhibits a dual mechanism modulating both pro-inflammatory and immunoregulatory pathways that holds potential as a novel therapeutic option for inflammatory bowel disease.^{1,2} Oral administration of GLPG3970 in colitis mouse models reduced disease activity scores, inhibited pro-inflammatory cytokine release and improved histological endpoints including protection of goblet cell health and MUC2 expression.^{2,3}

Mechanistic investigations demonstrated a broad immunomodulatory activity on colonic immune cell types. It remains unclear whether SIK2/SIK3 inhibition exerts a direct therapeutic activity on intestinal epithelial cell types or if these effects result indirectly from modulating pro-inflammatory and immunoregulatory mechanisms.³

Aims & Methods: We aimed to unravel the activity of SIK2/SIK3 inhibition using GLPG3970 in ulcerative colitis (UC) patient-derived epithelial cells focusing on SIK target engagement markers, inflammation and mucus production. Differentiated intestinal organoids from patients with UC were exposed to vehicle control, GLPG3970 (3 μ M and 20 μ M) or PGE2 (20 μ M; positive control) for 24 hours (gene expression) or 48 hours (immunohistochemistry). Gene expression was evaluated in organoid cultures derived from five patients with UC, with or without 24 hours of pro-inflammatory stimulation (using a mix of 100 ng/mL TNF α , 20 ng/mL IL-1 β and 1 μ g/mL flagellin)⁴ prior to 24 hours of exposure in combination with the compound, and measured by RT-qPCR compared with vehicle control (Friedman, Dunn's multiple comparison). Immunohistochemistry was performed for MUC2, DAPI, CK14 (n = 3 patients, minimum 10 images/condition, 3 replicates). Randomized images were analysed by Imaris Software by sectioning regions of interest (two-way ANOVA, Dunnett's multiple comparison).

Results: Upon GLPG3970 exposure, UC patient-derived organoids showed transcriptional upregulation of SIK target engagement markers such as the CREB¹ activation genes *NR4A1*, *NR4A2* and *NR4A3*. There was no effect with GLPG3970 on gene expression of inflammatory markers in colon epithelial cells, in the presence or absence of inflammatory stimulation, except for *IL-1 β* and *IL-8* upregulation after 24 hours of GLPG3970 exposure. Genes related to mucus production were upregulated in both non-inflamed (*MUC5AC*, 20 μ M, $p < 0.01$; *AGR2*, 20 μ M, $p < 0.05$) and inflamed conditions (*MUC2*, 20 μ M, $p < 0.01$; *MUC5AC*, 3 μ M and 20 μ M, $p < 0.01$) at the highest GLPG3970 concentration tested. Immunohistochemistry confirmed increased MUC2 secretion (secreted MUC2 surface $\times$ secreted MUC2 intensity) after 48 hours of GLPG3970 stimulation (3 μ M, $p < 0.05$; 20 μ M, $p < 0.01$); however, no significant increase was measured in absolute goblet cell number or goblet surface intensity compared with vehicle control.

Conclusion: SIK2/SIK3 inhibition by GLPG3970 showed a significant up-regulation of target engagement markers as measured by the CREB activation genes *NR4A1/2/3* in UC patient-derived colon epithelial cells, whereas

no direct downregulation of inflammatory markers was observed. Exposure of UC patient-derived colonic organoids to GLPG3970 20 μ M resulted in a signature of enhanced mucus secretion, both in the presence and absence of inflammation. Overall, these data indicate a direct impact of SIK2/SIK3 inhibition in intestinal epithelial cells with potential benefit in promoting barrier reinforcement via goblet cell mucus production in patients with active UC.

References: 1. Peixoto C *et al.* *J Med Chem* 2024;67:5233–58.

2. Pereira-Fernandes A *et al.* [abstract] *United European Gastroenterol J* 2021;9:S8.

3. Lavazais S *et al.* [abstract] *United European Gastroenterol J* 2021;9:S8.

4. Arnauts K *et al.* *Gastroenterology* 2020;159:1564–67.

Disclosure: This study was funded by Galapagos NV (Mechelen, Belgium). Editorial and publications management support was provided by PharmaGenesis London, London, UK, and was funded by Galapagos NV.

LG and KA are joint first authors.

LG and KA report no conflict of interest.

DM was an employee of Galapagos at the time of the work, and is now an employee of Novartis.

BV reports research support from AbbVie, Biora Therapeutics (formerly Progenity), Landos Biopharma, Pfizer, Sosei Heptares and Takeda; speaker fees from AbbVie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, Lilly, MSD, Pfizer, R-Biopharm, Sandoz, Takeda, Tillots Pharma, Truvion Healthcare and Viatrix; consultancy fees from AbbVie, Alfasigma, Alimentiv, Applied Strategic, AstraZeneca, Atheneum, BenevolentAI, Biora Therapeutics (formerly Progenity), Boxer Capital, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Lilly, Mylan, Inotrem, Ipsos, Janssen Pharmaceuticals, Pfizer, Sandoz, Sanofi, Santa Ana Bio, Sapphire Therapeutics, Sosei Heptares, Takeda, Tillots Pharma and Viatrix; and stock options from Vagustim.

SV reports speaker and/or consultancy fees from AbbVie, Abivax, AbolentS Pharma, AgomAb Therapeutics, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Biora Therapeutics (formerly Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, Gilead Sciences, GSK, Hospira, IMIDomics, Janssen Pharmaceuticals, Johnson & Johnson, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic Therapeutic, MRM Health, MSD, Mundipharma, Pfizer, ProDigest, Prometheus Biosciences, Roberts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillots Pharma, VectivBio, Ventyx Biosciences and Zealand Pharma; grants from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; and participation on a data safety monitoring board for Sanofi.

SDV is an employee of Galapagos.

MP113

UROLITHIN A ENHANCES INTESTINAL BARRIER FUNCTION VIA SECRETORY MUCIN PRODUCTION

T. Yasuda^{1,2}, T. Takagi¹, K. Uchiyama¹, R. Inoue³, Y. Itoh¹, Y. Naito⁴

¹Kyoto Prefectural University of Medicine, Molecular Gastroenterology and Hepatology, Kyoto, Japan, ²Akashi City Hospital, Gastroenterology, Akashi, Japan, ³Setsunan University, Department of Applied Biological Sciences, Faculty of Agriculture, Osaka, Japan, ⁴Kyoto Prefectural University of Medicine, Human Immunology and Nutrition Science, Kyoto, Japan

Contact E-Mail Address: everyday.enjoy29@gmail.com

Introduction: Maintaining the mucus layer is crucial in the innate immune system, and MUC2 is a significant component of the mucus layer in the intestinal tract. Urolithin A (Uro A) is a gut microbiota-derived metabolite from ellagic acid, commonly found in pomegranates and raspberries.

Recently, it has been described that the administration of Uro A enhances barrier function via the tight junction. However, the intestinal protective effect via mucin production has yet to be elucidated.

Aims & Methods: This study aimed to elucidate the effect of Uro A on mucin synthesis in the colon and to investigate the underlying molecular mechanisms. First, in vivo experiments were performed using wild-type mice (C57BL/6), NF-E2-related factor 2 (Nrf2) deficient mice, and wild-type mice treated with an aryl hydrocarbon receptor (AhR) antagonist. After Uro A administration, gut microbiota composition was analyzed, and short-chain fatty acid concentration was also measured. Next, in vitro assays using mucin-producing cells (LS174T) were conducted to assess mucin production upon Uro A treatment.

Results: The thickness of the MUC2-positive mucus layer in the Uro A group was significantly increased compared with that in the control group ($p < 0.01$). MUC2 protein levels in the colonic mucosal epithelium were significantly higher in the Uro A group than in the control group ($p = 0.041$). In Nrf2 deficient mice, Uro A treatment did not increase MUC2 protein levels in the colonic epithelium ($p = 0.309$). Similarly, in mice treated intraperitoneally with an AhR antagonist, MUC2 protein levels did not increase in the colonic epithelium after treatment with Uro A ($p = 0.222$). In experiments using Fluorescein isothiocyanate- Dextran, Uro A administration suppressed the mucosal permeability. Meanwhile, Uro A administration did not significantly upregulate tight junction protein expression in the epithelium. Hence, increased intestinal mucus appears to suppress leaky gut by a mechanism distinct from upregulating tight junction protein. After the treatment with Uro A, short-chain fatty acid-producing bacteria such as family *S24_7*, and genus *Ruminococcus* significantly increased. In addition, the propionic acid concentrations in stools were significantly increased after UroA administration. The treatment of Uro A was also beneficial for dextran sulfate sodium (DSS)-induced colitis in the mice model. The Uro A group showed a marked reduction in the disease activity index (DAI) after DSS administration ($p = 0.033$), and in the control group, the intestinal length was significantly shortened ($p = 0.018$). Hematoxylin and eosin staining of tissue sections showed that inflammatory cell infiltration and destruction of gland duct structures were mild in the Uro A group. In vitro data using LS174T cells demonstrated that the MUC2 mRNA level and the MUC2 protein levels in LS174T cells significantly increased after Uro A administration ($p = 0.02$ and $p < 0.01$, respectively). Fluorescence immunostaining showed that the strength of MUC2 fluorescence in LS174T cells after treatment with Uro A was significantly higher than that in the control group. In addition, MUC2 fluorescence expression did not increase after treatment with an Nrf 2 inhibitor. Similarly, MUC2 fluorescence did not increase after treatment with AhR antagonist.

Conclusion: Uro A promoted the up-regulation of MUC2 synthesis through the AhR and Nrf2 pathway, leading to the enhancement of the mucosal barrier function and the inhibition of the development of murine colitis. These findings involve alternating the intestinal microbiota and SCFA.

Disclosure: Tomohisa Takagi received collaborative research funds from Mitsubishi Tanabe Pharma Corporation and PreMedica, Inc. Yuji Naito received scholarship funds from EA Pharma Co., Ltd.; a collaboration research fund from Taiyo Kagaku Co., Ltd.

MP114

A NOVEL ROLE FOR FREE FATTY ACID RECEPTOR 3 IN MODULATING INFLAMMATORY SIGNATURE OF MACROPHAGES IN IBD

C. O'Mahony¹, J. Toman¹, A. Amamou¹, S. Ghosh¹
¹APC Microbiome, College of Medicine, Cork, Ireland

Contact E-Mail Address: 121126891@umail.ucc.ie

Introduction: As many as 40% of IBD patients do not respond to targeted therapies¹. Enhancing the efficacy of these therapies is a key priority, and defective host-microbe interplay is often thought to underpin a proportion of mechanistic therapeutic failure. Interactions of macrophages with the microbial-derived SCFAs (Butyrate, Propionate and Acetate) in particular; may be critical for disease remission. Therefore, we examined the manner that macrophages interacted with, and changed their behaviour according to exposure to SCFAs in order to identify new therapeutic targets.

Aims & Methods: This study aimed to explore phenotypic changes of macrophages upon sensing of SCFAs in the context of IBD. We hypothesised that SCFAs would alter the inflammatory signature of macrophages, and that de-orphanized transmembrane G-protein receptor Free-fatty acid receptor 3 (FFA3) expressed by immune cells in GI tract would be critical for this process, and furthermore that effective sensing of SCFAs would be necessary for shaping macrophage phenotype. THP-1 and monocyte-derived macrophage models were developed for exploring inflammatory signatures in the presence of 1mM or 4mM of each SCFA (Butyrate/Propionate/Acetate). By using a pharmacological activator of FFA3 (AR420626) we aimed to identify whether this receptor play an important role in directing macrophage phenotype. Secretion of (type-I Interferon) IFN-I and pro-inflammatory cytokines were measured using ELISA. Expression of Interferon-stimulated genes (ISGs) was quantified using RT-PCR. Subsequent experiments aimed to validate our findings with a knock-down model of FFA3.

Results: We demonstrated that polarisation of macrophages with LPS & IFN- γ rapidly led to the induction of type-I interferon responses and release of pro-inflammatory cytokines. This heightened secretion of IFN-I was almost entirely muted in the presence of butyrate and propionate (1mM and 4mM). As IFN-I drives the expression of ISGs through activation of IFNAR1-JAK/STAT axis, we quantified expression of the ISGs MX1 and IFIT1 as an indirect measure of bioactive IFN. Induction of MX1 and IFIT1, were strongly repressed by butyrate and propionate. Based on these observations, we determined that these responses to both SCFAs were being mediated by FFA3. Intriguingly, our results were closely mimicked by pharmacological intervention with AR420626 in a dose-dependent manner (10 – 50 μ M), suggesting that IFN-I secretion could be attenuated through activation of FFA3. Introducing a knock-down to our model, we validated our findings, and macrophages displayed impaired sensing of SCFA in the absence of FFA3.

Conclusion: We identified that macrophages reduce IFN-I release in the presence of butyrate and propionate, which is partly mediated through FFA3, and FFA3 ligands may be helpful for dampening inflammation in the gut mucosa in IBD.

References: (1). Ben-Horin, S., Kopylov, U. & Chowers, Y. Optimizing anti-TNF treatments in inflammatory bowel disease. *Autoimmun. Rev.* **13**, 24–30 (2014).

Disclosure: Nothing to disclose.

MP115

CANNABIDIOL, WHEN COMBINED WITH OLSALAZINE, OFFERS A NOVEL TREATMENT APPROACH FOR ULCERATIVE COLITIS

D. Thapa¹, L. Warne^{1,2}, M. Patil¹, R. Carlessi¹, M. Falasca³

¹Curtin University, Curtin Medical School, Curtin Health Innovation Research Institute (CHIRI), Bentley, Australia, ²Little Green Pharma (P) Ltd, Research and Development, West Perth, Australia,

³University of Parma, Department of Medicine and Surgery, Parma, Italy

Contact E-Mail Address: dinesh.thapa@postgrad.curtin.edu.au

Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized primarily by colon inflammation, significantly impacting quality of life. Current treatment options, including aminosalicylates such as olsalazine, often result in adverse effects and reduced efficacy over time, providing symptomatic relief rather than a cure. This underscores the urgent need for new, effective therapies.

The endocannabinoidome, the body's endogenous lipid signalling system comprising cannabinoid receptors, endogenous ligands, and metabolic enzymes, is emerging as a novel target for treating various inflammatory and metabolic disorders, including IBD (1).

Cannabidiol (CBD), a non-psychoactive compound found in Cannabis, exhibits anti-inflammatory and analgesic properties, including in IBD, through modulation of the endocannabinoidome. However, the clinical efficacy of CBD in IBD remains uncertain despite numerous trials (2).

Aims & Methods: This study aims to investigate the efficacy of CBD in combination with a sub-therapeutic dose of a clinically used drug for ulcerative colitis, olsalazine, in a refined and translationally relevant murine acute and chronic colitis model (3).

For induction of the acute colitis model, female BALB/c mice, aged 8-10 weeks, were challenged with 4% dextran sodium sulfate (DSS) in drinking water for 7 days, followed by 3 days of normal water. For the chronic model, 2% DSS was administered for 7 days, followed by 1% DSS for 10 days and again 2% for another 7 days. CBD (10, 30, and 60 mg/kg), and olsalazine (50 mg/kg) were administered intraperitoneally or orally once a day from day 1 to day 11 in the acute model whereas in the chronic model, these drugs were administered from days 1 to 10 and days 18 to 24. For the combination treatments, 50 mg/kg olsalazine was combined with 10 mg/kg CBD and delivered orally in both acute and chronic models.

Daily monitoring, including body weight, stool consistency, and occult blood/rectal bleeding, was recorded to calculate the disease activity index (DAI) score.

On endpoints (day 11 or day 24), whole blood was collected, and mice were euthanized to assess inflammation in different organs including the colon, spleen, kidneys, and liver. The tissues were flash frozen in liquid nitrogen and stored at -80°C. Frozen tissues were used to measure cytokines and chemokines using multiplex assays and neutrophils using myeloperoxidase (MPO) activity assays.

Results: Mice challenged with DSS in both acute and chronic models exhibited increased DAI scores, decreased colon length, increased cytokines and chemokines expression, increased MPO activity, and increased liver, spleen, and kidney weight. CBD treatment at 60 mg/kg, but not at 10 and 30 mg/kg, significantly reduced acute colitis as demonstrated by decreased DAI scores, decreased MPO activity and cytokines and chemokines expression, and increased colon length. Administration of olsalazine alone at 50 mg/kg orally did not produce any beneficial effects, but when combined with 10 mg/kg of CBD, there was a significant reduction in all colitis markers in both acute and chronic models.

Conclusion: While using CBD alone for treating colitis is ineffective, and high doses of olsalazine used in the clinics often come with adverse effects and lose effectiveness over time, our data show that combining low doses

of CBD and olsalazine significantly reduces colitis without adverse effects. Therefore, the low-dose combination of CBD and olsalazine offers a promising novel treatment for ulcerative colitis.

References: 1. Lian J, Casari I, Falasca M. Modulatory role of the endocannabinoidome in the pathophysiology of the gastrointestinal tract. *Pharmacol Res.* 2022 Jan;175:106025. doi: 10.1016/j.phrs.2021.106025. Epub 2021 Dec 7. PMID: 34883211

2. Hoffmann M, Schwertassek U, Seydel A, et al. A refined and translationally relevant model of chronic DSS colitis in BALB/c mice. *Laboratory Animals.* 2018;52(3):240-252. doi:10.1177/0023677217742681

3. Thapa D, Warne LN, Falasca M. Pharmacohistory of Cannabis Use-A New Possibility in Future Drug Development for Gastrointestinal Diseases. *Int J Mol Sci.* 2023 Sep 28;24(19):14677. doi: 10.3390/ijms241914677. PMID: 37834122; PMCID: PMC10572150.

Disclosure: The work presented here is partly funded by Little Green Pharma (LGP) Pty Ltd.

MP116

SINGLE-CELL TRANSCRIPTOMIC ANALYSIS REVEALS INSIGHTS INTO THE MECHANISM OF ACTION OF GRANULOCYTE-MONOCYTE APHERESIS WITH ADACOLUMN®

D. Kioroglou¹, J.L. Cabriada Nuño², U.M. Marigorta¹,

I. Rodríguez-Lago²

¹CIC bioGUNE, Bilbao, Spain, ²Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain

Contact E-Mail Address: iago.r.lago@gmail.com

Introduction: Granulocyte-monocyte apheresis (GMA) with Adacolumn® is a non-pharmacological treatment approved for the management of ulcerative colitis (UC), especially in steroid-dependent cases. The precise mechanism of action and immunological changes associated with GMA are still not fully understood. Gene expression analysis at the single-cell level (through scRNA-Seq) has emerged as a key tool to characterize drug responses at the molecular level.

Aims & Methods: We used scRNA-Seq to investigate the transcriptomic effects and immune cell population alterations induced by GMA. We generated scRNA-Seq from peripheral blood mononuclear cells (PBMC) of six ulcerative colitis (UC) patients undergoing GMA treatment.

Our analyses focused on gene expression profiles obtained at three key timepoints, namely

- i) immediately before the start of the first session,
- ii) immediately after the end of the first session (and hence, with a 2-hour gap from the first timepoint), and
- iii) after 5 sessions of GMA treatment. We examined a total of 12 samples, including three patients with data available for all three timepoints. The analytical pipeline comprised standard steps in scRNA-Seq, including quality control, filtering and integration by cell-type annotation, differential gene expression analysis and pathway enrichment profiling.

Results: We report three main results. First, we observed alterations in cell types directly impacted by GMA treatment in UC patients, including expansions of IFN γ -producing plasmacytoid dendritic cells (pDC) and subtype composition changes in central components of the innate system such as Natural Killers. Second, our analysis of short-term effects within the first session highlights significant changes in non-classical monocytes, including upregulation of pathways associated with hypoxia and glycolysis. Finally, evaluation after 5 sessions of treatment unveiled more widespread changes affecting various regulatory pathways and extending across cell types. In particular, we detect alterations in T cell populations, including upregulation of key pathways in response to inflammation in regulatory T cells.

Conclusion: For the first time, we have generated 12 single-cell transcriptomic profiles to characterize the effects of GMA treatment on peripheral blood of UC patients. Our analyses reveal significant alterations in gene regulation and cell type composition among patients undergoing GMA treatment, observed both in the short-term after the first 2-hour session and over the course of 5 sessions. By examining three key timepoints, we provide insights into the longitudinal changes and molecular mechanisms underlying the response to GMA treatment.

Disclosure: Nothing to disclose.

MP117
HYPERBARIC OXYGEN THERAPY FOR SURGICAL FISTULA CLOSURE IS FEASIBLE IN PERIANAL FISTULIZING CROHN'S DISEASE

L.G.M. Mulders¹, K. Beek², J. Tielbeek³, J. Stoker², G.R. D'Haens¹, C.J. Buskens⁴, R. van Hulst⁵, K.B. Gecse¹, AMFIBIO study group
¹Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Department of Radiology and Nuclear Medicine, Amsterdam, Netherlands, ³Spaarne Gasthuis, Department of Radiology and Nuclear Medicine, Haarlem, Netherlands, ⁴Amsterdam UMC, Department of Surgery, Amsterdam, Netherlands, ⁵Amsterdam UMC, Department of Anesthesiology, Amsterdam, Netherlands

Contact E-Mail Address: l.mulders@amsterdamumc.nl

Introduction: Perianal fistulas occur in up to 30% of patients with Crohn's disease (pCD) and frequently require a combined medical and surgical treatment approach. Hyperbaric Oxygen Therapy (HBOT) has previously shown benefit in treatment-refractory pCD.

Aims & Methods: In this pilot study, we aim to assess the feasibility of surgical fistula closure 4 weeks after HBOT, and efficacy of combining surgical closure and 8 weeks HBOT.

Patients with complex pCD refractory to at least 6 months of anti-TNF therapy were included in this study. All patients received a seton prior to starting treatment with 40 sessions (8 weeks) of HBOT (each lasting 110 minutes, with 5-minute air breaks) with 100% oxygen at 2.4 atmosphere. At week 4 the seton was removed, and surgical closure of the internal fistula opening was attempted. All patients continued stable dose of medical treatment during the study. Response was assessed by the fistula drainage assessment (FDA) and the perianal disease activity index (PDAI) at week 9, 26 and 52, and by pelvic MRI at week 9 and 26. MRI response was defined as a decrease of 2 points in MAGNIFI-CD score, MRI remission as a MAGNIFI-CD ≤6. (Serious) Adverse Events (AE) were reported for 52 weeks. Univariate logistical regression was used to explore potential variates associated with PDAI response (≤4) at week 26.

Age (years), mean (95%CI)	30.5 (23.7 – 27.3)
Female, n (%)	9 (90)
Crohn's disease duration (years), median [IQR]	9.0 [1.8 – 14.5]
Perianal disease duration (years), median [IQR]	3.5 [1.8 – 7.3]
Proctitis at baseline, n (%)	2 (20)
Internal fistula openings, n (%)	1: 7 (70) 2: 3 (30)
Primary fistula location, n (%)	anterior: 3 (30) lateral: 3 (30) posterior: 4 (40)
Fistula tracts, mean (95%CI)	3.5 (2.8 – 6.3)
Previous fistula surgeries, mean (95%CI)	4.1 (2.5 – 5.7)
Perianal fistula classification (Geldof et al.; class 1 – 4b), n (%)	2a: 3 (30) 2b: 1 (10) 2c-i: 1 (10) 2c-ii: 5 (50)

Table 1. Patient and fistula characteristics (n=10).

Results: Ten patients completed treatment and were analyzed (Table 1). All patients completed HBOT and underwent a technically successful surgical procedure at week 4. No proctitis was encountered at week 4 during examination under anesthesia. PDAI response was achieved by 30%, 60%, 58% at week 9, 26 and 52, respectively. FDA response/remission was achieved in 50%/20%, 80%/40% and 80%/50% of patients at week 9, 26 and 52, respectively. MRI response/remission was achieved in 60%/10% and 60%/20% of patients at week 9 and 26, respectively. No significant parameters were associated with PDAI response at week 26 in univariate logistical regression. (S)AEs included one patient with a potential oxygen toxicity seizure without long term effects, and one patient reported claustrophobia, no new AEs were reported.

Conclusion: HBOT is feasible in combination with surgical therapy in patients with complex pCD refractory to anti-TNF therapy. Patients had long-lasting benefit of the combined treatment approach. Further translational data are currently analyzed to clarify mechanisms of action and to explore potential biomarkers for therapy response.

Disclosure: LM, KB, JT and RvH have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this abstract. JS is President-elect of the European Society of Gastrointestinal and Abdominal Radiology. GD has served as consultant for AbbVie, Astrazeneca, Alimentiv, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion, Cosmo, Eli Lilly, Galapagos, GSK, Johnson and Johnson, Takeda, Pfizer Inc, Polpharma, Prometheus Biosciences, Tillotts and Ventyx; received speaker fees from AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly, Johnson and Johnson, Takeda, Pfizer Inc and Tillotts. CB has received grants from Boehringer Ingelheim and Roche; speakers honoraria from AbbVie, Janssen, Galapagos, Takeda, and Tillotts. KG has received grants from Pfizer Inc, Celltrion and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunic Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis and Takeda and speaker's honoraria from Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda and Tillotts.

MP118
DEVELOPMENT AND CHARACTERIZATION OF SPY003, A NOVEL EXTENDED HALF-LIFE MONOCLONAL ANTIBODY DRUG CANDIDATE TARGETING IL-23 FOR THE TREATMENT OF IBD

B. Kang¹, M. Alam¹, J. Milligan¹, S. Oliveira¹, J. Friedman², D. Nguyen², A. Spencer², J. Oh¹, H. Shaheen¹
¹Paragon Therapeutics, Waltham, United States of America, ²Spyre Therapeutics, Waltham, United States of America

Contact E-Mail Address: andy.spencer@spyre.com

Introduction: The cytokine IL-23 is secreted by activated macrophage and dendritic cells (DC) and promotes the expansion and/or activity of Th17 cells, CD8+ T cells, macrophages, and DCs. Its pathogenic role in IBD is suggested by genetic association and has been confirmed in clinical trials demonstrating IL-23 antagonism as an effective and safe treatment for Crohn's disease (CD) and ulcerative colitis (UC). SPY003 is a novel, extended half-life humanized IgG1 monoclonal antibody (mAb) that binds IL-23 with high affinity and specificity and potentially inhibits IL-23-mediated signaling.

Aims & Methods: SPY003 was evaluated in multiple *in vitro* and *ex vivo* assays compared to risankizumab (RIS) and guselkumab (GUS). Binding affinity to IL-23 was determined by surface plasmon resonance (SPR) and kinetic exclusion assays (KinExA). Antagonism of IL-23 signaling was measured via a STAT3 reporter cell line and phospho-STAT3 ELISA. SPY003-induced reduction of IL-17 secretion in response to human IL-23 was assessed in mouse splenocytes and human peripheral blood mononuclear

cells (PBMC). The binding epitope of SPY003 to IL-23 was determined using cryogenic electron microscopy. Half-life extension was measured via pharmacokinetic analysis in cynomolgus monkeys given a single bolus of SPY003 by intravenous and/or subcutaneous (SC) administration.

Results: SPY003 binds specifically to IL-23 with picomolar affinity. It inhibits STAT3 activity and phosphorylation with IC_{50} values $< 1nM$, as well as IL-17 secretion in IL-23-stimulated mouse splenocytes and human PBMC. IL-23 binding potency and IC_{50} values for IL-23 antagonism are comparable to those of RIS and GUS. Cryo-EM demonstrates the binding epitope of SPY003 within IL-23. The half-life of SPY003 is significantly extended in cynomolgus monkeys compared to both RIS and GUS. Based on allometric scaling of the clearance of SPY003 observed in this study, predictive simulations of SPY003 PK in humans suggest that Q3M-Q6M+ SC dosing will achieve therapeutic exposures in patients across a wide range of body weights and albumin concentrations.

Conclusion: SPY003 exhibits high selectivity and affinity for IL-23 and potentially inhibits downstream cellular signaling. With an extended half-life in NHP, SPY003 demonstrates therapeutic potential for effective and safe treatment of CD and UC with the potential advantage of twice a year SC dosing. Further preclinical and clinical studies are warranted to demonstrate this potential.

Disclosure: BK, MA, JM, SO, JO, and HS are employees of Paragon Therapeutics.

JF, DN, and AS are employees of Spyre Therapeutics.

MP119

UNVEILING THE STRONG SAFETY PROFILE AND HIGH TARGET ENGAGEMENT OF OPM-101, A FIRST-IN-CLASS ORALLY AVAILABLE RIPK2 INHIBITOR, IN A PHASE 1 CLINICAL TRIAL IN HEALTHY VOLUNTEERS

L. Peyrin-Biroulet¹, B. Robin², J. Hoflack², P. Genne²

¹Nancy University Hospital, Nancy, France, ²Oncodesign Precision Medicine, Dijon, France

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: Oncodesign Precision Medicine (OPM) has designed and developed OPM-101, an orally available macrocyclic small synthetic molecule with high affinity and specificity for binding and inhibiting RIPK2. The NOD2/RIPK2 pathway is a key driver of inflammatory bowel disease (IBD) as its hyperactivation results in an over production of proinflammatory cytokine, including tumor necrosis factor (TNF)- α , which plays an essential role in initiating and perpetuating inflammation and tissue damage in the intestine. Targeting RIPK2 has emerged as a promising therapeutic strategy for reducing inflammation, disease progression, and normalizing proinflammatory cytokines generation in IBD. Blocking RIPK2 pathway could become a possible therapeutic strategy for severe steroid refractory or dependent IBD patients. The main objective of this phase 1 study was to assess the safety and tolerability of OPM-101 in healthy volunteers.

Aims & Methods: The safety, pharmacokinetic (PK), and pharmacodynamic (PD) properties of OPM-101 were determined in a Single Ascending Dose (SAD) part of the study in male and female healthy volunteers. A single dose (5-1,000 mg) was administered to male healthy volunteers and a dose of 150 mg in female volunteers. A group of male volunteers received two single doses of 150 mg in fasted and in fed conditions a week apart. OPM-101 safety and tolerability were monitored throughout the study considering the following parameters: physical examination, any adverse events, clinical laboratory values, safety and 12-lead ECG, cardiac echography, Holter monitors, vital signs, and digestive tolerability. Blood samples were collected at pre-defined timepoints to determine the PK parameters and to assess the target engagement. Target engagement was determined *ex vivo* on whole blood samples by the percentage of in-

hibition of the L18-MDP-induced TNF α production. L18-MDP is a specific activator of the NOD2 pathway.

Results: In the SAD part of the study, 72 healthy volunteers were randomized in 9 cohorts. Volunteers were randomized 3:1 between OPM-101 (n=6) and placebo (n=2) in each cohort. The overall safety profile of OPM-101 was very good with only 8.3% of participants reporting a total of eight treatment-related TEAE (6 mild and 2 moderate).

OPM-101 is orally bioavailable, rapidly absorbed (T_{max} is between 2-4h), with a long terminal half-life of 12-15h. Female volunteers tended to have higher exposure than male volunteers receiving the same dose. When OPM-101 was administered after intake of a high fat breakfast, the exposure was twice that observed in fasted conditions, and variability of absorption was lower. The target engagement, observed with doses as low as 60 mg, was $>80\%$ over 24h and showed an immunomodulatory property inducing normalization of TNF α levels.

Conclusion: Following a single administration in both male and female healthy volunteers, OPM-101 exhibited a highly favorable safety profile. Its pharmacokinetic properties are well-suited for oral administration, demonstrating rapid target engagement after a single oral dose leading to an immunomodulation. This phase 1 study unveils OPM-101 as a potent RIPK2 inhibitor paving the way for groundbreaking therapeutic advancements in inflammatory colitis.

Disclosure: B. Robin, J. Hoflack and P. Genne are employees of OPM. Prof. L. Peyrin-Biroulet is advisor for OPM.

MP120

WITHDRAWN

Complications in end stage liver disease

15:30-16:30 / Poster Stage 3

MP121

OPTIMAL TIME FOR FOLLOW-UP AFTER VARICEAL BAND LIGATION IN CIRRHOTIC PATIENTS: A MULTI CENTER RANDOMIZED CONTROLLED TRIAL

A. Eliwa¹, M. Alborai¹, O. Elshaarawy², A. Abu-Elfath³, M. Aamr⁴, M. Ahmed Medhat³, A. Alzamzamy⁵, M. Zaghloul⁶, M. Sayed⁷, F. El-Raey⁸, A. Altonbary⁹, M. Saad¹⁰, E. Mahran¹¹, A. Eid¹², N. Makhoul³, S. Abdel-Salam¹³, M.-N. Wafi¹⁴, E. Bahbah¹⁵, M. Elbasiony¹⁶

¹Al-Azhar University, Internal Medicine, Cairo, Egypt, ²Royal Liverpool University Hospital, Gastroenterology and Hepatology, Liverpool, United Kingdom, ³Assiut University, Tropical Medicine and Gastroenterology, Faculty of Medicine, Assiut, Egypt, ⁴Shebin Teaching Hospital, GOTH, Hepatogastroenterology and Endoscopy, Shebin El Kom, Egypt, ⁵Military Medical Academy, Gastroenterology and Hepatology, Cairo, Egypt, ⁶Faculty of Medicine, Kafrelsheikh University, Hepatology, Gastroenterology and Infectious Diseases, Kafrelsheikh, Egypt, ⁷Aswan University, Tropical Medicine and Gastroenterology, Aswan, Egypt, ⁸Al-Azhar University, Hepatogastroenterology and Infectious Diseases, Damietta, Egypt, ⁹Mansoura Specialized Medical Hospital, Gastroenterology and Hepatology, Mansoura, Egypt, ¹⁰Specialized Medical Hospital Mansoura University, Internal Medicine, Mansoura, Egypt, ¹¹New Valley University, Faculty of Medicine, New Valley, Egypt, ¹²Al-Azhar University, Hepatogastroenterology and Infectious Diseases, Cairo, Egypt, ¹³Tanta University, Tropical Medicine and Infectious Diseases, Tanta, Egypt, ¹⁴Cairo University, Internal Medicine, Hepatogastroenterology Unit, Kasr Al-Ainy School of Medicine, Cairo, Egypt, ¹⁵Al-Azhar University, Faculty of Medicine, Damietta, Egypt, ¹⁶Mansoura University, Gastroenterology, Dakahleya, Egypt

Contact E-Mail Address: alborai@earth-eg.org

Introduction: Esophageal varices can lead to morbidity and mortality in patients with chronic liver diseases. There is a debate about the frequency of endoscopic variceal band ligation sessions needed for the eradication of esophageal varices.

Aims & Methods: We aimed to explore the optimal interval for endoscopic variceal band ligation sessions needed to obliterate esophageal varices. This study enrolled 374 patients with liver cirrhosis indicated for endoscopic variceal band ligation. After the first variceal band ligation, patients were randomly assigned to one of four groups regarding the interval of subsequent band ligation sessions:

Group 1 (subsequent band ligation every week),

Group 2 (subsequent band ligation every two weeks),

Group 3 (subsequent band ligation every three weeks), and;

Group 4 (subsequent band ligation every four weeks).

Patients were followed up till the point of eradicating esophageal varices with reporting of complications in the form of bleeding or post-banding ulcers.

Results: The studied groups had insignificant variations in terms of the mean number of sessions needed to eradicate varices completely and the mean number of subsequent band ligation sessions. Post-banding ulcers were highly incident in Group 1 (52.9%), followed by Group 2 (22.8%), Group 3 (8.0%), and Group 4 (2.7%), with a statistically significant difference between the studied groups ($p < 0.001$). The incidence of bleeding after the first band ligation session was only reported in Group 2 (1.3%). Patients with higher number of sessions needed to obliterate esophageal varices (sessions) were associated with lower hemoglobin (9.75 ± 1.60 vs.

10.48 ± 2.19 ; $p = 0.003$), lower INR (1.26 ± 0.24 vs. 1.35 ± 0.31 ; $p = 0.009$), and larger spleen diameter (15.52 ± 3.58 vs. 14.65 ± 3.31 ; $p = 0.011$) when compared with patients needed lower number of sessions to obliterate esophageal varices.

Conclusion: The four-week interval of elective variceal band ligation sessions is effective in achieving complete esophageal varices eradication with a lower rate of complications.

References: 1- Iwakiri, Y., J. Trebicka, *Portal hypertension in cirrhosis: Pathophysiological mechanisms and therapy*. JHEP Rep, 2021. 3(4): p. 100316.

Disclosure: Nothing to disclose.

MP122

IDENTIFICATION OF SUBPHENOTYPES OF SEPTIC PATIENTS WITH LIVER CIRRHOSIS

J. Lin¹, J. Zhu¹, R. Li²

¹First affiliated hospital of Soochow university, Department of Gastroenterology, Suzhou, China, ²Soochow University, Suzhou, China

Contact E-Mail Address: jxlin@stu.suda.edu.cn

Introduction: Septic patients with liver cirrhosis exhibits considerable heterogeneity.

Aims & Methods: The objective of current study was to identify subphenotypes of liver cirrhosis with sepsis among intensive care unit (ICU) patients. A retrospective study was performed based on the Medical Information Mart for Intensive Care (MIMIC-IV 2.0) database. Using unsupervised clustering, we identified distinctive subphenotypes based on 37 clinical variables obtained on admission. Primary outcomes were 28-day mortality. Cox regression was applied to quantify the risk associated with each subphenotype concerning clinical outcomes. A machine learning (ML) prediction model was developed and made available online, capable of identifying these subphenotypes from fundamental clinical variables.

Results: Our study enrolled a total of 1087 septic patients with liver cirrhosis, revealing two unique subphenotypes via k-means clustering algorithm. Subphenotype 1 was assigned to 719 patients (66%) and subphenotype 2 to 368 patients (34%). The subphenotype 2 was characterized by higher levels of hepatic injury, higher SOFA scores (average SOFA scores were 12.5), and worse clinical outcomes (28-day mortality, 49%). Subphenotype 2 showed significantly increased risk of 28-day mortality compared to Subphenotype 1 (hazard ratio [HR] = 2.14 [95%CI 1.69 – 2.71], $p < 0.001$). The ML model integrated seven variables could predict subphenotypes accurately.

Conclusion: This study differentiated and stratified subphenotypes among septic patients with liver cirrhosis, laying a foundation for more personalized therapeutic strategies. The predictive ML model developed has the potential to bolster clinical decision-making pertaining to these patients within the ICU setting.

Disclosure: The authors declare that they have no conflict of interest.

MP123

TRENDS IN MANAGEMENT AND OUTCOMES OF CIRRHOTIC PATIENTS WITH VARICEAL BLEEDING IN THE UNITED KINGDOM – 15 YEARS APART: A COMPARATIVE ANALYSIS OF 2007 AND 2022

G. Nigam¹, J. Grant-Casey², K. Oakland³, S. Hearnshaw⁴, V. Jairath⁵, S. Travis⁶, M.F. Murphy², L. Estcourt², A. Douds⁷, J. Leithead⁸, A. Stanley⁹, UK upper GI bleed group
¹Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ²NHS Blood and Transplant, Oxford, United Kingdom, ³HCA Healthcare UK, Clinical, Oxford, United Kingdom, ⁴Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom, ⁵Alimentiv Inc., Gastroenterology, London, Canada, ⁶John Radcliffe Hospital, Gastroenterology Department, Oxford, United Kingdom, ⁷Queen Elizabeth Hospital, Gastroenterology, Fakenham, United Kingdom, ⁸Forth Valley Royal Hospital, Larbert, United Kingdom, ⁹Glasgow Royal Infirmary, Department of Gastroenterology, Glasgow, United Kingdom

Contact E-Mail Address: gaurav.nigam@nhs.net

Introduction: This study revisits the management and outcomes of acute upper gastrointestinal bleeding (AUGIB) in cirrhotic patients across the United Kingdom, allowing comparisons with the last UK wide audit undertaken in 2007.¹

Aims & Methods: Focusing on cirrhotic patients with variceal bleeding, we analyze patient profiles, investigations, treatments, and outcomes, drawing comparisons with the 2007 study. A prospective multi-center observational study of adults (>16 years) presenting to 152 UK hospitals with AUGIB between 3 May - 2 Jul 2022.

Results: 744/5101 (15%) presenting with AUGIB had known cirrhosis (Child-Pugh categories: A:1%, B: 47%, C: 11%).with median age of 59yrs (IQR 49.7-69). 73%(547/744) were new admissions. Glasgow-Blatchford score(GBS), stratified patients into, 22% medium-risk(GBS 2-6),47% high-risk(7-11),and 30% very high-risk(≥12). For pre-endoscopy management: 58%(433) received proton pump inhibitors (PPI), 50%(371) terlipressin/vasopressor and 44%(326) antibiotics.

An endoscopy was performed for 91%(679/744). Time to endoscopy from presentation was: 0-12 hrs in 25%, 12-24 hrs in 25%, & 24-48 hrs in 21%. 45% (307/679) were identified to have varices (91% - oesophageal, 15% - gastric and 2% - duodenal) and 33%(224/679) had non-variceal findings. Median age of patients with varices (n=307) was 57 yrs (IQR 49-68). Stigmata of recent bleed were noted for 72%(222) - 45% blood in the upper GI tract and 65% high risk markings on varices and endotherapy was applied for 78%(241). Variceal therapy applied in 70%(214 - 93% banding, 12% injection therapy), Danis stent 2%(5) and Sengstaken tube 6%(14). 18% (55) had evidence of further in-patient bleeding after index endoscopy. During inpatient stay, 26%(81) needed >1 endoscopy, and 2%(6) underwent transjugular intrahepatic portosystemic shunt(TIPSS). 67%(206) were transfused ≥1 packed red blood cells, 17%(53) platelets and 22%(68) fresh frozen plasma for AUGIB. Median length of stay was 7days (IQR 5-11) and in-hospital mortality was 13%(40).

Comparisons with the 2007 audit for patients with varices revealed an increased average age (58yrs vs 54.5 yrs), increased pre-endoscopic use of PPI (62% vs 50%),vasopressors (70% vs 57%) and antibiotics (61% vs 27%). There was a significant increase in those receiving endotherapy (78% vs 64%) and undergoing TIPSS (2% vs .8%), along with a lower likelihood of further in-patient bleeding after an index endoscopy (18% vs 26%), and numerically lower in-hospital mortality (13% vs 15.2%).Comparisons with the 2007 audit are presented in table 1.

Outcome	2007 (n=526)	2022 (n=307)	p value
Mean age	54.5 yrs	57.7 yrs	-
Pre-endoscopy treatment			
Proton pump inhibitors	57%	62%	<0.05
Terlipressin/ vasopressor	57%	70%	<0.05
Antibiotics	27%	61%	<0.05
Endoscopy outcomes			
Stigmata of recent bleed	65%	72%	<0.05
Endotherapy	64%	78%	<0.05
Further bleeding	26%	18%	<0.05
TIPSS	0.8%	2%	<0.05
Transfusion >1 unit			
Packed red cells	73%	67%	<0.05
Fresh frozen plasma	35%	22%	<0.05
Platelets	14%	17%	0.26
Median LOS	9 days (IQR 5-21)	7 days (IQR 5-11)	-
In-hospital mortality	15.2%	13%	0.32

Table 1: Comparative analysis with 2007 audit of main outcomes for variceal bleeds.

Conclusion: Compared with 2007 patients presenting with variceal haemorrhage were more likely to receive optimal treatment, had reduced length of stay, reduced rebleeding and a trend towards reduced mortality. Our data suggests that further improvements in pre-endoscopic management and provision of TIPSS are required.

References:

1. Hearnshaw et al *Gut* 2011

Disclosure: Nothing to disclose.

MP124

USE OF PROTON PUMP INHIBITORS IN PATIENTS WITH LIVER CIRRHOSIS AND ANTICOAGULANT THERAPY, A RETROSPECTIVE STUDY

R. Eftimie Spitz¹, T. Surdea-Blaga²

¹University of Medicine and Pharmacy “Iuliu Hatieganu” Cluj-Napoca, Snd Department of Internal Medicine, Cluj-Napoca, Romania, ²University of Medicine and Pharmacy “Iuliu Hatieganu” Cluj-Napoca, 2nd Medical Department, Cluj-Napoca, Romania

Contact E-Mail Address: RAPHAEL.SPITZ@YAHOO.FR

Introduction: Proton Pump Inhibitors (PPIs) are commonly prescribed for gastrointestinal disorders. Several studies have reported an overprescription of PPIs in patients with liver cirrhosis^{1,2}, yet their use in these patients increases the risk of spontaneous bacterial peritonitis and mortality rates. HAS-BLED score is a tool used to evaluate bleeding risk in individuals on chronic anticoagulation therapy, and cardiologists use it to prescribe PPIs in patients on anticoagulants, to reduce the risk of gastrointestinal bleeding³.

Aims & Methods: This study aimed to assess the appropriateness of PPI prescriptions in patients with liver cirrhosis and anticoagulant treatment. A secondary objective was to investigate whether the guidelines for administering PPIs based on a patient's HAS-BLED score align with the indications for PPI prescription recommended in established gastroenterological guidelines.

This study was retrospective. From January 2022 to December 2023, we included consecutive cirrhotic patients who had anticoagulant treatment for various indications (atrial fibrillation, deep vein thrombosis, pulmonary embolism). All patients were counted only once, even if hospitalized multiple times. To establish the validity of PPI prescription, we used the current guidelines⁴⁻⁷. Anticoagulant treatment alone, is not a valid indication for PPI prescription in patients with liver cirrhosis, in the absence of concomitant antiplatelet treatment⁴. HAS-BLED scores were calculated⁸, and patients with a score ≥ 4 were considered at high risk for bleeding.

We looked for an association between high HAS-BLED score and PPI prescription, and whether these prescriptions were aligned with the current gastroenterological guidelines.

Results: We found 577 hospitalizations for cirrhosis, among these, 61 patients (mean age 71.3 years old $\pm$ 8.88, 46 males) were under chronic anti-coagulant treatment. We identified 32 patients on PPIs during the hospital stay. Fourteen (43.7%) had no valid indication, but 5 had a high HAS-BLED score. The remaining patients (n=18) were prescribed PPIs for the following reasons: gastritis (n=10), antiplatelet with high risks (n=3), NSAID and corticosteroid (n=2), peptic ulcer disease (n=2), gastroesophageal reflux disease (n=1). In our cohort, 27 (44.3%) patients had a high HAS-BLED score. Among these patients, 18 were on PPI. In the patients with low HAS-BLED (n=34), 14 were on PPIs, and 9 of them didn't have a valid indication based on current gastroenterological guidelines. We computed the Chi2 statistic to assess the association between PPI prescription and a high HAS-BLED score: the chi-square statistic yielded 3.921 (p=0.048). A similar association was observed at discharge: the chi-square statistic was 3.994 (p=0.046). No association was observed between HAS-BLED score and inappropriate PPI prescription (Chi2 = 0.147, p = 0.7).

		Low HAS-BLED score	High HAS-BLED score
During hospitalization	PPI	14	18
	No PPI	29	9
At discharge	PPI	7	12
	No PPI	27	15

Conclusion: In our cohort of patients with liver cirrhosis, over 50% were prescribed PPIs during their hospital stay, with 43.7% lacking a valid indication. An association was observed between the HAS-BLED score and the prescription of PPIs; however, only a portion of the non-valid indications can be attributed to the high HAS-BLED score.

References: 1. Gamelas Vet al. Prescription Pattern of Proton Pump Inhibitors at Hospital Admission and Discharge. *GE Port J Gastroenterol*. 2019;26(2):114-120. doi:10.1159/000488506

2. Ct C, et al. Inappropriate use of proton pump inhibitors in a local setting. *Singapore Med J*. 2014;55(7). doi:10.11622/smedj.2014087

3. Pistors R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010;138(5):1093-1100. doi:10.1378/chest.10-0134

4. Scarpignato C et al. Italian Society of Pharmacology, and the Italian Association of Hospital Gastroenterologists. Effective and safe proton pump inhibitor therapy in acid-related diseases - A position paper addressing benefits and potential harms of acid suppression. *BMC Med*. 2016;14(1):179. doi:10.1186/s12916-016-0718-z

5. <http://www.ncbi.nlm.nih.gov/books/NBK552570/>

6. Lanza FL, et al, Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol*. 2009;104(3):728-738. doi:10.1038/ajg.2009.115

7. Freedberg et al. The Risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert Review and Best Practice Advice From the American Gastroenterological Association. *Gastroenterology*. 2017;152(4):706-715. doi:10.1053/j.gastro.2017.01.031

8. Gallego P et al. Relation of the HAS-BLED bleeding risk score to major bleeding, cardiovascular events, and mortality in anticoagulated patients with atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2012;5(2):312-318. doi:10.1161/CIRCEP.111.967000

Disclosure: Nothing to disclose.

MP125
HEPATIC EXTRACELLULAR VESICLES-INDUCED CGAS-STING SIGNALING PROMOTES SKELETAL MUSCLE INFLAMMATION AND ATROPHY IN CIRRHOSIS

Y. 彭¹, X. Fan¹, L. Yang²
¹West China Hospital, Sichuan University, Division of Gastroenterology & Hepatology, Chengdu, China, ²West China Hospital of Sichuan University, Gastroenterology, Chengdu, China

Contact E-Mail Address: 2023224020021@stu.scu.edu.cn

Introduction: Sarcopenia, an important component of malnutrition, is linked to poor prognosis in cirrhotic patients. Recent studies have indicated that chronic muscle inflammation plays a pivotal role in the progression of sarcopenia, although the mechanism underlying the association between cirrhosis and chronic muscle inflammation remains poorly understood. Therefore, this study aimed to elucidate the specific mechanism by which hepatic-derived extracellular vesicles (EVs) promote proinflammatory responses in muscle macrophages via circulation, leading to the advancement of muscle inflammation during cirrhosis.

Aims & Methods: Liver fibrosis was induced by carbon tetrachloride injection and bile duct ligation. EVs from cirrhotic liver were isolated and characterized. Proteomics was utilized to identify functional mitochondrial components in EVs. Lastly, we conducted a cross-sectional study on patients with cirrhosis to validate these findings.

Results: Treatment of EVs from cirrhotic liver promoted inflammation in macrophages and muscle inflammation progression via activating the STING pathway. The Sting inhibitor in cirrhotic mice abolished the role of cirrhotic-derived EVs in muscle inflammation. In addition, hepatic-specific deletion of *Rab27a* and the inhibitor of EV—GW4869, significantly alleviated cirrhosis-induced muscle inflammation progression in cirrhotic mice. The proteomics results showed that mitochondrial proteins and mtDNA were enriched in EVs from cirrhotic liver. Furthermore, mitochondrial damage in hepatocytes caused by mitochondrial membrane potential decline led to mitochondrial DNA leakage, which caused macrophage inflammation through the STING pathway. Moreover, EVs from peripheral veins and hepatic veins who underwent transjugular intrahepatic portosystemic shunt in patients with cirrhosis and EV-mtDNA expression were associated with the severity of cirrhosis.

Conclusion: Hepatocyte-derived EVs promote inflammation in macrophages in muscle and facilitate muscle inflammation progression via the mtDNA-cGAS-STING signaling pathway. Reducing EV secretions in cirrhotic liver or targeting STING may be potential therapeutic approaches to slow the progression of cirrhosis-driven muscle inflammation.

Disclosure: Nothing to disclose.

MP126

ENDOSCOPIC CYANOACRYLATE INJECTION IMPROVES THE EFFICACY OF ENDOSCOPIC MANAGEMENT OF ESOPHAGEAL VARICEAL BLEEDING IN GOV TYPE I

X. Huang¹, L. Wu¹, S. Chen¹

¹Zhongshan Hospital, Fudan University, Endoscopy Center and Endoscopy Research Institute, Shanghai, China

Contact E-Mail Address: huangxiaoquan1010@aliyun.com

Introduction: The European Society of Gastrointestinal Endoscopy Guideline (ESGE) suggests endoscopic variceal ligation for treating acute esophageal variceal hemorrhage, and either endoscopic cyanoacrylate injection or EVL for GOV1-specific bleeding. However, some experts propose treating GOV1 similarly to esophageal varices since varices along the lesser curvature share a similar natural history.

Thus, data on endoscopic obstruction of gastric varices in GOV1 patients with esophageal variceal bleeding are limited. The efficacy of EVL for esophageal varices combined with cyanoacrylate injection for gastric varices in GOV1 appears promising.

Aims & Methods: In this multi-center retrospective cohort study, we aimed to access the efficacy of blocking gastric varices in the managing bleeding from esophageal varices in patients with GOV1. Cirrhotic patients experiencing bleeding from esophageal varices and having GOV I gastric varices in four centers were screened. All included patients were followed up for 180 days, or until death.

Results: A total of 93 cirrhotic patients with GOV I and bleeding esophageal varices were included. Among them, 58 patients underwent endoscopic cyanoacrylate injection (ECI) for gastric varices in addition to treatment for esophageal varices (EV) treatment, while the remaining 35 patients received treatment for EV only. Kaplan-Meier analysis demonstrated that the cumulative 180-day rebleeding rate was significantly lower in the ECI plus EV treatment group (7.9%) compared to the EV treatment group (30.7%) ($p=0.0031$). The cumulative incidence of 180-day mortality rate was 1.9% in the ECI plus EV treatment group and 23.9% in the EV treatment group ($p=0.0010$). Multivariable Cox regression analysis revealed that concomitant ECI treatment was an independent protective factor against for 180-day rebleeding and overall mortality.

Conclusion: In conclusion, obstruction of gastric varices in addition to endoscopic treatment for bleeding from esophageal varices in patients with GOV 1 proved superior to endoscopic treatment alone for esophageal variceal bleeding.

References: 1, de Franchis R, Bosch J, Garcia-Tsao G et al. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol* 2022; 76: 959-974. doi:10.1016/j.jhep.2021.12.022

2, Gralnek IM, Camus Duboc M, Garcia-Pagan JC et al. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2022; 54: 1094-1120. doi:10.1055/a-1939-4887

3, Kaplan DE, Bosch J, Ripoll C et al. AASLD practice guidance on risk stratification and management of portal hypertension and varices in cirrhosis. *Hepatology* 2023. doi:10.1097/hep.0000000000000647]

Disclosure: Nothing to disclose.

MP127

GUT MICROBIOME DYSBIOSIS IS NOT ASSOCIATED WITH THE PRESENCE OF PORTAL VEIN THROMBOSIS IN PATIENTS WITH END-STAGE LIVER DISEASE

R. Aleksandrova¹, L. Nieuwenhuis¹, N. Karmi², S. Zhang³, J.C. Swarte⁴, J.R. Bork³, R. Gacesa³, H. Blokzijl², R.K. Weersma², J. Lisman⁵, E.A.M. Festen², V.E. de Meijer¹

¹University of Groningen, University Medical Center Groningen, Department of Surgery, Section of Hepatobiliary Surgery and Liver Transplantation, Groningen, Netherlands, ²University of Groningen, University Medical Center Groningen, Department of Gastroenterology & Hepatology, Groningen, Netherlands, ³University of Groningen, University Medical Center Groningen, Department of Gastroenterology & Hepatology, Department of Genetics, Groningen, Netherlands, ⁴University Medical Centre Groningen, Internal Medicine, Groningen, Netherlands, ⁵University of Groningen, University Medical Center Groningen, Surgical Research Laboratory, Department of Surgery, Groningen, Netherlands

Contact E-Mail Address: r.r.aleksandrova@umcg.nl

Introduction: The gut-liver axis, the anatomical and physiological connection between the gut and liver, is hypothesized to contribute to the development of portal vein thrombosis (PVT) in patients with end-stage liver disease (ESLD). It has been proposed that the portal vein in patients with ESLD is an inflammatory vascular bed due to the translocation of endotoxins and proinflammatory cytokines from the gut.

We hypothesized that a pro-inflammatory gut microbiome in ESLD patients, and elevated levels of the gut microbiota-derived metabolite trimethylamine N-oxide (TMAO) which is an established driver of thrombosis, may contribute to the development of PVT.

Aims & Methods: In this cross-sectional study we investigated whether differences in gut microbiome diversity, bacterial species, metabolic pathway abundances, and TMAO blood levels are associated with presence of PVT in ESLD patients. Fecal samples, serum samples and data from patients with ESLD, as well as living kidney transplant donors ('healthy controls'), were collected from the TransplantLines Biobank and Cohort Study (NCT02811835). PVT was defined as presence of a thrombus in the portal vein assessed by either radiology or during surgery within a year prior to or after fecal sample collection.

We analyzed the fecal samples using Shotgun Metagenomic Sequencing to assess and compare microbiome diversity, microbial taxonomy, and metabolic pathways abundances. TMAO levels were measured in serum samples using a Vantera® Clinical Analyzer (LabCorp, Morrisville, NC, USA).

Results: A total of 102 ESLD patients, of which 23 had PVT, and 246 healthy controls were included. We found no significant difference in microbiome diversity between patients with PVT (median Shannon Diversity Index (SDI): 2.08), and without PVT (median SDI: 1.84; $P=0.18$). Both ESLD groups had lower microbiome diversity compared to healthy controls (median SDI: 2.55; both $P<0.05$). A Beta Diversity Analysis confirmed that the gut microbiome of ESLD patients was markedly distinct from that of healthy controls.

After false discovery rate correction, *Bacteroides fragilis* and three species from the family Clostridiales were increased in abundance in ESLD patients with PVT compared to those without PVT. No altered metabolic pathways abundances were observed between both ESLD groups.

Overall, altered abundances of 29% ($n=49$) and 51% ($n=86$) bacterial species, and 18% ($n=96$) and 35% ($n=191$) metabolic pathways were observed between patients with and without PVT, respectively, when compared to healthy controls. TMAO levels were higher in both ESLD patients

with (3.30µm) and without PVT (3.00µm) compared to healthy controls (2.70µm) (P = 0.13 and P = 0.84 respectively), with a trend towards higher levels in patients with PVT (P = 0.19).

Conclusion: Although we observed a profound difference in gut microbiota composition between patients with ESLD and healthy controls, our analysis revealed minimal differences in the gut microbiome composition between ESLD patients with or without PVT. These results indicate that a gut microbiome-derived pro-inflammatory state was not associated with the presence of PVT in these patients.

Disclosure: Nothing to disclose.

MP128

FONTAN-ASSOCIATED LIVER DISEASE: CLINICAL FEATURES AND NATURAL HISTORY

E. Uclés Ramada¹, C. Sánchez Cano¹, M. García Eliz^{1,2,3}, C. Vinaixa Aunés^{1,2,3}, J. Rueda Soriano⁴, F. Buendía Fuentes⁴, M. Berenguer Haym^{1,2,3,5}, I. Conde Amiel^{1,2,3}, V. Aguilera Sancho-Tello^{1,2,3,5}

¹Hospital Universitari i Politècnic La Fe, Hepatology and Liver Transplant Unit, Valencia, Spain, ²Instituto de Investigación Sanitaria La Fe, Valencia, Spain, ³CIBERehd, Instituto de Salud Carlos III, Madrid, Spain, ⁴Hospital Universitari i Politècnic La Fe, Cardiology. Adult Congenital Heart Disease Unit, Valencia, Spain, ⁵Universitat de València, Medicine Department, Valencia, Spain

Contact E-Mail Address: eugenioucles@hotmail.com

Introduction: Fontan Procedure (FP) is a palliative surgical intervention designed to address congenital heart defects involving a single functioning ventricle. Fontan-Associated Liver Disease (FALD) refers to liver damage linked with hemodynamic shifts occurring in patients more than 10 years post-surgery. This condition encompasses structural alterations, liver lesions, and the onset of portal hypertension. Its progression can be categorized into three functional phases. The duration elapsed since the FP stands out as a significant predictor of FALD.

Aims & Methods: 1. To describe clinical, analytical, imaging and elastographic characteristics of a group of patients with FALD.

2. To correlate time since FP, type of procedure, and single ventricle morphology with stages 2 or 3 FALD related clinical events (ascites, esophageal varices, hepatic nodules, hepatocellular carcinoma-HCC) and with analytical variables.

Single-centre retrospective observational study of patients followed for FALD between 2020-2023 in the hepatology department. All patients were evaluated with abdominal ultrasound ± hepatic MRI and elastography. Upper endoscopy was performed in cases with thrombocytopenia <150,000 or elastographic values >20 kPa.

Results: Fifty-five patients, 51% men with a mean age of 27.75 ± 8.5 years were included. Median time since FP was 19 years. Stage 2 or 3 FALD was observed in 78.2% of patients. Median laboratory values were total bilirubin 0.98 mg/dL; albumin 4.8 g/dL; platelets 179,000/µL; INR 1.06. Median elastographic value was 18.3 kPa. Imaging findings compatible with cirrhosis were observed in 54.5% of patients. Hepatic lesions in MRI were found in 46.3% of patients (37% were focal nodular hyperplasia), but no HCC was detected. Esophageal varices were described in 20% of patients, but no bleeding was recorded. Ascites was the only form of hepatic decompensation (7.3% of patients). Time since FP was associated with thrombocytopenia, imaging findings of cirrhosis, portal hypertension findings on imaging or endoscopy; stage 2 or 3 FALD as well as FP failure (defined as functional deterioration which requires cardiac transplant evaluation) and death (p-value <0.05). No statistically significant associa-

tions were found between type of FP or single ventricle morphology and stage 2 or 3 FALD. Biological markers such as CA 125 and proBNP were associated with failure of the FP and development of ascites, respectively.

Conclusion: FALD comprises a group of hepatic alterations that require follow-up according to the functional stage. Time since FP is considered the main predictor of severe presentations. Although over half of our patients had signs of cirrhosis on imaging, a low rate of hepatic complications was observed, even in patients with a FP of over 20 years.

References: 1. Téllez L, Rodríguez de Santiago E, Albillos A. Fontan-Associated Liver Disease: Pathophysiology, Staging, and Management. *Semin Liver Dis.* 2021;41(04):538–50.

1. Deal BJ, Jacobs ML. Management of the failing Fontan circulation. *Heart.* 2012;98(14):1098–104.

Disclosure: Nothing to disclose.

MP129

SAFETY AND THERAPEUTIC MANAGEMENT OF ANTICOAGULATION IN LIVER VASCULAR DISEASE

D. Azzouzi¹, M. Kadiri², N. Lagdali¹, F.Z. Chabib¹, C. Berhili¹, M. Borahma¹, F.Z. Ajana¹

¹Mohamed V University, Gastroenterology C, Rabat, Morocco, ²Ibn Sina Hospital, Rabat, Rabat, Morocco

Contact E-Mail Address: azzouzidriss.ad@gmail.com

Introduction: Anticoagulation is one of the treatment options for patients with liver vascular disease. Given the potential severity of recurrent thrombosis and the high frequency of pro-thrombotic states in these patients, long-term anticoagulation may be necessary, but there are very few data on direct oral anticoagulants (DOACs) in this context. The aim of this study is to report our experience of the tolerability of DOACs and vitamin K antagonist (VKA).

Aims & Methods: This is a prospective, descriptive, preliminary, mono-centre study of patients with liver vascular disease who were treated with DOACs or vitamin K antagonists and who experienced an adverse event as a result of this therapy. Curative anticoagulation treatment with Rivaroxaban 20 mg or VKAs was initiated in patients at high risk of thrombosis or with DOACs 15 mg in patients at low risk. The aim of this study is to report our experience of the tolerability of DOACs and vitamin K antagonist (VKA).

Results: Out of a total of 142 patients followed for liver vascular disease, 62% of patients were on anticoagulation (n=88), 17% of them had undesirable effects to anticoagulants (n=15), including 10 patients on DOACs (27%) and 5 cases on VKA (10%). The mean age was 48.56 years, with a M/F sex ratio of 0.8%.

Concerning patients on AOD, 20% were being monitored for porto-sinosoidal vascular disease (n=2), 50% for portal cavernoma (n=5) and the remaining 30% for Budd-Chiari syndrome (n=3). The associated conditions were protein S and C deficiency in all patients, one of whom was also taking oestrogenic oral contraception (10%), and another hyperhomocysteinemia due to celiac disease (10%). All patients had preserved liver function. Average time to onset: 1 month. The following events occurred: 50% metrorrhagia (n=5); 40% had, in addition to metrorrhagia, haematemesis and gingivorrhagia (n=4), and 10% rectorrhagia. There was 1 death due to massive haemorrhagic shock caused by rupture of oesophageal varices.

Among patients on VKAs, one patient (20%) was being followed up for porto-sinosoidal vascular disease due to protein C and S deficiency, 2 patients were being followed up for portal cavernoma (40%), one due to coeliac disease and the other due to chronic myeloid leukaemia and 2 patients were being followed up for chronic portal thrombosis due to primary myelofibrosis and antiphospholipid syndrome, and another for chronic

portal thrombosis due to antiphospholipid syndrome. Average time to onset: 4 months. The following events occurred: 40% haematemesis (n=2); 40% each of gingivorrhagia and epistaxis (n=2) and 20% rectal bleeding. In terms of treatment, maintenance of the same treatment was envisaged in 40% with close clinical and biological monitoring, temporary cessation of treatment pending the completion of the necessary investigations in 13% (n=2), and switch to a VKA in 34% (n=5).

Conclusion: DOACs are associated with numerous adverse events, some of which are very severe and may lead to death. In our series, 27% of patients on DOACs had adverse events compared with 10% of patients on VKAs. This shows that VKAs could be an effective and safe alternative in patients with thrombosis even at low risk compared with DOACs. These results need to be confirmed by large prospective studies.

Disclosure: Nothing to disclose.

Endoscopic techniques

15:30-16:30 / Poster Stage 4

MP130

DOES EUS-FNB IMPROVE THE ICDC DIAGNOSTIC LEVEL IN SUSPECTED AIP PATIENTS? RESULTS FROM A PROSPECTIVE MULTICENTER STUDY

M.C. Conti Bellocchi¹, S.F. Crinò¹, T. Ikeura², S. Carrara³, D. Oh⁴, F. Caldart⁵, N. de Pretis⁵, L. Bernardoni¹, E. Manfrin⁶, L. Frulloni⁵

¹University of Verona, Gastroenterology- Diagnostic and Interventional Endoscopy of Pancreas, Verona, Italy, ²Kansai Medical University, Department of Gastroenterology and Hepatology, Osaka, Japan, ³Istituto Clinico Humanitas, Gastrointestinal Endoscopy, Milano, Italy, ⁴Asan Medical Center, Gastroenterology- Department of Internal Medicine, Seoul, South Korea, ⁵University of Verona, Gastroenterology, Verona, Italy, ⁶University of Verona, Department of Diagnostics and Public Health, Section of Pathology, Verona, Italy

Contact E-Mail Address: Mariacristina.contibellocchi@aovr.veneto.it

Introduction: According to the International Consensus Diagnostic Criteria (ICDC), histological evaluation is crucial in diagnosing autoimmune pancreatitis (AIP). However, it is challenging to obtain pre-operatively using standard fine needle aspiration (FNA). In the last decade, endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB), particularly new-generation needles with end-cutting design, has been demonstrated to outperform FNA in pancreatic solid lesions. More recently, their role in AIP definition has been evaluated with promising results. We aimed to assess the utility of EUS-FNB end-cutting needles in enhancing ICDC diagnostic levels in suspected AIP patients and in defining the specific AIP subtype.

Aims & Methods: Adult patients with suspected focal or diffuse AIP, classified as probable type 1, type 2, or NOS AIP according to ICDC, were prospectively and competitively enrolled in four different Centers. Definitive AIP, previously diagnosed AIP, and patients who had steroid administration within three months were excluded. All patients underwent EUS-FNB with a 22-gauge end-cutting needle. The capability of EUS-FNB in enhancing ICDC diagnostic level, the detection rates of level 1 or 2 of histologic criterion, the diagnostic accuracy of FNB in this setting, and the malignancy rate were calculated.

Histological parameters (ICDC) on FNB samples of AIP patients	Type 1 N=26	Type 2 N=12
Periductal lymphoplasmacytic infiltrate	23 (88.4%)	4 (33.3%)
Storiform fibrosis	23 (88.4%)	4 (33.3%)
Obliterative phlebitis	9 (34.6%)	0
IgG4+ cells	23 (88.4%)	1* (8.3%)
Granulocytic and lymphoplasmacytic acinar infiltrate	0	10 (83.3%)
GELs	0	7 (49%)
Level 1	19 (73.1%)	6 (50%)
Level 1+2	22 (84.6%)	11 (91.6%)

*<10 HPF

Results: A total of 52 suspected AIP were enrolled (75% male, mean age 57.9 ± 17.3), 50 with focal/segmental appearance and 2 with diffuse pancreatic involvement. The ultimate diagnosis was AIP in 39 (75%) patients (including 26 (50%) type 1 AIP, 12 (23.1%) type 2 and 1 (1.9%) type NOS) and malignancy in 7 (13.5%) (including 3 adenocarcinomas, 2 lymphomas, 1 neuroendocrine tumor and 1 metastasis). Chronic pancreatitis was diagnosed in the remaining 6 (11.5%) patients, with no recurrence or malignancy onset during a mean follow-up of 14 months (range 12-48). EUS-FNB improved the diagnostic level of AIP in 36 out of 39 (92.3%) patients with a final diagnosis of AIP, 29 (74.3%) definitive, and 7 (17.9%) probable, according to ICDC. Three patients received a final AIP diagnosis after a steroid trial (respectively, one type 1, one type 2 with subsequent IBD

diagnosis, and one type NOS). The rate of level 1 in type 1 and type 2 AIP was 73.1% and 50%, respectively. The level 1 or 2 rates in type 1 and type 2 AIP were 84.6% and 91.6%, respectively. The overall diagnostic accuracy of EUS-FNB was 94.2% [95% CI 84.1–98.8]. Two mild pancreatitis (3.8%) occurred after EUS-FNB in focal type 1 AIP located in the head.

Conclusion: EUS-FNB using end-cutting needles can enhance the existing diagnostic criteria, mainly in atypical and focal presentations, ruling out malignancy and defining the specific subtype in a relevant percentage of cases with an optimal accuracy (94.2%) and good safety.

Disclosure: Nothing to disclose.

MP131

BETWEEN VISION AND REALITY: RESULTS FROM A PAN-EUROPEAN SURVEY ON ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY TRAINING CONDITIONS

K. Hamesch^{1,2,3}, O. Cahyadi^{4,3}, S. Dimitriadis^{5,3}, M. Hollenbach^{6,3}, P. Acedo⁷, M. Ayari⁸, H. Dauvarte⁹, E. Dieninyte - Misiune^{10,11}, V. Domislovic¹², A. Dugic^{13,14,3}, M. Đuriček¹⁵, O. Elshaarawy^{16,17}, A. Fennessy¹⁸, M.E. Geissler^{19,3}, Z. Gorcheva²⁰, A. Hadi²¹, V. Hamza²², I. Hasukic²³, H. Heinrich²⁴, I.J.M. Levink²⁵, J. Král^{26,27}, L. Kunovský^{28,29,30}, M. Mandorfer³¹, M. Moris³², Y. Nikiforova³³, H. Ouaya³⁴, G. Pellino^{35,36}, A. Pisani³⁷, O. Qejvani³⁸, H. Sadigov³⁹, M. Salaga⁴⁰, O. Sidiropoulos⁴¹, C. Simsek⁴², P. Sousa⁴³, M. Stojkovic Lalosevic⁴⁴, K. Tepeš⁴⁵, A.M. Voiosu⁴⁶, L. Wauters⁴⁷, A. Zanetto⁴⁸, S. Schlosser^{49,3}, J.J. Staudacher^{50,51}, UEG YTG

¹University Hospital Aachen, Aachen, Germany, ²University Hospital RWTH Aachen, Interdisciplinary Endoscopy, Aachen, Germany, ³Junge Gastroenterologie (JuGa) - German Young Gastroenterology Study Group, Berlin, Germany, ⁴St. Josef-Hospital, a hospital of the Ruhr-University-Bochum, Gastroenterology, Essen, Germany, ⁵University Hospital Coventry and Warwickshire, Coventry, United Kingdom, ⁶Heidelberg University Hospital, 6 Department of Medicine IV, Heidelberg, Germany, ⁷University College London, Institute for Liver & Digestive Health, London, United Kingdom, ⁸Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia, ⁹East Tallinn Central Hospital, Gastroenterology, Tallinn, Estonia, ¹⁰Vilnius university Santaros Klinikos, Center of hepatology, gastroenterology and dietetics, Vilnius, Lithuania, ¹¹Vilnius university hospital Santara Clinics, Vilnius, Lithuania, ¹²University Hospital Centre Zagreb, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ¹³Heidelberg University Hospital, Department of Medicine IV, Heidelberg, Germany, Department of Internal Medicine IV, Heidelberg, Germany, ¹⁴Karolinska Institute, Department of Medicine Huddinge, Stockholm, Sweden, ¹⁵Jessenius Faculty of Medicine, University Hospital in Martin, Clinic of Internal Medicine - Gastroenterology, Martin, Slovakia, ¹⁶Royal Liverpool University Hospital, UK, Gastroenterology and Hepatology, Liverpool, United Kingdom, ¹⁷National Liver Institute, Menoufia University, Department of Gastroenterology and Hepatology, Menoufia, Egypt, ¹⁸St Vincent's University Hospital, Gastroenterology Department, Dublin 14, Ireland, ¹⁹Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden, Department of Visceral, Thoracic and Vascular Surgery, Dresden, Germany, ²⁰Saint Marina University Hospital, Clinic of Internal Diseases, Pleven, Bulgaria, ²¹Hvidovre University Hospital, Gastro Unit, Søborg, Denmark, ²²University Clinical Center of Kosova, Prishtine, Kosovo, ²³UKC Tuzla, Tuzla, Bosnia and Herzegovina, ²⁴Universitätsspital Basel, Department for Gastroenterology and Hepatology, Basel, Switzerland,

²⁵Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²⁶Institute for Clinical and Experimental Medicine, Dept. of Hepatogastroenterology, Prague, Czech Republic, ²⁷Second Faculty of Medicine, Charles University, Department of Internal Medicine, Prague, Czech Republic, ²⁸2nd Department of Internal Medicine – Gastroenterology and Geriatrics, University Hospital Olomouc, Faculty of Medicine, Palacky University Olomouc, University Hospital Brno, Faculty of Medicine, Masaryk University, Olomouc, Czech Republic, ²⁹University Hospital Olomouc, Faculty of Medicine and Dentistry, Olomouc, Czech Republic, ³⁰Masaryk Memorial Cancer Institute, Brno, Czech Republic, ³¹Medical University of Vienna, Department of Gastroenterology and Hepatology, Department of Internal Medicine III, Vienna, Austria, ³²Hospital Universitario Marqués de Valdecilla, GI, Santander, Spain, ³³Government Institution “L.T.Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine”, Department of the study of diseases of the digestive system and their comorbidity with the noncommunicable diseases, Kharkov, Ukraine, ³⁴tangier faculty of medicine / tangier mohamed VI university hospital, Gastroenterology and Endoscopy, Tangier, Morocco, ³⁵Università degli Studi della Campania “Luigi Vanvitelli”, General and Colorectal Surgery, Aversa (CE), Italy, ³⁶Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona UAB, Barcelona, Spain, ³⁷Mater Dei Hospital, Gastroenterology, Mosta, Malta, ³⁸University Hospital Center ‘Mother Teresa’, Tirana, Albania, ³⁹AZERBAIJAN MEDICAL UNIVERSITY, Baku, Azerbaijan, ⁴⁰Medical University of Lodz, Department of Biochemistry, Lodz, Poland, ⁴¹417 NIMTS, Internal Medicine, Cholongos, Greece, ⁴²Hacettepe University, Division of Gastroenterology, Hepatology and Endoscopy, Ankara, Turkey, ⁴³Tondela-Viseu Hospital Center, Dept. of Gastroenterology, Viseu, Portugal, ⁴⁴Clinical center of Serbia, Gastroenterology and Hepatology, Belgrade, Serbia, ⁴⁵Diagnostic center Rogaska, Department of gastroenterology, Rogaska Slatina, Slovenia, ⁴⁶Colentina Clinical Hospital Dept. of Gastroenterology, Gastroenterology, Bucharest, Romania, ⁴⁷University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ⁴⁸Gastroenterology/Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy, ⁴⁹Universitätsklinikum Regensburg, Department of Internal Medicine I, Gastroenterology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany, ⁵⁰Charité Universitätsmedizin Berlin, Department of Gastroenterology, Rheumatology and Infectiology, Berlin, Germany, ⁵¹Berlin Institute of Health at Charité, Berlin, Germany

Contact E-Mail Address: khamesch@ukaachen.de

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) remains the procedure with the highest complication rate underscoring the importance of high-quality training. Despite existing guidelines, real-world data regarding training conditions remain limited. This Pan-European survey aims to explore the perceptions surrounding ERCP training.

Aims & Methods: A survey was distributed through the friends of the Young United European Gastroenterologists (UEG) Talent Group network. Inclusion criteria were physicians working in a UEG member state and regularly performing ERCP. Likert-scales as well as single- and multiple-choice questions were utilized.

Results: 649 of 1035 respondents from 35 countries were eligible for analysis. 228 were identified as trainees, 225 as trainers, and 196 regularly performed ERCP without being in either category. The mean age was 43 years with 72.0%, 27.6%, and 0.3% identifying as male, female, and non-bina-

ry, respectively. 73% of all participants agreed that a structured training regimen is desirable. However, 64% of participants reported not having such a structured program at their institution (71% of trainees and 55% of trainers). Likewise, 80% of participants did not have a mandatory self-assessment before training initiation.

Majority of trainees (73%) and trainers (81%) favored that training should be concentrated within centers meeting certain quality metrics. For this, 64% of all participants indicated that a threshold of 200 annual ERCPs should be used. Using this threshold revealed that 32% of trainees pursued training in centers with <200 annual ERCPs and that a low annual caseload of <50 was more frequent at lower volume centers vs. higher volume centers (86% vs. 63%, respectively). Furthermore, 71% of trainees performed <50 ERCPs/year in stark contrast to 95% of trainers performing >50 ERCPs/year. While 27% of trainees in higher volume centers were female, all trainees in lower volume centers were of female gender.

Conclusion: The first Pan-European survey investigating ERCP training conditions revealed that structured training and concentration of training efforts within European centers meeting specific quality metrics are desirable but exposed the low availability of structured training programs and that around 30% of trainees are practicing at lower volume centers. These data could be interpreted as motivation to further standardize ERCP training conditions and ultimately improve patient care throughout Europe.

Disclosure: Nothing to disclose.

MP132

DIAGNOSTIC ACCURACY OF DIFFERENT CHOLANGIOSCOPY-GUIDED BIOPSY TECHNIQUES FOR THE DIAGNOSIS OF INDETERMINATE BILIARY DUCT STRICTURES

D.M. de Jong¹, P.J. de Jonge¹, P.M.C. Stassen¹, P. Karagoyozov², J.J. Vila³, I. Fernández-Urién Sainz³, M. James⁴, S.V. Venkatachalapathy⁴, K. Oppong⁵, A. Anderloni⁶, A. Repici⁷, R. Gabbiadini⁷, D. Joshi⁸, M. Ellrichmann⁹, L. Kylänpää¹⁰, M. Udd¹⁰, F. Van Der Heide¹¹, P. Hindryckx¹², G. Corbett¹³, K. Basiliya¹³, V. Cennamo¹⁴, S. Landi¹⁴, S. Phillpotts¹⁵, G. Webster¹⁵, M.J. Bruno¹

¹Erasmus MC University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands, ²Acibadem City Clinic University Hospital Tokuda, Clinic of Gastroenterology, Sofia, Bulgaria, ³Complejo Hospitalario de Navarra, Gastroenterology & Hepatology, Pamplona, Spain, ⁴Nottingham University Hospitals NHS Trust, and School of Medicine, University of Nottingham, NIHR Nottingham Biomedical Research Centre, Nottingham, United Kingdom, ⁵Newcastle Upon Tyne NHS Foundation Trust, Gastroenterology & Hepatology, Newcastle-upon-Tyne, United Kingdom, ⁶Fondazione I.R.C.C.S. Policlinico San Matteo, Gastroenterology and Digestive Endoscopy Unit, Pavia, Italy, ⁷Humanitas Research Hospital, Gastroenterology & Hepatology, Milano, Italy, ⁸King's College Hospital NHS Foundation Trust, Institute of Liver Studies, London, United Kingdom, ⁹University Hospital Schleswig-Holstein, Interdisciplinary Endoscopy, Medical Department 1, Kiel, Germany, ¹⁰Helsinki University Central Hospital, Surgery, Helsinki, Finland, ¹¹University of Groningen, University Medical Center Groningen, Gastroenterology & Hepatology, Groningen, Netherlands, ¹²University Hospital of Ghent, Gastroenterology & Hepatology, Ghent, Belgium, ¹³Cambridge University Hospitals NHS Foundation Trust, Gastroenterology & Hepatology, Cambridge, United Kingdom, ¹⁴Local Health Authority of Bologna, Gastroenterology & Interventional Endoscopy Unit, Bologna, Italy, ¹⁵University College London Hospitals, Gastroenterology, London, United Kingdom

Contact E-Mail Address: d.m.dejong@erasmusmc.nl

Introduction: Indeterminate biliary duct strictures (IBDS) pose a diagnostic dilemma, and digital single-operator cholangioscopy (d-SOC) has improved diagnostic accuracy by enabling targeted intra-ductal biopsies (1-3). There is no consensus on the optimal biopsy strategy, but data suggests that at least four single biopsies yields adequate specimen samples for pathological examination (4). Considering the desmoplastic character of cholangiocarcinoma obtaining larger and deeper samples may have a higher diagnostic yield.

The aim of this study was to compare the diagnostic yield of d-SOC guided single standard biopsies to those obtained via bite-on-bite-biopsy (BBB) technique in patients with IBDS.

Aims & Methods: This international, multi-center, prospective cohort study included patients with a diagnosis of IBDS who underwent d-SOC from November 2020 to August 2022 at fourteen European tertiary referral centers (Dutch Trial Register: NL9649). IBDS was defined as a bile duct stricture of indeterminate nature after previous laboratory work-up, imaging or endoscopic retrograde cholangiography with or without brush-cytology of fluoroscopy guided intra-ductal biopsies.

During d-SOC, in every patient sampling of the stricture(s) was performed by firstly obtaining at least 4 single biopsies, and secondly obtaining at least 1 BBB. Definitive diagnosis was established on pathology outcomes (biopsies or surgical resection specimens) and clinical follow-up of at least one year. Primary outcome was the accuracy of both biopsy techniques.

Results: Eighty-nine patients were included (62% male, median age: 66 years), 52 of whom had a hilar and 37 a distal stricture. Single and BBB biopsies were technically successful and with sufficient tissue for diagnosis in 82 (92.1%, median number of biopsies = 4) and 78 (87.6%, median number of BBB biopsies = 2), respectively. These biopsies confirmed malignancy in 31/82 and 29/78 of cases, respectively. Comparing the two biopsy techniques, these techniques yielded different results in 4/78 patients (5.1%).

In 82 (92.1%) patients follow-up was complete and malignancy was confirmed in 51 (62.2%) patients, resulting in an overall sensitivity, specificity and accuracy of 60.8%, 100% and 75.6% of both techniques combined. For both sampling techniques, sensitivity and accuracy decreased significantly if a stent was placed at a prior ERC (n = 37, 41.6%) or whenever prior intra-ductal tissue acquisition had been performed (n = 41, 46.1%). The number of BBB did not affect sensitivity or accuracy. No adverse events related to d-SOC guided biopsies were noted.

Conclusion: In this prospective study, BBB did not outperform at least four random single biopsies of IBDS. Prior manipulation of the IBDS, by stent placement or prior tissue acquisition, is associated with a decreased yield.

References:

1. Angsuwatcharakon P, Kulpatcharapong S, Moon JH, et al. Consensus guidelines on the role of cholangioscopy to diagnose indeterminate biliary stricture. *HPB (Oxford)*. 2022;24(1):17-29.
2. Navaneethan U, Hasan MK, Lourdasamy V, et al. Single-operator cholangioscopy and targeted biopsies in the diagnosis of indeterminate biliary strictures: a systematic review. *Gastrointestinal Endoscopy*. 2015;82(4):608-614.e602.
3. Almadi MA, Itoi T, Moon JH, et al. Using single-operator cholangioscopy for endoscopic evaluation of indeterminate biliary strictures: results from a large multinational registry. *Endoscopy*. 2020;52(7):574-582.
4. Bang JY, Navaneethan U, Hasan M, et al. Optimizing Outcomes of Single-Operator Cholangioscopy-Guided Biopsies Based on a Randomized Trial. *Clinical Gastroenterology and Hepatology*. 2020;18(2):441-448.e441.

Disclosure: P.J.F. de Jonge is a speaker and received a consultancy fee for Boston Scientific. J.J. Vila is a speaker for Pentax, Cook Medical, and Olympus and is a consultant for Boston Scientific. M.W. James received consultancy fees from Boston Scientific and Cook Medical. K.W. Oppong received research funding for investigator initiated studies from Medtronic, and received speaker fees from Medtronic and Boston Scientific. D. Joshi is a speaker and received consultancy fees from Boston Scientific, Cook Medical, and Mirum Pharmaceuticals. M. Ellrichmann received research funding for industry initiated studies from Boston Scientific. He received research funding for investigator initiated trials from Boston Scientific, He is a consultant to Boston Scientific, Microtech, Medwork and Olympus. L. Kylänpää received a speaker fee from Boston Scientific. F. van der Heide received a speaker fee from AbbVie. P. Hindryckx is a speaker and received consultancy fees from Medtronic, Boston Scientific, Viatrix, Fujifilm, and Medwork. V. Cennamo is a consultant and speaker for and received travel grants from Olympus Italia, Olympus Europe, and Euro-medical. G.J.M. Webster is a consultant and speaker for Boston Scientific, Cook Medical, Pentax Medical, and Olympus Europe. M.J. Bruno received research funding for industry initiated studies from Boston Scientific and Cook Medical. He received research funding for investigator initiated studies from Boston Scientific, Cook Medical, Pentax Medical, Interscope, Mylan, and ChiRoStim. He is a consultant to Boston Scientific, Cook Medical, and Pentax Medical. The remaining authors have no conflicts of interests to disclose.

MP133

FEASIBILITY AND SAFETY OF SINGLE ORAL CHOLEDOSCOPY COMBINED WITH ENDOSCOPIC RADIOFREQUENCY ABLATION FOR THE DIAGNOSIS AND TREATMENT OF UNRESECTABLE EXTRAHEPATIC BILE DUCT CARCINOMA

C. Le^{1,2,3,4}, J. Yang^{1,2,3,4,5}

¹Hangzhou First People's Hospital, Gastroenterology, Hangzhou, China, ²Department of Gastroenterology, Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, China, ³Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China, ⁴Hangzhou Institute of Digestive Diseases, Hangzhou, China, ⁵Key Laboratory of Clinical Cancer Pharmacology and Toxicology Research of Zhejiang Province, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: Among the diagnostic methods for EHCC, cell brush is the conventional method for EHCC diagnosis, but the sensitivity of cell brush and routine biopsy is low. The sensitivity and accuracy of EHCC diagnosis can be improved by single oral choledochoscopy. Radiofrequency ablation is a common and effective treatment for unresectable EHCC, providing local tumor control. Single oral choledochoscopy combined with radiofrequency ablation can improve the positive rate of pathological diagnosis.

Aims & Methods: To investigate the feasibility and safety of treating non-resectable extrahepatic cholangiocarcinoma (EHCC) with single resection combined with radiofrequency ablation (RFA).

A total of 149 patients with suspected extrahepatic cholangiocarcinoma treated in Hangzhou First People's Hospital from January 2013 to January 2023 were reviewed. According to the treatment process, 114 patients were eventually included and divided into two groups (n=48 cases): Single oral choledochoscopy was performed by ERCP and the lesion tissue was biopsied under direct vision. Intraoperative rapid pathologic examination was performed on the same stage RFA for the patients who were pathologically identified as malignant tumors. Regular times group (n = 66): first by endoscopic retrograde pancreatic angiography (endoscopic retrograde cholangiopancreatography, ERCP) + cells brush or a single biopsy samples by mouth choledochoscope examination, pathological results to obtain positive line of ERCP + RFA again; The operation success rate, postoperative liver function recovery, average ERCP number, postoperative adverse event incidence, length of hospitalization and cost were compared between the two groups.

Results: 1. Patients in both groups successfully completed the RFA, the operation success rate was 100% (114/114).

2. There was no significant difference in the overall incidence of postoperative adverse events between the two groups [39.58% (19/48) vs. 39.40% (26/66), $\chi^2=0.00$, $P=0.984$].

3. There was no significant difference in the proportion of patients with total bilirubin improvement between the two groups [41.67% (20/48) vs. 42.42% (28/66), $\chi^2=0.32$, $P=0.750$].

4. The average number of ERCP in the same group was significantly lower than that in the conventional group, and the difference was statistically significant (1.00±0.00 times/person vs. 2.64±0.49 times/person, $t=0.77$, $P<0.001$).

5. The average length of hospital stay in the same group was significantly longer than that in the conventional group, with statistical significance (8.40±3.63 days vs. 17.47±9.82 days, $t=6.21$, $P<0.001$).

6. The average hospitalization cost in the same group was significantly higher than that in the conventional group, and the difference was statistically significant (27718.31±9142.02 yuan versus 49112.76±16153.14 yuan, $t=7.38$, $P<0.001$).

Conclusion: Single oral choledochoscopy combined with biopsy and RFA in the diagnosis and treatment of unresectable EHCC can reduce the number of operations and does not increase the incidence of postoperative adverse events, which is a safe and effective method with a high cost-benefit ratio.

References: [1] Le V H, O'Connor V V, Li D, et al. Outcomes of Neoadjuvant Therapy for Cholangiocarcinoma: A Review of Existing Evidence Assessing Treatment Response and R0 Resection Rate [J]. *J Surg Oncol*, 2021, 123(1): 164-71.

[2] Chen R, Zheng D, Li Q, et al. Immunotherapy of Cholangiocarcinoma: Therapeutic Strategies and Predictive Biomarkers [J]. *Cancer Lett*, 2022, 546: 215853.

[3] Rizzo A, Ricci A D, Brandi G. Durvalumab: An Investigational Anti-Pd-L1 Antibody for the Treatment of Biliary Tract Cancer [J]. *Expert Opin Investig Drugs*, 2021, 30(4): 343-50.

[4] Sadeghi S. Infigratinib for Cholangiocarcinoma [J]. *Drugs Today (Barc)*, 2022, 58(7): 327-34.

[5] Vignone A, Biancanello F, Casadio M, et al. Emerging Therapies for Advanced Cholangiocarcinoma: An Updated Literature Review [J]. *J Clin Med*, 2021, 10(21).

[6] Jang D K, Kim J, Paik C N, et al. Endoscopic Retrograde Cholangiopancreatography-Related Adverse Events in Korea: A Nationwide Assessment [J]. *United European Gastroenterol J*, 2022, 10(1): 73-9.

[7] Hollenbach M, Hoffmeister A. Adverse Events in Endoscopic Retrograde Cholangiopancreatography (ErCP): Focus on Post-ErCP-Pancreatitis [J]. *United European Gastroenterol J*, 2022, 10(1): 10-1.

Disclosure: The authors declare that there are no conflicts of interest.

MP134

FACTORS AFFECTING FLUOROSCOPY DURATION AND RADIATION DOSE DURING ERCP: A RETROSPECTIVE ANALYSIS OF A PROSPECTIVE DATABASE IN A TERTIARY CENTER

P. Gkolfakis¹, M. Spinou¹, G. Kondylis¹, A. Spanogianni¹, A. Panagaki¹, G. Aggelopoulos¹, P. Aggelogiannopoulou², P. Paraskevopoulou², A. Paraskevopoulou², G. Tziatzios¹, V. Delatolas², V. Chatonidis², C. Triantopoulou², A. Giannakopoulos¹, K.D. Paraskeva¹

¹Konstantopoulion-Patision General Hospital of Nea Ionia, Department of Gastroenterology, Athens, Greece,

²Konstantopoulion-Patision General Hospital of Nea Ionia, Department of Radiology, Athens, Greece

Contact E-Mail Address: konparaskeva@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is associated with increased technical difficulty and can potentially contribute to prolonged procedural duration and excess exposure to ionizing radiation.

Aims & Methods: The purpose of the present study was to present descriptive information about fluoroscopy during ERCP from a large reference center and to investigate possible determinants of the radiation dose or fluoroscopy duration during ERCP. We examined a prospectively collected single-center database of adult patients undergoing ERCP between 09/2021 and 12/2023 in a tertiary greek public hospital. Detailed information concerning patient, endoscopist and procedural parameters including ERCP indication, degree of difficulty of ERCP (defined using the Schutz score), types of interventions and fluoroscopy were recorded retrospectively. Non parametric statistical methods were used (Mann-Whitney U-test and Kruskal-Wallis test) for the analysis.

Results: In total, data of 1051 ERCPs were collected at first, while 1028 ERCPs with complete information for fluoroscopy duration and radiation

dose were included (mean patient age 72.20 ± 14.02 years, 49.1% men) in the analysis. The mean procedure time was 34.22 ± 14.9 minutes, carried out by three different endoscopists ($n_1=321$, 31.4%, $n_2=338$, 33%, $n_3=363$, 35.6%). The majority of ERCPs were performed for treatment of choledocholithiasis (64.5%) and were classified as of intermediate difficulty according to Schutz scoring system [Schutz score 2 ($n=523$, 53.4%)]. Fluoroscopy was used in 1010 ERCPs (98.2%) and the median fluoroscopy duration was 2.4 minutes (IQR=2.6 min) and the median radiation dose was $1031.6 \mu\text{Gym}^2$ (IQR= $1237.5 \mu\text{Gym}^2$). ERCPs performed with an indication of biliary tract neoplasm (e.g. cholangiocarcinoma, liver metastases) were associated with prolonged fluoroscopy duration [5.05min (IQR=6.35 min), $p=0.008$] and increased radiation dose [$2372.75 \mu\text{Gym}^2$ (IQR= $2462.68 \mu\text{Gym}^2$), $p=0.003$] in comparison to the rest of the indications including choledocholithiasis, pancreatic neoplasm, obstructive jaundice and other indications. ERCP difficulty was also related with increased radiation; ERCPs with Schutz score ≥ 3 were associated with increased radiation dose and fluoroscopy duration compared with ERCP procedures evaluated as Schutz score ≤ 2 [3.3min (IQR=3.9 min) vs. 2.1min (IQR=2.15 min), $p<0.001$ and $1280.8 \mu\text{Gym}^2$ (IQR= $1836.8 \mu\text{Gym}^2$) vs. $937.6 \mu\text{Gym}^2$ (IQR= $820.25 \mu\text{Gym}^2$), $p<0.001$ respectively]. There was no significant difference of the fluoroscopy duration ($p=0.495$) and radiation dose ($p=0.950$) among the three performing endoscopists.

Conclusion: Increased difficulty of ERCP and the indication of biliary tract neoplasm were related to higher radiation dose and prolonged fluoroscopy duration. These factors could be utilized to predict ERCP procedures related to increased radiation exposure and may contribute to adoption of appropriate radiation reduction methods.

Disclosure: Nothing to disclose.

MP135

USE OF LUMEN-APPPOSING METAL STENTS IN SURGICALLY ALTERED ANATOMY

E. Gökçe¹, P. Hindryckx²

¹Ghent University Hospital, Dept. of Gastroenterology, Ghent, Belgium, ²Ghent University Hospital Dept. of Gastroenterology, Dept. of Gastroenterology, Ghent, Belgium

Contact E-Mail Address: Emine.gokce@ugent.be

Introduction: The introduction of lumen-apposing metal stents (LAMs) has revolutionized the field of therapeutic endoscopic ultrasound (EUS). In the last decade, its utilization for off-label indications has markedly increased, particularly among patients with surgically altered anatomy to establish access in the excluded segment of the gastrointestinal tract. Indications for anastomosis creation include EUS-directed transgastric endoscopic retrograde cholangiopancreatography (EDGE), EUS-directed transgastric intervention (EDGEI), or endoscopic reversal of Roux-en-Y gastric bypass (RYGB) for specific indications (see below).

Aims & Methods: This study aims to evaluate the effectiveness and safety of LAMS in patients with surgically altered anatomy for EDGE, EDGEI, and reversal of RYGB. We collected data on all LAMS procedures conducted in patients with surgically altered anatomy, between October 2019 and February 2024 at the University Hospital of Ghent.

We used our prospective LAMS database and retrieved missing data from retrospective analysis of the medical patient records. The main outcome data of interest were technical success, clinical success, and adverse events. Technical success was defined as a successful placement of LAMS in the desired position. Clinical success was defined as either successful endoscopic access to the intended excluded gastrointestinal segment or achievement of the intended therapeutic goal when RYGB reversal was necessary. Adverse events were classified according to the AGREE criteria.

Results: A total of 73 LAMS procedures were performed: 70 cases of EUS-guided gastro-gastrostomy in patients with RYGB and 3 cases of EUS-guided gastro-enterostomy in patients with hepaticojejunostomy. Indications for LAMS procedures included 55 (75.3%) cases of EDGE, 13 (17.8%) cases of EDGI (such as gastroduodenoscopy and EUS), and 5 (6.8%) cases of RYGB reversal. Reversal of RYGB was required for one cachectic patient due to metastatic cholangiocarcinoma, three patients with hyperinsulinemic hypoglycemia, and one patient with therapy-resistant small intestinal bacterial overgrowth (SIBO).

The overall technical and clinical success rates were very high at 97.3% and 95.9%, respectively. Adverse events were observed in 11 out of 73 (15.1%) cases, including 7 (9.6%) minor events (AGREE score < 3) and 4 (5.5%) major events (AGREE score ≥ 3). Major events included stent migration (N=1), persistent fistula (N=2), and respiratory desaturation (N=1). All events could be successfully managed, and there were no procedure-related deaths. In 69.9% of cases, our method involved a dual-step approach, strategically implemented to await fistula maturation and reduce the risk of perforation. The median LAMS dwell time was 38 days (range 7, 431). LAMS was removed in 72.6% of the cases. Loss of LAMS patency occurred in 1 out of 73 (1.4%) cases and was endoscopically managed.

Conclusion: In conclusion, our study demonstrates that EUS-GG and EUS-GE offer an effective and safe approach to create anastomoses between gastrointestinal (GI) segments when performed by experts. With high technical (97.3%) and clinical (95.9%) success rates, LAMS proves beneficial for accessing excluded GI segments and reversing RYGB. Adverse events (15.1%) were mostly minor and manageable, with no procedure-related mortality. The extended patency duration and low re-intervention rate highlight LAMS as a minimally invasive and durable option in therapeutic endoscopic ultrasound procedures. Further prospective studies are required.

Disclosure: Nothing to disclose.

MP136

ENDOLUMINAL RADIOFREQUENCY ABLATION WITH STENTING VS STENTING ONLY IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION: A META-ANALYSIS OF RANDOMISED TRIALS

D. Ramai¹, E.R Smith², M.F. Maida^{3,4}, Y. Wang⁵, M. Spadaccini^{6,7}, M. Previtera⁸, S. Chandan⁹, Y. Huang¹⁰, S. Tokmak¹¹, P. Bhandari¹², J. Dubroff¹, C. Ko¹, J.D. Morris¹, G. Marasco^{13,14}, S.F. Crinò¹⁵, A. Facciorusso¹⁶, B.P. Mangiavillano¹⁷, M.A Khashab¹⁸
¹University of Utah Health, Gastroenterology & Hepatology, Salt Lake City, United States of America, ²Baylor Scott & White Health, Department of Medicine, Round Rock, United States of America, ³Department of Medicine and Surgery, University of Enna 'Kore', Gastroenterology and Endoscopy Unit, Enna, Italy, ⁴Umberto I Hospital, Gastroenterology Unit, Enna, Italy, ⁵Perelman School of Medicine at the University of Pennsylvania, Division of Hospital Medicine, Philadelphia, United States of America, ⁶Humanitas University, Biomedical Science, Rozzano, Italy, ⁷Humanitas Clinical and Research Center -IRCCS, Endoscopy Unit, Rozzano, Italy, ⁸University of Cincinnati Libraries, Donald C. Harrison Health Sciences Library, Cincinnati, United States of America, ⁹CHI Health Creighton University Medical Center, Division of Gastroenterology & Hepatology, Omaha, United States of America, ¹⁰Mayo Clinic Florida, Division of Gastroenterology and Hepatology, Jacksonville, United States of America, ¹¹Duzce University, Gastroenterology, Duzce, Turkey, ¹²Lenox Hill Hospital, Department of Medicine, New York, United States of America, ¹³University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ¹⁴IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ¹⁵G.B. Rossi University Hospital, Digestive Endoscopy Unit, Verona, Italy, ¹⁶University of Foggia, Gastroenterology, Foggia, Italy, ¹⁷Humanitas - Mater Domini, Gastrointestinal Endoscopy Unit, Milano, Italy, ¹⁸The Johns Hopkins Hospital, Division of Gastroenterology, Baltimore, United States of America

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: Endoluminal radiofrequency ablation (RFA) is a palliative treatment option for patients suffering from malignant biliary obstruction.

Aims & Methods: We aimed to conduct a meta-analysis to evaluate the impact of RFA on stent patency, patient survival, and adverse events. Major databases were searched from inception until November 2023 for patients who underwent stenting with or without RFA for extra-hepatic malignant biliary obstruction.

A random effects model was employed for analysis and results conveyed using risk ratio (RR) and mean difference (MD) with 95% confidence interval (CI).

Results: Nine RCTs involving 750 subjects (n=374 RFA plus stent vs n=376 stent only) diagnosed with malignant biliary obstruction were included. Overall, there was no difference in stent patency between both groups (MD = 26 days [95% CI -2.63 – 54.85]; I²=53%, P=0.07), however, RFA showed improved overall survival (MD = 1.64 months [95% CI 0.21 – 3.07]; I²=100%, P=0.02).

Subgroup analysis showed that patients with cholangiocarcinoma experienced an overall survival benefit with RFA (MD = 4.86 months [95% CI 4.61 – 5.07]; I²=0%, P<0.001), however, stent patency was unaffected (P=0.08). Subgroup analysis comparing plastic versus uncovered metal stents showed no difference in stent patency (P=0.63), however, plastic stents were associated with improved survival (MD = 2.05 months [95% CI 0.60 – 3.50]; I²=91%, P=0.002). An increased incidence of cholecystitis was noted with RFA versus stenting only (5% vs 0.2%, respectively).

Conclusion: Combining endoluminal RFA and stenting may improve overall survival in patients with malignant biliary obstruction. RFA did not impact stent patency significantly.

Disclosure: Nothing to disclose.

MP137

OUTCOMES OF LUMEN APPOSING METAL STENT PLACEMENT IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: A MULTICENTER INTERNATIONAL EXPERIENCE

B.P. Mangiavillano¹, D. Ramai², M. Kahaleh³, A. Tyberg⁴, H. Shahid⁵, A. Sarkar⁶, J. Samanta⁷, J. Dhar⁷, M. Bronswijk⁸, S. van der Merwe⁹, P.H. Deprez¹⁰, J. Vargas-Madrigal¹¹, G. Vanella¹², P.G. Arcidiacono¹³, C. Robles-Medrandia¹⁴, J. Alcivar-Vasquez¹⁵, M.G. Arevalo Mora¹⁶, A. Fugazza¹⁷, A. Lisotti¹⁸, P. Fusaroli¹⁹, M. Mutignani²⁰, E. Forti²⁰, A. Larghi²¹, G. Rizzatti²², D. Galasso²³, C. Barbera²⁴, F. Di Matteo²⁵, S. Stigliano²⁶, C. Binda²⁷, C. Fabbri²⁸, K.D.-C. Pham²⁹, R. Di Mitri³⁰, M. Amata³⁰, S.F. Crinò³¹, A. Ofosu³², L. De Luca³³, A. Al-Lehibi³⁴, F. Auriemma¹, D. Paduano³⁵, C. Gentile¹, F. Calabrese¹, M. Fiacca¹, C. Hassan³⁶, A. Repici³⁷, A. Facciorusso³⁸

¹Humanitas Mater Domini, Gastroenterology and Digestive Endoscopy, Castellanza, Italy, ²University of Utah Health, Gastroenterology, Salt Lake City, United States of America, ³Robert Wood Johnson Medical School Rutgers University, Gastroenterology, New Brunswick, United States of America, ⁴Rutgers Robert Wood Johnson, New Brunswick, United States of America, ⁵Hackensack Meridian Hospital, New Jersey, United States of America, ⁶Postgraduate Institute of Medical Education and Research, Chandigarh, India, ⁷Post Graduate Institute of Medical Education and Research, Chandigarh, Gastroenterology, Kolkata, India, ⁸Imelda Hospital Bonheiden and University Hospitals Leuven, Gastroenterology and Hepatology, Keerbergen, Belgium, ⁹UZ Leuven, Leuven, Belgium, ¹⁰Cliniques Universitaire Saint-Luc, Université de Louvain - Dept. de Hepato-gastroenterologie, Clinique, Dept. de Hepato-gastroenterologie, Brussels, Belgium, ¹¹Hospital San Juan de Dios, San Jose, Costa Rica, ¹²IRCCS San Raffaele Institute, Pancreatobiliary Endoscopy and Endosonography Division, Milan, Italy, ¹³Ospedale San Raffaele, Pancreatobiliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Center, Milan, Italy, ¹⁴Instituto Ecuatoriano De Enfermedades Digestivas (IECED), Espiritu Santo University, Guayaquil, Ecuador, ¹⁵Instituto Ecuatoriano De Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ¹⁶Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Research, Guayaquil, Ecuador, ¹⁷Humanitas Research Hospital, Rozzano, Milan, Italy, Digestive Endoscopy Unit, Division of Gastroenterology, Milano, Italy, ¹⁸Hospital of Imola, University of Bologna, Gastroenterology Unit, Bologna, Italy, ¹⁹University of Bologna, Gastroenterology, Imola, Italy, ²⁰Ospedale Niguarda, Endoscopy, Milano, Italy, ²¹Policlinico Universitario A. Gemelli IRCCS, Digestive Endoscopy Unit, Rome, Italy, ²²Fondazione Policlinico Universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore, Rome, Italy, ²³Hopital Riviera Chablais Gastroenterologie, Rennaz, Switzerland, ²⁴Ospedale di Teramo, Gastroenterology, Teramo, Italy, ²⁵Campus Bio-Medico Of Rome, GI Endoscopy Unit, Roma, Italy, ²⁶Campus Biomedico, Digestive and liver disease, Roma, Italy, ²⁷AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena Hospitals, Forlì, Italy, ²⁸AUSL Romagna, Forlì-Cesena gastroenterology, Gastroenterology, Bologna, Italy, ²⁹Haukeland University Hospital, Medicine, Bergen,

Norway, ³⁰ARNAS Civico-Di Cristina-Benfratelli, Gastroenterology and Endoscopy Unit, Palermo, Italy, ³¹University of Verona, Digestive Endoscopy Unit, Verona, Italy, ³²University of Cincinnati, Cincinnati, United States of America, ³³ASST Santi Paolo E Carlo, Digestive Endoscopy Unit, Milano, Italy, ³⁴King Fahad Medical City, Riyadh, Saudi Arabia, ³⁵Humanitas - Mater Domini, Castellanza, Italy, ³⁶Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ³⁷Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy, ³⁸University of Foggia, Gastroenterology, Foggia, Italy

Contact E-Mail Address: francesco.auriemma.1987@gmail.com

Introduction: Lumen-apposing metal stents (LAMS) provide a conduit to access lumens close to the gastrointestinal tract to perform various interventions. While outcomes of LAMS placement in native anatomy have been reported, data on LAMS placement in surgically altered anatomy (SAA) is sparse.

Aims & Methods: We aim to assess technical, clinical, and safety outcomes of LAMS placement in patients with SAA for different indications. This was an international multicenter retrospective observational study at 25 tertiary-care centers through November 2023. Consecutive patients with SAA who underwent LAMS placement under endoscopic ultrasound guidance were included. Primary outcome was technical success defined as correct placement of LAMS. Secondary outcomes were clinical success and safety.

Results: 255 patients with SAA (118 males; average age 61 ± 15 years) underwent LAMS placement. Surgical anatomy included total gastrectomy (n=3; 1.2%) subtotal gastrectomy (n=8; 3.1%), billroth I (n=19; 7.5%) billroth II (n=23; 9.0%), sleeve gastrectomy (n=16; 6.3%), pancreaticoduodenectomy (n=72; 28.2%), total pancreatectomy (n=3; 1.2%), roux-en-y gastric bypass (n=106; 41.6%), partial gastrectomy with roux-en-y (n=3; 1.2%); esophagectomy with partial gastrectomy (n=2; 0.8%). Indications were malignant biliary obstruction (n=32; 12.5%), cholecystitis (n=12; 4.7%), drainage of peri-pancreatic fluid collections (n=46; 18.0%); EUS-guided creation of enteric anastomoses (n=74; 29.0%); endoscopic ultrasound-directed transgastric ERCP (EDGE) (n=82; 32.2%); others (n=9; 3.5%). Both technical and clinical success ranged between 50% to 100%. Overall adverse event rate was 10.6% (n=27/255).

Conclusion: This study shows that placement of LAMS is associated with varying technical and clinical success rates in patients with SAA. The rate of adverse events is noteworthy, and thus, these procedures should be performed by expert endoscopists at tertiary centers.

Disclosure: Nothing to disclose.

MP138

EUS-GUIDED BILIARY RENDEZVOUS AFTER FAILED CANNULATION, AND COMPARISON WITH A TRANSMURAL DRAINAGE COHORT: OUTCOMES AT A SINGLE TERTIARY-CARE CENTER

J.B. Gornals¹, A. Garcia-Sumalla¹, S. Quintana¹, D. Luna-Rodriguez¹, J.G Velasquez-Rodriguez¹, M. Puigcerver-Mas¹, J. Escuer Turu¹, S. Maisterra¹, M. Marin Melia², B. Laquente-Saez², J. Busquets-Barenys¹
¹Hospital Universitari De Bellvitge, Bellvitge Biomedical Research Institute (idibell), Barcelona, Spain, ²Hospital Duran i Reynalds, Institut Català d'Oncologia (ICO), Barcelona, Spain

Contact E-Mail Address: jgornals@bellvitgehospital.cat
Introduction: EUS-guided biliary rendezvous (RV) is an EUS-assisted technique described as a rescue method in cases of failed biliary cannulation via endoscopic retrograde cholangiography (ERC). Current literature remains unclear regarding its current role.
Aims & Methods: Aim: to evaluate the efficacy and safety of biliary EUS-RV (benign vs malignant) and compare outcomes with EUS-guided transmural drainage (TMD) in malignant biliary obstruction. Methods: Retrospective observational study with prospective consecutive inclusion in a specific database from a tertiary-center. All patients that underwent a EUS-assisted ERC between October-2010 and November-2022 for failed ERC were included. A comparison analysis between benign vs. malignant disorders was performed. The outcomes of the EUS-RV malignant group were compared with an EUS-TMD group. Main outcomes were technical/overall success and adverse events (AEs).
Results: A total of 69 patients who underwent EUS-RV procedures, with benign and malignant pathologies (n=40 vs n=29), were included. Technical/overall success and related-AEs were 79.7% (95%CI, 68.3-88.4)/74% (95%CI, 61-83.7) and 24% (95%CI, 15.1-36.5), respectively. Failed cases were mainly related with guidewire manipulation. Seven failed RV were successfully rescued by EUS-TMD. On multivariable analysis, EUS-RV and malignant pathology was associated with a greater failure rate (technical success: OR,0.21; 95%CI,0.05-0.72; p=0.017), and higher AEs rate (OR,3.46; 95%CI,1.13-11.5; p=0.034). Also, the EUS-TMD group had greater technical success (OR,16.96; 95%CI,4.69-81.62; p<0.001) and overall success (OR, 3.09; 95%CI,1.18-8.16; p<0.026) with a lower AEs rate (OR,0.30; 95%CI,0.11-0.78; p=0.014) than EUS-RV in malignant disorders.

EUS-guided assisted ERC: benign vs malignant						
		No	Yes	OR [95%CI]	P value	N
Overall technical success, n (%):	Benign	4 (10.0)	36 (90.0)	Ref.	Ref.	69
	Malignant	10 (34.5)	19 (65.5)	0.21 [0.05-0.72]	0.017	
Overall success, n (%):	Benign	7 (17.5)	33 (82.5)	Ref.	Ref.	69
	Malignant	11 (37.9)	18 (62.1)	0.35 [0.11-1.03]	0.067	
Overall adverse events rate, n (%):	Benign	34 (85.0)	6 (15.0)	Ref.	Ref.	69
	Malignant	18 (62.1)	11 (37.9)	3.46 [1.13-11.54]	0.036	

Table 1: Comparison of clinical outcomes between groups.

Conclusion: EUS-RV is a demanding technique with better outcomes in benign than in malignant disorders. Comparison of the EUS-TMD group on malignant disorders showed worse outcomes with EUS-RV. Therefore, EUS-RV might be reserved basically for benign cases.
References:
1. van der Merwe SW, van Wanrooij RLJ, Bronswijk M et al. Therapeutic endoscopic ultrasound: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2022; 54: 185-205.

2. Klair JS, Zafar Y, Ashat M et al. Effectiveness and safety of EUS rendezvous after failed biliary cannulation with ERCP: A systematic review and proportion meta-analysis. J Clin Gastroenterol. 2023; 57: 211-217.
Disclosure: Nothing to disclose.

MP139

IMPLEMENTATION OF A BEHAVIOURAL RADIATION REDUCTION PROTOCOL FOR ENDOSCOPISTS AND RADIOGRAPHERS TO ACHIEVE THE LOWEST REPORTED DOSE AT ERCP

S. Joglekar^{1,2}, S. Mackay^{1,2}, A. Fox^{1,2}, A. Sayed-Hassen^{1,2}, R. Cade^{1,2}
¹Eastern Health, Department of Hepatobiliary and Upper GI Surgery, Box Hill, Australia, ²Monash University, Eastern Health Clinical School, Box Hill, Australia

Contact E-Mail Address: shantjog@gmail.com
Introduction: Radiation exposure to patients and staff is unavoidable during endoscopic retrograde cholangiopancreatography (ERCP). International and contemporary Diagnostic Reference Levels (DRL, 75th centile) range from a Dose Area Product (DAP) of 3-40 Gy.cm², and fluoroscopy time (FT) over 3 minutes per ERCP¹. Effective doses for patients and high-volume practitioners can approach acceptable annual safety limits. Our group reports a baseline DAP DRL of 2.81 Gy.cm² from 1857 ERCP over 5 years, the lowest reported for a large series. Dose determinants include fluoroscopy settings, patient/C-arm positioning and patterns of fluoroscopy use². Along the lines of the ALARA principle, we evaluated the implementation of a protocol to optimize these factors. Our study is the first to standardize a language for ERCP fluoroscopy between endoscopist and radiographer.
Aims & Methods: Along the lines of the ALARA principle, we evaluated the implementation of a protocol to optimize these determinant factors. Our study is the first to standardize a language for ERCP fluoroscopy between endoscopist and radiographer. Endoscopists and radiographers developed a protocol from their collective best practices. Radiographers applied the lowest dose and frame rate settings. Patient positioning was optimized relative to the C-arm. Endoscopists were asked to minimize low-yield images and preference intermittent fluoroscopy. Commands were standardized to streamline communication between endoscopists and radiographers. The protocol was implemented using verbal and written cues in the ERCP suite. The primary outcome was the effect of the protocol on Air Kerma, DAP and FT compared to the baseline, pre-intervention cohort. The same mobile under-couch C-arm was used, and comparisons were made between the amongst the same core group of surgeon-endoscopists.
Results: The protocol was implemented over 10 months over 274 successful ERCPs. There was a 75% reduction in median Air Kerma (5.27mGy to 1.33mGy, p<0.0001) and DAP (1.35 Gy.cm² to 0.33 Gy.cm², p<0.0001). The DAP DRL we report is the world's lowest, at 0.79 Gy.cm². Median FT improved by 41% (42s to 24s, p<0.0001); the FT DRL under protocol conditions was 38s. Sizeable reductions in dose were seen in the upper quartile of cases. Multivariate analysis of the pre-intervention group identified sphincteroplasty, malignancy and certain endoscopists negatively influence DAP and FT (p<0.001). Use of our protocol minimized the effects of these variables on radiation doses at multiple linear regression. Temporal analysis showed that the protocol was effective from first implementation, but there were ongoing improvements in reducing the radiation used in the more complex, higher-dose cases.
Conclusion: We demonstrate that a protocol to modify the endoscopist and radiographer behavior is easy to adopt, and results in sizeable percentage improvements from an already low-dose baseline. Thus, we de-

scribe the lowest reported doses at ERCP. Such a protocol can be applied to any ERCP environment to achieve similar dose improvement, which will reduce the radiation-risks for patients and staff.

References: 1. Hayashi S., et al., *Radiation exposure during image-guided endoscopic procedures: The next quality indicator for endoscopic retrograde cholangiopancreatography*. World J Clin Cases. 2018 Dec 26;6(16):1087-1093.

2. Dumonceau, J.M., et al., *Radiation protection in digestive endoscopy: European Society of Digestive Endoscopy (ESGE) guideline*. Endoscopy, 2012. 44(4): p. 408-21.

Disclosure: Nothing to disclose.

Short bowel and nutrition therapies

15:30-16:30 / Poster Stage 6

MP140

PROTEIN-BASED ORAL REHYDRATION SOLUTIONS FOR PATIENTS WITH AN ILEOSTOMY: A RANDOMISED, DOUBLE-BLINDED CROSSOVER STUDY

C.L. Rud^{1,2}, M.K. Hvistendahl³, B. Langdahl⁴, F. Kraglund¹, S.M.D. Baunwall¹, S. La⁵, P.B. Jeppesen³, C.L. Hvas^{1,2}

¹Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ²Aarhus University, Department of Clinical Medicine, Aarhus, Denmark, ³Rigshospitalet, Department of Intestinal Failure and Liver Diseases, Copenhagen, Denmark, ⁴Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark, ⁵Salford Royal Foundation Trust, Intestinal Failure Unit, Salford, United Kingdom

Contact E-Mail Address: CHARRU@rm.dk

Introduction: Patients with an ileostomy are at increased risk of dehydration and sodium depletion.

Aims & Methods: We aimed to investigate if protein type or protein hydrolysis affects absorption from oral rehydration solutions (ORS) in patients with an ileostomy.

This was a randomised, double-blinded, active comparator-controlled 3x3 crossover intervention study. We developed three ORS with whey protein isolate, caseinate or whey protein hydrolysate. The ORS contained 40-48 g protein/L, 34-45 mmol sodium/L and had an osmolality of 248-270 mOsm/kg. The patients ingested 500 mL/d during three 4-week periods with a >2-week washout.

The primary outcome was wet-weight ileostomy output.

Results: Thirteen patients were included in the analyses. Wet-weight ileostomy output did not change and there was no difference between interventions (p=0.38). A series of statistically significant improvements were observed following intake of whey protein isolate ORS, including decreased faecal losses of energy (-365 kJ/d, 95% confidence interval (CI), -643 to -87, p=0.012), magnesium (-4.0 mmol/d, 95%CI, -7.4 to -0.7, p=0.020), plasma aldosterone (-4,674 pmol/L 95%CI, -8,536 to -812, p=0.019), and increased eGFR (2.8 mL/min/1.73m², 95%CI, 0.3 to 5.4, p=0.03).

Conclusion: Ingestion of 500 mL/d of three protein-based iso-osmolar solutions resulted in unchanged and comparable ileostomy outputs in patients with an ileostomy. Following whey protein isolate ORS, we observed discrete improvements in a series of absorption proxies in both faeces and blood. The protein-based ORS were safe and well-tolerated. Future studies are warranted to explore if different compositions or doses of protein-based ORS can improve absorption in patients with an ileostomy.

Disclosure: Aarhus University and Arla Foods Ingredients Group P/S financed the wages for CLR's doctoral studies, but in no way influenced the data collection, analyses, interpretation or publishing of the data. SMBD is an active member of the EurFMT alliance, a non-profit academic association, and has received a speaker honorarium from Takada on a subject unrelated to this manuscript. CLH has received lecture honoraria from Baxter and BMS on subjects unrelated to this manuscript, and is the Head of the board of the Danish Society for Clinical Nutrition. The other authors have no potential conflicts of interest to report.

MP141

LONG-TERM SAFETY AND EFFECTIVENESS OF TEDUGLUTIDE IN PAEDIATRIC PATIENTS WITH SHORT BOWEL SYNDROME-ASSOCIATED INTESTINAL FAILURE: AN OBSERVATIONAL, PROSPECTIVE, MULTICENTRE REGISTRY

P.B. Jeppesen¹, M. Kohl-Sobania², F. Joly³, J.B. Mason⁴, J.P. Allard⁵, U.-F. Pape⁶, L. Pironi⁷, G.E. Gondolesi⁸, L.K. Schwartz⁹, P. Zhang¹⁰, A. Gabriel¹⁰, S. Sabrdaran¹⁰, Y.W. Huang¹⁰

¹Rigshospitalet, Copenhagen, Denmark, ²University Hospital Schleswig-Holstein, Lübeck, Germany, ³Hôpital Beaujon, Clichy, France, ⁴Tufts Medical Center, Boston, United States of America, ⁵Toronto General Hospital, Toronto, Canada, ⁶Asklepios Medical School, Hamburg, Germany, ⁷St. Orsola Hospital, University of Bologna, Bologna, Italy, ⁸Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina, ⁹NYU Langone Medical Center, New York, United States of America, ¹⁰Takeda Development Center Americas, Inc., Cambridge, United States of America

Contact E-Mail Address: Palle.Bekker.Jeppesen@regionh.dk

Introduction: Short bowel syndrome (SBS) is the most common cause of intestinal failure (IF) in children and is generally managed using parenteral nutrition and/or intravenous fluids (PN/IV). Long-term PN/IV can cause potentially life-threatening complications. Patients may receive teduglutide (TED) to encourage adaptation of the remaining intestine and to reduce dependence on PN/IV. Short-term studies have shown that TED is effective and has an acceptable safety profile in children and adults with SBS-associated IF (SBS-IF). However, assessment of long-term treatment with TED in paediatric patients with SBS-IF is limited.

Aims & Methods: We report real-world long-term safety and effectiveness data of TED from a paediatric cohort enrolled in the prospective, multinational SBS Registry (NCT01990040; EUPAS7973). Data were analysed cumulatively for up to 6 years between enrolment and interim data cut-off (June 23, 2014 to June 30, 2023). Patients were categorised based on whether they received TED (ever-treated; received ≥ 1 dose of TED 0.05 mg/kg/day [median]) or never received TED (never-treated; received PN/IV for ≥ 6 months before study entry). Safety endpoints included: occurrence of colorectal cancer in patients with any remnant colon; other malignancy; colorectal polyps; and adverse events (AEs). Effectiveness endpoints included clinical response ($\geq 20\%$ reduction in PN/IV volume from baseline) and change from baseline in volume of PN/IV (per weight [L/kg]) and number of days/week receiving PN/IV.

Results: In total, 398 paediatric patients were enrolled: 266 never-treated, 132 ever-treated (per-protocol set, n=397; 266 never-treated, 131 ever-treated). Patients had a mean (standard deviation [SD]) age of 5.4 (4.01) years (ever-treated 6.8 [4.12] years; never-treated 4.8 [3.80] years) and the majority were male (63.7%; ever-treated 68.7%; never-treated 61.3%). The median (range) length of exposure in ever-treated patients was 29.0 (1.15–106.61) months.

No new cases of colorectal cancer or new/worsening colorectal polyps were reported between baseline and interim cut-off. New/worsening malignancies were reported for one never-treated patient. A greater proportion of ever-treated patients reported AEs (87.0% vs 74.4%) and serious AEs (SAEs; 72.5% vs 59.0%) than never-treated patients. AEs and SAEs related to TED were reported in 15.3% and 6.1% of ever-treated patients, respectively. There were no allergic or hypersensitivity reactions to TED. The most common TED-related AEs were vomiting (3.8%) and abdominal pain (2.3%). Fatal events were recorded for one ever-treated and three never-treated patients.

A greater proportion of ever-treated patients had achieved a clinical response (year 1, 18/30, 60.0%; year 3, 11/17, 64.7%) than never-treated patients (year 1, 23/100, 23.0%; year 3, 17/82, 20.7%). Ever-treated pa-

tients had a greater mean (SD) reduction from baseline in PN/IV volume (L/kg; ever-treated: year 1, -39.4% [35.97], n=19; year 3, -61.6% [23.64]; n=7; never-treated: year 1, -21.1% [50.70], n=80; year 3, -34.4% [36.83], n=49) and number of days/week receiving PN/IV (ever-treated: year 1, -1.6 [2.16], n=30; year 3, -1.5 [1.77], n=17; never-treated: year 1, -1.0 [2.22], n=100; year 3, -0.6 [1.51]; n=82) than never-treated patients.

Conclusion: This 6-year interim analysis of real-world data from a large cohort of paediatric patients with SBS-IF supports that the safety profile of TED is consistent with the previous 5-year follow-up and suggests that TED improves intestinal adaptation in paediatric patients with SBS-IF over a 3-year period.

Disclosure: Palle B Jeppesen: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; commercial relationships as consultant and speaker with Albumedix, ArTara Therapeutics, Baxter, Coloplast, Ferring Pharmaceuticals, Fresenius Kabi, GlyPharma Therapeutic, Ironwood Pharmaceuticals, Naia Pharmaceuticals, NorthSea Therapeutics, Novo Nordisk Foundation, Protara Therapeutics, Takeda, Therachon, VectivBio and Zealand Pharma.

Martina Kohl-Sobania: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; study investigator for NPS Pharmaceuticals and Takeda; honoraria from Aposan, Takeda and Tauro-Implant as a speaker; advisory board member for Takeda.

Francisca Joly: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; study investigator for NPS Pharmaceuticals, Takeda, VectivBio and Zealand Pharma; advisory board member for Alira Health, ArTara Therapeutics, Baxter, M3E Solutions, Takeda, Therachon, VectivBio and Zealand Pharma; commercial relationships as consultant and speaker for Baxter, B. Braun, Fresenius Kabi, Nestlé Health Sciences, Takeda, Therachon and Théradiol.

Joel B Mason: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; research support from Takeda as a site for the study; compensation from Care/of, a producer of nutritional supplements; honoraria from UpToDate, a web-based medical information platform, for authoring chapters.

Johane P Allard: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; fees from Takeda as a consultant and speaker, and research support from Takeda as a study site principal investigator (PI); research support from Fresenius Kabi and OMS as a PI; honoraria from Baxter as a speaker and consultant; research support from Zealand Pharma as a site PI.

Ulrich-Frank Pape: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; honoraria from Takeda as a consultant and speaker, and research support from Takeda, VectivBio and Zealand Pharma as a study site PI.

Loris Pironi: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; advisory board member for Baxter, NorthSea Therapeutics and Takeda.

Gabriel E Gondolesi: speaker for Takeda; compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; received investigator-initiated research grant from Takeda.

Lauren K Schwartz: compensation received from Takeda as a member of the Scientific Advisory Committee for the SBS Registry study; speaker for Bristol Myers Squibb; advisory board member for Takeda.

Pinggao Zhang, Sasan Sabrdaran and Yi Wen Huang: employees of Takeda Pharmaceuticals U.S.A., Inc. and receive stock and/or stock options.

André Gabriel: former employee of Takeda Pharmaceuticals U.S.A., Inc. who received stock and/or stock options.

Acknowledgements: This study was funded by Takeda Pharmaceuticals U.S.A., Inc., MA, USA. Medical writing support, funded by Takeda Pharmaceuticals U.S.A., Inc., was provided by Elizabeth Coe, PhD of PharmaGenesis Cardiff, Cardiff, UK.

DIETARY FOOD GROUPS AND NUTRIENTS IN INFLAMMATORY BOWEL DISEASE AND ITS ASSOCIATIONS WITH SYSTEMIC INFLAMMATION

T. Zhang¹, B. Tan¹, J. Mok¹, S.K. Pang¹, S.M. Sim², X. Cai², L. Liu², J.L. Hartono^{1,3}, J. Lee^{1,2,3}

¹National University Health System, Division of Gastroenterology and Hepatology, Singapore, Singapore, ²National University of Singapore, iHealthtech, Singapore, Singapore, ³National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore

Contact E-Mail Address: jonathanlee@nus.edu.sg

Introduction: Diet plays a pivotal role in inflammatory bowel disease (IBD) as it is postulated to mediate inflammation in the gut. Certain foods dysregulate the immune system by altering the intestinal mucosal layer, contributing to microbial dysbiosis¹.

There is emerging evidence that specific dietary interventions may promote remission in mild to moderate IBD. However, few studies investigate the role of specific diet patterns in the development of IBD.

Aims & Methods: We aim to describe the nutritional profile in multi-ethnic Asian patients with IBD and compare them to healthy controls. We also aim to demonstrate association of certain diet patterns with increased risk of IBD, by analysis of inflammatory proteins.

The study cohort was sequentially recruited from a single tertiary centre comprising 145 patients with IBD (58.6% Ulcerative colitis (UC) and 41.4% Crohn's disease (CD)), and 112 healthy control, who are individuals undergoing screening colonoscopy with no colonic pathology.

A semi-quantitative validated food frequency questionnaire² was administered and nutrients and food group intakes were calculated for patients in g/day. Unsupervised analysis of the nutrient and food group data was done through principal component analysis (PCA).

Multivariate linear regression was used to identify nutrients and food groups associated with IBD subtypes while adjusting for age, gender, BMI, and race. Serum protein profiling was performed using the *Olink* Target 96 Inflammation assay, and spearman correlation was used to associate serum cytokines with nutrient and food groups.

Results: Dietary composition of IBD patients differ significantly from the control as demonstrated by PCA, with discrepancy between PC1 ($p<0.0001$) and PC2 ($p=0.0063$) axes which account for 17.9% and 13.0% of the total dietary composition variance. There is no significant difference between UC and CD subgroups.

Participants with IBD were younger ($46.9(\pm 14.2)$ in UC, $44.7(\pm 15.9)$ in CD, $p<0.01$), with greater representation of males (72.6% amongst UC, 66.7% amongst CD, $p=0.03$), and lower proportion of Chinese (50.6% amongst UC, 56.7% amongst CD, $p<0.01$) as compared to controls. Adjusting for differences in age, gender and ethnicity, sweetened beverages and white bread were dietary elements significantly associated with UC and CD respectively, whereby both groups had increased intake of sweetened beverages and savory bread. (Table 1)

Using paired serum samples and dietary outputs, 39 significant cytokine-dietary elements were identified. Of note, increased consumption of sweetened beverages and fruit juice was associated with increased expression of matrix metalloproteinase-1 (MMP-10) ($p<0.01$) and reduced expression of interleukin-22 (IL-22) ($p=0.03$). MMP-10³ regulates the pro-inflammatory cytokines in IBD patients. Conversely, IL-22⁴ promotes mucosal healing, and hence reduced expression may worsen IBD.

White bread intake has also been associated with multiple inflammatory proteins including OSM⁵ ($p=0.03$), EN-RAGE⁶ ($p=0.03$), FGF-23 ($p<0.01$) and IL-17A ($p=0.04$), shown from previous studies to be proinflammatory in IBD.

	Nutrient type	Estimate	Standard error	Statistic	p-value	Adjusted p-value
UC	Sweetened beverage	0.233	0.0561	4.15	<0.0001	0.0006
	Savory bread	0.0783	0.0362	2.16	0.0316	0.1420
	Tea	0.148	0.0604	2.45	0.0151	0.0844
	Carbohydrate/day	0.0211	0.00897	2.36	0.0192	0.0950
	Other seafood	0.0772	0.0383	2.01	0.0451	0.1800
CD	Sweetened beverage	0.148	0.0613	2.41	0.0168	0.0896
	Savory bread	0.0843	0.0396	2.13	0.0343	0.1480
	White bread	0.154	0.0442	3.49	0.0006	0.0059
	White porridge	0.110	0.0472	2.33	0.0203	0.0968

Conclusion: Our study shows a unique dietary profile for patients with and without IBD. There is a direct correlation of certain foods with increased expression of inflammatory proteins in patients with IBD. This suggests dietary profile in patients may affect IBD activity. Further studies may elucidate new nutritional therapy for IBD patients.

References:

1. Scott Manski, Nicholas Noverati, Tatiana Policarpo, Emily Rubin, Raina Shivashankar, Diet and Nutrition in Inflammatory Bowel Disease: A Review of the Literature, Crohn's & Colitis 360, Volume 6, Issue 1, January 2024, otad077, <https://doi.org/10.1093/crocol/otad077>
2. Whitton C, Ho JCY, Tay Z, Rebello SA, Lu Y, Ong CN, van Dam RM. Relative Validity and Reproducibility of a Food Frequency Questionnaire for Assessing Dietary Intakes in a Multi-Ethnic Asian Population Using 24-h Dietary Recalls and Biomarkers. *Nutrients*. 2017 Sep 25;9(10):1059. doi: 10.3390/nu9101059. PMID: 28946670; PMCID: PMC5691676.
3. Fonseca-Camarillo G, Furuzawa-Carballeda J, Martínez-Benítez B, et al. Increased expression of extracellular matrix metalloproteinase inducer (EMMPRIN) and MMP10, MMP23 in inflammatory bowel disease: Cross-sectional study. *Scand J Immunol*. 2021 Jan;93(1):e12962.
4. Li LJ, Gong C, Zhao MH, Feng BS. Role of interleukin-22 in inflammatory bowel disease. *World J Gastroenterol*. 2014 Dec 28;20(48):18177-88. doi: 10.3748/wjg.v20.i48.18177. PMID: 25561785; PMCID: PMC4277955.
5. Sare Verstockt, Bram Verstockt, Kathleen Machiels, et al. Oncostatin M Is a Biomarker of Diagnosis, Worse Disease Prognosis, and Therapeutic Nonresponse in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2021 Oct 18;27(10):1564-1575.
6. Foell D, Kucharzik T, Kraft M, et al. Neutrophil derived human S100A12 (EN-RAGE) is strongly expressed during chronic active inflammatory bowel disease. *Gut* 2003;52:847-853

Disclosure: Nothing to disclose.

MP143

FUNCTIONAL RELEVANCE OF INDIVIDUAL BACTERIAL STRAIN SIGNATURES IN RESPONSE TO THERAPEUTIC INTERVENTION WITH EXCLUSIVE ENTERAL NUTRITION IN PEDIATRIC CROHN'S DISEASE

D. Häcker^{1,2}, K. Siebert³, B.J Smith⁴, N. Köhler⁵, A. Mahapatra⁶, H. Heimes¹, J. Nie¹, A. Metwally¹, H. Hölz³, Q. Manz⁷, F. De Zen³, J. Heetmeyer³, K. Socas³, G. Le Thi³, C. Meng⁸, K. Kleigrew⁸, J.K Pauling⁹, K. Neuhaus⁶, L. Markus⁷, K.S Pollard^{4,9,10}, T. Schwerd³, D. Haller^{1,2,11}

¹Technische Universität München, Chair of Nutrition and Immunology, TUM School of Life Science, Freising, Germany, ²TUMCREATE, Singapore, Singapore, ³Dr. von Hauner Children's Hospital, LMU, Department of Pediatrics, Munich, Germany, ⁴Gladstone Institutes, San Francisco, United States of America, ⁵Technische Universität München, LipiTUM, Chair of Experimental Bioinformatics, Freising, Germany, ⁶Technische Universität München, ZIEL Institute for Food & Health, Core Facility Microbiome, Freising, Germany, ⁷Technische Universität München, Data Science in Systems Biology, School of Life Science, Freising, Germany, ⁸Technische Universität München, Bavarian Center for Biomolecular Mass Spectrometry (BayBioMS), Freising, Germany, ⁹University of California, San Francisco, United States of America, ¹⁰Chan Zuckerberg Biohub, San Francisco, United States of America, ¹¹Technical University of Munich, School of Life Sciences co-affiliated with School of Medicine, Freising, Germany

Contact E-Mail Address: jiatong.nie@tum.de

Introduction: Exclusive enteral nutrition (EEN) is the first-line therapy for pediatric Crohn's disease (CD) and has been shown to impact the gut microbiome. However, the evidence for EEN-mediated functional changes in the gut microbiome as an underlying cause of therapeutic efficacy is still lacking.

Aims & Methods: Our aim is to assess the protective mechanisms of EEN through its impact on the modification of gut microbiome signatures in pediatric CD. We established a prospective pediatric IBD cohort (N=78) and longitudinally followed 20 treatment-naïve Crohn's disease patients undergoing EEN therapy for 6-8 weeks. Changes of fecal microbiota and metabolites was characterized using integrated multi-omics analysis with profiling data from 16S rRNA amplicon sequencing and untargeted mass spectrometry. To validate the functional changes of diet-exposed fecal microbiota on gut inflammation, we established a combined approach using gut chemostat cultures and microbiota transfer into germ-free *IL10^{-/-}* mice. Metagenomic analysis was applied to identify specific strain signatures associated with the protective effects of EEN in the pediatric cohort and the colonized mice.

Results: Treatment-naïve CD patients (18/20) achieved clinical remission in response to EEN therapy (90%) of which 8 experienced recurrent CD activity within 1 year. Integrated multi-omics analysis identified network clusters from individually variable microbiome and metabolomic profiles, with *Lachnospiraceae* and medium chain fatty acids as protective features. Exposure of fecal microbiota from selected Crohn's disease patients to EEN-like and fiber-repleted diets in the gut chemostat model, followed by the subsequent transfer of their conditioned microbiota into germfree *IL10^{-/-}* mice, prevented or induced IBD-like inflammation, respectively. Metagenomic analysis of 54 selectively colonized mice identified highly individualized strain signatures in the gnotobiotic mouse model, contrary to the more universal metabolite profiles discriminating inflamed from non-inflamed mice. Furthermore, differentially abundant species in humanized mice showed individual patterns associated with EEN and EEN cessation in the CD patient cohort, confirming the highly personalized strain-level dynamics in patients.

Conclusion: These findings demonstrate that EEN therapy mediates protective changes in individually variant microbiome profiles, leading towards personalized patient-to-patient species and strain signatures. Most importantly, we provide evidence that EEN creates explicit functional changes in temporally and individually variable microbiomes of Crohn's disease patients.

Disclosure: DHaller served on the Microbiome Expert Panel from Reckitt Benckiser Health Limited. TS received lecture honoraria from Nutricia and MSD and travel support from Abbvie and Ferring outside the submitted work.

MP144

THE EFFECT OF A2 MILK ON REDUCING ABDOMINAL DISCOMFORT AFTER MILK CONSUMPTION: A SINGLE-CENTER, RANDOMIZED, DOUBLE-BLIND, CROSS-OVER STUDY

Y. Choi¹, N. Kim^{1,2}, J.H. Lee¹, Y. Kim¹, S. Kim¹, D.-H. Lee^{1,2}
¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea

Contact E-Mail Address: moonsin12345@naver.com

Introduction: β -casein, a major protein in cow's milk, is divided into the A1 and A2 type variants. Digestion of A1 β -casein yields the peptide β -casomorphin-7 which could cause gastrointestinal (GI) discomfort but A2 milk containing only A2 β -casein might be beneficial than A1/A2 (regular) milk.

Aims & Methods: The aim of this study was to evaluate the differences in GI discomfort after ingestion of A2 milk and A1/A2 milk. A randomized, double-blind, cross-over human trial was performed in 40 subjects who experienced GI discomfort following milk consumption. For each intervention period, either A2 milk first (A2→A1/A2) or A1/A2 milk was first consumed for 2 weeks (A1/A2→A2) following a 2-week washout period. GI Symptom Rating Scale (GSRS) scores, questionnaire for digestive symptoms, and laboratory tests including fecal calprotectin were evaluated. For symptom analysis generalized estimating equations (GEE) gamma model was used.

Results: A2 milk increased bloating ($P=0.041$) and loose stools ($P=0.026$) compared to A1/A2 milk in GSRS. However, A2 milk caused less abdominal pain ($P=0.050$), fecal urgency ($P<0.001$) and borborygmus ($P=0.007$) compared to A1/A2 milk in questionnaire for digestive symptoms. In addition, fecal calprotectin also decreased or less increased after consumption of A2 milk compared to A1/A2 milk ($P=0.030$), and this change was more pronounced in males ($P=0.005$) than in females. There were no significant adverse reactions during the trial.

		A2 milk		^a P-value	A1/A2 milk		^a P-value	^b P-value
		Before	After		Before	After		
Period 1	Abdominal pain	2.00 ± 0.71	1.00 ± 0.00	1.000	1.00 ± 0.00	1.00 ± 0.00	1.000	0.050*
	Fecal urgency	2.50 ± 0.35	1.00 ± 0.00	0.813	1.00 ± 0.00	1.50 ± 0.31	0.375	< 0.001***
Period 2	Borborygmus	1.00 ± 0.00	1.25 ± 0.22	0.500	1.00 ± 0.00	2.00 ± 0.00	0.750	0.007**

Per protocol analysis.
Period 1, the consumption period for the first intervention milk; Period 2, the consumption period for the second intervention milk.
P-values were calculated using ^aWilcoxon signed rank test or Generalized estimating equation (gamma distribution). * $P<0.05$, ** $P<0.01$, *** $P<0.001$.
Values are presented as LS mean ± SE.

Conclusion: A2 milk alleviated digestive discomfort in Koreans following A2 milk consumption (ClinicalTrials.gov NCT06252636 and CRIS KCT0009301).

Disclosure: Nothing to disclose.

MP145

DIFFERENT COOKING METHODS ALTER HOST AND GUT MICROBIAL METABOLISM, A RANDOMIZED CROSS-OVER DIETARY TRIAL IN HEALTHY VOLUNTEERS

J. Wellens^{1,2}, E. Vissers², A. Dumoulin², S. Hoekx¹, J. Vanderstappen¹, J. Verbeke³, R. Vangoitsenhoven⁴, M. Derrien^{5,6}, B. Verstockt^{1,2}, M. Ferrante^{1,2}, C. Matthys^{3,4}, J. Raes^{6,5}, K. Verbeke², S. Vermeire^{1,2}, J. Sabino^{1,2}

¹Leuven University Hospital, Gastroenterology and Hepatology, Leuven, Belgium, ²KU Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ³KU Leuven, Department of Chronic Diseases and Metabolism, Clinical and Experimental Endocrinology, Leuven, Belgium, ⁴Leuven University Hospital, Department of Endocrinology, Leuven, Belgium, ⁵KU Leuven, Rega Institute, Microbiology, Immunology and Transplantation Department, Leuven, Belgium, ⁶VIB Center For Microbiology, Leuven, Belgium

Contact E-Mail Address: judith.wellens@kuleuven.be

Introduction: Ultra-Processed Foods (UPFs) have been associated with chronic diseases such as cancer, obesity and inflammatory bowel diseases (IBD). A typical feature of UPFs is the presence of Advanced Glycation End products (AGEs), including Carboxy-Methyl Lysine (CML), due to thermal treatments.

Aims & Methods: We studied to what extent different cooking methods affect cardiometabolic and inflammatory markers through differential dietary AGE intake.

In a randomized cross-over pilot trial, healthy participants sequentially consumed a diet prepared with cooking methods that generate either low or high amounts of AGEs. Recipes during both periods contained identical ingredients, but simply differed in their cooking methods (grilling and baking vs. steaming and raw foods). Daily food logs were kept using photo documentation and the smartphone application FatSecret during the one-week run-in (baseline diet) and the subsequent two-week intervention periods. Estimated AGEs levels were calculated based on the previously published database of Uribarri et al.¹ Anthropometric measurements and biological samples were taken at baseline and after each intervention period. Blood samples were collected for routine tests, Lipopolysaccharide-Binding Protein (LBP) ELISAs, serum proteomics (Olink Target 96 Inflammation and Cardiometabolic panels), and direct measurement of serum AGEs. Faecal calprotectin, 16S rRNA sequencing, and short chain fatty acids (SCFA) measurements were performed on stool samples. Small intestinal permeability was measured according to a 2-hour Lactulose Mannitol Ratio (LMR) protocol.

Results: Twenty healthy participants with a median age (IQR) of 28 (23.5-38) years, and a median BMI of 23.0 (20.9-25.4) kg/m² were included. The average estimated intake of CML during the high-AGEs diet was comparable to baseline (20,480.5 vs. 19,545 kU CML/day, Wilcoxon signed rank test, p>0.1), but significantly higher than during the low-AGEs period (10,590 kU CML/day, Wilcoxon signed rank test, p=3.8 x 10⁻⁶). Metabolically, total cholesterol values increased (paired Wilcoxon signed rank test, p=0.04) when changing from a low-to-high AGEs diet. After applying a linear mixed model per protein, eukaryotic initiation factor 4E-binding protein (4E-BP1), increased significantly after consumption of the low-AGEs diet (adjusted p=0.03). The gut microbiota composition was largely unaffected

by the diets, as was faecal calprotectin. Importantly, faecal butyrate concentrations increased after the high-AGEs study period in the low-to-high AGEs group (paired Wilcoxon signed rank test, p=0.04). The LMR was increased throughout the study in the high-to-low AGEs group, but not in the low-to-high AGEs group. Serum LBP showed no difference.

Conclusion: By conducting the first randomized cross-over cooking methods trial that focusses on both intestinal and systemic endpoints at a proteomic, gut microbiome and permeability level, we found that cooking methods generating different AGE levels have a differential impact on human and gut microbial metabolism. More specifically, we show a beneficial effect of the low-AGEs diet on lipid profiles and the serum protein 4E-BP1, a protein known to affect lifespan, metabolism, and cancer development. In contrast, the high-AGEs diet was associated with increased faecal butyrate levels, a SCFA that is studied for its beneficial and anti-inflammatory luminal properties. These results are instructive for diet-based interventions in the prevention and treatment of chronic diseases, including the metabolic syndrome and IBD.

References: 1. Uribarri J, Woodruff S, Goodman S, et al. AGE's in Foods and practical ways to reduce them. J Am Diet Assoc. 2010;110(6):911-916.

Disclosure: The authors have no direct conflicts of interest to disclose. However the general COIs can be found below for optimal transparency.

JW reports no conflict of interest.

EV reports no conflict of interest.

AD reports no conflict of interest.

SH received consultancy fees from Ferring, Takeda.

Julie Vanderstappen received consultancy fees from Ferring, Janssen.

Joke Verbeke reports no conflict of interest to disclose.

RV is a clinical investigator for Bayer, Eli Lilly, Boehringer Ingelheim, Novo Nordisk; he reports speaker's fees from Boehringer Ingelheim, Eli Lilly, Goodlife Pharma, Novo Nordisk, Prowell, Sanofi; consultancy fees from Boehringer Ingelheim, Eli Lilly, Sanofi; Financial compensation for these activities has been received by the institution (UZ/KU Leuven).

BV reports having received Research support from AbbVie, Biora Therapeutics, Landos, Pfizer, Sosei Heptares and Takeda. Speaker's fees from Abbvie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring, Galapagos, Janssen, Lily, MSD, Pfizer, R-Biopharm, Sandoz, Takeda, Tillots Pharma, Truvion and Viatris. Consultancy fees from Abbvie, Alimentiv, Applied Strategic, Atheneum, BenevolentAI, Biora Therapeutics, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Lily, Mylan, Inotrem, Ipsos, Janssen, Pfizer, Progenity, Sandoz, Santa Ana Bio, Sosei Heptares, Takeda, Tillots Pharma and Viatris.

MF reports to have received research grants from AbbVie, Amgen, Biogen, EG, Janssen, Pfizer, Takeda, and Viatris; consultancy fees from AbbVie, Agomab Therapeutics, Boehringer Ingelheim, Celltrion, Eli Lilly, Janssen-Cilag, Medtronic, MRM Health, MSD, Pfizer, Regeneron, Samsung Bioepis, Sandoz, Takeda, and Thermo Fisher; and speakers' fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Falk, Ferring, Janssen-Cilag, Lamepro, MSD, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda, and Truvion Healthcare.

CM is chair of the KU Leuven Fund 'Nutrition', a donation-based fund to stimulate research on nutrition. Recipient of travel/accommodation expenses and small participation fee (<100€/meeting) as member of working groups of the Belgian Superior Health Council and Belgian Federal Agency of the Safety of the Food Chain. Recipient of travel/accommodation expenses as member of the scientific advisory body of the EU Joint Programme Initiative Healthy Diet, Healthy Life, as co-chair ILSI Europe Task Force Dietary Intake and Exposure, as member ILSI Europe Task Force Nutrient Intake Optimisation. Recipient of honoraria (<500€/year) as active member of the advisory board of NutriNews (Belgian Nutrition Information Center). Recipient of honoraria as jury-member of nutrition-related awards and reviewing EU-grants. Recipient of royalties from a textbook (Handboek Voeding, ACCO). Honoraria are used to support research of PhD Students.

JR reports grants from Beneo, Cargill, Colruyt group, Danone, DSM, J&J, MRM/Prodigest, Nestle Pfizer, and Takeda; and has received consulting and/or speaking fees from Aphea, Biofortis, DSM, Ferring, GSK, Janssen Pharmaceuticals, Metagenics, MSD, MRM/Prodigest, Nutricia, Takeda, Tsumura

KV receives travel /accommodation expenses as co-chair of the ILSI Europe Prebiotic Task Force and travel expenses and a participation fee as a member of a working group of the Belgian Superior Health Council. Recipient of honoraria and travel/accommodation expenses as a reviewer of grants (NWO (The Netherlands), ANR (France) and EU grants). Recipient of speakers' fees from Yakult and Kintu.

SV received financial support for research from AbbVie, J&J, Pfizer, Takeda and Galapagos and receives speakers' and/or consultancy fees from AbbVie, Abivax, AboleraPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Surrozen, Takeda, Theravance, Tillots Pharma AG, VectivBio, Ventyx, Zealand Pharma.

JS reports speaker's fees from Pfizer, Abbvie, Ferring, Falk, Takeda, Janssen, Fresenius, and Galapagos; consultancy fees from Janssen, Ferring, Fresenius, Abbvie, Galapagos, Celltrion, Pharmacosmos, and Pharmanovia; and research support from Galapagos and Viatrix.

MP146

48-WEEK TREATMENT WITH THE LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 (GLP-2) ANALOG APRAGLUTIDE IS ASSOCIATED WITH INCREASED ORAL INTAKE AND IMPROVED ENERGY AND CARBOHYDRATE ABSORPTION IN SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE (SBS-IF) AND COLON-IN-CONTINUITY (CIC)

A. Verbiest^{1,2}, M.K. Hvistendahl³, F. Bolognani⁴, C. Li⁵, N.N. Youssef⁶, F. Joly⁷, P.B. Jeppesen³, T. Vanuytsel^{1,2}

¹University of Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ²University Hospitals Leuven, Leuven Intestinal Failure and Transplantation Center (LIFT), Leuven, Belgium, ³Rigshospitalet, Copenhagen University Hospital, Department of Intestinal Failure and Liver Diseases, Copenhagen, Denmark, ⁴VectivBio/Ironwood, Clinical Development, Basel, Switzerland, ⁵VectivBio/Ironwood, Data Science, Basel, Switzerland, ⁶VectivBio/Ironwood, Medical Affairs, Basel, Switzerland, ⁷Hôpital Beaujon, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support, Clichy, France

Contact E-Mail Address: astrid.verbiest@kuleuven.be

Introduction: SBS-IF is a severe organ failure with long-term parenteral support (PS) dependence. GLP-2 stimulates intestinal adaptation resulting in increased absorptive capacity. Apraglutide (APRA) is a novel, long-acting GLP-2 analog in development for SBS-IF. This study investigated the safety and efficacy of APRA in patients with SBS-IF and CiC.

Aims & Methods: STARS Nutrition is a 52-Week (W) multicenter, open-label, phase 2 study in 9 adult SBS-IF-CiC patients (pts) receiving weekly subcutaneous APRA injections (5mg). 72-h metabolic balance studies (MBS) were performed at baseline (BL), 4W and 48W; with stable PS at BL and 4W. During MBS, oral fluid intake was kept constant by adhering to an individual predefined drinking menu. Duplicates of meals and fluids (wet weight intake) were collected as well as urine and feces (fecal wet weight output). Pts were advised to keep oral food intake at 4W similar to BL, but not at 48W to explore the effect of APRA on spontaneous dietary intake.

Safety was the primary endpoint. Secondary endpoints included changes in wet weight, energy and macronutrient absorption at 4W and 48W. Data are presented as mean (95% CI) unless specified otherwise. Nominal p-values are calculated using paired T-tests with significance set at 0.05.

Results: Small bowel length was 19 (range 0-50) cm and median estimated residual colon was 79 (range 43-100) %. At BL, pts received a PS volume of 10 (range 4-21) L/W. APRA had an acceptable safety profile. At 4W, fecal output reduced significantly by 253 (68 – 437) g/day (p=0.013); resulting in a trend to increased wet weight absorption of 256 (-9 – 520) g/day (p=0.057) while energy absorption remained unaltered. At 48W, pts significantly increased their overall wet weight intake (p=0.047), carbohydrate (p=0.042) and nitrogen intake (p=0.024) resulting in a significantly increased energy intake (p=0.027). Fecal wet weight output remained constant despite the increased oral intake. There was a significant increase in wet weight absorption by 316 (21 – 611) g/day (p=0.039), energy absorption by 1134 (58 – 2210) kJ/day (p=0.041) and carbohydrate absorption by 56.1 (8.8 – 94.3) g/day (p= 0.024). Urine output and body weight remained stable throughout the study.

Conclusion: The STARS Nutrition MBS findings confirm the role of the colon in energetic recovery of carbohydrates and maintenance of the fluid balance in SBS-IF-CiC. In pts with SBS-IF-CiC, APRA treatment resulted in an early reduced fecal output and improved wet weight absorption. After 48 weeks, oral intake was increased despite stable fecal output, leading to increased energy and carbohydrate absorption.

Disclosure: Astrid Verbiest, Mark Krogh Hvistendahl – nothing to declare.

Palle Bekker Jeppesen – received grants/research support/honoraria or consultation fees from Agomab, Albumedix A/S, ArTara Therapeutics, Bainan Biotech, Baxter, Coloplast, Ferring, Fresenius Kabi, GLyPharma, Naia Pharma, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, The Novo Nordisk Foundation, Therachon, VectivBio and Zealand Pharma.

Francisca Joly – has received grants/research support/honoraria or consultation fees from Agomab, Baxter, Fresenius Kabi, Nestlé Health Sciences, BBraun, Theradial, Mayoli, Biocodex, mobile3e Consulting, Carembouche, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, Therachon, VectivBio and Zealand Pharma.

Tim Vanuytsel – has served on the speaker bureau for Abbott, Agomab, Baxter, Biocodex, Dr. Falk Pharma, Fresenius Kabi, Ipsen, Menarini, Microbiotica, MyHealth, Remedus, Takeda, Truvion, VectivBio and Zealand Pharma. TV has provided clinical advice to Baxter, Danone, Dr. Falk Pharma, MyHealth, NorthSea Therapeutics, Shire, Therachon, Takeda, VectivBio, Zealand Pharma. TV has received research grants from Danone, MyHealth, Takeda and VectivBio.

Federico Bolognani, Carrie Li and Nader N. Youssef – employees of VectivBio/Ironwood.

This research was supported by VectivBio AG/Ironwood.

MP147

MOLECULAR SIGNATURES OF MASS REJECTION IN THE SMALL INTESTINAL GRAFT PRECEDE HISTOLOGIC FEATURES

N. Karmi¹, R. Oelen², E. Bigaeva¹, S. de Jong¹, J.W. Haveman³, F. Van Der Heide¹, M. Hermoso^{4,1}, M.G. Van der Wijst², G. Kats-Ugurlu⁵, R.K. Weersma¹, E.A. Festen¹, W.T.C. Uniken Venema¹, G. Dijkstra⁶

¹UMCG, Gastroenterology and Hepatology, Groningen, Netherlands, ²UMCG, Genetics, Groningen, Netherlands, ³UMCG, Surgery, Groningen, Netherlands, ⁴Universidad de Chile, Innate Immunity Laboratory, Santiago, Chile, ⁵UMCG, Pathology, Groningen, Netherlands, ⁶University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands

Contact E-Mail Address: w.t.c.uniken.venema@umcg.nl

Introduction: Intestinal transplantation (ITx) is the only cure for patients with irreversible intestinal failure and complications of parenteral nutrition, however, 5-year graft survival is only ~50%. We currently do not know why graft failure is highly prevalent and hypothesize that disturbed repopulation of recipient cells in the graft is associated with this imbalance leading to rejection. So far, answering this question has been hampered by technical limitations and limited patient numbers.

Aims & Methods: We performed single-cell mRNA sequencing of 28 longitudinally sampled ileal graft biopsies of three transplanted patients from surgery up to six months post-transplantation, obtained through the TransplantLines Biobank. Using their differential genetic background, we identified 90,282 donor and recipient cells in the graft and characterized their composition and function during clinical follow-up and rejection.

Results: We found no consistent repopulation of recipient immune cells over time, nor disturbance of repopulation upon rejection. T cells in the graft were predominantly of donor origin (59% of donor immune cells) and myeloid cells originated from the recipient (16% of recipient immune cells). Induction therapy using anti-thymocyte globulin did achieve less than 50% T cell depletion in the graft. Instead, apoptotic pathways in epithelial cells during moderate rejection preceded pathology-defined mass rejection, indicating potential prognostic information in the transcriptomic profiles.

Conclusion: In conclusion, this is the first longitudinal study of the ITx graft at single-cell level. We see that molecular profiles precede histologic signs of mass rejection, which may be a useful biomarker for treatment intensification. Unexpectedly, we find no consistent repopulation of recipient immune cells and a variable response to drugs.

Disclosure:

E.A.M.F. and W.T.C.U.V. were sponsored by a NVGE Gastrostart Grant W.T.C.U.V., E.V.B., R.K.W. and E.A.M.F. were sponsored by an unrestricted research grant from Takeda Pharmaceuticals.

R.K.W.: acted as a consultant for Takeda and received an unrestricted grant from Johnson and Johnson pharmaceuticals and speaker fees from AbbVie, MSD, Olympus and AstraZeneca.

E.A.M.F.: is supported by a ZonMW Clinical Fellowship grant (project number 90719075) volgt

G.D.: received speaker's fees from Janssen-Cilag, Abbvie, Takeda, and Pfizer. Received research grants from Royal DSM and Janssen-Cilag. Furthermore, a De Cock Foundation Grant was applied.

N.K. supported by an MD/PhD trajectory grant (21-12) from the Junior Scientific Masterclass, University of Groningen.

The TransplantLines Biobank and Cohort study was supported by grants from Astellas BV (project code: TransplantLines Biobank and Cohort study), Chiesi Pharmaceuticals BV (project code: PA-SP/PRJ-2020-9136), and NWO/TTW via a partnership program with DSM, Animal Nutrition and Health, The Netherlands (project code: 14939). The project was co-fi-

nanced by the Dutch Ministry of Economic Affairs and Climate Policy by means of so-called PPP-allowances, made available by the Top Sector Life Sciences & Health to stimulate public-private partnerships (project code: PPP-2019-032 and PPP-2022-015). The funders had no role in the study design, data collection, analysis, reporting, or the decision to submit for publication.

R.O., E.B, S.J., J.W.H, F.H: have nothing to declare

MP148

ONE-YEAR TREATMENT WITH THE LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 (GLP-2) ANALOG APRAGLUTIDE RESULTS IN PARENTERAL SUPPORT WEANING, CLINICAL BENEFIT AND IMPROVED PATIENT REPORTED OUTCOMES IN SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE (SBS-IF) AND COLON-IN-CONTINUITY (CIC)

A. Verbiest^{1,2}, M.K. Hvistendahl³, F. Bolognani⁴, C. Li⁵, N.N. Youssef⁶, P.B. Jeppesen³, F. Joly⁷, T. Vanuytsel^{1,2}

¹University of Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ²University Hospitals Leuven, Leuven Intestinal Failure and Transplantation Center (LIFT), Leuven, Belgium, ³Rigshospitalet, Copenhagen University Hospital, Department of Intestinal Failure and Liver Diseases, Copenhagen, Denmark, ⁴VectivBio/Ironwood, Clinical Development, Basel, Switzerland, ⁵VectivBio/Ironwood, Data Science, Basel, Switzerland, ⁶VectivBio/Ironwood, Medical Affairs, Basel, Switzerland, ⁷Hôpital Beaujon, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support, Clichy, France

Contact E-Mail Address: astrid.verbiest@kuleuven.be

Introduction: SBS-IF is a severe organ failure with long-term parenteral support (PS) dependence. GLP-2 stimulates intestinal adaptation resulting in increased absorptive capacity. Apraglutide (APRA) is a novel long-acting GLP-2 analog in development for SBS-IF. This multicenter, open-label, phase 2 study in SBS-IF-CiC aims to investigate the safety and clinical efficacy of APRA at 52 weeks (W).

Aims & Methods: STARS Nutrition is a 52W open-label study in 9 adult SBS-IF-CiC pts receiving once-weekly subcutaneous APRA injections (5 mg). Metabolic balance studies were performed at baseline and 4W with stable PS, followed by a 48-W PS adjustment period. During monthly 48-hour fluid balance assessments, oral fluid intake was kept constant by adhering to an individual predefined drinking menu while measuring urine volume. PS was reduced according to an algorithm if an increase in mean daily urinary output of $\geq 10\%$ was observed. As part of patient-reported outcomes (PRO), Patient Global Impression of Change (PGIC) v2.0 (5-point verbal response scale from 2= much better to -2= much worse) was used to assess overall change in pts' status since APRA use. Safety was the primary endpoint. Secondary endpoints included changes in weekly PS volume, energy content, and PS days, proportion of clinical responders ($\geq 20\%$ PS reduction) and changes in PGIC at 52W. Data are presented as mean (95% CI) unless otherwise specified. Nominal p-values are calculated using paired T-tests with significance set at 0.05.

Results: APRA had an acceptable safety profile. All pts experienced ≥ 1 adverse event (AE); a total of 127 AEs were reported. Three pts experienced serious AEs. APRA was interrupted for 1 week in one pt with acute cholangitis and restarted successfully to trial completion. Absolute weekly PS volume decreased significantly by -4702 (-6539 to -2865) mL/week representing a 52% reduction from baseline ($p=0.0004$). Accordingly, PS energy content significantly decreased by -3510 (-4991 to -2029) kcal/week ($p=0.0006$). All pts qualified as clinical responders. Seven pts (78%) achieved ≥ 1 day off PS of whom two pts (22%) reached enteral autono-

my. Pts gained an additional 2.1 (0.7–3.6) days off per week. Total body and lean body weight; and daily urine output remained stable despite PS reductions. All pts experienced a subjective improvement of their general condition based on the PGIC: eight pts reported a score of 2 (much better) and one pt reported a score of 1 (little better).

Conclusion: STARS Nutrition prospectively shows evidence for clinical benefit of a long-acting GLP-2 analog in SBS-IF-CiC. APRA has an acceptable safety profile and is associated with significant reductions in PS needs in pts with SBS-IF-CiC resulting in days without PS and subjective improvement based on PRO.

Disclosure: Astrid Verbiest, Mark Krogh Hvistendahl – nothing to declare.

Palle Bekker Jeppesen – received grants/research support/honoraria or consultation fees from Agomab, Albumedix A/S, ArTara Therapeutics, Bainan Biotech, Baxter, Coloplast, Ferring, Fresenius Kabi, GLyPharma, Naia Pharma, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, The Novo Nordisk Foundation, Therachon, VectivBio and Zealand Pharma.

Francisca Joly – has received grants/research support/honoraria or consultation fees from Agomab, Baxter, Fresenius Kabi, Nestlé Health Sciences, BBraun, Theradial, Mayoli, Biocodex, mobile3e Consulting, Car-embouche, NPS Pharmaceuticals, NorthSea Therapeutics, Shire, Takeda, Therachon, VectivBio and Zealand Pharma.

Tim Vanuytsel – has served on the speaker bureau for Abbott, Agomab, Baxter, Biocodex, Dr. Falk Pharma, Fresenius Kabi, Ipsen, Menarini, Microbiotica, MyHealth, Remedus, Takeda, Truvion, VectivBio and Zealand Pharma. TV has provided clinical advice to Baxter, Danone, Dr. Falk Pharma, MyHealth, NorthSea Therapeutics, Shire, Therachon, Takeda, VectivBio, Zealand Pharma. TV has received research grants from Danone, MyHealth, Takeda and VectivBio.

Federico Bolognani, Carrie Li and Nader N. Youssef – employees of VectivBio/Ironwood.

This research was supported by VectivBio AG/Ironwood.

Disease evolution of IBD

17:00-18:00 / Poster Stage 1

MP149

CHARACTERIZATION OF A EUROPEAN POPULATION WITH RECENTLY DIAGNOSED CROHN'S DISEASE: RESULTS FROM THE PROSPECTIVE CROHN'S DISEASE COHORT (CROCO) STUDY

J. Burisch¹, J. Revés², G. Madsen³, N. Arebi⁴, C. Wong⁴, A. Buisson⁵, M. Bonnet-Dodel⁵, P. Ellul⁶, K. Gatt⁶, S. Vieujean⁷, I. Rodríguez-Lago⁸, I. Ordás⁹, I. Kaimakliotis¹⁰, D. Duricova¹¹, S. Sebastian¹², V. Hernandez¹³, I. Mocanu¹⁴, E.-A. Goldis¹⁵, M. Nachury¹⁶, M. Fumery¹⁷, M. Allocca¹⁸, N. Pedersen¹⁹, B. Barberio²⁰, A. Guedes²¹, R. Ribeiro²¹, R. Ungaro²², J.-Y. Mary²³, N.B. Bigot²³, J. Lambert²³, J.-F. Colombel²⁴, J. Torres²⁵

¹Copenhagen University Hospital, Gastrounit Medical Division, Hvidovre, Denmark, ²Hospital Beatriz Ângelo, Division of Gastroenterology, Loures, Portugal, ³Copenhagen University Hospital - Amager and Hvidovre, Gastrounit Medical Division, Hvidovre, Denmark, ⁴St Mark's National Bowel Hospital, Dept. of Gastroenterology, London, United Kingdom, ⁵CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France, ⁶Mater Dei Hospital, Department of Gastroenterology, Msida, Malta, ⁷University Hospital CHU of Liège, Gastroenterology, Liège, Belgium, ⁸Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ⁹Hospital Clinic of Barcelona, Gastroenterology, Barcelona, Spain, ¹⁰American Gastroenterology Center, Gastroenterology and Hepatologist, Strovolos, Cyprus, ¹¹ISCARE I.V.F. a.s., IBD Clinical and Research Center, Prague, Czech Republic, ¹²Hull University Teaching Hospitals NHS Trust, IBD unit, Hull, United Kingdom, ¹³Hospital Alvaro Cunqueiro, Gastroenterology, Vigo, Spain, ¹⁴Hospital Garcia de Orta, Gastroenterology, Almada, Portugal, ¹⁵Algomed Policlinic, Dept. of Gastroenterology, Timisoara, Romania, ¹⁶CHRU Lille, Gastroenterology and Hepatologist, Courbevoie Cedex, France, ¹⁷CHU Amiens-Picardie Hôpital Sud, Department of Hepato - Gastroenterology, Amiens, France, ¹⁸IRCCS Hospital San Raffaele, IBD Center, Milano, Italy, ¹⁹Slagelse Hospital, Gastroenterology, Slagelse, Denmark, ²⁰University of Padua, Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ²¹Hospital da Luz Learning Health, Investigation Center, Lisboa, Portugal, ²²Icahn School of Medicine at Mount Sinai, Gastroenterology, New York, United States of America, ²³ECSTRRA Unit, Centre of Research in Epidemiology and Statistics, UMR 1153, Inserm, Paris, France, ²⁴Icahn School of Medicine at Mount Sinai, Gastroenterology, Usa, United States of America, ²⁵Hospital da Luz, Gastroenterology, Lisbon, Portugal

Contact E-Mail Address: johan.burisch@regionh.dk

Introduction: CD is a chronic progressive disease associated with bowel damage and disability and with a globally increasing prevalence. Contemporary reports on the clinical presentation, disease outcomes, and treatment choices in newly diagnosed patients across Europe are important to inform physicians.

Aims & Methods: To describe the clinical characteristics in a contemporary European cohort of recently diagnosed CD patients. The Crohn's Disease Cohort (CROCO) is an ongoing multicentre, European, prospective cohort study of recently diagnosed CD patients (within 12 months following diagnosis) intended to characterize bowel damage progression and disability. Herin, we report on the characteristics of CD-patients at inclusion in the study.

Results: Between Aug/21-April/24, 316 patients (58% male, 47% smoker or ex-smokers) with a median age at diagnosis of 34.4 (IQR 24.8; 49.6), were recruited from 17 centres. The median delay between symptoms onset and diagnosis was 6.5 months (IQR 2; 17.5); median disease duration at the time of inclusion was 3.9 months (IQR 1.6; 7.6); Ileal involvement (L1/L3) was reported in 86%. Overall, 15% had perianal disease and 28% had extra-intestinal manifestations, the most frequent being arthritis/arthralgia. One-third (32%) had evidence of either stricturing (B2) (17%) or penetrating (B3) (15%) phenotype; 7% had an intestinal-related surgery, and 2% perianal surgery. Fifty-nine (21%) patients had at least one CD-related hospitalization. Median faecal calprotectin was 236µg/g (IQR 75; 731) and median C-reactive protein was 4mg/L (IQR 1.2; 11). Regarding the therapies received from diagnosis to inclusion, 54% of the patients had received systemic steroids, 18% 5ASA, 10% IM monotherapy, and 43% started biological therapy (126 anti-TNF, 6 anti-IL 12/23 and 3 anti-integrin).

Conclusion: In this prospective cohort of newly diagnosed CD-patients, more than one-third of the patients presented with a complicated phenotype despite a short delay between onset of symptoms and diagnosis. Steroids remain frequently used, however early and effective therapy was started in approximately in 40% of patients, highlighting the changing paradigm in CD treatment.

Disclosure: JB: Reports grants and personal fees from AbbVie, grants and personal fees from Janssen-Cilag, personal fees from Celgene, grants and personal fees from MSD, personal fees from Pfizer, grants and personal fees from Takeda, grants and personal fees from Tillots Pharma, personal fees from Samsung Bioepis, grants and personal fees from Bristol Myers Squibb, grants from Novo Nordisk, personal fees from Pharmacosmos, personal fees from Ferring, personal fees from Galapagos, outside the submitted work. NA: received speaker fees from Ferring and Janssen. PE: educational grants Janssen; SV: Speaker fees from Abbvie, Ferring, Janssen Takeda. IR-L: has received financial support for travelling and educational activities from or has served as an advisory board member for Abbvie, Adacety, Celltrion, Chiesi, Danone, Dr. Falk Pharma, Ferring, Faes Farma Janssen, Galapagos, MSD, Otsuka Pharmaceutical, Pfizer, Roche, Takeda, and Tillotts Pharma. IO: has served as speaker and/or consultant and has received educational funding from MSD, Abbvie, Pfizer, Takeda, Janssen, Faes Farma and Chiesi, and has received research funding from Abbvie and Faes Farma. DD: Lecture fee/consultancy from: Takeda, Pfizer, Janssen, Ferring, AbbVie, Eli-Lilly. SS: received consulting fees and advisory board fees from Takeda, AbbVie, Merck, Ferring, Pharmacocosmos, Warner Chilcott, Janssen, Falk Pharma, Biohit, TriGenix, Celgene, and Tillots Pharma; speaker honoraria from AbbVie, Takeda, Celltrion, Pfizer, Biogen, AbbVie, Janssen, Merck, Warner Chilcott, and Falk Pharma. VH: Has served as consultant, has served as speaker, has received travel support or research funding from MSD, AbbVie, Ferring, Dr. Falk Pharma, Tillotts Pharma, Pfizer, Takeda, Janssen, KernPharma Biologics, Adacety, Sandoz, Biogen, Fresenius-Kabi, FAES Farma and Galapagos. MN: received board membership, consultancy, or lecture fees from Abbvie, Amgen, Biogen, Celltrion, Ferring, Fresenius-Kabi, Galapagos, Janssen, Lilly, Mayo-Li-Spindler, MSD, Nordic Pharma, Pfizer, Takeda, Viatrix. MF: Lecture and consulting fees from Abbvie, Pfizer, Tillots, Takeda, Gilead, Arena, Sandoz, Celltrion, Galapagos, Celgene, Boehringer, Biogen, Viatrix, Amgen, Fresenius, Celltrion, CTMA, Ferring and Janssen. MA: Speaker and consulting fees from Abbvie, Pfizer, Ferring and Janssen. BB: Speaker and consulting fees from Janssen, Takeda, Sofar, Alfasigma, Doxapharma. BB: Speaker and consulting fees from Janssen, Takeda, Sofar, Alfasigma, Doxapharma. RCU: has received consulting and/or advisory board fees from AbbVie, Bristol Myers Squibb, Celltrion, Janssen, Lilly, Pfizer, Roivant, Takeda. JC: receiving research grants from AbbVie, Janssen Pharmaceuticals and Takeda; receiving payment for lectures from AbbVie, Amgen, Anaptysbio, Allergan, Inc. Ferring Pharmaceuticals, Shire, and Takeda; receiving

consulting fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, BMS, Celgene Corporation, Eli Lilly, Ferring Pharmaceuticals, Galmed Research, Genentech, Galxo Smith Kline, Japan Gastroenterological Endoscopy Society, Janssen Pharmaceuticals, Kaleido Biosciences, Imedex, Immunix, Iterative Scopes, Merck, Microba, Morgan, Lewis & Bockius LLP, Novartis, Otsuka Pharmaceutical Development PBM Capital, Pfizer, Protagonist Therapeutics Sanofi, Takeda, TiGenix, Vifor; and hold stock options in Intestinal Biotech Development. JT: Grant - AbbVie, Janssen Personal Fees - Pfizer, Janssen, Abbvie, sandoz.

MP150

DISTINCT PERTURBANCES IN METABOLIC PATHWAYS ASSOCIATE WITH DISEASE PROGRESSION EVENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A.R. Bourgonje¹, S. Ibing^{2,3}, C. Argmann⁴, B.E. Sands¹, M.C. Dubinsky¹, M. Suarez-Farinas⁵, S. Mehandru¹, J.-F. Colombel¹, B.Y. Renard³, R.C. Ungaro¹

¹Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America, ²Icahn School of Medicine at Mount Sinai, Hasso Plattner Institute for Digital Health at Mount Sinai, New York, United States of America, ³University of Potsdam, Hasso Plattner Institute - Digital Engineering Faculty, Potsdam, Germany, ⁴Icahn School of Medicine at Mount Sinai, Genetics and Genomic Sciences, New York, United States of America, ⁵Icahn School of Medicine at Mount Sinai, Center of Biostatistics, New York, United States of America

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Patients with inflammatory bowel diseases (IBD) exhibit distinct shifts in circulating metabolite levels that have been associated with clinical disease activity and disease phenotype. However, there are limited data on the impact of metabolomic changes on disease progression in IBD. In this study, we aimed to understand the association of circulating metabolite levels and related pathways with the risk of disease progression in patients with IBD. Furthermore, we aimed to predict disease progression in these patients using both clinical and metabolomic features.

Aims & Methods: We conducted an observational cohort study using the Mount Sinai Crohn's and Colitis Registry (MSCCR). Patients were prospectively enrolled with baseline questionnaires and biospecimens that were then linked to longitudinal electronic health record data. A total of 1,456 serum metabolites were measured in 277 patients with UC and 375 patients with CD using untargeted metabolomics. Disease progression was defined as any new steroid or biological prescriptions, IBD-related hospitalizations, or surgery. Multivariable Cox proportional hazards regression (CoxPH) models, adjusted for age, sex, smoking, biologic use, and surgery were used to explore metabolite associations with risk of disease progression. Metabolite set enrichment analysis (MSEA) was performed to identify underlying metabolic pathways associated with disease progression. Prediction analyses were performed using L1-regularized CoxPH models with Random Survival Forests (RSF), and applied using different preceding feature selection approaches. Clinical parameters and metabolites were used as input features individually and in combination. Models were evaluated using Harrell's C-index, the Brier Score, and the area under the curve (AUC) at 3-years follow-up time.

Results: During a median of 2-year follow-up (IQR 0.3-5.1 years), 375 patients (57.5%) had a disease progression event. Among CD, 151 metabolites significantly correlated with the composite outcome (FDR<0.1). Of these, 81 (53.6%) were linked to higher risk, mainly enriched in amino acids, purine, and pyrimidine metabolism, fibrinogen cleavage peptides,

and bile acid pathways. Additionally, 70 (46.4%) metabolites associated with lower risk with enrichment in fatty acid metabolism, steroid biosynthesis, histidine, tryptophan, and antioxidant pathways. In CD, aspartate metabolism was most significantly associated with increased risk and linoleic metabolism with decreased risk. In UC, 84 metabolites were significantly associated with disease progression (FDR<0.1), with 29 (34.5%) associated with increased and 55 (65.5%) with decreased risk. Metabolic pathways linked to higher risk were sphingolipid, benzoate, hydrogen sulfide, polyamine, and tyrosine metabolism, while protective metabolites were enriched in branched-chain amino acid (BCAA), steroid biosynthesis, histidine, and phenylalanine pathways. In UC, sphingolipid metabolism was prominently associated with increased risk and BCAA metabolism with decreased risk. The combination of metabolomic and clinical features best predicted disease progression in both CD and UC, with 20 and 25 features robustly selected, respectively.

Conclusion: Specific metabolites and metabolic pathways are associated with risk of disease progression in patients with IBD, highlighting potential prognostic metabolite biomarkers and pathways that may be important in modulating risk of disease progression. Metabolomic features improve overall model performance when predicting disease progression in IBD, with distinct metabolites showing high predictive value.

Disclosure: Nothing to disclose.

MP151

ADHERENCE TO DIAGNOSTIC AND TREATMENT RECOMMENDATIONS FOR THE MANAGEMENT OF ACUTE SEVERE ULCERATIVE COLITIS: A PROSPECTIVE AND MULTINATIONAL STUDY

I. Rodríguez-Lago¹, M. Frasson², T. Pinkey³, S. Blackwell⁴, K.B. Gecse⁵, C.J. Buskens⁶, C.H. Knowles⁷, O. Zmora⁸, M.J. Brookes⁹, G. Fiorino¹⁰, P. Nos Mateu¹¹, G. Gallo¹², F. Pata¹³, A. Verjee¹⁴, S. Leone¹⁵, G. Pellino¹⁶, J. P. Gisbert¹⁷, on behalf of MASC (Management of Acute Severe Colitis) collaborating group and ESCP (European Society of Coloproctology) Cohort Studies Group
¹Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ²Hospital Universitario y Politécnico La Fe, Colorectal Surgery, Valencia, Spain, ³Queen Elizabeth Hospital-University of Birmingham, Academic Department of Surgery, Birmingham, United Kingdom, ⁴Patient representative, Liverpool, United Kingdom, ⁵Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁶Academic Medical Center, Surgery, Amsterdam, Netherlands, ⁷Queen Mary University of London- Blizard Institute Knowles, Centre for Neuroscience-Surgery & Trauma, London, United Kingdom, ⁸Assaf Harofeh Medical Center, Division of General Surgery, Zerifin, Israel, ⁹Royal Wolverhampton NHS Trust, Gastroenterology, Wolverhampton, United Kingdom, ¹⁰IRCCS Ospedale San Raffaele and Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ¹¹Hospital Universitario y Politécnico La Fe, Gastroenterology, Gastroenterology, Valencia, Spain, ¹²Sapienza University of Rome, Surgical Sciences, Rome, Italy, ¹³Nicola Giannettasio Hospital, General Surgery Unit, Corigliano-Rossano, Italy, ¹⁴Patient representative, London, United Kingdom, ¹⁵AMICI Italia, Associazione nazionale per le Malattie Infiammatorie Croniche dell'Intestino, Patient representative, Milan, Italy, ¹⁶Università degli Studi della Campania "Luigi Vanvitelli", Advanced Medical and Surgical Sciences, Naples, Italy, ¹⁷Hospital Universitario de La Princesa - Instituto de Investigación Sanitaria Princesa - Universidad Autónoma de Madrid, Gastroenterology, Madrid, Spain

Contact E-Mail Address: iago.r.lago@gmail.com

Introduction: Acute severe ulcerative colitis (ASUC) is a serious, potentially life-threatening condition. Hospital admission and prompt medical therapy with intravenous steroids is crucial, but rescue medical therapy is frequently needed, and surgery is often required.

Aims & Methods: Our aim was to assess the adherence to main diagnostic and management recommendations within the MASC multinational study. MASC was a prospective, multinational cohort study, including all consecutive patients hospitalized for ASUC between February 2019-January 2020. The primary outcome was surgery during the first 90 days after admission. We used descriptive statistics to determine the proportion of patients fulfilling each diagnostic and treatment recommendation according to ECCO and AGA.

Results: A total of 823 patients from 123 centers in 32 countries in five continents were included (median age 39 years [IQR, 28-54], 56% male, 64% non-smokers; Table 1). Most cases (74%) had a previous diagnosis of ulcerative colitis, and around half (48%) with prior ASUC episodes. Upon admission, they were under 5-ASA therapy (60%), thiopurines (14%), or biologics (21%). They were mostly admitted to the Gastroenterology ward (74%). During the initial assessment, 112 patients (15%) did not have stool culture or C. difficile testing, and CMV was evaluated in 50% of cases. Endoscopic assessment was performed in 66% of patients, mainly by flexible rectosigmoidoscopy (74%).

Patient characteristics	Frequency N=823
Age at ASUC diagnosis, median (IQR)	39 years (28-54)
Gender, male, n (%)	463 (56%)
Smoking history, never, n (%)	528 (64%)
Previous UC diagnosis, n (%)	613 (74%)
Disease extension, n (%)	
E1	54 (7%)
E2	298 (36%)
E3	428 (52%)
Previous episodes of ASUC, n (%)	297 (48%)
Ward of admission, Gastroenterology, n (%)	612 (74%)
Treatment upon admission, n (%)	
Oral steroids	37 (6%)
Oral mesalazine	367 (60%)
Thiopurines	85 (14%)
Methotrexate	8 (1.3%)
Anti-TNF	100 (16%)
Vedolizumab	31 (5%)
Tofacitinib	17 (3%)
Calcineurin inhibitors	5 (1%)

Regarding treatment, 3.4% of patients received exclusive parenteral nutrition, 70% low molecular weight heparin, and 42% prophylactic antibiotics. Steroids were started after a median of 0 days (IQR, 0-1), mostly with methylprednisolone or hydrocortisone (64%), 26% with other steroids, and 7% were managed without steroids. Infliximab was started in 159 patients (19%) after a median of 6 days (IQR, 4-8) after starting steroids, with 27% after >7 days. Most of the patients (93%) had some type of tuberculosis screening done prior to infliximab. Twenty-eight patients (3.4%) started cyclosporine. Thirty-two patients (4%) received other rescue therapy different from infliximab or cyclosporin. Colectomy was performed in 25 patients (3%).

Conclusion: The diagnostic and medical management of ASUC remains heterogeneous and different from current recommendations. This context demands more evidence and consensus on the best management of ASUC.

Disclosure: Nothing to disclose.

MP152

IMPACT OF ADVANCED THERAPY ON BOWEL URGENCY IN INFLAMMATORY BOWEL DISEASE: A MULTICENTER STUDY

F. D’Amico¹, O.M. Nardone², A. Bruno¹, M. Allocca¹, A. Zilli¹, F. Furfaro¹, T.L. Parigi¹, F. Ungaro³, I. Faggiani¹, A. La Mantia⁴, G. Calabrese², G. Fiorino⁵, L. Peyrin-Biroulet⁶, L. Massimino³, F. Castiglione², S. Danese¹

¹IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ²University of Naples Federico II, Gastroenterology, Department of Public Health, Naples, Italy, ³IRCCS Ospedale San Raffaele, Experimental Gastroenterology Unit, Division of Immunology, Transplantation and Infectious Disease, Milan, Italy, ⁴University of Naples “Federico II”, Gastroenterology, Department of Public Health, Naples, Italy, ⁵San Camillo-Forlanini Hospital, IBD Unit, Department of Gastroenterology & Digestive Endoscopy, Rome, Italy, ⁶Nancy University Hospital, Department of Gastroenterology, Vandœuvre-lès-Nancy, France

Contact E-Mail Address: damico_ferdinando@libero.it
Introduction: Bowel urgency (BU) is a common symptom in patients with inflammatory bowel disease (IBD). More than 80% of patients with ulcerative colitis (UC) and more than 60% of patients with Crohn’s disease (CD) experience BU during their life. Although BU negatively impacts the quality of life and psychosocial status, currently it is an overlooked symp-

tom. Furthermore, there is little evidence of the effectiveness of available advanced therapies on BU.

Aims & Methods: We aimed to evaluate the impact of different advanced therapies for IBD in improving BU. This was a retrospective cohort study conducted at two third-level centers (IRCCS San Raffaele hospital and university of Naples Federico II) between April 2023 and April 2024. All consecutive patients with confirmed diagnosis of CD or UC who started an advanced therapy (any biological drug or small molecule) with available data regarding BU at baseline (before starting an advanced therapy) and after induction therapy were eligible. BU was assessed using the numeric rating scale urgency score (NRS-us), a validated tool for quantifying BU in IBD. BU was defined as ≥3 in NRS-us. All available clinical (partial Mayo score for UC and Harvey-Bradshaw Index (HBI) for CD), biochemical (fecal calprotectin (FC) and C-reactive protein (CRP)), endoscopic (Mayo endoscopic score or SES-CD score) and intestinal ultrasound data were collected before and after the induction of an advanced therapy. Patients with history of bowel surgery or radiotherapy were excluded. The primary endpoint was BU improvement, defined as an NRS-us ≤3 or a score reduction of at least 2 points. A logistic regression multivariate analysis was performed to identify any correlation between socio-demographic factors, disease features, and treatment at baseline and changes in NRS-us. Analyses were subjected to correction using the false discovery rate (FDR) method.

Results: In total, 159 patients were included (89 male (56%) with a median age of 36 years and a median BMI of 22,1, 104 (65,4%) UC) (Table 1). Patients were treated with infliximab (24,5%), adalimumab (24,5%), ustekinumab (22,6%), vedolizumab (13,2%), upadacitinib (9,4%), tofacitinib (3,1%), filgotinib (1,3%), golimumab (0,6%) risankizumab (0,6%). A small proportion of patients underwent concomitant steroid (8,8%) or immunosuppressant therapy (12,6%). At baseline the median NRS-us was 7. Approximately half of the patients (81, 50,9%) experienced BU improvement after induction with a mean reduction of NRS-us of 2,3 ± 2,9. In the multivariate analysis, improvement in BU was associated with clinical remission (FDR=0.009 for CD and FDR=0.01 for UC), normalization of fecal calprotectin (FDR=0.001) and CRP (FDR=0.008), and normalization of bowel wall thickness to IUS (FDR=0.0006). No statistically significant difference in obtaining an improvement in BU was identified between the different drugs investigated.

	Number (%)
Male	89/159 (56)
Median age (years)	36
UC diagnosis	104 (64)
Median BMI at baseline	22,1
Disease duration (months)	63,4
Median NRS urgency score at baseline	7
Median fecal calprotectin at baseline	500 µg/g
Median C-reactive protein at baseline	10 mg/dL

Conclusion: The available advanced therapies improve bowel urgency after the induction phase. Improvement in BU is associated with clinical, biochemical, and ultrasound remission.

Disclosure: Nothing to disclose.

MP153

ENDOSCOPIC RESPONSE AT 1-YEAR AND ASSOCIATION WITH LONG-TERM CROHN'S DISEASE OUTCOME: A POOLED CLINICAL TRIAL ANALYSIS ADJUSTING FOR 1-YEAR CLINICAL REMISSION STATUS

S. Neff-Baro¹, A. Gauthier¹, M. Sanon², S. Kachroo³, D. Wirth⁴, L. Eisele⁵, K. Gurjar¹, D. Naessens⁶

¹Amaris Consulting, Paris, France, ²Janssen Global Services, Horsham, United States of America, ³Janssen Scientific Affairs, Horsham, United States of America, ⁴Janssen Cilag GmbH, Neuss, Germany, ⁵Jan-Cil Germany, Neuss, Germany, ⁶Janssen-Cilag, Beerse, Belgium

Contact E-Mail Address: msanon@its.jnj.com

Introduction: Therapeutic goals and clinical guidelines in Crohn's disease (CD) have evolved to include endoscopic outcomes being a key prognostic parameter in disease management. STRIDE-II guidelines comprise of clinical and patient-reported outcome remission, along with biomarker normalization and endoscopic healing. While available publications have correlated achievement of endoscopic response with long-term outcomes, few if any have adjusted for clinical remission status. Moreover, most of the data comes from patients treated with immunomodulators and/or TNFs. The objective of this analysis was to assess the impact of endoscopic response at the end of maintenance and long-term outcomes while adjusting for clinical remission status at maintenance.

Aims & Methods: Data from two randomized clinical trials (GALAXI-1, NCT03466411 and IM-UNITI, NCT01369355) were pooled to assess the impact of endoscopic response at 1 year on long-term patient relevant outcomes including clinical response, clinical remission, quality of life as assessed by the Inflammatory Bowel Disease Questionnaire (IBDQ), and risk for hospitalizations/surgeries. This post-hoc analysis assessed endoscopic response at the end of maintenance (~48 weeks) and patient relevant outcomes in the long-term extension (LTE) duration (~96 weeks). Patients without LTE outcome data and placebo treated patients were excluded. Multivariate analyses with trial as a random effect were conducted and adjusted for treatment arm during maintenance, clinical remission status at end of maintenance (EOM), and endoscopic response at EOM.

Results: A total of 461 patients had available endoscopy and clinical remission status at EOM (IM-UNITI, N=177; GALAXI-1, N=284). The number of patients with available LTE outcomes ranged from 290 (IBDQ remission) to 383 (clinical remission/clinical response). Endoscopic response at EOM was significantly associated with higher odds of LTE clinical remission and IBDQ remission with ORs of 1.91 and 1.99 respectively, with corresponding p values below 0.05. Endoscopic response at EOM was also associated with lower odds of LTE C-reactive Protein abnormality (OR=0.46, p<0.005), a marker of inflammation and disease activity. Lastly, a greater percentage of patients without endoscopic response at EOM experienced hospitalizations/surgeries though the difference was not significant due to low event counts (16% versus 9%, p=0.1237).

Conclusion: This analysis uses clinical data from robust trials and adjusted for patients' clinical remission status at the end of maintenance to isolate the benefit of endoscopic response in predicting long-term outcomes. Endoscopic response is significantly associated with more patients reaching clinical remission and better quality of life. Further investigation in large datasets with longer follow-up is needed to better understand whether measures of endoscopic improvement are also good surrogates for reductions in hospitalizations and surgeries.

Disclosure: Janssen Global Services provided funding for this research and I am an employee of Janssen.

MP154

EFFECTIVENESS OF INTRAVENOUS VEDOLIZUMAB INDUCTION AND DOSE ESCALATION IN ULCERATIVE COLITIS AND CROHN'S DISEASE; A LARGE-SCALE, CANADIAN REAL-WORLD COHORT.

E.-J. Bernard^{1,2}, J.-F. LeBlanc^{3,2}, A.H. Steinhart⁴, A. Wadhwa⁵, R. Ward⁵, J. Weiss⁶, C. Pettengell⁶, B. Bressler⁷

¹CHUM, Montreal, Canada, ²Université de Montréal, Montréal, Canada, ³Sacre-Coeur Hospital, Montréal, Canada, ⁴University of Toronto, Toronto, Canada, ⁵Takeda Canada Inc, Toronto, Canada, ⁶Pentavere Research Group, Toronto, Canada, ⁷University of British Columbia, Vancouver, Canada

Contact E-Mail Address: jean-frederic.leblanc@mail.mcgill.ca

Introduction: Vedolizumab (VDZ) is a gut-selective anti-lymphocyte trafficking drug indicated for the treatment of CD and UC [1] administered by intravenous (IV) infusion at Weeks 0, 2, and 6 followed by IV infusions every 8 weeks (Q8W) or subcutaneous injections every 2 weeks [2,3]. For IV treated patients who experience a suboptimal or loss of response (LOR), dose escalation to every four-week infusions (Q4W) may recapture response to treatment [4] but there is a lack of large-scale real-world data describing outcomes of dose-escalated patients [5].

Aims & Methods: Patients with moderately to severely active UC or CD were prospectively followed in a patient support program in Canada from 2015 to 2023. Harvey-Bradshaw Index (HBI, CD) and Partial Mayo Scores (PMS, UC) were assessed 2, 6, and 14 weeks after treatment initiation to understand VDZ induction effectiveness. HBI or PMS were assessed 12 weeks post dose Q4W escalation to understand the effectiveness of dose escalation in the presence of suboptimal or LOR.

Results are presented for patients who dose escalated to Q4W from Q8W maintenance (Q8W > Q4W), initiated Q4W at week 14 (w14>Q4W), or at week 10 (w10>Q4W). Remission was defined as HBI <5, or PMS <3. Response was defined as achieving remission or an HBI decrease of ≥3 points from baseline, or a PMS decrease of ≥2 points and ≥25% from baseline.

Results: 1056 CD (45% bio-naïve) patients and 1959 UC patients (71% bio-naïve) were eligible for this study. The median follow up was 18 months (range 3-61). The median age was 48 years (range: 18-92), and 44 years (range:18-89) for CD and UC patients respectively. 60% of CD patients and 51% of UC patients were female. For CD patients the median baseline HBI score was 10 (range 8-40), and for UC patients the median baseline PMS score was 6 (range 5-20).

Disease duration prior to VDZ was longer in bio-experienced patients compared to bio-naïve; CD (Medians: 14 vs 4 years) and UC (Medians: 6 vs 4 years). To further characterise the patient cohort induction effectiveness is reported. For CD patients, remission and response were 25% and 56% at 2 weeks, 34% and 66% at 6 weeks and 40% and 68% at 14 weeks.

For UC patients, remission and response were 32% and 64% at 2 weeks, 48% and 78% at 6 weeks and 55% and 81% at 14 weeks. In CD, 39% (183 of 473) of bio-naïve patients and 52% (302 of 583) of bio-experienced patients dose-escalated to Q4W within the first two years. In UC, 37% (520 of 1399) of bio-naïve patients and 49% (275 of 560) of bio-experienced patients dose-escalated to Q4W within the first two years. At Q4W dose escalation, 319 CD patients (110 bio-naïve, 209 bio-experienced) and 514 UC patients (334 bio-naïve, 180 bio-experienced) were not in HBI or PMS remission. For these patients, remission and response 12-weeks post dose escalation to Q4W are presented in table 1.

Conclusion: IBD patients experienced clinically meaningful remission and response rates following induction with IV VDZ. For those that have a suboptimal or LOR this study demonstrates the real-world effectiveness of dose escalating VDZ to Q4W in Canadian patients with IBD to complement previous clinical trials, and real-world studies.

	CD Bio-Naïve (N =110)			CD Bio- Experienced (N =209)			UC Bio-Naïve (N =334)			UC Bio-Experienced (N =180)		
	Q8W> Q4W (N=58)	W14> Q4W (N=36)	W10> Q4W (N=16)	Q8W> Q4W (N=119)	W14> Q4W (N=45)	W10> Q4W (N=45)	Q8W> Q4W (N=163)	W14> Q4W (N=100)	W10> Q4W (N=71)	Q8W> Q4W (N=79)	W14> Q4W (N=56)	W10> Q4W (N=45)
In Remission N (%)	25 (47%)	4 (13%)	2 (15%)	27 (24%)	9 (23%)	27 (22%)	65 (42%)	31 (42%)	15 (29%)	27 (37%)	19 (40%)	8 (22%)
In Response N (%)	33 (62%)	13 (43%)	4 (31%)	52 (47%)	23 (59%)	21 (52%)	86 (56%)	44 (59%)	26 (50%)	42 (58%)	26 (55%)	14 (38%)
Missing	5	6	3	8	6	5	9	26	19	6	9	8

Table 1: 12-week remission and response rates for pts dose escalated to Q4W from maintenance (Q8W>Q4W), at week 14 (W14>Q4W) or at week 10 (W10>Q4W)

References: 1. Argollo, M., et al., *Novel therapeutic targets for inflammatory bowel disease*. J Autoimmun, 2017. 85: p. 103-116.
2. Sandborn, W.J., et al., *Vedolizumab as induction and maintenance therapy for Crohn's disease*. N Engl J Med, 2013. 369(8): p. 711-21.
3. Feagan, B.G., et al., *Vedolizumab as induction and maintenance therapy for ulcerative colitis*. N Engl J Med, 2013. 369(8): p. 699-710.
4. Varghese, D., et al., *P632 Vedolizumab dose escalation in patients with inflammatory bowel disease experiencing loss of response: A systematic review and meta-analysis of real-world evidence*. Journal of Crohn's and Colitis, 2020. 14(Supplement_1): p. S524-S525.
5. Peyrin-Biroulet, L., et al., *Loss of Response to Vedolizumab and Ability of Dose Intensification to Restore Response in Patients With Crohn's Disease or Ulcerative Colitis: A Systematic Review and Meta-analysis*.

Disclosure: Jessica Weiss - Employee of Pentavere Research Group Inc.
Dr. Christopher Pettengell - Employee of Pentavere Research Group Inc.
Dr. Jean-Frédéric LeBlanc - AbbVie, BMS, Janssen, Fresenius-Kabi, Pfizer, Sandoz, Takeda.
Dr. Edmond-Jean Bernard - Fees of SICLEO for my presentations, Participation in advisory boards or speaker services: Abbvie, Janssen, Takeda, Pfizer, Merck, Amgen, Pendopharm, Jamp, Fresenius, Kabi, Bausch Health, Celltrion, Eli Lilly, BMS, Grant/Research: Janssen, Abbvie, Any other investment or relationship that could be judged by a reasonable and knowledgeable participant to have the potential to influence the content of the training activity: Abbvie, Janssen, Takeda, Pfizer, Merck, Amgen, Pendopharm, Jamp, Fresenius, Kabi, Bausch Health, Celltrion, BMS
Dr. Brian Bressler: Advisor/Speaker: Ferring, Janssen, Abbvie, Takeda, Pfizer, BMS, Merck, Sandoz, Organon, Lifelabs, Celltrion. Advisor: Alimentiv, Gilead, Iterative Health, AMT, Celgene, Merck, Amgen, Pendopharm, Eli Lilly, BMS, Fresenius Kabi, Mylan, Viatrix, Bausch Health, Celltrion Healthcare, BioJamp Pharma, Eupraxia. Research support: Janssen, Abbvie, GSK, BMS, Amgen, Genentech, Merck. Stock Options: Qu Biologic
Dr. A. Hillary Steinhart: Advisory Board Membership/Consultant: Abbvie, Amgen, BioJAMP, BMS, Fresenius Kabi, Janssen, McKesson, Mylan Pharmaceuticals, Organon, Pendopharm, Roche, Pfizer, Sandoz, Takeda, Viatrix, Speakers' Bureau: Abbvie, Amgen, Ferring, Fresenius Kabi, Janssen, Organon, Pfizer, Sandoz, Takeda, Research Grants: Abbvie, Arena, Celgene/BMS, Genentech, Janssen, Roche, Takeda
Dr. Ryan Ward - Employee of Takeda
Abhinav Wadhwa - Employee of Takeda

MP155

THE CHOICE OF FIRST-LINE BIOLOGICAL THERAPIES IS HIGHLY IMPACTING THE EVOLUTION OF ULCERATIVE COLITIS AND CANNOT BE RESCUED BY LATER TREATMENTS: RESULTS FROM THE APPETISER STUDY

D. M'Baye¹, B. Pereira¹, A. Buisson¹

¹CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France

Contact E-Mail Address: a_buisson@hotmail.fr

Introduction: Therapeutic sequencing is a burning question in patients with ulcerative colitis (UC) requiring an advanced therapy. Whether starting with a less effective but safer and more convenient drug is a loss of chance for UC patients or can be rescued by later treatments is key point.

Aims & Methods: In the APPETISER study, we compared the effectiveness of two strategies based on the choice of the first biologic owing to either the drug efficacy in network meta-analyses and randomized controlled trials (vedolizumab or infliximab) or better acceptability (full subcutaneous therapy: adalimumab and golimumab) to induce and maintain steroid-free clinical remission during the first 24 months.

We collected real-world data from an IBD referral center including all consecutive UC patients ≥ 18 years-old who started a first line of biologic for active UC with follow-up > 6 months. Prior colectomy or severe acute colitis were excluded. Patients were included in either effectiveness-based sequencing (EBS) if they started with infliximab or vedolizumab, or in acceptability-based sequencing (ABS) if they received adalimumab or golimumab as first-line biologic.

The primary endpoint was remission defined according to PRO2 (PRO2-remission) as the absence of bleeding, normalization of transit (Mayo stool frequency subscore = 0) and no steroid. PRO2-remission was defined as a binary criterion each month (the statistical unit being the month and not the patient).

The secondary endpoints concerned the analysis by patient and were CFREM (partial Mayo score ≤ 2 without steroid) at week 12 and 52, endoscopic remission (CFREM + score Endoscopic Mayo ≤ 1) at week 12, time to drug discontinuation and time to colectomy.

All comparisons were adjusted using propensity scores on potential confounders. Analysis by month was performed using mixed models to account for repeated data.

Results: Overall, 130 patients were included including 60 patients in the EBS group (IFX= 50 and VDZ= 10) and 70 in the ABS group (ADA= 48 and GLM= 22).

The populations had similar characteristics at baseline apart from concomitant immunosuppressant more frequent in EBS group (55.9% vs 21.7%). 2nd line treatment was started in 26.7% of patients in EBS group (ADA in 48.8%, VDZ 25.5% and ustekinumab 18.8%) and 87.1% of patients in ABS group (IFX in 54.1%, VDZ 31.1%).

After adjustment, the rate of CFREM was significantly higher in EBS arm than in ABS arm at week 12 (70.8% vs 33.0%, p < 0.001) and week 52 (72.8% vs 42.1%, p = 0.017). The rate of endoscopic remission at W12 was 22.1% and 10.0% in EBS and ABS arms, respectively (p = 0.086).

For the primary endpoint, 3350 months were analyzed (1180 in EBS arm and 1175 in ABS arm). The percentage of months spent in PRO2-CFREM in the first 24 months (primary endpoint) was greater in EBS arm than in ABS arm (74.2% vs 46.6%; p<0.001). The percentage of months spent in CFREM was higher in the IV arm in the first 6 months (60.4% vs 18.9%), and was not rescued later: between M7 and M12 (73.1% vs 38.6%), M13 and M18 (79.9% vs 57.0%) or M19 and M24 (83.3% vs 64.6%) (p < 0.001 for all comparisons).

Regarding long-term data, EBS group had a lower risk to first-line biologic discontinuation (aHR=6.5 [2.8-15.3], p < 0.001) and a clear trend for lower risk of colectomy (aHR=4.5 [0.9-22.3], p = 0.068).

Conclusion: Our data highlight that the choice of first-line biological therapies is highly impacting the evolution of ulcerative colitis and cannot be rescued by later treatments. Thus, the results of the APPETISER study advocate for the use of the most effective therapeutic option as first line of biologic.

Disclosure: Anthony BUISSON: Consulting fees for Abbvie, Amgen, Arena, Biogen, Celltrion Healthcare, CTMA, Galapagos/Alfa Sigma, Gutycare/Resilience, Janssen, MSD, Nexbiome, Pfizer, Roche, Sandoz, Takeda, Tillotts. And Viatrix. Lecture fees for Abbvie, Amgen, Biogen, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Mayoli-Spindler, MSD, Nordic Pharma, Norgine, Pfizer, Roche, Takeda, Tillotts and Vifor Pharma. Research grants from: Abbvie, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Lesaffre, Lilly, Pfizer, Takeda.

MP156

EFFICACY OF SECOND-LINE TREATMENTS FOLLOWING FIRST-LINE VEDOLIZUMAB TREATMENT IN ULCERATIVE COLITIS: A RETROSPECTIVE MULTICENTER STUDY OF GETAID

L. Calmejane¹, C. Reenaers², A. Amiot³, S. Nancey⁴, A. Nuzzo⁵, L. Vuitton⁶, C. Atanasiu⁷, C. Stefanescu⁸, R. Altwegg⁹, L. Guillo¹⁰, G. Bouguen¹¹, M. Nachury¹², G. Le Cosquer¹³, X. Roblin¹⁴, V. Abitbol¹⁵, D. Laharie¹⁶, M. Fumery¹⁷, M. Cavicchi¹⁸, M. Charkaoui¹⁹, A. Buisson²⁰, B. Caron²¹, B. Coffin²², S. Geyl²³, M. Vidon²⁴, J. Kirchgesner²⁵, M. Uzzan²⁶

¹Université Paris Cité, Paris, France, ²Assistants en formation gastro, réseau Ulg - CHU Sart Tilman, Assistants en formation gastro, réseau, CHU Sart Tilman, Lantremange, Belgium, ³Henri Mondor Hospital, APHP Dept. of Gastroenterology, Dept. of Gastroenterology, Creteil, France, ⁴Lyon Sud, Dept. de Gastroenterologie, Pierre Benite, France, ⁵Beaujon Hospital, Intestinal Stroke Center unit, Department of Gastroenterology, IBD, Intestinal Failure, Paris, France, ⁶Besançon university hospital gastroenterology, Dept. of Gastroenterology, Courbevoie, France, ⁷Hôpital Saint-Joseph, Gastroenterology, Paris, France, ⁸Institut des MICI, Neuilly-sur-Seine, France, ⁹HOPITAL SAINT ELOI Hepatologie Gastro enterologie, Montpellier cedex 5, France, ¹⁰Hôpital Nord, Marseille, France, ¹¹CHU Pontchaillou, Service des Maladies de l'Appareil Digestif, Rennes, France, ¹²CHRU Lille, Gastroenterology, Courbevoie Cedex, France, ¹³CHU Toulouse, Toulouse, France, ¹⁴University of St. Etienne Dept. de Gastroenterologie, Saint Etienne, France, ¹⁵Hopital Cochin Gastroentérologie AP-HP, Paris Cedex 14, France, ¹⁶CHU de Bordeaux Hopital Haut-Leveque Dept. de Gastroenterologie, Pessac cedex, France, ¹⁷Amiens University Hospital, Gastroenterology department, Amiens, France, ¹⁸Hopital Henri Mondor, Creteil, France, ¹⁹CHU DIJON, Gastro enterology, Paris Cedex 12, France, ²⁰CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France, ²¹Hôpital de Haute-pierre, Strasbourg, France, ²²Hopital Louis Mourier, Dept. de Gastroentérologie, Colombes Cedex, France, ²³CHU Limoges, hepato-gastro-enterology, Limoges, France, ²⁴CHI Créteil, Créteil, France, ²⁵Saint-Antoine Hospital - Department of Gastroenterology, Department of Gastroenterology, Paris, France, ²⁶Hôpital Mondor, Gastroenterology, Paris, France

Contact E-Mail Address: louis.calmejane@aphp.fr

Introduction: As a first-line biotherapy, vedolizumab showed superior efficacy compared to adalimumab in the VARSITY trial, which, combined with a favorable safety profile, should position it in a privileged position in bionave patients with ulcerative colitis (UC). However, a proportion of

patients have an insufficient response and/or intolerance, resulting in the need for a 2nd line of advanced therapy. To date, there are no data on the efficacy of biotherapies and small molecules in the 2nd line treatment of UC, after vedolizumab has failed. The objective of our study was to compare the efficacy of anti-TNFs, ustekinumab and JAKi in 2nd line in UC, after prior exposure to vedolizumab.

Aims & Methods: We conducted a retrospective multicenter study in 27 French and Belgian GETAID centers. All UC patients treated with vedolizumab in the first-line setting who received a second-line of anti-TNFs, ustekinumab and JAKi were retrospectively included. The primary outcome was corticoid-free remission at induction (week 14) defined by a clinical partial Mayo score of 2 or less, with no subscore greater than 1, in patients still receiving 2nd line therapy. The response was defined as a decrease in partial Mayo score of at least 30%. We also assessed the persistence rate of second-line treatments using the Kaplan-Meier method.

Results: 203 patients were included with a median follow-up of 5 months (IQR: 3.0-11.0). Of the 203 patients, 123 (60.6%), 64 (31.5%) and 16 (7.9%) were treated with anti-TNF, ustekinumab and JAKi in the second-line setting. The median duration of disease progression was 39 months prior to the introduction of the second line (IQR 15-137.0). Vedolizumab was discontinued in 109 patients for primary failure (53.7%), 81 patients for secondary failure (34.9%), and 14 patients for adverse reaction (7.4%).

At week 14, 31/95 (32.6%) patients on infliximab, 7/27 (25.9%) on SC anti-TNF, 20/63 (31.7%) on ustekinumab and 7/16 (43.8%) treated with JAKi achieved corticosteroid-free remission. Remission rates were 37.9% for patients on infliximab, 33.3% on SC anti-TNF, 50% on JAKi, and 38.1% on ustekinumab. Response rates were 51.6%, 40.8%, 52.4%, and 62.5%, respectively, for the infliximab, anti-TNF SC, ustekinumab and JAKi groups. At 1-year, overall treatment persistence was 41.9% [IC 95% 34.7-50.6%]. Treatment persistence was 45.2% [35.0-58.4] in patients treated with infliximab, 43.3% [27.8-67.5] for anti-TNF SC, 40.4% [28.2-58.0] in the Ustekinumab group and 18.8% [5.5-64.3] for the JAKi.

Second-line therapy was discontinued in 37 patients (34.9%) for primary failure, 53 (50%) for secondary failure and 16 (15.1%) for adverse reaction. The overall adverse reaction rate was 31/203 (15.3%), of which 16 resulted in discontinuation (15.1%). In patients on infliximab, the overall rate was 19/96 (19.8%), and infliximab was discontinued in 10 patients (10.4%) due to adverse reactions. With JAKi, the overall rate was 1/16 (6.3%) with no cases of herpes zoster or thrombo-embolic events. Finally, in the 64 patients treated with ustekinumab, only 5 side effects especially arthralgias were reported (7.8%).

Conclusion: This is the largest real-world study of the efficacy of second-line treatments after vedolizumab in UC. Corticosteroid-free remission rates at induction appeared to be similar between the different treatment groups. About forty percent of patients remained on second-line treatment at one year. Discontinuation of second-line treatment was predominantly related to primary or secondary failures. Efficacy at induction appeared to be similar between the different treatment groups.

Disclosure: Nothing to disclose.

MP157

DURABILITY OF A SECOND-LINE ANTI-TNF α AGENT AFTER FIRST ANTI-TNF α FAILURE COMPARED TO A DIFFERENT MECHANISM OF ACTION IN ULCERATIVE COLITIS: CAMBIACU STUDY

M. López-Vico¹, A. Hernández Martínez², P. Soto-Escribano³, M. Rojas-Feria⁴, A.M Caballero-Mateos⁵, A.M. Traperro-Martínez⁶, A.D. Sanchez Capilla¹, M.J. Cabello Tapia¹, M.M. Martín Rodríguez¹
¹Hospital Universitario Virgen de las Nieves, Gastroenterology Unit, Granada, Spain, ²Hospital Universitario Torrecárdenas, Gastroenterology Unit, Almería, Spain, ³Hospital Universitario Reina Sofía, Gastroenterology Unit, Córdoba, Spain, ⁴Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ⁵Hospital Universitario Clínico San Cecilio, Gastroenterology Unit, Granada, Spain, ⁶Hospital Universitario de Jaén, Gastroenterology Unit, Jaén, Spain

Contact E-Mail Address: leunamlv@gmail.com

Introduction: After first anti-TNF α (aTNF) failure in ulcerative colitis (UC), switching to a different mechanism of action (MoA) could decrease the rates of failure and discontinuation compared to a second aTNF and with a better safety profile.

Aims & Methods: We performed a retrospective and multicenter study (6 Andalusian sites). Patients diagnosed of UC who had failed a first biological therapy with an aTNF and started a second-line biological therapy with another aTNF or a different MoA such as ustekinumab (UST), vedolizumab (VDZ), tofacitinib and filgobinib (JAK) were included. The aim of our study was to evaluate the long-term durability of a different MoA compared to a second aTNF after a first-line therapy failure with aTNF.

Results: 185 patients with UC were included. There were no significant differences between both groups in terms of age, sex, extension of disease, extraintestinal manifestations or IMIDs, smoking habit or HLA-DQA1*05. The only significant difference was disease duration (9 years MoA vs 12 years in second aTNF, $p=0.02$). 80 patients received a different MoA (37 VDZ, 24 UST, 19 JAK) and 105 a second aTNF (34 IFX, 60 ADA, 11 golimumab). Duration of first aTNF, although non-significant ($p=0.06$), tended to be shorter in the MoA group (7 months vs 12 months in aTNF group). The most frequent cause of suspension of first aTNF in the MoA group was primary failure (46% vs 31%, $p=0.02$) and in the second aTNF group was secondary failure (51% vs 35%, $p=0.02$). The follow-up mean was 22.4 months in the group of a different MoA and 23.3 months in the second aTNF group. 60% of patients discontinued the second-line biological treatment, 64% with aTNF vs 35% with a different MoA. Durability of therapies in the group of different MoA was significantly longer compared with second aTNF (50% vs 31.4%, $p=0.036$) (figure 1). UST showed the best durability (66.7%), followed by JAK (63.2%), IFX (52.9%), VDZ (32.4%), ADA (21.7%) and golimumab (18.2%), with significant differences ($p=0.03$). Reasons for discontinuation were primary failure in 29.7% (63.6% second aTNF vs 36.4% different MoA), secondary failure in 25.9% (64.5% second aTNF vs 35.5% different MoA) and intolerance or adverse events in 6.4% (66.6% second aTNF vs 34.4% different MoA). Adverse events were reported in 12 patients, 8 with aTNF and 4 with other MoA (2 vs 0 infusion reactions, 1 vs 1 mild infections, 2 vs 1 respiratory adverse effects, 1 vs 1 cutaneous reactions, 1 vs 0 musculoskeletal effects, 1 vs 1 neoplasia).

Conclusion: Our study shows that after a first aTNF failure in UC, a switch to a biological therapy with a different MoA achieves longer survival compared to switching to a second aTNF, with less primary and secondary failure.

Disclosure: Nothing to disclose.

MP158

THE IMPACT OF PROACTIVE AND REACTIVE DRUG MONITORING WITH POINT-OF-CARE METHOD ON THE MEDIUM-TERM COURSE OF INFLAMMATORY BOWEL DISEASE

E. Iványi¹, B. Farkas¹, T. Resál¹, P. Bacsur¹, A. Balint¹, K. Farkas¹, Z. Szepes¹, T. Molnár¹

¹University of Szeged, Albert Szent-Györgyi Medical Center, Department of Internal Medicine, Szeged, Hungary

Contact E-Mail Address: ivanyemese@gmail.com

Introduction: Anti-TNF therapy has revolutionised the treatment of patients with Crohn's disease (CD) and ulcerative colitis (UC). However, primary resistance or loss of efficacy are serious clinical challenges. Therapeutic drug monitoring (TDM) could help to manage these unfavourable therapeutic outcomes. The measurement of anti-TNF drug levels (DL) with point-of-care tests (POCT) is fast, simple tool to guide the therapy. TDM can be performed reactively in patients with active disease and proactively in asymptomatic patients. Nevertheless, the optimal utilization of TDM is still debated.

Aims & Methods: Our aim was to evaluate the impact of proactive and reactive TDM on the medium-term course of inflammatory bowel disease. We enrolled patients with UC and CD who were treated at our department with infliximab or adalimumab and underwent reactive or proactive TDM with POCT method between October 2021 and September 2023. We examined the types of therapeutic decision (dose intensification, switch within or out of class) were performed knowing DL and how the changes have affected the half-yearly outcome. Laboratory findings such as C-reactive protein (CRP), iron, albumin, haemoglobin, platelet, stool calprotectin level and calculated disease activity indices, Crohn's disease activity index (CDAI), Harvey-Bradshaw Index (HBI), partial Mayo score (pMayo) and Simple clinical colitis activity index (SCCAI) were analysed at baseline and after 6 months. Statistical analysis was carried out with Graphpad Prism and SPSS.

Results: 175 patients were enrolled, 80 men, 95 women, median age was 38 (IQR 30-50 years). 81 UC and 94 CD patients. In 79 cases proactive, in 96 cases reactive TDM was performed. In the reactive group the CRP (5.9 vs 12.2 mg/l, $p=0.010$), platelet count (278.3 vs 314.5 G/l, $p=0.024$) and the four activity indices (CDAI $p=0.004$, HBI $p=0.0004$, SCCAI $p<0.0001$, pMayo $p<0.0001$) were significantly higher, the albumin level (46.5 vs 45 g/l, $p=0.019$) was significantly lower compared to the proactive group at baseline. In the reactive group CRP (12.2 vs 5.7 mg/l, $p=0.0083$) and albumin level (46.5 vs 45 g/l $p=0.0186$) and all examined activity indices (CDAI $p<0.0001$, HBI $p=0.0003$, SCCAI $p<0.0001$, pMayo $p=0.0002$) changed significantly after 6 month from baseline. In the proactive group the lowering of SCCAI ($p=0.0232$), pMayo ($p=0.0077$) and CDAI ($p=0.0471$) were significant comparing baseline and 6-month parameters. Between the proactive and reactive groups no significant difference was found at month 6. In 41 (52%) cases in the proactive group subtherapeutic DL was found. Within these cases in CD patients CDAI ($p=0.035$, OR:1.02, 95%CI: 1.0-1.05) had a significant predictive value for the half-yearly outcome, in UC platelet count appeared to be nearly significant ($p=0.097$, OR: 1.07, 95%CI: 0.99-1.15) as a predictive factor. In 41 (52%) of the proactively measured cases no intervention was done, 27 (34%) dose-intensification, 5 (6%) de-escalation, 5 (6%) stop and 2 (3%) switch was carried out. In the reactively measured group 55 patients (57%) had subtherapeutic DL. In the reactive group no therapeutic change happened in 25 cases (26%), 42 (44%) underwent dose-intensification, 29 (30%) had switch (13 within class, 16 out of class).

Conclusion: We found no difference between the proactive and reactive drug level monitoring methods with POCT. Both affected the decision-making process and presented beneficial effect for medium-term and helped to achieve stride therapy goals.

Disclosure: Nothing to disclose.

Mechanisms and treatment of IBS

17:00-18:00 / Poster Stage 2

MP159

PSYCHOLOGICAL INTERVENTION USING VIRTUAL REALITY FOR IRRITABLE BOWEL SYNDROME: PRELIMINARY RESULTS OF A RANDOMISED, SINGLE BLINDED, PARALLEL, PLACEBO-CONTROLLED STUDY

A. Aguilar^{1,2}, A. Beneria^{3,4,5,6}, M. Oriol- Escudé³, C. Pérez-Galbarro³, D. Restoy³, C. Barber Caselles^{1,2}, L.G. Alcala Gonzalez^{1,2}, J. Santos^{1,2}, C. Malagelada^{1,2}, B. Lobo Alvarez^{1,2}, J.A. Ramos^{3,4,5,6}, J. Serra^{1,2}

¹Hospital Universitari Vall d'Hebron, Digestive System Research Unit, Barcelona, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (Ciberehd), Barcelona, Spain, ³Hospital Universitari Vall d'Hebron, Department of Mental Health, Barcelona, Spain, ⁴Vall d'Hebron Research Institute (VHIR), Group of Psychiatry, Mental Health and Addictions, Barcelona, Spain, ⁵Biomedical Network Research Centre on Mental Health (CIBERSAM), Barcelona, Spain, ⁶Universitat Autònoma de Barcelona, Barcelona, Spain

Contact E-Mail Address: ariadna.agca@gmail.com

Introduction: Psychological therapies have been shown to be effective for treatment of patients with disorders of gut-brain interaction like irritable bowel syndrome (IBS). However, these therapies are time and personnel demanding which limits the access to this therapeutic option for many patients. Virtual reality (VR) creates an immersive environment where psychological interventions can be self-administered by the patient at home, thereby facilitating the access of these interventions to a large number of patients with minimal costs.

Aims & Methods: Our aim was to evaluate the effect of a psychological intervention delivered using VR on digestive symptoms in patients with IBS. Thirty-six patients with IBS (mean age 42±2 years, 89 % female) were randomized to receive a VR-based psychological intervention or placebo, using a randomized, single blind, parallel study design. The psychological intervention consisted in a 6-week program that started with a session of psychoeducation using a specifically created VR-video, followed by weekly sessions of group psychotherapy applied on-line by a psychologist. During the 6 treatment weeks, patients were asked to perform 15-30-min VR-sessions at home every day following a pre-designed protocol that incorporated progressive psychological interventions using VR-videos developed by a specialized company (XRHealth, Massachusetts, USA). The placebo group took a pill containing 0.3 g of glucose once daily. The primary outcome was the improvement of gastrointestinal symptoms (assessed by IBS-SSS) at the end of the intervention (6 weeks). Secondary outcomes included psychological comorbidities using the HADS (Hospital Anxiety and Depression Scale) and PSS (Perceived Stress Scale) questionnaires.

Results: Twenty-one patients were randomized to VR and fifteen patients to placebo. After 6 weeks of treatment, patients receiving the psychological intervention had a significantly greater reduction in IBS-SSS scores (score change -39±12) compared to patients on placebo (score change 1±19; $p=0.009$). When analyzing the specific symptoms, abdominal pain had a significant reduction after psychological intervention (score reduction -8±3; $p=0.015$) and a tendency was identified for abdominal bloating (score reduction -6±5; $p=0.097$). Both symptoms remained unchanged after placebo (score change 1±6; $p=0.719$ and -0±6; $p=0.695$, pain and distension, respectively).

In addition, psychological intervention was followed by a greater improvement than placebo in HADS scores for anxiety (score change -2.35 ± 0.56; $p=0.041$ vs score change 0.00 ± 0.85 after placebo) and depression

(score change -1.40± 0.71; $p=0.005$ vs score change 1.36 ± 0.50 after placebo). Stress evaluation using PSS also showed a greater reduction in stress perception in patients on psychological intervention (score change -5.15 ± 1.50) compared with patients on placebo 0.07 ± 1.35 ($p=0.023$).

Conclusion: A psychological intervention delivered at home using virtual reality is superior to placebo in relieving IBS symptoms, an effect that is associated to a reduction in anxiety, depression and stress in patients with IBS. These findings open the door to development of treatments in patients own home, and should facilitate the access to these treatments in large populations of patients. NTC06318572

Disclosure: No potential conflict of interest of any author.

MP160

INVOLVEMENT OF EOSINOPHIL-DRIVEN INTESTINAL IMMUNE ACTIVATION IN THE RESPONSE TO THE DOMINO DIET IN PRIMARY CARE PATIENTS WITH IRRITABLE BOWEL SYNDROME

K. Van den Houte¹, K. Routhiaux¹, J. Toth¹, M. Ceulemans², M.P. Jones³, L. Balsiger¹, J. Raes⁴, T. Vanuytsel⁵, F. Carbone⁶, J. Tack⁷

¹KU Leuven, TARGID, Leuven, Belgium, ²KU Leuven, Translational Research Center for Gastrointestinal Disorders, Leuven, Belgium, ³Macquarie University, Psychology, North Ryde, Australia, ⁴Rega Instituut, Leuven, Belgium, ⁵KU Leuven, Department of Gastroenterology, Leuven, Belgium, ⁶University of Leuven, TARGID, Leuven, Belgium, ⁷University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: karen.vandenhoute@kuleuven.be

Introduction: The DOMINO diet app (diet) provides superior symptom relief to a spasmolytic agent (otilonium bromide, OB) in primary care Irritable Bowel Syndrome (IBS)¹. While the DOMINO diet aimed to provide a practical approach to lower intake of FODMAPs (fermentable oligo-, di-, monosaccharides and polyols), genetic polymorphisms in the eosinophil trafficking chemokine receptor CCR3 were associated with response to the diet². A correlation between fecal eosinophil-derived neurotoxin (F-EDN) and colonic mucosal eosinophil degranulation was previously reported in IBS³.

Aims & Methods: To assess a role for eosinophil-driven mucosal inflammation as a target for IBS therapy, we assessed changes in F-EDN levels in primary care patients treated with the DOMINO diet and OB, and their correlation with symptoms and inflammatory markers. In the DOMINO study, primary care physician-diagnosed IBS patients (70% fulfilling Rome IV, Rome+) were randomized to diet or OB. Analysis of gene polymorphisms, blood and stool samples were collected from 356 patients (86 IBS-C, 116 IBS-D, and 154 IBS-M) before and after treatment with diet and OB (respectively $n=147$ and 163). We compared and correlated F-EDN levels, demographic parameters, IBS symptom severity scoring (IBS-SSS), laboratory blood tests as well as biomarkers of inflammation in stool (secretory IgA/sIgA, Beta-defensin2, calprotectin). Statistical analysis was conducted using non-parametric tests; data were presented as median with interquartile range.

Results: Baseline F-EDN correlated negatively with presence of CCR3 polymorphism ($r=-0.13$, $p=0.02$), positively with sIgA ($r=0.27$, $p<0.0001$), but showed no significant associations with IBS-SSS scores or other stool parameters. Furthermore, a positive correlation was observed between F-EDN and glucose ($r=0.16$, $p=0.004$), insulin ($r=0.14$, $p=0.01$) and triglyceride ($r=0.12$, $p=0.03$) plasma levels and body weight ($r=0.16/p=0.002$). F-EDN decreased significantly in responders to the diet (≥ 50 -point improvement on IBS-SSS) ($n=104$, $0.44\mu\text{g/g}[0.16;0.88]$ vs. $0.32\mu\text{g/g}[0.15;0.72]$, $p=0.03$), but not to medication ($n=97$, $0.48\mu\text{g/g}[0.16;1.01]$ vs. $0.44\mu\text{g/g}[0.19;0.87]$,

$p=0.57$). In diet responders, baseline F-EDN levels correlated positively with calprotectin and sIgA (respectively $r=0.24$, $p=0.01$ and $r=0.37$, $p<0.001$). The significant decrease in F-EDN after diet was more pronounced in the subset of patients fulfilling Rome IV criteria ($n=86$, $0.47\mu\text{g/g}$ [0.17;0.91] vs. $0.34\mu\text{g/g}$ [0.16;0.75], $p=0.02$). Baseline F-EDN levels in this cohort correlated with the improvement in IBS-SSS ($r=0.21$, $p=0.04$).

Conclusion: In primary care IBS, response to the DOMINO diet, but not to OB, is associated with the presence and decrease of eosinophil-driven intestinal immune activation. Further research will focus on the ability of the DOMINO diet, besides its FODMAP-lowering properties, to improve atypical food allergic reactions involved in IBS pathophysiology.

References:

1. Carbone, Van den Houde et al. Gut. 2022
2. Balsiger et al. Gut. 2023
3. Casado-Bedmar et al. Journal of Leukocyte Biology. 2022

Disclosure: Nothing to disclose.

MP161

THE EFFICACY AND SAFETY OF COMPOUND GLUTAMINE ENTERSOLUBLE CAPSULE IN THE TREATMENT OF DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (IBS-D): A MULTICENTER RANDOMIZED, DOUBLE BLINDING, PLACEBO-CONTROLLED WITHDRAWAL TRIAL

T. Bai¹, X. Liu², X. Jiang³, Y. Guo³, M. Zheng⁴, W. Tang⁵, X. Fang⁶, C. Liu⁷, S. Wang⁸, Y. Wu⁹, J. Tang¹⁰, Y. Chen¹¹, H. Yu¹², J. Wu¹³, Y. Song¹⁴, Q. Zhao¹⁵, Q. Zhang¹⁶, Y. Wei¹⁷, Q. Tong¹⁸, H. Deng¹⁹, Y. Gu²⁰, D. Liu²¹, Y. Li²², M. Ma²³, X. Hou²

¹Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, ²Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Gastroenterology, Wuhan, China, ³The Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan, China, ⁴Central Hospital of Tongchuan Mining, Tongchuan, China, ⁵West China Hospital, Sichuan University, Chengdu, China, ⁶Wuhan Puren Hospital, Wuhan, China, ⁷Binzhou Medical University Hospital, Binzhou, China, ⁸Xian Yang Central Hospital, Xianyang, China, ⁹Beijing Friendship Hospital, Capital Medical University, Beijing, China, ¹⁰Zhumadian Central Hospital, Zhumadian, China, ¹¹Lianyungang Hospital of TCM, Lianyungang, China, ¹²Luo Yang First People's Hospital, Luoyang, China, ¹³The Second Affiliated Hospital of Shaanxi University of Chinese Medicine, Xian, China, ¹⁴The Second Norman Bethune Hospital Of Jilin University, Changchun, China, ¹⁵Kaifeng hospital of traditional Chinese medicine, Kaifeng, China, ¹⁶The First People's Hospital of Jingzhou, Jingzhou, China, ¹⁷The First People's Hospital of Xianyang, Xianyang, China, ¹⁸Yichang Central People's Hospital, Department Of Gastroenterology, Yichang, China, ¹⁹Shang Rao People's Hospital, Shangrao, China, ²⁰The People's Hospital of Chizhou, Chizhou, China, ²¹2nd Xiangya Hospital, Gastroenterology, Chang Sha, China, ²²Shengjing Hospital Of China Medical University, Shenyang, China, ²³The Second People's Hospital of Taizhou, Taizhou, China

Contact E-Mail Address: drbaitao@126.com

Introduction: Irritable bowel syndrome is one of the most common Disorders of gut-brain interaction, with diarrhea being the predominant subtype. At present, there are limited drugs for effective management of irritable bowel syndrome.

Compound glutamine entersoluble capsules are composed of traditional chinese medicine formulas Sijunzi Tang and L-glutamine. The Sijunzi Tang, which has been used in traditional complementary and alternative

integrated medicine, has been used for the treatment of irritable bowel syndrome for many years. However, there is a lack of evidence from modern evidence-based medicine, its clinical efficacy and safety need to be confirmed. L-glutamine has the function of repairing damaged intestinal mucosa.

Aims & Methods: This study performed a multicenter randomized double-blind placebo-controlled withdrawal trial to explore the effectiveness and safety of compound glutamine entersoluble capsules in the treatment of diarrhea predominant irritable bowel syndrome.

The selected participants received the investigational drug for four weeks during the first single arm stage. The responding participants were randomly assigned to the compound glutamine entersoluble capsules and placebo groups in a 1:1 ratio for another 4 weeks.

The primary efficacy endpoint of the study was the response rate of both the improvement in abdominal pain and bowel movements after treatment in randomized controlled trial subjects (50% of the treatment course met the requirement of at least 30% improvement in abdominal pain severity (NRS pain score) and a reduction of at least 50% in bowel movement days for Bristol 6 or 7 types).

Results: A total of 558 subjects in 22 centers, of which 493 subjects were successfully screened and entered the placebo introduction period. During the placebo introduction period, there were a total of 493 subjects, of which 481 subjects were successfully rescreened and entered the single arm period. 437 subjects entered the randomized controlled trial period and were randomly divided into a treatment group of 217 subjects and a placebo group of 220 subjects.

For the primary efficacy endpoint, the number of response cases in the experimental group and placebo group were 114 (54.55%) and 89 (41.20%), respectively ($P=0.0059$). For secondary efficacy endpoints: (1) The number of improvements in NRS pain scores in the experimental group and placebo group were 138 (66.03%) and 107 (49.54%), respectively ($P=0.0006$); (2) The number of improved bowel movements in the experimental group and placebo group were 157 (75.12%) and 118 (54.63%), respectively ($P<0.0001$); (3) The median (quartile) relative baseline change of IBS-SSS scale in the experimental group was -47.00 (-97.00, -14.00) points; The median (quartile) relative baseline change in the placebo group was -17.00 (-63.00, 16.00) points, and there was a statistically significant difference between the two groups ($P<0.0001$); (4) The median (quartile) relative baseline change of IBS-QOL in the experimental group was -11.46 (-43.01, 0.00) points; The median (quartile) relative baseline change in the placebo group was -3.57 (-39.43, 0.00) points ($P=0.0007$).

During the randomized controlled trial period, the incidence of all adverse events in the 217 subjects in the trial group was 18.89%, the placebo group was 22.27%, the incidence of TEAEs related to the drug in the trial group was 2.30%, and the placebo group was 3.18%.

Conclusion: Compound glutamine entersoluble capsule can effectively improve the clinical symptoms of diarrhea predominant irritable bowel syndrome with a satisfactory safety.

Disclosure: Nothing to disclose.

MP162

EXPRESSION OF TRANSIENT RECEPTOR POTENTIAL ANKYRIN-1 IN THE COLONIC MUCOSA AND ITS CORRELATION TO SYMPTOM SEVERITY IN IRRITABLE BOWEL SYNDROME

S. Groen^{1,2}, D. Keszthelyi^{1,2}, E. Wilms^{1,2}, J. Huig^{1,2}, P. Xu^{1,2}, M. Elizalde^{1,2}, L. Vork^{1,2}, D.M. Jonkers^{1,2}, Z. Helyes^{3,4,5}, A.A Masclee^{1,2}, Z.Z. Weerts^{1,2}
¹Maastricht University Medical Center, Division of Gastroenterology and Hepatology, Maastricht, Netherlands, ²Maastricht University, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht, Netherlands, ³University of Pécs, Department of Pharmacology and Pharmacotherapy, Pécs, Hungary, ⁴University of Pécs, HUN-REN Chronic Pain Research Group, Pécs, Hungary, ⁵National Laboratory for Drug Research and Development, Budapest, Hungary

Contact E-Mail Address: syl.groen@gmail.com

Introduction: Visceral hypersensitivity is a hallmark of irritable bowel syndrome (IBS). Transient receptor potential (TRP) channels are known as molecules involved in the pathogenesis of visceral hypersensitivity. A putative role for the Transient Receptor Potential Ankyrin 1 (TRPA1) channel in colonic nociceptor activation and mechanosensation has been shown in animal studies. We hypothesize there is a correlation in TRPA1 mRNA expression and the symptom-severity in IBS patients.

Aims & Methods: The main objective of this study was to determine TRPA1 mRNA expression in the colonic mucosa and ascertain its correlation with symptom-severity in IBS patients. Second, difference in TRPA1 mRNA expression between IBS patients and healthy controls along with regional differences in TRPA1 mRNA expression was analyzed. IBS patients (Rome III) and healthy controls were included. Sigmoid biopsies were obtained in all subjects. Additional biopsies of the proximal colon were obtained in 24/30 IBS patients. TRPA1 mRNA levels were measured in duplicate by quantitative reverse-transcriptase–polymerase-chain-reaction (Biorad), using primers from Biolegio and normalized to GAPDH. Levels of mRNA were expressed as relative mRNA values using the $-2^{\Delta\Delta Ct}$ method. A multivariate regression was utilized to compare mRNA-expression between IBS patients vs healthy controls. Symptoms in IBS patients were assessed using the Gastrointestinal Symptom Rating Scale (GSRS).

Results: 30 IBS patients (median age 39.0 yrs, 80% female) and 23 healthy controls (median age 22.7 yrs, 43.5% female) were included. Relative TRPA1 mRNA expression in the sigmoid was significantly higher in IBS patients compared to healthy controls ($P<0.001$), independent of age and gender. There was no significant difference in relative TRPA1 mRNA expression between IBS subtypes ($P>0.05$). Within IBS patients expression of TRPA1 mRNA of sigmoid-biopsies was significantly higher compared to biopsies of the proximal colon ($p<0.001$). No significant correlation between TRPA1 expression in sigmoid or proximal colon in GSRS scales ($n=27$) was found.

Conclusion: In IBS patients relative TRPA1 mRNA expression in colonic biopsies is significantly elevated compared to healthy controls. Furthermore, relative TRPA1 mRNA expression is higher in sigmoid colonic biopsies than in proximal colonic biopsies of IBS patients. These findings suggest a potential for the TRPA1 pathway as a target for IBS treatment in the future. However, no correlation between TRPA1 mRNA expression and symptom severity was found. Therefore, further research towards the clinical relevance of the increased TRPA1 mRNA-expression in IBS-patients along with its location-specific expression is warranted.

Disclosure: Nothing to disclose.

MP163

ABDOMINAL BLOATING AND DISTENTION IN IRRITABLE BOWEL SYNDROME ARE COMMON AND PARTLY RELATED TO GUT TRANSIT AND VISCERAL HYPERSENSITIVITY

N. Tornkvist¹, H. Törnblom², M. Simrén², A. Josefsson³
¹Sahlgrenska Universitetssjukhuset, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden, ²Inst of medicine, Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ³Sahlgrenska University Hospital, Department of gastroenterology, Göteborg, Sweden

Contact E-Mail Address: navkiran.tornkvist@gu.se

Introduction: Patients with irritable bowel syndrome (IBS) frequently report bothersome abdominal bloating and/or distention.

Aims & Methods: We aimed to investigate the association of these symptoms to overall symptom characteristics and gut sensorimotor function. We included patients with IBS (Rome II-IV criteria) from studies investigating the association between IBS symptoms and pathophysiologic mechanisms. Validated questionnaires were used to evaluate gastrointestinal (GI) (GSRS-IBS and IBS-SSS), extraintestinal (PHQ-12), and psychological symptoms (HAD). Significant symptoms of abdominal bloating and/or distention were defined as a GSRS-IBS score ≥ 4 (at least moderate) for any of these two symptoms. Abdominal bloating or distention as the most bothersome symptom was defined in those scoring GSRS-IBS questions on bloating or distention higher than all other GI symptoms. Visceral sensory function was measured by a rectal barostat test and oro-anal transit time (OATT) was measured by use of radiopaque markers. Local reference values were used to define visceral hypersensitivity or abnormal OATT.

Results: We included 1100 patients with IBS; median age 35 (IQR 27-47) years and 794 (72%) females. IBS subtype distribution was IBS-C 30%, IBS-D 38%, and IBS-nonCnonD 32%.

Questions on abdominal bloating, abdominal distention, and passing gas had the highest median score, 5 (moderately severe), of all GSRS-IBS items (IQR 4-6 for bloating and passing gas, IQR 3-6 for distention). Significant abdominal bloating and/or distention was reported by 91.6% and 81.2% respectively, with a female predominance (74% and 78% respectively) and were equally distributed across IBS-subtypes ($p=0.09$). Having significant symptoms of abdominal bloating or distention was associated with more extraintestinal symptoms (PHQ-12) and more severe IBS symptoms (IBS-SSS) ($p<0.001$ for both). In addition, significant abdominal bloating was also associated with increased psychological symptoms (HAD), while significant distention was not ($p<0.05$ and $p=0.22$ respectively). There was no association between having significant abdominal bloating/distention and abnormal OATT or visceral hypersensitivity (Table 1).

	Signi- ficant bloating	Not signi- ficant bloating	p- value	Bloating most bother- some symptom	Bloating not most bother- some symptom	p- value	Signi- ficant disten- tion	Not signi- ficant disten- tion	p- value	Distention most bother- some symptom	Disten- tion not most bother- some symptom	p- value
Delayed OATT n (%)	35 (8)	3 (4.6)		5 (25)	33 (6.8)		27 (7)	11 (9.2)		4 (8)	34 (7.5)	
Normal OATT n (%)	300 (68.5)	41 (63.1)	0.24	13 (65)	328 (68)	0.01	267 (69.7)	74 (61.7)	0.26	34 (68)	307 (67.8)	0.95
Accelerated OATT n (%)	96 (28.6)	21 (32.3)		2 (10)	122 (25.3)		89 (23.2)	35 (29.2)		12 (24)	112 (24.7)	
Visceral hypersensi- tivity n (%)	96 (28.6)	4 (13.8)	0.09	88 (25.6)	88 (25.6)	0.016	70 (25.7)	29 (31.5)	0.28	11 (29.3)	88 (27.7)	0.59

Abdominal distention was more common as the most bothersome symptom compared to abdominal bloating (13% vs. 5%), both with a female predominance (76% and 79% respectively). The severity of IBS, extrain-

testinal, and psychological symptoms were similar in patients with and without abdominal bloating or distention as the most bothersome GI symptom ($p=0.09$, 0.45 , and 0.76 for bloating and $p=0.21$, 0.13 , and 0.69 for distention). However, abdominal bloating as the most bothersome GI symptom was associated with delayed OATT and visceral hypersensitivity. No such difference was noted comparing those with and without abdominal distention as the most bothersome GI symptom. Table 1.

Conclusion: The presence of significant bloating or distention in IBS is common and associated to more severe IBS as well as increased symptom burden, regardless of it being the most bothersome symptom or not, while the presence of bothersome abdominal bloating is associated to a deviant gut sensorimotor function. Our results suggest that bloating and distention play an important role in both disease burden and in further understanding pathophysiological mechanisms in IBS.

Disclosure: No conflicts of interest to declare.

MP164

BOTHERSOMENESS OF BOWEL SYMPTOMS AND HEALTHCARE SEEKING IN A POPULATION-BASED COHORT OF INDIVIDUALS WITH IRRITABLE BOWEL SYNDROME (IBS)

T. Taft¹, O.S. Palsson², D. Drossman³, M. Simrén⁴, J. Tack⁵, S. Fukudo⁶, A. Mulak⁷, J. Santos⁸, D.L. Dumitrascu⁹, X. Fang¹⁰, V. Andresen¹¹, M.J. Schmulson Wasserman¹², D. Mario Rodrigues¹³, S.I. Bangdiwala¹⁴, A.D. Sperber¹⁵
¹The Rome Foundation Research Institute, Chapel Hill, United States of America, ²University of North Carolina, Chapel Hill, Dept. of Medicine, Chapel Hill, NC, United States of America, ³Drossman Gastroenterology - Drossman Gastroenterology, Drossman Gastroenterology; Chapel Hill/US, Drossman Gastroenterology, Chapel Hill, United States of America, ⁴Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Dept of Internal Medicine, Gothenburg, Sweden, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium, ⁶Tohoku University, Sendai, Japan, ⁷Katedra I Klinika Gastroenterologii I Hepatologii Uniwersytet Medyczny Wroclaw, Department of Gastroenterology and Hepatology, Wroclaw, Poland, ⁸Institut de Recerca Vall d'Hebron, Department of Gastroenterology, Barcelona, Spain, ⁹Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, 2nd Medical Dept., Cluj-Napoca, Romania, ¹⁰Peking Union Medical College Hospital, Beijing, China, ¹¹Israelitisches Krankenhaus Hamburg/DE, Department Of Medicine, Hamburg, Germany, ¹²Takeda Mexico, Naucalpan, Mexico, ¹³Queens University, Kingston, Canada, ¹⁴Population Health Research Institute, Hamilton, Canada, ¹⁵Ben-Gurion University of the Negev, Faculty of Health Sciences, Farod, Israel

Contact E-Mail Address: ttaft@theromefoundation.org

Introduction: IBS patients are often high healthcare utilizers. Symptom frequency, as well as psychological factors like neuroticism, anxiety, and depression, impact healthcare seeking. Bothersomeness, i.e., how distressing or disruptive symptoms are to a person's daily life, is a potential treatment-seeking motivator in IBS. We aimed to evaluate symptom bothersomeness in IBS and its potential influence on healthcare utilization.

Aims & Methods: Adults in 9 countries (Canada, China, Germany, Japan, Mexico, Poland, Romania, Spain, United States) completed an online survey that included IBS Rome IV Diagnostic Questions, lifetime healthcare utilization (HCU) for IBS (Yes/No); depression and anxiety; negative emotionality/neuroticism (NE), or a person's tendency to experience anxiety, anger, frustration, pessimism, or depressed mood; demographic

questions and the question "Is the [symptom] bothersome to you?" (yes/no) for each: abdominal pain, hard/lumpy stools, and soft/mushy stools. Three separate binary logistic regression models assessed the symptom's frequency, depression, anxiety, NE, sex, and age as predictors of bothersomeness for each of the key IBS symptoms. Three additional regression models evaluated each symptom's bothersomeness and frequency, depression, anxiety, NE, sex, and age as predictors of HCU.

Results: Of 17,663 participants, 1,389 (7.9%) met Rome IV criteria for IBS (mean age 41.6 (SD 14.7) years, 62.3% female; IBS sub-types: 32% C, 29% D, 36% M, 4% U). Of those with IBS, 65.7% had ever visited a doctor because of bowel problems. Abdominal pain was rated bothersome by 93% of people with IBS, hard stools by 80%, and mushy/watery stools by 78%, with no sex differences. Older people (ages 65+) reported only hard stools as more bothersome ($t(1236) = -3.40$, 95%CI: -5.54 to -1.49 , $p<.001$) than people of ages 18-39 or 40-64. Bothersomeness (yes/no) was predicted in regression analyses by higher frequencies of abdominal pain [Odds Ratio (OR) and 95% CI: 2.00 (1.46-2.74)], hard stools [1.33 (1.24-1.43)], and mushy stools [(1.24 (1.16-1.31))], but not by age, sex, or psychological variables. People with IBS were significantly more likely (χ^2) to have ever visited a doctor for bowel problems if they rated their pain ($p = .003$), hard stools ($p = .020$), and mushy stools ($p < .001$), as bothersome. Finding pain and mushy stools bothersome (yes/no) increased the odds of HCU for pain and mushy stools, but not for hard stools in the regression models (Table 1). Higher frequency of pain and hard stools (but not mushy stools) also increased HCU odds, and older people were more likely to consult for all 3 symptoms. Psychological variables and sex were not significant predictors of HCU.

	Dependent variable: Ever sought care for this symptom (yes/no)					
	1. Abdominal pain		2. Hard / lumpy stools		3. Mushy / watery stools	
Predictors:	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Symptom bothersomeness	1.82 (1.18-2.79)	.006	1.24 (0.92-1.67)	.160	1.81 (1.37-2.40)	<0.01
Symptom Frequency	1.16 (1.03-1.32)	.019	1.06 (1.00-1.11)	.036		.254
Age	1.02 (1.01-1.02)	<.001	1.01 (1.01-1.02)	.002	1.02 (1.01-1.03)	<.001
Sex		.725		.507		.510
Anxiety Score (PHQ-4)		.423		.562		.489
Depression Score (PHQ-4)		.974		.977		.717
Negative Emotionality Score		.135		.258	.96 (.94-1.00)	.040

Table 1. Binary regression analyses for predicting IBS lifetime doctor consulting for bowel symptoms

Conclusion: For persons with IBS, subjective experience of how bothersome symptoms are is strongly associated with symptom reporting and a driving factor to HCU regardless of gender, psychological distress, or negative emotionality. Providers need to assess symptom bothersomeness in their clinical decision-making.

Disclosure: Nothing to disclose.

MP165

TARGETING CONFOCAL LASER ENDOMICROSCOPY-IDENTIFIED GUT BARRIER DYSFUNCTION IN IRRITABLE BOWEL SYNDROME VIA MULTIMODAL INTEGRATIVE THERAPY IMPROVES BARRIER INTEGRITY AND SYMPTOM RELIEF – INSIGHTS FROM AN EXPLORATORY, PROSPECTIVE OBSERVATIONAL CLINICAL TRIAL

M. Bittel^{1,2}, S. Weyrauch^{1,2}, M.-L. Groh^{1,2}, J. Langhorst^{1,2}

¹Bamberg Hospital, Sozialstiftung Bamberg, Clinic for Internal and Integrative Medicine, Bamberg, Germany, ²University of Duisburg-Essen, Chair of Integrative Medicine - Focus: Translational Gastroenterology, Bamberg, Germany

Contact E-Mail Address: jost.langhorst@gmx.de

Introduction: Irritable bowel syndrome (IBS) imposes a substantial burden on patients and healthcare systems globally, with diverse gut symptoms. Its pathophysiology involves disorders in gut-brain interaction and gut barrier dysfunction related to diet and stress. Confocal laser endomicroscopy (CLE) can detect barrier dysfunctions in vivo. Multimodal integrative mind-body medicine-based (MBM) therapy, including stress management, exercise, relaxation, and nutrition, may enhance gut barrier function, symptoms and patient well-being.

Aims & Methods: This study aims to screen IBS patients for prevalent and food-induced gut barrier dysfunction via CLE and explore the impact of a multimodal integrative therapy on barrier integrity, IBS-symptom severity, -quality of life and psychological well-being.

Methods: IBS patients (N=119) admitted between 1 February 2021 and 1 July 2023 at a Clinic for Internal and Integrative Medicine for a two-week inpatient stay underwent esophagogastroduodenoscopy with confocal laser endomicroscopy (CLE) and local food challenge (standardized protocol for egg white, soy, milk, yeast or wheat) to test for a primary prevalent (1stCLE+) or secondary food-induced (2ndCLE+) duodenal barrier dysfunction – after exclusion of IgE-mediated food allergy and coeliac disease. All IBS patients received a multimodal MBM therapy. Patients with barrier dysfunction were recommended to adhere to an adjuvant pre-clinically-tested barrier-stabilising therapy with myrrh, chamomile and coffee charcoal (MYRRHINIL INTEST® 3x4 dragées/ day), and exclusion of CLE-identified barrier-disrupting foods until a voluntary follow-up CLE (2nd CLE). Pre (=1st CLE) and Post (=2nd CLE) intervention, IBS-symptom severity (IBS-SSS), IBS-quality of life (IBS-QoL) and psychological well-being via clinically validated questionnaires were additionally assessed.

Results: Of the 119 IBS patients included in the study, 62% (n=74) showed duodenal barrier dysfunction [1stCLE+: n=27 (23%); 2ndCLE+: n=47 (39%)]. Of those, N=35 IBS patients (47%) with barrier dysfunction at 1stCLE returned for a voluntary 2nd CLE after 6.3 ± 3.0 months [at 1st CLE: 1stCLE+: n=15 (43%), 2ndCLE+: n=20 (57%); n=25 (71%) female; age 42.9 ± 15.4 yrs, diagnosis age 32.1 ± 15.0 yrs; disease duration 11.1 ± 11.2 yrs].

Of returned IBS patients, n=25 (71%) showed an improved gut barrier integrity, of whom 16 (46%) achieved complete stabilisation of the gut barrier (CLE-).

Pre-intervention, IBS patients were clinically characterized by severe IBS symptom severity (IBS-SSS 304.8 ± 83.4), severely impaired IBS-related quality of life (IBS-QoL 42.7 ± 16.6) and concomitant severe level of anxiety and depression (HADS 19.2 ± 7.7), fatigue (MFI-20 66.8 ± 13.1) and perceived stress (PSS-10 31.3 ± 7.7).

Post-intervention, patients exhibited significant and clinically relevant (MCID) improvement in all of these clinical outcomes (IBS-SSS $p < .001$, IBS-QoL $p < .001$, HADS $p < .001$, MFI-20 $p < .001$, PSS-10 $p = 0.004$), even allowing the severity score level to be reduced from severe to moderate. Patients reported particular improvement in abdominal pain, change in stool frequency and consistency, abdominal cramps and nausea assessed via 5-point Likert scale.

Conclusion: IBS patients have a high prevalence of existing and food-induced duodenal barrier dysfunction (62%). A multimodal integrative therapy showed a stabilisation of the gut barrier in 71% of IBS patients in a 2nd CLE as well as significant and clinically relevant improvement in IBS-related symptom severity, quality of life and psychological well-being.

References: 1) Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology*. 2021;160(1):99-114. e3. doi:10.1053/j.gastro.2020.04.014

2) Martin CR, Osadchiy V, Kalani A, Mayer EA. The Brain-Gut-Microbiome Axis. *Cell Mol Gastroenterol Hepatol*. 2018 Apr 12;6(2):133-148. doi: 10.1016/j.jcmgh.2018.04.003.

4) Hanning N, Edwinston AL, Ceuleers H, Peters SA, De Man JG, Hassett LC, De Winter BY, Grover M. Intestinal barrier dysfunction in irritable bowel syndrome: a systematic review. *Therap Adv Gastroenterol*. 2021 Feb 24;14:1756284821993586. doi: 10.1177/1756284821993586.

5) Fritscher-Ravens A, Pflaum T, Mössinger M, Ruchay Z, Röcken C, Milla PJ, Das M, Böttner M, Wedel T, Schuppan D. Many Patients With Irritable Bowel Syndrome Have Atypical Food Allergies Not Associated With Immunoglobulin E. *Gastroenterology*. 2019 Jul;157(1):109-118.e5. doi: 10.1053/j.gastro.2019.03.046. Epub 2019 May 15.

6) Fritscher-Ravens A, Schuppan D, Ellrichmann M, Schoch S, Röcken C, Brasch J, Bethge J, Böttner M, Klose J, Milla PJ. Confocal endomicroscopy shows food-associated changes in the intestinal mucosa of patients with irritable bowel syndrome. *Gastroenterology*. 2014 Nov;147(5):1012-20.e4. doi: 10.1053/j.gastro.2014.07.046. Epub 2014 Jul 30.

7) Rosenthal R. et al. Myrrh exerts barrier-stabilising and -protective effects in HT-29/B6 and Caco-2 intestinal epithelial cells. *Int J Colorectal Dis* (2016)

Disclosure: Jost Langhorst

Fees and lecturing: Falk Foundation; Repha GmbH biological medicines; Dr. Willmar Schwabe; Medice Arzneimittel, Galapagos Pharma, Takeda Pharmaceutical, Janssen Cilag, Dr. Pflieger Arzneimittel

Research funding: Steigerwald Arzneimittelwerke GmbH, Falk Foundation, TechLab, Inc., Dr. Willmar Schwabe, Repha GmbH biological medicines,

Other financial or non-financial benefits: none

Consulting and expert activities: Medical Publishers Stuttgart; Steigerwald Arzneimittelwerke GmbH; Repha GmbH; Ferring Arzneimittel GmbH; Dr. Willmar Schwabe

Corporate investments: none

Other conflicts of interest: None

Miriam Bittel

Fees and lecturing: Falk Foundation; Weber & Weber GmbH

Research funding: Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung (DCCV)

Other financial or non-financial benefits: none

Consulting and expert activities: Weber & Weber GmbH

Corporate investments: none

Other conflicts of interest: None

The other co-authors: no conflicts of interest.

MP166

IMPACT OF MEAL-RELATED SYMPTOMS IN IRRITABLE BOWEL SYNDROME (IBS)

M. Cuffe¹, V. Goodoory¹, C.E. Ng², C. Black^{1,3}, A.C. Ford^{3,1}

¹Leeds Gastroenterology Institute, St James' University Hospital, Leeds, United Kingdom, ²County Durham and Darlington NHS Foundation Trust, Surgery, Darlington, United Kingdom, ³Leeds Institute of Medical Research, St James' University Hospital, Leeds, United Kingdom

Contact E-Mail Address: melanie.cuffe@nhs.net

Introduction: Patients with IBS often report meal-related symptoms. These symptoms can negatively affect IBS-related quality of life, psychological health, and lead to food-avoidant behaviours¹. Developing our understanding of the impact of meal-related symptoms in IBS could lead to better treatment.

Aims & Methods: We aimed to compare the characteristics of patients with and without meal-related symptoms in IBS. Participants were recruited from the NIHR research register ContactME-IBS². We collected data for demographics, gastrointestinal symptoms^{3,4,5}, psychological health⁶, quality of life^{7,8}, and impact on work and daily activities⁹ using validated questionnaires among adults with IBS, as defined using the Rome IV criteria. We dichotomised the cohort according to whether they experienced meal-related symptoms, defined as being present $\geq 50\%$ of the time, or not. We compared the characteristics of the two groups and used logistic regression to explore predictors of meal-related symptoms in IBS.

	Had meal-related symptoms (n = 561)	Did not have meal-related symptoms (n = 191)	P value*
Female (%)	501 (89.3)	154 (80.6)	0.002
Most troublesome symptom (%)			
Abdominal pain	121 (21.6)	48 (25.1)	0.008
Constipation	30 (5.3)	23 (12.0)	
Diarrhoea	90 (16)	27 (14.1)	
Bloating or distension	175 (31.2)	43 (22.5)	
Urgency	145 (25.8)	50 (26.2)	
VSI scores (%)			
Low	151 (26.9)	96 (50.3)	<0.001
Medium	198 (35.3)	49 (25.7)	
High	212 (37.8)	46 (24.1)	
IBS-QOL score (%)			
Low	194 (34.6)	45 (23.6)	<0.001
Medium	196 (34.9)	56 (29.3)	
High	171 (30.5)	90 (47.1)	
Functional dyspepsia (%)			
Epigastric pain syndrome	195 (34.8)	39 (20.4)	<0.001
Postprandial distress syndrome	274 (49.1)	57 (30.2)	
WPAI:IBS, median (IQR)			
Absenteeism	0 (0-2.67)	0 (0-4.7)	0.92
Presenteeism	40 (20-60)	30 (10-60)	0.08
Overall work impairment	33.3 (10-60)	27.4 (6-51.9)	0.04
Activity impairment	50 (20-70)	30 (20-60)	<0.001

Table 1. Characteristics of Individuals with Rome IV IBS according to presence or absence of meal-related symptoms.

*P value for Pearson χ^2 for comparison of categorical data, independent samples t-test for continuous data, and Mann-Whitney U test for all four dimensions of Work Productivity and Activity Impairment: IBS.

Results: Of 752 respondents with Rome IV IBS, 561 (74.6%) were affected by meal-related symptoms. 89.3% of individuals with meal-related symptoms were female vs 80.6% of those without ($p=0.002$). A significantly higher proportion of those with meal-related symptoms reported bloating or distension as their most troublesome symptom (31.2% vs 22.5%, $p=0.008$), and had a higher prevalence of functional dyspepsia, especially postprandial distress syndrome (49.1% vs 30.2%, $p<0.001$). Individuals affected by meal-related symptoms reported higher levels of

gastrointestinal symptom-specific anxiety, had lower levels of IBS-related quality of life, and significantly higher levels of work productivity and activity impairment ($p<0.001$ for all analyses). Logistic regression analysis controlling for all other data showed that females (OR 2.3, 95% CI 1.30 - 4.08) and those with functional dyspepsia, both post-prandial distress syndrome (OR 2.0, 95% CI 1.3 - 3.3) and epigastric pain syndrome (OR 2.0, 95% CI 1.19 - 3.22), were more likely to report IBS meal-related symptoms. Conversely, IBS sufferers with abnormal depression scores were less likely to report meal-related symptoms (OR 0.4, 95% CI 0.20 - 0.72). This could reflect low mood leading to poor appetite. Overall, the model explained 22.8% of the variance of the data.

Conclusion: Individuals with Rome IV IBS who report meal-related symptoms experience significantly worse gastrointestinal symptom-specific anxiety and are more adversely affected at work compared to those without meal-related symptoms. These findings suggest that people with IBS and meal-related symptoms may benefit from early multidisciplinary treatment with dietary and psychological therapies.

References: 1. Böhn L et al. Am J Gastroenterol. 2013 May;108(5):634-41.

2. ContactME-IBS. <https://www.contactme-ibs.co.uk/>.

Accessed 23/4/2024.

3. Palsson OS et al. Gastroenterology. 2016;150:1481-91.

4. Whitehead WE et al. Rome III: The functional gastrointestinal disorders. Virginia: Degnon Associates Inc 2006. p. 835-53.

5. Labus JS et al. Aliment Pharmacol Ther. 2004;20:89-97

6. Spiller RC et al. Aliment Pharmacol Ther. 2010;32(6):811-20

7. Patrick DL et al. Dig Dis Sci. 1998;43(2):400-11.

8. Drossman DA et al. Am J Gastroenterol. 2000;95(4):999-1007.

9. Reilly MC et al. Aliment Pharmacol Ther. 2004;20(4):459-67

Disclosure: Nothing to disclose.

MP167

COLONIC MOTOR PATTERNS AFTER INTRACOLONIC INFUSION OF FRUCTANS, FRUCTOSE AND MANNITOL IN HEALTHY VOLUNTEERS ASSESSED WITH HIGH-RESOLUTION COLONIC MANOMETRY

A. Verheyden¹, S. Dubrulle¹, T. Vanuytsel¹, J. Tack¹

¹KU Leuven, University Hospital Gasthuisberg, Translational Research center for Gastrointestinal Disorders, Leuven, Belgium

Contact E-Mail Address: annelies.verheyden@kuleuven.be

Introduction: Although irritable bowel syndrome (IBS) is defined as a motility disorder, there is a lack of studies assessing colonic motility in these patients and linking it to symptoms. A recent FODMAP (Fermentable Oligo-, Di-, Monosaccharides, and Polyols) reintroduction study showed that fructans and mannitol triggered IBS symptoms in the majority of patients, while fructose did not, but the mechanism is unclear. Therefore, we set up a study investigating how these FODMAPs trigger colonic motor patterns in healthy volunteers (HV).

Aims & Methods: HV were included in a randomized, double-blind, 3-way crossover study where a 200 mL solution of either fructose, fructans, or mannitol was administered during three study visits, each separated by ≥ 2 weeks of wash-out. Participants followed a low-FODMAP and low-fiber diet for 3 days before each study visit. On the study day, they received a 250mL tap water enema for HRCM catheter placement (36-sensor solid-state) via colonoscopy. After recovery of 1h, colonic pressure waves (PWs) were measured in a fasted state (1h), after a 20-min FODMAP infusion (2h), and after a standardized meal (1h). The number and propagation direction of short PWs (3 sensors), long PWs (≥ 4 sensors), cyclic PWs, and high-amplitude propagating (retrograde) contractions (HA(R)PCs) were analyzed.

Results: A total of 15 study visits from five HV (40%men, 38±8 years, BMI 23.7±1.6 kg/m²) who finished the full protocol were analyzed. Although none of the motor patterns occurred more frequently with one of the FODMAPs in the fasted state, during FODMAP infusion, 1h post-infusion and postprandially, the short anterograde PWs occurred more frequently in the 2h post-infusion period with fructans compared to fructose and mannitol (p=0.03). Additionally, long synchronous PWs occurred more frequently 1h post-infusion with fructans compared to the fasted state (p=0.01) and there was a trend toward a higher occurrence of long synchronous PWs (p=0.054) and cyclic retrograde PWs (p=0.06) with mannitol

Conclusion: At the current number of healthy volunteers finalizing all 3 visits, fructans and to a lesser extent mannitol but not fructose intracolonic infusions are associated with increased occurrence of synchronous and anterograde colonic motor patterns. Triggering of colonic motor patterns may contribute to symptom triggering by these FODMAPs in IBS.

Disclosure: Nothing to disclose.

MP168
OPIUM TINCTURE HAS ANTI-PROPULSIVE EFFECTS IN CHRONIC DIARRHEA PATIENTS: A RANDOMIZED PLACEBO-CONTROLLED CROSS-OVER TRIAL

L. Davidsen^{1,2}, T. Okdahl^{1,2}, K.L. Høyer³, C.S. Knoph^{1,2}, I.M. Larsen¹, C.L. Hvas³, K. Krogh³, A.M. Drewes^{1,2}
¹Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark, ²Clinical Institute, Aalborg University, Aalborg, Denmark, ³Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark

Contact E-Mail Address: l.davidsen@rn.dk

Introduction: Chronic diarrhea is a debilitating disorder affecting up to 5% of the population. Opioids inhibit gastrointestinal motility via μ-opioid receptors in the enteric nervous system, and opioids have been used in the management of diarrhea for centuries. However, a lack of clinical evidence regarding their efficacy, along with concerns about potential opioid-induced sedation and addiction, limits their use in the clinic. Opium tincture (raw opium dissolved in ethanol) has recently shown anti-propulsive effects in a healthy cohort (1), but no evidence of its effects on the enteric and central nervous system (CNS) in chronic diarrhea patients exists.

Aims & Methods: We aimed to investigate the anti-propulsive effects of opium tincture and its secondary effects on the CNS in a randomized, double-blinded, placebo-controlled, cross-over trial in subjects with chronic diarrhea (defined as a minimum of three daily bowel movements for the past week) refractory to loperamide and targeted treatment (if known etiology). Opium tincture or placebo was administered for seven days in two study periods separated by 14 days. The end titration daily dose was 30 drops (~15mg of oral morphine).

Bowel movements were assessed using the Bristol Stool Form Scale, while a wireless motility capsule recorded gastrointestinal transit times. CNS effects in terms of change in pupil size, reaction time, and working memory were also investigated. Signs of addiction were evaluated using the Subjective Opiate Withdrawal Scale.

Results: Eleven subjects (mean age: 45 ±17 years, 46% males) with chronic diarrhea were included (idiopathic: 4; bile acid malabsorption: 3; inflammatory bowel disease: 2; microscopic colitis: 1; irritable bowel syndrome: 1). The number of daily bowel movements was reduced during treatment with opium tincture compared to placebo (overall estimated difference between treatments: -0.7 (-1.1 - -0.3), p=0.002). In line with this, opium tincture prolonged the colonic transit time (opium tincture: median 17h

(interquartile range 15-40h) vs. placebo: 12h (4-16h), p=<0.001). Opium tincture induced miosis in most subjects, but no indication of sedation or addiction was found.

	Opium tincture (n=11)	Placebo (n=11)	p-value
Anti-propulsive effects	Daily bowel movements (#)	2 (1-3)	3 (2-5)
	Stool consistency (BSFS score)	5 (4-6)	5 (5-6)
	Gastric emptying time (hours)	3 (2-4)	3 (2-18)
	Small bowel transit time (hours)	6 (4-7)	7 (3-6)
Central nervous system effects	Colonic transit time (hours)	17 (15-40)	12 (4-16)
	Δ pupil size (mm)	0.1 ±0.5	-0.6 ±0.5
	Δ reaction time (ms)	-0.7 ±21.4	-2.5 ±19.4
	Δ working memory (DST score)	1.2 ±1.4	1.2 ±1.4
	Signs of addiction (SOWS score)	8.8 ±4.9	11.7 ±9.1

Summary data (mean ±standard deviation or median (interquartile range). Delta values (Δ): day 7 minus day 1. [†]Repeated measures mixed model. [‡]Wilcoxon signed-rank test. BSFS: Bristol Stool Form Scale; DST: Digit Span Test; SOWS: Subjective Opiate Withdrawal Scale.

Conclusion: Opium tincture induced anti-propulsive effects in subjects with chronic diarrhea refractory to standard treatment, evident as a reduced number of bowel movements and prolonged colonic transit. No CNS involvement besides miosis was observed. These results suggest that opium tincture is a relevant treatment strategy for selected patients with chronic diarrhea, especially because no evidence of opioid-induced sedation or addiction was found. However, studies on the long-term effects are needed.

References: 1. Okdahl T, Mark EB, Nedergaard RB, et al. Effects of opium tincture on the enteric and central nervous systems: A randomized controlled trial. Basic Clin Pharmacol Toxicol. 2023 Feb 27;

Disclosure: The study was sponsored by an unrestricted grant by Pharmanovia. Pharmanovia had no influence on the design, analysis, or reporting of the study.

Identification and mechanisms in SLD

17:00-18:00 / Poster Stage 3

MP169

PREDICTIVE VALUE OF ULTRASONOGRAPHIC SURROGATE MARKERS OF FIBROSIS: A RETROSPECTIVE COHORT STUDY

P.F. da Silva Mesquita¹, M.M. Estevinho¹, C. Costa¹, A. Ponte¹, T. Freitas¹

¹Centro Hospitalar Vila Nova de Gaia/Espinho, Gastroenterology, Vila Nova de Gaia, Portugal

Contact E-Mail Address: pedro.filipe.silva.mesquita@gmail.com

Introduction: Performance of liver ultrasound (US) in the detection of fibrosis has been compared in the past with histology, however non-invasive tests are today's standard of care. Additionally, most of these studies were conducted in a controlled setting with dedicated sonographers, which does not reflect clinical practice. We aim to determine the specificity and diagnostic accuracy of routine clinical ultrasound surrogate markers in the staging of liver fibrosis against fibroscan, in the real-world setting.

Aims & Methods: Retrospective cohort study of patients who underwent liver US and Fibroscan (Echosens®) within 3 months of each other, in the last 6 months. Patients with clinical signs of decompensated cirrhosis were excluded. Ultrasonographic keywords of chronic liver disease were collected and their accuracy, specificity, and AUROC for liver fibrosis was calculated.

Results: 251 patients met the inclusion criteria. Mean age was 58,2 ($\pm 13,05$) years, and 73% were male. The most common etiologies were MASLD (34,5%), MetAld (19,2%), Alcohol (15,1%), followed by HCV (12,8%) and HBV (12,4%). In our cohort 25,9% of patients had advanced fibrosis ($>10\text{Kpa}$). The most specific signs were severe coarseness of the parenchymal texture 100% (98,02-100%); major structural changes (parenchymal atrophy or left liver lobe/caudate lobe hypertrophy): 96.17% (92.28%-98.45%) and severe steatosis: 89,87% (84,34%-93,67%). The simultaneous presence of an altered liver edge and any degree of coarseness showed a specificity of 82,07% (75,75%-87,32%). Splenomegaly, hepatomegaly/globose liver, steatosis, or coarseness of any degree showed a specificity under 75%. The most accurate signs (considering a prevalence of 2,85% of advance fibrosis) were severe coarseness 97,42% (94,59-99,01%, AUC 93,7%); major structural changes 93.94% (90.23%-96.55%, AUC 66,4%), severe steatosis: 87,30% (82,50%-91,17%, AUC of 51,5%) and the combined presence of an altered liver edge/any degree of coarseness 82,49% (77,18%-87,01%, AUC 69.5%). BMI and the presence of diabetes were strongly correlated with advanced fibrosis.

Conclusion: In summary, ultrasound surrogate markers of fibrosis remain accurate in predicting advanced fibrosis, even in a real-world setting.

Disclosure: Nothing to disclose.

MP170

A SYSTEMATIC REVIEW AND META-ANALYSIS OF DIAGNOSTIC OUTCOMES OF ENDOSCOPIC ULTRASOUND GUIDED LIVER BIOPSY VERSUS PERCUTANEOUS LIVER BIOPSY

G. Rancatore¹, G.E.M. Rizzo¹, M. Traina¹, L. Carrozza¹, C. Celsa², D. Quintini¹, G. Cabibbo², V. Di Marco², I. Tarantino¹

¹IRCCS-ISMETT, Endoscopy Service, Department of Diagnostic and Therapeutic Services, Palermo, Italy, ²Policlinico Paolo Giaccone, Palermo, Section of Gastroenterology, DIBIMIS, Palermo, Italy

Contact E-Mail Address: gabriele.rancatore@gmail.com

Introduction: Despite the increasing diffusion of non-invasive tests for the diagnosis of liver diseases, histological assessment through liver biopsy (LB) is still often mandatory especially in unclear cases. Actually, percutaneous approach (PC-LB) is the gold standard. Nowadays, endoscopic ultrasound-guided liver biopsy (EUS-LB) has emerged as an established method to achieve liver tissue sampling. EUS-LB has several advantages such as: sampling of both liver lobes, it allows to obtain liver tissue sampling in case of ascites and to avoid damage to nearby organs and vessels.

Aims & Methods: e performed a systematic review with meta-analysis (MA) to evaluate the diagnostic outcomes and safety for liver tissue acquisition of PC-LB and EUS-LB in patients with liver diseases and focal liver lesions. Studies that compare diagnostic outcomes of PC-LB and EUS-LB were identified through literature search using MEDLINE, Embase and Scopus until January 2024. MA was performed according to a frequentist approach.

Results: Overall, diagnostic adequacy was 94 % (CI 95%, 0.91-0.98, $I^2 = 83.92\%$, $P < 0.001$) for EUS-LB, while 96 % (CI 95%, 0.93-0.99, $I^2 = 91.58\%$, $P < 0.001$) for PC-LB. Moreover, based on eight studies comparison between the two procedures showed an OR 1.89 (95% CI, 0.44 – 8.12, $I^2 = 62.33\%$, $P = 0.003$) when comparing PC-LB to EUS-LB. Based on four studies, pooled accuracy was OR 2.45 (95% CI, 0.38 – 15.97, $I^2 = 49.74\%$, $P = 0.0114$) when comparing PC-LB to EUS-LB. Regarding safety, based on nine studies, pooled rate of overall adverse events was slightly higher in PC-LB compared to EUS-LB, OR: 1.25 (CI 95%, 0.51 – 3.09 $I^2 = 26.13\%$, $P = 0.212$). Technical success for EUS-LB was 99 % (CI 95%, 0.99 – 1.00, $I^2 = 0\%$, $P = 0.973$) while 100 % (CI 95%, 0.99-1.00, $I^2 = 0\%$, $P = 0.973$) for PC-LB, with an OR 1.11 (95% CI, 0.26-4.70, $I^2 = 0\%$, $P = 0.988$) when comparing PC-LB to EUS-LB. Overall no differences between the two procedures were observed in term of total length specimen with a standardized mean difference of 0.89 (95% CI, -0.87 – 2.64, $I^2 = 98.95\%$, $P < 0.001$) and in term of complete portal tract with a standardized mean difference of 0.50 (95% CI, -0.55 – 1.55, $I^2 = 97.42\%$, $P < 0.001$).

Conclusion: In conclusion, our meta-analysis does not show significant differences between PC-LB and EUS-LB in terms of diagnostic outcomes, albeit EUS-LB is slightly safer than PC-LB.

Disclosure: Nothing to disclose.

MP171

ULTRASOUND ATTENUATION COEFFICIENT (ATT): A PROMISING COMPLEMENTARY TOOL FOR EARLY DETECTION OF HEPATIC STEATOSIS

J. Carlos Goncalves^{1,2,3}, M. Souto^{1,2,3}, A.I. Ferreira^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Unidade Local de Saúde do Alto Ave, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's - PT Government Associate Laboratory, Braga/ Guimarães, Portugal

Contact E-Mail Address: joaogoncalves92@gmail.com

Introduction: Metabolic Associated Steatotic Liver Disease (MASLD) affects 25-30% of the European population and is projected to rise further. These patients are at increased risk for liver-related complications and higher overall mortality, emphasizing the need for early detection to improve outcomes. While abdominal ultrasound serves as the primary imaging modality for suspected liver disease, its sensitivity for diagnosing mild steatosis is inadequate, and gold-standard methods for quantifying liver steatosis infiltration, such as magnetic resonance imaging or liver biopsy are impractical for widespread use.

Aims & Methods: This study aimed to assess the diagnostic accuracy of the Attenuation Coefficient (ATT) as a complementary method to B-mode ultrasound for early detection of hepatic steatosis. Consecutive patients referred for transient elastography were prospectively enrolled. Liver steatosis was graded using a 4-point scale (normal, mild, moderate, or severe) in B-mode ultrasound for each patient, and ATT was measured in accordance with manufacturer quality criteria instructions (Fujifilm®). Additionally, the Hepato-Renal Index (HRI) was calculated for each patient, and Controlled Attenuation Parameter (CAP, Fibroscan®) was measured.

Results: A total of 128 patients, 61.7% male, with a mean age of 56.8±12.8 years, were included. Among them, 78.1% exhibited at least one cardiometabolic risk factor. The main referral indications were fibrosis assessment in viral hepatitis (42.2%), MASLD (21.9%), and alcoholic liver disease (11.7%). The median vibration-controlled elastography result was 5.8kPa. B-mode ultrasound steatosis assessment classified 44.5% as normal, 10.2% with mild steatosis, 21.1% with moderate steatosis, and 24.2% with severe steatosis. The area under the ROC curve for steatosis detection was 0.796 for HRI, 0.894 for ATT, and 0.896 for CAP, highlighting robust diagnostic performance, particularly for the latter two methods. There was a strong correlation between ATT and CAP ($r=0.710$). Using a CAP>248dB/m to define steatosis, the area under the ROC curve for ATT was 0.890. For an ATT cutoff value ≥ 0.66 , Sensitivity, Specificity, Negative Predictive Value, and Positive Predictive Value were 82.7%, 77.3%, 72.3%, and 86.1%, respectively. The sensitivity of B-mode ultrasound for steatosis detection was 79.5%, increasing to 90.4% when combined with ATT measurement.

Conclusion: ATT demonstrated excellent accuracy for steatosis detection, comparable to CAP and superior to HRI. Importantly, combining B-mode ultrasound with ATT significantly improved the diagnostic sensitivity. These findings suggest that ATT has the potential to become a valuable non-invasive tool alongside ultrasound for early detection of hepatic steatosis, aiding in earlier intervention and improved patient outcomes.

References: Tamaki N, Koizumi Y, Hirooka M, et al. Novel quantitative assessment system of liver steatosis using a newly developed attenuation measurement method. *Hepatol Res.* 2018;48(10):821-828. doi:10.1111/hepr.13179

Bozic D, Podrug K, Mikolasevic I, Grgurevic I. Ultrasound Methods for the Assessment of Liver Steatosis: A Critical Appraisal. *Diagnostics.* 2022;12(10):2287. doi:10.3390/diagnostics12102287

Disclosure: Nothing to disclose.

MP172

COMPARING THE PROGNOSTIC VALUE FOR LIVER DISEASE SCREENING OF THREE LIVER FIBROSIS MARKERS IN THE WELSH POPULATION FROM 2000 TO 2017: A GENERAL POPULATION-BASED COHORT STUDY

T. Hill¹, J. West², C. Crooks¹, J. Morling²

¹University of Nottingham, Translational Medical Sciences, Nottingham, United Kingdom, ²University of Nottingham, Population and Lifespan Sciences, Nottingham, United Kingdom

Contact E-Mail Address: joe.west@nottingham.ac.uk

Introduction: To investigate the prognostic utility of three non-invasive liver fibrosis markers calculated opportunistically from routine blood tests in the Welsh primary care population for identification of those at risk of cirrhosis or hepatocellular carcinoma (HCC).

Aims & Methods: Using the Secure Anonymised Information Linkage (SAIL) Databank at Swansea University (2000-2017) we identified a cohort of people with opportunistic liver blood tests that allowed calculation of 3 commonly used liver fibrosis markers: the aspartate transaminase to alanine transaminase (AST/ALT) ratio, the AST to platelet ratio index (APRI) and the fibrosis-4 index (FIB-4). These markers were modelled as continuous measurements using fractional polynomial models. This allowed the absolute rates and 10-year cumulative incidence of cirrhosis/HCC to be calculated across a range of risk thresholds, and we could then compare their performance via decision curve analysis. In addition, we reassessed the performance of these markers in higher risk patient populations including those with diabetes, obesity, and those with a history of alcohol misuse.

Results: There were 204,753 people with available blood tests enabling calculation of FIB-4, APRI and AST/ALT. At the commonly utilised cut-points to detect advanced fibrosis/cirrhosis of 3.25, 1.5 and 1.0 for FIB-4, APRI and AST/ALT respectively, the 10-year risks of cirrhosis/HCC were 7%, 18% and <1%. Decision curve analysis demonstrated that the APRI has the greatest net benefit for detecting 10-year risk of cirrhosis/HCC in a general population when compared to the AST/ALT ratio or FIB-4. For example, at low threshold risks for cirrhosis of 1-3%, the APRI identifies more true positive cases via fewer referrals for further investigation compared to the FIB-4. If implemented at the 3% risk threshold, the APRI would generate 7,061 referrals for further investigation for every 100,000 patients screened and capture 53% of potential cirrhosis cases, with 6,579 (93%) of those referrals being false positives.

In the diabetic sub-group of 18,006 patients, the 10-year risks of cirrhosis at the cut-points of 3.25, 1.5 and 1.0 on the FIB-4, APRI and AST/ALT respectively were doubled at 14%, 34% and 2.5%. If we implemented the same 3% risk threshold in the above 100,000 pseudo-population but restricted to only the 8.8% who would be expected to have diabetes ($n = 8794$), the APRI would generate 1956 referrals and capture 115 (73%) of potential diabetic cirrhosis cases, with 1841 (94%) of those referrals being false positives.

Conclusion: Liver fibrosis markers in the general population are unlikely to be useful to identify those at later risk of cirrhosis or HCC, because the prognostic utility of the markers leads to too many false positive and false negative results. In higher risk populations, like those with diabetes, the markers had more acceptable sensitivity – i.e. identified more, true positives, and generated a similar proportion of unnecessary referrals. Combining liver fibrosis markers with another investigation in high-risk groups such as Fibroscan may therefore be feasible to reduce the number of false referrals whilst maximising opportunities to identify those at risk of severe liver disease.

References: 1. Ford DV, Jones KH, Verplancke JP, Lyons RA, John G, Brown G, Brooks CJ, Thompson S, Bodger O, Couch T et al: The SAIL Databank: building a national architecture for e-health research and evaluation. *BMC Health Serv Res* 2009, 9:157.

2. Jones KH, Ford DV, Jones C, Dsilva R, Thompson S, Brooks CJ, Heaven ML, Thayer DS, McNerney CL, Lyons RA: A case study of the Secure Anonymous Information Linkage (SAIL) Gateway: a privacy-protecting remote access system for health-related research and evaluation. *J Biomed Inform* 2014, 50(100):196-204.

3. Lyons RA, Jones KH, John G, Brooks CJ, Verplancke JP, Ford DV, Brown G, Leake K: The SAIL databank: linking multiple health and social care datasets. *BMC Med Inform Decis Mak* 2009, 9:3.

Disclosure: JRM receives salary support from a Medical Research Council Clinician Scientist Fellowship [grant number MR/P008348/1]. The funders had no role in the study execution and reporting.

TAH salary is 50% funded by the NIHR Nottingham Biomedical Research Centre (BRC).

In addition, all authors are affiliated with the NIHR Nottingham Biomedical Research Centre (BRC).

Acknowledgements: This study makes use of anonymised data held in the Secure Anonymised Information Linkage (SAIL) Databank. We would like to acknowledge all the data providers who make anonymised data available for research.

SAIL staff were not involved in the preparation of this abstract, interpretation of the data provided by the SAIL Databank is solely that of the authors.

This project was supported by the following NIHR Fellowship Award; *Earlier detection of chronic liver disease (CLD), NIHR-INF-1270*.

MP173

DIAGNOSTIC AND PROGNOSTIC PERFORMANCE OF THE LIVER RISK SCORE IN TERTIARY CARE

G. Semmler¹, L. Balcar¹, B. Simbrunner¹, L. Hartl¹, M. Jachs¹, M. Schwarz¹, B. Hofer¹, L. Fritz¹, A. Schedlbauer¹, K. Stopfer¹, D. Neumayer¹, J. Maurer¹, S. Gensluckner², B. Scheiner¹, E. Aigner², M. Trauner¹, T. Reiberger¹, M. Mandorfer¹

¹Medical University of Vienna, Division of Gastroenterology & Hepatology, Department of Internal Medicine III, Vienna, Austria,

²Paracelsus Medical University Salzburg, First Department of Medicine, Salzburg, Austria

Contact E-Mail Address: georg.semmler@meduniwien.ac.at

Introduction: The LiverRisk score has been developed as blood-based tool to estimate liver stiffness measurement (LSM) in the general population (i.e., in subjects without known chronic liver disease (CLD), and thus, detect compensated advanced chronic liver disease (cACLD; LSM ≥ 10 kPa) and stratify their risk of liver-related events. Notably, its utility in other settings is unclear as a one-size-fits-all blood-based test. We aimed to evaluate its diagnostic/prognostic performance in patients referred to specialized hepatology outpatient clinics (i.e., tertiary care).

Aims & Methods: Subjects with known/suspected CLD at first LSM (cohort-I, n=5897) or first referral & LSM (cohort-II, n=1558) were retrospectively included. Calibration/agreement of the LiverRisk score with LSM was assessed as well as its diagnostic accuracy for LSM-defined cACLD compared to FIB-4/APRI. Finally, its predictive performance for hepatic decompensation was evaluated.

Results: In cohort-I/II, mean age was 48.3/51.8 years, 44.2%/44.7% were female, predominant etiologies were viral hepatitis (51.8%)/MASLD (63.7%), median LSM was 6.9 [5.1-10.9]/ 5.8 [4.5-8.8] kPa, and 1690 (28.7%)/ 322 (20.7%) had cACLD.

Despite a moderate correlation (Pearson's r: 0.325/0.422), the LiverRisk score systematically underestimated LSM (mean difference according to the Bland-Altman-method: -2.9/-1.8 points $\pm$ kPa). Variation of observed differences was considerable (95%CI of agreement: 39.4 and 35.2

points $\pm$ kPa), and showed a clear pattern towards larger disagreement at higher values with lower LiverRisk score than LSM.

The diagnostic accuracy of the LiverRisk for cACLD (AUROC: 0.757 [95%CI: 0.744-0.770]/ 0.790 [95%CI: 0.762-0.819]) was comparable to FIB-4 (0.769/0.813) and APRI (0.747/0.765). The cut-off of 10 points $\pm$ kPa yielded an overall accuracy of 74.2%/81.2%, high specificity (91.9/93.4%), but low negative predictive value (76.6/84.5%) with false-negative results in 20.0%/13.5% in cohort-I/II, respectively.

In cohort-I, 208 (3.5%) patients developed hepatic decompensation (median follow-up: 4.7 years). The LiverRisk score showed a reasonable accuracy for predicting hepatic decompensation within 2 years (AUROC: 0.817); however, it was inferior to LSM (0.891, p<0.001) and FIB-4 (0.912, p<0.001). The strata of LiverRisk score (and of LSM/FIB-4) discriminated patient groups of distinct risks for hepatic decompensation.

Conclusion: While being a major step forward for screening subjects without known liver disease in primary care, the LiverRisk score was not superior (vs. FIB-4) for diagnosis of cACLD or (vs. FIB-4/LSM) for prediction of hepatic decompensation in a tertiary care setting, i.e., in cohorts with a higher pre-test probability of cACLD. Notably, FIB-4 even outperformed the LiverRisk score in terms of prognostic utility.

Disclosure: Nothing to disclose.

MP174

CANCER RISK IN FAMILY MEMBERS OF INDIVIDUALS WITH MASLD: A POPULATION-BASED MULTIGENERATIONAL COHORT STUDY

F. Ebrahimi¹, J. Sun², D. Bergman¹, J.F. Ludvigsson³

¹Karolinska Institute, Stockholm, Sweden, ²Karolinska Institutet, Stockholm, Sweden, ³Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden

Contact E-Mail Address: febrahimi@outlook.com

Introduction: Recent findings suggest a higher risk of progressive liver disease and hepatocellular cancer in first-degree relatives of individuals with metabolic dysfunction-associated steatotic liver disease (MASLD). The familial risk of extrahepatic cancer is, however, unclear.

Aims & Methods: We conducted a nationwide multigenerational cohort study involving all family members of Swedish adults with biopsy-proven MASLD (1969–2017) and of matched general population comparators.

We included 36,684 first-degree relatives (FDRs: parents, siblings, offspring) and 8,788 spouses of MASLD individuals as well as 190,501 FDRs and 44,694 spouses of matched comparators without previous diagnosis of any cancer. Cox proportional hazards models were used to calculate multivariable adjusted hazard ratios (aHR) and 95% CIs.

Results: Over a median of 24.6 years the incidence rate for any extrahepatic cancer was slightly higher in MASLD FDRs than in comparator FDRs (72.3 vs. 71.9/10,000 person years (PY); aHR 1.04, 95%CI, 1.01–1.08). They were also at slightly higher risk of cancer-related mortality (24.0 vs. 23.6/10,000PY; aHR 1.08, 95% CI, 1.01–1.16). Compared to FDRs of comparators, largest differences were observed in rates of esophagus/stomach cancer (1.8 vs. 1.5/10,000PY; aHR 1.26, 95% CI, 1.01–1.58) and lung cancer (4.9 vs. 4.3/10,000PY; aHR 1.18, 95% CI 1.03–1.35).

Across generations of FDRs, the risk of cancer was uniformly increased with no differences by relationship (i.e., parents, siblings, and offspring; p>0.05). MASLD spouses were also at a slightly increased risk of extrahepatic cancer (119.1 vs. 113.4/10,000PY; aHR 1.07, 95%CI, 1.00–1.14) and cancer-related mortality (43.9 vs. 38.8/10,000PY; aHR 1.21, 95%CI, 1.07–1.38).

Compared to spouses of comparators, largest differences were observed in rates of colorectal cancer (17.0 vs. 13.4/10,000PY; aHR 1.34, 95% CI, 1.15–1.56).

Conclusion: First-degree relatives and spouses of individuals with biopsy-proven MASLD were at slightly higher risks of incident extrahepatic cancers, suggesting that shared lifestyle factors may contribute to the associations. Absolute cancer risks for family members were low and thus do not motivate implementation of screening programs.

Disclosure: Dr F. Ebrahimi has served as an advisory board member for Boehringer Ingelheim. Dr Ludvigsson has coordinated an unrelated study on behalf of the Swedish IBD quality register (SWIBREG). That study received funding from Janssen Corporation. Dr Ludvigsson has also received financial support from MSD to develop a paper reviewing national health-care registers in China. Ludvigsson has also a research collaboration on celiac disease with Takeda. The other authors have nothing to disclose.

MP175

THE CONTRIBUTION OF THE MEDICAL EDUCATION OF THE PATIENT WITH METABOLIC-ASSOCIATED FATTY LIVER DISEASE ON THE THERAPEUTIC RESULTS

A.N. Gologan¹, M.K. Grumeza¹, D.S. Gologan¹, E. Gologan², G. Balan², G.-E. Gilca-Blanariu²

¹University of Medicine and Pharmacy Grigore T Popa, Iasi, Romania, ²University of Medicine and Pharmacy Grigore T Popa, Medicale I, Iasi, Romania

Contact E-Mail Address: gologanandrei18@yahoo.com

Introduction: Metabolic-associated fatty liver disease (MAFLD) requires complex treatment based on diet and lifestyle. The understanding of the disease by patients through medical education is an element that could bring them a therapeutic benefit. Since the process is time-consuming and medical factors all over the world are under pressure to use maximum time for diagnostic and therapeutic purposes, an important role can be played by the voluntary activity carried out by medical students, under the guidance of teaching staff, devoted to this purpose.

Aims & Methods: A group of 250 patients with MAFLD, non-cirrhotic, diagnosed in a gastroenterology outpatient clinic, were proposed to participate in an educational program consisting of 3 sessions of 2 hours of interactive course about MAFLD (including notions of anatomy, physiology, diagnosis, evolution, prognosis, complications, risks, treatment, follow-up) in order to appreciate the contribution of medical education to the effectiveness of treatment.

The patients did not receive medication but only recommendations regarding lifestyle changes and the Mediterranean diet. They were re-evaluated 6 months after the initial evaluation.

Results: Of the 250 patients, only 126 (50.4%) accepted participation in the educational plan after informed consent, a disappointing proportion; the subgroup of those who did not participate in the course was reported as a control group (the main reason of non-participation was the fact that most of these patients considered to have already enough knowledge about MAFLD), being also invited to be evaluate after 6 months.

Educational presentations were given by medical students under the guidance of teaching staff (power-point presentations and informative flyers designed to fix the knowledges about disease) and patients were clinically, laboratory, ultrasound and fibroscan evaluated by attending physicians.

Also a questionnaire about quality of life was completed by each patient. Finally, after 6 months, only 85 patients from the control group and 118 from the study group returned for the final evaluation.

The final evaluation focused on 4 elements: 1- changes in body mass (decrease of more than 7%), 2- liver ultrasonography (reduction of the degree of steatosis), 3- laboratory analyzes (liver and metabolic tests) and 4- quality of life. In the study group, significantly better results were ob-

tained for parameters 1, 3 and 4: (78%, 87.2%, 84.7%) compared to the reference group (38.8%, 54.1%, 62.3%) which confirms the fact that patient education is an important element in understanding the disease and its treatment. Only in parameter 2 (decrease of steatosis at ultrasonography) there were no significant differences between the two groups (50.8% vs 48.2%), probably due to the too short follow-up time of the patients.

Conclusion: Therapeutic education of patients with MAFLD can bring more efficiency to the treatment of the disease in non-cirrhotic patients, mainly on body mass control, liver laboratory tests and quality of life, if they accept to participate at educational program.

References: Koutny F, Aigner E, Datz C, Gensluckner S, Maieron A, Mega A, Iglseider B, Langthaler P, Frey V, Paulweber B, Trinkka E, Wernly B. Relationships between education and non-alcoholic fatty liver disease. Eur J Intern Med. 2023 Dec;118:98-107. doi: 10.1016/j.ejim.2023.07.039. Epub 2023 Aug 3. PMID: 37541922.

Lee WM, Bae JH, Chang Y, Lee SH, Moon JE, Jeong SW, Jang JY, Kim SG, Kim HS, Yoo JJ, Kim YS. Effect of Nutrition Education in NAFLD Patients Undergoing Simultaneous Hyperlipidemia Pharmacotherapy: A Randomized Controlled Trial. Nutrients. 2021 Dec 13;13(12):4453. doi: 10.3390/nu13124453. PMID: 34960005; PMCID: PMC8709046.

Disclosure: Nothing to disclose.

MP176

EFFECT OF CHOLECYSTECTOMY ON LIVER FAT AND FIBROSIS IN MAFLD PATIENTS. PROSPECTIVE STUDY

K. Amalou¹, H. Benmellouka¹, R. Rekab¹, K. Saidani¹

¹HCA, Gastroenterology, Algiers, Algeria

Contact E-Mail Address: amalou_kh@yahoo.fr

Introduction: MAFLD is highly prevalent worldwide. Experimental studies have shown that cholecystectomy(Chx) increases hepatic steatosis(HS) and is associated with NAFLD in large retrospective cohort studies.

Aims & Methods: Evaluate the effect of Chx on HS and fibrosis, to assess the prevalence of MAFLD and to identify its risk factors(RF) in this population.

213 MAFLD patients were included, divided into two groups Chx(n=103) and non-Chx(n=110). At least a 5 years follow-up is conducted.

Results: BMI increased in Chx group (30.15±4.08 to 31.58±4.64)Vs (31.90±4.07 to 30.03±4.16) in the control group(p<0.001). Median CAP increased from 300.77±47.42 to 314.17±44.7(Chx) and decreased from 325.06±41.74 to 296.36±56.51 (control)(p<0.01). HS/MRI moved from 14.22±8.64 and 18.55±8.57 at baseline to 15.98±7.93 and 13.88±8.12 at the end of the study(p<0.001). The biological scores of HS(FI,HSI and LAP) all progressed in the Chx group and regressed in the control group(p<0.001). The prevalence of HS was 42.38%(Chx).

RF associated with significant HS were metabolic syndrome(MS), Chx, HS/MRI and FI score. RF associated with advanced fibrosis are BARD score, stiffness and Chx. Stiffness, obesity, Chx, GGT and HS/MRI are associated with NASH lesions.

Conclusion: Chx increases HS and fibrosis. MAFLD prevalence in Chx group is higher than overall population.

Disclosure: Nothing to disclose.

MP177

HEPATIC EFFECTS OF A NOVEL GPR119 AGONIST AGENT PS297 IN DIET-INDUCED OBESE MICE

M. Patil¹, I. Casari¹, D. Thapa¹, L. Warne^{1,2}, E. Dallerba³, M. Massi³, R. Carlessi^{1,4}, M. Falasca⁵

¹Curtin University, Curtin Health Innovation Research Institute, Curtin Medical School, Perth, Australia, ²Little Green Pharma Pty Ltd, Perth, Australia, ³Curtin University, School of Molecular and Life Sciences, Perth, Australia, ⁴Harry Perkins Institute of Medical Research, QEII Medical Centre and Centre for Medical Research, Perth, Australia, ⁵University of Parma, Department of Medicine and Surgery, Parma, Italy

Contact E-Mail Address: mohan.patil@postgrad.curtin.edu.au

Introduction: G-protein coupled receptor-119 (GPR119) agonism is known to modulate non-alcoholic fatty liver disease physiology. However, due to off-target effects, challenges remain for successful GPR119 agonist pharmacotherapy.

Designing a non-systemic drug candidate that locally targets gut-located receptors for incretin secretion is suggested as a safer approach to minimise conventional side effects. This strategy may potentially limit the direct action on pancreatic β -cells; however, chronic use may lead to beneficial outcomes.

We developed a novel small-molecule agent as an oleoyl-lysophosphatidylinositol derivative that stimulates intestinal glucagon-like peptide-1 (GLP-1) secretion by coupling with gut receptors at the orthosteric site.

Aims & Methods: The present study was designed to investigate the chronic impact of novel GPR119 agonist agent ps297 alone and in combination with Sitagliptin on liver health in high-fat diet (HFD)-induced obese mice.

Five-week-old healthy male C57BL6/J mice were fed with HFD for 20 weeks. Normal control mice were maintained on a standard chow diet. A dose-escalation protocol was followed during the treatment phase. Oral administration of the test compound commenced with an initial dose of 10 mg/kg/day for the first week, followed by weekly dose escalations of 10 mg/kg for the subsequent ten weeks until reaching a maximum dose concentration of 90 mg/kg/day. Sitagliptin was gavaged at a fixed dose of 20 mg/kg/day. Vehicle control mice received an equal volume of 0.25% carboxymethyl cellulose in water.

After ten weeks of treatment, blood samples were collected from each 4-hour fasted mice. Biochemical parameters including plasma glucose, triglycerides (TG), cholesterol (CHO), alanine aminotransferase (ALT), and aspartate transaminase (AST) were analysed using an automated analyser. Plasmatic concentrations of metabolic hormones were determined in a multiplex assay platform. Hepatic TG, CHO, and hydroxyproline concentrations were determined in frozen liver tissue samples by colourimetric assay. Liver histology was studied in tissue stored in 10% neutral buffered formalin. Hepatic ballooning was assessed in hematoxylin and eosin-stained sections, imaged using a slide scanner.

Results: Ten-week co-administration of compound ps297 with sitagliptin resulted in higher plasmatic GLP-1 levels compared to the HFD control arm, which led to a significant ($p<0.05$) reduction in fasting plasma glucose levels in this group. Moreover, combination group exhibited a significant reduction in liver weights ($p<0.0001$), plasma CHO ($p<0.05$), ALT ($p<0.0001$), and AST ($p<0.01$) levels. Furthermore, combination treatment showed a significant reduction in hepatic TG ($p<0.0001$) and CHO ($p<0.001$) concentrations compared to the HFD control group. Elevated hepatic hydroxyproline levels in HFD control mice were attenuated by combination treatment.

Additionally, the hepatic ballooning score was found to be significantly reduced in the combination treatment mice.

Conclusion: Sitagliptin combination of ps297, improved glucose homeostasis in HFD-fed obese mice. Additionally, a prominent improvement in liver health status was observed in this group, as evident by reductions in liver weight, plasma liver enzymes, hepatic TG and CHO, and hydroxyproline levels. These findings were further supported by liver histological examination.

The overall findings suggest the pharmacological potential of the GPR119 agonist compound ps297 in combination with gliptins to alleviate fatty liver disease, warranting further molecular investigation in disease-specific animal models.

References: Paternoster S, Simpson PV, Kokh E, Kizilkaya HS, Rosenkilde MM, Mancera RL, Keating DJ, Massi M, Falasca M. Pharmacological and structure-activity relationship studies of oleoyl-lysophosphatidylinositol synthetic mimetics. *Pharmacol. Res.* 172 (2021) 105822.

Bahirat UA, Shenoy RR, Talwar R, Goel RJ, Nemmani KVS. Co-administration of APD668, a G protein-coupled receptor 119 agonist and linagliptin, a DPPIV inhibitor, prevents progression of steatohepatitis in mice fed on a high trans-fat diet. *Biochem Biophys Res Commun* 495 (2018) 1608-1613

Disclosure: MF and MM are inventors of a patent related to oleoyl-LPI mimetics. Curtin University received funding from Little Green Pharma Pty Ltd. to support MF to conduct the submitted work. LW is a paid employee of Little Green Pharma Pty Ltd. No other relationships or activities that could appear to have influenced the submitted work.

MP178

AKKERMANSIA MUCINIPHILA IN THE SMALL INTESTINE IMPROVES LIVER FIBROSIS AND HYPERAMMONEMIA

N. Oguri¹, J. Miyoshi¹, N. Nemoto¹, N. Kawamura¹, M. Matsuura¹, T. Hisamatsu¹

¹Kyorin University School of Medicine, Department of Gastroenterology and Hepatology, Tokyo, Japan

Contact E-Mail Address: n_oguri@ks.kyorin-u.ac.jp

Introduction: Liver cirrhosis (LC) is the end stage of liver fibrosis that leads to various critical conditions, including hepatic encephalopathy (HE). Although recent evidence indicates that liver fibrosis is reversible, there is no intervention to promote this recovery process to date. The gut microbiota is thought to be involved in the pathogenesis of LC and HE. Rifaximin (RFX), a nonabsorbable broad-spectrum antibiotic, is widely used for HE treatment. Although the efficacy of RFX for HE has been established, the underlying mechanism of the efficacy of RFX remains unclear, while this antibiotic is considered to affect the gut microbiome.

Since the microbial compositions are different between anatomical sites in the gastrointestinal (GI) tract, we hypothesized that the effects of RFX on the gut microbiome can vary among GI sites.

Hence, we conceived the present study investigating the impacts of RFX on the gut microbiome along the GI tract to clarify the mechanism of RFX as well as to explore the role of the gut microbiota in the pathophysiology of LC and HE.

Aims & Methods: To investigate the impact of RFX on the gut microbiota and clinical manifestations of LC, RFX was orally administered to a carbon tetrachloride (CCl_4)-induced LC murine model. Blood ammonia (NH_3) concentration, liver pathological findings, and endotoxin concentration in the portal vein were examined. In each GI site, bacterial loads using qPCR of the *Tuf* gene and the bacterial compositions with 16S rRNA gene amplicon sequencing were assessed. Shotgun metagenomic sequencing was performed for jejunal and ileal contents to analyze the functional pathways in the small intestinal microbiota. On the host side, the gene expressions of the intestinal mucosa were examined using qPCR. To explore the clinical efficacy of *A. muciniphila* as a microbial intervention, we orally adminis-

tered *A. muciniphila* ATCC BAA-835 (AKK) to the CCl₄-induced LC murine model. The analyses described above for investigating the impacts of RFX were also performed for animals.

Results: RFX administration improved blood NH₃ concentration, liver fibrosis, and endotoxin concentration in the portal vein. The 16S rRNA gene amplicon sequencing analyses showed that the changes in the bacterial compositions were larger in the small intestine (jejunum and ileum) compared to the cecum, colon, and stool. The genus-level analysis of the small intestinal microbiota demonstrated that increases in *Faecalibaculum*, *Akkermansia*, and *Muribaculaceae* were associated with the improvement of liver fibrosis. Shotgun metagenomic sequencing showed that RFX administration altered the metabolic functions of the small intestinal microbiota. On the host side, the mRNA expression levels of tight junction proteins, antimicrobial peptides, and toll-like receptors in the small intestinal mucosa were altered by RFX administration. In the analyses of a microbial intervention, AKK administration improved liver fibrosis and blood NH₃ concentration. In addition, AKK administration significantly changed the small intestinal bacterial compositions in the murine LC model. The mRNA expression levels of tight junction proteins, antimicrobial peptides, and toll-like receptors in the small intestinal mucosa were altered by AKK administration.

Conclusion: This study demonstrated that the small intestinal microbiota was involved in the pathophysiology of LC and HE and proposed a new concept of “small intestine-liver axis” in LC and HE. The present study also suggests that oral administration of *A. muciniphila* is promising as a microbial intervention for these pathological conditions.

Disclosure: Mitsubishi Tanabe Pharma Corp., Takeda Pharmaceutical Co., Ltd., Janssen Pharmaceutical K.K., AbbVie GK, EA Pharma Co., Ltd., Pfizer Japan Inc., Alfresa Pharma Corp., Kyorin Pharmaceutical Co., Ltd., Mochida Pharmaceutical Co., Ltd., Daiichi Sankyo CO., Ltd., JIMRO Co., Ltd.

Medical management of pancreatitis

17:00-18:00 / Poster Stage 4

MP179

NON-PANCREATIC HYPERLIPASEMIA: A PUZZLING CLINICAL ENTITY

K.E. Feher¹, D. Tornai¹, Z. Vitális¹, L. Dávida¹, N. Sipeki¹, M. Papp¹

¹University of Debrecen, Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Debrecen, Hungary

Contact E-Mail Address: feher.krisztina.eszter@med.unideb.hu

Introduction: Increased lipase level is a serological hallmark of the diagnosis of acute pancreatitis (AP) but can be detected in various other diseases associated with lipase leakage due to inflammation of organs surrounding the pancreas or reduced renal clearance and/or hepatic metabolism. This non-pancreatic hyperlipasemia (NPHL) is puzzling for attending physicians during the diagnostic procedure for AP. It would be clinically beneficial to identify the clinical and laboratory variables that hinder the accuracy of lipase diagnosis with the aim of improve it. A more precise description of the NPHL condition could potentially provide prognostic factors for adverse outcomes which is currently lacking.

Aims & Methods: We aimed to provide a detailed clinical and laboratory characterization of a large prospective NPHL patient cohort and assess parameters determining disease outcomes.

A Hungarian patient cohort with serum lipase levels at least three times higher than the upper limit of normal (ULN) was prospectively evaluated over 31 months. Patients were identified using daily electronic laboratory reports developed to support an ongoing observational, multicenter, prospective cohort study called the EASY trial (ISRCTN10525246) to establish a simple, easy, and accurate clinical scoring system for early prognostication of AP. Diagnosis of NPHL was established based on $\geq 3 \times$ ULN serum lipase level in the absence of abdominal pain or abdominal imaging results characteristic of pancreatitis.

Results: A total of 808 patients [male, $n = 420$ (52%); median age (IQR): 65 (51-75) years] were diagnosed with $\geq 3 \times$ ULN serum lipase levels. A total of 392 patients had AP, whereas 401 had NPHL with more than 20 different etiologies. Sepsis and acute kidney injury (AKI) were the most prevalent etiologies of NPHL (27.7% and 33.2%, respectively). The best discriminative cut-off value for lipase was ≥ 666 U/L (sensitivity, 71.4%; specificity, 88.8%). The presence of AKI or sepsis negatively affected the diagnostic performance of lipase. NPHL was associated with a higher in-hospital mortality than AP (22.4% vs 5.1%, $P < 0.001$). In multivariate binary logistic regression, not lipase but increased amylase level (> 244 U/L) and neutrophil-to-lymphocyte ratio (NLR) (> 10.37 , OR: 3.71, 95%CI: 2.006-6.863, $P < 0.001$), decreased albumin level, age, and presence of sepsis were independent risk factors for in-hospital mortality in NPHL.

Conclusion: NPHL is a common cause of lipase elevation and is associated with high mortality rates. Increased NLR value was associated with the highest mortality risk. The presence of sepsis/AKI significantly deteriorates the serological differentiation of AP from NPHL.

Disclosure: Nothing to disclose.

MP180

TRANSFORMING THE MANAGEMENT OF SEVERE ACUTE PANCREATITIS: A MULTIDISCIPLINARY TEAM'S IMPACT ON INTERVENTIONAL ENDOSCOPY TIMING AND FOLLOW-UP AT A TERTIARY HPB CENTRE

D. Baig¹, P. Ratna¹, T. Nagdee¹, M. Shibeika¹

¹Blackburn Teaching Hospital, Gastroenterology, Blackburn, United Kingdom

Contact E-Mail Address: daniyalbaig@doctors.org.uk

Introduction: Effective timing of endoscopic interventions and follow-ups is crucial in the management of severe acute pancreatitis. Implementing a multidisciplinary team (MDT) approach not only enhances this timing but also ensures consistent clinical care, providing rapid responses to complications and timely adjustments in treatment plans. This coordinated approach optimises recovery and improves patient outcomes by integrating timely diagnostics and interventions. The MDT's strategic involvement is vital for maintaining high standards of care and safety and ensuring consistent and effective treatment of severe acute pancreatitis.

Aims & Methods: This retrospective cohort study assessed the impact of a novel hub-and-spoke severe acute pancreatitis (SAP) multidisciplinary team (MDT) model at a tertiary hepato-pancreato-biliary (HPB) centre. The model, which included Gastroenterologists, Surgeons, Nurses, Dietitians, and Radiologists, focused on optimising clinical outcomes by enhancing the coordination of hospital transfers and precision in the timing of interventional endoscopies. The study compared patient outcomes before the MDT implementation (January 2022 to January 2023) and after (November 2023 to March 2024), to improve intervention scheduling and establish systematic follow-up protocols to ensure comprehensive care. The primary objective was to evaluate how the MDT model influenced the timing of interventions and follow-up procedures in severe acute pancreatitis management.

Results: This study evaluated clinical outcomes for acute pancreatitis across two cohorts, comprising 191 patients before the implementation of a multidisciplinary team (MDT) and 76 patients following the implementation. For the pre-MDT cohort, the aetiology of pancreatitis included gallstone-induced cases (n=50), alcohol-related (n=45), idiopathic (n=2), and unspecified (n=94), with 28.79% of the cohort having a history of gallstones. In the pre-MDT group, the scheduling of interventions lacked consistency. 10 patients required inpatient endoscopic procedures, with a median time from admission to intervention of 13.0 days and a mean time of 12.79 days.

Post MDT implementation, 7 patients required inpatient endoscopic procedures, with waiting times reduced to a median of 6.5 days and a mean of 6.3 days. All these inpatients (n=7/7) received their procedures within the first week. The median duration of hospital stays was reduced from 8 days (pre-MDT) to 5 days (post-MDT). Additionally, the proportion of inpatients discharged within the first week post-intervention increased from 30% (n=3/10) pre-MDT to 71.4% (n=5/7) post-MDT. The average clinic follow-up time decreased from 169 days pre-MDT to 43 days post-MDT. The median timing to outpatient endoscopy was reduced, with 68% of patients receiving it in a six-week window post-discharge.

Conclusion: The integration of a multidisciplinary team (MDT) has markedly improved the management of severe acute pancreatitis, enhancing the precision and efficiency of interventional endoscopies. This optimised coordination has reduced hospital stays and ensured timely interventions, significantly boosting patient outcomes. The MDT approach effectively addresses the complexities of the condition, transforming patient care with tailored and rapid treatment strategies.

Disclosure: No disclosures.

MP181

PROGNOSTIC FACTORS FOR A GASTROINTESTINAL TRACT FISTULA ASSOCIATED WITH WALLED-OFF PANCREATIC NECROSIS AND ITS SEVERITY: DATA FROM THE MULTICENTRE WONDERFUL CONSORTIUM

T. Saito¹, M. Okuno^{2,3}, Y. Iwasa², K. Iwata², T. Iwashita⁴, S. Uemura⁴, K. Yoshida⁵, A. Maruta⁵, T. Hamada⁶, M. Takenaka⁷, H. Shiomi⁸, H. Isayama⁹, I. Yasuda¹⁰, Y. Nakai^{11,12}, the WONDERFUL Study Group in Japan

¹The University of Tokyo, Department of Gastroenterology, Tokyo, Japan, ²Gifu Municipal Hospital, Department of Gastroenterology, Gifu, Japan, ³Matsunami General Hospital, Department of Gastroenterology, Gifu, Japan, ⁴Gifu University Hospital, First Department of Internal Medicine, Gifu, Japan, ⁵Gifu Prefectural General Medical Center, Department of Gastroenterology, Gifu, Japan, ⁶Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ⁷Kindai University, Department of Gastroenterology and Hepatology, Faculty of Medicine, Osaka, Japan, ⁸Hyogo Medical University, Division of Hepatobiliary and Pancreatic Diseases, Department of Gastroenterology, Hyogo, Japan, ⁹Juntendo University, Gastroenterology, Tokyo, Japan, ¹⁰University of Toyama, Third Department of Internal Medicine, Toyama, Japan, ¹¹The University of Tokyo, Endoscopy and Endoscopic Surgery, Tokyo, Japan, ¹²Tokyo Women's Medical University, Department of Internal Medicine, Institute of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: tomsaito623@gmail.com

Introduction: Fistula formation in the gastrointestinal (GI) tract associated with walled-off necrosis (WON) may complicate the clinical course of patients with acute pancreatitis. Identifying prognostic factors for this complication would help optimise the treatment algorithm for patients with WON and improve clinical outcomes.

Aims & Methods: In our multicentre cohort of 76 patients receiving endoscopic ultrasound-guided pancreatic fluid drainage (EUS-PFD) for WON between 2010 and 2023, we identified 27 patients with a GI tract fistula and examined prognostic factors for the development of this complication. We additionally examined factors for a severe GI fistula defined as a requirement of surgical management or death from uncontrollable infection presumably due to the fistula.

Results: Among the 27 cases with a GI fistula, there were 12, 9, and 5 cases with a fistula in the colon, duodenum, and small intestine, respectively. No statistically significant differences were noted between the groups with and without a GI fistula in terms of age (median; 65 vs. 69 years, respectively), female sex (19% vs. 27%, respectively), aetiology of pancreatitis (alcohol / ERCP-related / gallstone, 28%/28%/20% vs. 28%/20%/26%, respectively), maximum WON diameter (14 cm vs. 14.5 cm, respectively), or ascites (26% vs. 35%). WON extension to the paracolic gutter or the pelvic cavity was associated with a higher risk of a GI fistula with odds ratios of 3.3 (95% confidence interval, 1.2-8.8) and 5.6 (95% confidence interval, 1.9-16.7), respectively. Fistulas occurring in the colon were more likely to be severe compared to those occurring in the other sites. Compared to patients with non-severe or no GI fistula, patients with a severe GI fistula were more likely to undergo a longer hospitalisation with medians of 165 days vs. 57 days ($P < 0.01$). In an investigation of treatment outcomes between colonic and non-colonic fistulas, non-colonic fistulas were successfully managed by EUS-PFD and supportive care in all cases compared to 67% in colonic fistulas ($P = 0.03$). All four cases with unsuccessful endoscopic management of a colonic fistula were characterised by a fistula size of > 5 mm or penetrating to the bladder. Among the four cases, three cases required surgical resection of the colon, and one case died of uncontrollable infection despite an attempt of endoscopic fistula closure with an over-the-scope clip.

Conclusion: In this multicentre cohort study, WON extending to the paracolic gutter or pelvic cavity was a risk factor for the incidence of a GI fistula, and colonic fistulas were associated with unfavourable clinical outcomes.

A substantial proportion of endoscopic treatment failures were noted in patients with a colonic fistula, suggesting the necessity of considering treatment strategies for this subpopulation (including the timing of salvage surgery).

Disclosure: H.I. declares research funding from Boston Scientific Japan, Fujifilm, and Piolax Medical Devices; and honoraria from Boston Scientific Japan, Century Medical, Create Medic, Fujifilm, Gadelius Medical, Hitachi Medical, Japan Lifeline, Kaneka, Kawasumi Laboratories, Olympus Medical, Piolax Medical Devices, Sumitomo Bakelite, UMIDAS, and Zeon Medical; and contributions from Boston Scientific Japan, Gadelius Medical, Japan Lifeline, and Zeon Medical.

Y.N. declares research funding from Boston Scientific Japan, Century Medical, Fujifilm, Gadelius Medical, HOYA Pentax Medical, Hitachi Medical, Kaneka, and Medico's Hirata; and honoraria from Boston Scientific Japan, Fujifilm, Gadelius Medical, Hitachi Medical, J-MIT, Medico's Hirata, and Olympus Medical. This work was not supported by any of those companies. The other authors declare no conflicts of interest related to this article.

MP182

IDIOPATHIC ACUTE PANCREATITIS DIAGNOSTICS: A PANCREAS2000 INTERNATIONAL SURVEY

A.-O. Panaitescu¹, A. Aronen², L. Guilabert³, A. Hadi⁴, V. Kiudelis⁵, B. Włodarczyk⁶, J. Laukkanen⁷, S. Regnér⁸

¹Bucharest Clinical Emergency Hospital, Gastroenterology and Interventional Endoscopy Department, Bucharest, Romania,

²Tampere University Hospital, Department of Gastroenterology and Alimentary Tract Surgery, Tampere, Finland, ³Dr. Balmis General University Hospital from Alicante, Gastroenterology, Alicante, Spain, ⁴Copenhagen University Hospital-Amager and Hvidovre, Pancreatitis Center East, Gastrounit, Copenhagen, Denmark, ⁵Lithuanian University of Health Sciences, Gastroenterology, Kaunas, Lithuania, ⁶Medical University of Lodz, Department of Digestive Tract Diseases, Lodz, Poland, ⁷Tampere University Hospital, Dept. of Gastroenterology and Alimentary Tract Surgery, Tampere, Finland, ⁸Lund University, Surgery Research Unit, Department of Clinical Sciences Malmö, Malmö, Sweden

Contact E-Mail Address: afroditapanaitescu@gmail.com

Introduction: While understanding the cause is pivotal for managing acute pancreatitis (AP), there is currently no established protocol for determining its aetiology. Ongoing research aims to validate diagnostic protocols and integrate advanced tests for cases of idiopathic acute pancreatitis (IAP). This study evaluated current international opinion about diagnosis and follow-up of IAP.

Aims & Methods: An international survey was conducted through an online survey platform; the link was shared through social media, e-mails and conference presentations. Responses were collected anonymously. The 37 questions were developed by an international multidisciplinary team, part of a Pancreas2000 collaborative project.

Results: Respondents (n=247) were from over 35 countries; 39% of them had over 10 years of clinical experience; 73% were working in tertiary referral centres; 56% were gastroenterologists, 34% surgeons. An equal number of respondents (n=85, 34%) chose magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) as the first

test ideally performed in case of no suspected aetiology for AP after basic tests. When both investigations were available in the respondents' centre, 44% chose other tests, 30% MRCP and 27% EUS. If there is no evidence of biliary aetiology, 79% of respondents would not perform cholecystectomy; the rest would choose recurrent AP and a history of elevated liver enzymes as main indications. No correlation was found when comparing tertiary and non-tertiary centres in performing cholecystectomies, similarly when comparing centres with or without EUS availability.

Most respondents (90%) followed up on moderate and severe AP cases without an aetiology at index admission; 53% of centres followed up on all the IAP cases after first discharge. The follow-up was mostly done by gastroenterologists (62%); 33% of specialists would conduct a follow-up visit every 6 months, while 17% wouldn't recommend follow-up visits.

Conclusion: This international survey highlights the lack of standardisation for diagnosis and follow-up of IAP. Although MRCP and EUS were ideally chosen as first options in IAP diagnosis, respondents chose other investigations in their practice even when both were available. Only half of the centres schedule visits, showing a lack of consensus regarding follow-up. There is a need for international standardisation for diagnosis and follow-up of IAP.

Disclosure: Nothing to disclose.

MP183

BURDEN OF GLUCOCORTICOID USE AND ASSOCIATED TOXICITIES IN COMMERCIALLY INSURED ADULTS WITH IGG4-RELATED DISEASE IN THE UNITED STATES

Z.S Wallace¹, J. Park², E. Serra³, A. Guérin³, K.R. Patterson², H. Patel², V.K. Singh⁴

¹Massachusetts General Hospital, Harvard Medical School, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America, ²Amgen Inc., Thousand Oaks, United States of America, ³Analysis Group, Inc., Montréal, Canada, ⁴Johns Hopkins University School of Medicine, Division of Gastroenterology, Baltimore, United States of America

Contact E-Mail Address: vsingh1@jhmi.edu

Introduction: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory disorder that often affects multiple organs. Glucocorticoids (GCs) are often used first-line for the treatment of IgG4-RD.¹ Despite their therapeutic benefits, long-term GC use is known to be associated with toxicities that can affect several organ systems.¹ While the association between GC exposure and toxicities has been well characterized in other conditions, little is known about the real-world use of GCs and the associated clinical burden in the context of IgG4-RD.

Aims & Methods: Commercially insured adults (age ≥18 years) diagnosed with IgG4-RD were identified in the IQVIA PharMetrics® Plus database (01/01/2011-06/30/2022) using a validated algorithm. This algorithm considered IgG4-RD-related diagnoses, prescription medication fills, and medical procedures.²

The index date was defined as the first observed IgG4-RD-related diagnosis code, and the baseline and follow-up periods were defined as the 12 months before and after the index date, respectively. GC use during the follow-up period was calculated as the total cumulative prednisone equivalent dose divided by 365 days.

Patients were classified into two mutually exclusive cohorts based on GC use. The low GC use cohort comprised patients with a mean GC dose of <5 mg/day, including patients with no GC use; the high GC use cohort comprised those with a mean GC dose of ≥5 mg/day. Incident GC toxicities were defined as toxicities with ≥1 diagnosis during the follow-up period and no diagnosis during the baseline period. Demographic characteristics

were reported as of the index date; GC use and incident toxicities were reported during the follow-up period. Descriptive comparisons of incident toxicities between cohorts were analyzed using Chi-square tests.

Results: A total of 295 patients with IgG4-RD were identified, with 150 (50.8%) included in the low GC use cohort (mean age 48.9 years, 55.3% female) and 145 (49.2%) in the high GC use cohort (mean age 50.8 years, 45.5% female). In the first year after diagnosis, most patients (84.1%) received ≥ 1 GC fill, with a mean of 4.1 fills, corresponding to 3.9 months of treatment.

Patients in the low GC use cohort received a mean of 1.8 fills, corresponding to 1.4 months of treatment or a mean dose of 1.4 mg/day over the 12-month follow-up period. Patients in the high GC use cohort received 6.4 fills, corresponding to 6.5 months of treatments or a mean dose of 12.0 mg/day over the follow-up period.

Higher GC use was associated with higher rates of incident GC toxicities, such that patients in the high GC use cohort had a greater mean number of GC toxicities (1.8 vs. 1.2; $p < 0.01$) and were more likely to have ≥ 3 toxicities (29.0% vs. 13.3%; $p < 0.01$) than the low GC use cohort. In particular, cardiovascular (29.0% vs. 18.7%; $p = 0.04$), gastrointestinal (29.7% vs. 16.0%; $p < 0.01$), and infectious (31.0% vs. 17.3%; $p < 0.01$) toxicities were more commonly observed among patients with high GC use than low GC use.

Conclusion: In the first year after diagnosis, patients with IgG4-RD experienced a substantial GC burden, as evidenced by nearly half of them exposed to high GC use. Higher GC use was associated with an increased incidence of GC toxicities across multiple organ systems. These findings suggest an unmet need for safe and effective treatments to mitigate prolonged exposure to GCs and improve patient outcomes, particularly in the absence of targeted FDA-approved therapies for IgG4-RD.

References:

1. Yasir M, et al. 2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK531462/>.
 2. Wallace ZS, et al. ACR Open Rheumatol. 2022;4(4):371–7.
- Disclosure: Z.S. Wallace, E. Serra, A. Guérin, and V.K. Singh have received consulting fees from Amgen Inc.
- J. Park, K.R. Patterson, H. Patel are employees of Amgen Inc. and hold stock.
- Study and abstract were funded by Amgen Inc.

MP184

THE ASSOCIATION BETWEEN CHRONIC PROTON PUMP INHIBITOR USE AND 30-DAY MORTALITY IN ACUTE PANCREATITIS

M. Fischman¹, A. Elias², A. Klein³, Y. Cohen¹, Z.S. Azzam⁴, I. Gherisin³

¹Hebrew University of Jerusalem, Faculty of Medicine, Jerusalem, Israel, ²Rambam Health Care Campus, Cardiology, Haifa, Israel, ³Rambam Health Care Campus, Gastroenterology, Haifa, Israel, ⁴Rambam Health Care Campus, Medicine, Haifa, Israel

Contact E-Mail Address: fischmaya@gmail.com

Introduction: Proton pump inhibitors (PPI) are some of the most prescribed drugs. They are known to decrease pancreatic exocrine secretions and protect gastric mucosa. Therefore, there has been interest in the impact of their short-term in-hospital administration on acute pancreatitis outcomes, with disappointing results. However, it is yet to be described whether long-term use of PPI affects acute pancreatitis outcomes.

Aims & Methods: We aimed to investigate the association between chronic PPI use and short-term outcomes of AP.

In this retrospective observational study, we included all patients admitted with a primary diagnosis of acute pancreatitis between January 2008 and June 2021. Chronic medications including PPI were listed upon ad-

mission. Association between chronic PPI use and 30-day all-cause mortality was evaluated by univariate logistic regression.

Results: During the study period 2,308 patients were admitted due to acute pancreatitis. PPI were listed as a chronic medication for 708 of the patients. When compared to non-PPI patients, patients on chronic PPI were older (mean age 62.2 years vs. 53.7 years, $p < 0.001$), more likely to be female (51% vs. 46%, $p = 0.048$), with higher Charlson Comorbidity Index score (mean 4.1 vs. 2.2, $p < 0.001$) and higher Glasgow Imrie score (2.24 vs. 2, $p < 0.001$). Mortality rates at 30 days were 1.5% ($n = 11$) among chronic PPI users, compared to 4.6% ($n = 73$) among the non-PPI group, with an OR of 0.33 (95% CI, 0.16–0.6, $p < 0.001$).

Conclusion: Despite chronic PPI users being older with a greater comorbidity load, chronic PPI use was associated with significantly lower 30-day mortality rates among patients with acute pancreatitis.

Further studies examining this association, preferably prospective, are warranted.

Disclosure: Nothing to disclose.

MP185

EVALUATION OF THE EFFICACY AND SAFETY OF INTRAVENOUS LIDOCAINE IN THE ANALGESIC MANAGEMENT OF ACUTE PANCREATITIS: RESULTS OF A RETROSPECTIVE STUDY

L. Ghilardi¹, S. Hakim¹, F. Brazier¹, E. Nguyen-Khac¹, M. Fumery¹, C. Yzet¹

¹Amiens University Hospital, Gastroenterology, Amiens, France

Contact E-Mail Address: clara.yzet@gmail.com

Introduction: Pain in acute pancreatitis is the symptom to be treated urgently. There are currently no recommendations for analgesic management. Intravenous lidocaine has both analgesic and anti-inflammatory effects. Its use has never been evaluated for analgesia in acute pancreatitis. The aim of our study was therefore to evaluate the efficacy and safety of intravenous lidocaine in the management of acute pancreatitis resistant to level I and II analgesics.

Aims & Methods: We conducted a retrospective, monocentric study between January 2015 and December 2021. Patients visiting the emergency department for proven acute pancreatitis and presenting with pain resistant to group I and II analgesics, hospitalized in the hepato-gastroenterology department and treated with intravenous lidocaine, were included. Pain was assessed by retrospective collection of numerical pain scales (NPS) at the emergency department, and at each analgesic re-evaluation. Treatment efficacy was defined as the absence of need for a Level III analgesic (opioids).

Results: 154 patients, hospitalized in our gastroenterology unit for acute pancreatitis and presenting with pain refractory to level I and II analgesics treated with intravenous lidocaine were included. Patients were predominantly male, with a median age of 48.5 years [37.0; 58.0]. The main etiology of acute pancreatitis was ethylic in 36% of cases.

Acute necrotizing pancreatitis was present in 69% of patients. 44/154 patients received a bolus of opioid morphine in the emergency department before the administration of lidocaine. Lidocaine was prescribed in a continuous way at the dose of 2g/24h (intravenous administration with electric syringe).

The median NPS before prescription of lidocaine was 8.0 [7.00; 9.00]. Lidocaine treatment was effective in 88.7% of patients (136/154). 1.3% of patients experienced lidocaine-related adverse events such as skin rash and dysgeusia. In univariate analysis, patients requiring intensive care or developing an acute respiratory distress syndrome were significantly more likely to fail lidocaine (respectively OR = 5.83; CI [1.69; 20.06]; $p = 0.01$ and OR = 4.23; CI [1.44; 12.43]; $p = 0.009$).

Conclusion: Intravenous lidocaine administration appears to be effective and safe for pain control in 89% of patients failing to level I and II analgesia. Further prospective studies are needed to confirm these results.

Disclosure: Nothing to disclose.

MP186

DOES OPIOID DOSAGE FOR PAIN MANAGEMENT IMPACT ON SEVERITY OF ACUTE PANCREATITIS? A MULTICENTRE INTERNATIONAL PROSPECTIVE STUDY

C.S. Knoph^{1,2}, S. Schou Olesen^{1,2}, J. Samanta³, R. Talukdar⁴, G. Capurso^{5,6}, E. de-Madaria⁷, D. Yadav⁸, A. Siriwardena⁹, J. Windsor¹⁰, A.M. Drewes^{1,2}, M. Nayar^{11,12}, S. Pandanaboyana^{11,12}, PAINAP Collaborative

¹Aalborg University Hospital, Centre for Pancreatic Diseases, Department of Gastroenterology & Hepatology, Aalborg, Denmark,

²Aalborg University, Department of Clinical Medicine, Aalborg, Denmark, ³Post Graduate Institute of Medical Education and Research, Department of Gastroenterology, Chandigarh, India,

⁴Asian Institute of Gastroenterology, Hyderabad, India, ⁵San Raffaele Scientific Institute IRCCS, Pancreas Translational & Clinical Research Center, Milan, Italy, ⁶Vita-Salute San Raffaele University, Milan, Italy, ⁷Dr. Balmis General University Hospital, ISABIAL, Gastroenterology Department, Alicante, Spain, ⁸University of Pittsburgh Medical Centre, Division of Gastroenterology & Hepatology, Pittsburgh, United States of America, ⁹Manchester Royal Infirmary, HBP Unit, Manchester, United Kingdom,

¹⁰University of Auckland, Surgical and Translational Research Centre, Auckland, New Zealand, ¹¹Freeman Hospital, HBP and Transplant Unit, Newcastle upon Tyne, United Kingdom,

¹²Newcastle University, Population Health Sciences Institute, Newcastle Upon Tyne, United Kingdom

Contact E-Mail Address: c.siggaard@rn.dk

Introduction: Abdominal pain is the cardinal symptom of acute pancreatitis (AP), often requiring opioid therapy. We aimed to investigate the dose-response relationship between exposure to opioids and the development of moderately severe and severe AP.

Aims & Methods: This was a post-hoc analysis of the prospective PAIN-AP database, which recruited patients with first-time AP from 118 centres across 27 countries between April 1 and June 30, 2022. From this database, we extracted baseline patient characteristics, post-pancreatitis outcomes and information regarding the dosage of opioid treatment. The morphine-equivalent doses (MEDs) of each opioid administered were calculated based on daily doses and duration of treatment and subsequently summarized into total cumulative MEDs for each patient. Using multivariable regression analysis, we identified risk factors for developing moderately severe or severe AP.

Results: The final cohort for this post-hoc analysis consisted of 1,030 AP patients receiving various doses of opioids (51% male; median age 54 (IQR, 40–69) years). The median pain severity on admission was 7 (IQR, 6–8), and in 504 (50%) patients, the pre-admission duration of pain was more than 24 hours. Most patients (78%) had mild AP, whereas 14% and 8% of patients developed moderately severe and severe AP. On multivariable analysis, a high burden of comorbidity (CCI>2), alcohol aetiology, pre-admission pain duration >24 hours and higher pain severity on admission were independent risk factors for moderately severe or severe AP. There was a significant increase in the risk of moderately severe or severe AP, per mg MED (OR 1.00 (95% CI, 1.00–1.00), P=0.039). Accordingly, receiving >40 mg MED (compared to <10 mg MED) increased the risk of moderately severe or severe AP (OR, 3.51 (95% CI, 2.09–5.93), P<0.001).

Conclusion: The association between opioid exposure and severity of AP was dose dependent. Further studies are warranted to explore this association as this may have clinical implications for pain management in AP.

Disclosure: Nothing to disclose.

MP187

DIAGNOSTIC ACCURACY OF ENDOSCOPIC ULTRASOUND GUIDED SHEAR-WAVE ELASTOGRAPHY FOR EARLY CHRONIC PANCREATITIS: A PROPENSITY SCORE MATCHED ANALYSIS

S. Shintani¹, O. Inatomi¹

¹Shiga University of Medical Science, Division of Gastroenterology, Otsu, Japan

Contact E-Mail Address: ss0513@belle.shiga-med.ac.jp

Introduction: Early chronic pancreatitis is a preliminary stage of chronic pancreatitis in “Mechanistic Definition”. However, the diagnostic criteria consist of subjective factors. Endoscopic ultrasound guided shear-wave elastography (EUS-SWE) is a novel imaging modality for the quantification of tissue stiffness. In this study, objective clinical features of ECP patients were examined using EUS-SWE.

Aims & Methods: We selected 34 patients in the ECP group and 53 patients in the normal group who underwent EUS-SWE from April 2020 to December 2021. ECP was diagnosed by JPN criteria in 2019. We used propensity score matching with age and sex, and 22 patients in each group were included in the evaluation. Elastic velocity measured by EUS-SWE (Vs, m/s) in the pancreatic body at least 5 measurements were examined. Each Vs value had a reliability measurement (VsN, %) and >50% was considered reliable. ALOKA ARIETTA 850 (FUJIFILM, Tokyo, Japan) and GF-UCT260 (Olympus, Tokyo, Japan) were used.

Results: The patients were 14 (63.6%) males with a mean age of 66.6 years in both groups. Type 2 diabetes mellitus was observed 18.1% in the ECP group and 22.7% in the normal group, history of alcohol consumption (>60g/day) was 36.4% and 9.1%, respectively. Clinical signs included 90.9% of abdominal pain, 18.2% of a history of acute pancreatitis, and 22.7% of pancreatic exocrine insufficiency in the ECP group. In addition, EUS findings showed 100% of Hyperechoic foci and strands, 54.5% of Lobularity, 68.2% of Hyperechoic duct wall, and 50% of Dilated side branch. The overall kappa values (95% CI) of interobserver reliability (IOR) for each EUS findings was as follows; hyperechoic foci and strands: 0.95 (0.86–1.0), lobularity: 0.67 (0.40–0.94), hyperechoic main duct margin: 0.68 (0.43–0.92), dilated branch ducts: 0.56 (0.27–0.86). Vs values were 2.21±0.56m/s in the ECP group and 1.69±0.36m/s in the normal group, which were significantly higher in the ECP group (p<0.001). The area under the curve for ECP diagnosis was 0.82 (cut off: 2.10, 95%CI: 0.69–0.94). However, Vs values were not useful as a predictor of type 2 diabetes or pancreatic exocrine insufficiency (p>0.05). There was a positive correlation between Vs values and the number of EUS criteria (rs=0.63, p<0.001). In multivariate analysis, history of acute pancreatitis and EUS score (≥2 criteria) were independent factors to increase Vs value.

Conclusion: The tissue velocity evaluated by EUS-SWE showed high elasticity in ECP compared to the normal pancreas. Furthermore, the Vs value was strongly correlated with EUS findings.

Disclosure: Nothing to disclose.

MP188

EUS-GUIDED PORTAL VEIN SAMPLING FOR ISOLATION AND CHARACTERIZATION OF CIRCULATING TUMOUR CELLS IN PANCREATIC CANCER PATIENTS (EUPHORIC): A PILOT PROSPECTIVE STUDY

G. Vanella¹, F. Frigo¹, R. Leone^{1,2}, C. Felici³, D. Lazarevic³, G. Di Sario³, V. Rossella³, M. Morelli³, G. Tonon³, C. Doglioni^{4,2}, M. Reni^{5,2}, M. Falconi^{2,6}, G. Capurso^{2,1}, P.G. Arcidiacono^{2,1}

¹IRCCS San Raffaele Scientific Institute, Pancreatobiliary Endoscopy and Endosonography Division, Milan, Italy, ²Vita-Salute San Raffaele University, Milan, Italy, ³IRCCS San Raffaele Scientific Institute, Centre for Omics Sciences, Milan, Italy, ⁴IRCCS San Raffaele Scientific Institute, Pathology Department, Milan, Italy, ⁵IRCCS San Raffaele Scientific Institute, Medical Oncology Department, Milan, Italy, ⁶IRCCS San Raffaele Scientific Institute, Pancreatic Surgery Unit, Milan, Italy

Contact E-Mail Address: g.e.vanella@gmail.com

Introduction: Liquid biopsy in patients with pancreatic ductal adenocarcinoma (PDAC) has been challenged by the limited information obtained from systemic circulation (SC). Circulating Tumour Cells (CTCs) in portal circulation (PC) are deemed to be biologically relevant and potentially carrying prognostic significance, despite mostly been evaluated during surgery.

Aims & Methods: This prospective, single-centre, interventional study enrolled PDAC patients to assess the feasibility and safety of EUS-guided transgastric and transhepatic Portal Vein sampling (EUS-PVS) for isolating, enumerating, and characterizing CTCs. PC and paired SC samples underwent microfluidic enrichment and dielectrophoretic (DEP) single-cell sorting based on immunostaining for epithelial and mesenchymal biomarkers. Targeted next-generation KRAS sequencing was performed on CTC subpopulations in a subset of patients.

Results: Between May 2022 and October 2023, 20 PDAC patients (25% metastatic) underwent EUS-PVS with 100% feasibility and safety. CTCs were isolated in all patients from both districts, but the total CTC concentration was significantly higher in PC compared to SC (8.1 [5.8-21.3] vs. 4.1 [2.3-6] / 7.5 ml of blood, $p=0.01$), particularly for mesenchymal CTCs. No associations with baseline clinical variables or disease stage were observed. A subset of CTCs exhibited KRAS codon 12 mutations, undetected in paired white blood cells.

Conclusion: EUS-PVS is a feasible, safe, and effective method for portal blood sampling, supporting subsequent molecular investigations. Despite more sensitive enrichment modalities enhance the yield of peripheral CTCs evaluation, portal circulation remains more informative, especially for detecting epithelial-to-mesenchymal transition events. DEP single-cell sorting was feasible in all patients, providing libraries of viable cells with specific 100%-pure phenotypes, potentially suitable for downstream molecular applications.

Disclosure: Nothing to disclose.

New developments in upper GI endoscopy

17:00-18:00 / Poster Stage 5

MP189

ENDOSCOPIC VACUUM THERAPY OUTPERFORMS STENTS FOR UPPER GASTROINTESTINAL SURGICAL LEAKS AND FISTULAE: A NEW GOLD STANDARD ON THE HORIZON

D. Feijó¹, M. Costa¹, A. Silva¹, C. Chaves¹, E. Gravito-Soares¹, M. Gravito-Soares¹, P. Amaro¹, C. Agostinho¹, M. Ferreira¹, P. Narra Figueiredo¹

¹ULS Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: diogofeijo96@gmail.com

Introduction: Upper gastrointestinal tract leaks and fistulae following surgery present significant challenges, associated with high morbidity and mortality. Self-expanding metal stents (SEMS) have conventionally been utilized as the primary endoscopic treatment. However, endoscopic vacuum therapy (EVT) has emerged as a promising alternative.

Aims & Methods: This study aims to compare the efficacy and safety of EVT against SEMS in managing postoperative upper gastrointestinal tract surgical leaks/fistulae. We included 61 patients, 18 of whom underwent EVT from 2022-2024, and 43 who received SEMS treatment from 2014-2024. Demographic data, clinical characteristics, and treatment outcomes were retrospectively analyzed. Success rate, defined as complete closure of the leak/fistulae, as well as rates of complications, readmission, and mortality were compared between the two endoscopic modalities.

Results: There were no statistically significant differences regarding distribution by gender, age, benign vs malignant disease, time from surgery to endoscopic treatment and leak size ($p>0.05$). Larger leak size was associated with significantly lower likelihood of closure ($p=0.025$). EVT demonstrated a remarkable success rate, achieving complete closure of the leaks/fistulae in 94.4%, compared to 55.8% success with SEMS ($p<0.001$). EVT was associated with less endoscopic adjuvant therapy (22.2% vs. 46.5%, $p=0.009$), despite a higher number of treatment sessions (4 vs. 2, $p<0.001$). SEMS patients experienced higher rates of technique-related complications (76.7% vs. 5.5%, $p<0.001$), readmission (55.8% vs. 0%, $p=0.016$) and mortality (34.9% vs. 11.1%, $p=0.059$), although deaths were not related to endoscopic treatment.

Conclusion: This study results indicate that endoscopic vacuum therapy (EVT) significantly outperforms self-expanding metal stents (SEMS) in treating postoperative upper gastrointestinal leaks and fistulae. EVT achieved a notably higher success rate in terms of complete leak/fistula closure compared to SEMS, while also showing fewer technique-related complications, readmissions, and lower mortality rates. These findings suggest that EVT may represent a safer and more effective approach to managing these complex postoperative complications, potentially redefining the standard of care. Given its benefits, EVT could become the new gold standard for these entities, leading to improved patient outcomes and reduced healthcare burdens. Further research with larger patient cohorts is recommended to solidify the evidence supporting EVT's superiority in this clinical context.

Disclosure: Nothing to disclose.

MP190

PERSONAL PROTECTIVE EQUIPMENT INTERVENTION TRIAL FOR OESOPHAGOGASTRODUODENOSCOPY (PEPTIDE): A RANDOMISED CONTROLLED TRIAL TO ASSESS THE MEDICAL STAFFS' OCCUPATIONAL EXPOSURE TO INFECTIOUS PARTICLES EXHALED BY PATIENTS DURING OESOPHAGOGASTRODUODENOSCOPY

Z. Yan¹, Y. Zhang¹, S. Zhang¹, M. Duan², A. Yang¹, L. Liu²

¹Peking Union Medical College Hospital, Gastroenterology, Beijing, China, ²Tsinghua University, Building Science, Beijing, China

Contact E-Mail Address: NirvanaYn@outlook.com

Introduction: As an aerosol-generating procedure, oesophagogastroduodenoscopy (OGD) promotes the production and release of infectious particles exhaled by patients, which would result in occupational exposure of medical staff and community spread.

We conducted the first prospective two-arm RCT to quantify medical staff's multi-route exposure to infectious particles exhaled by patients during OGD and to determine the efficacy of personal protective equipment (PPE).

Aims & Methods: In the PEPTIDE trial (NCT05321056), enrolled patients were randomly allocated to either with (intervention group) or without (control group) PPE (surgical masks) in a 1:1 ratio. A 3D-print anthropomorphic model with respiratory morphology and function was used to simulate medical staff and was placed at a fixed position beside the patients during anesthetic OGD. The distance from the oral cavity of the patient to the oral cavity of the anthropomorphic model will be 0.8 ± 0.1 m, and the anthropomorphic model will wear or not wear a surgical mask, according to the group allocation of the participant being examined. 1.5 mL saline solution containing 3.0 mg Vitamin B₂ (VB₂) was dripped into each patient's buccal mucosa and all relevant events of the patient, such as sneezing, nausea, vomiting, and snoring and their time of occurrence during OGD, would be recorded.

After examination, potentially infectious particles labeled with VB₂ in the model's facial region (eyes) and respiratory tract (oronasal cavities, pharynx and small airway) would be sampled timely and the fluorescence intensity (FI) of each would be measured. The primary and secondary outcomes were the exhaled particle dosage at the model's airway and facial regions, respectively.

Results: 130 patients were enrolled and assigned randomly to the two groups with 65 each. A positive exposure is defined as the FI of each sample greater than 800 CPS. Based on this, 61.5% of the models in the control group (40 subjects) were positive, compared to 26.2% in the intervention group (17 subjects); the difference between the two groups is significant ($P < 0.001$). Notably, almost all of them appeared in the upper respiratory tract, except one from the eyes. The mean total inhalation dosage was $(5.74 \times 10^{-5} \pm 5.81 \times 10^{-5})$ and $(2.43 \times 10^{-5} \pm 4.80 \times 10^{-5})$ mg of VB₂ in the control group and intervention group, respectively ($P < 0.001$).

Besides, correlation analysis showed that the use of PPE ($P < 0.0001$) and the personal medical history (PMH) of rhinitis ($P = 0.045$) were both negatively correlated with exposure, while high Mallampati classifications ($P = 0.014$) and hiccups during OGD ($P = 0.036$) were positively correlated with exposure. Based on the 4 factors above, a predictive model was established with a sensitivity of 73.7%, a specificity of 71.2%, and an overall accuracy of 72.3%.

Conclusion: This RCT study found that OGD medical staff are at a certain risk of inhalation exposure to pathogens released from potential patients, while wearing a surgical mask can reduce it by 57.8% concerning exposure dose. In addition, the PMH of rhinitis is found to be a protective factor for occupational exposure, while a high Mallampati classification and hiccups are risk factors.

References: [1] Zhang S, Yan Z, Zhang Y, et al. Protocol of a randomised controlled trial to assess medical staff's inhalation exposure to infectious particles exhaled by patients during oesophagogastroduodenoscopy and the efficacy of surgical masks in this context. *BMJ Open* 2023;13(2):e068291.

[2] Moon J, Ryu BH. Transmission risks of respiratory infectious diseases in various confined spaces: A meta-analysis for future pandemics. *Environ Res* 2021;202:111679.

[3] Zhang S, Wu X, Pan H, et al. Gastrointestinal endoscopy infection control strategy during COVID-19 pandemic: experience from a tertiary medical center in china. *Dig Endosc* 2021;33:577–86.

[4] Qadeer MA, Abbas Z. A surgical mask worn by the patient in addition to the barrier box reduces the droplet spray during endoscopy. *J Pak Med Assoc* 2021;71:1703.

[5] Akahoshi K, Tamura S, Akahoshi K. Protection against aerosol droplets from the mouth using the mask plus vinyl bag method during esophagogastroduodenoscopy in the coronavirus disease-19 pandemic. *Dig Endosc* 2021;33:e100–1.

[6] Phillips F, Crowley J, Warburton S, et al. Aerosol and droplet generation in upper and lower gi endoscopy: whole procedure and event-based analysis. *Gastrointest Endosc* 2022;96:603–11.

Disclosure: Nothing to disclose.

MP191

FEASIBILITY AND EFFECTIVENESS COMPARATIVE ANALYSIS OF STANDARD ENDOSCOPIC ULTRASOUND VS NOVEL ADAPTABLE ENDOSCOPIC ULTRASOUND PROBE EVALUATION: A MULTI-INSTITUTIONAL PROSPECTIVE STUDY

C. Robles-Medrand¹, D. Cunto¹, M. Arevalo-Mora^{1,2}, M. Puga-Tejada¹, M. Egas-Izquierdo¹, J. Baquerizo-Burgos¹, J. Alcivar-Vasquez¹, R. Del Valle¹, M.J. Mehta³, A.V. Sahai^{4,5}, B. Lim^{6,7}, M. Paez A.⁶, H. Pitanga-Lukashok¹

¹Instituto Ecuatoriano De Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Larkin Community Hospital, South Miami, United States of America, ³University Health Alliance, Georgia, United States of America, ⁴Université de Montréal, Quebec, Canada, ⁵Centre Hospitalier de l'Université de Montréal (CHUM), QuebecCanada, Canada, ⁶United Medical Doctors, South California, United States of America, ⁷University of California Riverside School of Medicine, RiversideUnited, United States of America

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Endoscopic ultrasound (EUS) has broadened its diagnostic and therapeutic scopes, as it is able to target lesions <3mm. High-frequency radial EUS-miniprobe exhibit procedural time reduction, improving image quality and maneuverability. EndoSound Vision System (EndoSound, Oregon, USA) is a new EUS (N-EUS) portable device that fastens onto a standard gastroscope, enabling a free working channel. It is an affordable alternative to conventional-EUS devices; and a promising opportunity to shorten the difficult EUS learning curve.

Aims & Methods: We aim to determine the feasibility and effectiveness of N-EUS in terms of anatomical structures appropriate identification in comparison with conventional-EUS. This prospective study included patients ≥ 18 years-old undergoing EUS evaluation in June-November 2023 by eight endoscopists from different institutions from South and North America. Patients underwent two consecutive procedures: First, a conventional EUS with a linear-array echoendoscope (Pentax EG38-J1OUT, Pentax Medical, Germany). Then, a different endoscopist performed EUS using the N-EUS coupled to a video gastroscope with therapeutic access

(EG29-i10, Pentax Medical, USA). A post-procedure ad-hoc survey was completed by the second endoscopist, to assess N-EUS acceptability in terms of endoscopists' experience using this device.

Results: Thirty-one patients underwent conventional EUS and N-EUS: 16/31 performed by first-time N-EUS users, 15/31 by endoscopists with prior N-EUS exposure, with median procedural times of 30 and 15 minutes, respectively ($p=.04$). Main EUS indication was chronic dyspepsia (35.5%). Identified structures during N-EUS were the liver/gallbladder/common bile duct (30/31, 96.8%), full pancreas (29/31, 93.5%), kidneys/left kidney (24/31, 77%; 13/15 endoscopists with prior exposure vs 11/16 first-time N-EUS users; $p<.001$), left adrenal gland (20/31, 64.5%). Gallbladder (GB) was unobserved in 8 cases, 7/8 had prior cholecystectomy. Evaluation position was 54.8% supine; 3/31 switched to left lateral. All procedures were completed with 100% clinical and technical success, requiring navigation changes in 51.6%, mainly in first-time N-EUS users ($p=.001$). FNB tissue sampling was achieved in 100% cases. Endoscopists' experience was predominantly described as "meeting clinical expectations". The ad-hoc survey showed high psychometrics, with homogeneity among surveyed endoscopists, without redundancy (Cronbach's alpha of .91), and a good construct validity (Kaiser-Meyer-Olkin Criterion of .728 and Bartlett's test p -value $=.0005$). When comparing both procedures, appropriate identification of GB or lack of, full pancreas, left/both kidneys and left adrenal gland was 31/31 vs 30/31, 31/31 vs 29/31, 31/31 vs 24/31 ($p=.0233$), and 29/31 vs 20/31 ($p=.0158$), respectively. Considering conventional EUS as a gold standard, the observed agreement of N-EUS to identify these structures were 96.8%, 93.5%, 77.4% and 64.5%, correspondingly. Observed agreement for kidneys and left adrenal gland increased when sub-analyzing the cases assessed by endoscopists with prior N-EUS exposure: 81.2% and 76.9%, respectively.

Conclusion: N-EUS is a safe, effective, and feasible tool for EUS evaluation, with high acceptability by endoscopists. Prior ex-vivo training may be warranted for first-time N-EUS users.

References: 1. LeBlanc JK. An overview of endoscopic ultrasound equipment. *Minerva Gastroenterol Dietol*. 2008 Jun;54(2):177-87. PMID: 18319690 .
2. Varas Lorenzo, M.J., Abad Belando, R. and Sánchez-Vizcaíno Mengual, E. (2018), Miniprobe Endoscopic Sonography for Gastrointestinal Tract Assessment: A Case Series of 1451 Procedures. *J Ultrasound Med*, 37: 293-303. <https://doi.org/10.1002/jum.14330>
3. Deprez PH. Choice of endosonographic equipment and normal endosonographic anatomy. *Best Pract Res Clin Gastroenterol*. 2009;23(5):623-37. doi: 10.1016/j.bpg.2009.07.001 . PMID: 19744628 .

Disclosure: Carlos Robles-Medrandá is a key opinion leader and consultant for Pentax Medical, Boston Scientific, Steris, Medtronic, Motus, Micro-tech, G-Tech Medical Supply, CREO Medical, EndoSound, and md-consgroup. All other authors declare no conflicts of interest.

MP192

EUS-GE: INITIAL SINGLE CENTER EXPERIENCE

A. Hujova¹, P. Macinga¹, J. Jarosova¹, J. Spicak¹, T. Hucl¹

¹*Institute of Clinical and Experimental Medicine, Hepatogastroenterology, Prague, Czech Republic*

Contact E-Mail Address: alzbeta.hujova@ikem.cz

Introduction: Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) using a lumen-apposing metal stent (LAMS) is a novel endoscopic technique used to treat gastric outlet obstruction mostly caused by malignant disease such as pancreatic, gastric or biliary cancer. It is a technically challenging procedure with a high-risk of complications especially when performed by an endoscopist with limited experience.

Aims & Methods: We retrospectively analyzed our prospectively collected data of all EUS-GE performed in our center from 2021. Clinical success was defined by the gastric outlet obstruction scoring system (GOOSS). All procedures were done by one endoscopist with no previous experience with the technique.

Results: In total 30 patients were included in the study (16 men, 14 women, mean age 69 years (range 44-90)). The indication for EUS-GE was malignant disease (pancreatic cancer, cholangiocellular carcinoma, gastric cancer, gallbladder cancer, breast cancer, renal cancer, small bowel and liver cancer) in 28 cases and benign disease (chronic pancreatitis, aortic aneurysm) in 2 patients. The procedure was technically feasible in all but one patient (29/30, 96,7%). Clinical success when evaluated as restoration of solid oral intake was 86,2%

(25/29 patients) and 100% (29/29) when evaluated as restoration of at least liquid oral intake. The overall mean GOOSS achieved was 2,5 (1-3). Severe complications occurred in two patients (2/29, 6,9%). In one patient we experienced an unusual complication 6 months after the procedure when a gastrojejunocolic fistula developed, causing weight loss and fecal content vomiting. The fistula was successfully closed endoscopically. Another patient with a metastatic gastric cancer died one day after the intervention of a cardiac cause. Mean procedure time was 46 minutes (20-91) with no difference in mean time of the first and last five procedures. Mean survival post intervention was 135 days (1-560). No intervention for symptom recurrence was needed during a mean follow-up of 90 days.

Conclusion: EUS-GE is an efficient and safe technique in the treatment of gastric outlet obstruction even when performed by an endoscopist with no prior experience.

References: 1. Itoi T, Ishii K, Ikeuchi N, Sofuni A, Gotoda T, Moriyasu F, Dhir V, Teoh AY, Binmoeller KF. Prospective evaluation of endoscopic ultrasonography-guided double-balloon-occluded gastrojejunostomy bypass (EPASS) for malignant gastric outlet obstruction. *Gut*. 2016 Feb;65(2):193-5. doi: 10.1136/gutjnl-2015-310348. Epub 2015 Aug 17. PMID: 26282674
2. Antonelli G, Kovacevic B, Karstensen JG, Kalaitzakis E, Vanella G, Hassan C, Vilmann P. Endoscopic ultrasound-guided gastro-enteric anastomosis: A systematic review and meta-analysis. *Dig Liver Dis*. 2020 Nov;52(11):1294-1301. doi: 10.1016/j.dld.2020.04.021. Epub 2020 Jun 3. PMID: 32505567
3. Hujova A, Stirand P, Turza P, Spicak J, Hucl T. Endoscopic management of gastrojejunocolic fistula as an unusual complication of endoscopic ultrasound-guided gastroenterostomy. *Endoscopy*. 2023 Dec;55(S 01):E151-E152. doi: 10.1055/a-1937-9558. Epub 2022 Oct 28. PMID: 36307072; PMCID: PMC9829763.

Disclosure: Nothing to disclose.

MP193

PALLIATION OF GASTRIC OUTLET OBSTRUCTION IN CASE OF BILIARY OBSTRUCTION. A RETROSPECTIVE, MULTICENTER STUDY: THE B-GOOD STUDY

A. Fugazza¹, M. Andreozzi², C. Binda³, A. Lisotti⁴, I. Tarantino⁵, J.J. Vila⁶, C. Robles-Medrand⁷, A. Amato⁸, A. Larghi⁹, E. Perez-Cuadrado-Robles¹⁰, G. Aragona¹¹, F. Di Matteo¹², R. Badas¹³, C. Barbera¹⁴, B.P. Mangiavillano¹⁵, S.F. Crinò¹⁶, M. Colombo¹⁷, M. Spadaccini¹⁸, C. Fabbri¹⁹, P. Fusaroli²⁰, A. Facciorusso²¹, A. Anderloni²², A. Repici²³

¹Humanitas Research Hospital, Rozzano, Milan, Italy, ²Digestive Endoscopy Unit, Division of Gastroenterology, Milano, Italy,

³Humanitas Research Hospital, Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano, Milano, Italy, ⁴AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena Hospitals, Forlì, Italy, ⁵Hospital of Imola, University of Bologna, Gastroenterology Unit, Bologna, Italy, ⁶ISMETT, Gastroenterology, Palermo, Italy, ⁷Complejo Hospitalario de Navarra, Endoscopy Unit. Gastroenterology Dpt., Pamplona, Spain, ⁸Instituto

Ecuatoriano De Enfermedades Digestivas (IECED), Espiritu Santo University, Guayaquil, Ecuador, ⁹Gastroenterology Unit, Ospedale Valduce, Como, Italy, ¹⁰Dr., Como, Italy, ¹¹Policlinico Universitario A. Gemelli IRCSS, Digestive Endoscopy Unit, Rome, Italy, ¹²Georges-Pompidou European Hospital, Department of Gastroenterology, Paris, France, ¹³Gastroenterology unit, Piacenza, Italy, ¹⁴Campus Bio-Medico Of Rome, Gi Endoscopy Unit, Roma, Italy, ¹⁵Azienda Ospedaliera Universitaria di Cagliari, Cagliari, Italy, ¹⁶Sofar Ospedale ramazzini di carpi, Carpi (mo), Italy, ¹⁷Humanitas - Mater Domini, Gastrointestinal Endoscopy, Milano, Italy, ¹⁸Humanitas Research Hospital, Digestive Endoscopy Unit, Rozzano, Milano, Italy, ¹⁹Humanitas Research Hospital, Rozzano, Milano, Italy, ²⁰Humanitas University, Biomedical Science, Rozzano, Italy, ²¹AUSL Romagna, Forlì-Cesena gastroenterology, Gastroenterology, Bologna, Italy, ²²University of Bologna, Gastroenterology, Imola, Italy, ²³University of Foggia, Gastroenterology, Foggia, Italy, ²⁴Policlinico San Matteo Pavia, Gastroenterology, Pavia, Italy, ²⁵Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy

Contact E-Mail Address: marta.snpp@gmail.com

Introduction: EUS-guided gastroenterostomy (EUS-GE) is a novel and effective procedure for the management of malignant gastric outlet obstruction (GOO) with more durable results when compared to enteral stenting (ES). However, data comparing EUS-GE to ES in patients already treated with EUS-guided choledocoduodenostomy (EUS-CDS) for distal malignant biliary obstruction (DMBO) are lacking. We aimed to compare outcomes of EUS-GE and ES for the palliation of GOO in this specific population of patients.

Aims & Methods: A multicentre retrospective analysis of patients with DMBO treated by EUS-CDS and concomitant or subsequent GOO treated by EUS-GE or ES from 2016 to 2021 was conducted. Primary outcomes were overall AEs rate and dysfunction of the EUS-CDS after GOO treatment. Secondary outcomes included clinical success, technical success, procedure duration, length of hospital stay and relapse of GOO symptoms.

Results: 77 consecutive patients were included in the study: 25 patients underwent EUS-GE and 52 underwent ES. AEs rate and patency outcomes of the EUS-CDS after GOO treatment were comparable between the two groups (12,5% vs 17,3 %; p=0,74). No recurrence of GOO symptoms was registered in the EUS-GE group while 11,5 % of ES patients had symptoms recurrence after a mean follow-up period of 93,5 days.

Conclusion: EUS-GE and ES are both effective and safe for the palliation of GOO in patients already treated by EUS-CDS for DMBO with no difference in the biliary stent dysfunction rate and overall AEs. EUS-GE is associated with less recurrence of GOO symptoms.

Disclosure: Nothing to disclose.

MP194

HEPATICOGASTROSTOMY VERSUS HEPATICOGASTROSTOMY WITH ANTEGRADE STENTING FOR MALIGNANT BILIARY OBSTRUCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

P. Paraskevopoulos¹, M. Obeidat², D. Bednarik², P. Martinekova², P. Matrai², D.V. Sando², N. Faluhelyi², A. Mikó², P. Hegyi², B. Eross²

¹Center of Translational Medicine, Budapest, Hungary,

²Semmelweis University, Institute for Translational Medicine, Budapest, Hungary

Contact E-Mail Address: panag.parask@gmail.com

Introduction: Combining antegrade (AGS) stenting and hepaticogastrotomy (HGS) is an increasingly used endoscopic ultrasound-guided intervention when stenting by endoscopic retrograde cholangiopancreatography (ERCP) is impossible. We comprehensively assessed the benefits and downsides of combined antegrade stenting and hepaticogastrotomy (HGAS).

Aims & Methods: The aim of our study was the justification of the addition of AGS during HGS. Five electronic databases were searched for studies on HGS with or without AGS from inception until December 2023. The odds ratio (OR) and pooled rates were used for single and two-arm comparisons with 95% confidence intervals (CI).

Results: The pooled technical and clinical success was 94% [CI:92-96%] and 88% [CI:84-91%] for HGS and 87% [CI:81-91%] and 94% [CI:89-97%] for HGAS, respectively. Pooled OR of HGAS and HGS showed an OR=0.25 [CI:0.03-2.34] for technical success and an OR=1.02 [CI:0.50-2.06] for clinical success.

The pooled adverse event rates were 20% [CI:16-25%] for HGS and 14% [CI:9-21%] for HGAS, whereas pooled OR showed an OR=0.94 [CI:0.14-6.38]. For re-intervention, an OR=0.37 [CI:0.27-0.52] was found. Time to stent dysfunction increased, HGAS 330 [CI: 280-Not reached] and HGS 209 [CI: 120-325] with no change in overall survival HGS 117 [CI: 91-151] and HGAS 147 [CI: 105-175].

Conclusion: The use of HGAS appears to increase clinical success and reduce the need for re-intervention. Overall adverse event rates were similar but bile leakage prevalence was decreased. Time to stent dysfunction seems to increase with no change in overall survival.

Disclosure: None to declare.

MP195

WITHDRAWN

MP196

REALITY AUGMENTED GLASSES IMPROVES ERGONOMICS IN GASTROINTESTINAL ENDOSCOPY

S.H. Kim¹, H.-S. Choi², E.-S. Kim¹, B. Keum³, Y.-T. Jeon⁴, H.J. Chun⁵, B. Lee³

¹Korea University College of Medicine, Dept. of Gastroenterology, Seoul, South Korea, ²Korea University, College of Medicine, Seoul, South Korea, ³Korea University College of Medicine, Seoul, South Korea, ⁴Institute of Digestive Disease and Nutrition, Korea University College of Medicine, Department Of Internal Medicine, Division Of Gastroenterology And Hepatology, Seoul, South Korea, ⁵Institute of Digestive Disease and Nutrition, Korea University College of Medicine, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: bomee26288@gmail.com

Introduction: Endoscopists are at increased risk of musculoskeletal injuries (MSI). Poor endoscopic posture is known to cause MSI. In this study, we systematically evaluated the ergonomic benefits of medical augmented reality glasses (ARG) in gastrointestinal endoscopy.

Aims & Methods: Screening gastroscopies were performed with and without ARG. The subjective experience was evaluated using a questionnaire-based NASA-Task Load Index (NASA-TLX). Biomechanical loads during endoscopy were captured using electromyography (EMG) sensors and motion tracking sensors. Perceived discomfort, muscle activity and body position were compared between ARG wearing group and non- ARG group.

Results: Five endoscopists performed total of 200 upper gastrointestinal endoscopies; 100 procedures in ARG group and 100 procedures in non-ARG group. Mean NASA-TLX scores of the participants were lower when ARG was used compared to those with conventional monitor. ARG wearing group exhibited improvements in physical demand, effort, and frustration scores compared to non ARG group. Muscle activation was significantly lower in ARG group compared to non ARG group in sternocleidomastoid and trapezius muscles. IMU analysis showed a significant reduction in the proportion of high risk positions of the neck and torso in the ARG group.

Conclusion: ARG was effective in improving the ergonomics of the examiner by correcting the bad posture of neck and torso during endoscopy. It reduces muscle fatigue and significantly corrects high risk posture that causes pain during endoscopy. The use of ARG in gastrointestinal endoscopy is expected to improve ergonomics for endoscopists.

Disclosure: Nothing to disclose.

MP197

THE ERGONOMIC COMPARISON OF ENDOSCOPIST'S HAND/ARM MOVEMENT AND RELEVANT MUSCLE LOAD BETWEEN DIAGNOSTIC AND THERAPUTIC ENDOSCOPY

S. Nagano^{1,2}, K. Momose^{1,2}, Y. Ishii³, K. Yamashita², T. Saito², K. Tanaka², K. Yamamoto², T. Makino², T. Takahashi², Y. Kurokawa², H. Eguchi², Y. Doki², K. Nakajima^{1,2}

¹Osaka University Graduate School of Medicine, Department of Next Generation Endoscopic Intervention (Project ENGINE), Suita, Osaka, Japan, ²Osaka University Graduate School of Medicine, Department of Gastroenterological Surgery, Suita, Osaka, Japan, ³Castem Co., LTD, Hiroshima, Japan

Contact E-Mail Address: snnsk1224@gmail.com

Introduction: The ergonomics has been considered important in practicing surgical laparoscopy, and prior studies have shown significance of relevant factors e.g. operating room setup and design of surgical devices. However, little has been known in flexible endoscopy; How do endoscopists control flexible endoscopes? Which muscles are loaded during endoscopy? The deeper understanding of ergonomic aspects in flexible endoscopy is indispensable, since the number of endoscopies performed and its complexity are rapidly increasing.

Aims & Methods: We aimed to identify the differences of ergonomics between diagnostic endoscopy (EGD) and therapeutic endoscopy (ESD), by 1) multiple motion capture technology, and 2) wireless surface electromyography (EMG), in pre-clinical setting.

1) The multiple motion capture assessment

The control section of standard flexible endoscope (GIF-Q260J; Olympus, Tokyo, Japan), from the boot to the angulation knobs, was marked with 6 optical reflective markers. These markers were traced using a motion capture system (OptiTrack Flex13; NaturalPoint, OR) and the data were processed to generate 3-D coordinate data (The sternum manubrium of the endoscopist was setup as the coordinate origin; X: left-right axis, Y: cranio-caudal axis, Z: antero-posterior axis). EGD and ESD were performed with this motion capture system using live porcine models. For each endoscopist, mean±2SD for plotted coordinates from the origin was calculated in the three axes and described as a range of his/her arm/hand movement. The data were compared between EGD and ESD.

2) EMG assessment

Muscle activation of the left biceps brachii muscle, trapezius muscle, extensor carpi ulnaris muscle, flexor carpi radialis muscle, pronator teres muscle, thenar muscle, back neck muscle, and erector spinae muscle were recorded during endoscopic procedures using wireless surface EMG (BioLog DL-5500, DL-510A; S&ME, Tokyo, Japan). The maximal voluntary contraction (MVC) was obtained to normalize root-mean-square muscle activation as %MVC. We compared differences in muscle activity between EGD and ESD using %MVC.

Results: 1) The motion capture was performed on 15 board-certified endoscopists conducting EGD (n=13) and ESD (n=12). The movement range of endoscopist's left hand/arm holding endoscope is shown in the Table. On all three axes, the range of movement was significantly narrower during ESD than during EGD (X, p<0.001; Y, p=0.015; Z, p<0.001).

	EGD			ESD		
	X axis	Y axis	Z axis	X axis	Y axis	Z axis
Mean ± 2SD (cm)	-0.32±14.2	-24.3±11.0	12.8±11.6	-1.3±9.9	-22.8±9.8	7.9±8.9

2) The EMG was recorded during 15 EGDs and 8 ESDs. The %MVC was higher during ESD than EGD in an analysis including all muscles (LS-mean±SE; EGD, 28.9±1.5%; ESD, 34.1±2.6%; p=0.078). The comparison by each specific muscle showed that the extensor carpi ulnaris muscle (EGD, 34.6±3.5%; ESD, 47.8±5.8%; p=0.093) and the pronator teres muscle (EGD,

42.8±6.6%; ESD, 67.6±10.9%; p=0.092) had significantly larger %MVC during ESD (p<0.1 was considered statistically significant).

Conclusion: Our study has first shown that the range of endoscopis's movement was significantly narrower in therapeutic endoscopy than in diagnostic endoscopy. Furthermore, it was demonstrated that muscle activity, especially in left forearm muscles, was larger during therapeutic endoscopy. These data may help understanding the ergonomics in flexible endoscopy, and potentially contribute to optimize its working environment and further development of relevant medical devices.

Disclosure: Nothing to disclose.

Gastric mucosa: Basic science

17:00-18:00 / Poster Stage 6

MP198

CHIA DEFICIENCY IN THE CHIEF CELLS PROMOTES SPASMOLYTIC POLYPEPTIDE-EXPRESSING METAPLASIA THROUGH PYROPTOSIS MEDIATED M2 MACROPHAGE POLARIZATION

S. Liu¹, Z. Ma¹, Y. Zhao¹, C. Hu¹, T. Li², B. Tuo¹, X. Liu¹

¹Department of Gastroenterology, Digestive Disease Hospital, Affiliated Hospital of Zunyi Medical University, Zunyi, China,

²Department of General Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, China, Zunyi, China

Contact E-Mail Address: anhuimazhiyuan@163.com

Introduction: Loss of parietal cells causes the development of spasmolytic polypeptide-expressing metaplasia (SPEM) through transdifferentiation of chief cells. However, whether initial chief cell loss cause SPEN needs to be further investigated. Acidic mammalian chitinase (CHIA) belongs to the 18 glycosidase family and is expressed in epithelial cells in various organ, which can degrade chitin-containing pathogens, participate in Th2-mediated inflammation. CHIA is highly expressed in the chief cells, and our previous study showed that CHIA deficiency in the chief cells is the key event to induces SPEN and progress to gastric cancer, which is independent of parietal cell loss (Zhao et al., DDW 2023; Hu et al., KDDW 2021). However, the molecular role and mechanism of CHIA in the development of SPEN is need further investigated.

Aims & Methods: Aims: Explore new cellular origins and specific molecular mechanisms of SPEN occurrence.

Methods: PCR and single-cell sequencing (scRNA-seq) technology, histopathological and immunofluorescence (IF) with specific markers were performed in CHIA wild type (WT) mice and knockout (KO) mice. Multiple endoplasmic reticulum stress markers, macrophage polarization markers and cytokine-related markers were detected by qPCR in CHIA WT and KO.

Results: PCR and scRNA-seq technology data showed that increased M2 macrophage infiltration and SPEN formation, but remaining of parietal cells in CHIA KO mice, when compared to CHIA WT mice. Furthermore, deletion of CHIA in mice resulted in release of endoplasmic reticulum stress-triggered, including upregulation of endoplasmic reticulum stress markers (PERK, XBP-1, eIF2α/P-eIF2α, and GRP78), followed with upregulation of pyroptosis-related marker, including NLRP3, ACS, GSDMD, NEK7, Caspase1, Caspase11, IL-1β, and IL-18, as well as significantly increase-ment of IL33/IL-13 release. Moreover, Double immunofluorescence staining showed that upregulation and colocalization of NLRP3 and IL-33 induced M2 macrophage polarization markers, including F4/80 and CD163 in the gastric mucosal of CHIA KO mice. Notably, IF showed that CHIA deficiency caused the mucous neck cell marker SOX9 shifted from the cervical isthmus into the SPEN cells, and co-localized with the SPEN markers CD44v, TFF2 and MUC6, suggesting that the origin of SPEN cells may trans-differentiate from mucous neck cell after CHIA gene deletion.

Conclusion: CHIA deficiency in the chief cells promotes SPEN through the pyroptosis mediated M2 macrophage polarization. The origin of CHIA deficiency promotes injury may origin from the transdifferentiation of mucous neck mucus cells into SPEN cells.

Disclosure: The authors declare that they have no conflicts of interest.

MP199

NAD(P)H QUINONE OXIDOREDUCTASE 1 (NQO1) PREVENTS GASTROINTESTINAL EPITHELIUM AGAINST REDOX IMBALANCE AS A MOLECULAR TARGET OF ENDOGENOUS HYDROGEN SULFIDE (H₂S)-SIGNALING AND NOVEL OXIDATION-SENSITIVE H₂S-PRODRUGS

U. Glowacka¹, M. Szetela¹, E. Korbut¹, M. Wierdak², T. Vignane³, M.R Filipovic³, M. Suski⁴, K.G Fosnacht⁵, M.D Pluth⁵, Z. Śliwowski¹, M. Magierowski¹

¹Jagiellonian University Medical College, Cellular Engineering and Isotope Diagnostics Lab, Department of Physiology, Cracow, Poland, ²Jagiellonian University Medical College, 2nd Department of Surgery, Cracow, Poland, ³Leibniz-Institut für Analytische Wissenschaften-ISAS e.V., Dortmund, Germany, ⁴Jagiellonian University Medical College, Proteomics Laboratory, Centre for the Development of Therapies for Civilization and Age-Related Diseases, Cracow, Poland, ⁵University of Oregon, Department of Chemistry and Biochemistry, Materials Science Institute, Knight Campus for Accelerating Scientific Impact, and Institute of Molecular Biology, Eugene, Oregon, United States of America

Contact E-Mail Address: urszula.glowacka@uj.edu.pl

Introduction: NAD(P)H quinone oxidoreductase 1 (NQO1) is an oxidation-sensitive enzyme that protects cells against redox imbalance. Involvement of NQO1 in gastrointestinal (GI) health and disease has been poorly studied. Hydrogen sulfide (H₂S) is an endogenous and anti-oxidative molecule that exerts anti-oxidative activity due to the posttranslational persulfidation of proteins. Bioactivity of H₂S is related e.g. to the regulation of antioxidant response elements (AREs) in the nucleus that subsequently affect many molecular factors. We assume that this phenomenon could also include NQO1. Importantly, triggerable H₂S-prodrugs, activated by reactive oxygen species (ROS) are a new class and promising agents in therapeutic applications but remain poorly explored in GI pharmacology. Novel, click-and-release carbonyl sulfide/H₂S donor (Peroxy-TCM), in the presence of ROS is capable to rapidly release cytoprotective H₂S. Of note, oxidative stress and ROS generation have been linked to the development of Barrett's esophagus (BE) or acute gastric mucosal injuries.

Aims & Methods: Therefore, we verified the contribution of the interplay between NQO1 and H₂S-signaling in the pathogenesis of oxidation-dependent GI diseases. We assessed the therapeutic capacity of the novel "click-chemistry"-based pharmacology, implementing this approach in experimental gastroenterology.

Clinically, proteome profile and pathway-specific PSSH shifts were evaluated using recent chemoproteomic approach in 3 sets of endoscopic esophageal samples: BE, squamous segments exposed to gastroesophageal reflux (GERD), and squamous segments from patients w/o GERD. Experimentally, male Wistar rats were administered intragastrically (i.g.) with i) vehicle, ii) peroxy-TCM (4 mg/kg) as a novel ROS-activated COS/H₂S donor or iii) peroxy-CM, as a structural control w/o H₂S-releasing ability. Peroxy-TCM was also combined with pharmacological NQO1 inhibitor (dicumarol, applied i.g.). Next, animals underwent microsurgical ischemia/reperfusion (I/R), selectively targeting gastric mucosa. Gastric mucosal damage was assessed micro- and macroscopically. Bioavailability of H₂S and oxidative RNA damage reflected by 8-hydroxyguanosine (8-OHG) levels were assessed in gastric mucosa. Pathway-specific proteome changes in the gastric mucosa were evaluated using mass spectrometry-based proteomics.

Results: Clinically, NQO1 protein and its persulfidation was progressively increased at subsequent phases of BE pathogenesis. Experimentally, peroxy-TCM in contrast to its negative control, reduced gastric damage and RNA oxidation induced by I/R. Gastric mucosal I/R activated peroxy-TCM and evoked H₂S-release in gastric mucosa. Proteomic screening showed

that gastroprotective effect of peroxy-TCM was accompanied by the increased mucosal level of NQO1. Pharmacological inhibition of NQO1 attenuated beneficial effects of H₂S-prodrug.

Conclusion: NQO1 emerged as an important molecular target that contributes in anti-oxidative response of GI epithelium to pathology-driven redox imbalance. NQO1 and its persulfidation could be also considered as an early biomarker of BE development. NQO1 activity in gastric mucosa depends on the H₂S-bioavailability. Click-chemistry-based H₂S-therapeutics appeared here to selectively release this gaseous molecule in controllable-manner (only in the presence of ROS) when applied i.g. This therapeutic approach mechanistically activates gastric mucosal NQO1, increasing the ability of gastric epithelium to cope with oxidative stress. [Funding: National Science Centre (Poland)- 2019/33/B/NZ4/00616, 2023/07/X/NZ4/01052]

References:

1. Steiger, Andrea K et al. "Inhibition of Mitochondrial Bioenergetics by Esterase-Triggered COS/H₂S Donors." ACS chemical biology vol. 12,8 (2017): 2117-2123. doi:10.1021/acscchembio.7b00279
2. Levinn, Carolyn M et al. "N-Methylation of Self-Immolative Thiocarbamates Provides Insights into the Mechanism of Carbonyl Sulfide Release." The Journal of organic chemistry vol. 86,8 (2021): 5443-5451. Doi:10.1021/acs.joc.0c02778
3. Zhao, Yu, and Michael D Pluth. "Hydrogen Sulfide Donors Activated by Reactive Oxygen Species." Angewandte Chemie (International ed. in English) vol. 55,47 (2016): 14638-14642. doi:10.1002/anie.201608052
4. Zhao, Yu et al. "Kinetic Insights into Hydrogen Sulfide Delivery from Caged-Carbonyl Sulfide Isomeric Donor Platforms." Journal of the American Chemical Society vol. 139,45 (2017): 16365-16376. Doi:10.1021/jacs.7b09527
5. Gilbert, Annie K, and Michael D Pluth. "Subcellular Delivery of Hydrogen Sulfide Using Small Molecule Donors Impacts Organelle Stress." Journal of the American Chemical Society vol. 144,38 (2022): 17651-17660. doi:10.1021/jacs.2c07225
6. Zhao, Yu et al. "Fluorogenic hydrogen sulfide (H₂S) donors based on sulfenyl thiocarbonates enable H₂S tracking and quantification." Chemical science vol. 10,6 1873-1878. 10 Dec. 2018, doi:10.1039/c8sc05200j
7. Zivanovic, Jasmina et al. "Selective Persulfide Detection Reveals Evolutionarily Conserved Antiaging Effects of S-Sulfhydration." Cell metabolism vol. 30,6 (2019): 1152-1170.e13. doi:10.1016/j.cmet.2019.10.007

Disclosure: Nothing to disclose.

MP200

WITHDRAWN

MP201

GLUTATHIONE-S TRANSFERASE PI GENE POLYMORPHISMS MODIFY SUSCEPTIBILITY TO DEVELOPING *HELICOBACTER PYLORI* INFECTION

I. Pantic¹, S. Lugonja², D. Jerotic³, A. Savic-Radojevic³, T. Milovanovic⁴

¹Clinic of Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, Serbia, ²General Hospital "Djordje Joanovic", Department of Internal Medicine, Zrenjanin, Serbia, ³Faculty of Medicine, University of Belgrade, Institute of Medical and Clinical Biochemistry, Centre for Excellence for Redox Medicine, Belgrade, Serbia, ⁴University Clinical Center of Serbia, School of Medicine University of Belgrade, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia

Contact E-Mail Address: ilic.ivana04@gmail.com

Introduction: Several factors are known to affect the clinical presentation of *Helicobacter pylori* (*H. pylori*) infection including bacterial virulence factors, intensity of the immune response of the host, host's genetic factors, as well as different environmental factors. Complex interactions between *H. pylori* and the host's immunological response result in the production of various cytokines (interferon- γ , tumor-necrosis factor α , interleukin-1 β , and interleukin-8) and reactive oxygen species (ROS) which lead to prolonged inflammation and subsequent damage to the gastric mucosa. Various inflammation mechanisms have been studied in *H. pylori* infection, including those related to the NF- κ B signaling pathway, ROS, and more recently NLRP3 inflammasome.

When it comes to the multifunctional family of glutathione transferase enzymes, glutathione S-transferase omega (GSTO) and pi (GSTP) are known for their antioxidant, as well as signaling activity. Specifically, the regulatory effects of GSTO and GSTP1, on NLRP3 inflammasome and NF- κ B signaling pathway, respectively, have been extensively studied.

Aims & Methods: Based on the known catalytic and signaling functions of GSTO and GSTP and their effect on both redox homeostasis and inflammation, we proposed a possible modifying role of GSTO and GSTP1 polymorphisms in the individual susceptibility towards the development of *H. pylori* infection. The distribution of polymorphisms in GSTO1 (rs4925), GSTO2 (rs156697), and GSTP1 (rs1695 and rs1138272) were assessed in 101 *H. pylori*-positive and 107 *H. pylori*-negative patients, emphasizing their individual and haplotype effects on disease development. Polymorphisms were determined by the appropriate qPCR method.

Results: The obtained results showed no influence of GSTO1 (rs4925) and GSTO2 (rs156697) polymorphisms on *H. pylori* infection development in both individual and haplotype analyses ($p>0.05$). However, individuals carrying variant GSTP1 (rs1695 and rs1138272) genotypes exhibit up to three times higher odds of *H. pylori* infection development, compared to those carrying referent alleles (Table 1).

GSTP1 rs1695 genotype	HP negative, n (%)	HP positive, n (%)	OR (95% CI)	p
*A/A	47 (44)	35 (35)	1 ^a	
*A/G	53 (50)	50 (49)	1.27 (0.71-2.27)	0.427
*G/G	7 (6)	16 (16)	3.07 (1.14-8.26)	0.026
*A/G + *G/G	60 (56)	66 (65)	1.47 (0.84-2.58)	0.172
GSTP1 rs1138272 genotype				
*C/C	92 (87)	74 (73)	1 ^a	
*C/T	14 (13)	22 (22)	1.95 (0.93-4.08)	0.075
*T/T	0 (0)	5 (5)	/	/
*C/T + *T/T	14 (13)	27 (27)	2.39 (1.17-4.89)	0.016

Table 1. Distribution of GSTP1 genotypes in *H. pylori*-positive and *H. pylori*-negative patients.

HP – *Helicobacter pylori*; OR – odds ratio; CI – confidence interval

These findings are confirmed by further haplotype analysis. Carriers of H3 haplotype, comprising GSTP1*G and GSTP1*T variant alleles were at more than a 3-fold increased risk of *H. pylori* infection development ($p=0.012$).

Conclusion: GSTP1 polymorphisms modify susceptibility to developing *H. pylori* infection. Further studies are needed to clarify the specific roles of glutathione transferases in innate and acquired immune response in the context of *H. pylori* infection development and maintenance.

Disclosure: Nothing to disclose.

MP202

WITHDRAWN

MP203

HELICOBACTER PYLORI SEROPREVALENCE IN PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS *HELICOBACTER PYLORI* NEGATIVE AT HISTOLOGY

M. Vavallo¹, J. Butt², S. Cingolani¹, L. Dottori¹, G. Cozza¹, F.P. Schiavone¹, E. Dilaghi¹, L. Belloni¹, M. Franchitti¹, B. Annibale¹, T. Waterboer², E. Lahner¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea University Hospital, Gastroenterology Unit, Rome, Italy, ²German Cancer Research Center (DKFZ), Division of Infections and Cancer Epidemiology, Heidelberg, Germany

Contact E-Mail Address: ma1996.mv@gmail.com

Introduction: For autoimmune atrophic gastritis (AAG) two pathogenetic models are proposed: a pure autoimmune disorder or gastric autoimmunity triggered by *Helicobacter pylori* (Hp) infection. In AAG, the diagnosis of Hp infection with conventional methods is challenging due to oxyntic mucosa atrophy, hypochlorhydria, and gradual Hp clearance.

Formerly, Hp seropositivity in AAG with negative Hp histology was shown by Western blotting. A Hp multiplex serology assay allowing simultaneous detection of antibodies to several Hp proteins and virulence factors has not been used so far in sera of AAG pts to test for Hp exposure.

Aims & Methods: The aim was to assess seroreactivity against Hp proteins in AAG pts, Hp negative at histological evaluation of gastric biopsies and without history of Hp infection.

Single centre case-control study on 75 adults with histological AAG diagnosis, age 63 (18-88) yrs, F:M 2.4:1, parietal cell (PCA)-intrinsic factor auto-antibodies (IFA) positivity in 81.3%-41.3%. AAG pts were compared with 2 control groups: 62 healthy stomach subjects (HS), age 65.5 (23-90) yrs, F:M 1.1:1, and 16 controls with Hp-positive antral non-atrophic gastritis (NAHp), age 59.5 (31-78) yrs, F:M 1.7:1. All 153 subjects had gastroscopy with biopsies, according to the updated Sydney system, for clinical suspicion of AAG (anaemia or dyspepsia) or AAG follow-up. Frozen sera (-20°C) were analysed by Hp multiplex serology assay.

This assay is based on a glutathione-S-transferase (GST) capture immunosorbent assay combined with fluorescent bead technology measuring antibody responses to 13 Hp proteins (CagA, VacA, UreA, HP0875, NapA, HpaA, HyaA, HcpC, Cad, GroEL, HP0231, HP0305, HP1564). Median fluorescent intensity (MFI) values for each antigen were determined in a 1:1000 serum dilution. Seropositivity to individual antigens was defined as MFI above cut-off. Hp seropositivity was defined as being positive for >3 or more antigens.

Results: AAG pts showed a higher, but not significantly, Hp seropositivity than HS (n=16/21.3% vs n=6/9.7%, $p=0.06$), but a significantly lower seropositivity than NAHp (12/75%, $p<0.0001$). The number of participants positive to none of the Hp antigens was similar in AAG and HS

(n=22/29.3% vs n=24/38.7%, p=0.25), and significantly higher than in NAHp (n=1/6.2%, p=0.05). The number of seroreactive antigens was significantly higher in AAG than in HS (mean±SEM 2.2±0.3 vs 1.4±0.2, p=0.04), and lower than in NAHp (5.4±0.7, p<0.0001). Hp antigens seroreactive in >50% of the 16 Hp seropositive AAG pts included GroEL, NapA, CagA, HyaA, Catalase, HcpC, and HP1564; UreA and VacA were seropositive in 37.5%/16 seropositive AAG pts.

Severe corpus atrophy was significantly more frequent in the 22 AAG pts without any seroreactivity (0 Hp antigens) than in seropositives (p=0.019) suggesting more severe disease in pts never exposed to Hp. IFA positivity was nearly 2x in Hp seronegatives compared to seropositives (45.8% vs 25%, p=0.137) albeit not significant. An inverse relationship between anti-UreA and IFA titers was shown (Spearman's rho -0.25 (95%CI -0.46 to -0.03), p=0.03), suggesting an opposite trend of Hp immunoreactivity and gastric autoimmunity.

Conclusion: By Hp multiplex serology, 30% of histologically Hp negative AAG pts had complete absence of seroreactivity, likely belonging to the pure AAG type. In contrast, 20% of AAG pts showed exposure to Hp, indicating that infection might have played a role in triggering gastric autoimmunity. The remaining 50% of AAG pts showed a weak seropositivity, probably belonging to a grey zone, not definitively categorizable by this approach.

References: 1. Rugge M, et al. Autoimmune gastritis: histology phenotype and OLGA staging. s.l. : Aliment Pharmacol Ther., 2012. p. 1460-1466. Vol. 35.
2. D'Elis MM, et al. Helicobacter pylori and gastric autoimmunity. s.l. : Microbes Infect., 2004 . p. 1395-401. Vol. 6.
3. Bergman MP, et al. The story so far: Helicobacter pylori and gastric autoimmunity. s.l. : Int Rev Immunol., 2005. p. 63-91. Vol. 24.
4. Bergman MP, D'Elis MM. Cytotoxic T cells in H. pylori-related gastric autoimmunity and gastric lymphoma. s.l. : J Biomed Biotechnol., 2010. p. 104918. Vol. 2010.
5. Mini R, et al. Western blotting of total lysate of Helicobacter pylori in cases of atrophic body gastritis. s.l. : Clin Chem., 2006. p. 220-226. Vol. 52.
6. Annibale B, et al. CagA and VacA are immunoblot markers of past Helicobacter pylori infection in atrophic body gastritis. s.l. : Helicobacter., 2007. p. 23-30. Vol. 12.
7. Gao L, et al. Association between chronic atrophic gastritis and serum antibodies to 15 Helicobacter pylori proteins measured by multiplex serology. . s.l. : Cancer Res., 2009. p. 2973-2980. Vol. 69.
8. Michel A, et al. Helicobacter pylori multiplex serology. s.l. : Helicobacter, 2009. p. 525-535. Vol. 14.

Disclosure: Nothing to disclose.

MP204

WITHDRAWN

MP205

HELICOBACTER PYLORI-RELATED GENES ARE DETECTABLE IN GASTRIC BIOPSIES OF A MINORITY OF PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS

S. Cingolani¹, L. Belloni¹, G. Stendardo¹, G. Cozza¹, M. Vavallo¹, L. Dottori¹, J. Butt², F.P. Schiavone¹, T. Waterboer², B. Annibale¹, E. Lahner¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea University Hospital, Gastroenterology Unit, Rome, Italy, ²Infection and Cancer Epidemiology, Division of Molecular Diagnostics of Oncogenic Infections, German Cancer Research Center (DKFZ), Heidelberg, Germany

Contact E-Mail Address: cingolanisophia97@gmail.com

Introduction: Autoimmune atrophic gastritis (AAG) is an immune-mediated disorder characterized by corpus-restricted atrophy and pseudopyloric or intestinal metaplasia, associated with reduced hydrochloric acid and intrinsic factor production and heterogeneous clinical consequences. The aetiology of AAG is autoimmune, but the role of *Helicobacter pylori* (Hp) has been proposed, although not definitively proven.

A possible antigenic crossreactivity with H⁺,K⁺-ATPase, the main autoantigen in AAG, has been reported and Hp seropositivity has been described in histologically Hp negative AAG.

One study employed molecular biology techniques to characterize a cohort of AAG patients as definitively Hp naïve.

Aims & Methods: The aim was to assess the presence of Hp-related genes in corpus mucosa biopsies of pts with AAG and Hp-positive and negative ctr by using real-time PCR.

Single-centre, experimental molecular biology study on 55 pts with histologically diagnosed AAG, of whom at histology 52 were Hp negative (age 61.5, range 28-88 yrs, 75% F, 96.2% parietal cell (PCA) and 44.2% intrinsic factor antibodies (IFA) positive), while 3 were Hp positive (age 74,69,33 yrs; 1 F; all 3 PCA and 1 IFA positive). Ctr were 4 pts who underwent gastroscopy for non-ulcer dyspepsia, 2 with Hp-positive superficial antral gastritis (positive ctr), and 2 with a healthy stomach (negative ctr). Hp serology (ELISA or multiplex) was available from all pts.

DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) tissue sections of corpus mucosa biopsies and real-time PCR was performed using specific probes for UreA, UreC, and CagA Hp related genes; 16sRNA and Beta2 microglobulin (B2M) specific probes were used as amplification ctr of bacterial and human DNA (real-time PCR cycle threshold (CT) >28<38).

Results: In 4(7.7%) of the 52 histologically Hp negative AAG pts, Hp-related genes were detected, in 4(7.7%) UreC, in 3(5.8%) UreA, and in 1(1.9%) CagA. All of them (3 F, aged 88,85,58,56 yrs) had positive Hp serology and PCA, only one was IFA-positive.

The detectability of B2M and bacterial 16sRNA genes did not differ in UreC-positive or UreC-negative pts (B2M CT mean 29.6±1.2 for UreC positives vs 29.7±1.4 for UreC negatives, p=0.99; 16sRNA gene CT mean 29.9±1.2 vs 29.4±1.2, p=0.27) indicating that the not-detectability of Hp-related genes was unrelated to reduced amounts of gastric bacterial or human DNA.

Hp serology was positive in all 4 histologically Hp-negative AAG pts positive for UreC compared to 5/48(10.4%) UreC negative pts (p<0.0001) indicating previous exposure. PCA were present in all 4 UreC positive AAG pts compared to 46/48(95.8%) of UreC negatives (p=0.68).

IFA positivity in UreC negatives was nearly 2x higher than that of UreC positives (45.8% vs 25%, p=0.42) without reaching significance. In 2/3 pts with histologically Hp-positive AAG, Hp-related genes could be detected; in the remaining patient, nor UreA, UreC neither CagA gene could be found (M, 69 yrs, no anemia, PCA-IFA-Hp serology positive).

Conclusion: In >90% of histologically Hp-negative and PCA or IFA positive AAG pts, Hp-related genes cannot be retrieved in the gastric mucosa. In 10% of these Hp-genes negative AAG pts, previous exposure to Hp can be testified by positive serology.

Hp-related genes can be detected in gastric biopsies in <10% of histologically Hp-negative AAG patients and positive Hp serology further confirms the role of Hp in this group.

These findings show that primary, Hp naive AAG is the more common type, but in a subset of pts, AAG seems to be secondary to Hp infection.

References: Lenti MV, Nature Rev Dis Primer 2020,

Lahner E, Dig Liv Dis 2019,

Annibale B, Helicobacter ,

Mini R, Clin Chem 2007,

Dottori L, UEGW 2023

Rugge M, Gut 2022

Disclosure: Nothing to disclose.

MP206

HIGH NEUTROPHIL-TO-LYMPHOCYTE RATIO AT HELICOBACTER PYLORI ERADICATION INCREASES THE RISK OF ERADICATION FAILURE AND 5-YEAR INCIDENCE OF POST-ERADICATED GASTRIC CANCER

T. Yasuda^{1,2}, N. Yagi¹, H. Kutsumi², Y. Nakahata¹, Y. Yasuda¹, T. Omatsu^{1,3}, N. Sakamoto¹, Y. Murakami¹, A. Obora¹, T. Kojima¹

¹Asahi University Hospital, Gastroenterology, Gifu, Japan, ²Akashi City Hospital, Gastroenterology, Akashi, Japan, ³North Medical Center, Kyoto Prefectural University of Medicine, Gastroenterology, Kyoto, Japan

Contact E-Mail Address: everyday.enjoy29@gmail.com

Introduction: Vonoprazan (VPZ) has been used in Japan since 2015 to eradicate *Helicobacter pylori*. The level of acid inhibition required for *H. pylori* eradication is a pH > 5.0, and VPZ treatment maintains this state for an extended period. Accordingly, VPZ reportedly has a higher eradication success rate than conventional proton pump inhibitors. However, the incidence and risk factors of gastric cancer (GC) as well as long-term prognosis after VPZ eradication of *H. pylori* remain unclear. Neutrophil-to-lymphocyte ratio (NLR) is an indicator of asymptomatic chronic inflammation. NLR was reported to reflect the balance between the tumor-promoting environment and the anti-tumor immune status.

Aims & Methods: This single-center cohort study included 934 consecutive patients who underwent *H. pylori* eradication using a VPZ regimen between February 2015 and June 2017. The patients were followed up for 5 years after *H. pylori* eradication. The trial was registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN000046308). The eradication regimen included VPZ 40 mg/day, amoxicillin 1500 mg/day, and clarithromycin 400 mg/day for 1 week for primary eradication and VPZ 40 mg/day, amoxicillin 1500 mg/day, and metronidazole 500 mg/day for 1 week for secondary eradication.

We examined the NLR at the time of eradication and investigated whether it could be a predictive marker of eradication success, risk of post-eradication GC development, and long-term prognosis.

Results: The study cohort included 57.3% men and had a mean age of 57.8 (interquartile range, 49-67) years. Of them, 3.2% had a history of GC resection. Two-thirds of all patients (59.0%, n=551) had open-type atrophy. The mean (standard deviation) NLR was 1.99 (1.20). The successful eradication rates were 92.6% (intention-to-treat) and 98.7% (per-protocol). Minor side effects (e.g., rash, diarrhea) occurred in 2.0% of all patients. A multivariate analysis showed that high NLR (odds ratio [OR], 2.96; p=0.004) was significantly associated with eradication failure. During the 5-year observation period, twelve cases of stage IA GC developed. The

3-year incidence rate was 0.87% and the 5-year incidence rate was 1.67%. The average time from eradication to diagnosis was 40.5 (6.1) months. A multivariate analysis showed that a high NLR (OR, 6.0; p=0.026), history of GC (OR, 6.9; p=0.011), and history of hypertension (OR, 5.8; p=0.016) were significantly associated with GC development. In contrast, age ≥ 70 years (p=0.402) and open-type atrophy (p=0.120) were not significant factors of GC development. A receiver operating characteristic curve showed that the optimal NLR cut-off value for new GC development at the time of eradication was 1.95 (sensitivity; 0.82, specificity; 0.65). Twelve patients died during the study period, and no treatment- or GC-related deaths were observed. A high NLR was associated with a significantly higher mortality rate (Hazard ratio [6.47], p=0.002).

Conclusion: High NLR was associated with *H. pylori* eradication failure using the VPZ regimen. A high NLR, history of GC, and history of hypertension were risk factors for new-onset GC within 5 years post-eradication, while a high NLR was also associated with a poor long-term prognosis after *H. pylori* eradication.

Disclosure: Nothing to disclose.

MP207

UNVEILING THE MECHANISM OF HELICOBACTER PYLORI IN GASTRIC CANCER IMMUNE EVASION THROUGH SPATIAL TRANSCRIPTOMICS OF PATHOLOGICAL SAMPLES

B. Chen¹, W. Kang²

¹The Chinese University of Hong Kong, Hong Kong, Hong Kong,

²The Chinese University of Hong Kong, Anatomical and Cellular Pathology, Hong Kong, Hong Kong

Contact E-Mail Address: bonanchen@cuhk.edu.hk

Introduction: Gastric cancer remains a major health challenge globally, with *Helicobacter pylori* (*H. pylori*) infection being a well-known risk factor. Despite significant advances in understanding the pathological mechanisms of gastric cancer, the specific interactions between *H. pylori* and the host immune system within the tumor microenvironment are not fully elucidated. This study leverages cutting-edge spatial transcriptomic technologies to explore these interactions in gastric cancer samples.

Aims & Methods: This research aims to elucidate the mechanisms through which *H. pylori* contributes to immune evasion in the gastric cancer microenvironment. We utilized spatial transcriptomics on 71 gastric cancer samples, supplemented by single-cell transcriptomics on 10 of these samples to achieve a high-resolution view of cellular interactions. Advanced analytical techniques, including cell interaction networks, neighborhood analysis, and deconvolution mapping, were employed to dissect the complex interplay between tumor cells, immune cells, and *H. pylori*.

Results: Our results reveal a sophisticated mechanism by which *H. pylori* induces the recruitment and activation of cancer-associated fibroblasts (CAFs) and regulatory T cells (Tregs), facilitating an immunosuppressive tumor microenvironment. Spatial transcriptomics highlighted significant alterations in gene expression patterns conducive to immune evasion, primarily mediated by the interaction between *H. pylori*, CAFs, and Tregs. The integration of single-cell and spatial data provided a detailed map of the immune landscape, revealing key nodes and pathways involved in this process.

Conclusion: The findings of this study provide compelling evidence of *H. pylori*'s role in shaping the immune landscape of gastric cancer towards immunosuppression through the modulation of CAFs and Tregs. These insights underscore the potential benefits of immunotherapeutic strategies tailored for *H. pylori*-positive gastric cancer patients. Future therapeutic interventions could focus on targeting these specific interactions to enhance the efficacy of cancer immunotherapy in this cohort.

Disclosure: The authors declare no conflict of interest related to this study. Funding sources and affiliations have been reviewed to ensure no potential bias or influence on the research outcomes. All procedures followed were in accordance with ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

IBD management from (non-)pharmaceutical interventions to outcome definitions

10:00-11:00 / Poster Stage 1

MP208

EFFECTIVENESS OF IBD-BOOST, A DIGITAL COGNITIVE BEHAVIOURAL SELF-MANAGEMENT PROGRAMME FOR FATIGUE, AND/OR PAIN, AND/OR FAECAL INCONTINENCE IN INFLAMMATORY BOWEL DISEASE: MULTICENTRE RANDOMISED CONTROLLED TRIAL

R. Moss-Morris¹, C. Norton², A.L Hart³, F. Cleirigh Buttner⁴, T. Hamborg⁴, L. Miller⁴

¹King's College London, Health Psychology, London, United Kingdom, ²King's College London, Clinical Nursing Research, London, United Kingdom, ³St Mark's Hospital and Academic Institute, Gastroenterology, Harrow, United Kingdom, ⁴Queen Mary University of London, Pragmatic Clinical Trials Unit, London, United Kingdom

Contact E-Mail Address: ailsa.hart@nhs.net

Introduction: Many people with IBD experience fatigue, pain and faecal incontinence (FI), impacting quality of life (QoL). We developed an interactive digital online self-management intervention (IBD-BOOST) based on a theoretically informed logic model and cognitive behavioural techniques.

Aims & Methods: To evaluate IBD-BOOST we conducted a multi-centre two-arm parallel group randomised controlled trial (RCT) comparing IBD-BOOST with Care as Usual (CAU), recruiting patients from clinics and national registries who rated the impact of fatigue and/or pain and/or FI as $\geq 5/10$. Those in the IBD-BOOST arm received 6 months access to the 12-session IBD-BOOST programme, a 30-minute telephone support call and weekly in-site email messages for 3 months. The UK Inflammatory Bowel Disease Questionnaire (UK-IBDQ) and global rating of symptom relief (GRSR) at 6 months were dual primary outcomes ($\alpha=0.025$ was considered statistically significant with two primary outcomes). Other secondary outcomes, including individual symptoms, were measured at 6 and 12 months. Complier-averaged causal effects (CACE), sensitivity and pre-specified subgroup analyses were conducted.

Results: 780 participants were randomised, 432 with Crohn's disease; 520 (66.7%) were female, mean age 49 years. At 6 months, both UK-IBDQ and GRSR were similar between the BOOST and CAU arms, $p=0.19$ for IBDQ and $p=0.39$ for GRSR. Adverse events were similar between groups. FI score and EQ5D utility score (secondary outcomes) were in favour of IBD-BOOST at 6 months, but pain and fatigue were no different. 57% of the intervention group completed a pre-defined minimum "dose" of 4 sessions (i.e. compliers). The CACE analysis suggested that compliers were more likely to report better QoL ($p=0.03$). Subgroup analysis of those meeting criteria for irritable bowel syndrome (IBS) at baseline, showed that IBD-BOOST was more effective in improving IBDQ and GRSR at 6 months when compared with CAU for the IBD-IBS group ($p_{\text{interaction}}=0.015$ and 0.046 , respectively).

Conclusion: This large RCT found that IBD-BOOST did not improve IBDQ and GRSR in patients with IBD and fatigue and/or pain and/or FI relative to CAU. Participants reported less FI at 6 and 12 months. Those with IBD-IBS improved more than those without.

Trial registration: ISRCTN71618461

Disclosure: Nothing to disclose.

MP209

TRYPTOPHAN METABOLITES AS BIOMARKER FOR FATIGUE IN INFLAMMATORY BOWEL DISEASE

P.I. Metselaar¹, M. Lowenberg², G.R. D'Haens², W.J. de Jonge¹, A.A. te Velde¹, M. Ghiboub¹

¹Amsterdam University Medical Centers, University of Amsterdam, Tytgat Institute for Liver and Intestinal Research, Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ²Amsterdam University Medical Centers, University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: m.ghiboub@amsterdamumc.nl

Introduction: Fatigue represents one of the largest unmet clinical needs in inflammatory bowel disease (IBD), both during active and quiescent disease (1, 2). Tryptophan (Trp) metabolites play an important role in mediating mood regulation, intestinal homeostasis and immune responses (3, 4). Dietary Trp is metabolized in the intestines by three different pathways (i.e. kynurenine, serotonin and indole cascade). Previous studies have shown the importance of tryptophan/serotonin balance in fatigue and altered tryptophan serum levels have been reported in IBD patients (5, 6).

Aims & Methods: We aimed to explore changes in Trp metabolite plasma levels in fatigued IBD patients. In total, 40 IBD patients (22 Crohn's disease (CD) and 18 ulcerative colitis (UC) patients) in clinical and biochemical remission (21 females, HBI <5 , SCCAI ≤ 2 , CRP $<5\text{mg/l}$ and/or fecal calprotectin $<250\mu\text{g/g}$) and 25 patients (15 CD and 10 UC) with active disease (18 females; HBI >5 , SSCAI >2 , CRP $>5\text{mg/l}$ and/or fecal calprotectin $>250\mu\text{g/g}$) were included. Patients were classified as fatigued (and further classified as active vs remission: 17 vs 15 females, 6 vs 18 males) or non-fatigued (active vs remission: 1 vs 6 females, 1 vs 1 males) based on their Multi-dimensional Fatigue Inventory score (cut-off for fatigue: ≥ 40). Targeted quantitative analysis of 21 Trp metabolites was performed in plasma samples utilizing liquid chromatography coupled with quadrupole mass spectrometry. Receiving Operator Characteristic (ROC) curve and random forest analysis were used to assess the biomarker power of Trp metabolites for fatigue. Data were analyzed according to sex and fatigue status.

Results: 5-OH-Tryptophan (5-HTP) plasma concentrations, the direct precursor of serotonin, were significantly higher in fatigued compared to non-fatigued female IBD patients who were in remission ($p=0.02$), and this was not observed in male patients, independent of disease status nor in female patients with active disease. ROC analysis (area under the curve (AUC)=0.82) and Random Forest analysis showed that 5-HTP could distinguish between fatigue and no fatigue in females with quiescent IBD, as well as the 3-OH-Kynurenine/Indole-3-Aldehyde ratio (AUC=0.89).

Conclusion: 5-HTP might represent a novel biomarker for fatigue in female patients with quiescent IBD, but it should be acknowledged that the sample size of male patients and female patients with active disease was limited. The impaired balance between the kynurenine and serotonin pathway suggests a potential role for Trp metabolism in fatigued IBD patients. These results warrant a larger-scale, longitudinal study in male and female IBD patients, both with active and quiescent disease.

References: 1. Nocerino, et al. Fatigue in Inflammatory Bowel Diseases: Etiologies and Management. *Adv Ther.* 2020;37(1):97-112.

2. Truysens, et al. Effect of 5-Hydroxytryptophan on Fatigue in Quiescent Inflammatory Bowel Disease: A Randomized Controlled Trial. *Gastroen-*

terology. 2022;163(5):1294-305.e3.

3. Ghiboub, et al. Sustained Diet-Induced Remission in Pediatric Crohn's Disease Is Associated With Kynurenine and Serotonin Pathways. *Inflamm Bowel Dis.* 2023;29(5):684-94.

4. Ghiboub, et al. Nutritional Therapy to Modulate Tryptophan Metabolism and Aryl Hydrocarbon-Receptor Signaling Activation in Human Diseases. *Nutrients.* 2020;12(9).

5. Yamashita. Potential Role of Neuroactive Tryptophan Metabolites in Central Fatigue: Establishment of the Fatigue Circuit. *International Journal of Tryptophan Research.* 2020;13.

6. Borren, et al. Alterations in Fecal Microbiomes and Serum Metabolomes of Fatigued Patients with Quiescent Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol.* 2021;19(3):519-527.e5.

Disclosure: No conflict of interest.

MP210

FATIGUE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES ASSOCIATES WITH ALTERED ANTIBODY RESPONSES AGAINST EPSTEIN-BARR VIRUS

M. Griesbaum¹, T. Vogl², M.C. Visschedijk¹, H. van Dullemen¹, E.A.M. Festen¹, G. Dijkstra¹, R.K. Weersma¹, A.R. Bourgonje¹

¹University of Groningen, Gastroenterology & Hepatology, Groningen, Netherlands, ²Medical university of Vienna, Center for Cancer Research, Vienna, Austria

Contact E-Mail Address: m.griesbaum@umcg.nl

Introduction: Patients with inflammatory bowel diseases (IBD) frequently experience fatigue, affecting up to 80% of those with active disease and approximately 50% with quiescent disease (1). The exact cause of IBD-associated fatigue is often unknown, making clinical management very challenging. Previous studies have suggested the potential involvement of infectious triggers and host immune responses in the development of fatigue.

Aims & Methods: In this study, we aimed to explore whether patients with quiescent IBD reporting fatigue exhibit specific systemic antibody responses, which could provide insight into potential immune reactivities underlying fatigue.

Systemic antibody epitope repertoires were profiled leveraging PhIP-Seq against 344,000 rationally selected peptide antigens. Fatigue severity was assessed on a 10-point Likert scale, ranging from 1 (no fatigue) to 10 (highest fatigue severity). Quiescent IBD was defined as clinical (Harvey-Bradshaw Index [HBI] <5 or Simple Clinical Colitis Activity Index [SCCAI] <2.5) and biochemical remission (C-reactive protein [CRP] <5 mg/L) at time of sampling. Multivariable logistic regression analyses, allowing adjustment for potential confounding factors e.g. age, sex, and smoking, were performed to identify associations between fatigue and systemic antibody responses.

Results: In total, 327 patients with IBD (156 with Crohn's disease [CD]; 171 ulcerative colitis [UC]) were profiled. A total of 153 different antibody-bound peptides were identified in association with fatigue considering nominal significance (nominal P-value <0.05), in the absence of significant associations after adjustment for multiple comparisons. Among antibodies nominally significantly associated with fatigue, 56 antibody-bound peptides (36.6%) were found in lower frequency among highly fatigued patients (fourth quartile, Q4), while 97 peptides (63.4%) were identified as more frequent in highly fatigued patients compared to those with lower fatigue scores (<Q4). Among highly fatigued patients, elevated antibody responses were primarily directed towards viral antigens, with by far the strongest signal against several antigens from Epstein-Barr virus (EBV), mostly directed at the EBV nuclear antigens 1 (EBNA-1) and 3B (EB-

NA-3B). In addition, elevated antibody responses were observed against bacterial antigens, including functional proteins from *Streptococcus* and *Staphylococcus* species. Most findings remained materially unchanged when we repeated analyses solely in patients with quiescent IBD, although antibody responses against EBV were altered, e.g. showing lower responses directed against the BLRF/BMRF/EA-D pathway. Furthermore, these antibody signatures were distinct from those recently identified in association with chronic fatigue syndrome (CFS) (2).

Conclusion: Fatigue in IBD is not reflected by distinct antibody epitope repertoires. However, our study suggests a potential involvement of viral antigens, particularly EBV, in IBD-associated fatigue. Although larger confirmatory studies are needed to validate these findings, this study shows that a technology like PhIP-Seq may represent a valuable strategy to approach the investigation of immune responses underlying complex symptoms such as fatigue.

References:

1. D'Silva A, Fox DE, Nasser Y, Vallance JK, Quinn RR, Ronksley PE, et al. Prevalence and Risk Factors for Fatigue in Adults With Inflammatory Bowel Disease: A Systematic Review With Meta-Analysis. *Clinical Gastroenterology and Hepatology.* 2022;20(5):995-1009.e7. doi:10.1016/j.cgh.2021.06.034
2. Vogl T, Kalka IN, Klompus S, Leviatan S, Weinberger A, Segal E. Systemic antibody responses against human microbiota flagellins are overrepresented in chronic fatigue syndrome patients. *Sci Adv.* 2022;8(38). doi:10.1126/sciadv.abq2422

Disclosure: Nothing to disclose.

MP211

THE EFFECT OF A MULTIMODAL LIFESTYLE INTERVENTION ON FATIGUE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

R. Loveikyte^{1,2}, L.J.M. Koppelman¹, M.J.H. Blijleven³, N. Wilmsen³, M. Rodríguez-Girondo⁴, S. Bloem⁵, P.W. Voorneveld¹, A.E. Van Der Meulen - De Jong¹, S. van der Marel⁶, P.W.J. Maljaars¹
¹Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ³Voeding Lefte Non-profit Foundation, Amsterdam, Netherlands, ⁴Leiden University Medical Center, Department of Biomedical Data Sciences, Leiden, Netherlands, ⁵Nyenrode Business University, Center for Marketing & Supply Chain Management, Breukelen, Netherlands, ⁶Haaglanden Medical Center, Department of Gastroenterology and Hepatology, The Hague, Netherlands

Contact E-Mail Address: r.loveikyte@lumc.nl

Introduction: Lifestyle factors are significant contributors to fatigue, which affects approximately 45% of patients with Inflammatory Bowel Disease (IBD) in remission.

Aims & Methods: In this study, we evaluated the effect of a digital multimodal lifestyle intervention on fatigue in patients with IBD. Patients with IBD in biochemical remission (fecal calprotectin <150 mg/kg) were enrolled in a multicenter, non-randomized, controlled interventional study. The intervention group participated in a 12-month lifestyle program—provided by the non-profit organization Voeding Lefte—that included digital group meetings with a nutritionist and a lifestyle coach focusing on gradual and sustainable behavior change regarding nutrition, physical activity, sleep, and stress management. In addition, the program encouraged patients to exercise more self-control over their personal health. Following the initial six months, attendance at online sessions was not mandatory; however, patients could attend online sessions every six to 12 weeks to

stay motivated and foster the lifestyle habits they acquired throughout the course. Patients in the control group received standard care that included an informational leaflet about the potential causes of fatigue in IBD, the leaflet also included basic lifestyle information and advice to exercise more, eat a healthier diet, stop smoking, reduce alcohol intake, improve sleeping habits, and manage stress. The allocation to a study group was determined by the availability within the group and participant's ability to attend the scheduled intervention. Clinical data and patient-reported outcomes were collected. Fatigue was measured with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F); any increase in FACIT-F after six months was considered a positive response to the intervention. The Minimal Clinically Important Difference (MCID) for fatigue was at least a four-point increase in the FACIT-F score¹. Inverse probability treatment weighting was used to correct confounding by indication.

Results: Thirty-six patients in the intervention group and 32 in the control group were compared. After six months, more patients in the intervention group (82.1% of patients) than in the control group (54.2% of patients) experienced improvement in fatigue, $P = 0.029$. Likewise, significantly more patients in the intervention group (71.4% of patients) than the control group (33.3% of patients) achieved a MCID regarding fatigue; $P = 0.006$. The improvements in fatigue were sustained throughout the study period in the intervention group. Acceptance of the health status was a significant factor for improvement in fatigue (β 7.813, SE 1.908, $P < 0.001$). Compared to the control group, quality of life improved in the intervention group; these patients gained 0.05 more quality-adjusted life years throughout the study. Last but not least, significant improvements in dietary quality were observed as early as three months after the baseline in the intervention but not the control group; these improvements in the intervention group were sustained throughout the study period.

Conclusion: Multimodal lifestyle intervention improves fatigue, quality of life, and dietary quality in patients with IBD who are in remission. Acceptance of the health status appears essential for fatigue improvement; instruments evaluating acceptance could help to personalize treatment and maximize its effectiveness.

References: 1. Cella D, Yount S, Sorensen M, et al. Validation of the Functional Assessment of Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. *J Rheumatol* 2005;32:811-9.

Disclosure: AEvdMdJ received unrestricted research grants from Galapagos, Norgine, Vedanta, Nestle, including speaker's fees from Galapagos, Tramedico, Takeda, Ferring, and Janssen Pharmaceuticals. PWV has received speaker fee from Galapagos and Takeda and served on the advisory board of Lilly, Galapagos, Janssen, BMS, Takeda, and Abbvie. RL has received travel expenses from Galapagos and Cablon Medical and served on the advisory board at Cablon Medical. NW and MJHB are employed by the non-profit organization Voeding Leeft and were a part of the team that guided participants in the intervention group. All other authors have no conflicts of interest to declare.

MP212

WITHDRAWN

MP213

USE OF THE INFLAMMATORY BOWEL DISEASE DISK AS A PSYCHOLOGY REFERRAL SCREENING TOOL

P. Girod¹, L. Harpur¹, L. Kumar¹, C. Coe¹, M. Hanly¹, M. Buckley¹, J. Sheridan¹, G. Cullen¹, G.A Doherty¹

¹St. Vincent's University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: parker.girod@gmail.com

Introduction: The Inflammatory Bowel Disease (IBD) disk is patient-led symptom scoring system for use during clinic visits to give physicians an overview of quality-of-life status in areas such as Emotion, Body Image, Sleep, Energy, Interpersonal Relations, Abdominal Pain, Education and Work, Sexual Function, Joint Pain, and Regulating Defecation.

The disk can be used to assess the need for psychological intervention in those with chronic diseases that exhibit high Emotion scores.

Aims & Methods: Assessing the performance of the IBD disk as a screening tool in a clinic setting for referrals to the IBD Psychology service.

A prospective initiative was introduced in which all patients were given an IBD disk at their clinic visit. Those with Emotion scores ≥ 7 were offered a referral to the IBD Psychology service.

Retrospective review was performed on all referrals to the IBD Psychology service over eight clinical weeks. Baseline demographics were collected such as age, sex, disease sub-type, surgical history, and disease activity at the time of clinic visit. Outcomes that were analysed included the number of patients who were willing to engage in the psychology service, reasoning for declining the service, and overall Emotion scores as reported on the disk.

Results: Over eight clinics, all patients were invited to fill out an IBD disk ($n=234$) and 29% of these patients ($n=69$) were offered a referral to the IBD Psychology service. The median age of referred patients was 43 years, 59% were female ($n=41$), 57% had Crohn's Disease ($n=39$), and 75% had no history of surgery ($n=52$). Of the referrals, 88% of patients were offered a psychology referral on the basis of high Emotion score on their IBD disk ($n=61/69$). The remaining patients ($n=8/69$) were referred following consultation with their physician.

46% of patients that were offered a referral, accepted it ($n=32$), with 75% ($n=24/32$) in the IBD disk cohort and 25% ($n=8/32$) in the other referral cohort. The patients that declined referral did so due to already engaging with external psychological support ($n=12$), personal reasons ($n=12$), or unknown reasons ($n=13$). The patients in the other referral cohort were offered referrals due to them enquiring about the psychology service ($n=2$) or from further prompting about their emotions from their physicians ($n=6$).

The median age of both IBD disk and non IBD disk cohorts was 43. The IBD disk cohort was 62% female ($n=38/61$) versus 38% female ($n=3/8$) in the other referral cohort. 54% of patients had a diagnosis of Crohn's Disease ($n=33/61$), 38% Ulcerative Colitis ($n=23/61$), and 8% IBD-Undiagnosed ($n=5/61$) versus 75% Crohn's Disease ($n=6/8$), 13% Ulcerative Colitis ($n=1/8$), and 13% IBD-U ($1/8$) in the IBD disk cohort and other referral cohort respectively.

Only 25% ($n=17/69$) patients that were referred had a history of IBD related surgery and 54% ($n=37/69$) of those referred were experiencing active disease during their clinic appointments.

Conclusion: The IBD disk is a helpful tool identifying patients for referrals to the IBD Psychology service for high emotional needs. Additional prompting from the treating physician during clinic appointments may identify more patients who would benefit from a psychology referral.

References: IBD Disk from AbbVie SA/NV - BE-IMM-210029 (v2.0) - August 2022

Disclosure: Nothing to disclose.

MP214

PSYCHIATRIC DISORDERS AMONG 5800 PATIENTS WITH MICROSCOPIC COLITIS: A NATIONWIDE POPULATION-BASED MATCHED COHORT STUDY

D. Bergman¹, B. Roelstraete¹, J. Sun¹, F. Ebrahimi^{1,2}, A. Butwicki^{1,3,4}, D. Pardi⁵, J.F. Ludvigsson^{6,7,8}

¹Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, ²Clarunis University Center for Gastrointestinal and Liver Diseases, Department of Gastroenterology and Hepatology, Basel, Switzerland, ³Akershus University Hospital, Division of Mental Health Services, R&D Department, Lørenskog, Norway, ⁴Medical University of Lodz, Department of Biostatistics and Translational Medicine, Lodz, Poland, ⁵Mayo Clinic, GI, Rochester, United States of America, ⁶Karolinska institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, ⁷Örebro University Hospital, Department of Pediatrics, Örebro, Sweden, ⁸Columbia University College of Physicians and Surgeons, Department of Medicine, Kusa, United States of America

Contact E-Mail Address: david.bergman1@gmail.com

Introduction: Microscopic colitis (MC) is an inflammatory condition of the large intestine. Primarily diagnosed in middle-aged and older adults, the age-specific incidence of the disease peaks in patients 75-79 years of age. While MC is associated with a reduced quality of life, large-scale studies on the association with future psychiatric disorders are lacking.

Aims & Methods: Due to the burden of symptoms as well as inflammatory similarities between MC and certain psychiatric disorders, we hypothesized that patients with MC were at an increased risk of psychiatric disease. Using the nationwide histopathology cohort ESPRESSO, we identified 5,816 patients in Sweden with MC. These patients were matched, according to birth year, sex, and county, with reference individuals (n=21,509) from the general population. All individuals with previously recorded psychiatric disorders or dispensation of medication indicative of psychiatric morbidity were excluded. Our main outcome measure was a pre-devised collection of ICD-codes, all indicating psychiatric disease. Moreover, to control for the impact of intrafamilial confounding, full siblings to patients with MC were identified, and in a sensitivity analysis, used as reference population. Adjusted hazard ratios were computed using Cox proportional hazards modelling. Our main analysis included adjustments for the matching factors (birth year, county, sex) as well as educational attainment (as a proxy for socioeconomic status) and inflammatory bowel disease, celiac disease, and type 1 diabetes.

Results: From 2006-2021, 519 patients with MC and 1,313 reference individuals were diagnosed with psychiatric disorders (9.9 vs. 6.5 events per 1,000 person-years), corresponding to one extra case of psychiatric disorder in 29 patients with MC over 10 years. After adjustments, this represented a hazard ratio (HR) of 1.57 (95% confidence interval [CI]=1.42-1.74). We found significantly elevated estimates up to 10 years after MC diagnosis and similar HRs in lymphocytic and collagenous colitis. More specifically, we observed increased risks for unipolar depression, anxiety disorders, stress-related disorders, substance abuse, and suicide attempts in patients with MC.

Our result was robust across several sensitivity analyses (Table 1).

Conclusion: Patients with MC are at increased risk of incident psychiatric disorders compared to the general population. Specifically, this increased risk applies to unipolar depression, anxiety disorders, stress-related disorders, substance abuse, and suicide attempts. The increased risk was most pronounced among older patients with MC.

References: NA

Disclosure: Dr Ludvigsson has coordinated a study for the Swedish IBD quality register (SWIBREG). That study received funding from the Janssen Corporation. Dr Ludvigsson has also received financial support from MSD to develop a paper reviewing national healthcare registers in China. Dr Ebrahimi has served as an advisory board member for Boehringer Ingelheim. Dr Pardi has consulted for Immunic Therapeutics, Takeda, AbbVie, Boehringer Ingelheim, and Lilly.

MP215

PATIENT-CENTERED THERAPEUTIC TARGETS IN INFLAMMATORY BOWEL DISEASE: A PERSONALIZED APPROACH TO IBD MANAGEMENT

H. Kallel¹, N. Elleuch¹, A. Hammami¹, A. Braham Ep Krifa¹, A. Ben Slama¹, H. Jaziri¹, M. Ksiai¹

¹Sahloul University Hospital, Gastroenterology, Sousse, Tunisia

Contact E-Mail Address: hamedkallel@hotmail.com

Introduction: Patients with Inflammatory Bowel Disease (IBD) encounter a wide range of symptoms, from the bowel and other non-specific symptoms. Physicians tend to focus on mucosal healing as a treatment target while little is known about issues important to patients. The aim of our study is to identify critical aspects of the daily burden impacting patients with IBD.

Aims & Methods: Ten dimensions of IBD-related disability were assessed in a cross-sectional survey, including patients followed and hospitalized between April and September 2023, using the self-administered IBD-Disk questionnaire. Patients were then required to select the three items they perceived as the main therapeutic goals and the three items they deemed least important. Disease clinical activity was assessed using Partial Mayo Clinic for Ulcerative colitis (UC) and Harvey Bradshaw Index for Crohn's disease (CD). Percentages were compared using the Chi-square test.

Results: We included 81 patients, 60.5% were male and 71.6% had CD. The mean age was 38.9 ± 12.6 and 59.3% were ≤ 40 at the time of inclusion. Life in urban areas was observed in 71.6% of the patients, a tertiary education in 40.7% and a high socio-economic level in 38.3% of the cases. The IBD was clinically active in 58% of the patients and 65.8% were on biotherapy. The items most frequently perceived as therapeutic goals were "Regulating defecation", "Abdominal pain" and "Energy" with a selection rate of 60.5%, 43.2% and 42.0% respectively. "Interpersonal interaction", "Sexual functions" and "Body image" were the most frequently selected items as least important disability dimensions with a 56.8%, 45.7% and 42.0% respective rate. Men and patients ≤ 40 tended to perceive "Education and work" as more important than women and patients > 40 (80.8% vs 19.2%, p=0.010, 84.6% vs 15.4%, p=0.001 respectively). CD patients tended to select "Abdominal pain" (82.9% vs 17.1%, p=0.050) and "Regulating defecation" (63.3% vs 36.7%, p=0.039) more frequently than UC patients as therapeutic goals. Furthermore, patients undergoing biotherapy were significantly more concerned about "Interpersonal interaction" than other patients (100% vs 0%, p=0.013). Patients living in urban areas appeared to perceive "Regulating defecation" as a main treatment target more frequently than patients living in rural areas (63.3% vs 36.7%, p=0.039). In addition, patients with active disease tended to prioritize "Sleep" more often than patients with clinical remission (81% vs 19%, p=0.013). In our study, tertiary education and high socio-economic level did not seem to significantly influence the treatment priorities to IBD patients.

Conclusion: The findings from this study would contribute to the understanding of the challenges faced by individuals living with IBD, offering valuable insights for physicians to prioritize areas of concern and narrow the perception gap between healthcare providers and patients. This increased understanding has the potential to alleviate the overall disease burden experienced by individuals with IBD.

Disclosure: Nothing to disclose.

MP216

DEFINING PARTIAL RESPONSE IN INFLAMMATORY BOWEL DISEASE: A DELPHI CONSENSUS APPROACH

I. Rodríguez-Lago¹, L.A. Menchén Viso², J.G. Sánchez-Hernández³, J. Guardiola⁴, V. Merino⁵, B. Garcillán⁶, E. Moreno⁶, E. Vispo⁶, E. Domenech Morral⁷

¹Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ²Hospital Universitario Gregorio Marañón, Madrid, Spain, ³Hospital Universitario de Salamanca, Salamanca, Spain, ⁴Hospital Universitario de Bellvitge, Gastroenterology, L'Hospitalet de Llobregat (Barcelona), Spain, ⁵Hospital Universitario Virgen del Rocío, Sevilla, Spain, ⁶Medical Affairs, Johnson & Johnson, Madrid, Spain, ⁷Hospital Germans Trias i Pujol, CIBEREHD, Gastroenterology Unit, Badalona, Barcelona, Spain

Contact E-Mail Address: iago.r.lago@gmail.com

Introduction: Therapeutic goals in inflammatory bowel disease (IBD) are constantly evolving and becoming increasingly ambitious. However, there are still unmet clinical needs. The concepts of response and remission through activity indexes are well established. Nevertheless, there is a wide range of clinical situations where they have not been standardized yet. Many patients show some degree of improvement, or partial response, but fail to meet defined objectives within the desired timeframe, leading to suboptimal therapeutic management. Therefore, early identification of partial responders is crucial for timely intervention, improving disease prognosis and quality of life.

Aims & Methods: Aim: To reach a consensus on the concept of partial response for different profiles of patients with IBD.

Methods: Initially, a scientific committee comprising 4 gastroenterologists and 2 hospital pharmacists involved in IBD management performed a literature review, defined the clinical scenarios and created the content of the Delphi questionnaire. Statements regarding partial response definitions in the short, medium, and long-term were defined for four different patient profiles: moderately-active ulcerative colitis (UC), acute severe UC; luminal and perianal Crohn's Disease (CD). A group of 60 IBD experts in Spain participated in this Delphi consultation. Panelists rated their agreement on a likert scale. Consensus was reached when at least 70% of panelists agreed or disagreed with a statement. Statements without consensus in the first round proceeded to subsequent iterative rounds until a consensus was met.

Results: Consensus was reached on 18 out of 22 statements in the first round and 4 in the second. The consensus definitions for partial response in different patient profiles are as follows:

1. Moderate UC (outpatient treatment):

- Short term: Clinical improvement without achieving clinical response.
- Medium term: Improvement without achieving clinical remission, with persistently elevated biomarkers (e.g. fecal calprotectin).
- Long term: Improvement without achieving clinical remission, with persistent inflammatory activity in biochemical parameters, imaging procedures, or endoscopic examinations.

2. Acute severe UC (admission):

- Short term: Clinical improvement without clinical response.
- Medium term: Clinical response.
- Long term: Improvement without achieving clinical remission, with persistent inflammatory activity in biochemical parameters, imaging procedures, or endoscopic examinations.

3. Luminal CD:

- Short term: Clinical improvement without achieving clinical response.
- Medium term: Clinical improvement without achieving clinical remission, with persistent inflammatory activity in biochemical tests.
- Long term: Clinical improvement without achieving clinical remission,

with persistent inflammatory activity in biochemical parameters, imaging procedures, or endoscopic examinations.

4. CD with perianal involvement:

- Short/medium term: Clinical improvement in the perianal area without clinical response.
- Long term: Clinical response of the perianal disease, with persistent inflammatory activity in imaging procedures or drainage of external openings.

Conclusion: Broad consensus was achieved on partial response definitions for various patient profiles in IBD. These standardized criteria can guide healthcare professionals in decision-making and assessing therapeutic effectiveness, ultimately improving patient care and outcome assessment.

Disclosure: Eugenia Vispo, Beatriz Garcillán and Elia Moreno work for the Medical Affairs Department of Johnson & Johnson.

MP217

CLINICAL VALIDATION OF A NOVEL SOFTWARE TOOL TO GUIDE THE INTRAVENOUS-TO-SUBCUTANEOUS SWITCHING OF INFLIXIMAB IN INFLAMMATORY BOWEL DISEASES

Y. Hoffer¹, Z. Wang¹, M. Fumery², M. Nachury³, M. Bazoge⁴, A. Buisson⁴, E. Dreesen¹

¹KU Leuven, Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium, ²Amiens University Hospital, Gastroenterology department, Amiens, France, ³CHRU Lille, Gastroenterology, Courbevoie Cedex, France, ⁴Université Clermont Auvergne, 3iHP, CHU Clermont-Ferrand, Service d'Hépatogastroentérologie, Clermont-Ferrand, France

Contact E-Mail Address: yannick.hoffert@kuleuven.be

Introduction: Therapeutic drug monitoring (TDM) of intravenous (IV) infliximab is increasingly practiced to improve therapeutic outcomes of patients with inflammatory bowel diseases (IBD). Recently, a subcutaneous (SC) formulation of infliximab was approved for maintenance treatment of IBD [1]. In the present work, we introduce a software tool to guide infliximab dosing by predicting infliximab concentrations after switching to the SC formulation.

Aims & Methods: The infliximab population pharmacokinetics (popPK) model was previously developed using data from pivotal trials [2]. The popPK model code was reconstructed using R (v4.3.0). A software tool was developed using the *Shiny* package (v1.7.4). Bayesian forecasting was implemented using *mapbayr* (v0.10.0), which was used to estimate individual PK parameters through maximum a posteriori estimation.

External validation data were obtained from the prospective, multicenter REMSWITCH trial [3]. For each patient, a pre-switch infliximab trough concentration (TC) was used to predict a post-switch TC. Predicted and observed post-switch TCs were compared, and absolute and relative prediction errors (PE) were calculated. Prediction errors were compared between patients with and without relapse. Relapse was defined as an increase in fecal calprotectin ≥ 150 mg/g from baseline.

A simulation study was performed to demonstrate how the software tool can guide the IV-to-SC switch. Simulation conditions were:

- Dosing: 10 mg/kg IV every four weeks (q4w) to 240 mg SC every two weeks (q2w)
- Patient: 70 kg, no antibodies towards infliximab (ATI), no co-administration of methotrexate
- Pre-switch TC: 17.6 mg/L

Results: A total of 77 patients contributed one pre/post-switch TC pair each. Three patients had detectable ATI in the pre-switch sample. Three other patients were cotreated with methotrexate.

Predicted infliximab TCs were unbiased in the absence of relapse (Table 1). However, the model tended to overpredict infliximab TC in patients who experienced a relapse.

	No relapse (N=60)		Relapse (N=17)	
	Median	[IQR]	Median	[IQR]
aPE (mg/L)	-0.06	[-2.4-3.3]	+3.8	[-1.0-5.7]
rPE (%)	-0.6	[-20.1-30.2]	+34.3	[-10.0-67.1]

Table 1. Predictive performance of the model.
Abbreviations: aPE, absolute prediction error (calculated as; predicted - observed); IQR, interquartile range; N, number of patients; rPE, relative prediction error (calculated as; [predicted - observed] / observed * 100%).

In the IV-to-SC simulation case, individual PK parameters (clearance 0.44 L/day, central volume of distribution 2.9 L, peripheral volume of distribution 27.0 L, and intercompartmental clearance 13.0 L/day) resulted in a post-switch TC of 18.6 mg/L right before the third SC injection. The simulation thus predicted no drop in TC after switching, thus presenting a likely safe switch strategy (considering the general belief that TCs drive efficacy).

Conclusion: The clinically validated, in-house developed software tool (<https://lpmx.shinyapps.io/infliximab/>) allows interactive simulations and personalized predictions to guide infliximab dosing while switching formulations. Predictions for patients without relapse were unbiased yet precision is likely compromised by variable SC bioavailability or possibly by time-varying PK. Overprediction of TC is likely driven by increased disease activity, characterized by an increased infliximab clearance and thus lower-than-expected infliximab observations, serving as a clinical alarm signal and warranting closer monitoring [4,5].

References: [1] S. Schreiber *et al.*, “Randomized Controlled Trial: Subcutaneous vs Intravenous Infliximab CT-P13 Maintenance in Inflammatory Bowel Disease,” *Gastroenterology*, vol. 160, no. 7, pp. 2340–2353, Jun. 2021, doi: 10.1053/j.gastro.2021.02.068.

[2] “Remsima European Public Assessment Report.pdf.”

[3] A. Buisson *et al.*, “Effectiveness of switching from intravenous to subcutaneous infliximab in patients with inflammatory bowel diseases: the REMSWITCH study,” *Clin Gastroenterol Hepatol*, vol. 21, no. 9, pp. 2338–2346.e3, 2023, doi: 10.1016/j.cgh.2022.08.011.

[4] W. Kantasiripitak, Z. Wang, I. Spriet, M. Ferrante, and E. Dreesen, “Recent advances in clearance monitoring of monoclonal antibodies in patients with inflammatory bowel diseases,” *Expert Review of Clinical Pharmacology*, vol. 14, no. 12, pp. 1455–1466, Dec. 2021, doi: 10.1080/17512433.2021.2028619.

[5] J. F. Brandse *et al.*, “Loss of Infliximab Into Feces Is Associated With Lack of Response to Therapy in Patients With Severe Ulcerative Colitis,” *Gastroenterology*, vol. 149, no. 2, pp. 350–355.e2, Aug. 2015, doi: 10.1053/j.gastro.2015.04.016.

Disclosure: YH and ZW are supported by a research grant by Research Foundation Flanders–FWO (1SHAA24N, 1SF2922N). MF has received consulting/lecture fees from AbbVie, Amgen, Arena, Biogen, Celltrion Healthcare, CTMA, Galapagos, Janssen, MSD, Pfizer, Takeda, Tillotts. MSD, Gilead, Celgene, Sandoz, and Ferring. MN has received board membership, consultancy, or lecture fees from AbbVie, Adacety, Amgen, Arena, Biogen, CTMA, Celltrion Healthcare, Ferring, Fresenius-Kabi, Janssen, Mayoli-Spindler, MSD, Pfizer, and Takeda. AB has received consulting fees from AbbVie, Amgen, Arena, Biogen, Celltrion Healthcare, CTMA, Galapagos, Janssen, MSD, Nexbiome, Pfizer, Roche, Takeda, and Tillotts; and lecture fees from AbbVie, Amgen, Biogen, Galapagos, Janssen, Mayoli-Spindler, MSD, Norgine, Pfizer, Roche, Takeda, Tillotts, and Vifor Pharma. ED has received consultancy fees from Alimentiv and argenx, lecture fees from Galapagos and Celltrion, and financial support from Janssen, Prometheus, and Sandoz. The remaining authors disclose no conflicts.

Leaving CRC behind: Improving endoscopy and surgery

10:00-11:00 / Poster Stage 2

MP218

LONG-TERM ONCOLOGICAL OUTCOME OF COLONIC STENTING AS BRIDGE-TO-SURGERY IN MALIGNANT LARGE BOWEL OBSTRUCTION

L.Y.E. Chen¹, J.M.S. Lim², B.E.A. Kwek², L.M. Wang³, J.W. Li², W.C.K. Lin², T.L. Ang²

¹Changi General Hospital / Singhealth, Gastroenterology and Hepatology, Singapore, Singapore, ²Changi General Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ³Changi General Hospital, SingHealth, Department Of Laboratory Medicine, Pathology Section, Singapore, Singapore

Contact E-Mail Address: elizabeth.chen@mohh.com.sg

Introduction: The use of self-expandable metal stents (SEMS) as a bridge-to-surgery (BTS) for acute malignant large bowel obstruction has seen an increase in recent years, with high rates of technical and clinical success¹. However, the long-term oncological prognostic impact of colonic stenting has received mixed reviews in the literature, with concerns about lympho-vascular and perineural invasion at the tumour site, which could potentially lead to increased risk of metastatic recurrence and poorer long-term oncological outcomes.

Aims & Methods: We examined the risk of metastatic disease occurrence in a single tertiary centre in Singapore by performing an audit on outcomes over a 10-year period following SEMS insertion as BTS. Data of patients who underwent SEMS insertion for malignant bowel obstruction (MBO) between September 2013 – December 2023 were retrospectively reviewed. The occurrence of metastases on computed tomography (CT) scan was documented and the time to disease occurrence noted. Overall survival, metastases-free survival and occurrence of metastatic disease were analysed using Kaplan-Meier estimates.

Potential factors associated with metastatic occurrence, namely American Joint Committee on Cancer (AJCC) staging and completion of adjuvant chemotherapy, were analysed using Fisher’s exact test and Kaplan-Meier estimator respectively.

Results: A total of 132 patients underwent SEMS placement from September 2013 to December 2023 for MBO. We excluded 31 patients who had metastatic disease at diagnosis or who underwent colonic stenting for palliative decompression, and five who were lost to follow up. Of the 96 remaining patients who underwent colonic stenting as BTS, the mean age was 68.4 years and 47 (49.0%) were male. The median length of follow-up was 32 months.

Overall survival and disease-free survival were 90.9% and 66.2% respectively. Mean overall survival time was 86.8 months (95% CI [75.1-98.6]), mean metastases-free survival was 95.6 months (95% CI [88.7-102.5]). 24 patients (31%) developed distant metastases during the follow-up period. Median time to metastases was 14.1 months. Of these 24 patients, 20 (83.3%) were AJCC stage 3, and four patients (16.7%) were AJCC stage 2. In addition, 11 patients (45.8%) completed adjuvant chemotherapy; 13 patients (54.1%) declined adjuvant chemotherapy or had attenuated doses. Using Kaplan-Meier estimates, overall survival and occurrence of metastases were not found to be significantly associated with completion of adjuvant chemotherapy (P values of 0.056 and 0.114 respectively). Keeping in mind the relatively small sample size, these results need to be interpreted with caution. A positive association was found with higher AJCC staging and occurrence of metastases using Fisher analysis, with a P value of 0.037.

Conclusion: The rate of occurrence of distant metastases was similar to prior reported literature. The majority of patients who developed metastatic occurrence were AJCC stage 3 who declined or had attenuated adju-

vant chemotherapy. The data suggests that colonic stenting as BTS does not worsen long-term oncological outcome. Disease recurrence was related to disease stage and lack of effective adjuvant chemotherapy.

References: 1. Li, James Weiquan FRCPed, FAMS1; Ngu, James Chi-Yong FRCS, MBBS2; Lim, Kok Ren FRCS, MBBS2; Tay, Shu Wen MRCP, MBBS1; Jiang, Bochao MRCP, MBBS1; Wijaya, Ramesh FRCS, MBBS2; Yusof, Sulaiman FRCS, MBBS2; Ong, Calvin Jianming FRCS, MBBS2; Kwek, Andrew Boon Eu MRCP, MBBS1; Ang, Tiing Leong FRCPed, FAMS1. Colonic stenting in acute malignant large bowel obstruction: audit of efficacy and safety in a Singapore tertiary referral centre. *Singapore Medical Journal* 64(10):p 603-608, October 2023. | DOI: 10.11622/smedj.2021127

Disclosure: None.

MP219

NON-RESTORATIVE LOW ANTERIOR RESECTION IS ASSOCIATED WITH WORSENEO ONCOLOGICAL OUTCOMES AND SURVIVAL IN RECTAL CANCER PATIENTS UNDERGOING TOTAL MESORECTAL EXCISION

R.T. Geitenbeek^{1,2}, M. Broekman¹, M. Friebe³, T.A. Burghgraef^{1,2}, E.C. Consten^{1,2}, R. Hompes⁴

¹University Medical Center Groningen, Department of Surgery, Groningen, Netherlands, ²Meander Medical Center, Department of Surgery, Amersfoort, Netherlands, ³University Hospital of Heidelberg, Department of Surgery, Heidelberg, Germany, ⁴Amsterdam UMC, Department of GI Surgery, Amsterdam, Netherlands

Contact E-Mail Address: maikiefriebe@gmail.com

Introduction: The type of rectal cancer resection may impact oncological outcomes following total mesorectal excision. Non-restorative low anterior resection (NRLAR) may be performed in cases where anticipated functional outcomes are poor or technical challenges hinder anastomosis creation. Existing literature suggests that NRLAR may achieve inferior oncological outcomes compared to restorative low anterior resection (RLAR) and abdominoperineal resection (APR). Therefore, this study compared oncological and survival outcomes between NRLAR, RLAR, and APR at three years postoperatively.

Aims & Methods: This retrospective cohort study encompasses all elective NRLAR, RLAR, and APR procedures performed for non-metastatic primary rectal carcinoma across 11 Dutch centers between 2013 and 2020. The primary outcome measured was 3-year disease-free survival (DFS), while secondary outcomes included 3-year overall survival (OS) and local recurrence (LR). Data analysis employed Kaplan-Meier survival analysis, and results were juxtaposed using log-rank testing. The association between resection type (NRLAR, RLAR, and APR) was further explored using multivariate Cox regression analysis.

Results: A total of 2069 patients were analysed, with 258 (12.5%) undergoing NRLAR, 1153 (55.7%) RLAR, and 658 (31.8%) APR. NRLAR demonstrated a lower three-year DFS at 70.8%, compared to RLAR (82.3%) and APR (77.5%) ($p < 0.001$). Similarly, three-year OS and LR were inferior for NRLAR (82.4%) in contrast to RLAR (93.5%) and APR (90.2%) ($p < 0.001$), and 7.9% (NRLAR) versus 3.2% (RLAR) and 4.5% (APR) ($p = 0.003$), respectively. Multivariate Cox regression analysis revealed NRLAR to be independently associated with worse DFS (HR 1.353; 95% CI: 1.061 – 1.803; $p = 0.039$), OS (HR 1.594; 95% CI: 1.065 – 2.386, $p = 0.023$), and a higher LR risk (HR 2.879; 95% CI: 1.667 – 4.975; $p = < 0.001$).

Conclusion: NRLAR is independently correlated with unfavourable oncological and survival outcomes when compared to RLAR and APR.

Disclosure: R. T. J. Geitenbeek: None Declared, M. Broekman: None Declared, T. A. Burghgraef: None Declared, E. C. Consten Paid Instructor with: Proctor for Intuitive, R. Hompes: None Declared.

MP220

THE RELATION BETWEEN POSTOPERATIVE COMPLICATIONS AFTER PRIMARY COLON CANCER SURGERY AND LONG-TERM OUTCOMES

E. Rademaker^{1,2}, B.C. Aktas², E.C.J. Consten^{3,4}, P.J. Tanis², H.L. Van Westreenen¹, Dutch Complex Cancer Initiative and Dutch Snapshot Research Group

¹Isala, Surgery, Zwolle, Netherlands, ²Erasmus MC, Surgery, Rotterdam, Netherlands, ³Meander MC, Surgery, Amersfoort, Netherlands, ⁴UMCG, Surgery, Groningen, Netherlands

Contact E-Mail Address: e.rademaker@erasmusmc.nl

Introduction: It is widely acknowledged that postoperative complications after colon cancer resection are associated with postoperative mortality, but the association with long-term outcomes is controversial. This study examined the impact of postoperative complications on locoregional recurrence, defined as any intra-abdominal recurrence including peritoneal metastases, and overall survival.

Aims & Methods: This national, population-based cross-sectional cohort study was carried out in 46 Dutch hospitals. Patients who underwent colon cancer resection between January 2014 and December 2015 were eligible. Long-term outcomes were assessed in patients without synchronous metastases and a minimum follow-up of 6 months using logistic regression, Kaplan-Meier, log-rank test, and Cox regression analyses.

Results: A total of 8936 patients were included with a median follow-up of 59.6 months (IQR 28.0-65.6). Any complication occurred in 2649 (29.6%) patients, of whom 1576 had surgical complications (806 requiring re-intervention) and 1791 non-surgical complications. When looking into patients with stage 1 to 3 colon cancer with a minimum follow-up time of 6 months, 7.5% of the cohort without any complication versus 9.2% with a complication develop a locoregional recurrence ($p=0.023$). Independent risk factors for locoregional recurrence were surgical approach, emergency setting, tumour location, pT, pN and resection margin status. Five-year overall survival probability was 86.7% versus 76.1% for patients with or without complications respectively ($p<0.001$), which remained significant in multivariable analysis (HR 1.43, 95CI% 1.29-1.59).

Conclusion: This study showed worse overall survival after a complicated postoperative course in stage I-III colon cancer patients, but no independent association with locoregional recurrence was found.

Disclosure: Nothing to disclose.

MP221

HISTOPATHOLOGICAL R0 RESECTION IS AN UNRELIABLE PERFORMANCE INDICATOR FOR QUALITY OF EN BLOC RESECTION IN COLORECTAL ENDOSCOPIC RESECTION

A. Egbal¹, M.-A. Noreillie¹, O. Olabintan¹, H. Ayubi¹, J. Bhoday², M. Anand¹, A. Adeyeye², H. Rashid², S. Thrumurthy³, S. Gulati⁴, B. Hayee¹, A. Emmanuel⁵, A. Haji⁶

¹Kings College Hospital, Gastroenterology, London, United Kingdom, ²Kings College Hospital, Colorectal surgery, London, United Kingdom, ³Kings College Hospital, Upper gastrointestinal surgery, London, United Kingdom, ⁴King's College Hospital, Gastroenterology, London, United Kingdom, ⁵King's College Hospital, Colorectal Surgery, London, United Kingdom, ⁶Kings College Hospital, Colorectal Surgery, London, United Kingdom

Contact E-Mail Address: ali.egbal@nhs.net

Introduction: Endoscopic submucosal dissection (ESD) is increasingly employed for colorectal endoscopic resection (ER) in specialist units around the world. Abundant Japanese series and more recent western

series report the outcomes of ESD, invariably reporting en bloc resection and R0 resection rates as a quality reporting measure. Whilst en bloc resection is well established to result in very low levels of recurrent/residual adenoma, evidence for recommending R0 resection is lacking. Furthermore, determining R0 status is subject to variations in specimen processing and histopathological examination.

Aims & Methods: We aimed to determine the significance of histopathological R0 resection on residual/recurrent adenoma at 6 month surveillance. Patients with LNCP treated by ESD with en bloc resection at a tertiary referral centre between September 2011 and September 2023 and who had completed the first surveillance at 6 months (SC1) were included. During surveillance the scar from ER was identified and examined with magnification chromoendoscopy and NBI/BLI. Only abnormal scars were biopsy sampled.

The incidence of recurrent/residual adenoma at 6 months in patients who had confirmed histopathological R0 resection was compared with patients who did not have confirmed R0 resection.

Results: 1400 LNCP underwent an initial successful ER over the study period, 665 by ESD and 735 by EMR/pEMR. 796 LNCP were resected en bloc and were included for analysis. Of these, Histopathological R0 resection was confirmed in 690 (86.9%). The mean lesion size was 44.5mm +/-25.6 mm (median 38.5mm, range 20mm-210mm). 518 patients had undergone SC1. Only 4 patients had residual/recurrent adenoma (0.77%). Only 1 patient who did not have confirmed R0 resection experienced recurrence and there was no association between confirmed R0 resection and recurrence (OR 0.41, 95% CI 0.04-4.02, p=0.41).

Conclusion: Histopathological R0 resection has no impact on outcome. In the colorectum, the margins of LNCP are readily apparent and complete resection is straightforward to confirm during ESD. Therefore, if high quality ESD is performed by experienced practitioners, in many cases lack of confirmation of R0 resection is likely to be a result of the difficulties in histopathological interpretation of often very large specimens. Recurrent/residual adenoma rates at surveillance would be a better quality metric for ESD along with en bloc resection rate.

Disclosure: Nothing to disclose.

MP222

LONG-TERM ONCOLOGICAL OUTCOMES AND PATTERNS OF DISTANT METASTASIS IN T1 VERSUS T2 COLON CANCER

J. Hanevelt¹, E. Rademaker², B. Zamaray², R.M. Brohet³, L.M. Moons⁴, F.P. Vleggaar⁴, B.C. van de Laar⁵, E.C. Consten^{5,6}, P.J. Tanis⁷, W.H. de Vos Tot Nederveen Cappel¹, H.L. van Westreenen², on behalf of the Dutch Snapshot Research Group (DSRG), Dutch Complex Colon Cancer Initiative (DCCCI)
¹Isala, Department of Gastroenterology and Hepatology, Zwolle, Netherlands, ²Isala, Department of Surgery, Zwolle, Netherlands, ³Isala, Department of Epidemiology & Statistics, Zwolle, Netherlands, ⁴University Medical Center Utrecht, Department of Gastroenterology & Hepatology, Utrecht, Netherlands, ⁵Meander Medisch Centrum, Department of Surgery, Amersfoort, Netherlands, ⁶University Medical Center Groningen (UMCG), Department of Surgery, Groningen, Netherlands, ⁷Erasmus MC, Department of Surgical Oncology and Gastrointestinal Surgery, Rotterdam, Netherlands

Contact E-Mail Address: j.hanevelt@isala.nl

Introduction: Organ preservation using local resection techniques for early colon cancer (CC) is receiving increasing attention. However, there is a significant difference in the primary treatment approach between pT1 and pT2 CC.

Aims & Methods: The objective of this study was to assess whether the depth of tumor invasion (T-stage) correlates with the survival and recurrence rates among patients who underwent surgical treatment for T1 and T2 CC. A multicenter retrospective cohort study was conducted, including patients who underwent curative surgery for T1 or T2 CC between 2014 and 2015. Patients in this cohort were originally identified through the Dutch ColoRectal Audit (DCRA), a prospective national registry of all patients undergoing surgery for primary colorectal cancer. Long-term oncological follow-up data from the original patient records were added to the DCRA data by surgical residents affiliated with the DSRG from 61 participating hospitals. The primary outcome measures were 5-year overall and distant metastasis-free survival (OS/MFS). Survival outcomes were compared with the Kaplan-Meier method and log-rank test. Cox proportional hazard models were used to analyze risk factors associated with these outcomes.

Results: In total, 928 patients with pT1 CC and 1349 patients with pT2 CC were included. Lymph node metastases (LNMs) were identified in the resection specimen in 118 (12.7%) out of 928 patients in the pT1 cohort and in 252 (18.7%) out of 1349 patients in the pT2 cohort. Locoregional recurrences occurred in 3 (0.3%) of patients in the pT1 cohort and 20 (1.5%) of patients in the pT2 cohort (P = 0.07). Distant metastases were observed in 30 (3.2%) out of 928 pT1 patients and in 66 (4.9%) out of 1349 pT2 patients (P = 0.05). Most patients who developed distant metastases during follow-up initially had no LNMs and were therefore staged as N0. Specifically, in the pT1 cohort, 20 out of 30 patients (66.6%) with distant metastases were initially staged as pT1N0, while in the pT2 cohort, 38 out of 66 patients (57.6%) were staged as pT2N0. The 5-year OS did not differ between the pT1N0 and pT2N0 patients (85.2% vs. 86.9%, p = 0.49, multivariable HR for pT2 adjusted for age, gender, ASA score and tumor location; 0.8, 95% CI 0.57 - 1.009), and neither did the 5-year MFS (96.0% vs. 95.9%, p = 0.65, multivariable HR 1.2, 95% CI 0.7 - 2.0). For patients with pT1N+ and pT2N+ stage, 5-year OS was 83.5% vs. 81.6% (p = 0.59, multivariable HR adjusted for administration of adjuvant chemotherapy of 1.0, 95% CI 0.6 - 1.8) and MFS was 90.9% vs. 87.1% (p = 0.43, multivariable HR adjusted for pN-stage and administration of adjuvant chemotherapy of 0.8, 95% CI 0.6 - 1.2).

	T1 N0 n = 810	T2 N0 n = 1097	p value	T1 N+ n = 118	T2 N+ n = 252	p value
Recurrent disease, n (%)	22 (2.7)	43 (3.9)	0.15	11 (9.3)	34 (13.5)	0.25
Loco regional recurrence only	2 (0.2)	5 (0.5)		1 (0.8)	5 (2)	
Distant metastases only	19 (2.3)	34 (3.1)		8 (6.8)	24 (9.5)	
Loco regional recurrence + distant metastases	1 (0.1)	4 (0.4)		2 (1.7)	5 (2)	
5-Year Overall Survival	85.2%	86.4%	0.49	83.5%	81.6%	0.59
5-Year Metastasis free survival	96.0%	95.9%	0.65	90.9%	87.1%	0.43

Conclusion: In early colon cancer, the depth of tumor invasion (pT1 or pT2) does not significantly affect the patient's metastasis-free or overall survival after oncological resection. In both cohorts (pT1 and pT2), the majority of distant metastases arise in patients without LNMs at the initial time of surgery (N0). Therefore, it could be questioned whether segmental colon resection with lymph node dissection is of oncological and clinical benefit in all cases.

Disclosure: Nothing to disclose.

MP223

IMMUNOREACT 15: IMMUNE PREDICTORS OF RELAPSE AFTER ADJUVANT THERAPY IN RECTAL CANCER PATIENTS

A. Stepanyan¹, M. Scarpa², A. Kotsafti², F. Scognamiglio¹, D. Gregori¹, V. Pellegrini¹, R. Salmaso¹, O. De Simoni², G. Becherucci¹, S. Negro¹, C. Vignotto¹, G. Spolverato¹, C. Ruffolo¹, I. Angriman¹, F. Bergamo², V. Chiminazzo¹, I. Maretto¹, B. Salmaso¹, M. Zizzo³, F. Marchegiani¹, L. Facci¹, S. Brignola⁴, G. Businello⁵, L. Licia⁴, V. Guzzardo¹, L. Dal Santo¹, C. Carlotta¹, M. Massani⁶, A. Pozza⁶, I. Cataldo⁶, T. Stecca⁶, A.P. Dei Tos¹, V. Zagone², P. Pilati², B. Franzato², A. Scapinello², G. Pozza⁴, M. Godina⁴, G. Pirozzolo⁴, A. Recordare⁴, I. Mondì⁴, C. Da Lio⁴, R. Merenda⁴, G. Bordignon⁴, D. Verdi⁴, L. Saadeh¹, S. Guerriero⁷, C. Romiti⁷, A. Piccoli⁷, M. Scarpa¹, IMMUNOREACT Study Group
¹Azienda Ospedaliera Universitaria di Padova, Padova, Italy, ²Veneto Institute of Oncology IOV-IRCCS, Padova, Italy, ³Arcispedale Santa Maria Nuova di Reggio Emilia, Emilia-Romagna, Italy, ⁴Azienda ULSS 3 Serenissima, Venezia, Italy, ⁵Azienda ULSS 5 Polesana, Rovigo, Italy, ⁶Azienda ULSS 2 Marca Trevigiana, Treviso, Italy, ⁷Ospedale di Fermo, ASUR 4, Fermo, Italy

Contact E-Mail Address: stepanyan.astgh@gmail.com
Introduction: It has been suggested that the development of cancer chemotherapy resistance may result from the intricate interplay between gene regulation and external environmental factors. Immune biomarkers hold promise as prognostic indicators for the efficacy of chemoradiotherapy; nevertheless, to date, none have been successfully achieved in routine clinical practice.
Aims & Methods: This study is a sub-analysis of data from the prospective IMMUNOREACT 2 trial (NCT04917263) including all the patients who underwent adjuvant therapy. Healthy rectal mucosa adjacent to the cancer was collected during surgery. Gene expression profiling was performed with Nanostring technology using nCounter® PanCancer IO 360™ Panel. Prospectively collected rectal mucosa samples were subjected to flow cytometry to determine the proportion of epithelial cells (Cyt-20+) acting as antigen-presenting cells (expressing CD80, CD86, HLAABC), activated T cells (expressing CD25, CD28, CD38), regulatory T cells (CD4+CD25+FoxP3+) or exhausted T cells (CTLA-4+). Non-parametric tests were used for small sample size comparisons. This study aims to evaluate immune biomarkers' role in determining adjuvant therapy's effectiveness in rectal cancer (RC) patients.
Results: A total of 31 patients with RC who underwent adjuvant therapy included in the prospective IMMUNOREACT 2 cohort were analyzed; during a median follow-up time of 20.8 months, 7 patients experienced relapse. Preliminary gene expression analysis on 19 specimens revealed 25 differentially expressed genes between patients who relapsed (n=3) and those who did not (n=16) (Fig. 1 A, B). In particular, in the normal rectal mucosa of patients who relapsed, downregulation of genes associated with macrophages (CD163, CEBPB, MARCO, MS4A2, MS4A4A, MS4A6A, SIGLEC1), inflammation (CCL8, C5, C5AR1, IL11RA, TIE1) and lymphocytes stimulation (VTCN1, TNFSF13B) was observed. Relapse was associated with a high CD8+ CD28+ cytotoxic lymphocytes mean fluorescence intensity (MFI) (p= 0.05). The accuracy of predicting relapse was AUC=0.765 for CD8+CD28+ MFI (Fig. 2 A, B).
Conclusion: Our preliminary data suggest that the immune-related markers signature in the healthy peritumoral mucosa might be useful for predicting relapse after adjuvant therapy in rectal cancer patients. Moreover, relapsing patients showed lower stimulation of macrophages and lymphocytes, thus suggesting that impaired immune surveillance might influence adjuvant therapy outcomes. Sampling healthy mucosa might help the decision-making about adjuvant therapy after surgery for rectal cancer.
Disclosure: Nothing to disclose.

MP224

COMPARISON OF THE PROGNOSIS AND LYMPH NODE METASTASIS BETWEEN “NO TUMOR BUDDING” AND “LOW-GRADE TUMOR BUDDING” IN T1 AND T2 COLORECTAL CANCER

J.Y. Lee¹
¹Dong-A university, Gastroenterology, Busan, Republic of Korea, South Korea

Contact E-Mail Address: ljyhateo@gmail.com
Introduction: Tumor budding is a significant prognostic value in the management of colorectal cancer (CRC). There are grades of tumor budding: 0-4 buds as low, 5-9 buds as intermediate, and more than 10 buds as high. However, the specific prognosis difference between cases with 0 buds and those with 1-4 buds, is not well-established due to a lack of comparative studies.
Aims & Methods: The aim of this study is to examine and compare the rate of lymph node (LN) metastasis and prognosis by distinguishing between 0 buds and 1-4 buds within the low-grade category (0-4 buds) of tumor budding in T1 and T2 CRC. This study retrospectively identified a total of 224 cases of T1 and T2 CRC from 2015 to 2018 across three medical institutions using medical records. The pathology, including the assessment of tumor budding, was subsequently reconfirmed, and the recurrence and survival of patients were evaluated up to December 2023.
Results: Patients in the BD1 group exhibited a higher T stage compared to BD0, accompanied by significantly increased rates of lymphovascular invasion and perineural invasion. The prevalence of LN metastasis was 14.8%. No significant difference in LN metastasis was observed between BD0 and BD1. In a multivariate analysis exploring factors associated with LN metastasis, relevant factors included lymphatic invasion, perineural invasion, and 5 buds or more. (Table 1) There were no significant distinctions in 5-year survival and progression free survival rate between the BD0 and BD1 groups (P=0.971).

	Univariate analysis		Multivariate analysis	
	OR	P-value	OR	P-value
Lymphatic		0.000		0.025
Lv 0: Lv 1	1:10.557 (4.188-26.712)		1:3.843 (1.181-12.510)	
Perineural		0.000		0.000
Pn 0: Pn 1	1:31.167(8.073-120.328)		1: 35.774 (6.655-192.317)	
Tumor budding		0.000		0.000
BD 0	1	0.232	1	0.799
BD 1	2.226 (0.592-8.675)	0.000	0.817 (0.173-2.471)	0.001
BD 2,3	19.880 (5.457-72.418)		9.794 (2.471-38.815)	

Table 1. Univariate and multivariate analysis for risk factor of lymph node metastasis.

Conclusion: The study confirmed that there was no significant difference in LN metastasis and prognosis between BD0 and BD1.
References: 1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA: A Cancer Journal for Clinicians* 2023;73(1):17-48.
2. Lugli A, Kirsch R, Ajioka Y, Bosman F, Cathomas G, Dawson H, et al. Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016. *Mod Pathol* 2017;30(9):1299-311.
Disclosure: Nothing to disclose.

MP225

EFFICACY AND SAFETY OF PREOPERATIVE INTRAVENOUS IRON VERSUS STANDARD CARE IN COLORECTAL CANCER PATIENTS WITH IRON DEFICIENCY ANEMIA - SYSTEMATIC REVIEW AND META-ANALYSIS

B. Al-Quraishi¹, P. Sydhom¹, M. Shaaban Abdelgalil¹, N. Shehata¹, M. El-Shawaf¹, N. Naji¹, N. Awwad¹, M. Tarek Osman¹, A. Mahmoud¹, A. K. Awad¹

¹Ain Shams University, Cairo, Egypt

Contact E-Mail Address: pishoysydhom@gmail.com

Introduction: Colorectal cancer (CRC) patients commonly encounter anemia, with estimates indicating that up to 58% are affected and iron deficiency (ID) anemia being the most prevalent. This study aimed to compare the efficacy and safety of preoperative intravenous iron (IVI) with standard care (no iron or oral iron) in CRC patients with ID anemia.

Aims & Methods: We conducted a systematic search of the Cochrane Library, PubMed, Scopus, and Web of Science databases from inception to September 20, 2023, to identify studies comparing intravenous iron (IVI) versus standard care in colorectal cancer (CRC) patients with iron deficiency anemia. Pooled results were analyzed for changes in hemoglobin (Hb) levels from baseline, need for red blood cell (RBC) transfusions, mean number of RBC units transfused, overall survival (OS), disease-free survival (DFS), and complications. We evaluated randomized clinical trials using the Cochrane Risk of Bias 2 tool and observational studies using the Newcastle Ottawa Scale. Statistical analysis was performed using Revman software Version 5.4.1.

Results: We analyzed data from 11 studies, encompassing 2,024 patients, and found that IVI significantly increased Hb levels at various crucial time points: preoperative (MD=1.17, CI 95% [0.95, 1.40], P<0.01), postoperative day one (MD=1.32, CI 95% [0.89, 1.76], P<0.01), hospital discharge (MD=0.76, CI 95% [0.28, 1.24], P=0.002), and 30 days postoperative (MD=1.57, CI 95% [1.27, 1.87], P<0.01). The overall need for RBCT significantly decreased with IVI (RR=0.39, CI 95% [0.27, 0.56], P<0.01), particularly in the postoperative period (RR=0.69, CI 95% [0.52, 0.92], P=0.01). No significant differences were found between preoperative and intraoperative periods. IVI notably reduced transfused red blood cell units, total complications, and wound dehiscence. However, there were no significant differences in total death, hospital stay, OS and DFS.

Conclusion: Preoperative IVI significantly increased Hb levels at critical time points and markedly reduced the overall need for RBCT, complications, and wound dehiscence. To further validate these findings, more well-designed randomized controlled trials are warranted.

Disclosure: Nothing to disclose.

MP226

EVALUATING THE INCREMENTAL PREDICTIVE VALUE OF THREE FECAL HEMOGLOBIN CONCENTRATIONS COMPARED TO TWO FOR FUTURE PREDICTION OF COLORECTAL CANCER

L. Mwangi¹, A. Katsara¹, I. Lansdorp-Vogelaar¹

¹Erasmus MC University Medical Center, Public Health, Rotterdam, Netherlands

Contact E-Mail Address: l.mwangi@erasmusmc.nl

Introduction: The fecal immunochemical test (FIT), utilized for fecal hemoglobin (f-HB) detection in stool, stands as a recommended screening approach for colorectal cancer (CRC) (1). Prior research has shown the predictive ability of f-HB concentration over two previous screening rounds in predicting future risk of CRC (2). However, there remains a gap in literature on the additional benefit of incorporating more than two f-HB concentrations.

Aims & Methods: In this study, we aim to assess the added prognostic value of using three preceding rounds of f-HB concentrations compared to using two rounds in risk prediction of Advanced Neoplasia (AN) and CRC. In our analysis, we utilize data from the fourth round of the Dutch CRC screening program. We first develop a prognostic model for detecting AN and CRC, incorporating participants age, sex, and f-HB concentrations from rounds 1, 2, and 3 as predictor variables. Similarly, we develop a separate model using only f-HB concentrations from rounds 2 and 3, along with sex and age as predictors. Model performance is assessed using receiver operating curve (AUC) and visual calibration inspection. We further report on the net classification improvement (NRI) and integrated discrimination improvement (IDI) to quantify how the models with 3 rounds of f-HB levels enhance the reclassification of participants with and without AN or CRC. Positive values of both NRI and IDI with a p-value of <0.005 indicate a significant improvement in classification of participants.

Results: Among study participants, 56959 (4.7%) had a positive FIT result, 15170 (1.2%) had AN detected and 2465 (0.2%) had CRC. The model with three rounds of f-HB levels outperformed the model with two rounds in discriminating patients with AN and CRC. Specifically, AUCs for AN and CRC were 0.76 (95% CI, 0.75-0.77) and 0.73 (95% CI, 0.66-0.74) respectively for model with three rounds of f-HB levels. Both NRI and IDI were positive with p values of <0.005 indicating an improvement in classification of participants with and without AN and CRC when using three rounds of f-HB concentrations compared to using two rounds.

	Outcome	AUC model with age, sex f-HB levels 1, 2 & 3 rounds (95%CI)	AUC model with age, sex f-HB levels 2 & 3 rounds (95%CI)
Training data	AN	0.76 (0.75 - 0.77)	0.73(0.72- 0.74)
	CRC	0.73(0.70 - 0.74)	0.71 (0.69- 0.72)
Validation data	AN	0.76 (0.75 - 0.77)	0.73(0.72- 0.74)
	CRC	0.73 (0.66 - 0.74)	0.69 (0.66 - 0.71)

Table 1: Values for AUC for models with three and two rounds of f-HB levels with age and sex as predictor variables for risk of AN and CRC

Abbreviations: AUC, area under the curve; CI, confidence interval;

AN, advanced neoplasia; CRC, colorectal cancer; f-HB, Fecal Hemoglobin

Conclusion: Our findings suggest that the model integrating three f-HB levels surpasses the two-level model in discrimination and reclassification. Therefore, using more preceding rounds of f-HB concentrations could potentially enhance personalized screening of CRC within the Dutch screening program.

References: 1. Rex DK, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, Kaltenbach T, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol.* 2017;112(7):1016-30.

2. Meester RGS, van de Schootbrugge-Vandermeer HJ, Breekveldt ECH, de Jonge L, Toes-Zoutendijk E, Kooyker A, et al. Faecal occult blood loss accurately predicts future detection of colorectal cancer. A prognostic model. *Gut.* 2023;72(1):101-8.

Disclosure: All authors declare that they have no competing interests.

MP227

EFFICIENCY OF REAL-TIME COMPUTER-AIDED POLYP DETECTION IN SURVEILLANCE COLONOSCOPY: A PILOT STUDY

S. Morimoto¹, H. Tanaka¹, Y. Takehara¹, N. Yamamoto¹, F. Tanino¹, Y. Kamigaichi¹, A. Tsuboi¹, K. Yamashita¹, Y. Urabe¹, T. Kuwai¹, S. Oka¹

¹Hiroshima University Hospital, Department of Gastroenterology, Hiroshima, Japan

Contact E-Mail Address: smorimoto@hiroshima-u.ac.jp

Introduction: Computer-aided detection (CAdE) system increases the efficiency of adenoma detection during colonoscopy, which is expected to reduce the incidence of colorectal cancer as well as cancer treatment-associated medical costs. However, most lesions detected using CAdE have been reported to be diminutive adenomas that may not affect patient prognosis. Additionally, CAdE may impose an immediate economic burden because the system needs to be purchased. Consequently, the use of CAdE for all colonoscopy procedures seems impractical. This study aimed to evaluate the usefulness of CAdE in patients undergoing regular surveillance colonoscopy (SCS), to identify the characteristics of endoscopists and patients who may benefit significantly from CAdE.

Aims & Methods: Patients who underwent regular SCS with CAdE at Hiroshima University Hospital from January to March 2023 and had undergone colonoscopy at least twice in the previous three years using a conventional detection method were enrolled. Forty-eight endoscopists who had collectively performed ≥ 800 colonoscopies performed the examinations. Endoscopic resection was performed for lesions ≥ 6 mm in size, flat and depressed neoplastic lesions ≤ 5 mm in size, and lesions with suspected high-grade dysplasia or T1a carcinoma, according to Japanese guidelines. Diminutive polypoid adenomas ≤ 5 mm in size were followed up without resection. Lesions pathologically identified as adenomas > 6 mm or carcinomas were defined as index lesions (ILs). Lesions pathologically identified as adenomas ≥ 10 mm in size, tubulovillous adenomas, and high-grade dysplasia were defined as advanced adenomas (AAs). The clinicopathological findings of the lesions detected by CAdE were evaluated, and the outcomes were compared between the semi-clean colon (diminutive polypoid adenomas ≤ 5 mm in size followed up without resection) and clean colon (no adenomatous polyps) groups.

Results: Overall, 78 patients were included. CAdE identified 46 adenomas that were not detected by previous colonoscopy in 28 patients, including three ILs but no AAs. The mean withdrawal time was 824 ± 353 s, and the mean tumor diameter was 3.3 mm (range, 2–8 mm). The most common gross type was 0-Is (70%), followed by 0-Isp (17%) and 0-IIa (13%). Most tumors were located in the ascending and sigmoid colons (28%), followed by the transverse colon (26%), cecum (7%), descending colon (7%), and rectum (4%). The ILs were 0-Isp of 6 mm diameter in the ascending colon, 0-Is of 7 mm diameter in the transverse colon, and 0-Isp of 6 mm diameter in the descending colon, all of which were adenomas with lesions on the folds. Overall, 34.1% and 38.2% of the patients in the semi-clean and clean colon groups, respectively, had newly detected adenomas. No new neoplastic lesions were detected using CAdE in patients without a history of endoscopic resection. When comparing the clinical backgrounds of patients with and without new ILs detected in CAdE SCS, a significant difference was found in the IL detection rate at the previous SCS between the groups (67% vs. 12%, $p = 0.0319$).

Conclusion: CAdE may help detect adenoma in SCS for patients with semi-clean colons and those with clean colons and a history of endoscopic resection. Its effectiveness is considered more for patients with ILs at the previous SCS.

Disclosure: Nothing to disclose.

Epidemiology in MASLD

10:00-11:00 / Poster Stage 3

MP228

PREVALENCE AND RISK FACTORS OF METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE IN KOREAN AIR FORCE ARMY INCLUSIVE OF PILOTS: 2020-2022

D.H. Song¹, B. Ku²

¹Korean Air Force Aerospace medical center in South Korea, Department of Internal Medicine, Cheongju-si, South Korea, ²Korea Institute of Oriental Medicine, Daejeon-si, South Korea

Contact E-Mail Address: engus1026@gmail.com

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a disease that complements Nonalcoholic Fatty Liver Disease (NAFLD) and is newly defined in 2020. It is defined based on metabolic abnormalities, regardless of the presence of liver disease caused by other causes such as alcohol consumption. Regarding the newly defined MAFLD, there has not been many studies related to the prevalence and risk factors in Korea, and no studies were found targeting soldiers, especially pilots.

Aims & Methods: The purpose of this study is to identify prevalence and risk factors for MAFLD in Korean air force army inclusive of pilots. The subjects are 1044 soldiers who underwent health checkups in Korean Air Force Aerospace medical center from January 2020 to December 2022. The data was retrospectively collected including age, height, weight, body mass index, waist circumference, blood pressure, smoking, drinking, exercise intensity, various blood test results, presence of fatty liver, and degree of fatty liver. Risk factors were analyzed using logistic regression.

Results: There were 667 pilots (64%) in our study, of whom 477 (72%) were high-performing pilots. The prevalence of MAFLD was 316 (30%) in all soldier. There was difference in the prevalence of MAFLD between pilot and non-pilot group (pilot group: 185 (28%), non-pilot group: 131 (35%) p -value=0.018). According to the multivariate analysis, body mass index (BMI), diabetes, systolic blood pressure, triglycerides (TG), uric acid (UA), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), alanine aminotransferase (ALT) were a risk factor associated with MAFLD among the entire soldiers. When categorized into pilot and non-pilot group, risk factors were associated with BMI, diabetes, alcohol consumption, and ALT in the non-pilot group. In the pilot group, they were statistically associated with age, BMI, dyslipidemia, TG, UA, HDL and ALT. Among them, UA showed the largest difference between the non-pilot group and the test group (non-pilot group: 1.14 (95% CI: 0.80-1.62), pilot group: 1.80 (95% CI: 1.38-2.36)).

Conclusion: There was a difference in the prevalence of MAFLD between pilot and non-pilot group. In particular, UA could be used to predict MAFLD as a specific risk factor in pilots comparing with non-pilots.

Disclosure: Nothing to disclose.

MP229

LIVER STEATOSIS: A RISK FACTOR FOR THE DEVELOPMENT OF COLONIC ADENOMAS?

R. Abbas¹, E. Mikhael¹, M. Khanfour¹, S. Helou¹, L. Amer¹, K. Honein¹, R. Slim Karam¹, E. Mahfouz¹, J. Amara¹, C. Yaghi¹

¹Université Saint-Joseph, Beirut, Lebanon

Contact E-Mail Address: eliomikhael7@gmail.com

Introduction: Several studies have suggested a possible association between hepatic steatosis and colonic adenomas, positioning hepatic steatosis on the list of potential risk factors.

Aims & Methods: Our study aims to investigate the relationship between hepatic steatosis and the development of colonic adenomas. This is an observational study, with both a retrospective and a prospective arm, spanning from 2017 till 2023. Selected patients are those who underwent a Fibroscan and a colonoscopy during the same year. We collected demographic data, medical history, medication intake, and results of both Fibroscan and colonoscopy. Our population was divided in two: population A with a Controlled Attenuation Parameter (CAP)<258 and population B with a CAP³≥258. The main outcome was the presence of adenomas on colonoscopy.

Results: In total, our analysis included 232 patients. A ROC curve was obtained, determining that a CAP³≥258 was associated with the presence of adenomas on a colonoscopy with an AUC of 0.630 with a sensitivity and specificity of 65% and 64% respectively. From these 232, 125 patients had a CAP³≥258 (53.8%) and 107 patients had a CAP<258 (46.2%). Patients with a CAP³≥258 more frequently exhibited: hypertension (54% vs 35.7%, p=0.016), diabetes (36% vs 10.7%, p<0.001), and dyslipidemia (70.6% vs 29.8%, p<0.001) compared to those with a CAP<258. The BMI was higher (29.2 vs 26.7, p=0.001) in the group (CAP³≥258). Finally, adenomas were more frequent (46.4% vs 33.6%, p=0.025) in this same group.

A multivariate analysis was done. The presence of CAP³≥258 (OR 2.58, p=0.017), diabetes (OR=3.71, p=0.02), and older age (OR=1.04, p=0.017) are associated with the presence of adenomas on colonoscopy.

Conclusion: Hepatic steatosis is independently associated with the presence of adenomas with an OR of 2.58. Therefore, early screening for colorectal cancer might be warranted in patients with hepatic steatosis. Further studies are required to establish hepatic steatosis as a risk factor of colonic adenomas.

Disclosure: Nothing to disclose.

MP230

CLINICAL FEATURES AND STATE OF THE INTESTINAL MICROBIOTA IN CHILDREN WITH METABOLICALLY ASSOCIATED STEATOTIC LIVER DISEASE

N. Pavlenko¹, O. Babadzhanian¹, O. Belousova¹, O. Shutova², I. Solodovnichenko¹, L. Voloshyna¹, O. Hanzii¹

¹Kharkiv National Medical University, Kharkiv, Ukraine, ²Kharkov National Medical University, Department of Pediatrics No. 3 and Neonatology, Kharkov, Ukraine

Contact E-Mail Address: pavlenko.nat.v@gmail.com

Introduction: It is known that one of the markers of metabolically associated fatty liver disease is disruption of the intestinal microbiota and changes in intestinal permeability with the development of increased epithelial permeability syndrome. All this leads to the translocation of endotoxins, liposaccharides, harmful bacteria and reactive oxygen species from the intestinal lumen into the circulation, where they are absorbed by the liver, which can cause increased lipogenesis and inflammation, which in turn can provoke the development of MASLD and leads to its progression.

Aims & Methods: Aims: to study the features of clinical manifestations, physical development and disorders of the intestinal microbiota in children with MASLD.

Methods: 147 children with MASLD aged 6-18 years were observed. The diagnosis was verified based on the criteria of the EASL 2023 recommendations (markers of cholestasis, lipid profile, ultrasound of the liver and gallbladder), and the results of bacteriological examination of stool were assessed.

Results: The predominant complaints (in 87% of patients) were: increased fatigue, irritability, emotional lability, discomfort in the right hypochondrium not related to food intake; In 65%, slight hepatomegaly was detected by palpation. 18 children were overweight: 8 children were at risk of obesity (BMI – 25.0 – 29.9); 7 children with grade I obesity (BMI – 30.0 – 34.9); 3 children with second degree obesity (BMI – 35.0 – 39.9). 4 children had type I diabetes mellitus, 12 had type II diabetes mellitus, and 15 had impaired glucose tolerance. Symptoms of arterial hypertension were detected in 23 children. A biochemical study revealed an increase in markers of cholestasis in almost all children (141 out of 147): alkaline phosphatase and gamma-glutamyltranspeptidase; 22 children had cytolytic syndrome of moderate activity (2-3 norms) due to ALT, 59 had dyslipidemia due to cholesterol and triglyceride fractions; 31 children had hyperglycemia. All children underwent studies of markers of viral hepatitis, levels of transferrin, ferritin, ceruloplasmin, a-1-antitrypsin, ANA, AMA, SMA, LKM-1, which made it possible to exclude viral hepatitis, hemochromatosis, Wilson's disease, and a-1-antitrypsin deficiency, autoimmune liver diseases. During ultrasound examination, there was a phenomenon of attenuation of the ultrasonic wave, an increase in the brightness of the parenchyma and a deterioration in the visualization of the vessels and bile ducts of the liver.

When assessing the intestinal microbiota, a decrease (in 65%) of Bifidobacterium, Bacteroids, Lactobacillus and an increase in opportunistic bacteria were revealed: Enterobacteriaceae, Proteobacteria (Escherichia), Parabacteroids, Ruminococcaceae, Fusobacterium (impaired intestinal microbiocenosis degree I-II).

Conclusion: In the majority of children (87%) with MASLD, nonspecific complaints of general asthenia, minor hepatomegaly (65%) prevailed, a third had excess body weight, and occasionally (9.5%) impaired glucose tolerance. 96% of children have increased biochemical markers of cholestasis. Disturbances of the intestinal microbiota are often found in children with MAFLD; they can both provoke the development of MASLD and support the inflammatory process in the liver; they require adequate correction.

Disclosure: no conflict of interest.

MP231

PREDICTORS FOR MAJOR CARDIOVASCULAR EVENTS OR LIVER RELATED EVENTS IN LIVER BIOPSY PROVEN MASLD PATIENTS: A LONG-TERM FOLLOW-UP COHORT

S. Treeprasertsuk¹, P. Ananchuensook¹, K. Thanapirom¹, C. Phathong¹

¹Chulalongkorn University, Medicine, Patumwan, Thailand

Contact E-Mail Address: battan5410@gmail.com

Introduction: MASLD patients is increasing worldwide and the clinical outcomes of different phenotypes had shown varied especially the occurrence of liver related events (LRE) or major cardiovascular events (MACE) (Eslam M, et al. Hepato Inter 2020, 14:889–919). In addition, the prognostic factors for LRE, or MACE, are not well studied.

Aims & Methods: Aims: We aimed to study the rate of LRE, or MACE and the predictors for LRE, or MACE, in MASLD patients with liver biopsy proven.

Methods: In a single-tertiary-center prospective cohort, we collected data of MASLD patients with biopsy-proven who were followed up of at least 1 years at King Chulalongkorn Memorial Hospital during 2005-2022. The primary outcome was the presence of LRE. or MACE. which included cirrhotic complications: acute decompensations; EV/GV bleeding, ascites, hepatic encephalopathy or HCC or acute complications requiring liver transplantation or death. MACE was defined by the occurrence of stroke or acute coronary disease or myocardial infarction. Related baseline characteristics, LSM, FIB-4, and liver biopsy were collected.

Results: Among 286 MASLD patients, the MASLD patients with mean age of 50.1 +/- 14.5 years old (range 19-80 yr.) Male and female were 44% and 56 % respectively. MASLD patients were categorized into 3 groups which were type 2 diabetes mellitus (T2DM) in 119 (41.6%), overweight or obese group in 149 (52.1%), and lean MASLD (BMI<23) in 18 (6.3%). Their baseline characteristics were shown in Table 1.

The average BMI was 41.3 kg/m² (range 19.1-88.7). Other metabolic abnormalities were hypertension in 165 (57.7%), and dyslipidemia in 157 (54.9%). There were 6 cirrhotic cases (2.1%) at diagnosis. Presence of advanced liver fibrosis (TE>12KPA) was found in 15 cases (5.2%). After a mean follow-up of 9.5 years (range 1-19); there were 11 cases (3.8%) developed coronary artery disease and 3 cases (1%) developed stroke. LRE. were present in 7 cases (2.4%) which included acute decompensation (3 cases; 1%), HCC (3 cases; 1%), and death (1 cases; 0.3%). The overall complications of LRE. or MACE. were present in 16 cases (5.6%). By using multivariate analysis, the predictors of LRE. or MACE. were in presence of hypertriglyceridemia (aOR 1.01 (1.00-1.01); p =0.002) and older age (aOR 1.06 (1.01-1.11); p =0.023).

Variables	T2DM (n=119)	Overweight/Obese (n=149)	Lean (n=18)	P value
Age (years)	53.2±15.0	46.1±13.2	62.5±10.1	<0.001
BMI (kg/m ²)	41.2±16.4	43.6±14.0	23.2±1.4	<0.001
Presence of DLP	84 (70.6%)	66 (44.3%)	7 (38.9%)	<0.001
AST (U/L)	45.1±30.0	38.7±33.5	75.7±57.1	<0.001
ALT (U/L)	64.7±42.6	61.6±47.7	94.8±50.9	0.01
Presence of advance fibrosis by TE>12 KPA (n=97)	9 (18.4%)	5 (13.2%)	1 (10.0%)	0.70
Presence of LRE.	9 (7.6%)	6 (4.0%)	1 (5.6%)	0.46
Presence of MACE.	7 (5.9%)	4 (2.7%)	1 (5.6%)	0.32

Conclusion: The overall complication of LRE. or MACE. was not uncommon (5.6% of this cohort with a mean follow-up of 9.5 years). Older age and hypertriglyceridemia were predictors of LRE. or MACE. occurrence.

References: Eslam M, et al. Hepato Inter 2020, 14:889-919.

Disclosure: Nothing to disclose.

MP232

ASSOCIATION OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND ALCOHOL-RELATED STEATOTIC LIVER DISEASE WITH RISK OF GASTROINTESTINAL TRACT CANCERS IN DIABETIC PATIENTS: A NATIONWIDE POPULATION-BASED STUDY IN KOREA

S.-G. Im¹, C.M. Shin¹, K. Han², J.H. Jung³, H. Jo¹, J.J. Choi⁴, E.H. Jin⁵, Y.J. Choi⁶, S.J. Kang⁵, J.H. Lim⁷, D.H. Lee¹

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, South Korea, ²Soongsil University, Department of Statistics and Actuarial Science, Seoul, South Korea, ³Catholic University of Korea, Biostatistics, Seoul, South Korea, ⁴Cha University Bundang Medical Center, Department of Internal Medicine, Seongnam, South Korea, ⁵Seoul National University Hospital Healthcare System Gangnam Center, Department of Internal Medicine, Seoul, South Korea, ⁶National Cancer Center, Department of Internal Medicine, Goyang-si, South Korea, ⁷Seoul National University Hospital Healthcare System Gangnam Center, Internal Medicine, Seoul, South Korea

Contact E-Mail Address: larzarus89@gmail.com

Introduction: Recently, sub-classification of steatotic liver disease (SLD) has been updated by revising non-alcoholic fatty liver disease (NAFLD) as metabolic dysfunction-associated steatotic liver disease (MASLD). In this new nomenclature, emphasis was on the etiology of SLD, primarily at factors of metabolic syndrome and alcohol intake. However, associations between MASLD and gastrointestinal tract cancers other than liver cancer in relation to alcohol intake still require further analysis.

Aims & Methods: We investigated the relationship between the incidence of three gastrointestinal tract cancers (esophageal, stomach, and colorectal) and MASLD or alcohol related-SLD in diabetic patients. Using a retrospective screening cohort of National Health Insurance Service, individuals with type 2 diabetes from 2009 to 2012 were enrolled with their disease status being monitored until 2021. Fatty liver index (FLI) score described by Bedogni et al. (2006) was used to stratify the probability of hepatic steatosis. No steatosis (NS), indeterminate steatosis (IS), and steatosis-probable (PS) group were defined as FLI score 0 to < 30, 30< to ≤60, and >60, respectively. SLD was assumed if FLI score ≥ 30, and MASLD was defined as having at least 1 adult criteria provided by the American Association for the Study of Liver Diseases (AASLD). 2,746,079 subjects were classified into following subgroups: group 1: no steatosis, group 2: MASLD alone, group 3: MASLD with other liver disease, group 4: MASLD with heavy alcohol intake (metALD, 30-60g/d for men and 20-50g/d for women), and group 5: alcoholic liver disease (alcohol intake ≥ 60g/d for men and ≥50g/d for women) with metabolic syndrome. Adjusted hazard ratios (aHR) for each gastrointestinal tract cancer were estimated by incorporating multivariate Cox proportional hazards model.

Results: Compared with group 1 (reference), group 2 showed increased risks of stomach and colorectal cancers (aHR [95% confidence interval (CI)]: 1.06 [1.04-1.09] and 1.17 [1.14-1.19] respectively), but a decreased risk of esophageal cancer (0.81 [0.74-0.88]). In all gastrointestinal tract cancers, the risk of developing cancer compared to group 1 tended to increase from group 3 to group 5 (aHRs in groups 3, 4, 5: 1.40, 1.74, 2.36 in esophageal cancer; 1.13, 1.20, 1.22 in stomach cancer; 1.24, 1.33, 1.34 in colorectal cancer, respectively; all p for trend < 0.0001). Subgroup analysis by probability of steatosis in non-drinkers showed that stomach and colorectal cancer risk was positively correlated with higher likelihood of liver steatosis (aHR for NS, IS, PS: 1.00, 1.05, 1.11 for stomach cancer and 1.00, 1.15, 1.27 for colorectal cancer, respectively, p for trend < 0.05). However, this correlation was not demonstrated in esophageal cancer (aHR for NS, IS, PS: 1.00, 0.95, 1.08 for esophageal cancer).

Conclusion: In patients with diabetes, MASLD itself is associated with an increased risk of stomach and colorectal cancers but is likely associated with a reduced risk of esophageal cancer. Hepatic steatosis may be associated with higher risk of stomach and colorectal cancers, but not esophageal cancer. Amount of alcohol consumption is confirmed to increase the risk of these cancers regardless of the presence of SLD.

References: 1. Rinella, Mary E. "Examining the Nomenclature Change From NAFLD and NASH to MASLD and MASH." *Gastroenterology & Hepatology* 19.11 (2023): 697.

2. Bedogni, Giorgio, et al. "The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population." *BMC gastroenterology* 6 (2006): 1-7.

3. Dabo, Bashir, et al. "The association between diabetes and gastric cancer: results from the Stomach Cancer Pooling Project Consortium." *European Journal of Cancer Prevention* 31.3 (2022): 260-269.

4. Lee, Hokyoo, et al. "Metabolic Dysfunction-Associated Fatty Liver Disease Increases Colon Cancer Risk: A Nationwide Cohort Study." *Clinical and translational gastroenterology* 13.1 (2022): e00435.

Disclosure: Nothing to disclose.

MP233

RISK OF ALL-CAUSE MORTALITY AND ADVERSE OUTCOMES FROM STEATOTIC LIVER DISEASE AND ITS SUBGROUPS IN THE GENERAL POPULATION

M. Michel^{1,2}, A. Armandi^{3,2}, A. Gieswinkel⁴, A.K. Schuster⁵, T. Münzel^{4,6}, S. Konstantinides⁷, M. Michal⁸, B. Straub⁹, I. Schmidtmann¹⁰, O. Tüscher⁸, P. Wild^{4,6,11,12}, K. Lackner¹³, P.R. Galle¹⁴, J. Schattenberg^{1,2}

¹Department of Internal Medicine II, University Medical Center Saarland, Homburg, Germany, ²Metabolic Liver Research Program, University Medical Center Mainz, Mainz, Germany, ³University of Turin, Department of Medical Sciences, Torino, Italy, ⁴Preventive Cardiology and Preventive Medicine, Department of Cardiology, University Medical Center Mainz, Mainz, Germany, ⁵Department of Ophthalmology, University Medical Center Mainz, Mainz, Germany, ⁶Center for Cardiology - Cardiology I, University Medical Center Mainz, Mainz, Germany, ⁷Center for Thrombosis and Hemostasis, University Medical Center Mainz, Mainz, Germany, ⁸Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Mainz, Germany, ⁹Institute of Pathology, University Medical Center Mainz, Mainz, Germany, ¹⁰Institute of Medical Biostatistics, Epidemiology and Informatics, University Medical Center Mainz, Mainz, Germany, ¹¹German Center for Cardiovascular Research (DZHK), Partner site Rhine Main, Mainz, Germany, ¹²Institute of Molecular Biology (IMB), Mainz, Germany, ¹³Institute for Clinical Chemistry and Laboratory Medicine, University Medical Center Mainz, Mainz, Germany, ¹⁴I. Department of Medicine, University Medical Center Mainz, Mainz, Germany

Contact E-Mail Address: maurice.michel@icloud.com

Introduction: With the implementation of the new nomenclature on steatotic liver disease (SLD), three main subgroups consisting of metabolic dysfunction-associated liver disease (MASLD), MASLD with increased alcohol intake (MetALD), and alcohol-related liver disease (ALD) have been defined. However, the risk of SLD for all-cause mortality and adverse outcomes as well as the different risks between MASLD, MetALD, and ALD needs further clarification.

Aims & Methods: Data from 13,599 participants without cancer of the population-based Gutenberg Health Study (baseline enrollment between 2007 and 2012) were cross-sectionally and prospectively analysed. The

fatty liver index (FLI) with a score of ≥ 60 was used to define SLD. The subgroups of SLD (MASLD, MetALD, and ALD) were defined according to the new nomenclature based on five cardiometabolic criteria and alcohol consumption.

The fibrosis-4 score (FIB-4) was calculated to determine patients at risk of fibrosis (≥ 1.3). All-cause mortality (10-year follow-up) and several adverse outcomes (hepatic decompensation, major adverse cardiac events (MACE), extrahepatic cancer) were analysed and compared across the subgroups of SLD.

Cox regression models were used to estimate adjusted hazard ratios (aHR) and their 95% confidence intervals (CIs). Adjustments were made for age, sex, socioeconomic status, education, and smoking.

Results: The overall prevalence of SLD was 37.3% (n=5,074), whereas the prevalence of MASLD, MetALD, and ALD were 30.5% (n=4,154), 5.3% (n=717) and 1.5% (n=202), respectively. Almost half of the population were women (48.9%, n=6,644), and the mean age was 54.3 (± 11.0) years. An elevated FIB-4 ≥ 1.3 was present in 20.2% (n=1,021) with SLD compared to 13.9% (n=1,184) without SLD (p<0.0001).

The cumulative incidence of all-cause mortality was higher in SLD and all its subgroups MASLD, MetALD, and ALD compared to no SLD (p<0.0001). Stratification by FIB-4 ≥ 1.3 revealed a higher risk of all-cause mortality across all investigated SLD subgroups compared to FIB-4 <1.3 (p<0.0001).

Each subgroup of SLD was associated with a higher risk of all-cause mortality: MASLD (aHR 1.6, 95% CI 1.4-1.9, p<0.0001), MetALD (aHR 1.6, 95% CI 1.3-2.1, p=0.00024) and ALD (aHR 1.6 95% CI 1.0-2.5, p=0.033).

The risk of adverse outcomes was increased in MASLD (hepatic decompensation: aHR 1.2, 95% CI 1.0-1.5, p=0.0045; MACE: aHR 1.5, 95% CI 1.2-1.8, p<0.0001; extrahepatic cancer: aHR 1.2, 95% CI 1.1-1.4, p=0.0086), whereas no differences were seen for MetALD and ALD.

Conclusion: The prevalence of SLD and especially MASLD is high in the general population. Patients with SLD and any of its three main subgroups show a higher risk of all-cause mortality, whereas the risk for adverse outcomes is particularly increased in those with MASLD. These results highlight the importance of screening for SLD and related risk factors to improve outcomes.

Disclosure: Nothing to disclose.

MP234

NON-INVASIVE FIBROSIS ASSESSMENT IN TYPE 2 DIABETIC PATIENTS WITH MASLD: A RISK STRATIFICATION APPROACH

L. Khayat¹, I. Jemni², L. Safer³

¹CHU Fattouma Bourguiba, Monastir, Tunisia, ²CHU Fattouma Bourguiba, Gastroenterology, Monastir, Tunisia, ³CHU Fattouma Bourguiba, Les Berges Du Lac, Tunisia

Contact E-Mail Address: Lobnakhayat@gmail.com

Introduction: The development and validation of non-invasive fibrosis tests have transformed clinical practice in hepatology in recent years. Metabolic-associated fatty liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), is currently the most prevalent liver disease.

In this study, our aim was to evaluate the utility of non-invasive tests in the diagnosis and staging of fibrosis in type 2 diabetic (T2D) patients with hepatic steatosis.

Aims & Methods: This was a prospective cross-sectional study that included 122 T2D patients over a 10-month period. Hepatic steatosis was confirmed by abdominal ultrasound or a FLI score ≥ 60 . We used non-invasive tests including the serum marker FIB-4, transient elastography FibroScan®, and the combined Agile -3 score.

Interpretation of the scores was as follows:

For FIB-4, < 1.3 indicated a low risk of advanced fibrosis, 1.3–2.67 indicated an intermediate risk of advanced fibrosis, and > 2.67 indicated a high risk of advanced fibrosis. For FibroScan, minimal or absent fibrosis (F0-F1) was defined by a LSM value <8 kPa, moderate hepatic fibrosis (≥F2) by a LSM value between 8–9.6 kPa, and advanced fibrosis by a hepatic elasticity LSM >9.6 kPa. For the Agile -3 score, a value < 0.451 excluded advanced fibrosis (F3) and a value ≥ 0.679 confirmed advanced fibrosis (F3).

Results: The average age was approximately 60 years with a female predominance. The FIB-4 score ranged from 0.311 to 4.01, with an average of 1.0881. 73.77% of patients had a FIB-4 indicating no fibrosis. 2.45% had advanced fibrosis, and 23.77% were in an indeterminate FIB-4 score range. The FIB-4 score had a positive predictive value (PPV) of 42.86% and a negative predictive value (NPV) of 77.23% for detecting significant fibrosis. Regarding advanced hepatic fibrosis, FIB-4 had a PPV of 45.45% and an NPV of 75.67%. Hepatic elasticity ranged from 1.5 to 75 kPa with an average of 6.62 kPa. 82.78% had no fibrosis, 8.19% had significant fibrosis, and 9.01% had advanced fibrosis. To reduce the grey zone, we calculated the AGILE-3 score, which was observed in a range from 0.03 to 1. It reduced the grey zone by up to 40%. Among the 10 patients in the grey zone on FibroScan, 3 were reclassified to fibrosis F3 by the AGILE-3 score, 4 remained in the grey zone, and 3 were reclassified to absent or minimal fibrosis.

Conclusion: The implementation of approaches using non-invasive tests is generally a promising strategy in the management of MASLD in primary care, providing clinically effective and cost-effective pathways to identify patients at risk of advanced fibrosis and streamline referrals to secondary care, subsequently benefiting from accurate risk assessments without the need for liver biopsies. Our study suggests the sequential use of non-invasive tests, starting with FIB-4 which, according to our study, has an NPV of over 75% to rule out advanced or significant fibrosis, followed by sequential use of FibroScan and Agile 3+ score to better reduce the grey zone, hence limiting the need for liver biopsies.

References: Sanyal AJ, Foucquier J, Younossi ZM, Harrison SA, Newsome PN, Chan WK, et al. Enhanced diagnosis of advanced fibrosis and cirrhosis in individuals with NAFLD using FibroScan-based Agile scores. *Journal of Hepatology*. 1 févr 2023;78(2):247–59.

Ma X, Zhu Y, Yeo YH, Fan Z, Xu X, Rui F, et al. The impact of an increased Fibrosis-4 index and the severity of hepatic steatosis on mortality in individuals living with diabetes. *Hepatol Int* [Internet]. 22 janv 2024 [cité 21 avr 2024]; Disponible sur: <https://doi.org/10.1007/s12072-023-10625-7>

Disclosure: Nothing to disclose.

MP235

ALCOHOL-INDUCED DEREGLATION OF IMMUNE-METABOLIC FUNCTIONS EXACERBATES ATHEROSCLEROSIS DEVELOPMENT IN A NOVEL MURINE MODEL FOR METALD

C. Hoebinger¹, D. Rajčić¹, L. Goederle¹, T. Hendrikx¹

¹Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria

Contact E-Mail Address: constanze.hoebinger@meduniwien.ac.at

Introduction: The recently revised nomenclature of steatotic liver disease differentiates between metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease (ALD), besides introducing the newly termed MetALD for patients with MASLD combined with moderate alcohol consumption. While this re-classification acknowledges alcohol as an important contributor to liver disease pathogenesis, a better understanding of the underlying mechanisms that might distinguish MetALD is necessary to identify novel targets to improve diagnosis and intervention for these distinct patients.

Aims & Methods: Here, we aimed to investigate ethanol-mediated immune-metabolic effects by utilizing dyslipidemic low-density lipoprotein receptor-deficient mice (*Ldlr*^{-/-}) in a novel murine model for MetALD. Hence, *Ldlr*^{-/-} mice, displaying a human-like systemic lipid profile, were fed a high-fat, high-cholesterol (HFC) diet for eight weeks in combination with regular or ethanol-containing drinking water (alternating 10–20% v/v) to induce MASLD and MetALD, respectively. To investigate the contribution of ethanol-induced dysbiosis, additional cohorts underwent similar dietary interventions in combination with broad-spectrum antibiotics to deplete the microbiome.

Results: Despite a similar body weight gain, ethanol intake by HFC-fed *Ldlr*^{-/-} mice resulted in heavier liver weights and heightened hepatic lipid levels, indicating enhanced steatosis compared to mice receiving regular drinking water. Gene expression analysis revealed alterations in lipid metabolism in the livers of ethanol-consuming HFC-fed *Ldlr*^{-/-} mice. In line, *Ldlr*^{-/-} mice exposed to ethanol had increased cholesterol, triglyceride, and free fatty acid levels in circulation, suggesting systemically enhanced dyslipidemia upon alcohol consumption. Furthermore, ethanol-treated mice recruited more inflammatory Ly6C^{high} monocytes to the liver and displayed higher hepatic gene expression of various pro-inflammatory markers, including *Il1b*, *Cxcl2*, and *Ccl2*, suggesting accelerated liver disease progression in mice with MetALD. Moreover, elevated hepatic inflammation was reflected systemically as HFC-fed *Ldlr*^{-/-} mice consuming ethanol showed increased monocytois in circulation. Notably, this was associated with enlarged lesion size in the aortic root of HFC-fed *Ldlr*^{-/-} mice receiving ethanol, which occurred independently of the elevated dyslipidemia, indicating a direct immunomodulatory effect of ethanol on atherosclerosis progression in mice developing MetALD compared to MASLD. While ethanol intake induced intestinal dysbiosis, microbiome depletion with broad-spectrum antibiotics, either from the start or during the last two weeks of the dietary intervention, did not mitigate the enhanced progression of steatohepatitis and elevated systemic monocytois in our murine MetALD model compared to MASLD-developing *Ldlr*^{-/-} mice.

Conclusion: Our findings demonstrate that alcohol consumption during metabolically-associated dysfunction serves as a critical lifestyle factor with immunomodulatory effects, independent of microbiota alterations. Alcohol significantly influences the progression of steatotic liver disease and atherosclerosis, thereby suggesting a heightened risk of cardiovascular events in patients with MetALD.

Disclosure: Nothing to disclose.

MP236

PHASE 3 RANDOMISED, PLACEBO-CONTROLLED ESSENCE TRIAL OF SEMAGLUTIDE 2.4 MG IN PARTICIPANTS WITH NON-CIRRHOTIC NON-ALCOHOLIC STEATOHEPATITIS: BASELINE CHARACTERISTICS, IMPACT OF NEW METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE CRITERIA AND NON-INVASIVE TESTS

P.N. Newsome^{1,2}, E. Bugianesi³, V. Ratziu⁴, M.E. Rinella⁵,
M. Roden^{6,7,8}, K.A. Engebretsen⁹, I. Kliers⁹, L.H. Østergaard⁹,
D. Vanni⁹, J. Zacho⁹, A.J. Sanyal¹⁰

¹National Institute for Health Research, Birmingham Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust and Centre for Liver and Gastrointestinal Research, Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom, ²Institute of Hepatology, Faculty of Life Sciences and Medicine, King's College London and King's College Hospital, London, United Kingdom, ³Department of Medical Sciences, University of Turin, Turin, Italy, ⁴Sorbonne Université, Institute for Cardiometabolism and Nutrition, Hospital Pitié-Salpêtrière, INSERM UMRs 1138 CRC, Paris, France, ⁵Department of Medicine, University of Chicago, Chicago, IL, United States of America, ⁶Department of Endocrinology and Diabetology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, ⁷German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Germany, ⁸Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany, ⁹Novo Nordisk A/S, Copenhagen, Denmark, ¹⁰Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, VCU School of Medicine, Richmond, VA, United States of America

Contact E-Mail Address: michael.roden@ddz.de

Introduction: ESSENCE (NCT04822181) is an ongoing 247-week Phase 3, randomised, placebo-controlled trial evaluating the effect of the glucagon-like peptide-1 analogue, semaglutide 2.4 mg subcutaneous once weekly (OW) in participants with non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH). We report the baseline characteristics of the randomised participants.

Aims & Methods: Following a 14-week screening phase, 800 participants (part 1) of 1200 planned (part 2) with MASH and fibrosis stages 2/3 (F2/F3) were randomised 2:1 to receive semaglutide 2.4 mg subcutaneous OW or placebo OW added to standard of care. In part 1, the two primary endpoints at 72 weeks are resolution of steatohepatitis and no worsening of liver fibrosis, and improvement in liver fibrosis and no worsening of steatohepatitis. Based on a central pathologist evaluation, inclusion criteria were histological presence of steatohepatitis stages F2/F3 per the Non-alcoholic Steatohepatitis Clinical Research Network classification, and a non-alcoholic fatty liver disease activity score (NAS) of ≥ 4 , with a score of ≥ 1 in steatosis, lobular inflammation and hepatocyte ballooning.

Results: 800 participants (250 F2; 550 F3) were randomised. Mean (SD) age was 56 (11.6) years; 57.1% were female; $\geq 99\%$ had ≥ 1 cardiometabolic risk factor(s) in accordance with the metabolic dysfunction-associated steatotic liver disease (MASLD) definition. Mean (SD) NAS was 5.05 (0.95), and higher in F3 versus F2 (5.11 [0.95] vs 4.92 [0.93], respectively). Notably, participants with a higher NAS had more cardiometabolic risk factors for MASLD (52.9% with NAS ≥ 5 vs 45.3% with NAS 4). Similarly, a greater proportion of participants with F3 had all five cardiometabolic risk factors versus F2 (52.9% vs 44.8%, respectively). Although cardiometabolic comorbidities were highly prevalent, 44.5% of participants did not have type 2 diabetes (T2D), and 27.3% did not have obesity. Normal liver transaminases were observed in 26.3% of participants (28% F2; 26% F3). Mean

(SD) FibroScan liver stiffness was 12.8 (6.9) kPa, and values of < 8 kPa were observed in 15.3% of participants. Mean (SD) controlled attenuation parameter value was 329 (46) dB/m; mean (SD) enhanced liver fibrosis (ELF) score was 10.0 (1.0), and 43.5% of participants had an ELF score of < 9.8 . Overall, 8.8% and 9.0% of participants with/without T2D did not meet any of the following non-invasive criteria: Fibrosis-4 index ≥ 1.3 , vibration-controlled transient elastography ≥ 8.1 , or ELF ≥ 9.8 , and more participants with F2 (14.7–16.4%) did not meet these criteria versus F3 (4.5–6.7%).

Conclusion: The ESSENCE baseline population includes participants with significant fibrosis (F2 and F3) and approximately 91% of the trial population had ≥ 1 positive diagnostic non-invasive test. Cardiometabolic risk factors were found in $\geq 99\%$ of participants, and in increased numbers in those with higher NAS and fibrosis stages.

This is an encore of an abstract that will be presented for the first time at the European Association for the Study of the Liver (EASL) Congress, 5–8 June 2024, Milan, Italy.

Disclosure: The ESSENCE trial is funded by Novo Nordisk A/S.

PNN: reports grants from Novo Nordisk, and has received consulting fees from Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, Bristol Myers Squibb (BMS), Pfizer, Sun Pharma, Madrigal and GSK. PNN also reports honoraria as a speaker for Novo Nordisk and AICME; support for attending meetings for Novo Nordisk; and participation on an advisory board for Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, BMS, Pfizer, Sun Pharma, Madrigal and GSK.

EB: served as a consultant or advisory board member for Boehringer Ingelheim, Gilead, Intercept, Merck, Novo Nordisk, Pfizer, ProSclero, and as a speaker for Gilead, Intercept, Merck, Novo Nordisk and Pfizer. EB has also received a research grant from Gilead for fatty liver research.

VR: received consulting fees from Novo Nordisk, Sagimet, Madrigal, Enyo, Poxel, Northsea, Intercept and ProSclero, and research grants (to institution) from Gilead and Intercept.

MER: consults for Boehringer Ingelheim, CytoDyn, GSK, Novo Nordisk, HistoIndex, Intercept, Madrigal, NGM Bio and Sonic Incytes.

MR: reports grants from Boehringer Ingelheim and Novo Nordisk, and has received fees for consulting or participation in advisory boards for Boehringer Ingelheim, Echosens, Eli Lilly and Novo Nordisk. MR also reports honoraria as a speaker for AstraZeneca, Boehringer Ingelheim, Novo Nordisk and Madrigal.

AJS: consults for and advises Avant Santé and AstraZeneca. AJS also consults for and has received grants from Akero, BMS, Intercept, Eli Lilly, Madrigal and Novo Nordisk. AJS consults for and owns stock in Rivos, and also consults for AGED Diagnostics, Albireo, Alnylam, Altimune, Boehringer Ingelheim, 89Bio, Echosens, Genentech, Gilead, GSK, HistoIndex, Mallinckrodt, Merck, NGM Bio, Novartis, PathAI, Pfizer, Poxel, Regeneron, Salix, Siemens, Surrozen, Takeda, Terns and Zydus. AJS owns stock in Durect, Exalenz, Genfit, Indalo, Inversago and Tiziana, and has received royalties from Elsevier and Wolters Kluwer.

KAE, IK, LHØ, DV and JZ: employees and stockholders of Novo Nordisk A/S.

Pancreatic cancer: Clinical

10:00-11:00 / Poster Stage 4

MP237

BRANCH DUCT IPMN-ASSOCIATED ACUTE PANCREATITIS IN A LARGE SINGLE-CENTER COHORT STUDY

F. Caldart¹, S. Crucillà¹, M.S. Battan², A. Amodio¹, P. Campagnola¹, N. de Pretis¹, A. Gabbrielli³, S.F. Crinò⁴, M.C. Conti Bellocchi⁴, A. Marcon⁵, L. Martinelli⁵, L. Frulloni¹

¹University of Verona, Gastroenterology B Unit, Pancreas Institute, University Hospital Verona, Verona, Italy, ²University of Verona, School of Medicine, Gastroenterology B Unit, Pancreas Institute, University Hospital Verona, Verona, Italy, ³University of Trento, Gastroenterology and Endoscopy Unit, University Hospital "S. Chiara", Trento, Italy, ⁴University of Verona, Endoscopy Unit, Pancreas Institute, University Hospital Verona, Verona, Italy, ⁵University of Verona, Department of Diagnostics and Public Health, Verona, Italy

Contact E-Mail Address: federicocaldart94@gmail.com

Introduction: IPMN are considered a possible cause of acute pancreatitis (AP) due to a transient obstruction of the pancreatic duct by mucin. IPMN-associated-AP is considered a relative indication to surgery for both, prevention of recurrent attacks of pancreatitis and for a hypothesized increased risk of cancer. The published literature is based on surgical series with significant population heterogeneity including MD-IPMN, mixed-type-IPMN and BD-IPMN. No data are available on the clinical features of this particular type of AP, on the risk of recurrent pancreatitis and pancreatic cancer in patients with BD-IPMN-associated-AP.

Aims & Methods:

The aim of this study is the description of clinical and radiological features of BD-IPMN-related AP.

All patients with AP associated to BD-IPMN without "worrisome features" and "high risk stigmata" and no other identifiable causes of AP evaluated at Gastroenterology Unit of the University of Verona between January 1st 2012 and December 31st 2022 were retrospectively identified and analyzed.

Results: One-hundred-thirty-five patients were included (54.8% males and 45.2% females), with mean age at the first episode of AP of 55.8 ± 12.5 years. Pancreatic necrosis was diagnosed in 15 patients (11.1%) and only 1 patient (0.7%) was admitted in Intensive Care Unit. One-hundred-two (75.6%) had recurrent pancreatitis.

The median size of the largest BD-IPMN was 8 mm (IQR 7). None had mural nodules, thickened cystic walls, or dilated main pancreatic duct ≥ 5 mm. Eighteen patients (13.3%) developed main pancreatic duct dilation ≥ 5 mm. None developed dilation of main pancreatic duct ≥ 10 mm, mural nodules, thickened cystic walls, or jaundice. At Cox unadjusted analysis no BD-IPMN-related features were associated to increased risk of recurrent pancreatitis. Surgical resection was performed in 10 patients (7.4%). None developed pancreatic cancer or signs of chronic pancreatitis during follow-up.

Conclusion: BD-IPMN-associated AP has a benign clinical course. Cystic features are not related to increased risk of recurrence. Cancer risk appears extremely low in patients with BD-IPMN-associated-AP.

Disclosure: Nothing to disclose.

MP238

RISK FACTORS FOR PANCREATIC CANCER IN PATIENTS WITH DIABETES MELLITUS: A JAPANESE POPULATION-BASED STUDY USING THE SHIZUOKA KOKUHO DATABASE

T. Satoh^{1,2}, E. Nakatani², S. Kawaguchi¹, K. Ohno¹, T. Usui^{2,3}

¹Shizuoka General Hospital, Department of Gastroenterology, Shizuoka, Japan, ²Shizuoka Graduate University of Public Health, Graduate School of Public Health, Shizuoka, Japan, ³Shizuoka General Hospital, Research Support Center, Shizuoka, Japan

Contact E-Mail Address: tatsunori-sato@i.shizuoka-pho.jp

Introduction: Pancreatic cancer (PC) are associated with notably poor prognoses. The clinical practice guidelines for PC list several risk factors of PC, including diabetes among them. Diabetic patients, who regularly visit the hospital, present a practical opportunity for pancreatic surveillance. Effective surveillance for PC could be achieved by identifying diabetic patients at high-risk for PC who already require regular hospital visits. Nevertheless, there is a notable lack of research on pancreatic cancer risk factors within the diabetic population.

Aims & Methods: This study aimed to identify risk factors for pancreatic cancer in diabetic patients using a longitudinal cohort from the Shizuoka Kokuho database, spanning April 2012 to September 2021. Diabetic patients were identified and monitored for the onset of pancreatic cancer. Factors analyzed included age, sex, the Elixhauser comorbidity index, and specific comorbidities. Statistical analyses involved univariate and multivariate Cox proportional hazards regression.

Results: The Shizuoka Kokuho database, which comprises 2,654,567 individuals, identified 212,775 as diabetic patients. Of these patients, 1,755 developed pancreatic cancer during the observation period, which had a median duration of 5.1 years and a maximum of 8.5 years. The annual incidence rate of pancreatic cancer in this group was 166.7 cases per 100,000 person-years [95% CI: 158.9–174.5].

Identified candidate risk factors included older age, male sex, coexisting liver disease, cardiac arrhythmias, hypertension, chronic pancreatitis, and pancreatic cystic lesions, each with *p*-values below 0.05. These variables were subsequently incorporated into a multivariate model.

The multivariable regression results indicated that older age and male gender were associated with an increased risk of pancreatic cancer (HR: 1.267 [95% CI: 1.150–1.395]). Liver disease emerged as a notable risk factor (HR: 1.13 [95% CI: 1.01–1.26]). Significant correlations were found between the onset of PC and both chronic pancreatitis (HR: 1.98 [95% CI: 1.48–2.64]) and pancreatic cystic disease (HR: 4.79 [95% CI: 3.43–6.67]). Neither the type of diabetes nor the presence of diabetic comorbidities was associated with the onset of PC.

Conclusion: This cohort study has identified key risk factors for pancreatic cancer in diabetic patients. Findings indicate that advanced age, male sex, a history of liver disease, chronic pancreatitis, and pancreatic cystic lesions significantly increase the risk of pancreatic cancer in this population. These insights underscore the importance of targeted surveillance for early detection of pancreatic cancer in diabetic patients, particularly those with these risk factors.

Disclosure: Nothing to disclose.

MP239

PROGNOSTIC IMPACT OF THE CALLY INDEX IN PATIENTS WITH RESECTABLE PANCREATIC CANCER

S. Matsui¹, Y. Kato¹, K. Ohgi¹, R. Ashida¹, M. Yamada¹, S. Otsuka¹, K. Uesaka¹, T. Sugiura¹

¹Shizuoka Cancer Center Hepato-Biliary-Pancreatic Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Sunto-Nagaizumi, Japan

Contact E-Mail Address: 070681ms@gmail.com

Introduction: The prognostic significance of the preoperative C-reactive protein-albumin-lymphocyte (CALLY) index has been reported in various cancer types; however, its role in pancreatic cancer remains unclear.

Aims & Methods: A cohort of 339 patients with resectable pancreatic cancer (RPC) who underwent curative surgery between July 2012 and December 2019 was analyzed. The CALLY index was defined as (albumin × lymphocytes)/ (C-reactive protein × 10⁴). The cutoff value of the CALLY index was determined according to receiver operating characteristics analysis using survival status at the 3-year follow-up.

We investigated the association between the CALLY index with disease-free survival (DFS) and overall survival (OS) using univariate and multivariate analyses.

Results: The median CALLY index was 4.1, with an interquartile range of 1.4–11.7. The cutoff value of the CALLY index was set at 3.0, dividing the patients into the CALLY-high group (> 3.0; n = 198) and the CALLY-low group (≤ 3.0; n = 141). The DFS and OS in the CALLY-low group were significantly worse than those in the CALLY-high group ($p < 0.001$ and $p < 0.001$, respectively). Multivariate analysis, using the preoperative clinicopathological variables, indicated that the CALLY index ≤ 3.0 was an independent prognostic factor for DFS (Hazard Ratio [HR] 1.53, $p = 0.008$) and for OS (HR 1.69, $p = 0.002$).

Conclusion: In RPC, survival outcomes were significantly stratified by the CALLY index = 3.0, with < 3 being a significantly poor prognostic factor for DFS and OS. The CALLY index may be useful in predicting the long-term survival of patients with RPC.

Disclosure: Nothing to disclose.

MP240

DIAGNOSTIC AND PROGNOSTIC ACCURACY OF MICRORNAS IN PANCREATIC CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

F. Hasani¹, M. Masrour², S. Khamaki¹, K. Jazi³, S. Hosseini¹, H. Heidarpour¹

¹Golestan University of Medical Sciences, School of Medicine, Gorgan, Iran, ²Tehran University of Medical Sciences, Tehran, Iran, ³Medical University of Qom, School of Medicine, Qom, Iran

Contact E-Mail Address: fatemehassani2001@gmail.com

Introduction: Pancreatic cancer (PC) remains a significant contributor to cancer mortality globally, with limited effective diagnostic and prognostic tools. MicroRNAs (miRNAs) have emerged as promising biomarkers for PC diagnosis and prognosis due to their stable presence in body fluids and regulatory role in gene expression. This systematic review and meta-analysis aim to evaluate the diagnostic and prognostic accuracy of miRNAs in PC based on existing literature.

Aims & Methods: A comprehensive literature search was conducted in PubMed, Web of Science, and Scopus databases. Studies reporting sensitivity, specificity, or area under the curve (AUC) values for miRNAs in PC diagnosis, as well as hazard ratios (HRs) for survival evaluations for prognosis, were included. Data extraction and quality assessment were

performed following PRISMA guidelines. Meta-analyses were conducted using appropriate statistical methods. The protocol has been registered in PROSPERO.

Results: Diagnostic analysis included 290 evaluations, revealing an overall AUC of 0.8226 for PC diagnosis. Subgroup analyses based on specimen type demonstrated varying diagnostic accuracies, with blood and tissue specimens showing higher AUC values. Promising miRNAs with AUC values above 0.8 included miR-320, miR-1290, miR-93, miR-25, miR-451, miR-20, miR-21, miR-223, and miR-122.

Prognostic analysis encompassed 46 studies, indicating significant associations between miRNA expression and overall survival (OS) and progression-free survival (PFS). The combined hazard ratio (HR) for studies reporting OS HRs higher than one was 1.7613 (95% CI: 1.5394–2.0152, $p < 0.0001$; I² = 81.7%). Notable miRNAs with prognostic significance included miR-10 (Pooled HR [95% CI] 2.3538 [0.8241–6.7229]), miR-21 (Pooled HR [95% CI] 1.9027 [0.8293–4.3652]), and miR-221 (Pooled HR [95% CI] 1.5022 [1.1424; 1.9754]). Studies reporting OS HRs less than one had a pooled HR of 0.6805 (95% CI: 0.5862–0.7901, $p < 0.0001$; I² = 65.4%), indicating favorable prognostic significance.

Conclusion: MiRNAs hold promise as diagnostic and prognostic biomarkers for PC. Blood and tissue specimens offer superior diagnostic accuracy, while several miRNAs show potential for predicting patient outcomes. Further research and validation are warranted to establish miRNAs' clinical utility in PC management.

Disclosure: Nothing to disclose.

MP241

VALIDATION OF KYOTO CONSENSUS GUIDELINE FOR INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS IN SMALL UNCHANGED BD-IPMN AFTER 5 YEARS SURVEILLANCE

M. Marasco¹, M. Signoretti¹, R. Di Pangrazio¹, M. Casella¹, M. Rinzivillo¹, B. Annibale¹, F. Panzuto¹

¹Digestive Disease Unit, Sant'Andrea University Hospital, Department of Medical Surgical Sciences and Translational Medicine, Sapienza University, Rome, Italy

Contact E-Mail Address: matteomarasco93@gmail.com

Introduction: Intraductal papillary mucinous neoplasm (IPMN) of the pancreas represents around 80 % of incidental-discovered cysts and one of the most frequent causes of access for pancreatic clinical evaluation. Fukuoka guidelines (2017) have been the clinical reference point until the recently published Kyoto guidelines (2024) that bring out various new key points including “stop surveillance” concept as an appropriate approach in specific patients.

Aims & Methods: The aim of the study is to observe clinical validity of new recommendations of Kyoto guidelines, particularly in patients with unchanged BD-IPMN ≤ 20 mm after 5 years of surveillance. This is an observational retrospective single-center study. Patients were evaluated in our Digestive Disease Unit from Jan 2018 to Jan 2024 and they were handled according to Fukuoka guidelines.

Results: A total of 163 patients (M: F=56:107) with a median age of 70 y/o (44-92). BD-IPMN were 152 (93.5%), located in the pancreatic head (70, 46%), body (63, 41.4%) and tail (19, 12.5%). During surveillance, 29 (18%) and 3 (2.2%) patients developed, respectively, ‘worrisome features’ (WF) and ‘high-risk stigmata’ (HRS). Overall, 39 (23.9%) patients underwent surveillance for ≥ 5 years. Particularly, 20 (51.3%) of these patients had BD-IPMN ≤ 20 mm unchanged during a median time follow-up of 77 months (60-144): median IPMN dimension was 12 mm (7-20) and median age was 71 y/o (59-87). They performed a median of 7 (3-10) exams (RMN, CT, EUS) with no evidence of WF or HRS beyond 5 years of follow-up. How-

ever, in IPMN ≥ 20 mm with surveillance ≥ 5 years, 14 (35.8%) and 2 (5.1%) patients developed, respectively, WF and HRS at a median of 22 months (6-120) from diagnosis with consequent different timing of follow-up or surgical strategy.

Conclusion: Based on our experience, no one patient with BD-IPMN ≤ 20 mm during FU ≥ 5 years developed any WF or HRS. This confirmed the latest points of view of Kyoto guidelines, providing patients the possibility to stop surveillance. This could have an important role in the patient's psychological aspects and in decreasing request overload of radiological or endoscopic exams.

References: 1. Tanaka M et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatol.* 2017 Sep-Oct;17(5):738-753.

2. Ohtsuka T et al. International evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas. *Pancreatol.* 2024 Mar;24(2):255-270

Disclosure: Nothing to disclose.

MP242

A LEVERAGING SOCIAL PROGRAM FOR EARLY-STAGE PANCREATIC CANCER DIAGNOSIS: THE ONOMICHI PROJECT

K. Hanada¹, A. Shimizu¹, K. Tsushima¹, E. Hiraaki¹, Y. Yamashita¹, T. Nobuto¹, A. Oshita², D. Takei², H. Ohtsuka², T. Noriyuki², T. Kasai³, M. Danjo⁴, S. Masaoka⁵, H. Ohtagaki⁶, N. Matsumoto⁷, S. Tanaka¹, N. Sasaki⁸, Onomichi General Hospital

¹Onomichi General Hospital, Dept. of Gastroenterology, Onomichi, Japan, ²Onomichi General Hospital, Dept. of Surgery, Onomichi, Japan, ³Onomichi Municipal Hospital, Gastroenterology, Onomichi, Japan, ⁴Danjo Clinic, Onomichi, Japan, ⁵Masaoka Clinic, Onomichi, Japan, ⁶Ohtagaki Clinic, Onomichi, Japan, ⁷Hirahara Clinic, Onomichi, Japan, ⁸Onomichi Medical Association, Onomichi, Japan

Contact E-Mail Address: kh-ajpbd@nifty.com

Introduction: Early detection of pancreatic cancer (PC) can significantly improve patient outcomes.

Aims & Methods: In 2007, the Onomichi Medical Association initiated a social program aimed at enhancing early PC diagnosis by fostering collaboration between PC specialists from medical centers and general practitioners. Initially, specialists educated general practitioners on PC risk factors, emphasizing elevated serum pancreatic enzyme levels, ultrasound (US) findings such as pancreatic duct dilation, and the importance of magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) for detecting early-stage PC. Upon encountering suspicious cases, general practitioners referred patients to specialists for further evaluation. A retrospective study was conducted, involving patients who underwent surgery and were diagnosed with PC at Onomichi General Hospital between January 2007 and December 2022.

Results: During this period, 28,185 patients sought consultation for suspected PC, with 9,420 undergoing CT scans. Additionally, 11,781 patients with main pancreatic duct (MPD) dilation underwent MRCP. CT and MRCP identified features suggestive of PC, prompting EUS examinations in selected patients. EUS-guided fine needle aspiration (FNA) was performed in 808 cases where tumor lesions were detected and deemed suitable for sampling. For cases with negative EUS-FNA results, undetected lesions on EUS, or lesions too small for EUS-FNA, endoscopic retrograde cholangiopancreatography (ERCP) with pancreatic juice cytology was conducted in 945 cases. Histological diagnosis confirmed PC in 813 cases, with 334 patients undergoing surgery. Among them, 140 cases were early-stage PC,

comprising 41 stage 0 and 99 stage I cases. The 5-year survival rate for PC cases diagnosed from 2011 to 2016 was 17.9%, showing improvement to 21.4% for cases diagnosed in 2017.

Conclusion: This collaborative early diagnosis program, emphasizing risk factor awareness and interdisciplinary cooperation within regional healthcare networks, highlights promising prospects for enhancing PC prognosis.

Disclosure: Nothing to disclose.

MP243

RISK OF PANCREATIC CANCER IN FIRST-DEGREE RELATIVES OF INDIVIDUALS WITH PRECURSORS: A SWEDISH NATIONWIDE COHORT STUDY

Q.-L. Wang^{1,2,3}, J. Sun¹, C. Yuan², M. Vujasinovic^{4,5}, M. Löhr^{3,5}, B. Wolpin², J.F. Ludvigsson^{1,6,7,8}

¹Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, ²Dana-Farber Cancer Institute, Medical Oncology, Boston, United States of America, ³Karolinska Institutet, Clinical Science, Intervention, and Technology, Stockholm, Sweden, ⁴Karolinska Institutet, Medicine Huddinge, Stockholm, Sweden, ⁵Karolinska University Hospital, Upper Abdominal Diseases, Stockholm, Sweden, ⁶Örebro University Hospital, Pediatrics, Örebro, Sweden, ⁷Columbia University Medical Center, Medicine, New York, United States of America, ⁸University of Nottingham, Epidemiology and Public Health, Nottingham, United Kingdom

Contact E-Mail Address: qiaoli.wang@ki.se

Introduction: Pancreatic cancer is estimated to be the second leading cause of cancer-related deaths in Europe by 2030 and remains a significant challenge with limited risk factors. Pancreatic intraepithelial neoplasia (PanIN), intraductal papillary mucinous neoplasms (IPMN), and mucinous cystic neoplasia (MCN) are three common precursor lesions for this disease. The risk of pancreatic cancer in first-degree relatives (FDRs) of individuals with precursors however remains unknown.

Aims & Methods: This study aims to analyze the absolute incidence and relative risk of pancreatic cancer by family history of precursors using a population-based cohort study in Sweden. We included all patients who had been pathologically diagnosed with precursor lesions of pancreatic cancer between 1965 and 2016 in Sweden and up to 5 matched reference individuals from the general population based on birth year, sex, calendar year, and residency. We identified all their FDRs (parents, full siblings, and offspring) using the Swedish multigeneration registry. All FDRs were followed up through national registries from birth or year 1959 when cancer registry was launched, until the date of pancreatic cancer diagnosis, death, migration, or end of follow-up (January 1st, 2020). The absolute cancer incidence rate was computed as the number of observed cases divided by person-years and relative risk was calculated as multivariable-adjusted hazard ratio (HR) using Cox proportional hazards regression.

Results: A total of 27,862 FDRs were included in the analyses, among which 4647 were FDRs of 1036 precursor patients and 23,157 were FDRs of 5067 matched reference individuals. During the follow-up, 149 FDRs developed pancreatic cancer, with an incidence rate of 10 (95% CI 8-12) per 100,000 person-years for FDRs of reference individuals, and 21 (16-28) for FDRs of precursor individuals. Compared to FDRs of reference individuals, FDRs of precursor had a 2.24 (1.58-3.18) times higher risk of developing pancreatic cancer during their lifetime. When stratified by subtype of precursors, similar HRs were found for PanIN (2.37 [1.52-3.70]) and IPMN (2.31 [1.29-4.11]), but not for MCN (1.84 [0.89-3.78]). Individuals whose parents had been diagnosed with precursors had 4.94 (2.10-11.62) times higher

risk for pancreatic cancer than those without. To facilitate clinical application, we also assessed the association of pancreatic cancer risk after known diagnosis of precursors in FDRs. Compared to reference counterparts, an HR of 4.46 (2.37-8.38) was found for those with known precursors in FDRs.

Conclusion: A family history of precursor lesions of pancreatic cancer can be an indicative risk factor for pancreatic cancer and risk estimates varies by precursor subtypes and type of FDRs with precursors. Precursor lesions in FDR should be considered as a positive phenotype in individuals at risk.

Disclosure: Dr. Wolpin reported receiving grants from AstraZeneca, Celgene, Bristol Myers Squibb, Eli Lilly, Novartis, and Revolution Medicines and receiving personal fees from BioLineRx, Mirati, Ipsen, GRAIL, Celgene, Bristol Myers Squibb, and Third Rock Ventures. Dr. Ludvigsson has coordinated an unrelated study on behalf of the Swedish IBD quality register (SWIBREG). This study has received funding from the Janssen corporation. Dr Ludvigsson has also received financial support from MSD to develop a paper reviewing national healthcare registers in China. Dr Vujasinovic and Dr Löhr have received lecture fees from Abbott and Viatrix. Dr Vujasinovic and Dr Löhr have also received financial support for writing a scientific book from Viatrix. All other authors declare that they have no conflicts of interest and nothing to declare.

MP244

HISTORY OF USE OF ORAL CONTRACEPTIVES AND HORMONAL REPLACEMENT THERAPY SEEMS TO IMPACT PROGNOSIS OF WOMEN WITH PANCREATIC CANCER DIAGNOSIS

G. Lauri¹, L. Archibugi¹, R. Ponz de Leon Pisani¹, C. Fortuanto¹, L. De Carolis¹, L. Apadula¹, M. Reni², M. Falconi³, P.G. Arcidiacono¹, G. Capurso¹

¹San Raffaele Hospital, Pancreatico-Biliary Endoscopy and Endosonography Division, Milan, Italy, ²San Raffaele Hospital, Department of Oncology, Milan, Italy, ³San Raffaele Hospital, Pancreatic Surgery and Transplantation Division, Milan, Italy

Contact E-Mail Address: gaetanolauri.94@gmail.com

Introduction: Hormonal exposure influences cancer initiation and progression in several organs, including the pancreas. The association between gynecological factors and the onset of pancreatic adenocarcinoma (PDAC) is conflicting, with some studies showing a reduced risk of PDAC with the use of hormonal replacement therapy (HRT) or with having had a late-onset menopause. Nonetheless, the association between gynecological factors and disease prognosis has not yet been investigated. Our objective was to evaluate whether gynecological/reproductive factors affect PDAC prognosis.

Aims & Methods: This was a single-center retrospective analysis of a prospectively maintained database of PDAC patients. Risk factors were assessed via questionnaires regarding gynecologic/reproductive factors (age at menarche, menopause, years of fertility, breastfeeding, pregnancy, miscarriages, use of oral contraceptives (OC) or HRT), medical history, and prognosis were evaluated with follow-up visits and/or telephonic calls. Continuous variables were investigated using the Mann-Whitney test, and factors associated with survival probability were evaluated using Cox's proportional hazards model, adjusting for potential confounders.

Results: 228 PDAC women were analyzed, with mean age at diagnosis being 68. The most frequent stages were borderline resectable (35.9%) and locally advanced (25.4%), with a median overall survival (OS) of 14 months. The age of PDAC onset for patients with previous use of OC was significantly lower than that of non-users (63 years vs. 72; $p < 0.0001$), and OC use was associated with a trend toward increased survival (HR 0.6; 95%CI: 0.35-1.03; $p = 0.06$). In addition, previous use of HRT was associated

with a reduced risk of recurrence or progression (HR, 0.4; 95%CI: 0.26-0.99; $p = 0.001$). No differences in survival or progression-free probability were observed with the other factors.

Conclusion: This is the first study to evaluate whether gynecological/reproductive factors are associated with the prognosis of PDAC patients, with the use of OC and HRT being the most relevant factors. Previous OC users had a significantly lower onset age for PDAC and a borderline significant association was seen with increased survival. Additionally, HRT use is associated with a reduced risk of tumor recurrence or progression. These data need to be confirmed, and the potential mechanisms need to be elucidated.

Disclosure: Nothing to disclose.

MP245

PROTEIN N-GLYCOSYLATION TRAITS CAN ACCURATELY DISTINGUISH PANCREATIC CANCER CASES FROM A HETEROGENEOUS GROUP OF CONTROLS

A. Bogdanski^{1,2}, D. Klatte^{1,2}, Y. Bi¹, K. Clift¹, J. van Hooft², M. van Leerdam^{2,3}, M. Wührer⁴, M. Wallace¹, Y. van der Burgt⁴
¹Mayo Clinic, Gastroenterology and Hepatology, Jacksonville, United States of America, ²Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ³Netherlands Cancer Institute, Gastrointestinal Oncology, Amsterdam, Netherlands, ⁴Leiden University Medical Center, Center for Proteomics and Metabolomics, Leiden, Netherlands

Contact E-Mail Address: a.m.bogdanski@lumc.nl

Introduction: New methods are urgently needed to detect pancreatic ductal adenocarcinoma (PDAC) at an earlier stage to improve outcomes.¹

²We have previously reported six protein N-glycosylation traits (NGTs) and further grouped these into three biologically distinct ones to discriminate PDAC patients from healthy controls with an area under the curve (AUC) of 0.81-0.88.³ A subsequent longitudinal study revealed glycosylation differences up to 50 months prior to diagnosis, indicating potential for early detection.⁴ However, external validation is needed to determine accuracy of this biomarker panel. Moreover, it is unknown whether this panel can differentiate PDAC in a diverse group that resembles clinical practice better. Therefore, this study aims to validate the biomarker panel in a heterogeneous cohort.

Aims & Methods: Protein N-glycans in prospectively collected plasma samples from Mayo Clinic were analyzed by mass spectrometry at the Leiden University Medical Center using a semi-automated preparation protocol.⁵ Glycosylation profiles were determined and compared between PDAC cases and controls. The control group consisted of imaging-confirmed pancreatic disease-negative controls and individuals with benign pancreatic diseases, including (non)-mucinous cysts and pancreatitis. Logistic regression was performed to calculate odds ratios (ORs) for the six previously reported protein NGTs. Additionally, AUC, sensitivity and specificity were calculated to determine the accuracy of the three biologically distinct NGTs (antennarity (CA4), sialylation (A3F0L), and fucosylation (CFa)) in discriminating PDAC cases from controls.

Results: We included 232 individuals, of whom 42 (18.1%) were diagnosed with PDAC, and 190 (81.9%) served as controls. Among controls, 59 (31.1%) were pancreatic disease-negative and 131 (68.9%) had benign pancreatic diseases. Median age of PDAC cases and controls was 71.7 (IQR=14.5) and 65.5 years (IQR=17.6), respectively. Among PDAC cases, 19 (45.2%) were female, and 106 (52.2%) among controls. The BMI in PDAC cases and controls was equal (26.8 (IQR=7.0) and 26.6 (IQR=7.6), respectively). Table 1 shows ORs for the six NGTs and PDAC. The AUC for the three biologically distinct traits was 0.77 (95% CI: 0.69-0.86), with a sensitivity of

0.81 (95% CI: 0.69-0.93) and specificity of 0.70 (95% CI: 0.64-0.76). When comparing PDAC cases to pancreatic disease-negative controls, the AUC was 0.83 (95% CI: 0.74-0.92), with a sensitivity of 0.79 (95% CI: 0.64-0.90) and specificity of 0.80 (95% CI: 0.69-0.90).

Variables	PDAC compared to Heterogeneous cohort		PDAC compared to pancreatic disease-negative cohort	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
CA2	0.90 (0.85-0.95)	<0.001	0.86 (0.79-0.93)	0.001
CA4	1.59 (1.30-1.97)	<0.001	2.08 (1.49-3.10)	<0.001
CFa	1.76 (1.28-2.47)	0.004	3.40 (1.86-7.15)	0.002
A3F0L	0.91 (0.84-0.97)	0.043	0.82 (0.72-0.91)	0.005
A3F0E	1.17 (1.07-1.29)	0.004	1.37 (1.18-1.64)	0.001
A3FE	1.90 (1.39-2.66)	0.001	2.58 (1.69-4.23)	<0.001

Table 1: The odds ratios for six glycosylation traits distinguishing pancreatic ductal adenocarcinoma cases from a heterogeneous cohort, including pancreatic disease-negative and benign pancreatic diseases controls. A subanalysis was performed for disease-negative controls. The Bonferroni correction was used to account for multiple testing. Abbreviations: PDAC= pancreatic ductal adenocarcinoma, CI= confidence interval.

Conclusion: Distinctive NGTs from plasma protein differentiate PDAC from non-PDAC in a diverse group, consisting of cystic pancreatic diseases and pancreatitis. This panel holds potential for future early detection methods.

- References:** 1. Klatte DCF, Wallace MB, Löhr M, Bruno MJ, van Leerdam ME. Hereditary pancreatic cancer. *Best Pract Res Clin Gastroenterol.* 2022;58-59:101783.
2. Goggins M, Overbeek KA, Brand R, Syngal S, Del Chiaro M, Bartsch DK, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut.* 2020;69(1):7-17.
3. Vreeker GCM, Hanna-Sawires RG, Mohammed Y, Bladergroen MR, Nicolardi S, Dotz V, et al. Serum N-Glycome analysis reveals pancreatic cancer disease signatures. *Cancer Med.* 2020;9(22):8519-29.
4. Levink IJM, Klatte DCF, Hanna-Sawires RG, Vreeker GCM, Ibrahim IS, van der Burgt YEM, et al. Longitudinal changes of serum protein N-Glycan levels for earlier detection of pancreatic cancer in high-risk individuals. *Pancreatology.* 2022;22(4):497-506.
5. Vreeker GCM, Nicolardi S, Bladergroen MR, van der Plas CJ, Mesker WE, Tollenaar R, et al. Automated Plasma Glycomics with Linkage-Specific Sialic Acid Esterification and Ultrahigh Resolution MS. *Anal Chem.* 2018;90(20):11955-61.

Disclosure: Nothing to disclose.

MP246

REDUCED RISK OF PANCREATIC CANCER ASSOCIATED WITH REGULAR ASPIRIN USE IN TYPE 2 DIABETES PATIENTS

J.T. Tan¹, K.-S. Cheung^{1,2}, X. Mao^{2,1}, W.-K. Seto^{1,2}

¹The University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong, ²The University of Hong Kong-Shenzhen Hospital, Department of Medicine, Shenzhen, China

Contact E-Mail Address: tjt97@connect.hku.hk

Introduction: Diabetes mellitus (DM) is a substantial risk factor for pancreatic cancer (PC). Concurrently, aspirin has been implicated to have chemopreventive effect against cancer of digestive system. However, studies regarding the effect of aspirin on mitigating PC risk among DM populations remain scant.

Aims & Methods: We aimed to examine whether regular use of aspirin was associated with a reduced risk of PC after adjusting for known risk factors among type 2 diabetes (T2D) patients.

This was a territory-wide, retrospective cohort study of newly diagnosed T2D patients between 2001 and 2015 in Hong Kong. Exclusion criteria included <18 years old, history of PC, pancreatic neuroendocrine tumor, serous cystadenoma, chronic or acute pancreatitis, and pancreatic cyst. The outcome of interest was pancreatic cancer. Adjusted hazard ratios (aHRs) for outcomes associated with aspirin use were calculated using multivariable Cox regression models. Aspirin use was treated as a time-varying covariates (≥ 180 days use at each yearly interval) in the analysis to address and minimize immortal-time bias.

Results: We identified 342,920 T2D patients (52.2% male, mean age: 58.8 $\pm$ 11.6 years), including 43,634 (12.7%) aspirin users. During a mean follow-up of 11.1 $\pm$ 4.2 years, 1,114 (0.3%) patients developed PC, with an incidence rate of 2.92 per 10,000 person-years. Aspirin use was associated with a reduced PC risk (HR 0.55, 95%CI 0.46-0.66). When compared with the reference group (never use), a lower risk was observed with increasing frequency, with the exception of daily use. In addition, longer durations of aspirin use were associated with a progressively lower PC risks (HR 0.83, 95%CI 0.71-0.96, for less than five years of use; HR 0.56, 95%CI 0.45-0.69, for five to ten years of use; and HR 0.27, 95%CI 0.20-0.36, for ten or more years of use. Both frequency and duration of aspirin use demonstrated statistically significant trends ($P_{\text{trend}} < 0.001$) (Table 1).

Aspirin use	No. of patients (n=342,920)	No. of PC (n=1,114)	HR (95% CI)	P*	P _{trend}
Frequency					
Never user	219,674	736	ref	-	<0.001
<Monthly use	13,809	52	0.66 (0.50-0.88)	0.004	
Monthly to <weekly use	13,274	44	0.59 (0.43-0.80)	<0.001	
Weekly to <daily use	73,232	201	0.54 (0.46-0.63)	<0.001	
Daily use	22,931	81	0.90 (0.69-1.16)	0.401	
Duration (years)					
Never user	219,674	736	ref	-	<0.001
<5	54,029	223	0.83 (0.71-0.96)	0.015	
5 - <10	40,003	99	0.56 (0.45-0.69)	<0.001	
≥ 10	29,214	56	0.27 (0.20-0.36)	<0.001	

Table 1. HRs and 95% CIs for the association between frequency and duration of aspirin use and risk of pancreatic cancer.

*Cox proportional hazards model was used to calculate the P values. Adjusted covariates included age, sex, lifestyle factors (body mass index, smoking, and alcohol use), metabolic disorders (dyslipidemia and hypertension), time-weighted mean HbA1c, DM complications, cardiovascular diseases, other anti-diabetic medications, non-aspirin non-steroidal anti-inflammatory drugs, and statins.

Abbreviation: CI, confidence interval; HR, hazard ratios; PC, pancreatic cancer; ref, reference

Conclusion: Aspirin use was associated with a reduction in PC risk among T2D patients, which was dependent on both frequency and duration of use. Notably, this trend was observed with increased frequency of use, with the exception of daily use. Further studies are warranted to assess long-term effects and potential risks.

Disclosure: Nothing to disclose.

Coeliac disease: Part 2

10:00-11:00 / Poster Stage 5

MP247

METABONOMICS FINDINGS SUPPORT CELIAC DISEASE AS MULTIFACTORS DISORDER

J. Wu¹, X. Wu², W. Zhang³, Y. Li⁴, T. Shi⁵, W. Hui⁵, X. Ruan⁶, H. Bai⁷, Q. Wu⁶, F. Gao⁵, Gao Feng- Wu Jing Collaboration Group
¹Research Institute Of Chinese Medicine Of Nanjing University, Nanjing Drum Tower Hospital, Nanjing, China, ²Henan Province Hospital of Traditional Chinese Medicine, Gastroenterology Department, Zhengzhou, China, ³Drum Tower Clinical College of Nanjing University of Chinese Medicine, Department of Internal Medicine of Traditional Chinese Medicine, Nanjing, China, ⁴Hezhou Chinese Medicine Hospital, Gastroenterology department, Hezhou, China, ⁵People's Hospital of Xinjiang Uygur Autonomous Region, Department of Gastroenterology, Urumqi, China, ⁶Affiliated hospital of Nanjing University of Chinese medicine, Department of Gastroenterology, Nanjing, China, ⁷BDA Branch of Dongfang Hospital of Beijing University of Chinese Medicine, Department of General Internal Medicine, Beijing, China

Contact E-Mail Address: wujing@njucm.edu.cn

Introduction: Celiac disease (CeD) is a common autoimmune disease among Caucasian people. It had been occasionally reported in southern China. However, cases of celiac disease are more common in the north-west region.

Aims & Methods: In order to elucidate the potential pathogenesis of celiac disease in the Chinese patients, metabolomics could be the good approaches for primary study. We used pseudotargeted metabolomics techniques, such as ultra-high performance liquid chromatography-high resolution mass spectrometry (UHPLC-HRMS) and triple quadrupole mass spectrometry (TQMS) to compare the plasma metabolomics differences of 15 celiac disease patients in Northwest China with 15 healthy volunteers and 30 inflammatory bowel disease patients. We also investigated the dietary and nutritional status of research participants and used Linear mixed effects calibration to perform factor correction on metabolomics results. Informed consent was obtained from all participants, and the study was approved by the Ethics Committee at Affiliated Hospital of Nanjing University of Chinese Medicine(2019NL-085-02) and the ethics committee of the people's Hospital of Xinjiang Uygur Autonomous Region (KY20220311067).

Results: The average age of CeD patients is 43.9 years old, 13 female and 2 male. The average of tissue transglutaminase antibody, tTG is 1792 (CU). Under the condition of false discovery rate (FDR) < 0.05, variable importance projection (VIP) > 1.0, and fold change (FC) > 1.5 or < 2/3, we found 330 plasma differential metabolites with 200 positive ions and 130 negative ions in celiac disease when compared with healthy control. Then, with area under the curve (AUC) ≥ 0.85 and FC ≥ 2.5 or ≤ 0.4, 146 potential biomarkers were identified, such as, fructose-6-phosphate(F6P), D-Erythrose 4-phosphate, which belongs to the pentose phosphate pathway (the abundance decreased), and succinic acid, Citric acid, isocitric acid, which belongs to the citric acid cycle (the abundance increased). Other fatty acid metabolites, such as 13-Hydroxyoctadecadienoic acid (13-HODE) were also involved. Amino acid derivatives, such as phenylacetyl-L-glutamine were part of candidate biomarkers. D-ribose 1,5-bisphosphate, a compound which is not a naturally occurring metabolite in human was found as a significant differentiate substance in our study. The results of comparison between celiac disease and inflammatory bowel disease patients were quite similar to the results compared with healthy controls.

varID	Compounds	Fold Change (FC)	p(U test)	FDR	PLSDA_VIP	OPLSDA_VIP
V242	Phenylacetyl-L-glutamine	3.0134	0.000704022	0.0022697	1.438867152	0.988966277
V15	D-Ribulose 1,5-bisphosphate	25.053	2.92E-06	3.05E-09	2.098764965	0.130716763
V219	D-Erythrose 4-phosphate	0.30481	2.45E-05	7.59E-06	1.642712256	0.652725141
V106	Succinic acid	2.5617	0.002955761	0.0010333	1.386618477	0.712218748
V118	Citric acid	2.8584	2.92E-06	9.09E-14	2.024053652	2.724307005
V72	Isocitric acid	4.0564	2.92E-06	7.76E-12	1.974868662	1.139193882
V442	13-HODE	20.218	0.000603666	0.0003052	1.452028839	0.670034178
V61	F6P	0.19911	2.92E-06	8.16E-16	2.061747407	0.07517334

Table 1. Parts of potential biomarkers for Celiac disease when compared with healthy controls.

Conclusion: Metabonomics findings support celiac disease as multifactors disorder. The abundance of the main metabolites in the pentose phosphate pathway decreases and the abundance of the main metabolites in the citric acid cycle increases in the Chinese patients with celiac disease. Changes in central carbon energy metabolism are the main aspects of celiac disease. Environmental factors, which might be part of the human exposome, also could contribute for the development of CeD. Specific mechanism needs further exploration.

References: 1.Wu J, Xia B, von Blomberg BM, Zhao C, Yang XW, Crusius JB, Peña AS. Coeliac disease: emerging in China? Gut. 2010 Mar;59(3):418-9. doi: 10.1136/gut.2009.197863. PMID: 20207652.

2. Wu X, Liu K, Wu Q, Wang M, Chen X, Li Y, Qian L, Li C, Dai G, Zhang Q, Mu G, Wu J, Shan Z. Biomarkers of Metabolomics in Inflammatory Bowel Disease and Damp-Heat Syndrome: A Preliminary Study. Evid Based Complement Alternat Med. 2022 Jul 1;2022:3319646. doi: 10.1155/2022/3319646. PMID: 35815273; PMCID: PMC9270137.

3. Bernini P, Bertini I, Calabrò A, la Marca G, Lami G, Luchinat C, Renzi D, Tenori L. Are patients with potential celiac disease really potential? The answer of metabonomics. J Proteome Res. 2011 Feb 4;10(2):714-21. doi: 10.1021/pr100896s. Epub 2010 Dec 13. PMID: 21090607.

4. Martín-Masot R, Mota-Martorell N, Jové M, Maldonado J, Pamplona R, Nestares T. Alterations in One-Carbon Metabolism in Celiac Disease. Nutrients. 2020 Dec 2;12(12):3723. doi: 10.3390/nu12123723. PMID: 33276620; PMCID: PMC7761552.

Disclosure: Mr. Gao Feng is the first corresponding author. Ms. Wu Jing is the second corresponding author, who is also the first author and is responsible for submitting and presenting this work.

MP248

MODELLING ENTEROVIRUS-INDUCED PREDISPOSITION TO CELIAC DISEASE: SINGLE-CELL TRANSCRIPTOMIC ANALYSIS OF COXSACKIE B VIRUS-INFECTED ORGANOID

H. Hien Le¹, V. Dotsenko¹, A. Sioofy Khojine², J. Laiho², H. Hyöty², K. Viiri¹

¹Tampere University and Tampere University hospital, Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere, Finland, ²Tampere University, Faculty of Medicine and Health Technology, Tampere, Finland

Contact E-Mail Address: hien.le@tuni.fi

Introduction: Celiac disease (CeD) is an autoimmune disorder influenced by genetic and environmental factors, primarily triggered by dietary gluten in genetically predisposed individuals. Enterovirus infections, as an additional environmental factor, have been linked to the development of CeD. We aimed to model molecular mechanisms on how enterovirus infection predisposes to CeD.

Aims & Methods: We used single-cell RNA sequencing (scRNAseq) and one enterovirus, coxsackievirus B1 (CVB1) infection in human intestinal

organoids as a model to explore the comprehensive transcriptional response of the intestinal epithelium damage. A total of 3940 single epithelial cells were evaluated for lineage biomarkers, differentially regulated genes, receptors, inflammation- and antiviral responses.

Results: CVB1 infection induced innate immune antiviral response in the intestinal epithelium. Single cell transcriptional profiling of the epithelium indicated that the main response to CVB1 infection expectedly occurs through interferon (IFN) related pathways. CVB1 induced innate IFN-2/3 and IFN- β 1 and, surprisingly, also triggered high expression of transglutaminase 2 (TG2) in human intestinal organoids.

Conclusion: Our work provides mechanistic, single-cell level, detail how CVB infection can poise to gluten-induced inflammatory damage in CeD. We hypothesise that CVB infection-induced surge of innate interferons in the intestinal epithelium can predispose to CeD by inducing the TG2 gene expression in specific epithelial cells and accelerate gliadin deamidation, step necessary to CeD pathogenesis.

In addition, our pathway analyses provide insights as to how the intestinal epithelium responds to the enterovirus infection and can possibly reveal novel anti-viral drug targets to inhibit virus-host interaction in endeavors to prevent CeD.

Disclosure: Nothing to disclose.

MP249

PRE-NATAL EXPOSURE TO ANTIBIOTICS IS ASSOCIATED WITH INCREASED PREVALENCE OF CELIAC DISEASE

R. Nassar¹, E. Brav¹, G. Howard¹, G. Ling¹, B. Yerushalmi¹

¹Soroka University Medical Center, Pediatric Gastroenterology Unit, Beer Sheva, Israel

Contact E-Mail Address: raouf.n@gmail.com

Introduction: Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains in genetically susceptible individuals. The prevalence of CD has increased dramatically over the last decade, with a prevalence of 1%-3%. Several risk factors for CD are reported, including genetic, nutritional, infections, mode of delivery, and exposure to post-natal antibiotics.

Aims & Methods: The aim of the study is to examine the association between prenatal exposure to antibiotics and CD. In a retrospective cohort study, we enrolled all the children born between 2000 and 2023 to mothers who belong to "Clalit" HMO and compared the prevalence of the CD between the children whose mothers purchased one or more antibiotics during the pregnancy and the children who didn't.

Results: A total of 658,899 children have met the inclusion criteria; 5,706 children were diagnosed with CD during the study years, with a prevalence of 0.86:100. The prevalence of CD among the children whose mothers received one or more antibiotic treatments during pregnancy was higher compared to those who didn't (0.9:100 vs. 0.8:100, p-value=0.003). A multivariable regression including the mother's age, mode of delivery, and history of CD of the mother showed RR of 1.07 (95%CI 1.01-1.13).

Conclusion: Unlike previous studies, our study showed a positive association between prenatal exposure to antibiotics and CD.

This association can be explained by several theories, including the effect of antibiotics on the maternal microbiome and the stimulation of the immune system. Further studies are warranted to explore the mechanism of this association.

References: 1. Lebowitz B, Rubio-Tapia A. Epidemiology, Presentation, and Diagnosis of Celiac Disease. *Gastroenterology*. 2021;160(1):63-75. 2. Kołodziej M, Patro-Goląb B, et al. Association between early life (prenatal and postnatal) antibiotic administration and coeliac disease: a systematic review. *Arch Dis Child*. 2019;104(11):1083-1089.

3. Mustalahti K, Catassi C, Reunanen A, et al. The prevalence of celiac disease in Europe: Results of a centralized, international mass screening project. *Ann Med*. 2010;42(8):587-595.

4. Barada K, Bitar A, Mokadem MAR, et al. Celiac disease in middle eastern and North African countries: A new burden? *World J Gastroenterol*. 2010;16(12):1449-1457.

5. Ludvigsson JF, Bai JC, Biagi F, et al. Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology. *Gut*. 2014;63(8):1210 LP - 1228.

6. Mårild K, Ludvigsson J, et al. Antibiotic exposure in pregnancy and risk of coeliac disease in offspring: a cohort study. *BMC Gastroenterol*. 2014;14:75.

7. Mårild K, Kahrs CR, et al. Maternal Infections, Antibiotics, and Paracetamol in Pregnancy and Offspring Celiac Disease: A Cohort Study. *J Pediatr Gastroenterol Nutr*. 2017;64(5).

8. Fallani M, Young D, et al. Intestinal microbiota of 6-week-old infants across Europe: geographic influence beyond delivery mode, breast-feeding, and antibiotics. *J Pediatr Gastroenterol Nutr*. 2010;51(1):77-84.

Disclosure: Conflict of Interest: None.

MP250

THE IMPORTANCE OF SIMULATED INADVERTENT GLUTEN EXPOSURE IN CELIAC DISEASE CLINICAL TRIALS

J. Silvester¹, M. Schumann², J. Murray³, M. M. Leonard⁴, R. Mohrbacher⁵, S. Budree⁶, N. Cheinquer⁶, A. Halper⁶, K. Hillen⁵, Q. Lei⁶, R. Mueller⁵, D.A. Leffler⁶, D. Schuppan⁷

¹Celiac Disease Program, Children's Hospital, Boston, United States of America, ²Charité – University Medicine, Department of Gastroenterology, Rheumatology and Infectious Diseases, Berlin, Germany, ³Mayo Clinic, Gastroenterology & Hepatology, Rochester, United States of America, ⁴Massachusetts General Hospital, Harvard Medical School, Division of Pediatric Gastroenterology and Nutrition, Department of Pediatrics, and Center for Celiac Research and Treatment, Boston, United States of America, ⁵Dr. Falk Pharma GmbH, Department of Clinical Research, Freiburg, Germany, ⁶Takeda Development Center Americas, Inc., Cambridge, United States of America, ⁷Medical University Mainz - Institute of Translational Immunology, Medical University Mainz, Institute of Translational Immunology, Mainz, Germany

Contact E-Mail Address: detlef.schuppan@unimedizin-mainz.de

Introduction: There is an unmet need for adjunctive therapies for patients with celiac disease (CeD) who experience inadequate disease control while maintaining a gluten-free diet (GFD). The optimal trial design to assess CeD treatment efficacy is unclear and increased adherence to a GFD during trials may improve disease control. We assessed symptom severity changes during the screening and run-in periods (no treatment) of two phase 2b CeD trials, one using simulated inadvertent gluten exposure (SIGE) and one without.

Aims & Methods: In two concurrent ongoing phase 2 CeD trials (NCT05353985 and EudraCT2020-004612-97) daily gastrointestinal (GI) symptom severity was measured using the Celiac Disease Symptom Diary 2.1® during the screening and run-in periods (4 weeks each in NCT05353985; 6 weeks and 5 weeks, respectively in EudraCT2020-004612-97) before any treatment administration. In both trials, eligible patients had biopsy-confirmed CeD and were experiencing CeD-related symptoms and enteropathy despite following a GFD. NCT05353985 included food bars containing ~500 mg gluten, consumed 3-times weekly after Week 2, for 2 weeks during the run-in period (post randomization). EudraCT2020-004612-97 did not include gluten exposure. Mean GI symptom severity scores were calculated each week during the screening and run-in periods.

Results: From the start of the screening period through to the end of the run-in period, mean GI symptom severity scores improved significantly in EudraCT2020-004612-97 (0.96 at Week 1 of screening, and 0.75 at Week 5 of run-in) whereas changes were non-significant in NCT05353985 (0.96 at Week 1 of screening and 0.92 at Week 4 of run-in).

Conclusion: Clinical trial participation may result in an improvement in CeD-related GI symptoms due to better GFD adherence. Administration of SIGE can minimize such trial effects and does not worsen symptoms in patients with CeD.

Disclosure: SB, NC, AH, DAL and QL are employees and shareholders of Takeda.

KH RM and RM are employees of Dr. Falk Pharma GmbH.

JM reports grants (to institution) from, National Institutes of Health, Immunogenix, Takeda Pharmaceutical, Allakos, ProventionBio, Oberkötter Foundation, and 9Meters, Inc.; contract (to institution) from Kanyos Bio (a wholly owned subsidiary of Anokion); and consultancy fees from Johnson and Johnson, Bristol Myers Squibb, Intrexon Corporation, Dren Bio, Neoleukin, Reistone pharma, GSK, Immunic Therapeutics, Brightseed Bio, Chugai Pharma, Alimentiv, Equillium, Ukko, Medibeacon, Israel Biotech Fund, Precigen, triangle insights group, Sanofi, Zag Bio, Loop bio and Orbimed; and has received royalties from Evelo. MS has no funding to disclose relating to this study and is the Principal Investigator in the EudraCT2020-004612-97 clinical trial.

MS has no funding to disclose relating to this study and is the Principal Investigator in the EudraCT2020-004612-97 clinical trial.

ML receives research funding from Takeda and Moderna, and has previously acted as a consultant for Anokion and Amgen.

JS reports grants (to institution) from Celiac Disease Foundation, National Institutes of Health, Takeda Pharmaceutical, Allan Foundation and consultancy fees from Alimentiv and Takeda Pharmaceuticals.

DS received study related management/advisory fees from Dr. Falk Pharma.

MP251

INVESTIGATION OF BODY COMPOSITION PARAMETERS IN PATIENTS WITH CELIAC DISEASE ON A GLUTEN-FREE DIET. PROSPECTIVE, MULTICENTER, CASE-CONTROL STUDY (ARCTIC STUDY)

M.Z. Peresztegi¹, Z. Vereczkei², Z. Sipos³, N. Farkas^{3,3}, B. Máth⁴, K. Lemes⁵, Z. Lenart⁵, V. Papp⁶, E. Dakó⁷, S. Dakó⁶, J. Bajor⁸

¹University of Pécs Medical School, Pécs, Hungary, ²University of Pécs Medical School, Institute for Translational Medicine, Pécs, Hungary, ³University of Pécs Medical School, Department of Medical Statistics and Informatics, Pécs, Hungary, ⁴Semmelweis University, Budapest, Hungary, ⁵University of Szeged 1st Dept. of Internal Medicine, Szeged, Hungary, ⁶Semmelweis University, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary, ⁷Semmelweis University, Faculty of Health Sciences, Budapest, Hungary, ⁸University of Pécs, Medical School, 1st Department of Medicine, Department of Gastroenterology, Pécs, Hungary

Contact E-Mail Address: peresztegzis@gmail.com

Introduction: Body composition parameters in patients with celiac disease differ from the normal population, and in some cases, they do not completely normalize even with a gluten-free diet. Despite weight gain on the diet, the change in body composition is generally unfavorable (less increase in fat-free body mass, significantly higher increase in fat content). One reason for this is improved absorption, but the high calorie, sugar,

and fat content of the gluten-free diet can also lead to undesirable weight gain and unfavorable metabolic changes (dyslipidemia, fatty liver, insulin resistance) without dietary control.

Aims & Methods: In our prospective multicenter, case-control study (ARCTIC study), we examined body composition parameters and blood lipid levels of patients with celiac disease who had been on a gluten-free diet for at least 1 year and compared them to those of healthy control individuals.

Patients from three university centers with celiac disease participated in the study. Body composition analysis was performed using an Inbody 770 device, measuring the following parameters: body mass index (BMI), waist-hip ratio, Inbody score, Skeletal muscle mass (SMM), Percent body fat (PBF), Visceral fat area (VFA). Blood lipids including total cholesterol, LDL, and triglyceride levels were measured. Abdominal ultrasound was performed to assess the degree of hepatic steatosis. Fischer's exact test and Chi-Square test were used for categorical variables, and the Welch Two Sample t-test was used to assess continuous variables. A p-value less than 0.05 is considered statistically significant.

Results: 97 patients with celiac disease (78 female, 19 male) and 47 (40 female, 7 male) control individuals were included. The mean age of patients with celiac disease (36.2 years) was slightly higher than that of controls (32.5 years), but the difference was not significant. The mean waist and hip circumference were higher in patients with celiac disease but did not reach the significance threshold ($p=0.051$ and $p=0.10$). Among the body composition parameters, higher mean BMI, Skeletal muscle mass, Percent body fat, Visceral fat area, and lower Inbody score were observed, but the differences were not significant ($p=0.31$, 0.16, 0.72, 0.39, 0.62). Based on BMI, 9.3% of celiac patients were underweight, 54.7% had normal weight, 18.5% were overweight, and 17.5% were obese. These proportions for controls were: 8.5%, 66%, 19%, 6.5%. The mean total cholesterol level was lower in patients with celiac disease ($p=0.043$), while the mean triglyceride level was higher ($p=0.85$). We found significantly more cases of hepatic steatosis in celiac patients than in controls ($p=0.012$). Among them, 83% met the Metabolic Dysfunction-Associated Liver Disease (MASLD) criteria, while 60% of controls with hepatic steatosis did.

Conclusion: The body composition parameters of celiac patients on a gluten-free diet are less favorable compared to control cases, albeit not significantly. Our data suggest that for most of these patients, the problem is not caused by malabsorption and malnutrition. Preventing cardiovascular and metabolic complications poses a new challenge in patient care.

Disclosure: Funding: National Research, Development and Innovation Office (grant FK142942); ÚNKP-23-3-II-PTE-1855; PTE-KITEP-2023-311.

MP252

SYMPTOM SEVERITY AND QUALITY OF LIFE IN PATIENTS WITH CELIAC DISEASE FOLLOWING A GLUTEN-FREE DIET: A US PATIENT SURVEY

M. Arvizu¹, J.R. Marden², S. Sethi², D. Adams³, N. Cheinquer¹, M.G. Geller⁴, L. M. Meckley¹, D.A. Leffler^{1,5}, S. Ghura¹, E. Liu⁶, R. Saad¹

¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²Analysis Group, Inc., Boston, United States of America, ³Vanderbilt University Medical Center, Nashville, United States of America, ⁴Celiac Disease Foundation, Woodland Hills, United States of America, ⁵Celiac Center, Beth Israel Deaconess Medical Center, Harvard Medical School Celiac Research Program, Boston, United States of America, ⁶Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, United States of America

Contact E-Mail Address: mariel.arvizu-boy@takeda.com

Introduction: This study assessed typical symptoms (abdominal pain, bloating, diarrhoea, nausea, tiredness) in patients with celiac disease (CeD) following a gluten-free diet (GFD) and evaluated the association between symptom severity and quality of life (QoL) to address limited data in this area.

Aims & Methods: In the Virtual Celiac Symptoms Study (NCT05309330), patients reported daily symptoms using the Celiac Disease Symptom Diary 2.1[®] (CDS 2.1[®]) over 12 weeks and completed patient-reported outcome measures (PROMs), with 7-day look-back, at specified timepoints, including the Impact of Celiac Disease Symptoms Questionnaire (ICDSQ) and the Patient Global Impression of Severity (PGI-S) measure. Spearman's correlation coefficient (SCC) and generalized linear regression evaluated associations between symptom severity and QoL PROM scores and mean differences were adjusted for key demographics.

Results: In total, 480 participants completed the study (mean [standard deviation] age: 31 [15] years, 81.7% female, 93.8% White). For all CeD symptoms measured, there was a positive linear association between CDS 2.1[®] symptom severity and PROM scores ($p < 0.001$). The SCC between symptom severity and PROMs was 0.45–0.62 (PGI-S) and 0.33–0.56 (ICDSQ). The strongest correlations between gastrointestinal symptom severity (abdominal pain, bloating, diarrhoea, and nausea) and PROMs were between PGI-S score and abdominal pain (SCC: 0.62) and bloating (SCC: 0.59). Patients with severe/very severe abdominal pain versus none had mean (95% confidence interval [CI]) 63.1% (53.2–73.6) and 217.5% (165.1–280.2) greater PGI-S and ICDSQ scores, respectively.

Conclusion: The results indicate that higher symptom severity is strongly associated with worse QoL in patients with CeD following a GFD and that CDS 2.1[®] assesses patient-relevant symptom severity in CeD.

Disclosure: MA, NC, DAL, SG and RS are employees and shareholders of Takeda. LMM was an employee of Takeda at the time of the study. JRM and SS are employees of Analysis Group, Inc., which received research support from Takeda Development Center Americas, Inc. DA has served as a consultant for Takeda Pharmaceuticals and Ironwood Pharmaceuticals. MG is an employee of the Celiac Disease Foundation, which received financial support from Takeda Development Center Americas, Inc. EL serves as a consultant for Takeda Pharmaceuticals and is an author for UpToDate (celiac section) for which he receives royalties.

MP253

QUANTIFYING COELIAC DISEASE EXTENT ON CAPSULE ENDOSCOPY USING A NOVEL MACHINE LEARNING ALGORITHM

C. Johnson^{1,2}, M.G. Shiha^{1,2}, A. Bard^{3,4}, M. McAlindon^{1,2}, R. Sidhu^{1,2}

¹Sheffield Teaching Hospitals, Academic Unit of Gastroenterology, Sheffield, United Kingdom, ²Sheffield University, Division of Clinical Medicine, School of Medicine and Population Health, Sheffield, United Kingdom, ³Motilent Ltd, London, United Kingdom, ⁴William Harvey Research Institute, National Institute for Health Research (NIHR), Barts Biomedical Research Centre, Queen Mary University of London, London, United Kingdom

Contact E-Mail Address: calvin.johnson@nhs.net

Introduction: Machine learning algorithms (MLA) trained on capsule endoscopy (CE) images have shown high accuracy in detecting signs of villous atrophy in patients with coeliac disease. However, using MLA to quantify coeliac disease extent and the proportion of small bowel affected has not been studied.

Aims & Methods: We analysed CE videos of adult patients (≥ 18 years) with biopsy-proven coeliac disease from a large prospectively maintained database. Demographic, clinical, and biochemical data were collected for all patients. The extent of coeliac disease and the proportion of small bowel affected were calculated for each video by an expert human reader and by a trained MLA. The consistency of agreement between the expert human and the MLA was estimated by intraclass correlation coefficients (ICCs) using a two-way mixed-effects model.

Results: CE videos of 75 patients with CD (median age 59 years [IQR 41.5–68 years], 60% female) were included. The median gastric passage time and small bowel transit time were 16 (IQR 98–50.5) and 277 (IQR 217.5–252) minutes, respectively. Macroscopic features of CD, including scalloping, fissuring, mosaicism, nodularity, were identified beyond the first tertile in 34.7% of patients (extensive disease). The overall agreement between the expert human and MLA for the proportion of small bowel affected was good (ICC 0.799, 95% CI 0.572–0.893). Patients with extensive small bowel CD were significantly more likely to have anaemia or ferritin deficiency than those with proximal disease ($p < 0.01$ and 0.026 respectively).

Conclusion: Trained MLA can accurately quantify the extent of coeliac disease and the proportion of small bowel involvement on CE, showing a good agreement with expert human assessment. This machine learning quantification of coeliac disease extent allows closer monitoring for nutritional deficiencies associated with extensive disease and provides an objective and standardised endpoint on response to therapy in clinical trials. Larger training and validation datasets are required to optimise the performance of the MLA.

Disclosure: Nothing to disclose.

MP254

PREVALENCE OF AVOIDANT/ RESTRICTIVE FOOD INTAKE DISORDER AMONG PATIENTS WITH NEWLY DIAGNOSED CELIAC DISEASE

A. Trikola¹, E. Beka², I. Lappas¹, G. Emmanouilidou¹, M. Ellina¹, L. Chrisaugis¹, G. Kranidiotis¹, G. Stefanidis¹, N. Viazis²

¹Athens Naval Hospital, Gastrointestinal Department, Athens, Greece, ²Evangelismos Hospital, Gastroenterology, Athens, Greece

Contact E-Mail Address: artemis.trikola@yahoo.gr

Introduction: Patients with recently diagnosed celiac disease (CD), usually present with upper gastrointestinal manifestations, including bloating, abdominal pain and chronic diarrhea or constipation, thus adopting several restrictive tendencies, apart from the standard-of-care gluten-free diet (GFD). Avoidant/restrictive food intake disorder (ARFID) is a newly established eating disorder affecting primarily children, but with emerging evidence among adults. We aimed to examine the prevalence of ARFID and the eating attitude among adults with recently diagnosed celiac disease.

Aims & Methods: In a prospectively maintained cohort of adult patients with a recent diagnosis of celiac disease, we evaluated eating habits of patients with a recent diagnosis of CD who were under GFD through the Eating Attitudes Test (EAT-26) and the prevalence of ARFID through nine item avoidant/restrictive food intake disorder screen (NIAS), containing three subscales (picky eating, appetite, fear).

Results: A total of 28 patients were enrolled [mean age 37.07 years old (IQR 23.47), 22 females (78.6%)], with a mean body mass index (BMI) of 23.7kg/m² (mean weight 65.2 kg and mean height 1,70m). A self-reported suspected food intake disorder had been reported by 35.7% of patients, while 21.4% were referred to a specialized mental care professional and 7.1% had been diagnosed by a non-specific food disorder in the past 6 months. Physical activity was limited or absent in 78.6% of enrolled patients.

Both EAT-26 and NIAS questionnaires displayed acceptable values on reliability analysis (Cronbach's alpha score 0.618 and 0.658 respectively). A total of 14% (4 out of 28 patients, 100% females) met criteria for ARFID, with a mean score of 42 points on the total scale of NIAS. Patients with ARFID reported that other people think that they are too thin ($p=0.004$) and felt external pressure from others to eat ($p<0.001$).

Females reported to push significantly themselves to eat regularly or large amounts of food on a daily basis ($p=0.04$), significantly consumed more time and thought to food ($p<0.001$), enjoyed trying new rich foods ($p=0.02$) and suffered from eating binges ($p=0.003$) compared to males. However, there were no differences between BMI, the self-reported suspected food disorder and the diagnosed mental health conditions. Additionally, CD patients with suspected and diagnosed food disorder scored similarly to all given questionnaires.

Conclusion: In a small sample of patients with recently diagnosed CD, ARFID may present up to 15% and contribute to persistent symptomatology and food restrictive attitude, despite being on GFD. Although females were found to be more susceptible to ARFID, by reporting more binge eating symptomatology and external factors exerting pressure, no significant differences were found on age, gender, BMI in our cohort.

Disclosure: Nothing to disclose.

MP255

PREVALENCE OF PATHOLOGY IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

P. Oka¹, M.G. Shiha¹, A. Finta², L. Madácsy², T.L.M. Wong³, Y. Yuan³, J.Y.W. Lau³, R. Sidhu⁴, M. McAlindon¹

¹Sheffield Teaching Hospitals NHS foundation trust, Gastroenterology, Sheffield, United Kingdom, ²Endo-Kapszula Ltd., Endoscopy Unit, Szekesfehervar, Hungary, ³Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁴Sheffield Teaching Hospitals NHS foundation trust, Academic Dept of Gastroenterology, Sheffield, United Kingdom

Contact E-Mail Address: oka.priya@gmail.com

Introduction: Current guidelines suggest upper and lower GI endoscopy to investigate iron deficiency anaemia (IDA) because of a perceived low risk of small bowel pathology. This is the first study to investigate the entire gastrointestinal tract to localise lesions suspected of causing blood loss in patients with IDA.

Aims & Methods: Patients referred to three centres (Sheffield, Hong Kong and Szekesfehervar, Hungary) for the investigation of IDA underwent small bowel (SB) capsule endoscopy (Navicam, AnX Robotica, Plano, US) a week prior to upper and lower gastrointestinal endoscopy. All lesions were described using terms selected from a predetermined diagnostic list and according to the perceived likelihood of bleeding (P0: unlikely; P1: suspected; P2: likely. Saurin et al., Endoscopy 2003).

Results: Assuming a true prevalence of small bowel lesions of 10% in patients with IDA, a sample size required to have 80% power of getting a 95% confidence interval for the prevalence no wider than 10 percentage points is 160 patients. 164 patients (median age 61 years (IQR 48.2-72); 50.6% male) had a median haemoglobin of 102.0 g/L (IQR 90.0-116.0), ferritin 11(IQR 7- 18). Completion rates for gastroscopy, colonoscopy and capsule endoscopy were 99.3%, 95.7% and 85.9% respectively. Diagnostic yield of P1/P2 lesions by SB capsule (49.3%) was higher than gastroscopy (25.7%) and colonoscopy (26.8%); $p<0.0001$. Four patients had fresh blood seen on capsule the source of which was unclear. Four additional patients were given new diagnoses of coeliac disease at capsule endoscopy which was subsequently confirmed following duodenal biopsy. All lesions were defined by a three-person expert panel review by consensus with a 99.1% agreement.

Gastroscopy pathology	Small bowel (SB) pathology	Colonoscopy pathology
Oesophageal erosions	4	SB angiodysplasia 50
Oesophageal ulcers	4	Small bowel ulcers 18
Oesophageal Varices	2	Ulcerated stenosis 3
Gastric tumour	2	Eroded SB polyp 2
Gastric ulcers	5	Small bowel erosions 21
Gastric angiodysplasia	1	Colonic angiodysplasia 3
Gastric erosions	16	Colorectal cancer 9
Eroded gastric polyp	2	Friable colonic polyps 3
GAVE	3	Haemorrhoids 16
PHG	1	
Duodenal adenoma	1	
Duodenal ulcer	2	
Duodenal erosions	3	
Duodenal angiodysplasia	1	

Table-1: Number of patients with P1/P2 pathology identified at gastroscopy, SB capsule and colonoscopy.

Conclusion: Pathology suspected of, or likely to be, causing blood loss in patients with IDA appears to be commoner in the small bowel than the proximal GI tract or colon. Small bowel examination should be performed routinely to maximise diagnostic yield.

Disclosure: Capsules for the study were provided by AnX robotica.

Clinical presentation and impact on treatment in EoE

10:00-11:00 / Poster Stage 6

MP256

PREVALENCE OF INFLAMMATORY ESOPHAGEAL EXTENT IN EOSINOPHILIC ESOPHAGITIS AND IMPACT ON TREATMENT RESPONSE

A. Sorge¹, G. Aldinio¹, B. Marinoni², R. Penagini¹, D. Maniero³, M. Ghisa⁴, E. Marabotto⁵, N. de Bortoli⁶, P. Visaggi⁷, A. Pasta⁵, V. Dipace⁵, M. Vecchi², E.V. Savarino⁸, M. Coletta²
¹University of Milan, Pathophysiology and Transplantation, Milan, Italy, ²Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy Unit, Milan, Italy, ³University of Padova, Surgery, Oncology and Gastroenterology, Padova, Italy, ⁴S. Maria del Prato Hospital, Feltre, Gastroenterology Unit, DISCOG - UOC Gastroenterologia, Padova, Italy, ⁵OSP Policlinico San Martino, Genova, Italy, ⁶University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ⁷University of Pisa, Gastroenterology Unit, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ⁸University of Padua, Surgery, Oncology and Gastroenterology, Division of Gastroenterology, Padua, Italy

Contact E-Mail Address: andreasure6@gmail.com
Introduction: Eosinophilic esophagitis (EoE) presents with varying histologic extents, yet the impact of comorbidities on eosinophilic distribution and the implications on disease progression and treatment response remains poorly understood.^{1,2} This study aimed to investigate the prevalence of different EoE extents and their impact on disease progression and treatment response within a multicenter cohort.
Aims & Methods: Clinical, endoscopic, and histologic data from adult EoE patients actively followed up at four Italian referral centers from October 2022 to October 2023 were retrospectively collected. The primary endpoint was to assess the prevalence of different EoE histologic extents (proximal, distal, diffuse) based on the presence of a pathological eosinophilic infiltrate (³15 Eo/HPF) and evaluate their association with comorbidities (atopic diseases, gastroesophageal reflux disease), clinical characteristics, endoscopic features. The secondary objective was to compare treatment responses among different histologic extents of EoE.
Results: 149 patients were included (median age: 37 years [IQR 25-51], 38.2% males). Proximal EoE was observed in 8.1% (12/149), distal EoE in 27.5% (41/149), and diffuse EoE in 64.4% (96/149) of patients. In proximal-EoE, male patients were significantly more prevalent (91.7% vs. 68.3% distal-EoE vs. 55.5% diffuse-EoE, P=0.03). No significant differences were found in the rate of autoimmune comorbidities (8.3%, 14.6% distal-EoE, 10.4% diffuse-EoE; P=0.8). Only allergic rhinitis was significantly more prevalent in the distal and diffuse-EoE groups compared to the proximal group (33.3% vs. 72.5% vs. 61.5%, P=0.049). The prevalence of asthma, atopic dermatitis, oral allergy syndrome, and gastroesophageal reflux disease was similar among the three EoE extent groups. Endoscopic inflammatory features at diagnosis were significantly more prevalent in the proximal-EoE group, compared to the distal and diffuse-EoE groups (91.7% vs 53.8% vs 66%; P=0.05). Endoscopic fibrotic features at diagnosis were similar between all the groups (proximal-EoE 50%, distal 42.5%, and diffuse-EoE 51.1%; P=0.6) The clinical response after first-line therapy was comparable in all groups (75.0%, 70.7%, and 69.8%, P=0.93) and proton pump inhibitors were the most frequently prescribed therapy (77.8%). The endoscopic fibrotic remission rate after first-line therapy was higher in the proximal-EoE compared to the distal and diffuse-EoE groups (100.0% vs. 35.7% vs. 13.8%, P=0.0001).

	Overall N=149	Proximal-EoE N=12	Distal-EoE N=41	Diffuse-EoE N=96	P
Age, years, median (IQR)	37 (25-51)	38 (23-69.5)	39 (25-47.5)	37 (26-51)	0.54
Male sex, n (%)	57 (38.2)	11 (91.7)	28 (68.3)	53 (55.2)	0.03
Autoimmune disorders, n (%)	17 (11.4)	1 (8.3)	6 (14.6)	10 (10.4)	0.84
Asthma, n (%)	41 (27.8)	6 (50.0)	9 (22.5)	26 (27.1)	0.17
Atopic dermatitis, n (%)	13 (8.8)	1 (8.3)	4 (10.0)	8 (8.3)	0.90
Allergic rhinitis, n (%)	92 (62.2)	4 (33.3)	29 (72.5)	59 (61.5)	0.049
Oral allergy, n (%)	15(10.1)	0 (0.0)	3 (7.5)	12 (12.5)	0.51
Proven GERD at diagnosis, n (%)	21 (14.3)	1/11 (9.1)	3 (7.5)	17 (17.7)	0.26

Table 1. Demographics and clinical characteristics
EoE, eosinophilic esophagitis; IQR, interquartile range.

Conclusion: In adult patients with EoE, an increasing proximal-to-distal gradient of esophageal eosinophilic infiltrate was observed. There was no clear correlation between the histologic extent of EoE and comorbidities, development of fibrosis, and response to treatment.
References: 1. Ghooz H, Stancampiano FF, Valery JR, et al. Extent of eosinophilic esophagitis predicts response to treatment. *Endosc Int Open* 2021;9:E1234-e1242.
2. Godat A, Mueller R, Schenker D, et al. Eosinophil Distribution in Eosinophilic Esophagitis and its Impact on Disease Activity and Response to Treatment. *Clin Gastroenterol Hepatol* 2023.
Disclosure: Nothing to disclose.

MP257

THE TIME TO EOSINOPHILIC OESOPHAGITIS DIAGNOSIS FOR PATIENTS PRESENTING WITH UPPER GASTROINTESTINAL SYMPTOMS IN PRIMARY AND SECONDARY CARE

N. Umar¹, C. Turnbull², R. Jazrawi³
¹Sandwell and West Birmingham Hospitals NHS Trust, Gastroenterology, West Bromwich, United Kingdom, ²Dr. Falk Pharma GmbH, Bourne End, United Kingdom, ³Dr. Falk Pharma UK Ltd. Medical Department., Bucks, United Kingdom

Contact E-Mail Address: nosheen.umar@nhs.net
Introduction: Patients with eosinophilic oesophagitis often experience diagnostic delays. Untreated eosinophilic oesophagitis may result in fibrosis and stricture formation, leading to morbidity and impaired quality of life. Early diagnosis and treatment can potentially prevent these outcomes and reduce emergency admissions with food bolus obstruction. The reasons for these delays have not been examined in primary care previously. This study quantifies the time to eosinophilic oesophagitis diagnosis and examines factors associated with diagnostic delays.
Aims & Methods: A retrospective cohort study of incident eosinophilic oesophagitis patients between 1st Jan 2006 and 31st Dec 2022 was undertaken using Clinical Practice Research Datalink (CPRD AURUM) linked to hospital admission data in Hospital Episode Statistics. Patients were followed from first proton pump inhibitor (PPI) prescription or presentation with eosinophilic oesophagitis related symptoms (food bolus obstruction or dysphagia) identified from SNOMED CT codes for primary care and ICD-10 codes for secondary care to diagnosis. The association between patient level factors and time to eosinophilic oesophagitis diagnosis was examined using a Robust Poisson regression model.
Results: 2300 eosinophilic oesophagitis patients were studied (67.7% male; age 38 (IQR 30-49)). Median time to diagnosis was 3.6 years (IQR 0.5-8.7). 80.7% patients had a PPI prescription record in primary care prior to eosinophilic oesophagitis diagnosis with a time to eosinophilic oesophagitis diagnosis of 4.9 years (IQR 1.5- 9.7). Factors associated with more than 3 years to diagnosis included: female sex (adjusted risk ratio

1.18, 95% CI 1.10-1.27); smoking (1.11, 1.01-1.23); compared with baseline of elective endoscopy, urgent endoscopy for dysphagia (1.35, 1.18-1.54), urgent endoscopy for food bolus obstruction (1.26, 1.13-1.41), dysphagia presentation in primary care (1.16, 1.08-1.25), food bolus obstruction presentation in primary care (1.11, 1.00-1.23) and PPI prescription in primary care (3.08, 2.58-3.67). 77% of patients had PPI treatment prescribed after eosinophilic oesophagitis diagnosis. 21% patients with no history of asthma or chronic obstructive pulmonary disease were prescribed a steroid inhaler (presumably swallowed) after eosinophilic oesophagitis diagnosis.

Conclusion: Longer time to eosinophilic oesophagitis diagnosis was associated with being female, smoking, food bolus obstruction and dysphagia presentations in primary or secondary care and particularly PPI prescriptions in primary care.

Disclosure: Nothing to disclose.

MP258

MISDIAGNOSIS IS COMMON ON THE PATH TO EOSINOPHILIC ESOPHAGITIS

L. Biedermann¹, K. Dave², C. Zema³, D. Mascia⁴, T. Pennant⁴, J.W. Chang⁵

¹Department of Gastroenterology and Hepatology, Universitäts Spital Zürich, Zürich, Switzerland, ²Bristol Myers Squibb, Uxbridge, United Kingdom, ³Bristol Myers Squibb, Princeton, NJ, United States of America, ⁴Adelphi Real World, Bollington, United Kingdom, ⁵Division of Gastroenterology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, United States of America

Contact E-Mail Address: Luc.Biedermann@usz.ch

Introduction: Patients with eosinophilic esophagitis (EoE) commonly face diagnostic delays, often due to misdiagnosis of conditions with similar symptoms such as gastroesophageal reflux disease (GERD).¹⁻³ Diagnostic delay in EoE has been associated with stricture formation, food impaction, persistent symptoms with impaired quality of life, and potentially a decrease in response to treatment.

Aims & Methods: This study examined the path from first symptoms to EoE diagnosis from both physician and patient perspectives and the impact of misdiagnosis. Data were from the Adelphi EoE Disease Specific Programme™ (DSP), a real-world, cross-sectional survey of physicians and their patients with confirmed diagnosis of EoE in the US, UK, and EU (France, Germany, Italy, Spain) from July to December 2023, including clinical data abstracted from medical records.⁴

Physicians reported if patients had been misdiagnosed prior to EoE diagnosis and the timing of key milestones, such as first symptoms, first medical consultation, and referral. Patients also reported timings of key milestones. We completed a descriptive analysis and presented results for the subset of patients who completed the survey and had clinical data abstracted.

Results: Physicians (n=190; 73% gastroenterologists, 18% allergists, 4% internal medicine, 4% pediatric gastroenterologists, 1% pediatric allergists) abstracted data on 1141 patients with EoE (93% adults, 89% White), of which 285 also completed a survey (25% response rate). For 967 patients, physicians assessed if the patient was previously misdiagnosed; 28% (n=272) were misdiagnosed, and the majority (81%) were misdiagnosed with GERD prior to the EoE diagnosis. Physicians reported that those who were misdiagnosed had a longer time from (1) first documented symptoms to patient's first medical consultation (mean days [SD]: 368.7 [671.0] vs 175.6 [611.8]) and (2) first consultation to EoE diagnosis (mean days [SD]: 332.3 [503.2] vs 78.9 [149.9]) when compared with pa-

tients who were not misdiagnosed (n=695). Misdiagnosed patients themselves also reported longer time from first symptoms to first medical consultation (mean days [SD]: 622.2 [1161.3] vs 327.1 [1154.2]) (Table).

Conclusion: Diagnostic delay is a known challenge in the management and care of EoE. Not only is clinical presentation underrecognized, but patients with EoE are commonly misdiagnosed, often with GERD, and experience prolonged diagnostic delay. Patients with a physician-confirmed misdiagnosis prior to their EoE diagnosis had longer time from their first symptoms to diagnosis due to both patient delay in seeking medical care and diagnostic delay. These findings highlight the significant unmet need for physician and patient education regarding EoE symptoms in order to facilitate timely diagnosis of EoE, which could aid in appropriate treatment strategies and improve both short- and long-term outcomes for patients with EoE.

	Total (n=1141)	Misdiagnosed ^a (n=272)	Not misdiagnosed ^a (n=695)	Unknown ^a (n=174)
Age, mean [SD], years	36.6 [14.7]	36.8 [14.7]	35.7 [14.0]	40.1 [16.7]
Female, %	34	34	34	32
White/Caucasian, %	89	86	90	89
BMI, mean [SD]	24.1 [3.5]	24.2 [3.3]	24.0 [3.6]	24.2 [3.4]
Conditions that were misdiagnoses, %		GERD (81) Achalasia (8) Esophageal candidiasis (3) Hypereosinophilic syndrome (1) Connective tissue disease (1) Don't know (5)		
Physician-reported time from first symptom to first medical consultation, ^b n	n=214 248.9 [876.2] 61.0 0-11,688 153.2	n=50 367.6 [516.9] 198.0 0-2556 275.0	n=150 211.5 [994.3] 38.0 0-11,688 84.0	n=14 225.9 [410.2] 92.0 0-1595 186.8
mean [SD], days median min-max IQR				
Patient-reported time from first symptom to first medical consultation, ^c n	n=269 378.3 [1122.8] 91.2 1-10,950 304.2	n=58 566.1 [1191.3] 197.7 20-8030 501.9	n=171 339.6 [1213.3] 60.8 1-10,950 154.4	n=40 271.4 [318.30] 152.1 1-1460 307.7
mean [SD], days median min-max IQR				
Physician-reported time from first medical consultation to EoE diagnosis, ^d n	n=236 168.1 [351.0] 59.0 0-2256 102.8	n=57 442.0 [595.5] 183.0 0-2256 398.5	n=161 73.1 [126.3] 36.0 0-1350 53.0	n=18 149.9 [218.8] 58.5 0-911 197.7
mean [SD], days median min-max IQR				

IQR=interquartile range

^aPhysicians were asked „Was this patient misdiagnosed with any other condition(s) to explain their symptoms prior to a confirmed diagnosis of EoE? (Yes, No, Don't know).“

^bPhysician reported for patients that have abstracted clinical data and the subset that completed a survey (n=285).

N is based on those with non-missing data.

^cOnly a subset of patients (n=285) for which physician abstract data completed a survey. N is based on non-missing patient survey data.

^dPatients were not asked to report on the time from first medical consultation to EoE diagnosis.

Table.

References:

- Murray FR, Kreienbuehl AS, Greuter T, Nennstiel S, Safroneeva E, Saner C, Schindler V, Schlag C, Schoepfer AM, Schreiner P, Straumann A, Biedermann L. Diagnostic delay in patients with eosinophilic esophagitis has not changed since the first description 30 years ago: diagnostic delay in eosinophilic esophagitis. *Am J Gastroenterol*. 2022 Nov 1;117(11):1772-1779. doi: 10.14309/ajg.0000000000001950. Epub 2022 Aug 12. PMID: 35971224.
- Schoepfer AM, Safroneeva E, Bussmann C, Kuchen T, Portmann S, Simon HU, Straumann A. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner.

- Gastroenterology. 2013 Dec;145(6):1230-6.e1-2. doi: 10.1053/j.gastro.2013.08.015. Epub 2013 Aug 13. PMID: 23954315.
3. Schoepfer AM, Safroneeva E, Bussmann C, Kuchen T, Portmann S, Simon HU, Straumann A. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. *Gastroenterology*. 2013 Dec;145(6):1230-6.e1-2. doi: 10.1053/j.gastro.2013.08.015. Epub 2013 Aug 13. PMID: 23954315.
4. Anderson P, Higgins V, Courcy J, Doslikova K, Davis VA, Karavali M, Piercy J. Real-world evidence generation from patients, their caregivers and physicians supporting clinical, regulatory and guideline decisions: an update on Disease Specific Programmes. *Curr Med Res Opin*. 2023 Dec;39(12):1707-1715. doi: 10.1080/03007995.2023.2279679. Epub 2023 Dec 15. PMID: 37933204.

Disclosure: LB has received consulting/advisory board fees from AbbVie, Amgen, Bristol Myers Squibb, MSD, Vifor, Falk, Escap, Janssen, Lilly, Calypso, Ferring, Pfizer, Takeda Pharmaceuticals, Janssen, and Sanofi. KD and JM are employees of and shareholders in Bristol Myers Squibb. CZ is a contractor to Bristol Myers Squibb. DM and TP are employees of Adelphi Real World. JWC has received fees for consulting from Sanofi-Regeneron and Takeda Pharmaceuticals.

MP259

COMPARISON OF CLINICAL PROFILE AND TREATMENT OUTCOMES OF EOSINOPHILIC ESOPHAGITIS PATIENTS IN COMMUNITY VERSUS TERTIARY CARE HOSPITAL: A PROSPECTIVE, MULTICENTRE STUDY

V. Storer¹, M. Ghisa¹, G. Lorenzon², D. Maniero³, M. De Bona³, A. Buda³, P. Visaggi⁴, N. De Bortoli⁴, F. Ferrara¹, E.V. Savarino²
¹Padua University Hospital, Gastrointestinal Endoscopy Unit, Gastroenterology Department, Padova, Italy, ²University of Padua, Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ³Gastroenterology Unit, Department of Oncological Gastrointestinal Surgery, S. Maria del Prato Hospital, Feltre, Italy, ⁴Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy

Contact E-Mail Address: vittoriostorer95@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated oesophageal disease that is showing a skyrocketing increase of new diagnoses in last two decades. Although tons of papers have been published clarifying several aspects of this disease, most of the evidences come from high volume – referral centres that may be not representative of the whole EoE population. In fact, little is known about demographic and clinical features as well as treatment outcomes of patients managed in community hospitals.

Aims & Methods: Between January 2021 and June 2023, we prospectively enrolled all EoE patients evaluated for the first time at two different centres: 1) a high-volume tertiary-care centre, the University Hospital of Padua (PH), that represent a national referral centre; 2) a low-volume community hospital, the hospital of Feltre (FH), with a catchment area of about 25,000 people, both located in the North-East of Italy. The diagnosis of EoE was made according to the latest international guidelines. Endoscopic features were assessed according to EREFS score (0-8 points). Histological remission was considered for eosinophilic peak <15 eos/HPF. The main goals of our study were to compare the cohorts of EoE patients from a community and a tertiary care centre in terms of demographic and clinical features as well as to assess differences in the rate of histological response to medical treatments.

Results: Overall, 210 patients were consecutively enrolled, 177 (84.3%) in the tertiary centre (PH) and 33 (15.7%) in the community one (FH). We

did not find any significant difference between PH cohort and FH patients regarding age (34.80 vs 38.24 years, $p=0.193$), male prevalence (79.1% vs 72.7%, $p=0.491$), body mass index (22.55 vs 22.63, $p=0.906$), prevalence of non-atopic comorbidities (35.6% vs 21.2%, $p=0.158$), diagnostic delay (3.35 vs 2.62 years, $p=0.682$). A not significant trend in higher EREFS score values was found in PH (3.3 vs 2.7, $p=0.062$). There was a significant difference regarding the number of patients that were evaluated for a second opinion (77% vs 15%, $p<0.001$) and the prevalence of atopic comorbidities (68.9% vs 42.4%, $p=0.008$), both higher in PH court.

Regarding medical treatments 184 patients were treated with PPI (157, 88.7% at PH and 27, 81.8% at FH, $p=0.219$). There was a significant difference in the rate of PPI response comparing PH and FH patients (29.94% vs. 51.85%, $p=0.044$). No differences in terms of rate of responsiveness regarding swallowed flutotide puffer (44% vs 36%, $p=0.295$) and orodispersible budesonide (50.9% vs 61.5%, $p=0.564$).

Conclusion: This study elucidated several significant aspects regarding EoE. Firstly, it revealed that EoE patients treated in peripheral hospitals may exhibit a milder phenotype, characterized by less severe endoscopic features and fewer atopic comorbidities. Conversely, more complex cases tend to be referred to specialised centres, often seeking for a second opinion. Accordingly, the rate of PPIs responsiveness was found to be higher in community hospitals and, indeed, they still hold a significant as effective therapeutic option for EoE patients. Given that most of the evidence come from high-volume referral centres, it is crucial to keep in mind these differences when assessing the wide spectrum of EoE patients. Although the need for new therapies is still a fact, the increasing prevalence of EoE also necessitates a thorough evaluation of the financial implications of these drugs.

Disclosure: Nothing to disclose.

MP260

LONG-TERM OUTCOMES OF MAINTENANCE THERAPY IN ADULT AND PEDIATRIC EOSINOPHILIC ESOPHAGITIS: A SYSTEMATIC REVIEW AND METANALYSIS

A. Barchi¹, F.V. Mandarino¹, G. Dell'Anna¹, E. Fasulo¹, M.-R. Yacoub², L. Albarello³, L. Massimino¹, F. Ungaro¹, E.V. Savarino⁴, S. Passaretti¹, S. Danese¹, E. Vespa¹
¹IRCCS Ospedale San Raffaele, Gastroenterology and Digestive Endoscopy, Milano, Italy, ²IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milano, Italy, ³IRCCS San Raffaele Scientific Institute, Pathology Unit, Milano, Italy, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: barchi.alberto@hsr.it

Introduction: Long-term maintenance treatment efficacy, safety and tolerability in eosinophilic esophagitis (EoE) is still partially understood. The aim of this study was to evaluate long-term outcomes of maintenance treatment for EoE with various drugs and dose regimens in real-world observational studies and randomized controlled trials (RCTs).

Aims & Methods: Systematic search was performed on Pubmed-MEDLINE, Embase and Cochrane Central Register of Controlled Trials from inception to October 2023. Studies reporting histologic success of maintenance therapy for EoE patients > 48 weeks, following 8-12 weeks of induction therapy with the same drug were included. Primary outcome was pooled histologic success (defined as < 15 eosinophils/HPF) at the end of follow-up for both study designs. Risk Difference (RD) or Odds Ratio (ORs) for histological success of maintenance therapy versus placebo (PBO) (for RCTs) and versus induction (for both study designs), pooled drug-related

adverse events (AEs), endoscopic and clinical success rates were assessed as secondary outcomes. Random effects model metanalyses were performed. A-priori sub-group analyses were performed to address substantial inter-study heterogeneity (measured with I² statistic).

Results: From 3,916 full articles, 23 articles matched inclusion criteria (17 observational studies and 6 RCTs), 7 with pediatric patients only. Overall, 1,923 patients (M 70.1%; mean age 29.8±12.6 years). Mean follow-up time was 78.4 weeks. Budesonide (either oro-dispersible or viscous suspension) was administered in 7 studies (including 2 RCTs), PPI in 6 studies (all observational, 4 pediatric), Fluticasone in 5 studies (including 1 RCT with 4 cohorts), Dupilumab in 2 RCTs and Cendakimab in 1 RCT. Pooled rate of long-term histologic success for RCTs was 83% (95% CI, 77%-89%; I² 73.1%), while for observational studies attested at 53% (95% CI, 42%-65%; I² 93.5%) at a median follow-up of 97.8 weeks. Maintenance therapy in RCTs showed a RD of -0.71 (95% CI; -0.92-0.50; p<0.01; I² 88.9%) versus PBO, while a RD of -0.06 (95% CI; -0.11-0.01; p<0.016; I² 23.1%) compared with induction. Observational studies showed a non-significant (p=0.38) Odds Ratio (OR) of 1.37 (95% CI, 0.66-2.85; I² 81.3%) of losing histologic success during therapy de-escalation. Pooled clinical success among RCTs attested at 61% (95% CI, 51%-75%; I² 71.3%), comparable with observational studies (60% [95% CI, 42%-77%; I² 97.3%]). Biological therapy (either Dupilumab or Cendakimab at various regimens) ranked first for pooled histologic success rate among RCTs with 79% (95% CI; 71%-87%; I² 54.9%). In observational studies, PPI with histologic success of 64% (95% CI, 50%-78%; I² 88.7%) and clinical success of 79% (95% CI; 66%-93%; I² 85.2%) ranked first. Pooled rate of AEs among RCTs attested at 34% (95% CI; 22%-45%; I² 93.2%), with a pooled candidiasis infection rate of 6% (95% CI; 2%-10%; I² 61.9%), comparable with pooled AEs among observational studies (5% [95% CI, 2%-7%; I² 66.7%]). Pooled therapy discontinuation rate was 0.14 (95% CI, 0.073-0.210, I² 94.49%) in real-world data.

Conclusion: This is the first meta-analysis on efficacy and safety of long-term maintenance treatment (median 78 weeks) for EoE. All treatments showed good efficacy in maintaining long-term histological remission without clear disadvantage in de-escalating therapy during maintenance in real-world data. Biological therapies resulted the most effective in RCTs, while PPIs in observational studies. Low adverse events rates and low therapy discontinuation rates confirm long-term treatment is well tolerated.

References: 1. Nistel M, Andrews R, Furuta GT, Atkins D. Elimination Diet or Swallowed Topical Steroid Treatment of Pediatric Eosinophilic Esophagitis: Five-Year Outcomes. *J Allergy Clin Immunol Pract.* 2023 Aug;11(8):2516-2523.e2. doi: 10.1016/j.jaip.2023.05.036. Epub 2023 May 30. PMID: 37263351; PMCID: PMC10525024.

Disclosure: ES has served as speaker for Abbvie, Agave, AGPharma, Alfasigma, Aurora Pharma, CaDiGroup, Celltrion, Dr Falk, EG Stada Group, Fenix Pharma, Fresenius Kabi, Galapagos, Janssen, JB Pharmaceuticals, Innovamedica/Adacyte, Malesci, Mayoly Biohealth, Omega Pharma, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda, Tillots, Uni-farco; has served as consultant for Abbvie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, Diadema Farmaceutici, Dr. Falk, Fenix Pharma, Fresenius Kabi, Janssen, JB Pharmaceuticals, Merck & Co, Nestlé, Reckitt Benckiser, Regeneron, Sanofi, SILA, Sofar, Synformulas GmbH, Takeda, Unifarco; he received research support from Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, Zeta Farmaceutici.

Danese has served as a speaker, consultant and advisory board member for Schering-Plough, AbbVie, Actelion, Alphawasserman, AstraZeneca, Cellerix, Cosmo Pharmaceuticals, Fer-ring, Genentech, Grunenthal, Johnson and Johnson, Millenium Takeda, MSD, Nikkiso Europe, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos, UCB Pharma and Vifor.

MP261

PATIENTS WITH NONEROSIVE HEARTBURN (NEH) AND EPIGASTRIC PAIN SYNDROME (EPS) ARE NOT CLINICALLY DISTINGUISHABLE AND BOTH BENEFIT FROM THE MUCOSAL PROTECTIVE AGENT POLIPROTECT IN THE PPI DEPRESCRIPTION PHASE. A RCT POST HOC ANALYSIS

E.S. Corazzari¹, A. Gasbarrini², L. d'Alba³, V. D'ovidio⁴, O. Riggio⁵, S. Passaretti⁶, B. Annibale⁷, M. Cicala⁸, A. Repici⁹, G. Bassotti¹⁰, C. Ciacci¹¹, A. Di Sabatino¹², M. Neri¹³, M.C. Braga¹⁴, E. Ribichini¹⁵, G. Radocchia¹⁶, P. Iovino¹⁷, M. Marazzato¹⁸, S. Schippa¹⁶, D. Badiali¹⁹

¹Irrcs Humanitas Research Hospital, Dept. of Internal Medicine, Rozzano, Italy, ²Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ³Azienda Ospedaliera S. Camillo, Department of Gastroenterology, Roma, Italy, ⁴Ospedale S. Eugenio, Unit of Gastroenterology and Endoscopy, Roma, Italy, ⁵Policlinico Umberto I, Roma, Italy, ⁶San Raffaele University Hospital, Gastroenterology, Milano, Italy, ⁷University Hospital S. Andrea, Rome, Medical and Surgical sciences, Rome, Italy, ⁸Università Campus Bio Medico, Gastroenterologia, Roma, Italy, ⁹Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy, ¹⁰Università di Perugia, Department of Medicine and Surgery, Gastroenterology & Hepatology Section, Perugia, Italy, ¹¹University of Salerno, Medicine Surgery Dentistry, Scuola Medica Salernitana, Salerno, Italy, ¹²IRCCS Policlinico S. Matteo, Prima Clinica Medica, Pavia, Italy, ¹³Università di Perugia, Department of Medicine and Aging Sciences, Chieti, Italy, ¹⁴Università La Sapienza, Department of Gastroenterology, Roma, Italy, ¹⁵Sapienza University, Internal Medicine and Medical Specialties Gastroenterology Unit, Rome, Italy, ¹⁶Università La Sapienza, Roma, Italy, ¹⁷University of Salerno, Department of Medicine, Surgery & Dentistry, Scuola Medica Salernitana, Salerno (Sa), Italy, ¹⁸Sapienza University of Rome, Department of Public Health and Infectious Diseases, Rome, Italy, ¹⁹Sapienza Università di Roma, Roma, Italy

Contact E-Mail Address: enrico.corazzari@uniroma1.it

Introduction: Initial first-line therapy for NEH and EPS are often PPIs, that are not indicated for long-term use and should be considered for de-prescribing (AGA CPU, Gastro 2022;162:13341). However, discontinuation of prolonged PPI therapy is followed by rebound acid hypersecretion (RAHS) and often by symptom recurrence. Antacids, alginates, and mucosal protective agents (MPA) are often used to counteract RAHS, but no controlled trials addressed the treatment phase of PPI deprescription in NEH and EPS

Aims & Methods: AIM to assess the efficacy of Poliprotect, an MPA made of natural substances, in the PPI deprescription phase of an RCT.

METHODS were reported in a published RCT (Corazzari et al *Am J Gastro* 2023;118:1024). Briefly, patients with a negative upper Gi endoscopy and complaining of heartburn NEH (n=81, F 63%) or Epigastric Pain/Burning (EPS) (n=45, F 67%) assumed omeprazole (20mg q.d) for 4 weeks. At PPI withdrawal they assumed Poliprotect made from *Aloe vera*, *Malva sylv.*, *Althea off.*, *limestone*, *nahcolite*, *Glycyrrhiza glabra*, *Matricaria recutita* (*Aboca*, *Sansepolcro*, Italy) 1.55 g tablet on demand for 4 weeks. VAS assessed daily symptom severity. A 50% VAS decrease from basal values defined a responder. Antacid was rescue medicine. Statistics with Wilcoxon rank sum test, and 2-sample test for equality of proportions, with continuity corrections.

Results: Demography and clinical baseline variables did not differ between NEH and EPS. During deprescription, poliprotect on-demand intake was of 2.36 (2.14) (M±SD) tablets/day. VAS score was [M (95%CI)] 25.6(21.0-

30.2) and 25.2(18.5-31.9) at the end of PPI treatment and 25.7(20.8-30.5) and 21.4(15.1-27.7) at the end of the deprescription in NEH and EPS, respectively. Rescue medicine consumption was 9.1±12.1 sachets and 8.7±10.8 during the 4-week PPI treatment and 11.1±12.2 and 20.2±23.4, (M±SD;n.s) during the 4 weeks of deprescribing in NEH and EPS patients, respectively. Responders' rate was 48% and 51.3% at the end of PPI treatment and 51.3% and 55% at the end of the deprescription in NEH and EPS, respectively. Of the entire sample, non-responders were 43% at the end of PPI treatment and 33.3% of them became responders at the end of the deprescribing phase. At the end of deprescription, GSRS GI symptom, and GIQLI QoL, items improved not significantly compared to those at the end of PPI treatment in both NEH and EPS. Treatment satisfaction was reported on OTE questionnaire by 82.8% and 85.7% at the end of PPI treatment and 81.3% and 95% at the end of the deprescription phase in NEH and EPS, respectively.

Conclusion: 1. At PPI deprescription, Poliprotect at the mean daily intake of 2.3 tablets appears to be equally effective in non-erosive Heartburn and Epigastric Pain Syndrome patients in

- counteracting the rebound acid hypersecretion effect
- maintaining the beneficial effect obtained with the previous PPI treatment
- reverting one-third of PPI non-responders to responders without any additional request for antacid rescue medicine.

2. Upper endoscopy-negative patients with heartburn and EPS appear to belong to the same clinical-therapeutic category as they cannot be distinguished for demography, accompanying gastrointestinal symptoms, gastrointestinal, physical, mental, and social items of quality of life, symptom severity, and response to treatment. The clinical use of the symptoms of heartburn, epigastric pain, or burning to differentiate patients with typical reflux-like symptoms from epigastric pain syndrome is not supported by the present data.

Disclosure: Consultancy for Alfa Sigma spa, SOFAR spa, Aboca spa.

MP262

REAL WORLD EVIDENCE ON IMPACT OF GENERAL PRACTITIONER ALERTING MESSAGES ON NEW DGVS PPI DEPRESCRIBING GUIDELINES IN GERMAN PRIMARY CARE SETTINGS

K. Plehhova¹, J. Wray¹, M. Haering², P. Aluko¹, F. De Grey-Warter¹, E. Horvath¹, B. Kovacic¹, C. Coyle³

¹Reckitt Benckiser Healthcare, Hull, United Kingdom, ²Reckitt Benckiser, Heidelberg, Germany, ³Reckitt Benckiser, Dept. of Medical Marketing, Slough, United Kingdom

Contact E-Mail Address: kate.plehhova@reckitt.com

Introduction: The Deutsche Gastroenterologie, Verdauungs-und Stoffwechselkrankheiten (DGVS) guideline, issued in March 2023 in Germany, recommends limiting PPI therapy to 4-8 weeks' duration with aim of reducing unnecessary long-term use and potential adverse events, where an appropriate long-term indication is absent. Doses of long-term PPI should be regularly reviewed with the aim of prescribing minimum effective dose.

Aims & Methods: This study aims to assess the impact of targeted educational intervention using a General Practitioner (GP) alerting system at the point of prescription on recent PPI deprescribing guidelines. The study also sorts to identify patient prescribed PPIs while observing PPI prescription patterns pre and post guideline release.

A 12-month non-interventional real-world study was carried out leveraging GP alerting messages in the electronic medical record (EMR) containing non-commercial short messages on latest guidance, recommendations, and peer-reviewed publications around PPI deprescribing in the

management of Gastroesophageal reflux disease (GORD) and upper GI conditions. Baseline for this study was January to March 2023.

This study spans 54% of primary care practices in Germany with anonymised prescription data of GPs in 2400 private GP practices equipped with a GP information system. Data analysis was conducted in patients with ICD codes for uncomplicated reflux and diagnosed GORD to determine impact of this intervention on PPI prescription by comparing prescription numbers in terms of pack sizes, diagnosis codes and number of GPs reached monthly.

Results: Over the 12 months period, an average of 333 and 65 GPs were reached monthly for diagnosed GORD and uncomplicated reflux respectively. While there was variation in number of GPs reached monthly, analysis revealed a statistical significant difference in high numbers of PPI prescriptions without indicated diagnosis; mean difference of 15 GPs against those with diagnosis code (95%CI: 9.7-20.10; P<0.001) for uncomplicated reflux and 47 GPs for diagnosed GORD (95%CI: 19.7-74.3; P<0.0017). The ratio of patients with an ICD code per GP reached ranged from 0.34 to 0.47 for uncomplicated reflux and diagnosed GORD indicating that less than half of the patients per physician had documented diagnosis justifying PPI use. This highlights significant gap in guideline adherence. However, for diagnosed GORD, percentage of patients with diagnosis rose by approximately 10% from Q1 to Q4.

An analysis of the data also showed consistent large pack sizes being prescribed for both uncomplicated Reflux (ICD12) and Diagnosed GORD (ICD K21.0 and K21.9). For uncomplicated reflux, it was found that 86% of prescriptions after the intervention were for >3 months while uncomplicated reflux rose to 100%. This is consistent with the findings of Plehhova 2023¹, which found that between 2020 to 2021, more than 60% of PPI prescriptions were for > 3 months and Rückert-Eheberg 2022 which described high proportions of off-label use in Bavaria². This study also found that patients with diagnosed GORD and with uncomplicated reflux were often prescribed doses larger than 20mg, both before and after the messaging intervention.

Conclusion: Findings from this study suggest that a significant proportion of PPI prescriptions do not align with current guideline recommendations. This emphasises the need for continuous and multidimensional improvement strategies and interventions on alignment of prescribing practice with guidelines, particularly in high-pressure primary care settings.

References: ¹ Plehhova K, Haering M, Wray J, Coyle C, Ibáñez E, Kostev K. Prescribing Patterns of Proton Pump Inhibitors in Germany: A Retrospective Study Including 472 146 Patients. J Prim Care Community Health. 2023 Jan-Dec;14:21501319231221002. doi: 10.1177/21501319231221002. PMID: 38142444; PMCID: PMC10749518.

²Rückert-Eheberg IM, Nolde M, Ahn N, Tauscher M, Gerlach R, Güntner F, Günter A, Meisinger C, Linseisen J, Amann U, Baumeister SE. Who gets prescriptions for proton pump inhibitors and why? A drug-utilization study with claims data in Bavaria, Germany, 2010-2018. Eur J Clin Pharmacol. 2022 Apr;78(4):657-667. doi: 10.1007/s00228-021-03257-z. Epub 2021 Dec 8. PMID: 34877614; PMCID: PMC8927002.

Disclosure: All authors disclose that they are employees of Reckitt Benckiser (UK and Germany).

MP263

IMPACT OF ESOPHAGEAL HYPERVIGILANCE, SYMPTOM-SPECIFIC ANXIETY, AND ADAPTIVE BEHAVIOURS ON REPORTED DYSPHAGIA IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE STUDY

P. Visaggi¹, I. Solinas¹, F. Ovidi¹, G. Adamo¹, G. Del Corso², D. Stefani Donati¹, M. Bellini¹, S.S. Zeki³, E.V. Savarino⁴, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²Institute of Information Science and Technologies "A. Faedo", National Research Council of Italy (CNR), Pisa, Italy, ³St Thomas' Hospital, Gastroenterology, London, United Kingdom, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: There is a known discrepancy between symptoms reporting and histological disease activity in patients with eosinophilic esophagitis (EoE) such that patients with EoE in histological remission may still report symptoms while patients with histologically active EoE may report few or no symptoms. Esophageal symptom-specific anxiety, hypervigilance, and adaptive behaviours at mealtime may affect dysphagia reporting in EoE but this has not been investigated.

Aims & Methods: We investigated the role of esophageal symptom-specific anxiety, hypervigilance, and adaptive behaviours at mealtime on dysphagia reporting in patients with EoE.

Consecutive adults (>18 years) with histologically active or inactive EoE (i.e., ≥ 15 or < 15 eosinophils/high-power field) at their last upper endoscopy (EGD) were prospectively enrolled. For each patient, esophageal hypervigilance, anxiety, and adaptive behaviours were assessed prior to the EGD by a physician who was blind to patients' treatment status and histological disease activity. Esophageal anxiety and hypervigilance were assessed using the validated Esophageal Hypervigilance and Anxiety Scale (EHAS) with a 30-day recall, while the validated Dysphagia Symptom Questionnaire (DSQ) and Dysphagia Symptom Score (DSS) were used for quantification of dysphagia. A structured interview (Pisa adaptation questionnaire, PiEAQ) was used for the assessment of adaptive behaviours (including: drinking water to push the bolus, lubricating food, chewing for long, and blending food) over the 30 days prior to the EGD. Kruskal-Wallis Rank Sum Test and Pearson's Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to calculate the diagnostic accuracy (AUC). Significance threshold was $p < 0.05$.

Results: Seventy-one patients were included. Sixty-two percent ($n=44$) had histologically active EoE and 38% ($n=27$) were in histological remission. High anxiety, hypervigilance, and use of adaptive behaviours were found in 49.3%, 46.5%, and 56.3% of patients, respectively. Higher levels of anxiety were associated with an increased severity of dysphagia according to DSQ and DSS scores ($p=0.02$ and $p=0.003$, respectively), whereas this was not true for hypervigilance ($p=0.79$ and $p=0.24$, respectively). Adaptive behaviours were significantly more commonly used by histologically active EoE compared to EoE in remission (72.3% vs 29.6%, $p < 0.001$). The DSQ and DSS scores of patients using any or a combination of adaptive behaviours were comparable to those of patients not using any adaptive behaviour at mealtime ($p > 0.1$ for all comparisons), suggesting a marginal impact of adaptive behaviours on dysphagia reporting. Based on ROC curve analysis, the AUC of the DSQ for the assessment of histological disease activity was 0.72 (DeLong 95% CI, 0.60-0.83), while the AUC of the DSS was 0.69 (DeLong 95% CI, 0.56-0.82). Dysphagia reporting adjustments based on anxiety or hypervigilance sub-scores of the EHAS or on the presence of adaptive behaviours at mealtime did not modify the performance of the DSQ and DSS.

		Patients with high esophageal anxiety (n=35)	Patients with low esophageal anxiety (n=36)	p value
Full population n=71	DSQ	3 [0-5]	2 [0-3]	$p=0.02$
(EHAS subscore cut-off>8)	DSS	5 [0-6]	2 [0-3]	$p=0.003$
		Patients with high esophageal hypervigilance (n=33)	Patients with low esophageal hypervigilance (n=38)	
Full population n=71	DSQ	2 [0-3]	2 [0-3]	$p=0.79$
(EHAS subscore cut-off>11)	DSS	3 [0-6]	2 [0-4]	$p=0.24$

Conclusion: Esophageal anxiety, hypervigilance, and adaptive behaviours can be found in half of EoE patients regardless of histological disease activity. Esophageal anxiety contributes to dysphagia severity in patients with EoE, while hypervigilance does not. The use of adaptive behaviours is associated with histologically active EoE and represents a clinical marker of disease activity but does not affect dysphagia reporting.

Disclosure: Nothing to disclose.

MP264

CLINICAL EFFECTIVENESS AND SAFETY OF ESOPHAGEAL STRICTURE DILATION USING A NOVEL ENDOSCOPIC ATTACHMENT CAP (BOUGIECAP VERSION 2.0) IN ADULTS WITH EOSINOPHILIC ESOPHAGITIS

J. Wakim El-Khoury¹, L. Biedermann², A. Kreienbühl³, C. Saner¹, A. Straumann², T. Greuter⁴, E. Safroneeva⁵, A.M. Schoepfer⁶

¹Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland,

²USZ Zürich, Gastroenterology & Hepatology, Zürich, Switzerland,

³USZ, Zurich, Switzerland, ⁴Hospital Zürich, Gastroenterologie und Hepatologie, Zurich, Switzerland, ⁵Tillotts Pharma, Inst. für Sozial- und Preventive Medizin, Rheinfelden, Switzerland, ⁶Lausanne University Hospital, Gastroenterology And Hepatology, Lausanne, Switzerland

Contact E-Mail Address: Jeanine.Wakim-El-Khoury@chuv.ch

Introduction: The BougieCap (Ovesco Endoscopy AG, Tübingen, Germany) is a cone-shaped transparent plastic cap attached by an adhesive tape to the tip of the endoscope and allows optical and tactile feedback during stricture dilation. In 2021, our group published on a one-time esophageal stricture dilation using the first version of BougieCap in 50 adults with EoE and were able to show its efficacy and safety. However, one BougieCap got detached during endoscopy. Ovesco recently released an upgraded BougieCap (version 2.0) that is characterized by the following features: 1) improved adhesive power of the tape; 2) gradual dilation over two millimeters per cap; 3) improved fit of the connecting part of the cap with the endoscope. As of yet, the technical feasibility, safety and clinical effectiveness of BougieCap version 2.0 for stricture dilation in adult EoE patients is unknown.

Aims & Methods: EoE patients prospectively included in the Swiss EoE Cohort were dilated with BougieCap 2.0 in case of the presence of esophageal strictures and stricture-related symptoms. Symptoms were assessed before and two weeks after a single dilation session using the validated EESAI PRO tool (range 0-100 points). This is an investigator-initiated study. None of the authors has financial ties with Ovesco Endoscopy AG.

Results: Forty two patients (76.2% male, median age 40 years (IQR 31-54 years), median disease duration 5 years (IQR 4-8 years), median diagnostic delay of 4 years (IQR 3-5 years), 57.2% treated with swallowed topical corticosteroids, 19.1% with proton pump inhibitors, 9.5% without anti-eosinophil therapy, 7.1% with elimination diet, 4.8% treated with dupilumab, 2.4% treated with benralizumab) were evaluated. Endoscopic bougienage was technically successful in 100%. A stricture diameter of < 10 mm was found in 14.3% of patients. Strictures were located in 38.1% in the prox-

imal esophagus, in 57.4% in the distal esophagus, and in 4.8% in both proximal and distal esophagus. Median esophageal diameter increased from 12 mm (IQR 12-13) to 14mm (IQR 14-16, $p<0.001$). Median EEsAI PRO dropped from 35 points (IQR 27-42) to 0 (IQR 0-12, $p<0.001$) at 2 weeks post dilation. There was no bleeding necessitating endoscopic intervention. Temporary post-dilational thoracic pain was reported by 33.3% of patients. No esophageal perforation was observed and no BougieCap got detached. One BougieCap was used in 66.7% of dilations whereas two BougieCaps were used in 33.3% of procedures. Median esophageal peak eosinophil count was 10/hpf (IQR 0-24).

Conclusion: In adults with EoE, endoscopic treatment of esophageal strictures using the upgraded BougieCap version 2.0 is technically feasible, safe and offers symptomatic improvement in the short term.

Disclosure: Nothing to disclose.

MP265

INTERIM FEASIBILITY OUTCOMES FROM THE FIRST REAL-WORLD PROSPECTIVE CAPSULE SPONGE IN EOSINOPHILIC OESOPHAGITIS STUDY (COSIE)

A.A. Rai¹, F. Coli¹, P. Baker¹, K. Shaw¹, M. O'Donovan², D. Morris¹

¹Lister Hospital; East and North Hertfordshire NHS trust, Gastroenterology, Stevenage, United Kingdom, ²Cyted Laboratory, Cyted Pathology Laboratory, Cambridge, United Kingdom

Contact E-Mail Address: Ayeshaaslamrai@gmail.com

Introduction: Eosinophilic oesophagitis is a condition characterised by symptoms of dysphagia and/or food impaction in adults, with oesophageal histology showing a peak eosinophil count of >15 eosinophils/high power field (or >15 eosinophils/ 0.3mm^2 or >60 eosinophils / mm^2), and the absence of other causes¹. Recent BSG guidelines for the management of Eosinophilic oesophagitis (EOE) in adults recommend repeat endoscopy to ensure histological remission on treatment. This can require multiple procedures that are unpleasant for patients and are resource intensive. Capsule sponge is a minimally invasive oesophageal cell sampling technology that has been used in >15000 patients with Reflux symptoms and Barrett's oesophagus. To date it has not been used in adults with EOE in clinical practice. The COSIE study is a pragmatic prospective ongoing study of adults with non-stenotic EOE to evaluate capsule sponge in routine clinical practice.

Aims & Methods: All adult patients attending a monthly dedicated EOE clinic May 2023 to April 2024 in a non-specialist hospital, were screened by a single consultant. Patients were offered capsule sponge and same day gastroscopy at least 8 weeks after starting or changing therapy or after three weeks from first diagnostic gastroscopy to monitor disease response and activity. The Endosign device was used in all patients. The Dysphagia Symptom Questionnaire, cytological and histological eosinophil count and Endoscopic reference score (EREFS) were measured as part of the ongoing study. Qualitative outcomes including success rate of swallowing, satisfactory cell sample (sufficient squamous cells), evidence of sponge reaching the stomach (columnar cells seen), complications and patient feedback and test preference were collected patient satisfaction questionnaire was collected after the procedure on the same day. All sponge cytology were processed by CYTED laboratories and endoscopic histology as part of normal clinical practice.

Results: 138 patients with EOE attended the clinic between May 2023 and April 2024. 77 patients identified as suitable, 41/53 (75%) agreed to take part. 12/53 (25%) declined to take part in the study when our research nurse contacted them and 24 are awaiting testing. 31/41 (75.6%) were male and 10 (24.4%) females. Median age observed was 50 years, standard deviation 14.58, minimum was 19 years old and maximum age

recorded was 72 years. Of the 41 patients who attempted to swallow capsule sponge 5 (12%) failed to swallow after 2 attempts. There have been no complications and no sponge detachments. 36 /41 (87.8%) agreed to same day gastroscopy. On same day gastroscopy examination, 20/36(55.5%) had minor grade I or II visible abrasions. No mucosal tears were evident. There was evidence of the capsule sponge reaching the stomach in 29/32 (90.6%). Adequate squamous cytological specimen were produced in 32/32 (100%). 36 (87.8%) patients found test acceptable of which 28/37 (75.6%) of those who expressed a preference preferred capsule sponge to gastroscopy.

Conclusion: The preliminary results show that capsule sponge is feasible to use in routine clinical practice and can be used safely to sample the oesophagus in non-stenotic EOE, providing sufficient samples. It is well tolerated and patients preferred capsule sponge to gastroscopy. Ongoing work will assess clinical effectiveness and management outcomes, comparative eosinophil counts and will contribute to a multicentre QU-BIE (QUantitative Biomarker Identification for Eosinophilic oesophagitis) study to evaluate potential biomarkers in EOE.

References: Dhar A, Haboubi HN, Attwood SE, et al. British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. Gut 2022;71:1459-1487.

Disclosure: Nothing to disclose.

Surgical considerations in IBD

11:30-12:30 / Poster Stage 1

MP266

NETWORK META-ANALYSIS COMPARING EFFICACY OF CONVENTIONAL THERAPY AND BIOLOGICS TO PREVENT ENDOSCOPIC POSTOPERATIVE RECURRENCE IN PATIENTS WITH CROHN'S DISEASE

M. Hupé¹, N. Mathieu¹, B. Pereira², A. Buisson²

¹CHU de Grenoble, IBD Unit, Grenoble, France, ²CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France

Contact E-Mail Address: mariannehupe@hotmail.fr

Introduction: As no direct comparison between IBD drugs to prevent endoscopic postoperative recurrence (POR) in Crohn's disease (CD) are available, hierarchizing these therapeutic options remains challenging.

Aims & Methods: The objective of this network meta-analysis was to compare the effectiveness of treatments to prevent endoscopic POR of CD. We performed a systematic review and network meta-analysis of comparative studies conducted in adults, evaluating a treatment to prevent endoscopic POR after ileocecal resection. The selection of studies was made according to PRISMA guidelines. The primary endpoint was endoscopic POR at 6 months defined as Rutgeerts score $\geq$ i2.

The network meta-analysis was carried out according to a random effects model. The results are presented as odds ratio (OR) with 95% confidence interval, adjusted for risk factors of POR. The risk of bias of the studies was assessed according to the Cochrane risk-of-bias tool for randomized trials and overall statistical heterogeneity between studies was assessed using τ . The SUCRA ranking method (surface under the cumulative ranking) was used to rank the treatments.

Results: Twenty studies were included in this network meta-analysis, including a total of 2414 patients. Overall heterogeneity was moderate ($\tau = 0.34$). After adjustment for POR risk factors, ustekinumab (OR = 0.23 [0.07-0.70]), vedolizumab (OR = 0.17 [0.05-0.59]), infliximab (OR = 0.18 [0.36-0.88]) and adalimumab (OR = 0.17 [0.07-0.42]) were superior to placebo to prevent endoscopic POR, contrary to 5-ASA (OR = 0.79 [0.42-1.48]) and thiopurines (RR = 0.52 [0.22-1.24]) (Table 1). Ustekinumab (OR = 0.29 [0.08-0.99]), vedolizumab (OR = 0.22 [0.06-0.85]), infliximab (OR = 0.23 [0.09-0.54]) and adalimumab (OR = 0.22 [0.08-0.59]) were more effective than 5-ASA in preventing endoscopic POR. Adalimumab (OR = 0.33 [0.15-0.74]) and infliximab (OR = 0.34 [0.13-0.87]) were also more effective than thiopurines.

We observed no difference in efficacy between the 4 biologics (infliximab, adalimumab, ustekinumab and vedolizumab). The SUCRA ranking identified adalimumab (SUCRA = 0.81), infliximab (SUCRA = 0.80), vedolizumab (SUCRA = 0.79) and ustekinumab (SUCRA = 0.72) as the most effective treatments. The probability that thiopurines (SUCRA = 0.41), 5-ASA (SUCRA = 0.24), placebo (SUCRA = 0.16) and antibiotics (SUCRA = 0.08) were significantly higher weak.

Conclusion: This network meta-analysis confirms the efficacy of anti-TNF agents, vedolizumab and ustekinumab in preventing endoscopic CD POR without any difference between them. When prophylactic therapy is indicated, biologics appear as the best therapeutic option to prevent of endoscopic POR. Due to lower effectiveness, the use of 5-ASA and thiopurines should be limited in this situation.

Disclosure: Anthony BUISSON: Consulting fees for Abbvie, Amgen, Arena, Biogen, Celltrion Healthcare, CTMA, Galapagos/Alfa Sigma, Gutycare/Resilience, Janssen, MSD, Nexbiome, Pfizer, Roche, Sandoz, Takeda, Tillotts. And Viatrix. Lecture fees for Abbvie, Amgen, Biogen, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Mayoli-Spindler, MSD, Nordic Pharma, Norgine, Pfizer, Roche, Takeda, Tillotts and Vifor Pharma. Research grants from: Abbvie, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Lesaffre, Lilly, Pfizer, Takeda.

MP267

FUNCTIONAL OUTCOMES AFTER PRIMARY ILEOCECAL RESECTION FOR CROHN'S DISEASE

N. Grellier^{1,2}, J. Kirchesner¹, N. Chafai³, I. Nion Iarmurier¹, C. Debove³, A. Bourrier¹, C. Landman¹, P. McLellan¹, H. Sokol¹, J. Lefevre³, P. Seksik¹, L. Beaugier¹

¹Saint-Antoine Hospital - Department of Gastroenterology, Department of Gastroenterology, Paris, France, ²Poitiers University Hospital, Gastroenterology, Poitiers, France, ³Saint-Antoine Hospital, Digestive surgery, Paris, France

Contact E-Mail Address: nathan_grellier@yahoo.fr

Introduction: Ileocecal resection (ICR) is the most common surgical procedure for ileal Crohn's disease (CD). Data is growing to suggest ICR in localized disease as a first-line treatment instead of biologics to maintain long-term remission. However, removal of the ileocecal valve has a detrimental effect on bowel transit and disabling symptoms may occur after surgery. We aimed to assess the impact of a primary ICR on the daily symptoms of patients with CD.

Aims & Methods: All patients who underwent a primary ileocecal resection at the Saint-Antoine Hospital between January 2017 and December 2022 were included. Patients were followed up with post-operative visits before and after Rutgeerts score assessment. Patients' daily symptoms were recorded using a dedicated database (SUVIMIC), the routine software used at the Saint-Antoine Hospital that includes assessment of patient reported outcomes.

Results: Between 2017 and 2022, 110 patients underwent primary ICR for CD in relapse at the Saint-Antoine Hospital. The median disease duration at surgery was 6 years (IQR 1–11). The indications for surgery were fistulizing CD phenotype for 62 patients (56.4%) and strictures for 40 patients (36.4%). Only 7 patients (6.4%) had inflammatory phenotype at the time of first ICR. The median time to Rutgeerts Score assessment was 7 months showing 75 patients (68.2%) in remission defined as a score of i0, i1, i2a and 35 patients (31.8%) in relapse with a score of i2b to i4. Patients' daily symptoms reported at endoscopic assessment (6 – 12 months after surgery) are shown in Table 1.

Patients' daily symptoms	According to disease activity		According to small bowel removed		
	Remission n = 75	Relapse n = 35	Short resection $\leq$ 20 cm n = 47	Resection 21 – 40 cm n = 46	Long resection $\geq$ 41 cm n = 17
Liquid stools	44 (58.7)	19 (54.3)	29 (61.7)	21 (45.7)	13 (76.5)
> 3 liquid stools per day	7 (9.3)	6 (17.1)	7 (14.9)	2 (4.3)	4 (23.5)
Number of liquid stools per day mean (SD)	1.4 (1.5)	1.9 (1.5)	1.8 (2.4)	1.1 (1.5)	2.1 (1.7)
Fecal urgency	17 (22.7)	9 (25.7)	12 (25.5)	6 (13.0)	8 (47.1)
Fecal incontinence	1 (1.3)	3 (8.6)	1 (2.1)	1 (2.2)	2 (11.8)
Anti-diarrheal medications	17 (22.7)	7 (20.0)	9 (19.2)	11 (23.9)	4 (23.5)
Abdominal pain	21 (28.0)	14 (40.0)	15 (31.9)	12 (26.1)	8 (47.1)
Fatigue	24 (32.0)	14 (40.0)	15 (31.9)	16 (34.8)	7 (41.2)

Table 1. Daily symptoms of patients after primary ileocecal resection at endoscopic assessment

Symptoms are expressed in number of patients (%). Remission was defined as a Rutgeerts score i0, i1, i2a and relapse i2b, i3 and i4.

According to disease activity, the prevalence of diarrhea, defined as liquid stools, was 58.7% in patients in remission and 54.3% in patients in relapse. The prevalence of fecal urgency was 22.7% and 25.7%, respectively. Fecal incontinence was present in one patient in remission and three patients in relapse. According to the length of the resected small bowel, liquid stools

were observed in 61.7% of patients with short resections (≤ 20 cm), 45.7% of patients with resections between 21 - 40 cm and 76.5% of patients with long resections (≥ 41 cm). Fecal urgency was present in 25.5%, 13.0% and 47.1% respectively. Furthermore, the prevalence of abdominal pain was 31.8% and of fatigue 34.5% in the whole cohort.

Conclusion: The prevalence of digestive symptoms after primary ICR for CD is high, especially diarrhea and fecal urgency, even in patients in remission. Primary ICR for CD is an effective treatment for achieving long-term remission, but removal of the ileocecal valve leads to irreversible changes in bowel transit, which must be considered before proposing surgery.

Disclosure: Nothing to disclose.

MP268

LONG-TERM IMPACT OF EARLY MEDICAL PREVENTION OF POSTOPERATIVE RECURRENCE ON THE NEED FOR A SECOND INTESTINAL RESECTION IN PATIENTS WITH CROHN'S DISEASE. DATA FROM THE ENEIDA REGISTRY

G. Piñero¹, V. Pérez Torrado¹, P. Nos Mateu², E. Ricart³, M. Calafat Sard¹, S. Riestra⁴, F. Mesonero Gismero⁵, E. Iglesias-Flores⁶, I. Pascual-Moreno⁷, M.I. Vera Mendoza⁸, M.D. Martín-Arranz⁹, L. De Castro Parga¹⁰, C. Taxonera Samsó¹¹, M. Rivero¹², J. Guardiola¹³, J. Gisbert¹⁴, L. Arranz Hernández¹⁵, A. Giordano¹⁶, P. Varela Trastoy¹⁷, L. Arias García¹⁸, J. Barrio¹⁹, A. Gutiérrez²⁰, S. García-López²¹, X. Calvet Calvo²², C.J. Gargallo-Puyuelo²³, J.M. Huguet²⁴, L. Bujanda Fernández de Piñola²⁵, J.L. Pérez-Calle²⁶, I. Moraleja²⁷, L. Ramos Lopez²⁸, Y. Zabana²⁹, D. Carpo³⁰, M. Sierra³¹, M. Barreiro de Acosta³², F. Bermejo³³, R. Lorente Poyatos³⁴, Y. González Lama³⁵, M. Navarro-Llavat³⁶, L. Márquez Mosquera³⁷, R. Camargo Camero³⁸, M.F. García-Sepulcre³⁹, N. Rull Murillo⁴⁰, L. Zabalza San Martín⁴¹, P. Vega⁴², D.S. Ceballos Santos⁴³, E. Sesé⁴⁴, Á. Ponferrada-Díaz⁴⁵, D. Monfort Miquel⁴⁶, M. Mañosa Ciria¹, E. Domenech Morral¹, on behalf of the ENEIDA Project of GETECCU

¹Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ²Hospital Universitario y Politécnico La Fe, Valencia, Spain, ³Hospital Clinic Barcelona, Gastroenterology, Barcelona, Spain, ⁴Hospital Universitario Central de Asturias, Oviedo, Spain, ⁵Hospital Universitario Ramon y Cajal, Gastroenterology, Los Santos de la Humosa, Spain, ⁶Hospital Universitario Reina Sofía de Córdoba, Digestive, Córdoba, Spain, ⁷Hospital Clinico Universitario de Valencia, Valencia, Spain, ⁸Hospital Universitario Puerta de Hierro Majadahonda, Digestive, Madrid, Spain, ⁹Hospital Universitario La Paz, Gastroenterology, Madrid, Spain, ¹⁰Hospital Álvaro Cunqueiro, Vigo, Spain, ¹¹Hospital Clinico San Carlos, Madrid, Spain, ¹²Hospital Universitario Marques de Valdecilla, Gastroenterology, Santander, Spain, ¹³Hospital Universitari de Bellvitge, Gastroenterology, L'Hospitalet de Llobregat (Barcelona), Spain, ¹⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Digestive Services, Madrid, Spain, ¹⁵Hospital Universitario Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Spain, ¹⁶Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, ¹⁷Hospital Universitario de Cabueñes, Gijón, Spain, ¹⁸Hospital Universitario de Burgos, Burgos, Spain, ¹⁹Hospital Universitario Río Hortega, Valladolid, Spain, ²⁰Hospital General Universitario de Alicante, Alicante, Spain, ²¹Hospital Universitario Miguel Servet, Zaragoza, Spain, ²²Consorci Corporació Sanitària Parc Taulí de Sabadell, Unitat de Malalties Digestives, Barcelona, Spain, ²³Hospital Clínico Universitario Lozano Blesa, Zaragoza,

Spain, ²⁴Consorcio Hospital General Univeristario de Valencia, Valencia, Spain, ²⁵Hospital Universitario Donostia, San Sebastián, Spain, ²⁶Hospital Universitario Fundación de Alcorcón, Alcorcon, Spain, ²⁷Hospital Universitario de Galdakao, Bizkaia, Spain, ²⁸Hospital Universitario de Canarias, Tenerife, Spain, ²⁹Hospital Universitari Mútua Terrassa, Department of Gastroenterology, IBD Unit, Terrassa, Spain, ³⁰Complejo Hospitalaria de Pontevedra, Pontevedra, Spain, ³¹Complejo Asistencial Universitario de León, Gastroenterology, León, Spain, ³²Hospital Clínico Universitario de Santiago, Gastroenterology, Santiago de Compostela, Spain, ³³Hospital Universitario Fuenlabrada, Fuenlabrada, Spain, ³⁴Hospital General Universitario de Ciudad Real, Ciudad real, Spain, ³⁵Hospital Universitario 12 de Octubre, Madrid, Spain, ³⁶Hospital de Sant Joan Despí Moisès Broggi, Barcelona, Spain, ³⁷Hospital del Mar, Gastroenterology, Barcelona, Spain, ³⁸Hospital Universitario Virgen de la Victoria, Málaga, Spain, ³⁹Hospital General Universitario de Elche, Elche, Spain, ⁴⁰Hospital Universitario Son Llàtzer, Palma de Mallorca, Spain, ⁴¹Hospital Universitario de Navarra, Pamplona, Spain, ⁴²Complejo Hospitalario Universitario de Ourense, Gastroenterology Department, Ourense, Spain, ⁴³Hospital Universitario de Gran Canaria Dr Negrín, Las Palmas de Gran Canaria, Spain, ⁴⁴Hospital Universitario Arnau de Vilanova de Lleida, Lleida, Spain, ⁴⁵Hospital Universitario Infanta Leonor, Madrid, Spain, ⁴⁶Consorci Sanitari de Terrassa, Barcelona, Spain

Contact E-Mail Address: gipinero@gmail.com

Introduction: Postoperative recurrence (POR) in patients with Crohn's disease (CD) occurs mostly within the first year after ileocolic resection. POR can be prevented efficiently with early postoperative use of thiopurines or anti-TNF agents. Recently, it has been reported that medical prevention for POR might also reduce the risk of delayed POR.

Aims & Methods: Aims: To assess the long-term risk of a second intestinal resection for CD according to the use of early medical prevention of POR. Methods: Adult patients with CD who underwent a first ileocolic resection with ileocolic anastomosis between 1990 and 2020 and at least one year of clinical follow-up were identified from the Spanish ENEIDA registry. Patients in whom ileocolic resection was due to cancer were excluded. Medical prevention of POR was defined as any immunomodulator or biological agent started within the first 6 months after the ileocolic resection and maintained for at least 3 months. Medical treatment of POR was defined as any immunomodulator or biological agent started at least 6 months after the index surgery. Surgical POR was defined as the need for a second intestinal resection at least 6 months after the first ileocolic resection.

Results: A total of 5,084 patients were included. Main characteristics of the whole cohort were as follows: 51% men, 39% active smokers at the first surgery, 40% penetrating and 40% stricturing behaviour, 25% perianal disease. 34% exposed to immunomodulators and 25% to biologicals before the first surgery. Median disease duration at first surgery of 3 years (range, 0-46), median age at index surgery was 35 years (range, 9-89), median follow-up until second resection or last visit of 125 months (range 6-408). 55% followed medical prophylaxis (33% thiopurines, 10% biological monotherapy, 12% combotherapy). Surgical POR occurred in 17% of the whole cohort. Kaplan-Meier survival curves showed a significantly higher risk of surgical POR among patients who did not follow medical prevention ($P<0.0001$), whether with thiopurines ($P<0.0001$) or biologicals ($P<0.0001$). No differences in surgical POR were observed between medical prevention with biologicals in monotherapy or combotherapy ($P=0.588$) nor between thiopurines and biologicals ($P=0.114$). In the Cox regression analysis, medical prevention with thiopurines (HR 0.65, 95%CI 0.56-0.76; $P<0.0001$) and medical treatment with biologicals (HR 0.87, 95%CI 0.80-0.94; $P<0.0001$) or thiopurines (HR 0.88, 95%CI 0.78-0.99; $P<0.032$) were independent protective factors of surgical POR.

Conclusion: Early medical prevention (particularly with thiopurines) seems to have a long-term beneficial effect on preventing surgical POR. Our findings support the systematic use of early medical prevention instead of endoscopy-driven strategies in the postoperative setting of CD.

Disclosure: Nothing to disclose.

MP269

IMPACT OF TIMING OF PROPHYLAXIS THERAPY ON POST-OPERATIVE ENDOSCOPIC RECURRENCE IN A REAL-LIFE COHORT OF PATIENTS WITH CROHN'S DISEASE

A. Del Gaudio¹, G. Cuccia¹, D.V. Federica¹, G. Coppola¹, P. Puca¹, L. Laterza¹, L. Parisio¹, D. Pugliese¹, A. Papa¹, G. Cammarota¹, A. Gasbarrini¹, F. Scaldaferri¹, L.R. Lopetuso¹

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Rome, Italy

Contact E-Mail Address: delgaudioangelo@gmail.com

Introduction: Despite significant advancements in medical therapy, surgery remains a common option for managing Crohn's disease (CD), especially in cases of complicated disease, with a 10-year risk of surgical resection (SR) of approximately 50%. (1)

Furthermore, it is well-established that the majority of patients experience subsequent relapse after surgery, with up to 90% develop endoscopic post-operative recurrence (POR) within one year. (2)

Several guidelines for managing post-operative CD recommend using pre-operative risk factor stratification to determine the use of prophylactic biologic therapy against POR in high-risk individuals. However, the optimal timing for initiating biologic therapy after resection surgery has not been established, and the impact of a delayed start remains unclear, particularly outside the context of clinical trials. A recent study demonstrated that initiating an anti-TNF agent within 4 weeks after SR was associated with a reduction in POR. (3)

However, the comparison was made against patients receiving no prophylaxis with biologic drugs.

Aims & Methods: Our study aims to assess the impact of the timing of biologic therapy initiation on endoscopic recurrence after resection surgery in CD. We conducted a single-center, retrospective study evaluating endoscopic outcomes of CD patients who underwent ileo-colonic resection. All patients underwent their first endoscopic evaluation within 6-12 months after surgery to assess POR, using the Rutgeerts score (RS), with POR defined as RS $\geq$ 2. All patients received biological therapy for recurrence prevention within 16 weeks after surgery.

Results: We included 177 patients, with a median age at surgery of 38 years old. The primary indication for surgery was stenotic disease. 77% of patients had no prior history of bowel resection and 38% were bio-naïve. All patients had at least one risk factor for post-surgical recurrence, including smoking or penetrating disease. Prophylactic biologic therapy (22% Infliximab, 53% Adalimumab, 8% Vedolizumab, and 17% Ustekinumab) was administered to all patients, with initiation within 4 weeks, 4-8 weeks, 8-12 weeks, and 12-16 weeks in 20%, 32%, 15%, and 33% of patients, respectively. POR was observed in 50% of the entire cohort at 6-12 months.

Starting therapy within 12 weeks following SR was associated with a significantly lower recurrence rate than initiating therapy beyond 12 weeks (POR: 36% vs 64% $p < 0.01$).

Notably, induction within 8 weeks showed a lower recurrence rate than after 8 weeks (POR: 39% vs 61%; $p < 0.05$). There was no significant difference in recurrence rate between starting therapy within 4 weeks and 8 weeks, even when stratifying by risk factors for recurrence. Furthermore, for patients already on biologic therapy prior to SR, therapy was either

maintained unchanged, switched, or swapped in 54%, 18%, and 28% of patients, respectively. Investigating the impact of these strategies on POR, we noted significant differences, with less recurrence for those who continued the same therapy after SR (POR: 42% vs 61% vs 72%; $p < 0.05$). However, the mean time to therapy resumption in this group was also significantly shorter than in the others (weeks 9.7 vs 15 vs 13; $p < 0.05$).

Conclusion: In our a real-life cohort, we found that prophylaxis administered within 12 weeks after resection correlates more strongly with a reduced risk of post-operative recurrence. Furthermore, in this group, our results indicate a lower risk of recurrence in patients receiving prophylaxis within 8 weeks. However, larger clinical studies are needed to confirm these results.

References: 1-Frolkis AD, Dykeman J, Negrón ME, Debruyen J, Jette N, Fiest KM, Frolkis T, Barkema HW, Rioux KP, Panaccione R, Ghosh S, Wiebe S, Kaplan GG. Risk of surgery for inflammatory bowel diseases has decreased over time: a systematic review and meta-analysis of population-based studies. *Gastroenterology*. 2013 Nov;145(5):996-1006. doi: 10.1053/j.gastro.2013.07.041. Epub 2013 Jul 27. PMID: 23896172.

2-Bobanga ID, Bai S, Swanson MA, Champagne BJ, Reynolds HJ, Delaney CP, Barksdale EM Jr, Stein SL. Factors influencing disease recurrence after ileocolic resection in adult and pediatric onset Crohn's disease. *Am J Surg*. 2014 Oct;208(4):591-6. doi: 10.1016/j.amjsurg.2014.06.008. Epub 2014 Jul 18. PMID: 25110291.

3-Axelrad JE, Li T, Bachour SP, Nakamura TI, Shah R, Sachs MC, Chang S, Hudesman DP, Holubar SD, Lightner AL, Barnes EL, Cohen BL, Rieder F, Esen E, Remzi F, Regueiro M, Click B. Early Initiation of Antitumor Necrosis Factor Therapy Reduces Postoperative Recurrence of Crohn's Disease Following Ileocecal Resection. *Inflamm Bowel Dis*. 2023 Jun 1;29(6):888-897. doi: 10.1093/ibd/izac158. PMID: 35905032; PMCID: PMC10233395.

Disclosure: None.

MP270

INTERVENTIONS FOR THE MANAGEMENT OF COMPLICATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND PERMANENT ILEOSTOMY FOR THE ENDOTRIAL CONSORTIUM: A SYSTEMATIC REVIEW

S.K. Vuyyuru¹, V. Solitano^{2,3}, Y. Yuang⁴, N. Narula⁵, S. Singh⁶, C. Ma^{7,8,9}, V. Jairath^{4,2,10,11}

¹Alimentiv Inc., London, Canada, ²Division of Gastroenterology, Western University, London, Ontario, Canada, ³Medicine, London, Canada, ⁴Division of Gastroenterology and Gastrointestinal Endoscopy, IRCCS Ospedale San Raffaele, Università Vita-Salute San Raffaele, Milan, Italy, Milan, Italy, ⁵Lawson Health Research Institute, London, Ontario, Canada, London, Canada, ⁶McMaster University, Medicine, Hamilton, Canada, ⁷Division of Gastroenterology, Department of Medicine, University of California, San Diego, La Jolla, California, United States, California, United States of America, ⁸University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada, ⁹Alimentiv Inc., London, Ontario, Canada, London, Canada, ¹⁰Departments of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada, Calgary, Canada, ¹¹Alimentiv Inc., Gastroenterology, London, Canada, ¹¹Department of Epidemiology and Biostatistics, Western University, London, Ontario, Canada., London, Canada

Contact E-Mail Address: svuyyur@uwo.ca

Introduction: The evidence guiding management of patients with inflammatory bowel disease (IBD) and permanent ileostomy (PI) is limited. We aimed to summarize the evidence for interventional studies related to adjunctive ostomy care including management of high stoma output,

skin care, stoma appliances, adhesives, behavioural interventions, mental health, diet, nutrition and disease recurrence.

Aims & Methods: MEDLINE, Embase, and Cochrane CENTRAL were searched from inception to January 5, 2024. Eligible studies were randomized controlled trials (RCTs), non-randomized controlled studies, or comparative cohort studies in English. Studies predominantly recruiting participants with ulcerative colitis (UC) and/or Crohn's disease (CD) with PI were considered. Studies assessing temporary ileostomy, and ostomies other than PI such as colostomy, urostomy, and jejunostomy were excluded.

Authors, Year	Country	Study design	Number of participants	IBD subclass (n)	Intervention	Control	Outcomes	Conclusions
Tytgat, 1976	Netherlands	Double-blinded, RCT, cross over	20, ileostomy (total colonic resections with PI)	UC (12) CD (5) Polyposis coli (2) Adenocarcinoma (1)	Loperamide 8mg/day (first four days) and were allowed to increase the dose to 12mg/day for the next 3 days)	Placebo	Ileostomy fecal output	Daily fecal outputs were significantly lower with loperamide compared to placebo
Berghouse, 1984	United Kingdom	Unblinded, randomized, ileostomies cross over,	10 patients with	CD (5) UC (5)	Diet rich in refined carbohydrates	Diet with unrefined carbohydrates	Microbial composition of ileostomy output	Approximately 10-fold increase of total bacteria per gram of effluent when patients were on diet with unrefined carbohydrates. Significantly low wet and dry weight of ileostomy output with diet rich in refined carbohydrates
Sandberg-Gertzen, 1986	Denmark	Double-blinded RCT, placebo-controlled cross over	8 patients who underwent colectomy with a PI	UC	Azodisal sodium (1 g/day vs 2 g/day) or sulphasalazine (2 g/day) given for five day periods	placebo	Ileostomy fluid output. Prostaglandin levels in ileostomy output	Azodisal sodium but not sulfasalazine was associated with increased ileostomy output and was dose related. Azodisal sodium was not associated with increased prostaglandin levels in ileostomy output.
Jarnerot, 1988	Sweden	Double-blinded, placebo-controlled RCT cross over	8 patients who underwent colectomy with a PI	UC	Olsalazine sodium 0.75g twice a day	Placebo	Bile acids in ileostomy output	Bile acid excretion was not significant different between Olsalazine and placebo
Ecker, 2003	Germany	Double-blinded RCT	40 patients with ileostomy and with a high ileostomy output (>1000 ml/24)	CD	Oral budesonide 3mg tid x 8 days	Placebo	A >25% reduction in intestinal output during treatment was defined as response	60% (12/20) of patients showed a response compared to none in placebo group. 30.2% decrease in median output was seen in budesonide group compared to 0.3% decrease in placebo group
Rud, 2019	Denmark	Double-blinded, active ileostomy and comparator-independent controlled RCT cross over	8 patients with ileostomy and parenteral nutrition	UC (5) CD (2) Cancer (1)	Iso-osmolar (279 mOsm/kg) oral supplement 200ml x 4 times a day for two days	Hyper-osmolar (681 mOsm/kg) oral supplement 200ml x 4 times a day for two days	Difference in ileostomy output	No statistically significant changes in ileostomy output. Iso-osmolar supplement induced a statistically significant increase in urine volume and natriuresis

Table 1. Characteristics of interventional studies conducted in patients of inflammatory bowel disease and permanent ileostomy

CD: Crohn's disease, PI: permanent ileostomy, RCT: randomized controlled trial, UC: ulcerative colitis.

Results: A total of 3217 records were identified and independently screened of which six studies were eligible (Table 1). Five studies were published more than 20 years ago (1976-2003) with a small sample size (ranged from 8 to 40). Five studies were double blind RCTs with four studies incorporating a cross over design, and one was non-blinded RCT with a cross over design. Two studies exclusively included patients with UC, one study included CD and the remaining three studies included both UC and CD. No studies included patients with active CD. Four studies assessed pharmacological interventions (loperamide, 5-aminosalicylate [5-ASA], azodisal sodium, and oral budesonide), one assessed oral supplement with different osmolarities and one assessed dietary interven-

tion (unrefined vs. refined carbohydrate). Decrease in ileostomy output was primary outcome of interest in four studies (Loperamide, budesonide and azodisal sodium). Outcomes of the remaining two studies include changes in microbial composition and bile acid excretion. Loperamide and budesonide were associated with decreased stoma output. In a study assessing dietary intervention, patients receiving diet rich in unrefined carbohydrates had a ten-fold increase in bacterial load in stoma output compared to patients on a diet rich in refined carbohydrates. One study reported no difference in stoma output between iso- and hyper-osmolar supplements but iso-osmolar supplements were associated with increased natriuresis. The remaining studies were designed to explore the effect of 5-ASAs on ileostomy output in patients with UC and PI.

Conclusion: This study highlights that the evidence base to inform care for patients with IBD and PI is almost non-existent. There is an urgent need for focused research in this area to inform evidence-based treatment decisions. The items identified in this review as well as knowledge gaps will inform consensus steps for development of future care pathways and expert guidelines.

Disclosure: SKV none.

VS has none to disclose.

YY has none to disclose.

NN has been a speaker or advisor for Janssen, Abbvie, Takeda, Pfizer, Merck, Sandoz, Fresenius Kabi, Innomar, Iterative Scopes, Bristol Myers Squibb, Viatrix and Ferring.

SS has received consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB Inc, and Vifor; and lecture fees from AbbVie, Amgen, Ferring Pharmaceuticals Inc, Gilead, Janssen, Mylan, Pfizer, and Takeda.

CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche, Sanofi; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Ferring, Fresenius Kabi, Janssen, Takeda, Pendopharm, and Pfizer; royalties from Springer Publishing; research support from Ferring, Takeda, Pfizer.

FR is consultant to Adnovate, Agomab, Allergan, AbbVie, Arena, Boehringer-Ingelheim, Celgene/BMS, CDISC, Celsius, Cowen, Ferring, Galapagos, Galmed, Genentech, Gilead, Gossamer, Guidepoint, Helmsley, Horizon Therapeutics, Image Analysis Limited, Index Pharma, Janssen, Koutif, Mestag, Metacrine, Mopac, Morphic, Organovo, Origo, Pfizer, Pliant, Prometheus Biosciences, Receptos, RedX, Roche, Samsung, Surmodics, Surrozen, Takeda, Techlab, Theravance, Thetis, UCB, Ysios, 89Bio.

VJ has received consultancy/advisory board fees from AbbVie, Alimentiv Inc., Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, GlaxoSmithKline, Genentech, Gilead, Janssen, Merck, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Topivert, Ventyx, and Vividion; and speaker's fees from, Abbvie, Ferring, Galapagos, Janssen Pfizer Shire, Takeda, and Fresenius Kabi.

MP271

PERIOPERATIVE HYPERGLYCEMIA AND RISK OF SURGICAL COMPLICATIONS IN CROHN'S PATIENTS

F. Colombo¹, F. Porretta¹, D. Anselmi², C. Baldi³, F. Roufael³, S.G. Ardizzone⁴, P. Danelli¹, G.M. Sampietro³, G. Maconi⁴

¹Università degli Studi di Milano, Department of General Surgery, Department of Biomedical and Clinical Sciences 'L. Sacco', University of Milan, ASST Fatebenefratelli Sacco, Milan, Italy., Milano, Italy, ²Università degli Studi di Milano, Centro Cardiologico Monzino, Milano, Italy, ³Università degli Studi di Milano, Department of General Surgery, ASST Rhodense, Ospedale di Rho-Monumento dei Caduti, Milano, Italy, ⁴Università degli Studi di Milano, ASST Fatebenefratelli-Sacco, Gastrointestinal Unit, L. Sacco University Hospital, Department of Biochemical and Clinical Sciences, University of Milan, Italy, Milano, Italy

Contact E-Mail Address: francesco.colombo@asst-fbf-sacco.it

Introduction: Perioperative hyperglycemia, in diabetic and non diabetic patients undergoing surgery, is known to be associated with increased rates of surgical site infection (SSI), myocardial infarction, stroke and other postoperative adverse events^{1,2}. No data are available in literature regarding the potential relationship between hyperglycemia and postoperative complications in Crohn's patients. Aim of the paper is to study the association between perioperative hyperglycemia and adverse events in a surgical cohort from two IBD Tertiary Care hospitals.

Aims & Methods: This study is a retrospective analysis of a prospectively maintained database. All patients undergoing first surgery for ileo-colonic Crohn between 2012 and 2023 were included. Patient cohort was divided in three subgroups according to the preoperative serum level of glycemia: <100 mg/dL, 100-126 mg/dL and > 126mg/dL. All postoperative complications were collected and categorized according the Clavien-Dindo classification³.

Results: In the study period, 641 patients were included, 389 (60.7%) males and 252 (39.3%) females. 7 (1.1%) were known diabetic patients. The mean preoperative serum level of glycemia was 97.23 ± 22.1 mg/dL and the mean postoperative level was 107.92 ± 29.7 mg/dL. Preoperative glycemia > 100 g/dL was related to a significant more frequent rate of complications (p<0.01; OR 3.34). Also elderly age (> 65 years old) and preoperative serum albumin < 35 g/L were found significant risk factors for postoperative complications: respectively with p< 0.01 (OR 1.01) and p< 0.04 (OR 1.97). The percentage of complications was gradually increased with the augmentation of the preoperative hyperglycemia with a statistically significant difference: 22.6% in the group with <100 mg/dL, 47.9% in the 100-126 mg/dL group and 56.2% in >126 mg/dL group (p< 0.01). Wound infection, abdominal abscess and postoperative ileus were statistically more frequent in Crohn's patients with preoperative glycemia> 100 gm/dL, respectively with p<0.001, p< 0.01 and p< 0.013.

Conclusion: Our study confirms that the risk of post-operative adverse events for Crohn's patients, as previously highlighted for general surgical population, appears to be linked to preoperative hyperglycemia. A prompt control of glycemia levels in the perioperative period could help to reduce significantly the rate of surgical complications in this already challenging and demanding disease.

References:

1. Kotagal M, Symons RG, Hirsch et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. Ann Surg. 2015 Jan;261(1):97-103. doi: 10.1097/SLA.0000000000000688.
2. Kiran RP, Turina M, Hammel J et al. The clinical significance of an elevated postoperative glucose value in nondiabetic patients after colorectal surgery: evidence for the need for tight glucose control?. Ann Surg 2013; 258: 599-605.

3. Clavien PA, Barkun J, de Oliveira ML et al. The Clavien-Dindo surgical classification of surgical complications. Ann Surg 2009; 250 (2): 187-196. doi : 10.1097/SLA.0b013e3181b13ca2.

Disclosure: Nothing to disclose.

MP272

TEMPORAL TRENDS IN COLECTOMY AND MORTALITY RATES FOLLOWING SURGERY FOR ULCERATIVE COLITIS IN ENGLAND: 2005-2020

J. Couch¹, K. Thomas¹, T. Card¹, D. Humes¹

¹University of Nottingham, Nottingham, United Kingdom

Contact E-Mail Address: david.humes@nottingham.ac.uk

Introduction: The incidence of Ulcerative Colitis (UC) in the England has changed little over the last fifteen years (1,2). Medical and surgical management however has transformed during that period. Our aim was to investigate whether colectomy rates and 90-day mortality following surgery have changed in the last two decades.

Aims & Methods: This was a population-based cohort study using computerized health records from Clinical Practice Research Datalink linked to Hospital Episode Statistics and Office of National Statistics data. An incident cohort was defined as patients with a new diagnosis of UC between 2005-2020.

Time to first colectomy was calculated from diagnosis date. Cumulative incidence of colectomy and 90-day mortality was calculated using life tables. Colectomy rates following UC diagnosis were calculated annually for each year between 2005 and 2020 using the denominator of total person time contributing to that year. Rates were modelled using Poisson regression analysis. Cox regression was used to model the risk of surgery and 90-day mortality rates and the effect of gender, socioeconomic status and region. Analysis was performed using StataMP 18.

Results: 46,730 patients had an incident diagnosis of UC, 49.33% (23,055/46730) were female. 5.72% (2672/46730) underwent colectomy. The one year risk of colectomy was 2.32% (95% CI 2.19-2.47%), with a 5-year risk of 4.92% (95% CI 4.72-5.13%) and 10-year risk of 6.47% (95% CI 6.22-6.73%). 90-day mortality for emergency and elective colectomy was 3.54% (95% CI 2.73-4.58%) and 1.44% (95% CI 0.92-2.25%) respectively. Total colectomy rate fell from 17.15 per 1000 person-years in 2005 to 5.96 per 1000 person years in 2020 (IRR 0.35, 95% CI 0.27-0.45). Elective colectomy rates fell from 6.78 per 1000 person-years in 2005 to 2.75 per 1000 person-years in 2020, (IRR 0.41, 95% CI 0.27-0.60). Emergency colectomy rates fell from 10.37 per 1000 person-years in 2005 to 3.21 per 1000 person-years in 2020 (IRR 0.31, 95% CI 0.22-0.43).

Females were 30% less likely to undergo colectomy (HR 0.70, 95% CI 0.65-0.75). There was a statistically significant difference in risk of colectomy by region with London, South East, East of England and North West having lower colectomy rates than West Midlands and the North East. There was no significant difference between gender, region or socioeconomic status for 90-day mortality.

Conclusion: There has been a significant reduction in both elective and emergency colectomy rates between 2005-2020. There was gender and regional variation in risk of colectomy. Further work may attempt to correlate these findings with prescription rates of particular medications to elicit a cause for these findings.

References:

1. King D, Reulen RC, Thomas T, Chandan JS, Thayakaran R, Subramanian A, et al. Changing patterns in the epidemiology and outcomes of inflammatory bowel disease in the United Kingdom: 2000-2018. Aliment Pharmacol Ther. 2020;(December 2019):1-13.
2. Freeman K, Ryan R, Parsons N, Taylor-Phillips S, Willis BH, Clarke A. The incidence and prevalence of inflammatory bowel disease in UK primary

care: a retrospective cohort study of the IQVIA Medical Research Database. BMC Gastroenterol [Internet]. 2021;21(1):1–7. Available from: <https://doi.org/10.1186/s12876-021-01716-6>

Disclosure: Nothing to disclose.

MP273

DEFINING NORMALCY: FEATURES OF AN ULTRA-NORMAL POUCH PHENOTYPE

M. Fischman¹, L. Godny^{2,3}, A. Friedenberg^{2,3}, R. Barkan^{3,2}, H. Yanai^{2,3}, I. White^{3,4}, N. Wasserberg^{3,4}, I. Dotan^{2,3}, J.E. Ollech^{2,3}

¹Hebrew University of Jerusalem, Department of Military Medicine, Jerusalem, Israel, ²Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ³Tel Aviv University, Faculty of Medical and Health Sciences, Tel Aviv, Israel, ⁴Rabin Medical Center, Division of Surgery, Petah Tikva, Israel

Contact E-Mail Address: fischmaya@gmail.com

Introduction: Chronic complications are common among patients with ulcerative colitis (UC) undergoing Ileal Pouch-Anal Anastomosis (IPAA)^{1,2}. To predict who may benefit most from IPAA, we focused on patients maintaining a normal pouch phenotype for over a decade, seeking which biomarkers identify this unique group.

Aims & Methods: All patients with UC after IPAA who were followed at the Rabin Medical Center comprehensive pouch clinic and consented to prospective observational follow-up were included. Patients with familial adenomatous polyposis or ileostomy were excluded.

“Ultra-normal” pouch phenotype was defined as both clinically and endoscopically normal pouch phenotype, with no episodes of acute pouchitis over 10 years post-ileostomy closure. We assessed demographic data; disease course; peri-operative factors; and inflammatory, serology, and genetic markers. We compared “ultra-normal” patients to “rapid complicators”, defined by the development of chronic pouchitis or Crohn’s-like disease of the pouch within five years post-ileostomy closure.

Results: Of over 400 patients, 174 consented to prospective follow-up; of these, 18 were excluded due to FAP and 8 due to ileostomy. Of the 148 qualifying for final analysis, 26 (17.5%) maintained an “ultra-normal” phenotype over an average of 20±7.14 years since ileostomy closure, while 32 (21%) were classified as “rapid complicators”.

The “ultra-normal” group (mean age, 55.2±13.3 years; females: 50%) had an average age at UC diagnosis of 23.7±10.0 years and age at surgery of 34.9±12.3 years. In comparison, the “rapid complicators” group had an average age at diagnosis of 22.3±15.1 years (p=0.25) and age at surgery of 31.1±16.9 years (p=0.2).

Repeated measurements during our study follow-up period found that “ultra-normal” patients maintained an average BMI of 27.2±6.2 kg/m² and hemoglobin, C-reactive protein, and fecal calprotectin levels of 14.0±1.45 g/dL, 0.63±0.56 mg/dL, and 190.8±169.0 µg/g, respectively. Their average Short Inflammatory Bowel Disease Questionnaire (SIBDQ) score was 55.6±10.2; average Pouchitis Disease Activity Index (PDAI) score was 2.7±1.7. None required post-operative steroidal, immunomodulator, or biologic treatment. Probiotics were intermittently used by 12 patients (46%).

Non-Ashkenazi Jewish origin was more common in the “ultra-normal” group (62% vs. 34%) than Ashkenazi Jewish (38% vs. 41%) and Arabs (0% vs. 22%), p=0.016. No patient in the “ultra-normal” group had NOD2 polymorphism, compared to 3 heterozygotes among “rapid complicators” (p=0.23). Pre-operative disease extent was similar between groups (p=0.64), as was the indication for IPAA, with 77% of “ultra-normal” patients and 78% of “rapid complicators” having refractory or severe disease as the surgery indication (p>0.99). However, pre-operative biologic therapy, mostly with anti-tumor necrosis factor agents, was independently significantly more

common among “rapid complicators” (75% vs. 19% in “ultra-normal”, p<0.001).

Conclusion: “Ultra-normal”, uncomplicated pouch phenotype for two decades after IPAA is sustained in a minority (~ fifth) of patients. While similar to “rapid complicators” in pre-operative disease course and indication for surgery, patients with “ultra-normal” pouch received less pre-IPAA biologic therapy. These findings may contribute to post-IPAA prognostication and, if validated, may affect pre-operative treatment decisions.

References: (1) Yanai H, Ben-Shachar S, Mlynarsky L, et al. The outcome of ulcerative colitis patients undergoing pouch surgery is determined by pre-surgical factors. *Aliment Pharmacol Ther.* 2017;46(5):508-515. doi:10.1111/apt.14205

(2) Kayal M, Plietz M, Rizvi A, et al. Inflammatory Pouch Conditions Are Common After Ileal Pouch Anal Anastomosis in Ulcerative Colitis Patients. *Inflamm Bowel Dis.* 2020;26(7):1079-1086. doi:10.1093/ibd/izz227

Disclosure: Jacob E Ollech: Has received grant support from Pfizer, consulting fees from Takeda, and speaker fees from Abbvie, Janssen, Pfizer, Takeda, Novartis, and Bristol Myers Squibb.

Iris Dotan: consultation fee or honorarium from: Abbott, Abbvie, Athos, Arena, Altman

Research, Cambridge Healthcare, Celltrion, Celgene/BMS, Eli-Lilly, Ferring, Falk Pharma, Food

Industries Organization, Gilead, Galapagos, Iterative Scopes, Integra Holdings, Janssen,

Neopharm, Pfizer, Rafa laboratories, Roche/Genentech, Sangamo, Sublimity, Sandoz, Takeda,

Wildbio. Grants: Altman Research, BMS, Pfizer

MP274

COMPARATIVE ANALYSIS OF SHORT- AND LONG-TERM RESULTS BETWEEN REDO AND PRIMARY ILEAL-POUCH ANAL ANASTOMOSIS PROCEDURES: A CRITICAL EXAMINATION

T. Braquet¹, M. Collard¹, A. Challine¹, C. Debove¹, N. Chafai¹, Y. Parc¹, J. Lefevre¹

¹Hopital Saint-Antoine General and Digestive Surgery, Digestive Surgery, Paris, France

Contact E-Mail Address: lefevre.jeremie@gmail.com

Introduction: Redoing an ileal pouch-anal anastomosis (IPAA) is a rare scenario but the only solution to effectively manage chronic surgical failures. The aim was to compare short- and long-term outcomes after redo-IPAA.

Aims & Methods: All patients who underwent IPAA surgery (primary or redo-IPAA) between 2010 and 2023 were included in this single-center study. Morbidity and ileal-pouch survival were collected. Patients were also administered questionnaires assessing bowel function with the Ileal Pouch Severity Score (IPSS) and the quality of life with the SF36.

Results: 380 primary-IPAA were performed during the inclusion period. Among them, 4% (n=17) required a redo-IPAA. 15 patients were referred to our centre for redo-IPAA. Therefore, 32 patients with redo-IPAA were included. Indication for redo-IPAA were chronic leakage from the previous IPAA (n=15), endoscopically unresectable ileal pouch polyps in FAP patients (n=9), IPAA stenosis (n=4), poor functional results (n=2), twist of the ileal pouch (n=1), invasive adenocarcinoma of the ileal pouch (n=1). Patients had been operated initially for Ulcerative Colitis (n=11), Familial polyposis (n=18) or other causes (n=3).

Median time interval from primary to redo-IPAA was 1.1 years with a minimum of 0.3 year and a maximum of 36 years. The anastomosis was handsewn in 97% of redo-IPAA versus 79% of primary-IPAA (p=0.018).

Manoeuvres to increase mesenteric length were never required during redo-IPAA, whereas it was in 27% of primary-IPAA ($p<0.001$). A diverting stoma to protect the IPAA was performed in 44% of primary-IPAA and in 69% of redo-IPAA ($p=0.007$). Overall postoperative morbidity was lower after redo-IPAA (25%) compared to primary-IPAA (47%, $p=0.016$), as well as hospital stay duration (median 7 days versus 9 days, $p=0.003$). Severe morbidity (redo-IPAA: 16%, primary-IPAA: 21%, $p=0.458$) and anastomotic leakage rate (redo-IPAA: 6%, primary-IPAA: 14%, $p=0.286$) did not differ. Post-operative mortality was nil after redo-IPAA and was 0.3% (1 patient) after primary-IPAA. No patient developed short bowel syndrome.

After a median follow-up of 48 months, ileal-pouch survival was similar between redo-IPAA and primary-IPAA groups (5-year ileal-pouch survival: 82% versus 90% respectively, log-rank test: $p=0.250$). Long-term rate of anastomotic stenosis was similar after redo-IPAA (18%) compared to primary-IPAA (12%, $p=0.365$). Among patients with a technical success of the IPAA procedure, the rate of definitive stoma due to a poor bowel functional result was 14% after redo-IPAA versus 8% after primary-IPAA ($p=0.401$). Long-term bowel function was significantly worse after redo-IPAA (median IPSS score: 56/100) compared to primary-IPAA (median IPSS score: 41/100, $p=0.007$), without impacting quality of life measured by the SF36 score (physical component summary: redo-IPAA: 49/100, primary-IPAA: 50/100, $p=0.501$ and mental component summary: redo-IPAA: 41/100, primary-IPAA: 45/100, $p=0.078$).

Conclusion: Redo-IPAA is feasible with acceptable post-operative morbidity as it showed a similar rates of severe complications, anastomotic leakage, and ileal-pouch survival compared to primary-IPAA. Functional outcomes is worse compared to primary-IPAA but avoid a definitive ileostomy. After a technical success of redo-IPAA, 14% of patients asked for a definitive stoma due to a poor bowel function, thus 86% of patients preferred to maintain digestive continuity with the achieved functional outcome rather than opting for a permanent ileostomy.

Disclosure: Nothing to disclose.

MP275

FUNCTIONAL POUCH EVALUATION WITH DYNAMIC TRANSPERINEAL ULTRASOUND AND ANO-POUCH MANOMETRY IN ULCERATIVE COLITIS PATIENTS WITH RESTORATIVE PROCTOCOLECTOMY: PRELIMINARY RESULTS

M.L. Vaiano¹, F. Colombo², A. Dell'Era¹, G. Maconi¹, L. Cariola², S. Ardizzone¹, P.G. Danelli²

¹Ospedale Luigi Sacco, Department of Gastroenterology, Milano, Italy, ²Ospedale Luigi Sacco, Department of Surgery, Milano, Italy

Contact E-Mail Address: marialuigia.vaiano@hotmail.com

Introduction: Restorative proctocolectomy is the intervention of choice in patients with refractory or complicated Ulcerative Colitis (UC). Despite the high success rate of the procedure, a minority of patients experiences recurrent symptoms related to pouch dysfunction. To date, neither a gold standard for instrumental diagnosis of such disorders nor specific reference parameters for studying this population have been established.

Aims & Methods: The main aim of this study was to evaluate the role of dynamic transperineal ultrasound (DTPUS) and ano-pouch manometry (APM) in describing functional changes of the pouch and their correlation with clinical symptoms.

This is a prospective observational study conducted on a consecutive unselected sample of patients who underwent restorative proctocolectomy with J pouch for refractory and/or complicated UC in an Inflammatory Bowel Disease (IBD) Tertiary Care Centre. Included patients underwent ileostomy closure at least one year before enrollment. Patients were administered a questionnaire to assess the degree of pouch dysfunction,

followed by DTPUS and APM performed by different operators who were blind to clinical data. Retrospective data regarding surgery and postoperative course were also collected. Fisher's exact test or chi-square test were used for statistical evaluation of the correlation between variables.

Results: 18 patients were analyzed. Based on symptoms severity, they were divided into five groups according to the recently proposed Ileoanal Pouch Syndrome Severity (IPS) score: absence of pouch dysfunction (4), mild dysfunction (4), moderate dysfunction (3), severe dysfunction (2), and extremely severe dysfunction (5). Among DTPUS variables, resting length of puborectalis muscle showed a significant inverse correlation ($p=0.03$) with the degree of pouch dysfunction. More relevant perineal descent and shorter length of puborectalis muscle during strain were also observed in patients with significantly severe dysfunction, although these correlations were not statistically significant ($p=0.08$ and 0.13 respectively). High prevalence of dyssynergic defecation (61%) was also found in all groups, regardless of symptom severity. Among manometric variables, resting basal pressure of the anal sphincter showed an inverse correlation with the severity of pouch dysfunction, albeit without reaching statistical significance ($p=0.12$). Other characteristics observed in all groups, regardless of symptom severity, were a high prevalence of dyssynergic defecation (53%) and absence of the recto-anal inhibitory reflex (77%). Among surgical characteristics, the presence of complications after the first colectomy stage showed significant correlation ($p<0.02$) with subsequent development of clinically relevant pouch dysfunction.

	US FEATURES					P
	0 NO IPS	1 mild IPS	2 moderate IPS	3 severe IPS	4 extremely severe IPS	
Resting length of puborectalis muscle (expressed in mm)	60,4 ± 9,3	64,1 ± 6,7	69,1 ± 1,1	51,8 ± 0,1	53,7 ± 6,3	0,03
Perineal descent (expressed in mm)	9,7 ± 2,6	8,5 ± 6,8	3,3 ± 5,8	14,5 ± 5,7	13,1 ± 2,6	0,08

	MANOMETRIC FEATURES					P
	0 NO IPS	1 mild IPS	2 moderate IPS	3 severe IPS	4 extremely severe IPS	
Resting basal pressure of anal sphincter (expressed in mmHg)	82,2 ± 12,5	86 ± 15,3	74,5 ± 11,2	55,1 ± 26,3	70,6 ± 14,6	0,12

Conclusion: Our preliminary results seems to highlight the role of APM and DTPUS in the diagnosis of functional pouch disorders after restorative proctocolectomy in UC.

References: Ardalan ZS, Friedman AB, Con D, Chandran S, Gibson D, Pham A, De Cruz P, Tay K, Bell S, Rosella O, Sparrow MP, Gibson PR. Accuracy of Gastrointestinal Ultrasound and Calprotectin in the Assessment of Inflammation and its Location in Patients with an Ileoanal Pouch. *J Crohns Colitis*. 2022 Jan 28;16(1):79-90. doi: 10.1093/ecco-jcc/jjab125. PMID: 34302729.

Quinn KP, Busciglio IA, Burton DD, Inoue A, Lee YS, Heiken JP, Sheedy SP, Fletcher JG, Raffals LE. Defining normal pouch function in patients with ileal pouch-anal anastomosis: a pilot study. *Aliment Pharmacol Ther*. 2022 Jun;55(12):1560-1568. doi: 10.1111/apt.16859. Epub 2022 Mar 11. PMID: 35274320.

Beer-Gabel M, Carter D. Comparison of dynamic transperineal ultrasound and defecography for the evaluation of pelvic floor disorders. *Int J Colorectal Dis*. 2015 Jun;30(6):835-41. doi: 10.1007/s00384-015-2195-9. Epub 2015 Mar 31. PMID: 25820786.

Beer-Gabel M, Teshler M, Barzilai N, Lurie Y, Malnick S, Bass D, Zbar A. Dynamic transperineal ultrasound in the diagnosis of pelvic floor disorders: pilot study. *Dis Colon Rectum*. 2002 Feb;45(2):239-45; discussion 245-8. doi: 10.1007/s10350-004-6155-7. PMID: 11852339.

Disclosure: Nothing to disclose.

Cutting-edge modalities for endoscopic resections

11:30-12:30 / Poster Stage 2

MP276

COMPARATIVE EFFICACY OF DIFFERENT TECHNIQUES FOR COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): A NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

M.F. Maida^{1,2}, A. Facciorusso³, G. Marasco^{4,5}, G. Calabrese⁶, G. Ianiro^{7,8}, J. Jacques⁹, R. Maselli^{10,11}, C. Hassan^{10,11}, A. Repici^{10,11}, R. Di Mitri⁶, S. Sferrazza⁶

¹University of Enna 'Kore', Department of Medicine and Surgery, Caltanissetta, Italy, ²Umberto I Hospital, Gastroenterology Unit, Enna, Italy, ³University of Foggia, Gastroenterology Unit, Foggia, Italy, ⁴University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁵S.Orsola-Malpighi University Hospital, Bologna, Italy, ⁶Arnas Civico-Di Cristina-Benfratelli Hospital, Gastroenterology and Endoscopy Unit, Palermo, Italy, ⁷Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Catholic University of Rome, Digestive Disease Center, Rome, Italy, ⁸Catholic University of the Sacred Heart, Department of Translational Medicine and Surgery, Rome, Italy, ⁹CHU Limoges - Hepato-Gastro-Enterology, CHU Limoges; Limoges/FR, Hepato-Gastro-Enterology, Limoges, France, ¹⁰Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ¹¹Humanitas Clinical and Research Center -IRCCS, Endoscopy Unit, Rozzano, Italy

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: Endoscopic submucosal dissection (ESD) is an advanced technique that can provide a successful 'en-bloc' and R0 resection rate for large gastrointestinal (GI) lesions. To date, several ESD techniques have been proposed, but their comparative efficacy is still unclear.

Aims & Methods: This network meta-analysis aims to investigate and compare the efficacy and safety of different ESD techniques for resection of colonic lesions. MEDLINE, Embase, Scopus, and the Cochrane Library were systematically searched for randomized controlled trials (RCTs) comparing different ESD techniques through March 2024. The primary outcomes were 'en-bloc' and R0 resection rates. The secondary outcome was the incidence of procedure-related AEs. Direct and indirect comparisons were performed among different ESD techniques. Results were expressed as risk ratio (RR) and 95% confidence interval (CI), using the DerSimonian and Laird random-effects model. The relative ranking of the interventions for achieving the aforementioned outcomes was calculated as their surface under the cumulative ranking curve (SUCRA). The study quality was evaluated using the revised Cochrane risk-of-bias (RoB2) tool for randomized trials.

Results: After selection of studies, 9 RCTs were included in the systematic review.

On network meta-analysis for 'en-bloc' resection (9 RCTs, 872 patients, 5 techniques assessed), pocked with traction ESD (PT-ESD) (RR=1.02 - 95%CI=0.96-1.07) and pocket ESD (P-ESD) (RR=1.02 - 95%CI=0.98-1.05) showed higher efficacy, whereas hybrid ESD (H-ESD) (RR=0.94 - 95%CI=0.87-1.02) lower efficacy compared to conventional ESD (C-ESD).

On network meta-analysis for R0 resection (7 RCTs, 732 patients, 4 techniques assessed), PT-ESD (RR=1.05 - 95%CI=0.96-1.16) showed higher efficacy, and H-ESD (RR=0.97 - 95%CI=0.84-1.13) lower efficacy compared to C-ESD. Overall, P-ESD resulted the best technique for 'en-bloc' resection (SUCRA 0.70) and PT-ESD for R0 (SUCRA 0.83), while H-ESD showed the poorest performance for both outcomes (SUCRA 0.06 and 0.30, respectively) (Table 1).

On network meta-analysis for AEs (9 RCTs, 872 patients, 5 techniques assessed), PT-ESD (RR=0.35 - 95%CI=0.05-2.48) was associated with a lower

incidence of AEs, and H-ESD (RR=1.22 - 95%CI=0.30-5.01) with higher incidence of AEs, compared to C-ESD. Overall, PT-ESD resulted as the safest technique (SUCRA 0.83), followed by T-ESD (SUCRA 0.60), whereas H-ESD showed the poorest performance (SUCRA 0.28).

According to the RoB2 tool, none of the studies included was of poor methodological quality except for one.

'En-bloc'		R0		AEs	
P-ESD	0.70	PT-ESD	0.83	PT-ESD	0.83
PT-ESD	0.67	P-ESD	0.52	T-ESD	0.60
T-ESD	0.67	T-ESD	0.46	P-ESD	0.47
C-ESD	0.39	C-ESD	0.38	C-ESD	0.32
H-ESD	0.06	H-ESD	0.30	H-ESD	0.28

Table 1. SUCRA score ranking of different interventions in terms of 'en-bloc' resection rate, R0 resection rate and incidence of AEs.

Conclusion: The results of this network meta-analysis show a trend towards greater effectiveness and safety of PT-ESD for the removal of colonic lesions. H-ESD was associated with worse results and should be avoided, preferring other techniques.

Disclosure: Nothing to disclose.

MP277

ENDOSCOPIC RESECTION IN TERTIARY WESTERN PRACTICE PROVIDES SUPERIOR RESULTS FOR PATIENTS THAN TRANSANAL MICROSURGERY

A. Eqbal¹, O. Olabintan¹, H. Ayubi¹, M.-A. Noreillie¹, J. Bhoday², H. Rashid³, M. Anand¹, A. Adeyeye², S. Thrumurthy⁴, S. Gulati¹, B. Hayee⁵, A. Emmanuel², A. Haji²

¹King's College Hospital, Gastroenterology, London, United Kingdom, ²Kings College Hospital, Colorectal surgery, London, United Kingdom, ³King's College Hospital, Colorectal Surgery, London, United Kingdom, ⁴Kings College Hospital, Upper gastrointestinal surgery, London, United Kingdom, ⁵Kings College Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: ali.eqbal@nhs.net

Introduction: Resection of large non-pedunculated colorectal polyps (LNPCP) located in the rectum varies by institution and region with some, particularly colorectal surgeons, favouring TEM and others endoscopic resection (ER). There is a paucity of data directly comparing these strategies and the procedure of choice remains under debate. Our unit is a tertiary referral centre for complex polyps and early colorectal cancer. All rectal LNPCP were treated by TEM until a change in practice from 2011 when the first-line therapeutic strategy for rectal LNPCP changed to ER.

Aims & Methods: We aimed to report the outcomes of TEM and ER of rectal LNPCP from a large tertiary cohort. Large (≥20mm) rectal adenomas resected by TEM or ER (2009 – 2023) were analysed. From 2009-2011 all rectal adenomas were treated by TEM, after which the primary resection strategy changed to ER. Outcomes were compared between techniques. Given the difference in resection strategy, a composite outcome of septic complications included clinically significant perforation for ER (early or delayed perforation requiring any form of unplanned medical or surgical treatment) and septic complications for TEM (peritonitis or pelvic/anorectal sepsis).

Results: 704 rectal adenomas were resected by TEM (n=71), EMR (n=145) and ESD/Hybrid ESD (n=488) with a mean size of 45mm for TEM vs 55mm for ER (p<0.001). 100% of patients undergoing TEM required hospital admission vs 15% for ER (p<0.001), and 100% required general anaesthesia (GA) for TEM vs 26% for ER (GA or propofol sedation, p<0.001). En bloc resection was achieved for 96% of ESD resections, 54% of TEMs, 28% of EMR and 14% of hybrid ESD (p<0.001). The incidence of complications

were similar (9.9% for TEM versus 5.0% for ER, $p=0.10$). Recurrence occurred in 2.7% after ESD, 21.1% after EMR, 23.6% after Hybrid ESD and 36.4% after TEM ($p<0.001$). No patients undergoing ER or TEM required surgery as a result of a complication.

Conclusion: Despite significantly larger lesion sizes, ER in our institution provides far superior results for patients than TEM with relatively fewer patients requiring hospital admission and lower recurrence rates, especially with ESD. En bloc resection was more likely with ER as a result of the difficulty achieving en bloc resection for extremely large lesions with TEM, which can invariably be resected en bloc by ESD. These results have led to a policy of ER for all apparently benign rectal tumours regardless of size and, in recent years, ESD as the primary approach for all rectal lesions.

Disclosure: Nothing to disclose.

MP278

RISK FACTORS FOR METACHRONOUS COLORECTAL CANCER OR ADVANCED LESIONS AFTER ENDOSCOPIC RESECTION OF SERRATED POLYPS: A SYSTEMATIC REVIEW AND META-ANALYSIS

S. Baile Maxía¹, C. Mangas-Sanjuan¹, U. Ladabaum², C. Sanchez Ardila³, N. Sala Miquel¹, C. Hassan⁴, M.D Rutter⁵, M. Bretthauer⁶, P. Zapater⁷, R. Jover¹

¹Hospital General Universitario Dr Balmis de Alicante, Gastroenterology, Alicante, Spain, ²Stanford University School of Medicine, Division of Gastroenterology and Hepatology, Stanford, United States of America, ³Universidad Miguel Hernández, Alicante, Spain, ⁴Humanitas University, Gastroenterology, Rome, Italy, ⁵Population Health Sciences Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom, ⁶University of Oslo, Department of Medicine, Gastrointestinal Endoscopy, Oslo, Norway, ⁷Hospital General Universitario Dr Balmis de Alicante, Pharmacology, Alicante, Spain

Contact E-Mail Address: sandrabaaile@gmail.com

Introduction: Serrated polyps (SPs) are precursors to 15–20% of colorectal cancers (CRCs). However, there are uncertainties regarding which SPs require surveillance and at what intervals, with recommendations adapted from those for adenomas in the absence of solid evidence.

Aims & Methods: Our aim was to assess which SP risk characteristics relate to a higher risk of metachronous CRC or advanced polyps. We systematically searched PubMed, EMBASE, and Cochrane for cohort, case-control studies, and clinical trials from inception to Dec 31, 2023, for CRC or advanced polyps [advanced adenoma (AA) or advanced SP] incidence at surveillance stratified by baseline SP size, dysplasia, location, and multiplicity. CRC and advanced polyp incidence per 1,000 person-years (p-y) were estimated. We performed a meta-analysis by calculating pooled relative risks (RR) using a random-effects model.

Results: 5,903 studies were reviewed and 14 included, with 493,949 patients (mean age 59.5 years, 55% men). Mean follow-up was 4.9 years. CRC incidence per 1,000 p-y was 2.09 (95%CI 1.29–2.90) for advanced SP, 1.52 (0.78–2.25) for SP $\geq$ 10mm, 5.86 (2.16–9.56) for SP with dysplasia, 1.18 (0.77–1.60) for proximal SP, 0.52 (0.08–1.12) for $\geq$ 3SP, 0.50 (0.35–0.66) for non-advanced SP, and 0.44 (0.41–0.46) for normal colonoscopy. Metachronous CRC risk was higher in advanced SP vs non-advanced SP (RR 1.84, 95%CI 1.11–3.04), and vs normal colonoscopy (RR 2.92, 2.26–3.77); in SP $\geq$ 10mm vs <10mm (RR 2.61, 1.43–4.77), and vs normal colonoscopy (RR 3.52, 2.17–5.69); and in SP with dysplasia vs normal colonoscopy (RR 2.71, 2.00–3.67). No increase in CRC or advanced polyp risk was found in patients with proximal vs distal SP, nor in $\geq$ 3SP vs 1–2SP.

Conclusion: CRC risk is significantly higher in patients with baseline advanced SP after 4.9 years of follow-up, with risk magnitudes similar

to those described for AA, supporting the current recommendation for 3-year surveillance in patients with advanced SP.

Disclosure: RJ has received research grants from MSD, and has participated as an advisor to MSD, Norgine, Alpha-Sigma, and GISupply. UL has participated in the advisory board (UniversalDx, Lean Medical, Vivante, Kohler Ventures), and as consultant (Medtronic, Clinical Genomics, Guardant Health, Freenome, ChekCap). MDR has no COI since start of 2020 (Advisor for Norgine in 2019). The rest of authors have nothing to disclose.

MP279

LONG-TERM OUTCOMES OF GRADE 1 RECTAL NEUROENDOCRINE TUMORS AFTER INCOMPLETE ENDOSCOPIC RESECTION

J.S. Park¹, J.H. Park¹, G.H. Lee¹, S.G. Lim¹, S.J. Shin¹, K.M. Lee¹, C.-K. Noh¹

¹Ajou University School of Medicine, Gastroenterology, Suwon, South Korea

Contact E-Mail Address: goodparkjs@hanmail.net

Introduction: Although the prognosis of low-grade rectal neuroendocrine tumors (NET) is good, surveillance of patients with pathologically incomplete resection after endoscopic resection (ER) remains controversial.

Aims & Methods: This study aimed to evaluate the long-term outcomes of patients with grade 1 rectal NET after ER and the risk factors for incomplete resection. We retrospectively enrolled patients who were diagnosed with rectal NET grade 1 after endoscopic resection between January 2011 and December 2023. We divided the patients into two groups according to histopathological evaluation: complete resection and incomplete resection. Patients who were followed up for > 12 months were included in the analysis. Logistic regression analysis was performed to investigate the risk factors for incomplete resection after ER.

Results: In total, 454 patients were enrolled in this study. Mean (SD) lesion size was 5.7 (2.1) mm and lesion location (distance from anal verge) was 7.8 (3.1) cm from anal verge. The most common treatment method was endoscopic mucosal resection with strip biopsy method (EMR-S, n = 338, 74.4%). On histopathologic evaluation after ER, the complete resection rate was 80.6% (n = 366). Of the incomplete resections (n = 88, 19.4%), 82 (18.1 %) were margin positive and 11 (2.4%) were lymphovascular invasion. Mean follow up months were 38.8 (27.3) and 46.2 (30.2) months in entire patients and incomplete resection group, respectively. In logistic regress analysis showed the lesion size 5.1 – 10 mm (OR 1.9, 95% CI 1.021– 3.686, $P = 0.044$), multiple lesions (OR 8.9, 95% CI 1.454 – 71.165; $P = 0.021$), and retroflexion scope view (OR 4.3, 95% CI, 1.639 – 10.924; $P = 0.002$) were the independent risk factors associated with incomplete resection. During the follow-up period, despite the inclusion of patients with incomplete resection, no recurrence was observed.

Conclusion: Grade 1 rectal NET have a very good prognosis even with incomplete ER. Even if the resection is incomplete, progress can be observed without additional treatment.

Disclosure: Nothing to disclose.

MP280

A MULTICENTER, RANDOMIZED CONTROLLED TRIAL OF A SELF-ASSEMBLING HEMOSTATIC GEL TO PREVENT DELAYED BLEEDING FOLLOWING ENDOSCOPIC MUCOSAL RESECTION: THE PURPLE TRIAL

J. Drews¹, M. Zachäus², T. Kleemann³, J. Schirra⁴, O. Cahyadi⁵, O. Möschler⁶, C. Schulze⁷, I. Steinbrück⁸, E. Wedi⁹, O. Pech¹⁰, T. Weismüller¹¹, A. Küllmer¹², M. Abdelhafez¹³, J. Wedemeyer¹⁴, T. Beyna¹⁵, J. Riedel², U.P. Halm², C. Güther³, R. Vasapolli¹⁶, C. Torres Reyes⁵, D. Quast⁵, O. Bachmann¹⁷, I. Marchuk¹⁸, C. Frahm¹⁸, T. Steffen¹⁸, M.V. Wulff¹, P. Wohlmuth¹⁸, T. Bunde¹, N. Gessler¹⁸, T. von Hahn¹⁹

¹Asklepios Klinik Barmbek, Hamburg, Germany, ²Helios Park-Klinikum Leipzig, Klinik für Gastroenterologie, Hepatologie, Hämatologie, Onkologie und Palliativmedizin, Leipzig, Germany, ³Carl-Thiem-Klinikum, Klinik für Gastroenterologie und Rheumatologie, Cottbus, Germany, ⁴University of Munich, Department of Internal Medicine II, München, Germany, ⁵St. Josef-Hospital, a hospital of the Ruhr-University-Bochum, Gastroenterology, Essen, Germany, ⁶Niels-Stensen-Kliniken, Osnabrück, Germany, ⁷Siloah St. Trudert Klinikum, Pforzheim, Germany, ⁸Evangelisches Diakonienkrankenhaus Freiburg, Freiburg, Germany, ⁹Sana Klinikum Offenbach, Offenbach, Germany, ¹⁰Krankenhaus Barmherzige Brüder Klinik für Gastroenterologie und Interventionelle Endoskopie - Klinik, Klinik für Gastroenterologie und, Regensburg, Germany, ¹¹Vivantes Humboldt Hospital, Berlin, Germany, ¹²Universitätsklinikum Freiburg, Freiburg im Breisgau, Germany, ¹³Klinikum rechts der Isar, Technical University of Munich, II. Medizinische Klinik und Poliklinik, Munich, Germany, ¹⁴Klinikum Robert Koch Gehrden, Gehrden, Germany, ¹⁵Evangel. Krankenhaus Düsseldorf, Department of Internal Medicine, Düsseldorf, Germany, ¹⁶University Hospital LMU Munich, Department of Internal Medicine II, Munich, Germany, ¹⁷Siloah St. Trudert Klinikum, Dept of Internal Medicine 1, Pforzheim, Germany, ¹⁸Asklepios Proresearch, Hamburg, Germany, ¹⁹Asklepios Klinik Barmbek, Gastroenterologie, Hepatologie und Interventionelle Endoskopie, Hamburg, Germany

Contact E-Mail Address: t.hahn@asklepios.com

Introduction: Delayed bleeding is a frequently observed complication after endoscopic mucosal resection of large adenomas of colorectum and duodenum. Even though the associated mortality is low, delayed bleeding causes significant morbidity and use of health care resources. Clip closure of the resection field reduces delayed bleeding, but it is time consuming and often complete closure is not achieved. Hemostatic gels and powders can be applied quickly and easily. These agents are in use for the treatment of active bleeding, but it is unknown, whether they will also prevent delayed bleeding when applied to the resection field prophylactically.

Aims & Methods: We conducted a randomized controlled trial of patients undergoing hot-snare endoscopic mucosal resection of flat lesion in the duodenum and colorectum at 15 centers in Germany. Lesions had to be non-pedunculated and measure at least 10 mm in the duodenum and 20 mm in the colorectum. Immediately after resection was completed patients were randomized to hemostatic gel application (intervention group) or no prophylaxis (control group). The primary endpoint was clinically significant delayed bleeding rate (CSDB) within 30 days after resection. Secondary endpoints included transfusion requirements, other complications, wound healing and lesion recurrence.

Results: A total of 233 patients were included in the trial. We performed a planned interim analysis when 200 patients were available for evaluation of the primary end point; at this point we stopped enrollment in the trial due to futility. Of the 200 patients included in the interim analysis, 100

(88 colorectal, 12 duodenal) were included in the intervention group and 100 (88 colorectal, 12 duodenal) in the control group. Groups were comparable in terms of patient age, sex, comorbidities, and lesion localization. CSDB occurred in 13 cases (13%) in the intervention group and in 6 cases (6%) in the control group. This difference was not statistically significant ($p=0.146$ Fisher's Exact Test). CSDB rates for colorectal lesions were 10% vs. 4.5% (intervention vs. control group) and for duodenal lesions 33% vs. 17%. Follow-up for patients already enrolled is continuing and data lock for the full study cohort is expected in May 2024. The full data set will be presented at UEG Week.

Conclusion: The application of a hemostatic gel following endoscopic mucosal resection of large non-pedunculated lesions in the duodenum and colorectum does not reduce the rate of CSDB.

Disclosure: OM and TVH have received lecture fees from Puramatrix (the company producing Purastat gel). TW has received lecture fees from Fuji (the company marketing Purastat in Germany).

MP281

IMPACT OF AGE AND COMORBIDITIES ON COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION OUTCOMES: A STRATIFIED ANALYSIS

S. Sferrazza¹, G. Calabrese¹, A. Capogreco², R. de Sire², P. Cecinato^{3,4}, R. Sassatelli³, G. de Roberto⁵, F. Barbaro⁶, C. Spada⁶, M.F. Chiappetta⁶, F. Pugliese⁷, M. Manno⁸, P. Soriani⁸, E. Rosa-Rizzotto⁹, A. Gubbiotti¹⁰, G. Andrisani¹¹, F. Di Matteo¹¹, F. Azzolini¹², A. Repici^{13,14}, R. Di Mitri¹, R. Maselli^{13,14}, ERIN Study Group

¹ARNAS Civico, Gastroenterology and Endoscopy Unit, Palermo, Italy, ²Humanitas University, Gastroenterology and Digestive Endoscopy, Rozzano (MI), Italy, ³Arcispedale Santa Maria Nuova - Reggio Emilia, Gastroenterology and Digestive Endoscopy, Reggio Emilia, Italy, ⁴University of Bologna, Medical and Surgical Sciences, Bologna, Italy, ⁵European Institute of Oncology Division of Endoscopy, Milan, Italy, ⁶Fondazione Policlinico Universitario Agostino Gemelli, Digestive Endoscopy, Rome, Italy, ⁷ASST NIGUARDA, Operative Digestive Endoscopy, Milano, Italy, ⁸Ramazzini Hospital Carpi, Azienda AUSL Modena, Digestive Endoscopy Unit, Carpi, Italy, ⁹St. Anthony Hospital Gastroenterology Unit Dept. of Medicine, Internal Medicine, Padova, Italy, ¹⁰Azienda Ospedaliera di Padova, Department of Gastroenterological, Surgical and Oncological Science, Padua, Italy, ¹¹Campus Biomedico, Digestive Endoscopy Unit, Roma, Italy, ¹²IRCCS San Raffaele Hospital, Gastroenterology and Gastrointestinal Endoscopy, Milano, Italy, ¹³Humanitas Clinical and Research Hospital, IRCCS, Endoscopy Unit, Rozzano (MI), Italy, ¹⁴Humanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy

Contact E-Mail Address: giulicalabrese94@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is emerging as the standard treatment for suspected superficial submucosal invasion lesions. Considering the global population ageing, understating the feasibility of this approach in elderly patients is of the utmost importance. Studies in this field have shown a tendency towards reduced resection rates and higher rates of complications.

Aims & Methods: We sought to assess the effectiveness and safety of colorectal ESD for patients aged ≥ 80 yo compared to 65-79 yo patients. We prospectively enrolled consecutive patients aged >64 years undergoing colorectal ESD between January 2019 and December 2023 from ten Italian Tertiary Referral Centres. Patients were classified as Elderly Group (E-Group, age >80 yo) and non-elderly group (NE-Group, 65-79 yo). Proce-

dures outcomes and adverse events were compared between E-Group and NE-Group and between patients with comorbidities and healthy (1-CM-Group and H-Group).

Results: A total of 980 patients were included [269 (27.5%) in the E-Group and 711 (72.5%) in the NE-Group]. Table 1 summarises the principal data and outcomes.

	Elderly group (n=269)	Non-elderly group (n=711)	p-value
Female sex, n (%)	120 (44.6)	311 (43.7)	0.81
Age (years), median (IQR)	83 (81-85)	72 (68-75)	<0.001
CCI, median (IQR)	5 (4-6)	3 (3-4)	<0.001
At least one comorbidity, n (%)	159 (59.1)	110 (15.4)	<0.001
Multiple comorbidities, n (%)	69 (25.7)	83 (11.7)	<0.001
General anaesthesia, n (%)	50 (18.6)	163 (22.9)	0.17
Procedure time (minutes), median (IQR)	90 (57-120)	90 (60-125)	0.66
Hospitalization, n (%)	202 (75.1)	541 (63.4)	0.001
En bloc resection, n (%)	250 (92.9)	673 (94.7)	0.30
R0 resection, n (%)	235 (87.4)	651 (91.6)	0.05
Length of hospital stay (days), median (IQR)	3 (2-4)	2 (2-4)	0.27
Sepsis, n (%)	2 (0.7)	5 (0.7)	0.95
Fever, n (%)	16 (5.9)	38 (5.3)	0.71
CRP increase, n (%)	16 (5.9)	50 (7.0)	0.55
PCT increase, n (%)	1 (0.4)	9 (1.3)	0.21
HF, n (%)	0	2 (0.3)	0.38
AKI, n (%)	1 (0.4)	3 (0.4)	0.91
Intraprocedural AEs, n (%)			
Perforation	10 (3.7)	46 (6.5)	0.10
Bleeding	16 (5.9)	32 (4.5)	0.35
Cardiovascular	2 (0.7)	1 (0.1)	0.13
Pulmonary	2 (0.7)	1 (0.1)	0.13
Pain	19 (7.1)	43 (6.0)	0.56
Drug-related	0	1 (0.1)	0.54
Postprocedural AEs (within 14 days), n (%)			
Perforation	1 (0.4)	6 (0.8)	0.43
Bleeding	6 (2.2)	36 (5.1)	0.05
Cardiovascular	0	2 (0.3)	0.38
Pulmonary	0	2 (0.3)	0.38
Delirium	6 (2.2)	1 (0.14)	0.001
Systemic infections	3 (1.1)	12 (1.7)	0.51

En-bloc resection and R0 rate did not statistically differ ($p=0.30$; $p=0.05$) between E and NE-Groups. Oncological curative resection was achieved in the two groups without significant differences ($p=0.41$). Histological outcomes were comparable between the two groups, except for lymphovascular invasion [E:14 (5.2%) vs NE:14 (2.0%); $p=0.007$ – OR:2.9 (CI:1.3-6.6)]. Regarding clinical course, intraprocedural and 14 days-adverse events (AEs), no statistically significant differences were found between the two groups, except for a higher rate of post-procedure delirium in the E-Group [6 (2.2%) vs 1 (0.1%); $p=0.001$ –OR:16.2 (CI:1.9-135.2)]. 1-CM-Group showed a higher rate of intraprocedural bleeding ($p=0.001$), fever onset ($p<0.001$), C-reactive protein ($p=0.006$) and procalcitonin increase ($p=0.02$), delayed perforation ($p=0.03$) and systemic infections ($p=0.02$) compared to the H-Group. The presence of one or more comorbidity, but not the age, was associated with a poorer clinical course [$p<0.001$; OR:2.3 (CI:1.5-3.6)] and poor overall course (poor clinical course combined with 14 days AEs) [$p<0.001$; OR:2.1 (CI:1.4-3.0)]. ASA classification (OR: 1.36; CI:1.01-1.83), the presence of one comorbidity (OR: 1.73; CI:1.14-2.63), and procedure time (OR: 1.01; CI:1.00-1.01) were poor outcome predictors. After excluding patients with at least one comorbidity, still no differences in terms of poor overall course ($p=0.21$) were registered between E and NE-Group.

Conclusion: Colorectal ESD is an effective and safe procedure in elderly patients. Physicians should acknowledge delirium as a possible AE in patients aged over 80. The presence of comorbidities should drive the execution of a comprehensive pre-procedural assessment and post-procedural care, to optimize outcomes and minimize complications.

Disclosure: Nothing to disclose.

MP282

THE EVOLUTION OF MODERN ADVANCED COLORECTAL ENDOSCOPIC RESECTION PRACTICE: REAL WORLD EXPERIENCE OF INTRODUCING HIGH VOLUME ESD WITH FAVOURABLE OUTCOMES

A. Emmanuel¹, O. Olabintan², A. Eqbal², H. Ayubi², J. Bhoday¹, M.-A. Noreillie³, A. Adeyeye¹, S. Gulati⁴, S. Thrumurthy², B. Hayee⁵, A. Haji¹

¹King's College Hospital, Colorectal Surgery, London, United Kingdom, ²King's Institute of Therapeutic Endoscopy, Gastroenterology, London, United Kingdom, ³Leuven University Hospital, Gastroenterology, Leuven, Belgium, ⁴King's College Hospital NHS Foundation Trust, London, United Kingdom, ⁵King's College London, University of London, London, United Kingdom

Contact E-Mail Address: shraddha.gulati@nhs.net

Introduction: Endoscopic resection (ER) techniques for treating large non-pedunculated colorectal polyps (LNPCP) have advanced significantly and the relevance of early studies reporting outcomes may diminish with time. EMR remains the predominant therapeutic option for LNPCP in western practice, but ESD is increasingly employed. Limited studies demonstrate safety and efficacy for highly selected patients, but no studies examine the practical introduction of ESD (which has a steep learning curve) as a standard component of ER strategies in real-world practice.

Aims & Methods: Patients with LNPCP treated by ER at a tertiary referral centre between January 2011 and September 2023 were included. ERs were divided into 2 time periods (Period 1: January 2011 – May 2018 and Period 2: June 2018 – September 2023). Resection technique and outcomes including en bloc resection, successful single-session resection and complications were compared for procedures between Period 1 and Period 2.

Results: 1563 LNPCP were treated with ER over the study period. ER was successful in 1517 (97%). The mean lesion size was 46.9mm +/- 26.3mm (median 40mm, range 20mm–210mm). 774 LNPCP were resected using EMR/pEMR and 743 by ESD/Hybrid ESD. ESD was used to resect 476 (64%) LNPCP during Period 2 compared to 267 (34.7%) during Period 1 ($p<0.001$). Whilst introducing ESD into practice during Period 1, a combination of Hybrid ESD and ESD were used with an en bloc resection rate of 64%, but en bloc resection for ESD increased to 98% during Period 2 ($p<0.001$). 97% of rectal LNPCP were resected by ESD during period 2 compared to 62% during period 1 ($p<0.001$). 45% of colonic LNPCP were resected by ESD during period 2 compared to 17% during period 1 ($p<0.001$). Complications occurred less frequently in Period 2 compared to Period 1 (2.9% versus 5.1%, $p=0.04$) and there was no difference in the rate of clinically significant perforation (1.2% versus 1.0%, $p=0.76$) or post-procedure bleeding (1.5% versus 1.6%, $p=0.89$). Fewer patients were admitted to hospital during period 2 compared to period 1 (5.6% versus 14.8%). Training occurred more frequently in Period 2 with 258 (35%) ERs performed in part or completely by an endoscopy fellow compared to 126 (16%) in period 1. 105 (22%) ESDs were performed in part or completely by an endoscopy fellow during Period 2 compared to 30 (11%) during period 1.

Conclusion: These data demonstrate the evolving nature of endoscopic resection practice in modern advanced practice. Large volume ESD can safely be incorporated into standard practice with a near-exclusive policy of ESD to treat all rectal LNPCP and nearly half of colonic LNPCP resected by ESD. En bloc resection rates comparable to Japanese expert centres can be achieved with no effect on complications. Moreover, regular training in ESD can safely be introduced.

Disclosure: Nothing to disclose.

MP283

LATE FIRST ENDOSCOPIC SURVEILLANCE FOLLOWING PIECEMEAL
ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL POLYPS IS
NOT ASSOCIATED WITH INCREASED ADENOMA RECURRENCE

T. Arraf¹, Y. Gorelik¹, F. Mazzawi¹, S. Banna², R. Moalem², A. Klein¹
¹Rambam, Gastroenterology, Haifa, Israel, ²Holy Family Hospital,
Gastroenterology, Nazareth, Israel

Contact E-Mail Address: yurigorelik@gmail.com

Introduction: Piecemeal endoscopic mucosal resection (pEMR) is the preferred treatment for large non-pedunculated colorectal polyps (LNPCPs) [1,2]. A major limitation of pEMR is residual or recurrent adenoma (RRA), which was reported to in 15%-30% of cases at first surveillance colonoscopy (SC1)[3], performed 3-6 months after the index procedure, but is reduced to the range of 3%-5% by applying ablative measures to the post-EMR resection margin[4].

Aims & Methods: This study aimed to evaluate the effects of late SC1 on RRA.

This is an analysis of a prospectively collected cohort of adult patients referred for pEMR at two academic centers in Israel, from 2016 to 2023. We included all patients who underwent pEMR of LNPCPs and completed SC1.

We compared outcomes between patients who completed early SC1 at 3-6 months following the index procedure with patients who completed late SC1 later than 6 months. All procedures and surveillance colonoscopies were performed by experienced endoscopists trained in pEMR using high-definition scopes. EMR was followed by thermal ablation of the entire mucosal defect margin with snare soft tip coagulation, as previously described[4].

Scar evaluation at SC1 was performed with high-definition white light and chromoendoscopy. Our primary endpoint was RRA at SC1.

Analyses were performed per lesion. We compared baseline parameters and outcome rates between groups, and performed multivariate analysis to assess the adjusted association of months to SC1 with RRA.

Results: We analyzed 516 lesions that underwent index pEMR resection and subsequent SC1. Baseline parameters and recurrence rates are presented in Table 1. The early SC1 group (n=371) underwent SC1 at a mean of 5.1 months versus a mean of 11.1 months in the late SC1 group (p<0.01; Table 1). Polyp size in the early SC1 group was significantly larger than that in the late SC1 group (mean size 35.9 mm [SD 13.9] vs. 32.1 mm [SD 12.4], p<0.01; Table 1). The distribution of lesion location, granularity differed between the groups (Table 1). However, there were no significant differences in lesion Paris classification or rates of high grade dysplasia (Table 1).

	Early SC1 (n=371)	Late SC1 (n=145)	P value
Time to SC1, months	5.1 (1.1)	11.1 (5.6)	<0.01
Age, years	65.4 (10.4)	68.0 (10.2)	0.01
Female, n (%)	168 (45.4)	51 (35.2)	0.05
Lesion Size, mm	35.9 (13.9)	32.1 (12.4)	<0.01
Distal location, n (%)	111 (29.9)	29 (20.0)	0.03
Granular morphology, n (%)	230 (63.7)	74 (53.2)	0.04
Paris IIb/IIc/III, n (%)	39 (10.5)	15 (10.3)	1.00
High grade dysplasia, n (%)	97 (26.1)	33 (22.8)	0.49
Recurrence at SC1, n (%)	23 (6.2)	7 (4.8)	0.70

Table 1. Comparison of baseline variables and outcome between the early and late SC1.

SC1, First surveillance colonoscopy.

We found no statistically significant difference in the rate of recurrence at SC1 between the two groups (6.3% in the standard group versus 4.8% in the delayed group, p=0.64). Additionally, a sub-analysis comparing the

early SC1 group to patients with very late SC1 (>12 months – mean time to SC1 17.9 (SD [5.4] months) and did not reveal significant difference in recurrence at SC1 (6.2% in the early SC1 vs 6.3% in the very late group, p=1). Multivariate analysis, adjusted for lesion size, location, and high-grade dysplasia, showed that time to SC1 was not significantly associated with RRA (odds ratio 1.05, 95% confidence interval 0.98-1.13).

Conclusion: Late SC1 is not associated with an increased RRA. Hence, we suggest that high-quality pEMR with margin ablation may alleviate the need for early SC1, thereby reducing healthcare and patient burdens. Further interventional studies are required.

References: [1] Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2017; 49: 270–297. doi:10.1055/S-0043-102569/ID/JR15335-1/BIB
[2] Shaukat A, Kaltenbach T, Dominitz JA, et al. Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2020; 159: 1916-1934.e2. doi:10.1053/j.gastro.2020.08.050
[3] Belderbos TDG, Leenders M, Moons LMG, et al. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: Systematic review and meta-analysis. *Endoscopy* 2014; 46: 388–400. doi:10.1055/S-0034-1364970/ID/JR910-7/BIB
[4] Klein A, Tate DJ, Jayasekaran V, et al. Thermal Ablation of Mucosal Defect Margins Reduces Adenoma Recurrence After Colonic Endoscopic Mucosal Resection. *Gastroenterology* 2019; 156: 604-613.e3. doi:10.1053/j.gastro.2018.10.003

Disclosure: The authors report no conflict of interests.

MP284

IMPACT OF MARGIN THERMAL ABLATION AFTER ENDOSCOPIC
MUCOSAL RESECTION OF LARGE (≥20MM) NON-PEDUNCULATED
COLONIC POLYPS ON LONG TERM RECURRENCE

T. O'Sullivan^{1,2}, F.V. Mandarino¹, J. Gauci¹, A. Whitfield^{1,2}, C. Kerrison¹, C. Nascimento¹, S. Gupta^{1,2}, O. Cronin^{1,2}, A. Sakiris¹, J.F. Prieto Aparicio¹, S. Arndtz³, G. Brown³, S. Raftopoulos⁴, D.J. Tate⁵, E. Lee¹, S. Williams¹, N. Burgess^{1,2}, M.J. Bourke^{6,2}
¹Westmead Hospital, Department of Gastroenterology and Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia, ³THE ALFRED HOSPITAL, Gastroenterology, Prahran, Australia, ⁴Sir Charles Gairdner Hospital, Department of Gastroenterology, Perth, Australia, ⁵University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium, ⁶Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: EMR is the standard of care for the management of large (≥20mm) non-pedunculated colonic polyps (LNPCPs). However, its efficacy and cost effectiveness, are limited by recurrence and the necessity for scheduled surveillance. Consequently, current surveillance intervals are conservative. Margin thermal ablation (MTA) after EMR for LNPCPs has dramatically reduced the incidence of recurrence at first surveillance colonoscopy at six-months (SC1). If this effect is durable, then subsequent surveillance intervals in patients who have been cleared of synchronous polyps could be substantially lengthened. We prospectively evaluated long-term surveillance outcomes in a cohort of LNPCPs that have undergone MTA.

Aims & Methods: Consecutive patients with LNPCPs undergoing EMR and MTA from four academic endoscopy centres were prospectively recruited. All patients that underwent successful endoscopic resection received

SC1 six months post resection. EMR scars were carefully evaluated with high-definition white light, narrow band imaging with near focus and biopsy. In the absence of recurrence, second surveillance (SC2) colonoscopy was conducted at a subsequent interval of 12 months with the scar evaluation process repeated. The primary outcome was recurrence at SC2 in all LNPPCs with a recurrence-free scar at SC1.

Results: 1324 LNPPCs referred for EMR were enrolled over 90 months until October 2022. Following exclusions, 1163 LNPPCs underwent EMR with complete MTA. 856 LNPPCs underwent SC1. 32 additional synchronous LNPPCs were cleared at this procedure. 25/856 (2.9%) (95%CI 1.9-4.3%) LNPPCs demonstrated recurrence. 469 LNPPCs free of recurrence at SC1 (median size 35mm) underwent SC2 at a mean interval of 22.9 months (95%CI 21.9-23.95) after the index EMR. 468 demonstrated a bland scar without recurrence. Only one recurrence occurred (0.2% 95%CI 0-1.2%), related to a 0-IIa+Is 20mm granular TVA located on the ileocaecal valve.

Conclusion: LNPPCs that have undergone successful EMR with MTA and are free of recurrence at SC1 are very unlikely to develop recurrence in subsequent surveillance out to 2 years. Following EMR of LNPPCs with MTA, patients who are cleared of synchronous neoplasia and demonstrate no recurrence after careful scar examination, can potentially undergo next surveillance in 3-5 years. Such an approach would reduce costs and enhance patient compliance.

Disclosure: Michael Bourke: Research Support: Olympus Medical, Cook Medical, Boston Scientific

The remaining authors have no financial, professional, or personal conflicts of interest to disclose.

MP285

DOES A TRAINEE INVOLVEMENT INFLUENCES COLORECTAL ESD OUTCOMES?

F. Felice¹, V. Van der Voort², Z. Jean-Baptiste¹, L. Alfaroni², R. Olivier², M. Dahan², J. Albouys², F. Pinard³, T. Grainville³, L. Quénehervé³, A. Culetto², T. Kaighobadi², M. Bordet³, H. Lepetit², K. Marcel³, C. Juglard², O. Plomteux¹, M. Pioche⁴, R. Legros², T. Wallenhorst³, J. Jacques², P. Leclercq¹

¹Clinique MontLegia - CHC Groupe Santé, Gastroenterology, Liège, Belgium, ²CHU Limoges - Hepato-Gastro-Enterology, CHU Limoges; Limoges/FR, Hepato-Gastro-Enterology, Limoges, France, ³CHU de Rennes, Rennes, France, ⁴Hospices Civils de Lyon, Gastroenterology and Endoscopy, Lyon, France

Contact E-Mail Address: florence.felice@hotmail.com

Introduction: Colorectal endoscopic submucosal dissection (ESD) is spreading worldwide, with increasing demand for training. Standardized skills assessment has yet to be defined to guarantee the quality and safety of the results obtained by trainees during their learning curve. ESGE recommends that the first ESD procedures should be supervised by an ESD-proficient endoscopist. The impact of a trainee's active participation on these initial supervised ESD results should be addressed.

The first ESD procedures are recommended to be performed under the supervision of an endoscopist with ESD expertise as advised by the European Society of Gastrointestinal Endoscopy (ESGE). The impact of active participation of a trainee on the outcome of these initial supervised ESDs should be investigated.

Aims & Methods: Between 01/2017 and 01/2024, all consecutive colorectal ESD procedures were prospectively registered by 3 participating ESD training centers, and data were analyzed retrospectively. Trainee participation was tracked. A trainee was defined as having performed less than 50 ESD's on humans, alone or under supervision. We compared the main procedural outcomes with respect to the presence or absence of a trainee

involved in the colorectal ESD procedure. Multivariate analysis and propensity score matching (PSM) were performed.

Results: 2462 consecutive colorectal ESD were included, of which 543 procedures (22%) involved the active participation of a trainee (15 trainers/15 trainees). Rectal lesions were more often treated with participation of a trainee (56% vs 31%, $p<0.001$ *with-trainee vs trainer-alone* respectively). There was no significant difference in en-bloc, R0 and curative resection rates whether a trainee participated or not (95.8%, 85.9% and 84.9% vs 95.1%, 88.2% and 84.7%, *with-trainee vs trainer-alone* respectively). Participation of a trainee resulted in a significant decrease in dissection speed (29.4 mm²/min vs 43.9 mm²/min, $p<0.001$ *with-trainee vs trainer-alone* respectively). Rates of perforation, delayed bleeding and surgery for complications were 8.6%, 5.9% and 0.9% vs 9%, 4.5% and 0.7% for *with-trainee vs trainer-alone* respectively, without significant differences. After PSM, the presence of a trainee significantly decreased the dissection speed (29.4 mm²/min vs 42.7 mm²/min, $p<0.001$ *with-trainee vs trainer-alone* respectively), increased the perforation rate (8.7% vs 5%, $p=0.023$ *with-trainee vs trainer-alone* respectively), but did not influence the curative resection rate (84.9% vs 88.8%, $p=0.078$ *with-trainee vs trainer-alone* respectively).

Conclusion: Active participation of a trainee during colorectal ESD did not affect the curative resection rate. However slower dissection speed and higher perforation rates, without increasing the need for surgery, were observed.

Disclosure: Nothing to disclose.

MP286

THE PREDICTIVE ROLE OF AMMONIA IN LIVER-RELATED DECOMPENSATION AND MORTALITY IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE

J. Damasceno e Costa¹, L. Andrade², T. Carvalho¹, A. Guimarães¹, J. Neves¹, R.S. Costa¹, D. Costa¹, A.C. Caetano¹, R. Gonçalves¹

¹Braga Hospital, Gastroenterology Department, Braga, Portugal,

²Universidade do Minho, Escola de Medicina, Braga, Portugal

Contact E-Mail Address: jpdcosta.93@gmail.com

Introduction: Advanced chronic liver disease (ACLD) may present in different stages with distinct prognoses. Child-Pugh and MELD scores are commonly used models for predicting liver-related mortality and decompensation, but they have several limitations.

An alternative or complementary tool that is simple and cost-effective would be invaluable. Recently, some studies identified a potential role of ammonia in predicting liver-related outcomes.

Aims & Methods: Our primary objective was to explore the predictive role of plasma ammonia levels regarding liver-related complications and mortality. Our secondary aim was to validate a new measure that corrects baseline ammonia levels to the upper limit of normal (AMM-ULN) and test a cut-off which was proposed in the literature to define patients at higher risk of such outcomes (AMM-ULN ≥ 1.4).

This retrospective study included 278 patients with ACLD who had an ammonia measurement in our hospital between 2018 and 2022. ACLD patients were divided into compensated and decompensated stages, with the latter being subdivided into three stages, according to the type of decompensation. Outcomes of liver-related decompensation and mortality were assessed in each group. AMM-ULN was evaluated as a predictor of these outcomes both in compensated and decompensated patients. The predictive accuracy of AMM-ULN was then determined by identifying the best cut-off.

Results: Plasma ammonia levels and AMM-ULN were predictors of hepatic decompensation (HR = 1.453, 95%CI 1.085 – 1.945, $p = 0.012$) and mortality (HR = 1.010, 95%CI 1.003 – 1.017, $p < 0.001$) at 12 months, in the compensated patient group. The AUROC for AMM-ULN was 67.4% in 1-year decompensations and 69.5% in 1-year mortality, with similar results for ammonia levels. AMM-ULN ≥ 1.4 identified patients at higher risk of liver-related decompensation and mortality at 12 months ($p = 0.009$ and $p = 0.020$, respectively).

Conclusion: Both ammonia levels and AMM-ULN were predictors of hepatic decompensation and liver-related mortality in compensated patients, at 12 months of follow-up. AMM-ULN ≥ 1.4 identified patients at higher risk of liver-related decompensation and mortality at 12 months.

References:

- D'Amico, G., Garcia-Tsao, G., & Pagliaro, L. (2006). Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. *Journal of Hepatology*, 44(1), 217–231. <https://doi.org/10.1016/j.jhep.2005.10.013>
- Haj, M., & Rockey, D. C. (2018). Predictors of clinical outcomes in cirrhosis patients. *Current Opinion in Gastroenterology*, 34(4), 266–271. <https://doi.org/10.1097/MOG.0000000000000450>
- De Franchis, R. et al (2022). Baveno VII – Renewing consensus in portal hypertension. *Journal of Hepatology*, 76(4), 959–974. <https://doi.org/10.1016/j.jhep.2021.12.022>
- Shalimar, Sheikh, M. F. et al (2019). Prognostic Role of Ammonia in Patients With Cirrhosis. *Hepatology*, 70(3), 982–994. <https://doi.org/10.1002/hep.30534>

Tranah, T. H. et al (2022). Plasma ammonia levels predict hospitalisation with liver-related complications and mortality in clinically stable outpatients with cirrhosis. *Journal of Hepatology*, 77(6), 1554–1563. <https://doi.org/10.1016/j.jhep.2022.07.014>

Balcar, L. et al (2023). Impact of ammonia levels on outcome in clinically stable outpatients with advanced chronic liver disease. *JHEP Reports*, 5(4), 100682. <https://doi.org/10.1016/j.jhepr.2023.100682>

Elzeftawy, A. et al (2018). Evaluation of the blood ammonia level as a non-invasive predictor for the presence of esophageal varices and the risk of bleeding. *The Turkish Journal of Gastroenterology*. <https://doi.org/10.5152/tjg.2018.17894>

Disclosure: Nothing to disclose.

MP287

TARGETED BREATH BIOPSY® PROFILING OF INDUCED BIOMARKERS UNVEILS A METABOLIC ADAPTATION IN CIRRHOSIS TOWARD ALCOHOL PRODUCTION

G. Ferrandino¹, F. Ricciardi¹, A. Murgia¹, M. Manhota¹, D. Fonseca¹, L. Nicholson-Scott¹, C. Fitzpatrick¹, E. Crone¹, E. Piscitelli¹, O. Gandelman¹, M. Allsworth¹, B. Boyle¹, A. Smolinska^{1,2}, C.A Ginesta Frings^{3,4}, J. Contreras³, V. Gabrielli³, C. Asenjo-Lobos³, F. Bascur³, V. Barrientos⁴, N. Clavo⁴, M. Jerez⁵, L. Méndez^{3,4}

¹Owlstone Medical Limited, Cambridge, United Kingdom,

²Maastricht University, Maastricht, Netherlands, ³Clínica Alemana,

Santiago, Chile, ⁴Hospital Padre Hurtado, Santiago, Chile,

⁵Universidad de Las Américas, Santiago, Chile

Contact E-Mail Address: Elizabeth.Crone@owlstone.co.uk

Introduction: Subjects with chronic liver disease have shown higher circulating ethanol levels after fasting or carbohydrates ingestion. However, clinical functional data about the capability of the injured liver to cope with alcohols remain limited.

In this study we used exhaled breath analysis to explore the conversion of an alcohol to the corresponding ketone, and a ketone to the corresponding alcohol, to establish the suitability of potential metabolic alterations and identify subjects with cirrhosis using a non-invasive breath test.

Aims & Methods: 2-butanol, and 2-pentanone (the substrates) were selected as an alcohol and a ketone based on their safe profile for human consumption, their reported hepatic metabolism, and their presence in breath. Hepatic metabolism was confirmed by simultaneous treatment of human suspension hepatocytes with 10 ng/ μ l of 2-butanol, and 2-pentanone to measure their conversion to respectively 2-butanone, and 2-pentanone (the bioproducts) by using headspace analysis coupled with gas-chromatography mass-spectrometry (GC-MS). Clinical metabolism of these compounds was evaluated by measurement of the breath profile in 14 subjects with cirrhosis and 14 healthy controls before and at different timepoints (10 - 120 minutes) after simultaneous ingestion of 2-butanol (100 mg) and 2-pentanone (100 mg) using Breath Biopsy® OMNI.

Results: The bioproducts were present in the head space of primary hepatocytes treated with the substrates and absent in control conditions omitting primary hepatocytes or substrates. After an overnight fasting all the participants showed breath levels of investigated compounds with no differences between healthy and cirrhosis groups ($p > 0.05$). After ingestion of the substrates, all the subjects showed a > 100 -fold increase of investigated compounds within 10 minutes. Subjects with cirrhosis showed higher levels of 2-butanone and 2-pentanone ($p < 0.05$) compared to healthy controls between 20- and 90-minutes post-administration. An exploratory classification model built on these breath-induced biomarkers at 20 minutes showed an area under the ROC curve of 0.92.

Conclusion: 2-butanol and 2-pentanone are metabolized to the corresponding ketone and alcohol in primary hepatocytes, supporting previous findings reporting hepatic metabolism. Subjects with cirrhosis showed higher breath levels of secondary alcohols independently from administration of the alcohol or the corresponding ketone, suggesting that the hepatic function is more balanced toward the alcohol production compared to healthy controls. This metabolic adaptation may contribute to higher circulating ethanol levels observed in subjects with chronic liver disease and be exploited in a breath test for cirrhosis detection.

Disclosure: Giuseppe Ferrandino, Federico Ricciardi, Antonio Murgia, Menisha Manhota, Daniela Fonseca, Louise Nicholson-Scott, Chloe Fitzpatrick, Elizabeth Crone, Elena Piscitelli, Olga Gandelman, Max Allsworth, Billy Boyle, and Agnieszka Smolinska are employee of Owlstone Medical Limited

MP288

A NONINVASIVE AND EFFECTIVE STRATEGY TO QUANTIFY ESOPHAGEAL VARICES FOR MONITORING AND STRATIFYING BLEEDING RISK IN PATIENTS WITH PORTAL HYPERTENSION USING ARTIFICIAL INTELLIGENCE-ASSISTED CONTRAST-ENHANCED CT

J. Liu¹, K. Liao², J. Yang¹, K. Deng¹

¹West China hospital of Sichuan University, Gastroenterology and hepatology, Chengdu, China, ²West China hospital of Sichuan University, Radiology, Chengdu, China

Contact E-Mail Address: cqjlh1004@163.com

Introduction: Esophageal variceal bleeding is a serious and fatal complication of cirrhosis. Currently, efficient noninvasive monitoring strategies are lacking. By applying artificial intelligence (AI) to computed tomography (CT) imaging, we developed an innovative tool to meet clinical needs.

Aims & Methods: This is an ambispective cohort study conducted at West China hospital between April 2021 and December 2021, patients underwent endoscopy and enhanced CT were registered. Furthermore, 97 patients with radiomic and hepatic venous pressure gradient data were enrolled from a portal hypertension database. High-risk esophageal varices (HREV) were defined as either moderate-severe varicose (HREV-1) or EV requiring intervention (HREV-2). Deep learning was used to develop segmentation and EV quantification models. The EV bleeding prediction model was established using least absolute shrinkage and selection operator (LASSO) regression and logistic regression analysis. The area under the curve (AUC) was calculated for efficiency evaluation. This trial is registered with the Chinese Clinical Trial Registry (ChiCTR2300069865) and is completed.

Results: A total of 2291 patients in the retrospective (n=780) and prospective (n=1511) cohorts were included. The internal and external validation cohort AUCs were 0.976 and 0.951 for EV vs. non-EV, 0.986 and 0.951 for HREV-1, and 0.978 and 0.898 for HREV-2, respectively. We found that volume ($p=0.0348$) and AI-10 ($p=0.0196$) were closely related to portal pressure. We further analyzed the AI features and bleeding events for patients with cirrhosis in the retrospective (n=254) and prospective (n=569) cohorts and applied the EV bleeding prediction model (validation cohort AUCs of 0.669, 0.701 and 0.705 at 1, 3, and 6 months, respectively), which was not inferior to that of endoscopic signs ($p > 0.05$).

Conclusion: Enhanced CT assisted by AI is a promising noninvasive strategy for quantifying EV, recognizing HREV and predicting short-term bleeding risk and has the potential to replace simple gastroscopy for diagnosis or monitoring. This approach could decrease unnecessary gastroscopy to some extent.

Disclosure: The authors have declared no competing interests.

MP289

GUT FUNGAL ALTERATIONS IN PATIENTS WITH LIVER CIRRHOSIS

E. Kiudeliene^{1,2}, D. Nikitina², J. Skieceviciene², R. Gedgaudas^{1,2}, J. Kupcinskas^{1,2}, L. Kupcinskas^{1,2}

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Laboratory of Clinical and Molecular Gastroenterology, Kaunas, Lithuania

Contact E-Mail Address: R.gedgaudas@gmail.com

Introduction: Liver cirrhosis is a late stage of liver fibrosis characterized by progressive deterioration of liver function, leading to potentially life-threatening complications. Recent studies focusing on bacterial alterations of gut microbiota have shown their association with liver disease pathogenesis, decompensation, and hospitalization rates. Recently, there has been increasing recognition of the potential role of gut fungal changes in liver cirrhosis, however, further investigation in this field is warranted.

Aims & Methods: The aim of this study was to determine gut fungi composition changes in patients with liver cirrhosis and to assess whether these changes are related to liver disease severity. For the analysis were used DNA samples, extracted from the liver cirrhosis patients' and healthy controls' stool samples. Internal transcribed spacer (ITS) was amplified and sequenced using MiSeq Illumina sequencing machine. Bioinformatical and statistical analysis were performed to reveal the fungal profile of each study group.

Results: Forty-five patients with liver cirrhosis and 45 healthy controls were included in the study. No significant differences in age or gender were observed between the cirrhosis and control groups. Cirrhosis patients showed significantly reduced fungal richness compared to the control cohort. However, no difference was observed in the Shannon alpha diversity index. No significant alterations in fungal compositions were noted concerning gender and etiology within the cirrhosis group. Patients who had Child-Pugh B and C liver cirrhosis had a significant shift in stool fungi composition compared to those in the Child-Pugh A group. Patients with Child C liver cirrhosis had a significantly increased fungi abundance compared with the Child A group. In accordance with the MELD score, patients with score ≥ 15 , had significantly increased richness and fungal diversity. Furthermore, an elevated abundance of the *Candida* genus was observed in liver cirrhosis patients group, while *Saccharomyces* genus was increased in the control group.

Conclusion: Patients with liver cirrhosis had reduced richness in stool fungal composition and an increased abundance of the *Candida* genus when compared with healthy controls. Moreover, patients with worse liver function had significant shifts in fecal fungal composition, suggesting that fungal alterations may be associated with cirrhosis progression.

Disclosure: Nothing to disclose.

MP290

HIGH PREVALENCE OF CHOLELITHIASIS AND ASYMPTOMATIC GALLBLADDER WALL THICKENING IN PATIENTS WITH CIRRHOSIS

A. Protopapas¹, A. Tsankof¹, V. Kyritsi¹, C. Gogou¹, M. Kyziroglou¹, E. Papathanasiou¹, C. Chatzikosma¹, A. Michalopoulos¹, C. Savopoulos¹, A. Protopapas¹

¹Aristotle University of Thessaloniki, AHEPA University Hospital, First Propedeutic Department of Internal Medicine, Thessaloniki, Greece

Contact E-Mail Address: adoprot@hotmail.com

Introduction: Patients with cirrhosis have been shown to have an increased risk of developing gallstones. Simultaneously, gallbladder wall thickening constitutes a frequent accidental finding in patients with cirrhosis undergoing imaging studies.

Aims & Methods: Our study aimed to determine the frequency of cholelithiasis and asymptomatic gallbladder wall thickening in a population of hospitalised patients with cirrhosis. Consecutive hospitalised patients with cirrhosis who underwent imaging studies (ultrasound, computed tomography or magnetic resonance imaging) were prospectively enrolled. Patients with symptoms suggestive of acute biliary disease or biliary etiology of cirrhosis were excluded. Gallbladder wall thickening was defined as measurements > 3mm.

Results: A total of 128 patients were included. Patients had a mean age of 64 ± 12.2 years and were predominantly male (73.4%) and with decompensated liver cirrhosis (DeCi) (78.1%). Alcohol-associated liver disease (47.7%) and metabolic dysfunction-associated steatohepatitis (16.4%) were the leading causes of cirrhosis. Most patients were classified as Child-Pugh stage B (53.1%), followed by patients in stage C (32%) and stage A (14.8%). A significant percentage of the patients had cholelithiasis (39.8%), with DeCi patients being more likely to have gallstones (45%) than compensated patients (21.4%) (p=0.024). Furthermore, a significant number of patients had asymptomatic gallbladder wall thickening (32.8%), with almost half of them (42.9%) not concurrently having cholelithiasis. Patients with DeCi were significantly more likely to have gallbladder wall thickening (39%) than patients with compensated disease (10.7%) (p=0.005). There was no statistical correlation between etiology of cirrhosis and cholelithiasis or gallbladder wall thickening.

Conclusion: Patients with cirrhosis maintain a significant probability of developing gallstones while also frequently displaying gallbladder wall thickening in the absence of acute biliary disease. Clinicians should keep in mind the possibility of biliary complications in these patients while simultaneously refraining from rushing to a diagnosis of acute cholecystitis based on imaging alone.

Disclosure: Nothing to disclose.

MP291

RISK FACTORS FOR HEPATIC ENCEPHALOPATHY AFTER UPPER GASTROINTESTINAL BLEEDING: A PROSPECTIVE SINGLE-CENTER STUDY

A. Lancho Munoz¹, J.M. Lopez Tobaruela¹, E.J. Ortega-Suazo², C. Tendero Peinado¹, R. Fernandez García¹, M. López-Vico², J.G. Martínez-Cara³, E. Redondo-Cerezo⁴, R. Jiménez-Rosales⁵
¹Hospital Virgen de las Nieves, Department of Gastroenterology and Hepatology, Granada, Spain, ²Hospital Universitario Virgen de las Nieves, Department of Gastroenterology and Hepatology, Granada, Spain, ³Hospital Virgen de las Nieves, Endoscopy Unit, Granada, Spain, ⁴Hospital Universitario Virgen de las Nieves, Gastroenterology, Granada, Spain, ⁵Hospital Universitario Virgen de Las Nieves, Gastroenterology, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: Hepatic encephalopathy (HE) is a group of neuropsychiatric disorders caused by liver dysfunction or portosystemic shunting, and it is a common complication in the progression of liver cirrhosis. Pathophysiologically, there is an imbalance between the hepatic production and clearance of ammonia, leading to an increase in serum ammonium levels, which can lead to neurological dysfunction, intracranial hypertension, cerebral oedema and ultimately death (1).

There are multiple triggering factors; one of the most well-known is upper gastrointestinal bleeding (UGIB) (2). Therefore, we suggest that the coexistence of UGIB and HE is associated with an increased risk of in-hospital mortality and prolonged hospital stay. This study aims to analyse the risk factors for HE during an episode of UGIB and its impact on the patient's prognosis.

Aims & Methods: Retrospective analysis of a prospective registry of patients with UGIB treated at the Hospital Universitario Virgen de las Nieves (2013-2022). Statistical analysis was performed using R v4.3.2. Categorical variables were compared using the Chi-square or Fisher's exact test. Odds ratios (OR) and 95% confidence intervals (95%CI) were calculated using the Woolf-Haldane formula for significant variables. Continuous variables were assessed using the Shapiro-Wilk test for normality, and Levene's test was used to check for homogeneity of variances. The t-test for independent samples, with or without Welch's correction, and the Mann-Whitney U test were used for hypothesis testing. Multivariate analysis is performed to identify independent risk factors for variables with statistically significant differences, calculating Odds Ratios (OR) and their 95% confidence intervals (95%CI).

Results: A total of 343 patients with liver cirrhosis and UGIB were analysed, of whom 260 were male and 83 were female, with an overall mean age of 61.51 ± 12.38, developing HE in a total of 66 patients. After comparing the cirrhotic population that developed HE with those that did not, we observed a series of variables that correlated significantly, as shown in Table 1.

Hepatic encephalopathy	Present (means ± STD) N= 66	Missing (means ± STD) N= 277	P-value
Bilirubin	4,78 ±7,7	2,18 ± 3,24	0,000015
Albumin	2,63 ± 0,57	3,04 ±1,28	0,000056
INR	1,77 ± 0,62	1,65 ±0,82	0,0056
Creatinine	1,37 ± 0,7	1,6 ± 6,41	0,0036
Platelets	125945 ±72209	140502 ±94082	0,66
Ascites	48,07%	29,12%	0,015
Urea	95,72 ±57,69	70,53 ±42,63	0,00017
Days of admission	11,75 ± 12	10,43 ±12,22	0,32
Mortality rate	33%	16%	0,00016

Subsequently, after performing multivariate analysis, we noticed that only

four variables had a significant independent relationship: bilirubin with an OR (95% CI) of 1.07 (1-1.16) with $p=0.064$; albumin with an OR (95%CI) of 0.41 (0.23-0.7) with $p=0.0017$; ascites with an OR (95%CI) of 1.65(1.01-2.71) with $p=0.04$; and urea on admission with an OR (95% CI) of 1.01 (1-1.102) with $p=0.0005$.

Conclusion: We conclude that patients with cirrhosis admitted for UGIB and who develop HE have higher mortality rates during admission without an apparent increase in hospital stay. Our study indicates that bilirubin, albumin, ascites, and urea are the most accurate predictors of HE development. These findings aligns with Rattanasupar et al. (2), concluding that the Child-Pugh score, which also considers the abovementioned variables, best predicts hepatic encephalopathy after UGIB. Further research is necessary to explore additional risk factors that aid in predicting and modelling the disease based on our findings.

References: 1. Elsaid MI, Rustgi VK. Epidemiology of Hepatic Encephalopathy. Clinics in Liver Disease. 2020 May;24(2):157–74.

2. Rattanasupar A, Tiawijit N, Rachatapantakorn B. Predictive factor for hepatic encephalopathy in cirrhotic patients who presented with acute variceal bleeding. J Med Assoc Thai. 2014 Jun;97(6):567–73.

Disclosure: Nothing to disclose.

MP292

OUTCOMES AND RISK FACTORS OF EARLY LIVER INJURY AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

X. Wang¹, B. Kunyi¹, X. Luo¹

¹Sichuan University West China Hospital, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: xiaoze.wang@foxmail.com

Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) reduces the portal vein blood flow into the liver while declining portal venous pressure, resulting in liver ischemia injury and even liver failure.

Aims & Methods: This study aimed to verify the impact of the post-TIPS early liver injury on survival through large sample retrospective analysis and explore the risk factors of post-TIPS liver injury. The data of patients undergoing TIPS in West China Hospital from November 2009 to March 2021 were collected. We analysed the predictive ability of end-stage liver disease model score (MELD) on the 90-day, 1-year and 3-year survival rates after TIPS and screened out the independent predictive factors of post-TIPS liver injury by regression analysis.

Results: A total of 1108 patients were included. The post-TIPS MELD score was superior to other scoring systems, with a better predictive effect on the 90-day survival rate and 1-year survival rate. The 90-day survival rate (98.3% vs. 87.2%, HR 15.9, 95% CI 7.9-31.9, $P < 0.001$), 1-year survival rate (95.1% vs. 79.2%, HR 8.3, 95% CI 5.0-13.7, $P < 0.001$) and 3-year survival rate (86.5% vs. 68.8%, HR 4.0, 95% CI 2.8-5.7, $P < 0.001$) were significantly higher in patients with a post-MELD score less than 15. Preoperative total bilirubin, serum creatinine, INR and change of portosystemic pressure gradient were independent predictors of early liver injury after TIPS.

Conclusion: Baseline liver function and pressure reduction contribute to the occurrence of early liver injury after TIPS. Post-TIPS MELD score can accurately predict short-term and long-term survival.

Disclosure: Nothing to disclose.

MP293

SAFETY STATINS IN CIRRHOTIC PATIENTS WITH AN INDICATION FOR HIGH CARDIOVASCULAR RISK. RETROSPECTIVE COHORT

R.T. Hernández Rodríguez¹, M.G. Reyes Zermeno¹

¹Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Ciudad de México, Mexico

Contact E-Mail Address: roxana28t@gmail.com

Introduction: Cirrhosis is a chronic condition with a high mortality. Cirrhotic patients with portal hypertension frequently present with large esophageal varices with bleeding or need for endoscopic intervention. The choice of treatment for variceal hemorrhage is endoscopic ligation and beta-blockers, which can be used as secondary prophylaxis. The pleiotropic effects of statins have been reported for the treatment of cardiovascular diseases, but at the liver level they favor the reduction of the hepatic venous pressure gradient (HVPG), with a decrease in the number of variceal hemorrhage events; however, their use had been restricted in cirrhotic patients due to their association with elevations in liver biochemistries.

Aims & Methods: To evaluate the safety statins in cirrhotic patients with an indication for high cardiovascular risk. And as a secondary aim, determine the presence of variceal hemorrhage during follow-up. This retrospective cohort study was carried out by the "Centro Médico Nacional 20 de Noviembre" between 2018 to 2022. Child Pugh A and B cirrhotic patients with a history of variceal hemorrhage or large varices with endoscopic ligation intervention without active hemorrhage were included and observed over a period of 4 years. To determine adverse events, compatible clinical data and biochemical examinations were searched in the electronic record, and pharmacovigilance committee records were reviewed.

Characteristics	Statin treatment, % (n=53)	Without statin treatment, % (n= 53)	p
Sex			
Female	58.5 (31)	58.5 (31)	
Male	41.5 (22)	41.5 (22)	
Etiology			
MAFLD	11.3 (6)	15.1 (8)	
PBC	11.3 (6)	17 (9)	
AIH	9.4 (5)	13.2 (7)	
HCV	22.6 (12)	20.8 (11)	
HBV	1.9 (1)	1.9 (1)	
ALCOHOL	13.2 (7)	11.3 (6)	
CRYPTOGENIC	30.2 (16)	20.8 (11)	
Age (years)	63	61	0.320
Aspartate aminotransferase(U/L)	39.6	61	0.001
Alanine aminotransferase(U/L)	37.6	51.2	0.041
Albumin	3.8	3.6	0.045
Prothrombin time	12.7	14	0.002
Total cholesterol (mmol/L)	157.6	179.4	0.042
International normalized ratio	1.06	1.1	0.004

Table 1. Demographics, selected clinical characteristics, and outcomes of patients..

Results: A total of 106 patients were included, of which 53 with statin use and 53 without statins. The characteristics were 41.5% men (n=44), 58.5% women (n=62). The average age was 62 ± 10 years. In order of frequency, the causes were: cryptogenic 25.5% (n=27), hepatitis C virus (HCV) 21.7% (n=23), primary biliary cholangitis (PBC) 14.2% (n=15), metabolic dysfunction-associated fatty liver disease (MAFLD) 13.2% (n=14), alcohol 12.3% (n=13), autoimmune hepatitis (AIH) 11.3% (n=12), hepatitis B virus (HBV)

1.9% (n= 2). With Child Pugh A 67% (n=71) Child Pugh B 35% (n=33). In the statin and non-statin group, the average values of the following variables were PT 12.7 ±1.9 vs 14 ±2.2, AST 39.6 ±24 vs 61 ±40, ALT 37.6 ±28 vs 51 ±38, albumin 3.8 ±0.6 vs 3.6 ±0.5, total cholesterol 157.6 ±35 vs 179.4 ±68, INR 1.06 ±0.17 vs 1.1 ±0.18 (p< 0.05) (Table 1). In the group of patients with statin use in 18.4% (n=10) Variceal ligation was performed, and in the group without statins, 24.5% (n=13), with a RR of 1.075, 95% CI (0.8-1.3). In the group of patients with statin use, 9.5% (n=5) had a bleeding event, and in the group without statins, 7.5% (n=4) had a bleeding event, with an RR of 1.25, CI 95% (0.3-4.4). None of the participants had clinical adverse effects.

Conclusion: The use of statins in cirrhosis compensated with portal hypertension was safe. In this study we could not demonstrate the pleiotropic effect of statins, probably due to the sample size. Therefore, it is necessary to generate subsequent studies including a larger number of patients.

Disclosure: Nothing to disclose.

MP294

PROTON PUMP INHIBITORS IN CIRRHOTIC PATIENTS: ARE THEY A RISK FACTOR FOR SPONTANEOUS BACTERIAL PERITONITIS?

S.Ş. Juncu^{1,2}, H. Minea^{1,2}, E.C. Cojocariu^{1,2}, A. Trifan^{1,2}, A.-M. Sîngeap^{1,2}
¹University of Medicine and Pharmacy "Grigore T. Popa", Iaşi, Romania, Medical Semiology and Gastroenterology, Iaşi, Romania, ²"St. Spiridon" County Emergency Hospital, Institute of Gastroenterology and Hepatology, Iaşi, Romania, Gastroenterology, Iaşi, Romania

Contact E-Mail Address: simona.juncu@yahoo.com

Introduction: Spontaneous bacterial peritonitis (SBP) is a common bacterial infection in cirrhotic patients, which can lead to severe complication and even death. Proton pump inhibitors (PPIs), are associated with high susceptibility to enteric infections. The aim of this study is to assess if PPIs use in cirrhotic patients is a risk factor for developing SBP.

Aims & Methods: We conducted a retrospective study (January 2019 to March 2024) on all cirrhotic patients with ascites admitted in the Gastroenterology Department of "St. Spiridon" County Clinical Emergency Hospital Iaşi, a tertiary referral center. We identified all cases of SBP, defined as elevated ascitic fluid absolute PMN count > 250 cells/mm³, with or without positive ascitic fluid bacterial culture. We assessed previous PPI administration and their respective indications for all patients, to identify a potential risk correlation.

Results: Out of the 1530 cirrhotic patients, 832 (54,4%) were male and 698 (45,6%) were female, with a mean age of 54 years. One hundred and seventy-four patients (11.4%) were diagnosed with SBP. Among them, 50 patients (28.7%) presented previous treatment with PPIs, with a valid indication in 14 (28%) cases. Out of the 1356 cirrhotic patients with ascites but without SBP, 1098 (71.8%) patients had no history of PPIs use. Among the remaining 258 patients (16.9%) undergoing previous PPI treatment, 156 (60.5%) had a valid indication. PPIs were identified as a risk factor for SBP (OR 1.71 [95% CI 1.20 to 2.44]; P=0.0029).

Conclusion: Patients with cirrhosis and ascites who receive PPIs are at a significant risk of SBP, as previous studies have demonstrated. Moreover, given that most patients with SBP lacked a valid indication for PPIs, it is crucial to accurately assess their necessity for such treatment. These findings highlight once again the importance of a comprehensive clinical approach to managing cirrhotic patients.

Disclosure: Nothing to disclose.

MP295

EVALUATION OF NUTRITIONAL STATUS AND DIETARY INTAKE IN PATIENTS WITH LIVER CIRRHOSIS: A REAL-LIFE STUDY IN OUTPATIENTS AND HOSPITALIZED SUBJECTS

S. Khan¹, S. Sansoni¹, S. Di Cola¹, L. Lapenna¹, M. Merli¹
¹Sapienza University, Department of Translational and Precision Medicine, Rome, Italy

Contact E-Mail Address: saniya.khan@uniroma1.it

Introduction: Malnutrition and sarcopenia are two very frequent complications in patients with liver cirrhosis (LC). These conditions are associated with increased morbidity and mortality, particularly in advanced stages and require early investigation. Despite their significant impact on the prognosis, they are often overlooked and underdiagnosed.

Aims & Methods: Aim: To provide a general overview regarding the nutritional status and dietary intake in patients with LC and highlight any disparities in nutritional parameters between outpatients and hospitalized LC patients.

Methods: In this prospective observational study, all consecutive LC patients attending the portal hypertension clinic and those admitted to the gastroenterology ward at Policlinico Umberto I from May 2023 to January 2024 underwent nutritional screening. Demographic information, clinical characteristics, SARC-F questionnaire, anthropometric measurements, liver frailty index (LFI) parameters, 24-hour diet recall, and food frequency questionnaire were included in the screening. Data was analyzed using Student's t-test and chi-square test by Jamovi software version 2.3.28.

Results: Altogether 126 patients [male- 72.2%; age 63.7±10.7 years; etiology: Alcohol-53%, MASLD-19%, Viral-20%, Others-8%; MELD- 11.8±4.4; MELD Na- 13.6±5.5; 50% Child A] were enrolled. 36% of the patients were sarcopenic according to SARC-F questionnaire (score ≥ 4), with a mean LFI of 4.6±0.9. Although 65% of the patients consumed at least one protein source daily, only 15% achieved recommended daily protein intake, and 78% had lower energy intake than recommended. Of these 126 patients, 68.3% were outpatient and 31.7% were hospitalized, with comparable age and gender distribution. Hospitalized patients had a lower BMI (kg/m²) [24.7±4.1 vs 27.8±6.9; p=0.01], higher prevalence of frailty [5.1±1.1 vs 4.3±0.7; p=<0.001], lower TSF (mm) [12.4±6.8 vs 16.2±8.1; p=0.04], and lower MUAC (cm) [29.6±5.1 vs 32.2±5.6; p=0.02] than outpatients. Further, none of the hospitalized patients met adequate protein intake, contrasting with 22% of outpatients (p=0.01).

Variables	Outpatient (n=86)	Hospitalized patients (n=40)	p value
Age (years)	64.2 ± 9.8	62.6 ± 12.3	0.4
Gender (male)	68.6%	80%	0.1
BMI (kg/m²)	27.8 ± 6.9	24.7 ± 4.1	0.01
MELD	10.5 ± 3.4	14.7 ± 5.2	<.001
MELD-Na	11.9 ± 6.1	17 ± 4.4	<.001
CTP	A: 60% B: 39% C: 1%	A: 25% B: 50% C: 25%	<.001
Hand grip strength (kg)	22.3 ± 8.7	24.6 ± 9.1	0.4
Chair stands (sec)	14.4 ± 5.3	15.6 ± 4.6	0.4
LFI	4.3 ± 0.7	5.1 ± 1.1	<.001
Robust (≤ 3.2)	5%	0	
Pre-frail (3.3-4.4)	54%	38%	
Frail (≥ 4.5)	40%	62%	0.06

Table 1: Comparison between outpatient and hospitalized patients.

Conclusion: The impairment of nutritional status tend to increase in the more advanced stages of liver disease. There is a need for timely and routine assessment of nutritional status and implementation of targeted life-style interventions to optimize patient outcomes.

Disclosure: Nothing to disclose.

Acute pancreatitis

11:30-12:30 / Poster Stage 4

MP296

"LEAVE NO STONE UNTURNED" – THE IMPACT OF ENDOSCOPIC ULTRASOUND IN PATIENTS WITH "IDIOPATHIC" ACUTE PANCREATITIS

U. Akbani¹, A. Hussenbux¹, A. On¹, M.T. Huggett¹, S. Everett¹, B. Paranandi¹

¹St James' University Hospital, Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: drumairakbani@gmail.com

Introduction: Gallbladder microlithiasis (GBM), often undetected on conventional imaging, is accurately visualised by endoscopic ultrasonography (EUS). GBM is considered a potential cause of idiopathic acute pancreatitis (IAP). This study examines the incidence and outcomes of gallstone disease detected by EUS in patients with a GB in-situ and at least one prior episode of IAP.

Aims & Methods: The aim of this study was to assess the incidence and outcomes of gallstone disease detected by EUS in patients with IAP and intact gallbladders.

All IAP patients with an intact gallbladder referred for EUS between 2018-2020 were included and followed up for 3-6 years. EUS was conducted by 1 of 3 consultant gastroenterologists in a tertiary centre. Blood results and imaging findings were reviewed to identify predictive factors for GBM. Subsequent to EUS, outcomes including cholecystectomy and Endoscopic Retrograde Cholangiopancreatography (ERCP) were examined. Post-intervention incidence of gallstone-related complications and pancreatitis were recorded.

Results: 112 patients met the inclusion criteria (60 male and 52 female; median age 55 (IQR 21.8-70.1). 82/112 (73.2%) patients were diagnosed with definite GB and/or common bile duct (CBD) pathology at EUS. Diagnoses included GBM 67/82 (81.7%), GB stone 12/82 (14.6%) and CBD stone 3/82 (3.7%). Six patients were lost to follow and were excluded from further analysis.

104/112 patients had recorded blood results prior to EUS. 35/39 (89.7%) patients with transaminitis were subsequently found to have positive findings on EUS compared with 41/65 (63.1%) without transaminitis. (χ^2 8.81, $p < 0.01$). 55/112 (49.1%) patients had normal imaging prior to EUS. The most common finding was biliary dilatation (15/112, 13.4%) which was not associated with positive EUS findings (χ^2 1.26, $p = 0.26$).

Once diagnosed with stone related disease, 62/76 (81.5%) patients were referred for a surgical opinion. Of these, 52/62 (83.8%) underwent a cholecystectomy. Mean follow-up was 4.03 years (SD: 0.92). During this time 3/52 (5.7%) patients developed a further episode of AP and of the 20/76 patients managed non-surgically; 2/20 (10.0%) developed AP subsequently (χ^2 0.40, $p = 0.53$).

4/76 patients underwent ERCP (3 therapeutic, 1 prophylactic sphincterotomy); none developed further episodes of AP during the follow up period.

Conclusion: EUS is a useful diagnostic test in IAP patients. The most common EUS diagnosis in IAP is stone-related disease. A large proportion of patients diagnosed with GBM had a cholecystectomy, with a low incidence of AP and stone related complications during extensive follow up. A Pre-procedural transaminitis was associated with stone-related disease. Further prospective research is required to examine the benefits of cholecystectomy over conservative management.

Disclosure: Nothing to disclose.

MP297

EASY-APP IS A MORE RELIABLE PROGNOSTIC TOOL THAN BISAP IN ACUTE PANCREATITIS

J. Nemeth¹, E.R. Fürst², D. Tarján³, E. Tari³, E. Szalai¹, V. Vass¹, F. Maraczi¹, R. Molontay¹, J. Pintér¹, B. Eross⁴, P.J. Hegyi⁵, S. Bunduc¹, P. Hegyi¹

¹Semmelweis University, Centre of Translational Medicine, Budapest, VIII., Hungary, ²Semmelweis University, Institute for Pancreatic Diseases, Budapest, Hungary, ³Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁴Semmelweis University, Institute for Translational Medicine, Budapest, Hungary, ⁵Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, Pécs, Hungary

Contact E-Mail Address: nemethjazmin222@gmail.com

Introduction: Several scores are available for the prognosis evaluation of acute pancreatitis (AP) at diagnosis. However, each has limitations. We trained an artificial intelligence-based model called EASY (early achievable severity index) to predict AP course. This study compares the prognostic values of the EASY score and the widely used bedside severity index (BISAP).

Aims & Methods: The EASY model was previously trained in 1184 cases and validated on a cohort of 3543 patients using data generally accessible on admission (medical history, anamnestic data, physical examination, laboratory parameters, imaging results). The EASY score increases with severity and ranges from 0 to 1. We further defined a categorical EASY score ([0, 0.2] -> 0, [0.21, 0.4] -> 1, [0.41, 0.6] -> 2, [0.61, 0.8] -> 3, [0.81, 1] -> 4). The evaluated outcomes were mortality, severity (based on Atlanta classification), and a binary EASY variable used during model training (=1 if the case is severe or lethal and otherwise 0). We calculated the area under the ROC curve (AUROC), sensitivity, precision and accuracy of each score for predicting the outcomes of interest.

Results: 1073 cases were included in the analysis. EASY and EASY categorical performed similarly and were superior to BISAP for mortality prediction (AUROC -EASY: 0.755 CI(0,676-0,829), EASY-categorical: 0.739 CI(0,658-0,811), BISAP: 0.708 CI(0,639-0,765)). The results were similar for severity (AUROC -EASY: 0.772 CI(0,73-0,813), EASY-categorical: 0.767 CI(0,721-0,802) BISAP: 0.72 CI(0,683-0,768)). However, the BISAP had slightly higher precision in predicting all outcomes. (Mortality -BISAP: 0.163 CI(0,085-0,256), EASY:0.151 CI(0,101-0,203); EASY-categorical: 0.203 CI(0,133-0,279); Severity: BISAP: 0.388 CI(0,27-0,505), EASY:0.313 CI(0,257-0,362), EASY-categorical:0.382 CI(0,322-0,474)).

Conclusion: The EASY score is overall superior to BISAP in predicting mortality and severity in AP. Being highly reliable and using data easily collectable on admission, the EASY-APP has great premises for becoming a reference tool for AP prognosis evaluation.

Disclosure: Nothing to disclose.

FLUSHING THERAPY IN EXTERNALLY DRAINED NECROTIZING PANCREATITIS – RESULTS OF THE MULTICENTRE, RETROSPECTIVE DRACULA TRIAL

M. Vornhuel¹, S. Sirtl¹, Y. Xu², S. Klauss¹, E. Orgler¹, M. Bezmarevic³, M. Jovanovic³, C. Ricci⁴, M. Fernandez Y Viesca⁵, M. Arvanitakis⁵, A. Hadi⁶, A.P. Prahm⁶, D. Di Mauro⁷, D.A. Ruess⁸, J. Hamm⁹, C. Ammer-Herrmenau⁹, T. Cúrdia Gonçalves¹⁰, J. Gonçalves¹⁰, L. Calavrezos¹¹, M. Goetz¹¹, S. Stoerzer¹², M. Schmelzle¹², L. Nawacki¹³, C.A. Condori Mamani¹⁴, M. Seitzinger¹⁵, J. Seelig¹⁵, S. Chooklin¹⁶, S. Rasch¹⁷, V. Philipp¹⁷, S. Pandanaboyana¹⁸, R. Aljaberi¹⁸, M. Kuzman¹⁸, C. Meinhardt¹⁹, B. González De La Higuera Carnicer²⁰, D. Ruiz-Clavijo Garcia²⁰, B. Eröss²¹, P. Hegyi²², N. Kerbakh²³, T.V. Moga²⁴, K. Pawlak²⁵, N. Cało²⁵, K. Khalaf²⁵, M. Brunner²⁶, A. Kleger²⁷, L. Schulte²⁷, M.L. Ruiz Rebollo²⁸, U. Mansmann², H. Stubbe¹, J. Mayerle¹, G. Beyer¹, DRACULA study group

¹LMU University Hospital, Department of Medicine II, Munich, Germany,

²LMU Munich, Institute for Medical Information Processing, Biometry, and Epidemiology, Munich, Germany,

³Clinic for General Surgery, Military Medical Academy, University of Defense, Department of Hepatobiliary and Pancreatic Surgery, Belgrade, Serbia, ⁴University of Bologna, Department of medical and surgical science (DIMEC), Bologna, Italy, ⁵ERASME University Hospital, Dept. of Hepatogastroenterology, Brussels, Belgium,

⁶Copenhagen University Hospital, Hvidovre, Pancreatitis Centre East (PACE), Copenhagen, Denmark, ⁷University of Exeter, Exeter, United Kingdom, ⁸Medical Center University of Freiburg, II. Med. Klinik, Freiburg, Germany, ⁹University of Goettingen, Goettingen, Germany, ¹⁰Hospital da Senhora da Oliveira - Guimarães, Gastroenterology Department, Guimarães, Portugal, ¹¹Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, ¹²MH Hannover, Hannover, Germany, ¹³Collegium Medicum Uniwersytet Jana Kochanowskiego, Kielce, Poland,

¹⁴Bolivian Japanese Gastroenterology Institute, La Paz, Bolivia, ¹⁵University Hospital Leipzig, Leipzig, Germany, ¹⁶Lviv Regional Clinical Hospital, Department of Surgery, Lviv, Ukraine,

¹⁷Klinikum rechts der Isar der TU München, Klinik und Poliklinik für Innere Medizin II, München, Germany, ¹⁸Freeman hospital, Newcastle upon tyne, United Kingdom, ¹⁹Klinikum Oldenburg AöR, University Clinic of Internal Medicine - Gastroenterology, Oldenburg, Germany, ²⁰Complejo Hospitalario Navarra, Dept. of Digestive Disease, Pamplona, Spain, ²¹University of Pecs, Pecs, Hungary, ²²University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ²³Poltava State Medical University, Surgery #3, Poltava, Ukraine, ²⁴University of Medicine and Pharmacy "Victor Babes" Timisoara, Gastroenterology And Hepatology, Timisoara, Romania, ²⁵University of Toronto, Toronto, Canada, ²⁶University Hospital Erlangen, Erlangen, Germany, ²⁷University Hospital Ulm, Department for Internal Medicine 1, Ulm, Germany, ²⁸Hospital Clinico Universitario Servicio De Aparato Digestivo, Aparato Digestivo, Valladolid, Spain

Contact E-Mail Address: marlies.koepke@med.uni-muenchen.de

Introduction: Necrotic collections and especially infected necrotic collections, developing in 5-10 % of patients, drive mortality in severe acute pancreatitis. Minimally invasive drainage is indicated in infected necrotic collections. The mode of drainage depends on technical feasibility and local expertise and often percutaneous drainage is performed singly or in addition to endoscopic drainage. However, current guidelines do not provide specific recommendations on how to handle percutaneous drains.

Aims & Methods: This retrospective, multicenter analysis aims to investigate common practice of percutaneous drainage therapy of pancreatic necrotic collections (WOPN and ANC) in patients with acute pancreatitis. Our goal was to detect possible advantages of different flushing regimens in regard to the primary endpoint length of hospital stay. The secondary endpoint was in-hospital mortality. All patients hospitalized for necrotizing acute pancreatitis with at least one percutaneous drain from 01/2016 until 12/2022 were included. Length of hospital stay and survival times were compared using Restricted Mean Survival Time (RMST). Bias correction for confounding factors was performed (age, sex, etiology, severity, ICU stay, admission year, volume of study site, number of necroses, use of antibiotics, drainage number, maximal necrosis size, location, detection of microbiological content, lumen, drainage duration, and flushing).

Results: 612 patients (67 % males) in 29 centres from 15 countries in Europe and [MK1] America were included in the analysis. Alcohol and gallstones account for 64 % of pancreatitis cases, the vast majority of them being moderate (30 %) or severe (63 %) episodes according to RAC. 57 % of patients presented with one necrotic collection, the rest had two or more. 69 % of necrotic collections were flushed. The flushing regimen was 3x daily in about half of the cases. After bias correction for confounding factors, the length of hospitalization or mortality did not differ between the flushed and non-flushed group (RMST ratio 1.027; 95% CI: 0.979,1.078, p value 0.278 and RMST ratio 1.021; 95% CI: 0.996,1.047, p value 0.098 respectively) or between the externally drained and the externally plus internally drained group (RMST ratio 0.982; CI 95% CI: 0.923,1.045, p value 0.564 and RMST ratio 1.021; 95% CI: 0.996,1.047, p value 0.098 respectively). Flushing with saline compared to flushing with antiseptics/antibiotics was associated to a significantly shorter hospital stay (RMST ratio 0.876; 95% CI: 0.817,0.939, p value <0.01), yet no difference in mortality (RMST ratio of 0.999; 95% CI: 0.946,1.055, p value 0.972).

[MK1]ein Zentrum aus Kanada + ein Zentrum aus Bolivien

Conclusion: This large retrospective multicentre study comprising 612 patients reveals heterogenic therapeutic regimens in necrotizing pancreatitis. A specific irrigation regime or combination of internal and external drains was not associated with a shorter length of hospitalisation or lower in-hospital mortality. Flushing with antibiotics or antiseptics does not appear to provide an improvement over flushing with saline.

Disclosure: Nothing to disclose.

MP299

LUMACAFITOR/IVACAFITOR (ORKAMBI™) DECREASES THE SEVERITY OF ALCOHOLIC PANCREATITIS

V. Venglovecz^{1,2,3}, A. Grassalkovich², E. Tóth², A. Ébert¹, Z. Rakonczay⁴, J. Maléth⁵, Z. Galla⁶, P. Monostori⁶, P. Hegyi^{3,7,2,8}

¹University of Szeged, Department of Pharmacology and Pharmacotherapy, Szeged, Hungary, ²University of Szeged, Translational Pancreatology Research Group, Interdisciplinary Center of Excellence for Research Development and Innovation, Szeged, Hungary, ³University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ⁴University of Szeged, Department of Pathophysiology, Szeged, Hungary, ⁵University of Szeged, Momentum GI Research Group, Szeged, Hungary, ⁶University of Szeged, Department of Paediatrics, Szeged, Hungary, ⁷Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ⁸Semmelweis University, Institute for Pancreatic Disorders, Budapest, Hungary

Contact E-Mail Address: venglovecz.viktoria@med.u-szeged.hu

Introduction: Heavy alcohol consumption is one of the most common etiological factor in the development of acute pancreatitis (AP). We have previously shown that ethanol (EtOH) decreases the expression and activity of the cystic fibrosis transmembrane conductance regulator (CFTR) which plays a key role in alcohol-induced AP development. Orkambi (Ivacaftor and Lumacaftor) is available to correct the impaired CFTR function and expression in cystic fibrosis patients.

Aims & Methods: Our aim in this study was to investigate whether Orkambi is able to decrease the severity of experimental AP. Intact guinea pig pancreatic ducts (PDs) were treated with different concentrations of EtOH (30; 50; 100 mM) alone and in combination with Ivacaftor and/or Lumacaftor (1; 3; 5 and 10 μ M) for 3, 7, 9 and 12 hours and CFTR expression and activity were evaluated by immunostaining and patch clamp, respectively. Alcoholic AP was induced in Orkambi-treated guinea pigs and standard laboratory and histological parameters were measured.

Results: Ivacaftor (10 μ M) and Lumacaftor (10 μ M) alone or in combination dose-dependently restored the localization and activity of the EtOH-damaged CFTR channel, during 12 hours of treatment. Oral administration of Orkambi decreased the severity of EtOH-induced pancreatitis.

Conclusion: We showed for the first time that Ivacaftor and Lumacaftor are able to restore the CFTR defect caused by alcohol and decreases the severity of pancreatitis. These results indicate that Orkambi may represent a novel therapeutic option in the treatment of AP.

The research was funded by the National Research, Development and Innovation Office (SNN134497 to VV, K135874 to ZR and K131996 to PH) and the Translational Medicine Foundation.

Disclosure: Nothing to disclose.

MP300

CHANGES IN FLUID DISTRIBUTION AND HAEMODYNAMICS IN THE EARLY PHASE OF ACUTE PANCREATITIS

M.L. Lauritsen¹, M.P. Werge¹, M. Cihoric¹, H.L. Jørgensen², N.B. Foss³, J.G. Karstensen¹, L.L. Gluud⁴, S. Novovic¹

¹Hvidovre University Hospital, Gastro Unit, Hvidovre, Denmark, ²Hvidovre University Hospital, Clinical Biochemistry, Hvidovre, Denmark, ³Hvidovre University Hospital, Department of Anaesthesiology and Intensive Care, Hvidovre, Denmark, ⁴University Hospital Hvidovre, Gastro Unit, Hvidovre, Denmark

Contact E-Mail Address: morten.lauritsen@regionh.dk

Introduction: In the early phase of acute pancreatitis (AP), fluid resuscitation plays a crucial role. Changes in fluid distribution, increased capillary permeability, minimized intravascular volume, and loss of vascular resistance may lead to cardio-vascular and renal failure. On the other hand, overhydration is associated with cardiac decompensation and respiratory failure. Previously, intensive fluid therapy with large volumes of crystalloids was recommended without addressing individual needs for fluid therapy.

We used measurements of physiological parameters focusing on cardiac function and changes in body composition, to study the association between fluid therapy and physiological response, in the patient with AP.

Aims & Methods: This study aimed to assess fluid distribution in relation to fluid therapy, inflammation, and cardiac- and renal function in the early phase of AP.

This was a single-centre, prospective observational cohort study. On baseline, day 1, 2, 10 and 90 following were assessed: preload dependency (passive leg raise manoeuvre and defined as a >10% increase in stroke volume), hemodynamic parameters (stroke volume, cardiac output measured by non-invasive monitoring (Non-invasive LiDCOrapid™; LiDCO, London, UK)), bioimpedance variables (weight, extracellular water (ECW), total body water (TBW) by seca mBCA 525, Germany). White blood count (WBC), C-reactive protein (CRP), and creatinine were measured and Modified Marshall score was calculated on each time point. Data are presented as medians with interquartile range (IQR). [JK1] Pearson correlation coefficient was used to assess the relationship between changes in weight and haemodynamic and bioimpedance parameters.

Results: Eighty-eight patients with first-time AP were included. Median age was 58 years, 46 were females. Gallstones were the predominant etiology (55%). At baseline, 35 patients (40%) were preload dependent. However, the median increase in weight during the first 10 days of admission was 2.65 kg (IQR: 0.9;4.73). Across time points, patients in the fourth upper quartile of weight increase had significantly higher volume of ECW than patients in the 1-3. quartile ($p=0.02$). No differences were observed for stroke volume, nor cardiac output. CRP was significantly higher in patients in the fourth upper quartile of weight increase than in patients in quartile 1-3. No difference was found for WBC and creatinine.

We found a significant correlation between increasing bodyweight and extracellular water volume, $R=0.383$, ($p<0.0001$), but not between increasing bodyweight and stroke volume $R=-0.016$ ($p=0.783$) or cardiac output, $R=0.015$ ($p=0.796$). Also, a significant correlation was found between creatinine and increasing weight, $R=0.229$ ($p<0.0001$). Modified Marshall score was significantly correlated to increasing body weight, $R=0.159$ ($p=0.006$).

Conclusion: The assessment of hydration status in AP requires an in-depth knowledge of body fluid homeostasis. Our data provide physiological rationale for emerging evidence regarding more restrictive fluid resuscitation. Personalized- and goal directed therapy may be a promising novel way in the transition from necessary fluid resuscitation to harmful fluid volume accumulation in the early phase of AP.

References: The Interplay between Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. Dumnicka P, Maduzia D, Ceranowicz P, Olszanecki R, Drożdż R, Kuśnierz-Cabala B.

Int J Mol Sci. 2017 Feb 8;18(2):354. doi: 10.3390/ijms18020354.

Tenner S, Baillie J, DeWitt J, Vege SS;

American college of Gastroenterology guideline: management of acute pancreatitis

Am J Gastroenterol 2013; 108: 1400-16.27.

Working group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis

Pancreatol 2013; 13:Suppl 2:e1-e15

Disturbances of the microcirculation in acute pancreatitis.

Cuthbertson CM, Christophi C.

Br J Surg. 2006 May;93(5):518-30. doi: 10.1002/bjs.5316.

Fluid Resuscitation in Acute Pancreatitis - Going over the WATERFALL.

Gardner TB

N Engl J Med. 2022 Sep 15;387(11):1038-1039. doi: 10.1056/NEJMe2209132.

Disclosure: Nothing to disclose.

MP301

PANCREATIC EXOCRINE INSUFFICIENCY FOLLOWING ACUTE PANCREATITIS AS AN UNDERESTIMATED CONDITION THROUGHOUT THE COURSE OF THE DISEASE AND INFLAMMATORY, NUTRITIONAL AND IMMUNOLOGICAL PREDICTIVE FACTORS – A PROSPECTIVE LONGITUDINAL STUDY

M. Gravito-Soares¹, E. Gravito-Soares², N.P. Almeida², P. Narra Figueiredo²

¹Centro Hospitalar e Universitário Coimbra; Faculty of Medicine, University of Coimbra, Gastroenterology, Coimbra, Portugal,

²Centro Hospitalar e Universitário de Coimbra; Faculty of Medicine, University of Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: ms18498@gmail.com

Introduction: Acute pancreatitis (AP) is a potentially life-threatening disease that causes local and systemic inflammation with heterogeneity in terms of AP severity.

Aims & Methods: Prospective longitudinal study of total of consecutive patients diagnosed with first episode of AP. Excluded patients with previous pancreatic exocrine insufficiency (PEI) and follow-up <6 months until EPI diagnosis. The aim of this study is to determine if and when PEI occurs after AP and which inflammatory, nutritional and immunological factors determine its occurrence. The variables were the development of PEI (elastase fecal-1 levels <200µg/g) and pancreatic endocrine insufficiency (PENI) (diagnosed by fasting serum glucose, HbA1c and oral glucose tolerance test according to updated The American Diabetes Association criteria) over time and clinical, serum and fecal markers, imaging and outcome variables.

Results: A total of 78 patients were enrolled (69.2% (n=54) males; mean age: 62.4±2.0 yo), 75.6 with alcoholic/biliary etiology. AP was moderately-severe in 38.6% and severe in 15.4%. PEI was diagnosed in 43.6% (n=34; mean fecal elastase 1:149.2±167.4 vs. 435.6±100.3; p<0.001), being 73.5% at the time, 17.6% at 1 month, 14.7% at 3 months and 2.9% at 6 months of AP diagnosis. Thirteen (33%) PEI patients had mild AP. PENI was present in 27.1% (n=17) of patients and 19.2% (n=15) had previous diabetes mellitus. One patient died of pneumonia with respiratory failure acute pancreatitis-related before completing follow-up.

After univariate/multivariate analysis, the statistically significant predictive factors for PEI following AP were younger age (58.0±17.0 vs. 65.9±16.8; OR=0.028; p=0.017), severe AP (11.5 vs. 3.8%; OR=4.920; p=0.026), con-

comitant PENI (14.1% vs. 7.7%; OR=5.918; p=0.049), low sodium (135.6±5.4 vs. 138.2±2.8; OR=0.223; p=0.002), low potassium (3.9±0.4 vs. 4.2±0.63; OR=0.867; p=0.047), low osmolality (275.4±11.4 vs. 277.1±27.5; OR=0.004; p=0.029), high vitamin B12 (1196.8±1330.6 vs. 512.0±451.27; OR=0.001; p<0.001), high ferritin (924.3±847.8 vs. 465.5±360.9; OR=1.001; p=0.006), high triglycerides (707.9±105.5 vs. 105.5±43.1; OR=1.001; p=0.016), low magnesium (1.8±0.3 vs. 2.0±0.2; OR=0.174; p=0.022), high zinc (0.9±0.3 vs. 0.8±1.1; OR=1.055; p=0.021), high total lymphocytes (1699.8±663.2 vs. 1247.8±500.2; OR=1.001; p<0.001) and high CD3 lymphocytes (1248.4±558.6 vs. 886.3±467.3; OR=1.001; p=0.002).

Conclusion: PEI is frequent after AP, being >1/4 diagnosed up to 6 months follow-up and 1/3 in mild AP. Patients with severe AP, PENI (occurring in >1/4 of patients), low sodium, potassium, osmolality and magnesium, and high vitamin B12, ferritin, triglycerides, zinc, lymphocytes and CD3 lymphocytes have a higher risk of PEI. A closer follow-up of AP patients is crucial and should include severity, inflammatory, endocrinological, nutritional, and immunological assessment.

References: 1. van den Berg FF, Boermeester MA. Update on the management of acute pancreatitis. Curr Opin Crit Care. 2023;29(2):145-151.

2. Huang W, de la Iglesia-García D, Baston-Rey I, Calviño-Suarez C, Larriño-Noia J, Iglesias-García J, et al. Exocrine Pancreatic Insufficiency Following Acute Pancreatitis: Systematic Review and Meta-Analysis. Dig Dis Sci. 2019;64(7):1985-2005.

3. Tu J, Zhang J, Ke L, Yang Y, Yang Q, Lu G, Li B, Tong Z, Li W, Li J. Endocrine and exocrine pancreatic insufficiency after acute pancreatitis: long-term follow-up study. BMC Gastroenterol. 2017;17(1):114.

4. Zheng L, Xue J, Jaffee EM, Habtezion A. Role of immune cells and immune-based therapies in pancreatitis and pancreatic ductal adenocarcinoma. Gastroenterology. 2013;144(6):1230-40.

Disclosure: Nothing to declare.

MP302

QUESTIONNAIRE SURVEY ON ENDOSCOPIC TREATMENT STRATEGIES FOR PANCREATIC FLUID COLLECTIONS IN JAPAN

N. Hayashi¹, T. Saito², T. Hamada³, T. Iwashita⁴, M. Takenaka⁵, H. Shiomi⁶, A. Masuda⁷, T. Fujisawa⁸, S. Matsubara⁹, A. Maruta¹⁰, K. Iwata¹¹, T. Mukai¹², S. Omoto⁵, M. Tsujimae⁷, A. Sakai⁷, T. Sato³, R. Nakano⁶, S. Takahashi⁸, K. Suda⁹, S. Uemura⁴, K. Yoshida¹⁰, M. Okuno¹¹, Y. Iwasa¹¹, H. Isayama¹³, Y. Nakai¹⁴, I. Yasuda¹, the WONDERFUL study group

¹University of Toyama, Third department of internal medicine, Toyama, Japan, ²The University of Tokyo, Dept of Gastroenterology, Tokyo, Japan, ³The University of Tokyo, Dept. of Gastroenterology, Tokyo, Japan, ⁴Gifu University Hospital, First Dept Of Internal Medicine, Gifu, Japan, ⁵Kindai University, Dept of Gastroenterology, Osaka sayama, Japan, ⁶Hyogo Medical University, Division of Hepatobiliary and Pancreatic Diseases, Department of Gastroenterology, Hyogo, Japan, ⁷Kobe University, Division of gastroenterology, Kobe, Japan, ⁸Juntendo University, Dept of Gastroenterology, Tokyo, Japan, ⁹Saitama Medical Center, Saitama Medical University, Gastroenterology and Hepatology, Kawagoe, Japan, ¹⁰Gif Prefectural General Medical Center, Dept. of Gastroenterology, Gifu, Japan, ¹¹Gifu Municipal Hospital, Dept of Gastroenterology, Gifu, Japan, ¹²Kanazawa Medical University, Dept of Gastroenterological Endoscopy, Ishikawa, Japan, ¹³Juntendo University, Gastroenterology, Tokyo, Japan, ¹⁴Tokyo Women's Medical University Hospital, Dept of Internal Medicine, Institute of Gastroenterology,, Tokyo, Japan

Contact E-Mail Address: h.nobu.116@gmail.com

Introduction: Management of pancreatic fluid collection (PFC), a serious late complication of acute pancreatitis, is critical to the improvement of its prognosis. Technical innovations such as endoscopic ultrasound (EUS)-guided drainage, lumen-apposing metal stents (LAMSs), and endoscopic necrosectomy (EN) have facilitated the minimally invasive approach to symptomatic PFCs that previously required surgical interventions. Although there has been extensive research, there remains a lack of consensus on important aspects such as the optimal timing of interventions, stent selection, and indications for necrosectomy. A better understanding of the variations in the treatment strategies would help us to identify unmet needs in this setting and design clinical studies for the standardized treatment algorithm.

Aims & Methods: To clarify the current status of PFC management in Japan and address unresolved issues. A comprehensive questionnaire survey was e-mailed to 80 centers with pancreatobiliary interventional endoscopists in Japan. The questionnaire consisted of 40 questions about the criteria for treatment indications, stent selection, and direct endoscopic necrosectomy as well as 6 case vignettes.

Results: A total of 73 centers responded to the questionnaire (response rate, 91.3%). Regarding the timing of EUS-guided drainage, 48 centers (65.8%) initiated treatment when the encapsulation of a PFC was confirmed within 4 weeks of the onset of pancreatitis, while 18 centers (24.7%) did at the same timing even if the encapsulation was considered incomplete. It should be noted that despite the revision of the Atlanta Classification and the proposal to define encapsulation as pancreatic necrosis after 4 weeks, a significant number of centers chose to perform intervention before that time. For symptomatic walled-off necrosis (WON) with low-level liquification, 45 centers (61.6%) chose a LAMS, and 16 centers (21.9%) injected saline to facilitate the expansion of the proximal flange of LAMS. The criteria for LAMS placement varied, with 8 centers (11.0%) using a liquid component of 50% or more as a criterion. On the other hand, 6 centers (8.2%) tended to perform EN and place a LAMS de-

spite the prominent presence of necrotic material. Regarding the indications for necrosectomy, 44 centers (60.3%) chose it when there was no improvement after drainage, while 22 centers (30.1%) performed it during or immediately after the initial drainage session when necrotic material was prominent. Forty-nine centers (67.1%) performed necrosectomy between 2 and 7 days after endoscopic drainage. All centers confirmed the absence of pseudoaneurysms before drainage, with prophylactic transcatheter arterial embolization performed in 64 centers (87.7%).

Conclusion: This Japanese multicenter survey revealed considerable variations in treatment strategies for PFC in terms of the timing and indications of interventions and stent selection. The findings of this study emphasized the need for continuous data collection and analysis to fill current gaps in treatment approaches. Future research should aim to develop evidence-based guidelines that can clarify the optimal timing of treatment and intervention criteria.

Disclosure: Nothing to disclose.

MP303

SYSTEMATIC REVIEW AND META-ANALYSIS: ATRIAL FIBRILLATION AND QTC PROLONGATION ARE ASSOCIATED WITH HIGHER MORTALITY AND SEVERITY IN ACUTE PANCREATITIS

V. Lillik^{1,2}, M. Obeidat¹, Á. Zolcsák^{1,3}, P. Ferdinandy^{1,4}, E. Bodó¹, A. Pourrastegar¹, A. Moradi¹, P. Hegyi^{1,5,6,7}, R. Nagy^{8,1}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Szent György University Teaching Hospital of Fejér County, First Department of Internal Medicine,, Székesfehérvár, Hungary, ³Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁴Semmelweis University, Department of Pharmacology and Pharmacotherapy, Budapest, Hungary, ⁵Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁶University of Pécs Medical School, Institute for Translational Medicine, Pécs, Hungary, ⁷University of Szeged, Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, Szeged, Hungary, ⁸Heim Pál National Pediatric Institute, Budapest, Hungary

Contact E-Mail Address: lillikvera@gmail.com

Introduction: Acute pancreatitis (AP) is a systemic inflammatory disorder with rising incidence and high mortality in severe cases. Cardiac abnormalities, even heart failure, are commonly seen phenomena during and after AP-related hospitalization.

Aims & Methods: Our aim is to investigate the bidirectional association between cardiac changes and AP outcomes. The protocol was registered on PROSPERO (CRD42023479679, CRD42023479674). We conducted a systematic search on the 5th of November 2023 in three main databases (PubMed, Embase, CENTRAL) and selected the articles based on pre-defined selection criteria. We were searching for articles including patients with AP and cardiac abnormalities [e.g. atrial fibrillation (AF), echocardiographic changes] and looked at different clinical outcomes. Pooled odds ratios (pOR) with 95% confidence interval (CI) were calculated using a random-effects model.

Results: Nine eligible articles were included in our meta-analysis. By analyzing 1.3 million AP patients, those with AF have almost three-times higher odds for in-hospital death, than patients without AF (pOR: 2.89, CI: 1.26 - 6.66). Patients with severe AP have three-times higher odds for in-hospital QTc interval prolongation than patients in the non-severe category (pOR: 3.31, CI: 1.19 - 9.21).

Conclusion: Patients with AF face a threefold increased odds for death and those with severe AP are three times more likely to develop QTc in-

terval prolongation. Cardiology screening, including ECG, is crucial for AP patients. Longitudinal studies are needed to assess the long-term relationship between AP and cardiac abnormalities.

References: Working Group IAP/APA Acute Pancreatitis Guidelines Pancreatolgy 2013.

Iannuzzi JP, et al. Gastroenterology. 2022.

Czapári D et al. Gastroenterology. 2023

Chacón-Portillo et al. Rev Invest Clin. 2017.

Banks PA et al, Gut 2012.

Disclosure: Nothing to disclose.

MP304

METABOLIC SYNDROME AND HYPERTENSION INDIVIDUALLY WORSEN THE OUTCOME OF ACUTE PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

D. Dobszai^{1,2}, M. Obeidat¹, E.Á. Szalai^{1,3}, Á. Zolcsák¹, L. Havelda^{1,4}, R. Papp^{1,5}, A. Choi¹, B.C. Budai^{1,4}, D. Csajbók¹, A. Szentesi^{6,1}, P. Hegyi^{1,4,6,7}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²University of Pécs Medical School, Institute for Translational Medicine, Pécs, Hungary, ³Semmelweis University, Department of Restorative Dentistry and Endodontics, Budapest, Hungary, ⁴Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁵Semmelweis University, Department of Pharmacology and Pharmacotherapy, Budapest, Hungary, ⁶University of Pécs, Institute for Translational Medicine, Pécs, Hungary, ⁷University of Szeged, 6. Translational Pancreatolgy Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, Szeged, Hungary

Contact E-Mail Address: dobszai.dalma@gmail.com

Introduction: With the obesity epidemic, the number of related health conditions have also markedly increased. As a result, the prevalence of metabolic syndrome (MS) reached 25% in western countries. In the severe form of acute pancreatitis (AP), mortality rate may be as high as 50%. Earlier studies associated the elements of MS with more complications, increased severity and mortality in AP. The aim of our meta-analysis was to identify the most important risk factors by investigating the individual and synergistic effect of MS factors on AP outcome.

Aims & Methods: Our systematic search was performed in three databases (MEDLINE, Embase and CENTRAL) from inception to 1 November 2023. Articles were selected according to predefined eligibility criteria. We investigated the effect of four MS factors: obesity, hypertension, diabetes mellitus and hypertriglyceridemia on AP outcome. We calculated pooled odds ratios (OR) with 95% confidence intervals (CIs). Risk of bias assessment was carried out with the Quality in Prognostic Studies (QUIPS) tool. The protocol was registered in PROSPERO under number CRD42023471092.

Results: We identified 15,904 unique records, and after the selection process, 103 studies were included in our analysis. Based on the results of four articles with a total sample size of 137,000, patients with MS are more likely to have moderately severe and severe, rather than mild AP (OR=1.687, CI:0.593-4.803). The odds of developing severe AP is almost 40% increased in the MS patient group (OR=1.398, CI:0.918-2.129). The risk of mortality is also increased in the group with MS (OR=1.307, CI:0.240-7.102). When analyzed individually, hypertension was a statistically significant predictor of both mortality (OR=2.564, CI:1.392-4.723) and disease severity (OR=1.792, CI:1.399-2.296) in AP.

Conclusion: MS and hypertension individually worsen the outcome of AP and may serve as a clinical predictor of severity and mortality.

Disclosure: Nothing to disclose.

MP305

FROM WATERFALLS AND TRICKLES: A RETROSPECTIVE STUDY ON THE RIGHT MEASURE OF FLUID RESUSCITATION IN ACUTE PANCREATITIS

N. Schneider¹, M. Scharpf¹, B. Mayer², T. Seufferlein¹, A. Kleger¹, M. Müller¹, V. Hentschel¹

¹Ulm University Hospital, Department of Internal Medicine I, Ulm, Germany, ²Ulm University, Institute for Epidemiology and Medical Biometry, Ulm, Germany

Contact E-Mail Address: Nora.Schneider@uniklinik-ulm.de

Introduction: Acute pancreatitis is a multifactorial condition which despite showing a mild disease course in the majority of patients can be associated with significant morbidity and occasional fatality. Until lately, aggressive fluid expansion has been an undisputed aspect about managing the early stages of acute pancreatitis. Evidence produced by recent studies including the WATERFALL trial [1] supports a more conservative approach of fluid resuscitation given the fact that patients face significantly higher odds of relevant fluid overload while experiencing no benefit of their underlying condition. However, owing to strict inclusion criteria, results obtained from the WATERFALL trial only apply to patients with non-severe pancreatitis.

Aims & Methods: This retrospective monocentric study is thought to shed light on fluid-related complications in pancreatitis patients with any degree of severity. Altogether, n = 129 patients with all-cause acute pancreatitis including moderately severe and severe courses were enrolled and divided into 3 groups based on their cumulative fluid administration within the first 24 hrs (restrictive: < 3 L, moderate: 3 – 6 L, aggressive: > 6 L). Vital sign records and laboratory values were reported at defined time points (baseline, t = 48 hrs, t = 7 days). Fluid replacement was guided by institutional protocols with an initial bolus of 10 ml/kg, followed by a high-volume infusion rate of 4 ml/kg/h (< 24 hrs). Clinical response to fluid administration was monitored by changes in mean arterial pressure (> 65 mmHg), urine output (> 0,5 ml/kg/h), hematocrit (< 44 %), and blood urea nitrogen (< 25 mg/dl) at t = 12 and 24 hrs, respectively.

Results: The majority of patients were allocated to the group of moderate fluid resuscitation (n = 76, 58,9 %). At baseline, patients did not differ in systemic disease severity as indicated by SIRS and SOFA scores. Compared with a restrictive and moderate fluid regime, a significantly higher proportion of patients with moderately severe or severe pancreatitis associated with an acute peripancreatic fluid collection had previously been administered > 6 L fluids (> 6 L: 17/33, 52 % vs. < 3 L: 2/20, 10 % and 3 – 6 L: 24/76, 32 % vs., p = 0,001). Patients receiving > 6 L fluids were significantly more likely to show at least one radiological feature of pulmonary fluid overload (> 6 L: 15/33, 45 % vs. < 3 L: 2/10, 10 % and 3 – 6 L: 16/76, 21 %, p = 0,006), be transferred to intensive care unit (> 6 L: 18/33, 55 % vs. < 3 L: 2/20, 10 % and 3 – 6 L: 21/76, 28 %, p = 0,002), and require extended in-patient care (8, 6 – 11 days vs. 6, 4 – 7 days and 6, 4 – 10 days, p = 0,025). In addition, within 72 hrs after admission these patients had a significantly lower Horowitz ratio compared with restrictive and moderate group (> 6 L: 285, 239 – 337 vs. < 3 L: 360, 319 – 360 and 3 – 6 L: 337, 304 – 390, respectively, p = 0,003). At t = 48 hrs, C-reactive protein levels were significantly higher in patients with > 6 L (> 6 L: 164, 74 – 260 mg/l vs. < 3 L: 58, 4 – 162 mg/l and 3 – 6 L: 95, 13 – 183 mg/l) while serum albumin levels were significantly decreased (> 6 L: 30, 27 – 32 g/l vs. 3 6 L: 34, 31 – 36,5 g/l and 36, 33,5 – 41,5 g/l, p = 0,001).

Conclusion: Besides conferring a significantly higher risk of pulmonary edema, excessive fluid replacement is significantly associated with moderately severe or severe disease courses of acute pancreatitis, prolonged hospitalization, and need for intensive care. Although the retrospective design does not allow conclusions on causal relationships, results imply that excessive fluid resuscitation not only increases the risk of iatrogenic

fluid overload but may additionally aggravate pancreatic inflammation. Our data suggest that further investigation on the appropriate fluid management in patients with moderate and severe acute pancreatitis is required.

References: [1] de-Madaria E, Buxbaum JL, Maisonneuve P, García García de Paredes A, Zapater P, Guilabert L, Vaillo-Rocamora A, Rodríguez-Gandía MÁ, Donate-Ortega J, Lozada-Hernández EE, Collazo Moreno AJR, Lira-Aguilar A, Llovet LP, Mehta R, Tandel R, Navarro P, Sánchez-Pardo AM, Sánchez-Marín C, Cobreros M, Fernández-Cabrera I, Casals-Seoane F, Casas Deza D, Lauret-Braña E, Martí-Marqués E, Camacho-Montaña LM, Ubieto V, Ganuza M, Bolado F; ERICA Consortium. Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis. *N Engl J Med.* 2022 Sep 15;387(11):989-1000. doi: 10.1056/NEJMoa2202884. PMID: 36103415.

Disclosure: All authors confirm that they have no conflict of interest.

Nutrition and the gut: Mechanisms and therapies

11:30-12:30 / Poster Stage 5

MP306

CHITIN-GLUCAN IN IBS: FROM PATHOGENESIS TO A THERAPEUTIC TARGET

C. Valibouze¹, C. Dubuquoy², P. Chavatte³, M. Genin⁴, V. Maquet⁵, S. Modica⁵, P. Desreumaux³, C. Rousseaux², E. Louis⁶, Gastrap Study Group

¹Université de Lille - CHU, Department of Digestive Surgery and Transplantation, Lille, France, ²Intestinal Biotech Development, Lille, France, ³Université de Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, Univ. Lille, Inserm, CHU Lille, Lille, France, ⁴Université and CHU de Lille, ULR2694 - METRICS: Évaluation des Technologies de Santé et des Pratiques Médicales, CHU Lille, Lille, France, ⁵Kitozyme SA, Herstal, Belgium, ⁶Centre Hospitalier Universitaire de Liège - CHU, Service de Gastroentérologie, Hépatologie, Onco. digestive, Liège, Belgium

Contact E-Mail Address: Edouard.Louis@uliege.be

Introduction: Irritable bowel syndrome (IBS) is a highly prevalent and challenging condition with limited therapeutic options. Chitin-glucan (CG) is a novel dietary prebiotic considered as a safe food ingredient by EFSA. To provide an alternative approach to the management of IBS patients, we evaluated in preclinical studies the roles of CG on visceral analgesia, intestinal inflammation and barrier function and performed an open-label trial in IBS patients.

Aims & Methods: Analgesic effect of CG used at a human equivalent dose (HED) of 1.5-3 g/d was evaluated in rats and compared to negative-tap water and positive-phloroglucinol control groups. Mice with DSS-induced colitis were used to analyze the anti-inflammatory properties of CG. Molecular mechanisms underlying analgesic, anti-inflammatory, and intestinal barrier-strengthening functions of CG were evaluated in human intestinal HT-29 epithelial cells. CG molecular modeling was developed to study its interactions with microbial cell walls.

A multicenter open-label trial was conducted in 120 patients with IBS (Rome IV criteria) treated with CG 1.5 g/d and simethicone 0.75 mg/d for 4 weeks. The primary endpoint was the responder rate, defined as the number of patients whose abdominal pain score decreased by $\geq 30\%$ from baseline at week (W) 4. The analysis was performed using the per-protocol set. Cardinal symptoms, impact of global symptoms on daily life, change in stool consistency, and improvement in defecatory disorders were evaluated.

Results: CG in animals was well tolerated. CG at 3g/d HED significantly decreased visceral perception by 14% after 2 weeks ($p < 0.01$) and reduced inflammation by 50% promoting mucosal regeneration in DSS-induced colitis mice. CG at 1.5g/d HED reduced visceral pain perception by 20% after 5 weeks of treatment ($p < 0.01$). At 3g/d HED, this analgesic effect was superior to phloroglucinol with a faster onset of action and a 50% inhibition of pain perception ($p < 0.0001$). The molecular mechanisms contributing to these analgesic and anti-inflammatory effects of CG involved a significant induction of μ -opioid receptor (MOR), cannabinoid-2 (CB2) receptor, IL-10 and a significant decrease of pro-inflammatory cytokines IL-1b and IL-8 mRNA. CG also significantly up-regulated barrier-related genes like muc5AC, claudin-2 and ZO-2. CG molecular modelling revealed a new property of the molecule as a chelator of gram-negative lipopolysaccharide (LPS), gram-positive lipoteichoic acid (LTA) and phospholipomannan (PLM) in fungi.

Overall, 100 IBS patients were evaluated. At week 4, 67% were abdominal pain responders (score: 5.8 ± 2.4 vs. 2.9 ± 2.0 , $p < 0.0001$). Similar improvements were observed for bloating (8.0 ± 1.7 vs. 4.7 ± 2.9 , $p < 0.0001$); 60%

responders), abdominal distension (7.2 ± 2.1 vs. 4.4 ± 3.1 , $p < 0.0001$; 53% responders), and impact of global symptoms on daily life (7.1 ± 2.0 vs. 4.6 ± 2.9 , $p < 0.0001$; 54% responders). Stool consistency improved in most patients (90% and 57% for patients with liquid and hard stools, respectively). Overall, 42% of patients with defecatory disorders reported very much/considerable improvements by 2 weeks. No severe adverse event occurred, and tolerability was rated “good” or “very good” by 93%.

Conclusion: CG decreased visceral perception and intestinal inflammation. It also impacted master genes regulation and direct binding of microbial products. CG-simethicone was well tolerated and improved IBS symptoms in an uncontrolled trial. A placebo-controlled trial with longer follow-up is now ongoing to confirm the benefits of CG in IBS patients.

Disclosure: Prof Pierre Desreumaux is President of the Scientific Board of BiOkuris SA

Prof Edouard Louis is member of the Scientific Board of BiOkuris SA.

MP307

THE IMPACT OF DIET ON BRAIN STRUCTURAL AND FUNCTIONAL NETWORKS

R. Rajiah¹, Q. Aziz¹, P. Nachev², J. Ruffle²

¹Wingate Institute for Neurogastroenterology, Centre for Neuroscience, Surgery and Trauma, London, United Kingdom,

²University College London, UCL Queen Square Institute of Neurology, London, United Kingdom

Contact E-Mail Address: rebekah.rajiah@gmail.com

Introduction: Diet is an essential regulator of brain function, evidenced by longstanding associations between nutrient intake and neuronal function, synaptic plasticity, and neurotransmitter release. Recent studies have suggested that diet may impact mental health and cognition and even convey susceptibility to neurodegenerative disease. However, there is little related neuroimaging evidence to date.

Aims & Methods: Our aim was to delineate the association between diet, brain structure and function. We studied 518 healthy participants from the Cambridge Centre for Aging and Neuroscience (CAM-Can) repository (261 male and 257 female, mean age $53 \pm .79$ years). Participants were clustered via their self-reported dietary intakes using K-means clustering. Resting-state functional, white matter tractography, and grey matter volumetry networks conditional to dietary cluster were analysed using network-based statistics, controlling for participant age and sex as nuisance covariates. Relevant clinical data comprising BMI and Hospital Anxiety and Depression Score (HADS) were compared between diet clusters using Welch's t-test.

Results: Four distinct dietary intake patterns were identified: balanced, meat-predominant, vegetarian, and raw vegetable-predominant diets. Specific dietary types – balanced, meat-predominant and vegetarian – were associated with increased functional, grey matter or white matter connectivity between regions comprising the bilateral insula, frontomedial cortex (FMC) and bilateral anterior cingulate cortex (ACC) ($p < 0.04$). A balanced diet was associated with significantly increased functional, structural, and white matter connectivity between frontal brain regions, including the orbitofrontal cortex (OFC), superior frontal gyri (SFG), and FMC ($p = 0.04$) when compared to other diet clusters. A balanced diet was associated with a significantly reduced depression score (HADS-D) ($p = 0.03$), compared to a meat-predominant one. The meat-predominant diet cluster was correlated with increased structural connectivity at the bilateral ACC ($p = 0.03$) and significantly increased BMI ($p = 0.01$), when compared to vegetarian diets.

Conclusion: In the largest study of its kind, we reveal the structural and functional connectomic brain associations of diet. Notably, the set of brain regions implicated have broader established roles across interocep-

tion, emotion, memory, reward and addiction. Our findings imply a possible physiological correlate for diet-induced changes in behaviour, weight, mood, and cognition previously observed in the literature, and pave the way for future research.

References: 1.Zhang R, Zhang B, Shen C, Sahakian BJ, Li Z, Zhang W, et al. Associations of dietary patterns with brain health from behavioral, neuroimaging, biochemical and genetic analyses. *Nat Ment Health*. 2024 Apr 1;1–18.

2.Gaynor AM, Varangis E, Song S, Gazes Y, Noofory D, Babukutty RS, et al. Diet moderates the effect of resting state functional connectivity on cognitive function. *Sci Rep*. 2022 Sep 27;12(1):16080.

3.Jensen DEA, Leoni V, Klein-Flügge MC, Ebmeier KP, Suri S. Associations of dietary markers with brain volume and connectivity: A systematic review of MRI studies. *Ageing Res Rev*. 2021 Sep 1;70:101360.

4.Rolls ET, Feng R, Cheng W, Feng J. Orbitofrontal cortex connectivity is associated with food reward and body weight in humans. *Soc Cogn Affect Neurosci*. 2023 Jan 1;18(1):nsab083.

5.Tan HE, Sisti AC, Jin H, Vignovich M, Villavicencio M, Tsang KS, et al. The gut–brain axis mediates sugar preference. *Nature*. 2020 Apr;580(7804):511–6.

6.Rolls ET. Functions of the anterior insula in taste, autonomic, and related functions. *Brain Cogn*. 2016 Dec 1;110:4–19.

7.Frank S, Kullmann S, Veit R. Food related processes in the insular cortex. *Front Hum Neurosci*. 2013 Aug 23;7:499.

Disclosure: No conflicts of interest.

MP308

EFFECT OF DIFFERENT FORMS OF TENOFOVIR ON DUODENAL ENTEROCYTES – A HYPOTHESIS ON DIFFERENT EFFECT OF TDF AND TAF ON BODY WEIGHT AND PLASMA LIPIDS

K. Kauppinen^{1,2}, I. Aho^{2,1}, N. Sjöblom^{3,1}, O. Tynnenen^{3,1}, A. Suomalainen^{4,5,6}, U. Schwab^{7,8}, F. Zhao¹, P. Arkkila^{9,1}, J. Sutinen^{2,1}

¹University of Helsinki, Helsinki, Finland, ²Helsinki University Hospital, Helsinki, Finland, Department of Infectious Diseases, Inflammation Center, Helsinki, Finland, ³Helsinki University Hospital, Department of Pathology, Helsinki, Finland, ⁴University of Helsinki, Stem Cells and Metabolism research program, Faculty of Medicine, Helsinki, Finland, ⁵University of Helsinki, HiLife, Helsinki, Finland, ⁶Helsinki University Hospital, HUS Diagnostic Center, Helsinki, Finland, ⁷University of Eastern Finland, School of Medicine, Institute of Public Health and Clinical Nutrition, Kuopio, Finland, ⁸Kuopio University Hospital, Wellbeing Services County of North Savo, Department of Medicine, Endocrinology and Clinical Nutrition, Kuopio, Finland, ⁹Helsinki University Hospital, Abdominal center, department of gastroenterology, Helsinki, Finland

Contact E-Mail Address: kai.kauppinen@hus.fi

Introduction: Tenofovir disoproxil fumarate (TDF) when compared to tenofovir alafenamide (TAF) leads to lower body weight and plasma lipid concentrations; the mechanisms of these effects are unknown. (1-3) TDF as opposed to TAF is processed into free tenofovir (TFV) within enterocytes when absorbed from proximal duodenum. (4) The effect of TFV in enterocytes is unknown, but in kidney proximal tubular cells it may cause mitochondrial damage. (5,6) We hypothesize that TDF may damage enterocytes leading to reduced absorption of nutrients from this anatomical site.

Aims & Methods: People living with HIV without known gastrointestinal diseases receiving stable TDF (n=12) or TAF (n=12) containing regimen underwent gastroscopy with biopsies from proximal and distal duodenum.

Biopsy samples were scanned with Leica GT450 scanner and measurements taken in Neagen's neaLink digital pathology solution. Serum intestinal fatty acid-binding protein (I-FABP) was measured as a circulating marker of enterocyte damage. Plasma/serum concentrations of nutrients absorbed from proximal duodenum were measured. COX/SDH histochemical staining and electron microscopy (EM) were conducted to evaluate mitochondria.

Results: All participants were male. TDF and TAF groups were matched for third antiretroviral agent (58% integrase strand transfer inhibitor, 42% non-nucleoside reverse transcriptase inhibitor) and age (mean (SD) TDF group 55 (12) and TAF group 57 (16) years). Five patients in TDF group (celiac disease, helicobacter gastritis and 3 cases of esophagitis) and 2 patients in TAF group (2 cases of esophagitis) had a pathological macroscopic or histologic finding ($p=0.178$). The patient with newly diagnosed celiac disease was excluded from the rest of the analyses. Villi were flatter (337 (59) vs. 397 (42) μm , $p=0.016$), crypts deeper (200 (46) vs. 176 (27) μm , $p=0.243$), and villus to crypt ratio lower (1.5 (0.42) vs. 2.5 (0.51), $p=0.009$) in TDF vs. TAF group. I-FABP concentration was significantly higher in TDF vs. TAF group (3.0 (1.07) vs. 1.8 (0.53) ng/ml, $p=0.003$). TDF group had numerically but not statistically lower concentrations of folate; vitamins A, B1, D and E. COX/SDH staining showed signs of mitochondrial damage in 10 participants in TDF and 11 in TAF group. EM-studies showed similar mitochondrial damage in both groups.

Conclusion: TDF group displayed signs of villous damage especially in proximal duodenum when compared to TAF group. This together with increased I-FABP suggest enterocyte damage and may contribute to the clinical effect of TDF on lowering body weight and plasma lipid concentrations when compared to TAF. Our data do not support mitochondrial toxicity as the culprit behind the mucosal damage, as COX/SDH histochemistry suggested mitochondrial dysfunction and EM showed similar signs of abnormalities in mitochondrial ultrastructure in both groups. Larger studies are needed to evaluate concentrations of nutrients absorbed from proximal duodenum among TDF users.

References: 1.) Kauppinen KJ, et al. Switching from tenofovir alafenamide to tenofovir disoproxil fumarate improves lipid profile and protects from weight gain. *AIDS* 2022; 36(10):1337-1344.

2.) Mayer KH, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet* 2020; 396(10246):239-254.

3.) Sax PE, et al. Tenofovir alafenamide vs. tenofovir disoproxil fumarate in single tablet regimens for initial HIV-1 therapy: a randomized phase 2 study. *J Acquir Immune Defic Syndr* 2014; 67(1):52-58.

4.) Ruane PJ, et al. Antiviral activity, safety, and pharmacokinetics/pharmacodynamics of tenofovir alafenamide as 10-day monotherapy in HIV-1-positive adults. *J Acquir Immune Defic Syndr* 2013; 63(4):449-455.

5.) Kohler JJ, et al. Tenofovir renal proximal tubular toxicity is regulated by OAT1 and MRP4 transporters. *Lab Invest* 2011; 91(6):852-858.

6.) Herlitz LC, et al. Tenofovir nephrotoxicity: acute tubular necrosis with distinctive clinical, pathological, and mitochondrial abnormalities. *Kidney Int* 2010; 78(11):1171-1177.

Disclosure: Nothing to disclose.

MP309

DECODING CODES EARLY – IS GENETICS THE MISSING LINK?

S. T. A¹, D. Janakiraman¹, N. Deivamani¹

¹*Institute Of Child Health/Madras Medical College, Paediatric Gastroenterology, Chennai, India*

Contact E-Mail Address: tasindhu1989@gmail.com

Introduction:

Congenital Diarrhea and Enteropathies (CODEs) pose significant challenge for diagnosis and management. Genetic sequencing for children with CODEs has important implication in early diagnosis.

Aims & Methods: Among children with chronic diarrhea those suspected to have CODEs clinically and endoscopically during the period of March 2023 to Feb 2024 were included.

Clinical profile, endoscopic, histological and genetic analysis were studied in all children with suspected CODEs.

Results: Total 15(n=15) cases were included. Overall male preponderance 80%(n=12) was noted. Age at onset ranged from 2days of life to 15months with mean age of 4months. Of them, 10(66%) children had watery diarrhea, 4(26%) children had bloody diarrhea and 1(6.6%) child had fatty diarrhea.

Endoscopic and histological yield in CODEs children were found in 40%(n=4) and 30%(n=3) respectively in children with watery diarrhea, and in all children with fatty or bloody diarrhea.

Out of 10 children with watery diarrhea two children had syndromic facies, woolly hair and café-u-lait spots were diagnosed as Syndromic Diarrhea-Trichohepatoenteric Syndrome (THES). 3 of them had protein losing enteropathy(PLE) with two among 3 showing normal endoscopy and biopsy, finally turned out to be *enterokinase deficiency*, while one child with endoscopically viewed whitish speckled mucosa with patchy vacuolated surface on histology had *DGAT 1 mutation*.

Two children with watery diarrhoea had microvillous atrophy (*MYO5B*) and one with severe watery diarrhea had *NEUROG3* mutation. Glucose galactose malabsorption (*GGM*), and Congenital Tufting Enteropathy (*CTE*) were seen in other two children. Among children with bloody diarrhea, two had proctocolitis on histology confirming Very Early Onset Inflammatory Bowel Disease(VEO-IBD) with genetic mutation showing *CARMIL 2* and *RIPK1* mutation. Two children with bloody diarrhoea suspected to have IBD had chronic colitis with thrombotic complications suggesting *CD55 deficiency* with Hyperactivation of complement, Angiopathic thrombosis, and PLE (CHAPLE syndrome). child with fatty diarrhoea with endoscopic findings suggestive of intestinal lymphangiectasia and histology of duodenal biopsy showing lipid droplets was clinically and genetically diagnosed Abetalipoproteinemia and started on fat free diet with MCT oil and vitamin A,D,E,K supplements.

Genomic analysis are the final stand of diagnosing CODEs due to the overlap of the clinical phenotypes and lack of appropriate biomarkers. Genetic Analysis had 100% yield when CODEs were suspected. Overall mortality rate was 26%(n=4) in 1year follow-up in our study group.

Conclusion: Single gene disorders are common among CODEs patients. Early Genetic testing helps in accurate diagnosis and initiating appropriate therapy as endoscopy and histology has poor yield.

References: •Lee, Kun Song et al. "How to do in persistent diarrhea of children?: concepts and treatments of chronic diarrhea." *Pediatric gastroenterology, hepatology & nutrition* vol. 15,4 (2012): 229-36. doi:10.5223/pghn.2012.15.4.229

•Thiagarajah, Jay R et al. "Advances in Evaluation of Chronic Diarrhea in Infants." *Gastroenterology* vol. 154,8 (2018): 2045-2059.e6. doi:10.1053/j.gastro.2018.03.067

•Bourgeois, P., Esteve, C., Chaix, C., Beroud, C., Levy, N., THES Clinical Consortium, Fabre, A., Badens, C. Tricho-hepato-enteric syndrome mutation

update: mutations spectrum of TTC37 and SKIV2L, clinical analysis and future prospects. Hum. Mutat. 39: 774-789, 2018

Disclosure: Nothing to disclose.

MP310

CLINICAL OUTCOME OF THREE DIFFERENT TECHNIQUES OF ENDOSCOPIC GASTROPLASTY. RESULTS AT 18 MONTHS FOLLOW-UP FROM A SINGLE CENTER, RANDOMIZED CONTROLLED TRIAL

S.F. Vadalà di Prampero¹, C. Rocchi², M. Massidda², V. Cosseddu³, P. Bazzu³, F. Di Maio³, N. Panic⁴, A. Malenkovic⁴, J. Formichetti³, S. Masia³, G. Faleschini⁵, G. Manzoni³, P. Giustacchini⁶, P.M. Rinaldi⁷, G. Costamagna^{1,6}, M. Bulajic¹
¹Isola Tiberina - Gemelli Isola Hospital, Digestive Endoscopy Unit, Center of Excellence for Gastrointestinal and Metabolic Disorders, Rome, Italy, ²Mater Olbia Hospital, Gastroenterology and Digestive Endoscopy Department, Olbia, Italy, ³Mater Olbia Hospital, Olbia, Italy, ⁴Dr Dragisa Misovic-Dedinje, Center for Digestive Endoscopy, Belgrade, Serbia, ⁵Spital STS AG, Bern, Switzerland, ⁶Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy, ⁷Mater Olbia, Department of Radiology, Olbia, Italy

Contact E-Mail Address: vadaladiprampero@gmail.com

Introduction:

Endoscopic Gastroplasty (EG) is an endoscopic therapy to treat obese patients focusing on gastric body remodeling. We considered three different techniques: Endoscopic Sleeve Gastroplasty (ESG), Endoluminal Vertical Gastroplasty (EVG), and distal Primary Obesity Surgery Endoluminal (POSE2).

Aims & Methods:

This was a single center, randomized controlled trial (ClinicalTrials.gov NCT04854317) of obese patients who underwent EG (through ESG or EVG or POSE2) or a low-calorie Mediterranean diet (1600 and 1400 Kcal/day). Outcomes included technical success rate, serious adverse event rate, and efficacy of the three EG procedures at inducing weight loss, improving obesity related comorbidities and quality of life (QoL), compared to diet.

Results: From July 2020 to May 2022, 240 obese (body mass index 37.5 ± 3.5 kg/m²) patients (mean age 46 ± 10 years; females 87.8%; obesity class II 58.3%; hepatic steatosis as the main comorbidity in 70%) underwent EG (through ESG, EVG or POSE2, with 60 patients for each procedure, 180 patients in total) or a low-calorie diet (60 patients). In the EG group the technical success rate was 100%. The serious adverse event rate was 1.1%. The follow-up visit was attended by 100/180 (55.6%), 48/180 (26.7%) and 19/180 (10.6%) patients at 6, 12 and 18 months, respectively. They experienced $16.1 \pm 6.1\%$, $13.7 \pm 9.0\%$ and $14.1 \pm 11.0\%$ total body weight loss (TBWL) and $39.7 \pm 15.4\%$, $35.3 \pm 23.4\%$ and $34.7 \pm 27.3\%$ excess weight loss (EWL) at 6, 12 and 18 months, respectively, with no significant difference among the three techniques in both parameters ($p > 0.62$ in TBWL% and $p > 0.94$ in EWL% ANOVA tests) at 18 months follow-up. Concerning the low-calorie diet group, 31/60 (52%), 13/60 (22%) and 4/60 (6%) patients attended their 6, 12 and 18 months follow-up; they experienced $1.1 \pm 4.7\%$ TBWL ($p < 0.001$ versus EG group) and $2.3 \pm 9.8\%$ EWL ($p < 0.001$ versus EG group) at 18 months. Ninety seven of one hundred (97.0%), 37/48 (77.1%) and 16/19 (84.2%) patients achieved at least 5% TBWL, while 86/100 (86.0%), 32/48 (66.6%) and 15/19 (78.9%) achieved at least 25% EWL in the EG group at 6, 12 and 18 months follow-up, compared to 4/31 (12.9%), 1/13 (7.6%) and 0/4 (0%), and 3/31 (9.7%), 1/13 (7.6%) and 0/4 (0%) in the diet group, at 6, 12 and 18 months. Fatty liver disease, hypertension, hyperlipidemia, diabetes, and obstructive sleep apnea improved after the EG procedure at 18 months, while no improvement was observed in the

diet group. Also, the QoL measured by EQ-5D test improved at 18-month follow-up ($p < 0.01$) in the EG group, while no significant improvement was detected in the diet group.

Conclusion: EG through ESG, EVG and D-POSE are technically feasible and safe, and appear to be effective for the treatment of obese patients, compared to diet, at a medium term follow-up.

Disclosure: The following authors have completed their 2024 DDW disclosure: Salvatore Vadalà di Prampero: Disclosure completed | Chiara Rocchi: Disclosure completed | Marco Massidda: Disclosure completed | Valentina Cosseddu: Disclosure completed | Paola Bazzu: Disclosure completed | Federica Di Maio: Disclosure completed | Jessica Formichetti: Disclosure completed | Simona Masia: Disclosure completed | Giacomo Faleschini: Disclosure completed | Nikola Panic: Disclosure completed | Gabriella Manzoni: Disclosure completed | Piero Giustacchini: Disclosure completed | Guido Costamagna: Disclosure completed | Milutin Bulajic: Disclosure completed

MP311

LONG-TERM RESULTS OF ENDOSCOPIC SLEEVE GASTROPLASTY BY OBESITY CLASS

M.V. Matteo¹, V. Bove², G. Carlino³, V. Pontecorvi⁴, L. Gualtieri¹, M. De Siena¹, C. Spada², I. Boskoski¹
¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, ²Fondazione Policlinico Universitario A. Gemelli, Roma, Italia - IRCCS, Digestive Endoscopy Unit, Roma, Italy, ³Policlinico Universitario Agostino Gemelli, Università Cattolica Del Sacro Cuore, 00168, Italy, ⁴IRCSS Fondazione Policlinico Gemelli, Endoscopia Digestiva Chirurgica, Rome, Italy

Contact E-Mail Address: mariavaleria31191@gmail.com

Introduction: Obesity is a chronic and recurrent disease. In the past few years, Endoscopic sleeve gastroplasty (ESG) has emerged as a minimally invasive technique to fill the therapeutic gap between medical and surgical approaches to obesity. ESG consists of full-thickness suturing of the gastric body to restrict gastric volume and impair gastric motility.

Most of the published data on ESG are limited to 12-24 months¹⁻⁶. In this study, we aim to report long-term results of ESG to implement further the evidence of long-term effectiveness in each BMI class.

Aims & Methods: A post-hoc analysis was performed on a prospective database including patients with obesity (BMI ≥ 30 kg/m²) who underwent ESG between May 2017 and May 2021 at a single tertiary Center. Before ESG, all patients were evaluated and identified as eligible for the bariatric procedure by the local bariatric multidisciplinary team. Weight loss outcomes (%EWL, %TBWL) were evaluated during follow-up and stratified according to obesity class. We evaluated the percentage of patients achieving %EWL $>25\%$, the current threshold defining the efficacy of a primary bariatric endoscopic procedure⁷, as well as percentage of patients achieving %TBWL $>10\%$, the minimum threshold associated with obesity-related comorbidities improvement⁸. All patients were included in a multidisciplinary follow-up scheduled at 1, 3, 6, and then every 6 months, as per routine clinical practice.

Results: Between May 2017 and May 2021, 252 subjects (73% Female) underwent ESG with a median BMI of 37.2 (35.3 - 40.8) kg/m² at baseline and a median age of 45 (36-54) years. No severe procedure-related adverse events occurred. Of 252 subjects, 58 (23%) had obesity class I (BMI 30-34.9), 120 (48%) had obesity class II (BMI 35-39.9), and 74 (29%) had class III obesity (BMI ≥ 40). Follow-up rate was 90.5% (228/252) at 12 months, 60.3% (152/252) at 24 months, and 30.2% at 30-36 months. Overall, 58% (44/76) of patients showed an %EWL $>25\%$ at 30-36 months of follow-up,

respectively. Similarly, 71% (54/76) of subjects showed a %TBWL > 5% 30-36 months after ESG. Weight loss results according to BMI class are reported in Table 1.

	Overall	Class I Obesity	Class II Obesity	Class III Obesity
%EWL 12mo	46.6 (27.9-63.2)	49.7 (30.4-66.3)	50.8 (32.7-64.0)	45.2 (27.8-57.1)
%EWL 24mo	39.3 (17.6-58.4)	39.3 (18.1-58.6)	41.5 (14.4-60.8)	31.3 (17.5-49.3)
%EWL 30-36mo	36.4 (21.0-66.3)	31.3 (6.4-54.7)	31.4 (13.0-54.8)	31.4 (13.0-54.8)
%TBWL 12mo	15.6 (10.3-21.3)	12.5 (6.5-19.4)	16.3 (10.5-22.4)	16.2 (10.5-22.6)
%TBWL 24mo	12.8 (6.4-19.4)	15.9 (10.3-21.3)	13.8 (4.5-18.9)	15.1 (7.6-22.9)
%TBWL 30-36mo	13.3 (6.7-23.8)	11.1 (4.5-18.3)	10.7 (4.4-18.2)	10.7 (4.4-18.2)
% of patients with %EWL > 25% (30-36mo)	58% (44/76)	77% (10/13)	68% (20/32)	42% (13/31)
% of patients with %TBWL > 5% (30-36mo)	71% (54/76)	77% (10/13)	75% (24/32)	61% (19/31)

%EWL and %TBWL are reported as median (Q1-Q3)
 %EWL: percentage of excess weight loss; %TBWL: percentage of total body weight loss; mo: months.

Conclusion: Despite limited by the follow-up loss, a common issue in clinical practice for obesity cohorts, our experience confirms that ESG in the setting of a multidisciplinary approach is a safe and effective procedure for the treatment of obesity, associated with sustained weight loss in all obesity classes.

References: 1. Sharaiha RZ, Kumta NA, Saumoy M, et al. Endoscopic Sleeve Gastroplasty Significantly Reduces Body Mass Index and Metabolic Complications in Obese Patients. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2017;15(4):504-510.
 2. Lopez-Nava G, Sharaiha RZ, Vargas EJ, et al. Endoscopic Sleeve Gastroplasty for Obesity: a Multicenter Study of 248 Patients with 24 Months Follow-Up. *Obes Surg.* 2017;27(10):2649-2655.
 3. Graus Morales J, Crespo Pérez L, Marques A, et al. Modified endoscopic gastroplasty for the treatment of obesity. *Surg Endosc.* 2018;32(9):3936-3942.
 4. Alqahtani A, Al-Darwish A, Mahmoud AE, Alqahtani YA, Elahmedi M. Short-term outcomes of endoscopic sleeve gastroplasty in 1000 consecutive patients. *Gastrointest Endosc.* 2019;89(6):1132-1138.
 5. Sharaiha RZ, Hajifathalian K, Kumar R, et al. Five-Year Outcomes of Endoscopic Sleeve Gastroplasty for the Treatment of Obesity. *Clin Gastroenterol Hepatol.* 2021;19(5):1051-1057.e2.
 6. Abu Dayyeh BK, Bazerbachi F, Vargas EJ, et al. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. *Lancet Lond Engl.* 2022;400(10350):441-451.
 7. Ginsberg GG, Chand B, Cote GA, et al. A pathway to endoscopic bariatric therapies. *Gastrointest Endosc.* 2011;74(5):943-953.
 8. Ryan DH, Yockey SR. Weight Loss and Improvement in Comorbidity: Differences at 5%,10%,15%, and Over. *Curr Obes Rep.* 2017;6(2):187-194.

Disclosure: Nothing to disclose.

MP312

DAILY ERYTHRITOL CONSUMPTION FOR FIVE WEEKS SHOWS NO IMPACT ON GLYCEMIC CONTROL IN HEALTHY ADOLESCENTS

A. Altstädt^{1,2}, V. Bordier^{1,2}, E. Flad^{1,2}, J. Drewe³, C. Beglinger⁴, A.C. Meyer-Gerspach^{1,2}, B.K. Wölnerhanssen^{1,2}

¹St. Clara Research Ltd., Basel, Switzerland, ²University of Basel, Basel, Switzerland, ³University Hospital Basel, Basel, Switzerland, ⁴University Hospital Basel, Division of Gastroenterology, Arlesheim, Switzerland

Contact E-Mail Address: anita.altstaedt@unibas.ch

Introduction: There is a close relationship between the rise in obesity and the increase in consumption of sugar-sweetened beverages. According to a report by the World Health Organization (WHO), about 18% of children and adolescents worldwide are affected by overweight or obesity. Sweet

beverage consumption is particularly high in this age group. The WHO recommends reducing sugar intake to prevent and treat obesity. Reduction of sugar intake can be achieved through partial substitution with alternative sweeteners. Erythritol is a naturally occurring non-caloric bulk sweetener. Unlike sugar, erythritol does not affect plasma glucose and insulin concentrations yet stimulates the release of gastrointestinal satiation hormones.

Aims & Methods: This study aimed to evaluate the impact of daily erythritol versus sucrose intake over 5 weeks on parameters of glycemic control, food intake and gastrointestinal symptoms in healthy adolescents.

In this randomized, double-blind, parallel trial, 30 healthy, lean adolescents (15 per group: mean $\pm$ SD; age: 16.9 $\pm$ 1.5 years; BMI: 20.9 $\pm$ 1.8 kg/m²) were included. For a duration of 5 weeks, they received a daily total of 36 g of erythritol (divided into two portions of 18 g in 150 mL tap water; ERY), or 25 g of sucrose (divided into two portions of 12.5 g in 150 mL tap water; SUC). During the week before and the last week of intervention, food intake was assessed by food records. Before and after the intervention period, an oral glucose tolerance test was carried out and blood samples were collected at fixed time points to measure plasma glucose and insulin. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and Homeostatic Model Assessment of Insulin Sensitivity (HOMA-%S) were calculated. The Gastrointestinal Symptom Rating Scale (GSRS) was applied to assess gastrointestinal symptoms at 3 timepoints (before, during week 3, and after the intervention).

Results: In the erythritol-group, parameters of glycemic control were not significantly different in response to the intervention. In the sucrose-group Cmax for blood glucose was not significantly different but Cmax for blood insulin (PRE_{SUC}: 91.67 $\pm$ 33.71 mIU/L vs. POST_{SUC}: 127.38 $\pm$ 68.24 mIU/L; p = 0.030) and HOMA-IR (PRE_{SUC}: 1.79 $\pm$ 0.74 vs. POST_{SUC}: 2.51 $\pm$ 0.74; p < 0.001) were significantly increased, while HOMA-%S (PRE_{SUC}: 70.5 $\pm$ 47.3 vs. POST_{SUC}: 43.2 $\pm$ 12.5; p = 0.016) was significantly reduced after the intervention period. In the erythritol-group, total sugar intake (PRE_{ERY}: 90.3 $\pm$ 34.0 g vs. POST_{ERY}: 71.0 $\pm$ 36.0 g; p = 0.034) and total carbohydrate intake (PRE_{ERY}: 256.8 $\pm$ 54.8 g vs. POST_{ERY}: 211.1 $\pm$ 71.0 g; p = 0.038) were significantly reduced after the intervention period, while total caloric intake (PRE_{ERY}: 2113.7 $\pm$ 495.4 kcal vs. POST_{ERY}: 1855.1 $\pm$ 495.7 kcal; p = 0.068) showed a trend of reduction. In the sucrose-group, total sugar intake (PRE_{SUC}: 75.4 $\pm$ 31.2 g vs. POST_{SUC}: 92.4 $\pm$ 24.7 g; p = 0.073) showed a trend of increase after the intervention period, while total carbohydrate and total caloric intakes were not significantly different. The total score of GSRS was not significantly different between the groups but increased significantly over time in both groups (p = 0.045).

Conclusion: Daily erythritol intake in healthy, lean adolescents over 5 weeks did not affect parameters of glycemic control but led to a significant reduction of total carbohydrate and total sugar intake. In contrast, the sucrose intervention resulted in a significant increase in maximum insulin concentration and HOMA-IR, along with a significant decrease in HOMA-%S.

Disclosure: Nothing to disclose.

MP313

THE ROLE OF NUTRITION AND MATERNAL MICROBIOTA IN THE DEVELOPMENT OF THE INFANT GUT MICROBIOTA

G. Rocchi¹, A. Altomare^{1,2}, C. Terranova³, D. Luvero³, F. Ferravante⁴, F. Del Chierico⁵, L. Putignani⁶, S. Emerenziani⁴, P. Ferrara⁷, R. Angioli³, C. Bartolucci⁸, M. Cicala^{2,9}, M.P.L. Guarino^{9,2}

¹Campus Bio-medico University, Departmental Faculty of Sciences and Technology for Sustainable Development and Human Health, Rome, Italy, ²Campus Bio Medico University, Gastroenterology Unit, Rome, Italy, ³Fondazione Policlinico Campus Bio-Medico di Roma, Gynecology and Obstetrics Unit, Rome, Italy, ⁴Fondazione Policlinico Campus Bio-Medico of Rome, Clinical Nutrition Unit, Rome, Italy, ⁵Bambino Gesù Children's Hospital, IRCCS, Research Unit of Human Microbiome, Rome, Italy, ⁶Bambino Gesù Children's Hospital, IRCCS, Unit of Microbiomics and Research Unit of Human Microbiome, Rome, Italy, ⁷Fondazione Policlinico Campus Bio-Medico of Rome, Pediatric Unit, Rome, Italy, ⁸Fondazione Comitans, Rome, Italy, ⁹Fondazione Policlinico Campus Biomedico di Roma, Gastroenterology and Endoscopy Unit, Roma, Italy

Contact E-Mail Address: giulia.rocchi@unicampus.it

Introduction: The extreme dynamism of the microbial ecosystem in the early years of life represents a crucial stage for undertaking targeted interventions to contribute to proper immune structuring and reduce susceptibility to chronic disorders. One of the main factors involved is maternal diet, which can influence the infant's gut microbiome through vertical transfer of maternal microbes to infants during vaginal delivery and breastfeeding. In this study, the association between maternal gut microbiota, maternal diet during pregnancy and lactation, and infant gut microbiota was analysed.

Aims & Methods: Healthy pregnant women in the 3rd trimester (baseline) were enrolled and nutritional counselling interventions were carried out. Stool samples and clinical data of mother and child were collected at baseline (T0), at birth (T1), and at 3 months (T2). A Food Diary and the MDSS (≥ 16) index assessed nutrient intake. Gut microbiota analysis on faecal samples from mothers and offspring was obtained by MiSeq 16rRNA Illumina. Statistical analysis will be performed using GraphPad Prism 9.0.

Results: 14 pregnant women with pre-gravid BMI 22.9 ± 3.2 kg/m² and pre-gravid TEE 2030 ± 137.3 Kcal/day were included. 75% of the infants were term-born vaginally and exclusively breastfed. Pregnant women had a dietary pattern not adhering to Mediterranean diet with an improvement following the nutritional intervention (MDSS T₀: 13 ± 2.5 ; T₁: 16 ± 0.7). At T₁, following nutritional counselling, the assessment of nutritional intakes showed an improving trend in energy intake of carbohydrates, lipids, and fiber, compared to dietary reference value. At baseline, maternal gut microbiota showed an important abundance of Proteobacteria phyla. At T₁, a positive trend in increasing abundances of Verrucomicrobiaceae, *Akkermansia* and *Fecalibacterium* was observed. Analysis of the infant gut microbiota at T1 and T2, showed increased α -diversity values over time, driven by the appearance of new bacterial species. A structural difference in microbial species, such as *E. coli*, *Bifidobacterium* and *Staphylococcus*, *Veillonella*, was observed between infants born via vaginal or caesarean delivery.

Conclusion: Preliminary data suggests that a nutritional counselling intervention in the 3rd trimester of pregnancy could be a potential protective factor that positively influences intestinal bacterial colonization in offspring.

Disclosure: Nothing to disclose.

MP314

MILK FAT GLOBULE MEMBRANE ENHANCES NEONATAL INTESTINAL EPITHELIAL MATURATION

J.W.M. de Kleer¹, J.L.M. Vermeulen¹, V. Dijkstra-Muncan^{1,2}, B. Sovran^{1,2,3}, T.T. Lambers⁴, W.J. de Jonge^{1,5}

¹Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, University of Amsterdam, Gastroenterology and Metabolism, Amsterdam, Netherlands, ²Emma Center for Personalized Medicine, Amsterdam University Medical Center (UMC), University of Amsterdam, Amsterdam, Netherlands, ³Amsterdam Reproduction and Development Research Institute, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam and Vrije Universiteit Amsterdam, Pediatric Surgery, Amsterdam, Netherlands, ⁴FrieslandCampina, Amersfoort, Netherlands, ⁵University of Bonn, Surgery, Bonn, Germany

Contact E-Mail Address: j.w.m.dekleer@amsterdamumc.nl

Introduction: Preterm birth complications such as sepsis and necrotizing enterocolitis (NEC), are the leading cause of death among neonates. (1) Preterm birth is likely associated with dysbalanced microbial colonization and immature intestinal epithelium at birth, which impacts functionality, and barrier function of epithelia once microbial colonization occurs. Both structural and functional maturation of the intestinal epithelium are required for sufficient digestion and absorption of nutrients. (2) Breastmilk (BM) has been shown to significantly reduce the risk of developing NEC in preterms, in contrast to infant formula (IF). (3) We hypothesize that this is partly explained by the fact that BM contains a unique fat component, the milk fat globule membrane (MFGM), absent in IF. MFGM comprises a triple membrane of polar lipids, embedding bioactive components such as proteins, phospholipids and gangliosides. MFGM has shown to induce elevated epithelial cell differentiation and enhanced barrier integrity in an allergic mouse model and an early life rat model. (4, 5) However, the effects of MFGM on human intestinal maturation are unknown. We studied the effects of MFGM on human intestinal maturation using *in vitro* human neonatal small intestinal organoids.

Aims & Methods: Primary human neonatal organoids were derived from ileal tissue collected during neonatal surgeries (age 5 weeks - 4 months). Three-dimensional organoids were exposed continuously for 7 days to either 0.25wt% MFGM-enriched whey or 0.25wt% whey protein isolate (WPI; whey protein control not containing MFGM). Differences in growth and morphology were assessed by brightfield microscopy. Organoid growth was assessed by quantification through ImageJ analyses. Epithelial maturation was defined by longitudinal expression of brush border enzymes sucrase isomaltase (Sis), lactase (Lct) and intestinal alkaline phosphatase (ALPI), epithelial differentiation into secretory Paneth cells (Lysozyme; Lyz) and Goblet cells (Mucin-2; Muc2), and decreased stemness (Lgr5). Epithelial maturation was assessed by immunohistochemical (IHC) staining and qPCR.

Results: Neonatal organoids stimulated with MFGM displayed slower growth rate and decreased Lgr5 expression compared to WPI and medium control. This was accompanied with a 15-fold increase in gene expression of ALPI and 18-fold increase in Sis, two brush border enzymes associated with epithelial maturation. Expression of Muc2 was increased in MFGM stimulated conditions compared to medium control. Additionally, IHC stainings showed higher expression of Lyz in MFGM stimulated organoids compared to control and WPI. This suggest that MFGM stimulation enhances maturation by increasing expression of brush border enzymes and epithelial differentiation, while reducing stemness.

Conclusion: Our data suggest that MFGM enhances epithelial maturation by enhancing expression of brush border enzymes and cell differentiation in a human primary neonatal organoid model.

References: 1. Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL, et al. Global, regional, and national causes of under-5 mortality in 2000-19: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet Child Adolesc Health*. 2022;6(2):106-15.

2. Frazer LC, Good M. Intestinal epithelium in early life. *Mucosal Immunol*. 2022;15(6):1181-7.

3. Altobelli E, Angeletti P, Verrotti A, Petrocelli R. The Impact of Human Milk on Necrotizing Enterocolitis: A Systematic Review and Meta-Analysis. *Nutrients*. 2020;12:1322.

4. Bhinder G, Allaire JM, Garcia C, Lau JT, Chan JM, Ryz NR, et al. Milk Fat Globule Membrane Supplementation in Formula Modulates the Neonatal Gut Microbiome and Normalizes Intestinal Development. *Sci Rep*. 2017;7:45274.

5. Gong H, Li T, Liang D, Gao J, Liu X, Mao X. Milk fat globule membrane supplementation protects against β -lactoglobulin-induced food allergy in mice via upregulation of regulatory T cells and enhancement of intestinal barrier in a microbiota-derived short-chain fatty acids manner. *Food Science and Human Wellness*. 2024;13(1):124-36.

Disclosure: Nothing to disclose.

MP315

DOES SMALL BOWEL BACTERIAL OVERGROWTH (SIBO) HAS A ROLE IN UNEXPLAINED PERSISTENT HALITOSIS?

A. Yusuf¹, A. Ahmed^{1,2}, R. Ahmed¹

¹City Hospital, Gastroenterology, Hargeisa, Somalia, ²City Hospital, Hargeisa, Somalia

Contact E-Mail Address: abdyus12@gmail.com

Introduction: Halitosis is a relatively common condition with significant psychosocial impact on patients. The aetiology of halitosis is multifactorial and can be due to oro-dental, ENT, pulmonary or gastrointestinal conditions.

Aims & Methods: We wanted to test if SIBO can play a role in unexplained persistent halitosis. We prospectively collected data on all patients who were referred or self-presented to our GI specialist unit with halitosis over a two-year period. The inclusion criteria for the study were all patients should have had a negative dental and ENT check. We excluded all patients with chronic pulmonary and GI conditions, and those who have had any antibiotic therapy in the preceding four weeks. The patients were tested for SIBO using Bedfont-UK Gastrolyzer system with Lactulose 10 g as a substrate. A ≥ 20 ppm rise in hydrogen by 90 minutes was considered positive as per the North American Consensus on Breath Testing.

Results: From August 2021 to August 2023, a total of 53 patients (males 56.7%, females 43.3%, average 40.9 years) with persistent unexplained halitosis met the inclusion criteria for the study. A total of 21 patients (39.6%) had a positive test for SIBO (males 38.1%, females 61.9%, average age 44.2 years). All patients with a positive test result were treated with either oral Co-amoxiclav or a combination of oral Ciprofloxacin and Metronidazole for a 14-day period, and were followed up at three months (table 1).

	Type of antibiotic therapy	Patients with full response at 3 months	Number of patients with partial response at 3 months	No response at 3 months	Lost to follow up
Positive SIBO test (n = 21)	Cipro/Metro (n = 13, (61.9%))	8 (61.5%)	3 (23.1%)	1 (7.7%)	1 (7.7%)
	Co-amox (n = 8, (38.1%))	5 (62.5%)	2 (25.0%)	1 (12.5%)	0

Table 1: Treatment outcomes for patients with positive SIBO test.

Conclusion: SIBO might be an important factor in patients with unexplained persistent halitosis, and their symptoms seem to respond well to antibiotic therapy. It would be prudent to carry out further larger studies with longer follow up period in order to establish the role of SIBO in patients with unexplained persistent halitosis.

Disclosure: Nothing to disclose.

Diagnosis and endoscopic treatment of upper GI neoplasms

11:30-12:30 / Poster Stage 6

MP316

HANDHELD MAGNETICALLY ASSISTED WHOLE GASTROINTESTINAL TRACT CAPSULE ENDOSCOPY EFFECTIVELY DETECTS OESOPHAGOGASTROCOLORECTAL TUMOURS AND POLYPS: A RANDOMIZED CONTROLLED TRIAL

N. Ohmiya¹, K. Tashiro², T. Omori³, S. Banno⁴, T. Tsukamoto⁵, T. Mizuno², MagCam study group

¹Fujita Health University School of Medicine, Departments of Gastroenterology and Advanced Endoscopy, Toyoake, Japan, ²Shinshu University Faculty of Engineering, Department of Electrical and Computer Engineering, Nagano, Japan, ³Fujita Health University School of Medicine, Department of Gastroenterology, Toyoake, Japan, ⁴Fujita Health University School of Medicine, Center for Clinical Trial and Research Support, Toyoake, Japan, ⁵Fujita Health University School of Medicine, Department of Diagnostic Pathology, Toyoake, Japan

Contact E-Mail Address: nohmiya@med.nagoya-u.ac.jp

Introduction: Capsule endoscopy screening for pangastrointestinal tumours during a single procedure is expected. Here, we developed a handheld guiding device using a neodymium magnet through which a conventional colon capsule endoscope without an internal magnet can be manipulated.

Aims & Methods: We aimed to determine its effectiveness and safety. In a randomized controlled trial, 96 patients harboring superficial oesophageal carcinomas, gastric tumours, or colorectal polyps or tumours (CRTs) were enrolled; 47 and 49 patients were allocated to the S group using a nonmagnetic sham device and the M group using this magnetic device, respectively. The primary outcomes were the per-patient diagnostic yields for the representative tumours or polyps and the per-lesion yields. The secondary outcomes were the observation rate at each gastric site, adverse events, and acceptability using a subjectively categorized questionnaire survey.

Results: Although the per-patient sensitivity and specificity of the representative gastric tumours in the S and M groups were 95.2% and 100.0%, respectively ($P=.4773$); and 96.2% and 92.3%, respectively ($P>.9999$), the per-lesion sensitivity of gastric polyps was significantly greater in the M group ($P < 0.0001$), especially those localized in the upper and middle portions and <5 mm in size. There were significantly distinct observation rates of total gastric sites in the S and M groups (87% vs. 98%, $P < 0.0001$). In both groups, the per-patient sensitivity and specificity of CRTs ≥ 6 mm and ≥ 10 mm were 90.9% and 96.7%, respectively; 92.5% and 98.2%, respectively; and 77.8% and 71.4%, respectively, for superficial oesophageal carcinoma.

There were no adverse events associated with magnetic guidance. The proportions of patients who reported “not at all” and “almost none” or “quite easy” and “fairly easy” for embarrassment, abdominal pain, and fear were higher than 80% and who desired CE at the next examination were 62.5% (60/96) in total.

Conclusion: This study provides evidence supporting the effectiveness, safety, and acceptability of magnetically assisted CE for pangastrointestinal cancer screening.

Japan Registry of Clinical Trials, JRCTs042180150.

References: 1. Tashiro K, Kutsuna S, Wakiwaka H, and Ohmiya N. Design of the Magnetic Guide Magnet for Magnetic Guide of a Capsule Endoscope. Journal of the Japan Society of Applied Electromagnetics and Mechanics 2017;25:100-105.

2. Matsushashi K, Ozawa Y, Tashiro K, Wakiwaka H, Mizuno T, and Ohmiya N. Design of Planar Array Magnet for Magnetic Guide of a Capsule Endoscope. Journal of the Japan Society of Applied Electromagnetics and Mechanics 2021;29:13-18.

Disclosure: Nothing to disclose.

MP317

CAN WESTERN EXPERTS DISTINGUISH T1A AND T1B ESOPHAGEAL ADENOCARCINOMA BASED ON OPTICAL EVALUATION: AN INTERNATIONAL INTER-OBSERVER AGREEMENT STUDY

S. Gupta^{1,2}, F.V. Mandarino¹, J. Gauci¹, A. Whitfield^{1,2}, C. Kerrison¹, P. Selvanathan³, P. Kumar¹, H. Messmann⁴, M. Wallace⁵, A. Repici⁶, M. Dinis-Ribeiro⁷, G. Haber⁸, A. Taylor⁹, I. Waxman¹⁰, P.D. Siersema¹¹, R.E. Pouw¹², A. Lemmers¹³, R. Bisschops¹⁴, J.D. Mosko¹⁵, C. Teshima¹⁵, K. Ragunath¹⁶, T. Rösch¹⁷, O. Pech¹⁸, T. Beyna¹⁹, P. Sharma²⁰, E. Lee¹, S. Williams¹, N.G Burgess^{1,2}, M.J. Bourke^{1,2}

¹Westmead Hospital, Gastroenterology & Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia, ³Princess Alexandra Hospital, Gastroenterology and Hepatology, Woolloongabba, Australia, ⁴Uniklinik Augsburg, III. Medizinische Klinik, Augsburg, Germany, ⁵Mayo Clinic, Gastroenterology, Ponte Vedra Beach, United States of America, ⁶Ist. Clinico Humanitas Rozzano, Dept. of Gastroenterology, Milano, Italy, ⁷IPO Porto, Dept. of Gastroenterology, Porto, Portugal, ⁸NYU Langone Health, New York, United States of America, ⁹St Vincent's Hospital Melbourne, Melbourne, Australia, ¹⁰Rush University Medical Center, Chicago, United States of America, ¹¹Erasmus MC – University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands, ¹²Amsterdam UMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ¹³Hôpital Univ. Erasme, Gastroenterology Department, Bruxelles, Belgium, ¹⁴Katholieke Universiteit Leuven, Gastroenterology, Leuven, Belgium, ¹⁵St Michael's Hospital, Therapeutic Endoscopy, Toronto, Canada, ¹⁶Royal Perth Hospital, Department of Gastroenterology, Perth, Australia, ¹⁷Clinic for Interdisciplinary Endoscopy, Klinik für Interdisziplinäre Endoskopie, Hamburg, Germany, ¹⁸Krankenhaus Barmherzige Brüder Klinik für Gastroenterologie und Interventionelle Endoskopie - Klinik, Klinik für Gastroenterologie und, Regensburg, Germany, ¹⁹Evangel. Krankenhaus Düsseldorf, Department of Internal Medicine, Düsseldorf, Germany, ²⁰University of Kansas School of Medicine Dept. of Gastroenterology, Gastroenterology, Leawood, United States of America

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: Distinguishing T1a and T1b oesophageal adenocarcinoma is imperative under current treatment paradigms. Piecemeal EMR is suggested to be acceptable for T1a oesophageal adenocarcinoma whereas en bloc R0 excision is required for in T1b disease, offering a potential cure and mitigate recurrence. Thus, we sought to ascertain whether internationally renowned expert Barrett's endoscopists were able to make this distinction based on optical evaluation.

Aims & Methods: A set of 60 endoscopic images of histologically confirmed high grade dysplasia (HGD), T1a and T1b disease (n=20 for each) were compiled from consecutive patients at a single institution. Each set contained four images, and were standardized to include an overview, a close-up in high-definition white light, a near-focus magnification image, and a narrow-band image. Experts were blind to histology and invited to predict it for each set of images – HGD vs T1a vs T1b.

Results: 19 experts from 8 countries (Australia, USA, Italy, Netherlands, Germany, Canada, Belgium, and Portugal) participated. The majority have been practicing for >20 years, with a median annual case volume for Barrett's EMR of 50 (IQR 18-75), and Barrett's ESD of 25 (IQR 10-45). Oesophageal adenocarcinoma (T1a/b) could be distinguished from HGD, with a pooled sensitivity of 89.1% (95% CI: 86.7-91.2). When predicting the T-stage for T1b adenocarcinoma cases, the pooled sensitivity was 43.8% (95% CI: 38.5-49.2). Fleiss' kappa was 0.421 (95% CI: 0.399-0.442, P<0.001).

Conclusion: Expert Barrett's endoscopists can reliably differentiate T1a/T1b oesophageal adenocarcinoma from HGD. Although there is fair-to-moderate agreement for T-staging, T1a disease cannot be reliably distinguished from T1b disease. This may have implications on clinical decision making and selection of endoscopic treatment methods.

Disclosure: Michael J. Bourke: Research Support: Olympus, Cook Medical, Boston Scientific.

MP318

ESD FOR THE TREATMENT OF EARLY BARRETT'S NEOPLASIA (ESTEBAN), A PROSPECTIVE, MULTICENTRIC DESCRIPTIVE STUDY

G. Bergez¹, V. Lepilliez², M. Pioche³, T. Wallenhorst⁴, N. Chapelle⁵, J. Jacques⁶, P.H. Deprez⁷, A. Berger⁸, G. Vanbiervliet⁹, S. Leblanc¹⁰, R. Coriat¹¹, F. Prat¹², M. Barret¹³

¹Université de Paris-Cité, Department of Gastroenterology and Digestive Oncology, Cochin Hospital, Assistance Publique - Hôpitaux de Paris, France, Paris, France, ²Hôpital Jean Mermoz, Lyon, France, ³Hospices civils de Lyon, Gastroenterology and endoscopy, Lyon, France, ⁴CHU Pontchaillou, Endoscopy Unit, Rennes, France, ⁵University Hospital of Nantes, Service d'hépatogastroentérologie - Institut des Maladies de l'Appareil Digestif, Nantes, France, ⁶CHU Limoges - Hepato-Gastro-Enterology, CHU Limoges; Limoges/FR, Hepato-Gastro-Enterology, Limoges, France, ⁷Cliniques Universitaire Saint-Luc, Université de Louvain - Dept. de Hepato-gastroentérologie, Clinique, Dept. de Hepato-gastroentérologie, Brussels, Belgium, ⁸Centre hospitalier universitaire de Bordeaux, Department of Gastroenterology and Digestive Oncology, University Hospital of Bordeaux, Bordeaux, France, ⁹CHU, Hôpital L'Archet 2 Gastroentérologie - Gastroenterology, CHU, Hôpital L'Archet 2 Gastroentérologie, Gastroenterology, Nice, France, ¹⁰Hôpital Privé Jean Mermoz, Sainte Foy Les Lyon, France, ¹¹Cochin University Hospital, Gastroenterology Unit, Paris, France, ¹²Assistance Publique Hôpitaux De Paris And Paris-Cité University, Dept. Of Gastroenterology, Clichy, France, ¹³Cochin Hospital, Gastroenterology, Paris, France

Contact E-Mail Address: guillaumeberge@yahoofr

Introduction: The safety of endoscopic submucosal dissection (ESD) in the context of resecting superficial tumors on Barrett's esophagus (BE) has been well assessed. However, there is limited knowledge regarding the oncological follow-up of BE and Barrett's esophagus after a combination of endoscopic resection and radiofrequency ablation.

Aims & Methods: A prospective, multicentric study involving 141 patients, enrolled between December 2016 and January 2019, and followed for three years. These patients underwent ESD for suspicious neoplasia lesions on BE, either alone or in combination with BE ablation.

The primary outcome measure was the R0 resection rate for adenocarcinoma and high-grade dysplasia (HGD). Secondary outcome measures included rates of en bloc resection rate, R0 resection rate for adenocarci-

noma or low-grade dysplasia, adverse event rate, overall and recurrence free survival at one and at three years, and the rate of complete remission of intestinal metaplasia at one year and three years.

Results: The R0 resection rate for carcinoma and HGD was 84,6% (110/130). R0 resection rate for invasive carcinoma was 80,8% (80/99). Seven early complications (< 48 hours) were observed, including 5 cases of bleeding and 2 cases of aspiration pneumonitis. No perforations occurred. Seventeen cases of esophageal strictures were reported. Recurrence was observed in 10 patients at 3 months, including 5 at the resection site, 5 at 12 months, and 3 at 36 months, totaling 18 recurrences over 3 years. 14 patients died during the follow-up, with 3 deaths attributed to esophageal carcinoma. The Complete Response to Intervention Monitoring (CRIM) was 63.7% in patients treated for Barrett's esophagus.

Conclusion: Endoscopic submucosal dissection is a safe and effective technique for treating early neoplastic lesions on BE, especially when combined with residual BE ablation. This study, one of the largest prospective studies on the subject, not only confirms the safety and efficacy of ESD but also provides valuable insights into post-resection tumor follow-up.

Disclosure: Nothing to disclose.

MP319

IS DUAL ENDOSCOPIC SCREENING A VALID STRATEGY TO REDUCE CANCER? PREVALENCE OF PRE-NEOPLASTIC LESIONS ON OPPORTUNISTIC GASTROSCOPY AT TIME OF COLONOSCOPY IN A HIGH-RISK AGE GROUP

C. Deane^{1,2,3}, R. Connaughton¹, O. Kelly^{3,1}, C. O'Morain^{2,4}

¹Connolly Hospital, Gastroenterology, Dublin, Ireland, ²Beacon Hospital Research Institute, Dublin, Ireland, ³Royal College of Surgeons Ireland, Dublin, Ireland, ⁴Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: cdeane4@gmail.com

Introduction: Gastric cancer is the 5th most common cancer globally(1). Europe's Beating Cancer Plan recognises the urgent need for a gastric cancer screening strategy(2). One promising approach, outlined in the Maastricht VI/Florence consensus report, suggests integrating screening modalities for gastric cancer, such as gastroscopy with colorectal cancer screening (3). This method holds the potential for cost-saving benefits through combined screening efforts (4).

Aims & Methods: We aimed to determine the prevalence of preneoplastic and neoplastic lesions in a high-risk age group, in those who underwent gastroscopy at the time of colonoscopy. Our secondary aims were to determine a) the quality of endoscopy performed and b) the endoscopic burden for pathology that required follow-up.

This was a single-centre review and audit of key performance indicators in a colorectal cancer screening centre. The age group targeted was 50-74, i.e. the target group for colon cancer screening in Europe. We included those undergoing colonoscopy for polyp surveillance or as part of the national colon cancer screening programme. Participants with red flag symptoms (iron deficiency anaemia, weight loss, dysphagia), family history of gastric cancer, established diagnosis of Barrett's, intestinal metaplasia, dysplasia or who had a gastroscopy in the last 3 years were excluded. The sample size required for a 95% confidence interval with a presumed positivity rate of 5-7% was 101. Descriptive statistics, correlations and associations were examined using Stata software.

Results: 101 patients were included; the median age was 59;38% were male. Indications for gastroscopy included abdominal pain (45%), chronic reflux (37%), chronic dyspepsia (7%) and other (9%). All patients had

a technically complete gastroscopy (D2 intubation rate 100%, retroflexion 100%), the median procedure length was 7 minutes (range 4–21). 93% of patients had a macroscopic finding at the time of gastroscopy. Findings included gastritis (chronic superficial, chemical) (60%), hiatal hernia (50%), oesophagitis (28%), duodenitis (24%), gastric body polyps (10%), Barrett's mucosa (8%), benign gastric or duodenal ulceration (9%), Schatzki ring (4%), erosions (4%), intestinal metaplasia (IM) (1%), oesophageal candidiasis (1%) and varices (1%). 59% had biopsies taken from two topographical sites as per MAPS guidelines. On biopsy, *Helicobacter pylori* infection was found in 15% (15/101), 7% had intestinal metaplasia (IM); no atrophy, dysplasia or cancer was detected. In those with IM who had MAPS biopsies (5/7), all were focal IM. In those with suspected Barrett's (n=8), 88% had biopsies taken in accordance with the Seattle protocol and the Prague classification was used in 50% of cases. Additional pathology encountered included histological evidence of antral gastritis (56%), body gastritis (53%), reflux oesophagitis (21%), Barrett's without dysplasia (4%), duodenitis (3%), and eosinophilic oesophagitis (1%). There was no statistical difference in age ($p<0.82$) or gender ($p<0.32$) in those with pre-neoplastic changes on gastroscopy.

Conclusion: 11% of individuals within the target age bracket exhibited a pre-neoplastic condition on gastroscopy and/or histology (i.e. gastric intestinal metaplasia, gastric atrophy or Barrett's oesophagus), a further 15% were diagnosed and treated for *Helicobacter pylori* infection, the leading cause of gastric cancer. Among these cases, 4–7% necessitated subsequent surveillance gastroscopy. Our findings support the role of dual endoscopic screening with quality gastroscopy as a potential strategy for gastric cancer screening.

References: 1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021;71(3):209–49. doi: 10.3322/caac.21660. Epub 2021 Feb 4.

2. Commission E. Europe's Beating Cancer Plan - Communication from the commission to the European Parliament and the Council. 2021.

3. Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut.* 2022.

4. Libanio D, Antonelli G, Marijnissen F, Spaander MC, Hassan C, Dinis-Ribeiro M, Areia M. Combined gastric and colorectal cancer endoscopic screening may be cost-effective in Europe with the implementation of artificial intelligence: an economic evaluation. *Eur J Gastroenterol Hepatol.* 2024;36(2):155–61. doi: 10.1097/MEG.0000000000002680. Epub 2023 Nov 15.

Disclosure: Nothing to disclose.

MP320

WITHDRAWN

MP321

PERFORMANCE OF AN ASSISTANT PROGRAM FOR DIAGNOSING THE DEPTH OF EARLY GASTRIC CANCER USING ENDOSCOPIC IMAGES

S. Hirata¹, K. Hamada², Y. Kawahara², S. Kuraoka¹, D. Uchida³, Y. Kono¹, M. Iwamuro¹, S. Kawano¹, M. Otsuka¹

¹Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Department of Gastroenterology and Hepatology, Okayama, Japan, ²Okayama University, Department of Practical Gastrointestinal Endoscopy, Okayama, Japan,

³Okayama University Hospital, Department of Regenerative Medicine, Center for Innovative Clinical Medicine, Okayama, Japan

Contact E-Mail Address: shchr.hirata327@gmail.com

Introduction: The depth of early gastric cancer is an important factor in determining the treatment plan such as endoscopic resection or surgery. We developed an artificial intelligence (AI) program using deep neural networks to diagnose mucosal and submucosal cancers using endoscopic images. Performance evaluation tests were conducted for clinical applications.

Aims & Methods: A validation dataset was established comprising 204 patients with early gastric cancer who underwent endoscopic resection or surgery at our hospital during 2018–2021. The lesion sites were the upper part in 16 (8%), middle part in 106 (52%), and lower part in 82 (40%) patients. The median lesion size (range) was 14 (2–90) mm; the lesion depth was mucosal cancer in 136 (67%) and submucosal cancer in 68 (33%) patients. Five white-light images per case at a minimum were used (median: 8, range: 5–22). The primary endpoint was sensitivity of mucosal cancer, defined as the lower limit of the 95% confidence interval (CI) > 75%, based on previous reports on the depth diagnosis of early gastric cancer. The secondary endpoints were specificity and accuracy.

Results: Sensitivity of this program for the diagnosis of mucosal cancer was 91.2% (95% CI: 85.2%–94.9%), indicating the usefulness of this program. Specificity was 66.2% (95% CI: 54.3%–76.3%), and accuracy was 82.8% (95% CI: 77.1%–87.4%).

Conclusion: The AI program developed for diagnosing the depth of early gastric cancer is useful and expected to be applied clinically in the near future.

Disclosure: Nothing to disclose.

MP322

UTILITY OF A FOLLOW-UP ENDOSCOPY AFTER A DIAGNOSIS OF OESOPHAGEAL ULCER AND PREDICTORS OF MALIGNANCY AND DYSPLASIA

R. Osborne¹, M. Elphick¹, T. Archer¹, C.W. Sin^{1,2}, C. Winters^{1,2}, N. Mohammed^{1,2}, B. Rembacken¹, R. Sood^{1,2}, V. Goodoory^{1,2}

¹Leeds Gastroenterology Institute, St. James's University Hospital, Leeds, United Kingdom, ²Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, United Kingdom

Contact E-Mail Address: miren.elphick1@nhs.net

Introduction: Oesophageal ulceration (OU) is a frequent finding at oesophago-gastro-duodenoscopy (OGD). Despite limited data on the benefit of a repeat endoscopy, current guidelines recommend a follow-up OGD after six weeks to exclude underlying malignancy¹.

Aims & Methods: Aims: We aimed to explore the utility of a follow-up endoscopy after a diagnosis of oesophageal ulcer and identify predictors of oesophageal malignancy and dysplasia. Secondary aims were to estimate the environmental and financial impact of a follow-up endoscopy.

Methods: We collected demographic, endoscopy, and histology data from patients diagnosed with OU over a 5-year period (from 1st January 2016 to

31st December 2020 inclusive) at Leeds Teaching Hospitals NHS Trust. We collected data from the index OGD, follow-up OGD, and from their medical records up to 3 years after a diagnosis of OU at their index OGD. We examined the proportion of patients who were diagnosed with dysplasia or malignancy at follow-up or up to 3 years after their index OGD. Binary logistic regression was performed to identify predictors of oesophageal malignancy or dysplasia at index OGD, follow-up OGD, or 3 years after the index OGD. NHS national cost data for OGD, and carbon dioxide (CO₂) emissions were estimated for all unnecessary follow-up OGDs^{2,3}.

Results: In total, 409 patients were diagnosed with OU. Of these, 33 patients were diagnosed with oesophageal cancer or dysplasia, with 30 diagnoses (90.9%) made at the index OGD and the remaining 3 (9.1%) at either the follow-up OGD or within 3 years of the index OGD. Of those 3 patients, one was diagnosed with oesophageal carcinoma, one with low grade dysplasia, and one with high grade dysplasia, all within a segment of Barrett's oesophagus already diagnosed at the index OGD. Those who were diagnosed with oesophageal malignancy or dysplasia, compared to those who were not, were more likely to have larger ulcers (mean size (SD), mm, 15.9 (17.2) vs 9.50 (11.1), $P = 0.003$), endoscopic features suspicious for malignancy (69.7% vs 8.0%, $P < 0.001$), Barrett's oesophagus (54.5% vs 14.4%, $P < 0.001$), and biopsies taken at index OGD (100% vs 64.1%, $P < 0.001$), and less likely to have a proton pump inhibitor prescribed (57.6% vs 86.4%, $P < 0.001$) after the index OGD. Following logistic regression controlling for all data, those with endoscopic features suspicious for malignancy (OR = 45.9; 95% CI 10.3 to 204) and those with Barrett's oesophagus at index OGD (OR = 5.29; 95% CI 1.56 to 18.0) were more likely to be diagnosed with oesophageal cancer or dysplasia up to 3 years after the index OGD. A total of 376 unnecessary OGDs were undertaken over a 5-year period, the costs of which were estimated at £140,248 and 10.6 tonnes of CO₂ emissions.

Conclusion: Repeat OGD to exclude underlying malignancy following a diagnosis of oesophageal ulcer may only be required in those with endoscopic features suspicious for malignancy and those with Barrett's oesophagus. Larger prospective multi-centre studies, with cost and carbon footprint analyses, are required to confirm our results and to inform guidelines.

References:

1. Beg S. et al. (2017). Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS), *Gut*, 66(11):1886-1899. DOI: 10.1136/gutjnl-2017-314109
2. NHS (2023): National tariff payment system documents, annexes and supporting documents. Available at: <https://www.england.nhs.uk/publication/national-tariff-payment-system-documents-annexes-and-supporting-documents/>
3. Lacroute, J. et al. (2023), The carbon footprint of ambulatory gastrointestinal endoscopy, *Endoscopy*, 55(10): 918–926. DOI: 10.1055/a-2088-4062

Disclosure: Nothing to disclose.

MP323

LONG-TERM OUTCOMES IN ELDERLY PATIENTS WHO UNDERWENT ADDITIONAL THERAPY AFTER ENDOSCOPIC RESECTION FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

A. Dobashi¹, T. Futakuchi¹, M. Ito¹, Y. Hasegawa¹, M. Fukuda¹, N. Tada¹, M. Kobayashi¹, K. Sumiyama¹

¹The Jikei University School of Medicine, Endoscopy, Tokyo, Japan

Contact E-Mail Address: akira.dobashi1980@gmail.com

Introduction: Oesophageal squamous cell carcinoma (OSCC) necessitates additional therapy such as surgical resection or chemoradiotherapy following non-curative endoscopic resections, considered the gold standard treatment. However, in elderly patients, decisions regarding additional therapy tend to be conservative due to concerns about increased invasiveness and its impact on prognosis.

Aims & Methods: The aim of this study was to investigate the long-term outcomes in elderly patients (aged 75 and above) with OSCC diagnosed pathologically as non-curative following endoscopic resections. A retrospective analysis was conducted on OSCC patients treated with endoscopic resection, evaluating pathology findings and prognosis based on medical records. Non-curative resection was defined as pathology revealing SCC invading the muscularis mucosa (MM) or submucosa (SM). Exclusion criteria included patients with other active malignancy, those with less than 12 months of follow-up, and those pathologically classified as having positive vertical margins (VM1) or margins difficult to evaluate (VMX). T1a-MM OSCC with lymphovascular invasion (LVI) or T1b-SM OSCC often requiring additional therapy were considered as index lesions.

Results: Twenty patients were excluded from the study (other active malignancy: n=16, dropout: n=3, VM1/VMX: n=1). A total of 120 cases were analyzed, with 27 elderly patients and 93 non-elderly patients. The proportion of SM lesions was higher in elderly patients compared to non-elderly patients (44.4% vs. 20.4%, $p < 0.05$). Additional therapy was administered exclusively to the index lesions. There was no significant difference in the rate of additional therapy for index lesions between elderly and non-elderly patients (76.2% [16/21] vs. 63.5% [33/52], $p = 0.295$), although non-elderly patients were more likely to undergo surgery (30.8% [16/52] vs. 3.7% [1/27], $p < 0.01$). The median follow-up periods for elderly and non-elderly patients were 72.6 vs. 78.4 months, respectively, with no significant difference ($p = 0.11$). During follow-up, no metastatic recurrences were observed in elderly patients, with 3 deaths unrelated to OSCC. In non-elderly patients, metastatic recurrences were observed in 8 cases. Among patients with T1a-MM without LVI who did not receive additional therapy (41 cases), 3 experienced metastatic recurrence, and 2 deaths were attributed to OSCC. Two cases (10.5% [2/19]) with additional therapy for T1a-MM and 3 cases (21.4% [3/14]) with T1b-SM had recurrence. Among those who experienced recurrence, 60% (3/5) succumbed to OSCC. In non-elderly patients, 16 deaths occurred, with 6 attributed to OSCC. The 5-year overall survival rates for elderly and non-elderly patients were 100% and 86.1%, respectively ($p = 0.81$), with 5-year disease-specific survival rates of 100% and 93.5%, respectively ($p = 0.19$). The 5-year disease-specific survival rates for elderly and non-elderly patients with index lesions followed by additional therapy were 100% and 90.4%, respectively, with no significant differences ($p = 0.213$).

Conclusion: The long-term outcomes of elderly patients who underwent additional therapy after endoscopic resection for OSCC were comparable to those of non-elderly patients.

Disclosure: Nothing to disclose.

MP324

ENDOSCOPIC ULTRASOUND-GUIDED VERSUS SURGICAL GASTROENTEROSTOMY FOR MALIGNANT GASTRIC OUTLET OBSTRUCTION – A RETROSPECTIVE PROPENSITY SCORE-MATCHED ANALYSIS

M. Ellrichmann¹, L.M. Weymar¹, L. Grossmann², T. Veiser², T. Heuer³, C. Gerges⁴, H. Neuhaus², T. Beyna², C.C. Conrad¹

¹University Hospital Schleswig-Holstein, Interdisciplinary Endoscopy, Medical Department 1, Kiel, Germany, ²Evangelisches Krankenhaus Düsseldorf, Department of Gastroenterology, Düsseldorf, Germany, ³St. Bernhard Hospital, Department of Gastroenterology, Kamp-Lintfort, Germany, ⁴University Hospital Essen, Department of Endoscopy, Essen, Germany

Contact E-Mail Address: l.m.grimm@icloud.com

Introduction: Malignant gastric outlet obstruction (GOO) can arise from a spectrum of malignancies, including gastroduodenal, pancreaticobiliary, colorectal, breast, and lung cancers. Typically, GOO heralds a grim prognosis and manifests with symptoms such as nausea, bloating, vomiting, and abdominal pain. Presently, laparoscopic gastroenterostomy (L-GE) stands as the preferred therapeutic modality; however, endoscopic ultrasound-guided gastroenterostomy (EUS-GE) employing lumen apposing metal stents has emerged as a promising minimally invasive alternative. Comparative studies directly assessing the efficacy of EUS-GE versus L-GE remain scarce.

Aims & Methods: We aimed to compare EUS-GE with L-GE for the treatment of GOO using a propensity score-matched analysis.

In a retrospective, multicenter analysis, consecutive patients were enrolled between April 2019 and April 2024 from two academic centers and one primary care facility. To mitigate selection bias, propensity score matching was employed, taking into account factors such as underlying malignancy, tumor stage, and clinical performance status. Clinical success, defined as a reduction of gastric outlet obstruction (GOO) symptom scores by ≥ 1 , served as the primary outcome measure. Secondary endpoints included technical success, time to oral intake, occurrence of adverse events (AEs), length of hospital stay, and 30-day mortality.

Results: A total of 94 patients underwent EUS-GE, while 78 patients underwent L-GE, as per initial screening. Propensity score matching resulted in 72 patients allocated to each group in a 1:1 ratio. The mean age of the study cohort was 68.2 ± 12.3 years, with 59.7% being female. Clinical success rates were 90.2% for EUS-GE and 82.2% for L-GE ($p=0.25$). Technical success rates were 95.2% for EUS-GE and 100% for L-GE ($p=0.06$). The mean duration of hospital stay was significantly shorter for EUS-GE compared to L-GE (10.1 ± 13.4 days vs. 15.5 ± 10.5 days; $p<0.001$). Less AE were observed in the EUS-GE group compared to the L-GE group, both in total (4.8% vs. 22%; $p=0.01$) and in serious AE (1.6% vs. 6.7%; $p=0.3$). The 30-day mortality rate was 11.3% in the EUS-GE group and 17.8% in the L-GE group.

Conclusion: In patients presenting with malignant GOO, EUS-GE showed a tendency towards enhanced clinical success, although not statistically significant, while maintaining comparable technical success rates to L-GE. Notably, clinical recovery post-intervention and hospital stay duration were notably shorter in the EUS-GE cohort, accompanied by a significantly lower incidence of adverse events. Consequently, EUS-GE stands poised to emerge as a preferred therapeutic option for GOO. Nevertheless, further prospective, randomized trials are imperative to validate these retrospective findings.

Disclosure: ME, CG, TB, HN received consultation fees and study support from Boston Scientific, USA. The other authors have nothing to declare.

MP325

THE CAUSES OF POST ENDOSCOPY UPPER GASTROINTESTINAL CANCER IN PATIENTS UNDERGOING DIAGNOSTIC ENDOSCOPY: PILOT RESULTS FROM THE ENGLISH NATIONAL ROOT CAUSE ANALYSIS PROJECT

A. Srinivasa¹, R. Fiadeiro², T. Rahman², S. Goel², T. Gentry², A. Moore³, B. Colley⁴, G. Longcroft-Wheaton⁵, D. Mukherjee⁶, M. McCord⁷, M. Fullard⁸, R. Tighe⁹, A. Dhar¹⁰, C. Healey¹¹, M. Banks¹², N.E Burr¹³, R. Valori¹⁴, N. Trudgill¹

¹Sandwell and West Birmingham NHS Trust, Gastroenterology, West Bromwich, United Kingdom, ²Health Data Insight CIC, Cambridge, United Kingdom, ³Royal Liverpool and Broadgreen University Hospital NHS Trust, Gastroenterology, Liverpool, United Kingdom, ⁴Royal United Hospital, Bath, United Kingdom, ⁵Portsmouth Hospitals NHS trust, Gastroenterology, Hampshire, United Kingdom, ⁶BARKING, HAVERING AND REDBRIDGE UNIVERSITY HOSPITALS NHS TRUST, Romford, United Kingdom, ⁷Heartburn Cancer UK, Basingstoke, United Kingdom, ⁸WEST HERTFORDSHIRE HOSPITALS NHS TRUST, Watford, United Kingdom, ⁹Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom, ¹⁰Darlington Memorial & Bishop Auckland Hospitals, Gastroenterology, Darlington, United Kingdom, ¹¹Airedale Nhs foundation trust, Gastroenterologist, Keighley, United Kingdom, ¹²University College London Hospital NHS Trust (UCLH), Endoscopy Unit, Gastrointestinal services, London, United Kingdom, ¹³Leeds Institute for Biomedical and Clinical Sciences, Gastroenterology, Leeds, United Kingdom, ¹⁴Gloucestershire NHS Foundation Trust - Medicine, Gloucestershire NHS Foundation Trust; Cheltenham/GB, Medicine, Cheltenham, United Kingdom

Contact E-Mail Address: amarsrinivasa@nhs.net

Introduction: Post endoscopy upper gastrointestinal cancers (PEUGIC) can be missed opportunities to diagnose upper GI cancer earlier or even prevent cancer. Up to 71% are potentially avoidable but identifying and investigating PEUGIC is challenging. A process for identifying PEUGIC and performing root cause analysis was piloted and the results are described.

Aims & Methods: The aims of the project were to develop a system to identify all PEUGIC in the English NHS and to allow endoscopy providers to conduct standardised root causes analysis of their PEUGIC via an online platform. This study allows local learning from PEUGIC and quantifies the reasons why PEUGIC occur at a national level.

PEUGIC occurring 3-36 months after a non-diagnostic (index) endoscopy between 2017 and 2023 were identified from the final or provisional registration in National Cancer Registration and Hospital Episode Statistics Datasets held by the National Cancer Registration and Analysis Service. Data for root cause analysis were uploaded onto a secure root cause analysis portal following local hospital review. PEUGIC following surveillance or therapeutic endoscopies were excluded.

Results: 305 PEUGIC were examined by local reviewers in 13 hospitals in England. 40 were excluded, mainly due to errors in provisional cancer data. Data were available for 220 PEUGIC (83%). 136 (62%) PEUGIC followed diagnostic, follow-up or screening endoscopies. PEUGIC sites were oesophagus 63% and stomach 37%.

Table 1 shows the PEUGIC root cause analysis based on the World Endoscopy Organisation categorisation and Kamran Endoscopy 2022. A lesion detected but inadequate assessment or decision making occurred in 15% and a possible missed lesion with inadequate endoscopy or decision making in 17%.

Diagnoses on index endoscopy in oesophageal PEUGIC: pre-malignant lesion 21% (e.g. Barrett's), no abnormal finding 51%, focal lesion 22% and

cancer associated lesion 6% (e.g. ulcer). Findings on index endoscopy in gastric PEUGIC: no abnormal finding 38%, cancer associated lesion 30%, focal lesion 22% and pre-malignant lesion 10% (e.g. gastric atrophy). Gastric PEUGIC tended to present more with advanced cancer (41% stage 4 vs 33% oesophageal PEUGIC). 13% of oesophageal and 12% of gastric PEUGIC were considered potentially avoidable by reviewers. Treatment appeared adversely affected in 45% of oesophageal and 38% of gastric PEUGIC. Reviewer considered that 9% of PEUGIC led to premature death.

PEUGIC categorisation	Number of cases
1. Lesion detected, adequate assessment and decision making but PEUGIC occurred	45 (33%)
2. Lesion detected, inadequate assessment and decision making	20 (15%)
3. Possible missed lesion, endoscopy and decision making adequate	48 (35%)
4. Possible missed lesion, endoscopy or decision making inadequate	23 (17%)

Table 1 Root causes of PEUGIC examined.

Conclusion: Abnormalities in the area of the later cancer were detected in 45% of oesophageal PEUGIC and 52% of gastric PEUGIC. Inadequate lesion assessment, endoscopy and/or decision making was noted in 32% of PEUGIC. Many patients had incurable disease when later diagnosed and treatment appeared adversely affected in 42%.

References: Kamran U, King D, Abbasi A, Coupland B, Umar N, Chapman WC, Hebbbar S, Trudgill NJ. A root cause analysis system to establish the most plausible explanation for post-endoscopy upper gastrointestinal cancer. *Endoscopy*. 2023 Feb;55(2):109-118. doi: 10.1055/a-1917-0192. Epub 2022 Aug 31. PMID: 36044914.

Disclosure: Nothing to disclose.

JAK inhibitors in the treatment of IBD

13:00-14:00 / Poster Stage 1

MP326

CLINICAL OUTCOMES OF JAK INHIBITOR THERAPY FOR PATIENTS HOSPITALISED WITH ACTIVE ULCERATIVE COLITIS (UC) IN A REAL-WORLD MULTI-CENTRE COHORT

C. White¹, M. Samaan¹, K.B. Kok², A. Walsh³, J.K. Limdi⁴, S. Honap⁵, P. Irving¹, E. Davis³, M. Colwill⁵, K.V. Patel⁵, J.H. Yeo⁶, P. Harrow⁶, A. Elford⁷, C.W. Lees⁸, C. Higgins⁹, P. Khan⁹, S. Fong⁹, K. Sethi-Arora⁴, E. Johnston¹⁰, K. Butler¹¹, M.F. Hale¹¹, L. Dean¹², P. Blaker¹², K. Shah², L. Pillay¹³, T. Raine¹³, C. Radia¹⁴, P. Harvey¹⁵, C. Patel¹, X.Y. Choon¹, S. Ray¹

¹Guy's and St Thomas' NHS Foundation Trust, Dept. of Gastroenterology, London, United Kingdom, ²Barts Health, Royal London Hospital, Gastroenterology, London, United Kingdom, ³John Radcliffe Hospital, Oxford, Gastroenterology, Oxford, United Kingdom, ⁴The Northern Care Alliance Hospitals NHS Foundation Trust, Gastroenterology, Bury, Greater Manchester, United Kingdom, ⁵St George's University Hospitals NHS Foundation Trust, Gastroenterology, London, United Kingdom, ⁶University College London Hospitals NHS Foundation Trust, Gastroenterology, London, United Kingdom, ⁷Western General Hospital, NHS Lothian, Gastroenterology, Edinburgh, United Kingdom, ⁸University of Edinburgh, Edinburgh IBD Unit, Edinburgh, United Kingdom, ⁹East Sussex Healthcare NHS Trust, Gastroenterology, Saint Leonards-On-Sea, United Kingdom, ¹⁰West Middlesex University Hospital, Gastroenterology, London, United Kingdom, ¹¹Sheffield Teaching Hospitals NHS Foundation Trust, Gastroenterology, Sheffield, United Kingdom, ¹²Maidstone and Tunbridge Wells NHS Trust, Gastroenterology, Tunbridge Wells, United Kingdom, ¹³Cambridge University Hospital NHS Foundation Trust, Gastroenterology, Cambridge, United Kingdom, ¹⁴King's College Hospital NHS Foundation Trust, Gastroenterology, London, United Kingdom, ¹⁵Royal Wolverhampton NHS Trust, Gastroenterology, Wolverhampton, United Kingdom

Contact E-Mail Address: christopher.white5@nhs.net

Introduction: Janus Kinase (JAK) inhibitors are licensed for the treatment of ulcerative colitis with the benefits of a fast onset of action and a short half-life.[i] This makes them a potential treatment option for patients hospitalised with UC, including those previously treated with, or unsuitable for, infliximab or cyclosporine. There is currently limited published evidence in this setting, drawn from small case series.

Aims & Methods: We performed a retrospective analysis of data collected at 14 sites in the United Kingdom, including both tertiary IBD centres (n=10) and general hospitals (n=4) between January 2019 to January 2024. We included patients who were hospitalised due to active UC and commenced a JAK inhibitor for that indication during the same admission. Baseline data included disease duration and extent, prior exposure to advanced therapies, clinical and endoscopic assessments of disease activity and laboratory parameters. We reviewed treatments administered during the same admission, including corticosteroids and advanced therapies. Coprimary endpoints were colectomy rate at 30 days and 12 months. 12 week, 6 month and 12month persistence data was collected. Adverse outcomes and treatment persistence at the same time points were also recorded.

Results: 80 patients (filgotinib (n=15), tofacitinib (n=25) and Upadacitinib (n=40) were included, with a minimum of 12 weeks follow-up. 43/80 (54%) were male, mean age was 37±14, mean admission albumin 35 and CRP 52. Extent of disease was E1 1/80 (1%), E2 31/80 (39%) and E3 48/80 (60%).

63/80 (79%) of patients had prior anti-TNF exposure (infliximab 47/80 (59%), including 13/80 (16%) of whom had received it as a previous rescue therapy). 31/80 (39%) were on prednisolone at admission. 50/80 (63%) had a baseline endoscopic assessment within 72 hours of admission, of which 34/50 (68%) had severe (Mayo 3) endoscopic activity. During admission, prior to JAK inhibitor administration, treatments given included IV hydrocortisone (93%), methylprednisolone (5%), infliximab (4%) and cyclosporine (1%).

Colectomy rates were 8% and 14% at day 30 and week 12 respectively. In patients for whom 12-month follow-up data were available, 5/34 (15%) had undergone a colectomy at that timepoint.

There was one recorded herpes zoster infection and no recorded thromboses or major adverse cardiovascular events.

JAK Inhibitor	Started during admission (%)	12 week persistence (%)	6 month persistence (%)	12 month persistence (%)
Filgotinib	15/80 (19)	13/15 (87)	9/14 (64)	7/10 (70)
Tofacitinib	25/80 (31)	18/25 (72)	9/25 (36)	8/23 (35)
Upadacitinib	40/80 (50)	32/40 (80)	14/21 (66)	0/1 (0)

Table 1. JAK Inhibitor & Treatment Persistence.

Conclusion: JAK inhibitors appear to offer a valuable treatment option for patients hospitalised with active UC. This appears to be the case even in patients with prior anti-TNF exposure. 86% of patients avoided colectomy at 12 weeks, with a similar proportion colectomy-free at 12-months. The risk of adverse events was small. Our study is, to our knowledge, the largest dataset examining the initiation of JAK inhibitors for those hospitalised with UC.

References: [1] Agrawal M, Kim ES, Colombel J-F. JAK inhibitors safety in ulcerative colitis: practical implications. *Journal of Crohn's and Colitis*. 2020;14(Supplement_2):S755-S60.

Disclosure: Nothing to disclose.

MP327

CLINICAL EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS BY PREVIOUS BIOLOGIC EXPOSURE

R. Panaccione¹, S. Danese², G. Parkes³, I. Blumenstein⁴, D.T. Rubin⁵, K. Takeuchi⁶, R. Vladea⁷, V. Remple⁷, J. Klaff⁷, E. Cheng⁷, S. Suravaram⁷, C.T.J. Holweg⁷, S. Vermeire⁸
¹University of Calgary, Medicine, Calgary, Canada, ²Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ³The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom, ⁴Goethe University Frankfurt, Frankfurt, Germany, ⁵The University of Chicago Medicine, Inflammatory Bowel Disease Center, Chicago, United States of America, ⁶IBD Center, Tsujinaka Hospital Kashiwanoha, Department of Gastroenterology and Hepatology, Kashiwa City, Japan, ⁷AbbVie, R&D, North Chicago, United States of America, ⁸University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: rpanacci@ucalgary.ca

Introduction: Many patients (pts) with moderately to severely active ulcerative colitis (UC) treated with biologics fail to respond or lose response and require alternative therapy.^{1,2} Upadacitinib (UPA), an oral reversible JAK inhibitor approved for treatment of adults with moderately to severely active UC, has shown efficacy in pts with an inadequate response, loss of response or intolerance to ≥ 1 biologic (biologic failure) or anti-TNF agent.³⁻⁵ However, data on the efficacy of UPA by the number and type of prior biologic therapies are limited.

Aims & Methods: This post hoc analysis evaluated clinical, endoscopic and safety outcomes of UPA in pts with UC with biologic failure by the number and type of prior biologics. After 8 weeks' (wks') induction therapy in the Phase 3 U-ACHIEVE or U-ACCOMPLISH trials, pts with clinical response to UPA 45 mg once daily (QD) were randomised to placebo (PBO), UPA 15 mg QD (UPA15) or UPA 30 mg QD (UPA30) for 52 wks in U-ACHIEVE Maintenance. In this study, efficacy was analysed by number (0 prior biologics failed [Non-Bio-IR], 1 or ≥ 2) of prior biologics. Outcomes were assessed after 8 wks' induction (pooled) and 52 wks' maintenance. Results are presented using non-responder imputation incorporating multiple imputation to handle missing data.

Results: Baseline pt (induction [n=988]; maintenance [n=681]) characteristics were similar across treatment arms in each subgroup by number of prior biologics, except pts who failed ≥ 2 prior biologics who had longer disease duration. Clinical and endoscopic outcomes were achieved by more pts who received UPA vs PBO after induction and maintenance, and by more pts who received UPA30 vs UPA15 in the ≥ 2 prior biologics group after maintenance. Furthermore, more pts who received UPA30 vs UPA15 and failed ≥ 2 prior biologics maintained clinical remission from Wk 0 of maintenance to Wk 52 (Table).

Adverse events (AEs) occurred at numerically higher rates for pts receiving UPA who failed ≥ 2 biologics in induction and maintenance studies. During induction, no malignancies or major adverse cardiovascular events (MACE) were reported, and there was 1 venous thromboembolic event (VTE) in the PBO group. During maintenance, across subgroups, rates of AEs of special interest were: malignancies (Non-Bio-IR: UPA15, 1.0 events/100 PY [E/100 PY]; UPA30, 1.8 E/100 PY; 1 prior biologic: PBO, 3.3 E/100 PY; UPA30, 5.5 E/100 PY; ≥ 2 prior biologics: UPA30, 1.8 E/100 PY), MACE (Non-Bio-IR: UPA30, 0.9 E/100 PY; 1 prior biologic: PBO, 3.3 E/100 PY) and VTE (Non-Bio-IR: UPA30, 1.8 E/100 PY), respectively. No AEs leading to death occurred in either study.

Efficacy endpoints n, (%)	Induction (8 weeks)						Maintenance (52 weeks)								
	Non-Bio-IR N=481		1 prior biologic N=203		≥2 prior biologics N=304		Non-Bio-IR N=345		1 prior biologic N=142		≥2 prior biologics N=194				
	UPA 45 mg QD	PBO	UPA 45 mg QD	PBO	UPA 45 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD	
	n=161	n=320	n=65	n=138	n=102	n=202	n=116	n=122	n=49	n=50	n=43	n=67	n=59	n=68	
Clinical remission per Adapted Mayo score ^a	12 (7.5)	116 (36.3)	0 (0)	39 (28.4)	2 (2.3)	42 (20.8)	16 (15.0)	49 (42.0)	65 (53.2)	4 (8.2)	28 (55.1)	23 (53.1)	4 (6.2)	15 (24.7)	39 (55.5)
Clinical response per Adapted Mayo score ^{a,b}	59 (36.6)	259 (80.8)	13 (20.2)	102 (73.9)	14 (13.7)	125 (61.9)	31 (28.5)	79 (68.3)	97 (79.4)	9 (17.3)	38 (76.0)	31 (71.7)	9 (13.7)	26 (44.1)	49 (72.0)
Endoscopic improvement ^c	20 (12.5)	156 (48.9)	2 (3.3)	53 (38.6)	3 (3.3)	56 (27.8)	23 (21.3)	61 (52.8)	82 (67.0)	4 (8.6)	29 (57.1)	25 (57.3)	4 (6.5)	19 (32.6)	41 (60.4)
Endoscopic remission ^c	4 (2.5)	69 (21.5)	0 (0)	13 (9.4)	1 (1.1)	24 (11.9)	10 (9.7)	33 (28.7)	38 (31.4)	<0.1 (<0.1)	12 (24.3)	10 (22.8)	3 (4.7)	10 (17.7)	18 (26.8)
HEMI ^d	15 (9.4)	130 (40.6)	2 (3.2)	44 (32.0)	3 (3.0)	47 (23.3)	20 (18.7)	50 (43.0)	70 (57.2)	3 (6.5)	26 (51.1)	22 (50.9)	4 (6.2)	16 (26.7)	39 (57.1)
Maintenance of clinical remission ^{b,e}	—	—	—	—	—	—	13 (26.5)	21 (48.2)	33 (61.5)	2 (10.0)	13 (76.5)	10 (75.6)	1 (6.3)	7 (43.8)	15 (21.5)
Steroid-free remission ^{d,f}	—	—	—	—	—	—	13 (26.5)	21 (48.2)	32 (59.6)	2 (10.0)	12 (70.6)	10 (75.6)	1 (6.3)	7 (43.8)	15 (21.5)

^aAdapted Mayo score ≤ 2 , with stool frequency subscore ≤ 1 and not greater than baseline. RBS=0 and ES ≤ 1 without friability.

^bThe overall clinical response rate at Week 8 or Week 16 of UPA 45 mg QD induction therapy was 81.8%.

^cA decrease in Adapted Mayo score ≥ 2 points and $\geq 30\%$ from baseline, and a decrease in RBS ≥ 1 point or an absolute RBS of ≤ 1 .

^dES ≤ 1 without friability.

ES=0.

ES ≤ 1 without friability and Geboes Score ≤ 3.1 .

^eFor Non-Bio-IR, n=49, 43 and 53 for PBO, UPA 15 mg QD and UPA 30 mg QD, respectively. For 1 prior biologic: n=20, 17 and 13 for PBO, UPA 15 mg QD and UPA 30 mg QD, respectively. For ≥ 2 prior biologics: n=16, 16 and 21 for PBO, UPA 15 mg QD and UPA 30 mg QD, respectively.

^fClinical Remission per Adapted Mayo score at Week 52 among patients who achieved clinical remission at the end of induction therapy.

^gClinical remission per Adapted Mayo score at Week 52 and corticosteroid free for ≥ 90 days before Week 52 among patients who achieved clinical remission at the end of induction therapy.

ES, endoscopic subscore; HEMI, histologic endoscopic mucosal improvement; Non-Bio-IR, 0 prior biologics failed; PBO, placebo; QD, once daily; RBS, rectal bleeding subscore; UPA, upadacitinib.

Table. Efficacy after 8 weeks' induction and 52 weeks' maintenance therapy.

Conclusion: Clinical and endoscopic improvements were seen with UPA vs PBO in induction and maintenance therapy in pts with moderately to severely active UC, regardless of the number of prior biologics failed.

During maintenance, numerically greater treatment benefits were seen with UPA30 vs UPA15 in the ≥ 2 prior biologics group. AEs occurred at numerically higher rates in pts who failed more biologics.

References: 1. Koo HM, et al. *Ther Adv Gastroenterol* 2023;16:17562848231201728

2. Ma C, et al. *J Clin Gastroenterol* 2015;49:675–82

3. Danese S, et al. *Lancet* 2022;399:2113–28

4. Sandborn WJ, et al. *Gastroenterology* 2020;158:2139–49

5. Vermeire S, et al. Presentation at ECCO 2023, March 1–4, Copenhagen, Denmark (OP04)

Disclosure: RP has received consulting fees, speaker fees and research support from Abbott, AbbVie, Abivax, Alimentiv, Allergan, Amgen, AnaptyBio, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Cosmos Pharmaceuticals, Eisai, Élan, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Landos, LyfemD, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Sanofi, Satisfai Health, Spyre, Sublimity Therapeutics, Takeda, Theravance, Union Therapeutics and Ventyx.

SD has received consultancy fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Gilead, Hospira, Janssen, Johnson & Johnson, MSD, Mundipharma, Pfizer, Roche, Sandoz, Takeda, TiGenix, UCB and Vifor Pharma.

GP has received personal payments/honoraria/speaker fees and/or accepted travel grants or fellowships from AbbVie, Allergan, Bristol Myers Squibb, Celltrion, Ferring, Galapagos, Janssen, Napp, Takeda and Tillotts; and is a director and shareholder in Ampersand Health.

IB has received consulting fees from AbbVie, Amgen, Arena, Biogen, Bristol Myers Squibb, Celltrion, Ferring, Galapagos, Janssen, Pfizer, Shire and Takeda; and speaker fees from AbbVie, Amgen, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Ferring, Galapagos, Janssen, Mylan, Pfizer, Shire and Takeda.

DTR has received grant support from Takeda; and has served as a consultant for AbbVie, Altrubio, Arena, Bristol Myers Squibb, Genentech/Roche, Gilead, Iterative Scopes, Janssen, Lilly, Pfizer, Prometheus Biosciences, Takeda and Techlab Inc.

KT has received consulting fees from Thermo Fisher Diagnostics K.K.; research grants from AbbVie and Takeda; and has served as a speaker for AbbVie, Celltrion, EA Pharma, Janssen, Kyorin, Mochida, Takeda, Tanabe Mitsubishi and Zeria.

RV, VR, JK, EC, SS and CH are full-time employees of AbbVie and may hold AbbVie stock and/or stock options.

SV has received grant support from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; and consulting and/or speaking fees from AbbVie, Abivax, Alimentiv (formerly Robarts Clinical Trials), Arena, Avaxia, Boehringer Ingelheim, Celgene, Dr. Falk Pharma, Ferring, Galapagos, Genentech/Roche, Gilead, Hospira, Janssen, MSD, Mundipharma, Pfizer, Prodigest, Progenity, Prometheus Biosciences, Second Genome, Shire, Takeda, Theravance and Tillotts.

Acknowledgments/Funding: AbbVie and the authors thank all of the trial investigators and patients who participated in these clinical trials. AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, review and approval of this publication. All authors had access to relevant data and participated in the drafting, review and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by Carl Davies, MSc, of 2 the Nth (Cheshire, UK) and was funded by AbbVie.

MP328

REAL-WORLD EFFECTIVENESS AND SAFETY OF UPADACITINIB FOR THE TREATMENT OF MODERATE TO SEVERE CROHN'S DISEASE IN A BELGIAN MULTI-CENTRIC REFRACTORY COHORT

A. Pavlidis¹, B. Verstockt², T. Lobaton Ortega³, S. Vieujeun⁴, F. Baert⁵, O. Dewit⁶, J.F. Rahier⁷, R. Ouziel⁸, A. Hoyois⁹, T. Holvoet¹⁰, F. Couturier¹¹, B. Willandt¹², P. Bossuyt¹³, M. Somers¹⁴, M. Salame¹⁵, A. Verreth¹⁶, D. Franchimont¹, A. Cremer¹

¹Erasme University Hospital, Department of Gastroenterology, Brussels, Belgium, ²University Hospitals Leuven, Department of Gastroenterology, Leuven, Belgium, ³University Hospital Ghent, Department of Gastroenterology, Ghent, Belgium, ⁴University Hospital CHU of Liège, Department of Gastroenterology, Liège, Belgium, ⁵AZ Delta, Department of Gastroenterology, Roeselare, Belgium, ⁶Cliniques Universitaires Saint-Luc, Department of Gastroenterology, Brussels, Belgium, ⁷CHU UCL Namur site Mont-Godinne, Department of Gastroenterology, Yvoir, Belgium, ⁸CHU Marie Curie, Department of Gastroenterology, Charleroi, Belgium, ⁹CHU Saint-Pierre, Department of Gastroenterology, Brussels, Belgium, ¹⁰VITAZ Hospital, Department of Gastroenterology, Sint-Niklaas, Belgium, ¹¹GZA Hospital, Department of Gastroenterology, Antwerp, Belgium, ¹²AZ St. Jan Brugge, Department of Gastroenterology, Brugge, Belgium, ¹³Imelda General Hospital, Dr. Bonheiden, Belgium, ¹⁴University Hospital Antwerp, Department of Gastroenterology, Antwerp, Belgium, ¹⁵Centre Hospitalier Régional Haute Senne, Soignies, Belgium, ¹⁶AZ Voorkempen, Department of Gastroenterology, Malle, Belgium

Contact E-Mail Address: anaspavl@gmail.com

Introduction: In the recent years, the therapeutic options for inflammatory bowel disease (IBD) have expanded. Multiple Janus kinase (JAK) inhibitors have been licensed: First Tofacitinib (TOFA) for Ulcerative Colitis (UC), followed, most recently, by Filgotinib (FIL) in UC and Upadacitinib (UPA) in UC and Crohn's Disease (CD).

Aims & Methods: The aim of the study was to explore the real-world effectiveness and safety of UPA in a multicenter Belgium refractory cohort of patients with moderate-to-severe CD.

This is an observational, national, retrospective multicenter study including all patients with active CD initiating UPA between September 2022 and January 2024 from 16 Belgian centers. Clinical remission and response were defined using the two-component patient reported outcome. Endoscopic response was defined as a decrease in baseline Simple Endoscopic Score (SES-CD) with $\geq 50\%$. Endoscopic remission was defined as SES-CD ≤ 4 or disappearance of baseline ulcers. Effectiveness endpoints were evaluated at week 12, 24 and 52, while CD-related hospitalization, surgery and safety were assessed throughout follow-up.

Results: Of the 66 patients who started UPA, 52 patients were analysed (6 excluded for ostomy and 8 for not having yet reached 24 weeks of follow-up) with a median follow-up of 21 weeks (IQR: 4-24). Patients were predominately female (54%), median age at baseline was 37 years old (IQR: 19-62) and median disease duration was 13 years (IQR: 0-29). 12% of the patients had ileal CD, 12% colonic CD, 76% ileocolonic CD with 17% concomitant upper gastrointestinal CD and 42% concomitant perianal disease. The majority of the patients (87%) was exposed to ≥ 3 biologics and 54% had previously undergone a CD-related surgery.

At week 24, 58% and 44% of overall eligible patients achieved steroid-free clinical response and remission, respectively. Endoscopic data were available in 17 out of the 52 patients of whom 65% and 47% reached endoscopic response and remission respectively within the first 24 weeks. Sixteen out of eighteen patients that used concomitant steroids at baseline were able to stop it by week 24.

Overall, 21 patients (40%) discontinued their treatment during follow-up with a median exposure duration of 16 weeks (IQR: 4-24): 11 due to primary non response, 3 due to secondary loss of response, 7 due to adverse event (AE). Among these 21 patients, 4 patients underwent CD-related surgery (2 intestinal resections and 2 diverting ostomies) after a median duration of 15 weeks (IQR: 11-24), while the others switched to another medical therapy. In total, 21% (11/52) patients required hospitalization within 24 weeks.

Twenty-seven AEs were reported in 19 (37%) patients, with 7 leading to treatment discontinuation (2 allergic skin rash, 1 severe acne, 1 folliculitis, 1 lip oedema, 1 severe stomatitis and 1 loss of appetite). The most common reported AEs were herpes simplex reactivation, respiratory tract infection, cutaneous reactions and acne. No herpes zoster infection, thrombotic or cardiovascular event were reported.

Conclusion: In this real-world cohort of highly refractory CD patients, UPA effectively induced steroid-free clinical remission and endoscopic remission by week 24 and was relatively well tolerated with respect to adverse events.

Disclosure: Dr Anneline Cremer has received lecture and advisory board fees from Galapagos, Abbvie, Janssen (2009-2014); lecture fees from Celltrion (2019-2024), Pfizer (2018-2023); advisory board fees from Takeda (2018-2023).

Dr Denis Franchimont has received lecture and/or advisory board fees from Abbvie, AstraZeneca, Dr. Falk Pharma, Ferring, Janssen, Mundipharma, MSD, Pfizer, Takeda, Amgen and research grants from Abbvie, Janssen, Takeda, Celltrion and Amgen (2019-2024).

Dr Sophie Vieujean received speaker's fees from Abbvie, Celtrion, Ferring, Janssen and Takeda.

Dr Jean-Francois Rahier has received lecture fees from Pfizer, AbbVie, Bristol Myers Squibb, Celltrion, Galapagos, Janssen and Takeda, and advisory board fees from Pfizer, AbbVie, Celltrion, Amgen, Glaxo Smith Kline, Galapagos, Janssen.

MP329

REAL-WORLD INDUCTION PERIOD DATA IN ULCERATIVE COLITIS PATIENTS INITIATING FILGOTINIB THERAPY: FINDINGS FROM THE PROSPECTIVE FILGOCOLITIS STUDY ON CLINICAL EFFECTIVENESS AND NOVEL WEARABLE-DERIVED OUTCOMES

B. Bokemeyer^{1,2}, S. Plachta-Danielzik³, T. Hellms⁴, W. Landry⁵, M. Kahl⁶, R. Ehehalt⁷, L. Zimmermann⁸, A. Schiffelholz⁹, P. Efken¹⁰, J. Reiner¹¹, L. Grasskemper³, K. Schmidt³, E. Gilman³, T. Wenske³, S. Schreiber¹²

¹Interdisciplinary Crohn Colitis Center, Gastroenterology, Minden, Germany, ²University Hospital Schleswig-Holstein, Campus Kiel, Clinic of General Internal Medicine I, Kiel, Germany, ³Competence Network IBD, Kiel, Germany, ⁴University Hospital Hannover, Department of Gastroenterology, Hepatology and Transplant Medicine, Hannover, Germany, ⁵MVZ Dachau, Dachau, Germany, ⁶Gastroenterology Practice, Hamburg, Germany, ⁷Praxis für Gastroenterologie Prof. Dr. R. Ehehalt, Heidelberg, Germany, ⁸Gastroenterology Practice, Magdeburg, Germany, ⁹Gastroenterology Practice, Augsburg, Germany, ¹⁰Gastroenterology Practice, Minden, Germany, ¹¹University Hospital Rostock, Gastroenterology, Rostock, Germany, ¹²University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany

Contact E-Mail Address: bernd.bokemeyer@t-online.de

Introduction: In this induction period analysis of the FilgoColitis study, we report on clinical effectiveness and psychosocial outcomes in ulcer-

ative colitis (UC) patients newly initiated on filgotinib (FIL) therapy in a real-world setting. In addition, this study attempts to define novel patient-based outcomes monitored by wearable devices.

Aims & Methods: FilgoColitis is a prospective, multi-centre, non-interventional, 24-month observational study in patients with active UC newly initiated on FIL therapy. The study evaluates patients with active UC receiving FIL in terms of disease activity (pMayo score), quality of life (QoL), and - in a subset - physical activity using two different wearable devices (Garmin® smartwatch and SensMotion® accelerometer). pMayo-defined clinical remission was related to physical activity (steps), mean heart rate, and stress levels in UC patients with complete wearable data available for the four days immediately following both baseline and week 10 (n=32). Data were considered complete if more than 50% of daily data were recorded from 6 am to 10 pm on at least 3 out of 4 days.

Results: The study enrolled 202 patients with UC who were newly treated with FIL. Six patients were excluded due to incomplete baseline data. Out of the participants with complete baseline data (n=196), 106 (54.1%) used at least one wearable device during the study. To validate the smartwatch, all steps measured in parallel by both the smartwatch and the conventional accelerometer system were compared halfway through the recruitment period and showed good agreement with a positive correlation of 0.88 (p<0.001). 168 patients with complete baseline and week 10 data were available for the induction period (week 10) analysis. Of these, 61.3% were male, and the median time since diagnosis was 8.0 years. Prior to treatment with FIL, 85.1% of patients had received biologic or small molecule therapies, and 54.8% had used immunosuppressants. After 10 weeks of induction therapy with FIL, a clinical response rate of 50.9% and a clinical remission rate of 29.2% were observed (Tab. 1). Clinical remission was 36.0% in biologic-naïve (n=25) and 28.0% in biologic-experienced patients (n=143) (p=0.564). The median baseline score on the EQ-VAS was 60, which increased to 75 by week 10, reflecting a significant improvement in QoL (p<0.001). There was no association between general biometric stress readings or step counts and clinical remission at week 10. However, heart rate at week 10 was significantly associated with clinical remission status, with a mean heart rate of 71.5 beats per minute (bpm) observed in patients in remission and 85.4 bpm in those not in remission (p=0.005). Sensitivity analysis identified a threshold of 80 bpm as optimal for discriminating clinical remission status, yielding a specificity of 0.778 and a sensitivity of 0.857.

Conclusion: In this real-world study, filgotinib demonstrated a response rate of 51% and a clinical remission rate of 29% in active UC at week 10. Using wearable device data, heart rate was identified as a suitable discriminator for categorising remission status. Subsequent analyses over the maintenance period will evaluate the utility of heart rate and additional wearable parameters in assessing clinical remission.

Outcome at week 10	all	bio-naïve	bio-experienced	p
n	168	25	143	
Clinical response modified, n (%)	84 (50.9)	14 (58.3)	70 (49.6)	0.571
Clinical remission, n (%)	49 (29.2)	9 (36.0)	40 (28.0)	0.564
Steroid-free remission, n (%)	43 (25.6)	8 (32.0)	35 (24.5)	0.584

Table 1. Remission and response to filgotinib therapy in UC patients at week 10.

References: 1. Plachta-Danielzik S, Grasskemper L, Schmidt K, Schreiber S, Bokemeyer B; Health Status, Quality of Life, Psychosocial Well-being, and Wearables Data of Patients With Active Ulcerative Colitis Receiving Filgotinib Therapy (FilgoColitis Study): Protocol for a Real-world Observational Study; JMIR Res Protoc 2023;12:e42574

Disclosure: Conflicts of Interest

BB has received consulting fees from AbbVie, MSD, Shire, Ferring, Hospira, Takeda, Movetis, Shield Therapeutics, Pfizer, Biogen, Janssen, Hexal, and

Celgene; received financial support for lectures and teaching from AbbVie, Ferring, MSD, Merckle, Falk, HLR, Shield Therapeutics, Pfizer, Celltrion, Takeda, Janssen, and Mundipharma; and received grant and financial support for research from AbbVie and Ferring. SS has received personal fees from AbbVie, Arena, BMS, Biogen, Celltrion, Celgene, IMAB, Gilead, MSD, Mylan, Pfizer, Fresenius, Janssen, Takeda, Theravance, Provention-Bio, Protagonist, and Falk.

MP330

EARLY REAL-WORLD OUTCOMES WITH FILGOTINIB IN PATIENTS WITH ULCERATIVE COLITIS: A PROSPECTIVE, OBSERVATIONAL STUDY (GALOCEAN)

M. Lowenberg¹, J.P. Seenan², M.L. Høivik^{3,4}, C. Gilletta De Saint Joseph⁵, W. Reinisch⁶, A. Armuzzi^{7,8}, S. Schreiber⁹, E. Ricart^{10,11}, G.A. Doherty¹², R. Saldana¹³, W. Sawyer¹⁴, A. Jus¹⁴, M. Zignani¹⁴, S. Vermeire¹⁵

¹University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam UMC, Amsterdam, Netherlands, ²Queen Elizabeth University Hospital, Department of Gastroenterology, Glasgow, United Kingdom, ³Oslo University Hospital, Department of Gastroenterology, Oslo, Norway, ⁴University of Oslo, Institute of Clinical Medicine, Oslo, Norway, ⁵Toulouse University Hospital, Gastroenterology and Pancreatology Department, Toulouse, France, ⁶Medical University of Vienna, Division of Gastroenterology and Hepatology, Vienna, Austria, ⁷IRCCS Humanitas Research Hospital, Inflammatory Bowel Disease Center, Rozzano, Milan, Italy, ⁸Humanitas University, Department of Biomedical Sciences, Milan, Italy, ⁹University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel University, Kiel, Germany, ¹⁰Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Gastroenterology Department, Hospital Clínic, Barcelona, Spain, ¹¹Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain, ¹²University College Dublin, Centre for Colorectal Disease, St. Vincent's University Hospital and School of Medicine, Dublin, Ireland, ¹³European Federation of Crohn's and Colitis Associations, Brussels, Belgium, ¹⁴Galapagos NV, Mechelen, Belgium, ¹⁵University Hospital Leuven, Department of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: m.lowenberg@amsterdamumc.nl

Introduction: Filgotinib (FIL) is an oral, JAK1 preferential inhibitor approved for the treatment of ulcerative colitis (UC). Although the clinical efficacy of FIL in UC has been demonstrated in the SELECTION trial,¹ real-world data are limited.

Aims & Methods: In total, 600 adult patients with moderately to severely active UC who initiate FIL treatment in routine clinical care will be enrolled in GALOCEAN (NCT05817942), an ongoing, European, multi-site, prospective, observational study. Here, we report baseline characteristics of the first 100 enrolled patients and effectiveness data from patients who reached week 10. Baseline demographics, disease characteristics, prior UC-related treatment and reasons for starting FIL were collected. At week 10, mean changes from baseline (CFBs) in the partial Mayo Clinic Score (pMCS) and the PRO-2 score, and the proportions of patients in pMCS remission (pMCS of ≤ 2) or PRO-2 remission (rectal bleeding subscore of 0 and stool frequency subscore of ≤ 1) were assessed. Mean CFBs at week 10 in patient-reported outcomes (Short Inflammatory Bowel Disease Questionnaire [SIBDQ], Urgency Numerical Rating Scale [NRS] and Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-Fatigue] scores) were also calculated. Safety was evaluated by documenting adverse events.

Results: As of January 2024, 100 patients (FIL 200 mg, 97% [97/100]; FIL 100 mg, 3% [3/100]) were enrolled, and had baseline data available; out of which 55 reached week 10. Baseline characteristics are shown in the **Table**. In total, 70% of patients (67/96) had up to moderate disease activity (pMCS of ≤ 6) and 30% (29/96) had severe disease activity (pMCS of ≥ 7) at baseline; 42% (42/100) were biologic-naïve. The most common cardiovascular risk factor was active or prior smoking (37% [37/100]). FIL was used as monotherapy in 47% of patients (47/100). At week 10, the mean (standard deviation [SD]) CFB in the pMCS was -2.7 (2.5; n=43), and 58% of patients (25/43) achieved pMCS remission. The mean (SD) CFB in the PRO-2 score at week 10 was -1.8 (1.7; n=46), and 72% of patients (33/46) achieved PRO-2 remission. Mean (SD) CFBs in patient-reported outcomes at week 10 were 10.1 (12.4; n=42) for the SIBDQ score, -1.3 (2.8; n=38) for the Urgency NRS score and 4.0 (9.3; n=42) for the FACIT-Fatigue score. Overall, 10 patients discontinued FIL because of adverse events, lack of effectiveness or physician decision. No new safety signals were identified. **Conclusion:** In this first interim report of GALOCEAN, week 10 data show that FIL improves symptoms in patients with UC in real-world clinical practice and has beneficial effects on health-related quality of life and fatigue. GALOCEAN is ongoing and long-term data with higher patient numbers will be evaluated to further characterize the real-world effectiveness of FIL in UC.

Characteristic	Total ^a (N=100)
Age, years, median (min-max)	37.0 (19-67)
Female, n (%)	52 (52)
UC duration, years, median (min-max)	5.9 (0-26)
UC type, n (%)	
Proctitis	13 (13)
Left-sided colitis	49 (49)
Pancolitis	34 (34)
Unknown	3 (3)
Disease activity and patient-reported outcomes, mean (SD)	
pMCS	5.3 (2.0)
PRO-2 score	3.3 (1.6)
SIBDQ score	38.0 (11.5)
Urgency NRS score	4.5 (2.6)
FACIT-Fatigue score	28.6 (11.7)
CRP, mg/L, median (min-max)	3.3 (0-50)
Prior biologic therapy, n (%)	58 (58)
Number of prior biologic therapies, n (%) ^b	
0	42 (42)
1	23 (23)
2	23 (23)
3	7 (7)
≥ 4	5 (5)

^aThe number of patients with missing data was n=1 for UC duration and UC type, n=4 for pMCS and PRO-2 score, n=11 for SIBDQ score, n=16 for urgency NRS score, n=11 for FACIT-Fatigue score and n=43 for CRP.

^bMultiple uses of the same therapy were counted once.

CRP, C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; pMCS, partial Mayo Clinic Score; NRS, Numerical Rating Scale; PRO-2, patient-reported outcome-2; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; UC, ulcerative colitis.

Table. Baseline characteristics.

References:

1. Feagan BG et al. *Lancet* 2021;397:2372-84.

Disclosure: The GALOCEAN study was sponsored by Galapagos NV (Mechelen, Belgium), who funded these analyses.

Medical writing support for the development of this abstract was provided by Risha Bulusu, MBiochem, of PharmaGenesis London, London, UK, and was funded by Alfasigma S.p.A.

WS, AM, MZ are employees of Alfasigma S.p.A at the time of abstract submission.

AA reports consulting and/or advisory board fees from AbbVie, Allergan,

Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, Lionhealth, MSD, Mylan, Nestlé, Pfizer, Roche, Samsung Bioepis, Sandoz and Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, Mitsubishi Tanabe Pharma Corporation, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda and Teva Pharmaceuticals; and research grants from Biogen, MSD, Pfizer and Takeda.

CGdSJ reports speaker and/or consultancy fees from AbbVie, Alfasigma, Amgen, Celltrion, Janssen, Galapagos, MSD, Pfizer and Takeda.

ER reports speaker fees from AbbVie, Faes Farma, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, Kern Pharma, MSD, Pfizer and Takeda; and consulting fees from AbbVie, Eli Lilly, Fresenius Kabi, Galapagos, Janssen Pharmaceuticals, MSD and Pfizer.

GD reports research/educational grants from Abbott, AbbVie, Celltrion, Genuity, Janssen Pharmaceuticals, MSD, Pfizer, Takeda and Tillotts Pharma; and speaker/personal fees from AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Dr Falk Pharma, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, MSD, Pfizer, Takeda/Shire and Tillotts Pharma.

JPS reports speaker fees from AbbVie, Fresenius Kabi, Galapagos, Janssen-Cilag, Pharmacosmos, Takeda and Tillotts Pharma; and advisory board fees from AbbVie, Bristol Myers Squibb, Dr Falk Pharma and Galapagos.

ML reports consultancy/lecture fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Galapagos, Janssen-Cilag, Johnson & Johnson, Medtronic, Pfizer, Takeda, and Tillotts, grants from

Galapagos and NFU and central reading services for Alimentiv.

MLH reports research grants from Ferring, Janssen, Pfizer, Tillotts, and Takeda, speaker fees from AbbVie, Ferring, Galapagos, Meda, MSD, Tillotts and Takeda; and advisory board fees from AbbVie, Eli Lilly, Galapagos, Janssen, MSD, Pfizer and Takeda.

RS reports no financial disclosures or conflicts of interest.

SV reports financial support for research from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; speaker and/or consultancy fees from AbbVie, Abivax, AbolterS Pharma, AgomAb Therapeutics, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Bior Therapeutics (formerly Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cytokine Pharma, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Genentech-Roche, Gilead Sciences, GSK, Hospira, IMiDomics, Janssen Pharmaceuticals, Johnson & Johnson, Materia Prima, Mestag Therapeutics, MiroBio, Morphee Therapeutic, MRM Health, MSD, Mundipharma, Pfizer, ProDigest, Prometheus Biosciences, Roberts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma AG, VectivBio, Ventyx Biosciences and Zealand Pharma.

SS reports personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos/Gilead Sciences, Hikma Pharmaceuticals, I-Mab, Janssen Pharmaceuticals, Morphee Therapeutic, MSD, Mylan, Pfizer, Protagonist Therapeutics, Provention Bio, Sandoz/Hexal, Takeda, Theravance Biopharma and Ventyx Biosciences.

WR reports speaker fees from AbbVie, Celltrion, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, MEDICE, MSD, Pfizer, Roche, Sobi and Takeda; consulting fees from AbbVie, Amgen, AOP Health (formerly AOP Orphan), Boehringer Ingelheim, Bristol Myers Squibb, Calyx, Celltrion, Eli Lilly, Galapagos, Gilead Sciences, InDex Pharmaceuticals, Janssen Pharmaceuticals, MedAhead, Microbiotica, Pfizer and Takeda; advisory board fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Galapagos, Janssen Pharmaceuticals and Pfizer; and research funding from AbbVie, Janssen Pharmaceuticals, Sandoz, Sanofi and Takeda.

AJ and WS were employees of Galapagos NV (former study sponsor), and are now employees of Alfasigma S.p.A (current study sponsor).

MZ was an employee and shareholder of Galapagos NV (former study sponsor), and is now an employee of Alfasigma S.p.A (current study sponsor).

MP331

TOFACITINIB VERSUS VEDOLIZUMAB IN ULCERATIVE COLITIS WITH PRIOR ANTI-TNF FAILURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

N.J. Milioli¹, V. Antunes², O. Martins³, T. Correa⁴, A.A. Prata⁵, A.C. Coan⁵, A.M. Reis⁶, E. Bulhões⁷, P. Romeiro⁸, M.V. Fernandes²
¹Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ²Federal University of Health Science of Porto Alegre, Porto Alegre, Brazil, ³Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁴Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁵Federal University of Espirito Santo, Vitória, Brazil, ⁶State University of Campinas, Campinas, Brazil, ⁷College of Higher Education of the United Amazon, Redenção, Brazil, ⁸Department of Medicine, University Center of Maceió, Maceió, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction:

Anti-TNF agents play a significant role in the induction and maintenance therapy of moderate to severe ulcerative colitis. However, at least 30% of patients experience loss of response within the first year of treatment.

Aims & Methods: This study aims to compare Tofacitinib versus Vedolizumab in patients with ulcerative colitis in the setting of previous anti-TNF failure. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for randomized and non-randomized studies comparing Tofacitinib versus Vedolizumab in this population. The primary outcome was colectomy rate. The secondary outcomes were thromboembolic event rate and infectious incidence. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I² statistics.

Results: The meta-analyses included 6 studies and 2,241 patients. There was a significant difference favoring Vedolizumab in colectomy rate (OR 2.03; 95% CI 1.30 to 3.16, p=0.002; I²=0%). There were no difference in thromboembolic event rate (OR 0.90; 95% CI 0.39 to 2.06; p=0.798; I²=0%) and infection incidence (OR 0.83; 95% CI 0.56 to 1.25; p=0.378; I²=0%).

Conclusion: In patients with ulcerative colitis with prior anti-TNF failure, tofacitinib showed higher colectomy rate compared to vedolizumab, with no difference in thromboembolic and infectious events between both groups. Considering this, vedolizumab seems to be a reasonable option in this population.

References: 1. Straatmijer T, Biemans V, Visschedijk MC, Hoentjen F, De Vries A, Van Bodegraven AA, et al. SUPERIOR EFFECTIVENESS OF TOFACITINIB COMPARED TO VEDOLIZUMAB IN ANTI-TNF EXPERIENCED ULCERATIVE COLITIS PATIENTS: A NATIONWIDE DUTCH REGISTRY STUDY. *United Eur Gastroenterol J.* 2022;10((Straatmijer T., t.straatmijer@amsterdamumc.nl; De Boer K.H.N.) Amsterdam UMC, Amsterdam, Netherlands):390–1.

2. Buisson A, Serrero M, Altwegg R, Guilmoteau T, Bouguen G, Nachury M, et al. Real-world comparison of effectiveness between tofacitinib and ustekinumab in patients with ulcerative colitis exposed to at least one anti-TNF agent: Results from the TORUS study. *J Crohns Colitis.* 2023;17((Buisson A.; Guilmoteau T.) CHU Clermont-Ferrand, IBD Unit, Clermont-Ferrand, France):i707.

3. Adimadhyam S, Lewis JD, Simon AL, Wolfe AE, Smith S, Hou L, et al. Real-world Evidence Comparing Tofacitinib and Vedolizumab in Anti-TNF-experienced Patients With Ulcerative Colitis. *Inflamm Bowel Dis.* 2024 Apr 3;30(4):554–62.

4. Hyun HK, Zhang HS, Yu J, Kang EA, Park J, Park SJ, et al. Comparative effectiveness of second-line biological therapies for ulcerative colitis and Crohn's disease in patients with prior failure of anti-tumour necrosis factor treatment. *BMC Gastroenterol.* 2022 Mar 27;22(1):143.

Disclosure: Nothing to disclose.

MP332

FIRST MECHANISTIC STUDY TO COMPARE THE EFFECTS OF JAK INHIBITOR AND ANTI-TNF THERAPY ON MICROVASCULAR FUNCTION. DOES THE MECHANISM OF THE DRUG PLAY A ROLE?

A. Kleynerman¹, E. Birch^{2,3}, S. N. Hader^{2,3}, Y. Nishijima^{2,3}, A. M. Beyer^{2,3,4}, P. Sinh⁵

¹Medical College of Wisconsin, Milwaukee, United States of America, ²Medical College of Wisconsin, Department of Medicine, Milwaukee, United States of America, ³Medical College of Wisconsin, Cardiovascular Center, Milwaukee, United States of America, ⁴Medical College of Wisconsin, Department of Physiology, Milwaukee, United States of America, ⁵Medical College of Wisconsin, Division of Gastroenterology and Hepatology, Department of Medicine, Milwaukee, United States of America

Contact E-Mail Address: akleynerman@mcw.edu

Introduction: Inflammatory bowel disease (IBD) has been associated with increased major adverse cardiac events (MACE). The ORAL Surveillance study reported increased risks of MACE in older adults with rheumatoid arthritis and cardiovascular (CV) risk factors (RFs) when treated with a Janus kinase inhibitor (JAKi) versus anti-tumor necrosis factor (anti-TNF) therapy. These results have prompted revisions in the guidelines on the utilization of JAKi in patients with IBD. However, the mechanisms behind the reported adverse outcomes associated with JAKi have not been fully elucidated. Microvascular dysfunction (MVD) is an independent, well-defined predictor of future MACE. Nitric oxide (NO) serves as the primary vasodilatory metabolite in healthy microcirculation, but in pathologic states like coronary artery disease (CAD) and diabetes mellitus (DM), this role shifts to hydrogen peroxide (H₂O₂).

Aims & Methods: We aimed to investigate the mechanistic effects of JAKi and anti-TNF drugs on microvascular endothelial function. Flow-mediated dilation (FMD), pharmacologically induced endothelial-dependent dilation to acetylcholine (ACh), and smooth muscle-dependent dilation to papaverine (ex vivo) were examined in vessels from healthy (≤ 3) and high-risk (≥ 4 CV RFs) subjects. To assess the effect of NO synthase blockade and H₂O₂ scavenging, we incubated vessels with L-NAME and PEG-Catalase (peg-cat), respectively. Isolated arterioles from surgical discard tissue were incubated in an endothelial culture medium containing vehicle (control), JAKi (Tofacitinib Citrate, CP-690550, Selleckchem), or anti-TNF (Infliximab, Y0002047, Sigma-Aldrich). Video microscopy was used to measure dilator function. Data are expressed as % max. diameter $\pm$ SE for n = 3-5 per condition, *p<0.05, **p<0.01, ***p<0.001. Statistical significance was established using two-way ANOVA.

Results: In isolated vessels from both healthy and high-risk subjects, neither anti-TNF nor JAKi treatments impaired FMD, ACh-mediated dilation, or papaverine-mediated dilation when compared to historic controls. Interestingly, in healthy vessels treated with JAKi, FMD was significantly blocked by peg-cat (at 100 cmH₂O, JAKi: 87 $\pm$ 10%, n = 3 vs. JAKi + peg-cat: 58 $\pm$ 12%, n = 3, p = 0.01), suggesting a mechanistic switch from NO to pathologic H₂O₂-mediated vasodilation, similar to the phenotype observed in patients with CAD. Additionally, treatment with anti-TNF partially restored L-NAME-inhibitable dilation in vessels from individuals with elevated CV risk (at 100 cmH₂O, anti-TNF: 68 $\pm$ 8%, n = 5 vs. anti-TNF + L-NAME: 36 $\pm$ 13%, n = 5, p = 0.116), suggesting a potential beneficial

effect on microvascular function. Results did not change with sub-group analysis of patients with and without CAD and DM, both recognized factors impacting MVD.

Conclusion: Our preliminary findings suggest that JAKi and anti-TNF drugs may have different mechanistic effects on microvascular endothelial function in vessels from healthy and high-risk patients. Further studies examining the impact of IBD medications on microvascular endothelial function pathways may provide a novel approach to guide therapeutic management in IBD patients with varying CV profiles.

Disclosure: Nothing to disclose.

MP333

EFFECT OF UPADACITINIB ON LIVER ENZYMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE OR ULCERATIVE COLITIS: POOLED ANALYSIS OF PHASE 3 INDUCTION AND MAINTENANCE STUDIES

M.C. Dubinsky¹, M. Reguerio², C. Ha³, G.Y. Melmed⁴, A. Armuzzi⁵, P. Irving⁶, S. Anyanwu⁷, E. Dubcenco⁷, F. Aponte⁷, I. Shah⁷, T. Wang⁷, S. Suravaram⁷, H. Palac⁷, D.T. Rubin⁸

¹Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ²Cleveland Clinic Foundation, Cleveland, United States of America, ³Mayo Clinic Arizona, Scottsdale, United States of America, ⁴Cedars Sinai Medical Center, Los Angeles, United States of America, ⁵IBD Center, IRCCS Humanitas Research Hospital, Gastroenterology, Rozzano, Milan, Italy, ⁶Guy's and St Thomas' Hospital, Dept. of Gastroenterology, London, United Kingdom, ⁷AbbVie, North Chicago, United States of America, ⁸University of Chicago Medicine, Chicago, United States of America

Contact E-Mail Address: drubin@uchicago.edu

Introduction: Upadacitinib (UPA) is an oral, reversible Janus kinase inhibitor (JAKi) approved for the treatment of moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC).¹⁻⁴ Abnormal levels of liver enzymes are frequently encountered in patients with inflammatory bowel disease. However, data on liver enzyme elevations in UC and CD patients treated with JAKi are limited.

Aims & Methods: This post hoc analysis evaluated changes in liver enzymes over time in phase 3 trials of UPA in CD (U-EXCEL, U-EXCEED, U-ENDURE) and UC (U-ACCOMPLISH, U-ACHIEVE). Patients were randomized 2:1 to receive once-daily (QD) UPA 45 mg (UPA45) or placebo (PBO) induction therapy for 12 weeks (wks) in the CD trials and 8 wks in the UC trials.^{3,4} Patients who achieved clinical response to UPA induction therapy were rerandomized (1:1:1) to PBO, UPA 15 mg (UPA15), or UPA 30 mg (UPA30) QD for the 52-wk maintenance studies.^{3,4} Data from the induction studies were pooled, as were data from the maintenance studies. Least-squared (LS) mean changes from baseline (BL) in alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (TBili) were calculated using ANCOVA models with treatment as a main factor, and BL and indication as covariates for induction and maintenance periods. The proportions of UPA-treated patients with Grade 3-4 liver enzyme elevations (ALT, AST, and ALP: >5.0 x upper limit normal [ULN]; TBili: >3.0 x ULN) were assessed.

Results: This analysis included 2,118 patients. At induction, BL mean [SD] ALT (PBO 19.4 [15.7] U/L; UPA45 18.2 [15.4] U/L, AST (PBO 19.5 [26.4] U/L; UPA45 17.8 [13.4] U/L, ALP (PBO 74.5 [25.8] U/L; UPA45 74.7 [35.2] U/L, and TBili (PBO 6.9 [4.4] μ mol/L; UPA45 6.8 [4.0] μ mol/L) were similar across treatment arms and within normal ranges. LS mean changes [SE] from BL in ALT, AST, ALP, and TBili were 4.7 [0.4] U/L, 4.7 [0.5] U/L, -8.7 [0.5] U/L, and 1.8 [0.1] μ mol/L, respectively, by wk 4 of UPA induction and remained relatively stable across all treatment groups through

wk52 of maintenance (Table). Incidences of Grade 3 or 4 elevations in liver enzymes were low throughout induction and maintenance (ALT: UPA45 1.1%, UPA15 2.1%, UPA30 1.0%; AST: UPA45 1.4%, UPA15 1.3%, UPA30 1.5%; ALP: UPA45 <0.1%, UPA15 0%, UPA30 0.2%; TBili: UPA45 0.4%, UPA15 0.4%, UPA30 0.6%). There were no events of drug-induced liver injury (DILI) in CD; 1 event was reported in UPA45 in UC induction, 1 event each in UPA15 and UPA30 in UC maintenance, all were nonserious and possibly attributed to other underlying conditions (i.e., alcohol) and/or concomitant medications (i.e., isoniazid, estrogen-containing contraceptive) (see Table footnotes).

Induction, LS Mean Change (SE)			Maintenance, LS Mean Change (SE)		
Parameter Timepoint	PBO (n = 725)	UPA45 (n = 1393)	Parameter Timepoint	PBO (n = 468)	UPA15 (n = 471) UPA30 (n = 480)
ALT, U/L			ALT, U/L		
Week 4	0.0 (0.6)	4.7 (0.4)	Week 12	2.5 (1.1)	5.1 (1.0)
Week 8	0.5 (0.6)	4.7 (0.5)	Week 52	2.2 (1.6)	7.7 (1.2)
AST, U/L			AST, U/L		
Week 4	-0.4 (0.7)	4.7 (0.5)	Week 12	2.6 (0.9)	6.2 (0.8)
Week 8	0.2 (0.5)	4.7 (0.3)	Week 52	2.4 (1.1)	7.5 (0.8)
ALP, U/L			ALP, U/L		
Week 4	0.3 (0.7)	-8.7 (0.5)	Week 12	1.7 (2.1)	-9.3 (1.9)
Week 8	1.9 (0.9)	-11.0 (0.7)	Week 52	5.2 (1.8)	-8.0 (1.3)
TBili, μ mol/L			TBili, μ mol/L		
Week 4	0.0 (0.1)	1.8 (0.1)	Week 12	0.4 (0.2)	1.9 (0.2)
Week 8	0.6 (0.2)	2.5 (0.1)	Week 52	3.0 (0.6)	5.5 (0.4)
DILI, n (%)	n = 378	n = 719	DILI, n (%)	n = 245	n = 250
[SSA%]	0	1 (0.1) [0.2] ^a	[SSA%]	0	1 (0.4) [0.4] ^b

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CD, Crohn's disease; DILI, drug-induced liver injury; LS, least square; PBO, placebo; SSA, study site adjusted; TBili, total bilirubin; UC, ulcerative colitis; UPA, upadacitinib.

Pooled UC+CD data are reported as LS mean change from baseline (standard error). Baseline is defined as the last nonmissing observation before their first dose of study drug. The denominators for DILI are from patients in the UC program only, as there were no reports in CD.

^a Liver damage due to concomitant isoniazid use for latent tuberculosis in 52-year-old female with 24 years of UC and was a current alcohol user. Event was reported on day 15 of UPA exposure.

^b Drug-induced hepatitis moderate in severity in 32-year-old male with 11 years of UC who was receiving concomitant Mesalazine medication and was a former alcohol user. Event was reported on day 140 of UPA exposure. Study drug was interrupted.

^c Drug-induced hepatopathy mild in severity in 28-year-old female with 6 years of UC who was receiving concomitant Pentasa and Triquilar medications. Event was reported on day 259 of UPA exposure. Patient withdrew from treatment.

Conclusion: Patients with moderately to severely active CD or UC receiving UPA experienced early changes in liver enzymes, which remained stable thereafter. Grade 3-4 elevations were rare and nonserious. Further evaluations of these liver enzyme changes and association with UPA benefit/risk over long-term extension studies are warranted.

References: 1. Danese S, Vermeire S, Zhou W, et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. *Lancet*. May 26 2022;399:2113-2128.

2. Loftus EV, Jr., Panés J, Lacerda AP, et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. *N Engl J Med*. May 25 2023;388(21):1966-1980. doi:10.1056/NEJMoa2212728

3. AbbVie. Rinvoq (Upadacitinib): Highlights of Prescribing Information [Package Insert]. AbbVie. Accessed March 21, 2024, //efaidnbmnnnibpcajpcglclefindmkaj/https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211675s015lbl.pdf

4. AbbVie. Rinvoq (Upacitinib): Summary of Product Characteristics [Package Insert]. AbbVie. Accessed March 21, 2024, efaidnbmnnnibpcajpcglclefindmkaj/https://www.ema.europa.eu/en/documents/product-information/rinvoq-epar-product-information_en.pdf

Disclosure: AbbVie Disclosure: AbbVie Inc. funded these studies (U-EXCEL, NCT03345849; U-EXCEED, NCT03345836; U-ENDURE, NCT03345823) and UC (U-ACCOMPLISH, NCT03653026; U-ACHIEVE, NCT02819635) and

participated in the study design, research, analysis, data collection, interpretation of data, reviewing, writing and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.

Acknowledgments: AbbVie and the authors thank all the trial investigators and the patients who participated in these clinical trials. Paulette Krishack, PhD, and Jeanie Meckes, PhD, of AbbVie, provided medical writing assistance for the development of this publication.

Disclosure:

Marla Dubinsky is a consultant for AbbVie, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Eli Lilly, Gilead Sciences, Janssen Pharmaceuticals, Pfizer, Prometheus Labs, Sanofi, Shire, Takeda, and receives research grants from AbbVie and Janssen Pharmaceuticals.

Miguel Regueiro has served as a consultant, speaker and advisory board member for AbbVie

Christina Ha has received financial support from advisory board fees from AbbVie, Bristol Myers Squibb, Bausch Health, Roivant, Janssen, Pfizer, and Takeda; consultant fees from AbbVie; educational grant funding from Bristol Myers Squibb, Pfizer, Janssen, AbbVie and the Helmsley Charitable trust.

Gil Y. Melmed is a consultant for AbbVie, Arena, Boehringer Ingelheim, Bristol Myers Squibb, Dieta, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Lilly, Janssen, Oshi Health, Pfizer, Prometheus Labs, Samsung Bioepis, Shionogi, Takeda, and Techlab, Viatrix He has received research grants from Pfizer.

Alessandro Armuzzi has received consulting and/or advisory board fees from AbbVie, Allergan, Amgen, Arena, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, Lionhealth, MSD, Mylan, Nestlé, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, and Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, Merck & Co, Mitsubishi Tanabe, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda and Tigenix; and research grants from Biogen, Merck & Co, Pfizer, and Takeda.

Peter M. Irving has received lecture fees from AbbVie, BMS, Celgene, Celltrion, Falk Pharma, Ferring, Galapagos, Gilead, MSD, Janssen, Pfizer, Takeda, Tillotts, Sapphire Medical, Sandoz, Shire, Warner Chilcott; Financial support for research: Celltrion, MSD, Pfizer, Takeda; Advisory fees: AbbVie, Arena, Boehringer Ingelheim, BMS, Celgene, Celltrion, Genentech, Gilead, Hospira, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor Pharma, and Warner Chilcott.

Samuel I. Anyanwu, Elena Dubcenco, Fernando Aponte, Isheeta Shah, Tao Wang, Smitha Suravaram, and Hannah Palac are AbbVie employees and may own AbbVie stock and/or stock options.

David T. Rubin has served as a consultant for AbbVie, Altrubio, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dizal Pharmaceuticals, Galapagos, Ichnos Sciences S.A., InDex Pharmaceuticals, Iterative Health, Janssen, Lilly, Pfizer, Prometheus Biosciences, Reistone, Syneos, and Takeda. He has received grant support from Takeda.

MP334

THE ADDITION OF HIGH-DOSE INTRAVENOUS BOLUS OF METHYL-PREDNISOLONE ADDED TO ORAL CORTICOSTEROIDS DOES NOT IMPROVE EFFICACY IN MODERATELY ACTIVE ULCERATIVE COLITIS: RESULTS OF A RANDOMISED, CONTROLLED STUDY OF GETECCU.

G. Piñero¹, J. Llaó¹, M. Mañosa Ciria¹, E. Martín-Arranz², Y. Zabana³, M. Navarro-Llavat⁴, E. García-Planella⁵, D. Busquets Casals⁶, D. Monfort Miquel⁷, J.R. Pineda⁸, A. Villoria Ferrer⁹, A. Gutiérrez¹⁰, L. Menchén¹¹, G. Bastida¹², F.J. García-Alonso¹³, M. Rivero¹⁴, M. Chaparro¹⁵, S. Riestra¹⁶, O. Merino Ochoa¹⁷, I. Rodríguez-Lago¹⁸, M. Barreiro de Acosta¹⁹, E. Domenech Morral²⁰,

on behalf of the ENEIDA project of GETECCU.

¹Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ²Hospital Universitario La Paz, Gastroenterology, Madrid, Spain, ³Hospital Universitari Mútua Terrassa, Department of Gastroenterology, IBD Unit, Terrassa, Spain, ⁴Hospital Moisès Broggi, Barcelona, Spain, ⁵Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, ⁶H. DE GIRONA DR. J. TRUETA/ICO GERONA, Gastroenterology, Girona, Spain, ⁷Consorci Sanitari de Terrassa, Barcelona, Spain, ⁸Hospital Álvaro Cunqueiro, Vigo, Spain, ⁹H. parc tauli, Gastroenterology, Sabadell, Spain, ¹⁰Hospital General Universitario de Alicante, Alicante, Spain, ¹¹Hospital Gregorio Marañón, Madrid, Spain, ¹²Hospital Universitario y Politécnico La Fe, Valencia, Spain, ¹³Hospital Río Hortega, Valladolid, Spain, ¹⁴Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain, ¹⁵Hospital Universitario de La Princesa, Gastroenterology Unit, Madrid, Spain, ¹⁶Hospital Central Universitario Asturias, Oviedo, Spain, ¹⁷Hospital Universitario de Cruces, Bilbao, Spain, ¹⁸Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ¹⁹University Hospital of Santiago, Gastroenterology, Santiago de Compostela, Spain, ²⁰Hospital Germans Trias i Pujol, Gastroenterology Unit, Badalona, Spain

Contact E-Mail Address: gipinero@gmail.com

Introduction: Oral corticosteroids remain the treatment of choice for moderately active ulcerative colitis (UC). However, only 30-60% of patients achieved clinical remission in controlled studies. In severe systemic diseases such as systemic lupus, the administration of high-dose intravenous methyl-prednisolone bolus accelerates and enhances clinical response.

Aims & Methods: Aims: To assess the impact of adding high-dose intravenous methyl-prednisolone bolus to oral corticosteroids for the treatment of moderately active UC.

Methods: Prospective, multicentre, controlled, randomised and open study. To be included, patients had to fulfil all the following criteria: 1) moderately active UC (complete Mayo score -cMS- of 6-10); 2) distal or extensive UC extent; 3) naïve to immunosuppressant and biological agents; and 4) absence of steroid-dependency criteria. Patients were randomised to receive either oral prednisone 60mg/day (ORAL) or the same regimen preceded by a 500mg intravenous bolus of methyl-prednisolone for three days (BOLUS). Patients were stratified according to UC onset or not and baseline oral mesalazine use. Oral prednisone regimen included a tapering schedule from week 2 to week 8. Once reaching the prednisone dose of 20 mg/day all patients started 2g/day of oral mesalazine. The main endpoint was clinical and endoscopic remission (cMS <3 with no value >1) at weeks 8 and 54, without needing rescue therapy or additional corticosteroid exposure.

Results: A total of 75 patients were included (39 in ORAL group, 36 in BOLUS group), with 24% at UC onset, 51% having extensive disease, 68% on maintenance oral mesalazine and 31% having received corticosteroids previously. Baseline cMS was 9 (7-9), C-reactive protein 9.25 mg/L (3.85-

20.17), and serum albumin 39.5 g/L (36.6-42.9), with no significant differences in clinical-epidemiological characteristics between both treatment groups. Overall, 48% (36 patients) achieved clinical-endoscopic remission at week 8 and 28% (21 patients) at both weeks 8 and 54 without needing additional steroid courses or rescue treatments. Among these, 11/36 (30.5%) were in the BOLUS group and 10/39 (25.6%) were in the ORAL group (P = 0.636). No significant differences between treatment groups were found in secondary endpoints including clinical-endoscopic remission at week 8 (58.3% vs. 38.5%; p = 0.085), clinical remission at week 54 (38.9% vs. 35.9%; P = 0.789), and endoscopic remission at week 54 (36.1% vs. 30.8%; P = 0.624).

Conclusion: The addition of three high-dose intravenous corticosteroids at the beginning of a conventional oral prednisone regimen does not improve the efficacy of treating moderately active UC in short nor in the medium term.

Disclosure: Nothing to disclose.

MP335

BROADENED REPRESENTATION OF PATIENTS WITH ULCERATIVE COLITIS, BUT NOT CROHN'S DISEASE, IN CONTEMPORARY RANDOMISED CONTROLLED TRIALS

J. Hanzel¹, E. Hamersak², T. Kodric², T. Vovk², D. Drobne¹

¹University Medical Centre Ljubljana, Department of

Gastroenterology and Hepatology, Ljubljana, Slovenia,

²Faculty of Pharmacy, Department of Biopharmaceutics and Pharmacokinetics, Ljubljana, Slovenia

Contact E-Mail Address: jurij.hanzel@gmail.com

Introduction: Patients enrolled in randomised controlled trials (RCT) of advanced therapeutics in inflammatory bowel disease (IBD) may differ from the target population of patients given these same drugs in routine practice. Prior research from 2012 indicated that only approximately a third of patients would theoretically qualify for enrolment in an RCT (1). We aimed to re-evaluate the overlap between patients in routine practice and those in contemporary RCTs.

Aims & Methods: We evaluated all patients with active IBD at our institution who were considered for treatment with a biologic or small molecule (both de novo and switching). Their characteristics were compared against inclusion and exclusion criteria of recently completed or ongoing RCTs: ozanimod, upadacitinib, risankizumab, golimumab-guselkumab, guselkumab (Crohn's disease [CD] only), filgotinib, mirikizumab, and etrasimod (ulcerative colitis [UC] only for the latter three drugs). We calculated the percentage of patients ineligible for all evaluated trials and identified the commonest criteria for ineligibility.

Trial	Crohn's disease (n = 155)	Ulcerative colitis (n = 131)
Ozanimod	46 (29.7%)	22 (14.2%)
Upadacitinib	24 (15.5%)	34 (21.9%)
Risankizumab	17 (11.0%)	42 (27.1%)
Guselkumab	24 (15.5%)	/
Golimumab-guselkumab	13 (8.4%)	32 (20.7%)
Filgotinib	/	11 (7.1%)
Mirikizumab	/	19 (12.3%)
Etrasimod	/	45 (29.0%)
At least one trial	53 (34.2%)	62 (47.3%)

Table 1. Number of patients (n, %) with inflammatory bowel disease eligible for participation in a randomized clinical trial.

Results: We evaluated 286 patients (155 CD, 131 UC); 16 additional patients with IBD unclassified were ineligible for trial participation by default. Among patients with CD, 34.2% (53/155) would have been eligible

for participation in at least one RCT; among patients with UC, 47.3% (62/131) would have been eligible for participation in at least one RCT (Table 1). Patients with CD would have been excluded mainly due to the presence of stricturing or penetrating disease, the presence of ostomies, comorbidities, including history of malignancy, and insufficient symptoms despite endoscopic activity. Patients with UC would have been excluded mainly due to insufficient symptoms despite endoscopic activity, ulcerative proctitis, newly diagnosed disease, and comorbidities, including history of malignancy.

Conclusion: Only a minority of patients with IBD from routine practice would be eligible for participation in contemporary RCTs, although the percentage has increased for patients with UC compared to past studies.

References: 1. Ha C et al. Patients enrolled in randomized controlled trials do not represent the inflammatory bowel disease patient population. *Clin Gastroenterol Hepatol* 2012;10:1002-7.

Disclosure: JH received speaker's fees from Abbvie, Janssen, and Takeda; consulting fees from Alimentiv Inc.

EH declares no conflict of interest.

TK declares no conflict of interest.

TV declares no conflict of interest.

DD has served as a speaker, consultant, and/or advisory board member for MSD, Abbvie, Takeda, Pfizer, Janssen, Krka, Eli Lilly, Otkal Pharma, Roche, Novartis, Amgen, and Lek.

IBD in pregnancy and paediatric patients

13:00-14:00 / Poster Stage 2

MP336

THE IMPACT OF PRE-DIAGNOSIS DIET AND OTHER ENVIRONMENTAL FACTORS ON INFLAMMATORY BOWEL DISEASE- RESULTS FROM THE PROSPECTIVE POPULATION-BASED COPENHAGEN IBD INCEPTION COHORT

M. Attauabi^{1,2,3}, G. Madsen^{2,3}, F. Bendtsen^{2,3,4}, J. Burisch^{2,3,4}, J.B. Seidelin^{1,4}

¹Copenhagen University Hospital, Herlev Hospital, Department of Gastroenterology and Hepatology, Herlev, Denmark, ²Copenhagen University Hospital - Hvidovre Hospital, Gastroint, Medical Section, Hvidovre, Denmark, ³Hvidovre Hospital, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents, and Adults, Hvidovre, Denmark, ⁴Faculty of Health and Medical Sciences, University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark

Contact E-Mail Address: mohamed.attauabi.02@regionh.dk

Introduction: The influence of environmental factors in the course of inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is unclear.

Aims & Methods: We aimed to investigate the role of environmental factors in disease activity, severity, and initial course of IBD.

Since May 1st, 2021, all adult and pediatric patients with incident IBD within a catchment area encompassing 20% of the Danish population were enrolled in the prospective population-based Copenhagen IBD Inception Cohort.¹ Upon diagnosis, all adult patients diagnosed between May 2021 and May 2023 were asked to report environmental factors using the International Organisation of IBD (IOIBD) and HeartDiet questionnaires.

A severe disease course was defined as a composite of a need for either oral glucocorticoids, immunomodulators, biologics, or intestinal resection within three months of disease. Severe disease activity was defined either endoscopically (UC: Mayo Endoscopic Score=3, CD: Simple Endoscopic Score-CD>16) or as a composite of biochemical activity (f-calprotectin>1800 µg/ g or C-reactive protein > 10 mg/L) and clinical activity (UC: Simple Clinical Colitis Activity Index (SCCAI)>10, CD: Harvey-Bradshaw Index (HBI)>7).

Clinical remission was defined as SCCAI<3 or HBI<5 points. All findings were adjusted for gender, age, and disease phenotype in multivariable logistical analysis yielding adjusted odds ratios (aOR (95% confidence interval)).

Results: The population consisted of 208 and 128 patients with incident UC and CD (67.5% and 63.1% of the original cohort), respectively, who completed the questionnaires within a median of 1.3 months (IQR 0.4 – 3.4 months) from diagnosis. No clinical differences were between participants and non-participants. During six months of follow-up, 128 (61.5%) and 77 (60.2%) patients with UC and CD, respectively, achieved clinical remission. In patients with UC, low intake of saturated fatty acids was associated with reduced probability of achieving clinical remission at follow-up (aOR= 0.42 [0.18;0.95]). In patients with CD, a high intake of whole meal bread was significantly associated with a reduced risk of severe activity (aOR=0.40 [0.16;0.98]), while high intake of fruits (aOR=0.27 [0.07;0.99]), vegetables (aOR=0.27 [0.09;0.80]), or fibers (aOR=0.30 [0.09;0.96]) were associated with lower risk of stricturing or penetrating phenotypes.

A severe disease course of UC was significantly and inversely associated with active smoking (aOR=0.28 [0.08;0.95]), intake of minced meat (aOR=0.38, [0.15;0.97]), and ultra-processed food (aOR=0.22 [0.06;0.78]). Conversely, minced meat was associated with elevated risk of a severe course of CD (aOR=3.59 [1.41;9.10]). In addition, active smoking was associated with increased risk of CD-related hospitalization (aOR=11.89

[2.53;55.92]) and stricturing phenotype (aOR=5.28 [1.76;15.85]). On the other hand, previous pregnancy (aOR=0.28 [0.09;0.93]) was associated with a reduced risk of a severe course of CD.

Among childhood factors, appendectomy was associated with increased risk of UC-related hospitalization (aOR=5.46 [1.05;28.34]), CD-related hospitalizations (aOR=11.89 [2.53;55.92]), and CD-related resections (aOR=19.48 [4.20;90.35]).

Conclusion: In conclusion, our prospective population-based study unveiled distinct environmental exposures to be associated with important clinical endpoints in UC and CD. These findings hold clinical value as they inform personalized patient counseling on lifestyle factors that might influence outcomes of IBD.

References: 1. Attauabi M, Madsen GR, Bendtsen F, et al. Influence of Genetics, Immunity and the Microbiome on the Prognosis of Inflammatory Bowel Disease (IBD Prognosis Study): the protocol for a Copenhagen IBD Inception Cohort Study. *BMJ Open*. 2022;12(6):e055779. doi:10.1136/bmjopen-2021-055779

Disclosure: Mohamed Attauabi: None

Gorm Roager Madsen: Personal fees from Tillotts

Flemming Bendtsen: Tillotts, Ferring

Jakob Benedict Seidelin: has received research grants from Takeda, Janssen, the Danish Research Council, and the Capital Region Denmark, and is national coordinator of studies from AbbVie, Arena Pharmaceuticals, Ely Lilly, and Boehringer Ingelheim.

Johan Burisch: reports grants and personal fees from AbbVie, grants and personal fees from Janssen-Cilag, personal fees from Celgene, grants and personal fees from MSD, personal fees from Pfizer, grants and personal fees from Takeda, grants and personal fees from Tillotts Pharma, personal fees from Samsung Bioepis, grants and personal fees from Bristol Myers Squibb, grants from Novo Nordisk, personal fees from Pharmacosmos, personal fees from Ferring, personal fees from Galapagos, outside the submitted work.

MP337

PREGNANCY OUTCOMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THREE UNIVERSITY MEDICAL CENTERS IN THE NETHERLANDS

D.G. Bouwknegt¹, G. Dijkstra¹, W.A. van Dop², C.J. van der Woude³, M.C. Visschedijk¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Radboud University Medical Center, Gastroenterology and Hepatology, Nijmegen, Netherlands, ³Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: diannebouwknegt@gmail.com

Introduction: As inflammatory bowel disease (IBD) is frequently diagnosed in young adults, the disease often coincides with pregnancy. About one in four female patients will have their first pregnancy after diagnosis. Current guidelines advise treatment through specialized clinics for IBD patients wishing to conceive, which are increasingly implemented. However, recent outcome data from these centers is scarce. In this study we therefore describe the pregnancy-course in three specialized Dutch IBD university clinics.

Aims & Methods: For this multicenter, retrospective cohort study, all adult female IBD-patients who had been pregnant during treatment in any of the three participating Dutch university medical centers between the inception of the respective electronic patient records and 2022 were included. Data on patient- and disease characteristics, lab values, medication usage and pregnancy outcomes was extracted from the electronic pa-

tient records. Topics relevant to pregnancy were logged, including intoxications, the use of folic acid and vitamin D, and gestational weight gain.

Results: Data was collected on 620 women who had been pregnant in the study period, including 376 (60.6%) with Crohn's disease (CD), 230 (37.1%) with ulcerative colitis (UC), and 13 (2.1%) with inflammatory bowel disease unclassified (IBDU). Of the CD-patients, 68 (18.1%) had a history of perianal disease. The mean age at conception of the first pregnancy was 29.9 years. Altogether, 983 pregnancies were included, of which 10.3% was conceived using assisted reproductive technologies, including in vitro fertilization (IVF) in 3.6% of pregnancies. During 9.8% of pregnancies, the mother actively smoked tobacco at conception. Medication was used during 71.0% of pregnancies, most often consisting of thiopurines (27.1%) and amino salicylates (24.4%). Appropriate gestational weight gain was achieved in 31.1% of pregnancies. 152 (15.5%) pregnancies resulted in miscarriage, 12 (1.2%) pregnancies were ectopic. In the remaining pregnancies, 511 (62.4%) newborns were delivered vaginally. A caesarean section (CS) was performed in 234 cases (23.8%). Overall, 54 mothers (23.1%) who underwent a CS had perianal disease. An adverse pregnancy outcome was noted in 159 (21.3%) of pregnancies, including low birth weight in 78 (10.5%), prematurity in 85 (11.4%) and dysmaturity in 89 (11.9%). Adverse outcomes occurred more often in the group of women who experienced disease activity in any point during pregnancy, but this difference was not statistically significant (30.8% vs 21.7%, p=0.120). Two patients developed deep venous thromboembolism during or within six weeks after pregnancy.

Conclusion: In IBD the mean age at conception and the rate of pregnancies conceived using IVF were comparable with the general Dutch population. A CS was performed more frequently in this cohort when compared to healthy pregnancies in the Netherlands (23.8% vs 17.6%). In these specialized centers low birth weight (10.5% vs 5.7%), prematurity (11.4% vs 6.6%) and dysmaturity (11.9% vs 9.7%) occurred more often in comparison to the known rates in Dutch pregnancies, emphasizing that adequate counseling before and during pregnancy in IBD is essential.

Disclosure: Nothing to disclose.

MP338

WITHDRAWN

M.J. Casanova¹, J. P. Gisbert¹, A. Amiot², H. Gordon³, G. Fiorino⁴, E. Flanagan⁵, P.G. Kotze⁶, A. Sokic-Milutinovic^{7,8}, E. Sonnenberg⁹, P. Núñez¹⁰, A. Blesl¹¹, I. Catalan-Serra^{12,13}, P. Bossuyt¹⁴, R. Filip^{15,16}, A. Bar-Gil Shitrit¹⁷, A. Kagramanova^{18,19}, Z. Krznaric²⁰, P. Molander²¹, G.J. Mantzaris²², P. Juillerat^{23,24}, T. Molnár²⁵, K.B. Gecse²⁶, J. Torres^{27,28}, P. Myrelid^{29,30}, U. Mahadevan³¹, J.R. Márquez³², B.M. Iade-Vergara³³, A. Rausch³⁴, D. Duricova³⁵, M. Chaparro^{*1}, M. Julsgaard^{*36,37}, ^{*}co-last authors

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Gastroenterology, Madrid, Spain, ²Bicetre University Hospital, Université Paris Saclay, AP-HP, CESP-INSERM U108, Le Kremlin Bicetre, Gastroenterology, Paris, France, ³Newham University Hospital, Barts Health NHS Trust, Gastroenterology, London, United Kingdom, ⁴IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Department of Gastroenterology and Digestive Endoscopy, Milan, Italy, ⁵St Vincent's Hospital Melbourne, Gastroenterology, Melbourne, Australia, ⁶Pontificia Universidade Católica do Paraná, Colorectal Surgery Unit, Curitiba, Brazil, ⁷School of Medicine University of Belgrade, Belgrade, Serbia, ⁸Clinic for Gastroenterology and Hepatology, University Clinical Center of Serbia, Belgrade, Serbia, ⁹Charité-Universitätsmedizin Berlin, Department of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany, ¹⁰Clínica Universidad de los Andes, Digestive Disease Center, Universidad de Chile, Facultad Medicina Occidente, Hospital San Juan de Dios, Santiago de Chile, Chile, ¹¹Medical University of Graz, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Graz, Austria, ¹²Levanger Hospital, Nord-Trøndelag Hospital Trust, Gastroenterology, Trondheim, Norway, ¹³Centre of Molecular Inflammation Research (CEMIR), Norwegian University of Science and Technology (NTNU), Department of Molecular Medicine, Trondheim, Norway, ¹⁴Imelda GI Clinical Research Center, Imelda General Hospital, Dr. Bonheiden, Belgium, ¹⁵Institute of Medicine, Medical College of Rzeszow University, Rzeszow, Poland, ¹⁶Clinical Hospital No. 2, Gastroenterology with IBD Unit, Rzeszow, Poland, ¹⁷Digestive Diseases Institute, Shaare Zedek Medical Center, affiliated with the Faculty of Medicine, the Hebrew University, IBD MOM Unit, Jerusalem, Israel, ¹⁸Moscow Clinical Scientific Center named after A. S. Loginov, Moscow, Russian Federation, ¹⁹Research Institute of Health Organization and Medical Management, Moscow, Russian Federation, ²⁰University Hospital Centre Zagreb, Zagreb, Croatia, ²¹Helsinki University Hospital HUS and Helsinki University, Abdominal Center, Gastroenterology, Helsinki, Finland, ²²White Cross Hospital, and HYGEIA Hospital, Gastroenterology, Athens, Greece, ²³Clinic for Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Gastroenterology, Bern, Switzerland, ²⁴Crohn and Colitis Center, Gastro-entérologie Beaulieu SA, Lausanne, Switzerland, ²⁵Gastroenterology Center, University of Szeged, Szeged, Hungary, ²⁶Amsterdam University Medical Center, Amsterdam, Netherlands, ²⁷Hospital Beatriz Ângelo, Division of Gastroenterology, Loures, Portugal, ²⁸Hospital da Luz, Lisbon, Portugal, ²⁹Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden, ³⁰Linköping

University Hospital, Department of Surgery, Linköping, Sweden, ³¹Division of Gastroenterology, Department of Medicine, University of California, San Francisco, United States of America, ³²Instituto de Coloproctología ICO, Medellín, Colombia, ³³Working Group on Inflammatory Intestinal Disease of Uruguay, Crohn's and Ulcerative Colitis Association of Uruguay, Montevideo, Uruguay, ³⁴Hospital Británico de Buenos Aires, Gastroenterology, Buenos Aires, Argentina, ³⁵IBD Clinical and Research Centre, ISCARE a.s., Prague, Czech Republic, ³⁶Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ³⁷Center for Molecular Prediction of Inflammatory Bowel Disease [PREDICT], Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark

Contact E-Mail Address: mjcasanova.g@gmail.com

Introduction: Inflammatory bowel disease (IBD) often affects patients during their reproductive years. The management of patients wishing to conceive or during pregnancy requires specialized counseling.

Aims & Methods: Our aim was to have a global perspective on the management of IBD by gastroenterologists (GIs) during preconception, pregnancy, breastfeeding and neonatal period.

An anonymous survey (75 questions) was developed to investigate different facets of clinical practice concerning the management of pregnant and breastfeeding in patients with IBD. A national representative from each European country, USA, Latin America, Australia and New Zealand was selected to distribute the survey to their GIs colleagues who treat IBD patients (irrespective of their experience).

Results: A total of 856 GIs from 36 countries participated in the survey. Among the participants, 63% had over a decade of experience as GIs, and 61% identified themselves as IBD specialists. The most relevant survey results and sub-analyses based on expertise are presented in tables 1 and 2. In the management of pregnant patients in remission, treatment discontinuation occurred either consistently or occasionally as follows: 20% thiopurines, 37% vedolizumab, 31% ustekinumab, and 96% small molecules. Notably, 13% did not always discontinue small molecules in patients contemplating pregnancy. Safety was the main reason for discontinuing IBD therapy during pregnancy. Contrary to the recommendations in clinical practice guidelines, many GIs avoid starting oral or rectal budesonide, anti-TNF, vedolizumab or ustekinumab during a disease flare. Further, a third of GIs would start thiopurines for a flare during pregnancy. Moreover, 13% will never perform a colonoscopy in a pregnant patient to guide decision making. Half of GIs implemented a dedicated outpatient follow-up program for pregnant patients in remission, with 87% enrolling all pregnant patients in this program. Concerning breastfeeding, 14% believed that all drugs can be used while breastfeeding. Regarding offspring's vaccination, about 20% recommend against the administration of non-live vaccines and only 50% recommended avoiding live vaccines during the first 12 months for children exposed to anti-TNF in-utero. Among those GIs who recommended delaying vaccines in such cases, only 41% recommended testing the infant for detectable anti-TNF levels if live vaccines were required. Among the surveyed GIs, only a minority had a referral obstetrician, and only 35% referred patients with active or complicated IBD, while 45% had a referral paediatrician with expertise in IBD. The main results regarding the medical management and monitoring of IBD during pregnancy, as well as advice on birth outcomes, breastfeeding, and vaccination, are detailed in Table 1.

Conclusion: The management of IBD during pregnancy, lactation, and neonatal period is notably suboptimal, even among GIs specifically dedicated to IBD. It is crucial to address this current need and implement urgent educational measures in this area.

Questions	Global N=856	By expertise		
		IBD specialists N=315	General GIs N=521	P
Pregnant patients in remission				
Discontinued of different types of drugs (always or sometimes), n (%)				
- Thiopurines	162 (20)	79 (15)	79 (27)	<0.001
- Allopurinol if combination with thiopurines	244 (75)	177 (77)	64 (70)	>0.05
- Thiopurines if combination with anti-TNF	337 (45)	207 (42)	122 (49)	>0.05
- Anti-TNF	354 (43)	210 (41)	113 (39)	0.03
- Methotrexate	698 (99.6)	446 (99.6)	238 (100)	>0.05
- Vedolizumab	370 (37)	177(36)	90 (40)	>0.05
- Ustekinumab	264 (31)	178 (38)	82 (43)	>0.05
- Small molecules	468 (96)	336 (97)	125 (95)	>0.05
Discontinue small molecules if contemplating pregnancy (always, sometimes), n (%)				
	460 (87)	328 (88)	124 (87)	>0.05
Pregnant patients with disease flare				
Initiate the following therapies in case of disease flare during 1 st , 2 nd or 3 rd trimester, n (%)				
- Systemic steroids	779 (91)	488 (94)	274 (87)	<0.001
- Oral budesonide	647 (76)	410 (79)	225 (71)	0.01
- Rectal budesonide	632 (74)	402 (77)	222 (71)	0.03
- Oral 5-ASA	736 (86)	471 (90)	253 (80)	<0.001
- Rectal 5-ASA	697 (81)	446 (86)	239 (76)	<0.001
- Thiopurines	237 (28)	152 (29)	82 (26)	>0.05
- Allopurinol	18 (2)	11 (2)	6 (2)	>0.05
- Methotrexate	3 (0.4)	1 (0.1)	2 (0.2)	>0.05
- Cyclosporine	92 (11)	75 (14)	17 (5)	<0.0001
- Anti-TNF	699 (82)	465 (89)	222 (70)	<0.0001
- Vedolizumab	471 (55)	326 (63)	135 (43)	<0.0001
- Ustekinumab	425 (50)	312 (60)	107 (34)	<0.0001
- Tofacitinib	11 (1)	4 (1)	6 (2)	>0.05
- Filgotinib	2 (0.2)	1 (0.2)	0 (0)	>0.05
- Upadacitinib	7 (0.8)	4 (0.8)	2 (0.6)	>0.05
- Ozanimod	1 (0.1)	1 (0.2)	0 (0)	>0.05
- Risankizumab	2 (0.2)	2 (0.3)	0 (0)	>0.05
Recommend urgent surgery, if indicated , n (%)				
- Yes, if clinically indicated regardless gestational age	726 (94)	461 (95)	252 (93)	
- Depends on the pregnancy trimester	25 (4)	15 (3)	10 (4)	>0.05
- Only if C-section could be performed	19 (3)	10 (2)	9 (3)	
Consider C-section indicated (always or if previous episodes of faecal incontinence) in case of, n (%):				
- Inactive perianal disease	500 (71)	324 (72)	167 (69)	>0.05
- Active perianal disease	745 (98)	472 (98)	256 (97)	>0.05
- Inactive rectovaginal fistula	642 (90)	401 (89)	228 (91)	>0.05
- History of ileal-pouch anastomosis	565 (84)	368 (84)	185 (84)	>0.05
Disease monitoring during pregnancy				
Perform a colonoscopy in case of disease flare if results will change the treatment, n (%)				
	725 (87)	444 (87)	267 (87)	>0.05
Order a CT scan in case complications or disease activity needs to be ruled out like in a non-pregnant patient, n (%)				
	290 (36)	77 (20)	50 (21)	>0.05
Order a MRI in case complications or disease activity needs to be ruled out like in a non-pregnant patient, n (%)				
	787 (93)	461 (94)	255 (91)	>0.05
Advice about adverse birth outcomes				
Who is the main person responsible for providing counselling regarding IBD in pregnancy, n (%)				
-Gastroenterologist	427 (50)	269 (52)	149 (47)	
-Obstetrician	18 (2)	7 (1)	11 (4)	>0.05
-Both (gastroenterologist and obstetrician)	387 (45)	232 (45)	145 (46)	<0.0001
-The nurse	8 (1)	7 (1)	1 (1)	
-Other	15 (2)	5 (1)	9 (3)	
Provide pre-conception counselling to fertile patients, n (%)				
-Yes, to all fertile patients	325 (38)	212 (41)	106 (35)	
-Yes, but only to those who request it	344 (40)	222 (43)	118 (39)	<0.0001
- No, not in generally	166 (20)	84 (16)	76 (26)	
Provide counselling to pregnant patients, n (%)				
-Yes, to all pregnant patients	587 (69)	382 (74)	200 (67)	
-Yes, but only to those who request it	153 (18)	88 (17)	59 (20)	<0.0001
- No, not in generally	90 (11)	47 (9)	39 (13)	
Breastfeeding				
Advice against the following drugs during breastfeeding, n (%)				
- 5-ASA	11(1)	5 (1)	6 (2)	0.002
- Systemic steroids	30 (4)	13 (3)	17 (5)	0.03
- Oral budesonide	17 (2)	9 (2)	8 (2)	>0.05
- Thiopurines	74 (9)	28 (5)	43 (14)	<0.0001
- Allopurinol	207 (24)	128 (25)	74 (23)	>0.05
- Methotrexate	579 (68)	343 (66)	223 (71)	>0.05
- Cyclosporine	337 (39)	188 (36)	140 (44)	0.02
- Ciprofloxacin	237 (28)	136 (26)	100 (32)	>0.05
- Metronidazole	228 (27)	126 (24)	101 (32)	0.01
- Anti-TNF	26 (3)	5 (1)	21 (7)	<0.0001
- Vedolizumab	38 (4)	13 (2)	23 (7)	0.001
- Ustekinumab	50 (6)	18 (4)	30 (9)	<0.0001
- Tofacitinib	504 (59)	325 (62)	169 (54)	0.01
- Filgotinib	493 (58)	324 (62)	162 (51)	0.002
- Upadacitinib	485 (57)	320 (61)	157 (50)	0.001
- Ozanimod	458 (54)	302 (58)	150 (48)	0.004

Vaccination				
Recommend no live vaccines during the first 12 months of life in a child exposed to anti-TNF in-utero, n (%)	423 (50)	288 (55)	129 (41)	<0.0001
Recommend no live vaccines during the first 12 months of life in a child exposed to vedolizumab in-utero, n (%)	303 (35)	214 (41)	84 (27)	<0.0001
Recommend no live vaccines during the first 12 months of life in a child exposed to ustekinumab in-utero, n (%)	332 (39)	241 (46)	87 (28)	<0.0001
Vaccines you recommend against in a child exposed to anti-TNFs in-utero, n (%)				
- Hepatitis B, tetanus, Haemophilus influenza type B	181 (21)	114 (22)	62 (20)	>0.05
- Tetanus, pertussis, diphtheria	196 (23)	119 (23)	72 (23)	>0.05
- Measles, mumps, rubella, rotavirus	373 (44)	239 (46)	125 (40)	>0.05
- BCG-vaccine	405 (47)	262 (50)	133 (42)	0.02
- Rotavirus	351 (41)	253 (49)	91 (29)	<0.001
Advice against live-vaccines vaccination beyond 12 months if the child is exposed to the following biologics during breastfeeding, n (%)				
- Infliximab				
- Adalimumab	120 (14)	71 (14)	46 (15)	>0.05
- Golimumab	120 (14)	71 (14)	46 (15)	>0.05
- Certolizumab	109 (13)	67 (13)	39 (12)	>0.05
- Vedolizumab	88 (10)	49 (9)	36 (11)	>0.05
- Ustekinumab	72 (8)	37 (7)	33 (10)	>0.05
	77 (9)	41 (8)	34 (11)	>0.05
Anti-TNF: antitumor necrosis factor, GI: gastroenterologist, IBD: inflammatory bowel disease, 5-ASA: 5-aminosalicylates, CT: computed tomography, MRI: magnetic resonance image, BCG: bacillus Calmette-Guérin.				

Table 1. Medical management and disease monitoring during pregnancy, advice birth outcomes, breastfeeding, and vaccination.

Disclosure: María José Casanova, has received education funding from Pfizer, Takeda, Janssen, MSD, Dr. Falk, Shire, Ferring, Galápagos and Abbvie.

Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene/Bristol Myers, Gilead/Galapagos, Lilly, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Norgine and Vifor Pharma.

Aurelien Amiot has received consulting fees from Pfizer, Janssen, Tillotts Pharma, Takeda, and Adacyte as well as lecture fees and travel accommodations from Abbvie, Janssen, Biogen, Fresenius kabi, Takeda Pfizer, Tillotts pharma, Sandoz and Celltrion.

Hannah Gordon has received speaker fees from Janssen, Ferring, AbbVie, IBDscope and consultancy fees from Galapagos

Paulo Kotze has receive consultancy and speaking honorarium for Abbvie, Janssen, Pfizer and Takeda.

Andreas Blesl has served as speaker, consultant, and advisory member for or has received research funding from Abbvie, Aengus, Boston Scientific, Bristol-Myers Squibb, Dr. Falk Pharma, Genericon, Gilead, Janssen, Lilly, MSD, Olympus, Pfizer, Takeda, Vifo

Ignacio Catalán-Serra has received research grants and/or speaker and advisory fees from: Tillots, Takeda, Ferring, Elli Lilly, Bristol-Myers-Squidd, Janssen and Abbvie

Peter Bossuyt has received financial support for research: AbbVie, Amgen, Janssen, Viatrix, Pfizer. Lecture fees: AbbVie, Bristol Myers Squibb, CAG, Celltrion, EPGS, Galapagos, Globalport, Janssen, Lilly, Materia Prima, Pentax, Scope, Takeda. Advisory board fees: AbbVie, Arena, Bristol Myers Squibb, Celltrion, CIRC, Dr Falk Benelux, Galapagos, Janssen, Eli Lilly, Pentax, PSI-CRO, Roche, Takeda, Tetrameros

Ariella Bar Gil Shitrit reports consulting/advisory fees from Takeda, Janssen, Neopharm Pfizer and AbbVie; Speaking and teaching fees from Takeda, Janssen, AbbVie, Neopharm, Rafa, BMS, Lilly and Pfizer, and research support from Takeda and Janssen.

Paulina Molander has received speaker and consultancy fees from Abbvie, Orion Pharma, Pfizer, Sandoz, Takeda, Tillotts Pharma, and advisory board member fees from BMS, Gilead and Janssen-Cilag

G Mantzaris: has served as advisory board member for AbbVie, Celgene, Celtrion, Ferring, Genesis, Hospira, Janssen, Millennium Pharmaceuticals, Merck Sharp & Dohme, Mylan, Pharmacosmos, Pfizer, Takeda, and Vianex;

has served as a speaker for AbbVie, Angelini, Falk Pharma, Ferring, Galenica, Cenesys, Hospira, Janssen, Merck Sharp & Dohme, Omega Pharma, Takeda, and Vianex; has served as a consultant for Merck Sharp & Dohme and Takeda; and has received research support from AbbVie, Galenica, Genesis, Menarini Group, and Merck Sharp & Dohme.

Pascal Juillerat has received research grant from Vifor Pharma, consulting/ Board/speaker from AbbVie, Arena, Amgen, BMS, Ferring, Gilead, Janssen, Lilly, MSD, Pfizer, Pierre Fabre, Roche, Sandoz, Takeda, Tillots, UCB Pharma.

Krisztina B. Gecse has received research grants from Abbvie, Pfizer Inc, Celltrion and Galapagos, consultancy fees and speaker's honoraria from AbbVie, Celltrion, Ferring, Galapagos, Immunic Therapeutics, Janssen Pharmaceuticals, Pfizer Inc., Samsung Bioepis, Takeda and Tillotts.

Pär Mirelyd has received paid lectures from Abbvie, Tillotts, Galapagos, Janssen and Pfizer

Uma Mahadevan has received consultant fees from Abbvie, Arena, BMS, Boehringer Ingelheim, Celltrion, Enveda, Gilead, Janssen, Lilly, Merck/Prometheus Laboratories, Pfizer, Rani Therapeutics, Roivant, Takeda.

Beatriz Iade has served as speaker from Abbvie and Janssen.

Dana Duricova has received lecture fee/ consultancy from Janssen, Takeda, Abbvie, Pfizer, Ferring, Eli-Lilly

Mette Julsgaard has received research grants for other investigator-driven studies from Takeda and Novo Nordisk Foundation (grant no. NN-F23OC0081717), has received consultation fees from Ferring and Takeda, and has received speaker's fees from MSD, Ferring, Tillotts Pharma, and Takeda.

María Chaparro has served as speaker, consultant or research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Biogen, Gilead and Lilly.

MP340

THE MODERATING ROLE OF ADVERSE CHILDHOOD EXPERIENCES IN THE RELATIONSHIP BETWEEN CROHN'S DISEASE ACTIVITY AND THE DEVELOPMENT OF PTSD SYMPTOMS

G. Spagnolo¹, F. Di Vincenzo², M. Vecchione³, A.M. D'Onofrio⁴, G. Camardese⁴, G. Sani⁴, A. Gasbarrini⁵, G. Cammarota⁶, D.P.R. Chieffo⁷, D. Ferrarese¹, F. Scaldaferrì²

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Unit of Clinical Psychology, Roma, Italy, ²Fondazione Policlinico Universitario "A. Gemelli" IRCCS, IBD Unit- UOS Malattie Infiammatorie Croniche Intestinali, CEMAD, Digestive Diseases Center, Roma, Italy, ³Sapienza University of Rome, Department of Social and Developmental Psychology, Roma, Italy, ⁴Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Department of Neuroscience, Section of Psychiatry, Roma, Italy, ⁵Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁶Catholic University, Fondazione Policlinico Gemelli, Internal Medicine and Gastroenterology, Rome, Italy, ⁷Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Clinical Psychology Unit, Roma, Italy

Contact E-Mail Address: federica.divincenzo30@gmail.com

Introduction: Crohn's disease (CD) is a type of chronic inflammatory bowel disease (IBD) characterized by transmural granulomatous inflammation, skip lesions, and a relapsing-remitting course, which affects the entire gastrointestinal tract, from the mouth to the anus. Patients with chronic illness are at an increased risk for traumatic stress because of the medical trauma. Previous evidence suggests that many patients perceive

the chronic nature of the disease and related diagnostics and therapeutic procedures as traumatic events. Initial studies on post-traumatic stress (PTS) in patients with inflammatory bowel disease have found that approximately one-third of patients may experience significant PTS symptoms, including flashbacks, nightmares, hypervigilance, disrupted sleep, and low mood, potentially leading to the development of post-traumatic stress disorder (PTSD).

Aims & Methods: The aim of this work is to assess the moderating role of adverse childhood experiences in the relationship between CD activity and PTSD symptoms.

In this cross-sectional study, the revised version of the Impact of Event Scale (IES-R) and the Adverse Childhood Experiences (ACEs) Questionnaire were administered to consecutive CD outpatients afferent to Fondazione Policlinico Universitario "A. Gemelli", IRCCS, Rome. The clinical disease activity of patients was assessed according to the Harvey-Bradshaw index (HBI). Data were analyzed using Pearson correlation coefficients and moderated regression analyses in SPSS software (version 27).

Results: A total of 172 CD patients were included in the study, with 154 completing the IES and 148 the ACEs questionnaire. Forty-eight patients (31.2% of the sample) exhibited a score of 33 or more on the IES-R, suggestive of a PTSD. Correlation analyses revealed that ACEs scores correlated significantly with all subscales of the IES-R: intrusion ($r=.405$, $p < .001$), avoidance ($r=.348$, $p < .001$), and hyperarousal ($r=.363$, $p < .001$). Moreover, patients with higher adverse childhood experiences (i.e., with high scores on the ACEs) had significantly more severe disease activity ($r=.272$, $p < .001$). Notably, the highest scores of ACEs were observed for the items related to feeling undervalued and ignored by one's family. Further results from regression analysis demonstrated that the relationship between CD activity and the overall IES-R score was significantly stronger among patients with high ACEs scores ($b = .21$, $p < .001$) compared to those with medium ($b = .12$, $p = .005$) or low scores ($b = .06$, $p = .291$).

Conclusion: Our study revealed that ACEs play a moderating role in the relationship between disease activity and the development of PTSD symptoms in the CD patient population. Patients with higher PTS symptoms and more ACEs are less likely to be in remission and may utilize more outpatient gastrointestinal services. These findings underscore the importance of a psychological assessment to enhance the management of these patients. Intervention trials to mitigate PTS symptoms in patients with IBD are warranted.

Disclosure: Nothing to disclose.

MP341

INCREASED FAMILIAL RISK OF IBD OVER THIRTY YEARS BASED ON TWO POPULATION-BASED IBD INCIDENT COHORTS CONDUCTED IN SOUTH-EASTERN NORWAY IN 1990-1994 (IBSEN) AND IN 2017-2019 (IBSEN III)

T.B. Aabrekk^{1,2}, G. Aamodt³, Ø. Asak⁴, R. Boyar⁵, T.E. Detlie^{6,7}, S.O. Frigstad⁸, K.I.A. Holten^{7,9}, G. Huppertz-Hauss¹⁰, I. Johansen^{11,12}, V.A. Kristensen^{7,13}, R. Opheim^{12,14}, V. Strande^{7,15,16}, R. Torp¹⁷, S. Vatn¹⁸, C. Lund^{7,13}, P. Ricanek¹⁶, M.L. Høivik^{13,7}, M.B. Bengtson¹

¹Sykehuset i Vestfold Med. Clinic Dept. of Medicine, Medical dept, Tønsberg, Norway, ²Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ³LANDSAM, Norwegian University of Life Sciences, Ås, Norway, ⁴Innlandet Hospital Trust, Department of gastroenterology, Lillehammer, Norway, ⁵Diakonhjemmet Hospital, Department of Internal Medicine, Oslo, Norway, ⁶Akershus University Hospital, Department of gastroenterology, Nordbyhagen, Norway, ⁷Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ⁸Bærum Hospital, Vestre Viken Hospital Trust, Department of Internal Medicine, Gjetsum, Norway, ⁹Østfold Hospital Trust, Department of Gastroenterology, Sarpsborg, Norway, ¹⁰Telemark Hospital, Dept. of Gastroenterology, Skien, Norway, ¹¹Faculty of Health, Welfare and Org., Østfold University College, Fredrikstad, Norway, ¹²Institute of Health and Society, University of Oslo, Department of Public Health Science, Oslo, Norway, ¹³Oslo University Hospital, Department Of Gastroenterology, Oslo, Norway, ¹⁴University of Oslo, Department of Gastroenterology, Oslo University Hospital, Oslo, Norway, ¹⁵Lovisenberg Diakonale Sykehus, Unger-Vetlesens Institutt, Oslo, Norway, ¹⁶Lovisenberg Diaconal Hospital, Department of Gastroenterology, Oslo, Norway, ¹⁷Sykehuset Innlandet, Hamar Medical, Sykehuset Innlandet, Hamar, Norway, ¹⁸Innlandet Hospital Trust, Department of Internal Medicine, Gjøvik, Norway

Contact E-Mail Address: tbaabrekk@msn.com

Introduction: The highest risk factor of inflammatory bowel disease (IBD) is having a first-degree relative (FDR) with IBD. Although the prevalence of IBD in Norway is among the highest in the world, its incidence has remained steady throughout the 21st century.

Aims & Methods: In this era of stable incidence, we wanted to explore the role of a positive family history of IBD. The rate of having at least one FDR with IBD in the adult IBD population was estimated in two population-based IBD incidence cohorts conducted in South-Eastern Norway. One in 1990-1994 (IBSEN) (0.9 M inhabitants in 1992) and the second 30 years later, in 2017-2019 (IBSEN III) (2.95 M inhabitants in 2017). We compared the phenotype of IBD, age at diagnosis (AAD) with standard deviation, the distribution of disease and severity of IBD, between sporadic and familial cases of IBD in the two cohorts. Severe disease was defined as extensive colitis in Ulcerative colitis (UC), and the presence of perianal, stricturing, or penetrating disease in Crohn's disease (CD). Further, those who reported more than one FDR with IBD in the IBSEN III cohort were invited to participate in a multiplex-family IBD study. In this multiplex-family cohort, we explored the generational differences in AAD, the severity of disease, and the association between the length of shared household and the phenotype of IBD. Chi-square and t-test were used for categorical and continuous variables, respectively. Tests of equal proportions were performed to compare the rate of familial IBD in the IBSEN and IBSEN III cohorts.

Results: Overall 785 adults aged >18 years were included in the IBSEN cohort (1990-1994) and 1561 in the IBSEN III cohort (2017-2019), of whom 7.3 % (57) and 10.9% (170) reported a positive family history of IBD, respec-

tively. The rate of familial IBD increased by 49.3% ($p=0.008$) over 30 years. In the IBSEN III cohort, there were no significant differences in mean AAD between familial, 38.7 (14.5) and sporadic cases, 39.1 (15.0) of IBD ($p=0.739$), nor between mean AAD in familial CD, 39.4 (14.0) and UC, 38.4 (14.7) ($p=0.664$), compared to sporadic CD, 40.4 (15.8) ($p=0.678$) and UC, 39.2 (15.0) ($p=0.587$).

Among familial and sporadic cases of IBD, 45/170 (26.5%) and 449/1391 (32.3%) had severe disease, respectively ($p=0.124$). Of familial IBD with severe disease, 10/55 (18.2%) and 35/115 (30.4%) suffered from CD and UC, respectively ($p=0.090$).

Among sporadic cases of IBD, 87/451 (19.3%) with CD and 362/940 (38.5%) with UC suffered from severe disease ($p<0.001$). In the multiplex IBD cohort, we included 30 children and 18 parents with familial IBD. The mean AAD was 25.1 years (13.0) among the children and 33.3 years (16.5) among the parents ($p=0.063$). Eight of twenty-six children (30.8%) and 9/16 (56.3%) among the parents reported severe disease ($p=0.102$). The length of shared households within multiplex families from the initial IBD diagnosis among FDRs to subsequent diagnoses of CD or UC in others, was 11.78 years and 17.14 years, respectively ($p=0.026$).

Conclusion: The rate of a positive family history of IBD has increased substantially over thirty years, underscoring the importance of shared environmental factors for the development of the IBD diagnosis. Severe disease was associated with UC among familial cases as well as among sporadic cases of IBD. Shorter time of shared household was significantly associated with development of familial CD.

Disclosure: Vendel A. Kristensen has reported advisory boards from Takeda and Tillotts Pharma, consultant fees from Janssen Cilag, Takeda, and speaker fees from Thermo Fischer Scientific.

Marte Lie Høivik has reported investigator-initiated research grants from Takeda, Pfizer, Tillotts, Ferring and Janssen, speaker honoraria from Takeda, Tillotts, Ferring, AbbVie, Galapagos, MSD and Meda and Advisory board Takeda, Galapagos, MSD, Lilly, Janssen, Pfizer and AbbVie.

The other authors of this abstract have no Conflict of Interest.

K.B. Gecse¹, M. Chaparro², M.T. Abreu³, Y. Leung⁴, E. Sonnenberg⁵, A. McDonnell⁶, K. Lazin⁷, J. Wu⁸, C. Smith⁹, M. Dulcine¹⁰, K. Wosik¹¹, U. Mahadevan¹²

¹Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Gastroenterology, Madrid, Spain, ³University of Miami Miller School of Medicine, Department of Medicine, Division of Gastroenterology, Crohn's and Colitis Center, Miami, United States of America, ⁴University of British Columbia, Department of Medicine, Vancouver, Canada, ⁵Charité-Universitätsmedizin Berlin, Medizinische Klinik m. S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ⁶Pfizer Ltd, Sandwich, United Kingdom, ⁷Pfizer AG, Zürich, Switzerland, ⁸Pfizer Inc, Cambridge, United States of America, ⁹Pfizer Inc, Collegeville, United States of America, ¹⁰Pfizer Brazil, São Paulo, Brazil, ¹¹Pfizer Canada, Kirkland, Canada, ¹²University of California San Francisco, Colitis and Crohn's Disease Center, San Francisco, United States of America

Contact E-Mail Address: krisztina.gecse@gmail.com

Introduction: Etrasimod is an oral, once-daily, selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC) and in development for the treatment of other immune-mediated inflammatory diseases. Based on animal studies at clinically relevant doses, etrasimod may cross the placenta and cause foetal harm. This analysis describes pregnancy outcomes in patients with maternal or paternal exposure to etrasimod during its clinical development.

Aims & Methods: Reports of pregnancy or partner pregnancy during etrasimod exposure were identified from all phase 1–3 completed or ongoing open-label studies up to 31 October 2023. These studies included healthy volunteers or patients with UC, Crohn's disease, atopic dermatitis, eosinophilic esophagitis or alopecia areata. In all studies, pregnancy was an exclusion criterion, women of childbearing age were required to use contraception and study drug was discontinued in any female patient that became pregnant. Pregnancy outcomes were categorised as healthy newborn, medical termination, foetal death, congenital malformation, spontaneous abortion or lost to follow-up.

Results: In total, 2091 unique patients were exposed to etrasimod in clinical trials; 593 (28.4%) were females of childbearing age (aged 16–44). There was a total of 14 pregnancies with exposure to etrasimod (nine maternal, five paternal). All pregnancy exposures were limited to the first trimester. Median (range) age of women with maternal etrasimod exposure was 28.0 (18–36) years. Estimated length of maternal etrasimod exposure (from last menstrual period until last etrasimod dose) ranged from 22 to 79 days. Of the nine maternal exposures, pregnancy outcomes were two healthy newborns, four medical terminations (two for unknown reasons, one due to an anembryonic gestation and one following “signs of a missed pregnancy”) and one each resulting in a congenital malformation (open [patent] foramen ovale), spontaneous abortion and loss to follow-up (Table). Of the five paternal exposures, there were two healthy newborns, two spontaneous abortions and one lost to follow-up (Table).

	Foetal death	Congenital malformation	Spontaneous abortion	Healthy newborn	Medical termination	Lost to follow-up
Maternal exposure, n (%) (N = 9)	0	1 (11.1) ^a	1 (11.1)	2 (22.2) ^b	4 (44.4) ^{c,d,e}	1 (11.1) ^f
Paternal exposure, n (%) (N = 5)	0	0	2 (40.0)	2 (40.0)	0	1 (20.0)

Data on pregnancy events and outcomes were taken from the Pfizer internal data warehouse on serious adverse events that included pregnancy.

^aPremature 34-week delivery due to premature rupture of membranes, open (patent) foramen ovale (heart) with circulatory failure and transient tachypnoea of the newborn, which were all considered non-serious concomitant events.

^bBoth patients had full-term birth, caesarean delivery.

^cReasons for medical termination were not known in two cases.

^dOne patient with an anembryonic gestation where umifenovir (received for a respiratory tract infection) was a co-suspected drug. Umifenovir is contraindicated for use in pregnancy.

^eOne patient was reported as having “signs of a missed pregnancy at 5 weeks and 6 days” the day prior to elective medical pregnancy termination.

^fPatient was diagnosed as having an ectopic pregnancy prior to being lost to follow-up.

N, total number of patients; n, number of patients with a given outcome.

Table. Pregnancy outcomes during the etrasimod clinical development programme.

Conclusion: Few pregnancies have been reported in the etrasimod clinical programme, with no clear trends on the risk of maternal or paternal etrasimod exposure. Ongoing etrasimod studies and larger post-marketing registries will further inform on the safety of etrasimod during pregnancy. Women of child-bearing potential should use birth control while on etrasimod.

Disclosure: KBG has received research support from Celltrion, Galapagos, and Pfizer Inc; speakers' honoraria and/or consulting fees from AbbVie, Celltrion, Ferring Pharmaceuticals, Immunic Therapeutics, Janssen, Novartis, Pfizer Inc, Samsung Bioepis, Takeda, and Tillotts. MC is a consultant/advisor for Gilead, Janssen, Lilly, Pfizer Inc, Takeda and Tillotts; has received grant/research support from Galapagos, Janssen and Pfizer Inc; is an investigator for AbbVie, Boehringer Ingelheim Ltd., Celgene, F Hoffman La Roche, Genentech, Hospira, Janssen Cilag International LV, Janssen Cilag International NV, Millenium Pharmaceuticals, Shield, Shire and Takeda and principal investigator for AbbVie, Ferring Pharmaceuticals, Janssen, MSD and Takeda. MTA is a consultant for Janssen, Prometheus Bioscience, Takeda, Gilead, Eli Lilly, AbbVie Inc, Amgen, Arena Pharmaceuticals, Bristol Myers, Celsius, Microba Life Sciences, Pfizer, UCB Biopharma, Prometheus and Janssen Biotech Inc. YL is an advisory committee/board member for Takeda, Pfizer, Eli Lilly, Janssen, AbbVie, Celltrion, Sandoz and consultant for Takeda, Pfizer, Eli Lilly, Janssen and AbbVie. ES is a consultant for AbbVie and Janssen and has received speaker fees from Biogen, Dr. Falk Pharma, Janssen, AbbVie, Takeda, BMS, Celltrion and CED Service GmbH. AM is an employee of Pfizer Ltd and shareholder of Pfizer Inc. KL is an employee of Pfizer AG and shareholder of Pfizer Inc. JW, CCS and MD are employees and shareholders of Pfizer Inc. KW is an employee and shareholder of Pfizer Canada Inc. UM is an advisory/committee board member for Merck (DSMB) and Rana Therapeutics; consultant for AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Enveda, Gilead, Janssen, Lilly, Pfizer, Protagonist, Roivant and Takeda and has received grant/research support from Leona and Harry Helmsley Trust.

MP344

RISK OF RAPIDLY PROGRESSIVE DISEASE COURSE IN PATIENTS WITH PEDIATRIC-ONSET ULCERATIVE COLITIS

G. D'Arcangelo¹, T. Raso¹, F. Ammattatelli¹, M. Distante¹, S. Rotulo¹, F. Zucconi¹, M. Aloï¹

¹Sapienza University of Rome, Pediatric Gastroenterology Unit, Rome, Italy

Contact E-Mail Address: giuliadarcangelo87@gmail.com

Introduction: Ulcerative colitis (UC) disease course is unpredictable at the diagnosis and its management is still based on a "one-size-fits-all" approach.

Aims & Methods: We aimed to investigate the predictive factors of a rapidly progressive disease course in pediatric UC.

This was a retrospective case-control study conducted at the Pediatric Gastroenterology Unit of Umberto I Hospital in Rome. We included newly diagnosed UC patients aged < 18 years, with a minimum follow-up of 24 months. Demographic data, clinical features, laboratory, endoscopic and histologic findings at the diagnosis were collected and compared between patients with indolent UC and those with a rapidly progressive (RP) course. Children were classified as having a RP course if they experienced at least one of the following within the first 24 months after diagnosis: acute severe colitis, need for colectomy, necessity to transition to anti-TNF- α therapy, or initiation of second-line biologic therapy.

Results: One hundred-sixteen patients were included, 67 (58 %) with a RP course and 49 (42 %) with an indolent disease. RP Children had higher age (11.5 vs 9, $p=0.0008$), PUCAI (50 vs 40, $p=0.0005$) and UCEIS (4 vs 3, $p=0.002$) at the diagnosis than those with indolent course. Hemoglobin was lower in the RP group (11.5 vs 12.3 g/dL, $p=0.05$). RP children had higher rate of cecal patch at endoscopy (18 % vs 2 % $p=0.007$) and a lower rate of sclerosing cholangitis (0 vs 8.2%, $p=0.02$). No differences were observed for all other clinical, laboratory, and histologic findings. Multivariate analysis confirmed that age and the presence of a cecal patch were associated with the risk of RP course ($p=0.02$, and $p=0.04$, respectively).

Conclusion: Among the clinical and easily obtainable information at the diagnosis in children with UC, an older age at the diagnosis, along with an endoscopic finding of a cecal patch seem associated with the risk of a more aggressive disease. Such results warrant confirmation in larger prospective cohorts for a future personalized approach to UC.

Disclosure: Nothing to disclose.

MP345

RISK OF RELAPSE AFTER ANTI-TNF WITHDRAWAL IN PAEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASES: A POPULATION BASED-STUDY

D. Ley¹, A. Leroyer², K. Bouhout³, C. Dupont-Lucas⁴, D. Turck¹, V. Bertrand⁵, N. Guillon², P. Wils⁶, N. Richard⁷,

C. Gower-Rousseau⁸, G. Savoye⁹, H. Sarter², M. Fumery¹⁰

¹Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE, Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Lille, France, ²Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE, Public Health, Epidemiology and Economic Health Unit, Lille, France, ³CHU Lille, Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Lille, France, ⁴Caen University Hospital, Pediatrics, Caen, France, ⁵Le Havre Hospital, Department of Pediatrics, Le Havre, France, ⁶Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE, Division of Gastroenterology, Lille, France, ⁷CHU Rouen, Gastroenterology, Rouen, France, ⁸CHU Reims, Research Unit and Public Health, Reims, France, ⁹CHU Rouen, UMR 1073 University of Rouen Normandy, Gastroenterology Unit, Rouen, France, ¹⁰Amiens University Hospital, Gastroenterology Department, Amiens, France

Contact E-Mail Address: delphine.ley@chru-lille.fr

Introduction: Anti-TNF are the first biologic treatment option in inflammatory bowel diseases (IBD). Few data is available on the long term risk of relapse after anti-TNF withdrawal in paediatric-onset IBD, especially at the population level.

Aims & Methods: All paediatric-onset (<17 years) IBD diagnosed between 1988 and 2011 were included in a prospective population-based study and were retrospectively followed until 2013. Among patients treated with first-line anti-TNF, the cumulative probability of relapse after anti-TNF withdrawal was evaluated using a composite outcome (intestinal resection, and/or flare-related hospitalization, and/or IBD treatment initiation, and/or active disease). Factors associated with relapse were investigated with a Cox model.

Results: Among a total of 1,344 patients (Crohn's disease (CD): $n=1,007$; Ulcerative colitis (UC): $n=337$), 562 were treated with anti-TNF. Anti-TNF was stopped in 73 patients (CD: $n=66$; UC: $n=7$) during remission defined by Harvey-Bradshaw score < 4 in CD and Mayo score ≤ 2 in UC. Among them, median time to anti-TNF initiation was 1.6 years (IQR, 0.7-4.0) and median duration of treatment was 1.0 year (0.3-1.7). The first line anti-TNF therapy was infliximab in 68 (93%) patients. At anti-TNF withdrawal, 47 (64%) patients received immunosuppressant. The cumulative probability of relapse after anti-TNF withdrawal at 1, 3 and 5 years was respectively 62%, 85% and 93%. Median delay of relapse was 9.5 months (7.5-12.0). The cumulative probability of flare-related hospitalization at 1, 3 and 5 years was respectively 7%, 7% and 8%. No patient required intestinal resection after a median follow-up of 8.7 (5.8-13.8) years. In multivariate analysis, median time to anti-TNF initiation >1 year was the only factor associated with the risk of relapse (HR 0.58, CI95% [0.35-0.97], $p=0.036$). Among relapsers, 46 (63%) were retreated with anti-TNF. Retreatment with anti-TNF was effective in 45 (98%) patients after a median delay of 3.9 months (3.5-10.0). Infusion reaction occurred in only 2 patients.

Conclusion: In a population-based cohort of paediatric-onset IBD, the risk of relapse after anti-TNF withdrawal was high, but was not associated with major complication. Retreatment with anti-TNF was effective and well tolerated.

Disclosure: Consultant fees from Sandoz and AbbVie.

HPB: Autoimmune pancreas and liver

13:00-14:00 / Poster Stage 3

MP346

CHRONIC LIVER DISEASE PATIENTS PRESENT A WEAK SARS-COV-2-SPECIFIC CELLULAR IMMUNE RESPONSE

C.S. Palma¹, M. Henrique¹, A.L. Simão¹, A.G. Santos¹, M. Cardoso¹, D.A. Fernandes¹, S. Carvalhana², M. Carneiro de Moura², J. Gonçalves¹, H. Cortez-Pinto³, R. Castro¹
¹Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal, ²Hospital de Santa Maria Dept. of Gastroenterology, Lisboa, Portugal, ³Faculdade de Medicina de Lisboa, Centro Hospitalar Lisboa Norte, HSM, Clínica Universitária de Gastroenterologia, Laboratório de Nutrição, Departamento de Gastroenterologia, Lisbon, Portugal

Contact E-Mail Address: carolina-palma@campus.ul.pt

Introduction: Patients with chronic liver disease (CLD), particularly those with cirrhosis, exhibit increased risk of developing severe illness when infected with SARS-CoV-2, primarily due to their underlying immune dysfunction and coexisting conditions. As such, vaccination plays a crucial role in safeguarding this population. Here, to fully assess the efficacy COVID-19 vaccination in patients with CLD, we thoroughly characterized the overall and SARS-CoV-2-specific cellular immune response of these patients.

Aims & Methods: Blood samples were systematically collected from patients with CLD (n=22) and healthy volunteers (n=12) at various intervals spanning one year after the initial administration of the BNT162b2 vaccine. Peripheral blood mononuclear cells (PBMCs) were isolated and stained with a panel of 22 surface markers and a viability dye, allowing for the detection of 28 immune cell subsets. In parallel, we analysed the presence of cells specific against SARS-CoV-2 peptide tetramers. Samples were analysed by flow cytometry with acquisition on a four-laser Cytex Aurora® spectral analyzer.

Results: Prior to vaccination, patients with CLD patients were already displaying fewer T cells and an increased number of B cells, comparing to healthy subjects. Within the T cell subsets, differences were significant for CD4+ T cells and the Naïve and Central Memory CD4+ subsets. At both 6-months and 1- year after vaccination, variances between groups were no longer observed. Rather, at 1-year postvaccination, T, CD8+ and CD4+ cells, as well as monocytes were found increased in both groups, suggesting that the vaccination is critical for inducing a strong cellular immune response. Analysis of SARS-CoV-2 epitope-specific cells demonstrated significantly lower frequencies of monocytes, CD4+ and CD8+ T cells, B cells, NK T cells, and NK cells including the regulatory and cytotoxic subsets recognizing the peptide tetramers in CLD patients, in comparison with healthy controls.

Conclusion: Together, these results indicate that CLD patients are capable of mounting a satisfactory immune cellular response following COVID-19 vaccination. However, the SARS-CoV-2-specific response is significantly weaker in CLD patients comparing with healthy individuals. These results reinforce the need for prioritization and/or booster vaccination for CLD patients. (Supported by 2022.08837.PTDC, FCT).

Disclosure: Nothing to disclose.

MP347

IMMUNOSUPPRESSIVE THERAPY ENABLES HEPATIC RECOMPENSATION IN DECOMPENSATED CIRRHOSIS DUE TO AUTOIMMUNE HEPATITIS – A PILOT STUDY

B. Hofer^{1,2,3,4}, L. Burghart⁵, S. Treiber¹, E. Halilbasic^{1,4}, M. Mandorfer^{1,2}, M. Trauner^{1,4}, T. Reiberger^{1,2,3,4}, A.F. Stättermayer^{1,4}

¹Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Vienna, Austria, ²Medical University of Vienna, Hepatic Hemodynamic Laboratory, Vienna, Austria, ³Medical University of Vienna, Christian Doppler Lab for Portal Hypertension and Liver Fibrosis, Vienna, Austria, ⁴Rare Liver Diseases (RALID) Center of the ERN RARE-LIVER at the Vienna General Hospital, Vienna, Austria, ⁵Klinik Ottakring, Wiener Gesundheitsverbund, Vienna, Austria

Contact E-Mail Address: Benedikt.S.Hofer@meduniwien.ac.at

Introduction: Autoimmune hepatitis (AIH) is associated with an increased risk of developing cirrhosis and progressing to hepatic decompensation. While a successful treatment of the underlying aetiology has been shown to enable hepatic recompensation in some aetiologies of cirrhosis, implications of recompensation have not yet been assessed in decompensated cirrhosis due to AIH.

Aims & Methods: In this pilot study, we assessed the incidence and prognostic role of hepatic recompensation in patients with decompensated cirrhosis (F3/F4 histology) due to AIH (simplified AIH score ≥ 6). Patients were included at first hepatic decompensation, marked by the first occurrence of ascites, variceal bleeding or hepatic encephalopathy (HE). Patients with acute liver failure were excluded due to the indication of the high urgency liver transplantation. In accordance with the Baveno VII criteria, recompensation was defined as (i) resolution of ascites and HE despite cessation of all diuretics and anti-HE therapies, (ii) absence of variceal bleeding and (iii) sustained improvement in hepatic synthetic function (bilirubin, albumin, INR) to Child-Pugh A values. Successful aetiological control in AIH was defined as a complete biochemical response under immunosuppressive therapy, i.e., a normalisation of transaminases and immunoglobulin G.

Results: Twenty-one patients with cirrhosis due to AIH (90.5% female, age: 54.6 [39.8-61.6] years) were included at time of first decompensation (85.7% ascites, 14.3% variceal bleeding) and followed for a median of 80.4 (14.6-133.0) months. The median MELD at decompensation was 15 (11-18). Clinically, decompensation occurred in two scenarios, resulting in two distinct patient subgroups: In the first subgroup (n=10; 47.6%), patients had already been diagnosed with AIH prior to hepatic decompensation and decompensation occurred despite ongoing immunosuppressive treatment (median treatment duration: 128 [70-164] months). Decompensation in this subgroup was primarily the result of an insufficient biochemical response and none of these patients achieved hepatic recompensation. In the second subgroup, which included 11 patients (52.4%), the diagnosis of AIH was first established in the context of index decompensation. Out of these 11 patients, 5 (45.5%) did not receive immunosuppressive treatment until more than 1 month after decompensation. This delay was mainly a consequence of a delayed diagnosis and none of these patients recompensated. In contrast, in the other 6 patients (54.5%), both the diagnosis of AIH and immunosuppressive treatment were established within less than 1 month after decompensation, resulting in hepatic recompensation in 4 patients. Notably, all recompensated patients achieved a 50% decrease in transaminase levels after 4 weeks of treatment. With regard to clinical outcomes, the 4 recompensated patients survived for 62.6, 101.3, 106.3 and 202.3 months, respectively, without the need for liver transplantation. In contrast, 6 of the 17 patients who remained de-

compensated died (35.3%, all liver-related) after a median of 32.8 (15.1-58.5) months and 4 (23.5%) required liver transplantation (after median 37.5 [15.9-57.1] months).

Conclusion: In AIH patients who first present with decompensated cirrhosis, a timely diagnosis followed by a prompt initiation of immunosuppressive treatment is associated with a higher probability of recompensation and improved survival. In contrast, decompensation despite ongoing immunosuppressive therapy is associated with a poorer prognosis.

Disclosure: MM served as a speaker and/or consultant and/or advisory board member for AbbVie, Collective Acumen, Gilead, and W. L. Gore & Associates and received travel support from AbbVie and Gilead.

MT has received research grants from Albireo, Alnylam, Cymabay, Falk, Gilead, Intercept, MSD, Takeda and Ultragenyx and travel grants from AbbVie, Falk, Gilead, Intercept and Janssen. He further has advised for AbbVie, Albireo, BiomX, Boehringer Ingelheim, Falk Pharma GmbH, Genfit, Gilead, Hightide, Intercept, Janssen, MSD, Novartis, Phenex, Pliant, Regulus, Siemens and Shire and has served as speaker for BMS, Falk, Gilead, Intercept, Madrigal and MSD. He is a co-inventor of patents for the medical use of norUDCA (nor-ursodeoxycholic acid/norucholic acid) filed by the Medical Universities of Graz and Vienna.

TR received grant support from AbbVie, Boehringer-Ingelheim, Gilead, MSD, Philips Healthcare, Gore; speaking honoraria from AbbVie, Gilead, Gore, Intercept, Roche, MSD; consulting/advisory board fee from AbbVie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from Boehringer-Ingelheim, Gilead and Roche.

MP348

IMMUNOREGULATORY MYELOID CELLS COUNTERACT T CELL HYPERACTIVATION-INDUCED LIVER INFLAMMATION BY EXTRACELLULAR VESICLE-MEDIATED PURINE METABOLIC REGULATION

F. Yang¹, R. Men¹, J. Lin¹, J. Liu², L. Yang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology and Laboratory of Gastrointestinal Cancer and Liver Disease, Chengdu, China, ²West China Hospital of Sichuan University, NHC Key Laboratory of Transplant Engineering and Immunology, Frontiers Science Center for Disease-related Molecular Network, Chengdu, China

Contact E-Mail Address: 2021181620212@stu.scu.edu.cn

Introduction: Dysregulated T-cell immune response-mediated inflammation is implicated in various liver diseases, yet mechanisms governing liver immune homeostasis control and therapies for limiting T-cell overactivation remain unclear. This study aims to elucidate the role of immunoregulatory myeloid cells (Mregs) in liver injury and their potential to modulate CD4⁺ T-cell hyperactivation via extracellular vesicle (EV)-mediated metabolic regulation.

Aims & Methods: Concanavalin A (ConA) mice and autoimmune hepatitis (AIH) patients were examined for alterations in purine metabolism associated with liver injury severity and therapeutic response. The expression of extracellular purine catabolism nucleases, such as CD39 and CD73, on CD11b⁺Gr-1⁺ myeloid cells (MCs) was assessed, with particular focus on liver injury conditions. The study investigated the natural expansion of the CD39⁺CD73⁺Gr-1^{high}CD11b⁺ regulatory MC (Mreg) subset during early liver injury phases and its effects on CD4⁺ T-cell hyperactivation and liver injury through in vitro and in vivo experiments. Mechanistic insights into Mreg-mediated immunosuppression were explored, particularly regarding the release of CD73^{high} EVs and their impact on extracellular AMP conversion, cAMP pathway activation, and inhibition of glycolysis and cytokine secretion in activated CD4⁺ T cells.

Results: Alterations in purine metabolism were observed in ConA mice

and AIH patients, correlating with liver injury severity and therapeutic response. CD39 and CD73 expression was markedly upregulated on CD11b⁺Gr-1⁺ myeloid cells under liver injury conditions. The CD39⁺CD73⁺Gr-1^{high}CD11b⁺ Mreg subset expanded naturally during early-stage liver injury and demonstrated efficacy in suppressing CD4⁺ T-cell hyperactivation and liver injury both in vitro and in vivo. The release of CD73^{high} EVs by Mregs facilitated extracellular AMP conversion to immunosuppressive metabolites (e.g., adenosine and inosine), activating the cAMP pathway and inhibiting glycolysis and cytokine secretion in activated CD4⁺ T cells.

Conclusion: These findings shed light on the mechanisms governing immune homeostasis during early liver injury and suggest that Mreg or Mreg-EV therapy may offer a targeted approach for preventing diverse liver diseases induced by T-cell overactivation.

Disclosure: Nothing to disclose.

MP349

ASSOCIATION OF SARCOPENIA ASSESSED BY CT/MRI WITH TREATMENT RESPONSE AND CLINICAL OUTCOMES IN NONCIRRHOTIC PRIMARY BILIARY CHOLANGITIS PATIENTS

L. Zhou¹, B. Li², X. Ao¹, X. Wang¹, Y. Zheng¹, Q. Deng¹, X. Fan¹, L. Yang¹

¹West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology and Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, Chengdu, China, ²West China Hospital, Sichuan University, Department of Radiology, Chengdu, China

Contact E-Mail Address: reciyazhou@foxmail.com

Introduction: Research about sarcopenia in primary biliary cholangitis (PBC) patients is limited while sarcopenia commonly occurs in cirrhotic patients. Concomitant sarcopenia in noncirrhotic PBC patients has been rarely explored yet.

Aims & Methods: This study aimed to investigate the prevalence of sarcopenia and the associations between concomitant sarcopenia at baseline and biochemical response to UDCA treatment and clinical outcomes in noncirrhotic primary biliary cholangitis (PBC) patients.

Between January 2009 and July 2022, consecutive PBC patients were retrospectively enrolled. Sarcopenia was assessed via pretreatment CT or MRI scans at the L3 level by the skeletal muscle index. Baseline characteristics, the response rate after 6 and 12 months of ursodeoxycholic acid (UDCA) administration, liver-related adverse events and baseline CRP and IL-6 levels in liver tissue and serum were evaluated.

Results: A total of 142 noncirrhotic PBC patients were included, with sarcopenia identified in 58 (40.8%) patients. The median duration of follow-up was 5.25 (3.23, 6.50) years. The group of PBC patients with sarcopenia demonstrated a lower biochemical response rate (44.9% vs. 64.8%; P=.031) according to the Paris-II criteria after 12 months of UDCA treatment, as well as higher incidence of new-onset ascites (28.1% vs. 13.1%, P=.027) during follow-up. Higher expression levels of baseline CRP and IL-6 in liver tissue and serum were observed in PBC patients with sarcopenia (P<.05).

Conclusion: Sarcopenia was highly prevalent in noncirrhotic PBC patients. Expression levels of baseline CRP and IL-6 in liver tissue and serum were elevated in noncirrhotic PBC patients with sarcopenia. Concomitant sarcopenia at baseline may adversely affect the biochemical response to UDCA treatment and occurrence of liver-related adverse events in PBC patients without cirrhosis.

Disclosure: Nothing to disclose.

MP350

DESIGN AND STUDY POPULATION OF MITIGATE: THE FIRST MULTINATIONAL RANDOMIZED CONTROLLED CLINICAL TRIAL IN IGG4 RELATED DISEASE, EVALUATING THE EFFICACY AND SAFETY OF THE CD19 B CELL DEPLETING AGENT INEBILIZUMAB

E.L. Culver¹, A. Khosroshahi², W. Zhang³, E. Della-Torre⁴, K. Okazaki⁵, Y. Tanaka⁶, M. Löhr⁷, N. Schleinitz⁸, L. Dong⁹, H. Umehara¹⁰, M. Lanzillotta⁴, Z.S. Wallace¹¹, M. Ebbo⁸, G. Webster¹², Y. Wu¹³, D. Cimbora¹³, N. Rampal¹³, J.H. Stone¹¹
¹John Radcliffe Hospital Translational Gastroenterology, Nuffield Department of Medicine, Oxford, United Kingdom, ²Emory University School of Medicine, Division of Rheumatology, Atlanta, United States of America, ³Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, National Clinical Research Center for Dermatologic and Immunologic Diseases, Department of Rheumatology and Clinical Immunology, Beijing, China, ⁴San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy, and Rare Diseases, Milan, Italy, ⁵Kansai Medical University, Department of Gastroenterology and Hepatology, Osaka, Japan, ⁶University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan, ⁷Karolinska Institutet, Center for Digestive Diseases, Stockholm, Sweden, ⁸Aix-Marseille Université, Département de Médecine Interne Hôpital de la Timone, AP-HM, Marseille, France, ⁹Tongji Hospital of Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China, ¹⁰Nagahama City Hospital, Shiga, Japan, ¹¹Massachusetts General Hospital, Harvard Medical School, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America, ¹²University College Hospital, Pancreatobiliary service, Gastrointestinal services, Endoscopy Unit, London, United Kingdom, ¹³Amgen Inc., Rockville, United States of America

Contact E-Mail Address: emma.culver@ndm.ox.ac.uk

Introduction: The roles of B cells in the pathophysiology of IgG4 Related Disease (IgG4-RD) and existing clinical experience suggest that B cell depletion may be an effective therapeutic avenue. Inebilizumab is a humanized, glycoengineered CD19-directed monoclonal antibody that effectively and selectively depletes B cells. The Phase 3 MITIGATE trial (NCT04540497) is a randomized, double-blinded, placebo-controlled trial that aims to demonstrate the efficacy and safety of inebilizumab monotherapy in reducing the risk of IgG4-RD relapse.

Aims & Methods: The MITIGATE study is being conducted at 80 sites in 22 countries. The study enrolled adult IgG4-RD patients who met the ACR/EULAR Classification Criteria for IgG4-RD with a score of at least 20 as determined by an Eligibility Committee (EC). Eligibility criteria included a history of multiorgan disease and active disease at the time of screening to increase the risk of flares for the primary endpoint. Subjects were stratified based on newly diagnosed (46%) vs. recurrent (54%) disease to control for potential differences in flare risk.

The primary endpoint is time to first Adjudication Committee-determined and investigator-treated IgG4-RD flare during the 12-month randomized controlled period. The study is event-driven and is powered on the accrual of 39 disease flares, which was anticipated to require 160 subjects.

To permit evaluation of inebilizumab as monotherapy, other immunosuppressive agents are prohibited. Glucocorticoids were normalized to 20 mg/day prednisone at the time of randomization and were tapered to discontinuation at the end of study week 8.

Results: Enrolment completed in April 2023 with 135 subjects enrolled. The mean age was 58.2 years and 65% were male. Time since diagnosis ranged from 0.1 to 20.5 years (median 0.9 years). Baseline ACR/EULAR

Classification Criteria scores ranged from 20 to 74. The number of organs affected by IgG4-RD up to the time of enrolment varied from 2 to 13, with 2-3 organs affected in 41% of subjects and ≥ 6 organs affected in 24% of subjects. The pancreas, bile ducts, and liver were affected in 52%, 31%, and 7% of subjects respectively. Hepatobiliary disease was accompanied by pancreatic involvement in 95% of cases, but only 59% of those with pancreatic involvement also had hepatobiliary disease. The submandibular, lacrimal, and parotid glands, lymph nodes, kidney, sinuses, and lungs were each affected in at least 20% of the study population. These findings suggest that the study population carries substantial pancreatic and hepatobiliary disease burden and is representative of real-world IgG4-RD cohorts.

Conclusion: MITIGATE enrolled a representative IgG4-RD population in terms of both number and distribution of organs affected. More than half of participants had hepato-pancreato-biliary disease, and hepatobiliary disease without pancreatic involvement was rare. Trial results are expected in 2024 and aim to establish the safety and efficacy of CD19-targeted B cell depletion by inebilizumab in IgG4-RD, potentially leading to the first approved treatment for this disease.

Disclosure: E.L. Culver, A. Khosroshahi, W. Zhang, M. Lanzillotta, Z.S. Wallace have received consulting fees from Amgen Inc. E. Della-Torre received consulting fees from Amgen Inc. and Horizon Therapeutics as member of Advisory Boards and of the Adjudication Committee during the MITIGATE Trial. Y. Tanaka has received speaking fees and/or honoraria from Eli Lilly, AstraZeneca, Abbvie, Gilead, Chugai, Behringer-Ingelheim, GlaxoSmith-Kline, Eisai, Taisho, Bristol-Myers, Pfizer, Taiho, received research grants from Mitsubishi-Tanabe, Eisai, Chugai, Taisho. N. Schleinitz has participated in advisory boards and received consulting fees from Viela Bio and Horizon Therapeutics. K. Okazaki, M. Löhr, L. Dong, H. Umehara, M. Ebbo, G. Webster have nothing to disclose. Y. Wu, D. Cimbora, and N. Rampal are employees of Amgen Inc. and hold stock. J.H. Stone has consulted for Amgen on the topics of IgG4-related disease, vasculitis, and glucocorticoid toxicity.

Study and abstract were funded by Amgen Inc. with medical writing support provided by Amy Cohen, PhD, Amgen Inc.

MP351

THE ROLE OF TRANSIENT ELASTOGRAPHY AND ENHANCED LIVER FIBROSIS SCORE IN THE HEPATO-PANCREATO-BILIARY PHENOTYPE OF IGG4-RELATED DISEASE

S. Kaur¹, R. Motta², C. Mercer¹, E. Culver²

¹Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, ²University of Oxford, Translational Gastroenterology and Liver Unit, Nuffield Department of Medicine, Oxford, United Kingdom

Contact E-Mail Address: rodrigo.vieiramotta@ndm.ox.ac.uk

Introduction: IgG4-related disease of the liver, pancreas, and bile ducts (IgG4-HPB) can lead to fibrosis and organ damage. Liver stiffness measurement (LSM) by vibration-controlled transient elastography and Enhanced liver fibrosis (ELF) score are validated, non-invasive methods for measuring liver fibrosis in other chronic liver diseases, but little is known about their utility in IgG4-HPB.

Aims & Methods: The aim of this study is to assess LSM using Fibroscan® and ELF in patients with IgG4-HPB. This is a retrospective observational cohort of patients meeting the ACR/EULAR classification criteria for IgG4-Related Disease at Oxford University Hospitals. Clinical data collected included demographics, organ involvement, clinical flares, serum biomarkers and organ damage. LSM was recorded in 55 IgG4-HPB patients, and sequential LSM was recorded in 32 patients. Serum ELF was

measured in 23 patients. Wilcoxon rank, Mann-Whitney U, and Fisher's exact tests were performed.

Results: Ninety-seven patients with IgG4-HPB were included; median age was 68 years $\pm$ 19, and 79% were male. Among the entire cohort, 69% had established organ dysfunction and/or damage and, when subdivided by organ involvement, damage was present in 72% of those with liver and biliary disease (IgG4-HB) and 65% of those with pancreatic disease only (IgG4-AIP) (Table 1).

	Overall cohort (n = 97)	HPB cohort (n = 57)	AIP cohort (n = 40)	p-value
Median age (IQR)	67.5 (19)	68.5 (19)	65.5 (18)	0.91
Men	77 (79%)	44 (77%)	33 (82%)	0.61
Established organ damage	67 (69%)	41 (72%)	26 (65%)	>0.99
Diabetes	33 (34%)	26 (46%)	12 (29%)	0.14
Cardiometabolic disease	41 (42%)	22 (39%)	20 (49%)	0.11
MASLD	19 (20%)	13 (23%)	6 (15%)	0.59
Mean cumulative steroid dose (SD)	7326 (17468)	9012 (21263)	4260 (3074)	0.32
Median number of flares (IQR)	1 (2)	1 (2)	0 (1)	0.25

LSM was recorded in 55 patients: IgG4-HB (n = 38) had a higher mean LSM compared with IgG4-AIP (n = 17) (6.1 kPa vs 5 kPa, p = 0.04). IgG4-HB were risk-stratified by LSM: 66% had LSM <8kPa, 21% had LSM $\geq$ 8 but <12kPa, and 13% had LSM $\geq$ 12kPa. There was a higher prevalence of metabolic associated steatotic liver disease (MASLD) and its metabolic factors (diabetes, hypertension, hypercholesterolemia, and ischaemic heart disease) in those with more advanced liver fibrosis (LSM $\geq$ 12 kPa). Furthermore, survival analysis showed that patients with LSM $\geq$ 8kPa develop organ damage faster than those with LSM < 8kPa (p=0.0086).

In longitudinal analysis, 32 patients with IgG4-HPB had serial LSMs. Of those with IgG4-HB (n = 22), 23% showed an increase in LSM over a median of 2 years (IQR 1-4). The proportion of patients meeting criteria for MASLD increased from 20% to 25% over a median of two years. In those with paired readings during active disease and remission (n = 8), there was no discernible variation in LSM.

Twenty-three patients with IgG4-HPB had an ELF test and were stratified by the score: 13/23 (56%) <9.8 and 10/23 (43%) $\geq$ 9.8. ELF accurately identified patients with more significant liver fibrosis; no patient with LSM $\geq$ 8kPa was seen in the <9.8 group (p = 0.0021). There was no association of ELF with disease activity or serum biomarkers.

Conclusion: This is the first study assessing the role of LSM by Fibroscan® and of ELF score in patients with IgG4-HPB. An increased LSM over time was associated with the accumulation of cardiometabolic risk factors, evidence of MASLD, and end-organ damage, while ELF score ruled out advanced fibrosis in this cohort concurrently.

Disclosure: EC: Speaking Fees: Horizon Therapeutics, Advanz (Intercept), Albireo, Dr Falk Pharma, Gilead, GSK; Consulting Fees: Advanz (Intercept), Horizon Therapeutics, Ipsen, Mirum, Moderna, Sanofi, Zenus Pharma; Grant Support: Jansen, Innovate UK, PSC Support, Wellcome Trust; Institutional Funding Support: BRC Oxford NIHR (UK), Oxford Charitable Fund, Research Capability Fund.

SK, RM and CM have nothing to declare.

MP352

DECODING THE ROLE OF NEUTROPHIL EXTRACELLULAR TRAPS IN AUTOIMMUNE HEPATITIS: IMPACTS ON MACROPHAGE EFFEROCYTOSIS AND MTOR PATHWAY INTERACTIONS

S. Wang¹, D. Tian¹

¹Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Contact E-Mail Address: d202282081@hust.edu.cn

Introduction: Autoimmune hepatitis (AIH) is a chronic liver disease characterized by elevated immunoglobulin G (IgG), autoantibodies, and interface hepatitis. Its incidence is rising globally, while current treatments often fall short and carry significant adverse effects. In AIH, hepatocytes are prone to apoptosis from immune attacks, yet impaired clearance leads to inflammation from accumulated apoptotic cells.

Neutrophil extracellular traps (NETs) contain granule proteins, DNA, and RNA, playing a role in autoimmune responses. They can expose self-antigens, potentially worsening autoimmune reactions. NETs' role in AIH and their effect on apoptotic cell clearance require further exploration. Macrophage efferocytosis is key for immune tolerance in the liver, with disruption leading to broader inflammation and efferocytosis escape. This study investigates the impact of NETs on macrophage efferocytosis and metabolism in AIH, seeking therapeutic targets to enhance liver health.

Aims & Methods: This study aims to explore the role of NETs in the pathogenesis of AIH, elucidating the molecular mechanisms by which NETs influence efferocytosis in hepatic macrophages within the context of AIH.

Six-to-eight-week-old male C57 mice were used to create AIH models in a specific-pathogen-free (SPF) setting. Flow cytometry was used to measure changes in neutrophil levels in the liver of AIH model mice and in the peripheral blood of patients. NETs levels in serum and liver tissue were determined through ELISA and immunohistochemistry. Macrophage phagocytosis of apoptotic cells was evaluated using multiplex immunofluorescence with confocal microscopy and flow cytometry. Glycolysis levels in macrophages were assessed with a Seahorse metabolic analyzer, and transcriptomic sequencing explored underlying mechanisms, with confirmation through Western blot analysis. Histopathological changes in the liver were examined with hematoxylin and eosin (H&E) staining, while Sirius Red staining assessed fibrosis. Serum levels of alanine transaminase and aspartate transaminase were used to gauge liver damage.

Results: Autoimmune hepatitis (AIH) features a reduced efferocytosis index in the liver, with fewer macrophages conducting efferocytosis and increased apoptotic cells. AIH mouse models reveal a significant rise in liver neutrophils, while AIH patients show an accumulation of neutrophil extracellular traps (NETs) in their livers and peripheral blood. Macrophages pretreated with NETs exhibit decreased phagocytosis of apoptotic cells. When DNase I clears NETs in AIH mice, liver inflammation and fibrosis are reduced, and apoptotic cells decrease. A comparison between AIH model mice with and without NETs clearance demonstrates a significant increase in efferocytosis by macrophages, while unengulfed apoptotic cells decline. Glycolysis in macrophages is significantly inhibited after NETs intervention, with the mTOR pathway showing downregulation, confirmed by Western blot analysis. However, when macrophages are pretreated with an mTOR-specific agonist, glycolysis levels and efferocytosis are restored compared to controls.

Conclusion: In AIH, increased levels of NETs or their components in the liver bind to TLR8 receptors, leading to downregulation of the mTOR pathway in hepatic macrophages. This interaction triggers metabolic reprogramming, inhibiting glycolysis and affecting cytoskeletal integrity. The resulting suppression of efferocytosis leads to an abnormal accumulation of apoptotic cells, which contributes to AIH progression.

Disclosure: Nothing to disclose.

MP353

CD177⁺ NEUTROPHILS EXERT PROTECTIVE EFFECT IN EXPERIMENTAL AUTOIMMUNE HEPATITIS

Y. Shen¹, T. Jia¹, C. Huang¹, M. Shen¹, X. Fan¹, R. Men¹, L. Yang¹

¹West China Hospital, Department of Gastroenterology and Hepatology and Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, Frontiers Science Center for Disease-related Molecular Network, West China Hospital, Sichuan University, Chengdu, China

Contact E-Mail Address: 156450779@qq.com

Introduction: Neutrophils could be recruited into liver in autoimmune hepatitis (AIH) and experimental AIH (Concanavalin A induced hepatitis), but the role of neutrophils in these kinds of immune related hepatitis has rare research to clarify. As previous reports, CD177 expressed exclusively on neutrophils, CD177⁺ neutrophils could alleviate inflammation in inflammatory bowel disease, and it could produce neutrophil extracellular traps that promote biliary atresia. However, there is no report about CD177⁺ neutrophils involved in AIH or experimental AIH.

Aims & Methods: In this study, we wanted to explore to role of neutrophils in AIH and wondered whether CD177⁺ neutrophils exert protective effect in it. We collected clinical samples of AIH patients and healthy control (HC), and established experimental AIH animal model by using Concanavalin A (ConA). Anti-Ly6G antibody was used as pretreatment to depleting neutrophils before ConA injection. Wild type (WT) and CD177 knock out (KO) C57BL/6J female mouse were used to construct different experimental AIH model. Flow cytometry analysis was used to detect the percentage of neutrophils in blood and liver. Detected serum biochemical indicators (ALT: alanine aminotransferase, AST: aspartate aminotransferase) and performed staining in liver tissues to evaluate liver injury.

Results: For AIH patients, CD177⁺ neutrophils in peripheral blood were significantly increased ($P < 0.05$). And for immunohistochemistry (IHC), the positive areas of CD66b (a surface marker of neutrophils) and CD177 were more obvious in liver tissues of AIH patients ($P < 0.05$). For animal experiment, we successfully established model of experimental AIH. In this model, liver injury was significant in ConA group than in normal control (NC) group, which showed prominent liver necrosis in hematoxylin-eosin (HE) staining and higher serum ALT and AST ($P < 0.05$). Positive IHC areas of Ly6G and CD177 were more obvious in liver tissues of ConA group, which meant the increased infiltration of neutrophils. We found that distributions of neutrophils were different in different organ. Compared to NC group, the amount of neutrophils in ConA group was decreased in bone marrow and increased in peripheral blood and liver, and its increase in liver trended to be more obvious ($P = 0.096$). So, we speculated that neutrophils mainly migrated to liver from marrow in ConA model. After depleting neutrophils, we through flow cytometry analysis to verify the depletion of neutrophils (CD11b⁺ Ly6G⁺ cells) in anti Ly6G-ConA group was thorough. HE staining showed liver injury appearances in ConA group and Ly6G isotype-ConA group were more severe than that in normal saline (NS) group and in anti Ly6G-ConA group. Similarly, ConA group and Ly6G isotype-ConA group had higher levels of serum ALT and AST than the other two groups. Finally, we used CD177 KO mouse to determine the role of CD177⁺ neutrophils in ConA model. HE staining showed the area of liver necrosis in CD177 KO-ConA group was largest. As for liver function, CD177 KO-ConA group also had the highest levels of serum ALT and AST ($P < 0.05$), which improve that the liver injury in this group was the most severe.

Conclusion: Neutrophils involved in AIH and experimental AIH. In experimental AIH, depletion of neutrophils could alleviate liver injury, and CD177⁺ neutrophils could exert protective effect in it.

Disclosure: Nothing to disclose.

MP354

PROSPECTIVE EUROPEAN REFERENCE NETWORK REGISTRY (R-LIVER) SUPPORTS IMPROVEMENT IN BONE DISEASE CARE DELIVERY AT THE LOCAL LEVEL FOR PATIENTS WITH AUTOIMMUNE LIVER DISEASES AND ENABLES DETAILED DESCRIPTION OF RISK FACTORS

B. Bozsó¹, S. Mogyorossy², P. Kovats¹, N. Sipeki¹, F. Olah¹, P. Antal-Szalmas³, Z. Vitális¹, I. Tornai¹, D. Tornai¹, C. Schramm⁴, M. Papp¹

¹University of Debrecen, Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Debrecen, Hungary, ²University of Debrecen, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Debrecen, Hungary, ³University of Debrecen, Department of Laboratory Medicine, Faculty of Medicine, Debrecen, Hungary, ⁴Universitätsklinikum Hamburg-Eppendorf, Medizinische Klinik und Poliklinik (Gastroenterologie mit Sektionen Infektiologie und Tropenmedizin), Hamburg, Germany

Contact E-Mail Address: bozsobogi24@gmail.com

Introduction: Bone loss is a frequently observed complication in patients with autoimmune liver diseases (AILD). The exact risk of osteopenia and osteoporosis is unclear. Risk factors of bone loss require clarification. DEXA is both the screening method and the treatment guide. According to the EASL CPG currently in force, DEXA should be performed for all AILD patients at presentation and during follow-up visits. The outline standard is 80% assessment within 5 yrs.

Aims & Methods: Since 2017, the University of Debrecen (UNIDEB) prospectively collected data of AILD patients. In 2019, UNIDEB joined the prospective, multicenter, quality-controlled R-LIVER Registry on rare liver diseases launched by The European Reference Network for Hepatological Diseases (ERN RARE-LIVER). A total of 209 prospective AILD patients were included. Clinical, laboratory, imaging, and DEXA data were collected at the time of diagnosis and during yearly follow-up visits. A retrospective AILD patient cohort (n=176, 2010-2016) was used as a control group for monitoring guideline-adherence and clinical care standards of bone loss. We aimed to 1) assess bone loss at the time of diagnosis during the follow-up; 2) define risk factors of bone loss; 3) evaluate the accomplishment of quality objectives for the diagnosis of bone loss and analyze how the R-LIVER Registry supported quality improvement in the local level.

Results: According to DEXA results, 55.7% of patients had some degree of bone loss and 24.5% had osteoporosis at the time of diagnosis with the highest prevalences detected in PBC (67.5% and 32.5%, respectively). Older age (OR:1.050), post-menopausal status (OR:4.821), presence of significant liver fibrosis ($>9.2\text{kPa}$; OR:3.966, $p < 0.01$ for all) and elevated γGT levels (OR:1.001; $p = 0.041$) were risk factors for osteoporosis at diagnosis in the pooled patient group. mHAI was a risk factor in AIH, but degree of cholestasis was not in PSC and PBC separately. 171 patients had at least 1 year follow-up and 56 of them had repeated DEXA. Significantly more patients had DEXA assessment in line with the EASL CPG after joining ERN RARE-LIVER compared to the previous period. DEXA at diagnosis improved from 8.5% (retro) to 23.7% (2017-2018) then to 66% (all ERN), reaching 73.7% in 2023. In patients who had DEXA at diagnosis, guideline adherence of DEXA follow-up steadily improved from 42.9% (2017-2018) to 56.3% (2019-2020) and 88.6% (2021-2022). The outline standard was not achieved prior accession (17% had DEXA in 5 yrs retro and 50.8% between 2017-2018), but thereafter DEXA assessment was 72.7% after only 2 yrs of median follow-up (IQR: 0.75-4.1).

Conclusion: Bone loss was a frequent complication in our prospective AILD patient cohort. We identified several general and liver disease related risk factors, which warrant validation in the whole ERN cohort. After joining ERN RARE-LIVER program, gradual and significant improve-

ment was observed in the diagnosis of bone loss in AILD that verifies quality-controlled prospective registries as important tools for implementation of complex care in the clinical practice at local level.

Disclosure: Nothing to disclose.

Patient outcome: Pancreas

13:00-14:00 / Poster Stage 4

MP355

“ENHANCING SURVIVAL WITH PRECISION: EFFICACY AND SAFETY OF ENDOSCOPIC ULTRASOUND-GUIDED RADIOFREQUENCY ABLATION IN UNRESECTABLE PANCREATIC ADENOCARCINOMA – A PROSPECTIVE ANALYSIS”

M.F. Castro¹, J. Vargas¹, A. Ochoa Palominos²

¹*Caja Costarricense del Seguro Social, Hospital San Juan De Dios, San Jose, Costa Rica*, ²*Hospital Calderón Guardia, San José Costa Rica, Gastroenterology, Escazú, Costa Rica*

Contact E-Mail Address: mfcastr@ccss.sa.cr

Introduction: Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) has emerged as a promising minimally invasive technique for the management of unresectable pancreatic adenocarcinoma. Despite its potential, the practical outcomes and overall survival implications of this technique require thorough assessment in real-world settings.

Aims & Methods: This prospective study aimed to evaluate the feasibility, safety, and efficacy of EUS-RFA in patients with locally advanced or metastatic pancreatic adenocarcinoma. For the procedure, an RFA 19-g needle with an electrode active tip length of 10 mm was introduced into the tumor through the working channel of the echoendoscope. The generator settings were set at 35 W, and energy was applied from the distal to the proximal margin of the tumor until the entire lesion was treated. (video 1 EUS RFA PADC.mp4) The primary endpoints were technical success, complication rate, and overall survival.

Results: Twenty consecutive patients (58% female; average age 60 +/- 11.5 years; average tumor diameter, 37 +/- 16.7 mm) underwent EUS-RFA combined with subsequent chemotherapy. Sixteen patients (80%) were diagnosed with locally advanced adenocarcinoma, while four (20%) had metastatic disease. Technical success was achieved in 100% of the cases. The median overall survival was 15 +/- 2.2 months. No adverse events were reported. It should be noted that a patient with locally advanced adenocarcinoma downstaged after multimodal therapy and underwent surgical resection.

Conclusion: EUS-RFA is a feasible and safe treatment modality for patients with unresectable pancreatic adenocarcinoma, with high technical success and low complication rates. Future studies with larger cohorts are needed to confirm these findings and optimize treatment protocols.

Disclosure: Nothing to disclose.

MP356

HEPATOPANCREATODUODENECTOMY FOR EXTRAHEPATIC CHOLANGIOCARCINOMA -A SERIES OF 100 CONSECUTIVE CASES FROM AN EXPERT CENTER IN JAPAN-

T. Sugiura¹

¹*Shizuoka Cancer Center, Division of Hepato-Biliary-Pancreatic Surgery, Sunto-Nagaizumi, Japan*

Contact E-Mail Address: t.sugiura@scchr.jp

Introduction: Hepatopancreatoduodenectomy (HPD) is indicated for widely spreading cholangiocarcinomas. However, the procedure remains controversial due to high morbidity and mortality, as well as uncertain oncological benefits.

Aims & Methods: The aim of this study is to evaluate the efficacy and safety of HPD for extrahepatic cholangiocarcinoma. A total of 100 patients who underwent HPD between 2003 and 2020 were reviewed. Short- and long-term outcomes were compared with those of patients who under-

went hepatectomy with extrahepatic bile duct resection (HT-B) (n=203) and pancreatoduodenectomy (PD) (n=209) for extrahepatic cholangiocarcinoma during the same period.

Results: The median operating time and blood loss of HPD were 668 min and 1842 mL, which were significantly longer and greater in comparison to the HT-B (552 min and 1264 mL) and PD (457 min and 911 mL) groups. The rate of clinically relevant postoperative complications (Clavien-Dindo grade ≥ 3) after HPD was 82%, which was significantly greater in comparison to the HT-B (39%) and PD (68%) groups. However, the mortality rate was 2% and was almost comparable to the HT-B (2.5%) and PD (1.4%) groups. The 3- and 5-year survival rate, and median survival time were 59.0%, 40.7%, and 50 months, respectively, in the HPD group; 61.1%, 41.8%, and 45 months in the HT-B group; and 60.7%, 45.4%, and 48 months in the PD group. No significant differences were observed between the groups. Thirty-six patients who underwent HPD survived for 5-years.

Conclusion: Although HPD is technically demanding and forces stress on patients, it can be performed with acceptable mortality and survival rate. HPD for widely spreading cholangiocarcinoma should be considered a standard procedure in expert hepato-pancreato-biliary centers.

Disclosure: Nothing to disclose.

MP357

WITHDRAWN

MP358

MEASURING INEQUALITY AND SPATIAL DISTRIBUTION OF CHRONIC LIVER DISEASE MORTALITY IN EUROPE FROM 2013 TO 2018 USING DATASET LINKAGE OF ROUTINELY COLLECTED NOMENCLATURE OF TERRITORIAL UNITS FOR STATISTICS (NUTS) 2 REGIONAL LEVEL DATA

E. Meehan¹, J. Enticott²

¹Western Health, Gastroenterology, Footscray, Australia,

²Monash University, Monash Centre for Health Research and Implementation, Melbourne, Australia

Contact E-Mail Address: ejmeehan@gmail.com

Introduction: Health disparities in the burden of chronic liver disease (CLD) exist across socioeconomic, geographic, and ethnic lines.¹ However, the extent and nature of disparities in European patients with CLD has been minimally explored.

Aims & Methods: This study aims to evaluate socioeconomic and geographic disparities in CLD mortality across Europe between 2013 and 2018. We analysed 6 years of standardized death rates for CLD in NUTS 2 regions within current European Union (EU) member states. NUTS 2 regions are subnational areas containing between 800,000 and 3,000,000 inhabitants, used for standardizing cross-border comparisons.² We linked Eurostat datasets of 'Gross Domestic Product (GDP) Purchasing Power Standards (PPS) per inhabitant' and 'Causes of death'. Standardized death rates were weighted against the European Standard Population, and CLD mortality was defined using the codes K70, K73, and K74 from the International Classification of Diseases, 10th Revision. We chose a start date of 2013 as it coincided with Croatia's accession into the EU and the first reporting of CLD mortality in several regions. We chose an end date of 2018 due to significant missing data in subsequent years. Regions were divided into quintiles from most to least disadvantaged based on GDP PPS per inhabitant, and summary statistics were calculated for each quintile. Concentration indices and curves were generated in Stata, using GDP PPS per inhabitant to rank regions by socioeconomic status. Finally, choropleth maps were generated to visually compare CLD mortality across NUTS

2 regions. We adhered to REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement guidelines.³

Results: Of the 242 NUTS 2 regions in current EU member states, GDP data was complete for all regions, but CLD mortality data was unavailable in 3 Croatian regions in all years and 1 French region in 2013. 238 (98.4%) regions were therefore analysed in 2013, and 239 (98.8%) were analysed in all other years. In 2013, median GDP PPS per inhabitant was \$23,550 (IQR: \$17,600 to \$30,000), and median standardized death rate across all regions was 12.94 per 100,000 (IQR: 8.46 to 17.64). The rate in the most disadvantaged quintile was 1.38 times higher than this, at 17.9, and 1.43 times higher than the rate in the least disadvantaged quintile (12.52). Concentration indices and curves indicated that the burden of CLD mortality was concentrated in regions with lower GDP PPS per inhabitant. Indices ranged from -0.11 to -0.13, with $p < 0.001$ in all years indicating significant inequality. Choropleth maps showed higher death rates in Eastern and Central Europe. The top 6 regions by CLD mortality were all located in Romania. The highest in all years was the Sud-Est region, where the rate ranged from 59 to 64 deaths per 100,000.

Conclusion: We identified socioeconomic disparities in the distribution of CLD mortality and found a high burden of disease in Eastern European nations. The concentration of mortality in the poorest quintile, with a death rate 1.38 times higher than the overall population, is similar to findings in Australia, where the poorest quintile's death rate is 1.42 times higher than the population at large.⁴ Limitations included a retrospective design and a lack of granular data on sub-classifications of CLD and potential confounders such as rural status. Ultimately, our findings identify potential targets for health promotion and contribute to an understanding of how disadvantage contributes to health disparities in CLD.

References: 1. Kardashian A, Serper M, Terrault N, Nephew LD. Health disparities in chronic liver disease. *Hepatology*. 2023; 77(4):1382-1403. doi: 10.1002/hep.32743.

2. Frédéric Gouardères. Common classification of territorial units for statistics (NUTS). European Parliament. Updated March, 2024. Accessed April 12, 2024. <https://www.europarl.europa.eu/factsheets/en/sheet/99/common-classification-of-territorial-units-for-statistics-nuts>

3. Benchimol EI, Smeeth L, Guttman A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med*. 2015; 12(10):e1001885. doi: 10.1371/journal.pmed.1001885

4. Australian Institute of Health and Welfare. (2011). Mortality Over Regions and Time (MORT) books: Socioeconomic Group 2017-2021. Australian Government. Retrieved February 28, 2024. <https://www.aihw.gov.au/reports/life-expectancy-deaths/mort-books/contents/mort-books>

Disclosure: Nothing to disclose.

MP359

COMPARING PLASTIC VS BIODEGRADABLE PANCREATIC STENTS FOR THE PREVENTION OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS: PRELIMINARY RESULTS OF A SINGLE-CENTER RANDOMIZED CONTROLLED TRIAL

C. Robles-Medrandá¹, D. Cunto¹, M. Egas-Izquierdo¹, M. Puga-Tejada¹, R. Del Valle¹, J. Baquerizo-Burgos¹, M. Arevalo-Mora^{1,2}, H. Alvarado-Escobar¹, H. Pitanga-Lukashok¹, J. Alcivar-Vasquez¹

¹Instituto Ecuatoriano De Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Larkin Community Hospital, South Miami, United States of America

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) stands as the primary choice for treating pancreatobiliary disorders. Among its complications, post-ERCP pancreatitis (PEP) is the most frequent, with a prevalence ranging from 4-10%, and reaching up to 15% in high-risk patients. To mitigate the hydrostatic pressure contributing to PEP in high-risk patients, the insertion of a pancreatic duct stent is considered a preventive measure. The available options for pancreatic duct stenting include plastic pancreatic stents (PPS) and biodegradable stents (BDS) placement; However, currently, there is no available data on their efficacy, nor the best setting for choosing between the two.

Aims & Methods: Our aim is to compare the effectiveness of PPS vs BDS for the preventing PEP. A single-center, prospective, randomized controlled trial (RCT) in patients with biliary tract disease requiring ERCP was conducted from January/2022 to June/2023. Subjects ≥ 18 years-old, with a non-manipulated pancreatic papilla and written informed consent were included in the study. Patients not requiring or failed stenting, hemodynamically unstable, pregnant or nursing subjects, at risk of fluid overload, cholangitis, sepsis, acute/flare-up chronic pancreatitis, recent biliary tract manipulation, uncontrolled coagulopathy, kidney or liver failure or comorbidities impacting the cardiac-risk assessment were excluded. During ERCP, PPS (5F $\times$ 4cm) or BDS (6F $\times$ 4cm or 6F $\times$ 6cm) were randomly selected and placed. At three-days and five-weeks post-procedure, the patients required follow-up assessment to rule-out PEP based on physical examination findings, laboratory tests (amylase, lipase, PCR, WBC and total bilirubin), abdominal ultrasound, and history of any post-ERCP hospitalization.

Results: Ninety-seven patients were enrolled (54 BDS and 43 PPS), with a median age of 53 years, 63.9% females. The main indication for ERCP was choledocholithiasis (89.7%). The median time for biliary cannulation was 5 minutes, requiring sphincterotomies in 90/97 patients. Additionally, from the 43/97 PPS cohort, biliary stents simultaneous placement was required in 13/43 (30.2%), compared to 4/54 from BDS cohort (7.4%; $p=.0076$). It was shown that median post-ERCP total bilirubin was significantly lower in both PPS (1.04 vs 0.96; $p=.0338$) and BDS cohort (1.04 vs 0.52 mg/dL; $p=.0044$). The same was observed for median C-reactive protein in PPS (7.03 vs 4.10 mg/dL; $p=.0338$) and BDS (11.2 vs 5.1 mg/dL; $p=.01$). Meanwhile, median post-ERCP lipase was significantly higher in both PPS (47 vs 54.8 mg/dL; $p=.05$) and BDS (48.5 vs 110 mg/dL; $p=.0134$). PEP was noticed in 8/97 (8.2%), with no significant difference in prevention when PPS and BDS were compared (14% vs 3.7%; $p=.133$).

Conclusion: A lower but non-significant rate of PEP prevention using BDS vs PPS was noticed. The significant reduction on total bilirubin levels, mainly in the BDS cohort, deserves further studies that must be conceived around this endpoint.

References: 1. Cahyadi O, Tehami N, de-Madaria E, Siau K. Post-ERCP Pancreatitis: Prevention, Diagnosis and Management. *Medicina* (Kaunas). 2022 Sep 12;58(9):1261. doi: 10.3390/medicina58091261 .

2. Borrelli de Andreis F, Mascagni P, Schepis T, Attili F, Tringali A, Costamagna G, Boškoski I. Prevention of post-ERCP pancreatitis: current strategies and novel perspectives. *Therap Adv Gastroenterol*. 2023 Mar 6;16:17562848231155984. doi: 10.1177/17562848231155984 .

3. Thiruvengadam NR, Kochman ML. Emerging Therapies to Prevent Post-ERCP Pancreatitis. *Curr Gastroenterol Rep*. 2020 Nov 13;22(12):59. doi: 10.1007/s11894-020-00796-w .

4. Johnson KD, Perisetti A, Tharian B, Thandassery R, Jamidar P, Goyal H, Inamdar S. Endoscopic Retrograde Cholangiopancreatography-Related Complications and Their Management Strategies: A "Scoping" Literature Review. *Dig Dis Sci*. 2020 Feb;65(2):361-375. doi: 10.1007/s10620-019-05970-3 . Epub 2019 Dec 2.

Disclosure: Carlos Robles-Medrandá is a key opinion leader and consultant for Pentax Medical, Steris, Medtronic, Motus, Micro-tech, G-Tech Medical Supply, CREO Medical, EndoSound, and mdconsgroup. All other authors declare no conflicts of interest.

MP360

TIME TO SURGERY DOES NOT AFFECT THE SURVIVAL OUTCOME IN PATIENTS WITH PERIHILAR CHOLANGIOCARCINOMA

Y. Tohmatsu¹, K. Ohgi¹, R. Ashida¹, M. Yamada¹, S. Otsuka¹, Y. Kato¹, K. Uesaka¹, T. Sugiura¹

¹Shizuoka Cancer Center Hepato-Biliary-Pancreatic Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Sunto-Nagaizumi, Japan

Contact E-Mail Address: y.tohmatsu@scchr.jp

Introduction: Patients with perihilar cholangiocarcinoma (PHC) often require lengthy preoperative management, resulting in a long time to surgery (TTS). However, the relationship between the TTS length and postoperative survival outcome remains unknown.

Aims & Methods: This retrospective single-center study included 224 patients with PHC (2011–2020). TTS was defined as the period from the date of the diagnosis by computed tomography to the date of surgery; the median TTS was 64 (range, 19–212) days. The patients were divided into 2 groups with a TTS cutoff value of 64 days. The surgical and oncological outcomes were then compared between the long- (n=116) and short-TTS (n=108) groups.

Results: Radical resection rate was 74% in long-TTS group and 84% in short-TTS group. The frequencies of preoperative biliary infection (52% vs. 33%, $P=0.004$) and portal vein embolization (84% vs. 49%, $P<0.001$) were significantly higher in the long-TTS group than in the short-TTS group. There was no marked difference in the postoperative mortality rate (2% vs. 3%, $P=0.697$) and histopathological findings, such as lymph node metastasis (41% vs. 43%, $P=0.871$) and R1 resection rate (15% vs. 9%, $P=0.193$), between the groups. The overall survival was comparable between the groups (median survival time, 47 vs. 43 months, $P=0.627$). In the multivariate analysis, only lymph node metastasis was an independent prognostic factor (hazard ratio, 1.494; $P=0.044$), although TTS was not associated with the survival.

Conclusion: TTS did not affect the survival outcomes of patients who underwent surgical resection for PHC. It is essential to achieve radical resection safely with appropriate preoperative management, regardless of the length of TTS.

Disclosure: Nothing to disclose.

MP361

BREAKING BOUNDARIES: SCARLESS CHOLECYSTECTOMY ACHIEVED WITH A NOVEL FLEXIBLE ENDOSCOPIC ROBOTIC PLATFORM

S. Perretta^{1,2}, G. Carlino^{3,1}, J. Marescaux¹

¹IRCAD, University of Strasbourg, Institute for Research on Cancers of the Digestive Tract, Strasbourg Cedex, France, ²IRCAD-IHU, Surgery, Strasbourg, France, ³Policlinico Universitario Agostino Gemelli, Università Cattolica Del Sacro Cuore, Surgical Digestive Endoscopy, 00168, Italy

Contact E-Mail Address: silvana.perretta@ircad.fr

Introduction: While robotic surgery has enhanced the precision of laparoscopy, its rigid instrumentation presents limitations. Flexible endoscopic instruments offer potential advantages in reach and access, yet have historically lacked the stability and force needed for human application. The advent of a flexible robotic platform holds promise in providing the necessary visualization, stability, and instrumentation for safe and effective procedures in humans. This video demonstrates the proof of concept for cholecystectomy using a novel flexible robotic platform.

Aims & Methods: In a porcine in-vivo model, a flexible robotic platform was used to perform a cholecystectomy. The platform is a master-slave system with a physician console, patient cart, an 18mm wide, 45cm long flexible shaft, and two 6mm robotic effector arms with 7 degrees of freedom. A 2cm incision was made at the level of the umbilicus to introduce the platform. Once in position, an atraumatic grasper and scissors were introduced under endoscopic control of the cobra camera. Cholecystectomy was performed in a hybrid format, using flexible instruments with one additional 5mm laparoscopic grasper to optimize exposure of the operating field. The triangle of Calot and gallbladder were successfully dissected, and the cystic duct and artery were clipped and divided with the flexible endoscopic instruments. A 5mm laparoscopic camera was used to enhance lighting in the peritoneal cavity beyond the cholecystectomy site, facilitating comprehensive monitoring of the entire procedure and platform in action.

Results: Total operative time was 22 minutes. There were no intraoperative complications. Cholecystectomy was performed safely and completely with the flexible endoscopic instruments.

Conclusion: Single incision cholecystectomy with this novel flexible robotic platform is safe and feasible. The approach may combine the best technical aspects of laparoscopic, robotic, and endoscopic surgery, minimizing trauma and external scars although improvement in exposure and lighting are desirable. Clinical investigation with this promising technology is ongoing.

Disclosure: Silvana Perratta is a member of EndoQuest's Clinical Advisory Board

Jacques Marescaux is a member of EndoQuest's Scientific Advisory Board.

MP362

SUSTAINABLE SURGERY - QUANTIFYING THE CARBON FOOTPRINT OF A LAPAROSCOPIC CHOLECYSTECTOMY: A LIFE-CYCLE ASSESSMENT STUDY (CO₂SURG-STUDY)

S. Bluiminck¹, D.J. Comes¹, E. Kooistra², L. De Nes³, F. Van Workum⁴, H. Touw², M.M. Eussen⁵, N.D. Bouvy⁵, T. Stoberneck², P.R. De Reuver¹

¹Radboud University Medical Centre, Surgery, Nijmegen, Netherlands, ²Radboud University Medical Centre, Intensive Care, Nijmegen, Netherlands, ³Maasziekenhuis Pantein, Surgery, Beugen, Netherlands, ⁴Canisius Wilhelmina Ziekenhuis, Surgery, Nijmegen, Netherlands, ⁵Maastricht University Medical Centre, Surgery and NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht, Netherlands

Contact E-Mail Address: stijn.bluiminck1@radboudumc.nl

Introduction: The Dutch healthcare sector is responsible for over 7% of the national carbon footprint and 4% of all produced waste, with a substantial contribution of the surgical community. (1-2) Numerous sustainability initiatives have emerged, each targeting specific aspects of surgical procedures such as utilization of disposables, waste management, and use of inhalation anaesthesia.

However, for the surgical team to gain insights into the environmental impact of procedures and to identify the primary contributors guiding mitigation strategies, a comprehensive assessment of the surgical procedures is imperative.

This study aimed to assess the carbon footprint of laparoscopic cholecystectomy (LC) and identify mitigation options by performing a life-cycle assessment (LCA).

Aims & Methods: A multicentre observation study of 15 elective LCs was conducted in 3 hospitals. This LCA studied the entire life cycle of processes and materials involved in the surgical procedure including all surgical instruments (i.e., reusable, and disposable instruments), medication (including anaesthesia), sterilisation process of reusable equipment, energy consumption, operating room (OR) scrubs and linen, and travel movements of operating room personnel and patients. The primary outcome measure was the carbon footprint in kg CO₂ equivalents (eq.) of the operation. Secondary outcomes were identifying major contributing factors and mitigation options. Based on feasible mitigation measures, the carbon footprint of a best-case scenario was determined. The LCA was performed according to ISO14040 guidelines and ReCiPe 2016 methodology. (3-4)

Results: The carbon footprint of a LC was 56.5 kg CO₂ eq. The main contributors were disposable materials, accounting for 40% of the total carbon footprint (22.7 kg CO₂ eq. IQR 21.5-24.6), energy consumption (11%, 6.1 kg CO₂ eq.; IQR 5.4-7.9), and transport of personnel (13%, 7.1 kg CO₂ eq.; IQR 5.5-9.6). Reusable products made up 22% (12.5 kg CO₂ eq.; IQR: 12.5-12.5) with 81% attributable to the sterilisation process. Medication made up 3.0 kg CO₂ eq. (5%, IQR: 0.08-5.9), with inhalation anaesthetic, sevoflurane responsible for 96% of the carbon footprint. The Best-case scenario included transitioning to reusable instruments, reducing surgical drapes, adopting total intravenous anaesthesia, and switching to 100% green energy, reducing the total footprint by 23%.

Conclusion: This study showed the carbon footprint of a LC and provided insights in the most important contributing factors. A substantial reduction in the carbon footprint can be achieved by replacing disposable surgical instruments (trocars and clipper) with reusable alternatives, reducing surgical drapes, switching to total intravenous anaesthesia, and transitioning to 100% green energy. The results of this study extend beyond LC and can be used to accelerate and provide guidance for sustainability initiatives, an essential step towards sustainable surgical care.

Moreover, the most impactful approach to reduce the carbon footprint lies in avoiding unnecessary procedures. Recent studies have shown that a restrictive or conservative strategy for uncomplicated gallstone disease is comparable to cholecystectomy as a treatment option in terms of quality of life and biliary-related complications (5-6). Therefore, we are currently conducting a carbon footprint effectiveness analysis in the United Kingdom and the Netherlands to determine the carbon footprint reduction potential of a conservative or restrictive strategy for uncomplicated gallstone disease. We anticipate being able to present the results at the congress.

- References:** 1. Steenmeijer MA, Rodrigues JFD, Zijp MC, et al. The environmental impact of the Dutch health-care sector beyond climate change: an input-output analysis. *Lancet Planet Health*. 2022;6(12):e949-e57.
2. MacNeill AJ, Lillywhite R, Brown CJ. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. *Lancet Planet Health*. 2017;1(9):e381-e8.
3. ISO 14040:2006(en) Environmental management — Life cycle assessment — Principles and framework 2006.
4. Huijbregts MAJ, Steinmann ZJN, Elshout PMF, et al. ReCiPe2016: a harmonised life cycle impact assessment method at midpoint and endpoint level. *The International Journal of Life Cycle Assessment*. 2017;22(2):138-47.
5. Ahmed I, Hudson J, Innes K, et al. Effectiveness of conservative management versus laparoscopic cholecystectomy in the prevention of recurrent symptoms and complications in adults with uncomplicated symptomatic gallstone disease (C-GALL trial): pragmatic, multicentre randomised controlled trial. *Bmj*. 2023;383:e075383.
6. van Dijk AH, Wennmacker SZ, de Reuver PR, et al. Restrictive strategy versus usual care for cholecystectomy in patients with gallstones and abdominal pain (SECURE): a multicentre, randomised, parallel-arm, non-inferiority trial. *Lancet*. 2019 Jun 8;393(10188):2322-2330. doi: 10.1016/S0140-6736(19)30941-9. Epub 2019 Apr 27. Erratum in: *Lancet*. 2019 May 11;393(10184):1936. PMID: 31036336.

Disclosure: Nothing to disclose.

MP363

CLINICAL OUTCOMES OF CHOLANGIOPANCREATOSCOPY-ASSISTED LITHOTRIPSY AND FREY SURGERY FOR DIFFICULT PANCREATIC DUCT STONES: EXPERIENCE OF A MEDICAL CENTER

W.-H. Huang¹, C.-Y. Yang², S.-C. Chuang², H.-H. Cheng^{2,2}, T.-L. Hsieh², P.-C. Huang², Y.-C. Chang², C.-Y. Peng²

¹China Medical University Hospital, Internal Medicine, Taichung, Taiwan, ²China Medical University Hospital, Taichung, Taiwan

Contact E-Mail Address: u97766.huang@msa.hinet.net

Introduction: Difficult pancreatic duct stones, including large and/or impacted pancreatic duct stones, cannot usually be treated by conventional endoscopic retrograde cholangiopancreatography (ERCP). Extracorporeal shock wave lithotripsy (ESWL) and surgery including Frey operation are the main treatment for such difficult pancreatic duct stones. Recently, cholangiopancreatography-assisted lithotripsy using electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) provides an alternative modality for ductal clearance.

Aims & Methods: We aimed to evaluate the clinical outcomes of cholangiopancreatography-assisted lithotripsy and Frey surgery in patients with difficult pancreatic duct stones.

From January, 2018 to December, 2023, a total of 12 (10 male and 2 female) consecutive patients, 51 (38-71) years old, with large and/or impacted pancreatic duct stones undergoing single-operator cholangiopancreatography-assisted lithotripsy using EHL and/or LL, and 14 (10 male and 2

female) consecutive patients, 48 (33-62) years old, undergoing Frey surgery in a medical center were retrospectively analyzed. Clinical outcomes including stone size, lithotripsy and surgery procedures, ductal clearance, complications, and length of hospital stay were evaluated.

Results: In the group of cholangiopancreatography-assisted lithotripsy, 11 (91.7%; 11/12) patients were successfully treated in 19 (median 2; range 1-3) sessions including LL (n=16) and EHL (n=3) to achieve ductal clearance (Clinical success). The technical success rate was 94.7% (18/19). Six (50%; 6/12) patients with pancreatic duct stones were successfully treated at the first session of cholangiopancreatography-assisted lithotripsy. After the procedure, mild pancreatitis occurred in 5 (26.3%; 5/19) patients. The median length of hospital stay was 4 (2-9) days. In the group of Frey surgery, 11 (78.6%; 11/14) patients underwent the surgery successfully. Adverse events after Frey surgery occurred in 3 (21.3%; 3/11) patients, including intra-abdominal abscess, peritonitis and bacteremia, respectively. The median length of hospital stay was 16 (7-58) days.

Conclusion: Cholangiopancreatography-assisted lithotripsy is an effective and safe modality for difficult pancreatic duct stones. Comparing with Frey surgery, cholangiopancreatography-assisted lithotripsy can be an initial therapy.

Disclosure: The authors declare no conflicts of interest.

MP364

ACCURACY OF TRANSABDOMINAL ULTRASOUND 2D SHEAR WAVE ELASTOGRAPHY COMPARED TO ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS OF CHRONIC PANCREATITIS

C.F.M. Jung¹, C. Binda¹, E. Liverani¹, E. Dajti², C. Abbatiello³, L. Cristofaro², L.V. Alemanni⁴, A. Sartini⁵, C. Coluccio¹, G. Gibiino⁴, S. Fabbri⁴, C. Serra⁶, C. Fabbri¹

¹Gastroenterology and Digestive Endoscopy, Forlì-Cesena Hospitals, AUSL Romagna, Italy, Forlì-Cesena, Italy, ²Alma Mater Studiorum Università di Bologna, Italy, Bologna, Italy, ³AOU San Giovanni di Dio e Ruggi D'Aragona, Endoscopia Digestiva, Durazzano, Italy, ⁴Gastroenterology and Digestive Endoscopy, Forlì-Cesena Hospitals, AUSL Romagna, Italy, Forlì-Cesena, Italy, ⁵Gastroenterology and Digestive Endoscopy, Forlì - Cesena Hospitals, AUSL Romagna, Italy, Forlì-Cesena, Italy, ⁶S.Orsola-Malpighi Hospital, Interventional, Diagnostic and Therapeutic Ultrasound Unit, Bologna, Italy

Contact E-Mail Address: cecilia.binda@gmail.com

Introduction: Diagnosis of chronic pancreatitis (CP) is challenging, especially in early stages when typical clinical signs and parenchymal changes are lacking. To date, evaluation by endoscopic ultrasound (EUS) using Rosemont criteria (RC) is the gold standard for the diagnosis of CP, but represents an invasive method with still suboptimal accuracy. Therefore, it is of crucial interest to develop non invasive, widely applicable tests for the diagnosis of CP. Recently the Gemelli chronic pancreatitis ultrasound score (USCP) has been developed to fill this gap (1). Comparable to liver stiffness measurement, transabdominal ultrasound (US) with 2D shear wave elastography (2D SWE) could represent an additional alternative for the diagnosis of CP. It uses measurement of tissue stiffness, which increases naturally with chronic inflammatory changes, present in CP (2).

Aims & Methods: We conducted a single center prospective case control study where all the included subjects underwent EUS first (for the suspicious of CP or other reasons such as lithiasis), with RC defined patient cohorts with chronic pancreatitis or absence of parenchymal changes. Patients with and without CP subsequently underwent US with evaluation of the pancreas using 2D SWE (in m/s) and characterization by the USCP score (LogiqE10, GE Healthcare). Primary outcome was agreement

between the different evaluation techniques, namely RC and 2D SWE. Secondary outcome was the evaluation of a cut off value of SWE differentiating values in CP from normal values. Main exclusion criteria were patients with liver cirrhosis, acute pancreatitis and inability to visualize the pancreas with US.

Results: 51 patients with CP and 51 without CP were included. Median SWE were statistically different between groups (no CP 1.50m/s; IQR 1.34-1.63 and with CP 1.83 m/s; IQR 1.68-2.08; $p<0.0001$). Patients with RC indeterminate for CP had lower SWE values compared to patients with RC consistent with CP (Median 1.67m/s, IQR 1.52-1.72 vs. 1.90 m/s, IQR 1.72-2.12, $p<0.0001$). Median USCP Score significantly differed between groups (no CP 0-1 points, with CP 3-9 points, $p<0.0001$). SWE values did not correlate with age, BMI, HbA1c or stool elastase levels, but correlated significantly with USCP score ($p<0.001$) and RC ($p<0.001$). USCP Score significantly correlated with BMI ($p=0.011$), stool elastase levels ($p<0.001$), HbA1c ($p=0.002$) as well as RC ($p<0.0001$). We defined a cutoff- SWE value of <1.42 m/s to rule out CP with a sensitivity of 97% (NPV 98%) and a SWE cut off >1.97 ms/s to diagnose CP with a specificity of 97% (PPV 92%).

Conclusion: Transabdominal ultrasound evaluation of the pancreas with 2D SWE is a promising, widely applicable and non-invasive tool for the diagnosis of CP. More studies with larger cohorts confirming the results are necessary.

References: 1)Pagliari D, et al. A new ultrasound score for the assessment and follow-up of chronic pancreatitis: The 'Gemelli USCP score'. *Dig Liver Dis.* 2020 Jun;52(6):644-650.

2) Yashima Y et al. Acoustic radiation force impulse elastography for noninvasive assessment of chronic pancreatitis. *J Gastroenterol.* 2012 Apr;47(4):427-32.

Disclosure: Nothing to disclose.

Challenges in upper GI oncology

13:00-14:00 / Poster Stage 5

MP365

SCREENING FOR GASTRIC CANCER IN PORTUGAL: A MULTICENTER CROSS-SECTIONAL STUDY IN PRIMARY HEALTHCARE

P. Pimentel-Nunes¹, R.P. Bastos¹, T. Moreira¹, M. Coelho-Rocha¹, R.F. Veloso¹, D. Libânio¹, C. Bernardes¹, T. Pinto-Pais¹, M. Bento-Miranda¹, F. Barreto¹, L. Prado¹, A. Maia-Gonçalves¹, L. Rafael¹, R. Panzeri-Rodrigues¹

¹Unilabs Portugal, Porto, Portugal

Contact E-Mail Address: pedronunesml@gmail.com

Introduction: Gastric cancer screening is not formally recommended in Portugal, despite having an incidence rate of 26/100,000 inhabitants, which contrasts with recommendations from other countries with moderate incidence.

Aims & Methods: Aims: To assess the frequency of screening indications and correspondent diagnoses in patients referred for upper endoscopy from primary healthcare.

Methods: A multicenter cross-sectional study including patients who underwent upper endoscopy at 13 national endoscopy units from January to March 2024.

Results: 6320 patients were included (57% male, mean age 58). Cancer screening was the indication for upper endoscopy in 1775 patients (28% of total; 52% male, mean age 60). Biopsies of the antrum and corpus were performed in 91% of those exams, and virtual chromoendoscopy was used in 19% of screening endoscopies (vs 34% for atrophic gastritis surveillance, $p<0.05$). Endoscopic staging for intestinal metaplasia was performed in 13%. By regions, screening indication was more common in Minho (35%) and less in the Lisbon region (15%, $p<0.05$ vs other regions). Only 21% of exams were considered normal, with the main findings being: erythematous gastritis (31%); atrophic gastritis (16%, 1% autoimmune gastritis), reflux esophagitis (15%), papular gastritis (10%), erosive gastritis (8%), gastric polyps (5%), erosive duodenitis (3%), peptic ulcers (3%), subepithelial lesions (1.5%) and Barrett's esophagus (0.5%). Histologically, 30% of patients had intestinal metaplasia, 5% in both the antrum and corpus. Fourteen neoplastic lesions (0.8%) were identified: 5 gastric neoplasms (0.3%), 4 superficial gastric lesions (0.2%), 2 esophagus/junction neoplasms (0.1%), 2 superficial junction lesions (0.2%), and 1 ampulloma (0.1%). Ten percent of patients would require future endoscopic surveillance.

Conclusion: A significant proportion of upper endoscopies in Portugal are already performed for cancer screening, which seems justifiable given the high proportion of clinically relevant alterations identified. The low proportion of exams with chromoendoscopy suggests that measures are needed to increase the use of this technique in clinical practice.

Disclosure: Nothing to disclose.

MP366

OPTIMAL ENDOSCOPIC SCREENING STRATEGY FOR THE DETECTION AND TREATMENT OF GASTRIC CANCER: A COST-EFFECTIVENESS ANALYSIS

F. Ishibashi¹, S. Suzuki², K. Kobayashi³, T. Kawakami³, R. Tanaka⁴, K. Mochida², T. Morishita²

¹International University of Health and Welfare Ichikawa Hospital, Department of Gastroenterology, Chiba, Japan, ²International University of Health and Welfare Ichikawa Hospital, Department of Gastroenterology, Ichikawa, Japan, ³Koganei Tsurukame Clinic, Endoscopy Center, Tokyo, Japan, ⁴Shinjuku Tsurukame Clinic, Digestive Disease Center, Tokyo, Japan

Contact E-Mail Address: f.jazzmaster@gmail.com

Introduction: The risk of gastric cancer is expected to decrease with reduced *Helicobacter pylori* (*H. pylori*) infection rate. Although periodic endoscopic screening for gastric cancer is widely performed in East Asia, the optimal screening strategy remains unclear. Cost-effectiveness analysis (CEA) is an effective method to objectively compare different screening methods. However, no studies have compared the cost-effectiveness of endoscopy-based screening strategies.

Aims & Methods: This study aimed to determine the most cost-effective endoscopic screening strategy for the detection and treatment of gastric cancer in a modern Japanese cohort.

This study consisted of two phases: clinical data collection and analysis, followed by simulation model development. The following data was retrospectively extracted from participants who received screening endoscopy between April 2019 and March 2023: age, *H. pylori* infection status, presence of intestinal metaplasia, pathological diagnosis of gastric cancer, and the interval between the most recent endoscopies. A Markov state transition model was constructed based on the cohort data.

In this model, the prevalence of *H. pylori* infection and intestinal metaplasia, the transition probabilities between each state, and the probabilities of incidence of gastric cancer and treatment were defined. In the base-case analysis, the cost-effectiveness of 15 strategies with different starting ages (40/50/60 years) and screening intervals (1/2/3/4/5 years) was compared.

The net monetary benefit (NMB) and incremental cost-effectiveness ratio (ICER) of quality-adjusted life-years (QALY) gained by treatment were used as outcomes. The NMB is a measure of the difference between the cost required for a strategy and the cost threshold for the same effect; the larger the NMB of a strategy, the more cost-effective it is. In contrast, a lower ICER is considered more cost-effective.

	Dominance	Cost (JPY/USD)	Incremental Cost (JPY/USD)	Effectiveness (QALY)	Incremental effectiveness (QALY)	ICER (JPY/USD) /QALY	NMB (JPY/USD)
Every 4-year screening strategy (50 years old)	Reference	116,960 /791	Reference	19.4632	Reference	Reference	97,199,068 /657,461
Every 5-year screening strategy (40 years old)	Undominated	144,615 /978	27,655 /187	19.5066	0.0434	637,874 /4,315	97,388,189 /658,741
Every 4-year screening strategy (40 years old)	Undominated	147,443 /997	2,827 /19	19.5098	0.0032	871,875 /5,897	97,401,578 /658,831
Biennial screening strategy (40 years old)	Undominated	203,815 /1,379	56,372 /381	19.5124	0.0026	21,863,477 /147,886	97,358,097 /658,537
Annual screening strategy (40 years old)	Undominated	321,606 /2,175	117,791 /796	19.5131	0.0007	173,642,337 /1,174,529	97,243,698 /657,763

Results: A simulation model was constructed based on the cohort data of 94,137 participants (mean age 54.5 years, males 57.9%; 74.4% *H. pylori*-naïve, 94.2% intestinal metaplasia-negative). The results of the base-case analysis showed that the screening strategy of 4-year intervals starting at the age of 40 years had the highest net monetary benefit (97,401,578 yen) (Table). Based on the Monte Carlo simulation, the cost-effectiveness acceptability curve demonstrated that the 4-year interval screening strategy starting at the age of 40 years was superior to the other strategies when the willingness-to-pay was set at 5,000,000 yen. In one-way sensitivity analysis with a varying probability of *H. pylori* infection status transition, the incremental cost-effectiveness ratio was superior in the screening strategy every 4 years, starting at age 40 years.

Conclusion: Gastric cancer screening strategies can be modified in terms of cost-effectiveness in a modern Japanese cohort. Our simulation showed that endoscopic screening at 4-year intervals starting at 40 years was the most cost-effective method.

Disclosure: Nothing to disclose.

MP367

GENOMIC MARKERS FOR ENHANCED RISK STRATIFICATION IN BARRETT'S ESOPHAGUS PATIENTS WITH LOW GRADE DYSPLASIA

P. Stougie¹, N. Frei¹, V. Pappalardo², A. Khoshiwal¹, H. Yu³, R. Menezes², L. Duits¹, J.J. Bergman¹, M. Stachler³

¹Amsterdam UMC, Dept. of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Netherlands Cancer Institute, Biostatistics Centre and Department of Psychosocial and Epidemiological Research, Amsterdam, Netherlands, ³University of California, Department of Pathology, San Francisco, United States of America

Contact E-Mail Address: p.stougie@amsterdamumc.nl

Introduction: Current risk stratification of Barrett's esophagus (BE) patients, based on histological identification of dysplasia, lacks reliability due to poor interobserver agreement and the limited predictive value of low-grade dysplasia (LGD).

Aims & Methods: This study aims to identify genomic factors enhancing risk stratification for BE patients with a community diagnosis of LGD.

Progressors to early esophageal adenocarcinoma and non-progressors were identified in a randomized controlled trial screening cohort of community-based LGD patients. Sequencing used a targeted capture-based panel to detect mutations and copy number changes (CNV). Detected mutations, homozygous deletions, and high-level amplifications underwent filtering for likely pathogenic events. We performed logistic regression, covariate analysis, and penalized mixed-effect models. A joint model for survival and mixed effects was applied for spatiotemporal data analysis. The model's performance was compared with that of general and expert pathologists to evaluate its clinical relevance.

Results: 220 samples, comprising 28 progressors with a median time to progression of 1.2 (IQR 0.4-2.2) years and 95 non-progressors with a median progression-free follow-up of 7.9 (IQR 5.9-10.6) years, all with a median C3M5 BE, were analyzed. Multiple factors were associated with progression, including *TP53* ($p < 0.0001$, Hazard Ratio (HR) = 13.39, 95% confidence intervals (CI) 5.64-31.78), chromosomal arm 17p loss ($p < 0.0001$, HR = 10.24, 95% CI 4.82-21.76), mutational burden ($p < 0.001$, HR = 1.52, 95% CI 1.21-1.90), and total number of CNVs ($p < 0.0001$, HR = 1.48, 95% CI 1.34-1.64). Several other alterations trended to be associated with progression, including *APC* mutation and presence of an oncogenic amplification. The combined influence of *TP53* and 17p loss enhanced the accuracy of risk prediction. However, high correlation precluded their use as cumulative risk. Patients with samples containing ≥ 3 mutations had a very high risk of

progression (HR = 10.33, 95% CI 2.22-48.01). Presence of any genetic variant—amplification, deletion, CNV, or mutation— indicated progression risk (p<0.0001, HR = 1.15, 95% CI 1.11-1.21). Samples lacking any genetic variants showed no progression. A combined *TP53* and CNV model effectively identifies progression risk with a sensitivity of 64.3%, specificity of 94.7%, and an AUC of 0.837, distinguishing 89 out of 94 non-progressors. In contrast to traditional assessments, this model demonstrates substantial improvements (p=0.002) compared to the expert pathologist assessment (median sensitivity of 67.9 % [0.321, 0.821], median specificity of 80.4% [0.606, 0.957], k value: 0.47).

	Predicted non-Progressive	Predicted Progressive
True Non- Progressors	91	4
True Progressors	10	18

Conclusion: This study not only reinforces the well-established role of *TP53* mutations but also introduces crucial novel genomic markers. The addition of 17p loss emerges as indispensable for enhanced risk assessment.

Furthermore, distinct genetic variations, including CNVs and total mutations, individually and collectively signify a significantly higher risk. Intriguingly, patients without any distinctive genetic abnormalities did not progress. A combined genomic model could consistently accurately risk stratify BE patients with a community-based LGD diagnosis, highlighting its enhanced and reliable predictive accuracy.

Disclosure: NA.

MP368

THE INCREASING TRUE PREVALENCE OF OXYNTIC GLAND NEOPLASIA: HIDING IN PLAIN SIGHT

T. Takao¹, H. Asahara², M. Asahara³, Y. Asahara³, D. Motomura⁴, Y. Shimamoto¹, T. Yoshizaki¹, N. Jinbo⁵, Y. Morita¹, T. Toyonaga¹, R. Kushima⁶, Y. Kodama¹
¹Kobe University Hospital, Department of Gastroenterology, Kobe city, Japan, ²Kobe Red Cross Hospital, Department of Gastroenterology, Kobe city, Japan, ³Asahara Clinic, Akashi city, Japan, ⁴University of British Columbia, Vancouver, Canada, ⁵Kobe University Hospital, Department of Pathology, Kobe city, Japan, ⁶Shiga University Hospital, Department of Pathology, Otsu city, Japan

Contact E-Mail Address: t.takao1234@gmail.com

Introduction: Oxyntic gland neoplasms (OGNs) are rare gastric lesions that mainly show differentiation to chief cells [1, 2]. In the fifth edition of the WHO classification, the OGN entity includes oxyntic gland adenoma and gastric adenocarcinoma of fundic gland type [3]. Though these subtypes are classically considered more benign, interest has been developing in a third group, gastric adenocarcinoma of fundic-gland mucosa type (GA-FG-M). GA-FG-M are distinct among OGN in that they more commonly show lymphovascular invasion on histology and are thus considered more aggressive lesions with higher malignant potential. Although interest in OGNs has been gradually increasing in the past few years, most studies had involved cases collected by tertiary referral centers, leading to a gap in the knowledge of the true disease frequency in the real-world setting. To address this issue, we previously reported the incidence of OGNs in 7488 patients in a large outpatient clinic in Japan between 2017 and 2021. However, the absolute number of OGNs was limited and the incidence of GA-FG-M was unknown [5].

Aims & Methods: The goal of this study was to more accurately characterize the disease frequency and clinicopathological characteristics of OGNs by including more than three times the number of lesions discovered since the previous report. We also aim to include an estimate for the GA-FG-M subtype. All upper gastrointestinal endoscopies performed at a high-volume outpatient clinic between December 2017 and December 2023 were retrospectively reviewed, and new cases of histologically diagnosed OGN were identified. Patient demographics, endoscopic and histopathological details are presented.

Results: During the study period, 9431 patients underwent 22322 procedures, with 85 patients having a total of 106 OGNs, resulting in a point prevalence of 0.9% (85/9431). GA-FG-M was identified in 3 patients, leading to a prevalence of 0.03% (3/9431). Fifteen patients (18%) had multiple lesions simultaneously or metachronically. Forty-six patients (54%) had a history of *H. Pylori* infection. Forty-nine lesions underwent endoscopic management, with 11 resected via ESD and 38 via EMR-C. The median tumor diameter was 3mm (range 2-9). Fourteen of the resected lesions had evidence of submucosal involvement. In this subset, the deepest penetration ranged from 10-950um into the submucosal layer. Median Ki67 index value was 2% (range 1-15). Thus far, there has been no evidence of recurrence on clinical follow up.

Conclusion: Though the most recent WHO classification states the prevalence of OGNs remains unknown [3], our data supports that these lesions are more common than once thought. Initial reports had suggested rates of <0.01% [6], and our previous study had found a community point prevalence of 0.36% [5]. However, in two years since that study period, the amount of lesions identified has more than tripled, leading us to a more accurate prevalence estimate of 0.9%. In addition, we clarified the prevalence of GA-FG-M to be 0.03%. It is possible this number may continue to rise in the future, as knowledge about this atypical form of gastric neoplasia is further disseminated amongst gastroenterologists and pathologists.

References: [1] Tsukamoto, Tetsuya, et al. “Gastric adenocarcinoma with chief cell differentiation.” *Pathology international*. 2007, 57(8): 517-522.
[2] Ueyama H, Yao T, Nakashima Y, et al. Gastric adenocarcinoma of fundic gland type (chief cell predominant type): proposal for a new entity of gastric adenocarcinoma. *Am J Surg Pathol*. 2010, 34(5):609-619.
[3] Yao T, Vieth, M. Oxyntic gland adenoma. *Digestive system tumours*. In *World Health Organization Classification of Tumours 5th edition* (ed. WHO Classification of Tumours Editorial Board) 83–84, (International Agency for Research on Cancer, World Health Organization, 2019).
[4] Ueyama H, Yao T, Akazawa Y et al. Gastric epithelial neoplasm of fundic-gland mucosa lineage: proposal for a new classification in association with gastric adenocarcinoma of fundic-gland type. *J Gastroenterol*. 2021, 56(9):814-828.
[5] Asahara, Hikari, et al. “Clinicopathological Features and the Prevalence of Oxyntic Gland Neoplasm: A Single-center Retrospective Study.” *Internal Medicine* (2023): 0552-22.
[6] Tohda G, Osawa T, Asada Y, et al. Gastric adenocarcinoma of fundic gland type: Endoscopic and clinicopathological features. *World J Gastrointest Endosc*. 2016, 25(4):244-251.
Disclosure: There are no COIs to disclose in relation to this presentation.

MP369

SLC26A9 GOVERNS GASTRIC PARIETAL CELL IDENTITY AND FUNCTIONS AS AN IMPORTANT PROTECTIVE ROLE IN THE INJURY-INDUCED METAPLASIA

Z. Ma¹, E. Wu^{2,3}, T. Li³, B. Tuo³, X. Liu⁴

¹Department of Gastroenterology, Affiliated Hospital of Zunyi Medical University, Zunyi, China, ²Affiliated Hospital of Zunyi Medical University, Zunyi, American Samoa, ³Affiliated Hospital of Zunyi Medical University, Zunyi, China, ⁴Affiliated Hospital of Zunyi Medical University, Hannover, China

Contact E-Mail Address: anhuimazhiyuan@163.com

Introduction: Gastric injury induces metaplasia is based on parietal cells loss and reprogramming chief cells into proliferative, mucin-rich spasmolytic polypeptide-expressing metaplasia (SPEM) cells. Previously, we demonstrated that parietal cell-selective Slc26a9 deficiency in mice promotes the development of SPEM and progress to gastric intraepithelial neoplasia in mice (Liu et al., Cellular oncology; 2022; Deng et al., DDW2023). However, the exact role of Slc26a9 in injury-induced metaplasia is need further investigated.

Aims & Methods: We used immunostaining to characterize the expression pattern of Slc26a9 during murine gastric development, homeostasis, and injury in homeostasis, after conditional genetic deletion of Slc26a9. Furthermore, to reveal the functional role of Slc26a9, Injury-induced metaplasia was established in Slc26a9^{fl/fl} mice and Slc26a9^{fl/fl}/Atp4b-Cre mice with high-dose tamoxifen.

Results: Mice with parietal cell selective Slc26a9 deficiency first developed spontaneous parietal cell damage, which subsequently led to SPEM. Parietal cell injury was associated with the release of typical pyroptosis factors, including NLRP3, Caspase-1, ASC, GasderminD, IL-1 β and IL-18. At the same time, SLC26A9 colocalized with caspase1, NLRP3, GSDMD, and NLRP3 and GSDMD, and produced a large number of reactive oxygen species (ROS), markers of mitochondrial damage, thereby expanding membrane perforation of GSDMD-N fragments and amplifying inflammasome-mediated parietic cell pyrodeath. At the same time, electron microscopy showed that after the knockout of the Slc26a9 gene, the mitochondria of the murine wall cells were obviously swollen, the cell membrane structure was blurred and damaged, the matrix was more dissolved, the ridge was broken and disappeared, and there were many bubble protrusions. This suggests that parietal cell specific SLC26A9 gene deletion may lead to parietal cell scorch death through mitochondrial damage mediated by GSDMD. However, with a large number of parietal cell damage and loss, gastric hypergastrinemia stimulates Tuft cell proliferation and migration to the gastric mucosa for colonization, and secretes a series of alarm hormones such as IL-25, IL-33, HMGB1.

Moreover, ILC2 cell secretory factors such as IL-17RA and IL-17RB, GATA3, CD90, CD25 were up-regulated. M2 macrophage polarization-related markers such as Arg1, Fizz1, Ym1, Klf4 and secreted chemokines such as CCL24 and CCL22 were significantly up-regulated. The immunofluorescence staining of F4/80+ and CD163+ was significantly increased. This suggests that the spontaneous injury of parietal cells caused by the deletion of SLC26A9 gene in gastric parietal cells may lead to gastric dysfunction (hypoacid and hypergastrinemia) and mucosal epithelial injury, which may promote the occurrence of SPEM through IL-25 mediating the activation of ILC2 cells to regulate the cellular immune mechanism of macrophage M2 polarization.

Conclusion: Slc26a9 target deletion in parietal cells leads to spontaneous damage and scorch death of parietal cells, which is the core target and cell origin of initiating SPEM. After parietal cell specific Slc26a9 gene deletion leads to spontaneous injury of parietal cells, gastric dysfunction and mucosal injury result in the release of alarm hormone IL-25, which pro-

motes the development of SPEM by activating IL-25-ILC2-macrophage M2 polarization axis. Slc26a9 plays an important protective role in stabilizing gastric epithelial cell differentiation and gastric mucosal immune homeostasis.

Disclosure: No conflict of interest.

MP370

LUTEOLIN TARGETING STAT3 DOWN-REGULATES LCN2 EXPRESSION AND INHIBITS THE GASTRIC PRECANCEROUS STATUS

X. Hao¹, J. Ning¹, Y. Lang¹, X. Han¹, Q. Meng¹, Y. Xiong¹, W. Fu¹, J. Zhang¹, C. Wang², S. Ding¹

¹Peking University Third Hospital, Department of gastroenterology, Beijing, China, ²Synthetic and Functional Biomolecules Center, Peking University, Beijing, China

Contact E-Mail Address: njing2006@aliyun.com

Introduction: During gastric cancer (GC) progression, two types of metaplasia, spasmolytic polypeptide-expressing metaplasia (SPEM) and intestinal metaplasia (IM), are considered key pre-tumour events crucial for malignant transformation to GC. Currently, no effective therapeutic strategies target these events.

Aims & Methods: This study was performed to investigate the inhibitory efficacy and mechanism of action of luteolin (Lut) on SPEM and IM. An in vivo SPEM model was established by intraperitoneal injection of high-dose tamoxifen (TAX) in mice, and the IM models were established by treating GES-1 cells and rats with chenodeoxycholic acid (CDCA). To reveal the mechanism of action of Lut, we performed transcriptomic analysis of Lut-treated gastric corpus specimens, and quantitative chemoproteomic profiling to identify key targets of Lut.

Results: Lut-treated mice exhibited remarkable resistance to oxyntic atrophy and emergence of SPEM. Significant numbers of Lut-treated rats entered remission from IM. Transcriptomic analysis revealed that up-regulated LCN2 expression in the injured mucosal region in SPEM model mice could be downregulated by Lut. LCN2 knockdown also inhibited high-dose TAX-induced SPEM formation. Quantitative chemoproteomic profiling results suggest that STAT3 is a key target of Lut and that STAT3 inhibition partially abolishes the beneficial effect of Lut.

Conclusion: Lut is a novel therapeutic candidate for SPEM and IM that can target STAT3 by downregulating LCN2 expression. These findings reveal a novel strategy for inhibiting gastric precancerous conditions.

Disclosure: Nothing to disclose.

MP371

OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE TREATMENT OF OESOPHAGEAL SQUAMOUS DYSPLASIA AND EARLY SQUAMOUS CELL CARCINOMA IN THE WEST

S. Gupta¹, F.V. Mandarino¹, J. Gauci¹, A. Whitfield¹, T. O'Sullivan¹, O. Cronin¹, C. Kerrison¹, A. Tang¹, E. Lee¹, S. Williams¹, N.G. Burgess¹, M.J. Bourke¹

¹Westmead Hospital, Sydney, Australia

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: Endoscopic submucosal dissection (ESD) has evolved to become a viable treatment option for oesophageal squamous dysplasia (SD) and early squamous cell carcinoma (ESCC). Although en bloc, R0, excision has the potential to yield an endoscopic cure, surgery remains the standard of care in the West. Furthermore, Western data pertaining to endoscopic outcomes is limited. We aimed to assess the efficacy and safety of ESD for SD and ESCC in a single tertiary referral centre.

Aims & Methods: We conducted a prospective observational cohort study over 87 months until November 2023 in consecutive patients undergoing ESD for SD or ESCC. The primary outcomes were enbloc, R0 and curative resection rates. Secondary outcomes included procedure duration, tumor recurrence and adverse events.

Results: 112 consecutive patients were referred for treatment and underwent ESD (median age 73 [IQR 68-78]; 50% male; Table 1). Median lesion size was 30 mm (IQR 20-50mm) and Paris IIa was the most common morphology (58.9%). Enbloc resection was achieved in 109 (97.3%) and R0 excision in 87 (77.7%). Curative resection in cases of LGD and HGD, where margins were clear of dysplasia, was 7/11 (63.6%) and 31/34 (91.2%) respectively. In those with T1a/T1b SCC, the curative resection rate was 20/61 (32.8%). In T1a SCC lesions, 11/20 (55.0%) had a curative ESD. Of the remainder, 6/9 were poorly differentiated, 1/9 had LVI, and 2/9 had positive margins (1 deep, 1 peripheral). In T1b SCC lesions, 9/41 were curative (22.0%). The remainder were either poorly differentiated, >T1b-SM1, LVI positive or a combination. In those with T1a/T1b disease, without adverse tumor biology, ESD achieved curative resection in 20/22 (90.9%). In the 41/61 (67.2%) T1a/T1b patients that did not meet criteria for cure, subsequent treatment included surgery (n=5), radiotherapy (n=5) and chemoradiotherapy (n=1). After MDT discussion, the remaining 30 were managed conservatively, due to advanced age or comorbidities. In these, recurrence occurred in 6/30 patients (1 local, 3 nodal, 2 metastatic) at a median follow up of 12 months (6-18 months). The median hospital length of stay was 1 day (IQR 1-3). Oesophageal strictures occurred in 46 patients (41.1%), requiring a median of 3 dilations (IQR 1-8). There were 2 cases of delayed bleeding. There were no perforations.

	Median (IQR) OR n (%)
Age (years)	73 (IQR 68-78)
Male gender	56 (50%)
Lesion Size (mm)	30 (IQR 20-50)
Morphology (Paris classification)	
Paris IIa	66 (58.9%)
Paris Is / IIa+Is	20 (17.9%)
Paris IIb	17 (15.2%)
Paris IIc component	8 (6.2%)
Other	1 (0.9%)
Histology	
Reactive squamous hyperplasia	6 (5.4%)
Low grade dysplasia	11 (9.8%)
High grade dysplasia	34 (30.4%)
T1a squamous cell carcinoma	20 (17.9%)
T1b squamous cell carcinoma	41 (36.5%)
ESD defect length (cm)	7 (IQR 5-9)
ESD defect circumferential extent (%)	60 (IQR 50-83.3)
Procedure duration (mins)	90 (IQR 60-120)
Hospital length of stay (days)	1 (IQR 1-3)

Table 1.

Conclusion: ESD is curative for low and high-grade dysplasia. In a Western setting, ESD offers definitive T-staging and has the potential to yield a cure in almost 33% of T1a and T1b SCC cases. Due to a high risk of disease recurrence, adjuvant therapy should be considered in cases of a non-curative resection.

Disclosure: Nothing to disclose.

MP372

FOXC1 MAY UNDERGO LIQUID-LIQUID PHASE SEPARATION AND INVOLVED IN THE DEVELOPMENT OF GASTRIC CANCER

W. Jing^{1,2,3}, K. Deng^{2,3}, J. Yang^{2,3}
¹Department of Gastroenterology & Hepatology, Chengdu, China, ²West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China, ³Sichuan University-Oxford University Huaxi Gastrointestinal Cancer Centre, Department of Gastroenterology & Hepatology, Chengdu, China

Contact E-Mail Address: daisyjingwn@163.com

Introduction: Recently, liquid-liquid phase separation (LLPS) of transcription factor has been found to play a critical role in the development of tumors [1-3]. Meanwhile, Forkhead box C1 (FOXC1), a transcription factor protein with intrinsically disordered regions (IDRs), is related with the prognosis of gastric cancer [4]. However, whether FOXC1 could undergo LLPS and whether FOXC1 involved in the development of gastric has not been studied until now.

Aims & Methods: Therefore, we aimed to investigate whether FOXC1 could undergo LLPS and the potential role of FOXC1 in gastric cancer. We analyzed different expression gene of gastric cancer samples from The Cancer Genome Atlas dataset and the sequencing results of our own samples. The protein sequence prediction website (Disprot - Database of Protein Disorder) was used to predict the IDRs of FOXC1. Besides, fluorescence recovery after photobleaching (FRAP) and cellular immunofluorescence were used to explore whether FOXC1 could undergo LLPS. What's more, cell proliferation assay, cell apoptosis assay and cell migration assay were utilized to investigate the potential role of FOXC1 in gastric cancer.

Results: In the different expression gene analysis of the TCGA database and our own data, it was found that the expression level of FOXC1 in gastric cancer was significantly higher than that of paracancer tissue (Figure 1 A-B), which was proved by RTq-PCR (Figure 1 C). Knockdown of FOXC1 in gastric cancer cell resulted in decreased proliferation (Figure 2A), decreased migration (Figure 2B), and increased apoptosis (Figure 2C). In the prediction of protein structure, it can be found that the IDRs region of FOXC1 accounts for more than 50% (Figure 3).

After the fluorescence bleaching of the droplet formed by FOXC1 with Ac-GFP in AGS cell, the fluorescence gradually recovers within a few minutes (Figure 4C). What's more, endogenous FOXC1 could form puncta with irregular distribution in nuclear (Figure 4D), which also proves that FOXC1 can undergo LLPS.

Conclusion: Overall, knockdown of FOXC1 in gastric cancer cell can inhibit the development of gastric cancer by decreasing proliferation and migration, increasing apoptosis. FOXC1 can also undergo LLPS in vitro and in vivo. Therefore, we speculate that FOXC1 may promote the development of gastric cancer through LLPS.

References: [1] Kondo H, Mishiro K, Iwashima Y, Qiu Y, Kobayashi A, Lim K, Domoto T, Minamoto T, Ogawa K, Kunishima M, Hazawa M, Wong RW. Discovery of a Novel Aminocyclopropanone Compound That Inhibits BRD4-Driven Nucleoporin NUP210 Expression and Attenuates Colorectal Cancer Growth. Cells. 2022 Jan 18;11(3):317. doi: 10.3390/cells11030317. PMID: 35159127; PMCID: PMC8833887.

[2] Boeynaems S, Alberti S, Fawzi NL, et al, Polymenidou M, Rousseau F, Schymkowitz J, Shorter J, Wolozin B, Van Den Bosch L, Tompa P, Fuxreiter M. Protein Phase Separation: A New Phase in Cell Biology. Trends Cell Biol. 2018 Jun;28(6):420-435. doi: 10.1016/j.tcb.2018.02.004. Epub 2018 Mar 27. PMID: 29602697; PMCID: PMC6034118.

[3] Peng Q, Tan S, Xia L, et al. Phase separation in Cancer: From the Impacts and Mechanisms to Treatment potentials. Int J Biol Sci. 2022 Aug 1;18(13):5103-5122. doi: 10.7150/ijbs.75410. PMID: 35982902; PMCID: PMC9379413.Liu Z, Li L, Li X, Hua M,

[4] Xu Y, Shao QS, Yao HB, Jin Y, Ma YY, Jia LH. Overexpression of FOXC1 correlates with poor prognosis in gastric cancer patients. *Histopathology*. 2014 Jun;64(7):963-70. doi: 10.1111/his.12347. Epub 2014 Feb 12. PMID: 24329718.

Disclosure: Nothing to disclose.

MP373

TRANSCRIPTOMIC-BASED MOLECULAR SIGNATURE TOWARDS EARLY DETECTION OF GASTRIC CANCER IN INTERMEDIATE-RISK POPULATIONS

C. Lopes^{1,2,3}, A. Brandao⁴, J. Costa⁵, D. Libânio^{1,6}, M. Dinis-Ribeiro^{1,6}, A.C. Pereira¹

¹Research Center of IPO Porto (CI-IPOP)/CI-IPOP@RISE (Health Research Group), Portuguese Institute of Oncology of Porto (IPO Porto)/Porto Comprehensive Cancer Center Raquel Seruca (Porto.CCC), Precancerous Lesions and Early Cancer Management Group, Porto, Portugal, ²Center for Health Technology and Services Research (CINTESIS@RISE), Porto, Portugal, ³ICBAS – School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal, ⁴Research Center of IPO Porto (CI-IPOP)/CI-IPOP@RISE (Health Research Group), Portuguese Institute of Oncology of Porto (IPO Porto)/Porto Comprehensive Cancer Center Raquel Seruca (Porto.CCC), Cancer Genetics Group, Porto, Portugal, ⁵Portuguese Institute of Oncology of Porto, Department of Pathology, Porto, Portugal, ⁶Portuguese Institute of Oncology of Porto, Department of Gastroenterology, Porto, Portugal

Contact E-Mail Address: catarina.p.lopes@ipoporto.min-saude.pt

Introduction: The asymptomatic nature of precancerous lesions, namely low- and high-grade dysplasia (LGD and HGD, respectively), constitutes a major clinical challenge that precludes a timely detection of gastric cancer (GC) in curable stages. The identification of novel and accurate biomarkers holds the promise of a better risk assessment and citizens stratification for an early diagnosis. In this exploratory study, we proposed to characterize the transcriptomic landscape of gastric lesions (GL) towards the definition of a molecular profile for early screening of GC in Western populations.

Aims & Methods: RNA-Sequencing analysis was conducted on RNA extracted from 39 formalin-fixed paraffin-embedded (FFPE) samples: 20 “normal-appearing” mucosa controls and 19 gastric lesions (GL), including LGD, HGD, and adenocarcinoma. Differential expression analysis, functional enrichment analysis, least absolute shrinkage and selection operator (Lasso) regression, and the machine-learning extreme gradient boosting (XGBoost) algorithm were employed to identify potential biomarkers and assess the predictive value of the molecular signature of the top dysregulated genes.

Results: A total of 1171 differentially expressed genes (DEGs) were identified in GL. Remarkably, 867 of these genes (74%) showed exclusive dysregulation in lesions compared to stage I GC samples from The Cancer Genome Atlas (TCGA) stomach adenocarcinoma (STAD) cohort. These unique biomarkers predominantly participate in translation, as well as metabolic and biosynthetic processes. In contrast, DEGs from TCGA-STAD cohort were primarily enriched in immunity-related processes. Notably, the eight best genes model, comprising *ADAMTSL1*, *CLDN2*, *ENC1*, *GSR*, *IQNC*, *PER1*, *PRR33*, and a novel transcript corresponding to a long non-coding RNA (lncRNA, ENSG00000227218), achieved an area under the curve (AUC) of 0.938 (95% CI: 0.815-1.000), with a sensitivity of 87.5% and specificity of 100% to classify GL samples.

Conclusion: This preliminary study identified over 800 DEGs exclusively in GL compared to stage I GC. Moreover, it unveiled a molecular-based signature that effectively discriminates patients with GL in an intermediate-risk

population. This discovery paves the way for enhancing early GC screening strategies, particularly for those who can be treated through minimally invasive, nonsurgical procedures.

Disclosure: Nothing to disclose.

MP374

ENHANCING EARLY DETECTION OF OESOPHAGEAL SQUAMOUS CELL CARCINOMA THROUGH SHALLOW WHOLE-GENOME SEQUENCING AND NON-ENDOSCOPIC SPONGE SAMPLING

A. Yusuf¹, M. Turkot², S. Malhotra³, M. di Pietro¹, M. O'Donovan³, N. Pilonis⁴, K. Nowicki-Osuch⁵, A. Mroz^{2,6}, M. Lenarcik^{2,6}, M. Mikula⁷, M. Wójtowicz-Popiel^{6,4}, J. Reguła^{2,4}, M. Kamiński^{2,4}, R. Fitzgerald¹, W. Januszewicz^{2,4}

¹University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom, ²Medical Centre for Postgraduate Education, Department of Gastroenterology, Hepatology and Clinical Oncology, Warsaw, Poland, ³Cambridge University Hospitals NHS Foundation Trust, Department of Histopathology, Cambridge, United Kingdom, ⁴Maria Skłodowska-Curie National Research Institute of Oncology, Department of Gastroenterological Oncology, Warsaw, Poland, ⁵German Cancer Research Center (DKFZ), Heidelberg, Germany, ⁶Medical Centre for Postgraduate Education, Department of Pathomorphology, Warsaw, Poland, ⁷Maria Skłodowska-Curie National Research Institute of Oncology, Department of Genetics, Warsaw, Poland

Contact E-Mail Address: ay327@cam.ac.uk

Introduction: Oesophageal squamous cell carcinoma (OSCC) represents approximately 90% of the nearly half-million annual cases of oesophageal cancer globally. The invasiveness and high costs associated with traditional upper endoscopy limit its use in the routine surveillance of at-risk populations, including individuals with a history of head and neck cancer (HNC). Previous data suggest that copy number abnormalities (CNAs) are a feature of OSCC development.

Aims & Methods: This study explored the efficacy of shallow whole-genome sequencing (sWGS) to detect genome-wide CNAs in cells collected using a non-endoscopic sponge pan-oesophageal sampling device. Our objective was to develop and validate a predictive model for the early detection of oesophageal squamous dysplasia and neoplasia, aiming to improve disease prognosis through timely intervention.

We prospectively collected oesophageal specimens from 178 participants using the Cytosponge device as part of the EDEN and OSCAR projects: OSCC (n = 24), high-risk individuals (n = 61), and healthy controls with dyspeptic symptoms (n = 93). The samples underwent 1.5-2x sWGS as well as H&E staining for atypia assessment and p53 immunohistochemistry (IHC) which were performed by two gastrointestinal (GI) pathologists who were blinded to the reference endoscopic diagnoses. Through penalised regression analysis, we identified significant CNAs indicative of dysplasia or early neoplasia. These critical genomic insights were then used to develop and refine a logistic regression model aimed at predicting dysplasia or early neoplasia in cytosponge-derived specimens. The predictive accuracy of the model was subsequently confirmed through validation against sWGS in microdissected ESD samples which represented known pathological states.

Results: Key genomic indicators for oesophageal squamous dysplasia and early neoplasia were identified, including significant CNAs in chromosome arms chr2q, chr3q, chr9p, and chr11q along with the Genome-Wide Instability Score (GWIS), a percentage-based metric quantifying genomic instability across the genome. Our logistic regression model, which integrated these genomic biomarkers, achieved an Area Under the Receiver

Operating Characteristic Curve (AUROC) of 0.947, with sensitivity and specificity rates of 89% and 88.2%, respectively. This model outperformed another that utilised only pathological data (definite squamous atypia and p53 IHC), which achieved an AUROC of 0.880, with a sensitivity and specificity of 83.6% and 84.6%, respectively. However, when pathological data were combined with the genomic indicators, the diagnostic performance of our model improved significantly, resulting in an AUROC of 0.969 with enhanced sensitivity and specificity of 95.9% and 90.5%, respectively. Further validation of the genomic model against microdissected ESD samples with known pathological states reinforced its robustness, achieving an AUROC of 0.879, which improved to 0.905 when low grade dysplasia (LGD) samples were excluded, highlighting the diagnostic challenges and variability in LGD classification.

Conclusion: The integration of shallow whole-genome sequencing with non-endoscopic sponge sampling has the potential for the early detection of OSCC. This approach is particularly valuable in high-risk populations and settings where traditional endoscopy is impractical.

Disclosure: Nothing to disclose.

AI and beyond

13:00-14:00 / Poster Stage 6

MP375

NAVIGATING COELIAC DISEASE WITH ARTIFICIAL INTELLIGENCE: A PATH TOWARDS ENHANCED PATIENT AND PHYSICIAN SUPPORT

A. Achemlal¹, C. Hiji¹, S. Berrag¹, S. Azammam¹, M. Amine¹, S. Oualaalou¹, S. Ouahid¹, C. Jioua¹, S. Akir¹, N. Fouad¹, T. Adioui¹, M. Tamzaourte¹

¹Mohamed V Military Training Hospital, Gastro Enterology 1, Rabat, Morocco

Contact E-Mail Address: achemlal.amine@gmail.com

Introduction: The prevalence of celiac disease is increasing and represents a growing global health issue. The disease profoundly affects patients' quality of life through the multitude of symptoms and complications, as well as the necessity for strict adherence to a gluten-free diet. Gastroenterologists face persistent challenges in diagnosing and managing celiac disease amidst its complexities.

In this context, the integration of artificial intelligence (AI) emerges as a promising advancement, offering potential to revolutionize the landscape of celiac disease management.

Our objective is to evaluate the effectiveness of AI as a reliable and useful asset for patients and gastroenterologists in the management of celiac disease.

Aims & Methods: Research was carried out on the Google Trends website to identify the 5 most searched-for keywords (from 2004 to March 2024) related to celiac disease: gluten-free diet, diagnosis, serologies, associated diseases, complications.

We asked 10 gastroenterologists and 10 celiac patients to formulate all the questions they had about celiac disease in relation to these key words. Eighty questions were generated based on their responses (40 questions formulated by each group).

The questions were inputted into the "prompt" section of an artificial intelligence (Google GEMINI version 20/02/2024) and the answers were evaluated using a 7-point Likert-type reliability and usefulness scale by two independent celiac disease experts.

Statistical analyses were performed using JAMOVI version 2.3 software. Inter-observer agreement was assessed using Intra-class correlation coefficient [ICC], and Student t-test was used to compare differences between two groups. The significance level for this study was set at $p < 0.05$.

Results: The intra-class correlation coefficient values for both reliability and usefulness scores demonstrated excellent agreement between the two experts.

Indeed, for answers intended to help gastroenterologists, we observe (Reliability: ICC=0.918, 95% CI : 0.852-0.956 Usefulness: ICC=0.887, 95% CI : 0.798-0.939).

For answers intended for celiac patients (Reliability: ICC=0.935, 95% CI : 0.881-0.965 and ICC=0.926, 95% CI : 0.865-0.960)

The average scores given by experts n°1 and n°2 were: Reliability 4.83 ± 1.58 vs. 5.03 ± 1.54 ($p=0.04$) and Usefulness 4.75 ± 1.39 vs. 5.00 ± 1.26 ($p=0.01$), suggesting that AI had limitations in providing reliable but also useful answers to healthcare professionals about celiac disease.

However, when it came to answering celiac patients' questions, we noted that AI gave better scores, this time with no statistically significant difference between the two experts: 5.60 ± 1.15 vs 5.63 ± 1.17 ($p=0.78$) and 5.67 ± 1.33 vs 5.78 ± 1.27 ($p=0.23$).

Finally, there was a statistically significant difference between the two groups (gastroenterologist and celiac patients), concerning the reliability and usefulness of AI responses for expert n°1 ($p=0.008$ and $p=0.001$ respectively) as well as for expert n°2 ($p=0.045$ and $p=0.003$ respectively).

Conclusion: The results suggest that AI, particularly Google GEMINI, can

be a particularly useful tool in managing celiac disease, especially for celiac patients, by providing reliable and useful answers to questions related to gluten-free diet, diagnosis, serologies, associated diseases, and complications. However, the results are less satisfactory when it comes to answering healthcare professionals, highlighting the need for constant updates and reliance on reliable and up-to-date sources.

Disclosure: Nothing to disclose.

MP376

COPY NUMBER ALTERATIONS BASED MACHINE LEARNING IN PREDICTING PROGNOSIS FOR BARRETT'S ESOPHAGUS PATIENTS WITH LOW-GRADE AND INDEFINITE DYSPLASIA

L. Wu¹, G. Devonshire¹, B. Walker-Smith¹, A. M. Frankell¹, M. O'Donovan¹, M. di Pietro¹, R. Fitzgerald¹

¹University of Cambridge, Cambridge, United Kingdom

Contact E-Mail Address: lw748@cam.ac.uk

Introduction: Accurate estimation of cancer risk in patients with Barrett's esophagus (BE) and low-grade dysplasia (LGD) or indefinite for dysplasia (ID) is difficult, leading to potential under- and over-treatment. We aimed to evaluate the utility of machine learning (ML) and copy number alterations (CNAs) assessed by shallow whole genome sequencing (SWGS) on standard formalin-fixed paraffin-embedded (FFPE) samples for precise risk stratification in this group of BE patients.

Aims & Methods: We conducted a retrospective analysis on a cohort of 164 BE patients encompassing 990 tissue samples with SWGS (~0.4X) data from 2001-2018. These included 215 samples with LGD or ID from 64 patients, of which 38 progressed to high-grade dysplasia (HGD) or cancer at later timepoints (P), and 26 who did not progress (NP). CNAs were quantified using QDNASeq, and outlier bins were determined by Tukey's fences. Subsequently, the CNAs of 64 esophageal cancer driver genes were compared between P and NP groups using t-tests and ranked by p-values. A random forest (RF) ML model was developed on the CNAs of the 64 genes, employing nested 5-fold cross-validation split by patients and iterated 100 times to mitigate bias. The model's performance was compared against routine p53 immunohistochemistry (IHC), a decision tree that incorporates p53 followed by the ML model, and the current ESGE clinical guideline recommending treatment after LGD is identified in two endoscopies. Both the model and model+p53 were assessed across 100 test sets derived from the cross-validation.

The guideline's performance was evaluated using a historical extended cohort comprising 253 LGD patients, of which 32 progressed, and underwent at least one surveillance endoscopy after LGD diagnosis and before HGD/cancer diagnosis. According to the guideline, two occurrences of LGD result in a positive prediction.

Results: Significant variance was observed in the distribution of relative CNAs across genomic bins between P- and NP-LGD/ID samples, with the proportions of outliers at 2.15% (95% CI: 1.88%, 2.42%) vs. 1.35% (95% CI: 1.26%, 1.44%).

The most divergent genes included TP53, ABCB1, MET, BRAF, and SIN3A, exhibiting higher CNAs in progressed samples. Among the 215 samples, the RF model achieved an average sensitivity of 73.4% and specificity of 80.2%.

Of these, 160 samples were tested for p53 IHC staining, where p53 alone showed a sensitivity of 22.1% and specificity of 100%, and a combined analysis of p53 and model increased the sensitivity of model alone (81.5% vs. 78.1%, $p<0.001$) while maintaining the same specificity at 78.9%. As a benchmark, the performance of the current ESGE guideline on biopsy diagnosed LGD patients demonstrated a sensitivity of 75.0% and specificity of 59.6%.

Conclusion: Our findings affirm the utility of ML and CNAs in predicting progression in BE patients with LGD or ID. Incorporating p53 followed by ML can further improve the performance. Molecular biomarkers would allow anticipation of intervention in high-risk cases and reduction of over-treatment in low-risk cases.

Disclosure: Nothing to disclose.

MP377

ARTIFICIAL INTELLIGENCE IMPROVES ENDOSCOPISTS' VESSEL DETECTION DURING THIRD SPACE ENDOSCOPY

M. Scheppach¹, R. Mendel², A. Muzalyova¹, R. David², A. Probst¹, S. Nagl¹, C. Römmele¹, H.C. Yip³, L.H.-S. Lau⁴, S. Gölder⁵, A. Schmidt⁶, K. Kouladourous⁷, M. Abdelhafez⁸, B. Walter⁹, M. Meinikheim¹⁰, P.W.Y. Chiu¹¹, C. Palm², H. Messmann¹, A. Ebigo¹

¹University Hospital of Augsburg, Internal Medicine III - Gastroenterology, Augsburg, Germany, ²Ostbayerische Technische Hochschule Regensburg, Regensburg Medical Image Computing (ReMIC), Regensburg, Germany, ³The Chinese University Of Hong Kong, Hong Kong, Hong Kong, ⁴The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁵Ostalb Klinikum, Department of Internal Medicine I - Gastroenterology, Aalen, Germany, ⁶Robert-Bosch-Krankenhaus, Department of Gastroenterology, Stuttgart, Germany, ⁷Universitätsmedizin Mannheim, Zentrale Interdisziplinäre Endoskopie, Mannheim, Germany, ⁸Klinikum rechts der Isar, Technical University of Munich, II. Medizinische Klinik und Poliklinik, Munich, Germany, ⁹Universitätsklinikum Ulm, Klinik für Innere Medizin I, Ulm, Germany, ¹⁰University Hospital of Augsburg, Department of Gastroenterology, Augsburg, Germany, ¹¹Chinese University of Hong Kong, Department of Surgery, Hong Kong, Hong Kong

Contact E-Mail Address: markus.scheppach@uk-augsburg.de

Introduction: Artificial intelligence (AI) algorithms aid endoscopists in detecting and characterizing colonic polyps in clinical practise and lead to an improved adenoma detection rate. AI may also support therapeutic procedures by detecting and marking anatomical structures during complex procedures like endoscopic submucosal dissection (ESD) ¹. However, a possible effect of AI on the intraprocedural blood vessel detection rate during third space endoscopy remains unclear.

Aims & Methods: This study aimed at evaluating the impact of a newly developed AI algorithm for real time intraprocedural vessel detection on the vessel detection performance of endoscopists during ESD. To this end, 5470 single images from 59 full length third space endoscopy videos were annotated for submucosal blood vessels. Together with 179681 additional unlabeled images this dataset was utilized for the training of a DeepLabV3+ neural network. The trained algorithm detected and marked submucosal blood vessels on the endoscopic image in real time. Consequently, a video test consisting of 101 video clips with 200 predefined blood vessels was used for the evaluation of the algorithm alone, as well as 19 endoscopists with and without AI support.

Results: The algorithm showed a vessel detection rate (VDR) of 93.5% and a median vessel detection time (VDT) of 0.3 sec. AI support was associated with an elevation of endoscopists' VDR from 56.4% to 72.4% ($p<0.001$). VDT decreased from 6.7 to 5.2 sec with AI support ($p<0.001$). False positive detections were measured on 4.5% of single frames. They had a significantly shorter duration than true positive findings (0.7 vs. 6.0 sec, $p<0.001$).

Conclusion: AI support led to increased VDR and reduced VDT of endoscopists. False positive findings were easily distinguishable from true positives by their short duration. Future research may elucidate a possible

effect of AI on clinical parameters like intraprocedural complication rates or procedure times.

References: 1. Ebigo A, Mendel R, Scheppach MW, et al. Vessel and tissue recognition during third-space endoscopy using a deep learning algorithm. *Gut* 2022.

Disclosure: Nothing to disclose.

MP378

DIFFERENT BIOPSY RATE BRINGS DIFFERENT APPLICATION EFFECTIVENESS FOR ARTIFICIAL INTELLIGENCE DEVICE IN DETECTING GASTRIC NEOPLASMS IN REAL WORLD

L. Huang¹, L. Wu², H. Yu³

¹Renmin Hospital of Wuhan University, Wuhan, China, ²Renmin Hospital of Wuhan university, Wuhan, China, ³Renmin Hospital of Wuhan University, Gastroenterology, Wuhan city, China

Contact E-Mail Address: huangli9707@163.com

Introduction: The implementation of computer-aided detection (CAD) devices in esophagogastroduodenoscopy (EGD) could autonomously identify gastric precancerous lesions and neoplasms, and reduce the miss rate of gastric neoplasms in prospective trials. However, there is still insufficient evidence of their use in real-life clinical practice.

Aims & Methods: A real-world, two-center, large-volume, pragmatic study was conducted at Wenzhou Central Hospital (WCH) and Renmin Hospital of Wuhan University (RHWU). Random biopsy and target biopsy were adopted and CAD devices were applied in 2019 and 2021 at WCH and RHWU, respectively. We compared differences in gastric precancerous and neoplasm detection of EGD before and after the use of CAD devices in the first half of the year.

Results: A total of 33885 patients were included and 32886 patients were ultimately analysed. In WCH of which biopsy rate > 95%, with the implementation of CAD, more early gastric cancer detection rate (0.35% vs. 0.59%, $p=0.028$, $OR(95\%CI) = 1.65(1.06-2.60)$) was found while gastric neoplasm detection rate (1.39% vs. 1.36%, $p=0.897$, $OR(95\%CI) = 0.98(0.76-1.26)$) remained stable. In RHWU of which biopsy rate < 20%, the gastric neoplasm detection rate (1.78% vs. 3.23%, $p<0.001$, $OR(95\%CI) = 1.84(1.33-2.54)$) nearly doubled after the implementation of CAD while there was no significant change in the early gastric cancer detection rate.

Conclusion: In our study of large-volume tertiary centers with varied biopsy strategies, we observed that diagnostic benefits differed depending on the application conditions, and each biopsy approach offered distinct advantages. In healthcare center with a high biopsy rate exceeding 95%, the CAD device appeared to enable endoscopists to conduct more precise, targeted biopsies, leading to an increased detection of early gastric cancer. However, the overall gastric neoplasm detection rate remained consistent. In contrast, at institutions like RHWU, which employed a targeted biopsy strategy resulting in an average biopsy rate less than 20%, the incorporation of CAD in routine EGD demonstrated a notable increase in the overall gastric neoplasm detection rate, particularly for low-grade intraepithelial neoplasia.

References: 1. Sung, H., et al., *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries*. *CA Cancer J Clin*, 2021. 71(3): p. 209-249.

2. Correa, P., *Human gastric carcinogenesis: a multistep and multifactorial process--First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention*. *Cancer Res*, 1992. 52(24): p. 6735-40.

3. Leung, W.K. and J.J. Sung, *Review article: intestinal metaplasia and gastric carcinogenesis*. *Aliment Pharmacol Ther*, 2002. 16(7): p. 1209-16.

4. Correa, P., et al., *A model for gastric cancer epidemiology*. *Lancet*, 1975. 2(7924): p. 58-60.

5. Ling, T., et al., *A deep learning-based system for identifying differentiation status and delineating the margins of early gastric cancer in magnifying narrow-band imaging endoscopy*. *Endoscopy*, 2021. 53(5): p. 469-477.

6. Gong, E.J., et al., *Deep learning-based clinical decision support system for gastric neoplasms in real-time endoscopy: development and validation study*. *Endoscopy*, 2023. 55(8): p. 701-708.

7. Wu, L., et al., *Deep learning system compared with expert endoscopists in predicting early gastric cancer and its invasion depth and differentiation status (with videos)*. *Gastrointest Endosc*, 2022. 95(1): p. 92-104.e3.

8. Guimarães, P., et al., *Deep-learning based detection of gastric precancerous conditions*. *Gut*, 2020. 69(1): p. 4-6.

Disclosure: Nothing to disclose.

MP379

NEW MACHINE-LEARNING MODELS OUTPERFORM CONVENTIONAL RISK ASSESSMENT TOOLS IN GASTROINTESTINAL BLEEDING

E. Boros^{1,2}, K.G. Prószéky³, R. Molontay^{3,4}, J. Pintér^{3,4}, N. Vörhendi^{5,1}, O.A. Simon^{6,1}, B. Teutsch^{7,1,8}, D. Palinkas^{9,7}, L. Frim¹, E. Tari^{10,7}, E.-B. Gagy^{11,7}, I. Szabó⁶, R. Hágendorn⁶, Á. Vincze⁶, F. Izbéki², Z. Abonyi-Tóth⁷, A. Szentesi¹, V. Vass¹, P. Hegyi^{1,7,10}, B. Eross^{7,10,1}

¹University Of Pécs, Institute For Translational Medicine, Pécs, Hungary, ²Fejér County Szent György University Teaching Hospital, Székesfehérvár, Hungary, ³Budapest University of Technology and Economics, Department of Stochastics, Institute of Mathematics, Budapest, Hungary, ⁴Budapest University of Technology and Economics, HUN-REN-BME Stochastics Research Group, Budapest, Hungary, ⁵Hospital and Clinics of Siófok, Internal Medicine, Siófok, Hungary, ⁶Medical School, University of Pécs, First Department of Medicine, Pécs, Hungary, ⁷Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ⁸Semmelweis University, Department of Radiology, Medical Imaging Centre, Budapest, Hungary, ⁹Central Hospital of Northern Pest – Military Hospital, Department of Gastroenterology, Budapest, Hungary, ¹⁰Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ¹¹Semmelweis University, Selye János Doctoral College for Advanced Studies, Budapest, Hungary

Contact E-Mail Address: boroseszter987@gmail.com

Introduction: Acute gastrointestinal bleeding (GIB) is a common reason for hospitalization, with a 2%–20% risk of mortality. Identification of patients at high risk of death is essential to make fast and adequate decisions on their management.

Aims & Methods: We developed two machine-learning (ML) models to calculate the risk of in-hospital mortality in patients admitted due to overt GIB.

The prospective, multicenter Hungarian GIB Registry's data were analyzed. We focused on in-hospital mortality and applied statistical binary classification. The predictive performance of XGBoost and Catboost machine-learning algorithms was compared with the Glasgow-Blatchford (GBS) and pre-endoscopic Rockall scores. We evaluated our models using five-fold cross-validation, and performance was measured by area under receiver operating characteristic curve (AUC) analysis with 95% confidence intervals (CI). The individual predictions and the variables' contribution to the outcome were calculated via the SHapley Additive exPlanations (SHAP) method.

Results: Overall, we included 1,021 patients in the analysis; 52% had nonvariceal upper GIB, 30% had lower GIB, and 9% had variceal bleeding. The median age was 70 years; 60% were men. In-hospital death occurred in 108 cases (11%). We selected 19 of 96 input variables in both final ML

models. The XGboost and the Catboost model identified patients who died with an AUC of 0.84 (CI: 0.76-0.90; 0.77-0.90; respectively) in the internal validation set, whereas the GBS and pre-endoscopic Rockall clinical scoring system's performance was significantly lower, AUC values of 0.68 (CI: 0.62 - 0.74) and 0.62 (CI: 0.56 - 0.67), respectively. The XGBoost model had a specificity of 0.96 (CI: 0.92-0.98) at a sensitivity of 0.25 (CI: 0.10-0.43) compared with the CatBoost model, which had a specificity of 0.74 (CI: 0.66-0.83) at a sensitivity of 0.78 (CI: 0.57-0.95). In the CatBoost model, the most influential variables contributing to the prediction were CRP level, smoking, melena, minimum systolic blood pressure, previous GIB, Glasgow Coma Scale and hemoglobin level.

Conclusion: The new ML models identified patients with high mortality risk significantly better than GBS and pre-endoscopic Rockall scores. Due to its better sensitivity, we prefer the CatBoost model in determining the in-hospital mortality risk of GIB.

Disclosure: Nothing to disclose.

MP380

HUMAN-COMPUTER INTERACTION: EXAMINING THE INFLUENCE OF ARTIFICIAL INTELLIGENCE ON THE DIAGNOSTIC CONFIDENCE OF ENDOSCOPISTS IN THE EVALUATION OF BARRETT'S ESOPHAGUS

D.A. Roser¹, M. Meinikheim¹, R. Mendel², C. Palm², A. Muzalyova¹, D. Rauber², T. Rückert², N. Parsa^{3,4}, M. Byrne^{4,5}, H. Messmann¹, A. Ebigbo¹

¹University Hospital Augsburg, Department of Gastroenterology, Augsburg, Germany, ²Ostbayerische Technische Hochschule Regensburg, Regensburg Medical Image Computing, Regensburg, Germany, ³Mayo Clinic, Division of Gastroenterology and Hepatology, Scottsdale, United States of America, ⁴Satisfai Health, Vancouver, Canada, ⁵Vancouver General Hospital, The University of British Columbia, Department of Gastroenterology, Vancouver, Canada

Contact E-Mail Address: David.Roser@uk-augsburg.de

Introduction: Human-computer interactions (HCI) can substantially influence the performance of Artificial Intelligence (AI). Studies indicate that although endoscopists, when assisted by AI, demonstrate significant improvements in assessing Barrett's esophagus (BE), their performance does not reach the stand-alone level achieved by AI. A critical aspect of HCI is the impact of AI on the certainty and confidence exhibited by endoscopists. Indirectly, diagnostic confidence when utilizing AI may be associated with the trust and acceptance of AI. In a study focusing on BE videos, our objective was to examine the influence of AI on endoscopists' diagnostic confidence and explore potential correlations with diagnostic performance.

Aims & Methods: Twenty-two endoscopists from twelve centers, with varying levels of BE experience, reviewed ninety-six standardized endoscopy videos. The endoscopists were categorized as experts and non-experts and were randomly assigned to evaluate the videos with and without AI. Participants were divided into two arms: Arm A assessed videos initially without AI and then with AI, while Arm B followed the opposite order. Evaluators were tasked with identifying BE-related neoplasia and providing confidence ratings both with and without AI on a scale from 0 to 9. The study was followed up by a survey.

Results: In Arm A (without AI first, with AI second), the use of AI significantly increased confidence levels for both experts and non-experts ($p < 0.001$). Notably, only non-experts experienced a significant improvement in sensitivity and specificity ($p < 0.001$ bzw. $p < 0.05$) with the assistance of AI. While experts exhibited higher confidence levels without AI compared to non-experts with AI, there was no significant difference in accuracy be-

tween these two groups. In Arm B both groups demonstrated a significant reduction in confidence ($p < 0.001$), while maintaining consistent accuracy levels. In addition, in 9% of the choice changes with AI, the wrong choice was made despite correct indications made by AI.

Conclusion: AI significantly boosted confidence levels for both expert and non-expert endoscopists - an effect that was reversible in the study model. Furthermore, experts consistently displayed higher confidence levels, with or without AI, compared to non-experts with AI, despite comparable outcomes. It was further observed that in 9% of the choice changes the investigators ignored the AI in disadvantage of the patient. These findings highlight the potential role of AI in enhancing diagnostic confidence during endoscopic assessments.

Disclosure: Nothing to disclose.

MP381

A SELECTIVE RESECTION ALGORITHM FOR BARRETT'S NEOPLASIA OPTIMIZES ONCOLOGICAL OUTCOMES

S. Gupta^{1,2}, F.V. Mandarino¹, A. Sakiris¹, J. Gauci¹, M. Sidhu^{1,2}, A. Whitfield^{1,2}, O. Cronin^{1,2}, T. O'Sullivan^{1,2}, C. Kerrison¹, E. Lee¹, N.G. Burgess^{1,2}, M.J. Bourke^{1,2}

¹Westmead Hospital, Gastroenterology & Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: Accepted oncological principles advise enbloc, R0, excision of cancer to provide a cure. In Barrett's neoplasia, this includes T1a and T1b disease, where histology is favorable. While treatment options include endoscopic mucosal resection (EMR) and submucosal endoscopic dissection (ESD), a mechanism for appropriate technique selection has not been described.

Aims & Methods: We conducted a prospective observational study to evaluate the performance of a selective resection algorithm for Barrett's neoplasia (SRAB). To achieve an enbloc resection, ESD was selected if there was a suspicion for $\geq$ T1a disease and the lesion was >15 mm (January 2017 to April 2023). This was compared with a conventional EMR predominant approach (CEA), where ESD was only performed in cases suspicious for deep submucosal invasion or T1b disease (February 2013 to December 2016). The primary outcome was curative oncologic resection (R0 resection with favorable histologic features).

Results: A total of 298 resections were performed in 298 patients (68 UEA, 230 SRAB). Median lesion size was 20 mm (IQR 15-30). T1a adenocarcinoma was identified in 83 (27.9%) and T1b in 58 (19.5%), of which 31 (10.4%) were SM1. Comparing T1a and T1b disease, the rate of enbloc resection (CEA 12 [46.2%] vs SRAB 103 [90.4%]; $P < 0.001$), R0 excision (CEA 7 [26.9%] vs SRAB 86 [74.8%]; $P < 0.001$) and curative resection (CEA 6 [23.1%] vs SRAB 58 [50.4%]; $P = 0.011$) was higher in the SRAB group. Among all T1a and T1b-SM1 cases with favorable histology, which underwent ESD, 39/46 (84.8%) were R0 excisions and are likely cured. There were no significant differences in adverse events ($P > 0.788$ for all).

Conclusion: A selective resection algorithm optimizes oncologic outcomes for Barrett's adenocarcinoma and mitigates the risk of piecemeal resection of cancers.

Disclosure: Michael J. Bourke: Research Support: Olympus, Cook Medical, Boston Scientific.

MP382

WITHDRAWN

MP383

NOVEL AI-ENABLED ASSESSMENT OF HISTOLOGIC REMISSION AND EARLY RESPONSE TO THERAPY IN A PHASE 2 CLINICAL TRIAL UC COHORT

M. Iacucci¹, G. Santacroce¹, P. Meseguer^{2,3}, A. Diéguez², R. Del Amor², W.J. Eastman⁴, I. Zammarchi¹, B. Hayes⁵, R. Crotty⁵, Y. Maeda¹, M. Puga-Tejada¹, I. Ditonno¹, B.B. Kolawole⁶, U. Chaudhari⁶, V. Vadori⁶, L. Burke⁵, S. Ghosh¹, E. Grisan⁶, V. Naranjo²
¹APC Microbiome Ireland, College of Medicine and Health, University College of Cork, Cork, Ireland, ²Instituto Universitario de Investigación e Innovación en Tecnología Centrada en el Ser Humano, HUMAN-tech, Universitat Politècnica de València, València, Spain, ³valgrAI – Valencian Graduate School and Research Network of Artificial Intelligence, Valencia, Spain, ⁴Eli Lilly and Company, Indianapolis, United States of America, ⁵Department of Histopathology, Cork University Hospital, Cork, Ireland, ⁶School of Engineering, London South Bank University, London, United Kingdom

Contact E-Mail Address: iacuccim@yahoo.it

Introduction: Achieving Histologic Remission is a key therapeutic target in ulcerative colitis (UC) and is predictive of favourable clinical outcomes. Predicting consistent therapy responses in clinical trials and practice is an unmet need crucial for improving therapeutic decisions in UC patients.

Aims & Methods: Thus, our study aimed to develop a novel AI model for assessing histologic disease activity and predicting early therapy response in a Phase 2 Clinical trial UC cohort. We used 302 whole slide images (WSIs) from moderate-to-severe active UC patients enrolled in a phase 2 mirikizumab (anti-IL23 mAb) clinical trial to train a novel deep neural network (DNN) model for WSIs. 106 WSIs from baseline, 106 from 12 weeks of treatment and 90 from 52 weeks of treatment were included. The ability of the model to predict remission/activity and response to therapy at 12 and 52 weeks was assessed. The system output was compared with human assessment. Histologic remission was defined as Geboes <2.0 and histologic improvement as Geboes <3.0. An early response to therapy at different time points was based on histologic remission or histologic improvement.

Results: Using all available WSIs, the system distinguished histologic activity/remission with sensitivity, specificity, and accuracy of 89%, 86% and 88%, respectively. The DNN predicted response to therapy based on histologic remission with 79% sensitivity, 78% specificity, and 78% accuracy at week 12 and 80% sensitivity, 92% specificity, and 87% accuracy at week 52. Furthermore, the model predicted response to therapy based on histologic improvement with 79% sensitivity, 76% specificity, 77% accuracy at week 12 and 80% sensitivity, 92% specificity, and 87% accuracy at week 52.

	HR	Response to therapy			
		HR week 12	HR week 52	HI week 12	HI week 52
Sensitivity	88.5%	78.6%	79.5%	79.3%	79.5%
Specificity	86.4%	78%	92.2%	75.5%	92.2%
Accuracy	87.8%	78.3%	86.7%	77.4%	86.7%

Abbreviations: HI, histological improvement; HR, histological remission.

Conclusion: Our study shows the remarkable ability of this novel AI histology model to distinguish histologic remission and activity in a clinical trial cohort. Notably, the model accurately predicted response to therapy at weeks 12 and 52. This AI model represents a promising tool in clinical trials and potentially in practice, offering objective guidance for personalized management in UC patients.

Disclosure: Nothing to disclose.

MP384

SUBSTANCE P AND NK1R – A NOVEL NEUROIMMUNE PATHWAY IN GASTRO-OESOPHAGEAL REFLUX DISEASE

T. Leech¹, P. Woodland², D. Kellsell³, D. Blaydon³, M. Peiris⁴
¹Queen Mary University of London, Wingate Institute of Neurogastroenterology, London, United Kingdom, ²Queen Mary University Barts & the London, Wingate Institute of Neurogastroenterology, London, United Kingdom, ³Queen Mary University of London, Blizard Institute, London, United Kingdom, ⁴Blizard Institute, Queen Mary University of London, Centre for Neuroscience, Surgery and Trauma, Wingate Institute of Neurogastroenterology, London, United Kingdom

Contact E-Mail Address: t.leech@qmul.ac.uk

Introduction: Gastro-oesophageal reflux disease (GORD) is characterised by visceral pain hypersensitivity, manifesting as heartburn, and distal oesophageal inflammation. In the oesophageal mucosa of GORD patients, even without visible inflammation (non-erosive reflux disease; NERD) there is increased innervation of sensory nerve fibres containing Substance P (SP) (Xu et al., 2013). SP may be released in response to luminal refluxate or inflammatory mediators to potentiate neuro-immune pathways relevant to GORD pathogenesis. We aimed to investigate the contribution of SP and its receptor NK1R to GORD symptoms.

Aims & Methods: To assess expression of NK1R on native tissue epithelium, biopsies were collected from healthy controls (HC), functional heartburn (FH), NERD and erosive reflux disease (ERD) patients following informed consent (Royal London Hospital ethics number: 19/LO/1506) and prepared for immunohistochemistry. NK1R was co-stained with epithelial cell marker E-Cadherin, pan-leukocyte marker CD45, and general T lymphocyte marker CD3. NK1R protein level was determined by mean fluorescence intensity of 3 FOVs. Cells of the NE-1 oesophageal epithelial cell line were incubated with media containing 100 nM and 300 nM SP for 30 minutes. Cells were lysed and intracellular inflammatory pathway activation was determined by p-NF-κB/NF-κB ratio through Western blot. mRNA levels of the inflammatory cytokine CXCL8 were determined via qPCR with 18S rRNA as a housekeeping gene.

Results: Quantification of mucosal tissue samples showed NK1R mean fluorescence intensity was significantly higher in NERD (fold-change 1.52; $p<0.05$) and ERD (fold change 1.70; $p<0.01$) oesophageal mucosa compared to healthy control (n=6-8). Interestingly, NK1R was also found expressed in a sub-group of CD3+ T lymphocytes specifically in the papillae and epithelium of GORD patients. In NE-1 oesophageal epithelial cells, 30 minutes exposure to 100 nM (fold change 1.41; $p<0.05$) and 300 nM (fold change 1.92; $p<0.0001$) SP induced phosphorylation of NF-κB in a dose dependent manner (n=7-8). CXCL8 expression in NE-1 cells exposed to 30 nM, 100 nM, or 300 nM SP for 30 minutes resulted in significantly higher mRNA expression at the highest concentration (fold change 6.29; $p<0.05$), although a dose-dependent trend was observed at lower concentrations (n=3).

Conclusion: The significant increase in NK1R expression in NERD and ERD patients compared to healthy volunteers, combined with expression on T lymphocytes provides evidence, for the first time, that SP may have a critical role in potentiating pain sensation in the oesophagus. Indeed, SP directly induces NF-κB phosphorylation and increases transcription of inflammatory cytokine IL-8 in oesophageal epithelial cells. This demonstrates a novel neuroimmune pathway regulated by SP and NK1R that may be critical in GORD symptom generation.

References: Xu, X., Li, Z., Zou, D., Yang, M., Liu, Z., & Wang, X. (2013). High expression of calcitonin gene-related peptide and substance P in esophageal mucosa of patients with non-erosive reflux disease. *Dig Dis Sci*, 58(1), 53-60. doi:10.1007/s10620-012-2308-z

Disclosure: Nothing to disclose.

Monitoring disease activity in IBD

14:30-15:30 / Poster Stage 1

MP385

PREDICTING ENDOSCOPIC IMPROVEMENT IN ULCERATIVE COLITIS WITH THE ULCERATIVE COLITIS SEVERITY INDEX: A POST-HOC ANALYSIS OF UPADACITINIB PHASE 3 TRIAL DATA

N. Narula¹, E.C. Wong¹, P.S. Dulai², J.K. Marshall¹, V. Jairath³, E. Cheng⁴, C.H. Chung⁴, X. Phaleng⁴, W. Reinisch⁵

¹McMaster University, Farncombe Family Digestive Health Research Institute, Division of Gastroenterology, Department of Medicine, Hamilton, Canada, ²Northwestern University, Division of Gastroenterology, Chicago, United States of America, ³Western University, Division of Gastroenterology, Department of Medicine, London, Canada, ⁴AbbVie Inc., Chicago, United States of America, ⁵Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Vienna, Austria

Contact E-Mail Address: walter.reinisch@meduniwien.ac.at

Introduction: The recently developed Ulcerative Colitis Severity Index (UCSI) has been previously reported to be more accurate than the Mayo Clinic score to predict 1-year endoscopic improvement (EI) at baseline (defined as a Mayo endoscopic score ≤ 1) for patients with moderate-to-severe ulcerative colitis (UC), using data from the UNIFI ustekinumab phase 3 clinical trial.¹ Validation of the UCSI with additional therapies is needed to elucidate the potential of the UCSI to improve UC treatment by predicting long-term outcomes.

Aims & Methods: To further evaluate the utility of the UCSI as a predictive tool to determine EI, this study reports the predictive value of the UCSI using upadacitinib (UPA) phase 3 trial data in patients with moderate-to-severe UC (ClinicalTrials.gov identifier: NCT02819635).² This post-hoc analysis assessed the intention-to-treat population receiving UPA 45 mg once daily 8-week induction treatment and randomized to UPA 30 mg or UPA 15 mg in maintenance (n=444). Baseline UCSI scores for 409 participants (35 were missing data) were calculated as the sum of 6 subscores derived from prior biologic failure, albumin <40 g/L, C-reactive protein >5 mg/L, endoscopic erosions/ulcerations, histology structural/architectural changes, and Mayo stool frequency scores. Receiver Operating Characteristic (ROC) analysis was conducted for all specified efficacy endpoints. Area under the curve (AUC) and 95% confidence interval were calculated for 7 endpoints, including 1-year EI predicted by baseline UCSI and Mayo Clinic score. A nonparametric approach was used to compare AUC between UCSI and Mayo Clinic score, and to calculate p-values. The UCSI cut-off to predict 1-year EI was determined using the Youden index (defined as Youden = Sensitivity + Specificity - 1), which is the maximum potential effectiveness of a diagnostic or predictive test that maximizes the distance between the chance diagonal line and the point (x,y) on the ROC curve, a point farthest from random.

Likelihood of endoscopic improvement	Number of participants achieving EI out of total (%)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Low (UCSI score ≥ 10)	120/239 (50.2)	44 (37.8-51.1)	62 (54.8-68.5)	56.5 (49.0-63.9)	49.8 (43.5-56.1)	1.16 (0.9-1.5)	0.90 (0.8-1.1)
High (UCSI score <10)	96/170 (56.4)						

CI, confidence interval; EI, endoscopic improvement; ITT, intention-to-treat; MES, Mayo Endoscopic Score; OD, once daily; UCSI, Ulcerative Colitis Severity Index; UPA, upadacitinib.

*The ITT population (UPA 45 mg OD group) comprises participants who received UPA 45 mg OD 8-week induction treatment and who were enrolled under the protocol for the 52-week maintenance treatment period in Cohort 1 and randomized to UPA 30 mg or 15 mg OD.

Table. Accuracy of the UCSI for Prediction of 1-year Endoscopic Improvement (MES ≤ 1) in the ITT* Population, Based on a Threshold Score of 10.

Results: In AUC-ROC analyses of the UCSI and Mayo Clinic score to predict 1-year efficacy outcomes, the UCSI and Mayo Clinic score were similar (p-values ranging from 0.36 to 0.84). Both were considered poor with AUC-ROC ranging from 0.51 to 0.57. A cut-off point of 13 for UCSI based on the Youden index yielded low prediction capabilities. A cut-off of 10 was found in the initial derivation paper to dichotomize the likelihood of EI ('Low' as UCSI score ≥ 10 , 'High' as UCSI <10).¹ Using this cutpoint, there was again no difference in rates of EI (56.4% vs 50.2%, respectively) (Table).

Conclusion: The UCSI did not predict endoscopic outcomes when tested with this phase 3 dataset for UPA in UC, with UPA achieving EI regardless of the likelihood of achieving this outcome at 1 year, based on the UCSI threshold of 10. Further analysis with other datasets is needed to explore the predictive value of the UCSI for other therapies. The re-randomization study design might have affected the predictive value of the UCSI, and further analyses on treat-through studies are needed.

References: ¹Wong CL, Dulai PS, Marshall JK, et al. Predicting endoscopic improvement in ulcerative colitis using the Ulcerative Colitis Severity Index. *Inflamm Bowel Dis.* 2024;30:370-381. Doi:10.1093/ibd/izad074; ²Vermeire S, Danese S, Zhou W, et al. Efficacy and safety of upadacitinib maintenance therapy for moderately to severely active ulcerative colitis in patients responding to 8 week induction therapy (U-ACHIEVE Maintenance): overall results from the randomised, placebo-controlled, double-blind, phase 3 maintenance study. *Lancet Gastroenterol Hepatol.* 2023;8:976-989. Doi: 10.1016/S2468-1253(23)00208-X

Disclosure: NN has received honoraria from Janssen, AbbVie, Takeda, Pfizer, Merck, Sandoz, Novartis, and Ferring. ECLW reports no conflicts of interest. PSD has received consulting and/or research support from Takeda, Pfizer, Janssen, BMS, Gilead, Novartis, and Lilly; owns stock options in DigbiHealth; and has received royalties from PreciDiag. JKM has received honoraria from Janssen, AbbVie, Allergan, Bristol Myers Squibb, Ferring, Janssen, Lilly, Lupin, Merck, Pfizer, Pharmascience, Roche, Shire, Takeda, and Teva. VJ has received consulting/advisory board fees from AbbVie, Alimentiv Inc, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, SCOPE, Second Genome, Sorriso, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; and has received speaker's fees from AbbVie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, and Fresenius Kabi. WR has served as a speaker for Abbott Laboratories, AbbVie, Aesca, Aptalis, Astellas, Centocor, Celltrion, Danone Austria, Elan, Falk Pharma GmbH, Ferring, Immundiagnostik, Mitsubishi Tanabe Pharma Corporation, MSD, Otsuka, PDL, Pharmacosmos, PLS Education, Schering-Plough, Shire, Takeda, Therakos, Vifor, and Yakult; served as a consultant for Abbott Laboratories, AbbVie, Aesca, Algernon, Amgen, AM Pharma, AMT, AOP Orphan, Arena Pharmaceuticals, Astellas, AstraZeneca, Avaxia, Roland Berger GmbH, Bioclinica, Biogen IDEC, Boehringer Ingelheim, Bristol Myers Squibb, Cellerix, Chemocentryx, Celgene, Centocor, Celltrion, Covance, Danone Austria, DSM, Elan, Eli Lilly, Ernst & Young, Falk Pharma GmbH, Ferring, Galapagos, Genentech, Gilead, Grünenthal, ICON, Index Pharma, Inova, Janssen, Johnson & Johnson, Kyowa Hakkō Kirin Pharma, Lipid Therapeutics, LivaNova, Mallinckrodt, Medahead, MedImmune, Millennium, Mitsubishi Tanabe Pharma Corporation, MSD, Nash Pharmaceuticals, Nestle, Nippon Kayaku, Novartis, Ocera, OMass, Otsuka, Parexel, PDL, Periconsulting, Pharmacosmos, Philip Morris Institute, Pfizer, Procter & Gamble, Prometheus, Protagonist, Provention, Roberts Clinical Trial, Sandoz, Schering-Plough, Second Genome, Seres Therapeutics, SetPoint Medical, Sigmoid, Sublimity, Takeda, Therakos, Theravance, Tigenix, UCB, Vifor, Zealand, Zyngenia, and 4SC; and served

as on the advisory board for Abbott Laboratories, AbbVie, Aesca, Amgen, AM Pharma, Astellas, AstraZeneca, Avaxia, Biogen IDEC, Boehringer Ingelheim, Bristol-Myers Squibb, Cellerix, Chemocentryx, Celgene, Centocor, Celltrion, Danone Austria, DSM, Elan, Ferring, Galapagos, Genentech, Grünenthal, Inova, Janssen, Johnson & Johnson, Kyowa Hakko Kirin Pharma, Lipid Therapeutics, MedImmune, Millenium, Mitsubishi Tanabe Pharma Corporation, MSD, Nestlé, Novartis, Ocera, Otsuka, PDL, Pharmacosmos, Pfizer, Procter & Gamble, Prometheus, Sandoz, Schering-Plough, Second Genome, SetPoint Medical, Takeda, Therakos, Tigenix, UCB, Zealand, Zyn-
genia, and 4SC. EC, CHC, and XP are employees of AbbVie Corporation.

MP386

ENHANCING DIAGNOSTIC PRECISION IN CROHN'S DISEASE: EVALUATING THE IMPACT OF SMALL BOWEL CAPSULE ENDOSCOPY IN ISOLATED PERIANAL DISEASE

S. Ponte¹, D.G. Ferreira¹, M. Salgado^{1,2}, A.T. Ferreira¹, S. Archer¹,
M.L. Rocha¹, C. Caetano¹, P. Lago¹, I. Pedroto¹

¹Unidade Local de Saúde de Santo António, Department
of Gastroenterology, Porto, Portugal, ²Instituto de Ciências
Biomédicas Abel Salazar da Universidade do Porto, Porto,
Portugal

Contact E-Mail Address: sofiafonte1995@gmail.com

Introduction: Crohn's disease (CD) may manifest as perianal disease (PD) in up to 36% of cases. In the majority, PD occurs simultaneously or after the diagnosis of small bowel CD. Diagnosing CD in patients with isolated PD can be challenging. Small bowel capsule endoscopy (SBCE) has been shown to have a higher diagnostic yield for small bowel findings compatible with CD than other modalities.

Aims & Methods: This study aimed to assess the impact of SBCE as a diagnostic tool for CD in patients with isolated PD.

Retrospective cohort study spanning 2008 to 2023. Adult patients with isolated PD (recurrent fissures, trans-/supra-/extra-sphincteric fistula or abscess) and negative conventional workup for CD (ileocolonoscopy and cross-sectional imaging) who underwent SBCE (Pillcam, Given®) were included. Patients using nonsteroidal anti-inflammatory drugs or with a CD history were excluded. Demographics, biomarkers, SBCE findings and subsequent management were recorded and analyzed.

Results: Forty patients (mean age 40.2 years, 67.5% females) were included. SBCE identified findings compatible with small bowel CD (aphthous ulcerations, linear/circumferential ulcers and stenosis) in 32.5% (13 patients), enabling diagnosis and subsequent treatment in all of them, based on disease severity. In this group, mean previous fecal calprotectin (FC) was 722.2µg/g, but FC was inferior to 200µg/g in 46.2% (6 patients). In 4 patients (10%) with negative SBCE, isolated perianal CD was assumed and immunosuppressors were started. There was no statistically difference in FC of the patients with positive and negative SBCE. Laboratory findings (C-reactive protein, albumin), tobacco use and family history of CD/ulcerative colitis did not show significant associations with SBCE findings.

Conclusion: For patients with PD and a negative conventional CD workup, SBCE demonstrated a 32.5% incremental diagnostic yield, leading to therapy initiation based on severity.

Disclosure: Nothing to disclose.

MP387

DEVELOPMENT AND VALIDATION OF THE IBD LIFE QUESTIONNAIRE: A WORLD-WIDE PATIENT-CENTRED APPROACH

J. van Oostrom¹, S. Anjie¹, M. Braad¹, J. Horrigan², N. Karimi³,
B. Adi⁴, G. Ganesh⁴, S.-K. Yang⁵, J.S. Lasa⁶, M.L. Parks⁷, C. Broër⁸,
A. de Kruif⁹, P. Olivera Sendra^{10,6}, B.D. Ye¹¹, R. Banerjee⁴,
L. Peyrin-Biroulet¹², S. Connor^{13,3}, C.A. Siegel², K.B. Gecse¹,
G.R. D'Haens¹

¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Dartmouth Hitchcock Medical Center, Gastroenterology and Hepatology, Lebanon, United States of America, ³South West Sydney Clinical Campuses, UNSW Medicine and Health, UNSW Sydney, Australia and South Western Sydney IBD Research Group, Ingham Institute for Applied Medical Research, Sydney, Australia, ⁴Asian Institute of Gastroenterology, Hyderabad, India, ⁵Asan Medical Center, University of Ulsan, College of Medicine, Seoul, South Korea, ⁶Centro de Educación Médica e Investigación Clínica (CEMIC), IBD Unit, Gastroenterology Section, Department of Internal Medicine, Ciudad Autónoma Buenos Aires, Argentina, ⁷Hospital Británico, Gastroenterology Department, Buenos Aires, Argentina, ⁸University of Amsterdam, Faculty of Sociology, Amsterdam, Netherlands, ⁹Free University, Faculty of Science, Methodology and Applied Biostatistics, Amsterdam, Netherlands, ¹⁰Mount Sinai Hospital, Gastroenterology, Toronto, Canada, ¹¹Asan Medical Center, Gastroenterology and Inflammatory Bowel Disease Center, Seoul, South Korea, ¹²Nancy University Hospital, Inserm U 1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ¹³Liverpool Hospital, Department of Gastroenterology, Sydney, Australia

Contact E-Mail Address: j.m.vanoostrom@amsterdamumc.nl

Introduction: For patients living with inflammatory bowel diseases (IBD), the ultimate treatment goal is to live a "normal life." However, no validated patient-reported outcome measurement (PROM) exists yet to measure this. Moreover, most PROMs were developed by western healthcare professionals, lacking a global, patient-centred approach.

Aims & Methods: Through a world-wide patient-centred approach, we aimed to develop and validate a PROM that identifies and measures normality of life for patients with IBD, the "IBD LIFE."

IBD patients without an ostomy, pouch or significant other comorbidities could participate in the project. The development phase included 6-10 patients with Crohn's disease (CD) and 6-10 patients with ulcerative colitis (UC) from each of the participating countries (Argentina, Australia, India, the Netherlands, South-Korea and the USA).

The development phase consisted of (i) semi-structured qualitative interviews about living a normal life with IBD, (ii) an online Delphi round to rate item importance, (iii) a focus group to clarify wording, categorisation and scales, (iv) pilot-testing and (v) cross-cultural translation.

For the validation phase, 200 adult IBD patients are recruited per language (100 CD, 100 UC). At baseline (BL), we assessed clinical disease activity (using the Harvey Bradshaw Index (HBI) or Simple Clinical Colitis Activity Index (SCCAI)) and asked patients to complete a PROM set including the IBD LIFE, a general quality of life (QoL) PROM and an IBD-specific QoL PROM (Short-Form-36 (SF-36) and IBD Questionnaire (IBDQ)). In addition, 30 consecutive patients per language were asked to complete a second PROM set 2 weeks after baseline (W2), comprising of the IBD LIFE, IBDQ and question 2 from the IBD-control.

Internal consistency was assessed using Cronbach's α . Test-retest reliability was assessed through the intraclass correlation coefficient (ICC) by comparing IBD LIFE scores at BL and W2 in patients with stable QoL (de-

fined as <10% difference in the IBDQ score and the IBD control question 2 answered “no change”). Construct validity was assessed at BL through Spearman’s correlation coefficients between the IBD LIFE, the comparator QoL PROMs and disease activity indices.

Results: The IBD LIFE consists of 23 questions divided into 5 categories: physical items, activities, social items, psychological items and circumstances.

For the validation phase, we report on the first 364 included patients (200 Dutch, 100 Spanish and 64 English speaking patients, 187 UC and 177 CD, median disease duration 10 years [5-18], see table 1). In CD, median HBI was 2 [1-5] and in UC, median SCCAI was 1 [0-2]. PROM response percentage was 85%. 38 patients completed W2 visit, of whom 71% had stable QoL. The IBD LIFE showed excellent internal consistency (Cronbach’s $\alpha = 0.95$). Test-retest reliability was good (ICC = 0.94 [95% CI 0.88-0.98]). The IBD LIFE exhibited good construct validity, depicted by a strong correlation with IBD-specific QoL (IBDQ $r = 0.90$), and general QoL (SF-36 $r = 0.84$) and a moderate correlation with clinical disease activity (HBI $r = 0.58$; SCCAI $r = 0.54$).

	n = 364
Demographics	
Gender (male), n (%)	160 (41%)
Age (year), median [IQR]	41 [30-54]
Employment status (employed), n (%)	328 (90%)
Disease characteristics	
Diagnosis (CD), n (%)	177 (49%)
Median disease duration (year), median [IQR]	10 [5-18]
Naïve to advanced therapies, n (%)	215 (59%)
Crohn's disease	
Underwent CD-related surgery, n (%)	186 (51%)
HBI, median [IQR]	2 [1-5]
Ulcerative colitis	
Underwent UC-related surgery, n (%)	51 (14%)
SCCAI, median [IQR]	1 [0-2]

Table 1. Baseline characteristics.

Conclusion: The IBD LIFE is a novel, valid and reliable PROM that has been developed through a rigorous process with maximal patient involvement. Further validation in English, Spanish, Hindi, French and Korean is ongoing, as well as responsiveness analyses and cross-cultural validation.

Disclosure: This project was supported by an unrestricted grant from Eli Lilly and Company.

Joep van Oostrom has received speaker’s fees from Tillotts
 Neda Karimi has received grant support from Janssen and conference attendance support from Ferring, and Pfizer.
 Juan Lasa has received consulting fees and honoraria from Abbvie; honoraria from Janssen; honoraria from Takeda Pharmaceuticals; consulting fees from Glaxo Smith Kline.
 Pablo A. Olivera has received consulting fees from AbbVie, Takeda, and Janssen; honoraria from Takeda and Janssen; and financial support for attending meetings, travel, or both from AbbVie, Takeda, Janssen, and Ferring.
 Byong Duk Ye has served on advisory boards for AbbVie Korea, Celltrion, Daewoong Pharma, Ferring Korea, Janssen Korea, Pfizer Korea, and Takeda Korea; has received research grants from Celltrion and Pfizer Korea; has received consulting fees from Chong Kun Dang Pharm., CJ Red BIO, Cornerstones Health, Daewoong Pharma, IQVIA, Kangstem Biotech, Korea United Pharm. Inc., Medtronic Korea, NanoEntek, and Takeda; and has received speaking fees from AbbVie Korea, Celltrion, Ferring Korea, IQVIA, Janssen Korea, Pfizer Korea, Takeda, and Takeda Korea.
 Rupa Banerjee has served on advisory boards of Jansen, Takeda, Pfeizer India, Cipla, Menarini, Sun pharma, Abbott , Ferring pharma, MSN labs , Dr. Reddys , Zydus and Cadila She has received research support from DRL, Microlabs, Takeda, J & J at the IBDENC. She has grants from The Leona M and Harry B Helmsley Charitable Trust.

Susan J Connor has received honoraria for Advisory Board participation, speaker fees, educational support and/or research support from: Abbvie, Amgen, BMS, Celltrion, Chiesi, DrFalk, Eli-Lilly, Ferring, Fresenius Kabi, GSK, Janssen, MSD, Novartis, Organon, Pfizer, Sandoz, Takeda, Agency for Clinical Innovation, Gastroenterological Society of Australia, Medical Research Future Fund, South Western Sydney Local Health District, Sydney Partnership for Health, Research and Enterprise (SPHERE) and The Leona M and Harry B Helmsley Charitable Trust..

Corey A Siegel has received grant support from Abbvie, Janssen, Pfizer and Takeda; has served as a consultant for Abbvie, BMS, Lilly, Janssen, Napo Pharmaceuticals, Pfizer, ProciseDx, Prometheus Biosciences, Takeda, and Trellus Health; has served as a speaker for CME activities for Abbvie, Janssen, Pfizer and Takeda; has received licensing fees from Takeda for intellectual property created by MiTest Health, LLC; and is a co-founder of MiTest Health, LLC.

Laurent Peyrin-Biroulet reports personal fees from Galapagos, AbbVie, Janssen Pharmaceuticals, Genentech, Alimentiv, Ferring Pharmaceuticals, Tillots Pharma, Celltrion, Takeda, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Inotrem, Allergan, MSD, Roche, Arena Pharmaceuticals, Gilead Sciences, Amgen, BMS, Vifor Pharma, Norgine, Mylan, Eli Lilly, Fresenius Kabi, OSE Immunotherapeutics, Enthera, Theravance, Pandion Therapeutics, Gossamer Bio, Viatrix, and Thermo Fisher; grants from AbbVie, MSD, Takeda, and Fresenius Kabi; and stock options from Clinical Trials Mobile Application.

Krisztina Gecse has received grants from Pfizer Inc, Celltrion and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunic Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis and Takeda and speaker’s honoraria from Abbvie, Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda and Tillotts.

Geert D’Haens has served as a consultant and/or received speaker’s fees from AbbVie, Alimentiv, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion Healthcare, Cytoki Pharma, Eli Lilly, Ferring, Galapagos, Glaxo SmithKline, Gossamer Bio, Immunic, InDex Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Takeda, Tillotts, Ventyx Biosciences.

Suzanne Anjie, Marlou Braad, Jamie Horrigan, Bhargavi Adi, Girish Ganesh, Suk-Kyun Yang, Christian Broër, Anja de Kruif and Rupa Banerjee report no conflicts of interest.

MP388 ULTRASOUND VERSUS ENDOSCOPY IN ULCERATIVE COLITIS: A HEAD-TO-HEAD STUDY

M. Allocca¹, F. Furfaro¹, A. Zilli¹, F. D’Amico¹, T.L. Parigi¹, L. Peyrin-Biroulet², G. Fiorino³, S. Danese¹
¹IRCCS Hospital San Raffaele and University Vita-Salute San Raffaele, IBD Center, Milano, Italy, ²Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 “Inflammation/Cellular Stress and Exposure to Environmental Risks”, Vandoeuvre-les-Nancy, France, ³San Camillo-Forlanini Hospital, Gastroenterology and Digestive Endoscopy, Rome, Italy

Contact E-Mail Address: mariangela.allocca@gmail.com
Introduction: Endoscopic confirmation of treatment response is recommended in ulcerative colitis (UC). However, colonoscopy (CS) is not well accepted by patients and approximately 50% of patients starting treatment do not undergo CS in the following 2 years. Fecal calprotectin (FC), a non-invasive biomarker of mucosal inflammation, is widely available, but a universal cut-off value applicable to all patients is not yet known.

Intestinal ultrasound (IUS) is emerging as an accurate tool for monitoring treatment response. In particular, the Milan ultrasound criteria (MUC) is a validated score to assess endoscopic activity in UC. $MUC \leq 6.2$ accurately detects Mayo endoscopic score (MES) ≤ 1 (REF 1 e 2).

Aims & Methods: The aim of this study was to evaluate the performance of non-invasive approaches in detecting treatment response in UC in an outpatient setting, using CS as reference standard.

All consecutive patients with UC seen in the outpatient clinic in one week and scheduled for a colonoscopy the following week were eligible. Treatment response was graded according to: a) symptoms (partial Mayo score, $PMS \leq 2$), b) biomarkers ($FC \leq 250$ mcg/g and C-reactive protein, $CRP \leq 5$ mg/L), c) Milan Ultrasound Criteria ($MUC \leq 6.2$) and d) combined approach with MUC and FC ($MUC \leq 6.2 + FC \leq 50$ mcg/g or $MUC \leq 6.2 + FC \geq 50 \leq 250$ mcg/g). Receiver Operating Characteristic (ROC) curve analysis was used to compare the non-invasive approaches, using Mayo endoscopic score as reference standard (response defined by $MES \leq 1$).

Results: 97 patients with UC were enrolled (60 males, median age 39 years). 77 patients were in biologics or small molecules, 29 in steroids and 5 in immunosuppressants. Response to treatment (defined by $MES \leq 1$) was correctly identified in 64% of cases based on symptoms, 68% using biomarkers, 80% using MUC, and 83% with a combined approach. Biomarkers-based detection was not superior to symptoms (0.695 vs. 0.671; $p = 0.74$). Ultrasound-based detection was superior to both symptoms (0.822 vs 0.671; $p = 0.015$) and biomarkers (0.822 vs 0.695; $p = 0.046$). Combined approach was superior to symptoms (0.825 vs 0.671; $p = 0.016$) and biomarkers (0.825 vs 0.695; $p = 0.004$), but not to IUS (0.825 vs 0.822; $p = 0.943$).

Conclusion: The use of an ultrasound-based approach in combination with FC increases our ability to assess treatment response in UC patients in real time, possibly avoiding CS.

References: 1) Allocca M, Fiorino G, Bonovas S, et al. Accuracy of humanitas ultrasound criteria in assessing disease activity and severity in ulcerative colitis: A prospective study. *J Crohns Colitis* 2018;12:1385–91. doi:10.1093/ecco-jcc/jjy107.

2) Allocca M, Filippi E, Costantino A, et al. Milan ultrasound criteria are accurate in assessing disease activity in ulcerative colitis: external validation. *United Eur Gastroenterol J* 2021;9:438–42. doi:10.1177/2050640620980203.

Disclosure: Nothing to disclose.

MP389

DEFINING DIAGNOSTIC ULTRASONOGRAPHIC PARAMETERS IN ULCERATIVE COLITIS: A LONGITUDINAL PROSPECTIVE MULTICENTER STUDY

F. Zorzi¹, M. Fraquelli², C. Bezzio³, F. Castiglione⁴, A. Rispo⁴, M. Allocca⁵, E. Cuccagna¹, F. Furfaro⁵, F. Caprioli², M. Ventura⁶, A. Testa⁴, S. Saibeni⁷, G. Maconi⁸, E. De Cristofaro¹, G. Monteleone¹, E. Calabrese¹

¹University of Rome Tor Vergata, Gastroenterology Unit, Department of Systems Medicine, Roma, Italy, ²Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Gastroenterology and Endoscopy Unit, Milan, Italy, ³IBD Centre, IRCCS Humanitas, Research Hospital, Rozzano, Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy, ⁴Federico II University, Naples, Italy, ⁵IRCCS Hospital San Raffaele and University Vita-Salute San Raffaele, IBD Center, Milano, Italy, ⁶National Institute for Health, Migration and Poverty (INMP), Rome, Italy, ⁷ASST Rhodense, Gastroenterology Unit, Rho, Italy, ⁸Luigi Sacco University Hospital Gastroenterology Unit Biomed and Clinical Sciences, Department of Biomedical and Clinical Sciences – L.Sacco University Hospital, Milan, Italy

Contact E-Mail Address: emma.calabrese@uniroma2.it

Introduction: Data on Intestinal Ultrasonography (IUS) in ulcerative colitis (UC) are growing especially in monitoring colonic lesions after therapies. Ultrasonographic parameters derived from studies in Crohn's disease populations.

Aims & Methods: Aim of our multicenter study was to define IUS parameters of normality and activity in UC patients compared to a healthy control group (HC). Secondary aim was to evaluate severity of colonic lesions using endoscopy as reference standard.

From July 2022 to Oct. 2023, we conducted a multicenter study at 6 IBD centers. Patients (pts) with UC and indication to perform colonoscopy were longitudinally enrolled. HC [no gastrointestinal symptoms, no anemia and normal fecal calprotectin (FC)] were enrolled to establish normal values. The analysis was performed per patient and per segment evaluating colonic wall thickening (CWT), colonic wall flow, Milan Ultrasound Criteria (MUC), Mayo endoscopic score (MES) and partial/full Mayo score. The sample size for UC cohort and HC, the area under (a ROC) curve, Spearman's correlation among clinical data, FC, IUS and endoscopy were calculated.

Results: 180 UC patients and 80 HC were enrolled. In the UC cohort, 53% were male with a median age of 40 years (range 18–78), 64% had extensive colitis and 36% had left colitis. In the HC, 44% were male with a median age of 29 years (range 19–70). Median CWT in comparison to MES in UC patients and median CWT in HC were shown in Table 1. Rectum wall thickening showed higher values than other colonic segments. A $CWT \geq 2.75$ mm showed a sensitivity, specificity, NPV and PPV of 54%, 96%, 48% and 97%, respectively, in differentiating UC patients from HC [AUC=0.72]. A rectum wall thickening >4.55 mm showed a sensitivity, specificity, NPV and PPV of 67%, 84%, 56% and 89%, respectively, in differentiating UC patients from HC [AUC=0.82]. A $CWT \geq 3.5$ mm showed a sensitivity, specificity, NPV and PPV of 57.4%, 94.3%, 86% and 78%, respectively, in differentiating activity from remission in UC patients [AUC=0.84]. A rectum wall thickening >5 mm showed a sensitivity, specificity, NPV and PPV of 57.5%, 85.7%, 41% and 92%, respectively, in differentiating UC rectal activity from remission [AUC=0.81]. The correlation of the CWT or MUC vs MES was better than clinical data and FC.

Conclusion:

	CWT mm median; (range)			
	Right colon	Transverse colon	Left colon	Rectum
Healthy control N=80	1.9; (1.2-3.4)	1.8; (1.3-5)	2; (1.3-3)	3.8; (1.5-5.5) [§]
MES 0 N=36	2.3; (1.1-4)	2.25; (1.4-4.2) [°]	3; (1.5-4.2)	4; (3-6) [*]
MES 1 N=32	1.65; (0.9-3.8)	1.7; (1.2-3.2) [°]	2.6; (1.5-6)	4.95; (1.9-8) [*]
MES 2 N=45	2.1; (1-4)	2.3; (1.3-5.7) [°]	3.5; (1.3-5.5)	5.15; (3-10) [*]
MES 3 N=67	3; (1-7)	3; (1.3-7) [°]	5.3; (2.7-8.5)	5.5; (3.2-9.7) [*]

[§]Data available in 25 pts, [°]Data available in 108 pts, ^{*}Data available in 178 pts

IUS, importantly CWT as the most relevant parameter, is highly accurate to diagnose and detect activity in UC patients.

Disclosure: Nothing to disclose.

MP390

LOW-INTENSITY PULSED ULTRASOUND: A NEW GUT LIQUID BIOPSY APPROACH TO PREDICT DISEASE ACTIVITY IN ULCERATIVE COLITIS

S.E. Pineda Chavez¹, A.A. Carriles Lineares¹, G. Rizzo^{2,3}, A. Cafarelli^{4,5}, M. Wozny¹, G. Mori², A. Sorriento^{4,5}, L. Loy⁶, A. Dal Buono⁶, R. Gabbiadini⁶, C. Bezzio⁶, P. Spaggiari⁷, F. Hrvat¹, G. Vignolle⁸, L. Ciglar⁸, K. Vierlinger⁸, C. Nöhammer⁸, D. Lucchetti^{9,10}, A. Sgambato^{9,10}, F. Colella¹⁰, T. Canu¹¹, A. Esposito^{11,12}, S. Recchia¹³, R. Bisogno¹⁴, F. Tran^{15,16}, N. Baran¹⁶, M. Pruijt^{17,18}, L. Oldenburg^{17,18}, G. D'Haens^{17,18}, P. Rosenstiel^{15,16}, S. Schreiber^{15,16}, A. Repici^{1,19}, A. Armuzzi^{1,6}, L. Ricotti^{4,5}, S. Vetrano^{1,2}

¹Humanitas University, Department of Biomedical Sciences, Milan, Italy, ²Humanitas Research Hospital IRCCS, Department of Gastroenterology, Laboratory of Gastrointestinal Immunopathology, Rozzano, Italy, ³University of Cagliari, Department of Medical Science and Public Health, Cagliari, Italy, ⁴Scuola Superiore Sant'Anna, The BioRobotics Institute, Pisa, Italy, ⁵Scuola Superiore Sant'Anna, Department of Excellence in Robotics & AI, Pisa, Italy, ⁶Humanitas Research Hospital IRCCS, IBD Unit, Department of Gastroenterology, Rozzano, Italy, ⁷Humanitas Research Hospital IRCCS, Department of Pathology, Rozzano, Italy, ⁸AIT Austrian Institute of Technology GmbH, Center for Health and Bioresources, Competence Unit Molecular Diagnostics, Vienna, Austria, ⁹Università Cattolica del Sacro Cuore, Department of Translational Medicine and Surgery, Rome, Italy, ¹⁰Fondazione Policlinico Universitario 'Agostino Gemelli' IRCCS, Rome, Italy, ¹¹IRCCS San Raffaele Scientific Institute, Experimental Imaging Center, Milan, Italy, ¹²Vita Salute San Raffaele University, School of Medicine, Milan, Italy, ¹³University of Insubria, Department of Science and High Technology, Como, Italy, ¹⁴Humanitas Medical Care, Unit of Diagnostic Imaging, Milan, Italy, ¹⁵University Medical Center Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ¹⁶University Medical Center Schleswig-holstein, Campus Kiel, Institute of Clinical Molecular Biology, Kiel, Germany, ¹⁷University of Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁸University of Amsterdam, Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ¹⁹Humanitas Research Hospital IRCCS, Department of Gastroenterology, Endoscopy Unit, Rozzano, Italy

Contact E-Mail Address: samuel.eliaspineda.chavez@gmail.com

Introduction: Ulcerative Colitis (UC) diagnosis relies on invasive endoscopic biopsy collection for histological assessment. There is a critical need for specific, easy-to-detect and non-invasive approaches to assessing disease activity such as liquid biopsy. Extracellular vesicles (EVs) carrying tissue-specific miRNAs are a promising means of liquid biopsy for

detection in blood. However, the low detectability of these EV-derived miRNAs hinders their clinical application. Low-intensity pulsed ultrasound (LIPUS) has the potential to modulate EV biogenesis and enhance their release carrying UC-specific miRNAs.

Aims & Methods: We explored Low-intensity Pulsed Ultrasound (LIPUS) technology to boost the release of mucosal miRNAs carried by extracellular vesicles (EVs) as UC biomarkers, potentially enabling disease activity monitoring through a blood test.

We conducted a simulation framework to estimate the optimal energy dosage, *in-vitro* defined, reaching the colon *in-vivo*. LIPUS stimulation was performed during the active and recovery phase of acute and chronic colitis models. Murine models of colitis were obtained by dextran sodium sulfate (DSS) administration to C57BL/6 female mice, whilst DSS cycles were stopped for recovery. Four and 35 UC patients were enrolled for *ex-vivo* gut biopsy stimulation and for blood collection respectively, stratified by disease activity defined by endoscopic mayo (e-Mayo) score. EV-miRNA isolated were profiled by next-generation sequencing and microarray.

Results: Our study demonstrates that LIPUS at 38 kHz, 150 mW/cm² for 180s effectively promotes miRNA release reflecting the chronic and acute inflammatory status of mucosa in experimental colitis models. *Ex-vi-vo* LIPUS stimulation of UC patient gut biopsies not only confirmed the association of murine miRNAs with disease activity in humans, but also enhanced additional 19 miRNAs, displaying their potential main role in the mucosal inflammatory process. Remarkably, the validation in a large cohort of UC patients' blood corroborated LIPUS-induced miR-532-3p to solely correlate with disease severity, while other miRNAs were either highly variable or undetectable without LIPUS stimulation.

Conclusion: Therefore, LIPUS is a safe, non-invasive method to enhance the detection of rare biomarkers in blood, potentially paving the way for a new era of gut liquid biopsy for monitoring UC disease progression.

Disclosure: A. Dal Buono has received speaker's fees from AbbVie, Galapagos and Celltrion. R. Gabbiadini has received speaker's fees from Pfizer, MSD and Celltrion. C. Bezzio received lecture fees and served as a consultant for Takeda, MSD, Ferring, Abbvie, Galapagos and Janssen. A.Armuzzi Consulting/advisory board fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, Lionhealth, MSD, Mylan, Nestlé, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda, Tillots Pharma; Speaker's fees from AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda, Teva Phaceutical and received research grants from MSD, Takeda, Pfizer, Biogen.

MP391

INTESTINAL ULTRASOUND IN NEWLY DIAGNOSED CROHN'S DISEASE: SONOGRAPHIC FINDINGS AND PREDICTIVE VALUE OF EARLY TRANSMURAL HEALING

G. Madsen^{1,2}, M. Attuabi^{2,1,3}, R. Wilkens^{1,4}, J. Fremberg Ilvemærk^{1,3,2}, K. Theede^{2,1}, J. Wium Bjerrum³, F. Bendtsen^{1,2}, J.B. Seidelin³, T. Boysen^{1,2}, J. Burisch^{1,2}
¹Copenhagen University Hospital - Amager and Hvidovre, Gastrounit, Hvidovre, Denmark, ²Copenhagen University Hospital - Amager and Hvidovre, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre, Denmark, ³Copenhagen University Hospital - Herlev, Department of Gastroenterology and Hepatology, Herlev, Denmark, ⁴Bispebjerg Hospital, Unit of Gastroenterology, Department of Medicine, Copenhagen, Denmark

Contact E-Mail Address: gormmadsen@hotmail.com

Introduction: A major difficulty in treating Crohn's disease (CD) lies in the unreliable association between clinical symptoms and underlying inflammation, hindering effective monitoring. Intestinal ultrasound (IUS) has emerged as a valuable, non-invasive, and well tolerated tool for assessing inflammatory activity in CD. The "Selecting Therapeutic Targets in Inflammatory Bowel Disease" (STRIDE-II) guidelines recognize the transformative impact of IUS in inflammation assessment but hesitate to endorse transmural healing as a primary treatment target due to current limitations of available therapies in achieving this outcome. However, limited data exist on the applicability of IUS in patients with newly diagnosed CD who might not have developed irreversible fibrotic alterations.

Aims & Methods: The primary aim of this study was to characterize the sonographic features of CD at diagnosis and throughout the initial year post-diagnosis. Additionally, we sought to assess the predictive capability of IUS herein.

We conducted a prospective, population-based cohort study involving newly diagnosed patients with CD. Patients were systematically monitored using IUS in tandem with symptomatic, biochemical, and endoscopic evaluations throughout the first year following diagnosis. Transmural remission (TR) was defined as BWT $\leq$ 3 mm without colour Doppler signal, and symptomatic remission as Harvey-Bradshaw Index $\leq$ 4.

Results: During the study period (May 2021 – May 2023), 201 patients with adult-onset CD were included. No significant associations were observed between sonographic characteristics of inflammation and diagnostic delay.

At three months post-diagnosis, TR was achieved in 38% of patients, with a higher proportion observed in those with colonic disease (L1: 33%, L2: 52%, L3: 27%; $p = 0.05$). TR at three months was significantly associated with symptomatic remission at subsequent follow-ups during the first year (3 months: 87% vs. 51%, $p < 0.001$; 6 months: 87% vs. 61%, $p = 0.004$; 9 months: 76% vs. 49%, $p = 0.012$; 12 months: 87% vs. 64%, $p = 0.013$), as well as a reduced risk of treatment escalation (20% vs. 65%, $p < 0.0001$) during this period.

By 12-month, 41% of patients achieved TR, with no significant association observed with disease location. In a multivariable analysis adjusted for age, sex, smoking, disease location, and baseline sonographic inflammation, a higher body mass index (BMI) significantly decreased the likelihood of achieving transmural remission (overweight: Odds ratio (OR) = 0.13, 95% confidence interval (CI): 0.02–0.93; obesity: OR = 0.06, 95% CI: 0.01–0.64).

Among the 126 patients with ileal or ileocolonic disease, 16 (13%) underwent ileocecal resection (ICR) within the first year. In an analysis of receiver operating characteristic area under the curve (ROC AUC), which included endoscopic, symptomatic, sonographic, and biochemical findings, the

International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) in the terminal ileum at diagnosis emerged as the most accurate predictor of ICR during this period: IBUS-SAS 63 (AUC = 0.92, sensitivity = 100%, specificity = 73%).

Conclusion: The findings of this study highlight TR as an attainable goal for newly diagnosed CD patients with a positive impact on the disease course. Moreover, the negative influence of high BMI on the likelihood of achieving TR underscores the necessity for further investigation into the impact of weight on the disease course of IBD. The study also reveals that sonographic inflammation in the terminal ileum at diagnosis is the most accurate predictor of the need of ICR within the first year.

Disclosure: Nothing to disclose.

MP392

A NOVEL SWITCHING-MULTIMODAL ARTIFICIAL INTELLIGENCE TO SIMULTANEOUSLY CONVERT DIFFERENT ENDOSCOPIC ENHANCEMENT MODALITIES FOR ACCURATE ASSESSMENT OF INFLAMMATION AND HEALING IN ULCERATIVE COLITIS

M. Iacucci¹, G. Santacroce¹, I. Zammarchi¹, U. Chaudhari², B.B. Kolawole², R. Del Amor³, P. Meseguer^{3,4}, V. Naranjo³, A. Buda⁵, R. Bisschops⁶, S. Ghosh¹, E. Grisan², PICaSSO group
¹University College Cork, APC Microbiome Ireland, College of Medicine and Health, Cork, Ireland, ²London South Bank University, School of Engineering Computer Science and Informatics, London, United Kingdom, ³Universitat Politècnica de València, Instituto de Investigación e Innovación en Bioingeniería, HUMAN-tech, Valencia, Spain, ⁴valgrAI - Valencian Graduate School and Research Network of Artificial Intelligence, Valencia, Spain, ⁵Santa Maria del Prato Hospital, Department of Gastrointestinal Oncological Surgery, Feltre, Italy, ⁶University Hospitals Leuven, Division of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: giovanni.santacroce01@universitadipavia.it

Introduction: Virtual Chromoendoscopy (VCE) has proven effective in predicting disease activity in Ulcerative Colitis (UC), although challenges persist regarding local availability and expertise. Artificial intelligence (AI) models applied to VCE have demonstrated a remarkable ability to rapidly, objectively, and accurately predict inflammation. Nonetheless, training machine algorithms across different enhancement modalities remains challenging. Hence, this study pioneers a novel machine model designed to simultaneously detect different VCE enhancement modalities and facilitate the transition between images to improve and standardise AI-based assessment of inflammation in UC.

Aims & Methods: Endoscopic videos from 302 UC patients recruited in the international real-life prospective PICaSSO study were analysed. The endoscopic assessment of the rectum and sigmoid colon was performed using white-light endoscopy (WLE), iScan 2 and iScan 3 modalities (Pentax, Japan). In the study's first phase, a switching AI model that detects and converts images across different modalities was developed. A neural network (NN) to identify the acquisition modality of each frame was trained and tested with 1531 (510 WLE, 518 iScan 2, and 503 iScan 3) and 321 (103 WLE, 109 iScan 2, 109 iScan 3) randomly extracted frames, respectively. Subsequently, a CycleGAN model was trained with 900 images per modality to allow inter-modality image switching. In the second phase, 240 annotated videos (4605 frames) were selected, with endoscopic activity assessed by experts using the UC Endoscopic Index of Severity (UCEIS) for WLE and the Paddington International Virtual Chromoendoscopy Score (PICaSSO) for VCE. Videos were switched to missing modalities and used to train a previously developed deep-learning model for inflammation assessment.¹ Four models were trained: three using a single modality as

input and one combining all modalities. Model performance in predicting inflammation was evaluated by computing accuracy, sensibility, specificity and AUC.

Results: The switching model showed a remarkable ability to classify and convert images across different endoscopic modalities, achieving a 92% NN classifier accuracy on the test set. The deep learning model showed a sensitivity of 80% (95% CI 59%-93%), specificity of 94% (95% CI 82%-99%), accuracy of 89% (95% CI 79%-95%) and AUC of 0.91 in predicting inflammation when combining images obtained through the switching model. This multimodal approach improved the performance of single-modality models.

Conclusion: This study introduces an innovative multimodal "AI-switching" model capable of accurately detecting and simultaneously switching between different endoscopic enhancement modalities. Combining the images obtained through this model enables precise assessment of inflammation in UC patients, exhibiting promising potential for application in clinical trials and clinical practice.

Modality	Accuracy, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC
Unimodal - WLE	82 (71-90)	81 (54-96)	82 (70-91)	0.84
Unimodal - iSCAN2	82 (71-90)	71 (49-87)	88 (75-95)	0.86
Unimodal - iSCAN3	82 (71-90)	73 (50-89)	86 (73-94)	0.88
Unimodal - WLE + iScan2 + iScan3	89 (79-95)	80 (59-93)	94 (82-99)	0.91

Table 1. Performance measures of the switching AI model in predicting inflammation.

References: ¹ Iacucci M et al. *Endoscopy*. 2023;55:332-341.

Disclosure: Nothing to disclose.

MP393

COMPREHENSIVE AI-POWERED ASSESSMENT OF WHOLE SLIDE IMAGING WITH SMART TILING AND HEATMAPS IN ULCERATIVE COLITIS: FEASIBILITY STUDY

D.T. Rubin¹, V.H. Koelzer^{2,3}, W. Xiong⁴, B. Hussaini⁵, C. Pereira da Costa⁶, J. Himoff⁶, A. Shashi⁵, M. Freire⁵, L. Peyrin-Biroulet⁷, O. Kubassova⁶

¹University of Chicago Medicine, Chicago, United States of America,

²University Hospital Zurich, Pathology and Molecular Pathology, Zurich, Switzerland, ³University Hospital Basel, Institute of Medical Genetics and Pathology, Basel, Switzerland, ⁴University of British Columbia, Medicine, Vancouver, Canada, ⁵Takeda, Zurich, Switzerland, ⁶Image Analysis Group, London, United Kingdom,

⁷Nancy University Hospital and Inserm U 1256, Nutrition-Genetics and Environmental Risk Exposure, Vandoeuvre-les-Nancy, France

Contact E-Mail Address: drubin@uchicago.edu

Introduction: Histopathological analysis of mucosal biopsies in ulcerative colitis (UC) is currently performed by pathologists on digital whole slide images (WSIs) or under the microscope; but established grading scales are not routinely employed and are subject to well-described intra- and inter-observer variations. Previously, we demonstrated that our Artificial Intelligence (AI) Tool can assign a Nancy Index (NI) [1] to a biopsy case with accuracy comparable to an expert pathologist [2].

Here we introduce the novel concepts of "smart tiling" and HeatMaps for comprehensive AI-powered assessment of WSIs and deploy these to describe a sample of WSIs.

Aims & Methods: We refer to a high-power location in a WSI as a 'tile', a fixed size region of interest of 1024 by 1024 pixels, with 0.5 microns per pixel in WSI with 20-fold magnification. Our previously validated AI Tool identifies tissue types, cell types (neutrophils, lymphocytes, plasmacytes), cell

density, crypts, and ulcerations, and calculates an NI with high degree of agreement [2]. In this analysis, we 'mapped' the WSIs on a tile-by-tile basis and using the NIs, created a HeatMap of grades from NI 0 to 4. The NI for the WSI was selected on the basis of the most frequently appearing NI. We included fixed size tiles that contained more than 15% of tissue in them and excluded the rest. In this feasibility study, we processed 11 WSIs received from 2 different scanners, which resulted in a 1175 tile database.

Results: The average number of tiles per WSI was 107, with a range from 30 tiles (WSI with NI=0) to 203 tiles (WSI with NI=4). Every WSI contained multiple tiles with a variety of NIs. WSIs scored as NI= 3 or 4 contained on average 53 tiles of NI=4, 36 with NI=3, 16 with NI=2, and 8 with NI=1 and 8 with NI=0. WSIs scored as NI= 0-2 contained on average 16 tiles of NI=4, 5 with NI=3, 34 with NI=2, and 10 with NI=1 and 18 with NI=0. The average neutrophil or eosinophil / lymphocyte / plasmacyte counts per tile were: in WSIs with NI=0 15/22/52, in WSIs with NI=2 22/35/88, in WSI with NI=3 57/53/125, in WSI with NI=4 73/31/85. The average sum of neutrophils divided by the number of tiles in WSIs with NI=0 0.83, in WSIs with NI=2 1.92, in WSI with NI=3 20.3, in WSI with NI=4 25.6.

Conclusion: This is the first description of novel concepts for histopathological analysis of mucosal biopsies in UC with smart tiling and HeatMaps. We identified significant heterogeneity and variation among tiles and within WSIs in both degree of inflammation by the AI-determined NI, but also in cell types. These novel findings and automatic assessments provide new insight into the pathophysiology of UC and may allow for more reliable clinical assessments in our patients.

References: 1. Marchal-Bressenot, A et al. Development and validation of the Nancy histological index for UC. *Inflammatory Bowel Disease* (2014). <https://doi.org/10.1136/gutjnl-2015-310187>

2. Peyrin-Biroulet, L et al. An artificial intelligence-driven scoring system to measure histological disease activity in ulcerative colitis. *United European Gastroenterology Journal* (2024) <https://doi.org/10.1002/ueg2.12562>

3. Tanevski et al. Learning tissue representation by identification of persistent local patterns in spatial omics data. *bioRxiv* (2024). <https://doi.org/10.1101/2024.03.06.58369>

Footnote: David T Rubin and Viktor H Koelzer share joint first authorship. Laurent Peyrin-Biroulet and Olga Kubassova share joint last authorship.

Disclosure: DTR has received grant support from Takeda; and has served as a consultant for Abbvie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. He serves on the Board of Trustees for the Crohn's & Colitis Foundation and is on the Board of Directors for Cornerstones Health.

VHK has been a speaker for Indica Labs; has received research support/grants from Image Analysis Group and Roche; and other support from Sharing Progress in Cancer Care (invited chair).

WX has no disclosures.

BH, SA, and MF are employees of Takeda. CPdC, JH, and OK are employees of Image Analysis Group.

LPB has received consulting fees from AbbVie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, Bristol Myers Squibb, Celltrion, Connect Biopharm, Cytoki, Eli Lilly, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Gossamer Bio, H.A.C. Pharma, Image Analysis Group, InDex, Inotrem, Janssen, Medac, Merck Sharp and Dohme, Mopac, Morphic, Norgine, Novartis, OM Pharma, Ono Pharmaceutical, OSE Immunotherapeutics, Pandion, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, TiGenix, Tillotts, Viatrix, Vifor, and Ysopia; grants from Celltrion, Fresenius Kabi, and Takeda; lecture fees from AbbVie, Amgen, Arena, Biogen, Celltrion, Eli Lilly, Ferring, Galapagos, Genentech, Gilead, Janssen, Medac, Merck Sharp and Dohme, Pfizer, Sandoz, Takeda, Tillotts, Viatrix, Vifor, and Ysopia; travel support from AbbVie,

Amgen, Celltrion, Connect Biopharm, Eli Lilly, Ferring, Galapagos, Genentech, Gilead, Gossamer Bio, Janssen, Medac, Merck Sharp and Dohme, Pfizer, Sandoz, Takeda, Thermo Fisher, and Tillotts.

Funding: This study was sponsored by Takeda.

Acknowledgements: Medical writing support was provided by Paul Hassan, PhD, of Excel Scientific Solutions, and was funded by Takeda.

MP394

DEVELOPMENT OF AN INTEGRATED ARTIFICIAL INTELLIGENCE SOFTWARE PLATFORM TO DETERMINE THE EXTENSION AND ACTIVITY OF ULCERATIVE COLITIS

A. Andrade¹, M. Garcias², I. Tarrio¹, R. Ribeiro¹, H. Ribeiro¹, S. Ponnusamy³, P. Ravindran⁴, L. Lopes^{1,5,6}

¹Hospital de Santa Luzia, ULS Alto Minho, Gastroenterology Department, Viana do Castelo, Portugal, ²School of Medicine, University of Minho, Braga, Portugal, ³Oasis Health LDA, Chennai, India, ⁴Mobius Knowledge Services, Chennai, India, ⁵Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ⁶ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: aldajaandrade@gmail.com

Introduction: Over the past few years, the incidence of Ulcerative Colitis (UC) has been increasing worldwide. In the clinical management of UC, assessing its severity based on disease activity and extension is particularly relevant, as it allows for the differentiation of patients into various groups and facilitates therapeutic optimization. Therefore, the development of an Artificial Intelligence (AI) platform capable of identifying UC extension and activity from hospital clinical notes significantly aids gastroenterologists in their daily healthcare practices and supports hospital research endeavors.

Aims & Methods: We aimed to assess the accuracy of an integrated AI software platform in evaluating the colonic extent and endoscopic activity of UC using unstructured data from hospital medical records.

A model based on natural language processing and keyword-based extraction was developed for determining the extent and activity of UC. For algorithm development, training, validation, and testing, clinical records from 465 patients diagnosed with UC at a university-affiliated hospital between January 2005 and February 2023 were utilized.

Results: A total of 556 episodes from 16 patients (31.3% men; median age 47 ± 21.5 years) were used to test the model. Concerning the colonic extension, the model demonstrated an accuracy of 0.99, precision of 0.93, recall of 0.90, and F1 score of 0.92. Regarding endoscopic activity, the model achieved an accuracy of 0.95, precision of 0.89, recall of 0.91, and F1 score of 0.90.

Conclusion: The AI platform effectively identified the extent and endoscopic activity of UC within unstructured data from hospital medical reports. The algorithm demonstrated promising results, with high accuracy and excellent performance metrics in the variables studied, positioning it as a potential candidate for future clinical applications.

Disclosure: Nothing to disclose.

Towards the cure of CRC

14:30-15:30 / Poster Stage 2

MP395

MULTIMERIN-2 LOSS FAVORS COLORECTAL CANCER CELLS DISSEMINATION

E. Poletto¹, L. Camicia¹, E. Andreuzzi², G. Carobolante¹, G. Schinello¹, E. Di Siena¹, I.V. Albergati³, A. Piruzza³, M.G. Nadin⁴, S. Maiero⁴, S. Realdon⁴, S.L. Croce³, R. Cannizzaro^{3,4}, M. Mongiat¹
¹Centro di Riferimento Oncologico - Aviano - I.R.C.C.S., Division of Molecular Oncology, Aviano, Italy, ²IRCCS Materno Infantile "Burlo Garofolo", Trieste, Italy, ³University Of Trieste, Dipartimento Universitario Clinico di Scienze mediche, chirurgiche e della salute, Trieste, Italy, ⁴Centro di Riferimento Oncologico - Aviano - I.R.C.C.S., Oncological Gastroenterology, Aviano, Italy

Contact E-Mail Address: evelina.poletto@cro.it

Introduction: Metastasis is the major cause of mortality among colorectal cancer (CRC) patients and represents a crucial cancer research challenge. Metastasis is the results of an intimate crosstalk between cancer cells and the surrounding tumor microenvironment, where neoplastic cells exploit the inefficient and leaky tumor vessels to disseminate to secondary organs¹. In this context, the extracellular matrix protein Multimerin-2, specifically deposited by endothelial cells (EC), is instrumental for the maintenance of vascular homeostasis, ensuring the proper formation of cell-cell junctions via the VEGFR2 signaling².

Aims & Methods: We observed that Multimerin-2 is down modulated in tumors both at transcriptional and post-translational levels. Thus we hypothesized that Multimerin-2-devoid vessels may enhance cancer cell dissemination, being characterized by a compromised endothelial barrier. Multimerin-2 expression was analyzed in human CRC samples through IHC, ELISA and *in silico* by the tnmplot.com tool. The effects of Multimerin-2 loss were assessed *in vitro* through transmigration assays upon Multimerin-2 down-regulation in EC cells and the molecular mechanism verified by WB and qRT-PCR. The putative Multimerin-2-affected metastatic dissemination was assessed through intravenous injection of MC38 colon cancer cells in *wt* and *Multimerin-2*^{-/-} mice.

Results: Multimerin-2 expression is significantly reduced within the tumor tissue respect to the normal counterpart among CRC patients, despite at variable degree. Importantly, *in vitro*, we found an increased number of CRC cells transmigrating through a Multimerin-2-depleted endothelium. This phenomenon was not VEGFR2-dependent since the use of a VEGFA blocking agents did not affect the extravasation of tumor cells. Indeed, under tumor-mimicking conditions, the knock-down of Multimerin-2 in ECs induces the upregulation of the vascular adhesion molecule VCAM1, a molecule exploited also by cancer cells to transpass the endothelium³. Accordingly, the intravenous injection of B16F10 syngeneic melanoma cells, as well as MC38 colon cancer cells, in *Multimerin-2*^{-/-} mice led to the formation of a higher number of metastatic lesions in the lungs.

Conclusion: Overall, these data indicate that Multimerin-2 expression is required to maintain vascular stability and halt the escape of cancer cells, suggesting that the Multimerin-2-devoid tumor vessels may represent a preferential route for metastatic dissemination, during CRC progression.

References: ¹Lugano R. et al, Tumor angiogenesis: causes, consequences, challenges and opportunities, *Cell Mol Life Sci.*, 2020

²Pellicani R. et al, Multimerin-2 Maintains Vascular Stability and Permeability, *Matrix Biol.*, 2020

³Wieland E. et al, Endothelial Notch1 Activity Facilitates Metastasis, *Cancer Cell* 2017

Disclosure: Nothing to disclose.

MP396

SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS WERE ASSOCIATED WITH LOWER RISK OF COLORECTAL CANCER AND ADENOMA THAN METFORMIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

K.S. Cheung^{1,2}, X. Mao¹, J.-T. Tan¹, W.-K. Leung¹, W.-K. Seto^{1,2}

¹The University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong, ²The University of Hong Kong-Shenzhen Hospital, Department of Medicine, Shenzhen, China

Contact E-Mail Address: mongolhorse2002@gmail.com

Introduction: The American Gastroenterological Association has recommended metformin as chemopreventive agent for colorectal cancer (CRC).

Aims & Methods: We aimed to compare sodium-glucose cotransporter-2 inhibitors (SGLT-2i) (either as monotherapy or combination therapy with metformin) to metformin monotherapy on CRC risk in type 2 diabetes (T2D) patients.

Using the territory-wide electronic healthcare database in Hong Kong, we identified all adults with T2D aged ≥ 18 years initially receiving SGLT-2i or metformin between January 2015 and June 2022. Index date was defined as the first date of study medication prescription and a 180-day lead-in period was used to categorize patients into SGLT-2i(+)/metformin(-), SGLT-2i(+)/metformin(+), and SGLT-2i(-)/metformin(+) groups. Primary outcome was CRC development. Secondary outcomes were (i) CRC-related mortality, (ii) colonic adenoma (any, non-advanced and advanced) development. Advanced adenoma was defined as adenoma with villous histology or high-grade dysplasia. Overlap weighting was applied to balance baseline characteristics, including age, sex, body mass index, smoking, alcohol, hemoglobin A1c, T2D duration, comorbidities (dyslipidemia, hypertension, stroke, heart failure, coronary artery disease, atrial fibrillation), prior colonoscopy, other anti-diabetic medications, aspirin, and statins. The intention-to-treat design was applied, and multivariable Cox regression models were conducted to estimate adjusted hazard ratios (aHRs) of outcomes with SGLT-2i use. Dose-response relationship was investigated according to defined daily dose (DDD), with one DDD being equivalent to daily use of dapagliflozin 10 mg, canagliflozin 200 mg, empagliflozin 17.5 mg, or ertugliflozin 10 mg. Duration-response relationship was investigated according to the proportion of SGLT-2i use, derived by dividing the treatment duration by follow-up duration.

Results: Among 436,890 T2D patients (mean [SD] age: 64.3 [11.6] years; 48.7% male), there were 8,481 (1.9%) SGLT-2i(+)/metformin(-), 48,008 (11.0%) SGLT-2i(+)/metformin(+), and 380,401 (87.1%) SGLT-2i(-)/metformin(+) users. During a median follow-up of 6.3 years [interquartile range: 3.2–7.8], there were 4,976 (1.1%) incident CRC cases and 1,311 (0.3%) CRC-related deaths. When compared with SGLT-2i(-)/metformin(+), both SGLT-2i(+)/metformin(+) and SGLT-2i(+)/metformin(-) were associated with a lower CRC risk (aHR:0.51, 95%CI:0.36-0.73; and aHR:0.46, 95%CI:0.25-0.86, respectively). There was no difference in CRC risk between SGLT-2i(+)/metformin(+) and SGLT-2i(+)/metformin(-) (aHR:1.11, 95%CI:0.54-2.26). When metformin was used as the reference group, a stepwise decreasing risk of CRC was observed for SGLT-2i 0.5-0.9 DDD (aHR:0.76, 95%CI:0.64-0.90) and 1 DDD or above (aHR:0.46, 95%CI:0.35-0.60) ($P_{\text{trend}} < 0.001$). Similarly, a duration-response relationship existed – SGLT-2i use proportion $< 80\%$ with aHR:0.73 (95%CI:0.57-0.94) and $\geq 80\%$ with aHR:0.62 (95%CI:0.52-0.74) ($P_{\text{trend}} < 0.001$). In addition, SGLT-2i was associated with lower risk of CRC-related mortality (aHR:0.45, 95%CI:0.29-0.68), any adenoma (aHR:0.81, 95%CI:0.75-0.88), non-advanced adenoma (aHR:0.84, 95%CI:0.77-0.91) and advanced adenoma (aHR:0.59, 95%CI:0.48-0.72) than metformin monotherapy.

Conclusion: SGLT-2i, either as monotherapy or combination therapy with metformin, associated with lower risk of CRC than metformin monotherapy, in a dose- and duration-response manner. Randomized clinical trials

investigating effect of SGLT-2i on colonic polyp are warranted to validate our study findings.

Disclosure: Nothing to disclose.

MP397

LOXL2 IN COLORECTAL CANCER SUPPRESSES ANTI-TUMOUR IMMUNITY THROUGH RECRUITING AND ACTIVATING MDSCS AND IS A THERAPEUTIC TARGET FOR IMMUNOTHERAPY

J. Cheng^{1,2}, Q. Zhou^{1,2}, L. Lei^{1,2}, X. Zhang^{1,2}, Y. Du^{1,2}, Q. Li³, H. Deng^{1,2}, G. Li^{1,2,4}, X. Bai^{1,2}

¹Department of General Surgery, Nanfang Hospital, The First School of Clinical Medicine, Southern Medical University, Guangzhou, China, ²Guangdong Provincial Key Laboratory of Precision Medicine for Gastrointestinal Tumour, Guangzhou, China, ³Dermatology Hospital, Southern Medical University, Guangzhou, China, ⁴Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China

Contact E-Mail Address: baixiaowudocor@foxmail.com

Introduction: Colorectal cancer (CRC) is the third-most common malignancy worldwide. Lysyl oxidase-like protein 2 (LOXL2), which promotes crosslinking of collagen and elastin, contributes to tumor progression in different tumour entities, but its role in CRC has not been evaluated. Here, we unraveled the role of LOXL2 in regulating tumour immune microenvironment of CRC and identified LOXL2 as a potential target for immunotherapy.

Aims & Methods: We analyzed the expression of LOXL2 in the Cancer Genome Atlas (TCGA) data. The effect of LOXL2 on CRC cell growth was determined by cell viability and colony formation assays. In vivo models were established by subcutaneous injection of colorectal cancer cell lines into immunodeficient NOD-SCID- γ (NSG) mice and immunocompetent wild-type BALB/c mice. Flow cytometry and immunohistochemistry were used to analyze immune cell composition. The collagen fibers in the extracellular matrix (ECM) were observed by masson staining, second harmonic generation imaging (SHG), and two-photon fluorescence imaging.

Results: Survival prognosis analysis revealed that high LOXL2 expression was correlated with poor survival of patients with CRC in TCGA cohort. However, we found that LOXL2 overexpression in human (HCT116 and DLD1) and mouse (CT26 and MC38) CRC cell lines had little effect on tumor growth *in vitro* and in immunodeficient mice. But its overexpression in mouse CRC cell lines could significantly promote tumor growth in immunocompetent mice ($p < 0.05$). Overexpression of LOXL2 led to CXCL1 upregulation in the supernatant of CRC cells and CRC tumor tissues; subsequently, upregulation of CXCL1 induced more migration of myeloid-derived suppressor cells (MDSCs) *in vitro* and recruited more MDSCs in the tumor microenvironment. On the other hand, LOXL2 increased the crosslinking of collagen fibers *in vitro* and in the tumor microenvironment, which subsequently activated the function of MDSCs (up-expression of Arg1, IDO1, and INOS) and increased the oncostatin M (OSM) secreted by MDSCs. In turn, OSM secreted by MDSCs induced the expression of LOXL2 in CRC cells. The accumulation and activation of MDSCs in the tumor microenvironment inhibited the infiltration and function of CD8⁺ T cells, which suppressed the anti-tumour immunity of the host. Targeting of LOXL2 with a neutralizing antibody or inhibitor (PAT-1251) significantly impaired tumor growth ($p < 0.05$) and MDSC infiltration and activation ($p < 0.05$) in immunodeficient mice. Finally, PAT-1251 boosted anti-PD1 efficacy in colorectal cancer, suggesting that it could be repurposed to improve immunotherapy efficacy.

Conclusion: Our findings revealed that LOXL2 exerted a pro-tumorigenic role in CRC. LOXL2 recruited and activated MDSCs through CXCL1 and

crosslinking of collagen fibers, respectively, subsequently reducing infiltration and activation of anti-tumor CD8⁺ T cells in the tumor microenvironment. Targeting this axis with PAT-1251 improved the efficacy of immunotherapy in colorectal cancer.

Disclosure: Nothing to disclose.

MP398

LOSS OF MULTIMERIN-2 IN COLORECTAL CANCER ALTERS VASCULAR EFFICIENCY AND IMMUNITY

L. Camicia¹, E. Andreuzzi², E. Poletto¹, G. Carobolante¹, G. Schinello¹, E. Di Siena¹, I.V. Albergati³, A. Piruzza³, M.G. Nadin⁴, S. Maiero⁴, S. Realdon⁴, L.S. Crocè³, R. Cannizzaro^{4,3}, M. Mongiat¹
¹Centro di Riferimento Oncologico - Aviano - I.R.C.C.S., Division of Molecular Oncology, Aviano, Italy, ²IRCCS Materno Infantile "Burlo Garofolo, Trieste, Italy, ³University Of Trieste, Dipartimento Universitario Clinico di Scienze mediche, chirurgiche e della salute, Trieste, Italy, ⁴Centro di Riferimento Oncologico - Aviano - I.R.C.C.S., Oncological Gastroenterology, Aviano, Italy

Contact E-Mail Address: lucricamicia@gmail.com

Introduction: Tumor angiogenesis is considered as a hallmark of cancer¹ and plays a critical role in colorectal cancer (CRC) development and progression^{2,3}. Tumor vasculature promotes tumor growth and metastasis since it not only provides nutrients and oxygen for the rapid proliferation of cancer cells as well as a route for metastatization, but also affects the infiltration of immune cells to the tumor site. Thus, the targeting of angiogenesis has become an attractive strategy against various human malignancies, including CRC⁴. In fact, tumor-associated vessels are leaky and poorly efficient due to the dismantlement of the basement membrane and the loss of pericytes, thus preventing proficient drug delivery to the tumor⁵. In this context, we demonstrated that Multimerin-2, an extracellular matrix glycoprotein deposited along the blood vessels in juxtaposition between endothelial cells and pericytes, mural cells fundamental in vessels stabilization, is key in the maintenance of vascular homeostasis⁶. However, the effects of this molecule on pericytes biology and its putative impact on the immune cells' recruitment are still poorly understood. Since, many vessels associated with CRC lose Multimerin-2 expression, thus we aimed at verifying the effects of this loss in pericyte recruitment, vascular stability, and the surrounding tumor microenvironment.

Aims & Methods: Immunohistochemistry analysis on colorectal cancer patients' biopsies revealed that colon cancer associated vessels display a downregulated expression of Multimerin-2. Thus, we aimed at verifying the extent of pericyte recruitment by Multimerin-2-devoid vessels in a colon cancer model and at evaluating how Multimerin-2 loss affects the surrounding tumor microenvironment. Human umbilical vein endothelial cells (HUVEC) and Human brain vascular pericytes (HBVP) were used as *in vitro* models for proliferation, functional assays, transcriptomic and proteomics analyses. Wild type and *Multimerin-2*^{-/-} C57BL/6 mice were subcutaneously injected with the syngeneic colon cancer MC-38 cells and pericyte coverage and microenvironmental features were assessed in tumor sections by immunofluorescence as well as drug delivery following cisplatin treatment six hours prior sacrifice.

Results: We demonstrated that Multimerin-2 promotes pericytes migration, adhesion, and proliferation. Consistently, MC-38 xenografts from Multimerin-2 mice displayed a decreased pericytes coverage along the vessels as well as increased intratumoral hypoxia, suggestive of vascular inefficiency. In fact, upon treatments we counted less DNA \cisplatin adducts in tumors from *Multimerin-2*^{-/-} mice. Interestingly, tumors from Multimerin-2 mice also displayed an altered CD68 cells infiltrate, suggesting that Multimerin-2 loss can affect macrophages recruitment to the tumor

site. Accordingly, a higher number of the monocytic-like cells THP-1 migrated through a Multimerin-2-depleted endothelium. Furthermore, we observed that the loss of Multimerin-2 also associates with the expression of cytokines involved in macrophages recruitment.

Conclusion: These results suggest that Multimerin-2 loss impairs the pericyte recruitment, adhesion and proliferation. As a result, the vasculature lacking Multimerin-2 is utterly destabilized leading to increased intratumoral hypoxia and poorly efficient drug delivery. Importantly, the absence of Multimerin-2 also impairs the immune response suggesting that different Multimerin-2 expression in CRC tumor associated vessels could represent a promising biomarker to predict the efficacy of chemotherapy and/or immune therapy in CRC patient treatment

References: 1. Hanahan, D. Hallmarks of Cancer: New Dimensions. *Cancer Discovery* 12, 31–46 (2022).

2. Weis, S. M. & Cheresh, D. A. Tumor angiogenesis: molecular pathways and therapeutic targets. *Nat Med* 17, 1359–1370 (2011).

3. Angiogenesis Factors Involved in the Pathogenesis of Colorectal Cancer. *Current Health Sciences Journal* 5–11 (2013) doi:10.12865/CHSJ.40.01.01.

4. Liu, Z.-L., Chen, H.-H., Zheng, L.-L., Sun, L.-P. & Shi, L. Angiogenic signaling pathways and anti-angiogenic therapy for cancer. *Sig Transduct Target Ther* 8, 198 (2023).

5. Carmeliet, P. & Jain, R. K. Principles and mechanisms of vessel normalization for cancer and other angiogenic diseases. *Nat Rev Drug Discov* 10, 417–427 (2011).

6. Pellicani, R. *et al.* Multimerin-2 maintains vascular stability and permeability. *Matrix Biology* 87, 11–25 (2020).

Disclosure: Nothing to disclose.

MP399

WITHDRAWN

MP400

THE ADHESION G PROTEIN-COUPLED RECEPTOR F5 IS A CRUCIAL REGULATOR OF CD4⁺ T CELL FUNCTION: IMPLICATION FOR COLITIS AND COLON CANCER

D. Jacenik¹, M. Zielinska², E.J. Beswick³, J. Fichna²

¹University of Lodz, Faculty of Biology and Environmental Protection, Department of Cytochemistry, Lodz, Poland,

²Medical University of Lodz, Faculty of Medicine, Department of Biochemistry, Lodz, Poland, ³University of Kentucky, Department of Internal Medicine, Division of Digestive Diseases and Nutrition, Lexington, United States of America

Contact E-Mail Address: damian.jacenik@biol.uni.lodz.pl

Introduction: T cells, are a major regulator and source of pro-inflammatory cytokines, which may promote colitis, but be protective in some cancers^{1,2}. Nevertheless, limited efforts have been made to explore factors which determine the phenotype of T cells and their impact on the above-mentioned phenomena. The adhesion G protein-coupled receptor F5 (ADGRF5) belongs to seven-transmembrane receptor subfamily and may be related to development of some cancer types³.

Aims & Methods: The aim of the study was to assess the significance of ADGRF5 for T cell function and its impact on colitis and colon cancer progression. WT and ADGRF5 knockout CD4⁺ T cells were examined for cytokine genes and proteins using real-time PCR, Western blot and multiplex analysis. Tumor killing assay and flow cytometry analysis were performed to evaluate tumor killing properties of T cells co-cultured with MC38 colon cancer cells. ADGRF5 WT and KO mice were utilized to examine the impact of ADGRF5 on colitis, colitis-associated cancer development and colon

cancer growth. Adoptive transfer of WT and ADGRF5 knockout CD4⁺ and CD8⁺ T cells were examined in tumor models to assess their role in disease progression.

Results: In murine model of colon cancer, animals with ADGRF5 knockout developed significantly smaller tumors which was accompanied by enhanced CD3 expression and hyperproduction of cytokines related to T cell action compared to wild type mice. *Ex vivo* analysis of two main population of T cells obtained from spleen of wild type and ADGRF5 knockout mice revealed that activated CD4⁺ but not CD8⁺ T cells with ADGRF5 were manifested by increased production of major anti-cancer molecules such as interferon γ (IFN- γ), perforin and granzyme B, and were characterized by secretion profile of cytokines related to mixed phenotype of T helper (T_H) 1 and T_H2 cells. Moreover, we documented higher proportion of apoptotic cells in co-culture of MC38 colon cancer cells with ADGRF5 knockout but not wild type CD4⁺ T cells. Finally, in the murine model of colon cancer adoptive transfer of CD4⁺ T cells with ADGRF5 knockout led to a significant reduction of tumor volume which was reversed by administration of antibody against IFN- γ . Nevertheless, ADGRF5 knockout in mice with colitis-associated colorectal cancer and colitis was related to significantly higher number of colon tumors and worse disease activity index compared to wild type animals, respectively. These results together with the analysis of gene expression signature in inflamed colons suggest opposite role for ADGRF5 in colitis than in the allograft colon cancer.

Conclusion: ADGRF5 is a critical regulator of T cell function and specific knockout of ADGRF5 reprograms CD4⁺ T cells into the pro-inflammatory phenotype. Our *in vitro* and *in vivo* studies indicated that ADGRF5 knockout in T cells promote pro-inflammatory cytokines, which prevent gastrointestinal cancer progression while boost both colitis and colitis-associated colorectal cancer development.

References: 1. Jacenik D., Karagiannidis I., Beswick E.J. 2022. *T_H2 cells inhibit growth of colon and pancreas cancers by promoting anti-tumorigenic responses from macrophages and eosinophils.* Br J Cancer. 128: 387-397. doi: 10.1038/s41416-022-02056-2.

2. Shale M., Schiering C., Powrie F. 2013. *CD4⁺ T cell subsets in intestinal inflammation.* Immunol Rev. 252: 164-82. doi: 10.1111/imr.12039.

3. Jacenik D., Hikisz P., Beswick E.J., Fichna J. 2023. *The clinical relevance of the adhesion G protein-coupled receptor F5 for human diseases and cancers.* Biochim Biophys Acta Mol Basis Dis. 1869: 166683 doi: 10.1016/j.bba-dis.2023.166683.

Disclosure: The work was supported by the National Science Centre, Poland under research project no 2019/32/C/NZ5/00064 (DJ).

MP401

A DYNAMIC MOLECULAR LANDSCAPE AT SINGLE-CELL RESOLUTION AND THE IMPORTANCE OF LIGAND-RECEPTOR GENES THROUGH THE PROGRESSION OF COLORECTAL CANCER

J. Sheng¹, N. Li², Y. Liao¹, Y. Zhang¹, H. Chen¹, M. Tu¹, G. Zhong¹, C. Xiong¹, Z. He¹, Y. Lei², P. Zheng², L. Wang³, X. Gao³, Y. Zhu², J. Liu², H. Fan¹

¹Yichun People's Hospital, Yichun, China, ²The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, China, ³Yunnan Agricultural University, Kunming, China

Contact E-Mail Address: ndyfy10307@ncu.edu.cn

Introduction: As common precursors to colorectal cancer (CRC), polyps and adenomas in the large intestine may develop into malignancy over time through a cascade known as the "normal-polyp-adenoma-carcinoma" sequence. Colorectal cancer (CRC) is the third most common cancer and the leading cause of cancer-related death worldwide, with an estimated increase to 3.2million new cases and 1.6million deaths by 2040

. The high mortality of CRC is largely due to the late diagnosis, incomplete molecular understanding of pathological progression, and limited treatment options for patients with advanced disease stage. Therefore, the identification of novel biomarkers at early (pre-cancerous) phase, thorough elucidation of pathological mechanisms, and development of effective therapies is crucial for CRC diagnosis and treatment.

Aims & Methods: Here we have utilized 10x genomics scRNA-seq platform to perform a high-resolution transcriptomic analysis of three normal colorectal tissues, two samples with inflammatory polyps, two specimens with adenomatous polyps and three CRC samples.

Results: By analyzing the scRNA-seq data of the ten human colorectal samples, which represent the four phases of colorectal pathogenesis, in combination with validation by immunofluorescence staining using expanded clinical samples, and together with verification using large scale TCGA and Kaplan-Meier data, we revealed a dynamic molecular landscape and for the first time demonstrated the importance of ligand-receptor genes, transcription factors and genes encoding multiple immunoglobulins and heat shock proteins driving the colorectal carcinogenesis.

Besides the heterogeneity of (sub-) cell types and difference of the transcriptomic profiling across the four stages, one of the most interesting and novel findings of this study is that the expression of ligand-receptor genes can be used to determine the cell types and even cell sub-types, at least for the colorectal tissues collected in this study, not the expressions of other gene sets, such as cell surface receptor signaling pathways, cell-cell signaling, transcription factors, cytokines, cell activation factors, cell signaling factors, or extracellular matrix, implying that ligand-receptor pairs are fundamentally important for the cell type determination and cell-cell communications in colorectal tissues.

We found that some genes encoding immunoglobulin members are highly expressed in the T cells (*IGHA1*, *IGHA2*, *IGKC* and *IGLC2*) and in the fibroblasts (*IGHA1*, *IGHA2*, *IGLC1*, *IGLC2*, *IGKC* and *JCHAIN*) from normal colorectal tissues, while some genes encoding heat shock proteins are highly expressed in T cells (*HSP90AA1*, *HSP90AB1*, *HSPA1B*, *HSPD1*, *HSPE1* and *HSPH1*) and plasma cells (*HSP90AA1*, *HSPA1A*, *HSPA1B*, *HSPA6*, *HSPB1* and *HSPD1*) from abnormal colorectal samples, especially in the ones with adenomatous polyps.

Furthermore, IgG plasma cells can be grouped into two sub-types, characteristic of high expression of immunoglobulin-encoding genes *IGKC* and *IGLC1/IGLC2*, respectively. In addition, the six clusters of IgA plasma cells can also be characterized based on the combinatory expression level of some immunoglobulin-encoding genes (*IGHA1*, *IGHA2*, *IGKC*, *IGLC1*, *IGLC2* and *IGLC3*). In summary, our analyses suggested the potential distinct functional importance of immunoglobulins and heat shock proteins in immunity and microenvironment during the colorectal malignancy.

Conclusion: Our transcriptome data provides valuable insights and a useful resource for better understanding the molecular pathological landscape in CRC to achieve more effective diagnosis and treatments.

References: Siegel, R.L., Wagle, N.S., Cercek, A., Smith, R.A., and Jemal, A. (2023). Colorectal cancer statistics, 2023. CA Cancer J Clin 73, 233-254. 10.3322/caac.21772.

2. Morgan, E., Arnold, M., Gini, A., Lorenzoni, V., Cabasag, C.J., Laversanne, M., Vignat, J., Ferlay, J., Murphy, N., and Bray, F. (2023). Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. Gut 72, 338-344. 10.1136/gutjnl-2022-327736.

3. Huck, M.B., and Bohl, J.L. (2016). Colonic Polyps: Diagnosis and Surveillance. Clin Colon Rectal Surg 29, 296-305. 10.1055/s-0036-1584091.

4. He, D.G., Chen, X.J., Huang, J.N., Chen, J.G., Lv, M.Y., Huang, T.Z., Lan, P., and He, X.S. (2022). Increased risk of colorectal neoplasia in inflammatory bowel disease patients with post-inflammatory polyps: A systematic review and meta-analysis. World J Gastrointest Oncol 14, 348-361. 10.4251/wjgo.v14.i1.348.

5. Rudy, D.R., and Zdon, M.J. (2000). Update on colorectal cancer. *Am Fam Physician* 61, 1759-1770, 1773-1754.

6. Heumos, L., Schaar, A.C., Lance, C., Litinetskaya, A., Drost, F., Zappia, L., Lucken, M.D., Strobl, D.C., Henao, J., Curion, F., et al. (2023). Best practices for single-cell analysis across modalities. *Nat Rev Genet* 24, 550-572. 10.1038/s41576-023-00586-w.

Disclosure: Nothing to disclose.

MP402

ROLE OF AUTOPHAGY IN THE HOST RESPONSE TO INFECTION BY PATHOGENIC ESCHERICHIA COLI ASSOCIATED WITH COLORECTAL CANCER

C. Desseux¹, A. Da Silva¹, J. Delmas¹, A. Tassini¹, P. Sauvanet¹, N. Barnich¹, G. Dalmasso¹, H.T.T. Nguyen¹

¹Université Clermont Auvergne, UMR 1071 Inserm, Clermont-Ferrand, France

Contact E-Mail Address: coline.desseux@uca.fr

Introduction: In patients with colorectal cancer (CRC), intestinal dysbiosis has been observed, with abnormal colonization of the colonic mucosa by pathogenic *Escherichia coli* strains producing a cyclomodulin named cytotoxic necrotizing factor (CNF). Cyclomodulins are bacterial toxins capable of altering the cell cycle of the infected cell. One of the mechanisms involved in host defence against pathogens and in carcinogenesis is autophagy. However, the role of autophagy in the host response to the infection by CNF-producing *E. coli*, designated as CyPEC, has not yet been described.

Aims & Methods: Thus, the aim of this study was to investigate the role of autophagy in colorectal carcinogenesis in the context of CyPEC infection. Mice predisposed to CRC development with autophagy deficiency specifically intestinal epithelial cells (*Apc^{Min/+}/Atg16l1^{ΔIEC}* mice) and their control littermates with functional autophagy (*Apc^{Min/+}* mice) were infected with the clinical CyPEC strain 21F8. Tumor size and number were determined using a dissecting microscope. The mouse colons were collected and used for histological score assessment, and to analyse the levels of markers of autophagy, cell proliferation, apoptosis and inflammation by immunoblot, immunohistochemical staining and ELISA.

Results: We showed that in *Apc^{Min/+}/Atg16l1^{ΔIEC}* mice, infection with the CyPEC 21F8 strain led to increases in the number and the size of colonic tumours, compared with the uninfected condition. However, this was not observed in *Apc^{Min/+}* mice. The increase in tumorigenesis in *Apc^{Min/+}/Atg16l1^{ΔIEC}* mice upon 21F8 infection versus uninfected condition was associated with increased pro-inflammatory cytokine production, enhanced cellular proliferation and decreased apoptosis in colonic epithelial cells.

Conclusion: Our results suggest that autophagy is necessary to limit the pro-carcinogenesis effects of the CyPEC 21F8 strain, thereby decreasing colorectal tumorigenesis. In another word, autophagy deficiency could be a susceptibility factor for the development of CRC in a host with colonization by CyPEC strains.

Disclosure: Nothing to disclose.

MP403

NUCLEAR TRANSLOCATION OF CNPY3 FACILITATES COLORECTAL CANCER PROGRESSION VIA ENHANCING E3 LIGASE TRIM21-MEDIATED UBIQUITINATION AND DEGRADATION OF P53 PROTEIN

X. Li¹, S. Xie¹, M. Yin¹, S. Zhu¹, S. Zhang¹

¹Beijing Friendship Hospital, Capital Medical University, Beijing, China

Contact E-Mail Address: xue_li95@126.com

Introduction: Canopy FGF signaling regulator 3 (CNPY3) is a protein predominantly localized in the endoplasmic reticulum. Its expression is increased in several cancers, including colorectal cancer (CRC). However, how CNPY3 affects CRC progression and the function of CNPY3 translocation to the nucleus in CRC is not clear.

Aims & Methods: This study aimed to investigate the role of CNPY3 in the development of CRC. In vitro, the impacts of CNPY3 on CRC growth were evaluated by 5-Ethynyl-2'-deoxyuridine staining, colony formation, wound healing, transwell migration, and apoptosis assay. Tumor xenograft mouse models and orthotopic mouse models of colorectal cancer metastasis were used to assess in vivo. Furthermore, the underlying mechanism of CNPY3 in CRC was revealed by RT-qPCR, western blot, LC-MS/MS analysis, immunofluorescence staining, coimmunoprecipitation, GST-pulldown, confocal microscopy, ubiquitination assays, and rescue experiments.

Results: CNPY3 was significantly upregulated in CRC tissue and cell lines, correlating with their poor prognosis. Functional experiments demonstrated that CNPY3 enhances CRC proliferation, migration, invasion, and tumor growth. Notably, our investigation reveals a nucleus translocation of *cnpy3* by activation of nuclear localization sequences through protein conformational changes. Meanwhile, nuclear localization of CNPY3 promotes the binding of TRIM21 and p53 and forms a CNPY3-TRIM21-p53 complex, thereby promoting the ubiquitination-proteasomal degradation of wild-type p53 protein, inhibiting the related genes of the TP53 signaling pathway, and promoting apoptosis of tumor cells. In vivo and in vitro, inhibiting the degradation of p53 was able to suppress CNPY3 in cancer-promoting tumors, whereas the knockdown of CNPY3 in p53^{-/-} HCT116 cells did not significantly inhibit CRC.

Conclusion: CNPY3, after nuclear translocated, binds to TRIM21 and p53 and stabilizes the TRIM21-p53 interaction. This CNPY3-TRIM21-p53 complex facilitates TRIM21-mediated p53 ubiquitination and causes p53 proteasome degradation.

Collectively, these findings support that CNPY3, an oncogene with CRC progression and poor prognosis, serves as a biomarker and therapeutic target correlated to suppress p53 function.

References: 1. Wakabayashi Y, Kobayashi M, Akashi-Takamura S, et al. A protein associated with toll-like receptor 4 (PRAT4A) regulates cell surface expression of TLR4. *J Immunol.* 2006;177(3):1772-9.

2.

3. Xiao L, Li XX, Chung HK, Kalakonda S, et al. RNA-Binding Protein HuR Regulates Paneth Cell Function by Altering Membrane Localization of TLR2 via Post-transcriptional Control of CNPY3. *Gastroenterology.* 2019;157(3):731-743.

4. Ghait M, Husain RA, Duduskar SN, et al. The TLR-chaperone CNPY3 is a critical regulator of NLRP3-inflammasome activation. *Eur J Immunol.* 2022;52(6):907-923.

5. Zhou YQ, Bao TS, Xie JX, et al. The SLITRK4-CNPY3 axis promotes liver metastasis of gastric cancer by enhancing the endocytosis and recycling of TrkB in tumour cells. *Cell Oncol (Dordr).* 2023;46(4):1049-1067.

6. Reddy BA, van der Knaap JA, Bot AG, et al. Nucleotide biosynthetic enzyme GMP synthase is a TRIM21-controlled relay of p53 stabilization. *Mol Cell.* 2014;53(3):458-70.

7. Liu J, Zhang C, Xu D, et al. The ubiquitin ligase TRIM21 regulates mutant p53 accumulation and gain of function in cancer. *J Clin Invest*. 2023;133(6):e164354.

Disclosure: Nothing to disclose.

MP404

CD3 POSITIVE T CELL, IMMUNOSCORE AND CLINICOPATHOLOGICAL FEATURES OF EARLY-ONSET COLORECTAL TUMORS

N. Akimoto¹, A. Tatsuguchi¹, O. Goto¹, A. Hoshimoto¹, Y. Shimazu¹, R. Inoue², S. Nakagome¹, T. Habu¹, Y. Ishikawa¹, E. Koizumi¹,

K. Higuchi¹, T. Nishimoto¹, J. Omori¹, R. Ohashi², K. Iwakiri¹

¹*Nippon Medical School, Graduate School of Medicine, Gastroenterology, Tokyo, Japan*, ²*Nippon Medical School, Graduate School of Medicine, Integrated Diagnostic Pathology, Tokyo, Japan*

Contact E-Mail Address: naohiko.akimoto07@gmail.com

Introduction: The incidence of early-onset colorectal cancer is increasing alarmingly worldwide, and countermeasures against this issue are urgently needed. Although previous studies suggested age-related molecular pathological changes, the association between the roles of Immunoscore using the ration of CD3+ and CD8+ T cells in anti-tumor immune responses and early-onset colorectal cancer and adenoma resected by endoscopy remains unclear.

This study aimed to investigate the association of Immunoscore using the ratio of CD3+ and CD8+ T cells and clinicopathological characteristics mainly focused on early-onset tumors. We defined early-onset colorectal tumors as those that occurred at less than 50 years of age at diagnosis and later-onset as those that occurred at 50 years of age or older in this study.

Aims & Methods: The aim of this study was to investigate the association between Immunoscore and clinicopathological features of early-onset colorectal tumors. Utilizing a molecular pathological database of 169 colorectal cancer and adenoma cases, we analyzed 306 colorectal lesions including 214 early-onset tumors resected by endoscopic procedures including cold snare polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection from February 2017 to January 2020 at Nippon Medical School Hospital in Japan.

After collecting formalin-fixed paraffin-embedded (FFPE) tissue blocks, CD3 and CD8 immunostaining was performed, and the number of CD3+ and CD8+ cells was quantified in each area of tumor, stromal, and normal. One to five fields of view (median 5 fields) were selected depending on the size of the lesion using a fluorescence microscope BZ-X800 (KEYENCE) at 200x magnification, and the average number of CD3+ and CD8+ cells was calculated by automatic counting.

Counting stromal and normal cells was limited to those specimens for which the excised specimens were large enough to contain sufficient stromal and normal portions in addition to the tumor portion. Immunoscore was calculated by the ratio of CD8+/CD3+ positive T cells. Clinicopathologic characteristics were also evaluated retrospectively. Chi-square test was used to compare categorical variables, Spearman's test to examine correlation, Mann-Whitney U test to compare continuous variables, and Kruskal-Wallis test to compare the three groups.

Results: The tumor location was 126 (41%)/142 (47%)/37 (12%) in the proximal/ distal colon/rectum. The number of CD3+T cells decreased significantly with increasing tumor diameter ($P<0.001$). The number of CD3+T cells was predominantly lower in type Ip (protruding type) compared to type non-Ip ($P<0.001$). The distribution of Immunoscore measured in tumor area was significantly different among tumor locations ($P<0.05$).

Conclusion: Using endoscopically resected specimens, we suggest that the anti-tumor immune response may differ according to tumor size, gross type, and location. Further studies are warranted to stratify early-onset tumors requiring careful surveillance after endoscopic resection in terms of the anti-tumor immune response in T cells.

Disclosure: Nothing to disclose.

New clinical aspects in hepatology

14:30-15:30 / Poster Stage 3

MP405

ANTICOAGULANT THERAPY FOR PORTAL VEIN THROMBOSIS IN CIRRHOSIS: WHAT IS THE PROGNOSTIC IMPACT?

L. Faty¹, O. Elmqaddem¹, H. Koulali², Z. Abdelkrim³, G. Kharrasse⁴, Z. Ismaili⁵
¹Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Department of Hepato-Gastroenterology, Oujda, Morocco, ²Mohammed VI University Hospital, Hepatogastroenterology, Oujda, Morocco, ³Mohammed VI University Hospital, Mohammed the First University, CHU Med VI Oujda, Oujda, Morocco, ⁴Faculty of Medicine Oujda, Avicenne, Oujda, Morocco, ⁵Medical School, Hepato Gastroentetology, Oujda, Morocco

Contact E-Mail Address: lamrani.fati12@gmail.com

Introduction: Portal vein thrombosis is a common complication of cirrhosis regardless of etiology. Medical management with anticoagulant treatment was a subject of debate with many questions about the balance between bleeding risk and therapeutic benefit. Recently, it has been proven that anticoagulant treatment improves the prognosis of liver disease and portal hypertension, without any additional bleeding risk.

Aims & Methods: The aim of our study is to identify the prognostic impact of anticoagulant treatment for portal vein thrombosis in cirrhotic patients.

It is a retrospective study including all patients followed for cirrhosis at our institution between January 2017 and August 2022. The diagnosis and monitoring of portal vein trunk recanalization were performed by Doppler ultrasound and computed tomography scan. Treatment was decided on a case-by-case basis and was dependent on the stage of liver disease, patient age, and extension of thrombus. Patients excluded: patients with portal cavernoma. upper endoscopy was systematically performed before treatment. The prognosis improvement rate was determined by the Child-Pugh score at baseline and at completion of the study.

Results: A total of 53 patients with portal vein thrombosis were included among 285 cirrhotic patients followed during this period. Portal vein thrombosis was diagnosed in 11.3% (n = 6). The mean age was 54 years, with a male-to-female ratio of 0.7 (22 males/31 females).

The etiology of cirrhosis included chronic hepatitis B in 11.3% (n = 6), chronic hepatitis C in 5.6% (n = 3), primary biliary cholangitis in 3.7% (n = 2), autoimmune hepatitis in 1.8% (n = 1), Budd-Chiari syndrome in 1.8% (n = 1), Wilson's disease in 1.8% (n = 1), and idiopathic causes in 73.5% (n = 39). Before PVT diagnosis, the Child-Pugh score was classified as follows: A in 71.6% (n = 38), B in 24.5% (n = 13), and C in 3.7% (n = 2).

The main cirrhosis decompensations were bleeding related to portal hypertension in 67.9% (n = 36), ascites in 54.7% (n = 29), and hepatocellular carcinoma (HCC) in 3.7% (n = 2).

Anticoagulant treatment was indicated in 47.1% (n = 25) of cases, 48% of patients (n = 12) were treated with low molecular weight heparin (LMWH), 44% (n = 11) with direct oral anticoagulants (DOACs), and 8% (n = 2) with acenocoumarol. Among patients treated with anticoagulants, 68% (n = 17) had hemorrhagic decompensation, 56% (n = 14) had ascitic decompensation, 8% (n = 2) had hepatic encephalopathy, and 4% (n = 1) had hepatocellular carcinoma.

	Treated Patients (n=25)	Non-Treated Patients (n= 28)	P value
Child Pugh Score Stability	40 % (n= 10)	42 % (n=12)	>0.001
Child Pugh Score Deterioration	32 % (n= 8)	35 % (n=10)	>0.001
Child Pugh Score Improvement	28% (n=7)	21,4 % (n=6)	>0.001

Table 1: Outcomes of Patients Treated with Anticoagulants vs. Untreated Patients

Conclusion: In our study, 71% of patients had a Child Pugh A score at the time of PVT diagnosis. 40% of patients maintained a stable Child score during follow-up and 28% even improved their prognostic stage.

References: <https://doi.org/10.1016/j.jhep.2023.02.023>
<https://doi.org/10.1016/j.jhep.2023.10.002>
<https://doi.org/10.1016/j.jhep.2023.03.022>
<https://doi.org/10.1016/j.jhep.2023.05.040>

Disclosure: Nothing to disclose.

MP406

PHYSICAL FRAILITY IS A MAJOR RISK FACTOR FOR ADVERSE OUTCOMES IN HOSPITALIZED PATIENTS WITH CIRRHOSIS.

F. D'Arcangelo¹, A. Zanetto¹, A. Ferrarese¹, M. Grasso¹, M. Bucci¹, M. Gambato¹, G. Germani¹, F.P. Russo¹, M. Senzolo¹, J. Lanari², U. Cillo², P. Burra¹
¹Gastroenterology/Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy, ²Hepato-Biliary-Pancreatic and Liver Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy

Contact E-Mail Address: francesca.darcangelo02@gmail.com

Introduction: Recent evidence indicates that physical frailty, as assessed by liver frailty index (LFI), is an independent predictor of mortality in patients with cirrhosis. However, majority of data are from North American cohorts of patients in the outpatient clinic setting.

Aims & Methods: We prospectively investigated characteristics and impact of frailty in all patients with cirrhosis who were admitted to our unit between October 1st, 2021 and March 31st, 2023. Exclusion criteria were: age<18 or>70 years; known musculoskeletal disease; history of liver transplantation. LFI was calculated at admission and previously established thresholds were used to assess physical frailty: <3.2 (robust); between 3.2 and 4.5 (pre-frail); >4.5 (frail). Primary outcome was liver related death.

Results: One hundred-fifteen patients with cirrhosis were included (median age 60 years; 72% male), median MELD score 22 (IQR 14-26). 68.5 % of patients were CHILD C class. Presence of ascites were the most frequent sign of significant clinical portal hypertension (79.3% of patients). Alcohol was the most common aetiology of cirrhosis (62%). At time of inclusion, 42% of patients were frail (median LFI 4.23; IQR 3.62-4.72). During hospitalization patients with CHILD C class and frailty were admitted to the ICU for further decompensation of liver disease more frequently than patients with CHILD A/B class (11% vs. 0% p=0.034) and without frailty (19.1% vs. 6.3%, p=0.037). When discharged, patients with frailty were more frequently re-hospitalized when compared with patients without frailty (78.8% vs. 55.8%, p=0.028). No differences in rate of re-hospitalization were observed according to Child class (p=0.474). Fifty-eight patients (50% Child C) died during follow up of which 66.7% were frail and 33.3 % not frail (p=0.003), median time of follow up were 279 days (IQR 59-513). At univariate analysis Meld score>22, presence of ascites and presence of frailty were found to be associated with shorter survival, however at multivariate analysis, MELD score (OR:2.74; 95% CI 1.478-5.059 p=0.001) and frailty (OR:3.45; 95% CI 1.83-6.52, p=0.000) were the only independent predictor of death.

Conclusion: Frailty is frequent among hospitalized patients with cirrhosis, with a higher rate of ICU admission during hospitalization and re-hospitalization after discharge. The presence of frailty resulted strongly associated with an increased risk of death; This study opens the need of larger and multicentric studies looking

at physical frailty in the context of hospitalized patients with cirrhosis. Understanding the contribution of frailty to outcomes can ultimately optimize the management of patients during hospital stay especially in those who may benefit from early interventions including physical rehabilitation and nutritional supports.

References: Lai JC, Covinsky KE, Dodge JL, Boscardin WJ, Segev DL, Roberts JP et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. *Hepatology* 2017;66(2):564-574.

Lai JC, Covinsky KE, McCulloch CE, Feng S. The Liver Frailty Index Improves Mortality Prediction of the Subjective Clinician Assessment in Patients With Cirrhosis. *Am J Gastroenterol* 2018;113(2):235-242.

Tandon P, Montano-Loza AJ, Lai JC, Dasarathy S, Merli M. Sarcopenia and frailty in decompensated cirrhosis. *J Hepatol.* 2021 Jul;75 Suppl 1(Suppl 1):S147-S162. doi: 10.1016/j.jhep.2021.01.025. PMID: 34039486; PMCID: PMC9125684.

Disclosure: Nothing to disclose.

MP407

ENDOSCOPIC ULTRASOUND-GUIDED LIVER BIOPSY QUALITY COMPARED TO PERCUTANEOUS AND TRANSJUGULAR TECHNIQUES: A NETWORK META-ANALYSIS

M. Puga-Tejada¹, M. Arevalo-Mora^{1,2}, R. Oleas^{3,1}, C. Torres-Herrera^{4,5}, F. Ferber-Reyes¹, A. Perez², N. Martin², J. Baquerizo-Burgos¹, M. Egas-Izquierdo¹, D. Cunto¹, H. Alvarado-Escobar¹, R. Del Valle Zavala¹, J. Alcivar-Vasquez¹, H. Pitanga-Lukashok¹, C. Robles-Medrandia¹

¹Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Larkin Community Hospital, South Miami, United States of America, ³Cook County Health and Hospitals System, Chicago, United States of America, ⁴Hospital DIPRECA, Internal Medicine, Santiago de Chile, Chile, ⁵Universidad Diego Portales, Santiago de Chile, Chile

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Percutaneous liver biopsy (PC-LB) is the gold standard for the study of chronic liver disease. However, it is limited to patients with appropriate clinical and hematological conditions. Transjugular liver biopsy (TJ-LB) represents a less invasive yet less available technique. Endoscopic ultrasound-guided liver biopsy (EUS-LB) has emerged as a minimally invasive readily available technique. To the best of our knowledge, no network meta-analysis has compared LB quality and related adverse events among these techniques.

Aims & Methods: A systematic search was run in PubMed, Embase, Web of Science and Cochrane. The search included studies from inception to November 2023, in adult patients, which compared at least two of the following techniques: EUS-LB, PC-LB or TJ-LB. The analyzed endpoints were mean total sample length (TSL), mean number of complete portal triads (CPT), rate of appropriate sample for diagnosis, sample fragmentation and major adverse events (hematomas, bleeding, perforation, death). There was no distinction regarding study design, biopsy needle type or assistance with additional imaging methods. The studies with insufficient data, without any reported endpoint, or case series were excluded. The PC-LB was the reference. Data was analyzed in Rv4.0.

Results: Over the last thirty years (1993 to 2023), 21 original studies were analyzed being: 18/21 full manuscripts; 15/21 retrospective, 3/21 prospective, 3/21 randomized clinical trials (RCT); 11/21 EUS-LB, 21/21 PC-LB and

16/21 TJ-LB; 5/21 EUS-LB vs PC-LB, 10/21 PC-LB vs TJ-LB, and 6/21 compared the three techniques. We scrutinized 620 EUS-LB patients, 3347 PC-LB, and 1901 TJ-LB. TSL pooled mean for EUS-LB, PC-LB, and TJ-LB was 28.6 ± 10.6 mm, 23.3 ± 13.5 mm, and 15.7 ± 9.0 mm, respectively. Pooled rate of appropriate sample for diagnosis was 96.6%, 89.2%, and 85.4%, with a major adverse events pooled rate of 4%, 2.9%, and 3.5%, respectively. Between 14 studies and 24 pairwise comparisons, TSL EUS-LB mean was 0.17 mm longer (p=.932), but TJ-LB 4.93 mm shorter (p=.0025) (I²=95%). Between 3 studies and 5 pairwise comparisons, relative risk (RR) of sample fragmentation was significantly higher for EUS-LB (RR 4.55; 95% CI 2.72 – 7.61; p<.001) and TJ-LB (RR 2.72; 95% CI 1.54 - 4.80; p<.001) (I²=0%). There was not significant difference among mean number of CPT (I²=97.3%), rate of appropriate sample for diagnosis (I²=48.7%) or major adverse events (I²=10.5%).

Conclusion: EUS-LB quality is comparable to PC-LB and superior to TJ-LB in terms of TSL. These techniques are comparable in terms of the mean number of CPT, rate of appropriate sample for diagnosis, and major adverse events. Further original studies are needed to define the sample fragmentation rate of the aforementioned.

References: McCarty TR, Bazarbashi AN, Njei B, Ryou M, Aslanian HR, Muniraj T. Endoscopic Ultrasound-Guided, Percutaneous, and Transjugular Liver Biopsy: A Comparative Systematic Review and Meta-Analysis. *Clin Endosc.* 2020 Sep;53(5):583-593. doi: 10.5946/ce.2019.211. Epub 2020 Sep 29. PMID: 33027584; PMCID: PMC7548145.

Chandan S, Deliwala S, Khan SR, Mohan BP, Dhindsa BS, Bapaye J, Goyal H, Kassab LL, Kamal F, Sayles HR, Kochhar GS, Adler DG. EUS-guided versus percutaneous liver biopsy: A comprehensive review and meta-analysis of outcomes. *Endosc Ultrasound.* 2023 Mar-Apr;12(2):171-180. doi: 10.4103/EUS-D-21-00268. PMID: 36204798; PMCID: PMC10237604.

Disclosure: Nothing to disclose.

MP408

THE IMPACT ON SURVIVAL OF INFECTION BY MULTIDRUG-RESISTANT MICROORGANISMS IN PATIENTS WITH LIVER CIRRHOSIS - ANALYSIS OF A RETROSPECTIVE COHORT

M. Francisco¹, L. Martins Figueiredo¹, G. Alexandrino¹, M. Cardoso¹, J. Carvalho e Branco¹, M.N. Costa¹, R. Carvalho¹, A.M. Martins¹

¹Hospital Prof. Doutor Fernando Fonseca, Gastroenterology, Amadora, Portugal

Contact E-Mail Address: monicafrancisco96@gmail.com

Introduction: Infection is the main cause of decompensation in liver cirrhosis (LC) and contributes to high mortality. Infection by multidrug-resistant microorganisms (MDRO) is becoming increasingly prevalent, and there is evidence that it reduces survival in LC.

Aims & Methods: A 6-year retrospective analysis was carried out on a cohort of patients with LC admitted due to infection between October 2017 and March 2018. MDRO was defined as resistance to at least 3 antibiotic classes. The survival time in weeks from the date of MDRO isolation or date of hospitalization to the date of death was evaluated. SPSS was used to reproduce Kaplan-Meier (KM) survival curves.

Results: 31 patients were included, 17 of whom had MDRO isolation vs. 14 without MDRO isolation (N-MDRO) during the 2017-2018 period. After the analysis period, 30 patients had died. A lower survival rate was observed in patients with MDRO isolation, with a mean survival rate of 37.9 weeks vs. 61.5 weeks for N-MDRO, although without statistical significance (p=0.7). From the subgroup analyses carried out, there was also a statistically non-significant lower average survival in the MDRO group: analyzing patients without a diagnosis of hepatocellular carcinoma (23 patients),

there was an average survival of 47.9 weeks in the MDRO (12 patients) vs 75.7 weeks in the N-MDRO group ($p=0.74$); and in the subgroup with Child Pugh <C (12 patients), there was an average survival of 29.6 weeks in the MDRO (9 patients) vs 110.6 weeks in the N-MDRO group ($p=0.18$).

Conclusion: The results of this cohort, although not statistically significant, suggest that MDRO infection has an impact on the decreased survival of patients with LC, particularly in patients who would expect a longer survival.

References: Kaplan Meier curves of survival will be presented.

Disclosure: Nothing to disclose.

MP409

THE OUTCOME PREDICTION ROLE OF RED CELL DISTRIBUTION WIDTH IN 1000 HOSPITALIZED CIRRHOTIC EGYPTIAN PATIENTS

M. Abdel-Samiee¹, M. Kohla¹, M.F. Ragab², H.S. Ghanem³, A.K. AbouGabal¹, E. Abdelsameea¹

¹National Liver Institute-Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt, ²El-Minshawy Hospital, Department of Microbiology, Tanta, Egypt, ³National Liver Institute - Menoufia University, Clinical Pathology Department, Menoufia, Egypt

Contact E-Mail Address: drmohammed100@yahoo.com

Introduction: A systemic inflammatory response syndrome (SIRS) is linked to red cell distribution width (RCDW), which produces pro-inflammatory signals that act directly on hematopoietic stem cells in the bone marrow. This stimulation may cause alterations in the membrane of red blood cells (RBCs), as assessed by RCDW, which have been linked to increased morbidity and death in a number of systemic disorders.

Aims & Methods: This study aims to evaluate RCDW as a predictor of outcome in hospitalized cirrhotic patients.

This prospective cross-sectional study was conducted on 1000 patients. The outcome was assessed by days of hospitalization; mortality in hospitalized patients or during short-term follow-up (3 months) and rehospitalization during follow-up of 6 months.

	Child score			Test of sig Kruskal- Wallis Test	p- value
	A	B	C		
MELD SCORE					
Mean±Std.	21.866±15.1499	24.685±11.944	40.819±18.587	438.2	0.0001*
N	212	388	400		
Median (Mini-Maxi)	15.952(10.009-90.215)	21.810(16.189-90.013)	35.182(13.214-90.555)		
days of hospitalization					
Mean±Std.	2.55±2.673	10.23±4.642	17.67±5.296	652.7	0.0001*
N	212	388	400		
Median(Mini-Maxi)	1.00(1-10)	9.00(1-28)	16.00(7-30)		
number of hospitalization during follow up					
Mean±Std.	0.17±0.509	1.58±0.994	3.29±0.753	681.7	0.0001*
N	212	388	400		
Median(Mini-Maxi)	0.00(0-2)	2.0(0-4)	3.0(0-4)		
CRP					
Mean±Std.	15.32±32.870	30.00±37.731	84.87±53.172	536.8	0.0001*
N	212	388	400		
Median(Mini-Maxi)	5.00(0-140)	18.30(5-227)	72.15(8-230)		
PCV					
Mean±Std.	33.101±7.058	31.871±20.735	28.963±6.423	52.86	0.0001*
N	212	388	400		
Median(Mini-Maxi)	33.300(14.1-46.5)	29.9(14.7-221.3)	28.4(13.8-43.7)		

Table 1. Relation between outcome of patient and its relation to child score

Results: Male represented 69.6%. Mean age was 57.67 ± 13.07 years old. Baseline co-morbidities were recorded as the presence of diabetes mellitus (200 patients) and hypertension (400 patients). Hepatitis C virus was the commonest etiology of the diseased liver (90%). Child-Pugh classes A, B and C of studied patients represented (21.2%, 38.8% and 40%). The survived patients during follow-up represented 63.3%. Area under the curve for RCDW was 0.923 (95% CI, 0.904–0.943), 0.910 for C-reactive protein (95% CI, 0.890–0.930), 0.904 for Hb (95% CI, 0.883–0.925) and 0.903 for platelets (95% CI, 0.882–0.924). RCDW cutoff point at 21.35 for predicting survival had sensitivity 93%, specificity 91%, accuracy 92%, positive predictive value 85 and negative predictive value 96. Regression analysis revealed a significant positive association between both RCDW and white blood cells with mortality.

Table 1 shows that there was a significant difference among the groups (child A.B.C) regarding outcome which represented by MELD score days of hospitalization and number of hospitalization during follow up as MELD score was highest in child C patient (40.8) compared with child B patient (24.6) and group A (21.8) and also hospitalization days was highest in child C (17.8) compared with child B (10.23) and group A (2.55)

Conclusion: RCDW could provide useful information for predicting the length of hospitalization and survival in hospitalized cirrhotic patients.

References: Moreau R. Acute-on-chronic liver failure: a new syndrome in cirrhosis. Clin Mol Hepatol 2016; 22:1–6.

Bernal W, Jalan R, Quaglia A, Simpson K, Wendon J, Burroughs A. Acute-on-chronic liver failure. Lancet 2015; 386:1576–1587.

Jalan R, Pavesi M, Saliba F, Amorós A, Fernandez J, Holland-Fischer P, et al; CANONIC Study Investigators; EASL-CLIF Consortium. The CLIF Consortium Acute Decompensation score (CLIF-C ADs) for prognosis of hospitalised cirrhotic patients without acute-on-chronic liver failure. J Hepatol 2015; 62:831–840.

Gustot T, Fernandez J, García E, et al. Shortterm (28-day) clinical course and transplant-free mortality in acute-onchronic liver failure (ACLF): evidence for reversibility of AC

Disclosure: Nothing to disclose.

MP410

EMERGING ROLE OF SPLEEN STIFFNESS MEASUREMENT IN PREDICTION OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION: A SINGLE CENTER EXPERIENCE

M. Capasso¹, S. Albano¹, F. Mazzitelli¹, F. Capozzi¹, L. Ranieri¹, A.G. Rutigliano¹, M. Guarino¹, V. Cossiga¹, F. Morisco¹

¹University of Naples Federico II, Department of Clinical Medicine and Surgery, Diseases of the Liver and Biliary System Unit, Naples, Italy

Contact E-Mail Address: luisa.ranieri92@gmail.com

Introduction: According to Baveno VII, non-invasive-based criteria is useful to rule in or out for clinically significant portal hypertension (CSPH) in advanced chronic liver disease (ACLD). Liver stiffness measurement (LSM) and platelet count (PLT) are the two parameters considered in this field, particularly LSM ≥ 25 kPa is highly predictive for CSPH, while LSM ≤ 15 kPa plus PLT ≥ 150 G/L exclude CSPH. Spleen Stiffness Measurement (SSM) can be used in ACLD patients, identifying patients with a low probability (SSM <40 kPa) of having high-risk varices.

Aims & Methods: The aim of our study is to explore the utility of SSM in predicting endoscopic signs of portal hypertension and its added value compared to LSM and platelet count. This retrospective study was conducted at the University of Naples “Federico II”. All patients with ACLD (for any etiologies) with at least LSM ≥ 10 who underwent esophagogastroduo-

denoscopy (EGD) for portal hypertension assessment within one year before Spleen Stiffness measurement were enrolled. Exclusion criteria were patients < 18 yrs, PLT>150*10³/cc, liver transplantation, HCC patients, portal vein thrombosis and incomplete data. The study population was divided in three groups: the first includes patients with LSM≥25, the second patients with LSM≥15 and <25 and the third patients with LSM≥10 and <15. **Results:** Sixty-nine patients (41 male, mean age 62.7±14.8 years old) were recruited. The main etiology was virus-related (30 patients, 43.4%) followed by metabolic (13 patients, 18.8%), alcohol (12 patients, 17.4%), autoimmune (7 patients, 10.1%) and other (7 patients, 10.1%). Fifty-five patients were Child A and 14 patients were Child B. Overall, mean LSM was 24.7±12.9 kPa, mean SSM was 59.8±23.5 kPa and mean PLT count was 102±50*10³/cc. The groups were composed by 25, 27 and 17 patients, respectively. Eighteen out of 25 patients (69.2%) belonging to the first group had endoscopic sign of PH and almost all of them (17/18, 94.4%) had SSM≥40kPa. In the second group a lower rate of endoscopic sign of PH was found (14/27, 51.8%), although SSM had a high diagnostic performance (100%). Finally, in the third group, in which according to Baveno VII the pre-test probability of CSPH is low, 5 out of 17 (29.4%) had endoscopic sign of PH and, among them, 60% of patients (3/5) had SSM>40kPa. Indeed, SSM demonstrated a better positive correlation with the presence of endoscopic sign of PH (Pearson coefficient r=0.4) than LSM (r=0.3). **Conclusion:** SSM enhances the diagnostic performance of LSM and PLT assessment proposed by Baveno VII in predicting portal hypertension in patients with ACLD.

Disclosure: Nothing to disclose.

MP411

ADDITION OF NON-SELECTIVE BETA-BLOCKERS TO ENDOSCOPIC COMBINED TREATMENT FOR SECONDARY PROPHYLAXIS OF CIRRHOTIC VARICEAL BLEEDING

L. Wu^{1,2}, X. Huang¹, F. Li^{1,3}, D. Schuppan^{2,4}, S. Chen^{1,3}

¹Zhongshan Hospital, Fudan University, Department of Gastroenterology and Hepatology, Shanghai, China,

²University Medical Center, Johannes Gutenberg University, Institute of Translational Immunology and Research Center for Immunotherapy, Mainz, Germany, ³Minhang Hospital, Fudan University, Department of Gastroenterology, Shanghai, China, ⁴Beth Israel Deaconess Medical Center, Harvard Medical School, Division of Gastroenterology, Boston, United States of America

Contact E-Mail Address: 20111210043@fudan.edu.cn

Introduction: Gastroesophageal varices are present in approximately 50% of cirrhotic patients¹. The cirrhosis-related age-standardized mortality is high². Gastroesophageal variceal bleeding is a medical emergency with a mortality rate of approximately 10-20% at six weeks¹, and rebleeding incidence ranged from 32% to 84%³, and even higher, around 90%, in patients receiving no antiviral therapy⁴. Endoscopic variceal ligation (EVL) and endoscopic variceal obliteration (EVO) with cyanoacrylate are recommended for patients with acute variceal bleeding⁵, but both treatments have no impact on portal pressure⁶. Portal hypertension is the primary pathophysiological mechanism underlying gastroesophageal varices. Non-selective beta-blockers (NSBBs) induce vasodilation by targeting beta-receptors on blood vessels and the heart, reduce cardiac output through negative inotropic effects, thereby reducing portal blood flow and associated portal pressure^{7,8}. Gastroesophageal varices type 1 (GOV1) and type 2 (GOV2) are varices in direct continuity from the esophagus to the stomach (lesser and greater curvatures, respectively)⁹. We chose EVL after EVO for treatment of GOV1 and GOV2, which tended to have a better secondary prophylactic effect according to our clinical experience. How-

ever, no prior research has evaluated the effect of additional NSBB under these circumstances. It remains unclear whether the addition of NSBB provides further benefit after *combined* use of tissue adhesive and endoscopic variceal ligation for bleeding gastroesophageal varices.

Aims & Methods: We retrospectively analyzed cirrhotic patients (mainly due to hepatitis B and C) who received endoscopic combined treatment of gastroesophageal varices and were assigned or not to NSBB treatment as a second prophylaxis. Subanalysis was done for ascites, portal vein thrombosis, splenectomy, and Child-Pugh grade. 5-year overall survival and rebleeding rates were compared between treatment groups.

Results: A total of 490 patients were analyzed, and 130 patients received additional NSBB treatment. Although the additional NSBB treatment did not lead to a statistically significant difference in overall 5-year survival (Log-rank test, p = 0.133), it did reduce the 5-year rebleeding rate from 45.7% to 30.64% (Log-rank test, p = 0.002, univariate COX analysis, HR 0.57, 95% CI 0.39-0.82), consistent with the comparison after propensity score matching. Neither overall survival nor bleeding differed significantly between propranolol and carvedilol. NSBB (HR 0.54, 95% CI 0.37-0.79, p = 0.001) and splenectomy (HR 0.65, 95% CI 0.44-0.96, p = 0.030) were independent factors in reducing rebleeding, rather than improving survival, in cirrhotic patients who received combined endoscopic treatment. In patients without splenectomy, NSBB treatment improved overall survival (Log-rank test, p = 0.019, univariate COX analysis, HR 0.43, 95% CI 0.21-0.89) and reduced rebleeding rates (Log-rank test, p = 0.001, univariate COX analysis, HR 0.52, 95% CI 0.34-0.78).

Conclusion: We show for the first time that adding NSBB to *combined* endoscopic therapy significantly reduced recurrent variceal bleeding (GOV1 & GOV2) in cirrhotic patients, yet did not improve overall survival, except for patients without splenectomy. The addition of NSBB for patients receiving *combined* endoscopic treatment of gastroesophageal varices provides benefits but does not prolong overall survival.

References: 1. Jakab SS, Garcia-Tsao G. Evaluation and Management of Esophageal and Gastric Varices in Patients with Cirrhosis. Clin Liver Dis 2020;24:335-50.

2. Collaborators GBDC. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 2020;5:245-66.

3. de Franchis R, Primignani M. Natural history of portal hypertension in patients with cirrhosis. Clin Liver Dis 2001;5:645-63.

4. He L, Ye X, Ma J, et al. Antiviral therapy reduces rebleeding rate in patients with hepatitis B-related cirrhosis with acute variceal bleeding after endotherapy. BMC Gastroenterol 2019;19:101.

5. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol 2022;76:959-74.

6. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69:406-60.

7. Baiges A, Hernández-Gea V, Bosch J. Pharmacologic prevention of variceal bleeding and rebleeding. Hepatol Int 2018;12:68-80.

8. Reiberger T, Mandorfer M. Beta adrenergic blockade and decompensated cirrhosis. J Hepatol 2017;66:849-59.

9. Alqahtani SA, Jang S. Pathophysiology and Management of Variceal Bleeding. Drugs 2021;81:647-67.

Disclosure: Nothing to disclose.

MP412

THE RESPONSE OF GUT MICROBIOTA TO ARSENIC METABOLISM IS INVOLVED IN ARSENIC-INDUCED LIVER INJURY, WHICH IS INFLUENCED BY THE INTERACTION BETWEEN ARSENIC AND METHIONINE SYNTHASE

Z. Weng¹

¹Nanjing Medical University, School of Public Health, China

Contact E-Mail Address: wengzhenkun@njmu.edu.cn

Introduction: Arsenic, a potent environmental toxin, has been widely reported to cause significant health problems, including liver damage and disturbances in the metabolic processes. One of the lesser-understood facets of arsenic toxicity is its impact on gut microbiota, the community of microorganisms living in the intestinal tract, which plays a crucial role in host metabolism and overall health. Previous studies have indicated that arsenic exposure can alter the composition of gut microbiota, potentially affecting the host's metabolism of arsenic and exacerbating its toxic effects. Despite ongoing research, the mechanisms underlying the interaction between arsenic exposure, gut microbiota changes, and arsenic metabolism remain inadequately defined.

Aims & Methods: The primary objective of this study was to elucidate the dynamics of gut microbiota changes under varying levels of arsenic exposure and to understand how these changes affect arsenic metabolism and subsequent liver toxicity. We used C57BL/6 mice as a model system, exposing them to 0, 5, or 10 ppm sodium arsenite (NaAsO₂) in their drinking water over a period of six months. We conducted a comprehensive analysis of the gut microbiota, focusing on folic acid (FA)/vitamin B12 (VB12)- and butyrate-synthesizing communities. Additionally, molecular interactions between arsenic and methionine synthase (MTR), an enzyme crucial for FA/VB12 utilization, were assessed using 3D molecular simulations and biochemical assays. The intervention model involved supplementation of FA and VB12 to evaluate their protective effects against arsenic-induced disturbances.

Results: Exposure to NaAsO₂ significantly altered gut microbiota, with a notable increase in the abundance of FA/VB12- and butyrate-synthesizing microbiota. This shift was hypothesized to compensate for the disrupted utilization of these nutrients due to arsenic exposure. In higher arsenic exposure levels, however, the microbiota changes were inconsistent, suggesting a potential threshold beyond which the compensatory mechanism may be overwhelmed. Biochemical assays confirmed that arsenic binds to MTR, disrupting its function and further impacting FA/VB12 metabolism. The interaction was substantiated by SEC-UV-DAD and fluorescence-labeled arsenic studies, which demonstrated that arsenic directly interacts with MTR in both non-cellular and cellular systems. Our intervention model using FA and VB12 supplementation showed that it was possible to mitigate the disturbances in gut microbiota, restore MTR levels, enhance arsenic metabolism, and reduce liver injury.

Conclusion: This study provides significant insights into the interaction between arsenic exposure and gut microbiota. We demonstrated that changes in gut microbiota are not merely a consequence of arsenic exposure but are intricately linked to the metabolic processes affected by arsenic, particularly through the disruption of MTR function. The supplementation of FA and VB12 proved effective in blocking these disturbances, suggesting potential therapeutic strategies to combat arsenic toxicity. The findings emphasize the importance of considering gut microbiota in the management and treatment of arseniasis and underscore the complex interplay between environmental toxins, gut microbiota, and host metabolism. Future studies should focus on further delineating the specific pathways and mechanisms by which microbiota influence arsenic metabolism and exploring the potential for microbiota-targeted therapies in arsenic-related diseases.

Disclosure: Nothing to disclose.

MP413

PARAPTOSIS - A NOVEL BACTERIAL-INDUCED CELL DEATH IN INTESTINAL EPITHELIAL CELLS WITH IMPACT ON SPONTANEOUS BACTERIAL PERITONITIS

M. Ernst¹, C. Steindl¹, C. Brochhausen², C. Kunst¹, K. Gülow¹, M. Müller-Schilling¹

¹University of Regensburg, Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology, Rheumatology, and Infectious Diseases, University Hospital Regensburg, Regensburg, Germany, ²University of Heidelberg, Medical Faculty Mannheim, Institute of Pathology, Mannheim, Germany

Contact E-Mail Address: Martha.Ernst@stud.uni-regensburg.de

Introduction: Spontaneous bacterial peritonitis (SBP) is a severe complication of liver cirrhosis, carrying life-threatening consequences. Pathophysiologically, SBP emerges from bacterial translocation from the gut to the peritoneal cavity. The mechanisms of bacterial interaction with intestinal epithelial cells remain incompletely understood. We showed that patients with liver cirrhosis exhibit a thinner intestinal mucus layer, facilitating direct interaction between bacteria and epithelial cells. This interaction results in the degradation of cell junctions, tissue damage, and cellular stress (Haderer et al., Gut 2022). p53 and its family members p63 and p73 are important regulators of cellular stress responses. This study investigates the relationship between expression of p53 family members and paraptosis, a bacterial-induced form of programmed necroptotic cell death.

Aims & Methods: HCT-116 cells with different p53/p73 status (p53KO, p73KO, p53/p73 double KO) were co-cultured *Escherichia coli* (*E. coli*) O6:Hnt and harvested in 30-minute intervals for up to 4 hours. We investigated cell death mechanisms using specific inhibitors (zVAD, actinomycin D). Cell death rates were determined by flow cytometry using Annexin V / DAPI staining. Protein expression of p53 and p73 was evaluated by Western Blot. Changes in cell morphology were examined via electron microscopy.

Results: Bacterial co-culture induced paraptosis in intestinal epithelial cells, characterized by distinct morphological alterations such as mitochondrial swelling, dilatation of the endoplasmic reticulum, cytoplasmic vacuolization, and chromatin condensation at the nuclear membrane. Bacterial-triggered cell death was accompanied by a paraptosis-specific protein profile. Actinomycin D effectively inhibited paraptosis in HCT-116 cells irrespective of their p53/p73 status. Notably, upon bacterial contact, protein levels of p53 and p73 were initially upregulated, followed by gradual degradation. CRISPR/Cas9-mediated knockout of p53 family members resulted in modified kinetics of cell death progression, with the absence of either p53 or p73 delaying paraptosis induction.

Conclusion: Bacterial co-culture induces paraptosis in intestinal epithelial cells, with the p53 family influencing the kinetics of cell death. A comprehensive molecular characterization of this process is of crucial clinical relevance, as the p53 status in the intestinal epithelium influences paraptosis susceptibility. Induction or stabilization of p53 and p73 could thus be a therapeutic option for the prevention and treatment of SBP.

References: Haderer et al., Gut 2022

Disclosure: Nothing to disclose.

MP414

EXPLORING HEPATOCELLULAR CARCINOMA RISK IN HEPATITIS C VIRUS PATIENTS WITH SUSTAINED VIROLOGICAL RESPONSE: INSIGHTS FROM A REAL-WORLD COHORT

A.T. Ferreira¹, S. Bizarro Ponte¹, N. Gonçalves², F. Craveiro³, M. Dupont⁴, T. Guedes^{1,5}, L. Maia¹, J.M. Ferreira¹, I. Pedrito^{1,5}

¹Unidade Local de Saúde de Santo António, Department of Gastroenterology, Porto, Portugal, ²Portuguese Oncology Institute of Porto, Department of Gastroenterology, Porto, Portugal, ³Unidade Local de Saúde de Matosinhos, Department of Gastroenterology, Matosinhos, Portugal, ⁴Unidade Local de Saúde de Trás-os-Montes e Alto Douro, Department of General Surgery, Vila Real, Portugal, ⁵Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal

Contact E-Mail Address: anatmendesferreira@gmail.com

Introduction: Direct-acting antivirals (DAA) have revolutionized the treatment landscape for chronic hepatitis C (CHC), yielding notably high sustained virological response (SVR) rates. While SVR is associated with reduced hepatocellular carcinoma (HCC) risk, recent studies emphasize the importance of ongoing surveillance, particularly in patients with advanced fibrosis (F3-F4), mainly within the initial three years post-SVR.

Aims & Methods: The aim of this study was to assess the risk of hepatocellular carcinoma over a five-year period following DAA-induced SVR in a real-life cohort of F3-F4 patients.

Data were retrospectively collected from CHC F3-F4 patients initiating DAA treatment between February 2015 and January 2017 at a tertiary center. Statistical analysis was performed with SPSS 29.0 (significance level ≤ 0.05).

Results: Out of 239 patients included (69.5% male; median age: 58 years), a SVR at 12 weeks rate of 96.6% was achieved. Among those with SVR and continued follow-up (n=229), 5.2% (n=12) developed HCC over the five-year period, with 50% occurring more than three years post-SVR.

The annual HCC incidence rate was 1.1 cases/100 person-years (33.3% HCC-related mortality rate). Most HCC cases occurred in males (75%) and cirrhotic patients (75%, Child-Pugh A: 77.8%). The mean alpha-fetoprotein level at HCC diagnosis was 156.1 ng/mL. Additionally, 75% of patients who developed HCC had other co-factors for liver disease, mainly metabolic. Comparing the presence of other liver disease co-factors, no statistically significant difference was found between those who developed HCC and those who did not during the five-year follow-up period (p-value 0.267).

Conclusion: The incidence rate of HCC post-SVR has been reported to be 0.9-2.96/100 person-years for DAA therapy, consistent with the findings of this investigation. Nevertheless, our study underscores that the risk of HCC persists for at least five years following SVR, warranting long-term surveillance. Contrary to previous research, there is insufficient evidence to support the involvement of other co-factors in HCC development.

Disclosure: Hsu CC, Gopalakrishna H, Mironova M, Lee MH, Chen CJ, Yang HI, Wiese M, Chang KM, Wright EC, Abijo T, Feld JJ, Kaplan DE. Risk of Hepatocellular Carcinoma After Spontaneous Clearance of Hepatitis C Virus and in Noncirrhosis Chronic Hepatitis C Patients With Sustained Virological Response: A Systematic Review. Clin Infect Dis. 2023 Aug 14;77(Suppl 3):S245-S256. doi: 10.1093/cid/ciad380. PMID: 37579210; PMCID: PMC10425144.

Li M, Li Y, Zhang Y, Wang X, Lin C. Five-year follow-up of sustained virological response with hepatitis C infection after direct-acting antiviral therapy: A single-center retrospective study. Medicine (Baltimore). 2024 Feb 16;103(7):e37212. doi: 10.1097/MD.00000000000037212. PMID: 38363923; PMCID: PMC10869073.

Outcomes and implications of pancreatic disease

14:30-15:30 / Poster Stage 4

MP415

PREVALENCE OF ASYMPTOMATIC CHRONIC PANCREATIC HYPERENZYMEMIA (CAPH) IN A TERTIARY CARE CENTER

L. Piermarini¹, G. Scalese¹, D. Carlomagno¹, A. Schirinzì¹, C. Severi¹, F. Covotta¹

¹Sapienza, University of Rome, Department of Translation and Precision Medicine, Roma, Italy

Contact E-Mail Address: leonardo.piermarini@gmail.com

Introduction: Blood elevation of pancreatic enzymes is generally associated with clinical symptoms and represent biological sign of pancreatic pathology. Occasionally, serum elevation of pancreatic enzymes can be found in asymptomatic patients while performing routine laboratory tests and be related to a condition termed Chronic Asymptomatic Pancreatic Hyperenzymemia (CAPH).

Aims & Methods: The purpose of this study was to evaluate the diagnostic management of asymptomatic chronic pancreatic hyperenzymemia and to assess the true prevalence of CAPH in a tertiary care center. Patients who referred to the specialist outpatient pancreatic clinic at the University Hospital Policlinico Umberto I in Rome for asymptomatic pancreatic hyperenzymemia, from September 2021 to September 2023, were enrolled. Inclusion criteria were: age over 18 years, 2 years of follow-up with availability of at least 2 magnetic resonance cholangiopancreatography, and serial determination of serum pancreatic enzymes in the absence of known pancreatic pathology. Subjects with positive history of pancreatic pathology, known causes of hyperenzymemia and history of alcohol intake greater than 40 g/day (males) and 20 g/day (females) were excluded. At the end of two years, the diagnosis of CAPH was made in asymptomatic subjects with persistent pancreatic enzyme elevation who had no relevant pancreatic changes on imaging.

Results: 41 patients were included in the study [median age 68 (31-84) years, 15 Males and 26 Females]. In 22/41 (54%) patients, organic pancreatic alterations were found on the 2nd level imaging examination, 54.5% (12/22) of them requiring specific follow-up: 9/22 (41%) patients had intraductal papillary mucinous neoplasms (IPMNs) and 3 (14%) chronic pancreatitis. Additional findings were 4 (29%) ectasia of the pancreatic ductal system, 3 (14%) sphincter and ampullary abnormalities, 2 (9%) cases of pancreas divisum and 1 (4%) cystadenoma. In the remaining 19/41 (46%) patients, monitored for 24-months follow-up, no pancreatic organic changes were found and a diagnosis of CAPH was made. No differences in risk factors for pancreatic diseases were found between patients with organic alterations and patients with CAPH: smoking 27 vs 26%, alcohol consumption below the exclusion limits 13 vs 21%, BMI 24.5 vs 23, respectively. A positive family history for pancreatic diseases was found in 50% of the subjects for each group, without any specific familiarity for asymptomatic chronic pancreatic hyperenzymemia.

Conclusion: A comprehensive diagnostic work-up is essential in cases of occasional asymptomatic findings of elevated pancreatic enzymes; more than half of the patients underlying organic pancreatic disease that requires specific periodic follow-up. After 2 years of follow-up, the diagnosis of CAPH was made in the other half of patients.

Disclosure: Nothing to disclose.

MP416

TRIGLYCERIDE GLUCOSE INDEX: CAN IT PREDICT PANCREATIC STEATOSIS?

Z.n. Harput¹, S. Yaraş², M. Cindoruk³, E. Kasap⁴, H. Ünal⁵, A.Ş. Köksal⁶, A.E. Yıldırım⁷, B. Özşeker⁸, N. Oruç⁹, M. Soytürk¹⁰, S. Kaçar¹¹, M. Kaya¹², K. Irak¹³, Y. Gökden¹⁴, D. öğütmen koç¹⁵, O. Özdoğan¹, E. Altıntaş¹, N. Ekmen³, M. Saruç⁵, Ş. Acar¹⁶, M. Polat¹⁷, S. Barutçu¹⁸, G. Bengi¹⁹, V. Gökbulut¹¹, N.G. Ünal²⁰, D. Oğuz²¹, O. Sezgin¹

¹Mersin University, Department of Gastroenterology, Mersin, Turkey, ²Mersin University, Department of Gastroenterology, Mersin, Mersin, Turkey, ³Gazi University, Department of Gastroenterology, Ankara, Turkey, ⁴Celal Bayar University, Department of Gastroenterology, Manisa, Turkey, ⁵Acibadem Mehmet Ali Aydınlar University Faculty of Medicine, Department of Gastroenterology, İstanbul, Turkey, ⁶Sakarya University Faculty of Medicine, Department of Gastroenterology, Sakarya, Turkey, ⁷Memorial Bahçelievler Hospital, University of Gaziantep Faculty of Medicine,, Department of Gastroenterology, İstanbul, Turkey, ⁸Johns Hopkins Hospital and Health System, Department of Medicine, Baltimore, Maryland,, United States of America, ⁹Ege University Faculty of Medicine, Department of Gastroenterology, İzmir, Turkey, ¹⁰Dokuz Eylül University Faculty of Medicine, Department of Gastroenterology, İzmir, Turkey, ¹¹Yüksek İhtisas Education and Research Hospital, Department of Gastroenterology, Ankara, Turkey, ¹²Dicle University Faculty of Medicine, Diyarbakır, Turkey, Department of Gastroenterology, Diyarbakır, Turkey, ¹³İstanbul Kanuni Sultan Süleyman Training and Research Hospital, Department of Gastroenterology, İstanbul, Turkey, ¹⁴University of Health Science Okmeydanı Training and Research Hospital, Department of Gastroenterology, İstanbul, Turkey, ¹⁵Gaziosmanpaşa Taksim Education and Research Hospital, Department of Gastroenterology, İstanbul, Turkey, ¹⁶Ministry of Health Amasya Sabuncuoğlu Şerefeddin Education and Research Hospital, Department of Gastroenterology, Amasya, Turkey, ¹⁷Şanlıurfa Mehmet Akif İnan Education and Research Hospital, Department of Gastroenterology, Şanlıurfa, Turkey, ¹⁸University of Gaziantep, Gaziantep, Department of Gastroenterology, Gaziantep, Turkey, ¹⁹Dokuz Eylül University Faculty of Medicine, İzmir, Turkey, Department of Gastroenterology, İzmir, Turkey, ²⁰Ege University Faculty of Medicine, Department of Gastroenterology, İzmir, Turkey, ²¹Kırıkkale University Faculty of Medicine, Department of Gastroenterology, Kırıkkale, Turkey

Contact E-Mail Address: zeknurzek@gmail.com

Introduction: Triglyceride glucose (TyG) index is a new biomarker for metabolic disorders. The relationship between diabetes mellitus (DM), obesity, non-alcoholic fatty liver disease and TyG index has been determined in recent studies, but there is no study on pancreatic steatosis, which is a relatively new entity. This study aimed to determine the relationship between TyG index and pancreatic steatosis.

Aims & Methods: This study was conducted based on the data of patients included in the 'Turkey Pancreatic Steatosis Prevalence Study' conducted by the TGD Pancreas Study Group. Demographic data and clinical information of the patients were collected. TyG index was calculated with the formula 'ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2]'. Pancreatic steatosis was evaluated with abdominal ultrasonography (USG) by experts in this area.

Results: 1700 patients were included in the study. There were 967 women (56.9%) and 733 men (43.1%). Mean ages, respectively; 48.6±24, and 47.25±15 years. Body mass indexes (BMI) were 27.3±5.6 and 27.05±4.04.

347 (26.4%) of the participants were diagnosed with metabolic syndrome (MS), 230 (17.2%) were diagnosed with DM, and 319 (23.9%) were diagnosed with hypertension. Hepatosteatois was detected in 943 (55.5%) and pancreatosteatois was detected in 1132 (69.9%) in USG. Mean TyG index was 4.69±0.32. A statistically significant, positive ($r=0.334$, $r=0.383$, $r=0.206$, $r=0.299$, respectively) correlation was detected between the TyG index and BMI, waist-hip circumference and HOMA-IR ($p<0.05$). Mean TyG index; It was significantly higher in individuals with HT, DM, MS and pancreatic steatosis ($p<0.05$).

Conclusion: TyG index is a relatively new biomarker that indicates the metabolic profile. This is the first study conducted between pancreatic steatosis, which awareness has just increased and TyG index. TyG index was found to be statistically significantly higher in individuals with pancreatic steatosis.

Disclosure: Nothing to disclose.

MP417

THE COMBINATION OF YKL-40 AND INTERLEUKIN 6 PREDICTS MORE ACCURATELY THE SEVERITY OF ACUTE PANCREATITIS THAN EITHER BIOMARKER ALONE: A CROATIAN SINGLE-CENTER PROSPECTIVE OBSERVATIONAL STUDY.

N. Blazevic¹, S. Pelajic¹, D. Rogic², V. Trkulja³, M. Miler⁴, M. Nikolic¹, M. Zivkovic¹, N. Barsic¹, D. Hrabar¹, T. Pavic¹

¹Sestre milosrdnice University Hospital Center, Zagreb, Croatia, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ²University Hospital Center Zagreb, Zagreb, Croatia, Department of Laboratory Diagnostics, Zagreb, Croatia, ³University of Zagreb School of Medicine, Zagreb, Croatia, Department of Pharmacology, Zagreb, Croatia, ⁴Sestre milosrdnice University Hospital Center, Zagreb, Croatia, Department of Clinical Chemistry, Zagreb, Croatia

Contact E-Mail Address: nina.blazevic05@gmail.com

Introduction: Acute pancreatitis (AP) often has unpredictable and complicated clinical course. Numerous biochemical predictors may aid in the risk stratification of AP (including interleukin 6 (IL-6)), but none of them are accurate. YKL-40 is glycoprotein playing mayor role in inflammation and angiogenesis, with reported average serum concentrations of ≥ 190 ng/mL in inflammatory diseases. It has been shown that IL-6 stimulates the production of YKL-40 and, in reverse, YKL-40 (at least in some tissues) induces the production of IL-6.

Aims & Methods: The aim of our study is to assess whether combined concentrations of both YKL-40 and IL-6 could be more informative in risk stratification of developing more severe form of AP than concentrations of either biomarker alone.

We included 150 consecutive consenting adults with AP admitted to Sestre milosrdnice UHC, Zagreb (June 2020-June 2023). Patients with any acute/chronic diseases known to be associated with dysregulated expression of YKL-40 were excluded. Alongside routine laboratory studies (including C-reactive protein (CRP)), 7 mLs of blood were withdrawn for determining YKL-40 and IL-6 concentrations on admission and 48h after. Severity of disease was defined using revised Atlanta classification. Blood samples for YKL-40 and IL-6 quantification in 30 consenting non-AP adults consistent with previously mentioned exclusion criteria were withdrawn. They were matched 1:1 by age and sex to randomly selected 10 patients from each of AP severity categories. Analysis were performed using enzyme-linked immunosorbent assays. AP patients were classified into 2 categories for each biomarker (based on YKL-40 and IL-6 concentrations on admission and 48h after): 1. for YKL-40: low (<190 ng/mL) and high (≥ 190 ng/mL); 2. for IL-6: low (<42 pg/mL) and high (≥ 42 pg/mL). Cumulative multimodal logit models were fitted to ordinal outcome "AP severity" – using raw data,

and data after entropy balancing undertaken to balance the two categories of YKL-40 and IL-6 concentrations on age, sex, time between symptom onset and admission, and CRP concentrations.

Results: The results showed lower YKL-40 (<50 ng/mL) and IL-6 (<20 pg/mL) concentrations in 30 non-AP adults compared to AP patients. At both time points (on admission and 48h after), odds of more severe AP were clearly higher with YKL-40 and IL-6 concentrations above vs. below the cut-off values (190 ng/mL and 42 pg/mL, respectively), and were particularly higher in patients with both cytokines above the cut-off vs. patients with both cytokines below the cut-off. The same relationship was maintained with adjustments for age, body mass index, days elapsed since symptom onset and admission, and for CRP concentrations – however, the strength of association was lower. This is in line with the fact that high CRP concentration predicts more strongly severe AP forms when taken 48h after compared to admission.

This phenomenon was apparent also when the interaction term was included in the model: at CRP concentrations 45 mg/L, neither YKL-40, or IL-6 or their combination above the cut-off values were associated with the outcome; at CRP concentrations 90 mg/L, odds were higher, and were particularly high for a combination of high YKL-40 and high IL-6. The same was observed at CRP concentrations 180 mg/L.

Conclusion: Overall, data suggest that combined YKL-40 and IL-6 concentrations in acute AP, taken either on admission or 48h after, predict more strongly moderate and/or severe (vs. mild) AP than either cytokine alone, and do so 'on-top' of the CRP concentrations.

References: 1. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG et al. Classification of acute pancreatitis - 2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102–111.

2. van den Berg FF, de Bruijn AC, van Santvoort HC, Issa Y, Boermeester MA. Early laboratory biomarkers for severity in acute pancreatitis; A systematic review and meta-analysis. *Pancreatology*. 2020;20(7):1302-1311.

3. Tizaoui K, Yang JW, Lee KH, Kim JH, Kim M, Yoon S et al. The role of YKL-40 in the pathogenesis of autoimmune diseases: a comprehensive review. *Int J Biol Sci*. 2022;18(9):3731-3746. doi: 10.7150/ijbs.67587.

4. Blazevic N, Rogic D, Pelajic S, Miler M, Glavcic G, Ratkajec V et al. YKL-40 as a biomarker in various inflammatory diseases: A review. *Biochem Med*. 2023;34(1):010502.

Disclosure: Nothing to disclose.

MP418

DEEP VENOUS THROMBOSIS IN ACUTE PANCREATITIS: PREVALENCE AND CLINICAL IMPLICATIONS

F. Amri¹, H. Bouamar¹, O. Elmqaddem¹, H. Koulali¹, A. Zazour¹, Z. Ismaili¹, G. Kharrasse¹

¹Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Department of Hepato-Gastroenterology, Oujda, Morocco

Contact E-Mail Address: fakh.amr@gmail.com

Introduction:

In patients with acute pancreatitis (AP), prolonged hospitalization and pro-inflammatory processes create conditions conducive to deep vein thrombosis (DVT) formation. Despite this, there is a scarcity of research on the incidence and risk factors specific to DVT development in hospitalized AP patients.

Aims & Methods: We conducted a retrospective analysis of 402 medical data from patients who were hospitalized with AP at our gastroenterology department of a university hospital from January 2018 to December 2023. The study included patients who underwent abdominal and pelvic

computed tomography (CT) and our objective was to determine the prevalence of DVT in hospitalized AP patients and evaluate its influence on morbidity and mortality.

Results: Among 402 patients with acute pancreatitis (AP), 5.5% (n=22) developed DVT, with Portal vein thrombosis in 54.5%, Splenic vein thrombosis in 32%, and Superior mesenteric vein thrombosis in 13.6%. The mean age among patients with DVT was 58 ± 22 years compared to 56 ± 18 years (P=0.03). DVT incidence was significantly higher among patients with a Computed Tomography Severity Index score of ≥ 3 (63.6%, P=0.02). Among patients with pleural effusion, 13.7% without thrombosis and 31.8% with thrombosis were observed (P=0.02). An association was found between Systemic Inflammatory Response Syndrome (SIRS) and thrombosis, with 16.1% of patients with persistent SIRS not developing thrombosis compared to 40.9% with thrombosis (P=0.006). Similarly, among patients with a Bedside Index for Severity score > 2, 15.0% without thrombosis and 31.8% with thrombosis were observed (P=0.03). Among patients with WON, 6.9% without thrombosis and 35.0% with thrombosis were observed (P<0.001). The mean CRP level was significantly higher in patients with thrombosis (187 ± 100 vs 130 ± 107 mg/dL, P=0.02). Hypoalbuminemia was significantly more frequent in cases of thrombosis (P=0.002). During follow-up, among patients with pancreatic insufficiency, 0.9% without thrombosis and 10.0% with thrombosis were observed (P=0.001). However, no significant association was observed between thrombosis and mortality rate.

Conclusion: In summary, our study reveals the prevalence of DVT in AP patients, emphasizing its clinical significance. Factors such as higher severity scores and association with systemic inflammation underscore the importance of proactive management to mitigate DVT risk and enhance patient outcomes.

Disclosure: Nothing to disclose.

MP419

CLINICAL AND BIOCHEMICAL OUTCOMES OF AGGRESSIVE FLUID RESUSCITATION VERSUS CONSERVATIVE FLUID RESUSCITATION IN PATIENTS WITH ACUTE PANCREATITIS

I.O. Vargas Olmos¹, M.C. Peláez Luna²

¹The American British Cowdray Medical Center, Internal Medicine - Gastroenterology, Mexico City, Mexico, ²The American British Cowdray Medical Center, Gastroenterology, Mexico City, Mexico

Contact E-Mail Address: issac_vargas@hotmail.com

Introduction: Acute pancreatitis is one of the most frequent and critical gastrointestinal diseases, therefore adequate management is essential to impact the prognosis of patients. Despite advances in the understanding of the pathophysiology of the disease and its complications, management remains a challenge and is mainly based on fluid resuscitation, pain management and early enteral nutrition.

Fluid resuscitation is the cornerstone of initial management, and acute pancreatitis treatment guidelines recommend early and aggressive hydration, however, evidence regarding what type of solution as well as what velocity of infusion should be used, is limited. There is not an established dose of intravenous fluids to prevent or reverse progression to multiple organ failure and reduce overload complications.

Aims & Methods: The main objective is to compare the clinical and biochemical outcomes of patients with acute pancreatitis who receive aggressive fluid resuscitation versus those who receive conservative fluid resuscitation after the first 48 hours of treatment.

195 patients were included, which were divided into two groups: 30 patients who received aggressive fluid resuscitation (more than 2.5 ml/kg/h) and 165 patients who received conservative fluid resuscitation (less than

2.5 ml/kg/h) during the first 48 hours of hospitalization. A second division of groups was performed based on 48-hour fluid balance: 129 patients who had a global fluid balance more than (>) positive 4000 ml and 66 patients who had a global fluid balance less than (<) positive 4000 ml.

Results: Patients with aggressive fluid resuscitation had a statistically significant smaller increase in C-reactive protein delta compared to conservative fluid resuscitation (+ 5.2 vs + 6.8, p 0.035) at 48 hours of treatment. Patients who had a 48-hour fluid balance > 4000 ml had a significantly greater increase in C-reactive protein delta (+ 11.46 vs + 3.94, p 0.012) compared to < 4000 ml 48-hour fluid balance, as well as longer time to start oral intake (79.36 vs 55 hrs, p 0.024) and greater requirement for loop diuretics (33.3% vs 14.8%, p 0.006).

Outcome	Global balance	Mean	p	Fluid resuscitation	Mean	p
C-reactive protein delta at 48 hours (mg/dl)	< 4000 ml	+3.94	0.012	< 2.5 ml/kg/h	+6.86	0.035
	> 4000 ml	+11.46		> 2.5 ml/kg/h	+5.2	
Creatinine delta at 48 hours (mg/dl)	< 4000 ml	-0.27	0.86	< 2.5 ml/kg/h	-0.14	0.73
	> 4000 ml	+0.26		> 2.5 ml/kg/h	+0.25	
BUN delta at 48 hours (mg/dl)	< 4000 ml	-3.53	0.177	< 2.5 ml/kg/h	-1.47	0.66
	> 4000 ml	+3.62		> 2.5 ml/kg/h	+2.11	
Leukocyte delta at 48 hours (10 ⁹ /L)	< 4000 ml	-1.87	0.171	< 2.5 ml/kg/h	-1.68	0.30
	> 4000 ml	-1.14		> 2.5 ml/kg/h	-1.3	
In-hospital days	< 4000 ml	5.81	0.237	< 2.5 ml/kg/h	5.83	0.30
	> 4000 ml	6.48		> 2.5 ml/kg/h	6.87	
Analgesia requirement (h)	< 4000 ml	67.62	0.147	< 2.5 ml/kg/h	73.39	0.64
	> 4000 ml	97.63		> 2.5 ml/kg/h	105.44	
Oral intake time (h)	< 4000 ml	47.5	0.024	< 2.5 ml/kg/h	55.48	0.28
	> 4000 ml	79.8		> 2.5 ml/kg/h	79.36	
Requirement for loop diuretics (%)	< 4000 ml	14.8	0.006	< 2.5 ml/kg/h	12	0.67
	> 4000 ml	33.3		> 2.5 ml/kg/h	19	

A multivariate analysis was performed and we found a significantly greater decrease in hematocrit percentage at 48 hours in patients with aggressive fluid resuscitation compared to the conservative resuscitation group, which was concordant with greater hemodilution and higher doses of intravenous fluids.

Conclusion: Aggressive fluid resuscitation is associated with lower changes in levels of C-reactive protein delta compared to conservative fluid resuscitation, as long as patients do not have a 48-hour fluid balance greater than 4000 ml at 48 hours, because at this point the levels of delta C-reactive protein and delay in starting oral intake are greater compared to patients with a global balance less than 4000 ml, in addition to requiring loop diuretics in a higher percentage.

References: 1.- Xiu-Wei Li. et al. Comparison of clinical outcomes between aggressive and non-aggressive intravenous hydration for acute pancreatitis: a systematic review and meta-analysis. *Critical Care* (2023) 27:122.

2.- Crosignani et al. Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review *Annals of Intensive Care* (2022) 12:98.

3.- Marcello Di Martino, et al. Systematic review and meta-analysis of fluid therapy protocols in acute pancreatitis: type, rate and route, *HPB* 2021, 23, 1629–1638.

4.- James L. Buxbaum, et al. Early Aggressive Hydration Hastens Clinical Improvement in Mild Acute Pancreatitis. *Am J Gastroenterol* 2017; 112:797–803.

5.- E de-Madaria et al., Fluid resuscitation with lactated Ringer's solution vs normal saline in acute pancreatitis: A triple-blind, randomized, controlled trial, *United European Gastroenterology Journal* 2018, Vol. 6(1) 63–72.

6.- A. Aggarwal, M. Manrai, R. Kochhar. Fluid resuscitation in acute pancreatitis *World J Gastroenterol* 2014 December 28; 20(48): 18092-18103.

7.- S. Zhou, C. Buitrago, A. Foong et al. Comprehensive meta-analysis of randomized controlled trials of Lactated Ringer's versus Normal Saline for acute pancreatitis *Pancreatology* 21 (2021) 1405-1410.

Disclosure: Nothing to disclose.

MP420

CHANGES IN BODY COMPOSITION AND DEVELOPMENT OF SARCOPENIA AS A SEQUELAE OF ACUTE PANCREATITIS

S. Bhattarai¹, M. Bhowmick², J. Samanta², P. Gupta³, H.S Mandavdhare², S. Shruti⁴, S. Roy², S.K Sinha²

¹Post Graduate Institute of Medical Education and Research, Internal Medicine, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ³Post Graduate Institute of Medical Education and Research, Radio Diagnosis and Imaging, Chandigarh, India, ⁴Government Medical College, Chandigarh, India

Contact E-Mail Address: sushmii88official@gmail.com

Introduction: Changes in body composition of patient with acute pancreatitis (AP) may stem from various causes such as anorexia secondary to proinflammatory state, abdominal pain, vomiting, ileus, sepsis etc and they can have a considerable effect on the disease outcome.

Aims & Methods: This study aimed to evaluate changes in body composition and development of sarcopenia in patients with moderately severe acute pancreatitis (MSAP) and severe acute pancreatitis (SAP) over short term follow up. This was a Single-centre observational study conducted in a tertiary care centre in northern India. Body composition analysis was done using bioelectrical impedance (BIA) method and sarcopenia assessment was done with hand grip strength (HGS) using digital hand dynamometer and skeletal muscle index (SMI) at 3rd lumbar vertebral (L3) level using computed tomography (CT) at baseline (admission) and after 8 weeks.

Results: A total of 40 patients were included (MSAP-22 and SAP-18). Mean age was 39.4 ± 14.6 years and 75% (30) were males. The predominant etiologies were alcohol (47.5%) and gallstone disease (37.5%). The mean BISAP score was higher in SAP than MSAP (2.17 ± 0.71 vs 1.05 ± 0.79, P < 0.001) and most common organ failure in SAP was acute lung injury (88.9%). In both MSAP and SAP there was significant change in body mass index (BMI), body fat percentage, subcutaneous fat percentage, whole body muscle percentage and visceral fat level between baseline and after 8 weeks. There was significant reduction in SMI at 8 weeks in both MSAP and SAP (47.5 ± 10.5 vs 41.5 ± 7.3, p < 0.001 and 48.9 ± 10.2 vs 41.2 ± 8.5 p < 0.001 respectively) but no significant difference in HGS was observed in both MSAP and SAP over 8 weeks follow up. On comparison between MSAP and SAP patients, the decline in BMI tend to be more pronounced in SAP, however the difference did not reach significant level (Table 1). Using European consensus definition, prevalence of probable sarcopenia and sarcopenia in MSAP and SAP at follow up were (68% and 22.7%) and (66% and 22.1%) respectively.

Body composition parameters	Moderately severe acute pancreatitis (22)	Severe acute pancreatitis(18)	P value
BMI(Kg/m2)			
Baseline	22.1 ±4.3	25.3 ±5.2	0.05
Follow up	20.5 ±3.8	22.4±5.2	
Mean change	-1.6±1.6	-2.8±2.3	
P value	<0.001	<0.001	
Body fat (%)			
Baseline	23.5±8.1	27.2±9.7	0.89
Follow up	21±8	24.4±6.4	
Mean change	-2.5 ±4.5	-2.7±5.24	
P value	0.01	0.03	
Whole body subcutaneous fat(%)			
Baseline	16.8±5.7	20.7±8.6	0.47
Follow up	14.9±5.9	18.6±7.1	
Mean change	-1.9±2.7	-2.6±3.4	
P value	0.003	0.01	
Whole Body Skeletal Muscle (%)			
Baseline	30.9±3.9	29.2±4.7	0.2
Follow up	30.7±4.7	30.2±4.7	
Mean change	-0.2±4.3	1.04±2.49	
P value	0.81	0.09	
Visceral fat level			
Baseline	6.1±5.2	9.6±6.9	0.4
Follow up	4.5±4.3	6.5±5.4	
Mean change	-1.5±1.8	-3±2.8	
P value	<0.001	<0.001	
Hand grip strength (HGS)			
Baseline	23.5±8.2	22.5±10	0.14
Follow up	25.4±8.4	21.9±8.5	
Mean change	1.9±5.2	-0.6±5.4	
P value	0.09	0.59	
Skeletal muscle index (SMI)			
Baseline	47.5±10.5	48.9±10.2	0.3
Follow up	41.5±7.3	41.2±8.5	
Mean change	-5.9±7.2	-7.7±5.7	
P value	<0.001	<0.001	
Probable sarcopenia (follow up)	68%	66%	
Sarcopenia (follow up)	22.7%	22.1%	

Table 1 – Body composition and sarcopenia variables in Moderately severe acute pancreatitis and Severe acute pancreatitis

*Follow up (8 weeks)

Conclusion: Acute pancreatitis is associated with significant changes in body composition variables and development of sarcopenia. This may have a significant bearing on the planning of nutritional rehabilitation of these patients to prevent adverse health outcome.

Disclosure: Nothing to disclose.

MP421

PREVALENCE AND CLINICAL IMPACT OF SARCOPENIA, PANCREATIC EXOCRINE INSUFFICIENCY AND OSTEOPATHY IN CHRONIC PANCREATITIS

H. Döngelli¹, G. Bengi², R.C. Yarol³, C. Altay³, S. Dolu², N. Danis², Ö. Selahattin Topalak², H. Akpınar⁴, M. Soytürk²

¹Dokuz Eylül University Hospital, Internal Medicine, İzmir, Turkey,

²Dokuz Eylül University Hospital, Department of Gastroenterology, İzmir, Turkey, ³Dokuz Eylül University Hospital, Radiology, İzmir, Turkey, ⁴Dokuz Eylül University Hospital, Gastroenterology, İzmir, Turkey

Contact E-Mail Address: suleyman.dolu@deu.edu.tr

Introduction: Chronic pancreatitis (CrP) is a fibroinflammatory disease that progresses with the loss of both exocrine and endocrine parenchyma of the pancreas due to fibrosis resulting from chronic inflammation (1). Chronic abdominal pain is the most common clinical feature in CrP, which is a malnutrition syndrome (2). Alcohol is the most common cause of CrP (3).

Sarcopenia is defined as a decrease in total body muscle mass (4). Sarcopenia is associated with adverse outcomes in CrP patients.(5).The prevalence of sarcopenia is increased in CrP patients compared to the normal population(6). In a study by Olesen et al., the frequency of sarcopenia in CrP patients was found to be 17%, and they found that sarcopenia was associated with a decrease in the general health. In this study, PEI, smoking and narcotic analgesic use were defined as risk factors for sarcopenia (7). Pancreatic exocrine insufficiency (PEI) is one of the most common complications of chronic pancreatitis. In a study by Kempeneers et al., mild and severe PEI in CrP patients were reported %31 and %46, respectively (8). The prevalence of osteopathy is high in patients with CrP and may increase the risk of fractures. In a meta-analysis of 19 studies by Amanda Koh et al., it was shown that 19% of the patients diagnosed with chronic pancreatitis were osteoporotic and 37% were osteopenic (9).

Aims & Methods: The prevalence of sarcopenia, pancreatic exocrine insufficiency (PEI) and osteopathy is high in chronic pancreatitis (CrP), and these are important complications with adverse consequences. The aim of our research is to evaluate the prevalence and risk factors of sarcopenia, PEI and osteopathy in CrP patients.

83 CrP patients were included in the study.

The surface area of the paravertebral muscles was measured from the third lumbar region of the cross-sectional images; PVMl was used to assess sarcopenia. PFE was used to evaluate PEI, and results were reported as no PEI, mild, or severe. DEXA was used to evaluate osteopathy. EORTC PAN26 and a semiotic questionnaire were performed. CBC, routine biochemical tests and vitamin/mineral levels were measured at the same time of PFE.

Results: The prevalence of sarcopenia, PEI, and osteoporosis was found to be 19 (22.9%), 56 (67.5%), and 18 (21.7%), respectively.

Male gender (OR:4.9 and p=0.044), severe PEI (OR:4.2 and p=0.043), smoking (OR:4.6 and p=0.040) and zinc deficiency (OR:2.2 and p=0.029) were defined as risk factors for sarcopenia.

Of the 83 patients, 20 were diagnosed with mild and 36 with severe PEI, and PEI was not detected in 27 patients. Severe PEI was determined to be associated with osteoporosis/osteopenia (p=0.010), DM (p=0.001), heavy narcotic analgesic use (p=0.030), sarcopenia (p=0.016) and zinc deficiency (p=0.012).

Osteoporosis was detected in 18 patients and 42 patients had osteopenia. PAN26 scores were higher in individuals with osteoporosis (p=0.029). Female gender (OR:7.8 and p=0.004), severe PEI (OR:8.1 and p=0.003) and sarcopenia (OR:5 and p=0.037) were identified as independent risk factors for osteopathy.

Conclusion: The prevalence of sarcopenia, PEI and osteopathy are increased in CrP. Smoking, zinc deficiency, PEI, and male gender are defined as risk factors for sarcopenia. The prevalence of osteopathy increases in patients with sarcopenia and is associated with decreased quality of life. PVMl was used for the first time to evaluate sarcopenia in CrP patients.

In studies evaluating sarcopenia using cross-sectional imaging methods, zinc deficiency was identified as a risk factor for sarcopenia for the first time in the literature.

References:

- 1-Etemad, Babak, and David C. Whitcomb. "Chronic pancreatitis: diagnosis, classification, and new genetic developments." *Gastroenterology* 120.3(2001):682-707.
- 2-Kleeff, Jorg, et al. "Chronic pancreatitis." *Nature reviews Disease primers* 3.1(2017):1-18.
- 3- Hirota, Moriguchi, et al. "The seventh nationwide epidemiological survey for chronic pancreatitis in Japan: clinical significance of smoking habit in Japanese patients." *Pancreatology* 14.6(2014):490-496.
- 4-Cruz-Jentoft, Alfonso J., et al. "Sarcopenia: revised European consensus on definition and diagnosis." *Age and ageing* 48.1(2019):16-31.
- 5- Yuan, Shuai, and Susanna C Larsson. "Epidemiology of sarcopenia:

Prevalence, risk factors, and consequences.” *Metabolism: clinical and experimental* vol. 144(2023):155533.

6-Fasullo, Matthew et al. “Sarcopenia in Chronic Pancreatitis - Prevalence, Diagnosis, Mechanisms and Potential Therapies.” *Current gastroenterology reports* vol. 24,4(2022):53-63.

6-Dodds, Richard Matthew, et al. “The epidemiology of sarcopenia.” *Journal of Clinical Densitometry* 18.4(2015):461-466.

7-Olesen, Søren S., et al. “Sarcopenia associates with increased hospitalization rates and reduced survival in patients with chronic pancreatitis.” *Pancreatology* 19.2(2019):245-251.

8-Kempeneers, Marinus A et al. “Natural Course and Treatment of Pancreatic Exocrine Insufficiency in a Nationwide Cohort of Chronic Pancreatitis.” *Pancreas* vol. 49,2(2020):242-248.

9-Koh, Amanda et al. “Risk of osteopaenia, osteoporosis and osteoporotic fractures in patients with chronic pancreatitis: A systematic review and meta-analysis.” *Clinical nutrition (Edinburgh, Scotland)* vol. 42,7(2023):1086-1094.

Disclosure: Nothing to disclose.

MP422

EFFICACY AND SAFETY OF ERCP IN PATIENTS WITH SYMPTOMATIC PANCREAS DIVISUM

R. Ben Haj Ali¹, M. Yakoubi¹, A. Ben Mohamed¹, G. Gharbi¹, M. Mahmoudi¹, A. Khsiba¹, M. Medhioub¹, M.L. Hamzaoui¹

¹Mohamed Taher Maamouri Hospital, Gastroenterology and hepatology department, Nabeul, Tunisia

Contact E-Mail Address: rayen2.benhajali@gmail.com

Introduction: Pancreas divisum is the most frequent congenital anomaly of the pancreas. It arises from failed fusion of the dorsal and ventral pancreatic ducts. In symptomatic patients, the endoscopic intervention is proposed as first-line treatment via retrograde cholangiopancreatography (ERCP). In case of failure, surgery remains a feasible option.

Aims & Methods: The aim of this research was to evaluate the efficacy and safety of ERCP in the treatment of patients with symptomatic pancreas divisum.

We conducted a retrospective and descriptive study including ERCP procedures performed between January 2014 and February 2024. We collected clinical and radiological data regarding patients in whom the diagnosis of symptomatic pancreas divisum was confirmed. The success of ERCP was defined by the ability to perform minor papilla sphincterotomy with or without dorsal duct stent insertion. The adverse events of ERCP as well as the long term outcome of each patient were collected during follow up.

Results: During the study period, 22 procedures were carried out in patients with this anomaly. The median age was 44.5 years (14 years - 72 years) with a male-to-female ratio of 0.83. The diagnosis was made during the exploration of recurrent acute pancreatitis in 10 patients, a first episode of acute pancreatitis in 8 patients, recurrent abdominal pains in 3 patients and chronic pancreatitis in one patient. The most observed variant of the anomaly was complete pancreas divisum in 15 patients. The incomplete variant was observed in 3 patients. The variant with isolated dorsal duct was found in 2 patients and 1 case of pancreas divisum associating an ansa pancreatica was identified. Endoscopic treatment was successful in 15 patients with a success rate of 77.3%. The main therapeutic option was sphincterotomy of the minor papilla alone in 13 patients and, in addition, placement of a stent in the dorsal pancreatic duct in the other 2 patients. Intervention failure was mainly associated with the inability to catheterize the minor papilla in 5 patients. Failure to visualize the minor papilla and stenosis of the duodenal bulb were the other causes of failure.

No subsequent complications post-ERCP were reported. During follow up, no endoscopic reintervention due to symptoms reoccurrence was necessary.

Conclusion: In our study, endoscopic treatment of pancreas divisum in symptomatic patients was successful in 77.3% of the cases. Sphincterotomy alone or with stent placement were the preferred therapeutic options, allowing symptom relief in all patients. Although these techniques carry numerous risks, no complications occurred during the subsequent patient follow-up.

Disclosure: Nothing to disclose.

MP423

A MULTICENTER COMPARATIVE ANALYSIS OF A LUMEN-APPPOSING STENT VS. PLASTIC STENTS FOR ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE OF A PANCREATIC PSEUDOCYST: THE WONDERFUL STUDY GROUP IN JAPAN

T. Saito¹, S. Omoto², M. Takenaka², M. Tsujimae³, A. Sakai³, A. Masuda³, T. Sato¹, T. Hamada¹, R. Nakano⁴, H. Shiomi⁴, S. Takahashi⁵, T. Fujisawa⁵, S. Kentaro⁶, S. Matsubara⁶, S. Uemura⁷, T. Iwashita⁷, K. Yoshida⁸, A. Maruta⁸, Y. Iwasa⁹, M. Okuno^{9,10}, K. Iwata⁹, N. Hayashi¹¹, T. Mukai¹², H. Isayama¹³, I. Yasuda¹¹, Y. Nakai^{14,15}, the WONDERFUL Study Group in Japan
¹The University of Tokyo, Department of Gastroenterology, Tokyo, Japan, ²Kindai University, Department of Gastroenterology and Hepatology, Faculty of Medicine, Osaka, Japan, ³Kobe University, Division of Gastroenterology, Department of Internal Medicine, Hyogo, Japan, ⁴Hyogo Medical University, Division of Hepatobiliary and Pancreatic Diseases, Department of Gastroenterology, Hyogo, Japan, ⁵Juntendo University Graduate School of Medicine, Department of Gastroenterology, Tokyo, Japan, ⁶Saitama Medical Center, Saitama Medical University, Department of Gastroenterology and Hepatology, Saitama, Japan, ⁷Gifu University Hospital, First Department of Internal Medicine, Gifu, Japan, ⁸Gifu Prefectural General Medical Center, Department of Gastroenterology, Gifu, Japan, ⁹Gifu Municipal Hospital, Department of Gastroenterology, Gifu, Japan, ¹⁰Matsunami General Hospital, Department of Gastroenterology, Gifu, Japan, ¹¹University of Toyama, Third Department of Internal Medicine, Toyama, Japan, ¹²Kanazawa Medical University, Department of Gastroenterological Endoscopy, Kanazawa, Japan, ¹³Juntendo University, Department of Gastroenterology, Tokyo, Japan, ¹⁴The University of Tokyo Hospital, Department of Endoscopy and Endoscopic Surgery, Tokyo, Japan, ¹⁵Tokyo Women's Medical University, Department of Internal Medicine, Institute of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: tomsaito623@gmail.com

Introduction: It is unknown how stent types relate to clinical outcomes of endoscopic ultrasound (EUS)-guided drainage of pancreatic pseudocysts. This multicenter retrospective study aimed to compare the clinical outcomes between a lumen-apposing metal stent (LAMS) and a plastic stent.

Aims & Methods: Among 357 patients with pancreatic fluid collections in a large multi-institutional WONDERFUL consortium, we included 123 patients who received EUS-guided drainage of a pancreatic pseudocyst (16 and 107 cases with LAMS and plastic stent(s), respectively). We examined clinical treatment success, procedure-related adverse events, and pseudocyst recurrence.

Results: There were no differences between the groups regarding demographics (e.g., age and sex) and disease characteristics (e.g., size, encapsulation status, and the timing of drainage in relation to the onset of acute

pancreatitis). The clinical success rates were comparable between the LAMS and plastic stent groups (94% vs. 87%, respectively; $P = 0.40$). The stent types were not associated with the time to clinical success (median, 25 days vs. 22 days for the LAMS and plastic stent groups, respectively; $P = 0.56$), the overall rate of procedure-related adverse events (0% vs. 5.6%, $P = 0.33$), or the rate of recurrence following clinical success (6.7% vs. 17%, $P = 0.19$).

Conclusion: In patients receiving EUS-guided drainage of pancreatic pseudocysts, clinical outcomes appeared to be comparable between the LAMS and plastic stent groups. If validated, our findings would support the feasibility of plastic stents in this patient population, which is a more cost-effective treatment modality than LAMSs. We, the WONDERFUL study group, have launched a randomized non-inferiority trial of plastic stents compared to a LAMS in this setting (NCT#06133023).

Disclosure: H.I. declares research funding from Boston Scientific Japan, Fujifilm, and Piolax Medical Devices; and honoraria from Boston Scientific Japan, Century Medical, Create Medic, Fujifilm, Gadelius Medical, Hitachi Medical, Japan Lifeline, Kaneka, Kawasumi Laboratories, Olympus Medical, Piolax Medical Devices, Sumitomo Bakelite, UMIDAS, and Zeon Medical; and contributions from Boston Scientific Japan, Gadelius Medical, Japan Lifeline, and Zeon Medical. Y.N. is an editorial board member of *Digestive Endoscopy* and declares research funding from Boston Scientific Japan, Century Medical, Fujifilm, Gadelius Medical, HOYA Pentax Medical, Hitachi Medical, Kaneka, and Medico's Hirata; and honoraria from Boston Scientific Japan, Fujifilm, Gadelius Medical, Hitachi Medical, J-MIT, Medico's Hirata, and Olympus Medical. This work was not supported by any of those companies. The other authors declare no conflicts of interest related to this article.

MP424

DOES CONTRAST-ENHANCED ENDOSCOPIC ULTRASOUND GUIDED TISSUE ACQUISITION IMPROVE THE DIAGNOSTIC RATE OF PANCREATIC CANCER COMPARED TO ENDOSCOPIC ULTRASOUND GUIDED TISSUE ACQUISITION IN PATIENTS WITH FEATURES OF CHRONIC PANCREATITIS?

R.G. Jeler¹, E.C. Seulean¹, R.I. Orzan^{1,2}, V. Rednic¹, C. Pojoga^{1,3}, C. Hagiu^{1,2}, I. Rusu^{1,2}, G. Molnar¹, N. Al Hajjar^{1,2}, A. Seicean^{1,2}

¹Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor", Cluj-Napoca, Romania, ²"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania,

³Babes-Bolyai University, UBB Med, Cluj-Napoca, Romania

Contact E-Mail Address: edina.seulean01@gmail.com

Introduction: Chronic pancreatitis represents a risk for pancreatic cancer with an estimated effect of 16 in the first 2 years, 7.9 in the first 5 years and over 3 in 9 years. The sensitivity of endoscopic ultrasound fine needle aspiration (EUS-FNA) in diagnosing pancreatic malignancy in cases with and without chronic pancreatitis drops from 91.5% to 65.3%. Although contrast-enhanced fine needle aspiration (CH-EUS-FNA) was not statistically superior to standard EUS-FNA in diagnosing solid pancreatic lesions, some emphasis was placed on the usefulness of CH-EUS-FNA in cases of pancreatic masses on chronic pancreatitis.

Aims & Methods: Aim. To assess and compare the diagnostic rate of CH-EUS tissue acquisition (CH-EUS-TA) compared to standard EUS-TA in cases of solid pancreatic masses with features of chronic pancreatitis.

Material and methods. This is a retrospective unicenter study from 2020 to 2022 that included solid pancreatic masses (solid component > 80%) that required EUS-guided sampling and features of chronic pancreatitis that needed EUS tissue acquisition. We excluded patients with previous

surgery or chemotherapy for pancreatic diseases, contraindications for tissue sampling or without 1-year follow-up in negative cases. We divided patients in two groups: group 1 with CH-EUS-FNA and group 2 with standard FNA, both using 22G needles. The final diagnosis was based on FNA or surgery results or on 1-year follow-up.

Results: There were 13 patients included in group 1 and 27 patients included in group 2. The sensitivity for malignancy was 85% in group 1 and 80% in group 2. No difference was proved regarding size or mass location, percentage of definitive chronic pancreatitis between groups. The most common lesion location was the head of the pancreas (60%), while the mean mass size was 2,4 cm. Less than 50% of patients (42%) were classified as "Definitive Chronic Pancreatitis" according to Rosemont Criteria. Regarding the severity of disease according to Cambridge Severity Score, the largest group (45% of patients) was the "Cambridge 3" group. 45% of the patients required main bile duct stenting for main bile duct stenosis. A small percent of patients (15%) showed signs of portal hypertension. In group 1, the hypo-enhancement was observed in 38.4% of patients.

Conclusion: In this retrospective series, the CH-EUS-FNA proved to perform similarly with EUS-FNA when chronic pancreatitis features were noticed. Further studies using EUS fine needle biopsy (EUS-FNB) contrast guided procedures are needed in this category of patients.

References:

1. Kirkegard J et al. Chronic Pancreatitis and Pancreatic Cancer Risk: A Systematic Review and Meta-analysis. *Am J Gastroenterol* 2017
2. Abdallah MA, et al. Endoscopic Ultrasound Guided Fine-Needle Aspiration for Solid Lesions in Chronic Pancreatitis: A Systematic Review and Meta-Analysis. *Dig Dis Sci*. 2022

Disclosure: The authors have no conflicts of interest to declare.

H.pylori treatment: Part 1

14:30-15:30 / Poster Stage 5

MP425

A LARGE-SCALE SURVEY REVEALING LEVELS OF KNOWLEDGE AND PUBLIC PERCEPTION FOR HELICOBACTER PYLORI IN JAPAN

H. Saito^{1,2}, C. Matsumoto¹, T. Uchiyama¹, Y. Nishikawa^{3,4}, T. Kakiuchi⁵, Y. Eguchi⁶, M. Tsubokura¹, Y. Mizuno⁷

¹Fukushima Medical University School of Medicine, Department of Radiation Health Management, Fukushima, Japan, ²Soma Central Hospital, Department of Internal Medicine, Soma, Japan, ³Kyoto University, Health Informatics, Kyoto, Japan, ⁴Hirata Central Hospital, Hirata, Japan, ⁵Saga University, Department of Pediatrics, Faculty of Medicine, Saga, Japan, ⁶Loco-Medical General Institute, Ogi, Japan, ⁷Ma-ru Clinic Yokosuka, Yokosuka, Japan

Contact E-Mail Address: h.saito0515@gmail.com

Introduction: *Helicobacter pylori* (*Hp*) infection is one of the major causes of gastric cancer and represents a significant global public health challenge. In Japan, where the incidence of gastric cancer is high, reducing the risk through the eradication of *Hp* is deemed crucial. While enhancing awareness about *Hp* is thought to encourage testing and contribute to treatment, there is a lack of evaluation regarding the Japanese population's awareness of *Hp*.

Aims & Methods: In this cross-sectional study, we aim to assess baseline knowledge and attitude towards *Hp* among Japanese population. Participants were recruited through an online survey platform (Macromill, Inc), with ages ranging from 20 to 69, reflecting the age demographic composition of Japan equally across genders. Referencing the existing surveys on *Hp*¹⁻³, we assessed knowledge on five key aspects related to *Hp*: risk of infection (scored out of 7), diseases caused by *Hp* (scored out of 7), methods of testing (scored out of 5), benefits and side effects of *Hp* eradication (scored out of 8), and knowledge of gastric cancer prevention (scored out of 10). Attributes of participants, socioeconomic factors, and health literacy (HLS-14)⁴ were also evaluated to study their correlation with knowledge about *Hp*.

Results: A total of 3,095 individuals participated. Of these, 56.3% reported having some knowledge about *Hp*. 865 participants (28.0%) had undergone *Hp* testing, 354 (11.4%) confirmed *Hp* infection, and 283 (9.1%) had received treatment for *Hp*. About 55.6% (1,722 participants) consider that the treatment for *Hp* posed a significant financial burden. The average correct response rate across all knowledge items was 45.6% (SD: 19.0%). The individual correct response rates were 57.3% for risk of *Hp* infection, 50.9% for diseases caused by *Hp*, 24.5% for methods of testing, 45.6% for benefits and side effects of *Hp* eradication, and 44.4% for knowledge of gastric cancer prevention. Higher scores were significantly associated with having an income over 4 million yen, a family history of *Hp*, personal *Hp* testing history, *Hp* treatment history, and higher health literacy. Over 80% of respondents acknowledged that understanding the relationship between *Hp* and stomach symptoms, recognizing *Hp* as a gastric cancer risk, and knowing that *Hp* eradication reduces future gastric cancer risk influenced their decision on the need for eradication. Similarly, the same proportion reported that believing that the harshness of the treatment exceeds the current symptoms and the high costs of testing and treatment influenced their decisions for eradication.

Conclusion: The level of understanding of *Hp* among the Japanese population is moderate and influenced by income level, health literacy, and personal experience with the *Hp* infection. Many consider testing and treatment burdensome. Enhancing correct understanding of *Hp* could potentially increase testing and treatment rates, contributing to the future reduction of gastric cancer in Japan.

References: 1. Kimberly S Bailey, et al., *Helicobacter pylori* treatment knowledge, access and barriers: a cross-sectional study. *Helicobacter* 2023;28(2):e12954.

2. You Wu, et al., Awareness and attitudes regarding *Helicobacter pylori* infection in Chinese physicians and public population: A national cross-sectional survey. *Helicobacter* 2020;25(4):e12705

3. Thomas Zheng Jie Teng, et al., *Helicobacter pylori* knowledge and perception among multi-ethnic Asians. *Helicobacter* 2021;26(3):e12794.

4. Machi Suka, et al., The 14-item health literacy scale for Japanese adults (HLS-14). *Environ Health Prev Med.* 2013;18(5):407-15.

Disclosure: Nothing to disclose.

MP426

A NOVEL MULTI-EPITOPE-BASED VACCINE AGAINST *HELICOBACTER PYLORI*; EVALUATION OF THE IMMUNOGENICITY AND PROTECTIVE EFFECT

B. Kalali^{1,2}, H. Moeini¹, A. Mostafazadeh³, A. Yadegar⁴, V. Wedershoven¹, C. Schulz², P. Malfetheriner²

¹Iguana Biotechnology GmbH, Munich, Germany, ²Ludwig Maximilian University, Department of Medicine 2, Munich, Germany, ³Medical University of Babol, Babol, Iran, ⁴Shahid Beheshti University of Medical Sciences, Tehran, Iran

Contact E-Mail Address: bk@iguana-biotec.com

Introduction: The development of gastric cancer is strongly linked to *Helicobacter pylori* infection. Therefore, early diagnosis and eradication of *H. pylori* infection can significantly lower the risk, as studies consistently show reduced cancer rate with these measures. The success in achieving such a goal depends on widespread early detection and treatment, plus effective prevention of new infections. To date, there is no effective certified vaccine against *H. pylori* available. This study describes the development of a novel multi-epitope *H. pylori* vaccine consisting of B- and T-cell epitopes from six conserved virulence factors of the bacteria.

Aims & Methods: Through comprehensive bioinformatic analysis, sixteen B- and T-cell epitopes were carefully selected, considering both MHC classes I and II for the T-cell epitopes. The recombinant Multi-Epitope-Unit antigen (MEU) was combined with flagellin as adjuvant. Additionally, recombinant Modified Vaccinia virus Ankara (MVA) encoding the MEU antigen was generated. The vaccine candidates were tested in mice. To this end, two sets of animal experiments were designed. One set to evaluate the immunogenicity of the new MEU construct, while the second set to assess the protective effect of the vaccine candidates. In the vaccination protocol, both protein- and MVA-based vaccine candidates were administered intramuscularly (IM) to C57/BL6 mice on days 0, 7 and 14. Two weeks after the last immunization, mice in the prevention groups were challenged with three doses of the mouse adapted *H. pylori* SS1 strain. The groups, allocated for evaluating the immunogenicity of the new vaccine, were not exposed to infection with *H. pylori* or any further treatments prior to the analysis. Humoral (antibody) and cellular immune responses, along with the levels of protection and infection, were evaluated at two or four weeks post-immunization or -infection respectively. Bacterial load in prevention groups was determined through culturing of the gastric samples. The reactivity of anti-MEU antibodies, raised in immunized animals, to the *H. pylori* clinical isolates was also assessed via ELISA employing crude antigens of a set of 30 clinical isolates.

Results: The MEU antigen, whether adjuvanted with flagellin or in MVA construct, was observed to elicit significant antibody levels in mice, capable of reacting with crude antigens from *H. pylori*. The most substantial antibody response was detected towards the individual epitopes from Urease and Flid (hook-associated protein 2 homologue).

Both vaccine protocols, using the flagellin-adjuvanted MEU and the recombinant MVA, demonstrated complete protection against *H. pylori* infection compared to non-immunized animals. This protection was achieved through either a schedule of immunization with the protein-based vaccine candidate followed by MVA boost or two administered doses of MVA.

Conclusion: The novel MEU-based vaccine demonstrated significant immunoreactivity against *H. pylori* antigens. Our findings indicate a complete protection against *H. pylori* infection in the mice immunized with the multi-epitope unit antigen, regardless of the vaccination protocols. The reactivity of these antibodies with the bacteria native crude antigens suggests the antigen's correct processing by the mammalian immune system. Moving forward, our next step involves assessing the therapeutics effects of the vaccine candidate.

Disclosure: Nothing to disclose.

MP427

THE INFLUENCE OF INDICATIONS FOR *HELICOBACTER PYLORI* INVESTIGATION ON PRESCRIPTIONS AND EFFECTIVENESS: EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

S.J. Martínez-Domínguez^{1,2,3}, O. P. Nyssen⁴, A. Lanas⁵, E. Alfaro⁶, L.V. Jonaitis⁷, U. Mahmudov⁸, I. Voynovan⁹, G. Babayeva¹⁰, L.R. Rodrigo Sáez¹¹, G. Fiorini¹², Á. Pérez-Aisa¹³, J. Tejedor-Tejada¹⁴, B. Tepeš¹⁵, L. Vologzanina¹⁶, E. Mammadov¹⁷, F. Lerang¹⁸, Q.F. Vidadi Oğlu¹⁹, N. Bakulina²⁰, R.A. Abdulkhakov²¹, T. Ilchishina²², T.J. Butler²³, A.S. Silkanovna Sarsenbaeva²⁴, R. Bumane²⁵, A.J. Lucendo²⁶, M. Romano²⁷, L. Bujanda Fernández de Piérola²⁸, S. Abdulkhakov²⁹, O. Zaytsev³⁰, M. Pabón-Carrasco³¹, A. Keco-Huerga³¹, M. Denkovski³², J.M. Huguet³³, M.C. Perona Vincenti³⁴, O. Núñez Martínez³⁵, M. Pavoni³⁶, G. Fadieienco³⁷, S. Alekseenko³⁸, S. Smith³⁹, L. Hernández Villalba⁴⁰, J. Kupcinskas⁴¹, D.S. Bordin⁴², M. Leja⁴³, A. Gasbarrini⁴⁴, O. Gridnyev⁴⁵, A. Cano-Català⁴⁶, P. Parra⁴⁷, L. Moreira Ruiz⁴⁸, F. Megraud⁴⁹, C. O' Morain⁵⁰, J. Gisbert⁵¹, on behalf of the Hp-EuReg investigators

¹Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ²Aragón Health Research Institute, Zaragoza, Spain, ³Facultad de medicina, Universidad de Zaragoza, Zaragoza, Spain, ⁴Hospital Universitario de La Princesa, IIS-IP, and CIBERehd, Gastroenterology Unit, Madrid, Spain, ⁵University of Zaragoza University Hospital Dept. of Medicine-Gastroenterology, Dept. Medicine & Gastroenterology, Zaragoza, Spain, ⁶Hospital Clínico Universitario Lozano Blesa, Gastroenterology/ Digestivo, Zaragoza, Spain, ⁷Lithuanian University of Health Sciences Dept. of Gastroenterology, Gastroenterology, Kaunas, Lithuania, ⁸Modern Hospital, Baku, Azerbaijan, ⁹A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ¹⁰Azerbaijan State Advanced Training Institute for doctors named after A.ALIYEV, Terapiya, Baku, Azerbaijan, ¹¹University of Oviedo, Oviedo, Spain, ¹²Sant'Orsola Hospital Dept. of Internal Medicine, Dept. of Medical and Surgical sciences, Bologna, Italy, ¹³Agencia Sanitaria Costa del Sol, , Marbella, Spain, ¹⁴Hospital Universitario de Cabueñes, Gijón, Spain, ¹⁵DC ROGASKA d.o.o., Gastroenterology, Rogaska Slatina, Slovenia, ¹⁶Gastrocenter, Perm, Russian Federation, ¹⁷Azerbaijan State Advanced Training Institute for Doctors named by A.Aliyev, Baku, Azerbaijan, ¹⁸Central Hospital of Ostfold, Medicine, Grålum, Norway, ¹⁹National Oncology Centre, Baku, Azerbaijan, ²⁰North-Western State Medical University n. a. I. I. Mechnikov, St. Petersburg, Russian Federation, ²¹Kazan State Medical University, Kazan, Russian Federation, ²²SM-clinic, Saint-Petersburg, Russian Federation, ²³Trinity College Dublin, Dublin, Ireland, ²⁴Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁵Digestive Diseases Centre GASTRO, Riga, Latvia, ²⁶Hospital General de Tomelloso, Tomelloso, Spain, ²⁷Università Vanvitelli, Dept. of Internal Medicine, Napoli, Italy, ²⁸Instituto Biodonostia, San Sebastián, Spain, ²⁹I. I. Mechnikov North-Western State Medical University of the Ministry of Health of the Russian Federation, Saint Petersburg, Russian Federation, ³⁰First Clinical Medical Centre, Kovrov, Russian Federation, ³¹Hospital Universitario de Valme, Sevilla, Spain, ³²Diagnostic centre, Bled, Slovenia, ³³Hospital General Universitario de Valencia, Valencia, Spain, ³⁴Hospital Quiron Marbella, Dept. of Gastroenterology, Marbella, Spain, ³⁵Hospital Sanitas La Moraleja, Gastroenterology, San Sebastian De Los Reyes, Spain, ³⁶University of Bologna, Bologna, Italy, ³⁷Government Institution L.T. Malaya Therapy National Institute of NAMS of Ukraine, Kharkiv, Ukraine, ³⁸Far Eastern State Medical University, Khabarovsk, Russian Federation, ³⁹Trinity College

Dublin/Tallaght University Hospital, Clinical Medicine (Trinity College Dublin) & Gastroenterology (Tallaght University Hospital), Dublin, Ireland, ⁴⁰Santos Reyes, Gastroenterology, Aranda de Duero, Spain, ⁴¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ⁴²A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ⁴³University of Latvia, Digestive Diseases centre GASTRO, Riga, Latvia, ⁴⁴Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁴⁵National institute of therapy named L.T.Malaya NAMS of Ukraine, Department of the Study of Digestive System Diseases and their Comorbidity with Non-communicable Diseases, Kharkiv, Ukraine, ⁴⁶Althaia Xarxa Assistencial Università de Manresa, Manresa, Spain, ⁴⁷Hospital de la Princesa, Madrid, Spain, ⁴⁸Hospital Clinic de Barcelona, Gastroenterology, Gava, Spain, ⁴⁹Hopital Pellegrin, Laboratoire de Bacteriologie, Bordeaux, France, ⁵⁰Trinity College Dublin, Faculty of Health Sciences, Dublin, Ireland, ⁵¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Digestive Services, Madrid, Spain

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: The role of indications for *Helicobacter pylori* investigation on prescriptions and effectiveness is uncertain.

Aims & Methods: To assess the appropriateness of indications for *H. pylori* treatment, and its influence on prescriptions and effectiveness. International, prospective, non-interventional registry of the management of *H. pylori* infection by European gastroenterologists (Hp-EuReg). Treatment-naïve patients registered from 2013 to July 2023 at e-CRF AEG-REDCap were included. Effectiveness was evaluated by modified intention-to-treat analysis.

Results: Overall, 53,636 treatment-naïve patients from 34 countries were analyzed. Indications were inappropriate in 2,989 (5.6%) cases. Most common indications were: dyspepsia with normal endoscopy (49%), non-investigated dyspepsia (20%), duodenal ulcer (11%), gastric ulcer (7.7%), and gastroesophageal reflux disease (GERD) (2.6%). Treatment effectiveness varied by indication: duodenal ulcer (91%), gastric ulcer (90%), preneoplastic lesions (90%), dyspepsia with normal endoscopy (89%), GERD (88%), and non-investigated dyspepsia (87%); $p<0.001$. Bismuth quadruple therapies reached 90% effectiveness in all indications except GERD. The effectiveness with PPI-bismuth-metronidazole-tetracycline (quadruple-BMTc) was lower in patients treated for non-investigated dyspepsia as compared to those with dyspepsia with normal endoscopy, however, in all cases cure rates were optimal (91.8% vs. 93.9%, $p=0.047$). In Spain, these latter results were also confirmed in the same indications (92% vs. 94%, $p<0.05$), and similar scenario was observed for quadruple-BMTc in patients with dyspepsia from Russia and Italy, but did not reach statistical significance. PPI-clarithromycin-amoxicillin-bismuth showed similar effectiveness rates for dyspepsia with normal endoscopy and non-investigated dyspepsia (93%), also confirmed in Spain, Russia and Azerbaijan. Concomitant clarithromycin-amoxicillin-tinidazole/metronidazole (CAT-CAM) achieved 90% except in patients with non-investigated dyspepsia. Most of concomitant-CAT-CAM therapies (36%) were prescribed in Spain, where the effectiveness was suboptimal in patients with non-investigated dyspepsia (87%), dyspepsia with normal endoscopy (89.8%) and GERD (89%) ($p<0.001$). Triple therapies showed suboptimal eradication rates in all indications with the exception of Lithuania, where optimal effectiveness was observed in patients with non-investigated dyspepsia (99%, $p=0.009$). Adverse events were higher in patients treated for dyspepsia with normal endoscopy as compared to duodenal ulcer (23% vs. 28%, $p<0.001$). Therapeutic compliance was higher in patients with duodenal ulcer and preneoplastic lesions (98% and 99%, $p<0.001$).

Indications, n (%)	Spain	Russia	Azerbaijan	Italy	Slovenia	Lithuania	Others	Total
Triple-CA								
Non-investigated Dyspepsia	577 (75.3)†	348 (84.9)	37 (92.5)	31 (68.9)†	378 (89.6)	68 (96.6)*	920 (82.1)†	2,359 (82.1)†
Dyspepsia with normal endoscopy	1,208 (86.2)*	847 (82.8)	1,532 (90.9)	76 (87.4)	900 (90.7)	799 (85.4)	1,027 (86.4)	6,389 (87.4)*
Duodenal Ulcer	341 (89.5)*	302 (81.8)	134 (93.7)	21 (91.3)	199 (94.8)	65 (78.3)†	279 (90.6)*	1,341 (88.4)*
Gastric Ulcer	217 (88.2)	268 (82.0)	232 (91.0)	12 (92.3)	128 (87.1)	38 (88.4)	183 (88.0)	1,078 (87.0)
Preneoplastic lesions	94 (83.9)	52 (92.9)	2 (100.0)	0 (0.0)	18 (94.7)	1 (50.0)	125 (88.0)	292 (87.4)
GERD	35 (89.7)	69 (75.8)	27 (96.4)	5 (83.3)	282 (92.5)	7 (87.5)	44 (83.0)	469 (88.5)
Total	2,472 (83.9)	1,886 (82.9)	1,964 (91.2)	145 (82.9)	1,905 (90.9)	978 (85.7)	2,578 (85.4)	11,928 (86.4)
p-value	<0.001	0.119	0.713	0.015	0.127	0.009	0.001	<0.001
Concomitant-CAT-CAM								
Non-investigated Dyspepsia	1,974 (86.8)†	1 (100.0)	0 (0.0)	57 (95.0)	3 (75.0)	0 (0.0)	220 (92.1)	2,255 (87.5)†
Dyspepsia with normal endoscopy	2,097 (89.8)	30 (88.2)	0 (0.0)	219 (95.2)	9 (90.0)	0 (0.0)	456 (94.8)	2,811 (90.9)
Duodenal Ulcer	767 (94.1)*	19 (90.5)	0 (0.0)	6 (85.7)	1 (100.0)	0 (0.0)	72 (90.0)	865 (93.6)*
Gastric Ulcer	331 (91.9)	10 (83.3)	0 (0.0)	14 (87.5)	1 (100.0)	1 (100.0)	32 (91.4)	389 (91.5)
Preneoplastic lesions	123 (94.6)	0 (0.0)	0 (0.0)	4 (80.0)	0 (0.0)	0 (0.0)	6 (100.0)	133 (94.3)
GERD	73 (89.0)	1 (100.0)	0 (0.0)	34 (97.1)	0 (0.0)	0 (0.0)	20 (95.2)	128 (92.1)
Total	5,365 (89.5)	61 (88.4)	0 (0.0)	334 (94.6)	14 (87.5)	1 (100.0)	806 (93.5)	6,581 (90.2)
p-value	<0.001	-	-	1.000	-	-	0.265	<0.001
Quadruple-BMTc								
Non-investigated Dyspepsia	1,762 (91.5)†	38 (92.7)	0 (0.0)	153 (93.9)	0 (0.0)	0 (0.0)	149 (92.0)	2,102 (91.8)†
Dyspepsia with normal endoscopy	2,144 (94.1)*	125 (94.0)	0 (0.0)	403 (96.7)	2 (100.0)	0 (0.0)	350 (90.7)	3,028 (93.9)*
Duodenal Ulcer	525 (94.8)	21 (91.3)	0 (0.0)	23 (85.2)†	0 (0.0)	0 (0.0)	44 (83.0)	613 (93.3)
Gastric Ulcer	302 (92.9)	16 (100.0)	0 (0.0)	30 (96.8)	0 (0.0)	0 (0.0)	56 (87.5)	404 (92.7)
Preneoplastic lesions	83 (92.2)	2 (66.7)	0 (0.0)	23 (100.0)	0 (0.0)	0 (0.0)	10 (100.0)	118 (93.7)
GERD	70 (90.9)	0 (0.0)	0 (0.0)	19 (90.5)	0 (0.0)	0 (0.0)	8 (80.0)	97 (89.8)
Total	4,886 (93.1)	202 (93.5)	0 (0.0)	651 (94.9)	2 (100.0)	0 (0.0)	617 (90.1)	6,358 (93.0)
p-value	0.017	0.722	-	0.049	-	-	0.259	0.047
Quadruple-CAB								
Non-investigated Dyspepsia	274 (91.6)	219 (94.4)	2 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	25 (100.0)	524 (93.2)
Dyspepsia with normal endoscopy	455 (91.5)	2,069 (93.3)	157 (98.7)	0 (0.0)	0 (0.0)	31 (83.8)	92 (81.4)	2,804 (92.7)
Duodenal Ulcer	99 (96.1)	389 (91.3)	243 (99.2)*	0 (0.0)	0 (0.0)	3 (100.0)	31 (72.1)†	765 (93.3)
Gastric Ulcer	45 (97.8)	348 (94.3)	227 (96.2)†	0 (0.0)	1 (100.0)	3 (100.0)	10 (100.0)	634 (95.3)
Preneoplastic lesions	26 (86.7)	132 (91.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	49 (96.1)*	208 (91.6)
GERD	13 (86.7)	58 (89.2)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	72 (88.9)
Total	912 (92.1)	3,215 (93.1)	629 (98.0)	0 (0.0)	2 (100.0)	42 (87.5)	207 (85.5)	5,007 (93.1)
p-value	0.195	0.296	0.034	-	-	-	0.001	0.113

Table 1. Overall effectiveness (by modified intention-to-treat) of first-line treatment schemes.

A: Amoxicillin, B: Bismuth salts, C: Clarithromycin, GERD: gastroesophageal reflux disease, M: Metronidazole, Tc: Tetracycline. Group “Success” (*) or “Failure” (†) statistically significant.

Conclusion: In Europe, indications for *H. pylori* investigation could be improved in 5.6% of patients. Higher effectiveness was observed in patients treated for gastric or duodenal ulcers and preneoplastic lesions. Bismuth and non-bismuth quadruple therapies reached optimal results in almost all indications.

Disclosure: Dr. Samuel J. Martínez-Domínguez has served as a speaker for Juvisé. Dr. Ángel Lanas has served as a speaker for Juvisé. Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin, Biocodex, Juvisé and Richen. Dr. Nyssen has received research funding from Mayoly, Allergan, Diasorin, Biocodex, Juvisé and Richen.

MP428

EFFECTIVENESS AND SAFETY OF FIRST-LINE EMPIRICAL NON-BISMUTH CONCOMITANT THERAPY VERSUS SINGLE-CAPSULE BISMUTH QUADRUPLE THERAPIES IN SPAIN: ANALYSIS OF 12,000 PATIENTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, N. Montes², Á. Pérez-Aísa³, S.J. Martínez-Domínguez⁴, L. Rodrigo⁵, A.J. Lucendo⁶, J.M. Huguet⁷, J. Tejedor-Tejada⁸, A. Garre¹, L. Bujanda⁹, M. Pabón-Carrasco¹⁰, M. Castro-Fernández¹⁰, M. Perona¹¹, Ó. Núñez¹², B.J. Gómez Rodríguez¹³, A. Moreno Loro¹⁴, M. Soledad Marcos¹⁵, J. Barrio¹⁶, F. Bermejo¹⁷, J. Gomez-Camarero¹⁸, A. Keco-Huerta¹⁰, M. Planella¹⁹, M. Fernandez-Bermejo²⁰, E. Iyo²¹, P. Mata-Romero²², D. Martin-Holgado²², R. Pajares Villarroya²³, V. Flores²⁴, A.B. Pozo Blanco²⁵, B. Velayos²⁶, S. Montori²⁷, N. Alcaide²⁶, T. Angueira²⁸, E. Barreiro Alonso²⁹, L. Fernández-Salazar²⁶, A. Cuadrado³⁰, I. Pérez Valle³¹, B. Hermida Pérez³², M. Sánchez Alonso³³, P. Pazo Mejide³⁴, M. Jiménez-Moreno³⁵, E. Barba³⁶, E. Albéniz²⁷, L. Hernández³⁵, A. Cano-Catalá³⁷, P. Parra¹, L. Moreira³⁸, F. Megraud³⁹, C. O'Morain⁴⁰, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM),

and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Unidad de Metodología, IIS-Princesa; Servicio de Reumatología, Hospital Universitario de La Princesa; Plant Physiology, Pharmaceutical and Health Sciences Department, Faculty of Pharmacy, Universidad San Pablo-CEU, CEU-Universities, Boadilla del Monte, Spain, ³Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ⁴Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁵Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ⁶Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ⁷Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ⁸Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ⁹Department of Gastroenterology, Biodonostia Health Research Institute, Department of Medicine, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ¹⁰Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ¹¹Department of Gastroenterology, Hospital Quirón Marbella, Marbella, Spain, ¹²Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ¹³Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ¹⁴Department of Gastroenterology, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ¹⁵Department of Gastroenterology, Hospital 12 de Octubre, Madrid, Spain, ¹⁶Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ¹⁷Department of Gastroenterology, Hospital Universitario de Fuenlabrada, Fuenlabrada, Spain, ¹⁸Department of Gastroenterology, Hospital Universitario de Burgos, Burgos, Spain, ¹⁹Department of Gastroenterology, Hospital Universitari Arnau de Vilanova, Institut de Recerca Biomèdica de Lleida (IRBL), Lleida, Spain, ²⁰Hospital Parque San Francisco, Cáceres, Spain, ²¹Department of Gastroenterology, Hospital Comarcal de Inca, Inca, Spain, ²²Department of Gastroenterology, Hospital Universitario de Cáceres, Cáceres, Spain, ²³Department of Gastroenterology, Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain, ²⁴Department of Gastroenterology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ²⁵Department of Gastroenterology, Hospital Arnau Vilanova-Lliria, Valencia, Spain, ²⁶Department of Gastroenterology, Hospital Clínico de Valladolid, Valladolid, Spain, ²⁷Department of Gastroenterology, Hospital Universitario de Navarra, Navarrabiomed, Universidad Pública de Navarra, Pamplona, Spain, ²⁸Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain, ²⁹Department of Gastroenterology, Hospital Central de Asturias, Department of Pharmacology, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ³⁰Gastroenterology and Hepatology Department, Marqués de Valdecilla University Hospital, Clinical and Translational Research in Digestive Diseases, Valdecilla Research Institute (IDIVAL), Santander, Spain, ³¹Department of Gastroenterology, Hospital Central de Asturias, Oviedo, Spain, ³²Department of Gastroenterology, Hospital Valle del Nalón, Langreo, Spain, ³³Department of Gastroenterology, Hospital Universitario Santa Bárbara, Puertollano, Spain, ³⁴Department of Gastroenterology, Hospital Universitario de

Cruces, Barakaldo, Spain, ³⁵Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁶Department of Gastroenterology, Neurogastroenterology and Motility Unit, Hospital Clínic de Barcelona, University of Barcelona, Barcelona, Spain, ³⁷Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ³⁸Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ³⁹INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴⁰School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: The V Spanish Consensus Conference on *H. pylori* recommends as first-line treatment either a non-bismuth quadruple concomitant regimen (PPI, clarithromycin, amoxicillin, and metronidazole) for 14 days or a bismuth-containing quadruple therapy (PPI, bismuth, tetracycline, and metronidazole in a single-capsule) for 10 days. The superiority of one treatment over the other is currently not established.

Aims & Methods: To compare the effectiveness and safety of first-line empirical concomitant treatment versus bismuth quadruple therapy as single-capsule in Spain.

All treatment-naïve patients registered in AEG-REDCap in the Spanish cohort of the European *H. pylori* Registry (Hp-EuReg) from 2013 to 2023, treated with either concomitant therapy or the single-capsule, were evaluated. First, a set of pre-selected variables evaluated variations in prescriptions, observing significant differences in following: year of visit, geographical region, and patient age. Therefore, a propensity score analysis (SMR) was conducted and included in the multivariate logistic regression model to determine the modified intention-to-treat effectiveness (mITT) of both treatments. Additionally, a multivariate analysis with 10,000 bootstrap replicas was performed, balancing for geographical region and including associated variables.

Results: A total of 11,720 treatments were analysed: 6,293 (54%) with concomitant therapy (for 10 and 14 days) and 5,427 (46%) consisting of single-capsule (10 days). Concomitant therapy, both for 10 and 14 days, was associated with lower mITT effectiveness (88%; OR=0.53; [95% CI 0.43-0.66]; and 90%; OR=0.62; [0.53-0.73], respectively) compared to single-capsule therapy (93% mITT, $P<0.001$). Compliance (OR=6.81; [5.05-9.15]), presence of ulcer (OR=1.49; [1.17-1.91]), and central geographical region (OR=2.51 [1.94-3.29]) were the variables associated with greater eradication success ($P<0.001$). However, there was no demonstrated benefit of using high-dose (equivalent to 80 mg omeprazole twice daily) PPI compared to standard dose (equivalent to 40 mg omeprazole twice daily). Compliance was higher with single-capsule (98%) compared to 10- and 14-days concomitant therapy (both 97%). The incidence of adverse effects was lower with concomitant therapy for 10 days (25%) than for 14 days (33%); and the latter was significantly higher than with single-capsule (25%) ($P<0.0001$). Regarding serious adverse effects, 9 (0.1%) and 7 (0.1%) cases were reported with concomitant therapy and single-capsule therapy, respectively.

Conclusion: In Spain, bismuth-containing quadruple therapy prescribed as single-capsule is more effective and better tolerated than non-bismuth quadruple concomitant treatment.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

MOST FREQUENT *HELICOBACTER PYLORI* FIRST-LINE EMPIRICAL ERADICATION THERAPIES: DATA FROM THE LATIN AMERICAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-LATAMREG).

D. Reyes-Placencia¹, J.M. Remes-Troche², O. Laudanno³, W. Otero⁴, A. Piscoya⁵, G. Otoyá⁶, C. von Muhlenbrock⁷, J. Ramirez Garcia⁸, C. Campos Nuñez⁹, H. Cedron¹⁰, I. Hanna-Jairala¹¹, D. Cabrera Hinojosa¹², C. Vargas-Alayza¹³, W. Araujo-Gil¹³, P. Medel-Jara¹⁴, G. Latorre¹, J. Chahuán Abde¹, A. Arenas¹⁵, R. Candia¹, R. Mansilla-Vivar¹⁶, J.I. Vargas¹, F.J. Bosques Padilla¹⁷, E. Coss-Adame¹⁸, J.A. Velarde-Ruiz Velasco¹⁹, F. Higuera de la Tijera²⁰, M.S. Gonzalez Huevo²¹, R. Raña-Garibay²², A.R. Flores Rendon²³, O. Gomez-Escudero²⁴, J.K. Yamamoto-Furusho²⁵, E.I. Juárez Valdés²⁶, N. Ortiz-Olvera²⁷, M. Pizarro¹, F. Martinez²⁸, M.V. Binder²⁸, F. Silva²⁸, G. Ahumarán²⁹, P.C. Rodriguez³⁰, O.A. Bedini³¹, F. Ustares³², L. Otero³³, H. Marulanda⁴, E. Otero³³, A. Trespalcacios³⁴, A. Cano-Català³⁵, L. Moreira Ruiz³⁶, P. Parra³⁷, O. P. Nyssen³⁷, J. P. Gisbert³⁷, A.J. Riquelme Pérez³⁸

¹Pontificia Universidad Católica de Chile, Departamento de Gastroenterología, Facultad de Medicina, Santiago, Chile, ²Universidad Veracruzana, Veracruz, Mexico, ³Instituto Doctor Alfredo Lanari, Buenos Aires, Argentina, ⁴Universidad Nacional de Colombia, Bogota, Colombia, ⁵Hospital Guillermo Kaelin de la Fuente, Lima, Peru, ⁶Hospital Guillermo Almenara Irigoyen, Lima, Peru, ⁷Clinica Universidad de los Andes, Santiago, Chile, ⁸Clinica Liga contra el Cancer, Lima, Peru, ⁹Hospital Clinica Biblica, San Jose, Costa Rica, ¹⁰Clinica Anglo Americana, Lima, Peru, ¹¹Hospital Miguel Hilario Alcivar, Guayaquil, Ecuador, ¹²Hospital Nacional Dos de Mayo, Lima, Peru, ¹³Hospital de Chulucanas, Piura, Peru, ¹⁴Pontificia Universidad Católica de Chile, Programa de Doctorado en Epidemiología, Departamento de Salud Pública, Santiago, Chile, ¹⁵Clinica Alemana de Santiago - Universidad del Desarrollo, Departamento de Gastroenterologia, Santiago, Chile, ¹⁶Hospital de Puerto Montt - Universidad San Sebastian, Puerto Montt, Chile, ¹⁷Tecnologico de Monterrey, Monterrey, Mexico, ¹⁸Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Ciudad de Mexico, Mexico, ¹⁹Hospital Civil de Guadalajara, Guadalajara - Jalisco, Mexico, ²⁰Hospital General de México, Gastroenterology and Hepatology, Mexico City, Mexico, ²¹Instituto de Seguridad Social del Estado de Mexico y Municipios, Toluca, Mexico, ²²Hospital Español de Mexico, Ciudad de Mexico, Mexico, ²³Baja California Instituto de Seguridad y Servicios Sociales de los Trabajadores del Gobierno y Municipios del Estado de Baja California, Tijuana, Baja California, Mexico, ²⁴Hospital Angeles Puebla, Puebla, Mexico, ²⁵Hospital Medica Sur, Ciudad de Mexico, Mexico, ²⁶Hospital Juárez de México, Gastroenterología, Ciudad de Mexico, Mexico, ²⁷UMAE CMN Sigle XXI IMSS, Ciudad de Mexico, Mexico, ²⁸Pontificia Universidad Católica de Chile, Escuela de Medicina, Facultad de Medicina, Santiago, Chile, ²⁹Clinica Monte Grande, Buenos Aires, Argentina, ³⁰Instituto Modelo Cordoba, Cordoba, Argentina, ³¹Centro de Endoscopia Digestiva, Rosario, Argentina, ³²Sanatorio Lavalle, Jujuy, Argentina, ³³Centro de Gastroenterología y Endoscopía, Bogota, Colombia, ³⁴Pontificia Universidad Javeriana, Bogota, Colombia, ³⁵Fundacio Institut de Recerca i Innovacio en Ciencies de la Vida i de la Salut a la Catalunya Central, Vic, Spain, ³⁶Hospital Clinic de Barcelona, Gastroenterology, Barcelona, Spain, ³⁷Hospital Universitario de la Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid,

Spain, ³⁸Pontificia Universidad Católica de Chile, Departamento de Gastroenterología-CECAN: Centro para la prevención y el control del cáncer, Santiago, Chile

Contact E-Mail Address: diegoresplacencia@gmail.com

Introduction: In Latin America, the *Helicobacter pylori* infection is a common problem (prevalence of 47-63%)^{1,2}. There is limited information regarding the best approach for *Helicobacter pylori* infection management in Latin America.

Aims & Methods: Our aim was to describe the most frequent eradication therapies, their effectiveness, adherence, and safety.

A multicenter, prospective, international registry (Hp-LATAMReg; Hp-WorldReg partner) was conducted. Information about therapies used by gastroenterologists in seven countries (Argentina, Chile, Colombia, Costa Rica, Ecuador, Mexico, and Peru) from 2015 to 2024 was registered at e-CRF AEG-REDCap platform. The modified intention-to-treat (mITT) effectiveness, safety, and adherence were analysed for the first-line regimens. The length of the treatment and the proton pump inhibitor (PPI) dose prescribed were also evaluated.

Results: Overall, 2,511 patients were registered, of which 2,323 (93%) were treatment-naïve. The most commonly prescribed first-line therapies (n=2,216, 88%) were: standard clarithromycin-based triple therapy (PPI-amoxicillin-clarithromycin; n=801, 30%), PPI-clarithromycin-amoxicillin-metronidazole (n=369, 14%), dual therapy (PPI-amoxicillin; n=274, 10%), PPI-metronidazole-doxycycline-bismuth (n=201, 7.6%), PPI-metronidazole-tetracycline-bismuth (n=186, 7.1%), PPI-amoxicillin-metronidazole-bismuth (n=156, 5.9%), PPI-clarithromycin-amoxicillin-bismuth (n=119, 4.5%), and PPI-amoxicillin-levofloxacin (n=110, 4.2%). Most of those regimens (n=2,055, 93%) were optimized, that is prescribed for 14 days and almost 50% of the patients were administered high-dose PPIs (54 to 128 mg omeprazole equivalents b.i.d.) (n=967, 46%) with significant differences between schemes (p<0.01) (Table 1).

	Prescription (% , n)							
	PPI-C-A (27%, n=801)	PPI-C-A-M (15%, n=366)	PPI-A (11%, n=274)	PPI-M-Tc-B (7.3%, n=185)	PPI-C-A-B (4.2%, n=118)	PPI-A-M-B (6.7%, n=156)	PPI-A-L (3.7%, n=109)	PPI-M-D-B (7.9%, n=201)
mITT eradication rate (% , n) (p<0.01*)	75%, n=595	89%, n=327	88%, n=241	87%, n=160	79%, n=93	95%, n=148	74%, n=81	87%, n=172
Side effects rate (% , n) (p<0.01*)	35%, n=281	41%, n=151	7.3%, n=20	12%, n=23	18%, n=21	47%, n=72	20%, n=22	48%, n=97
Adherence rate (% , n) (p<0.01*)	98%, n=779	99%, n=363	98%, n=269	97%, n=181	98%, n=117	97%, n=152	99%, n=109	96%, n=193
High-dose PPIs use (% , n) (p<0.01*)	25%, n=192	31%, n=105	98%, n=267	73%, n=132	22%, n=25	65%, n=100	43%, n=44	52%, n=102
High-dose PPIs mITT cure rate (% , n) (p<0.01*)	69%, n=131	85%, n=88	88%, n=236	93%, n=123	72%, n=18	97%, n=97	77%, n=34	83%, n=85
14 days use (% , n) (p<0.01*)	89%, n=697	98%, n=358	99%, n=273	99%, n=184	95%, n=105	100%, n=156	90%, n=99	97%, n=195
14-days and high-dose PPIs use (% , n) (p<0.01*)	23%, n=185	26%, n=96	99%, n=266	71%, n=131	21%, n=25	64%, n=100	37%, n=40	49%, n=98
14-days and high-dose PPIs mITT cure rates (% , n) (p<0.01*)	74%, n=115	90%, n=84	89%, n=236	93%, n=122	72%, n=18	97%, n=97	80%, n=32	85%, n=83

Table 1. Effectiveness by modified intention-to-treat, safety, and compliance of first-line empirical therapy.

*Chi square test. mITT = modified intention to treat; PPI = Proton pump inhibitor; C = clarithromycin; A = amoxicillin; B = bismuth salts; M = metronidazole; L = levofloxacin; Tc = tetracycline; D = doxycycline; high-dose PPIs (54 to 128 mg omeprazole equivalents b.i.d.).

The first-line mITT overall effectiveness ranged from 74% to 95%, being the PPI-amoxicillin-metronidazole-bismuth the only therapy achieving optimal (90%) cure rates. However, when therapies were optimised (i.e.; 14 days and high-dose PPIs) the following also provided optimal (>90%) effectiveness: PPI-clarithromycin-amoxicillin-metronidazole (90%); PPI-metronidazole-tetracycline-bismuth (93%) and PPI-amoxicillin-met-

ronidazole-bismuth (97%). The dual therapy PPI-amoxicillin provided encouraging mITT results (89%) and had the lowest incidence rate of side effects (7.3%); whereas the highest was reported with PPI-metronidazole-doxycycline-bismuth (48%). Good adherence, defined as >90% of drug intake, was observed in 98% (n=2,163) of cases (Table 1).

Conclusion: In Latin America, bismuth quadruple therapy with PPI-amoxicillin-metronidazole-bismuth and optimized (14-day and high-dose PPIs) quadruple therapies either with PPI-clarithromycin-amoxicillin-metronidazole and PPI-metronidazole-tetracycline-bismuth provided optimal (>90%) effectiveness. Dual therapy with PPI-amoxicillin provided encouraging results (close to 90% cure rates) and had the lowest incidence rate of adverse events.

References: 1. Li Y, Choi H, Leung K, Jiang F, Graham DY, Leung WK. Global prevalence of *Helicobacter pylori* infection between 1980 and 2022: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2023 Jun;8(6):553–64.

2. Curado MP, de Oliveira MM, de Araújo Fagundes M. Prevalence of *Helicobacter pylori* infection in Latin America and the Caribbean populations: A systematic review and meta-analysis. *Cancer Epidemiol*. 2019 Jun;60:141–8.

Disclosure: Nothing to disclose.

MP430

AN UPDATE OF THE *HELICOBACTER PYLORI* DIAGNOSTIC TESTS AND INDICATIONS FOR TREATMENT FROM THE LATIN AMERICAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-LATAMREG)

D. Reyes-Placencia¹, J.M. Remes-Troche², O. Laudanno³, W. Otero⁴, A. Piscoya⁵, G. Otoyá⁶, C. von Muhlenbrock⁷, J. Ramirez Garcia⁸, C. Campos Nuñez⁹, H. Cedron¹⁰, I. Hanna-Jairala¹¹, D. Cabrera Hinojosa¹², C. Vargas-Alayza¹³, W. Araujo-Gil¹⁴, P. Medel-Jara¹⁴, G. Latorre¹, J. Chahuán Abde¹, A. Arenas¹⁵, R. Candia¹, R. Mansilla-Vivar¹⁶, J.I. Vargas¹, F.J. Bosques Padilla¹⁷, E. Coss Adame¹⁸, J.A. Velarde Ruiz Velasco¹⁹, F. Higuera de la Tijera²⁰, M.S. Gonzalez Huezo²¹, R. Raña-Garibay²², A.R. Flores Rendon²³, O. Gomez-Escudero²⁴, J.K. Yamamoto-Furusho²⁵, E.I. Juárez Valdés²⁶, N. Ortiz-Olvera²⁷, M. Pizarro²⁸, M. Bustamante²⁹, E. Dukes²⁹, F. Silva²⁹, G. Ahumarán³⁰, P.C. Rodriguez³¹, O.A. Bedini³², F. Ustares³³, L. Otero³⁴, H. Marulanda⁴, E. Otero³⁴, A. Trespalacios³⁵, A. Cano-Català³⁶, L. Moreira Ruiz³⁷, P. Parra³⁸, O. P. Nyssen³⁸, J. P. Gisbert³⁸, A.J. Riquelme Pérez³⁹, on behalf of the Hp-LATAMReg investigators.

¹Pontificia Universidad Católica de Chile, Departamento de Gastroenterología, Facultad de Medicina, Santiago, Chile, ²Universidad Veracruzana, Veracruz, Mexico, ³Instituto Doctor Alfredo Lanari, Buenos Aires, Argentina, ⁴Universidad Nacional de Colombia, Bogotá, Colombia, ⁵Hospital Guillermo Kaelin de la Fuente, Lima, Peru, ⁶Hospital Guillermo Almenara Irigoyen, Lima, Peru, ⁷Clinica Universidad de los Andes, Santiago, Chile, ⁸Clinica Liga contra el Cancer, Lima, Peru, ⁹Hospital Clinica Biblica, San Jose, Costa Rica, ¹⁰Clinica Anglo Americana, Lima, Peru, ¹¹Hospital Miguel Hilario Alcivar, Guayaquil, Ecuador, ¹²Hospital Nacional Dos de Mayo, Lima, Peru, ¹³Hospital de Chulucanas, Piura, Peru, ¹⁴Pontificia Universidad Católica de Chile, Programa de Doctorado en Epidemiología, Departamento de Salud Pública, Santiago, Chile, ¹⁵Clinica Alemana de Santiago - Universidad del Desarrollo, Departamento de Gastroenterología, Santiago, Chile, ¹⁶Hospital de Puerto Montt - Universidad San Sebastian, Puerto Montt, Chile, ¹⁷Tecnologico de Monterrey, Monterrey, Mexico, ¹⁸Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Ciudad de Mexico, Mexico, ¹⁹Hospital Civil de Guadalajara, Guadalajara - Jalisco, Mexico, ²⁰Hospital General de México, Gastroenterology and Hepatology, Mexico City, Mexico, ²¹Instituto de Seguridad Social del Estado de Mexico y Municipios, Toluca, Mexico, ²²Hospital Español de Mexico, Ciudad de Mexico, Mexico, ²³Baja California Instituto de Seguridad y Servicios Sociales de los Trabajadores del Gobierno y Municipios del Estado de Baja California, Tijuana, Baja California, Mexico, ²⁴Hospital Angeles Puebla, Puebla, Mexico, ²⁵Hospital Medica Sur, Ciudad de Mexico, Mexico, ²⁶Hospital Juárez de México, Gastroenterología, Ciudad de Mexico, Mexico, ²⁷UMAE CMN Sigle XXI IMSS, Ciudad de Mexico, Mexico, ²⁸Pontificia Universidad Católica de Chile, Department of Gastroenterology, Faculty of Medicine, Santiago, Chile, ²⁹Pontificia Universidad Católica de Chile, Escuela de Medicina, Facultad de Medicina, Santiago, Chile, ³⁰Clinica Monte Grande, Buenos Aires, Argentina, ³¹Instituto Modelo Cordoba, Cordoba, Argentina, ³²Centro de Endoscopia Digestiva, Rosario, Argentina, ³³Sanatorio Lavalle, Jujuy, Argentina, ³⁴Centro de Gastroenterología y Endoscopia, Bogotá, Colombia, ³⁵Pontificia Universidad Javeriana, Bogotá, Colombia, ³⁶Fundacio Institut de Recerca i Innovacio en Ciencies de la Vida i de la Salut a la Catalunya Central, Vic, Spain, ³⁷Hospital Clinic de Barcelona, Gastroenterology,

Barcelona, Spain, ³⁸Hospital Universitario de la Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ³⁹Pontificia Universidad Católica de Chile, Departamento de Gastroenterología-CECAN: Centro para la prevención y el control del cáncer, Santiago, Chile

Contact E-Mail Address: diegoreyesplacencia@gmail.com

Introduction: In Latin America, the *Helicobacter pylori* infection is a common problem (prevalence of 47-63%)^{1,2}. There is limited information regarding the best approach for *Helicobacter pylori* infection management in Latin America.

Aims & Methods: Our aim was to describe the *H. pylori* diagnostic tests and treatments' indications in Latin America.

A multicenter, prospective, international registry (Hp-LATAMReg; Hp-WorldReg partner) was conducted. Data were collected by gastroenterologists in seven countries (Argentina, Chile, Colombia, Costa Rica, Ecuador, Mexico, and Peru) from 2015 to 2024 and registered at e-CRF AEG-REDCap platform. The most frequent indications for treatment and diagnostic tests before and after eradication treatment were evaluated.

Results: Overall, 2,497 patients were registered, of which 1,680 (67%) were female. The mean (SD) age of the patients was 53 (14) years, with 1,087 patients (44%) from Mexico, 446 (18%) from Peru, 343 patients (14%) from Chile, 274 (11%) from Argentina, 200 (8%) from Colombia, 104 (4.2%) from Costa Rica, and 43 (1.7%) from Ecuador. Among those, 2,186 (88%) were treatment-naïve cases. The most frequent indications for treatment were non-investigated dyspepsia (n=995, 40%) and dyspepsia with normal endoscopy (n=690, 28%) (Table 1). The main *H. pylori* diagnostic methods before the eradication treatment were histology (n=1,642, 66%), rapid urease test (n=354, 14%) and ¹³C-urea breath test (UBT) (n=298, 12%). One diagnostic test was used in 2,471 (99%) cases, and 1,985 (80%) patients were diagnosed with invasive tests. To assess post-treatment eradication, the most frequent *H. pylori* diagnostics tests used were stool antigen monoclonal test (n=1,016, 41%), ¹³C-UBT (n=635, 25%) and ¹⁴C-UBT (n=516, 21%). There were statistical differences between the countries regarding the indication for treatment and the diagnostic methods before and after the eradication therapy.

Country	Argentina (n=274)	Chile (n=343)	Colombia (n=200)	Costa Rica (n=104)	Ecuador (n=43)	Mexico (n=1,087)	Peru (n=446)	Overall (n=2,497)
Indication of <i>Helicobacter pylori</i> eradication	p<0.001*							
Non- investigated dyspepsia	27 (9.9%)	45 (4.5%)	36 (18%)	2 (1.9%)	0 (0%)	700 (65%)	185 (42%)	995 (40%)
Dyspepsia with normal endoscopy	201 (74%)	202 (58%)	16 (8%)	15 (14%)	1 (2.3%)	33 (3%)	176 (39%)	644 (26%)
Duodenal Ulcer	13 (4.8%)	8 (2.3%)	5 (2.5%)	8 (7.7%)	1 (2.3%)	45 (4.1%)	9 (2%)	89 (3.6%)
Gastric Ulcer	13 (4.8%)	7 (5.1%)	13 (6.5%)	8 (7.7%)	7 (16%)	75 (6.9%)	14 (3.1%)	137 (5.5%)
Preneoplastic lesions	0 (0%)	2 (0.6%)	0 (0%)	19 (18%)	31 (67%)	67 (6.1%)	33 (7.4%)	152 (6.1%)
First-degree relatives of patients with gastric cancer	2 (0.7%)	12 (3.5%)	9 (4.5%)	10 (9.6%)	2 (4.7%)	19 (1.8%)	16 (3.6%)	70 (2.8%)
Screening to prevent gastric cancer	0 (0%)	0 (0%)	0 (0%)	1 (1%)	1 (2.3%)	17 (1.6%)	10 (2.2%)	29 (1.2%)
Other	6 (2.2%)	64 (19%)	109 (54%)	41 (39%)	0 (0%)	121 (11%)	2 (0.4%)	343 (14%)

Conclusion: This is an update³ of the first multicenter international registry on *H. pylori* management in Latin America (Hp-LATAMReg). There was marked heterogeneity between the countries regarding the main treat-

ment indications and the most frequently used diagnostic tests for *H. pylori* infection. The inclusion of more countries is necessary to improve the representativeness of the region.

References: 1. Li Y, Choi H, Leung K, Jiang F, Graham DY, Leung WK. Global prevalence of *Helicobacter pylori* infection between 1980 and 2022: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2023 Jun;8(6):553–64.

2. Curado MP, de Oliveira MM, de Araújo Fagundes M. Prevalence of *Helicobacter pylori* infection in Latin America and the Caribbean populations: A systematic review and meta-analysis. *Cancer Epidemiol*. 2019 Jun;60:141–8.

3. European *Helicobacter* and Microbiota Study Group (EHMSG). *Abstracts. Microb Health Dis* 2023; 5: e857. DOI: 10.26355/mhd_20239_857

Disclosure: Nothing to disclose.

MP431

H. PYLORI: BISMUTH QUADRUPLE THERAPY WITH DOXYCYCLINE IS AN EFFECTIVE THERAPY IN AN IRISH COHORT

C. Costigan^{1,2}, D. Scaiscia², M. Comerford², R. Whitmarsh³, G. Madders², J. O’Connell², O. Costigan², T. Butler¹, F. O’Hara², S. Ismail³, D. McNamara^{2,1}

¹Trinity College Dublin, Clinical Medicine, Dublin, Ireland, ²Tallaght University Hospital, Gastroenterology, Dublin, Ireland, ³Cavan & Monaghan Hospital, Department of Gastroenterology, Cavan, Ireland

Contact E-Mail Address: conorcostigan92@gmail.com

Introduction: There has been a reduction in the rate of successful eradication for *H. pylori* in recent years, which has been largely attributed to increasing antibiotic resistance to traditional therapies. In areas of high clarithromycin & metronidazole resistance such as ours, Bismuth Quadruple Therapy (BQT) is a recommended first line therapy. In Ireland BQT has only recently been adopted, with doxycycline rather than tetracycline being employed for reimbursement reasons.

Aims & Methods: We aimed to assess efficacy of BQT therapy for *H. pylori* eradication in an Irish cohort.

All patients testing positive for *H. pylori* via OGD or UBT in a 2 Irish tertiary centres were treated prospectively with BQT (Bismuth 120mg QDS, Metronidazole 400mg TDS, Doxycycline 100mg BD & Esomeprazole 40mg BD x 14 days) over a period of 8 months. Eradication was confirmed with UBT at least 4 weeks after cessation of therapy (A delta-over-baseline >4% was considered positive) or by stool antigen testing, as available. Patient demographics and treatment outcomes were recorded, analysed and controlled for basic demographics and prior *H. pylori* treatment

Results: To date 122 BQT-treated patients with post-eradication testing were identified, 60(49%) female, mean age 50 years, 99 (80%) patients were treatment-naïve. Overall, 108 (89%) had successful *H. pylori* eradication. There was no association between successful eradication and age or gender (p= 0.1546 and 0.0336 respectively).

BQT first line treatment success was significantly higher than for subsequent treatments (92/99) 93% versus (16/23) 70% OR 5.7, 95%CI 1.7 – 18.6, p <0.00 3. Neither age nor gender were significant predictors of outcome (p=0.0594)

Conclusion: BQT as first line therapy for *H. pylori* infection is highly effective in a high dual resistance population. Doxycycline substitution for tetracycline still achieved > 90% eradication. BQT as second line treatment as expected performed less well, and should no longer despite the complicated regime be reserved for rescue therapy.

Disclosure: Nothing to disclose.

MP432

EFFICACY AND SAFETY OF POTASSIUM COMPETITIVE ACID BLOCKER BASED THERAPIES VS PROTON-PUMP INHIBITOR BASED THERAPIES IN H. PYLORI ERADICATION: A META-ANALYSIS

M. Soriano¹, M. Baldeo¹, M.L. Sy-Janairo¹, E. Aguila¹

¹St Lukes Medical Center, Taguig, Philippines

Contact E-Mail Address: mybaldeo@stlukes.com.ph

Introduction: H. pylori infection has affected approximately 50% of the world's population with the rates being higher in developing countries than in developed ones. Conventional proton-pump inhibitors (PPIs) have been used as first-line treatment for this condition. However, potassium competitive acid blockers (PCABs) were recently developed which may offer beneficial effects than PPIs.

Aims & Methods: This meta-analysis aims to assess the effectiveness of Potassium competitive acid-blocker against Proton pump inhibitors for the eradication of H. pylori among adults with H. pylori infection.

Electronic search of randomized controlled trials comparing H pylori eradication rate of P-CAB and PPI-based therapy was done. Quality assessment used the Modified Cochrane risk-of-bias tool, and statistical analysis was performed using ReviewManager 5.4.1

Results: Fifteen RCTs with 4129 participants who received H pylori eradication therapy comparing potassium competitive acid blockers (Tegoprazan, Vonoprazan, and YH808) with proton pump inhibitors were analyzed. H. pylori eradication rate of potassium competitive acid blocker-based therapy was higher than that of PPI-based triple therapy RR 1.04, CI 1.10-1.18, P < 0.05.

Subgroup analysis showed that PCABs based regimens had significantly higher eradication rates than PPI in treatment naive patients (RR 1.14, 95% CI 1.1-1.18, pP < 0.05) and that Vonoprazan based regimen in particular had superior eradication rates compared to PPI based regimens (RR 1.16 95% CI 1.12-1.20 P < 0.05).

No significant differences were seen between the Tegoprazan and YH4808 groups compared to the PPI group. Adverse events were also lower in the PCAB group compared to the PPI group.

Conclusion: A significant challenge that is being faced by current PPIs include nocturnal acid reflux despite treatment with twice daily PPI, and additional dosage of H2-receptor blocker at bedtime which deters successful control of gastritis under PPI treatment.

Our study shows that potassium competitive acid blockers are effective and have significantly higher eradication rates compared to PPI, with lower incidence of adverse events.

References: Yu, K. et al. (2020). Randomized clinical trial: tegoprazan, a novel potassium competitive acid blocker or lansoprazole in the treatment of gastric ulcer. *Aliment Pharmacol Ther.* 2020 Sept;52(5):789-797
Tan, N. et al. (2023). Efficacy and safety of keverprazan compared with lansoprazole in the treatment of duodenal ulcer: a phase III, randomized double blind multicenter trial. *Clinical and Translational Gastroenterology.* 2023 Jul; 14(7)

Kim, J. et al. (2023). Efficacy of tegoprazan-based bismuth quadruple therapy compared with bismuth quadruple therapy for Helicobacter pylori infection: A randomized, double-blind, active-controlled study. *Helicobacter.* 2023 June; 28(3)

Zhou, S. et al. (2023). Keverprazan, a novel potassium-competitive acid blocker: Single ascending dose safety, tolerability, pharmacokinetics, pharmacodynamics and food effect in healthy subjects. *European Journal of Pharmaceutical Sciences* 190(1)2023;2-12

Zhou, B. et al. (2023). Vonoprazan-amoxicillin dual therapy for Helicobacter pylori eradication: A systematic review and meta-analysis of randomized controlled trials. *Saudi J Gastroenterol.* 2023 Nov-Dec; 29(6): 347-357.

Yang, C. et al. (2022). Effectiveness and safety of vonoprazan-based regimen for Helicobacter pylori eradication: A meta-analysis of randomized clinical trials. *J Clin Pharm Ther.* 2022 Jul;47(7):897-904

Disclosure: authors have no conflict of interest.

MP433

PRESCRIPTIONS AND EFFECTIVENESS OF 3,351 EMPIRICAL RESCUE THERAPIES ON THIRD AND SUBSEQUENT LINES: DATA FROM THE EUROPEAN REGISTRY ON HELICOBACTER PYLORI MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, M. Pavoni², A. Garre¹, D. Boltin³, Á. Pérez-Aísa⁴, L. Rodrigo⁵, L. Jonaitis⁶, P.S. Phull⁷, S.J. Martínez-Domínguez⁸, I. L. P. Beales⁹, J. Barrio¹⁰, L. Bujanda¹¹, V. Milivojevic¹², A.J. Lucendo¹³, J.M. Huguet¹⁴, B. Tepeš¹⁵, F. Lerang¹⁶, M. Pabón-Carrasco¹⁷, G. Losurdo¹⁸, M. Areia¹⁹, M. Castro-Fernández¹⁷, P. Bogomolov²⁰, J. Gomez-Camarero²¹, J. Tejedor-Tejada²², M. Denkovski²³, A. Gasbarrini²⁴, B.J. Gómez Rodríguez²⁵, P. Mata-Romero²⁶, F. Bermejo²⁷, D. Martín-Holgado²⁶, G.M. Buzás²⁸, A. Keco-Huerta¹⁷, M. Domínguez Cajal²⁹, M. Perona³⁰, Ó. Núñez³¹, I. Voynovan³², S. D Georgopoulos³³, L. Hernández³⁴, J. Kupcinkas⁶, R. Marcos-Pinto³⁵, D.S. Bordin³⁶, V. Papp³⁷, M. Leja³⁸, T. Rokkas³⁹, A. Cano-Català⁴⁰, P. Parra¹, L. Moreira⁴¹, F. Megraud⁴², C. O'Morain⁴³, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ³Department of Gastroenterology, Rabin Medical Center, Tel Aviv University, Tel Aviv, Israel, ⁴Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ⁵Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ⁶Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania, ⁷Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom, ⁸Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁹Norwich Medical School, University of East Anglia, Norwich, United Kingdom, ¹⁰Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ¹¹Department of Gastroenterology, Biodonostia Health Research Institute, Department of Medicine, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ¹²Clinical Center of Serbia and School of Medicine, University of Belgrade, Belgrade, Serbia, ¹³Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ¹⁴Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ¹⁵Department of Gastroenterology, DC Rogaska, Rogaska Slatina, Slovenia, ¹⁶Østfold Hospital Trust, Grålum, Norway, ¹⁷Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ¹⁸Department of Gastroenterology, Department

of Precision and Regenerative Medicine and Ionian Area, University of Bari, Bari, Italy, ¹⁹Department of Gastroenterology, Portuguese Oncology Institute of Coimbra, Faculty of Medicine of the University of Porto (FMUP), Center for Health Technology and Services Research (CINTESIS), Coimbra, Portugal, ²⁰Universal Clinic Private Medical Center, Moscow, Russian Federation, ²¹Department of Gastroenterology, Hospital Universitario de Burgos, Burgos, Spain, ²²Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ²³Interni oddelek, Diagnostic Centre, Bled, Slovenia, ²⁴Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ²⁵Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ²⁶Department of Gastroenterology, Hospital Universitario de Cáceres, Cáceres, Spain, ²⁷Department of Gastroenterology, Hospital Universitario de Fuenlabrada, Fuenlabrada, Spain, ²⁸Department of Gastroenterology, Ferencváros Health Center, Budapest, Hungary, ²⁹Department of Gastroenterology and Hepatology, Hospital Universitario San Jorge, Huesca, Spain, ³⁰Department of Gastroenterology, Hospital Quirón Marbella, Marbella, Spain, ³¹Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ³²A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ³³Athens Medical, P. Faliron General Hospital, Athens, Greece, ³⁴Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁵Gastroenterology Department, Centro Hospitalar do Porto, Universidade do Porto, Instituto De Ciências Biomédicas de Abel Salazar, Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal, ³⁶Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow clinical scientific center, Department of outpatient therapy and family medicine, Tver State Medical University, Department of propaedeutic of internal diseases and gastroenterology, Russian University of Medicine, Moscow, Russian Federation, ³⁷Department of Surgery, Transplantation and Gastroenterology, Semmelweis University, Budapest, Hungary, ³⁸Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia, ³⁹Gastroenterology Clinic, Henry Dunant Hospital, Athens, Greece, ⁴⁰Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ⁴¹Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ⁴²INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴³School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es
Introduction: *Helicobacter pylori* treatment's effectiveness decreases as treatment eradication attempts fail.
Aims & Methods: To evaluate the use and effectiveness of empirical rescue therapies on third and subsequent lines, in Europe.
Sub-study of the the European Registry on *H. pylori* Management (Hp-Eu-Reg), an international, multicenter, prospective, non-interventionist registry starting in 2013 aiming to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists (38 countries, 400 researchers). All infected adult patients were systematically registered at AEG-REDCap e-CRF until December 2023, all cases with three or more

eradication attempts were extracted. Only the empirically prescribed therapies were considered. Effectiveness was analysed by modified intention-to-treat (mITT) and per protocol (PP). Data were subject to quality review.
Results: In total, 3,351 rescue treatments were included: 2,349, 688, 228 and 86 in third-, fourth-, fifth- and sixth-line treatments, respectively. Mean age was 51 years, 68% of patients were women and 5.3% were allergic to penicillin. Sixty-eight different treatment schemes were used, being the three-in-one single-capsule bismuth quadruple therapy the most commonly prescribed (Table). Overall effectiveness was 73% by mITT, and 74% by PP analyses. Bismuth quadruple therapy as single-capsule provided the highest mITT overall cure rate (84%) and achieved 87% when optimised with high-dose PPIs ($p>0.05$). Quadruple PPI-bismuth-tetracycline-metronidazole achieved optimal eradication rate (91% by mITT), only when high-dose PPIs and 14-day prescriptions were used. The use of doxycycline instead of tetracycline was associated with lower eradication rates in classical bismuth quadruple therapies ($p<0.05$).

Rescue therapy	Use, N (%)	n	Modified intention-to-treat	n	Per-protocol
			Effectiveness, % (95% CI)		Effectiveness, % (95% CI)
PPI-Single capsule B-Tc-M	796 (25%)	741	84 (81-87)	718	85 (83-88)
Triple PPI-A-L	486 (15%)	380	80 (76-84)	374	81 (77-85)
Triple PPI-A-R	363 (11%)	317	70 (65-75)	309	71 (66-76)
Quadruple PPI-A-L-B	275 (8.7%)	246	74 (69-80)	239	75 (70-81)
Quadruple PPI-B-Tc-M	243 (7.7%)	230	68 (62-74)*	222	69 (63-75)
Quadruple PPI-C-A-M	147 (4.7%)	137	65 (57-73)	134	66 (57-74)
Quadruple PPI-B-D-M	120 (3.8%)	116	63 (54-72)	112	63 (54-73)
Triple PPI-C-A	75 (2.4%)	66	59 (46-72)	64	59 (47-72)
Triple PPI-A-M	68 (2.2%)	61	59 (46-72)	59	59 (46-73)
Overall	3,161 (100%)	2,964	73 (71-74)	2,875	74 (72-76)

mITT, modified intention-to-treat; PP, per-protocol; N, total number of patients analysed; 95% CI - confidence interval; PPI, Proton Pump Inhibitor; A, amoxicillin; B, bismuth; C, clarithromycin; D, doxycycline; L, levofloxacin; M, metronidazole; Tc, tetracycline; R, rifabutin; *, achieved over 90% effectiveness when optimised (high-dose PPIs and 14-days length).

Table 1. Effectiveness of the most frequently prescribed empirical therapies on third and subsequent treatment lines.

Conclusion: Empirical rescue treatments in third and subsequent lines obtain, in general, suboptimal eradication rates in Europe; however, bismuth quadruple therapy as single-capsule obtained encouraging results. Only the optimised bismuth quadruple therapy achieved $\geq 90\%$ effectiveness.
Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.
Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

Dysphasia: Diagnostics and therapeutics

14:30-15:30 / Poster Stage 6

MP434

DEVELOPMENT OF A QUESTIONNAIRE FOR 'INABILITY TO BELCH' AND FIRST EVALUATION AGAINST HIGH RESOLUTION IMPEDANCE MANOMETRY WITH BELCH PROVOCATION TEST

K. Raymenants¹, T. Guedens¹, J. Arts^{1,2}, Y. Kjöller³, H. Van Gucht³, M. Mukherjee³, N. Rommel⁴, T. Vanuytsel¹, J. Tack¹
¹UZ Leuven, KU Leuven, Translational Research Center for Gastrointestinal Disorders, Department of Neurogastroenterology and Motility, Leuven, Belgium, ²AZ Sint-Lucas Brugge, Gastroenterology and Hepatology, Brugge, Belgium, ³UZ Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ⁴University of Leuven, Department of Neurosciences, Leuven, Belgium

Contact E-Mail Address: karlienraymenants@gmail.com

Introduction: 'Inability to Belch', also called retrograde cricopharyngeal dysfunction (R-CPD), is a syndrome characterized by inability or impaired ability to belch, gurgling noises from the chest or lower neck, thoracic or abdominal pain, bloating and flatulence (1). Although awareness of the disorder is increasing, little is known about its cause, characteristics or epidemiology.

Besides recognition of typical symptoms, high resolution impedance manometry (HRIM) is increasingly used to confirm the diagnosis in suspected cases (2, 3).

Aims & Methods: Our aim was to design a diagnostic questionnaire based on the cardinal symptoms, and to validate this questionnaire against the only available objective diagnostic tool at present, i.e. HRIM with belch provocation test (sparkling water) (2, 3).

The questionnaire was developed based on medical history taking of patients that presented to our center with 'inability to belch' (4). Fifteen symptoms were included: inability to belch, gurgling noises, thoracic pain, abdominal pain, nausea, fullness, early satiety, bloating, flatulence, heartburn, regurgitation, frequent or painful hiccups, dysphagia, and difficulty to vomit.

These were questioned for frequency, severity, bothersomeness and the trigger or timing at which they occurred. A first draft of the questionnaire was evaluated in a cognitive debriefing of the first three R-CPD patients, after which some clarifying changes were made.

Subsequently, the questionnaire was filled out during HRIM prospectively by R-CPD and control patients, each of whom underwent belch provocation test as described by our group (3).

Wilcoxon signed rank test was used to compare between groups. A logistic model was used to compute probabilities with their 95% confidence interval (CI).

Results: The questionnaire was completed by 17 patients reporting inability to belch, and 47 control patients, during HRIM with belch provocation test. In 13 out of 17 patients (sensitivity 76%, positive likelihood ratio of HRIM: 8.44), R-CPD was confirmed with typical findings on HRIM. The indication for HRIM in control patients was GERD (n=27), dysphagia (n=9), chest pain (n=3), known achalasia (n=2), belching (n=1), globus (n=1) and dyspepsia (n=1). In the control patient group, 4 patients were excluded from further analysis because of abnormalities on HRIM similar to R-CPD (specificity 91%, negative likelihood ratio: 0.26).

Using HRIM as a gold standard, we identified the following questions that were significantly different in R-CPD patients vs. controls: frequency of inability to belch ($p < 0.001$, probability of abnormal HRIM when present: 0.6000 CI 0.380:0.786), gurgling noises ($p = 0.0019$, probability when present 0.4000, CI 0.230:0.597), and dysphagia ($p = 0.003$, probability when present 0.065, CI 0.016:0.022). Even though these symptoms were often

present in R-CPD, chest pain, abdominal pain, nausea, fullness, early satiety, bloating, heartburn, regurgitation, hiccups and vomiting did not differ significantly between both patient groups.

Conclusion: We designed a diagnostic questionnaire to help identifying R-CPD. Based on a comparison between R-CPD patients with a control population with a variety of upper motility disorders, the presence of 'inability to belch', gurgling noises; and the absence of dysphagia were significantly different between R-CPD patients and controls.

Pending further validation, this questionnaire provides a basis for developing a scoring system for patients with 'inability to belch' and it can be used to explore the epidemiology of this peculiar syndrome.

References: 1. Bastian RW, Smithson ML. Inability to Belch and Associated Symptoms Due to Retrograde Cricopharyngeus Dysfunction: Diagnosis and Treatment. *OTO Open*. 2019;3(1):2473974x19834553.

2. Oude Nijhuis RAB, Snelleman JA, Oors JM, Kessing BF, Heuveling DA, Schuitmaker JM, et al. The inability to belch syndrome: A study using concurrent high-resolution manometry and impedance monitoring. *Neurogastroenterol Motil*. 2022;34(5):e14250.

3. Karlien Raymenants FV, Stijn Arnaert, Jan Tack, Tim Vanuytsel, Filip Baert, Lieve Delsupehe, Joris Arts Manometric diagnosis and treatment of retrograde cricopharyngeus dysfunction (R-CPD). *United European Gastroenterology Journal*. 2023;11.

4. Arnaert S, Arts J, Raymenants K, Baert F, Delsupehe K. Retrograde Cricopharyngeus Dysfunction, a New Motility Disorder: Single Center Case Series and Treatment Results. *J Neurogastroenterol Motil*. 2024;30(2):177-83.

Disclosure: Nothing to disclose.

MP435

SYMPATHETIC AROUSAL IS DIFFERENT IN RESPONSE TO MENTAL STRESS IN PATIENTS WITH GLOBUS PHARYNGEUS COMPARED TO HEALTHY CONTROLS

P. Liptak¹, I. Tonhajzerova², Z. Visnovcova³, N. Ferencova³, J. Hoferica¹, M. Ďuriček⁴, P. Banovcin⁴

¹University Hospital in Martin, Clinic of Internal Medicine-Gastroenterology, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia, ²Jessenius Faculty of Medicine in Martin, Comenius University, Department of Physiology, Martin, Slovakia, ³Jessenius Faculty of Medicine in Martin, Comenius University, Biomedical Centre Martin, Martin, Slovakia, ⁴Jessenius Faculty of Medicine, University Hospital in Martin, Clinic of Internal Medicine - Gastroenterology, Martin, Slovakia

Contact E-Mail Address: liptak@jfm.uniba.sk

Introduction: Globus pharyngeus is one of the more common Disorder of Gut Brain Interaction (DGBIs). The pathophysiological mechanisms of DGBIs are complex. However, data considering possible cause of globus pharyngeus are scarce. Accumulating evidence indicates that autonomic dysregulation contributes to DGBI but whether this is true for globus is still unknown. The symptoms are often triggered by stress associated with sympathetic overexcitation, however, the mechanisms of sympathetically linked regulation in these disorders, especially in response to stress are incompletely understood.

Aims & Methods: The aim of this study was to assess potential changes of cognitive stress-related sympathetic regulation of different effector responses (skin conductance and alpha-adrenergic vasomotor activity) in patients suffering from globus pharyngeus. Studied population included 15 patients diagnosed with globus and 12 sex- and age-matched healthy controls. All patients were diagnosed according to ROME IV criteria for Dis-

orders of gut brain interaction. Continuous electrodermal activity (EDA) was recorded with sampling frequency of 256 Hz (required by hardware) (FlexComp Infinity Biofeedback, Thought Technology, Canada). The EDA signal was monitored by two dry, Ag-AgCl, bipolar electrodes placed on the middle phalanges of two fingers on the left (non-dominant) hand, and continuous “beat-to-beat” blood pressure (BP) was recorded using Finometer MIDI (FMS, Netherlands) during complex stress response: rest - mental arithmetic test - recovery. Each period lasted 5 minutes. Evaluated parameters: 1) spectral power in low-frequency band of systolic BP variability (LF-SBP) reflecting sympathetic alpha-adrenergic stimulation of vascular smooth muscles, 2) skin conductance level (SCL) calculated as a mean of tonic EDA reflecting sympathetic cholinergic regulation and emotional arousal in response to cognitive stress. Moreover, reactivity of both parameters was calculated.

Results: LF-SBP (reflecting sympathetic function) was normal at baseline, but significantly increased in response to mental arithmetic test in globus group compared to controls ($p < 0.001$), but in recovery phase LF-SBP parameter was without significant between-group changes. Surprisingly, no differences were found in SCL parameter during complex stress response. Reactivity of both parameters was similar and without significant changes.

Conclusion: Our results revealed significantly increased LF-SBP indicating alpha-adrenergic vasomotor overactivity during cognitive stressor associated with a return to basal values in patients with globus pharyngeus compared to controls. In contrast, EDA was without between-group changes during all phases of stress response which may point to remaining emotional and sympathetic arousal in patients with globus pharyngeus. These findings revealing subtle and discrete abnormalities in alpha-adrenergic sympathetic regulatory network evoked only by cognitive stress and can contribute to clarifying the pathomechanisms and psychophysiological pathways leading to sympathetic and emotional dysregulation in patients with globus pharyngeus. We believe that this represents a fundamental step for personalized and specific non-invasive therapy in patients with globus pharyngeus such as biofeedback.

Support: Slovak Scientific Grant Agency [VEGA 1/0048/24]

Disclosure: Nothing to disclose.

MP436

MANAGEMENT IN PRIMARY CARE OF PATIENTS UNDER 50 PRESENTING WITH SYMPTOMS OF FOOD BOLUS OBSTRUCTION OR DYSPHAGIA

N. Umar¹, C. Turnbull², R. Jazrawi³, N. Trudgill¹

¹Sandwell and West Birmingham Hospitals NHS Trust, Gastroenterology, West Bromwich, United Kingdom, ²Dr. Falk Pharma GmbH, Bourne End, United Kingdom, ³Dr. Falk Pharma UK Ltd., Medical, Bucks, United Kingdom

Contact E-Mail Address: nosheen.umar@nhs.net

Introduction: Symptoms of dysphagia are common in the community and younger patients may not be referred for endoscopy if symptoms are not suggestive of malignancy. We have examined the management of patients under 50 with dysphagia in primary care.

Aims & Methods: Retrospective study using primary care data (Clinical Practice Research Datalink AURUM) linked to hospital admission data (Hospital Episode Statistics) between 2010 and 2022. All patients 18-50 years presenting in primary care with dysphagia or food bolus obstruction were studied. Patients with upper gastrointestinal (UGI) cancers were excluded. Referral rates for OGD and biopsy and proton pump inhibitor (PPI) prescription were examined. Patient level factors associated with referral rates within 1 year of symptom onset and PPI prescription within 30 days of a symptom record in primary care were studied using Robust Poisson regression models.

Results: Of 59,878 symptomatic patients, 98.2% had dysphagia and 1.8% had food bolus obstruction (median age 39 (IQR 30-46) years; 57.7% female). 7871 (3.2%) patients with UGI cancer were excluded. Of 696 diagnosed eosinophilic oesophagitis patients (1.2%), 92% presented with dysphagia and 8% with food bolus obstruction. 12,341 (21%) of patients with dysphagia and 248 (23.6%) of patients with FBO were not referred for endoscopy or gastroenterology assessment and simply prescribed a PPI. Factors associated with not being referred included: younger age adjusted relative risk 0.62, 95% CI 0.61-0.64, comparing 47-50 years (4th quartile) to 18-30 (1st quartile); black ethnicity 1.06, 1.03-1.09; and PPI prescription 1.09, 1.08-1.11. Factors associated with PPI prescription after dysphagia presentation included: increasing age adjusted relative risk 1.66, 1.60-1.73, comparing 47-50 years (4th quartile) to 18-30 (1st quartile); increasing deprivation 1.05, 1.01-1.10; smoking 1.05, 1.01-1.08; obesity 1.22, 1.18-1.26; and asthma 1.13, 1.10-1.16.

Factors associated with not being referred for food bolus obstruction included: black ethnicity 1.35, 1.16-1.58; a history of atopy 1.20, 1.08-1.32; and PPI prescription 1.43, 1.31-1.56. Endoscopy was performed in only 33% of patients with a FBO presentation in primary care, of which 62% had oesophageal biopsies taken.

Conclusion: In patients <50 presenting in primary care, 66% of food bolus obstruction and 67% of dysphagia patients were not referred for endoscopy despite risk factors for eosinophilic oesophagitis including atopy or asthma, representing a missed opportunity to diagnose eosinophilic oesophagitis. 24% of food bolus obstruction and 21% of dysphagia patients were just treated with a PPI without further investigation.

Disclosure: Nothing to disclose.

MP437

THE CHARACTERISTICS OF RAPID DEVELOPMENT ACHALASIA COMPARED TO LONGSTANDING ACHALASIA

A. Kurosugi¹, T. Matsumura¹, M. Sonoda¹, S. Takahashi¹, T. Kaneko¹, K. Okimoto¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Chiba, Japan

Contact E-Mail Address: akanekurosugi1125@chiba-u.jp

Introduction: Achalasia is an esophageal motility disorder associated with impaired relaxation and peristalsis of the lower esophageal sphincter (LES). Although it has been reported to be associated with autoimmune diseases, viral infections, and eosinophilic esophagitis, the cause has not yet been elucidated. The course of the achalasia is also unknown. Although it was thought to be a longstanding disease, the existence of rapid development achalasia associated with SARS-CoV-2 infection has been reported recently [1][2]. This suggests that the progression pattern may be different depending on its underlying cause.

Aims & Methods: The aim of this study was to investigate the characteristics of the development of achalasia to find new insights into the cause and course of the disease. A total of 148 patients diagnosed with achalasia by high-resolution manometry (HRM) were included in this study. Questionnaires and medical records were reviewed to assess initial symptoms, progression patterns, and comorbidities. The relationships between HRM results and progression way of symptoms were also investigated. Rapid development was defined as a case in which a progressive course within few weeks was clearly answered.

Results: The type of achalasia was Type I in 79 cases, Type II in 56 cases, and Type III in 13 cases. Median age at onset was 45 (range 32-64), median age of diagnosis was 53 (range 40-72), and sex ratio (M:F) was 73:75. The mode of onset of symptoms was rapid development in 38 patients (25.7%), longstanding in 92 (62.2%), and unknown in 18 (12.1%). Among

the rapid development cases, three cases presented anhidrosis at the same time, which was significantly more than longstanding type (8% vs 0%, $P=0.02$, Fisher's exact test). Two cases of anhidrosis in this study were diagnosed as autoimmune autonomic ganglionopathy in which viral infection suggested involvement [3]. No significant differences were observed in progression patterns, resting LES pressure or IRP.

Conclusion: Achalasia may exhibit either rapid development or longstanding progression. Unlike longstanding cases, rapid development cases exhibited potential associations with anhidrosis in some cases. Although further case accumulation is needed, the results suggest that rapid growth achalasia may have a distinctive background such as anhidrosis compared to longstanding achalasia.

References: 1. Samo S, Hamo F, Hamza A, et al. Rapid Development of Achalasia After SARS-CoV-2 Infection: PCR Analysis of Esophageal Muscle Tissue. *Am J Gastroenterol*. 2024; Online ahead of print

2. Wasim AU, Khan MW, Khan OA, et al. Acute-Onset Achalasia Following a Recent COVID-19 Infection: A Case Report. *Cureus*. 2023;15:e38803.

3. Nakane S, Mukaino A, Higuchi O, et al. A comprehensive analysis of the clinical characteristics and laboratory features in 179 patients with autoimmune autonomic ganglionopathy. *J Autoimmun* 2020;108:102403.

Disclosure: Nothing to disclose.

MP438

EVALUATION OF DIET AND EATING HABITS IN PATIENTS WITH ESOPHAGEAL ACHALASIA

A. Cesarini¹, G. Scalese¹, E. Ribichini¹, C. Mocci¹, D. Badiali¹

¹Sapienza University, Departement of Traslational and Precision Medicine, Rome, Italy

Contact E-Mail Address: chiaramocci94@gmail.com

Introduction: Esophageal Achalasia (EA) is a rare esophageal motility disorder, characterized by impaired peristalsis and incomplete relaxation of the Lower Esophageal Sphincter (LES) in response to swallowing. Key symptoms of the disease include dysphagia, food regurgitation, and retrosternal pain, significantly impacting the quality of life (QoL) and often leading patients to restrict their food intake. Consequently, EA patients often adopt self-managed dietary practices that may result in nutritional imbalances and deficiencies, given the lack of specific dietary guidelines.

Aims & Methods: This retrospective study aimed to describe and evaluate the dietary patterns, eating habits, and nutritional status of achalasic patients. Additionally, the secondary aim was to explore potential associations between food rheology and symptomatology. Patients with a manometric diagnosis of EA were recruited from our outpatient gastrointestinal pathophysiology center. Disease severity was assessed with Eckardt Symptoms Score (ESS), symptoms were evaluated with Modular Questionnaire Roma IV and QoL with the MD Anderson Dysphagia Inventory (MDADI). The MDADI outcomes were stratified into severe, moderate, mild and not perceived disability. Patients also filled out a food diary for 15 days, recording ingested food for each meal and symptoms onset. Estimated caloric intake and macronutrient composition were compared to those recommended by the Italian Society of Human Nutrition (SINU).

Results: Forty-three achalasic patients were included (M 24, F 19, mean age 56.7 ± 15.8 yrs). The median BMI was 23.7 (18.8-32.2), 34 patients (79%) had an active disease (ESS ≥ 3). Most patients reported mild to moderate disability (respectively 42% and 35%), while 21% reported severe disability and 2% perceived no disability. Disease activity, measured by ESS, strongly correlated with perceived disability ($r=0.59$; $p<0.0001$), while no significant correlation was found between ESS and BMI. The diary analysis showed a mean caloric intake of 1572±373 kcal versus the estimated needs of 2293,71±374 kcal based on anthropometric parameters

and physical activity, resulting in a mean caloric deficit of 720 ± 416 kcal ($p<0.0001$). Macronutrient analysis also reported an unbalanced distribution: carbohydrates 43.3%±7.3 vs recommended 55-59%, protein 18.2%±4.5 vs 15-18%, total fat 37.6%±7.7 vs 26-27% and fibre 14g±5.2 vs 25-30g. Solid food caused significantly more symptoms than semiliquid and liquid ones: dysphagia (35.5% vs 3.5% vs 5.7%, $p<0.0001$), chest pain (10% vs 12.1% vs 0.2%, $p<0.0001$), regurgitation (8.9% vs 1.4% vs 1.9%, $p=0.001$), cough (5% vs 0.2% vs 0.6%, $p=0.0002$). Bread, pasta, and pizza (50-60%), fresh fruit (44%), lean meat (39.5%), crackers, snacks, and vegetables (30-35%) were the most commonly reported triggers of dysphagia. Additionally, 60% of patients reported worsened symptoms with cold foods, while 53% reported improvement with hot foods.

Conclusion: This study underscores the significant impact of EA on QoL, influenced by disease activity. Achalasic patients tend to modify their diets to minimize symptoms, favoring easily swallowable soft and fatty foods while reducing intake of solid foods rich in carbohydrates and fiber. Thus, comprehensive nutritional assessment is strongly recommended for EA patients to mitigate dietary imbalances and manage possible deficiencies promptly.

Disclosure: Nothing to disclose.

MP439

COMPARATIVE LONG-TERM OUTCOMES OF PERORAL ENDOSCOPIC MYOTOMY IN TREATMENT-NAÏVE ACHALASIA VERSUS PATIENTS WITH PRIOR SURGICAL INTERVENTIONS

M. Ito¹, N. Tada¹, H. Matsui¹, A. Dobashi¹, T. Masuda², F. Yano², K. Sumiyama¹

¹The Jikei University School of Medicine, Endoscopy, Tokyo, Japan,

²The Jikei University School of Medicine, Surgery, Tokyo, Japan

Contact E-Mail Address: mamoru.ito1222@gmail.com

Introduction: Peroral endoscopic myotomy (POEM) has become a standard endoscopic treatment for patients with achalasia, with many studies reporting on its long-term effectiveness. However, the impact of a patient's previous surgical history on the long-term outcomes of POEM remains unknown.

Aims & Methods: This study aims to compare the long-term efficacy of POEM in achalasia patients with and without prior surgical interventions. A single center, retrospective review was conducted on achalasia patients who underwent POEM between January 2016 to December 2020. Clinical, demographic, radiographic, endoscopic, and manometric data were collected. Patients with less than two years of follow-up without noted failure were excluded. The analysis compared outcomes between first-time POEM patients (naïve POEM) and those undergoing POEM following failed surgical treatments (redo POEM). The primary outcome was the clinical success rate, defined as an Eckardt Score of 3 or less at final follow-up and no need for additional interventions. Secondary endpoints included the prevalence of postoperative gastroesophageal reflux disease (GORD), the necessity for acid suppression medications, and additional interventions for achalasia.

Results: Data were collected on 47 naïve POEM and 26 redo POEM patients. After excluding 17 naïve POEM patients and 8 redo POEM patients who did not meet the criteria for long-term follow-up, a total of 30 naïve POEM patients and 18 redo POEM patients were analyzed. In the redo POEM group, 77.8% (14/18) of the patients underwent Heller myotomy with Dor fundoplication, while the surgical details for the remaining patients were unknown. The median length of symptoms was 5 (IQR 3-10) years for naïve patients and 6 (IQR 1.2-17.5) years for redo patients ($p=0.29$). According to the Chicago classification v4.0, the achalasia subtypes in the naïve POEM group were Type I in 9 patients (30%), Type II in

12 (40%), Type III in 3 (10%), and other types in 6 (20%). For the redo POEM group, subtypes were Type I in 9 patients (50%), Type III in 2 (11.1%), and unspecified in 7 (38.9%). Barium esophagram revealed no significant differences in the maximum diameter between the groups (naïve POEM 45.8 ± 21.4 mm vs. redo POEM 44.9 ± 15.4 mm, $p=0.89$). Long-term success rates were 76.7% (23/30) in naïve POEM and 83.3% (15/18) in redo POEM, with no significant difference between the groups ($p=0.72$). Postoperative GORD was noted in 63.3% (19/30) in the naïve POEM versus 67% (12/18) in the redo POEM ($p=0.06$), with newly prescribed acid suppression medication in 23.3% (7/18) and 55.6% (10/18), respectively ($p=0.02$). Additional interventions for achalasia were required in 10% (3/30) in the naïve POEM versus 11.1% (2/18) in the redo POEM, with no significant difference between the groups ($p=1.0$). In the naïve POEM group, one patient required a second POEM, another was hospitalized due to achalasia recurrence, and a third underwent Heller myotomy with Dor fundoplication. In the redo POEM group, one patient underwent endoscopic balloon dilatation, and another required esophagectomy.

Conclusion: POEM is an effective long-term treatment for achalasia, demonstrating similar success rates in patients undergoing either their first or redo POEM procedures. The overall efficacy and safety profiles support POEM as a recommended treatment for managing achalasia regardless of prior surgical treatment failures.

Disclosure: Nothing to disclose.

MP440

REDOPOEM: EFFICACY AND SAFETY AFTER FAILURE OF A FIRST POEM

A. D'Angelo¹, F. Zerbib¹, M. Barret², C. Gronnier¹, M. Saunier¹, J. Levy³, A.-s. Philippe⁴, T. Degand⁵, L. Caillio⁶, M. Pioche⁷, T. Wallenhorst⁸, J.-M. Gonzalez⁹, M. Schaefer¹⁰, J. Jacques¹¹, G. Vanbiervliet¹², P. Onana Ndong¹², E. Coron¹³, G. Velut¹³, G. Rahmi¹⁴, A. Aidibi¹⁴, A. Berger¹

¹CHU de Bordeaux - Hôpital Haut Leveque, Hépatogastroentérologie, Pessac, France, ²Cochin Hospital, Gastroenterology, Paris, France, ³Clinique des Cèdres, Gastro-entérologie, Cornebarrieu, France, ⁴Centre Hospitalier Intercommunal de Toulon - La Seyne-sur-Mer, Hépatogastro-Entérologie, La Seyne Sur mer, France, ⁵CHU De Dijon, Gastroenterology, Dijon Cedex, France, ⁶CHU DE NIMES, Gastro enterology, Nîmes, France, ⁷Hospices civils de Lyon, Gastroenterology and endoscopy, Lyon, France, ⁸CHU Pontchaillou, Endoscopy Unit, Rennes, France, ⁹APHM - North Hospital, Dept. de Gastroenterologie, Marseille, France, ¹⁰Centre Hospitalier Régional Universitaire De Nancy, Hepatogastroentérologie, Nancy, France, ¹¹CHU Limoges - Hepatogastro-Enterology, CHU Limoges; Limoges/FR, Hepatogastro-Enterology, Limoges, France, ¹²CHU, Hôpital L'Archet 2 Gastroentérologie - Gastroenterology, CHU, Hôpital L'Archet 2 Gastroentérologie, Gastroenterology, Nice, France, ¹³Hôpital Hotel Dieu Et Hme, Digestive Diseases Institute, Nantes Cedex 1, France, ¹⁴Hôpital Européen Georges Pompidou Dept. de Gastroenterologie, Gastroenterology, Paris, France

Contact E-Mail Address: amaury.dangelo@yahoo.fr

Introduction: Per-oral endoscopic myotomy (POEM) has been widely employed as a treatment for esophageal motility disorders since 2008, exhibiting an efficacy rate of approximately 80-90% and a safety rate of 90%. Nevertheless, approximately 10% of patients remain symptomatic after treatment, with limited data available on second-line strategies. Our aim was to determine the validity of redoPOEM as a second line therapy after POEM failure.

Aims & Methods: We conducted a retrospective multicenter study involving 15 French expert centers, including all patients who underwent redoPOEM up to the end of September 2023. Patients were classified as experiencing primary failure if their Eckardt score exceeded 3 at 3 months post-procedure, and as experiencing secondary failure if their Eckardt score exceeded 3 at the last follow-up or if additional treatment was necessary. Safety was assessed using the AGREE classification, with events of grade II or higher considered significant.

Results: Ninety-one patients were included in the study, 44% were female, the average age was 54.6 ± 18.0 years. Patients were followed for a mean duration of 22 months (range 3,5 – 69,5 months). The mean Eckardt score before redoPOEM was 5.8 ± 2.0 . No technical failure was reported. At the 3-month follow-up, 79% of patients had achieved clinical success, with an average Eckardt score of 2.05 ± 2.0 . Long-term success was observed in 60.5% of all patients, and among those who had achieved clinical success at the 3-month mark, the long-term success rate was 77%. Additionally, 25% of the patients required a complementary treatment, such as botulinum toxin injections, endoscopic dilation or Heller myotomy. A low Eckardt score before redoPOEM was associated with clinical success at the 3-month follow-up in univariate analysis, whereas an Eckardt score of 5 or higher before redoPOEM appeared to be a risk factor for primary failure. Multivariate analysis did not show any predictive factors of failure. The safety rate was 90%, with no reported deaths within one month following the procedure. Nine patients experienced grade II or higher adverse event: four patients were treated with antibiotics for pneumonia or mucosal breach without further complications, while four others underwent a new endoscopy due to mucosal breach, with covered esophageal stents or hemostatic clips used to manage the situation. One patient experienced multiorgan failure.

Conclusion: RedoPOEM proves to be an effective strategy for managing patients who experience primary failure or symptomatic relapse following a POEM. It demonstrates promising efficacy and safety outcomes, supported by the largest cohort reported to date for redoPOEM. Further research is warranted to compare redoPOEM with Heller myotomy and endoscopic dilation as second-line treatments for esophageal motility disorders.

Disclosure: Nothing to disclose.

MP441

SUBMUCOSAL INJECTION-GUIDED SEPTOMYOTOMY (SING TECHNIQUE) FOR THE MANAGEMENT OF ZENKER DIVERTICULUM: RESULTS FROM A PROSPECTIVE MULTICENTRIC STUDY

G. Dell'Anna¹, F.V. Mandarino¹, G. Testa², F. Frigo², D. Arese², M.C. Verga¹, D. Esposito¹, E. Fasulo¹, A. Barchi¹, R. Barà¹, E. Viale¹, L. Fuccio³, F. Coppola², S. Danese¹, M. Spandre², F. Azzolini¹

¹IRCCS San Raffaele Scientific Institute and University, Gastroenterology and Gastrointestinal Endoscopy Unit, Milan, Italy, ²Ospedale San Giovanni Bosco, Digestive Endoscopy Unit, Division of Gastroenterology, Turin, Italy, ³S. Orsola-Malpighi University Hospital, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: g.dellanna93@gmail.com

Introduction: Endoscopy is the first-line approach for managing Zenker's Diverticulum (ZD). Various endoscopic techniques, each with its own advantages and limitations, have been described. We have proposed a new technique, which we have named Submucosal Injection-Guided septomyotomy (SING technique).

Aims & Methods: The performance of SING technique was evaluated in a prospective observational cohort of patients with ZD who underwent the

procedure at two Italian hospitals: San Raffaele Hospital (Milan, Italy) and San Giovanni Bosco Hospital (Turin, Italy).

SING technique involves a classic septotomy, which consists of a mucosal incision with a Hook-Knife in the middle of the septum and a cricopharyngeal myotomy for all the length of the Zenker's Diverticulum and beyond 10 mm into the esophageal proper muscular layer. The novelty of the technique lies in the submucosal injection during the septomyotomy on both the esophageal and diverticular sides, which helps to better delineate the muscular layer and guide the complete myotomy, without the need for bilateral submucosal tunnelling.

Clinical success (CS) was defined as a Dakkak and Bennet Dysphagia Score (DBDS) of ≤ 1 and a Kothari-Haber Score (KHS) of < 2 at 3 months. Recurrence was defined as an increase in DBDS of > 1 after achieving CS or a KHS of ≥ 2 after CS. Follow-up included clinical evaluations at 3 and 6 months, and then annually. Adverse Events (AEs) are classified according to the AGREE Classification.

Results: 42 patients with ZD underwent SING technique between March 2021 and January 2024 (median age 74 [IQR 67-80], 66.7% males, BMI 24.6 [IQR 21-27]). The median diverticula depth was 30mm (IQR 25-45) with a median septum length of 20mm (IQR 14-30). Median KHS at diagnosis was 4 (IQR 4-6), dysphagia for solids (42.9%) was the most common symptom, with a median symptom duration of 12 months (IQR 6-24). While a technical success rate was observed in all cases (42/42, 100%), a clinical success rate was observed in 40/42 patients (95.2%). In the 2/42 (4.8%) cases of clinical failure, endoscopic evaluation revealed the presence of a minimal residual muscular septum successfully treated with septomyotomy. Median procedural time was 34 minutes (IQR 29-60), with a hospital stay of 2 days (IQR 2-2). No AEs were recorded. After a median follow-up of 370 days (IQR 297-747), no cases of symptom recurrence were recorded.

Conclusion: SING technique is a safe and effective technique for the endoscopic treatment of ZD. It improves and enhances the efficacy of traditional endoscopic septotomy and can also be utilized as rescue therapy.

Disclosure: Nothing to disclose.

MP442

COMPLETE MYOTOMY OF THE CRICOPHARYNGEAL MUSCLE WITH THE 'CLUTCH CUTTER' SCISSORS: THE BENEFIT OF Z POEM WITHOUT THE ASSOCIATED MORBIDITY IN SYMPTOMATIC ZENKER'S DIVERTICULA

M. Harb¹, J.-B. Danset¹, C. Medlij¹, O. Marty¹, D. Levoir¹, B. El Khoury¹, C. Souaid¹, Y. Le Baleur¹

¹Hospital Saint Joseph de Paris, Paris, France

Contact E-Mail Address: marc_harb@hotmail.com

Introduction: Several therapeutic modalities, including surgery, rigid and flexible endoscopy, have been described for the management of symptomatic Zenker's diverticulum (ZD). Symptom relief such as dysphagia and regurgitation constitute the primary goal of treatment. The ESGE (European Society of Gastrointestinal Endoscopy) recommends as first-line treatment the performance of a septotomy, which has a higher safety profile compared to Z POEM (Zenker's Peroral Endoscopic Myotomy). Septotomy is most commonly performed using a dissection knife or a needle knife, stopping the section 5 mm from the bottom of the diverticulum, leaving muscle fibers intact, which may contribute to some of the recurrences in the medium and long term. The aim of this retrospective study was to evaluate the safety and efficacy at 12 months of complete myotomy of the diverticular septum using a dissection scissor.

Aims & Methods: A septotomy with sectioning of the cricopharyngeal muscle fibers was performed in 43 patients presenting with a symptomatic Zenker's diverticulum of the upper third of the esophagus using the following technique: After oro-tracheal intubation in a patient lying

supine, gastroscopy with a single-channel gastroscope equipped with a transparent hood was performed. Once the hood was positioned over the septum, an incision with a clutch cutter (Fujifilm) was made at two points on the diverticular wall, 5 mm apart, extending 2 mm into the mucosa and submucosa.

The next step involved avulsion of the mucosal and submucosal hood using a 10 mm diathermic loop by mucosectomy without injection to expose the cricopharyngeal muscle. Subsequently, complete sectioning of all muscle fibers using the clutch cutter under traction, followed by closure of the defect along its entire height using clips, was performed.

The symptoms were analyzed before the intervention as well as at 3, 6 months, and 1-year post-intervention using a comprehensive questionnaire with each patient serving as their own control before and after the procedure.

The following data were collected: peri- and post-procedural complications (hemorrhage, perforation, infection, others), procedure duration, immediate technical success, and clinical success at 3 months, 6 months, and 1 year.

Results: The average size of the Zenker's diverticulum was 25.6 mm, and the average procedure duration was 48 minutes.

No peri- or post-procedural complications were observed, although one patient experienced an injury to the piriform sinus. Patient follow-up was conducted at 3, 6, and 12 months post-intervention. During follow-up consultations, patients assessed the improvement of their symptoms as a percentage.

At 3 months, 92% of patients experienced a 100% improvement in their preoperative symptoms. By 6 months, 94% of patients reported a 100% improvement, which further increased to 97% at 12 months.

This series, the largest ever reported of complete cricopharyngeal myotomy using the Clutch cutter with complete closure of the defect, achieves an equivalent of "open" Z POEM without detachment of the cervical or mediastinal adipose spaces, with very low morbidity and a recurrence rate lower than that of classical septotomy.

Conclusion: The technique of complete cricopharyngeal muscle sectioning using the Clutch Cutter dissection tool is safe, effective, and associated with low morbidity, along with a very low recurrence rate at one year. It could potentially be considered as a first-line treatment for symptomatic Zenker's diverticula in patients who have not undergone prior treatment.

Disclosure: I can affirm that there is no conflict of interest associated with the study I conducted.

MP443

REPEAT PERORAL ENDOSCOPIC MYOTOMY: TECHNICAL DIFFICULTY AND RISK FACTORS

L. Ma¹, Z.-Q. Liu¹, Q.-L. Li¹, P.-H. Zhou¹

¹Zhongshan Hospital, Fudan University, Endoscopy Center and Endoscopy Research Institute, Shanghai, China

Contact E-Mail Address: maly14@fudan.edu.cn

Background and aims: Repeat peroral endoscopic myotomy (Re-POEM) appeared to be a promising salvage option for patients with persistent/recurrent symptoms after initial POEM, but it may be more.

Aims & Methods: Between July 2012 and October 2023, 158 achalasia patients underwent Re-POEM were retrospectively enrolled in this study. Another 2978 patients without prior myotomy were selected for naïve POEM. After propensity score matching (PSM), procedure-related parameters were compared between the two groups. Univariable and multivariable analyses were performed to reveal risk factors for difficult Re-POEM.

Results: With similar baseline characteristics between two groups after PSM, the procedure time was comparable between Re-POEM and naïve

POEM groups (61.4±27.0 vs. 59.3±29.9, $p=0.496$). The Re-POEM group showed shorter esophageal myotomy length (7.0±2.1 vs. 8.2±1.1, $p<0.001$) and longer gastric myotomy length (2.3±0.6 vs. 2.1±0.4, $p=0.017$), compared with the naïve POEM group. Mucosal injury in Re-POEM group was slightly higher, which was not statistically significant (20.3% vs. 13.9%, $p=0.135$). No differences were found in the incidence of gas-related adverse events (AEs), major AEs, and technical difficulty. Multivariate analysis determined mucosal edema (OR=4.942, 95% CI, 1.554-15.714, $p=0.007$) and submucosal fibrosis (OR=3.817, 95% CI, 1.333-10.931, $p=0.013$) to be independent risk factors for difficult Re-POEM.

Conclusion: Re-POEM appears safe and feasible as a salvage option after initial POEM failure, with comparable procedure duration, incidence of AEs and technical difficulty to naïve POEM. Mucosal edema and submucosal fibrosis were associated with difficult Re-POEM.

Disclosure: Nothing to disclose.

Identifying drug targets in IBD: Part 1

16:00-17:00 / Poster Stage 1

MP444

NON-INVASIVE TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION (NITAVNS) DEMONSTRATES SPATIALLY SPECIFIC REGULATION OF IMMUNE CELL DISTRIBUTION IN A PRECLINICAL MODEL OF ULCERATIVE COLITIS

F. Hesampour¹, D. Tshikudi¹, A. Veysel Özden^{2,3},

C.N. Bernstein^{4,5}, J.-E. Ghia^{1,5,4,6}

¹University Of Manitoba, Immunology, Winnipeg, Canada,

²Bahcesehir University, Istanbul, Turkey, ³Vagustim, Istanbul,

Turkey, ⁴University of Manitoba, Internal Medicine, Winnipeg,

Canada, ⁵University of Manitoba, Inflammatory Bowel Disease

Clinical & Research Centre, Winnipeg, Canada, ⁶Children's Hospital

Research Institute of Manitoba, Winnipeg, Canada

Contact E-Mail Address: jeghia@yahoo.fr

Introduction: Decreased vagus nerve activity and increased inflammatory immune cells are observed in ulcerative colitis (UC) (1, 2). Due to its anti-inflammatory and protective properties, vagus nerve stimulation (VNS) has garnered attention for UC therapy (3). Non-invasive transcutaneous auricular vagus nerve stimulation (NitaVNS), devoid of the side effects associated with invasive techniques, demonstrates protective anti-inflammatory effects in our mouse UC-like model of colitis (4), although the specific cellular mechanisms remain unclear.

Aims & Methods: To evaluate the effects of NitaVNS on the distribution of granulocytes, macrophages, natural killer (NK) cells, and CD4⁺ and CD8⁺ T cells in the colon tissue, spleen, and mesenteric lymph nodes of a UC-like colitis mouse model, NitaVNS was administered to C57BL/6 male mice daily for 10 min, beginning one day before colitis induction with 5% dextran sulfate sodium for 5 days in water (the control group received regular water). This continued until the end of the study, with no stimulation in sham mice. The daily disease activity index (DAI) was evaluated along with distal macroscopic scores at the time of sacrifice. The frequencies of granulocytes (Ly6G), macrophages (F4/80), NK cells (NK1.1), CD4⁺ T cells (CD3, CD4), and CD8⁺ T cells (CD3, CD8) were analyzed in the cecum, proximal, mid and distal colon, spleen, and mesenteric lymph nodes (MLNs) using flow cytometry.

Results: NitaVNS in colitic mice significantly improved the DAI and macroscopic scores related to rectal bleeding, colon bleeding, fecal consistency loss, and shortened colon length compared to sham-stimulated colitic mice. In contrast, no changes were observed in the non-colitic mice. While NitaVNS did not alter the frequency of Ly6G⁺ cells in the cecum, mid/distal colon, and MLNs, it significantly decreased the positivity of these cells in the proximal colon and spleen of mice with colitis without affecting non-colitic mice. NitaVNS significantly decreased the frequency of F4/80⁺ cells in the mid-colon but did not influence these cells in the cecum, proximal and distal colon, spleen, or MLNs. In colitic conditions, NitaVNS significantly increased NK cell frequency in the spleen without affecting non-colitic mice. Moreover, NitaVNS did not alter the frequency of NK cells in the colon or MLNs in colitic or non-colitic mice. Additionally, NitaVNS did not induce changes in CD4⁺ and CD8⁺ T cell distribution in the colon tissue, spleen, or mesenteric lymph nodes of colitic and non-colitic mice.

Conclusion: These results suggest that NitaVNS could potentially reduce inflammation in colitic mice, locally and systemically, by decreasing the frequency of granulocytes in the colon and spleen and colonic macrophages. Additionally, NitaVNS increased the number of splenic NK cells, potentially contributing to its systemic effects. These findings indicate promising therapeutic potential for NitaVNS.

References: 1. Ghia JE, Blennerhassett P, Kumar-Ondivveeran H, Verdu EF, Collins SM. The vagus nerve: a tonic inhibitory influence associated

with inflammatory bowel disease in a murine model. *Gastroenterology*. 2006;131(4):1122-30.

2. Wiese JJ, Manna S, Kühl AA, Fasci A, Elezkurtaj S, Sonnenberg E, Bu-beck M, Atreya R, Becker C, Weixler B, Siegmund B, Patankar JV, Prüß MS, Schumann M. Myenteric Plexus Immune Cell Infiltrations and Neurotransmitter Expression in Crohn's Disease and Ulcerative Colitis. *J Crohns Colitis*. 2024 Jan 27;18(1):121-133.

3. Verma N, Mudge JD, Kasole M, Chen RC, Blanz SL, Trevathan JK, Lovett EG, Williams JC, Ludwig KA. Auricular Vagus Neuromodulation-A Systematic Review on Quality of Evidence and Clinical Effects. *Front Neurosci*. 2021 Apr 30;15:664740.

4. Hesampour F, Tshikudi D, Veysel Özden A, Bernstein CN, Ghia JE. A54 The impact of non-invasive transcutaneous auricular nerve stimulation (NitaVNS) on the development of experimental colitis in mice. *J Can Assoc Gastroenterol*. 2023 Mar 7;6(Suppl 1):30.

Disclosure: F. Hesampour: None Declared, D. Tshikudi: None Declared, A. Veysel Özden: The employee of the company providing the stimulator, C. N. Bernstein: None Declared, J-E. Ghia: None Declared.

MP445

DEVELOPMENT OF AN INFLAMMATORY AND ENDOPLASMIC RETICULUM STRESS MIX TO PRIME PATIENT-DERIVED ORGANIDS TO FACILITATE PRECLINICAL COMPOUND EVALUATION IN INFLAMMATORY BOWEL DISEASE

L. Giorio¹, K. Arnauts¹, J. Sabino^{1,2}, M. Ferrante^{1,2}, S. Vermeire^{1,2}, B. Verstockt^{1,2}

¹KU Leuven, Department of Chronic Diseases and Metabolism (CHROMETA), Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ²KU Leuven, University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium

Contact E-Mail Address: lorenzo.giorio@kuleuven.be

Introduction: Patient-derived organoids represent a valuable tool to unravel disease- and patient-specific mechanisms in inflammatory bowel diseases (IBD). We previously showed that organoids from patients with ulcerative colitis (UC) lose their acute inflammatory phenotype, and consequently established an inflammatory mix to re-induce inflammation in undifferentiated intestinal organoids¹. However, inducing solely inflammation might not be sufficient to study IBD-specific pathways as, for example, endoplasmic reticulum (ER) stress has been shown a role in the pathogenesis of IBD, and targeting the ER protein folding homeostasis of epithelial cells could be a new treatment target².

Aims & Methods: To effectively use organoids as a pre-clinical model for IBD, there is a critical need to 1) enable prolonged exposure to preclinical compounds, in an inflammatory setting, to decipher their mechanism of action and 2) establish different disease phenotypes to study disease mechanisms. To this aim, we optimized two mixes tailored to induce either an inflammatory (INF) or ER stress-driven inflammatory phenotype in differentiated intestinal organoids. Intestinal organoid cultures, isolated from endoscopy-derived non-inflamed colonic biopsies of nine patients with UC were expanded, mechanically dissociated, followed by culturing in an human expansion media³ for two days. Next, the cultures were subjected to a differentiation media (human expansion media without the addition of WNT3a, nicotinamide and SB202190) for four consecutive days. On day six, organoids were exposed to either the differentiation media only, an INF mix (50 ng/ml TNF- α , 20 ng/ml IL-1 β , 1 μ g/ml Flagellin) or an ER stress mix (10 ng/ml TNF α , 20 ng/ml IL-1 β , 1 μ g/ml Flagellin, Tunicamycin 25ng/ml) for 48 hours in differentiation media. RNA was extracted and sequenced by Illumina Truseq mRNA (HiSeq4000). Differential gene expres-

sion and pathways were studied through DESeq2 and Ingenuity Pathway Analysis ($|\log_2FC| > 2$, FDR < 0.05).

Results: Transcriptomic analysis demonstrated a clear separation on principal component analysis of the untreated control and INF and ER mix exposure upon 48 hours of exposure. The INF mix exposure resulted in the upregulation of 324 and the downregulation of 148 genes compared to the untreated control, while the ER mix exposure resulted in 368 and 138 genes being up- and downregulated respectively compared to the untreated control. Inflammatory markers (CXCL1, CXCL2, CXCL11, IL1 β , IL8) were significantly upregulated following exposure to both the INF mix and the ER stress mix. However, only organoids challenged with the ER stress mix showed a strong upregulation of ER stress markers (PDIA4 HSP90B1, HSPA5, DDIT3, all within $|\log_2FC| > 2$). Ingenuity Pathways Analysis (IPA) of the contrast of the ER stress mix versus the INF mix highlighted the up-regulation of ER stress-related pathways including ATF6 (ATF6-alpha) activates chaperone genes and ATF4 activates genes in response to endoplasmic reticulum stress.

Conclusion: Exposure of UC patient-derived differentiated colonic organoids for 48 hours to either the INF mix or ER stress mix significantly upregulated INF markers, while ER stress markers only resulted in being significantly upregulated after exposure to the ER stress mix. IPA confirmed that the dysregulated genes were part of ER stress-related pathways. These results will facilitate the use of organoids to mimic an INF or ER stress phenotype and will promote their use to study pre-clinical compounds for prolonged exposures (48 hours) in a disease-representative IBD model.

References:

1. Arnauts et al., *Gastroenterology*, 2020
2. Cao et al., *Inflammatory Bowel Diseases*, 2016

Disclosure: LG and KA report no conflict of interest.

JS reports financial support for research from Galapagos and Viatrix; receives speakers' fees from Abbvie, Falk, Takeda, Pfizer, Galapagos, Ferring, Janssen, and Fresenius; and does consultancy for Janssen, Ferring, Fresenius, Abbvie, Galapagos, Celltrion, Pharmacosmos, and Pharmanovia.

MF reports financial support for research from AbbVie, Amgen, Biogen, EG, Janssen, Pfizer, Takeda, and Viatrix; receive speakers' fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Falk, Ferring, Janssen-Cilag, Lampro, MSD, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda, and Truvion Healthcare; and does consultancy for AbbVie, Agomab Therapeutics, Boehringer Ingelheim, Celltrion, Eli Lilly, Janssen-Cilag, Medtronic, MRM Health, MSD, Pfizer, Regeneron, Samsung Bioepis, Sandoz, Takeda, and Thermo Fisher

SV reports speaker and/or consultancy fees from AbbVie, Abivax, AbolentIS Pharma, Agomab Therapeutics, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Biora Therapeutics (formerly Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, Gilead Sciences, GSK, Hospira, IMIDomics, Janssen Pharmaceuticals, Johnson & Johnson, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic Therapeutic, MRM Health, MSD, Mundipharma, Pfizer, ProDigest, Prometheus Biosciences, Roberts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma, VectivBio, Ventyx Biosciences and Zealand Pharma; grants from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; and participation on a data safety monitoring board for Sanofi.

BV reports research support from AbbVie, Biora Therapeutics (formerly Progenity), Landos Biopharma, Pfizer, Sosei Heptares and Takeda; speaker fees from Abbvie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, Lilly, MSD, Pfizer, R-Biopharm, Sandoz, Takeda, Tillots Pharma, Truvion Healthcare and Viatrix; consultancy fees from Abbvie, Alfasigma, Alimentiv, Applied Strategic, AstraZeneca, Atheneum, BenevolentAI, Biora Therapeutics (formerly Progenity), Boxer Capital, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Lilly, Mylan, Inotrem, Ipsos, Janssen Pharmaceuticals, Pfizer

er, Sandoz, Sanofi, Santa Ana Bio, Sapphire Therapeutics, Sosei Heptares, Takeda, Tillots Pharma and Viartis; and stock options from Vagustim. This study was funded by Landos Biopharma.

MP446

THE NOVEL AMINO ACID-BASED PAI-1 INHIBITOR, LDN-071 SIGNIFICANTLY REDUCES THE SEVERITY OF ACUTE AND CHRONIC INFLAMMATION IN COLITIS MODELS

B. Jójárt^{1,2,3,4}, N. Csákány-Papp^{2,3,4}, H. Laub^{1,2}, B. Vasas⁵, B. Barta⁶, V. Szabó^{2,3,4}, L. Kajári³, M. Bagyánszki⁶, K. Farkas^{2,7}, I. Mándity^{1,8}, G. Heltovics¹, P. Pallagi^{1,2,3,4}, J. Maléth^{1,2,3,4}
¹Ladon Therapeutics Ltd, Szeged, Hungary, ²University of Szeged, Albert Szent-Györgyi Medical School, Department of Medicine, Szeged, Hungary, ³University of Szeged, ELKH-USZ Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ⁴University of Szeged, HCEMM-USZ Molecular Gastroenterology Research Group, Szeged, Hungary, ⁵University of Szeged, Albert Szent-Györgyi Medical School, Department of Pathology, Szeged, Hungary, ⁶University of Szeged, Faculty of Science and Informatics, Department of Physiology, Anatomy and Neuroscience, Szeged, Hungary, ⁷University of Szeged, HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary, ⁸Research Centre for Natural Sciences, Institute of Materials and Environmental Chemistry, Artificial Transporters Research Group, Budapest, Hungary

Contact E-Mail Address: jojart.boldizsar@gmail.com

Introduction: Inflammatory Bowel Diseases (IBD) are chronic inflammatory disorders characterized by alterations of acute relapses and remission. The past decades have brought substantial advances in the pharmacological management of IBD by a wide range of medicines. However, the sustained efficacy of the currently available anti-inflammatory therapies is still far from optimal. Therefore, the development of novel therapies represents a major unmet clinical need in this field. Recently, the enrichment of the coagulation pathway genes and among these, Plasminogen activator inhibitor 1 (PAI-1) was described in IBD, whereas PAI-1 emerged as a link between the epithelium and inflammation. Moreover, the genetic deletion of PAI-1 prevented the severity of experimental colitis in mice.

Aims & Methods: Based on these, we aimed to develop and test novel PAI-1 inhibitors for the treatment of IBD.

The novel, amino acid-based PAI-1 inhibitor, LDN-071 was synthesized by the A³SMO[®] platform. The inhibitory potential and cytotoxicity effects of the peptide were determined by *in vitro* assays. Acute and chronic colitis was induced in mice with DSS and 10 mg/bwkg LDN-071 was administered *per os*. The changes of body weight, spleen weight, and colon length were measured. Haematoxylin eosin (HE) and Periodic acid-Schiff (PAS) staining were performed for histology. ELISA and qRT-PCR measurements were applied to analyze the cytokine expressions. Hydroxyproline assay was used to quantify the mucosal collagen deposition. *In vivo*, the toxicity of LDN-071 was determined in mice. Human colon organoid and fibroblast (FB) cell cultures were generated from IBD patients and the effects of LDN-071 were observed.

Results: LDN-071 significantly inhibited PAI-1 *in vitro* without decreasing the cell viability in a concentration range of 1 μM–1 mM. In the acute mice model, the administration of 10 mg/bwkg LDN-071 in the DSS-treated mice prevented the body weight loss, the development of bloody diarrhea, the decrease of colon length, and the increase of the spleen weight, which were displayed by the DSS+vehicle-treated animals. The histological analysis of the colon revealed that DSS treatment induced severe transmural inflammation, ulceration, loss of crypt structures, and goblet

cell depletion. Importantly, all these parameters were significantly ameliorated by the administration of 10 mg/bwkg LDN-071 in the acute and chronic models as well. Additionally, mucosal gene and protein expressions of TNF-α, IL-1β, and IL-6 were significantly decreased by PAI-1 inhibition in the acute phase. Besides, the LDN-071 treatment significantly reduced the inflammation, epithelial erosion, and fibrosis caused by chronic administration of DSS. However, the collagen deposition was significantly lower in the PAI-1-inhibited DSS mice. Importantly, no signs of toxicity were observed in mice exposed to 100 mg/bwkg LDN-071 for 7 days. In our *in vitro* models, the PAI-1 inhibition reduced the protein level and gene expression of pro-inflammatory cytokines in human colon organoid of IBD patient. Moreover, the gene expression of fibrosis-related genes significantly decreased after the LDN-071 treatment in IBD patients-derived human FB cell culture.

Conclusion: Our results showed that LDN-071, a novel amino acid-based inhibitor of PAI-1, significantly ameliorated the severity of acute and chronic colitis in mice. However, the LDN-071 reduced the expression of inflammation- and fibrosis-related genes and proteins *in vitro* human models. We propose that the inhibition of PAI-1 could be a potential novel therapeutic strategy in IBD.

Disclosure: LDN-071 PAI-1 inhibitor is owned by Ladon Therapeutics Ltd.

MP447

TEV-48574, AN ANTI-TL1A ANTIBODY IN DEVELOPMENT FOR USE IN CROHN'S DISEASE AND ULCERATIVE COLITIS, DEMONSTRATES TARGET ENGAGEMENT THROUGH A PROFOUND RAPID AND SUSTAINED REDUCTION IN FREE TL1A LEVELS

T. Angeles¹, R. Balyan¹, A. Papp², T. Ung¹, K. Olah-Varga², Y. Liu¹, J. Dreyman³, O. Dotan³, S. Li¹, S. Rohatagi¹, R. Singh¹, L. Rabinovich-Guilatt³, G. Raphael¹
¹Teva Branded Pharmaceutical Products R&D, Inc., West Chester, United States of America, ²Teva Pharmaceutical Works Private Ltd. Co., R&D, Debrecen, Hungary, ³Teva Pharmaceutical Industries Ltd., Netanya, Israel

Contact E-Mail Address: Thelma.Angeles@tevapharm.com

Introduction: Tumor necrosis factor-like ligand 1A (TL1A) has been implicated in numerous immune-mediated and fibrotic diseases, such as inflammatory bowel disease (IBD) and asthma, making it an ideal target for therapeutic intervention. TEV-48574 is a human IgG1 monoclonal antibody with a novel mechanism of action that preferentially inhibits binding of TL1A to the Death Receptor 3 (DR3), involved in proinflammatory signaling, with a greater potency compared to the Decoy Receptor (DcR3), which could preserve the natural homeostatic mechanism. TEV-48574 has been shown to reduce fibrosis, inflammation, and mortality in animal models of IBD and asthma.¹ A phase 1 first-in-human (FIH) study, comprised of a single ascending dose (SAD) and a multiple ascending dose (MAD) phase, assessed safety, tolerability, immunogenicity, pharmacodynamic and pharmacokinetics of TEV-48574 amongst healthy participants and those with asthma. It has also been assessed in a phase 2A uncontrolled T2 low/non T2 asthma proof-of-concept (POC) study, where results from an interim analysis met predefined futility criteria leading to early termination. TEV-48574 is in clinical development as a potential treatment for ulcerative colitis and Crohn's disease. This analysis aims to evaluate target engagement; free TL1A levels were measured in phase 1 and phase 2A TEV-48574 studies.

Aims & Methods: Free TL1A levels were measured using a ligand binding assay in the FIH and POC studies. In the FIH SAD phase, healthy participants were administered TEV-48574 as a single dose (1–1000 mg) or placebo by subcutaneous (SC) route. In the FIH MAD phase, mild asthmatic

patients were randomized to active (up to 2300 mg) or placebo SC treatment. The phase 2A POC study was a 16-week randomized, double-blind, parallel-group trial to evaluate the efficacy, tolerability, and safety of a single dose regimen of TEV-48574 compared to placebo.

Results: In the FIH study, following SAD and MAD administration, while unchanged in the placebo group, free TL1A levels showed a rapid reduction at the first analyzed time point (1 hour after dose) in the active treatment groups. The free TL1A levels in the MAD phase of the FIH study remained suppressed up to day 92 (63 days after last dose, pooled result for doses), despite extremely low remaining TEV-48574 concentrations. In the POC study, TEV-48574 resulted in reduction of free TL1A levels, sustained up to ~10 weeks after the last dose. An analysis of patients who received all doses showed a persistent pharmacodynamic effect, demonstrated by continued suppression of free TL1A despite decreasing concentrations of TEV-48574 after the last dose on day 98.

Conclusion: Target engagement was shown by a rapid and sustained TEV-48574-mediated suppression of free TL1A that persisted longer than the drug exposure. Given that TL1A has been implicated in the pathogenesis of immune-mediated and fibrotic diseases, such as IBD¹, the data here-in support further development of TEV-48574 in patients with ulcerative colitis and Crohn's disease.

References: 1. Clarke AW, et al. mAbs. 2018;10:4664-77.

Disclosure: All other authors are employees of Teva Pharmaceuticals. TEV-48574 is being developed in a partnership between Teva and Sanofi.

MP448

ROSNILIMAB, A PD-1 AGONIST ANTIBODY IN CLINICAL DEVELOPMENT FOR ULCERATIVE COLITIS, REDUCES PATHOGENIC PD-1+ T CELLS AND INFLAMMATORY CYTOKINE SECRETION IN PATIENT BLOOD AND IN A MOUSE MODEL OF ULCERATIVE COLITIS

S. Parmley¹, C. Haines¹, P. Soroosh¹, R. Frank¹, M. Hsu¹, P. Brodsky¹, J. Michaels¹, P. Lizzul¹, M. Dahl¹

¹AnaptysBio, San Diego, United States of America

Contact E-Mail Address: mdahl@anaptysbio.com

Introduction: Checkpoint agonism represents a promising class of therapies for the treatment of autoimmune and inflammatory diseases, including ulcerative colitis (UC), where unmet needs persist. Engagement of checkpoint receptor PD-1 by its natural ligand PD-L1 is critical for regulation of T cells. Rosnilimab is an investigational PD-1 agonist IgG1 antibody designed to optimize inhibitory signaling through PD-1, does not block PD-1 binding to PD-L1, and depletes PD-1^{high} pathogenic T cells while agonizing remaining PD-1+ T cells. The percentages of PD-1+ T cells in the peripheral blood of moderate and severe UC patients are higher than in mild UC patients (1-4). Reduction of elevated PD-1^{high} Tph cells in both UC colon and peripheral blood correlates with remission (2). Therapeutic reduction of PD-1^{high} Tph cells and inflammatory cytokines from PD-1+ T cells, by depletion and agonism signaling together, has the potential to reduce overactive immune responses and induce remission.

Aims & Methods: The potency of the agonism and depletion mechanisms of rosnilimab was evaluated in vitro using peripheral blood mononuclear cells (PBMCs) from UC patients. Rosnilimab is a human IgG1 antibody with Fc effector function. A version of rosnilimab that lacks Fc effector function was generated by mutating the IgG1 Fc domain at L234A and L235A (LALA). PBMCs from UC patients were activated with anti-CD3 and anti-CD28, cultured for several days with rosnilimab IgG1, rosnilimab IgG1-LALA, or isotype control and analyzed for the number of PD-1+ T cells and levels of inflammatory cytokines. In addition, the therapeutic potential of depletion and agonism of pathogenic PD-1+ T cells was evaluated in a mouse model of UC using a surrogate of rosnilimab. The surrogate consists of the fab do-

mains of rosnilimab formatted with a mouse IgG2a Fc domain which enables immune cell depletion in mice. On Day 0, hPD1 CD4+CD45Rb+ T cells donor cells were adoptively transferred into Rag2^{-/-} recipients to elicit UC-like disease. Starting on Day 21, 10 mpk of isotype control mIgG2a, rosnilimab-mIgG2a, or control anti-mIL-12 p40 were dosed intraperitoneally twice weekly for 4 weeks. This model system allowed assessment of the therapeutic potential of depletion and agonism mechanisms of rosnilimab on hPD1+ T cells, with a depletion-enabled mouse IgG2a isotype, in the context of T cell-driven gut inflammation and pathology.

Results: In PBMCs from UC patients, at therapeutically relevant concentrations, rosnilimab IgG1 reduced PD-1^{high} T cells by 90%, while rosnilimab IgG1-LALA reduced PD-1^{high} T cells by 14%. Isotype control did not reduce T cells. Furthermore, rosnilimab IgG1 reduced secretion of inflammatory cytokines interferon gamma (IFN-γ) and CXCL13 compared to rosnilimab IgG1-LALA or isotype control. In the hPD-1 mouse model of UC, rosnilimab mIgG2a reduced body weight loss, colon pathology, IFN-γ and CXCL13 as assessed by spatial transcriptomics of the colon, and infiltration of hPD-1 CD4+ T cells into the colon as assessed by immunofluorescence, compared to isotype control. In addition, rosnilimab mIgG2a demonstrated efficacy comparable to anti-IL-12 p40 antibody treatment.

Conclusion: Rosnilimab, a PD-1 checkpoint agonist antibody, functions to reduce pathogenic PD-1+ T cells by both depletion and agonism. These in vivo and in vitro results are consistent with the mechanisms of depletion and agonism and support the strong rationale for evaluating the therapeutic potential of rosnilimab in an ongoing phase 2 study in UC (NCT06127043).

References:

1. Shi W, Zhang Y, Hao C, Guo X, Yang Q, Du J, Hou Y, Cao G, Li J, Wang H, Fang W. PeerJ. 2023; May 31;11:e15481.
2. Long Y, Xia C, Sun Y, Ma Y, Xu L, Song Y, Liu C. Immunol Lett. 2021; 233:2-10.
3. Roosenboom B, Horjus Talabur Horje CS, Smids C, Leeuwis JW, van Koolwijk E, Groenen MJM, Wahab PJ, van Lochem EG. Scand J Gastroenterol. 2021; 56(6):671-679.
4. Nguyen J, Finkelman BS, Escobar D, Xue Y, Wolniak K, Pezhouh M. Hum Pathol. 2022; 126:19-27.

Disclosure: All authors are employees and shareholders of AnaptysBio, Inc.

DIFFERENTIAL MODULATION OF INFLAMMATORY CYTOKINE PROFILES AMONG EARLY RESPONDERS AND NON-RESPONDERS IN A PHASE 1B STUDY OF THE NUCLEOTIDE-BINDING OLIGOMERIZATION DOMAIN, LEUCINE RICH REPEAT CONTAINING X1 (NLRX1) AGONIST NX-13 IN ULCERATIVE COLITIS

B. Siegmund¹, S. Vermeire², A. Yarur³, S. Schreiber⁴, S. Danese⁵, R. Mosig⁶, F. Cataldi⁷, B. Verstockt², M.C. Dubinsky⁸
¹Charité - Universitätsmedizin Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ²University Hospitals Leuven and KU Leuven, Translational Research in Gastrointestinal Disorders - IB, Department of Gastroenterology and Hepatology and Department of Chronic Diseases, Metabolism and Aging, Leuven, Belgium, ³Cedars Sinai Medical Center, Division of Gastroenterology and Hepatology- Center for Inflammatory Bowel Diseases, Los Angeles, United States of America, ⁴University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ⁵Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁶Landos Biopharma, Inc, Blacksburg, United States of America, ⁷Landos Biopharma America, Beverly, United States of America, ⁸Mount Sinai Hospital, Mount Sinai, New York City, United States of America

Contact E-Mail Address: britta.siegmund@charite.de

Introduction: Inflammatory cells and cytokines play an instrumental role in the pathogenesis and disease course of ulcerative colitis (UC) and are thus accepted therapeutic targets. NX-13 is a first-in-class, orally active, once-daily, gut-selective NLRX1 agonist in development for UC. NLRX1 is a mitochondrial associated protein with a novel, bimodal, immunometabolic mechanism which upregulates mitochondrial metabolism, reduces oxidative stress, and decreases pro-inflammatory cell differentiation and cytokine release broadly in mouse models of IBD¹. NX-13 was well tolerated and showed gut selectivity with low systemic drug exposure in Phase 1 studies reported previously^{2,3}. We now present data from the phase 1b study describing changes in tissue cytokine levels and related to clinical response.

Aims & Methods: In this double-blind phase 1B trial (NCT04862741)³, 36 patients with active UC (Total Mayo Score 4-10; Mayo endoscopic subscore 2-3) were randomly assigned to NX-13 250mg Immediate Release (IR), 500mg IR, 500mg Delayed Release (DR) or Placebo QD for 4 weeks. Protein levels of IFN γ , IL-10, IL-12(p40), IL-17, IL-4, IL-6, IL-8, MCP1, and TNF α in colonic tissue from NX-13 treated patients collected at screening (baseline) and week 4 of treatment were determined by Human Cytokine/Chemokine Panel – Immunology Multiplex Assay (Millipore Sigma) normalized to total protein concentrations. Patients from all NX-13 dose groups with paired baseline and week 4 samples (n=18) were included in this analysis. Mann-Whitney U testing was used for comparisons between responders (Resp) and non-responders (NR).

Results: Baseline cytokines levels were not different between Resp (change from baseline of at least -3, or -30% in total Mayo Score) and NR. NX-13 treatment resulted in a decrease of multiple proinflammatory cytokines at week 4 compared to baseline in most patients, and especially in Resp. compared to NR at week 4 (Table 1). Primarily, the reduction (% change from baseline) of Th1 cytokines IL-12(p40) and IFN γ was greater in NX-13 treated patients with clinical response compared to NR, resulting in significantly lower values in Resp compared to NR at the end of the 4-week study. Similarly, IL-6 also tended to be lower among Resp. after 4 weeks of treatment with NX-13. Additionally, Th2 cytokine IL-4 values were significantly lower after 4 weeks of NX-13 in patients in clinical response

compared to NR. Myeloid cell recruitment may also have been affected by cytokine changes induced by NX-13 as IL-8 and MCP levels were lower in clinical Resp. Reduced myeloid cell recruitment is consistent with higher levels of histologic remission in NX-13 treated patients³.

Cytokine	Primary Function	Mean % CFB (95% CI)			Mean Value Week 4 / End of Study (95% CI)		
		NR (n=7)	Resp (n=11)	p=	NR (n=7)	Resp (n=11)	p=
IL-12 (p40)	Th1	199 (-5.83-404)	-2.42 (-45.0-40.1)	0.03*	12.3 (1.2-23.5)	2.0 (1.2-2.9)	0.005**
IFN γ	Th1	1208 (-837-3253)	53.4 (-164-271)	0.004**	143.4 (-135.6-422.3)	6.3 (0.03-12.6)	0.01*
IL-6	Th1	3864 (-3044-10771)	63.7 (-126-253)	ns	120.4 (-17.5-258.4)	4.5 (1.4-7.6)	0.06#
IL-4	Th2	390 (-262-1041)	-13.7 (-61.9-34.4)	ns	31.0 (3.7-58.3)	3.7 (1.7-5.6)	0.01*
IL-8	Chemoattractant	1207 (-648-3063)	568 (-817-1954)	0.07#	204.3 (-0.1-408.6)	29.4 (7.4-51.4)	0.06#
MCP-1	Chemoattractant	968 (-769-2726)	7483 (-9258-24225)	ns	1684.2 (454.9-2913.4)	475.0 (145.6-804.4)	0.05#

CFB = Change from Baseline; NR= Clinical Non-Responder; Resp = Clinical Responder defined as CFB of at least -3, or -30% in total Mayo Score; **p $\leq$ 0.005, *p $\leq$ 0.05, #p $\leq$ 0.10. ns p $>$ 0.10 by Mann-Whitney U testing.

Conclusion: Broad changes in tissue cytokine expression were specifically observed in patients that responded to NX-13- after 4 weeks of treatment, compared to non-responders. These changes mirror those seen in preclinical mouse colitis models where a broad array of cytokines is reduced¹. The early onset of cytokine shifts associated with clinical response to NX-13 at week 4 is notable and will be assessed in the ongoing phase 2 NEXUS study in patients with moderate to severe UC (NCT05785715).

References: ¹Leber, et al. J Immunol 203(12); ²Leber, et al. UEGW J 9(Supp); ³Verstockt, et al. JCC epub 11NOV2023

Disclosure: BS has received grant support from Pfizer (to institution); served as a consultant (served as a representative of Charité) for AbbVie, Arena, BMS, Boehringer, Celgene, Endpoint Health, Falk, Galapagos, Janssen, Landos, Lilly, Pfizer, PredictImmune, and Takeda; and has received speaker's fees (served as a representative of Charité) from AbbVie, CED Service GmbH, Falk, Ferring, Galapagos, Janssen, Lilly, Pfizer, and Takeda; support for attending meetings/travel from Falk; and served as president of ECCO. | SV has received grants from AbbVie, J&J, Pfizer, Takeda, and Galapagos; consulting and/or speaking fees from AbbVie, Abivax, AbolentS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, MiroBio, Morpich, MrM-Health, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance, Tillots Pharma AG, and Zealand Pharma. | AY reports consulting fees from Takeda, Prometheus Labs, Arena Pharmaceuticals, and Bristol Myers Squibb; and speaker bureau fees from Bristol Myers Squibb. | SS has received personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Dr Falk Pharma, Ferring, Fresenius, Galapagos, Genentech, GSK, Gilead, I-MAB Biopharma, Janssen, Lilly, Merck, Novartis-Sandoz, Pfizer, Protagonist, Takeda, and Theravance. | SD reports consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB Inc., and Vifor; he reports lecture fees from Abbvie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, and Takeda. | RM is an employee of Landos. | FC is an employee of Landos. | BV has received grants from Abbvie, Biora Thera-

peutics, Landos, Pfizer, Sosei Heptares, and Takeda; Speaker's fees from Abbvie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring, Galapagos, Janssen, MSD, Pfizer, R-Biopharm, Takeda, Truvion and Viatris. Consultancy fees from Abbvie, Alimentiv, Applied Strategic, Atheneum, Biora Therapeutics, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Mylan, Inotrem, Ipsos, Janssen, Progenity, Sandoz, Sosei Heptares, Takeda, Tillots Pharma and Viatris. | MCD reports consulting fees from Abbvie, Arena, Bristol Myers Squibb, Celgene, Eli Lilly, Genentech, Gilead, Janssen, Pfizer, Prometheus Labs, and Takeda; and is founder and a shareholder of Trellus Health.

MP450

CHARACTERIZATION OF TWO NOVEL EXTENDED HALF-LIFE MONOCLONAL ANTIBODY DRUG CANDIDATES TARGETING TL1A FOR THE TREATMENT OF IBD

E. Zhu¹, D. Rios¹, J. Milligan¹, J. Ministro¹, B. Kang¹, J. Friedman², D. Nguyen², A. Spencer², M. Rose², J. Oh¹, H. Shaheen¹

¹Paragon Therapeutics, Waltham, United States of America, ²Spyre Therapeutics, Waltham, United States of America

Contact E-Mail Address: joshfriedman@me.com

Introduction: Tumor necrosis factor (TNF)-like ligand 1A (TL1A) mediates a broad spectrum of pro-inflammatory and fibrotic effects and is implicated in the pathogenesis of several immunologic disorders. A pathogenic role for TL1A in IBD is suggested by genetic association. Blockade of the interaction of TL1A with its cognate receptor, DR3, has been shown to ameliorate disease activity in patients with Crohn's disease (CD) and ulcerative colitis (UC). We have characterized SPY002-091 and SPY002-072, two novel TL1A-specific fully human IgG1 monoclonal antibodies (mAbs) with extended pharmacokinetic (PK) half-life. Both antibodies bind soluble and membrane-bound TL1A with high affinity and potentially inhibit TL1A-mediated signaling.

Aims & Methods: SPY002-091 and SPY002-072 were evaluated in multiple *in vitro* and *ex vivo* assays and compared to other anti-TL1A mAbs in clinical development (MK-7240, RG6631, and TEV-48574). Binding affinity to soluble TL1A was determined by surface plasmon resonance and binding to membrane-bound TL1A was confirmed by flow cytometry (FACS). Competitive blockade of TL1A binding to cell-surface DR3 was determined by FACS, and competition against the decoy receptor, DcR3, was evaluated by ELISA. The binding epitopes of SPY002-091 and SPY002-072 were determined using cryogenic electron microscopy (cryo-EM). TF-1 cell apoptosis and a primary human whole blood-based assay measuring IFN γ secretion were used to assess functional blockade of TL1A. Half-life extension was measured via pharmacokinetic analysis in cynomolgus monkeys given a single bolus of either SPY002 mAb by intravenous and/or subcutaneous (SC) administration.

Results: SPY002-091 and SPY002-072 each bind to distinct epitopes on TL1A with sub-nanomolar affinity but do not bind the related TNF super family proteins TNF, FasL, TRAIL, or LIGHT. Both antibodies bind soluble TL1A and TL1A expressed on the surface of human embryonic kidney (HEK) cells. Both antibodies potentially inhibit TL1A-induced apoptosis in human TF-1 cells and TL1A-induced secretion of IFN γ in human whole blood, with IC₅₀ values comparable to those of RG6631 and TEV-48574, and a substantially lower IC₅₀ than that of MK-7240.

In cynomolgus monkeys, both SPY002-091 and SPY002-072 exhibit a pharmacokinetic half-life of approximately 25 days compared to an observed half-life of 9-12 days for RG6631 and MK-7240. Structural studies employing cryo-EM show that each SPY002 mAb targets an epitope within a single TL1A subunit enabling binding to both monomeric and trimeric TL1A. Based on allometric scaling of SPY002-091 and SPY002-072 clearance in

NHPs, predictive simulations of their human PK properties suggest that Q8W-Q12W SC dosing will achieve therapeutic exposures in patients across a wide range of body weights and albumin concentrations.

Conclusion: We have characterized two anti-TL1A antibodies that exhibit high selectivity and affinity for TL1A, demonstrate effective blockade of the TL1A interaction with DR3, and potentially inhibit downstream cellular signaling. With an extended half-life observed in NHP, both SPY002-091 and SPY002-072 demonstrate therapeutic potential for effective and safe treatment of CD and UC with the advantage of infrequent SC dosing. Further preclinical and clinical studies are warranted to demonstrate this potential.

Disclosure: EZ, DR, JM, JM, BK, JO, and HS are employees of Paragon Therapeutics.

JF, DN, AS, and MR are employees of Spyre Therapeutics.

MP451

AQ312, A POTENT SMALL MOLECULE ARYL HYDROCARBON AGONIST, DEMONSTRATES EFFICACY IN EXPERIMENTAL MODELS OF INFLAMMATORY BOWEL DISEASE

W. Russell¹, M. Johansson¹, M. Hultqvist¹, J. Lund¹

¹Aqilion AB, Helsingborg, Sweden

Contact E-Mail Address: wayne.russell@aqilion.com

Introduction: Despite approval of several therapeutic approaches for the treatment of IBD, current treatments do not extend clinical response beyond the 40% 'therapeutic ceiling' and many patients do not achieve clinical remission.

The aryl hydrocarbon receptor (AhR) is a cytosolic ligand-dependent transcription factor that is expressed in many cell types. Activation of the receptor regulates many pathophysiological functions, including immune homeostasis and barrier integrity. AQ312 is a potent and selective AhR agonist undergoing preclinical development for the treatment of IBD.

Aims & Methods: The aim of the work was to determine the potency of AQ312 and evaluate the effects of AQ312 in preclinical animal models of IBD.

Cellular potency of AQ312 was determined using the human, mouse and rat AhR/ARNT reporter gene assay and compared to reference AhR agonists (Indigo Biosciences). The pharmacokinetics of AQ312 were measured in rats after acute administration (P.O.). Acute colitis was induced in C57Bl/6 mice by administration of DSS in the drinking water. Chronic colitis was induced in SCID mice by transfer of CD4⁺ T cells obtained from spleens of Balb/c mice. AQ312 was administered perorally (P.O.) at 1mg/kg, daily (d-7 to d9 in DSS and d0-d48 T cell transfer). Body weight was monitored throughout the study whilst colon weight and length, and inflammatory cells (flow cytometry) and cytokines (Luminex) in the colon were determined at necropsy. In addition, expression of cytochrome P450 1A1 (CYP1A1) was determined in colon tissue by RT-PCR to demonstrate AhR activation.

Results: AQ312 was a selective and potent activator of AhR, with similar potency for human, mouse and rat receptors (EC50 of 4.3, 2.1 and 3.9nM respectively). In rats, a single dose of AQ312 was rapidly cleared (T_{0.5}=1h) with little systemic exposure after 4h. Induction of acute or chronic experimental colitis in mice led to marked colon edema, immune cell infiltration and increased production of inflammatory cytokines. These effects were significantly reduced after per oral treatment with AQ312.

Conclusion: AQ312 is a potent and selective small molecule AhR agonist that is rapidly cleared in rodents. The molecule has demonstrated therapeutic benefit in 2 models of experimental colitis. AQ312 has the potential to be the 'best in class' AhR agonist for the treatment of IBD.

Disclosure: Nothing to disclose.

MP452

DIRECT INTESTINAL INFECTION WITH SARS-COV2 LEADS TO SYSTEMIC DISSEMINATION IN MICE

L. Casorla Perez¹, G. Oliva Escudero¹, K.A. Toth¹, D.M. Alvarado¹, C. Karl¹, L. Thackray¹, M.S. Diamond¹, S. Ding¹, M. Ciorba¹

¹Washington University School of Medicine, Saint Louis, United States of America

Contact E-Mail Address: mciiorba@wustl.edu

Introduction: SARS-CoV-2 exhibits an extra-pulmonary tropism, with up to 70% of COVID-19 patients experiencing at least one gastrointestinal (GI) symptom. Persistent viral presence has been observed in intestinal biopsies months after the virus has been cleared from the respiratory tract, which has been implicated in the development of long COVID symptoms. Despite these observations, the dynamics of SARS-CoV-2 infection within the intestine, as well as its potential to act as a viral reservoir and source of ongoing pathogenesis, remain largely unknown.

Aims & Methods: We recently established a robust mouse model to study the dynamics of intestinal SARS-CoV-2 infection by exposing the distal ileum of mice through ventral laparotomy and administering the virus directly into the lumen.

Results: In wild-type (WT) C57Bl/6 mice, after perfusion, viral RNA was detected throughout the GI tract at 7 days post infection (dpi), not only at the site of initial infection, but also in other regions such as the esophagus, stomach, duodenum, jejunum, colon, and rectum. Moreover, viral RNA was also found in extra-intestinal sites, including the salivary gland, liver, and brain. In *Stat1*^{-/-} mice with impaired type I, II, and III interferon signaling, the levels of viral RNA as well as nucleocapsid antigens in the GI tract were 10 to 100 times higher than those in WT mice. Virus also successfully disseminated to systemic organs such as the heart, lung, kidney, brain, and spleen. Viral shedding in feces was observed from 3 to 7 dpi in *Stat1*^{-/-} mice but not WT mice. Notably, rapid secretory diarrhea was observed in these mice, marking the first instance of diarrhea induced by SARS-CoV-2 infection in a mouse model. Additional studies are ongoing to further characterize these findings, including the assessment of the timing of viral replication, titration of infectious viruses, detailed histological analysis, and immunological profiling.

Conclusion: These results emphasize the usefulness of this mouse model in exploring the mechanisms underlying the impact of SARS-CoV-2 on the intestines locally and systemically. The study also underscores the critical role of interferon signaling in restricting intra-intestinal replication and preventing the virus from spreading to other organs. This has important clinical implications, particularly for individuals taking JAK inhibitor medications, which could affect the interferon response and potentially increase susceptibility to more severe outcomes from SARS-CoV-2 infection.

Disclosure: M.S.D. is a consultant for Inbios, Vir Biotechnology, Ocugen, Topspin Therapeutics, GlaxoSmithKline, Moderna, and Immunome. The Diamond laboratory has received unrelated funding support in sponsored research agreements from Vir Biotechnology, Emergent BioSolutions, and Moderna.

MP453

MITOCHONDRIAL PERTURBATION OF THE INTESTINAL EPITHELIUM CAUSES INFLAMMATION-RELATED TRANSCRIPTIONAL RESPONSES AND MICROBIOTA-DEPENDENT TISSUE INJURY

E. Urbauer¹, D. Aguanno¹, N. Mindermann¹, H. Omer¹, A. Metwaly¹, T. Faro², M. Remke³, S. Reitmeier¹, S. Bärthel^{4,5,6}, J. Kersting⁷, Z. Huang⁷, F. Xian⁸, D. Saur^{4,5,6}, B. Stecher^{9,10}, M. List^{7,11}, D. Gómez-Varela⁸, K. Steiger³, M. Allez¹², E. Rath¹, D. Haller^{1,13}

¹Technical University of Munich, Chair of Nutrition and Immunology, Freising-Weihenstephan, Germany, ²LMU Munich, Department of Pediatrics, Dr. von Hauner Children's Hospital, University Hospital, Munich, Germany, ³Technical University of Munich, Institute of Pathology, Munich, Germany, ⁴German Cancer Research Center and German Cancer Consortium, Division of Translational Cancer Research, Heidelberg, Germany, ⁵Technical University of Munich, Center for Translational Cancer Research (TranslaTUM), School of Medicine, Munich, Germany, ⁶Technical University of Munich, Institute of Experimental Cancer Therapy, Klinikum Rechts der Isar, School of Medicine, Munich, Germany, ⁷Technical University of Munich, Data Science in Systems Biology, TUM School of Life Sciences, Freising-Weihenstephan, Germany, ⁸University of Vienna, Systems Biology of Pain, Division of Pharmacology & Toxicology, Department of Pharmaceutical Sciences, Faculty of Life Sciences, Vienna, Austria, ⁹Ludwig-Maximilians University of Munich, Max von Pettenkofer-Institute for Hygiene and Clinical Microbiology, Munich, Germany, ¹⁰Partner site LMU Munich, German Center for Infection Research, Munich, Germany, ¹¹Technical University of Munich, Munich Data Science Institute, Garching, Germany, ¹²Hopital Saint-Louis APHP, Université Denis Diderot Paris 7, Gastroenterology, Paris, France, ¹³Technical University of Munich, ZIEL Institute for Food & Health, Freising-Weihenstephan, Germany

Contact E-Mail Address: nora.mindermann@tum.de

Introduction: The intestinal epithelium is the most regenerative tissue in the human body and an essential interface between the microbial ecosystem and the underlying mucosa, orchestrating both immune-mediated and metabolic functions. Mitochondrial signaling and metabolism controls the phenotype and function of intestinal epithelial cells (IECs) and mitochondrial perturbation is associated with chronic inflammation. We hypothesize that disruption of microbial-metabolic circuits and impaired metabolic flexibility of IECs contribute to the initiation and progression of tissue injury underlying chronic inflammation.

Aims & Methods: To address the role of mitochondrial impairment in epithelial homeostasis, conditional deletion of Heat shock protein 60 (Hsp60) was induced in the epithelium of Hsp60^{ΔAIEC} and Hsp60^{ΔAIEC};*Il10*^{-/-} mice under specific pathogen free and germfree conditions. Blinded histological analysis was used to assess metabolic injury and tissue inflammation. Additional 16S rRNA and shallow shotgun sequencing as well as metaproteomic analysis were performed to identify microbiome changes at the compositional and functional levels. Nanostring analysis and single-cell RNA sequencing (scRNA-seq) were used to identify epithelial cell population-specific transcriptional responses and to validate these gene signatures in resected tissues from Crohn's disease patients.

Results: Hsp60 deletion in IECs leads to the disruption of mitochondrial metabolism and the development of irregular crypt architecture, referred to as metabolic injury. Tissue lesions and IBD-related colitis are accelerated in Hsp60^{ΔAIEC};*Il10*^{-/-} mice. Germfree mice are protected from injury and inflammation, demonstrating a causal contribution of bacteria to metabolic injury. Mitochondrial perturbation in Hsp60^{ΔAIEC} mice is associated with microbial dysbiosis, including an increased abundance of *Bacteroi-*

des spp., which are maintained during sustained inflammation in Hsp60^{ΔIEC}/110^{-/-} mice. Consistently, *B. caecimuris* triggers tissue aberration in monocolonized-Hsp60^{ΔIEC} mice, supporting its deleterious role in tissue homeostasis. Furthermore, metaproteomic analysis revealed a metabolic adaptation of *B. caecimuris* in response to tissue injury. Importantly, the clinical relevance of *Bacteroides spp.* is confirmed in a combined analysis of three IBD cohorts (N=560 patients). Transcriptional profiling of the epithelium identified a gene signature in injury-associated sub-populations, including *Ido1*, *Nos2* and *Duox2*. Remarkably, the identified metabolic injury gene signature discriminates inflamed (N=196) versus non-inflamed (N=147) mucosa in CD patients, thus validating the human relevance of epithelial mitochondrial disruption in IBD.

Conclusion: Bacterial presence is a key driver of intestinal injury and metabolic injury associates with dysbiotic changes, notably expansion of *Bacteroides spp.* and their metabolic adaptation. Furthermore, mitochondrial perturbation induces a metabolic injury signature, which differentiates inflamed versus non-inflamed mucosa in IBD patients, strengthening the hypothesis of unresolved metabolic injury as a novel concept in the pathogenesis of intestinal inflammation.

Disclosure: Nothing to disclose.

Deciphering cancer

16:00-17:00 / Poster Stage 2

MP455

LYNCH SYNDROME AND THYROID NODULES: A SINGLE CENTER EXPERIENCE

I. Spinelli¹, S. Moffa¹, F. Fianchi¹, T. Mezza¹, F. Cinti¹, G. Di Giuseppe¹, C. Marmo¹, G. Ianaro¹, F.R. Ponziani¹, A. Tortora², M.E. Riccioni¹, A. Giaccari¹, A. Gasbarrini¹

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy,

²Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy

Contact E-Mail Address: irenespinelli1@gmail.com

Introduction: Lynch syndrome (LS) is an autosomal dominant genetic disease associated with germ-line mutations of genes involved in mismatch repair (MLH1, MSH2, MSH6 and PMS2) and the EPCAM gene. LS patients are at increased risk for colorectal cancer and other malignancies (especially endometrial, ovarian, and gastric cancer). There are few reported cases of thyroid cancer in patients suffering from LS.

Aims & Methods: To systematically investigate the presence of thyroid nodules in LS patients, to assess their cytologic classes and to explore its association with genetic features of the disease. A retrospective and descriptive analysis was conducted to include all LS patients followed at CEMAD (Centro Malattie Apparato Digerente) of Fondazione Policlinico Universitario A. Gemelli IRCCS. For each patient, characteristics of LS disease and previous history of thyroid disease were evaluated. Majority of patients underwent thyroid ultrasound (US) and nodule cytology was performed when needed. Gene mutations were reviewed for each patient with thyroid nodules and previous history of thyroid disease.

Results: A total of 139 LS patients, 52 males and 87 females, were included in the study. 103 patients (74%) underwent thyroid ultrasound examination, and 7 patients (5%) had a previous history of thyroid disease (cancer or multinodular goitre). For these two groups, mean age was 51.9 years. 29 patients (21%) did not already perform US at the time of analysis. Thyroid nodules were found in 62 patients (60%) who underwent US and 9 of them (14%) had suspicious features of malignancy inducing fine-needle aspiration biopsy. Cytologic analysis classified 7 of 9 cases (78%) as TIR2 and 2 (22%) as TIR3a. Between patients with nodular thyroid disease (single nodule, multinodular goitre and cancer), most of them (25 patients, 36% of total) were carriers of MSH6 mutation, while 22 (32%), 17 (24%) and 5 (7%) had MSH2, MLH1 and PMS2 mutations, respectively.

Conclusion: A high prevalence of thyroid nodules is found in patients with Lynch Syndrome, especially in MSH6 carrier patients. Performing at least one thyroid ultrasound examination is suggested for detection of nodular thyroid disease in LS patients. Systematic investigations are needed to estimate their prevalence, features, and risk of malignant transformation.

References: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Genetic/Familial High-Risk Assessment: Colorectal Version 2.2023 — October 30, 2023

Verrienti A, Carbone A, Sponziello M, Pecce V, Cito DS, Bruno R. Papillary thyroid carcinoma as first and isolated neoplastic disease in a Lynch syndrome family member with a germline MLH1 mutation. *Endocrine*. 2022 Jun;77(1):199-202. doi: 10.1007/s12020-022-03048-1. Epub 2022 Apr 12. PMID: 35415788.

Pacini F, Basolo F, Bellantone R, Boni G, Cannizzaro MA, De Palma M, Durante C, Elisei R, Fadda G, Frasoldati A, Fugazzola L, Guglielmi R, Lombardi CP, Miccoli P, Papini E, Pellegriti G, Pezzullo L, Pontecorvi A, Salvatori M, Seregini E, Vitti P. Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. *J Endocrinol Invest*. 2018 Jul;41(7):849-876. doi: 10.1007/s40618-018-0884-2. Epub 2018 May 4. PMID: 29729004.

Disclosure: Nothing to disclose.

MP456

CLINICOPATHOLOGIC SIGNIFICANCE OF OSBPL3 AS A SURVIVAL PREDICTOR IN COLORECTAL CANCER

J.H. Kim¹, S. Han², S. Jeong³, Y.H. Han¹, H. Lee¹, J.-W. Chung¹, K.O. Kim¹, K.A. Kwon¹

¹Gachon University Gil Medical Center, College of Medicine, Gachon University, Department of Internal Medicine, Incheon, South Korea,

²Jeju National University Hospital, Jeju National University College of Medicine, Jeju National University, Department of Internal Medicine, Jeju, South Korea, ³Gachon Medical Research Institute, Gachon University Gil Medical Center, College of Medicine, Gachon University, Gachon Biomedical Convergence Institute, Incheon, South Korea

Contact E-Mail Address: junghokimm@gilhospital.com

Introduction: Colorectal cancer (CRC) is one of the most common malignancies worldwide. Oxysterol binding protein 3 (OSBPL3) is a protein involved in lipid binding and transport and is known to play an essential role in tumorigenesis. However, its expression and function in colorectal cancer (CRC) is unclear.

Aims & Methods: This study included patients who underwent CRC surgery at Gachon University Gil Medical Center between April 2010 and January 2013. We analyzed 448 patients with primary colorectal cancer (CRC) who underwent surgery and had preserved paraffin blocks. Using immunohistochemical staining, a clinically applicable, rapid, and highly accurate assay method, we aimed to detect OSBPL3 expression in CRC and correlate it with clinicopathologic characteristics, prognosis, and survival to identify novel patient-specific biomarkers.

Results: The 5-year event-free survival (EFS) and disease-specific survival (DSS) hazard ratios (HRs) of the OSBPL3^{High} subgroup were 1.65 (95% confidence interval (CI): 0.99-2.76, $p = 0.05$) and 1.49 (95% CI: 0.89-2.61, $p = 0.20$), respectively. When tumor node metastasis (TNM) staging and OSBPL3 expression were combined, the 5-year EFS and DSS HRs of patients with CRC with OSBPL3^{High} expression cancer at the same TNM stage (stage III/IV) were 4.06 (95% CI: 2.72-6.07, $p = 0.001$) and 4.41 (95% CI: 2.91-6.68, $p = 0.001$), respectively, compared to those with OSBPL3^{Low} expression cancer, indicating a poor prognosis. Therefore, OSBPL3^{High} expression is associated with poor prognosis and survival rate in CRC patients. Combining OSBPL3 expression with TNM staging can predict CRC prognosis and survival rate more accurately.

Conclusion: Our data show that increased expression of OSBPL3 is associated with poor prognosis and survival rate in CRC patients. By combining OSBPL3 expression with TNM staging, we can more accurately predict the prognosis of CRC.

Disclosure: Nothing to disclose.

MP457

ANTI-TUMOR EFFECT OF WEE1 INHIBITOR AZD1775 ON COLORECTAL CANCER

M. Ariyoshi¹, H. Takigawa¹, Y. Kitadai¹, D. Shimizu¹, R. Miyamoto¹, Y. Hiyama¹, Y. Urabe¹, S. Oka¹

¹Hiroshima University Hospital, Department of Gastroenterology, Hiroshima, Japan

Contact E-Mail Address: misa4235@hiroshima-u.ac.jp

Introduction: Wee1 negatively regulates the G2/M checkpoint of the cell cycle, inhibiting cells with DNA damage from entering mitosis and inducing apoptosis. Although efficacy of Wee1 inhibitors as single agents or in combination with other agents has been reported in a variety of carcinomas and the association between Wee1 inhibitors and tumor immunity

has been reported, the effect of Wee1 inhibitors on the tumor immune microenvironment in colorectal cancer (CRC) has not been clarified. Since *p53* and *KRAS* are involved in cell cycle regulation at the G1/S checkpoint, mutations in them may increase dependence on the G2/M checkpoint for DNA repair, making Wee1 inhibitors more effective.

Aims & Methods: This study aimed to clarify the association between Wee1 expression and clinicopathological features in CRC and the effect of Wee1 inhibitors on the tumor immune microenvironment in CRC. Study 1: We performed immunostaining on 152 CRC cases surgically resected at our hospital between May 2013 and February 2015, and classified them into positive and negative groups according to the degree of Wee1 expression and investigated the association between Wee1 expression and clinicopathological features. Study 2: We measured Wee1 expression levels by Realtime PCR on 10 human-derived CRC cell lines and 2 mouse-derived CRC cell lines. We examined the effect of Wee1 inhibitor (AZD1775) on cell proliferation using Timelapse system. We examined the effect of Wee1 inhibitor on cell cycle using Cell Cycle Analysis Kit. We examined the effects of Wee1 inhibitor on apoptosis induction were examined using the Apoptosis Detection Kit. Study 3: We created the CRC orthotopic transplantation mouse model by transplanting the CRC cell line MC38 derived from C57BL/6 mice into the cecum of mice, comparing the tumor sizes of the control and treatment groups treated with Wee1 inhibitor for 21 days, and evaluating the effect of Wee1 inhibitor on the tumor immune microenvironment by immunostaining and RNA sequencing of mice tumor specimens.

Results: Study 1: No significant association was found between Wee1 expression and clinicopathological features or prognosis. However, overall survival rate was significantly higher in Wee1 positive and *KRAS*-mutant patients compared to Wee1 negative and *KRAS* wild-type patients. Study 2: Real time PCR showed that Wee1 expression was higher in most CRC cell lines than in normal colon mucosa. Wee1 inhibitor attenuated cell proliferation in a concentration-dependent manner in all CRC cell lines, and the effect was independent on Wee1 expression level. Cell cycle analysis showed that the percentage of cells in G2/M phase increased after exposure to Wee1 inhibitor, especially in cell lines with both *p53* and *KRAS* mutations. In addition, the number of apoptotic cells increased after exposure to Wee1 inhibitor, but in the cell lines with *KRAS* mutation and *p53* wild type, the number of apoptotic cells did not increase. Study 3: In the orthotopic transplanted mouse model, tumor volume was significantly smaller in the treated group compared to the control group, and immunohistological examination and RNA sequencing of mice tumor specimens showed enhanced tumor immunity and suppressed stromal reaction.

Conclusion: Wee1 inhibitor attenuated CRC cell proliferation through modulating cell cycle, especially in cell lines with *p53* mutation and attenuated tumor growth via enhancement of tumor immune response and suppression of stromal reaction in orthotopic transplanted mouse model. Wee1 inhibitor AZD1775 could be the promising treatment option for CRC.

Disclosure: Nothing to disclose.

MP458

ENDOSCOPIC FINDINGS FOR EACH MUCIN PHENOTYPE IN SUPERFICIAL NONAMPULLARY DUODENAL EPITHELIAL TUMORS

A. Nakayama¹, M. Kato², Y. Imura², S. Murata², D. Minezaki¹, A. Tojo², H. Sakurai², K. Iwata¹, K. Miyazaki¹, T. Masunaga¹, M. Mizutani², T. Akimoto¹, Y. Takatori¹, S. Kawasaki², N. Matsuura¹, T. Sujino², K. Takabayashi², N. Yahagi¹

¹Keio University, Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Tokyo, Japan,

²Keio University School of Medicine, Center for Diagnostic and Therapeutic Endoscopy, Tokyo, Japan

Contact E-Mail Address: anakayama34@keio.jp

Introduction: In the endoscopic diagnosis of superficial nonampullary duodenal epithelial tumor (SNADET), it is not easy to differentiate carcinoma from adenoma. On the other hand, SNADETs can be classified into gastric and intestinal phenotypes of mucin phenotype, and it has been reported that carcinomas of the gastric phenotype in particular show a poor prognosis. If the mucin phenotype can be predicted only by endoscopic findings, it may be possible to estimate the biological malignancy of SNADETs. Then, the following studies were conducted, focusing on it as a new endoscopic diagnosis.

Aims & Methods: The aim of this study was to clarify the endoscopic findings of SNADET in each mucin phenotypes. Between August 2018 and April 2021, 500 cases of suspected SNADET in our hospital were prospectively entered for analysis. Finally, 401 cases with 401 lesions that were treated endoscopically and pathologically diagnosed as SNADET were included and analyzed. Two pathologists with expertise in gastrointestinal pathology performed histological diagnosis according to the Vienna Classification (VCL) and evaluation of mucin phenotypes based on the results of immunostaining for CD10, MUC2, MUC5AC, and MUC6. Each endoscopic finding was compared between gastric and intestinal phenotype, and multivariate analysis was performed using a logistic regression model.

Results: With regard to pathological evaluation, 289 (72.1%) cases were diagnosed as VCL category 3 and 112 (27.9%) cases were diagnosed as VCL category 4/5. The details of mucin phenotypes in this SNADETs were as follows: 44 pure gastric, 11 gastric predominant, 18 mixed gastrointestinal, 159 intestinal predominant, and 180 pure intestinal phenotypes, respectively, and the percentages of VCL category 4/5 were 63.6%, 54.5%, 38.9%, 30.8% and 16.1%, respectively ($P < 0.01$, Cochran-Armitage trend test). Compared in the two groups of gastric phenotype (pure gastric and gastric predominant) and intestinal phenotype (pure intestinal and intestinal predominant), there were significant differences in location (from the bulb to the proximal descending part (hereafter, proximal side): 82.2% vs 29.0%, $P < 0.01$), lesion diameter (20.0 mm vs 15.0 mm, $P < 0.05$), macroscopic type (Type 0-I: 60.0% vs 14.8%, $P < 0.01$), redness (present: 68.9% vs 32.8%, $P < 0.01$), surface structure (closed-loop structure (CLS): 84.4% vs 29.6%, $P < 0.01$), white opaque substance (WOS) (absent: 51.1% vs 11.0%, $P < 0.01$). In multivariate analysis, location (proximal side: OR 4.5, 95%CI 1.8-10.9), macroscopic type (Type 0-I: OR 2.5, 95%CI 1.1-5.7), surface structure (CLS: OR 5.4, 95%CI 2.1-13.8), WOS (absent: OR 2.9, 95%CI 1.3-6.7) were independently and significantly associated with being gastric phenotype of SNADET.

Conclusion: This study showed that SNADETs with gastric and intestinal phenotypes were found to show different endoscopic findings.

Disclosure: There is no conflict of interest in this study.

MP459

THE SIGNIFICANCE OF CD13 DETECTION IN GASTRIC JUICE EXOSOMES FOR EARLY GASTRIC CANCER SCREENING AND DIAGNOSIS

J. Ning¹, Y. Lang¹, X. Hao¹, Y. Wang¹, Y. Xiong¹, M. Zu¹, J. Zhang¹, S. Ding¹

¹Peking University Third Hospital, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: njing2006@aliyun.com

Introduction: Gastric cancer is one of the most common malignant tumors with high morbidity and mortality. Manifestations of early gastric cancer often lack specificity, leading to delayed diagnosis, with a majority of cases progressing to advanced stages upon identification. Additionally, traditional tumor markers such as CEA, CA19-9, and CA72-4 exhibit limited sensitivity and specificity. Hence, there exists an urgent imperative to discover novel predictive and diagnostic markers for early-stage gastric cancer. Unlike gastric mucosal tissue biopsy, which is restricted to localized sampling, gastric juice offers a more comprehensive and representative reflection of the overall gastric environment. However, the acidic nature of gastric juice and the presence of multiple digestive enzymes present challenges for the direct detection of protein markers in gastric juice. Exosomes, characterized by lipid bilayer membranes, serve to stabilize proteins and facilitate their transportation within the microenvironment and distant regions, thereby exerting regulatory functions and offering potential diagnostic significance.

Aims & Methods: In this study, we endeavored to identify protein markers within gastric juice exosomes of early gastric cancer patients with enhanced sensitivity and specificity. Briefly, gastric juice samples were collected from early gastric cancer patients and chronic gastritis patients matched for age and gender, who underwent gastroscopy at Peking University Third Hospital. Exosomes were isolated through ultracentrifugation. Following protein quality control, label-free quantitative proteomics was employed to investigate the differential protein composition between the two groups. Additionally, we conducted further analysis to explore the interaction among the differential proteins in the two groups with KEGG enrichment analysis. Moreover, immunohistochemical (IHC) staining, western blot and electron microscopy immunocolloid gold staining were conducted to validate the proteomic findings.

Results: The results of differential protein expression analysis indicated the presence of 21 up-regulated proteins and 32 down-regulated proteins in gastric juice exosomes of the early gastric cancer group compared to the gastritis group (fold change >2 , $P < 0.05$). Further KEGG pathway enrichment analysis revealed that the differentially expressed proteins were primarily enriched in pathways related to glucose and lipid metabolism, immunomodulation, and the PPAR signaling pathway. In comparison to the gastritis group, the levels of CD13 protein in gastric juice exosomes were significantly increased by 7.45-fold ($P = 0.043$) in early gastric cancer patients. IHC staining was conducted and the results demonstrated significantly higher expression levels of CD13 in gastric mucosa tissues of gastric cancer patients compared to those of patients with gastritis, consistent with those in gastric juice exosomes. Additionally, Western blot confirmed elevated levels of CD13 in gastric juice exosomes of the early gastric cancer group compared to the gastritis group, further corroborating the proteomics findings. Furthermore, electron microscopy immunocolloid gold staining revealed predominant expression of CD13 on the membrane of gastric juice exosomes, providing a crucial basis for its subsequent direct detection through antigen-antibody recognition.

Conclusion: In summary, our findings suggested that CD13 in gastric juice exosomes may serve as a promising marker for early gastric cancer screening, aiming to facilitate early diagnosis and treatment interventions.

Disclosure: Nothing to disclose.

MP460

DEVELOPMENT AND VALIDATION OF A URINARY EXOSOMAL MIRNA DIAGNOSTIC PANEL FOR EARLY DETECTION OF ESOPHAGEAL CANCER

T. Murano^{1,2}, H. Yamashita¹, Y. Kano¹, K. Takeuchi³, T. Yoshimoto⁴, H. Fujiwara⁵, S. Namiki², H. Yamaguchi⁶, Y. Ando⁶, Y. Nishiyama⁶, M. Mizunuma⁶, Y. Ichikawa^{6,7}, T. Yano¹

¹National Cancer Center Hospital East, Department of Gastroenterology and Endoscopy, Chiba, Japan, ²Tokyo Metropolitan Tama Medical Hospital, Department of Gastroenterology, Tokyo, Japan, ³Tsujinaka Hospital Kashiwanoha, Department of Gastroenterology, IBD Center, Chiba, Japan, ⁴Medical Corporation Doyukai Kasuga Clinic, Tokyo, Japan, ⁵Tokyo Medical and Dental University, Department of Gastrointestinal Surgery, Tokyo, Japan, ⁶Craif Inc., Nagoya, Japan, ⁷Nagoya University, Institute of Innovation for Future Society, Nagoya, Japan

Contact E-Mail Address: tatmuran@east.ncc.go.jp

Introduction: Esophageal squamous cell carcinoma (ESCC) is the most common histological type of esophageal cancer in eastern Asia and Africa. Diagnosis at early stage is crucial to reduce the mortality of ESCC. Currently, esophagogastroduodenoscopy (EGD) is the golden standard for screening ESCC, however, the patient compliance rate has been low due to the invasiveness and high cost of EGD. Thus, there is an unmet need for the development of diagnostic modality that enables non-invasive early detection of ESCC.

Aims & Methods: The purpose of this study is to construct a urinary exosomal miRNA panel as a least invasive test that can detect ESCC with high accuracy and validate its performance in a prospective cohort enriched with early ESCC. We prospectively collected urine samples from 161 ESCC patients and 180 healthy controls (HC) at five institutions from September 2019 to March 2023. Exosomes were extracted from urine specimens by polymer precipitation method, and exosomal miRNAs were subjected for comprehensive expression analysis by small RNA seq. Of the 341 total samples, 309 samples (90.6%) that passed the QC check were selected for subsequent data-analysis. In the training cohort (100 samples of ESCC and 98 samples of HC), we measured the expression of 328 miRNAs to identify candidate biomarker miRNAs. A miRNA diagnostic panel was constructed using machine learning analysis, and diagnostic performance was evaluated using a 5-fold cross-validation method. In the validation cohort (50 samples of ESCC and 61 samples of HC), the diagnostic performance of the urinary miRNA diagnostic panel was verified with blind to clinical information.

Results: In the RNAseq analysis of the training cohort (ESCC; mean age 68.2 years, 77.9% male; HC; mean age 58.1 years, 76.3% male), 33 out of 328 miRNAs were differentially expressed between ESCC and HC. Out of the 33 dysregulated miRNAs, 21 were upregulated and 12 were down-regulated. A multi-miRNA biomarker panel composed of miRNAs that were individually significant and non-significant between ESCC and HC had a diagnostic performance of AUC 0.89 (95% CI 0.84 to 0.94) by 5-fold cross-validation. In the validation cohort (ESCC; mean age 63.0 years, 78.0% male, median size 32mm, Stage I/II/III/IV 54/10/26/10%, HC; mean age 51.0 years, 52.5% male), The diagnostic performance of the miRNA diagnostic panel was AUC 0.85(95% CI 0.80 to 0.90), with a sensitivity of 84%, specificity of 73.8%, and accuracy of 78.4% at a pre-defined cutoff value. There was no confounding of diagnostic performance by age, gender, BMI, history of alcohol consumption or smoking. The sensitivity by clinical stage of ESCC was 88.9/80.0/77.8/80% for Stage I/II/III/IV.

Conclusion: We developed and validated a urinary exosomal miRNA diagnostic panel, which may be a new non-invasive diagnostic method that contributes to the early detection of ESCC.

Disclosure: Tomonori Yano received research funding from Craif Inc.

MP461

CLINICOPATHOLOGICAL FEATURES AND CARCINOGENIC POTENTIAL OF SERRATED POLYPOSIS SYNDROME

R. Hirai¹, H. Kinugasa¹, M. Otsuka¹

¹Okayama University Hospital, Gastroenterology and Hepatology, Okayama, Japan

Contact E-Mail Address: ryosukehirai1122@gmail.com

Introduction: Serrated Polyposis Syndrome (SPS) is a disease characterized by multiple serrated lesions (SLs), such as sessile serrated lesions (SSL), traditional serrated adenomas (TSA), and hyperplastic polyps (HP). Although it has been suggested that SPS may be a high risk for developing colorectal cancer, it may have been frequently missed in the past due to low recognition and diagnostic complexity. Epidemiological investigations and studies on its pathogenesis are extremely limited, especially with the new WHO classification revised in 2019¹.

Aims & Methods: This study aimed to characterize the clinicopathological and molecular features of carcinogenesis in SPS. We retrospectively reviewed the findings of colonoscopy of 640 patients who underwent endoscopic/surgical resection of one or more serrated lesions at Okayama University Hospital between January 2012 and October 2023. Patients were classified into two groups: those matching the diagnosis of SPS (SPS group) and others (Sporadic SL group). The control group consisted of patients who underwent colonoscopy as a screening examination between January and December 2022 and had no serrated lesions. Patient background, incidence of colorectal cancer, and clinicopathological findings of all resected lesions including tubular adenoma (TA) were evaluated in the above three groups. Genomic DNA was extracted from FFPE tissues of all colorectal cancers, and mutation analysis of KRAS (codon 12 and 13) and BRAF (codon 600) were performed by direct sequencing of the PCR products. Microsatellite instability (MSI) analysis was performed by coelectrophoretic sequencing of five quasi-monomorphic mononucleotide markers (NR-21, NR-22, NR-24, BAT-25, and BAT-26).

Results: The subjects were 55 in the SPS group, 585 in the Sporadic SL group, and 368 in the control group. There were no significant differences in age, sex, or history of cancer in other organs. The incidence of colorectal cancer was 18 (32.7%) in the SPS group, 98 (16.8%) in the Sporadic SL group, and 20 (5.4%) in the control group, showing a significant difference among the three groups ($p < 0.001$). Details of 21 colorectal cancer lesions in 18 patients in the SPS group were as follows: left/right side, 15 lesions/6 lesions; early/advanced cancer, 16 lesions/5 lesions. Four of the six (67%) right-sided lesions were MSI-high and/or had BRAF mutations, suggesting carcinogenesis via the serrated neoplasia pathway. In contrast, 12 of the 15 (80%) lesions on the left side were histologically coexistent with adenoma components and/or had KRAS mutations, suggesting carcinogenesis via the adenoma-carcinoma pathway. In addition, of the 640 patients with SLs (SPS group and Sporadic SL group), 458 (71.6%) had concomitant TAs and the incidence of colorectal cancer was significantly higher in patients with TAs (96/458, 21.0%) than in those without TAs (20/182, 11.0%) ($p = 0.003$).

Conclusion: SPS has a high incidence of colorectal cancer, and the coexistence of SLs and TAs is suggested to be a risk factor for cancer development. Interestingly, carcinogenesis via the adenoma-carcinoma pathway from comorbid TAs, rather than the serrated-neoplasia pathway, is dominant in SPS.

References: Dekker E, Bleijenberg A, Balaguer F. Update on the World Health Organization Criteria for Diagnosis of Serrated Polyposis Syndrome. *Gastroenterology* 2020; 158:1520-1523.

Disclosure: Nothing to disclose.

MP462

STAT2-MEDIATED CONTROL OF COLORECTAL CANCER DEVELOPMENT AND ANTI-TUMOR THERAPY

M.T. Chiriac^{1,2,3}, Z. Hracsko¹, C. Becker^{1,2,3}, M.F. Neurath^{1,2,3,4}

¹University of Erlangen-Nuremberg, Department of Medicine 1, Erlangen, Germany, ²Deutsches Zentrum Immuntherapie (DZI), University Hospital Erlangen, Erlangen, Germany, ³Comprehensive Cancer Center Erlangen-EMN, University Hospital Erlangen, Erlangen, Germany, ⁴Ludwig Demling Endoscopy Center of Excellence, University Hospital Erlangen, Erlangen, Germany

Contact E-Mail Address: mircea.chiriac@uk-erlangen.de

Introduction: Colorectal cancer, with an estimated two million new cases each year worldwide, poses a significant socioeconomic burden on modern society. It is the second leading cause of cancer-related deaths, accounting for nearly one million premature deaths annually.

Aims & Methods: The role of Signal Transducer and Activator of Transcription 2 (STAT2) in this context is not yet understood, and no therapies targeting this transcription factor are currently being pursued. We explored the function of STAT2 in colorectal cancer by employing experimental mouse models, as well as conducting functional assays with three-dimensional tumoroids in the context of anticancer therapy.

Results: In vivo studies showed that Stat2KO mice were more resistant to developing tumors in both inflammation-driven and inflammation-independent models of experimental colorectal cancer. This unexpected outcome could not be reconciled with the known role of STAT2 in inducing cell death downstream of type I interferon signaling. We consequently performed ex vivo experiments with tumoroids derived from Stat2KO mice carrying the multiple intestinal neoplasia (Min) mutant allele of the adenomatous polyposis coli (Apc) gene. These tumoroids exhibited slower growth, were generally smaller in size, and showed a higher degree of differentiation compared to those derived from ApcMin/+ wildtype mice. Remarkably, when treated with anti-tumor agents that induce cell death through various mechanisms, tumoroids derived from ApcMin/+ Stat2KO mice were found to be highly sensitive. Additional functional studies indicated that the underlying mechanism might involve a STAT2-dependent disruption of innate immune DNA sensing.

Conclusion: Our results establish STAT2 as a promoter of colorectal cancer and a contributor to resistance against anti-tumor therapy. These findings suggest that targeting STAT2-dependent signaling could be a promising therapeutic strategy for patients with colorectal cancer.

Disclosure: Nothing to disclose.

MP463

PCR-BASED MICROSATELLITE INSTABILITY TESTING: PITFALLS AND STRATEGIES FOR ENHANCING ACCURACY

M. Kessler^{1,2,3}, M. von Knebel Doeberitz^{1,2}, A. Ahadova^{1,2}, M. Kloor^{1,2}

¹University Hospital Heidelberg, Institute of Pathology, Department of Applied Tumor Biology, Heidelberg, Germany, ²German Cancer Research Centre (DKFZ), Cooperation Unit Applied Tumor Biology, Heidelberg, Germany, ³University Hospital Heidelberg, National Center for Tumor Diseases, Heidelberg, Germany

Contact E-Mail Address: maria--kessler@t-online.de

Introduction: The detection of microsatellite instability (MSI) in tumor tissue is of high relevance for (1) identifying patients eligible for immune checkpoint blockade and (2) Lynch syndrome carriers. Gold standard for MSI analysis are DNA-based methods that are encompassing PCR-based amplification of short repetitive sequence stretches (microsatellites) and assessing length variations in the respective amplicons.

However, diagnostic complications can arise due to potential artifacts known as stutter bands, which are erroneous insertions or deletions occurring in PCR amplification that make it difficult to detect the true length of the microsatellite fragment. Correctly distinguishing these artifacts from true genetic insertion/deletion (indel) mutations in microsatellites *in vivo* is crucial for accurate MSI fragment length assessment. Factors such as PCR cycle number, laboratory conditions, and DNA quality can influence the occurrence of stutter bands. A thorough understanding of these factors is vital for preventing diagnostic errors. Moreover, improving our knowledge of changes during PCR amplification can advance our understanding of the evolution of these mutations in microsatellites *in vivo*.

Aims & Methods: Fluorescent multiplex PCR for the BAT25, BAT26, BAT40, and CAT25 microsatellite fragments was performed on multiple microsatellite stable and microsatellite unstable samples across different PCR cycle counts. Peak distribution was assessed for each reaction, and peak profiles were evaluated in relation to cycle numbers for different template DNA samples analyzed. In addition, we analyzed peak profiles to infer the potential fragment lengths prior to amplification, i.e. closest to the original sample.

Results: We analyzed the formation of stutter bands during PCR analysis in microsatellite fragments and were able to highlight a shift in the distributions of PCR peaks with increasing cycle count. Amplified fragment sizes tended to be of shorter length with higher numbers of cycles. This was paralleled by an increase of stutter bands in high compared to low cycle reactions. Additionally, *in silico* modeling of our peak data demonstrates how the length of microsatellite markers, the read depth and the number of PCR cycles affect the reliability and interpretability of MSI detection PCR.

Conclusion: Our results indicate that optimizing reaction conditions is a critical step to standardizing MSI detection by PCR. This may have important implications in MSI diagnostic procedures, particularly when assessing small samples with low DNA template concentration or tumors with borderline MSI status. Our observations suggest that a comprehensive understanding of the peak data produced in fluorescent multiplex PCR can significantly improve diagnostic capability in detecting MSI status in tumor samples and can further insight into the development of MSI mutations *in vivo*. Developing mathematical models that describe cycle-wise changes of peak distributions is the next step to improve the accuracy of PCR-based MSI testing.

Disclosure: Nothing to disclose.

Management of hepatobiliary cancer

16:00-17:00 / Poster Stage 3

MP464

TRANSARTERIAL CHEMOEMBOLIZATION PLUS APATINIB WITH OR WITHOUT CAMRELIZUMAB: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CONTROL-MATCHED STUDIES

M.V. Fernandes¹, V. Antunes¹, O. Martins², T. Correa³, A.A. Prata⁴, A.M. Reis⁵, A.C. Coan⁴, E. Bulhões⁶, P. Romeiro⁷, N.J. Milioli⁸
¹Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ²Federal University of Juiz de Fora, Juiz de Fora, Brazil, ³Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁴Federal University of Espírito Santo, Vitória, Brazil, ⁵State University of Campinas, Campinas, Brazil, ⁶College of Higher Education of the United Amazon, Redenção, Brazil, ⁷Department of Medicine, University Center of Maceió, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction:

Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related deaths. Unresectable HCC can be treated with transarterial chemoembolization (TACE), which causes hypoxia and induces the expression of vascular endothelial growth factor (VEGF). Antiangiogenic drugs can be useful in this setting.

Aims & Methods: This study aims to compare TACE plus Apatinib (antiangiogenic drug, TACE+A) versus TACE plus Apatinib plus Camrelizumab (immune checkpoint inhibitor, TACE+AC). We performed a systematic review in PubMed, Embase, Cochrane and Web of Science databases, searching for studies comparing TACE+A versus TACE+AC in patients with unresectable HCC. The primary outcomes were overall survival and disease-free progression survival. The secondary outcomes were treatment response and adverse events grade III or IV. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I^2 statistics.

Results: The meta-analyses included 3 studies and 1,134 patients. There was a significant difference favoring TACE+AC in overall survival (HR 0.41; 95% CI 0.28 to 0.60; $p < 0.01$; $I^2 = 87\%$) and in disease-free progression survival (HR 0.29; 95% CI 0.15 to 0.55; $p < 0.01$; $I^2 = 0\%$) compared to TACE+A. There is no difference in adverse events grade III or IV between groups (OR 1.08; 95% CI 0.83 to 1.40; $p = 0.586$; $I^2 = 0\%$).

Conclusion: In patients with unresectable HCC, TACE+AC demonstrated superior efficacy compared to TACE+A. The two combinations showed similar safety profiles.

References: 1. Duan X, Li H, Kuang D, Chen P, Zhang K, Li Y, et al. Transcatheter arterial chemoembolization plus apatinib with or without camrelizumab for unresectable hepatocellular carcinoma: a multicenter retrospective cohort study. *Hepatol Int.* 2023 Aug;17(4):915–26.
2. Liu H, Yu Q, Gu T, Qu P, Ma X, Zhou S, et al. Transarterial Chemoembolization plus Apatinib with or without Camrelizumab for the Treatment of Advanced HBV-related Hepatocellular Carcinoma. *J Gastrointest Liver Dis JGLD.* 2023 Jun 22;32(2):182–9.
3. Zhu D, Ma K, Yang W, Zhou HF, Shi Q, Ren JW, et al. Transarterial chemoembolization plus apatinib with or without camrelizumab for unresected hepatocellular carcinoma: A two-center propensity score matching study. *Front Oncol.* 2022;12:1057560.

Disclosure: Nothing to disclose.

MP465

FECAL MICROBIOTA TRANSPLANT COMBINED WITH ATEZOLIZUMAB PLUS BEVACIZUMAB IN PATIENTS WITH HEPATOCELLULAR CARCINOMA WHO PROGRESSED ON ATEZOLIZUMAB PLUS BEVACIZUMAB – INTERIM ANALYSIS OF THE FAB-HCC PHASE II PILOT STUDY

A. Frick¹, K. Pomej², B. Scheiner³, L. Balcar¹, L. Pajancic¹, A. Klotz¹, K. Regnat¹, K. Zinob¹, M. Trauner⁴, D. Tamandl⁵, C. Gasché¹, M. Pinter¹

¹Medical University Vienna, Division of Internal Medicine III, Department of Gastroenterology and Hepatology, Vienna, Austria, ²Medical University of Vienna, Gastroenterology and Hepatology, Vienna, Austria, ³Medical University Vienna, Division of Internal Medicine III, Department of Gastroenterology and Hepatology, Wien, Austria, ⁴Head of Division of Gastroenterology and Hepatology - Department of Medicine III, Head of Division of Department of Medicine III, Wien, Austria, ⁵Medical University of Vienna, Department of Biomedical Imaging and Image-guided Therapy, Vienna, Austria

Contact E-Mail Address: adrian.frick@meduniwien.ac.at

Introduction: The gut microbiota is often altered in chronic liver diseases and hepatocellular carcinoma (HCC), and increasing evidence suggests that it may influence response to cancer immunotherapy. Strategies to modulate the gut microbiome (i.e., fecal microbiota transplant (FMT)) may help to improve efficacy of immune checkpoint inhibitors (ICIs) or even overcome resistance to ICIs.

Aims & Methods: In this single-center phase II pilot study (ClinicalTrials.gov ID: NCT05750030), we plan to include 12 patients with advanced HCC who progressed on atezolizumab/bevacizumab. Patients will receive atezolizumab/bevacizumab every 3 weeks in combination with a single FMT via colonoscopy from donors with HCC who responded to PD-(L)1-based immunotherapy. The primary endpoint is safety, measured by incidence and severity of treatment-related adverse events (TRAEs). The main secondary endpoint is best overall response (BOR) according to RECISTv1.1 and mRECIST. Here, we report results of a preplanned interim analysis.

Results: Of 6 patients included so far, 5 were male, 5 had BCLC stage C, and 5 had Child-Pugh class A. All patients underwent successful FMT without any periinterventional complications. TRAEs related to FMT were all low-grade (grade 1-2) and included bloating (n=2), constipation (n=2), and diarrhea (n=1). TRAEs related to atezolizumab included one grade 2 pruritus, and TRAEs related to bevacizumab included arterial hypertension (one grade 3 and two grade 2) and proteinuria (one grade 3 and one grade 1). All patients had at least one follow-up imaging. Two patients had partial response, 3 patients had stable disease, and 1 patient had progressive disease as BOR according to both RECISTv1.1 and mRECIST, which corresponds to an objective response rate of 33% and a disease control rate of 83%.

Conclusion: Based on acceptable safety and promising efficacy results, the decision to continue recruitment in this trial was made. An update with longer follow-up will be presented at the meeting, including analyses of the gut microbiome.

Disclosure: AF received travel support from Takeda and Amgen, he received speaker honoraria from AbbVie
KP has nothing to disclose.

BS received travel support from AbbVie, AstraZeneca, Gilead and Ipsen, speaker honoraria from Eisai as well as grant support from AstraZeneca and Eisai.

BL received speaker honoraria from Chiesi and Gilead.

LP has nothing to disclose.

AK has nothing to disclose.

KR has nothing to disclose.

KZ has nothing to disclose.

MT received speaker honoraria from Albireo, BMS, Falk Foundation, Gilead, Intercept, Madrigal and MSD; he has advised for Abbvie, Albireo, BiomX, Boehringer Ingelheim, Falk Pharma GmbH, Genfit, Gilead, Hight-de, Intercept, Ipsen, Janssen, MSD, Novartis, Phenex, Pliant, Rectify Regulus, Siemens and Shire. He further received travel grants from Abbvie, Falk, Gilead Intercept and Janssen and research grants from Albireo, Almylam, Cymabay, Falk, Gilead, Intercept, MSD, Takeda and Ultragenyx. He is also co-inventor of patents on the medical use of NorUDCA filed by the Medical Universities of Graz and Vienna.

DT served as a speaker and/or consultant and/or advisory board member for Siemens, Roche, Sanova, Bristol-Myers Squibb and received travel support from Bayer and Siemens.

CG nothing to disclose.

MP received speaker honoraria from Bayer, BMS, Eisai, Ipsen, Lilly, MSD, and Roche; he is a consultant/advisory board member for AstraZeneca, Bayer, BMS, Eisai, Ipsen, Lilly, MSD, and Roche; he received grants from AstraZeneca, Bayer, BMS, and Roche; he received travel support from Bayer, BMS, Ipsen, and Roche.

MP466

ASAP SCORE MAY PREDICT HCC RECURRENCE AFTER COMPLETE RADIOLOGICAL RESPONSE TO LOCOREGIONAL TREATMENTS

L. Canova^{1,2}, M.A. Iavarone¹, E. Alimenti¹, R. Perbellini¹, S.C.U. Renteria³, R. D'Ambrosio¹, E. Degasperis¹, F. Facchetti¹, A.M. Ierardi⁴, A. Sangiovanni¹, C. Ferruccio³, P. Lampertico^{1,5}

¹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy,

²Università degli Studi di Milano, Milan, Italy, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Clinical Laboratory, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Radiology Department, Milan, Italy, ⁵CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Contact E-Mail Address: lorenzo.canova27@gmail.com

Introduction: Alpha fetoprotein (AFP) and prothrombin induced by vitamin K absence/antagonist II (PIVKA-II) are biomarkers for hepatocellular carcinoma (HCC), which have been extensively in the diagnosis of HCC, while their use in the prognosis prediction remains poorly assessed. Recently, a new algorithm (ASAP) - including age, gender, AFP and PIVKA-II - has been validated as an alternative to GALAD for prediction of HCC development with a cut-off of 0.52. The identification of predictors of HCC recurrence after curative treatment has always been relevant to patients' management, and now may have further utility with the arrival of adjuvant therapies.

Aims & Methods: The aim of our study was to evaluate the predictive role of AFP and PIVKA-II alone or combined in the ASAP score for HCC recurrence in patients who achieved a complete response (CR) after locoregional treatment. In this single-center, observational ongoing study, we have enrolled 156 consecutive patients with first diagnosis of HCC treated by ablation (MWTa) or chemoembolization (TACE). CR was evaluated by CT-scan 1 month after treatment, afterwards patients were evaluated every three months by CT-scan, clinical and biochemical features until recurrence, death or last follow up. PIVKA-II and AFP levels were measured at the day of treatment by Fujirebio assays, Japan.

Results: 81 (52%) patients with HCC who achieved CR after the first treatment were included: median age 66 (40-87); 83% men, 57% HCV-positive, 91% Child-Pugh A, 85% BCLC 0/A, 53% MWTa. The day of treatment, the

median AFP was 6.3 ng/mL (1.3-3,537), median PIVKA-II was 112 (16-5,090) mAU/mL, median ASAP score was 0.405 (-3.44-6.64; 47% with ASAP value > 0.52). During follow up, HCC recurred in 47 (58%) patients [median time to recurrence was 298 (41-1256) days after achieving CR]. PIVKA-II [HR 2.53 (95%CI 1.47-4.35), p<0.001] and age [HR 1.03 (95%CI 1.00-1.07), p=0.013] were the only independent predictors of overall HCC recurrence by a multivariable model for single variables only, while the ASAP score [HR 1.31 (95%CI 1.12-1.52), p<0.001] was the only independent predictor of recurrence in a multivariable model including only scores and algorithms. PIVKA-II [HR 2.14 (95%CI 1.09-4.18), p=0.026] was the only independent predictor of early recurrence in the first multivariable model, while platelet to lymphocyte ratio [PLR; HR 1.02 (95%CI 1.00-1.04)] and ASAP score [HR 1.30 (95%CI 1.03-1.64)] were independent predictors of early recurrence according to the second model. Adopting the ASAP cut-off of 0.52, the algorithm independently predicted HCC recurrence [HR 3.54 (95%CI 1.86-9.75), p<0.001], but did not predict HCC early recurrence [HR 1.95 (95%CI 0.87-4.34), p=0.103].

Conclusion: The ASAP algorithm may accurately predict HCC recurrence and early recurrence after complete radiological response, deserving further studies to refine the model.

Disclosure: Nothing to disclose.

MP467

THERAPEUTIC EFFICACY AND SAFETY OF ATEZOLIZUMAB PLUS BEVACIZUMAB TREATMENT IN 1000 JAPANESE PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA: INSIGHTS FROM REAL-WORLD CLINICAL PRACTICE

K. Murakawa¹, A. Hiraoka¹, S. Kakizaki^{2,3}, T. Hatanaka⁴, T. Tada⁵, K. Kariyama⁶, J. Tani⁷, H. Toyoda⁸, M. Kaibori⁹, A. Naganuma¹⁰, Y. Yata¹¹, H. Kuroda¹², F. Tada¹, K. Nouse⁶, T. Kumada¹³, Gastroenterology Center

¹Ehime Prefectural Central Hospital, Gastroenterology Center, Matsuyama, Japan, ²NHO Takasaki General Medical Center, Department of Clinical Research, Takasaki, Japan, ³Gunma University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Maebashi, Japan, ⁴Gunma Saiseikai Maebashi Hospital, Department of Gastroenterology, Maebashi, Japan, ⁵Japanese Red Cross Himeji Hospital, Department of Internal Medicine, Himeji, Japan, ⁶Okayama City Hospital, Department of Gastroenterology, Okayama, Japan, ⁷Faculty of Medicine, Kagawa University, Department of Gastroenterology and Neurology, Miki-cho, Kita-gun., Japan, ⁸Ogaki Municipal Hospital, Department of Gastroenterology and Hepatology, Ogaki, Japan, ⁹Kansai Medical University, Department of Surgery, Hirakata, Japan, ¹⁰NHO Takasaki General Medical Center, Department of Gastroenterology, Takasaki, Japan, ¹¹Hanwa Memorial Hospital, Department of Gastroenterology, Osaka, Japan, ¹²Iwate Medical University School of Medicine, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Morioka, Japan, ¹³Gifu Kyoritsu University, Department of Nursing, Ogaki, Japan

Contact E-Mail Address: kazumura.1994@outlook.jp

Introduction: Although atezolizumab plus bevacizumab treatment (AB) has been developed as the first immune therapy for unresectable hepatocellular carcinoma (u-HCC) based on the results of the IMbrave 150 trial, there have been few reports of the therapeutic efficacy and safety of AB for u-HCC in real-world clinical practice with a large cohort.

Aims & Methods: This study aimed to elucidate the therapeutic outcome of AB. From 2020 to 2023, 1016 Japanese patients with u-HCC treated with AB in our hospitals were enrolled (median age: 74 years, initial line use:

697, BCLC stage 0 or A:B:C:D=77:408:512:19). Child-Pugh classification and modified albumin-bilirubin (ALBI) grade, in which the middle grade was divided into 2 sub-grades by an ALBI score of -2.27, were used for the assessment of hepatic reserve function. The therapeutic efficacy and safety of AB were evaluated, retrospectively.

Results: The median observation period was 12.5 months (IQR 6.8-21.2). Child-Pugh class A included 920 patients, B included 95, and C included 1, while ALBI grade 1 comprised 360 patients, grade 2 comprised 641 (grade 2a:2b=266:375), and grade 3 comprised 15. The median progression-free survival (mPFS) and overall survival (mOS) in the entire cohort were 7.6 months (95% CI 6.7-8.3) and 22.3 months (95% CI: 19.2-25.5). The mPFS/mOS according to Child-Pugh class (A:B:C) were 7.8/24.5, 5.0/9.4, and 0.4/1.1 months, respectively, while those according to modified ALBI (1:2a:2b:3) were 10.6/31.0, 8.0/22.1, 5.9/14.1, and 5.3/10.5 months, respectively (each $P<0.001$). According to BCLC stage (0 or A:B:C:D), mPFS/mOS were 14.5/not reached, 9.1/25.1, 6.0/19.1, and 2.4/10.5 months, respectively (each $P<0.001$). When PFS and OS were compared between initial and later line use groups, significant differences were observed (mPFS/mOS=7.9/24.9 vs. 6.5/18.8 months, respectively, each $P<0.05$). Adverse events (any grade>10%/grade 3 or more, %) included urine protein (31.7/9.3), fatigue (23.4/2.7), appetite loss (20.2/2.8), hypertension (18.1/5.5), hepatic function abnormality (17.0/5.1), ascites/edema (13.0/3.4), fever (12.4/1.0), and rash (11.5/1.4), with AE grade 5 observed in 9 patients (0.9%) (liver injury 4, interstitial pneumonia 3, esophageal varices bleeding 1, and colitis 1). Immune-related AE, which required steroids, was occurred in 148 (15.4%).

Conclusion: In the clinical practice of Japanese u-HCC patients numbering over 1000, AB showed favorable therapeutic results and similar safety to those of the IMbrave150 trial (median observation period 8.6 months). The prognostic improvement effect of initial line use might be better than that of subsequent lines. To obtain a better prognosis, the introduction of AB is recommended in patients with better hepatic reserve function, if possible.

Disclosure: Nothing to disclose.

MP468

CIRCULATING BLOOD MICROBIOME SIGNATURES OF HEPATOCELLULAR CARCINOMA ARE ASSOCIATED WITH TREATMENT RESPONSE AND PROGNOSIS

R. Gedgaudas^{1,2}, E. Morkunas^{1,2}, R. Inciuraite², A. Link³, J. Skieceviciene², M. Alunni-Fabroni⁴, K. Schütte^{5,6}, P. Malferttheiner⁷, G. Varkalaite², J. Ricke⁷, J. Kupcinskas^{1,2}

¹Lithuanian University Of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University Of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³Otto-von-Guericke University of Magdeburg, Gastroenterology, Hepatology and Infectious Diseases, Magdeburg, Germany, ⁴Univeristy Hospital of LMU Munich, Department of Radiology, Munich, Germany, ⁵Marienhospital Osnabrück, Department of Internal Medicine and Gastroenterology, Osnabrück, Germany, ⁶Medizinische Hochschule Hannover, Department of Gastroenterology, Hepatology and Endocrinology, Hannover, Germany, ⁷Univeristy Hospital of LMU Munich, Department of Internal Medicine II, Munich, Germany

Contact E-Mail Address: R.gedgaudas@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer, predominantly diagnosed in patients with chronic liver diseases. The absence of specific biomarkers and the typically asymptomatic progression of the disease lead to delayed diagnosis. Patients with liver disease, including HCC, exhibit alterations in the gut

microbiome and increased bacterial permeability, factors that may influence disease progression and patient outcomes. In recent years, there has been a growing interest in exploring circulating microbiome signatures as potential indicators of liver disease status, providing a new avenue for understanding HCC.

Aims & Methods: Aims: To identify the signatures of the circulating blood microbiome associated with hepatocellular carcinoma, response to treatment and disease prognosis.

Methods: This study conducted a post-hoc analysis of the SORAMIC clinical trial utilizing peripheral blood plasma samples. For this analysis, blood plasma samples from a cohort of 71 patients with HCC were examined (25 treated with Sorafenib and 46 with SIRT/Sorafenib). Peripheral blood samples were collected at two time points: baseline (prior to the initiation of anti-tumor therapy) with all 71 patients included, and post-therapy (7 to 9 weeks after treatment) with 39 patients included. Additionally, peripheral blood samples were obtained from 52 control subjects, who were endoscopically diagnosed with colonic diverticulosis, to compare against the patient group. The composition of the circulating blood microbiome was assessed through 16S rRNA gene sequencing, targeting the V1-V2 hypervariable regions. Subsequent analyses focused on identifying associations with potential novel biomarkers for diagnosis, prognosis, and response to treatment.

Results: Patients with HCC had significantly diminished α -diversity of the circulating blood microbiome as compared to controls. Significant differences were also observed in between microbial communities of these two cohorts based on Bray-Curtis dissimilarity index. Patients with HCC had significantly higher levels of *Proteobacteria* and *Bacteroidetes* and lower levels of *Firmicutes* and *Campylobacterota*. Differential abundance analysis revealed that families of *Gordoniaceae*, *Cryomorphaceae*, *Burkholderiaceae*, *Comamonadaceae*, *Enterobacteriaceae* were significantly enriched in patients with HCC. At the genus level, patients with HCC had higher levels of *Gordonia*, *Fluviicola*, *Burkholderia*, *Limnohabitans* and *Escherichia/Shigella* and lower levels of *Corynebacterium*. HCC patients, who responded to treatment with SIRT/Sorafenib showed an increase in blood bacterial diversity, enrichment of families *Burkholderiales incertae sedis*, *Arcobacteraceae*, *Peptostreptococcaceae*, *Moraxellaceae*, genera *Sphaerotilus*, *Aliacrobacter*, *Rhodoluna*, *Giesbergeria*, *Microbacterium*, *Romboutsia*, *Arcicella*, *Pseudorhodofera* and depletion in families *Gordoniaceae*, *Cryomorphaceae* and genera *Cloacibacterium*, *Gordonia*, *Limnohabitans*, *Fluviicola* after the treatment. Levels of *Acinetobacter*, *Enhydrobacter* and *Micrococcus* in the blood before the HCC treatment were associated with patient prognosis.

Conclusion: Patients with HCC exhibit a unique circulating blood microbiome profile characterized by reduced bacterial diversity. Response to treatment is linked to an increase in α -diversity and changes in the circulating microbiome profile. Specific members of the circulating microbiome show potential prognostic capabilities, suggesting their utility as biomarkers for predicting disease progression and treatment outcomes in HCC.

Disclosure: Nothing to disclose.

MP469

EVALUATING TREATMENT STRATEGIES IN HEPATOCELLULAR CARCINOMA: A LONGITUDINAL ANALYSIS OF BCLC RECOMMENDATIONS AND PATIENT OUTCOMES

A. Eleonora¹, M.A. Iavarone^{1,2}, L. Canova¹, M. Bruccoleri¹, B. Antonelli³, A.M. Ierardi⁴, A. Sangiovanni¹, P. Lampertico^{1,2}

¹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy, ²University of Milan, Department of Pathophysiology and Transplantation, CRC "A. M. and A. Migliavacca" Center for Liver Disease, Milan, Italy, ³Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, General and Liver Transplant Surgery Unit, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Radiology Department, Milan, Italy

Contact E-Mail Address: eleonoralimenti@gmail.com

Introduction: In 2022 the BCLC staging and treatment algorithm for hepatocellular carcinoma (HCC) management has been updated (BCLC_2022), granting for higher flexibility and customized management for HCC patients as compared to the 2018 version.

Aims & Methods: Aim of the study was to evaluate the feasibility of BCLC_2022 in daily clinical practice (BCLC_2018 as benchmark), its impact on response to treatment and on overall survival (OS).

We retrospectively evaluated data of 798 prospectively followed (year 2006 to 2022) patients with de novo HCC: 187 0, 371 A, 132 B, 87 C and 21 D, according to BCLC. First line treatment allocations were discussed by a multidisciplinary team (MTD), following updated recommendations. All patients were followed until death or end of follow-up (12/2022).

Results: Overall, the feasibility if BCLC increased from 51% for the BCLC_2018 to 69% for the BCLC_2022 ($p<0.001$): 56% to 73% stage 0 ($p=0.001$), 45% to 72% stage A ($p<0.001$), 51% to 65% stage B ($p=0.02$), while no changes were registered for stage C and D. Among BCLC 0 /A patients, 130 (23%) were treated with TACE, which is a "lower priority option" for these stages according to BCLC_2022. The rate of "downward stage migration" was significantly lower with BCLC_2022 (33% to 16%, $p<0.001$). "Downward stage migration" without curative intent was associated with a lower proportion of complete response to first line treatment in the early stages (0% vs 77%, $p=0.003$ in BCLC0; 0% vs 57%, $p=0.001$ in BCLC A) and to a shorter OS [6 months (IQR 2-16) vs 82 months (IQR 42-132), $p<0.001$ in BCLC 0] as compared to BCLC_2022. Similarly in early stages patients treated with a "lower priority option" had a lower proportion of complete response (82% vs 60%, $p=0.01$ in BCLC 0 and 74% vs 20%, $p<0.001$ in BCLC A) and a shorter OS [33 (IQR 23-61) vs 74 months (IQR 42-137) $p<0.001$ in BCLC A] as compared to those undergoing first choice treatments. In BCLC B and C, an upward stage migration was associated to a higher achievement of complete response (17% vs 52%, $p<0.001$ in BCLC B and 2% vs 41% $p<0.001$ in BCLC C), and granted a longer OS [(63 months (IQR 36-72) vs 28 (IQR 18-44), $p=0.003$ in BCLC B and 21 months (IQR 15-44) vs 11 months (IQR 4-25) in BCLC C] as compared to BCLC 2022. In BCLC 0 and undergoing a "downward stage migration" without curative intent was an independent predictor of mortality [HR 6.94 (95% CI 2.27-21.20) $p=0.001$], alongside with age [HR 1.08 (95% CI 1.06-1.13), $p<0.001$] and ALBI grade 3 [HR 9.34 (95% CI 1.21-72.19), $p=0.03$. Conversely, "upward stage migration" was independently associated to a lower mortality risk both in BCLC B" [HR 0.46 (95% CI 0.27-0.80), $p=0.006$] and C [HR 0.50 (95% CI 0.27-0.92) $p=0.03$].

Conclusion: The BCLC_2022 updated version of HCC staging and treatment system allowed a greater adherence to the algorithm in clinical practice, without adversely affecting the survival of patients. Choosing a "cu-

orative option" for early HCC granted longer survival, as well as the access to treatments with curative intent permits a survival benefit in selected patients in more advanced stages.

Disclosure: Nothing to disclose.

MP470

EFFICACY OF POSTOPERATIVE ADJUVANT THERAPIES IN PATIENTS WITH RESECTED CHOLANGIOCARCINOMA

H. Shin¹, Y.-K. Jung¹

¹Korea University Ansan Hospital, Dept. of Internal Medicine, Gyeonggi, South Korea

Contact E-Mail Address: shg0715@nate.com

Introduction: Surgical resection is an only curative treatment in cholangiocarcinoma (CCC). However, despite curative resection, recurrences are frequent so that most of the patients undergo bad prognosis. Adjuvant therapy in surgically resected CCC has not proved its clinical benefit until now.

Aims & Methods: This study aimed to evaluate the benefit of adjuvant therapy on overall survival (OS) and disease free survival (DFS). We categorized a retrospective cohort of 159 patients who underwent surgical resection for CCC into two groups based on their chosen treatment approach: observation group ($n=66$) and adjuvant chemotherapy/chemoradiation group ($n=93$). OS and DFS were estimated using the Kaplan-Meier method.

Results: There were no significant differences in age, gender, tumor differentiation, resection margin status (R0, R1), lymphovascular invasion, perineural invasion, lymph node metastasis, TNM stage between two groups. Adjuvant treatment did not show a significant improvement in overall survival (OS) with a median OS of 59 months in the observation group and 41 months in the adjuvant treatment group ($p=0.35$). However, in subgroup analyses based on the presence of lymph node involvement and the status of resection margin, adjuvant treatment was found to statistically significantly improve OS in the subgroups with LN+ group and R1 group, respectively. Tumor recurrence rate was 56% in observation group, 53% in adjuvant treatment group. The median DFS in each groups were 44 and 37 months ($p=0.08$). Adjuvant treatment didn't significantly extend DFS in LN+ subgroup, but showed improvement of DFS in R1 group.

Conclusion: Our study suggested potential benefit of adjuvant therapy in the aspects of OS in the selective group with LN+ and R1 among patients with resected CCC. However, a positive impact was noted in DFS only for the R1 group. A further randomized well controlled prospective study is warranted.

Disclosure: Nothing to disclose.

MP471

SURVIVAL ANALYSIS OF ALPHA-FETO PROTEIN NEGATIVE METASTATIC HEPATOCELLULAR CARCINOMA: A POPULATION-BASED STUDY

M. Mortagy¹, T. Kaung¹, M. Liaqat¹, A. ElGehiny², A. Abdelhameed³, K. Elguzouli¹, D. Sheppard¹

¹Hampshire Hospitals NHS Foundation Trust, Gastroenterology Department, Winchester, United Kingdom, ²MD Anderson Cancer center, Houston, United States of America, ³Alexandria University Faculty of Medicine, Alexandria, Egypt

Contact E-Mail Address: muhammad.liaqat@hhft.nhs.uk

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer in incidence and the third in mortality worldwide. Its incidence is variable worldwide. Seventy-two percent of cases occur in Asia. It is more common in males. Alpha-Feto protein is negative in only 30% of patients with HCC. 60-months survival of HCC ranges from 70% (for early stages) to 20% (for advanced stages). The overall median survival of metastatic HCC is 11 months. Patients with negative AFP usually have better survival than those with positive AFP. The effect of AFP negativity on metastatic HCC survival duration and the factors affecting survival of this subgroup of patients is not well studied.

Aims & Methods: This study aims to identify the factors affecting the overall survival of patients with AFP negative metastatic HCC and their survival duration. A total of 1146 patients with AFP-negative metastatic HCC diagnosed between 1975 to 2020 were extracted from the U.S. Surveillance, Epidemiology and End-results (SEER) program databases. Univariable and Multivariable Cox regression were performed, associated hazards ratio (HR) and Kaplan Meier curves/statistics were generated for overall survival analysis.

Results: Most patients were males (78.8%). Their mean age was 65.6. Most patients were of white race (74.9%) and of non-Spanish-Hispanic-Latino origin (79.8%). Most patients lived in metropolitan areas (87.6%) and earned \$75,000+ (37.3%). Most patients were married (48.1%). The mean tumor size was 9.93 cm with 75.1% > 2cm in size. Most patients had T0/T1 stage (41.1%) followed by T3 (32.7%). Most patients had N0/Nx stage (72.7%). Most patients didn't receive chemotherapy (62.1%).

The median survival of the cohort was 5 months (95% confidence interval: 5-6 months). The survival of the cohort was 99%, 28.3%, 8.5%, 3.8% at 1,12, 36 and 60 months respectively. Univariable Cox regression was statistically significant for age (HR 1.01), grade III (HR 1.55), grade IV (2.75), receiving chemotherapy (HR 0.48), black race (HR 0.80). Univariable Cox regression was non-statistically significant for sex, T stage, N stage, origin, rurality, marital status. Grade wasn't included in multivariable cox regression due to missing data (71.9%). Multivariable cox regression model was only statistically significant for receiving chemotherapy (HR 0.49).

Conclusion: The overall survival of AFP-negative metastatic HCC is very poor. Chemotherapy may be associated with better survival. However, the chemotherapy variable in SEER is limited by data incompleteness and possible unmeasured causes for receiving or not receiving chemotherapy. It is unclear if patients with negative AFP metastatic HCC survive longer than those with positive AFP metastatic HCC. More studies are needed to study the effect of different biomarkers on the survival of HCC patients.

References: McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of Hepatocellular Carcinoma. *Hepatology*. 2021;73 Suppl 1(Suppl 1):4-13. doi:10.1002/hep.31288

Disclosure: Nothing to disclose.

MP472

CHRONIC LIVER DISEASE AND RADIATION-INDUCED SECOND PRIMARY LIVER MALIGNANCY

A. Ellaiithy¹, I. Ellaiithy²

¹Suez Canal University, Faculty of Medicine, Ismailia, Egypt,

²Cairo University, Faculty of Medicine, Cairo, Egypt

Contact E-Mail Address: asmaa.ellithy1@gmail.com

Introduction: Cancer survivors are at a high risk to develop second primary malignancy (SPM) which constitutes a serious threat for them. Radiotherapy is the cornerstone for the management of many cancers as a loco-regional treatment modality. Due to the low liver tolerance, cirrhotic patients are at a high risk of developing radiation-induced liver toxicities despite the modern safe radiation delivery techniques. Radiation damage cells through direct energy deposition and reactive free radical generation. Recent studies demonstrated a potential risk of SPMs following radiotherapy with further investigations for strategies to decrease radiation-induced SPMs. However, it is insufficiently addressed if developing liver SPMs is a serious adverse event following radiotherapy for cirrhotic patients.

Aims & Methods: We aimed to quantitatively assess the risk of gastrointestinal (GI) and liver SPMs following radiotherapy in patients with chronic liver disease. SEER.stat version 8.4.3 was used to obtain and analyze the data of patients with chronic liver disease diagnosed from 2000 to 2020. Using Ishak fibrosis score: F0-4 for no to moderate fibrosis and F5-6 for advanced or severe cirrhosis. We subgrouped the patient according to the history of receiving radiotherapy for prior cancer treatment in two groups and excluded patients with unknown radiotherapy administration history. We used MP-SIR session to calculate the Standardized Incidence Ratio (SIR) as Observed/Expected (O/E) with 95% confidence interval (CI). We calculated the Excess Risk (ER) per 10,000. Significance was achieved at 0.05.

Results: Out of 15,168 patients with advanced liver cirrhosis, 88.4% received no radiotherapy and 11.6% received systemic radiotherapy. We observed 215 cirrhotic patients developed GI SPMs (O/E=2.76, 95%CI: 2.41-3.16, P<0.05, ER= 45.51), 106 of them developed liver SPMs (O/E=8.80, P<0.05). Patients with liver cirrhosis who received radiotherapy had an increased risk for GI SPMs (Observed=24, O/E=3.34, 95%CI: 2.14- 4.96, P<0.05, ER= 64.43) compared to who received no radiotherapy (O/E=2.71, 95%CI: 2.34- 3.12, P<0.05, ER= 43.72). Liver SPMs after radiotherapy in cirrhotic patients had an O/E of 12.31 (Observed=13, P<0.05) while the group who received no radiotherapy had an O/E of 8.46 (Observed=93, P<0.05, ER=29.77). In non-cirrhotic patients, we observed 75 patients had GI SPMs with O/E of 3.13 (P<0.05), 30 of them had liver SPM (O/E= 8.44, P<0.05) and five patients had intrahepatic bile duct SPM (O/E= 10.59, P<0.05).

Conclusion: The results of this study give deep insights regarding the burden of SPMs in chronic liver disease. Liver cirrhosis with or without radiotherapy exposure have significantly increased the risk for GI SPMs. Cirrhotic patients who received radiotherapy had an increased risk for GI SPMs by three folds and a 12-fold increased risk for liver SPMs. However, who received no radiotherapy had an 8-fold increased risk for liver SPM. Thus, screening for HCC and GI SPMs in cirrhotic patients is a must for early detection and better management outcome especially after radiotherapy.

References: 1. Kong J, Yu G, Si W, Li G, Chai J, Liu Y, et al. Second Primary Malignancies in Patients With Hepatocellular Carcinoma: A Population-Based Analysis. *Front Oncol* [Internet]. 2021 Aug 23 [cited 2024 Apr 18];11:713637. Available from: /pmc/articles/PMC8420091/ 2. Koay EJ, Owen D, Das P. Radiation-Induced Liver Disease and Modern Radiotherapy [Internet]. Vol. 28, *Seminars in Radiation Oncology*. NIH Public Access; 2018 [cited 2024 Apr 18]. p. 321–31. Available from: /pmc/articles/PMC6402843/

3. Yang J, Gao J, Hu J, Hu W, Qiu X, Huang Q, et al. Carbon-ion radiotherapy in the treatment of radiation-induced second primary malignancies. *Ann Transl Med* [Internet]. 2022 Nov [cited 2024 Apr 18];10(22):1200–1200. Available from: /pmc/articles/PMC9761151/

Disclosure: Nothing to disclose.

MP473

FIB-4 IN PREDICTING HEPATOCELLULAR CARCINOMA DURING VIRAL HEPATITIS: A NOVEL INDICATION FOR AN OLD TOOL

M. Ayari¹, A. Chehaider¹, W. Khemiri¹, M.H. Douggu¹, T. Jomni¹

¹Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia

Contact E-Mail Address: ayari.myriam@hotmail.fr

Introduction: Hepatocellular carcinoma (HCC) is a severe outcome during liver disease with limited treatment options when diagnosed lately. It is the leading cause of death in patients with chronic hepatitis, particularly secondary to chronic viral hepatitis. Screening scores are continuously being developed and assessed to optimize early diagnosis.

Aims & Methods: The aim of this study was to investigate the correlation between FIB-4 score and HCC risk during treated chronic viral hepatitis in Tunisian patients. We conducted a single-center retrospective study analyzing data from patients with chronic viral hepatitis B and C. Patients with co-infection BD, D, VIH or associated nonalcoholic steatohepatitis were excluded. FIB4 score was calculated for each patient at presentation.

Results: In total, 88 consecutive patients were enrolled: 42 with chronic hepatitis B and 46 with chronic hepatitis C. The mean age at diagnosis was 51.5 ±12 years with a sex-ratio M/F of 1.31. At baseline, 37.2% of patients had already developed cirrhosis. Virological response was achieved in 92% of the population. HCC occurred in 16% (N=14) of patients after a mean follow-up period of 79. The stage of HCC was classified as 'A', 'B', 'C' and 'D' according to BCLC classification in 28.5%, 25%, 43% and 0.7% respectively. Univariate analysis identified: older age (p=0.02), low platelet count (p<0.0001), cirrhosis (p<0.0001), high bilirubin level (p=0.028) and high Fib-4 (p=0.01) as factors associated with the occurrence of HCC. When analyzing the receiver operating characteristic (ROC) curve, AUC of FIB4 score in predicting HCC was 0.845 (95% CI: 0.730–0.960, p<0.0001). The corresponding FIB-4 cut-offs for 90% sensitivities was 1.67, while the cut-offs for 90% specificities was 3.8.

Conclusion: In our study, high FIB-4 score was associated with increased HCC risk in patients with viral hepatitis. FIB-4 index is based on routinely clinical and biological data and showed highly predictive performances in predicting HCC allowing better stratification.

Disclosure: Nothing to disclose.

Pancreatic cancer: Clinical and basic science

16:00-17:00 / Poster Stage 4

MP474

TARGETING RHOA EXPRESSION WITH FORMONONETIN AND SALVIANOLIC ACID B TO MITIGATE PANCREATIC CANCER-ASSOCIATED ENDOTHELIAL CELLS CHANGES

Y. Chen^{1,2}, Y. Wang^{1,2}, X. Zhang^{1,2}, J. Yang^{1,2}, H. Jin^{1,2}

¹School of Medicine, Westlake University, Hangzhou, China,

²Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China

Contact E-Mail Address: wangyu@zcmu.edu.cn

Introduction: Pancreatic Cancer (PC), a highly lethal malignancy of the digestive system, is associated with a poor prognosis, as evidenced by a less than 7% 5-year survival rate [1]. Projections suggest that by 2030, PC will rank as the second leading cause of cancer-related deaths [2-3]. A crucial aspect of the progression of pancreatic cancer involves its crosstalk with endothelial cells (ECs), particularly in the regulation of vascular homeostasis [4]. Numerous studies have demonstrated the significant involvement of Vascular Endothelial Growth Factor (VEGF) in the process of ECs functional remodeling [5-6]. Activation of the PI3K/AKT signaling pathway has been shown to enhance VEGF-mediated vascular formation, thereby contributing to the normal development and repair of the vascular system [7-8]. Considering the aberrant vascular features observed in tumors, targeting specific pathways to revert immature and unstable vessels to a normal vasculature state appears to be a promising therapeutic strategy for the treatment of the disease. Previous studies have indicated that the combination of Formononetin and Salvianolic acid B (FcS) significantly inhibits pancreatic xenograft tumors *in vitro*. However, it remains unclear whether this combination can inhibit the abnormal vascularization of pancreatic tumors to achieve its anti-cancer effect.

Aims & Methods: This study aimed to investigate the efficacy of FcS in modulating the effects of pancreatic cancer on endothelial cells, explore the alterations in molecular mechanisms within these cells, and elucidate the intricate molecular mechanisms underlying this interaction.

To elucidate the interaction between endothelial cells and pancreatic cancer cells, a co-culture system using Human Umbilical Vein Endothelial Cells (HUVECs) and PANC-1 cells was established to investigate the potential of targeting abnormal vasculature as a promising avenue for anti-tumor therapy. The proliferation, migration, invasion, and lumen formation of HUVEC were compared in mono-culture (HUVECs) and co-culture with PANC-1 (H-P), followed by treatment of H-P with FcS to assess its anti-angiogenic properties. Then, molecular docking was utilized to predict the interactions between Formononetin and Salvianolic acid B with RhoA, and the expression of RhoA in HUVECs post-FcS treatment was assessed. Furthermore, the role of RhoA in the effects of FcS on HUVECs was explored using shRhoA lentivirus. *In vivo* investigations were conducted using a zebrafish xenograft tumor model to assess the anti-tumor effects of FcS, focusing on cancer cell proliferation, migration, apoptosis, and vascular sprouting.

Results: The treatment with FcS showed a dose-dependent inhibition of PANC-1-induced alterations in HUVECs, including proliferation, migration, invasion, and tube formation. Molecular docking analysis indicated potential interactions between FcS and RhoA. FcS downregulated the expression of RhoA and modulated the PI3K/AKT pathway in PANC-1-induced HUVECs. Furthermore, the inhibitory effects of FcS on HUVEC phenotypic changes were attenuated by RhoA knockdown. *In vivo* experiments using a zebrafish xenograft model demonstrated the anti-tumor effects of FcS, including the inhibition of proliferation, metastasis, and vascular sprouting, and promotion of tumor cell apoptosis.

Conclusion: This study illuminates the potential of FcS in inhibiting pancreatic cancer-induced changes in endothelial cells. FcS exhibits pronounced anti-abnormal vasculature effects, potentially achieved by downregulating RhoA expression, inhibiting the PI3K/Akt signaling pathway.

References:

1. Siegel, R. L., Giaquinto, A. N., Jemal, A., 2024. Cancer statistics, 2024. *CA Cancer J Clin.* Jan-Feb. 74, 12-49.
2. The Lancet Gastroenterology Hepatology, 2023. Cause for concern: the rising incidence of early-onset pancreatic cancer. *Lancet Gastroenterol Hepatol.* Apr. 8, 287.
3. Neoptolemos, J. P., Kleeff, J., Michl, P., Costello, E., Greenhalf, W., Palmer, D. H., 2018. Therapeutic developments in pancreatic cancer: current and future perspectives. *Nat Rev Gastroenterol Hepatol.* Jun. 15, 333-348.
4. Kishimoto, T., Saito, K., Ishikura, H., 1995. Mechanism of blood-borne metastasis in relation to the interaction between pancreatic carcinoma and endothelial cells. *Nihon Rinsho.* Jul. 53, 1765-9.
5. Goel, S., Duda, D. G., Xu, L., Munn, L. L., Boucher, Y., Fukumura, D., Jain, R.K., 2011. Normalization of the vasculature for treatment of cancer and other diseases. *Physiol Rev.* Jul. 91, 1071-121.
6. Jain, R.K., 2001. Normalizing tumor vasculature with anti-angiogenic therapy: a new paradigm for combination therapy. *Nat Med.* Sep. 7, 987-9.
7. Brazil, D. P., Hemmings, B. A., 2001. Ten years of protein kinase B signaling: a hard Akt to follow. *Trends Biochem Sci.* Nov. 26, 657-64.
8. Sarbassov, D. D., Guertin, D. A., Ali, S. M., Sabatini, D. M., 2005. Phosphorylation and regulation of Akt/PKB by the rictor-mTOR complex. *Science.* Feb. 18, 1098-101.

Disclosure: Nothing to disclose.

MP475

PROTEIN KINASE R REGULATES THE GROWTH OF PANCREATIC DUCTAL ADENOCARCINOMA BY MODULATING THE CELL CYCLE VIA GADD45A

Y. Numata¹, M. Koizumi¹, T. Watanabe¹, O. Yoshida¹, Y. Tokumoto¹, K. Marui¹, S. Ishikawa¹, M. Kokubu¹, Y. Okujima¹, Y. Imamura¹, T. Kumagi², Y. Hiasa¹

¹Ehime University Graduate School of Medicine, Gastroenterology and Metabolism, Shitsukawa, Japan, ²Ehime University Hospital, Postgraduate Medical Education Center, To-on, Japan

Contact E-Mail Address: donguri4949@gmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) has poor prognosis. This bleak outlook is due to the lack of effective drug therapies for PDAC. Therefore, there is an urgent need to develop new and effective medications for PDAC.

Protein kinase R (PKR) is a ubiquitously expressed serine-threonine kinase encoded by EIF2AK2 in humans. Recent studies have uncovered a dual role for PKR in cancer; it can act as either a promoter or suppressor, depending on the type of cancer. This paradoxical effect is thought to be due to variations in PKR expression and their diverse effects on cellular regulation in different tumor microenvironments.

Our study also revealed that PKR promotes the growth of hepatocellular carcinoma cells infected with hepatitis C virus. However, the role of PKR in PDAC remains to be elucidated.

Aims & Methods: This study aimed to identify the roles and mechanisms of action of PKR in PDAC by analyzing clinical evidence and *in vitro* data obtained from PDAC cell lines.

We used the human pancreatic cancer cell lines (PANC-1 and MIA PaCa-2) and verified PKR expression in PDAC cell lines using RT-PCR and Western

blotting. MTS assay was used to determine the effect of PKR on cell proliferation. To elucidate the mechanisms underlying the effect of PKR on PDAC, RNA-seq analysis was conducted. Flow cytometry was performed to investigate the effects of PKR knockdown on cell cycle progression and apoptosis in PDAC cells.

Additionally, we used the GEPIA database to compare the expression levels of PKR (EIF2AK2) in pancreatic cancer and normal pancreatic tissues. The Kaplan-Meier Plotter tool was used to analyze the relationship between individual PKR mRNA expression and disease-free survival (DFS) in patients with PDAC.

Results: PDAC cell lines exhibited significantly reduced proliferation when transfected with PKR-targeting siRNAs or treated with PKR inhibitors. RNA-seq analysis revealed a substantial upregulation of GADD45A expression when PKR expression was inhibited. After PKR silencing, cell cycle analysis indicated a pronounced accumulation of cells in the G1 phase, which is consistent with the known role of GADD45A as a cell cycle regulator.

Additionally, the inhibition of proliferation resulting from PKR knockdown was reversed upon downregulation of GADD45A, indicating an interactive effect between PKR and GADD45A in regulating PDAC cell growth. Furthermore, as mentioned above, PKR knockdown increased the percentage of cells in the G1 phase, and knockdown of both GADD45A and PKR returned the percentage of cells in the G1 phase to the same level as that in the control. These results indicated that the interaction between PKR and GADD45A plays a critical role in the proliferation of PDAC cells by regulating the cell cycle.

PKR mRNA expression levels in tumor and normal tissues were compared using the GEPIA database. Elevated PKR mRNA expression in tumor tissues compared with that in normal tissues was more pronounced in PDAC than in other carcinomas. We performed a prognostic analysis using the Kaplan-Meier Plotter database to explore the clinical significance of PKR in PDAC. The results showed that patients with elevated PKR mRNA expression had shorter disease-free survival (DFS; n=278; HR=1.84, 95% CI 1.36-2.5). In contrast, the group with high GADD45A expression showed a prolonged DFS. These data were consistent with our *in vitro* experimental results.

Conclusion: PKR promotes PDAC cell proliferation by modulating cell cycle via regulation of GADD45A expression. These results suggest that PKR is a potential novel therapeutic target for PDAC.

Disclosure: Nothing to disclose.

MP476

REAL LIFE ADHERENCE TO INTERNATIONAL GUIDELINES IN BD-IPMN MANAGEMENT. CLINICAL AND COSTS IMPACT OF DIVERGENT STRATEGIES IN BD-IPMN CARE. THE PACMANS STUDY

S. Kayali¹, E. Marabotto², S. Dibitetto³, S. Fantasia¹, A. Busatto⁴, S. Caprioli², A.P. Luzzi², E.V. Savarino⁴, L.A. Laghi¹, C.G. De Angelis⁵, E.G. Giannini²

¹University of Parma, Department of Medicine and Surgery, Parma, Italy, ²University of Genoa, Department of Internal Medicine, Genova, Italy, ³University of Turin, Division of Gastroenterology, Turin, Italy, ⁴University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ⁵'San Giovanni Battista' Hospital, University of Turin, Turin, Italy

Contact E-Mail Address: jstefanok@gmail.com

Introduction: Over the last two decades, there has been a rise in the diagnosis of Branch Duct Intraductal Papillary Mucinous Neoplasms (BD-IPMN), incidental findings posing potential neoplastic risks. Multiple guidelines, notably the International Association of Pancreatology (IAP)' revised in Fukuoka in 2017, have been suggested to optimize risk manage-

ment. However, the intricate nature of these guidelines makes adherence challenging, raising uncertainties regarding their application in clinical practice.

Aims & Methods: This study aimed to assess adherence to the 2017 IAP guidelines, identify factors associated with non-compliance, and analyze the impact of divergent strategies on clinical outcomes and costs. Clinical and histopathological data from 2017 to 2023 were retrospectively collected from four tertiary centers in Northern Italy, focusing on patients with suspected BD-IPMN. Multivariate logistic regressions were employed to analyze factors influencing divergent strategies from the IAP guidelines and assess their consequences on clinical outcomes, survival, and costs. Surveillance strategies were considered aggressive if deviating to a narrower surveillance timing or indicating higher-level examinations than recommended by the IAP guidelines. Conservative approach was defined as suggesting extended surveillance timing or indicating lower-level examinations than specified by the IAP.

Results: Of the 333 enrolled patients with a total of 1400 visits and a median follow-up of 4 years, 54% received recommendations deviating from the guidelines, predominantly in an aggressive direction (53.7%). Protective factors for deviation were an Age-adjusted Charlson Comorbidity Index (ACCI) above 4 (OR 0.44, 95% CI 0.33-0.58, $p < 0.001$) and larger initial IPMN size (OR 0.22, 95% CI 0.17-0.28, $p < 0.001$), while divergent approach increased by 25% every two years of follow-up (OR 1.25, 95% CI 1.11-1.41, $p < 0.001$). Conservative divergences, occurring in 25% of cases, were associated with the presence of High-Risk Stigmata (HRS) (OR 5.79, 95% CI 1.82-18.50, $p = 0.003$) and female gender (OR 1.55, 95% CI 1.25-2.04, $p = 0.001$). Notably, divergent strategies did not lead to different rates of IPMN-related mortality (2.5% vs 2.4%, $p = 1$). However, they resulted in increased surveillance costs, escalating from 720 [407-1253] to 878 [664-1181] euros per patient over three years ($p = 0.001$).

Conclusion: In conclusion, adherence to the IAP guidelines in clinical practice was low, predominantly exhibiting deviations in an aggressive direction. This non-adherence significantly increased costs compared to those projected by following the recommended guidelines.

Disclosure: Nothing to disclose.

MP477

WITHDRAWN

MP478

COMBINED ^{32}P IMPLANTATION AND CHEMOTHERAPY VERSUS CHEMOTHERAPY ALONE FOR LOCALLY ADVANCED PANCREATIC CANCER: A PROPENSITY-SCORE WEIGHTED LANDMARK ANALYSIS

A. Lim^{1,2}, D. Nitchingham², J. Bednarczyk^{3,2}, M. Bills⁴, L. Lanka⁵, B. Allen⁶, A. Tan⁶, W. Hsieh⁴, B. Crouch⁴, J. Zobel¹, J.-E. Thomson⁷, E. Neo⁷, R. Safaeian¹, E. Tse^{1,2}, C.K. Rayner^{2,1}, A. Ruszkiewicz^{2,8,9}, J. Wong¹⁰, N. Singhal¹¹, D. Bartholomeusz^{1,4}, F. Weilert¹², N.Q. Nguyen^{1,2}

¹Royal Adelaide Hospital, Department of Gastroenterology, Adelaide, Australia, ²University of Adelaide, Adelaide, Australia, ³South Australia Health and Medical Research Institute, SAHRMI Women and Kids, Adelaide, Australia, ⁴Royal Adelaide Hospital, Department of Nuclear Medicine, Adelaide, Australia, ⁵Waikato Hospital, Department of Radiology, Hamilton, New Zealand, ⁶Waikato Hospital, Department of Nuclear Medicine, Hamilton, New Zealand, ⁷Royal Adelaide Hospital, Department of Hepatobiliary Surgery, Adelaide, Australia, ⁸SA Pathology, Surgical Pathology, Adelaide, Australia, ⁹University of South Australia, Centre of Cancer Biology, Adelaide, Australia, ¹⁰Waikato Hospital, Department of Oncology, Hamilton, New Zealand, ¹¹Royal Adelaide Hospital, Department of Oncology, Adelaide, Australia, ¹²Waikato Hospital, Department of Gastroenterology, Hamilton, New Zealand

Contact E-Mail Address: amanda.hw.lim@gmail.com

Introduction: The combination of standard chemotherapy and phosphorus-32 (^{32}P) microparticle intra-tumoural implantation has revealed encouraging results for patients with locally advanced pancreatic cancer (LAPC). As no direct comparison has been made, our aim was to compare FOLFIRINOX alone and FOLFIRINOX with ^{32}P implantation in a propensity-score weighted analysis.

Aims & Methods: We conducted a retrospective cohort study comparing LAPC patients with combination chemotherapy and ^{32}P implantation at 2 centres with patients with chemotherapy only (discussed at hepatobiliary multidisciplinary team meetings or underwent diagnostic endoscopic ultrasound for pancreatic cancer) from a single centre, from August 2017 to January 2023. Landmark analysis was used to overcome immortal time bias. Propensity score weighting was further performed to minimise baseline confounders. Primary outcome was overall survival.

Results: 104 patients were considered. The landmark date was designated as 3 months after initiation of chemotherapy. After excluding patients who died before the landmark, 101 patients were included in the propensity-score weighted analysis (35 with ^{32}P implantation and chemotherapy, 66 with chemotherapy only). The restricted mean survival time (RMST) within 24 months after initiation of chemotherapy was estimated to be 112 days longer for patients with ^{32}P implantation and chemotherapy (459 days, 95%CI 393-536) compared to patients with chemotherapy only (347 days, 95% CI 308-392). The restricted mean local progression free time within 24 months after initiation of chemotherapy is estimated to be 112 days (95% CI 36-187) longer for patients with ^{32}P implantation and chemotherapy compared to patients with chemotherapy only. Average tumour size at 6 months was 12.8mm smaller (95% CI 4.69-20.9, $p=0.002$) with combination therapy than with chemotherapy only. The probability of downstaging if all patients were to be treated with combination therapy was 22.3% higher (95% CI 5.12%, 39.5%, $p=0.03$) than the probability with chemotherapy only.

Conclusion: This first comparative study between standard chemotherapy and chemotherapy with additional ^{32}P microparticles implantation has demonstrated significant survival, disease control and downstaging benefits of combination therapy with chemotherapy and ^{32}P microparticle implantation.

Disclosure: None.

MP479

EXPLORATORY BIOMARKER ANALYSIS FOR PREDICTING THERAPY SUCCESS OF SECOND LINE NAL-IRI/5-FU/FA CHEMOTHERAPY IN METASTATIC PDAC PATIENTS BASED ON THE PREDICT TRIAL (AIO-PAK-0216)

A. Lahusen¹, M.P. Lutz², M. Karthaus³, M. Kirchner⁴, K. Kluck⁴, P.F.-Y. Cheung⁵, S. Wisser⁶, N. Ansorge⁷, G. Barmashenko⁸, S. Hoefling⁹, C. Burkart¹⁰, T. Decker¹¹, L.F. von Weikersthal¹², T. Geer¹³, A. Gerhardt¹⁴, L. Jacobasch¹⁵, M. Koenigsmann¹⁶, T. Leidig⁹, M. Schulte⁹, N. Schulte¹⁷, A. Schwarzer¹⁸, G. Siegler¹⁹, D. Waldschmidt²⁰, J. Budczies⁴, J. Siveke⁵, A. Tannapfel⁶, A. Stenzinger⁴, T. Ettrich¹, T. Eiseler¹, S. R  th⁷, T. Seufferlein¹
¹University Hospital, Internal Medicine I, Ulm, Germany, ²Caritasklinikum St. Theresia, Innere Medizin, Saarbr  cken, Germany, ³M  nchen Klinik, Innere Medizin, Neuperlach, Germany, ⁴Universit  tsklinikum, Molekularpathologische Zentrum, Heidelberg, Germany, ⁵Universit  tsklinikum, Experimental Tumor Therapy, Essen, Germany, ⁶Ruhr-Universit  t, Pathologie, Bochum, Germany, ⁷St. Elisabeth-Krankenhaus, Innere Medizin, K  ln, Germany, ⁸AIO-Studien-gGmbH, Berlin, Germany, ⁹CROLL GmbH, N  rnberg, Germany, ¹⁰Schwarzwald-Baar-Klinikum, Innere Medizin, Villingen-Schwenningen, Germany, ¹¹Gemeinschaftspraxis, H  matologie und Onkologie, Ravensburg, Germany, ¹²Klinikum St. Marien, Innere Medizin, Amberg, Germany, ¹³Diakonie Klinikum, Innere Medizin, Schw  bisch Hall, Germany, ¹⁴Medizinisches Versorgungszentrum, Blut- und Krebserkrankungen, Potsdam, Germany, ¹⁵Gemeinschaftspraxis, H  matologie-Onkologie, Dresden, Germany, ¹⁶Ambulanzzentrum, Innere Medizin, Hannover, Germany, ¹⁷Universit  tsmedizin, Innere Medizin, Mannheim, Germany, ¹⁸Onkopraxi Probstheida, Leipzig, Germany, ¹⁹Klinikum Paracelsus, Innere Medizin, N  rnberg, Germany, ²⁰Universit  tsklinikum, Innere Medizin, K  ln, Germany

Contact E-Mail Address: a.lahusen1@googlemail.com

Introduction: The recent phase IIIb/IV PREDICT trial (NCT03468335) aimed to investigate the predictive value of 1st line chemotherapy (CTX, Gem-nabPac) for 2nd line CTX (nal-IRI/5-FU/FA) in metastatic PDAC patients (mPDAC Pts) and found an association of clinical parameters (e.g. CA19-9 level, leukocyte/neutrophil count) with 2nd line CTX time-to-treatment failure (TTF). Hence, this study had the objective to uncover molecular and phenotypic alterations within the tumor immune microenvironment (TiME) of treatment-na  ve Pts with shortest (S-) vs. longest (L-) TTF after 2nd line CTX and to identify corresponding liquid biomarkers (combined with clinical parameters) for predicting 2nd line CTX TTF.

Aims & Methods: Pts were stratified into two cohorts based on S- or L-TTF2 (n = 10 Pts per group, 80/20% quantiles, TTF2: 2nd line treatment start to treatment failure). PDAC tissue specimens from surgical resection (treatment-na  ve) were enriched for tumor cell content via laser microdissection and subjected to RNA (NanoStringTM, PanCancer IO360) profiling. Selected differentially regulated genes from the Omics results were used for screening PBMCs from 2nd line treatment-na  ve Pts on protein (flow cytometry, FC) or RNA (RT-qPCR) level. FC data was used for the generation of HyperGates (HG) via R-based single-cell clustering algorithms (x-Shift, FlowSOM, T-REX) and subsequent ML-based back-gating (HyperFinder in FlowJo) of most differential clusters. The Weka-based algorithm Wrapper-SubsetEval (WSE) with one of ten different classifiers (NB, KLR, LR, SMO, IBk, RT, RF, J48, FT, SPegasos) was used for feature selection and the classifier/subset with the best performance was used for classification (S-TTF vs. L-TTF, TTF: diagnosis mPDAC to failure of 2nd line CTX) of training (80%, n = 66) as well as validation (20%, n = 16) datasets.

Results: Comparisons of L-/S-TTF transcriptome data revealed significantly increased inflammation (upregulated 18-gene inflammation signature), immune cell activation (enriched signatures: activated CD8 T cells/B cells/CD4 T cells), immune cell infiltration signatures (CD8 T cells, Neutrophils, Tregs), and immune exhaustion (upregulation of PDCD1, LAG3, CTLA4, TIGIT, IDO1, CD96) for L-TTF tumors. Additionally, the favorable Bailey immunogenic subtype was enriched for the L-TTF group. Hence, PBMCs from blood samples of 2nd line CTX na  ve mPDAC Pts were screened for selected differentially regulated candidates from the Omics results. Analysis of eight separate FC panels including 19 candidates revealed 1198 differential clusters with corresponding HGs. Feature selection for this dataset combined with 50 additional features from RT-qPCR (relative expression and ratios for 12 candidates), 890 manual (classical) gates (MGs) for FC data, and 45 clinical parameters, unmasked a signature of 7 HGs and 2 MGs for 9 protein markers (CD4, CD62P, CD8, NKG2D, CD45, CD62L, CD121b, CD19, Nkp46). ML by using Na  ve Bayes successfully predicted S-TTF and L-TTF groups prior to 2nd line CTX with nal-IRI/5-FU/FA (ROC-AUC (training) > 0.90, ROC-AUC (validation) > 0.90).

Conclusion: In our study, we have identified a favorable TiME for L-TTF mPDAC Pts (2nd line CTX) showing CD8 T cell inflamed ("hot") tumor tissues prior to 2nd line CTX. We further present a 9-marker liquid biomarker panel including 9 flow cytometry PBMC population gates for early prediction of 2nd line nal-IRI/5-FU/FA therapy success in mPDAC Pts. With our findings, we aim to advance the personalized treatment of mPDAC Pts e.g. by additionally exploring the potential for immunotherapy in patients with a positive marker signature.

References: Lutz, M. P. et al. 1624P Predictive factors for treatment success of second-line Nal-IRI/5-FU/FA in patients with metastatic pancreatic ductal adenocarcinoma (PDAC) (AIO-PAK-0216). *Ann. Oncol.* 34, S899–S900 (2023).

Karthaus, M. et al. Prediction of early treatment failure of second-line nal-iri/5-FU/FA in patients with advanced pancreatic adenocarcinoma (AIO-PAK-0216). *J. Clin. Oncol.* 41, 721–721 (2023).

Disclosure: Conflict of interest (M. Lutz): Consulting and advisory role for Servier.

MP480

WITHDRAWN

MP481

IDENTIFYING DRUGGABLE TUMOR-IMMUNE INTERACTIONS IN ATM-DEFICIENT PANCREATIC CANCER

J. Ragg¹, E. Roger¹, E. Zimmer¹, D. Srinivasan¹, A. Härle¹, H.M. Mummey², Y. Lee², K.J. Gaulton², L. Perkhofer¹, J. Gout¹, A. Kleger¹

¹University Hospital Ulm, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Department of Pediatrics, UC San Diego, La Jolla, United States of America

Contact E-Mail Address: julia.ragg@uni-ulm.de

Introduction: The complex biology of pancreatic ductal adenocarcinoma (PDAC) remains a significant challenge and limits overcoming its dismal prognosis. The tumor microenvironment (TME), shaped by dynamic interactions between cancer-associated fibroblasts (CAFs), immune and tumor cells, plays a crucial role in PDAC pathogenesis. Our investigation into homologous recombination deficiency (HRD), caused by mutations in genes like *ATM*, revealed its role in promoting PDAC aggressiveness and triggering a pronounced desmoplastic reaction, suggesting a unique TME programming. We have shown that the loss of *ATM* in the neoplastic epithelium reprograms CAFs through the TGF β signaling to promote cancer aggressiveness. Additionally, preliminary data revealed distinct immune profiles in *ATM*-deficient and proficient tumors.

Aims & Methods: To capture the immune profiles of *ATM*-deficient PDACs, and decipher specific oncogenic tumor-stroma interactions, we first conducted single cell-resolved multiomics analyses of murine *ATM* and/or *P53*-depleted PDACs. Histopathological analyses and validation using publicly available human datasets were performed to further characterize *ATM* loss-specific immune patterns in pancreatic cancer.

Results: Mouse tumor analyses, using single-nucleus multiomics RNA/ATAC sequencing and multiplex immunostainings, revealed alterations in immune cell contents, e.g. reduced macrophage populations and reduced M2 polarization in *ATM*-deficient tumors. *ATM* loss-specific immune molecular signatures were further investigated and correlated with human PDAC RNA sequencing data (TCGA, PanCancer Atlas). Molecular signatures and cell-cell communication inference revealed *ATM*-specific tumor-TME interactions and identified the TGF β signaling as a core driver of the interplay between CAFs, immune cells, and a particularly aggressive EMT-like tumor cell subpopulation overrepresented in *ATM*-depleted tumors. Strikingly, we also observed distinct communication patterns between CAFs and immune cells. Finally, a combinatorial therapy targeting the TGF β -driven tumor-stroma dialog reversed the cancer-promoting TME remodeling and exacerbated the therapeutic response to FOLFIRINOX *in vivo*, exclusively in *ATM*-deficient HRD PDACs.

Conclusion: Through single cell-resolved multiomics analyses of *ATM*-deficient PDACs, and validation in human cases, we unveil transcriptional, translational, and secretory regulatory events, shed light on the intricate interplay between tumor genetics and PDAC microenvironment, and pave the way for the elaboration of novel personalized therapies.

Disclosure: Nothing to disclose.

MP482

FOLFIRINOX VERSUS GEMCITABINE/NAB-PACLITAXEL IN METASTATIC PANCREATIC CANCER: A REAL-WORLD DATA ANALYSIS INCLUDING NGS PANEL INSIGHTS

J. Kim¹, G. Leem¹, H.S. Lee¹, M.-J. Chung¹, J.Y. Park¹, S. Bang¹, S.W. Park¹, S.-Y. Song¹, J.H. Jo¹

¹Yonsei University College of Medicine, Division of Gastroenterology, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: jaratoll90@yuhs.ac

Introduction: FOLFIRINOX and Gemcitabine/Nab-paclitaxel are widely used 1st-line regimens in metastatic pancreatic cancer. We would like to present real-world data of 12 years of experience with both regimens including genomics insights

Aims & Methods: Patients with metastatic pancreatic cancer who received FOLFIRINOX or Gemcitabine/Nab-paclitaxel were retrospectively included from January 2010 to December 2022. Outcomes were overall survival (OS) and progression free survival (PFS). Median survival time was calculated using Kaplan-Meier estimates adjusted with 1:1 Propensity Score Matching (PSM). Additional tissue Next Generation Sequencing (NGS) panel data was analyzed.

Results: A total of 521 patients, 251 patients received FOLFIRINOX and 270 patients received Gemcitabine/Nab-paclitaxel as a first-line regimen. FOLFIRINOX group were younger (61.8 vs. 65.9, $p < 0.001$). Before PSM, FOLFIRINOX group showed prolonged median OS (11.1 vs 7.8 months) and PFS (8.8 vs. 5.8 months) ($p = 0.002$, both) compared to Gemcitabine/Nab-paclitaxel group. After PSM, FOLFIRINOX group still showed prolonged median OS (11.1 vs 9.0 months, $p = 0.010$) and PFS (9.2 vs 6.4 months, $p = 0.001$) than Gemcitabine/Nab-paclitaxel group. NGS was available from 31 and 22 patients in the FOLFIRINOX and Gemcitabine/Abraxane group, respectively. The most frequently mutated genes were KRAS (94.3%), TP53 (84.9%), CDKN2A (24.5%), SMAD4 (24.5%), ARID1A(13.2%) and RNF43(9.4%). On Cox Regression Analysis, RNF43 mutation was correlated with poor PFS with Gemcitabine/Nab-paclitaxel (HR, 4.849; 95% CI, 1.150-20.450, $P = 0.032$).

	FOLFIRINOX (N = 31)			Gemcitabine/Nab-P (N = 22)		
	cHR	95% CI	P value	cHR	95% CI	P value
KRSA	2.577	0.597-11.115	0.204	1.602	0.209-12.279	0.650
TP53	1.922	0.576-6.414	0.288	1.122	0.363-3.464	0.842
CDKN2A	1.698	0.708-4.074	0.236	1.103	0.409-2.973	0.846
SMAD4	0.678	0.274-1.677	0.400	0.701	0.264-1.860	0.475
ARID1A	0.670	0.158-2.848	0.588	1.919	0.610-6.034	0.265
RNF43	1.199	0.276-5.210	0.809	4.849	1.150-20.450	0.032

cHR, Crude hazard ratio; CI, confidence interval

Conclusion: FOLFIRINOX showed prolonged OS and PFS compared to Gemcitabine/Nab-paclitaxel. FOLFIRINOX can be considered 1st-line regimen in metastatic disease. The NGS data suggest RNF43 could be a potential predictive marker for the response to Gemcitabine/Nab-Paclitaxel, however, larger size confirmation study is needed to validate this finding.

Disclosure: Nothing to disclose.

MP483

EXPLOITING THE MEVALONATE PATHWAY AS A METABOLIC VULNERABILITY IN GEMCITABINE RESISTANT PANCREATIC CANCER

A.K. Beutel^{1,2}, S. Calderon¹, E. Nghiem¹, R. Singh¹, N. Yousefian¹, C. Anaraki¹, K. Gulay³, D. Juarez¹, G. Tong⁴, T. Seufferlein², E. Zimmer⁵, A. Muir⁶, C. Jang⁷, H. Tiriach³, T. Martinez⁴, A. Kleger^{2,5}, D. Fruman¹, C.J. Halbrook^{1,8}

¹University of California Irvine, Molecular Biology and Biochemistry, Irvine, United States of America, ²University Hospital Ulm, Internal Medicine 1, Ulm, Germany, ³University of California San Diego, Surgery, Moores Cancer Center, San Diego, United States of America, ⁴University of California Irvine, Pharmaceutical Sciences, Irvine, United States of America, ⁵University Hospital Ulm, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ⁶University of Chicago, Ben May Department for Cancer Research, Chicago, United States of America, ⁷University of California Irvine, Biological Chemistry, Irvine, United States of America, ⁸University of California Irvine, Chao Family Comprehensive Cancer Center, Orange, United States of America

Contact E-Mail Address: alicabeutel@hotmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy with a devastating prognosis. A lack of durable responses to chemotherapy renders its treatment particularly challenging. Gemcitabine, a pyrimidine anti-metabolite, is a key component in PDAC therapy, but resistance poses a major hurdle in clinical care. Multiple mechanisms of chemoresistance have been attributed to rewired metabolism in PDAC cells. Accordingly, we aim to target these altered metabolic pathways to improve response to treatment.

Aims & Methods: To investigate metabolic vulnerabilities, we generated an acquired gemcitabine resistance in murine PDAC cell lines. We performed RNA sequencing on parental and gemcitabine resistant cell lines to identify targetable transcriptomic programs that drive cell-intrinsic resistance.

Results: Our transcriptomic dataset demonstrated that PDAC cells re-wire several metabolic pathways upon the acquisition of gemcitabine resistance, including downregulation of nucleoside transporters required for gemcitabine uptake and gemcitabine activating enzymes, as well as upregulation of detoxification enzymes. We performed a customized screen of common metabolic inhibitors and observed that gemcitabine resistant cells were exquisitely susceptible to statins, inhibitors of the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, an observation consistent across multiple clinically available statins. Protein and RNA sequencing data showed a downregulation of the mevalonate biosynthesis pathway and its rate-limiting enzyme, HMG-CoA reductase, in gemcitabine resistance. Importantly, the sensitivity to statins correlated with the extent of the gemcitabine resistance, suggesting that targeting the HMG-CoA reductase is a metabolic vulnerability that is gradually gained in PDAC cells upon the acquisition of resistance. Downstream rescue experiments suggested that statins induce apoptosis through lowered levels of geranylgeranyl pyrophosphate and reduced protein geranylation of small GTPases. To validate our findings *in vivo*, we orthotopically implanted gemcitabine resistant murine PDAC cells into syngeneic mice that were fed with a modified diet precluding geranylgeraniol. Here, the combined treatment of gemcitabine and pitavastatin effectively inhibited tumor growth of resistant allografts.

Conclusion: Collectively, these data suggest that targeting the HMG-CoA reductase is a metabolic vulnerability that is gained in PDAC cells upon the acquisition of gemcitabine resistance. The treatment combination of gemcitabine and pitavastatin, two widely used compounds in patients, has potential to translate into an immediate clinical benefit and improve survival in this deadly disease.

Disclosure: Nothing to disclose.

Pharmaceutical treatment of EoE

16:00-17:00 / Poster Stage 5

MP484

EVALUATING PLACEBO RATES IN EOSINOPHILIC ESOPHAGITIS RANDOMIZED CONTROLLED TRIALS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Rivas¹, Y. Yuan², S. Ahmed¹, A. Qasim³, D.B. O’Gorman³, B.G. Feagan^{3,2,4}, V. Jairath^{2,4,3}, A.J. Bredenoord⁵, E.S. Dellon⁶, C. Ma^{7,3}

¹University of Calgary, Department of Medicine, Calgary, Canada,

²London Health Sciences Centre, Division of Gastroenterology, London, Canada, ³Alimentiv Inc., London, Canada, ⁴Western University, Department of Epidemiology and Biostatistics, London, Canada, ⁵Academic Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁶University of North Carolina School of Medicine, Center for Esophageal Diseases and Swallowing, and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Chapel Hill, United States of America, ⁷University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada

Contact E-Mail Address: Angelica.Rivas@albertahealthservices.ca

Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory and progressive fibrotic condition of the esophagus characterized by the infiltration of eosinophils into the esophageal mucosa and esophageal dysfunction. There remain limited treatment options for EoE and accordingly, a substantial unmet need for effective and safe medical therapies. Drug development in EoE has been hampered by heterogeneous placebo response rates, especially for clinical outcomes, and uncertainty regarding appropriate endpoint configurations. Accurate characterization of placebo response in EoE randomized controlled trials (RCTs) will help inform more future efficient trial designs.

Aims & Methods: To conduct a systematic review and meta-analysis to characterize symptomatic, endoscopic, and histologic placebo response rates in placebo controlled EoE RCTs.

Electronic database (CENTRAL, MEDLINE, EMBASE) searching (inception to 1 JAN 2024) identified placebo controlled RCTs evaluating medical therapies for adults with EoE. Studies were screened independently by 2 reviewers (AR and SA), and full texts were then reviewed for eligibility. The proportion of clinical, endoscopic, and histologic responders (improvement and remission) assigned to placebo were pooled using a random-effect model. The Stuart-Ord inverse double arcsine square root transformation method was used to compute 95% confidence intervals (CI) for point estimates of placebo response. Heterogeneity was evaluated using the *I*² method. Analyses were conducted in StatsDirect 3.3.6.

Results: A total of 25 placebo-controlled RCTs (placebo sample size range: N = 4–105) were included. The pooled proportion of patients receiving placebo who achieved clinical response was 41.0% (n = 11; 95% CI 29.7%, 52.8%) with substantial heterogeneity (*I*² = 74.9%). Definitions of clinical response varied between studies. The pooled proportion for histologic remission (peak eosinophil count [PEC] ≤ 6 eos per high power field [hpf]) was 4.3% (n = 20; 95% CI 2.6%, 6.2%) with low heterogeneity (*I*² = 23.6%), while a more stringent definition of histologic remission (PEC ≤ 1 eos/hpf) yielded a pooled placebo remission rate of 1.3% (n = 18; 95% CI 0.5%, 2.5%) with low heterogeneity (*I*² = 0%). The pooled histologic improvement rate was 6.2% (n = 15; 95% CI 3.3%, 10.0%) with substantial heterogeneity (*I*² = 50.6%). Limited studies reported on endoscopic improvement and remission (Table 1).

Conclusion: More than 1 in 3 patients assigned to placebo in EoE RCTs will achieve clinical response (substantial heterogeneity detected), while less than 1 in 10 of these patients will achieve histologic remission (low

heterogeneity detected). These findings highlight 1) the need to develop validated and responsive patient-reported outcome measures, which may be difficult due to the episodic nature of symptoms in EoE; and 2) the challenge of using a coprimary clinical and histologic outcome in EoE RCTs, given the discordance between symptoms and objective disease activity measures.

Outcome Measured in Placebo Patients (n = number of studies)	Sample Size (range)	Pooled Proportion% (95% CI)	Heterogeneity, I ² % (95% CI)
Clinical Response/Improvement (n = 11)	6 to 105	41.0 (29.7, 52.8)	74.9 (49, 84.8)
Clinical Remission (n = 9)	4 to 33	13.8 (5.9, 24.3)	66.2 (12.2, 81.6)
Endoscopic Response/Improvement (n = 3)	6 to 19	25.1 (12.4, 40.5)	0 (0, 72.9)
Endoscopic Remission (n = 3)	9 to 29	2.8 (0.06, 9.6)	9.1 (0, 75.3)
Histologic Response/Improvement (≤ 15 eos/hpf, n = 15)	6 to 105	6.2 (3.3, 10.0)	50.6 (0, 71.3)
Histologic Remission (n = 24)			
≤ 6 eos/hpf (n = 20)	6 to 105	4.3 (2.6, 6.2)	23.6 (0, 55.2)
≤ 1 eos/hpf (n = 18)		1.3 (0.5, 2.5)	0 (0, 43.7)

Table 1. Pooled proportion of placebo patients achieving measured outcomes in EoE studies.

Disclosure: AR: No conflicts of interest

SA: No conflicts of interest

YY: No conflicts of interest

AQ: Is an employee of Alimentiv Inc.

DBO: Is an employee of Alimentiv Inc.

BGF: consulting fees from AbbVie, Abivax, Adiso, AgomAB Therapeutics, Alliantera, Amgen, AnaptysBio, Arena Pharma, Avoro Capital Advisors, Atomwise, BioJamp, Biora Therapeutics, Blackbird Laboratories, Boehringer-Ingelheim, Boxer Capital, Celsius Therapeutics, Celgene/BMS, Celltrion, Connect BioPharma, Cytoki, Disc Medicine, Duality, EcoR1, Eli Lilly, Equillum, Ermium, First Wave, Forbion, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, Gossamer Pharma, GSK, Hinge Bio, Index Pharma, Imhotex, Immunic Therapeutics, Intercept, JAKAcademy, Janssen, Japan Tobacco Inc., Kaleido Biosciences, Klick Health, Landos Biopharma, Lenczner Slaght, LifeSci Capital, Lument AB, Mage Biologics, Mestag, Millennium, MiroBio, Monte Rose Tx, Morgan Lewis, Morpich Therapeutics, Mylan, Nexys Therapeutics, Nimbus Therapeutics, OM Pharma, OrbiMed Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics (Merck), Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Roivant/Televant, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Sobi, Spyre Therapeutics, Surrozen Inc., Sun Pharma, Synedgen, Takeda, Teva, Thelium, Tigenix, Tillotts, Triastek, TR1X Inc. Ventyx Biosciences, Zagbio, Zealand Pharma. Speaker fees from AbbVie, Janssen, Takeda.

VJ: consulting/advisory board fees from AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Anaptys Bio, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; and speaker's fees from, Abbvie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi.

AJB: AJB received research funding from Nutricia, Thelial, Sanofi/Regeneron, SST, and Dr. Falk Pharma and received speaker and/or consulting fees from Laborie, Medtronic, BMS, Dr. Falk Pharma, Calypso Biotech,

Eupraxia, Aqilion, Alimentiv, Sanofi/Regeneron, Reckitt and AstraZeneca ESD: Research funding: Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Shire/Takeda

Consultant: Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Apollo, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morpich, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio

Educational grant: Allakos, Aqilion, Holoclara, Invea

CM: consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Pendopharm, Pfizer, Prometheus Biosciences Inc., Roche, Sanofi, Takeda, Tillotts Pharma; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Eli Lilly, Ferring, Fresenius Kabi, Janssen, Organon, Pendopharm, Pfizer, Sanofi, Takeda, Tillotts Pharma; royalties from Springer Publishing; research support from AbbVie, Ferring, Pfizer.

MP485

MULTI-CENTRE REAL-WORLD UK EXPERIENCE OF ORO-DISPERSIBLE BUDESONIDE IN THE MAINTENANCE TREATMENT OF EOSINOPHILIC OESOPHAGITIS

J. Cooney¹, M. Galoni², Y. Sredharan³, H. Abdelrahim⁴, P. Appiahene¹, Z. Mrevlje-Simon⁵, H.N. Haboubi⁴, I. Mainie³, A. Dhar², J. Hayat¹

¹St George's University Hospitals NHS Foundation Trust, Gastroenterology, London, United Kingdom, ²County Durham and Darlington NHS Foundation Trust, Gastroenterology, Durham, United Kingdom, ³Belfast Health and Social Care Trust, Gastroenterology, Belfast, United Kingdom, ⁴Cardiff and Vale University Health Board, Gastroenterology, Cardiff, United Kingdom, ⁵University Hospitals Sussex NHS Foundation Trust, Gastroenterology, Brighton, United Kingdom

Contact E-Mail Address: josephcooney@doctors.org.uk

Introduction: Orodispersible budesonide (ODB) is an effective treatment for eosinophilic oesophagitis (EoE), with clinical trials reporting clinical remission rates of 75% at 48 weeks. Real-world data is lacking, particularly for longer term ODB maintenance treatment. We have conducted the first UK multicentre review of real-world outcomes on adults with EoE taking ODB from 5 tertiary hospitals.

Aims & Methods: Databases at 5 UK centres were screened to identify adults taking ODB. Audit approval was obtained by each centre. Electronic results and documentation were reviewed. Patients were telephoned and validated surveys completed to assess symptoms – Reflux Disease Questionnaire (RDQ), Hospital Odynophagia Dysphagia Questionnaire (HODQ) and Adult EoE Quality of Life Survey (EoE-QoLS). A numeric rating scale was used for pts to gauge their response to ODB.

Results: 104pts aged 24-86y (med 41y), 27F:77M, taking ODB for 3-60months (med8.5m, mean14.2m) were included.

97pts completed questionnaires – 98% reported ODB had improved their symptoms. Scores on ODB were low, suggesting clinical remission: RDQ 0-52 (med0), HODQ 0-29 (med2), and EoE-QoLS 37-120 (med60).

71% received PPI first line prior to ODB, of which 81% reported inadequate improvement in dysphagia and 94% did not achieve histological remission (HR, <15eos/hpf) on PPI prior to ODB. 21pts continued PPI in addition to ODB - 1/21 was not in HR.

82pts underwent OGD on ODB – 77% were in HR. 74% pts had fibrotic findings (stricture, trachealisation) which had improved or resolved for 49% on ODB. 78% pts had inflammatory findings (oedema, exudate, furrows) which had improved or resolved for 67% on ODB.

14% experienced oro-oesophageal candidiasis on ODB. ODB was not discontinued.

Following ≥8week induction with 1mg BD ODB, 51pts had tried a reduced maintenance dose of 1mg OD ODB – 77% reported no deterioration in their symptoms on 1mg OD vs BD. 10pts had undergone OGD on 1mg OD – 7/10 were in HR.

Conclusion: Symptomatic and histopathological remission rates on ODB in this multicentre UK study are comparable to clinical trial outcomes yet resolution of endoscopic signs was lower. 1mg OD ODB kept a majority with symptomatic control but this was not always accompanied by histological/endoscopic remission. QoL scores were not proportionately as low as symptom scores on ODB, suggesting a persisting psychological burden despite treatment and warrants further study.

References: Lucendo et al, Gastroenterology (2019)

Miehlke et al, UEG Journal (2022)

Straumann et al, Gastroenterology (2020)

Dhar et al, Gut (2022)

Disclosure: Nothing to disclose.

MP486

IMPLICATIONS FOR NON-INVASIVE BIOMARKERS OF EOSINOPHILIC ESOPHAGITIS BASED ON RESULTS FROM A PHASE 2 TRIAL OF CENDAKIMAB IN ATOPIC DERMATITIS

E.S. Dellon¹, J. Li², S. Harris², L. Gao², C. De Oliveira², C. Charriez², J. Silverberg³

¹Center for Esophageal Diseases and Swallowing, Division of Gastroenterology and Hepatology, School of Medicine, University of North Carolina, Chapel Hill, NC, United States of America,

²Bristol Myers Squibb, Princeton, NJ, United States of America,

³Department of Dermatology, School of Medicine and Health Sciences, George Washington University, Washington, DC, United States of America

Contact E-Mail Address: sarah.harris@bms.com

Introduction: Cendakimab is a recombinant, humanized, high-affinity, neutralizing monoclonal antibody that binds to interleukin 13 (IL-13) and blocks interaction with both its receptors, IL-13Rα1 and IL-13Rα2. IL-13 is a cytokine implicated in the pathogenesis of atopic dermatitis (AD) and is thought to be a key driver of the complex pathophysiology of eosinophilic esophagitis (EoE). IL-13 signals through both IL-13Rα1 and IL-13Rα2 to regulate cellular and molecular pathways across a variety of cell types. The binding of IL-13 to IL-13Rα1 promotes a Type 2 immune response and eosinophil recruitment, whereas the binding of IL-13 to IL-13Rα2 is believed to play a role in fibrosis and epithelial tissue remodeling. Several biomarkers associated with Type 2 inflammatory diseases are known to be regulated by IL-13. Eotaxin-3, a key biomarker, plays a central role in attracting eosinophils to the site of inflammation. Periostin, an extracellular matrix protein linked to activated fibroblasts, is implicated in tissue remodeling and fibrosis. Another enzyme governed by IL-13 is matrix metalloproteinase-12 (MMP-12)—this enzyme contributes to tissue remodeling and breakdown of extracellular matrix components. Here, we evaluate the pharmacodynamic effects of IL-13 inhibition with cendakimab on the key serum biomarkers eotaxin-3, periostin, and MMP-12 in patients with AD, with a focus on exploring potential implications for EoE.

Aims & Methods: In this phase 2, multicenter, global, randomized, double-blinded, placebo-controlled, parallel-group study (NCT04800315), 220

adults with moderate-to-severe AD received cendakimab 360 mg Q2W, 720 mg QW, 720 mg Q2W, or placebo for 16 weeks. Blood samples were collected, and a panel of biomarkers were assessed. The current analysis focuses on the assessment of serum levels of eotaxin-3, periostin, and MMP-12 using Proximity Extension Assay pre- and post-treatment on day 1 (baseline), at week 1 and week 2, and then biweekly until week 16. The least square mean percent change from baseline at week 16 for each treatment group was evaluated.

Results: For all 3 doses of cendakimab, there was a significant decrease from baseline in the levels of eotaxin-3, periostin, and MMP-12 as early as week 1 post-treatment and continued through week 16 of cendakimab treatment (Table). Compared with placebo, cendakimab resulted in significantly greater reductions in these biomarker levels through week 16.

Conclusion: Cendakimab decreased levels of key inflammatory and remodeling biomarkers over 16 weeks of treatment in patients with AD. These findings suggest that cendakimab modulates pathways of inflammation, fibrosis, and tissue remodeling in AD and add to the existing clinical evidence of its modulation in other Type 2 inflammatory diseases such as EoE.

Treatment	Eotaxin-3 LS mean percent CFB (95%CI)	Periostin LS mean percent CFB (95%CI)	MMP-12 LS mean percent CFB (95%CI)
Cendakimab 360 mg Q2W	-51.53 (-61.98 to -38.20)*†	-47.50 (-56.45 to -36.73)*†	-52.00 (-58.39 to -44.63)*†
Cendakimab 720 mg QW	-58.20 (-67.29 to -46.59)*†	-55.76 (-63.31 to -46.67)*†	-54.72 (-60.83 to -47.65)*†
Cendakimab 720 mg Q2W	-67.77 (-74.75 to -58.85)*†	-60.93 (-67.57 to -52.94)*†	-61.07 (-66.27 to -55.06)*†
Placebo	-5.80 (-26.63 to 20.94)	-23.92 (-37.15 to -7.90)*	-16.69 (-28.31 to -3.19)*

Table. Least square mean percent change from baseline in key serum biomarker levels at week 16 in patients with AD.

CFB, change from baseline; CI, confidence interval; LS, least square.

*P < 0.05 versus baseline.

†P < 0.01 cendakimab versus placebo

Disclosure: ESD served as a consultant for Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/ Bristol Myers Squibb, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GlaxoSmithKline, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio, received research funding from Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/ Bristol Myers Squibb, Regeneron, Revolo, Shire/Takeda, and received educational grant from Allakos, Aqilion, Holoclara, and Invea. JL, SH, LG, CDO, and CC are employees and stockholders of Bristol Myers Squibb. JS served as consultant for Abbvie, Alamar, Aldena, Amgen, AOBiome, Apollo, Arcutis, Arena, Asana, Aslan, Attovia, BioMX, Biosion, Bodewell, Boehringer-Ingelheim, Bristol Myers Squibb, Cara, Castle Biosciences, Celgene, Connect Biopharma, Corevitas, Dermavant, Eli Lilly, FIDE, Galderma, GlaxoSmithKline, Incyte, Invea, Kiniksa, Leo Pharma, Merck, My-Or Diagnostics, Nektar, Novartis, Optum, Pfizer, RAPT, Recludix, Regeneron, Sandoz, Sanofi-Genzyme, Shaperon, TARGET-RWE, Teva, Union, UpToDate, participated on a data safety monitoring board or advisory board for Biosion and Sanofi, received grants or contracts from Galderma, Incyte, Pfizer, received honoraria from Abbvie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme.

MP487

DUPILUMAB IS ASSOCIATED WITH IMPROVED HISTOLOGY, CLINICAL SYMPTOMS, AND ENDOSCOPIC FINDINGS IN ADULTS AND ADOLESCENTS WITH EOSINOPHILIC ESOPHAGITIS THROUGH 52 WEEKS REGARDLESS OF BASELINE DISEASE DURATION: POST-HOC SUBGROUP ANALYSIS OF THE PHASE 3 LIBERTY EOE TREET STUDY

N. Gonsalves¹, C. Schlag², C. Santander³, K. Peterson⁴, C. Xia⁵, T. Pela⁶, B. Raphael⁵, J.A. Jacob-Nara⁶, A. Radwan⁵

¹Northwestern University Feinberg School of Medicine, Division of Gastroenterology and Hepatology, Chicago, United States of America, ²University Hospital Zürich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ³Hospital Universitario de la Princesa, Department of Gastroenterology and Hepatology, Madrid, Spain, ⁴University of Utah, Division of Gastroenterology, Salt Lake City, United States of America, ⁵Regeneron Pharmaceuticals Inc., Tarrytown, United States of America, ⁶Sanofi, Bridgewater, United States of America

Contact E-Mail Address: christoph.schlag@gmx.de

Introduction: Eosinophilic esophagitis (EoE) is a chronic, progressive, type 2 inflammatory disease, with a substantial impact on quality of life; longer disease duration increases the risk of fibrostenosis, which may reduce both clinical and histologic response to therapy. Dupilumab, a fully human monoclonal antibody that blocks key drivers of type 2 inflammation, is approved for the treatment of EoE in adults and adolescents aged ≥12 years weighing ≥40 kg in the EU, and for patients aged ≥1 year, weighing ≥15 kg in the US.

Aims & Methods: The objective of this post-hoc subgroup analysis of the LIBERTY EoE TREET study (NCT03633617) was to assess the long-term efficacy of dupilumab in patients with EoE stratified by baseline disease duration. In Part B, patients received 24 weeks of dupilumab 300 mg once weekly (qw), dupilumab 300 mg once every 2 weeks, or placebo qw. Eligible patients who completed Part B received dupilumab through 52 weeks (Part C). This analysis focuses on patients who were originally randomized to dupilumab 300 mg qw or placebo. Co-primary endpoints were the proportion achieving peak esophageal intraepithelial eosinophil count (PEC) ≤6 eosinophils per high-power field (eos/hpf) and absolute change from baseline in Dysphagia Symptom Questionnaire (DSQ) total score. Key secondary endpoints included proportion achieving PEC <15 eos/hpf, and mean change from baseline in Endoscopic Reference Score (EREFS) total score and Histologic Scoring System (HSS) grade/stage scores. Data were stratified by baseline disease duration defined as time since diagnosis (≤5 years, >5-10 years, >10 years), as reported by the investigator.

Results: At Part B baseline (Week 0) in the dupilumab and placebo groups, respectively, 43 and 48 patients had EoE for ≤5 years, 22 and 13 patients had EoE for >5-≤10 years, and 15 and 18 patients had EoE for ≥10 years. Each of the co-primary endpoints—PEC ≤6 eos/hpf and DSQ total score at Week 24—favored dupilumab over placebo, regardless of disease duration (Table).

At Week 24, marked improvements with dupilumab vs placebo were also seen for EREFS and HSS grade/stage scores across all disease duration subgroups (Table). At Week 52, all patients who received continued dupilumab maintained improvement across all outcomes, including 88.6%, 73.7%, and 90.9% achieving ≤6 eos/hpf in the ≤5, >5-≤10, and ≥10 year subgroups, respectively. Regardless of subgroup, 100% of patients receiving continued dupilumab achieved PEC <15 eos/hpf at Week 52. Patients who switched from placebo to dupilumab at Week 24 showed improvement in all outcomes at Week 52, comparable to patients who received continued dupilumab.

	≤5 years		>5-≤10 years		>10 years	
	Placebo (n=48)	Dupilumab qw/ dupilumab qw (n=43)	Placebo (n=13)	Dupilumab qw/ dupilumab qw (n=22)	Placebo (n=18)	Dupilumab qw/ dupilumab qw (n=15)
Proportion achieving PEC ≤6 eos/hpf, n (%)	4 (8.3)	28 (65.1)	0 (0.0)	11 (50.0)	1 (5.6)	8 (53.3)
Proportion achieving PEC <15 eos/hpf, n (%)	5 (10.4)	37 (86.0)	0 (0.0)	19 (86.4)	1 (5.6)	10 (66.7)
Change from baseline in DSQ score	-14.6 (12.8)	-24.7 (16.5)	-9.3 (8.7)	-23.4 (17.9)	-17.0 (13.9)	-25.9 (15.0)
Change from baseline in EREFS total score	-0.9 (4.2)	-4.7 (3.9)	-0.6 (1.9)	-3.7 (3.0)	-0.1 (2.7)	-4.1 (2.7)
Change from baseline in HSS grade score	-0.1 (0.5)	-0.9 (0.5)	-0.1 (0.4)	-0.9 (0.4)	-0.1 (0.3)	-0.8 (0.5)
Change from baseline in HSS stage score	-0.1 (0.5)	-0.8 (0.4)	-0.1 (0.4)	-0.9 (0.4)	-0.1 (0.3)	-0.7 (0.5)

Data are reported as mean (SD) unless otherwise stated. DSQ, Dysphagia Symptom Questionnaire; eos/hpf, eosinophils per high-power field; EREFS, Endoscopic Reference Score; HSS, Histologic Scoring System; PEC, peak intraepithelial esophageal eosinophil count; qw, once weekly; SD, standard deviation.

Table. Co-primary and secondary endpoints at Week 24, stratified by baseline disease duration.

Conclusion: Dupilumab 300 mg qw demonstrated notable histologic response and substantial symptomatic and endoscopic improvements in adults and adolescents with EoE through 52 weeks. These results show that dupilumab 300 mg qw is an effective long-term treatment for patients with EoE, regardless of disease duration at baseline.

Disclosure: NG: Allakos, AstraZeneca, BMS, Regeneron Pharmaceuticals Inc., Exact Sciences, Sanofi, Takeda – consulting fees. Regeneron Pharmaceuticals Inc., Sanofi, Takeda – speaker bureau fees.

CSc: Adare Pharmaceuticals Inc., AstraZeneca, Calypso, Dr. Falk Pharma, EsoCap GmbH, Regeneron Pharmaceuticals Inc. – consulting fees
CSa: AstraZeneca, Doctaforum Medical Marketing S.L., Farma de Colombia SAS, Isomed Pharma S.L., Laborie/MMS, Medtronic Covidien AG, Menarini Consumer Healthcare – consulting fees. Adare Pharmaceuticals Inc., AstraZeneca, Celldex Therapeutics, Dr. Falk Pharma GmbH, EsoCap Biotech, International Marketing & Communication, Regeneron Pharmaceuticals Inc., S.A. – research funding.

KP: AGA, Alladapt, Allakos, AstraZeneca, BMS, Ellodi, Invea, Lucid, Nexstone, Peerview, Regeneron, Takeda, WebMD – consulting fees. Adare, Allakos, AstraZeneca, Celldex, Ellodi, Regeneron Pharmaceuticals Inc.-Sanofi, Revolo – research fees. AGA, Allakos, PeerView, Regeneron Pharmaceuticals Inc., Takeda, WebMD – speaker fees. Allakos, Chobani – grant support. Nexeos Bio – stock and options.

CX, BR, AR: Regeneron Pharmaceuticals Inc. – employees and shareholders.

TP, JAJ-N: Sanofi – employees, may hold stock and/or stock options in the company.

MP488

CENDAKIMAB ADMINISTRATION IMPROVES ESOPHAGEAL GENE EXPRESSION IN EOSINOPHILIC ESOPHAGITIS IRRESPECTIVE OF ENDOSCOPIC RESPONSE

J.M. Caldwell¹, A.Y. Ballaban¹, J. Li², R. Maddux², S. Harris², E.S. Dellon³, M.E. Rothenberg¹

¹Division of Allergy and Immunology, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, United States of America, ²Bristol Myers Squibb, Princeton, NJ, United States of America, ³Center for Esophageal Diseases and Swallowing, Division of Gastroenterology and Hepatology, Department of Medicine, University of North Carolina, Chapel Hill, NC, United States of America

Contact E-Mail Address: sarah.harris@bms.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic, progressive Type 2 inflammatory disease characterized by esophageal dysfunction and eosinophilic inflammation. Interleukin (IL)-13 is a key mediator in the pathogenesis of EoE. Cendakimab, a humanized monoclonal anti-IL-13 antibody, lowered esophageal eosinophil counts and improved dysphagia, histologic and endoscopic measures of inflammation, and fibrosis in a phase 2 trial of patients with EoE regardless of steroid response. Previous studies have shown that cendakimab reversed the expression of genes and molecular pathways involved in EoE pathogenesis vs placebo, including genes involved in IL-13 signaling, remodeling, and epithelial differentiation. Transcript changes correlated with histological and endoscopic findings.

In this substudy, we performed a detailed analysis of the relationship between endoscopic responder populations and changes in tissue transcript expression.

Aims & Methods: In a double-blind, placebo-controlled phase 2 trial (NCT02098473), patients with EoE received cendakimab 180 mg or 360 mg once weekly or placebo. This substudy evaluated the impact of systemic cendakimab treatment on local esophageal gene expression, as well as correlations between gene expression and endoscopic outcomes (endoscopic reference score [EREFS] range, 0–18). EoE-related transcripts were quantified in biopsies collected at baseline and at week 16.

Results: *POSTN* ($r=0.43$; $P<0.0001$) and *ALOX15* ($r=0.43$; $P<0.0001$) showed the strongest correlation with total EREFS across placebo and cendakimab groups. Endoscopic responders on cendakimab (post-treatment EREFS <2) exhibited improved expression of 33 genes vs baseline. Interestingly, endoscopic nonresponders showed improvement in the same 33 genes plus 6 additional genes (*ALOX12*, *GRPEL2*, *UPK1A*, *SPINK7*, *FAM25A*, *SPRR2D*).

Patients with endoscopic improvement (post-treatment EREFS decrease ≥ 4) showed normalization in a subset of genes ($n=15$, including *TPSB2*/*TPSAB1*, *CPA3*, and *TGFB1*) that did not reverse in patients showing less EREFS improvement. However, patients with less EREFS improvement (post-treatment EREFS decrease <4) showed corrected expression of 2 key epithelial genes, *SPINK7* and *UPK1A*, that did not reverse in patients with endoscopic improvement.

Conclusion: Molecular analysis of biopsies from patients with EoE demonstrates that after 16 weeks of treatment with cendakimab, endoscopic responders and nonresponders both show improvement in gene expression. Heterogeneous changes in inflammatory-, mast cell-, and epithelial-related genes may impact endoscopic findings. These findings indicate that cendakimab broadly modifies molecular biomarkers even in patients who do not show early endoscopic improvement, raising the possibility that biomarker improvement may precede endoscopic changes in some patients.

Disclosure: JMC, AYB, and MER have no relationship/activities/interests to disclose. JL, SH, and RM are employees at Bristol Myers Squibb. ESD served as a consultant for Abbott, Abbvie, Adare/Ellodi, Aimmune, Akeso-bio, Alfasigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, Astra-Zeneca, Avir, Biorasi, Calypso, Celgene/Receptos/ Bristol Myers Squibb, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GlaxoSmith-Kline, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Roberts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio, received research funding from Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/ Bristol Myers Squibb, Regeneron, Revolo, Shire/Takeda, and received educational grant from Allakos, Aqilion, Holoclara, and Invea.

MP489

BUDESONIDE ORODISPERSIBLE TABLETS EFFECTIVELY INDUCE CLINICO-HISTOLOGICAL REMISSION IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS PREVIOUSLY TREATED WITH SWALLOWED TOPICAL CORTICOSTEROIDS

P. Schreiner¹, A.M. Schoepfer², A. Straumann³, L. Biedermann³, A.J. Lucendo⁴, S. Miehlke⁵, M. Kernbauer-Hoelzl⁶, R. Mueller⁷

¹Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology, Vienna, Austria, ²Lausanne University Hospital, Gastroenterology And Hepatology, Lausanne, Switzerland, ³USZ Zürich, Gastroenterology & Hepatology, Zürich, Switzerland, ⁴Hospital General de Tomelloso, Dept. de Gastroenterology, Madrid, Spain, ⁵Facharztzentrum Eppendorf, CED-Schwerpunkt, Magen-Darm-Zentrumpraxis,, University professor of internal medicine, Hamburg, Germany, ⁶Dr. Falk Pharma Österreich, Department of Medical Affairs, Vienna, Austria, ⁷Dr. Falk Pharma GmbH, Clinical Research & Development, Freiburg, Germany

Contact E-Mail Address: philipp.schreiner@meduniwien.ac.at

Introduction: Budesonide orodispersible tablets (BOT) effectively induce and maintain clinical and histological remission in patients with eosinophilic esophagitis (EoE) (1, 2). A substantial fraction of patients recruited for the BUL-1 and BUL-2 studies had previously been treated with swallowed topical corticosteroids (STC) other than BOT. This *post-hoc* analysis aims to assess whether BOT was equally effective in adult EoE patients with and without prior use of STC (3).

Aims & Methods: This retrospective *post-hoc* analysis pooled 59 patients from the double-blind study phase of the BOT induction study (BUL-1) and 181 patients from the open-label induction phase of the BOT maintenance study (BUL-2). Patients were either STC-naïve ($n=103$) or had prior STC ($n=118$); for 19 patients previous treatment with STC was unknown. All patients received 1 mg BOT two times daily (BID) for 6 weeks. The primary efficacy end point was the rate of patients with clinico-histologic remission (≤ 2 points on numerical rating scales [0–10] each for dysphagia and odynophagia on each of the last 7 days prior to the end of treatment [EoT], and peak eosinophil count <16 eos/mm² hpf [corresponding to <5 eos/hpf]) at week 6/EoT.

Results: BOT showed similar efficacy in patients both with and without prior STC treatment. Clinico-pathologic remission was recorded for 67.8% ($n=67$) of patients with prior STC treatment and 65% ($n=80$) of patients with no prior STC (table 1).

Prior STC-treatment	Number (%) of patients achieving clinico-histological remission at week 6/EoT; [total number]		
	BUL-1 (1 mg BID)	BUL-2 (1 mg BID)	Overall
Unknown	2 (66.7) [n=3]	11 (68.8) [n=16]	13 (68.4) [n=19]
No	9 (52.9) [n=17]	58 (67.4) [n=86]	67 (65.0) [n=103]
Yes	23 (59.0) [n=39]	57 (72.2) [n=79]	80 (67.8) [n=118]

Conclusion: This *post-hoc* analysis of the BUL-1 and BUL-2 study program demonstrates that pre-treatment with STC other than BOT does not reduce the likelihood of achieving clinico-histological remission by treatment with BOT.

One explanation for successful induction of remission despite prior STC treatment is that initial relapse on STC may be due to insufficient delivery of STC to the esophageal mucosa, and/or insufficient equivalent dose of alternative topical steroid compound, rather than patients becoming truly corticosteroid-refractory. In addition, the specialized formulation of BOT that delivers budesonide precisely to the esophageal mucosa may also improve adherence, owing to a more standardized and convenient method of administration.

References: 1. Lucendo AJ, Miehke S, Schlag C, Vieth M, von Arnim U, Molina-Infante J, et al. Efficacy of Budesonide Orodispersible Tablets as Induction Therapy for Eosinophilic Esophagitis in a Randomized Placebo-Controlled Trial. *Gastroenterology*. 2019;157(1):74-86 e15.
2. Straumann A, Lucendo AJ, Miehke S, Vieth M, Schlag C, Biedermann L, et al. Budesonide Orodispersible Tablets Maintain Remission in a Randomized, Placebo-Controlled Trial of Patients With Eosinophilic Esophagitis. *Gastroenterology*. 2020;159(5):1672-85 e5.
3. Miehke S, Hruz P, Vieth M, Bussmann C, von Arnim U, Bajbouj M, et al. A randomised, double-blind trial comparing budesonide formulations and dosages for short-term treatment of eosinophilic oesophagitis. *Gut*. 2016;65(3):390-9.

Disclosure: Philipp Schreiner reports fees for consulting/advisory board from AbbVie, BMS, Dr. Falk Pharma, Janssen, Pfizer, Takeda, Galapagos and Sanofi. Alfredo J Lucendo has received research funding from Dr Falk Pharma; Stephan Miehke is a member of advisory boards for Celgene and EsoCap and has received speaker's fee from Dr Falk Pharma GmbH and Falk Foundation. Ralph Mueller and Markus Kernbauer-Hölzl are employees of Dr Falk Pharma GmbH; Alain Schoepfer is a member of an advisory board for Dr Falk Pharma GmbH, Adare Pharmaceuticals, Celgene Pharmaceuticals, and Regeneron Pharmaceuticals. He has received research funding from Dr Falk Pharma GmbH, Adare Pharmaceuticals, Celgene Pharmaceuticals, and Regeneron Pharmaceuticals. He has received speaker's fees from Dr Falk Pharma GmbH and Celgene Pharmaceuticals; Alex Straumann is a consultant of Calypso, EsoCap, Dr Falk Pharma GmbH, GSK, Receptos-Celgene, Regeneron-Sanofi, Shire and Tillotts, and has received speaker fees and research funding from Dr Falk Pharma GmbH. Luc Biedermann reports fees for consulting/advisory board from AbbVie, Amgen, BMS, MSD, Vifor, Dr. Falk Pharma, EsoCap, Janssen, Calypso, Ferring, Pfizer, Takeda, Janssen, and Sanofi.

MP490

DUPILUMAB LED TO RAPID AND SUSTAINED IMPROVEMENT IN DYSPHAGIA IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS AFTER SWITCHING FROM PLACEBO: RESULTS FROM PART C OF THE LIBERTY EOE TREET STUDY

E.S. Dellon¹, M. Chehade², A.J. Bredenoord³, J.M. Spergel⁴, C. Xia⁵, S.T. Tilton⁶, E. McCann⁵, T. Pela⁶, B. Raphael⁵, J. Jacob-Nara⁶, A. Radwan⁵

¹University of North Carolina School of Medicine, Chapel Hill, United States of America, ²Mount Sinai Center For Eosinophilic Disorders, Icahn School Of Medicine, New York, United States of America, ³Amsterdam University Medical Center, Amsterdam, Netherlands, ⁴Perelman School of Medicine at University of Pennsylvania School of Medicine, Department of Pediatrics, Philadelphia, United States of America, ⁵Regeneron Pharmaceuticals Inc., Tarrytown, United States of America, ⁶Sanofi, Bridgewater, United States of America

Contact E-Mail Address: mirna.chehade@mssm.edu

Introduction: Eosinophilic esophagitis (EoE) is a chronic type 2 inflammatory disease with increasing incidence and prevalence. Patients with EoE usually present with symptoms of dysphagia that impact their quality of life. In the 3-part, Phase 3 LIBERTY EoE TREET study (NCT03633617), dupilumab improved histologic, symptomatic, and endoscopic aspects of EoE up to 52 weeks.

Aims & Methods: The aim of this analysis was to assess the effect of dupilumab on symptoms of dysphagia in the 28-week extended treatment period of LIBERTY EoE TREET in patients who switched from placebo to dupilumab at 24 weeks. In Parts A and B, patients received dupilumab 300 mg or placebo weekly (qw) for 24 weeks. Patients who completed Parts A and B entered Part C - a 28-week extended treatment period in which all patients received dupilumab 300 mg qw; patients entering Part C remained blinded to their treatment in Parts A and B. Dysphagia Symptom Questionnaire (DSQ) score and number of days with dysphagia (assessed using the DSQ) were calculated over a 14-day period. Percent change in DSQ score and in number of days with dysphagia from Week 24 through Week 52 vs the Week 24 baseline were assessed for patients who switched from placebo to dupilumab 300 mg qw at Week 24 and or continued on dupilumab 300 mg.

Results: Mean (SD) DSQ score after 24 weeks of placebo was 24.7 (19.6) and 21.5 (18.4) in Parts A (n=37) and B (n=37), respectively. Significant improvements in DSQ score were observed within 4 weeks of the switch to dupilumab 300 mg qw (mean percent reduction: 31.5% and 29.9%). After 28 weeks (at Week 52), mean percent reduction in DSQ score was 63.6% and 59.7%. After 24 weeks of placebo, mean (SD) days with dysphagia was 6.6 (4.7) and 6.0 (4.7) in Parts A and B, respectively. At Week 52, there was a 63.2% and 46.8% mean reduction in the number of days with dysphagia.

Conclusion: In patients who initially received 24 weeks of placebo, weekly treatment with dupilumab 300 mg resulted in rapid (within 4 weeks) and sustained (up to 28 weeks) improvement in symptoms of dysphagia as assessed by the DSQ score. The magnitude of the improvement in dysphagia observed after switching from placebo to dupilumab was similar to that seen at 4 weeks in patients who originally initiated dupilumab in Parts A and B of the study.

Disclosure: Dellon ES. Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, AlfaSigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Dr. Falk Pharma, Eli Lilly, EsoCap, Eupraxia, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morpich, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio - consultant.

Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Shire/Takeda – research funding. Allakos, Aqilion, Holoclara, Invea – educational grants.

Chehade M. Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, BMS, Nexstone Immunology, Phathom, Recludix Pharma, Regeneron Pharmaceuticals Inc., Sanofi, and Shire/Takeda – consultant. Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, Celgene/BMS, Danone, Regeneron Pharmaceuticals Inc., and Shire/Takeda – research funding.

Bredenoord AJ. Alimentiv, Aqilion, AstraZeneca, Dr. Falk Pharma, Eupraxia, Laborie, Medtronic, Reckitt, Regeneron Pharmaceuticals Inc., and Sanofi – consultant. Dr Falk Pharma, Norgine, Nutricia, Sanofi, SST, Regeneron Pharmaceuticals Inc., and Thelial – research funding. Alimentiv, Aqilion, AstraZeneca, Dr Falk Pharma, Eupraxia, Laborie, Medtronic, Reckitt, Regeneron Pharmaceuticals Inc., and Sanofi – speaker fees.

Spergel JM. Allakos, DBV Technologies, Novartis, Regeneron Pharmaceuticals Inc., and Shire/Takeda – consultant. DBV Technologies and Regeneron Pharmaceuticals Inc. – research grant support.

Xia C, McCann E, Khodzhayev A, Radwan A. Regeneron Pharmaceuticals Inc. – employees and shareholders.

Tilton ST, Pela T, Jacob-Nara JA. Sanofi – employee, may hold stock and/or stock options in the company.

MP491

REAL-WORLD EVIDENCE OF THE EFFECTIVENESS AND SAFETY OF ORODISPERSIBLE BUDESONIDE FOR THE TREATMENT OF EOSINOPHILIC ESOPHAGITIS: A MULTICENTRE PROSPECTIVE STUDY EVALUATING THE INDUCTION PERIOD

D. Maniero¹, M. Ghisa¹, G. Lorenzon¹, G. Giorgini², E. Bendia², M. Coletta³, R. Penagini³, E. Vespa⁴, A. Barchi⁴, A. Mari⁵, N. de Bortoli⁶, E. Dilaghi⁷, B. Annibale⁷, P. Iovino⁸, M. Caminati⁹, S. Russo¹⁰, E.V. Savarino¹

¹University of Padova, Department of Surgery, Oncology and Gastroenterology, Padova, Italy, ²Ospedali Riuniti di Ancona, Digestive System Diseases, Digestive Endoscopy and Chronic Inflammatory Bowel Diseases, Ancona, Italy, ³IRCCS Ospedale San Raffaele, Milano, Italy, ⁴Vita Salute San Raffaele Hospital, Gastroenterology and Gastrointestinal Endoscopy, Modena, Italy, ⁵Nazareth Hospital EMMS, Gastroenterology Department, Nazareth, Israel, ⁶University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ⁷Digestive and Liver Disease Unit of Sant'Andrea Hospital-Sapienza University of Rome, Sapienza Univeristy of Rome, Department of Medical and Surgical Sciences and Translational Medicine, Scientific Disciplinary Area of Gastroenterology (MED/12), Rome, Italy, ⁸University of Salerno, Department Of Medicine, Surgery & Dentistry Scuola Medica Salernitana, Salerno (Sa), Italy, ⁹Azienda Ospedale Università di Verona, UOC Gastroenterology, Verona, Italy, ¹⁰Azienda Ospedaliero-Universitaria di Modena, UOC Gastroenterology, Modena, Italy

Contact E-Mail Address: dariamaniero@gmail.com

Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune antigen-mediated inflammatory disease, characterised by esophageal dysfunction and eosinophilic infiltration. The pharmacological treatments aim to achieve clinical, endoscopic and histological remission. Recently, a new budesonide orodispersible tablet (BOT) has become available, showing in the registration trials great efficacy compared to placebo in inducing clinical, endoscopic and histological disease remission. Only few real-life data are available in EoE setting.

Aims & Methods: This is a multicentre, prospective, observational study, aimed to evaluate in clinical practice (real-life setting) the safety profile and the clinical, endoscopic and histological effectiveness of BOT in EoE patients. Patients diagnosed with EoE, aged ≥ 18 years, treated with BOT 1mg bid as induction treatment for 12 weeks were enrolled. Clinical, demographic and medication data were collected at baseline. BOT treatment outcomes were evaluated after 12 weeks, considering EoE Endoscopic Reference Score (EREFS) for endoscopic appearance, and peak eosinophilic infiltration for histological assessment. Moreover, the Dysphagia Symptom Questionnaire (DSQ) and Health-Related Quality of Life (HRQoL) were also collected in order to evaluate clinical response.

Results: One-hundred and fifty-two patients (121 male; mean age 35) treated with BOT were enrolled, in 8 Italian Centres and 1 Israelian Centre. The most frequent symptoms at diagnosis were dysphagia (N=119, 78%) and food bolus impaction (N=106, 70%). Allergic comorbidities were present in 105 (69%) of patients. 129 patients were previously treated with PPI, with a positive histological response only in 42 (33%). After 12 weeks of treatment, endoscopic remission was achieved in 54% of patients, with a reduction of the mean EREFS score from 3.1±2 to 1.3±1.1 (p<0.0001). Histological remission was obtained in 91% of patients, with a mean peak of 33.3±29.9 of eosinophils/high power field (HPF) at the baseline vs 3.1±11.3 (p<0.0001). The DSQ shows a significant reduction from 20.3±23.5 vs 4.8±9.6 (p=0.001). HRQoL questionnaire score passed from 119.6±41.8 to 140±40.6 (p=0.02), which demonstrates an improvement in quality of life. Main data are resumed in Table 1. Side effects occurred in 22 out of 151 patients (15.6%), but only four of them needed to stop the treatment with BOT.

Study Population	N	%
Males	121/152	80
Symptoms		
Dysphagia	119/152	78
Food Bolus Impaction	106/152	70

EoE Features	N	Baseline	N	After Induction	p
EREFS Score (mean±SD)	144/152	3.1±2	114/152	1.3±1.1	<0.0001
Eosinophils/HPF (mean±SD)	142/152	33.3±29.9	109/152	3.1±11.3	<0.0001
DSQ (mean±SD)	53/152	20.3±23.5	52/152	4.8±9.6	0.001
HRQoL (mean±SD)	50/152	119.6±41.8	44/152	140±40.6	0.02

Conclusion: This study confirms the effectiveness of the treatment with BOT in the induction of EoE remission in a real-life setting, either considering clinical, endoscopic and histologic outcomes. Our data also showed a good safety profile, with a few patients requiring drug interruption. Further investigations are necessary to evaluate BOT effectiveness in the long-term period.

References: Miehke S et al.; International EOS-2 Study Group. Budesonide orodispersible tablets for induction of remission in patients with active eosinophilic oesophagitis: A 6-week open-label trial of the EOS-2 Programme. United European Gastroenterol J. 2022 Apr;10(3):330-343. doi: 10.1002/ueg2.12220.

Laserna-Mendieta EJ et al, EUREOS and EoE CONNECT research group: Swallowed topical corticosteroids for eosinophilic esophagitis: Utilization and real-world efficacy from the EoE CONNECT registry. United European Gastroenterol J. 2024 Jan 29. doi: 10.1002/ueg2.12533. Epub ahead of print. PMID: 38284792.

Disclosure: Prof. Savarino: Individual Scientific Consultant for Dr. Falk.

MP492

DUPILUMAB IMPROVES CAREGIVER-REPORTED EOSINOPHILIC ESOPHAGITIS SYMPTOMS IN CHILDREN AGED 1 TO <12 YEARS WITH EOE: 16-WEEK RESULTS FROM THE PHASE 3 EOE KIDS STUDY

M.E. Rothenberg¹, D. Ashok², S. Oliva³, C. Xia⁴, T. Pela⁵, S. Durrani⁴, J. Jacob-Nara⁵, A. Radwan⁴, S.T. Tilton⁵, R.B. Thomas⁴

¹Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati, United States of America, ²London Childrens Hospital, Pediatric Gastroenterology, London, Canada, ³Pediatric Gastroenterology and Liver Unit, Maternal and Child Health Department, Rome, Italy, ⁴Regeneron Pharmaceuticals Inc., Tarrytown, United States of America, ⁵Sanofi, Bridgewater, United States of America

Contact E-Mail Address: salvatore.oliva@uniroma1.it

Introduction: Eosinophilic esophagitis (EoE), a chronic, progressive, type 2 inflammatory disease. Dupilumab is a fully human monoclonal antibody that blocks interleukin (IL)-4 and IL-13, key drivers of type 2 inflammation.

Aims & Methods: The aim of this analysis was to assess the impact of dupilumab on caregiver-reported EoE symptoms in children aged 1 to <12 years with active EoE in the placebo-controlled Part A of the Phase 3 EoE KIDS trial (NCT04394351). This analysis was conducted in children randomized to dupilumab higher-exposure or placebo. The Pediatric Eosinophilic Esophagitis Symptom Score (PEESS) version 2.0 (caregiver version) comprises 20 items (items scored 0–4; higher scores indicate greater burden) assessing frequency (11 questions) and severity (9 questions) of symptoms and adaptive behaviors, containing 4 subdomains: dysphagia, nausea/vomiting, gastroesophageal reflux disease, and pain. PEESv2.0 was evaluated at baseline and Week 16 in EoE KIDS; total, frequency, severity, domain (all scored 0–100), and individual item scores were compared in patients treated with dupilumab higher-exposure or placebo. Reported p-values are nominal.

Results: Baseline characteristics were similar in dupilumab higher-exposure (n=37) and placebo (n=34) groups; baseline mean PEESv2.0 total scores were 38.0 and 38.3, respectively. At Week 16, PEESv2.0 total was reduced with dupilumab higher-exposure vs placebo (least squares [LS] mean change [95% confidence interval (CI)] -19.86 [-24.98, -14.74] vs -11.83 [-17.61, -6.05]; LS mean difference [95% CI] -8.03 [-15.39, -0.67], p<0.05). At Week 16, all domain subscores were at least numerically reduced with dupilumab higher-exposure vs placebo with nominal significance observed in LS mean scores for frequency (-22.47 vs -11.88 [p<0.01]), dysphagia (-23.38 vs -13.76 [p<0.05]), and nausea/vomiting (-29.08 vs -15.30 [p<0.05]) domains.

Conclusion: Dupilumab higher-exposure led to improvement in PEESv2.0 total score vs placebo at Week 16 in EoE KIDS. Frequency, dysphagia, and nausea/vomiting domains were improved with nominal significance, though all domains were improved numerically with dupilumab vs placebo.

Disclosure: Rothenberg ME: Allakos, AstraZeneca, BMS, Celldex, ClostraBio, EnZen Therapeutics, GSK, Guidepoint, Pfizer, PulmOne, Regeneron Pharmaceuticals Inc., Revolo Biotherapeutics, Sanofi, Santa Ana Bio, Serpin Pharma, Spoon Guru, and Uniquitybio – consultant; Allakos, Celldex, ClostraBio, EnZen Therapeutics, PulmOne, Santa Ana Bio, Serpin Pharma, Spoon Guru, and Uniquitybio – equity interest; Receives royalties from Mapi Research Trust (for PEESv2), Teva Pharmaceuticals (for reslizumab), and UpToDate; and is the inventor of patents owned by Cincinnati Children's Hospital.

Oliva S: Celgene/Receptos/BMS, Medtronic, Ocean Pharma, Sanofi/Regeneron – advisory board; Medtronic, Sanofi/Regeneron – speaker fees.

Ashok D: Sanofi – speaker fees.

Xia C, Durrani S, Radwan A, Thomas R: Regeneron Pharmaceuticals Inc. – employees and shareholders.

Pela T, Jacob-Nara J, Tilton ST: Sanofi – employee, may hold stock and/or stock options in the company.

MP493

EFFICACY AND SAFETY OF THE SELECTIVE SPHINGOSINE 1-PHOSPHATE RECEPTOR MODULATOR, ETASIMOD, IN ADULT PATIENTS WITH EOSINOPHILIC OESOPHAGITIS: PRIMARY RESULTS FROM THE PHASE 2 VOYAGE STUDY

E.S. Dellon¹, M.H. Collins², A.J. Bredenoord³, H. Philpott⁴, L. Biedermann⁵, M. Dulcine⁶, T. Nguyen-Cleary⁷, C. Su⁷, J. Yu⁷, F. Cataldi⁷, H. Zheng⁸, W. Wang⁷, J.C. Woolcott⁷, I. Hirano⁹

¹University of North Carolina School of Medicine, Center for Esophageal Diseases and Swallowing, and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, Chapel Hill, United States of America, ²Cincinnati Children's Hospital Medical Center, Division of Pathology and Laboratory Medicine, Cincinnati, United States of America, ³Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁴University of Adelaide, Northern Adelaide Local Health Network (NALHN), Department of Gastroenterology Lyell McEwin and Modbury Hospitals, Adelaide, Australia, ⁵University Hospital Zürich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ⁶Pfizer Brazil, São Paulo, Brazil, ⁷Pfizer Inc, Collegeville, United States of America, ⁸Pfizer Inc, New York, United States of America, ⁹Northwestern University, Kenneth C. Griffin Esophageal Center, Division of Gastroenterology and Hepatology, Feinberg School of Medicine, Chicago, United States of America

Contact E-Mail Address: luc.biedermann@usz.ch

Introduction: Etrasimod is an investigational, oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator in development to treat immune-mediated inflammatory disorders. Etrasimod regulates lymphocyte egress from secondary lymphatic organs and therefore may have promise in the immune cell mediated disease, eosinophilic oesophagitis (EoE).

Aims & Methods: This analysis aimed to investigate the efficacy and safety of oral etrasimod 1 and 2 mg QD vs placebo (PBO) in adults with active EoE. VOYAGE (NCT04682639) was a phase 2 study with a 24-week (wk) randomised, double-blind, PBO-controlled treatment period, followed by a 28-wk extension period. The primary efficacy endpoint was the percentage change from baseline (BL) (%CFB) in oesophageal peak eosinophil count (PEC) at Wk 16. Other efficacy endpoints assessed the effects of etrasimod on histological and endoscopic features and symptoms of EoE, and included proportion of patients (pts) who achieved PEC <15 and ≤6 eosinophils/high power field, absolute CFB in EoE-Histology Scoring System (EoE-HSS) grade and stage scores, EoE Endoscopic Reference Score (EREFS), Patient Global Impression of Severity (PGIS) and Dysphagia Symptom Questionnaire (DSQ; overall and by BL dilation history) at Wk 24. We present the findings from the double-blind treatment period.

Results: We randomised 108 pts with active EoE to etrasimod 2 mg QD (N=41), etrasimod 1 mg QD (N=39) or PBO (N=28); 47.2% of pts were female and BL average duration of EoE was 4.6 years, with 55.6% having a history of oesophageal dilation and 40.0% having prior corticosteroid treatment. Treatment with etrasimod 2 mg QD resulted in a 46.1% decrease from BL in PEC (PBO-adjusted) at Wk 16 (p=0.0103) and statistically significant reductions in %CFB in PEC at Wk 24, and reductions in absolute CFB in EoE-HSS grade and stage scores, EREFS, PGIS and, in pts without

BL dilation history, DSQ score (Table). In etrasimod 1 mg- vs PBO-treated pts, there were statistically significant reductions in %CFB in PEC and absolute CFB in EoE-HSS grade and stage scores at Wk 24. There were no serious treatment-emergent adverse events (TEAEs) reported up to Wk 24; 2 pts discontinued due to TEAEs (Table).

Visit/endpoint	Etrasimod 2 mg QD (N=41)			Etrasimod 1 mg QD (N=39)			PBO QD (N=28)	
	BL value, mean (SD)	CFB ^a	Difference from PBO, mean (SD) (p value)	BL value, mean (SD)	CFB ^a	Difference from PBO, mean (SD) (p value)	BL value, mean (SD)	CFB ^a
Wk 16								
PEC ^{c,e}	116.5 (82.6)	-38.3 (77.9)	-46.1 (p=0.0103)	106.3 (83.3)	40.3 (269.93)	32.5 (p=0.2861)	116.3 (71.9)	7.8 (87.77)
Proportion with PEC <15 eos/HPF, %		22.0			12.8			0.0
Proportion with PEC ≤6 eos/HPF, %		12.2			7.7			0.0
Wk 24								
PEC	116.5 (82.6)	-52.4 (59.66)	-113.7 (p<0.0001) -0.21	106.3 (83.3)	-27.4 (78.00)	-88.7 (p=0.0022) -0.19	116.3 (71.9)	61.3 (143.45)
EoE-HSS grade ^{d,e}	0.4 (0.18)	-0.2 (0.03)	(p<0.0001) -0.23	0.4 (0.19)	-0.1 (0.03)	(p<0.0001) -0.20	0.4 (0.16)	0.05 (0.03)
EoE-HSS stage ^{d,e}	0.4 (0.20)	-0.2 (0.03)	(p<0.0001) -0.91	0.4 (0.24)	-0.2 (0.03)	(p=0.0001) -0.61	0.4 (0.22)	0.03 (0.04)
EREFS ^{d,f}	3.7 (1.74)	-1.3 (0.26)	(p=0.0303) -0.48	3.2 (1.59)	-1.0 (0.26)	(p=0.1473) -0.28	4.3 (1.39)	-0.4 (0.32)
PGIS ^{d,g}	2.4 (0.6)	-0.7 (0.12)	(p=0.0121) 0.5	2.3 (0.5)	-0.5 (0.11)	(p=0.1312) -0.28	2.5 (0.6)	-0.2 (0.14)
DSQ	33.6 (12.9)	-18.6 (2.64)	-4.16 (p=0.3061)	32.0 (10.0)	15.7 (2.52)	-1.29 (p=0.7451)	32.7 (10.3)	-14.5 (3.08)
Overall ^h	34.9 (11.5)	-10.8 (4.40)	0.62 (p=0.8992)	31.6 (9.4)	-9.3 (4.22)	2.12 (p=0.6572)	37.8 (8.5)	-11.4 (5.10)
History of dilation = Yes	32.2 (14.5)	-21.6 (3.83)	-11.95 (p=0.0311)	32.5 (11.2)	-16.5 (3.82)	-6.84 (p=0.2014)	26.9 (9.2)	-9.6 (4.70)
History of dilation = No								
Proportion with PEC <15 eos/HPF, %		31.7			30.8			0.0
Proportion with PEC ≤6 eos/HPF, %		24.4			15.4			0.0
Summary of TEAEs up to Wk 24 in the VOYAGE study, n (%)ⁱ								
All causality TEAEs ^{j,k}		29 (70.7)			27 (69.2)			21 (75.0)
Serious TEAEs ^l		0 (0.0)			0 (0.0)			0 (0.0)
TEAEs leading to study treatment discontinuation		1 (2.4) ^m			0 (0.0)			1 (3.6) ⁿ
TEAEs occurring in ≥10% of pts ^o								
Nausea		6 (14.6)			3 (7.7)			3 (10.7)
Dizziness		4 (9.8)			4 (10.3)			1 (3.6)
COVID-19		3 (7.3)			4 (10.3)			5 (17.9)
Oesophageal food impaction		1 (2.4)			1 (2.6)			5 (17.9)
EoE		0 (0.0)			1 (2.6)			3 (10.7)
TEAEs leading to death		0 (0.0)			0 (0.0)			0 (0.0)

^a%CFB (mean [SD]) calculated for PEC, and absolute CFB (least squares mean [standard error]) calculated for EoE-HSS grade and stage, EREFS, PGIS and DSQ. All PBO-adjusted differences from PBO are expressed as least squares mean, except %CFB in PEC, which is expressed as the mean difference.

^bp values are from an analysis of covariance model for rank score of %CFB including factors for treatment group, BL history of oesophageal dilation (Yes/No), concurrent PPI therapy (Yes/No), and BL eosinophil PEC (eos/HPF) as a covariate.

^cFull analysis set, includes all randomised pts who received at least one dose of study treatment.

^dp values are from a linear mixed effects model for change from BL including factors for treatment group, visit, interaction of treatment-by-visit, BL history of oesophageal dilation (Yes/No), concurrent PPI therapy (Yes/No), and BL score as a covariate.

^eGrade and stage score ranges from 0–1.

^fScore ranges from 0–9.

^gScore ranges from 0–4.

^hScore ranges from 0–84.

ⁱSafety analysis set, includes all pts who were randomised and received at least one dose of study treatment.

^jSeverity was classified using CTCAE, version 5.0, ie, Grade 1 for mild, Grade 2 for moderate, Grade 3 for severe, Grade 4 for life-threatening and Grade 5 for death related to AE; most AEs were Grade 1 or 2.

^kFirst-dose, transient heart rate reductions and cardiac conduction aberrations are known on-target effects of sphingosine

1-phosphate receptor modulators. Bradycardia events were reported by 3 pts. One event occurred on Day 1 in a pt taking etrasimod 2 mg QD and was classed as Grade 2; one event occurred on Day 3 in a pt taking etrasimod 2 mg QD and was classed as Grade 1; one event occurred at the Wk-24 visit when the pt transitioned from PBO treatment to blinded etrasimod 1 or 2 mg QD (ie, Day 1 of etrasimod) and was classed as Grade 1. Two cases associated with the first etrasimod dose (asymptomatic with unremarkable electrocardiogram findings) resolved without any interventions at Hour 5 of the cardiac monitor procedure. The third case (without documented heart rate measurement) was associated with dizziness and nausea and was reported on Day 3. The pt continued study treatment and all AEs resolved without interventions on Day 23.

^lWhere seriousness was not entered/missing, the event was classified as serious.

^mBalance disorder, Grade 2.

ⁿDysphagia, Grade 2.

^oTEAEs occurred in ≥10% of pts in at least one treatment group.

%CFB, percentage change from baseline; AE, adverse event; BL, baseline; COVID-19, Coronavirus Disease 2019; CTCAE, Common Terminology Criteria for Adverse Events; DSQ, Dysphagia Symptom Questionnaire; EoE, eosinophilic oesophagitis; EoE-HSS, Eosinophilic Oesophagitis-Histology Scoring System; eos, eosinophils; EREFS, Eosinophilic Oesophagitis Endoscopic Reference Score; HPF, high power field; n, number of pts with event; N, number of pts in the treatment group; PBO, placebo; PEC, peak eosinophil count; PGIS, Patient Global Impression of Severity; PPI, proton pump inhibitor; pt, patient; QD, once-daily; SD, standard deviation; TEAE, treatment-emergent adverse event; Wk, Week.

Table. Change from BL (CFB) in PEC at Wk 16 (primary endpoint), additional efficacy endpoints at Wk 24 and a summary of TEAEs up to Wk 24 in the VOYAGE study.

Conclusion: Etrasimod 2 mg QD met the primary histologic endpoint and significantly improved endoscopic features of EoE, overall symptom severity and dysphagia (in pts without dilation history only) at Wk 24 and was well tolerated. This supports further evaluation of etrasimod in EoE.

Disclosure: ESD has received grant/research support from Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo and Shire/Takeda; has received consulting fees from Abbott, AbbVie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, EsoCap, Eupraxia, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, Lilly, LucidDx, Morphic, Nexstone Immunology, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE and Upstream Bio; and has received educational grants from Allakos, Holoclara and Invea. MHC has been a consultant for Alimentiv/Robarts, Allakos, Arena, BMS, EsoCap, Pfizer, Regeneron, Sanofi, Shire a Takeda company and AstraZeneca. AJB has received grant/research support from Nutricia, Norgine, Dr. Falk Pharma, Thelial, Sanofi/Regeneron and SST; lecture fees from Laborie, Medtronic, Dr. Falk Pharma, Reckitt, Aqilion, Eupraxia, Alimentiv, Sanofi/Regeneron and AstraZeneca; and has received consulting fees from Laborie, Medtronic, Dr. Falk Pharma, Reckitt, Aqilion, Eupraxia, Alimentiv, Sanofi/Regeneron and AstraZeneca. HP has received research grants from Hospital Research Foundation South Australia; is a speaker for Falk and GSK; and has received consulting fees from AusEE and Falk. LB has received consulting fees from AbbVie, Calypso, Esocap, Ewopharma, Falk, Ferring, Janssen, MSD, Pfizer Inc, Sanofi, Shire, Takeda and Vifor. MD, CS, JY, WW and JCW are employees and shareholders of Pfizer Inc. TNC and HZ were employees and shareholders of Pfizer Inc at the time the work was completed. FC was an employee of Arena Pharmaceuticals, San Diego, CA, USA; a wholly-owned subsidiary of Pfizer Inc, New York, NY, USA at the time of analysis. IH has received research/grants from NIH, Adare/Ellodi, Allakos, Arena, AstraZeneca, Meritage, Celgene/Receptos/BMS, Regeneron and Shire/Takeda; and consulting fees from Adare/Ellodi, Allakos, Amgen, Arena/Pfizer, Aslan, AstraZeneca, Celgene/Receptos/BMS, Celldex, EsoCap, Gossamer Bio, Nexstone Immunology, Parexel/Calyx, Phathom, Regeneron, Sanofi and Shire/Takeda.

Endoscopic resection for upper GI cancer

16:00-17:00 / Poster Stage 6

MP494

CANCER BURDEN CORRELATES WITH THE RISK OF RECURRENCE AFTER PIECEMEAL ENDOSCOPIC RESECTION OF EARLY-STAGE ADENOCARCINOMA IN BARRETT'S OESOPHAGUS

G. Hattersley¹, A.V Hadjinicolaou², A. Sorge³, D. Conceição⁴, S. Pan², V. Sujendran⁵, J. Ortiz-Fernández-Sordo⁶, M. di Pietro⁷
¹School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom, ²University Of Cambridge, Department Of Gastroenterology & MRC Cancer Unit, Cambridge, United Kingdom, ³Gent University Hospital, Gent, Belgium, ⁴Gastroenterologia ed Endoscopia digestiva, Milano, Italy, ⁵Portuguese Oncology Institute, Gastroenterology, Lisboa, Portugal, ⁶Cambridge Oesophago-Gastric Center, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, ⁷Nottingham University Hospitals Dept. of Gastroenterology, Digestive Dis. Biomedical Research, Nottingham, United Kingdom, ⁷University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom

Contact E-Mail Address: gjh49@cam.ac.uk

Introduction: Endoscopic resection (ER) is curative for Barrett's oesophagus-related early-stage oesophageal adenocarcinoma (EAC) without high-risk features, such as lymphovascular invasion (LVI), positive margins (R1), and deep submucosal invasion (T1b sm2-3). Piecemeal endoscopic mucosal resection (pEMR), often used for lesions larger than 15mm, prevents assessment of lateral margins and therefore complicates precise risk estimation for residual EAC at the first post-ER endoscopy. Thus, we investigated alternative clinical factors that could potentially be used to assess the risk for residual and recurrent EAC post-ER.

Aims & Methods: We performed a longitudinal cohort study of patients who underwent ER between 2006-2023. Inclusion criteria were: T1a or well/moderately differentiated T1b sm1 EAC; LVI-, and R0 resection. ER was categorised as pEMR (n=105) or en-bloc ER (n=22 en-bloc EMR, n=9 endoscopic submucosal dissection). The primary outcome was residual EAC at first post-ER endoscopy. Secondary outcomes were residual HGD at first post-ER endoscopy, recurrence of EAC and HGD at any post-ER endoscopy, and remission of EAC, HGD and intestinal metaplasia (IM) at latest endoscopy. Multivariate logistic regression, receiver operating characteristics, chi-squared, and Kaplan Meier analyses were performed to investigate possible associated risk factors.

	Univariate		Multivariate	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Age *	0.96 (0.90-1.01)	0.11	0.92 (0.87-0.99)	0.025
Sex, male *	0.96 (0.20-3.38)	0.95	0.40 (0.057-1.92)	0.30
High alcohol consumption (≥14 units weekly) *	0.65 (0.17-3.15)	0.55	0.44 (0.088-2.58)	0.32
Ever smoker *	1.93 (0.70-5.70)	0.21	2.09 (0.62-7.43)	0.24
Percentage of cancerous samples *†	1.25 (1.03-1.52)	0.026	1.32 (1.07-1.66)	0.013
Number of samples taken	1.11 (0.92-1.33)	0.25		
Differentiation *	1.19 (0.48-3.02)	0.71	1.05 (0.37-3.04)	0.93
Stage, T1b sm1 *	3.50 (0.44-22.79)	0.19	11.01 (1.01-106.05)	0.035

Table 1: logistic regression model for residual EAC at the first post-pEMR endoscopy

* : inclusion in multivariate analysis

† : odds ratio for a 10% increase in the percentage of cancerous samples

Bold indicates statistical significance.

Results: The cumulative incidence of recurrence of HGD was higher post-pEMR compared to en-bloc ER (HR = 2.43, 95% CI: 1.1-5.36; $p=0.021$), with residual EAC at first post-ER endoscopy accounting for 35% of such

post-pEMR recurrence. The percentage of pEMR specimens with EAC was an independent risk factor for residual EAC at first post-pEMR endoscopy ($p=0.013$, Table 1). A 53.5% cut-off of involved pEMR specimens was identified as the optimal threshold for residual EAC prediction (specificity=0.68, sensitivity=0.67, AUC=0.66). Indeed, rate of residual ($p=0.013$) and recurrent ($p=0.00041$) EAC were higher when EAC involvement was >50%. However, rates of remission of EAC ($p=0.13$), HGD ($p=0.20$) and IM ($p=0.81$) were unaffected by high EAC burden.

Conclusion: High burden of cancer in pEMR specimens correlates with increased risk of residual and recurrent EAC at post-pEMR endoscopy. Post-pEMR site check is recommended prior to endoscopic ablation, particularly in patients where more than 50% of pEMR specimens show EAC, where repeat ER should be performed in cases of flat subtle lesions. This will ensure eradication of any focus of residual disease and high success rates for treatment of early EAC using endotherapy.

Disclosure: Nothing to disclose.

MP495

WITHDRAWN

MP496

EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN ELDERLY PATIENTS WITH RELATIVE INDICATIONS OF EARLY ESOPHAGEAL SQUAMOUS CELL CARCINOMA

H. Yan¹, S. Wang¹, J. Yang^{1,2}

¹West China Hospital, Sichuan University, Chengdu, China, ²West China Hospital, Sichuan University, Chengdu, Christmas Island

Contact E-Mail Address: hailin_yan@163.com

Introduction: Endoscopic submucosal dissection (ESD) has been widely used to treat early esophageal squamous cell carcinoma (ESCC). Literature reported that the excellent 5-year survival rate of patients with early ESCC treated by ESD can reach more than 95%¹. However the premise of efficacy of ESD is that the esophageal lesions meet the indications of endoscopic therapy. Patients with absolute indications (AI) refer to those with tumor infiltrating into the epithelial layer (M1) or mucosal lamina propria layer (M2) or differentiation type of high grade intraepithelial neoplasia (HGIN), who have lower lymph node metastasis (LNM) rate than 5.6% and have excellent efficacy and safety of ESD². Patients with relative indications (RI) refer to those with tumor infiltrating into the mucosal muscle layer (M3) or submucosal superficial layer (SM1) but with no clinical evidence of LNM, who have significantly higher risk of LNM, about 8%-53%², and lack high-quality clinical evidence of the efficacy and safety of ESD.

After ESD, if the patients were at high risk of LNM, additional treatment including surgery, radiation or chemotherapy were recommended. However, some elderly patients often presented with multiple underlying ailments, experiencing organ decline that renders them unable to withstand surgical interventions. It's been reported that the overall survival rate of elderly patients with esophageal squamous after surgery is significantly lower than that of non-elderly patients³⁻⁴. There is lack of data reporting on the survival of elderly patients with RI who are at high risk of LNM after ESD.

Aims & Methods: Our target population is elderly patients with relative indications (RI) of endoscopic submucosal dissection (ESD) for esophageal squamous cell carcinoma (ESCC). They are limited on the performance of ESD and additional surgery after ESD because of severe complications and high mortality. We aim to investigate the efficacy, safety of ESD and benefits of additional surgery in these patients. We collected data of tar-

get population who received ESD in a tertiary hospital from January 2015 to March 2019. We divided them into elderly group (age $\geq$ 65 years, n=38) and non-elderly group (age<65 years, n=70).

Results: Two groups had no significant differences in the rates of bleeding (10.5% vs 12.9%, $P=0.517$), perforation (2.6% vs 2.9%, $P=0.938$), stenosis (31.6% vs 25.7%, $P=0.542$), en-bloc resection (94.9% vs 98.6%, $P=0.252$), R0 resection (61.5% vs 73.2%, $P=0.182$), recurrence (5.3% vs 2.9%, $P=0.088$) and metastasis (2.6% vs 2.9%, $P=0.938$). Kaplan-meier (K-M) analysis showed 5-year progression-free survival rate (5-PFS) (88.6% vs 92.4%, $P=0.755$) and 5-year overall survival rate (5-OS) (96.3% vs 94.9%, $P=0.613$) of elderly and non-elderly group. K-M analysis showed 5-OS of patients with and without additional surgery in elderly group (100% vs 94%, $P=0.724$) and non-elderly group (100% vs 95.8%, $P=0.451$). COX regression revealed tumor progression (including recurrence and metastasis) affected the survival of target population ($P=0.001$, HR=46.562 (4.839, 447.994)) independently. Univariate and multivariate analysis found positive horizontal margin(HM) affected tumor progression ($P=0.010$, HR=10.751(1.717, 67.334)) independently.

Conclusion: ESD showed excellent efficacy and safety in elderly patients with RI who didn't benefit significantly from additional surgery.

References:

1. Zhang YQ, Chen T, Zhang C, et al. Endoscopic Submucosal Dissection for Superficial Proximal Esophageal Neoplasia is Highly Successful. *Ann Surg* 2017;266:995–999.
2. Eguchi T, Nakanishi Y, Shimoda T, et al. Histopathological criteria for additional treatment after endoscopic mucosal resection for esophageal cancer: analysis of 464 surgically resected cases. *Mod Pathol* 2006;19:475–480.
3. Tapias LF, Muniappan A, Wright CD, et al. Short and long-term outcomes after esophagectomy for cancer in elderly patients. *The Annals of thoracic surgery* 2013;95:1741–1748.
4. Aoyama T, Hara K, Kazama K, et al. The Short- and Long-term Outcomes of Esophagectomy for Esophageal Cancer in Patients Older than 75 Years. *Anticancer Res.* 2020;40:1087–1093.

Disclosure: Nothing to disclose.

MP497

WITHDRAWN

MP498

THE USEFULNESS OF STEPWISE ESD TO PREVENT SEVERE STRICTURE AFTER ESD FOR CIRCUMFERENTIAL ESOPHAGEAL NEOPLASIA

I. Oyama¹, A. Takahashi¹

¹Saku Central Hospital Advanced Care Center, Endoscopy, Nagano, Japan

Contact E-Mail Address: oyama@coral.ocn.ne.jp

Introduction: Recently, ESD has become widespread, making it possible to safely remove large superficial esophageal cancers measuring 5 cm or more. However, severe stricture after circumferential ESD is a remaining major problem. Several treatment methods including local injection, oral administration of steroid, and stent insertion etc., have been reported. However, their effectiveness is insufficient.

We have reported the effectiveness of stepwise ESD to remove residual Barrett's mucosa to prevent metachronous cancer in UEGW2023. And, we expanded the indication of Stepwise ESD for circumferential SCC.

Aims & Methods: The aim of this study is to clarify the usefulness of Stepwise ESD for preventing severe stricture after ESD for circumferential esophageal neoplasias. Subjects were patients with circumferential

esophageal tumors, and underwent ESD at Saku Hospital from Jan. 2006 to Jan. 2024. Seventeen and fifty-one patients had adenocarcinoma (EAC) and Squamous cell carcinoma (SCC), respectively. The patients were divided into the En bloc (EB) group and the Stepwise (SW) group. In the EB group, a circumferential ESD was performed with or without triamcinolone injection. In the SW group, 2/3 of the circumference was resected in the first ESD, and 50–200 mg of TA was locally injected. And, the second ESD was performed 2–3 months later.

Results: Totally sixty-eight patients were enrolled into this study. 55 patients underwent en bloc resection and 13 patients underwent stepwise ESD. There was no significant difference in age, gender and location between two groups.

The mean diameters of the tumor, length of resected specimen and long axis mucosal defect in the EB and the first Stepwise ESD were 59 (30–130) and 50 (36–90) mm ($p=0.23$), 68 (29–150) and 71 (50–100) mm ($p=0.8264$), and 8 (5–15) and 8 (3–9) cm ($p=0.56$), respectively. There was no significant difference. And, the mean duration of ulcer healing in both groups were 137 (42–1028) and 46 (32–120) days ($p<0.0001$). The duration of ulcer healing was significantly shorter in SW group.

In the EB group, 47 of 55 patients developed severe stenosis and underwent EBD, whereas only 1 of 13 patients in the SW group required EBD. The median number of EBDs in both groups were 5 (0–33) and 0 (0–5), respectively (<0.0001).

Conclusion: The number of EBDs in the SW group was significantly less than that in the EB group. And, there were no severe complications. Therefore, stepwise ESD is an excellent treatment method that can prevent severe stenosis after endoscopic resection of circumferential esophageal neoplasia.

Disclosure: Nothing to disclose.

MP499

EFFICACY AND SAFETY OF COLD VS. HOT SNARE FOR GASTRIC POLYPECTOMY: A REAL-WORLD SINGLE-CENTER STUDY

L. Santos¹, A. Trigo¹, C. Borges Chaves¹, M. Cristiano¹, F. Lima¹, H. Ribeiro¹, M. Gravito-Soares^{1,2}, E. Gravito-Soares^{1,2}, D. Gomes^{1,2}, P. Figueiredo^{1,2}

¹Gastroenterology Department, Centro Hospitalar e Universitário de Coimbra, Unidade Local de Saúde de Coimbra, Coimbra, Portugal, ²Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Contact E-Mail Address: luispedroasantos@gmail.com

Introduction: Gastric polyps are detected in approximately 3–6% of patients undergoing routine upper endoscopy. The standard approach to managing most gastrointestinal polyps is through endoscopic polypectomy, although bleeding is a common adverse event. While cold snare polypectomy (CSP) has been reported as a safe alternative to hot snare polypectomy (HSP) for removing small colorectal polyps, further evidence is necessary to validate its effectiveness and safety specifically for gastric polyps.

Aims & Methods: Aim: Compare the efficacy and safety of CSP and HSP for removing small gastric polyps (5–15mm).

Materials and Methods: Cross-sectional study, with a prospective enrollment, including 330 consecutive gastric endoscopic polypectomies conducted in a tertiary center, between January 2021 and December 2023. Patients who underwent either CSP or HSP for gastric polyps ranging from 5 to 15 mm in size were enrolled, while those with underlying polyposis syndromes were excluded. Dedicated snares were utilized for CSP procedures. A 30-day phone survey was carried out to evaluate post-polypectomy adverse events. Statistical analysis was performed using the SPSS software v28.

Results: Overall, 330 gastric lesions in 218 patients were removed through snare polypectomy (CSP-165 lesions; HSP-165 lesions), mainly located in the body (51.5%). The median lesion size was 8.0 mm (IQR 4.0) and 8.0 mm (IQR 3.0) for CSP and HSP, respectively ($p=0.08$), ranging from 5 to 15 mm in both groups. The most common histological diagnoses were hyperplastic (58.2%) and fundic gland (29.4%) polyps. While the complete endoscopic resection rate was 100% in both groups, the *en-bloc* resection rate was slightly higher for CSP (CSP 98.2% vs. HSP 97.6%; $p=0.45$). At histological analysis, the complete (R0) resection rate was equal for both groups (CSP 98.2% vs. CSP 98.2%; $p=1.00$). Immediate bleeding, endoscopically treated, was more common with HSP (CSP 2.4% vs. HSP 3.6%; $p=0.52$). Delayed bleeding occurred exclusively in the HSP group (CSP 0.0% vs. HSP 1.2%; $p=0.16$). There were no perforations or procedure-related deaths. At univariate analysis, piecemeal resection (OR 64.6; 95%CI [3.5-1184.8]; $p=0.005$) was associated with a higher risk of delayed bleeding.

Conclusion: CSP demonstrates comparable effectiveness and potentially greater safety profile compared to HSP for gastric polypectomy. Consequently, CSP was non-inferior to HSP and may serve as an additional option for the removal of gastric polyps sized ≤ 15 mm. Piecemeal resection is a hypothetical risk factor for delayed post-polypectomy bleeding.

Disclosure: Nothing to disclose.

MP500

DEVELOPMENT AND VALIDATION OF A MODEL FOR PREDICTING ELECTROCOAGULATION SYNDROME AFTER ENDOSCOPIC FULL-THICKNESS RESECTION OF GASTRIC TUMORS

F. Liao¹, J. Liang¹, Y. Huang¹, J. Rong¹, Z. Zhu¹, X. Pan¹, C. Wang¹, S. Long¹, X. Zhou¹, G. Li¹, Z. Yin¹, Y. Chen¹, X. Shu¹

¹First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, China

Contact E-Mail Address: 459048754@qq.com

Introduction: Endoscopic full-thickness resection (EFTR) is a new endoscopic technique, which is mainly used to resect gastrointestinal tumors that are difficult to resect by conventional endoscopic resection methods¹. Post-endoscopic submucosal dissection electrocoagulation syndrome (PEECs) is one of the postoperative complications of endoscopic resection², but the incidence and risk factors of electrocoagulation syndrome after endoscopic full-thickness resection (EFTR) are still unclear. The aim of this research was to identify risk factors and develop a predictive nomogram for electrocoagulation syndrome after gastric EFTR.

Aims & Methods: Multivariate logistic regression was used to analyze the risk factors of electrocoagulation syndrome after gastric EFTR. A prediction nomogram was developed based on the above results, and bootstrap was employed for internal validation of the model.

Results: A total of 507 patients who underwent gastric EFTR were included, and the incidence of PEECs was 9.9%. Multivariate logistic regression showed that tumor size ≥ 10 mm, hot biopsy forceps for hemostasis, and operation time were independent risk factors of PEECs. A nomogram based on these risk factors showed good predictive ability, and the area under the ROC curve (AUC) was 0.769 (95% CI: 0.700-0.838). The calibration curve of the predictive model also demonstrated a good fit.

Conclusion: This study developed a predictive nomogram based on tumor size, hemostasis method, and operation time, which was used to identify high-risk patients with electrocoagulation syndrome after gastric EFTR.

References: 1. Dolan RD, Bazarbashi AN, McCarty TR, Thompson CC, Aihara H. Endoscopic full-thickness resection of colorectal lesions: a systematic review and meta-analysis. *Gastrointest Endosc.* 2022;95:216-24.e18. 2. Qiu J, Ouyang Q, Zhang Y, Xu J, Xie Y, Wei W, et al. Post-endoscopic sub-

mucosal dissection electrocoagulation syndrome: a clinical overview. *Expert review of gastroenterology & hepatology.* 2022;16:1079-87.

Disclosure: Nothing to disclose.

MP501

ESD FOR DUODENAL TUMORS – ESD VS. HYBRID ESD –

A. Takahashi¹, T. Oyama¹

¹Saku Central Hospital Advanced Care Center, Endoscopy, Nagano, Japan

Contact E-Mail Address: aurevoireurope@yahoo.co.jp

Introduction: ESD is an excellent endoscopic treatment with high en-bloc and R0 resection rate. However, duodenal ESD is technically difficult. And, it has been reported that the perforation rate of duodenal ESD is higher than that of ESD of other organs.

Hybrid ESD, which involves circumferential incision followed by removal of the lesion using a snare, may shorten the operation time, but detailed studies have not been conducted.

Aims & Methods: The aim of this study was to compare the treatment outcomes of ESD and hybrid ESD for duodenal tumors.

The subjects were superficial duodenal tumors that were resected at Saku Central Hospital from Dec.2002 to Dec. 2023, and diagnosed as grade 3 or 4 according to the Vienna classification.

ESD and Hybrid ESD were performed for 16 and 148 patients. Gender (Male/Female), age and location (1st, 2nd, 3rd) of both groups were 18/8, 106/42, 64 (39-84), 62 (37-84) and (4/18/4), 9/119/20, respectively. There was no significant difference.

Results: 1. Paris classification 0-I/IIa/IIb/IIc were 2/17/1/6 and 3/6/0/84, respectively.

2. En-bloc resection rate was 100% (26/26) and 89% (131/148), respectively ($p=0.07$). R0 resection rate was 100% (26/26) and 82% (121/148), respectively ($p=0.01$).

3. Size of tumor and specimen were 20 (5-63) / 9(2-27) and 28 (17-66) / 16 (8-34) mm, respectively ($P<0.001$, $P<0.001$).

4. Duration of procedure was 95 (34-265) and 30 (8-34), respectively ($P<0.001$).

5. Complications: Perforation, delayed perforation and delayed bleeding were 0% and 2.7% (4/148), 3.8% (1/26) and 2% (3/148), 0% and 0.7% (1/148), respectively. There was no significant difference.

6. Local recurrence rate was 0%, 0.7% (1/148), and the only local recurrent case was treated by HOT biopsy.

Hybrid ESD was useful for shortening treatment duration, however the R0 rate were significantly lower. Recently, under water EMR has been applied to the duodenal lesions, and it seems necessary to conduct a comparative study of hybrid ESD and under water EMR in the future.

Conclusion: ESD has excellent R0 resection rate, however it is technically difficult and has long treatment duration. On the other hand, hybrid ESD shortens treatment times but has lower R0 resection rates. Therefore, the indication of hybrid ESD is limited. Further examination including under water EMR should be performed.

References: None

Disclosure: Nothing to disclose.

FEASIBILITY OF EXTENDED GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE LESIONS WITH A NOVEL FLEXIBLE ENDOSCOPIC ROBOTIC PLATFORM

G. Carlino^{1,2,3}, P. Mascagni^{2,4}, P. Riva^{1,5}, G. Andrisani⁶, F. Barbaro², M. Pizzicannella⁷, H. Chung⁸, H. Inoue⁹, J. Marescaux¹, S. Perretta^{1,5,10}
¹IRCAD, University of Strasbourg, Institute for Research on Cancers of the Digestive Tract, Strasbourg Cedex, France, ²Policlinico Universitario Agostino Gemelli, Università Cattolica Del Sacro Cuore, Surgical Digestive Endoscopy, 00168, Italy, ³Università Cattolica del Sacro Cuore, Rome, Italy, ⁴Institut de Chirurgie Guidée par l'Image, Strasbourg, France, ⁵Nouvel Hôpital Civil, CHRU-Strasbourg, Department of General Surgery, Strasbourg, France, ⁶Università Campus Bio-Medico di Roma, Rome, Italy, ⁷Ospedale Cardinale G Panico, Endoscopy Unit, Tricase, Italy, ⁸Seoul National University, Seoul, South Korea, ⁹Showa University Koto Toyosu Hospital, Digestive Disease Center, Tokyo, Japan, ¹⁰IRCAD-IHU, Surgery, Strasbourg, France

Contact E-Mail Address: giorgio.carlino1996@gmail.com
Introduction: Endoscopic submucosal dissection (ESD) is the gold standard for superficial gastric cancer. Nonetheless, mastering ESD entails a steep learning curve requiring 30-50 procedures to achieve proficiency. An innovative robotic flexible endoscopic platform may have the potential to expedite the learning curve. The primary goal of this study was to compare a novel flexible endoscopic robotic platform (R-ESD) with conventional ESD (C-ESD) for safety and efficacy of removing large gastric lesions. The secondary aim was to compare beginners and expert performance.
Aims & Methods: A prospective comparative trial was conducted between R-ESD and C-ESD using large gastric lesions in an ex-vivo porcine model from November 2023 to January 2024. Four beginners (no or little endoscopic dissection experience) and four experts (> 500 ESD procedures) were assigned to perform 3 R-ESD and 3 C-ESD each during the study period. All were novices on the flexible robotic platform and underwent the same standardized one-day training. The main outcome measures were overall operative time, dissection speed, rates of en-bloc and curative resection (R0), and perforation. Secondary outcomes assessed the performance of beginners versus experts.

	Beginners	Expert	p
	R-ESD	C-ESD	
N	12	10	
Time (min)	57.8 (17.1)	52.6 (17.4)	0.489
Area (cm²)	42.1 (10.2)	42.9 (7.7)	0.840
Speed (cm²/min)	0.77 (0.20)	0.92 (0.43)	0.293
Perforation	0/12	0/10	1
Muscle Injury	0/12	0/10	1
R0 Dissection	12/12	10/10	1
En bloc Dissection	12/12	10/10	1

Table 1. Comparison between convention endoscopic submucosal dissection (ESD) performed by experts and robotic ESD performed by beginners. Data are reported as mean (standard deviation) value. A comparison was performed by a Two Sample T-Test. Data are reporting as mean (Standard deviation). Abbreviation: ESD=Endoscopic submucosal dissection; C-ESD=Conventional ESD; R-ESD= Robot-assisted ESD.

Results: In the study period forty-two 5x5cm lesions were resected- 22 R-ESD and 20 C-ESD. Overall the R-ESD and C-ESD groups had similar mean operative time (75.0 [SD 26.0] minutes versus 76.5 [36.3] minutes, respectively) and dissection speed (0.65 [0.21]cm²/min R-ESD versus 0.68 [0.48]cm²/min C-ESD; p=0.798). 100% of R-ESD were completed en-bloc

and with an R0 resection, while the C-ESD group had a 95% en-bloc and 85% R0 resection rate (p>0.05). The perforation rate in R-ESD was 0%, compared to 10% in C-ESD cases. While the disparity between experts and novices was notable for C-ESD, within the R-ESD cohort beginners demonstrated better operative times and dissection speeds, with rates of perforation, en-bloc and curative resection (R0) similar to experts, (Table 1).
Conclusion: Robotic ESD using a novel flexible endoscopic robotic platform proved to be safe, feasible, and equally effective as conventional ESD for managing large gastric lesions. The flexible endoscopic robotic platform empowered beginners to achieve safety and efficacy comparable to experts after just three procedures. This platform holds significant potential to democratize ESD, reducing variability among operators and expanding access to endoluminal organ-sparing therapies for patients.
Disclosure: Silvana Perretta is a member of EndoQuest’s Clinical Advisory Board
Jacques Marescaux is a member of Endoquest’s Scientific Advisory Board

IBD risk factors and outcomes

10:00-11:00 / Poster Stage 1

MP503

IDENTIFICATION OF SERUM METABOLITES AND LIPOPROTEINS PREDICTIVE OF RESPONSE TO INFLAMMATORY BOWEL DISEASE TREATMENT

P.J. Martínez¹, M. Baldán-Martín¹, R. Gil-Redondo⁴, I. Soletto¹, M. Orejudo¹, C. Ramírez¹, A.J. Lucendo⁶, C. Rodríguez⁷, A. Gutiérrez-Casbas¹, E. Martín-Arranz², L. Bujanda³, I. Rodríguez-Lago¹¹, R. De Francisco¹², E. Iglesias-Flores⁴, F. Bermejo⁵, M. Van Domselaar⁶, M.J. García⁷, L. Fernández-Salazar⁸, J. Barrio⁹, X. Calvet¹⁰, L. Torrealba²⁰, I. Bastón-Rey¹¹, H. Pallares Manrique²², Y. Ber Nieto²³, E. Leo-Carnerero²⁴, M.J. Casanova¹², O. Millet¹³, J.M. Mato¹³, M. Chaparro^{*12}, J. P. Gisbert^{*12}, *co-last authors

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Precision Medicine and Metabolism Lab, CIC bioGUNE, Derio, Spain, ³Hospital General de Tomelloso, Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), CIBERehd, Ciudad Real, Spain, ⁴Hospital Universitario de Navarra, Pamplona, Spain, ⁵Hospital General Universitario de Alicante, CIBERehd and Instituto Investigación Sanitaria y Biomédica de Alicante, Alicante, Spain, ⁶Hospital Universitario La Paz and Instituto de Investigación Sanitaria La Paz (IdiPaz), UAM, Madrid, Spain, ⁷Hospital Universitario Donostia and Instituto Biodonostia, Universidad del País Vasco (UPV/EHU), Donostia, Spain, ⁸Hospital Universitario de Galdakao, Biocruces Bizkaia HRI, Vizcaya, Spain, ⁹Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ¹⁰Hospital Universitario Reina Sofía, Córdoba, Spain, ¹¹Hospital Universitario de Fuenlabrada and IDIPAZ, Madrid, Spain, ¹²Hospital Universitario de Torrejón and Universidad Francisco de Vitoria, Madrid, Spain, ¹³Marqués de Valdecilla University Hospital and IDIVAL, Santander, Spain, ¹⁴Hospital Clínico de Valladolid, Valladolid, Spain, ¹⁵Hospital Universitario Río Hortega, Valladolid, Spain, ¹⁶Consorci Corporació Santitària Parc Taulí, CIBERehd, Sabadell, Spain, ¹⁷Hospital Universitario Dr. Josep Trueta, Girona, Spain, ¹⁸Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain, ¹⁹Hospital Juan Ramón Jiménez, Huelva, Spain, ²⁰Hospital San Jorge, Huesca, Spain, ²¹Hospital Universitario Virgen del Rocío, Sevilla, Spain

Contact E-Mail Address: paula_jmg@hotmail.com

Introduction: The therapeutic goal in inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is the control of the inflammatory process through drugs (biologic and JAK-inhibitor therapies) that generally have a high cost and may have side effects. Unfortunately, only one-third of patients respond to these treatments and there are no markers that accurately predict this response.

Aims & Methods: The aim of this study was to identify potential serum metabolic biomarkers predictive of response to different drugs for IBD at baseline (before treatment), which could facilitate the selection of the most appropriate therapy for each patient. For this purpose, a prospective

and multicenter study was conducted including CD and UC patients who initiate biologic (anti-TNF, ustekinumab or vedolizumab) or JAK-inhibitor (tofacitinib) therapies. Patients were assessed at 14 weeks to determine if they had achieved endoscopic response, based on the SES-CD and on the endoscopic sub score of the Partial Mayo Score. The analysis of the serum metabolome and deconvolution of the serum lipoprotein profile into 110 fractions were conducted using nuclear magnetic resonance for quantitative differential analysis comparing baseline serum samples of responders compared with non-responders.

Results: A total of 150 patients were included (30 CD anti-TNF, 30 UC anti-TNF, 30 CD ustekinumab, 30 UC vedolizumab, and 30 UC tofacitinib). Table 1 shows a summary of the most relevant results obtained during the metabolomic analysis, which revealed metabolites and lipoproteins (common or drug-specific) with significantly altered levels ($p < 0.05$) in the baseline serum samples of subsequent responders compared to non-responders. Moreover, based on ROC curves, potential biomarkers with good sensitivity and specificity for distinguishing between responders and non-responders before treatment were identified. Finally, our analysis identified alanine, aspartate, glutamate, arginine and butanoate metabolism, and the citrate cycle, as the main baseline altered metabolic pathways that could be associated with the response to IBD treatment.

Study group	Number of Biomarkers*		Best AUC values**
	Metabolites	Lipoproteins	
CD anti-TNF	2	3	0.83; 0.81; 0.78; 0.75; 0.74
UC anti-TNF	1	7	0.88; 0.84; 0.83; 0.77; 0.76; 0.73
CD ustekinumab	4	24	0.96; 0.95; 0.94; 0.91; 0.90; 0.89; 0.87; 0.80
UC vedolizumab	5	8	0.90; 0.79; 0.78
UC tofacitinib	3	8	0.98; 0.96; 0.91; 0.88; 0.87; 0.85

Table 1. Summary of identified potential metabolic biomarkers predictive of endoscopic response to IBD treatment.

*Biomarkers with significantly altered levels ($p < 0.05$) in the baseline serum of responders vs non-responders patients. **AUC corresponding to the biomarkers with the best sensitivity and specificity for distinguishing between responders and non-responders patients before treatment. AUC: Area Under the Curve calculated using the MetabolAnalyst software in univariate analysis; CD: Crohn's disease; IBD: Inflammatory bowel disease; UC: Ulcerative colitis.

Conclusion: The present study represents an effort towards personalized medicine in targeted therapy selection in IBD patients, which is an important unmet need. Although it needs further validation, we were able to identify a number of serum metabolites and lipoproteins with the potential of predicting response to biologic and JAK-inhibitor therapies.

Disclosure: Nothing to disclose.

MP504

THE SERUM IMMUNE PROFILE OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND SPONDYLOARTHRITIS

S. Veltkamp¹, F.A van Gaalen², J.N Samsom³,
A.E van der Meulen – de Jong¹, P. Voorneveld¹

¹Leiden University Medical Center (LUMC), Gastroenterology and Hepatology, Leiden, Netherlands, ²Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands, ³Erasmus University Medical Center - Sophia Children's Hospital, Lab of Pediatrics, div. Gastroenterol & Nutrition, on behalf of the Dutch TIMID consortium, Rotterdam, Netherlands

Contact E-Mail Address: s.h.c.veltkamp@lumc.nl

Introduction: Inflammatory bowel disease (IBD) is strongly associated with joint inflammation, as is highlighted by the high prevalence of spondyloarthritis (SpA) in patients with IBD (up to 13%) compared to the general population (0.2-1.6%) [1, 2].

IBD and SpA have many overlapping features, including genetic risk factors, changes in the gut microbiota, and therapies targeting TNF- α , IL-23, or JAK [3].

However, current therapies for both diseases are unable to break the cycle of chronic inflammation, and still a significant proportion of patients fail to respond. Disease heterogeneity likely plays a role in this [4, 5], underscoring the necessity to improve management and refine classification.

Aims & Methods: In this study, 92 inflammation-related proteins were quantified in serum of patients from one IBD and one SpA cohort using the novel Olink proteomics proximity extension assay. Fold changes (FC) in expression with $|\log_2 FC| > 0.5$ were considered meaningful, and false discovery rates (FDR) < 0.05 were considered significant. The IBD cohort existed of 255 IBD patients with (n=155) and without (n=100) self-reported joint complaints [8].

From the patients with joint complaints, 58 fulfilled any of the SpA criteria. The SpA cohort, or SPACE cohort, consisted of 169 patients with chronic back pain (≥ 3 months, ≤ 2 years) of unknown origin [9].

After 2 years of follow-up, 85 patients had proven axSpA. Serum samples were taken at baseline, and 167/169 samples from the SPACE cohort and 241/255 samples from the IBD cohort passed quality control and were included in the analysis.

Results: Thirty-four proteins were differentially expressed between 95 IBD patients without joint complaints and 85 proven axial SpA (axSpA) patients from the SPACE cohort, of which 14 were higher in IBD patients (including 4E-BP1, IFN- γ , TNF, FGF-21, CD8A, and CCL9), and 20 were higher in axSpA patients (including CASP-8, SIRT2, STAMBP, FGF-19, ST1A1, and EN-RAGE). In addition, the immune profile of IBD patients with joint complaints differed from IBD patients without joint complaints: 4E-BP1, CASP-8, STAMBP, SIRT2, AXIN1, and TNFSF14, were significantly upregulated in patients with joint complaints. Of note, if IBD patients without joint complaints were compared to the subgroup of 58 patients with joint complaints who met criteria for SpA, the same proteins showed significant upregulation, suggesting minimal difference between IBD patients with joint complaints who meet or who do not meet SpA criteria. Direct comparison of patients who met and who did not meet SpA criteria within the group of IBD patients with joint complaints indeed showed no noteworthy difference in serum immune profile. Within the SPACE cohort, comparison of patients with chronic back pain with and without axSpA diagnosis also showed no significant difference in serum protein expression.

Conclusion: This study shows that patients with axSpA versus patients with IBD without joint complaints have differing serum immune profiles. Within IBD patients with self-reported joint complaints and within patients with self-reported chronic back pain (from the SPACE cohort), no distinct difference in immune profile is observed, regardless of SpA diag-

nosis. The inflammation signatures of patients with chronic inflammatory diseases should be further investigated to provide insights for enhancing disease management in the future.

- References:** 1. Karreman, M.C., et al., *The Prevalence and Incidence of Axial and Peripheral Spondyloarthritis in Inflammatory Bowel Disease: A Systematic Review and Meta-analysis*. J Crohns Colitis, 2017. 11(5): p. 631-642.
2. Stolwijk, C., et al., *Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis*. Arthritis Care Res (Hoboken), 2016. 68(9): p. 1320-31.
3. Gracey, E., et al., *Revisiting the gut-joint axis: links between gut inflammation and spondyloarthritis*. Nat Rev Rheumatol, 2020. 16(8): p. 415-433.
4. van Unen, V., et al., *Mass Cytometry of the Human Mucosal Immune System Identifies Tissue- and Disease-Associated Immune Subsets*. Immunity, 2016. 44(5): p. 1227-39.
5. Gulino, G.R., M. Van Mechelen, and R. Lories, *Cellular and molecular diversity in spondyloarthritis*. Semin Immunol, 2021. 58: p. 101521.
6. van Erp, S.J., et al., *Classifying Back Pain and Peripheral Joint Complaints in Inflammatory Bowel Disease Patients: A Prospective Longitudinal Follow-up Study*. J Crohns Colitis, 2016. 10(2): p. 166-75.
7. Marques, M.L., et al., *Can rheumatologists unequivocally diagnose axial spondyloarthritis in patients with chronic back pain of less than 2 years duration? Primary outcome of the 2-year SPondyloArthritis Caught Early (SPACE) cohort*. Ann Rheum Dis, 2024. 83(5): p. 589-598.

Disclosure: FAG: grants from Stichting vrienden van Sole Mio and Stichting ASAS, grants and/or consulting fees from Abbvie, ASAS, BMS, Galapagos, Janssen, Lilly, Novartis, Pfizer, and UCB.

AEM: grants from Nestle, Norgine, Cablon, Galapagos, and ZonMW, ad boards/speaker fees from Tramedico, Janssen, Takeda, Galapagos, Vedanta, Ferring, AbbVie, and Dear Health.

PV: speaker fees from Takeda and Galapagos, advisory board: Takeda, Galapagos, Lilly, BMS, Janssen, and Abbvie.

MP505

AUTOIMMUNE THYROID DISORDERS ARE A RISK FACTOR FOR MICROSCOPIC COLITIS: A NATIONWIDE POPULATION-BASED MATCHED CASE-CONTROL STUDY

D. Bergman¹, X. Kang^{1,2}, J. Sun¹, F. Ebrahimi^{1,3}, J. Ludvigsson^{1,4,5}

¹Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, ²Yale School of Medicine, New Haven, United States of America, ³Clarunis University Center for Gastrointestinal and Liver Diseases, Department of Gastroenterology and Hepatology, BaselSwit, Switzerland, ⁴Orebro University Hospital, Pediatrics, Orebro Swe, Sweden, ⁵Columbia University College of Physicians and Surgeons, Department of Medicine, New York, United States of America

Contact E-Mail Address: david.bergman.1@ki.se

Introduction: Microscopic colitis (MC) is an inflammatory condition of the large intestine encompassing the subtypes lymphocytic colitis and collagenous colitis. MC has been linked to various autoimmune conditions, but reports on autoimmune thyroid disorders (AITD) have mostly been cross-sectional and none has included stratified results or corroborated the association with sensitivity analyses.

Aims & Methods: To examine the association of MC and its subtypes with prior diagnosis of AITD, a matched case-control study was performed using the nationwide ESPRESSO cohort in Sweden. Diagnosis of AITD was ascertained from either ICD-based records of Graves' disease or Hashimoto-specific prescribed drugs. All biopsy-confirmed MC patients diagnosed 2006-2017 were compared separately with regards to prevalent AITD to two groups: i) biopsy-free general population matched on birth year, sex

and county of residence at index year; and ii) biopsy-free full siblings to account for unmeasured confounders from common genetic risk and early environmental factors. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated via conditional logistic models stratifying on the matching variables or family groups and adjusting for education attainment, birth country, and history of celiac disease, inflammatory bowel disease, asthma, rheumatoid arthritis, psoriasis and type 1 diabetes. Sex difference in the association was tested via an “exposure × sex” interaction term. Separate analyses on MC subtypes and a sensitivity analysis of MC cases with at least 1-year follow-up before the index date (to minimize surveillance bias) were also carried out.

Results: A total of 10,448 MC cases and 49,935 controls were identified 2006-2017, among whom 1205 (11.5%) and 3791 (7.6%) were exposed to AITD, respectively. Compared to controls, MC patients were more frequently affected by at least one of the six other autoimmune comorbidities (8.3% vs 3.3%). As shown in Table 1, MC associated significantly with prevalent AITD at an OR of 1.60 (95% CI: 1.49-1.72) after adjusting for all covariates. This association appeared non-differential between collagenous colitis and lymphocytic colitis, and between males and females ($P_{\text{interaction}}=0.4$ for MC). When full siblings were compared to, the OR for MC association with AITD attenuated but remained statistically significant (OR: 1.22; 95% CI: 1.08-1.39). Sensitivity analyses also supported our main results.

	Population comparison			Sibling comparison
	MC	CC	LC	MC
Model 1	1.60 (1.49, 1.72)	1.63 (1.45, 1.84)	1.58 (1.45, 1.73)	1.64 (1.45, 1.85)
Model 2	1.60 (1.49, 1.72)	1.62 (1.43, 1.83)	1.59 (1.46, 1.74)	1.22 (1.08, 1.39)

Model 1 adjusted for only the matched or family group as stratum.

Model 2 further adjusted for birth country and education attainment in population analysis, and age, sex, index year as well as birth country and education attainment in sibling analysis, plus history of six autoimmune comorbidities in both analyses.

Abbreviations: CC, collagenous colitis; LC, lymphocytic colitis; MC, microscopic colitis.

Table 1. Odds ratios for the AITD-MC association.

Conclusion: Our findings corroborate the known association between MC and AITD and also support the notion that MC patients to a larger extent exhibit a predisposition towards autoimmune conditions. Our findings underscore the importance of investigating the underlying mechanisms of this association and emphasize the need for clinicians to consider MC in AITD patients presenting with diarrhoea.

Disclosure: Dr Ludvigsson has coordinated a study for the Swedish IBD quality register (SWIBREG). That study received funding from the Janssen Corporation. Dr Ludvigsson has also received financial support from MSD to develop a paper reviewing national healthcare registers in China, and has an ongoing study on celiac disease funded by Takeda. Dr Ebrahimi has served as an advisory board member for Boehringer Ingelheim.

This work was supported by the Karolinska Institutet (Ludvigsson), Stockholm County Council (Ludvigsson).

XK was supported by the Swedish Research Council (2022-00164).

JS was supported by the European Crohn's and Colitis Organization, the Stiftelsen Professor Nanna Svartz fond, and the Swedish Society for Medical Research.

FE was supported by the Swiss National Science Foundation (P500PM_210866).

None of the funding organisations has had any role in the design and conduct of the study, in the collection, management, and analysis of the data, or in the preparation, review, and approval of the manuscript.

MP506

GASTROINTESTINAL BACTERIAL INFECTIONS PRECEDE DISEASE ACTIVATION AND SIGNIFICANTLY INCREASE THE NEED FOR MEDICAL TREATMENT INTENSIFICATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

M. Kase¹, K. Vitikainen², C.-G. af Björkesten³, V.-J. Anttila⁴, L. Meriranta², P. Arkkila⁵, P. Molander⁶

¹University of Helsinki, Internal Medicine, Helsinki, Finland,

²University of Helsinki, Helsinki, Finland, ³Helsinki University Hospital, Abdominal Centre, Hus, Finland, ⁴University of Helsinki, Infectious Diseases, Helsinki, Finland, ⁵Helsinki University Hospital, Gastroenterology, Helsinki, Finland, ⁶Helsinki University Hospital, Peijas hospital, Helsinki, Finland

Contact E-Mail Address: merit.kase@hus.fi

Introduction: Enteric pathogens are a leading cause of diarrhea worldwide, even in high-income countries [1]. Moreover, patients with inflammatory bowel disease (IBD) are at an increased risk of infection [2,3] and gastrointestinal (GI) bacterial infections are commonly implicated as precipitants of IBD flares [4]. The diagnostic work-up therefore requires consideration of a wide variety of inflammatory or infectious diseases that mimic IBD.

Aims & Methods: Firstly, we aimed to evaluate in IBD patients factors that predispose to GI, secondly, factors that affect the severity of the GI infections and lead to hospitalization, and thirdly, how GI bacterial infections alter the activity of IBD further on.

This retrospective, observational, single-center, cohort study comprises 123 patients with ulcerative colitis (UC) or Crohn's disease (CD) with confirmed *Campylobacter* spp., *Yersinia* spp., *Salmonella* spp. or enterohemorrhagic *E. coli* (EHEC) infection, and their age and sex matched controls with IBD but without bacterial GI infection. We identified IBD patients with positive stool samples by performing a search combining the positive stool sample registry of the Hospital district of Helsinki and Uusimaa and the IBD registry of Helsinki University Hospital. Patient data from 1 January 2008 to 30 June 2023 was collected retrospectively from patient electronic charts.

Background factors, such as age, sex, IBD type and phenotype, previous surgical treatment, ongoing medication, previous IBD clinical activity, other comorbidities (based on Charlson Comorbidity Index [CCI]), smoking status, previous long-distance travelling, infectious symptoms, and need of medical consultations due to GI bacterial infection were evaluated. Follow-up data one to six months after the GI infection was analyzed. The results of the GI infection patients were compared with the controls.

Results: Out of 5194 IBD patients in the IBD registry, 123 patients were confirmed with *Campylobacter* spp., *Yersinia* spp., *Salmonella* spp. or EHEC infection. Of those with a GI bacterial infection, 64% (n=79) had UC and 36% (n=44) had CD. Patients with a GI bacterial infection diagnosis were more likely to have a flare and medication intensification in one to six months after the infection compared to the control group (37% vs 11%, p<0.001, and 37% vs 20%, p=0.006, respectively). Neither age, IBD phenotype, disease activity, CCI, IBD medication nor previous long-distance travelling to a lower hygiene country increased the risk of severe bacterial infection or the need hospital care.

Conclusion: IBD patients having GI bacterial infections are at a higher risk of experiencing an IBD flare and requiring an intensification in their IBD medication within one to six months after the infection. However, there is no significant association between different IBD medications or previous symptomatic IBD and the risk for hospitalization.

References: 1. Siciliano V, Nista EC, Rosà T, Brigida M, Franceschi F: Clinical Management of Infectious Diarrhea. *Rev Recent Clin Trials* 2020, 15(4):298-308.

2. Rahier JF, Magro F, Abreu C, Armuzzi A, Ben-Horin S, Chowers Y, Cotte M, de Ridder L, Doherty G, Ehehalt R *et al*: Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014, 8(6):443-468.

3. Kirchgessner J, Lemaitre M, Carrat F, Zureik M, Carbonnel F, Dray-Spira R: Risk of Serious and Opportunistic Infections Associated With Treatment of Inflammatory Bowel Diseases. *Gastroenterology* 2018, 155(2):337-346 e310.

4. Gecse KB, Vermeire S: Differential diagnosis of inflammatory bowel disease: imitations and complications. *Lancet Gastroenterol Hepatol* 2018, 3(9):644-653.

Disclosure: Nothing to disclose.

MP507

POPULATION-WIDE STUDY IDENTIFIES HLA-DRB1*01:03 AS A STRONG RISK FACTOR FOR SEVERE ULCERATIVE COLITIS DISEASE COURSE

M.V. Vestergaard^{*1}, K. Allin^{*1,2}, A.K. Nøhr^{*1}, J.V. Torresano Lominchar¹, H.S. Christensen¹, R.F. Brøndum¹, M. Bøgsted¹, H.B. Krarup³, K.R. Nielsen⁴, H.A. Jacobsen¹, L. Larsen^{**1,2}, A. Sazonovs^{**1}, T. Jess^{**1,2},
^{*}co-first authors ^{**}co-last authors
¹Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Aalborg University Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ²Aalborg University Hospital, Department of Gastroenterology & Hepatology, Aalborg, Denmark, ³Aalborg University Hospital, Molecular Diagnostics, Aalborg, Denmark, ⁴Zealand University Hospital, Department of Clinical Immunology, Roskilde, Denmark

Contact E-Mail Address: marievv@dcm.aau.dk

Introduction: We lack reliable biomarkers to identify patients with inflammatory bowel disease (IBD) at a greater risk of severe disease course. With emerging evidence that early step-down treatment in severe patients leads to better disease outcomes, alongside worries about overtreatment of mild patients, there is a clinical need to identify such biomarkers.

Aims & Methods: In this study, we explore genetic variants associated with severe disease course for ulcerative colitis (UC) in a nationwide cohort of 4491 patients from Denmark. We genotyped 4491 patients with UC (4153 from Danish birth blood spot archive; 338 from NorDIBD regional cohort), linking them with registry data capturing medical interactions throughout patients’ lifetimes. Patients who required 2+ IBD-related hospitalizations, 2+ IBD-related major surgeries, 1 IBD-related hospitalization and 1 IBD-related major surgery or use of systemic corticosteroids (≥5000 mg) in the first 3 years of diagnosis were defined as severe. We conducted a genome-wide association study comparing severe patients (N=1203) to those with a less severe disease course (N=3288).

Results: The GWAS identified a signal within the HLA region, with the HLA-DRB1*01:03 allele driving the association (OR=3.30 [2.23-4.87], P=2.08×10⁻⁹, UC carriage rate=2.8%). We did not observe an association with CD severity in a similarly ascertained cohort of 3688 individuals (P=0.79). Remarkably, carriage of DRB1*01:03 was associated with a seven-fold increase of major surgery risk (OR=7.05 [4.55-10.91], P=2.31×10⁻¹⁶) (Table 1). At the point of diagnosis, carriage of DRB1*01:03 was associated with higher CRP levels (β=2.68, P=1.70×10⁻⁷), f-cal levels (β=1.92, P=4.42×10⁻³) and a higher rate of hospitalization at diagnosis (OR=1.64, P=0.014), suggesting that the effect on severity is not limited to disease progression.

Outcome	N	OR [95% CI]	P-value
Main analysis	1203 vs. 3288	3.30 [2.23 - 4.87]	2.08E-09
≥5000 mg corticosteroids	821 vs. 3288	2.29 [1.42 - 3.69]	1.06E-03
≥2 hospitalizations	692 vs. 3288	5.16 [3.44 - 7.73]	1.72E-14
≥2 hospitalizations without major surgery	555 vs. 3288	5.93 [3.71 - 9.49]	2.28E-12
≥2 major surgeries	242 vs. 3288	7.24 [4.35 - 12.04]	1.49E-12
Major surgery	358 vs. 3266	7.05 [4.55 - 10.91]	2.31E-16
Intestinal resection	210 vs. 3266	7.42 [4.46 - 12.32]	2.33E-12
Enterostomy	151 vs. 3266	8.38 [4.67 - 15.03]	1.54E-10
Colectomy	338 vs. 3266	7.34 [4.73 - 11.40]	8.23E-17

Table 1: HLA-DRB1*01:03 has a consistent direction of effect and magnitude across different conditions that define patient severity; it is associated with multifaceted patient severity, rather than one particular factor entirely driving the association.

Conclusion: In this large-scale, unselected nationwide cohort study, we find that HLA-DRB1*01:03 is a biomarker of UC disease course that is associated with a more severe presentation at diagnosis, as well as higher subsequent risk of surgery and hospitalization. Demonstrating the association at a genome-wide significance level for the first time, this study revitalizes findings from smaller studies at the beginning of the genetic era which explicitly recruited severe patients and made estimating carriage effects difficult. While HLA-DRB1*01:03 is a low-frequency allele, patients who carry it are at a much higher risk of severe UC. As the cost of typing a single HLA allele is low (under 50 EUR) and several pharmacogenetic variants are beginning to be tested at diagnosis, we argue that it is a valuable addition to the arsenal of personalized healthcare tools.

Disclosure: Nothing to disclose.

INCIDENCE AND RISK FACTORS OF INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: LONGITUDINAL PROSPECTIVE INFEII REGISTRY OF GETECCU

Y. Zabana^{1,2}, I. Rodríguez-Lago³, B. Sicilia Aladrén⁴, R.M. de Francisco García⁵, M. Piqueras Cano⁶, M.L. De Castro Parga⁷, M. Chaparro^{8,2,9}, F. Gomollón^{2,10}, E. Domenech Morral^{2,11}, E. Sainz Arnau¹², L. Márquez-Mosquera¹³, A.J. Lucendo^{14,2}, O. García-Bosch¹⁵, X. Calvet Calvo^{16,2}, J. Gordillo¹⁷, D. Busquets Casals¹⁸, V.J. Morales Alvarado¹⁹, M. Rivero²⁰, J. Guardiola²¹, P. Navarro Cortés²², E. Iglesias-Flores²³, M. Iborra²⁴, R. Ferreira-Iglesias²⁵, F. Mesonero Gismero²⁶, E. Sesé²⁷, R. Vicente Lidón²⁸, R. Pajares²⁹, A. Algaba³⁰, O. Benítez¹, M. Aceituno^{1,2}, A. Rodríguez-Pescador³, L. Arias-García⁴, S. Riestra Menendez⁵, R. Mena⁶, L. Sanromán⁷, J. Gisbert^{31,2}, M.T. Arroyo-Villarino¹⁰, M. Mañosa Ciria^{32,2}, M. Teller¹², M.F. Murciano Gonzalo¹³, T. Angueira¹⁴, M. Esteve Comas^{1,2}, GETECCU

¹Hospital Universitari Mútua Terrassa, Department of Gastroenterology, IBD Unit, Terrassa, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain, ³Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ⁴H Universitario de Burgos, Gastroenterology, Burgos, Spain, ⁵Hospital Universitario Central de Asturias, Oviedo, Spain, ⁶Hospital Consorci Terrassa, Terrassa, Spain, ⁷Hospital Álvaro Cunqueiro-Complejo Hospitalario Universitario de Vigo, Gastroenterology, Vigo, Spain, ⁸Hospital Universitario de La Princesa, Gastroenterology Unit, Madrid, Spain, ⁹Instituto de Investigación Sanitaria Princesa (IIS-Princesa) and Universidad Autónoma de Madrid (UAM), Madrid, Spain, ¹⁰Hospital Clínico Universitario Lozano Blesa, Servicio de Aparato Digestivo, Zaragoza, Spain, ¹¹Hospital Germans Trias i pujol, Gastroenterology Unit, Badalona, Barcelona, Spain, ¹²Hospital Sant Joan De Déu - Althaia, MANRESA, Manresa, Spain, ¹³Servei de Digestiu-Hospital del Mar and Hospital del Mar Research Institute (IMIM), Barcelona, Spain, ¹⁴Hospital General de Tomelloso Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Dept. de Gastroenterology, Tomelloso, Spain, ¹⁵Hospital de Sant Joan Despí Moisès Broggi, Digestive Diseases Department, Sant Joan Despí, Spain, ¹⁶Hospital de Sabadell, Institut Universitari Parc Taulí, UAB, Unitat de Malalties Digestives, Barcelona, Spain, ¹⁷Hospital de la Santa Creu i Sant Pau, Gastroenterology Unit, Barcelona, Spain, ¹⁸H. DE GIRONA DR. J. TRUETA/ICO GERONA, Gastroenterology, Girona, Spain, ¹⁹Hospital General de Granollers, Gastroenterology/Endoscopy, Granollers, Spain, ²⁰Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain, ²¹Hospital Universitario de Bellvitge, IDIBELL and Universitat de Barcelona, Gastroenterology, L'Hospitalet de Llobregat (Barcelona), Spain, ²²Hospital Clínico de Valencia, Valencia, Spain, ²³Hospital Universitario Reina Sofía, Digestive, Córdoba, Spain, ²⁴La Fe University and Politecnical Hospital, Valencia, Spain, ²⁵University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²⁶Hospital Ramon y Cajal, Gastroenterology, Los Santos de la Humosa, Spain, ²⁷Hospital Arnau de Vilanova, Lleida, Spain, ²⁸H. U. MIGUEL SERVET, Zaragoza, Spain, ²⁹Hospital Infanta Sofía, Madrid, Spain, ³⁰Hospital Universitario de Fuenlabrada, Instituto de Investigación de La Paz (IdiPAZ), Fuenlabrada, Madrid, Spain, ³¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa, Digestive Services, Madrid, Spain, ³²Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain

Contact E-Mail Address: yzabana@gmail.com

Introduction: The true effect of having inflammatory bowel disease (IBD) in the development of infections has not been studied in depth since cohort studies are scarce and the results of studies are sometimes contradictory. Especially, this complication has not been addressed prospectively in an incident cohort of patients with IBD.

Aims & Methods: Aims: To assess, regarding infections in IBD: 1) incidence and type, 2) risk factors, 3) effect of type and the duration of IBD treatment, 4) impact in mortality 5) effect of IBD activity.

Methods: The INFEII registry (ClinicalTrials.gov: NCT02904590) is a prospective study promoted by GETECCU to determine the incidence and risk factors of infection in an inception cohort of patients with IBD and follow-up of at least 5 years. This longitudinal prospective study within the ENEIDA registry included incident cases with IBD. Patients were recruited between 2016 and 2020 with a planned follow-up of 5 years. All infections were detailed analysed. An infection was considered relevant when: 1) required hospital admission, 2) led to death or endangered the patient's life, 3) was treated with specific antibiotics, 4) occurred recurrently, and/or 5) required change/withdrawal of immunosuppressive treatment.

Results: The INFEII registry recruited 1456 patients from 28 centres throughout Spain. The median follow-up was 71 months (IQR 60-79 months). The description of the cohort is presented in Table 1. Of the 1456 patients, 580 (40%) presented at least one relevant infection. In total, 1321 infections were collected. One-hundred and seven infections (8%) required hospitalisation and four patients died (0.3%) over infection. Ninety-nine patients were lost to follow-up (22 died and 34 changed hospitals). The most prevalent infections were: ear-nose-throat in 238 cases, urinary tract infections in 237, respiratory in 234, COVID-19 in 133, skin infections in 127, dental in 64 and colitis/enteritis in 64. From the whole cohort and at some point, in time, 756 (52%) patients received 5ASA, 481 (33%) steroids (369 (25%) oral, 112 (7.7%) intravenous), 568 (39%) azathioprine, 72 (4.9%) methotrexate, 21 (1.4%) tofacitinib, 533 (37%) antiTNF, 141 (9.9%) ustekinumab and 77 (5.3%) vedolizumab. The effect of treatment and IBD activity in each infection is being analysed.

Variable (N%)	Total 1456	No infections 876	Any Infection 580	Univariate P
Gender (female)	668 (46)	378 (43)	290 (50)	0.01
Active smokers	314 (22)	177 (20)	137 (24)	0.09
Age at IBD diagnosis				
Mean (IQR)	42 (29-55)	42 (29-54)	41 (28-56)	0.74
>50 years	529 (36)	319 (36)	210 (36)	0.93
Unclassified colitis	27 (1.85)	20 (2.28)	7 (1.2)	0.14
Ulcerative colitis	781 (54)	484 (55)	297 (51)	0.14
Crohn's disease				
L1	648 (45)	372 (42)	276 (48)	
L2	280 (43)	153 (41)	127 (46)	
L3	122 (19)	77 (21)	45 (16)	
L4	235 (36)	133 (36)	102 (37)	0.29
	121 (19)	58 (16)	63 (23)	
Crohn's behaviour				
B1	486 (75)	284 (76)	202 (73)	0.34
B2	109 (17)	61 (16)	48 (17)	0.32
B3	61 (9)	33 (8.9)	28 (10)	0.32
perianal	123 (20)	65 (17)	58 (21)	0.28
History of severe infections (before IBD diagnosis)	36 (2.5)	13 (1.5)	23 (3.96)	0.004
Occupational risk	450 (31)	252 (29)	198 (34)	0.03
Comorbidity	256 (18)	143 (16)	113 (19)	0.12
Death (all causes)	22 (1.5)	11 (1.3)	11 (1.9)	0.33

Table 1. Clinical characteristics of patients included in the INFEII study.

Conclusion: Infections are frequent complications in patients with IBD, presented in 40% of them. Being a woman, having a history of past serious infections or occupational risk may be associated with infection

occurrence. It has to be determined if IBD activity and treatment pose a greater risk for infections. This paradigmatic study implies the first use of the ENEIDA registry in prospective research.

Disclosure: Nothing to disclose.

MP509

WITHDRAWN

MP510

LONG-TERM OUTCOMES OF NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS: RESULTS FROM THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

M. Chaparro¹, A. Garre¹, A. Núñez Ortiz², S. Rubio³, M.T. Diz-Lois Palomares⁴, S. Riestra⁵, H. Alonso-Galán⁶, E. Fernández-Salgado⁷, R. Ferreiro-Iglesias⁸, M. Vela⁹, Á. Ponferrada Díaz¹⁰, E. Sánchez Rodríguez¹¹, V. Hernández¹², L. Arias García¹³, J. Barrio¹⁴, J.M. Huguet¹⁵, D. Ginard¹⁶, M. Rivero¹⁷, I. Vera¹⁸, I. Alonso-Abreu¹⁹, J.M. Benítez²⁰, M. Aguas²¹, I. Rodríguez-Lago²², X. Calvet²³, L. Fernández-Salazar²⁴, A. Echarri²⁵, M.T. Arroyo²⁶, M. Navarro-Llavat²⁷, P. Vega²⁸, M. Sierra²⁹, E. Guerra del Río³⁰, R. Vicente³¹, M.J. Casanova¹, P. Navarro³², J. Ortiz de zarate³³, P. Varela Trastoy³⁴, K. Spicakova³⁵, A. Gutiérrez-Casbas³⁶, M.D. Martín-Arranz³⁷, C. Piñero³⁸, Á. Hernández-Martínez³⁹, E.A. Torrella Cortes⁴⁰, J.M. Marrero⁴¹, R. Lorente Poyatos⁴², L. Martí Romero⁴³, O. Bosch⁴⁴, J.M. Duque⁴⁵, M. Aceituno⁴⁶, H. Fernández⁴⁷, J.P. Gisbert¹, on behalf of the EpidemIBD group

¹Hospital Universitario de La Princesa, IIS-Princesa, UAM, and CIBEREHD, Gastroenterology Unit, Madrid, Spain, ²Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ³Hospital Universitario de Navarra, Gastroenterology Unit, Pamplona, Spain, ⁴Hospital Universitario A Coruña, Gastroenterology Unit, A Coruña, Spain, ⁵Hospital Universitario Central de Asturias and ISPA, Gastroenterology Unit, Oviedo, Spain, ⁶Hospital Universitario Donostia and Instituto Biogipuzkoa, Gastroenterology Unit, San Sebastián, Spain, ⁷Complejo Hospitalario Universitario de Pontevedra and Instituto de Investigación Sanitaria Galicia Sur, Gastroenterology Unit, Pontevedra, Spain, ⁸Complejo Hospitalario Universitario de Santiago and FIDIS, Gastroenterology Unit, Santiago de Compostela, Spain, ⁹Complejo Hospitalario Universitario Ntra. Sra. de Candelaria, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ¹⁰Hospital Universitario Infanta Leonor, Gastroenterology Unit, Madrid, Spain, ¹¹Hospital Ramón y Cajal, Gastroenterology Unit, Madrid, Spain, ¹²Hospital Álvaro Cunqueiro, Estrutura Organizativa de Xestión Integrada de Vigo, Gastroenterology Unit, Vigo, Spain, ¹³Hospital Universitario de Burgos, Gastroenterology Unit, Burgos, Spain, ¹⁴Hospital Universitario Río Hortega, Gastroenterology Unit, Valladolid, Spain, ¹⁵Consorcio Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ¹⁶Hospital Universitari Son Espases, Gastroenterology Unit, Palma de Mallorca, Spain, ¹⁷Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology Unit, Santander, Spain, ¹⁸Hospital Universitario Puerta de Hierro Majadahonda, Gastroenterology Unit, Madrid, Spain, ¹⁹Hospital Universitario de Canarias (H.U.C.), Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ²⁰Hospital Universitario Reina Sofía and IMIBIC, Gastroenterology Unit, Córdoba, Spain, ²¹Hospital Universitari i Politecnec La Fe, Gastroenterology Unit, Valencia, Spain, ²²Hospital

de Galdakao-Usansolo, Gastroenterology Unit, Galdakao, Spain, ²³Hospital de Sabadell, Institut Universitari Parc Taulí, Universitat Autònoma de Barcelona and CIBEREHD, Gastroenterology Unit, Sabadell, Spain, ²⁴Hospital Clínico Universitario de Valladolid, Gastroenterology Unit, Valladolid, Spain, ²⁵Complejo Hospitalario Universitario de Ferrol, Gastroenterology Unit, Ferrol, Spain, ²⁶Hospital Clínico Universitario Lozano Blesa, IIS Aragón and CIBEREHD, Gastroenterology Unit, Zaragoza, Spain, ²⁷Hospital de Sant Joan Despí Moisès Broggi, Gastroenterology Unit, Barcelona, Spain, ²⁸Complejo Hospitalario Universitario de Ourense, Gastroenterology Unit, Ourense, Spain, ²⁹Complejo Asistencial Universitario de León, Gastroenterology Unit, León, Spain, ³⁰Hospital Universitario de Gran Canaria Dr. Negrín, Gastroenterology Unit, Las Palmas de Gran Canaria, Spain, ³¹Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain, ³²Hospital Clínico Universitario de Valencia and Universitat de València, Gastroenterology Unit, Valencia, Spain, ³³Hospital Universitario de Basurto, Gastroenterology Unit, Basurto, Spain, ³⁴Hospital de Cabueñes, Gastroenterology Unit, Gijón, Spain, ³⁵Hospital Universitario de Araba (sede Txagorritxu y sede Santiago), Gastroenterology Unit, Vitoria, Spain, ³⁶Hospital General Universitario de Alicante and CIBEREHD, Gastroenterology Unit, Alicante, Spain, ³⁷Hospital Universitario La Paz, Universidad Autónoma de Madrid and IdiPAZ, Gastroenterology Unit, Madrid, Spain, ³⁸Hospital Universitario de Salamanca, Gastroenterology Unit, Salamanca, Spain, ³⁹Complejo Hospitalario de Especialidades Torrecárdenas, Gastroenterology Unit, Almería, Spain, ⁴⁰Hospital General Universitario J.M. Morales Meseguer, Gastroenterology Unit, Murcia, Spain, ⁴¹Hospital Universitario Insular de Gran Canaria, Gastroenterology Unit, Las Palmas de Gran Canaria, Spain, ⁴²Hospital General Universitario de Ciudad Real, Gastroenterology Unit, Ciudad real, Spain, ⁴³Hospital Francisc De Borja, Gastroenterology Unit, Gandía, Spain, ⁴⁴Hospital Universitario Fundación Jiménez Díaz, Gastroenterology Unit, Madrid, Spain, ⁴⁵Hospital San Agustín, Gastroenterology Unit, Avilés, Spain, ⁴⁶Hospital Universitari Mutua Terrasa and CIBEREHD, Gastroenterology Unit, Terrasa, Spain, ⁴⁷Hospital San Pedro, Gastroenterology Unit, Logroño, Spain

Contact E-Mail Address: mariachs2005@gmail.com

Introduction: IBD is a global health problem. It is necessary to understand the evolution and treatment exposure in a cohort of newly diagnosed IBD patients in the biologic era in the South of Europe

Aims & Methods: Aims: 1) To describe the main epidemiological and clinical characteristics of patients at IBD diagnosis and the long-term outcomes; 2) to analyse the use of drugs for IBD, and the need of hospitalisations and surgeries; 3) to compare IBD management based on the type of disease and the resources of the hospitals.

Methods: Prospective, population-based nationwide registry. Adult patients diagnosed with IBD —Crohn's disease (CD), ulcerative colitis (UC) or IBD unclassified— during 2017 in the 17 Spanish regions were included. Patients who consented were followed-up for 5 years (yr) after diagnosis. Treatment was grouped into 5 categories: mesalamine (oral or topical), steroids (intravenous, oral, or topical), immunomodulators (thiopurines, methotrexate or cyclosporine), biologics (anti-TNF, vedolizumab, ustekinumab) or JAK inhibitors (JAKi), and surgery. Hospitals were classified into high resources and low resources ones. Cumulative incidence of exposure to each of the studied treatments was estimated by Kaplan-Meier curves; curves were compared with log-rank test.

Results: A total of 3,301 incident cases of IBD diagnosed during 2017 in 108 hospitals, covering over 22 million inhabitants in Spain (about 50% of the population), were enrolled into the follow-up study. Main character-

istics of the cohort are summarised in table 1A and 1B. Median diagnosis delayed was 3.5 months (5.6 in CD and 2.7 in UC, $p<0.001$). During the 5-yr follow-up, 25% of UC patients progressed to more extensive involvement, while 8% of CD patients with inflammatory behaviour progressed to either stricturing or fistulising behaviour. Most of the patients who received mesalamine, corticosteroids, or immunomodulators initiated treatment within the first 2 years after diagnosis (figure 1). However, the cumulative incidence of biologics/JAKi usage steadily increased over time, reaching 49% by the 5-yr timepoint in CD. In terms of surgeries, a progressive increase in cumulative incidence was observed in CD; however, the incidence of colectomy remained stable in UC from the 2nd year post-diagnosis. The management and progression of IBD unclassified were similar to that of UC. Regarding the type of hospital, a higher cumulative incidence of biologics/JAKi usage, hospitalisations, and surgeries was observed in CD at high resources hospitals. No differences were observed in the use of other therapeutic resources or the management of UC.

	CD (N=1,526)	UC (N=1,633)	P-value
Median age at diagnosis, IQR (years)	40.9 (28.4-54.4)	45.6 (34.5-57.1)	<0.001
Median diagnosis delay, IQR (months)	5.6 (1.8 - 15.2)	2.7 (1.3 - 5.8)	<0.001
Male sex, n (%)	766 (50.2)	897 (54.9)	0.008
Symptoms at diagnosis, n (%)	13,61 (89.2)	15,38 (94.7)	<0.001
Family history, n (%)	272 (17.8)	214 (13.1)	<0.001
Extraintestinal manifestations, n (%)	294 (19.3)	157 (9.6)	<0.001
Former smoker, n (%)	364 (23.9)	765 (46.8)	<0.001
Mesalazine, n (%)	665 (43.6)	1,582 (96.9)	<0.001
Steroids, n (%)	1,205 (79.0)	843 (51.6)	<0.001
Immunomodulators, n (%)	878 (57.5)	309 (18.9)	<0.001
Biologics/JAK inhibitors, n (%)	675 (44.2)	281 (17.2)	<0.001
Hospitalisations, n (%)	657 (43.1)	430 (26.3)	<0.001
Surgery, n (%)	247 (16.2)	40 (2.5)	<0.001

Continuous variables are reported as median (p25-p75), and the number of non-missing values is provided. Categorical variables are reported as number of occurrences in each category. Percentages were calculated with the total sample as denominator, except subcategories of types of EII. P-values are calculated performing U Mann-Whitney tests for continuous variables and Pearson's χ^2 tests for categorical variables. IQR, interquartile range.

Conclusion: In the EpidemIBD large-scale epidemiological study, we have observed that the delay in diagnosing IBD is shorter than previously described. Approximately 50% of patients with CD and 20% of patients with UC end up receiving biologics/JAKi in the first 5 yrs following diagnosis. The percentage of patients undergoing surgery was lower than previously reported; in the case of UC, the majority of colectomies occurred within the first 2 yrs after diagnosis.

Disclosure: MDMA has received consulting and/or speaker fees from Abbvie, Pfizer, Takeda, Janssen, Tillotts Pharma and Galapagos; and has received research funding from Abbvie, Janssen and Pfizer.

RF-I has served as a speaker, advisory member or has received research funding from Takeda, MSD, Abbvie, Janssen, Pfizer, Palex, Shire Pharmaceuticals, TillottsPharma, Faes, Adacyte, Ferring and Casenrecordati.

R. Lorente has served as a speaker, or has received research or education funding from Abbvie, Pfizer, Takeda, Janssen and Galapagos.

IV has served as a Speaker, consultant and advisory member for and has received funding for: MSD, Abbvie, Pfizer, Ferring, Shire Pharmaceuticals, Takeda, Tillots, Janssen y Galápagos.

EF-S Tillotts Pharma (speaker and travel grants), Ferring (speaker and travel grants), Faes (travel grants), MSD (speaker and travel grants), Abbvie (speaker and travel grants), Falk (travel grants), Shire (speaker and travel grants), Takeda (speaker and travel grants).

LAG has served as speaker or has received research or education funding from MSD; Abbvie; Kern Pharma; Ferring; Faes Farma; Shire Pharmaceuticals; Pfizer; Takeda; Janssen; Tillots Pharma and Otsuka Pharmaceutical

MP511

PRIMARY SCLEROSING CHOLANGITIS AS RISK FACTOR FOR MORTALITY AND HOSPITALIZATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROPENSITY MATCHED COHORT STUDY

F. D'Amico¹, M. Allocca¹, T.L. Parigi¹, F. Rusconi², G. Hernandez², A. Segovia-Hilara³, A. Zilli¹, F. Furfaro¹, G. Fiorino⁴, P. Invernizzi⁵, L. Peyrin-Biroulet⁶, S. Danese¹

¹IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ²TriNetX Europe NV, Sint-Martens-Latem, Belgium, ³Universidad Politecnica de Madrid, Biomedical Informatics Group, Departamento de Inteligencia Artificial, ETSI Informaticos, Madrid, Spain, ⁴San Camillo-Forlanini Hospital, IBD Unit, Department of Gastroenterology & Digestive Endoscopy, Rome, Italy, ⁵Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca School of Medicine, Division of Gastroenterology, Monza, Italy, ⁶Nancy University Hospital, Department of Gastroenterology, Vandœuvre-lès-Nancy, France

Contact E-Mail Address: damico_ferdinando@libero.it

Introduction: There is a well-known association between inflammatory bowel disease (IBD) and primary sclerosing cholangitis (PSC). It is estimated that approximately 2% of IBD patients have PSC. However, there is little data regarding the impact of PSC on the prognosis of patients with IBD.

Aims & Methods: We conducted a retrospective cohort study using TriNetX, a multi-institutional database, to compare outcomes of patients with IBD and those with both IBD and concomitant PSC between 2003 and 2023. All patients with a confirmed diagnosis of Crohn's disease (CD), ulcerative colitis (UC), or indeterminate colitis with or without PSC were eligible. One-to-one propensity score matching was employed to balance demographic parameters, comorbid conditions, and IBD medications between cohort 1 (IBD) and cohort 2 (IBD and concomitant PSC). The primary endpoint was a composite endpoint including risk of mortality, hospitalization, and surgery. Secondary endpoints were the risk of mortality, IBD-related surgery, and IBD-related hospitalization. Risks were expressed as Hazard Ratio (HR) with a 95% confidence interval (CI).

Results: A total of 409,104 IBD patients were analyzed, including cohort 1 (405,923) and cohort 2 (3,181). After propensity score matching, 3007 patients from each group were included (mean age 48.1 ± 19.4 years, female 40%, UC 75%, CD 24,8%). Cohort 2 patients had an higher risk of experiencing the composite endpoint compared to cohort 1 group (HR 1.326, CI 1.232-1.428). Similarly, a higher risk of experiencing hospitalization and mortality was identified in subjects with IBD and concomitant PSC (HR 1.326, CI 1.224-1.436 and HR 1.697, CI 1.467-1.963 respectively). No difference was detected in terms of surgery between the two groups (HR 1.181, CI 0.970-1.438). Another analysis was performed to compare the outcomes of patients with CD or UC with or without concomitant PSC. Both CD and UC patients with concomitant PSC had an higher risk of achieving the composite endpoint (HR 1.186, CI 1.026-1.372 and HR 1.293, CI 1.189-1.408, respectively). An increased risk of mortality and hospitalization was found both in patients with CD (HR 2.164, CI 1.587-2.952, and 1.207, CI 1.031-1.412, respectively) and UC (HR 1.875, CI 1.578-2.228 and HR 1.279, CI 1.168-1.401, respectively) and concomitant PSC. In patients with CD or UC and concomitant PSC no increased risk of surgery was found (HR 0.954, CI 0.641-1.421 and HR 1.102, CI 0.886-1.369, respectively).

Conclusion: In the largest case series of patients with IBD and PSC, concomitant PSC increased risk of mortality and IBD-related hospitalization.

Disclosure: Nothing to disclose.

DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE DO NOT IMPACT GLP-1 ANALOGS EFFICACY: AN OBSERVATION FROM THE EPI-IIRN

Y. Gorelik¹, C. Friss², R. Lujan², Y. Loewenberg Weisband³, A. Ben Tov⁴, N. Ledderman⁵, E. Matz⁶, I. Dotan⁷, D. Turner⁸, H. Bar-Yoseph⁹
¹Rambam, Gastroenterology, Haifa, Israel, ²Shaare Zedek Medical Center, Juliet Keidan Institute of Pediatric Gastroenterology Hepatology and Nutrition, Jerusalem, Israel, ³Clalit Health Services, Clalit Research Institute, Tel Aviv, Israel, ⁴Sackler Faculty of Medicine, Tel Aviv University, Pediatric Gastroenterology Unit, Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Givatayim, Israel, ⁵Meuhedet Health Services, Tel Aviv, Israel, ⁶Leumit Health Services, Tel Aviv, Israel, ⁷Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ⁸Shaare Zedek Medical Center, Pediatric GI, Jerusalem, Israel, ⁹Rambam Health Care Campus, Gastroenterology, Haifa, Israel

Contact E-Mail Address: yurigorelik@gmail.com

Introduction: There is a global increase in the metabolic syndrome and inflammatory bowel diseases (IBD) prevalence, with a rise in patients who are being treated for both syndromes[1]. The growing use of GLP-1 analogs for both diabetes mellitus type 2 (DM2) and weight loss and the fact that these are originally gut-derived hormones with many gastrointestinal (GI) functions have raised concerns related to GLP-1 treatment in patients with IBD. We aimed to examine the efficacy of these agents in an Israeli nationwide cohort of IBD patients and matched controls (epi-IIRN).

Aims & Methods: IBD patients were identified using a previously validated algorithm and non-IBD matched controls (1:2-3 ratio) by year of birth, sex and jurisdiction. DM2 patients were identified if they had at least two occurrences of either any of the DM2 international classification of diseases 9 diagnoses, or a purchase of a non-insulin anti-diabetic medication. We included patients with GLP-1 dispensation for more than 6 months. The outcomes were changes in glycated hemoglobin (HbA1c) and body mass index (BMI), compared using Mann-Whitney test. Linear mixed effects models were constructed, with patients as random effects and change in either HbA1c or BMI (in each model) as outcomes. The models [HB1] were adjusted for sex, age, baseline HbA1c value, insulin and SGLT-2i treatment. Missing numeric values were carried forward from a previously recorded value for the same patient.

Results: Out of 1426 patients with diabetes who initiated GLP-1 agonists, 861 were treated for at least 6 months, 437 with IBD and 424 controls. IBD patients were significantly older, had lower BMI (<1 point difference), and were more likely to use glucocorticoids (Table 1). The change in HbA1c was not significantly different between IBD patients and controls (-0.3 [-1.1, 0.1] and -0.4 [-1.1, 0.1], respectively, p=0.74), neither was the change in BMI (-0.4 [-1.9, 0.5] and -0.5 [-2.3, 0.1], respectively, p=0.14). In the multivariate mixed effects models, IBD status in GLP-1 agonist users were not associated to change in HbA1c or change in BMI during treatment.

	IBD (n=437)	Non IBD (n=424)	P value
Follow up time, years	2.5 [1.3, 5.5]	2.8 [1.4, 6.0]	0.35
Age, years	61.4 [52.4, 67.6]	58.4 [50.2, 65.5]	<0.01
Male, n (%)	224 (51.3)	196 (46.2)	0.16
BMI	32.3 [29.8, 36.0]	33.5 [30.7, 37.6]	<0.01
HbA1c (baseline %)	7.9 [7.3, 8.8]	8.0 [7.3, 8.9]	0.93
Albumin, g/dL	4.2 [3.9, 4.3]	4.2 [4.0, 4.4]	0.6
Insulin	184 (42.1)	153 (36.1)	0.08
SGLT-2i	96 (22.0)	80 (18.9)	0.30
Glucocorticoids use	27 (6.2)	12 (2.8)	0.03

*data is presented as median [IQR] or n (%)

Conclusion: GLP-1 analogs show similar efficacy in patients with DM2 and IBD compared with patients without IBD. Further evidence is needed for their efficacy and tolerability in patients with IBD and overweight.
References: [1] Jess T, Jensen BW, Andersson M, et al. Inflammatory Bowel Diseases Increase Risk of Type 2 Diabetes in a Nationwide Cohort Study. Clin Gastroenterol Hepatol 2020; 18: 881-888.e1. doi:10.1016/j.cgh.2019.07.052
Disclosure: The authors report no conflict of interests.

Screening and surveillance of CRC: What's new

10:00-11:00 / Poster Stage 2

MP513

HIGH-RESOLUTION RECTOSCOPY USING DUAL-MODE MHZ OPTICAL COHERENCE TOMOGRAPHY - A STEP TOWARDS REAL TIME 3D ENDOSCOPY

B. Schulte¹, S. Burhan², A.P. Singh², W. Draxinger², S. Lotz², M. Heimke³, T. Heinze³, T. Wedel³, M. Rahlves², R. Huber², M. Ellrichmann¹

¹Interdisciplinary Endoscopy, Medical Department I, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany, ²Institute of Biomedical Optics, Universität zu Lübeck, Luebeck, Germany, ³Institute of Anatomy, Center of Clinical Anatomy, Christian-Albrechts University Kiel, Kiel, Germany

Contact E-Mail Address: Berenice.Schulte@UKSH.de

Introduction: In addition to colonoscopy and histology, endoscopic ultrasound (EUS) plays a pivotal role in assessing rectal cancer (T-staging). As new therapeutic options emerge, exact imaging of the tumor is essential for the primary diagnosis and the evaluation of therapeutic response. In this regard, optical coherence tomography (OCT) offers a superior axial and lateral resolution compared to conventional rectal EUS and may contribute to individualized therapeutic strategies.

Aims & Methods: Our study aimed to evaluate the imaging quality of our further refined OCT-rectoscope prototype, which integrates an extended range additional to the optimized standard mode.

We integrated a double ferrule design with a fiber optical switch into a MHz-OCT rectoscope.

The performance of this adjustable OCT-rectoscope was assessed in two human colons, post-mortem and *in situ*. The body donors were preserved using an ethanol-glycerol-lysoformin-based technique resulting in true-to-life tissue consistency.

Results: The extended range mode adjusted the focus depth and imaging range and ensured imaging quality despite varying colon diameters or altered total wall thickness. The optimized standard mode gave a detailed resolution of the different rectal wall layers. Compared to the former prototype MHz-OCT rectoscope and rectal EUS, the images stood out: The mucosa appeared as a broad pale gray band, exactly circumscribed by the lamina muscularis mucosae. The submucosa was visualized as an inhomogeneous, light gray broad area. Furthermore, the muscularis propria comprising the circular and longitudinal muscle layer manifested as two homogeneous dark gray bands. The serosa was displayed as a bright band.

Conclusion: The new dual-mode MHz-OCT design allows a fast change between the extended range and the optimized standard mode. The imaging quality in both modes was exceptional compared to the state of the art EUS, with clear delineation of the different rectal wall layers, providing ideal conditions for accurate staging of rectal cancer. Further imaging studies are warranted to evaluate this dual-mode MHz-OCT rectoscope in human colons *in vivo*. In the future, this technique could serve additionally in indications like inflammatory bowel disease to quantify inflammation more precisely. Moreover, it could be integrated into a colonoscope design to evaluate the whole colon.

References: B. Schulte*, M. Göb* et al., High-resolution rectoscopy using MHz optical coherence tomography: a step towards real time 3D endoscopy. Scientific Reports, 02/2024

AP. Singh et al., Virtual Hall sensor triggered multi-MHz endoscopic OCT imaging for stable real-time visualization. Opt express, 02/2024

Disclosure: Nothing to disclose.

MP514

ERIC, NEW VIRTUAL ASSISTANT FOR COLONOSCOPY: A PILOT STUDY

L.E. Del Vecchio¹, S. Pecere¹, F. Barbaro¹, L.G. Papparella¹, C. Spada¹

¹Catholic University of Rome, Gemelli Hospital, Gastroenterology and Digestive Endoscopy Unit, Roma, Italy

Contact E-Mail Address: livioenricodelvecchio@gmail.com

Introduction: A successful colonoscopy requires ideal stool preparation, yet the percentage of insufficient bowel preparation is still very high. Frequently, the patients use website information on colonoscopy preparation. Conversely, the daily activity of the hospital staff consists of spending time with patients, communicating with them and giving answers to a high number of questions coming from patients regarding the preparation for the procedure or the exam itself. Hence, the idea to adopt a rapid and intuitive patient-oriented digital service to respond to their needs, the virtual assistant Eric.

Aims & Methods: Endo-Chat is an automated online communication platform, powered by AI (Artificial Intelligence) with the use of the Natural Language Processing and Deep Learning technologies, that answers procedure-related questions in real-time. The engine is named ERIC, stands for "Endoscopy Robot for Intelligent Chat" and is an intelligent chatbot, capable of answering autonomously to most of the doubts of a patient who is supposed to undergo an endoscopic examination.

Results: Since the introduction of the conversational artificial intelligence system at the Policlinico Gemelli starting from 24th of January 2022 to the 16th of March 2023, Eric has been able to autonomously manage 94% of the questions sent by patients, thus forwarding only the remaining 6% (of the requests) to specialized human operators.

We calculated that in the pre-pilot phase, a large part of the daily activity of nurses was dedicated to communicating with patients, around 40 hours per week, while in the post-pilot phase, the time spent for communication was significantly reduced to 15 hours per week. According to OECD Health Statistics 2022, the average annual salary of a European nurse is 35,300 euros, with an annual hypothetical saving of 22,062 euros, comparable to a part-time contract.

Also, the number of cancelled procedures for poor patient preparation has fallen from 22 to 7 per week, considering a volume of 200 procedures per week.

Regarding patient's experience, users can leave voluntary feedback on their virtual assistant experience directly on the ERIC website, evaluating the quality of the service. Patient service evaluations were enthusiastic till now, as 63% rated the service as excellent.

Conclusion: In our observational pilot study, the first in Europe to our knowledge, we assessed the benefits measurement for patients and Hospital staff. Starting from these preliminary interesting results, we can speculate that the introduction of Endo-Chat in high-volume endoscopy service is feasible and useful not only for patients but also for hospital staff.

Disclosure: The authors declare no conflict of interest.

MP515

PREVALENCE OF COLONOSCOPY-RELATED ADVERSE EVENTS IN OLDER ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Q. Lu¹, X.-H. Lv¹, J.-L. Yang¹
¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: 237199636@qq.com

Introduction: The need for colonoscopies in the elderly has significantly grown compared to 20 years ago. Furthermore, the issue of advanced age has long been a concern to colonoscopists. Our study aimed to evaluate the occurrence of colonoscopy-related adverse events (AEs) in older individuals.

Aims & Methods: A detailed search was conducted on October 28th, 2023, using the Pubmed, Embase, and Cochrane Library databases. Meta-analyses were performed using the generalized linear mixed model and the results were expressed for pooled rate along with relevant 95% confidence intervals (CIs).

Results: We retrieved 14748 records, of which 34 studies were included. The overall pooled rate of colonoscopy-related perforation, bleeding and death in the elderly were 0.072% (95% CI 0.051-0.102; I²=82%), 0.184% (95% CI 0.093-0.364; I²=99%), and 0.026% (95% CI 0.002-0.431; I²=0%), respectively. Patients aged over 80 years had a 2.44-fold (RR 2.44; 95% CI 1.15-5.66; I²=79%) risk of perforation and 1.24-fold (RR 1.24 95% CI 1.04-1.49; I²=0%) risk of bleeding comparing with patients aged 80 years and under. For screening purposes, the pooled rate of perforation and bleeding were 0.086% (95% CI 0.071-0.103; I²=0%) and 0.170% (95%CI 0.049-0.591; I²=96%), respectively. The rates were 0.076% (95% CI 0.029-0.202; I²=0%) and 0.166% (95% CI 0.062-0.438; I²=54%) for diagnostic purposes, respectively. In comparison to non-therapeutic colonoscopies, therapeutic colonoscopies showed a higher rate of perforation (0.044% vs. 0.004%) and bleeding (0.167% vs. 0.004%).

Conclusion: We reported on the prevalence of colonoscopy-related AEs in older adults, emphasizing concerns over the safety of colonoscopy for those aged over 80 years.

Disclosure: Nothing to disclose.

MP516

RELIABILITY OF RECOMMENDATIONS ISSUED BY CHATGPT 3.5 AFTER A SCREENING COLONOSCOPY

E. Mikhael¹, S. Helou¹, R. Abbas¹, L. Amer¹, R. Slim Karam¹, E. Mahfouz¹, J. Amara¹, K. Honein¹, C. Yaghi¹
¹Université Saint-Joseph, Beirut, Lebanon

Contact E-Mail Address: eliomikhael7@gmail.com

Introduction: There is a steadily increasing interest among patients in obtaining medical information from electronic sources. ChatGPT, a conversational agent utilizing artificial intelligence, has been demonstrated as a reliable source of information for patients before a colonoscopy (1) as well as in various medical purposes.

Aims & Methods: The aim of this study is to determine the ability of ChatGPT 3.5 to issue recommendations after a screening colonoscopy for colorectal cancer. This is a single-center observational cross-sectional study conducted in 2023. Only colonoscopies for screening purposes were included. Colonoscopies performed for gastrointestinal bleeding, follow-up of chronic inflammatory bowel diseases, post-operative follow-up of colorectal cancer, or in patients under 40 years old were excluded. Colonoscopy reports and corresponding pathology reports were entered into a conversation with ChatGPT 3.5. The colonoscopy report includes the quality of colonic preparation, withdrawal time, results, and specimens sent

for histology. ChatGPT 3.5 was asked to determine the time interval for the follow-up colonoscopy using the Consensus of the American multisociety taskforce of 2020 (2). The answers from ChatGPT were compared to the recommendations, and were validated by two gastroenterologists. The answers were categorized as “correct”, “underestimated” if the interval recommended by ChatGPT is shorter than the one provided by the consensus, and “overestimated” if the interval recommended by ChatGPT is longer than the one provided by the consensus.

Results: A total of 1259 colonoscopies were considered for analysis. The average age at the time of colonoscopy was 61.6 ± 11.0 years old. Among the participants, 688 (54.6%) were women and 517 (45.4%) were men. ChatGPT® issued a correct recommendation in 892 cases (70.8%). The surveillance interval was underestimated in 260 (20.7%) cases and overestimated in 107 (8.5%) cases.

The accuracy of the recommendations for each identified category is represented in the table below.

Result	Correct answer N (%)	Incorrect, under- estimate interval N (%)	Incorrect, overestimate interval N (%)
Normal colonoscopy with adequate bowel preparation (n= 590)	544 (92.2%)	46 (11.8%)	0 (0%)
Inadequate bowel preparation (n= 190)	100 (52.6%)	0 (0%)	90 (47.4%)
1-2 tubular adenomas with low grade dysplasia (n= 180)	26 (14.4%)	154 (85.6%)	0 (0%)
3-4 tubular adenomas with low grade dysplasia OR hyperplastic polyp ≥ 1cm (n=58)	53 (91.4%)	3 (5.2%)	2 (3.4%)
Polyp with high grade dysplasie, with villous component, OR serrated with dysplasia or ≥ 1cm, OR 5 or more adenomas (n=121)	108 (89.3%)	7 (5.8%)	6 (4.9%)
Serrated polyp without dysplasia AND < 1cm (n=5)	5 (100%)	0 (0%)	0 (0%)
Polyp ≥2cm resected with piecemeal mucosectomy (n=7)	6 (85.7%)	0 (0%)	1 (14.3%)
Ten or more adenomas (n=8)	4 (50%)	0 (0%)	4 (50%)
Total (n=1259)	892 (70.8%)	260 (20.7%)	107 (8.5%)

Table 1. Accuracy of the recommendations issued by ChatGPT 3.5 according to the colonoscopy result.

Conclusion: ChatGPT appears to be a reliable tool for issuing recommendations after a screening colonoscopy. It is limited by the recognition of poor preparation requiring closer surveillance. Artificial intelligence could be exploited and integrated into colorectal cancer screening programs. It could also be used by a patient to remind them of their next colonoscopy, except in cases of poor colonic preparation.

References:

1. Lee TC, Staller K, Botoman V, Pathipati MP, Varma S, Kuo B. ChatGPT Answers Common Patient Questions About Colonoscopy. Gastroenterology. 2023;165(2):509-511.e7. doi:10.1053/j.gastro.2023.04.033
2. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc. 2020;91(3):463-485.e5. doi:10.1016/j.gie.2020.01.014

Disclosure: Nothing to disclose.

MP517

IMPACT OF THE SCREENING AND DIAGNOSTIC METHODS ON THE CONTINUOUS DECREASE OF THE COLORECTAL CANCER INCIDENCE AND MORTALITY IN THE CZECH REPUBLIC

S. Suchanek^{1,2}, O. Ngo^{3,4}, T. Grega^{1,2}, K. Hejzmanova^{3,4}, M. Ambrozova^{3,4}, R. Chloupkova^{3,4}, O. Majek^{3,4}, L. Dušek^{3,4}, M. Zavoral^{1,2}

¹Military University Hospital, 1st Faculty of Medicine, Charles University, Department of Internal Medicine, Prague, Czech Republic, ²Military University Hospital, 1st Faculty of Medicine, Charles University, Department of Gastrointestinal Oncology, Prague, Czech Republic, ³Institute of Health Information and Statistics of the Czech Republic, Prague, Czech Republic, ⁴Masaryk University, Faculty of Medicine, Institute of Biostatistics and Analyses, Brno, Czech Republic

Contact E-Mail Address: stepan.suchanek@uvn.cz

Introduction: The colorectal cancer (CRC) incidence and mortality might be influenced by the screening and diagnostic methods related to the pre-cancerous lesion (adenomatous polyps) and colorectal neoplasia identification. In the Czech Republic, there are two methods available. First is the annual (in age 50–54) or biennial (in age over 50) immunochemical fecal occult blood test (FIT), followed by FIT+ colonoscopy, if positive. The second one is screening colonoscopy (in age over 50) which might be repeated in 10 years interval. Besides these screening methods, diagnostic FIT and colonoscopy are available for symptomatic patients.

Aims & Methods: Evaluation of the CRC incidence and mortality trends between years 2000 (introduction of the screening program) and 2021 (most recent data available) and target population coverage (three years interval) by screening and diagnostic FIT and colonoscopy (CRC-affecting methods) in last 10 years (2012–2022). The analysis was performed using the National Registry of Reimbursed Health Services in the Czech Republic (data since 2010) and the Registry of Preventive Colonoscopies (data since 2006).

Results: In years 2000–2021, the decrease in CRC incidence and mortality by 31.6% and 46.3%, respectively, was noticed. Target population (individuals age over 50) coverage of all CRC-affecting methods have risen in years 2012–2022 from 43.0% to 47.8%. In year 2022, the target population consists of 4,140,725 individuals and screening FITs were performed in 1,490,661 persons (36.0%), screening colonoscopies in 109,200 individuals (2.6%), diagnostic FITs in 97,505 patients (2.4%) and diagnostic colonoscopies in 283,462 patients (6.8%). In years 2006–2022, 474,063 preventive colonoscopies were done, adenomas were removed in 179,478 patients (37.9%) and colorectal cancers were diagnosed in 13,428 patients (2.8%) (48.8% of them in stage I).

Conclusion: The indirect evidence shows the probable impact of the high numbers of the screening and diagnostic fecal immunochemical tests and colonoscopies performed, adenomas removed, and early-stage cancers diagnosed on the continuous decrease of the colorectal cancer incidence and mortality in the Czech Republic.

References: Supported by program projects of the Ministry of Health of the Czech Republic with reg. no. NU22-08-00424, MO1012 and Cooperatio.

Disclosure: Nothing to disclose.

MP518

WITHDRAWN

MP519

VARIATIONS IN USE OF FAECAL IMMUNOCHEMICAL TESTING (FIT) IN PRIMARY CARE IN ENGLAND: A POPULATION-BASED COHORT

A. Morton^{1,2}, C. Crooks^{1,2,3}, J. West^{1,2,3}, B.D. Nicholson⁴, D.J. Humes^{1,2,3}

¹University of Nottingham, Nottingham, United Kingdom, ²NIHR Nottingham Biomedical Research Centre, University of Nottingham and Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom, ³Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom, ⁴Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom

Contact E-Mail Address: alastair.morton1@nottingham.ac.uk

Introduction: The United Kingdom National Institute for Health and Care Excellence recommends Faecal Immunochemical Testing (FIT) for all patients presenting to primary care with symptoms suggestive of colorectal cancer. How use of this test varies across England is unknown, which this study aimed to quantify.

Aims & Methods: Routinely-collected primary care records (Clinical Practice Research Datalink Aurum) were used to assess variations in symptomatic FIT use in adults (≥18 years) between regions and over time in England from 2019 to 2023. Rates were calculated using the population registered to each primary care practice as the denominator, with analysis split by calendar year.

The first coded FIT test with a numerical result per patient each year was extracted from the primary care records. Rates of testing were calculated using Poisson regression, adjusted for other confounders. Results were described between groups, regions and years at the recommended threshold of ≥10 µgHb/g faeces (results above this threshold henceforth referred to as FIT10), describing the proportions likely to have a secondary care referral based on national guidance. Logistic regression was used to compare the impact of year, region, gender and age on the differences in FIT10.

Results: Between 01/01/2019 and 05/06/2023 there were 531,735 FIT results among 495,121 patients and a denominator population of 17,910,681. The number of completed FITs increased from 8,395 in 2019 to 237,708 in 2022 (the last complete year within the study), with a corresponding ~thirty-fold increase from 0.69 tests per 1000 person-years in 2019 (95%CI 0.68–0.71) to 19.57 per thousand person-years in 2022 (95%CI 19.50–19.65). There was large variation in testing between regions, with rates 3.6 times higher in the North East compared to the West Midlands (17.05 per thousand person-years, 95%CI 16.87–17.23 versus 4.72 per thousand person-years, 95%CI 4.67–4.76). These differences persisted to 2022, with less than half the rate in the West Midlands (11.32) compared to the North East (31.85 per thousand person-years).

20.4% of results were FIT10. Despite increased testing, the overall proportion FIT10 did not change over time. 51.7% of all tests FIT10 were in those over 70 years of age. The percentage FIT10 was lower in regions with higher rates of FIT testing, for example FIT10 ranged from 16.7% in the South West (rate of testing 14.62 per thousand person-years) to 25.3% in the South East (rate of testing 8.00 per thousand person-years). After adjusting for year, region, gender and age, this difference persisted (adjusted OR 0.57, 95%CI 0.55–0.58) comparing FIT10 in the South West to the South East. The difference in proportions FIT10 between regions showed some convergence over time, from a range of 16.6%–26.7% (10.1%) in 2021 to 15.8%–23.7% (7.9%) in 2023.

Conclusion: There has been a marked increase over time in the use of FIT for patients with symptoms in primary care, with large and persistent variations between regions of England. The overall proportion FIT10 has not decreased over time with increasing use, however there were large

differences in FIT10 between regions that correlated with rates of testing. These regional differences persisted but reduced over time as testing rates increased nationally. It is likely that clinical pathway differences in the implementation of FIT over time and between regions explain the variations we have observed. If used as a guide to referral, such variation could lead to inequalities in colorectal investigation and diagnosis.

Disclosure: Nothing to disclose.

MP520

TESTING GERMLINE MUTATIONS PATIENTS WITH 10-19 LIFETIME COLORECTAL ADENOMAS: IS IT NECESSARY?

P.F. da Silva Mesquita², J. Rodrigues¹, C. Costa², M.M. Estevinho², T. Freitas², A. Ponte²

¹Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal, ²Gastroenterology, Porto, Portugal, ³CHVNG/E, Gastroenterology, Vila Nova De Gaia, Portugal

Contact E-Mail Address: pedro.filipe.silva.mesquita@gmail.com

Introduction: The prevalence of pathogenic APC and biallelic MUTYH mutations, in patients with 10 to 19 cumulative colorectal adenomas (CRA), is stated to be 5% and 4%, respectively. ESGE and NCCN suggest referring patients with ≥ 10 CRA to genetic counseling, limiting direct testing to patients with ≥ 20 CRA. USMSTF states that patients with multiple CRA should be considered for genetic testing. BSG recommends testing all patients under 60 years-of-age with ≥ 10 CRA, and over 60 only patients with family history of colorectal cancer (FHC) or polyposis. Predictors are needed to further select patients and maximize the diagnostic yield.

Aims & Methods: To assess the prevalence and predictors of pathogenic APC and MUTHY mutations in patients with 10-19 lifetime adenomas to the date of the genetic test.

We retrospectively included all patients undergoing screening for APC and MUTYH mutations, in our center since 2010. Patients undergoing family screening or with a history of colorectal cancer (CRC) were excluded. Endoscopic, histological, and family history data was collected.

Results: 96 patients (36%) presented with 10-19 cumulative adenomas. Patients were on average 64,45 ($\pm 9,33$) years and 78.1% were male. FHC was present in 21,8%, diminishing to 19,7% when considering first-degree relatives only and to 4,2% applying ESGE familiar-CRC definition. On average patients had 5 advanced adenomas (size ≥ 10 mm, tubulovillous/villous histology or with high-grade dysplasia) and 66.7% had ≥ 10 CRA on a single colonoscopy. No patients were found to have pathogenic mutations of the APC and MUTYH genes.

Conclusion: Despite a combined expected prevalence of 7-12/100 patients, and the high presence of risk factors in our cohort, no pathogenic mutations were found. ESGE and NCCN criteria would have led to the referral of 96 patients to genetic counseling and BSG recommendations would trigger 42 genetic tests. We question the prevalence of these mutations in the Portuguese population and the cost-effectiveness of testing patients with 10-19 cumulative CRA.

Disclosure: Nothing to disclose.

MP521

EVALUATION OF THE INCIDENCE OF POST COLONOSCOPY COLORECTAL CANCER IN A SPECIFIC PATIENT POPULATION BY USING A NEWLY DEVELOPED DASHBOARD FOR REAL-TIME AND ONGOING MONITORING OF PATIENT OUTCOMES AND ENDOSCOPIST PERFORMANCE

S. Corneillie¹, W. Bruneel², J. Bossuyt², F. Dedeurwaerdere³, F. Marolleau⁴, D. De Wulf⁴, L. Desomer⁵

¹AZ Delta Rumbeke-Menen-Torhout, Clinical Nurse Specialist Endoscopy, Roeselare, Belgium, ²AZ Delta Rumbeke-Menen-Torhout, Data-Analysis, Roeselare, Belgium, ³AZ Delta Rumbeke-Menen-Torhout, Department of Histopathology, Roeselare, Belgium, ⁴AZ Delta Rumbeke-Menen-Torhout, Gastroenterology and hepatology, Roeselare, Belgium, ⁵AZ Delta Rumbeke-Menen-Torhout, Gastroenterology and Hepatology, Roeselare, Belgium

Contact E-Mail Address: sophie.corneillie@azdelta.be

Introduction: Colorectal cancer (CRC) poses a significant global health threat, with high incidence rates and a major impact on public health. Despite screening and diagnostic advances, CRC claimed 2,520 lives in Belgium in 2021. Colonoscopy helps identify and remove polyps, reducing CRC risk. However, post-colonoscopy CRC (PCCRC) cases still occur, influenced by factors like inadequate bowel preparation and short withdrawal time. Understanding these factors is vital for enhancing CRC screening and prevention. Utilizing a POWERBI dashboard can aid in collecting data on screening colonoscopies, including key performance indicators like withdrawal time and adenoma detection ratio (ADR).

Aims & Methods: This study aimed to create a comprehensive dashboard for analyzing PCCRC at our center. Secondary goals included identifying factors contributing to PCCRC in our patient population. We designed an integrated dashboard and analyzed coded data from electronic patient records, including colonoscopy findings matched with histopathological data. A retrospective analysis identified patients with PCCRC and factors possibly contributing to its development. Each case underwent detailed manual review. Colonoscopy indications analyzed were positive iFOBt, surveillance and screening.

Results: The dashboard was developed by a data analyst under the guidance of the clinical nurse specialist in endoscopy and the gastroenterologists in our center. The initial version of this dashboard consisted of the following data: demographics and comorbidities of the patients, number of colonoscopies and their indications, adenoma detection ratio per endoscopist, histopathology data coupled with the data from the endoscopy report, BBPS and withdrawal time. Using diagrams, an easy overview of the current available data is readily visualised.

From the 13200 screening colonoscopies performed between June 2019 and april 2024, 274 (2.08%) CRC's were detected. 16/274 (5.84%) were PC-CRC (9 males and 7 females), including 1 patient with Lynch syndrome, 1 Crohn's disease, and 1 signet ring cell carcinoma. The detected carcinomas were located in the ascending colon (1), hepatic flexure (2), transverse colon (1), cecum (5), sigmoid (5) and rectum (2). The median time to the detection of a PCCRC was 23 months (range 5 - 38). The mean age of individuals diagnosed with PCCRC was 70 years (range 37 - 88). The median withdrawal time at the index colonoscopy was 8.5 minutes (range 3 - 54). The Boston Bowel Preparation Score (BBPS) was utilized to assess bowel preparation quality of the index colonoscopy, with a median score of 9 (range 3 - 9). The median ADR in our center is 46.2%. Three patients died of PCCRC.

Conclusion: We identified and analysed PCCRC and interval cancers by using a newly developed dashboard. This dashboard extracts real-time coded data from patient files and allows for retrospective, real-time and ongoing monitoring. By using this tool as an audit, healthcare providers can take targeted actions to improve the quality of colonoscopies and aim

to reduce the incidence of PCCRC. In the future, expansion of this dashboard should allow to extract data allowing for comparing groups and analyse risk factors associated with PCCRC and interval cancer. Ideally, a dashboard should be considered to be integrated in all endoscopy reporting systems providing real-time data on endoscopist's performance and patient outcomes.

References: 1. Burr NE, Derbyshire E, Taylor J, et al.. Variation in post-colonoscopy colorectal cancer across colonoscopy providers in English National Health Service: population based cohort study. *BMJ* 2019;367:l6090. 10.1136/bmj.l6090
2. Rutter, M. D., Beintaris, I., Valori, R., Chiu, H. M., Corley, D. A., Cuatrecasas, M., Dekker, E., Forsberg, A., Gore-Booth, J., Haug, U., Kaminski, M. F., Matsuda, T., Meijer, G. A., Morris, E., Plumb, A. A., Rabeneck, L., Robertson, D. J., Schoen, R. E., Singh, H., Tinmouth, J., ... Sanduleanu, S. (2018). World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer. *Gastroenterology*, 155(3), 909–925.e3. <https://doi.org/10.1053/j.gastro.2018.05.038>
3. Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service.

Disclosure: Nothing to disclose.

MP522

A FAECAL MICROBIAL SIGNATURE TO OPTIMISE COLORECTAL CANCER SURVEILLANCE IN LYNCH SYNDROME

S. Taboada-López^{1,2}, M. Malagón¹, L.J. Garcia-Gil², M. Serra-Pegès¹, X. Aldegue^{3,4}, A. Bahi⁴, R. Moreira^{5,6,7}, A. Castells^{5,6,7}, T. Ocaña^{5,6,7}, J. Castillo^{5,6,7}, J. Guardiola⁸, N. Dueñas⁹, V. Piñol^{2,3}, M. Pineda⁹, G. Capellà⁹, S. Ramió-Pujol¹, L. Baldo^{10,11}, F. Balaguer^{5,6,7}, J. Brunet^{9,12}

¹GoodGut SLU, Girona, Spain, ²Universitat de Girona, Girona, Spain, ³Hospital Universitari de Girona Dr. Josep Trueta, Department of Gastroenterology, Girona, Spain, ⁴Institut d'Investigació Biomèdica de Girona, Salt, Spain, ⁵Hospital Clínic Barcelona, Department of Gastroenterology, Barcelona, Spain, ⁶Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain, ⁷University of Barcelona, Barcelona, Spain, ⁸Hospital Universitari de Bellvitge, Department of Gastroenterology, L'Hospitalet De Llobregat, Spain, ⁹Institut Català d'Oncologia de Bellvitge, Hereditary Cancer Program, Hospitalet de Llobregat, Spain, ¹⁰University of Barcelona, Department of Evolutionary Biology, Ecology and Environmental Sciences, Barcelona, Spain, ¹¹Institute for Research on Biodiversity (IRBio), Barcelona, Spain, ¹²Institut Català d'Oncologia de Girona, Hereditary Cancer Program, Girona, Spain

Contact E-Mail Address: sandra.taboada@goodgut.eu

Introduction: Colonoscopic surveillance reduces colorectal cancer (CRC) incidence and mortality in Lynch syndrome (LS) carriers. Still, its invasiveness and high costs highlight the need for a non-invasive approach to predict the presence of neoplastic lesions.

Aims & Methods: This study aimed to identify faecal bacterial biomarkers to discern between carriers with colorectal lesions and those with normal colon.

Two independent Spanish cohorts (a training and a validation cohort) were recruited through two multicenter studies (Table 1). Participants provided a faecal sample before surveillance colonoscopy to quantify the abundance of *F. prausnitzii* (FPRA) and its phylogroups I and II (PHGI and PHGII), *P. stomatis* (PTST), *B. fragilis* (BCTF), *B. thetaiotaomicron* (BCTT), B46 (best BLAST match *S. variabile*), *G. morbillorum* (GMLL), B48 (best

BLAST match *R. faecis*), and *E. coli* (ECO) through qPCR. Eubacteria (EUB) was quantified as the total bacterial load. Participants were classified based on colonoscopy findings as normal colonoscopy (NC), non-advanced adenoma (NAA), and advanced neoplasia (AN, including advanced adenoma and CRC). A bacterial signature for neoplasia prediction was defined and validated in the training and validation cohorts, respectively.

		Training cohort	Validation cohort
Age	mean (range)	51 (25-83)	47 (20-75)
Sex (female)	n (%)	32 (64.0)	75 (65.8)
Diagnosis	NC (%)	40 (80.0)	71 (64.5)
	NAA (%)	6 (12.0)	35 (31.8)
	AA (%)	3 (6.0)	3 (2.8)
	CRC (%)	1 (2.0)	1 (0.9)
Mutated gene	High penetrance	MLH1 (%) - MSH2 (%) - EPCAM (%)	18 (36.0) - 9 (18.0) - 0 (0.0)
	Low penetrance	MSH6 (%) - PMS2 (%)	37 (33.6) - 25 (22.9) - 1 (0.9)
Total		n	50
			110

Table 1. Main characteristics of the study participants. NC, normal colonoscopy; NAA, non-advanced adenoma; AA, advanced adenoma; CRC, colorectal cancer.

Results: The bacterial abundances were analysed in the training cohort according to age, sex, body mass index (BMI), germline mutation, and colonoscopy findings. Significant moderate positive correlations were identified between the abundances of BCTF and age ($r=0.325$, $p=0.040$), and PHGII and BMI ($r=0.399$, $p=0.010$). A significant negative correlation was identified between GMLL abundance and BMI ($r=-0.331$, $p=0.036$). Patients harbouring *MLH1* mutations exhibited a significantly higher abundance of FPRA compared to *PMS2* carriers ($p=0.048$). Patients with neoplasia (NAA+AN) presented significantly lower abundances of BCTF ($p=0.027$) and B48 ($p=0.038$) than patients with NC. Patients with AN presented a significantly lower abundance of PTST compared to patients with NC or NAA ($p=0.032$).

Although all the bacterial markers achieved a sensitivity of 100% to predict the presence of neoplasia, none of them presented a specificity higher than 25% by itself. To maintain sensitivity and increase specificity a bacterial signature was defined including ECO, BCTF, GMLL, FPRA, PHGI, PHGII, and B46 combined with the inherited mutation. The signature showed 100% sensitivity (SS), 52.50% specificity (SP), 34.48% positive predictive value (PPV), and 100% negative predictive value (NPV). This signature was subsequently validated demonstrating 100% SS, 56.45% SP, 53.44% PPV, and 100% NPV.

Conclusion: A new faecal bacterial signature to predict the presence of colorectal neoplasia in LS carriers has been identified, showcasing its potential usefulness to improve and personalise LS surveillance, optimising endoscopic resources, and providing a less invasive and cost-effective approach.

Disclosure: S. Taboada-López, M. Malagón, S. Ramió-Pujol and M. Serra-Pegès are employees of GoodGut.

MP523

EXPLORING THE POTENTIAL OF ORAL BUTYRATE SUPPLEMENTATION IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE: SUBGROUP INSIGHTS FROM AN INTERVENTIONAL STUDY

M. Mitrovic¹, A. Dobrosavljević¹, A. Milic¹, D. Zaric¹, P. Vuković¹, P. Svorcan¹

¹Kbc Zvezdara, Gastroenterology and hepatology, Belgrade, Serbia

Contact E-Mail Address: miloskbcz18@gmail.com

Introduction: Although the exact mechanism of metabolic dysfunction-associated steatotic liver disease (MASLD) development is unknown, new research indicates that the gut microbiota may significantly impact the disease's progression through one of its most vital functions—the synthesis of butyrate. Animal models have already demonstrated the positive effects of butyrate administration, but no studies have yet investigated the possible impact of oral butyrate supplementation in the population of MASLD patients.

Aims & Methods: We conducted an interventional study of 177 individuals diagnosed with MASLD. MASLD was defined by a baseline attenuation coefficient (ATT) obtained by point shear-wave elastometry (pSWE) of 0.63 dB/cm/MHz or higher and a baseline alanine-aminotransferase (ALT) of more than 40 IU/L. After diagnosis was made, a total of 121 patients were administered 1000 mg of calcium butyrate, whereas 56 patients were treated with 1000 mg of sodium butyrate. Patients were prescribed a Mediterranean diet regimen, which required an intake of 20–30 kilocalories per kilogram of body weight, split between 35–40% fat, 20% protein, and 40–45% carbs. At the start of the investigation, patients were requested to provide stool samples for stool short chain fatty acids (SCFA) analysis and blood samples for miRNA panel (miR-192, miR-885, miR-122) analysis. We also followed the elastometry parameter, ALT, lipidogram, high-sensitive C-reactive protein (hsCRP), tumor necrosis factor- α (TNF- α), interleukin-1, interleukin-6, and cytokeratin-18 dynamics during the 12-week treatment period.

Results: We did not observe a significant effect of butyrate supplementation on the level of liver steatosis (baseline vs. endpoint ATT- 0.78 vs 0.76 dB/cm/MHz, $p=0.33$) and ALT (baseline vs. endpoint ALT 72 vs 73 IU/L, $p=0.58$). No significant effects were observed in inflammatory markers or lipidogram dynamics. Neither calcium- nor sodium-butyrate showed superiority. However, the benefit of butyrate supplementation was observed in the population of patients with MASLD and body mass index below 25 kg/m² (baseline vs. endpoint ATT 0.80 vs 0.77 dB/cm/MHz, $p=0.043$; baseline vs endpoint hsCRP 3.7 vs. 2.4 mg/L, $p<0.001$), baseline SCFAs below 20 μ mol/g (baseline vs. endpoint ALT 78 vs. 74 IU/L, $p=0.0142$; baseline vs. Endpoint ATT 0.84 vs. 0.78 dB/cm/MHz, $p=0.002$), baseline hsCRP levels above 10 mg/L (baseline vs. endpoint hsCRP 14.6 $\pm$ 3 vs. 6.4 $\pm$ 1.4 mg/L, $p<0.001$) and patients with upregulated miR-192 (baseline vs endpoint TNF α 30.4 vs. 24.6 pg/ml; baseline vs. endpoint cytokeratin-18 229 vs. 211 IU/L, $p=0.025$).

Conclusion: Oral butyrate supplementation could benefit selected groups of patients with MASLD, especially in lean, those with higher inflammatory status, or low stool SCFAs.

Disclosure: Nothing to disclose.

MP524

SIMILAR WEIGHT LOSS WITH SEMAGLUTIDE REGARDLESS OF DIABETES AND CARDIOMETABOLIC PARAMETERS IN INDIVIDUALS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

M. Armstrong^{1,2,3}, T. Okanoue⁴, M. Palle⁵, A.-S. Sejlø⁵, M. Tawfik⁵, M. Roden^{6,7,8}, K. Opuni⁵

¹Queen Elizabeth University Hospital, Liver Unit, Birmingham, United Kingdom, ²National Institute for Health Research, Birmingham Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, ³Centre for Liver & Gastrointestinal Research, Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom, ⁴Saiseikai Suita Hospital, Department of Gastroenterology and Hepatology, Osaka, Japan, ⁵Novo Nordisk A/S, Søborg, Denmark, ⁶Division of Endocrinology and Diabetology, Medical Faculty, Heinrich-Heine University and University Hospital, Düsseldorf, Germany, ⁷Institute of Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Düsseldorf, Germany, ⁸German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Germany

Contact E-Mail Address: keep@novonordisk.com

Introduction: In the absence of any globally approved pharmacotherapy, current guidelines recommend lifestyle modification and weight loss in people with obesity and metabolic dysfunction-associated steatotic liver disease (MASLD), including metabolic dysfunction-associated steatohepatitis (MASH). Semaglutide, a glucagon-like peptide (GLP)-1 analogue indicated for management of body weight and type 2 diabetes (T2D), is under investigation in MASH. However, T2D seems to reduce GLP-1 analogue-mediated weight loss in people with overweight/obesity.

Aims & Methods: This study evaluated the impact of T2D and other cardiometabolic parameters on weight loss in randomised controlled trials of subcutaneous semaglutide in MASLD including MASH. Data were taken from adults in NCT03357380 (MASLD; semaglutide 0.4 mg or placebo once daily [OD] for 72 weeks), NCT02970942 (MASH and fibrosis stage [F] 1–3; semaglutide 0.1, 0.2 or 0.4 mg or placebo OD for 72 weeks) and NCT03987451 (MASH, F4 and compensated liver cirrhosis; semaglutide 2.4 mg or placebo once weekly [OW] for 48 weeks). This post-hoc analysis pooled data for semaglutide

(0.4 mg OD and 2.4 mg OW) and placebo, with weight changes grouped by baseline T2D status (previously diagnosed or glycated haemoglobin [HbA1c] $\geq 6.5\%$, pre-T2D [HbA1c $\geq 5.7 - < 6.5\%$] or no T2D [HbA1c $< 5.7\%$]). Mean on-treatment changes from baseline to 1 year were used to derive estimated treatment differences (ETDs) and 95% confidence intervals for semaglutide vs placebo. Impact of cardiometabolic factors including baseline fasting lipids, plasma glucose, diabetes duration and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) were assessed.

Results: Of the 300 participants included, 209 (70%) had T2D, 51 (17%) pre-T2D and 40 (13%) non-T2D. ETDs ranged from – 9.8 kg in the pre-T2D group to – 11.6 kg in the non-T2D group; there was no significant difference between the non-T2D vs pre-T2D, pre-T2D vs T2D and non-T2D vs T2D groups in terms of weight change (Table). Weight change was not influenced by known diabetes duration, or baseline HOMA-IR or glucose and lipid levels.

Conclusion: Unlike previously reported differences in weight change in people with and without T2D, the presence of T2D did not influence efficacious weight loss with semaglutide in individuals with MASLD including MASH.

Disclosure: MJA is a consultant for, and has received speaker fees from, Novo Nordisk and Norgine.

A-SS is an employee and shareholder of Novo Nordisk A/S.

MSP is an employee and shareholder of Novo Nordisk A/S.
MT is an employee of Novo Nordisk A/S.
MR is on advisory boards for and received speaker fees from Novo Nordisk.
TO has no interests to declare.

MP525

ANTIHYPERGLYCEMIC AGENTS AND METABOLIC ASSOCIATED FATTY LIVER DISEASE IN TYPE 2 DIABETES: FINDINGS FROM A PROSPECTIVE CROSS-SECTIONAL STUDY

L. Khayat¹, I. Jemni², L. Safer³

¹CHU FATTOUMA BOURGUIBA, Gastroenterology, Monastir, Tunisia,

²CHU FATTOUMA BOURGUIBA, Monastir, Tunisia, ³CHU FATTOUMA BOURGUIBA, Les Berges Du Lac, Tunisia

Contact E-Mail Address: Lobnakhayat@gmail.com

Introduction: Currently, there is no approved medication for the treatment of Metabolic Associated Fatty Liver Disease (MASLD). However, numerous clinical trials have examined the effect of antihyperglycemic agents on MASLD in type 2 diabetic (T2D) patients, given the close association between T2D and this hepatopathy, both of which are closely linked to insulin resistance.

Our aim is to evaluate and compare the therapeutic effects of different hypoglycemic agents in patients with MASLD and T2D.

Aims & Methods: This is a prospective cross-sectional study involving 200 T2D patients over a 6-month period. The presence of hepatic steatosis was confirmed by abdominal ultrasound and/or a Fatty Liver Index (FLI) score greater than 60 in 122 patients. Hepatic fibrosis was assessed using FibroScan in all patients with MASLD. Two comparative studies were conducted to identify the therapeutic effects of hypoglycemic medications on hepatic steatosis and significant fibrosis, defined by a LSM value ≥ 8 kPa.

Results: Patients were predominantly female (73.2%) with a median age of 59.76 ± 10 years. The duration of T2D, although longer in cases of steatosis, was not statistically significant. Glycemic control, assessed by fasting blood glucose and HbA1c levels, was less optimal in patients with MASLD, with an average HbA1c level of 8.98%, compared to patients without hepatic steatosis, who had an average HbA1c level of 8.74% ($p=0.002$). A similar trend was observed with fasting blood glucose levels (81.96% vs 73.07%), but it did not reach statistical significance.

Degenerative complications, regardless of their type, were comparable between the two groups.

The prescription of biguanides was associated with a reduced risk of hepatic steatosis ($p=0.05$), while insulin use was frequently observed in patients with steatosis, with a statistically significant correlation for long-acting human insulin and rapid-acting analogs (33.61% vs 19.23% in the absence of steatosis, $p=0.02$) and (4.92% vs 0% in the absence of steatosis, $p=0.05$) respectively. No other therapeutic modality, including different classes of oral antidiabetic agents, was correlated with the risk of steatosis.

The prescription of sulfonylureas and rapid-acting insulin analogs was associated with a higher risk of significant hepatic fibrosis, with p -values of 0.05 and 0.008 respectively. In contrast, the use of long-acting human insulin was less frequent in patients with significant fibrosis, with a statistical correlation of 0.03. No other treatment modality, including various types of oral antidiabetic agents, was associated with the risk of fibrosis.

Conclusion: The use of biguanides appears to reduce the risk of hepatic steatosis, while insulin therapy, particularly rapid-acting analogs, is associated with an increased risk of hepatic steatosis and fibrosis. These observations emphasize the importance of an individualized therapeutic approach to optimize the management of MASLD in type 2 diabetic patients. Further studies are needed to validate these associations

References: Tang W, Xu Q, Hong T, Tong G, Feng W, Shen S, et al. Comparative efficacy of anti-diabetic agents on nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized and non-randomized studies. *Diabetes Metabolism Res.* févr 2016;32(2):200-16.

Yan J, Yao B, Kuang H, Yang X, Huang Q, Hong T, et al. Liraglutide, Sitagliptin, and Insulin Glargine Added to Metformin: The Effect on Body Weight and Intrahepatic Lipid in Patients With Type 2 Diabetes Mellitus and Nonalcoholic Fatty Liver Disease. *Hepatology.* juin 2019;69(6):2414-26.

Disclosure: Nothing to disclose.

MP526

ASSESSMENT OF RESMETIROM EFFICACY (80 MG VS. 100 MG) STRATIFIED BY BASELINE BODY MASS INDEX AND WEIGHT IN PATIENTS FROM THE MAESTRO-NASH TRIAL

J. Schattenberg¹, R. Loomba², R. Taub³, D. Labriola³, S.A. Harrison⁴

¹Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Medizinische Klinik für Innere Medizin II, Homburg, Germany, ²University of California, MASLD Research Center, Division of Gastroenterology and Hepatology, San Diego, United States of America, ³Madrigal Pharmaceuticals, Inc., West Conshohocken, United States of America, ⁴Pinnacle Clinical Research,, San Antonio, United States of America

Contact E-Mail Address: Joern.schattenberg@uks.eu

Introduction: MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating the efficacy of resmetirom in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH) and fibrosis. 966 patients with biopsy confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo administered once daily. Histologic endpoints were assessed after 52 weeks. Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or ≥ 1 -stage reduction in fibrosis with no worsening of NAS (FI). Body weight is the major factor influencing exposure to resmetirom in patients with NASH/MASH.

Aims & Methods: This post-hoc analysis was performed to provide additional evidence of a relationship between resmetirom dose, baseline body weight and body mass index (BMI) and to assess the impact of baseline body weight and BMI on resmetirom response, we

stratified resmetirom efficacy data on the dual endpoints based on baseline patient body weight (≤ 100 and >100 kg) and BMI (≥ 35 and <35 kg/m²).

Results: For patients treated with resmetirom 80 mg who weighed ≤ 100 kg, the 30% PDFF response was 66.9%; and in patients with a Week 52 biopsy, 35.4% showed fibrosis improvement (FI) compared with 32% who showed no worsening of fibrosis (NR). In patients >100 kg, the 30% PDFF response was 56.7%; FI=22.5%; and NR=27%. For patients who received resmetirom 100 mg who were ≤ 100 kg, the 30% PDFF response was 71.7%; FI was 33.6% and NR was 35.8%; for patients >100 kg, PDFF=72.5%; FI=32.5%; NR=35.8%. Increases in FI were noted relative to placebo for patients who received resmetirom 80 mg (mITT population) who had BMI <35 : 13.0% (5.2, 20.8); NR=33.4% (14.2, 30.6); and in patients with BMI ≥ 35 : FI=7.0% (-0.7, 14.7); NR=9.8% (3.1, 16.6). Increases were also noted relative to placebo for patients who received 100 mg of resmetirom (mITT population) who had a BMI <35 : FI=11.8% (4.2, 19.4) NR=21.0% (13.4, 28.7); for patients with BMI ≥ 35 : FI=11.1% (3.4, 18.9); NR=20.0% (12.3, 27.7).

Conclusion: As shown in these stratified data, resmetirom 100 mg was consistently more effective than 80 mg in achievement of the dual primary endpoints in the sample of patients who had higher baseline body weight

and BMI. In patients with a lower BMI, there was no observed difference in efficacy between the 80 and 100 mg resmetirom doses.

Disclosure: Authors are investigators in the MAESTRO-NASH trial or employees of Madrigal Pharmaceuticals.

MP527

SEMAGLUTIDE IMPROVES CARDIOVASCULAR OUTCOMES IN PATIENTS WITH HIGH RISK FOR METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS – A SUBGROUP ANALYSIS FROM THE SELECT TRIAL

S. Meyhöfer^{1,2}, C. Bertrand³, C. Cercato⁴, H. Colhoun⁵, A.K. Duun-Henriksen⁶, I. Kliers⁶, M. Lincoff⁷, I. Lingvay⁸, M. Long^{6,9}, P. Newsome¹⁰, S. Nicholls¹¹, M. Quiroga Pelaez⁶, F. Santini¹², A.J. Sanyal¹³, S. Kahn¹⁴, **B. Ludvik**¹⁵

¹Clinical, Medical & Regulatory, Novo Nordisk Pharma GmbH, Mainz, Germany, Mainz, Germany, ²Department of Internal Medicine 1 - Endocrinology & Diabetes, University Medical Centre Lübeck, Lübeck, Germany, ³Nantes Université, CHU Nantes, CNRS, INSERM, l'institut du thorax, Nantes, France, Nantes, France, ⁴Obesity Unit, Department of Endocrinology, Hospital das Clínicas, University of São Paulo, São Paulo, Brazil, ⁵Institute of Genetics and Cancer, The University of Edinburgh, Edinburgh, United Kingdom, ⁶Novo Nordisk A/S, Copenhagen, Denmark, ⁷Department of Cardiovascular Medicine, Cleveland Clinic and Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, United States of America, ⁸Department of Internal Medicine/Endocrinology and Peter O'Donnell Jr. School of Public Health, University of Texas Southwestern Medical Center, Dallas, United States of America, ⁹Department of Medicine, Section of Gastroenterology, Boston University Chobanian & Avedisian School of Medicine, Boston, United States of America, ¹⁰Institute of Hepatology, King's College London and King's College Hospital, London, United Kingdom, ¹¹Victorian Heart Institute, Monash University, Melbourne, Australia, ¹²Obesity and Lipodystrophy Centre, University Hospital of Pisa, Pisa, Italy, ¹³Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University School of Medicine, Richmond, United States of America, ¹⁴Department of Medicine, VA Puget Sound Health Care System and University of Washington, Seattle, United States of America, ¹⁵1st Medical Department and Karl Landsteiner Institute for Obesity and Metabolic Disorders, Landstrasse Clinic, Vienna Healthcare Organization, Vienna, Austria

Contact E-Mail Address: bernhard.ludvik@gesundheitsverbund.at

Introduction: Cardiovascular (CV) risk is increased in people living with metabolic dysfunction-associated steatohepatitis (MASH). Although liver biopsy remains the gold standard to diagnose MASH, it is not practical to implement on a large scale. However, non-invasive tests, such as the Fibrosis-4 score (FIB-4), are useful for staging patients with fibrotic MASH and predict overall, CV- and liver-related mortality. In the SELECT CV outcome trial, which included patients with a body mass index ≥ 27.0 kg/m² and established CV disease but without diabetes, those treated with the glucagon-like peptide-1 receptor agonist semaglutide had a 20% CV risk reduction compared with those receiving placebo. We examined the CV benefits of semaglutide in a subgroup of participants at high risk of MASH as defined by FIB-4.

Aims & Methods: SELECT was a multicentre, randomised, double-blind, placebo-controlled, event-driven trial that enrolled 17,604 patients aged ≥ 45 years. Patients were randomly assigned in a 1:1 ratio to receive once-weekly subcutaneous semaglutide 2.4 mg or placebo in addition

to standard of care recommendations for CV disease prevention. This subgroup analysis for the primary composite endpoint of 3-point major adverse cardiovascular event (MACE; non-fatal myocardial infarction, non-fatal stroke, CV death) was performed for patients with increased MASH risk as indicated by FIB-4 ≥ 1.3 for patients aged < 65 years and FIB-4 ≥ 2.0 for patients aged ≥ 65 years, and for a second subgroup of patients of any age with FIB-4 > 2.67 , respectively. As identified by review of medical history and co-medication, patients with a cause of liver disease other than MASH were not included in this analysis.

Results: From the SELECT cohort, 3,665 patients (20.8% of all) aged < 65 years with FIB-4 ≥ 1.3 and aged ≥ 65 years with FIB-4 ≥ 2.0 were included in this analysis. The primary CV endpoint occurred in 140 of the 1,834 patients (7.6%) in the semaglutide group and in 176 of the 1,831 patients (9.6%) in the placebo group (hazard ratio [HR] 0.79; 95% confidence interval [CI] 0.63, 0.98; $p < 0.03$). In the subgroup of 475 patients with suspected MASH and advanced fibrosis (FIB-4 > 2.67 irrespective of age), there were 22 CV events in 235 patients treated with semaglutide 2.4 mg compared with 35 events in 240 placebo-treated patients, yielding an HR of 0.64 (95% CI 0.37, 1.08; $p = 0.10$).

Conclusion: In line with the primary analysis of the SELECT trial, use of semaglutide 2.4 mg in a subgroup of patients at high risk of fibrotic MASH as defined by FIB-4 produced a 21% reduction in MACE outcomes.

Disclosure: SM received consulting honoraria from Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, Daichii-Sankyo, esanum, Gilead, Ipsen, Lilly, Novartis, Novo Nordisk, Sandoz, Sanofi.

CB reports grants and personal fees from Amgen, Regeneron and Sanofi, and personal fees from Abbott, Akcea, AstraZeneca, Bristol Myers Squibb, Genfit, Gilead, Eli Lilly and Company, Merck (MSD) and Novo Nordisk.

CC served as advisory board for Novo Nordisk and reports having received research grants from Eli-Lilly, Novo Nordisk, Merck, Boehringer Ingelheim, Eurofarma, Fractyl, and EMS.

HC served on advisory panels for Novo Nordisk and Bayer; receiving research funding from Sanofi, Roche and IQVIA, and grants from Chief Scientist Office, Diabetes UK, European Commission, Juvenile Diabetes Research Foundation and Medical Research Council; serving on speaker's bureau for Novo Nordisk; and holding stock in Roche Pharmaceuticals and Bayer.

AKDH, IK and ML are employees and stockholders of Novo Nordisk A/S.

ML declares having received honoraria from Akebia, Alnylam, Ardelyx, Becton Dickinson, Brainstorm Cell, Eli Lilly, Endologix, FibroGen, GSK, Intarcia, Medtronic, Neovasc, Novo Nordisk, Provention Bio and ReCor, and for consulting activities and research funding to his institution from AbbVie, AstraZeneca, CSL Behring, Eli Lilly, Esperion and Novartis.

IL declares having received research grants from Boehringer Ingelheim, Merck, Mylan Pharmaceuticals Inc., Novo Nordisk, Pfizer and Sanofi US Services Inc., and has served as a consultant for AstraZeneca, Bayer Healthcare Pharmaceuticals Inc., Biomea Fusion, Boehringer Ingelheim, Carmot, Eli Lilly, Intarcia, Intercept Pharmaceuticals Inc., Janssen Global Services, LLC, Johnson & Johnson Medical Devices & Diagnostics Group - Latin America, L.L.C., MannKind Corporation, Merck, Novo Nordisk, Pfizer Inc., Sanofi US Services Inc., Shionogi Inc., Structure Therapeutics, Target pharma, Valeritas Inc., and Zealand Pharma A/S, and has received travel expenses from Boehringer Ingelheim, Eli Lilly and Company, Johnson & Johnson Medical Devices & Diagnostics Group - Latin America, L.L.C., Novo Nordisk, Sanofi US Services Inc. and Zealand Pharma A/S.

PN reports grants from Novo Nordisk, and has received consulting fees from Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, Bristol Myers Squibb (BMS), Pfizer, Sun Pharma, Madrigal and GSK. PNN also reports honoraria as a speaker for Novo Nordisk and AiCME; support for attending meetings for Novo Nordisk; and participation on an advisory board for Novo Nordisk, Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, BMS, Pfizer, Sun Pharma, Madrigal and GSK.

SN received research support from AstraZeneca, Amgen, Anthera, CSL Behring, Cerenis, Cyclarity, Eli Lilly, Esperion, Resverlogix, New Amsterdam Pharma, Novartis, InfraRedx and Sanofi-Regeneron and is also a consultant for Amgen, Akcea, AstraZeneca, Boehringer Ingelheim, CSL Behring, Eli Lilly, Esperion, Kowa, Merck, Takeda, Pfizer, Sanofi-Regeneron, Vaxxinity, CSL Sequiris, and Novo Nordisk.

MQP is an employee and stockholder of Novo Nordisk A/S.

FS worked as a consultant, participated in studies, and/or received travel funds from the following companies that are involved with obesity, lipodystrophy and/or diabetes: Aegerion/Amryt, Novo Nordisk, Lilly, Bruno Pharma, Boehringer, Pfizer, Bioltalia.

AJS consults for and advises Avant Santé and AstraZeneca. AJS also consults for and has received grants from Akero, BMS, Intercept, Eli Lilly, Madrigal and Novo Nordisk. AJS consults for and owns stock in Rivus, and also consults for AGED Diagnostics, Albireo, Alnylam, Altimmune, Boehringer Ingelheim, 89Bio, Echosens, Genentech, Gilead, GSK, HistoIndex, Mallinckrodt, Merck, NGM Bio, Novartis, PathAI, Pfizer, Poxel, Regeneron, Salix, Siemens, Surrozen, Takeda, Terns and Zydus. AJS owns stock in Durect, Exalenz, Genfit, Indalo, Inversago and Tiziana, and has received royalties from Elsevier and Wolters Kluwer.

SK, for the period over which SELECT was conducted, declares receiving advisory board/consulting fees from AltPep, Bayer, Boehringer Ingelheim, Casma Therapeutics, Eli Lilly, Intarcia, Merck, Novo Nordisk, Oramed, Pfizer and Third Rock Ventures.

MP528

SAFETY PROFILE OF SEMAGLUTIDE IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS: POST-HOC ANALYSIS OF DATA FROM TWO PHASE 2 STUDIES

L. Lotte Gluud¹, S.A. Harrison², M. Kurt Jara³, M. Skalskøi Kjær⁴, A. Lotfi⁴, K. Phonekeo⁴, M. Sundby Palte⁴, P.N. Newsome⁵, K. Opuni⁴

¹The Gastro Unit, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark, ²Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom, ³Novo Nordisk Inc., Plainsboro, United States of America, ⁴Novo Nordisk A/S, Søborg, Denmark,

⁵Centre for Liver and Gastrointestinal Research, Institute of Immunology and Inflammation, and National Institute for Health Research (NIHR) Birmingham Biomedical Research Centre, The Medical School, University of Birmingham, Birmingham, United Kingdom

Contact E-Mail Address: KEOP@novonordisk.com

Introduction: Semaglutide, a glucagon-like peptide-1 receptor analogue approved for treatment of type 2 diabetes (T2D) and overweight or obesity, is being investigated as a potential treatment for patients with metabolic dysfunction-associated steatohepatitis (MASH). Here, we present safety data from two phase 2 trials of subcutaneous semaglutide in patients with MASH with or without compensated cirrhosis.

Aims & Methods: This was a *post-hoc* analysis of two trials: NCT02970942 (320 patients with fibrosis stage F1–3 randomised 3:1 to once-daily semaglutide 0.1, 0.2 or 0.4 mg [n=80, 78 and 82] or placebo [n=80] for 72 weeks) and NCT03987451 (71 patients with compensated cirrhosis randomised 2:1 to once-weekly semaglutide 2.4 mg [n=47] or placebo [n=24] for 48 weeks). Patients received diet/lifestyle advice in both trials. Safety data were analysed descriptively.

Results: In NCT02970942, 18 patients discontinued semaglutide due to adverse events (AEs), with a similar proportion of patients discontinuing in the semaglutide 0.4 mg (5%; 4/82) and placebo arms (5%; 4/80). In NCT03987451, three patients from the semaglutide arm (6.4%) discontin-

ued due to AEs. In both trials, gastrointestinal (GI) disorders were the most common AEs with semaglutide (64–77% vs 33–45% with placebo); most GI AEs with semaglutide were non-serious and mild (55–71%) or moderate (22–36%). The proportion of patients with GI AEs with semaglutide in the MASH trials (63.8–76.9%) was similar to that seen in the weight management program STEP (63.5–82.8%), but higher than in the T2D development program SUSTAIN (34.4–52.0%).

There were no reported cases of acute pancreatitis. Overall, the proportion of patients with hepatic AEs (most frequently reported [in 0–3 patients per arm]: blood bilirubin increased, alanine transaminase increased, hepatic enzyme increased, international normalised ratio increased, transaminases increased, ascites) was 8–11% with semaglutide versus 4–14% with placebo. Few gallbladder-related AEs were reported. Four cholelithiasis events occurred in the semaglutide arms in the two trials; three were serious, of which two led to cholecystitis or cholangitis. All three serious events resolved with cholecystectomy. No cases of drug induced liver injury were reported. Throughout the trials (up to 72 weeks), three patients in the semaglutide group reported malignant neoplasms (breast cancer, endometrial adenocarcinoma and peripheral T-cell lymphoma) vs none with placebo; all events were judged as unlikely to be related to semaglutide.

Conclusion: Data from two phase 2 trials indicate that semaglutide is generally well tolerated in patients with MASH, including those with compensated cirrhosis. No new safety concerns were identified, and the safety profile was similar to that in patients with T2D and overweight/obesity. Data from the ongoing phase 3 trial (NCT04822181) will provide further knowledge about the safety of semaglutide in patients with MASH.

Disclosure: Funding: Novo Nordisk A/S.

Medical writing: Diana Marouco, PhD, of OPEN Health Communications, provided medical writing support, which was funded by Novo Nordisk A/S in accordance with Good Publication Practice (GPP) guidelines (www.ismpp.org/gpp-2022).

Lise Lotte Gluud is scientific advisor and consultant for Alexion, Becton Dickinson, Gilead, Norgine, Novo Nordisk, Pfizer, Sobi and Vingmed.

Philip N Newsome has received grants from Boehringer Ingelheim and Novo Nordisk and is a consultant for Astra Zeneca, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, Glaxo SmithKline, Intercept Pharmaceuticals, Novo Nordisk, Pfizer, Poxel Pharmaceuticals, Sagimet Terns and Theratechnologies.

Stephen A. Harrison is scientific advisor and consultant for Novo Nordisk. Mette Skalskøi Kjær is a full-time employee and shareholder of Novo Nordisk A/S.

Maximilian Kurt Jara, Amine Lotfi, Karina Phonekeo and Mads Sundby Palte are full-time employees of Novo Nordisk A/S.

Encore statement: This abstract was also presented at the European Association for the Study of the Liver (EASL) Congress, 21–24 June 2023 in Milan, Italy.

MP529

WITHDRAWN

MP530

MIR-21 ABLATION RESCUES SKELETAL MUSCLE FUNCTION IN A MOUSE MODEL OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

D.A. Fernandes¹, J. Rodrigues¹, M. Henrique¹, C.S. Palma¹, L. Izquierdo-Sanchez^{1,2,3}, J.M. Bañales^{3,4,2,5}, P.M. Rodrigues^{3,4,2}, R. Castro¹, A.L. Simão¹

¹iMed.Ulissboa - The Research Institute for Medicines, Liver Disease Diagnostic and Therapeutics, Lisbon, Portugal, ²Biogipuzkoa Health Research Institute, Liver and Gastrointestinal Diseases Area, San Sebastian, Spain, ³Carlos III National Institute of Health, Centre for the Study of Liver and Gastrointestinal Diseases (CIBERehd), Madrid, Spain, ⁴IKERBASQUE, Basque Foundation for Science, Bilbao, Spain, ⁵University of Navarra, Department of Biochemistry and Genetics, School of Sciences, Pamplona, Spain

Contact E-Mail Address: diogofernandes@gmail.com

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) presents as a complex multifactorial disease, in which dysregulation of metabolic homeostasis in the liver, as well as in distant organs, plays a substantial role. Recent evidence places skeletal muscle and the muscle-liver axis at the center of the MASLD pathogenic cascade. In fact, low muscle mass and muscle fat infiltration associates with increased risk of advanced MASLD, namely metabolic-associated steatohepatitis (MASH). In parallel, we showed that microRNA-21 (miR-21) is increased in the liver and skeletal muscle of MASH patients, with its abrogation ameliorating disease progression in vivo.

Aims & Methods: Here, we investigated the effects of miR-21 on muscle function in the context of experimental MASLD. *Mir21* whole body knock-out (KO); *Mir21*Alb-Cre KO (hepatocyte-specific KO) and wild-type (WT) mice were fed ad libitum with a high-fat/calorie diet (HFD) with high fructose/glucose corn syrup in drinking water for 20 weeks, or with a standard diet (SD), to recapitulate key, complementary metabolic features of human MASLD. Muscle phenotype and function were evaluated through grip strength and wheel running assays one week before sacrifice. In parallel, glucose tolerance test was also performed. At sacrifice, liver/muscle biopsies and total serum were collected for subsequent analyses.

Results: Both *Mir21*Alb-Cre KO and *Mir21* KO HFD-fed mice displayed significant lower weight increments throughout time, compared to WT HFD-fed mice. Moreover, all HFD-fed mice presented reduced voluntary wheel-running distance, except for *Mir21*KO HFD-fed mice, which showed SD-like wheel-running distance. *Mir21* KO mice also displayed a tendency to have grip strength levels higher than WT mice. Furthermore, both *Mir21*Alb-Cre KO and *Mir21* KO HFD-fed mice had AUC of glucose significantly lower than WT HFD-fed mice, and that was similar to WT SD-fed mice. In agreement, *Mir21* KO HFD-fed mice showed increased mRNA levels of MyoD and Pax7, two transcription factors responsible for the development and regeneration of skeletal muscle through the differentiation of myoblasts into myotubes, thereby counteracting the decrease observed in WT HFD-fed mice. Moreover, both *Mir21*Alb-Cre KO and *Mir21* KO HFD-fed mice had significantly decreased mRNA expression levels of *Mafbx* (atrofina-1), a ubiquitin ligase responsible for marking muscle cell proteins for degradation, when compared with WT mice.

Conclusion: Our results show that *Mir21* KO mice on a high-fat diet exhibit higher skeletal muscle function compared to their WT counterparts, further suggesting that the ablation of miR-21 contributes to muscle regeneration while inhibiting muscle degradation. These findings highlight the relevance of the muscle-liver axis in MASLD pathogenesis and, possibly, therapeutic targeting. (2022.08837.PTDC, FCT).

Disclosure: Nothing to disclose.

MP531

THE EFFECT OF SGLT2 INHIBITORS ON HEPATIC STEATOSIS DETECTED BY MRI-PDFF IN PATIENTS WITH TYPE 2 DM AND METABOLIC ASSOCIATED STEATOSIS LIVER DISEASE

M.A. Amin¹, N. Adly¹, H. Saad¹, M. Fawzi², H. Abdallah Elsheimy¹
¹Cairo University, Internal Medicine, Giza, Egypt, ²National liver institute, Radiology, Cairo, Egypt

Contact E-Mail Address: monasleman@hotmail.com

Introduction: Metabolic associated steatosis liver disease (MASLD) is the new nomenclature of non-alcoholic fatty liver diseases (NAFLD) which highlights its crucial effect on the cardiometabolic risk factors that lead to the development and progression to liver diseases. Recently SGLT2 inhibitors have been identified to reduce hepatic steatosis in patients with T2DM with MASLD

Aims & Methods: Our aim was to assess the effect of SGLT2 inhibitors on hepatic steatosis in patients with T2DM and MASLD, we enrolled 30 diabetic adults with hepatic steatosis on ultrasound confirmed and quantified by baseline magnetic resonance proton density fat fraction (MRI-PDFF) they started SGLT2 inhibitors added to the standard of care treatment for 6 months and assessment of the percentage change of hepatic steatosis with done by repeat MR-PDFF.

Results: There were statistically significant decreases in the mean body weight and BMI after treatment (86.7Kg, 33.313 Kg/m²) respectively compared to their levels before treatment (90.367kg, 35.144 Kg/m²) respectively, $P < 0.001$. Moreover, the mean serum fasting blood sugar and alanine transaminase decreased significantly after treatment (209.267, 22.633) compared to levels before treatment (220.566, 28.03) ($P = 0.017$, $P = 0.03$) respectively.

Regarding hepatic steatosis there was a statistically significant decrease in the mean MRI-PDFF measurement for hepatic steatosis after treatment (13.297 $\pm$ 7.15) compared to the mean levels before treatment (15.288 $\pm$ 8.72) with a mean difference (-1.9911, $P = 0.006$) of about 13.16% decrease of steatosis

Conclusion: Addition of SGLT2 inhibitors to the standard treatment in type 2 diabetic patients with MASLD could reduce the hepatic steatosis significantly after 6 months of treatment associated with decrease in body weight, BMI, fasting blood sugar. Thus, the therapeutic use of SGLT2 inhibitors is valuable in type 2 diabetic patients associated with MASLD

Disclosure: Nothing to disclose.

MP532

EFFECT OF SAROGLITAZAR ON METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE RELATED EARLY FIBROSIS AND STEATOSIS- A PROSPECTIVE, SINGLE CENTRE, REAL WORLD STUDY

R. Singh¹, G. Baweja²

¹J P Medical Centre, Gastroenterology, Chandigarh, India,

²J P Medical Centre, Chandigarh, India

Contact E-Mail Address: drrajdeep@gmail.com

Introduction: The new nomenclature of Non alcoholic fatty liver disease (NAFLD) as metabolic dysfunction-associated steatotic liver disease (MASLD), has an excellent concordance and 99% of individuals with NAFLD meet MASLD criteria. MASLD is becoming the most rapidly increasing contributor to the disease burden related to adverse liver outcomes, including cirrhosis, liver failure, and HCC. To curb this rising tide of MASLD (38.2% global prevalence), an early comprehensive and efficient management strategies are very crucial. Saroglitazar, a novel dual PPAR α/γ agonist operates through a multifaceted mechanism of action, targeting

key pathways driving the progression of MASLD, and have shown benefits at different stages of disease ranging from early to advance fibrosis and compensated cirrhosis.

Aims & Methods: We tried to evaluate the effect of Saroglitazar in MASLD associated early fibrosis, in a population where majority did not have diabetes and hypertension at baseline.

A prospective, real world study was conducted at a single centre setting in North India with 67 patients showing ultrasonographic evidence of fatty liver changes and dyslipidemia. Transient elastography was performed to reliably exclude advanced liver disease and treatment progression at 3 and 6 months after Saroglitazar 4 mg OD prescription. The Controlled Attenuation Parameter (CAP) and liver stiffness measurement (LSM) were assessed as primary treatment endpoints along with other markers of liver function and metabolic health as secondary efficacy parameters. Changes were evaluated using paired t-tests, from baseline to the 12 and 24 week mark. This rigorous methodology allowed for a comprehensive assessment of Saroglitazar's impact on both liver health and metabolic parameters.

Results: The 67 patients, who followed the study inclusion criteria and treated with Saroglitazar 4 mg OD, were evaluated on primary and secondary efficacy parameters. They had the mean age 50.34 ± 11.69 and mean body weight 82.1 ± 11.9 . Among them, 61.2% are males, 88.1% non diabetic, 89.6% non hypertensive, and 83.6% are not having any family history of NAFLD. 57.8% of them had F0-F1 fibrosis and 34.4% had F2 fibrosis at baseline. The mean reduction in CAP was 34.7 ($p < 0.001$) and 38.7 dB/m ($p < 0.001$) and mean reduction in LSM was 0.53 ($p = 0.043$) and 1.31 Kpa ($p < 0.001$), respectively at 12 and 24 weeks ($n = 32$). A significant and consistent reduction in AST, ALT, TG, LDL and HbA1c was also seen. No new safety signals were observed.

Parameters	Baseline Median (IQR)	12 Weeks (Mean change)	% Change	p value	24 Weeks (Mean change)	% change	p value
Weight (in Kg) (n=58)	80.5 (14.0)	-4.11	-5.01	0.0524	-5.2 (n=32)	-6.2	0.072
HbA1c (n=62)	6.6 (0.38)	-0.3	-4.54	<0.001	-0.55 (n=27)	-7.96	0.0014
LDL (n=62)	134 (65.0)	-35.37	-24.80	<0.001	-37.9 (n=19)	-24.6	<0.001
TG (n=58)	198.0 (82.0)	-59.91	-27.70	<0.001	----	----	----
SGOT (n=59)	52 (34.5)	-23.51	-38.04	<0.001	-27.7 (n=34)	-40.9	<0.001
SGPT (n=59)	58 (42.0)	-26.05	-39.12	<0.001	-39.5 (n=34)	-46.8	<0.001
CAP (n=64)	296.5 (34.3)	-34.67	-11.79	<0.001	-38.7 (n=32)	-13.2	<0.001
LSM (n=64)	7.4 (1.4)	-0.53	-6.85	0.0430	-1.31 (n=32)	-15.8	<0.001

Table: Absolute and percentage mean changes in Primary and secondary study parameters at 12 and 24 weeks.

Conclusion: Treatment with Saroglitazar 4 mg significantly reduces liver stiffness and steatosis, improves liver enzymes, and other metabolic parameters like serum glucose and lipid profile. It could be a crucial treatment component for an early comprehensive and efficient management of MASLD and helpful in curbing the rising tide of global MASLD burden. Saroglitazar treatment was safe.

References: 1. Targher G, Byrne CD, Tilg HMASLD: a systemic metabolic disorder with cardiovascular and malignant complications Gut 2024;73:691-702.

2. Lei Miao, Giovanni Targher, Christopher D. Byrne, Ying-Ying Cao, Ming-Hua Zheng, Current status and future trends of the global burden of MASLD, Trends in Endocrinology & Metabolism, 2024,ISSN 1043-2760, <https://doi.org/10.1016/j.tem.2024.02.007>.

3. Soto A, Spongberg C, Martinino A, Giovinnazzo F. Exploring the Multifaceted Landscape of MASLD: A Comprehensive Synthesis of Recent Studies, from Pathophysiology to Organoids and Beyond. Biomedicines. 2024; 12(2):397. <https://doi.org/10.3390/biomedicines12020397>

Disclosure: Nothing to disclose.

Managing bile duct disease

10:00-11:00 / Poster Stage 4

MP533

DOUBLE GUIDE-WIRE TECHNIQUE VERSUS TRANSPANCREATIC BILIARY SPHINCTEROTOMY FOR DIFFICULT BILIARY CANNULATION: A RANDOMIZED CONTROLLED TRIAL

K. Amalou¹, N. Benboudiaf¹, K. Saidani¹

¹HCA, Gastroenterology, Algiers, Algeria

Contact E-Mail Address: amalou_kh@yahoo.fr

Introduction: During endoscopic retrograde cholangiopancreatography (ERCP) for biliary indication, difficult biliary cannulation with an unintended access to the main pancreatic duct (PD) increases the risk of post-ERCP pancreatitis (PEP). Both double guidewire technique (DGW) and transpancreatic biliary sphincterotomy (TPBS) can be performed.

Aims & Methods: The purpose of this prospective, randomized, controlled trial is to compare the technical success and adverse events (AEs) rate of these techniques.

Method: Patients with native papilla and planned CBD cannulation were recruited from January 2021 and July 2023. An experienced endoscopist attempted CBD cannulation with wire-guided cannulation. If the procedure fulfilled the definition of difficult cannulation and a guidewire entered the pancreatic duct, randomization to either TPBS or to DGW was performed. If the randomized method failed, any method available was performed. The primary end point was the frequency of PEP and the secondary end points included successful cannulation with the randomized method.

Results: Overall, 1082 patients were recruited and 202 patients (56.3% males, mean age 64.2 years) were evaluated (98 DGW, 104 TPBS). Malignant biliary stricture was the most common ERCP indication (58.2%). The rate of success in deep biliary cannulation was significantly higher in the TPBS group (96.1%) compared to DGW(81.2%) at the first attempt ($p = 0.01$). No significant difference in AEs rate, particularly in PEP incidence was found between the two groups. PEP developed in 14/104 patients (13.5 %) in the TPBS group and 16/98patients (16.1 %) in the DGW group ($P = 0.71$). No difference existed in PEP severity between the groups.

Conclusion: In difficult biliary cannulation, TPBS demonstrated a higher success rate and similar safety profile compared with DGW. there was no difference in PEP rate between TPBS and DGW techniques. TPBS is a good alternative in cases of unintended PD cannulation of difficult cannulation.

Disclosure: Nothing to disclose.

MP534

ASSOCIATION BETWEEN FRAILTY AND 30-DAY OUTCOMES IN PATIENTS UNDERGOING ERCP

J. John¹, C.J. Foster², B. Blair³, L. Joo³, N. Dasu⁴, H. Suga³, M. Bakhit⁴, Y. Khalid⁵

¹Jefferson Health NJ, Internal Medicine, Cherry Hill, United States of America, ²Jefferson Health NJ, Interventional Gastroenterology, Cherry Hill, United States of America, ³Jefferson Health NJ, Gastroenterology, Cherry Hill, United States of America, ⁴Beth Israel Lahey Hospital and Medical Center, Interventional Endoscopy/Gastroenterology, Burlington, United States of America, ⁵Geisinger Health System/ Wright Center for GME, Scranton, United States of America

Contact E-Mail Address: nrdsu4@gmail.com

Introduction: Previous case reports and studies have shown frailty to be a risk factor for complications and poor outcomes following surgeries and endoscopic procedures. However, limited studies have examined the impact of frailty on endoscopic retrograde cholangiopancreatography (ERCP). Our study aims to compare patients undergoing ERCP with frailty to those without ERCP to understand the impact of frailty on ERCP better.

Aims & Methods: The NIS is a large, publicly available all-payer inpatient care database in the USA and was queried. We retrospectively analyzed the Nationwide Inpatient Sample (NIS) database for 2015-2019. Patients with a principal diagnosis of ERCP with and without frailty were identified using the ICD-10 codes. Multivariate regression analysis was used to calculate the odds ratios of in-hospital mortality, the average length of hospital stay (LOS), and hospital charges (TOTHC) using STATA 17 MP.

Results: Our study identified approximately 1,088,175 patients undergoing ERCP, of which 1,700 were frail.

On multivariate analysis, in patients undergoing ERCP and frailty as a co-morbidity, positive predictors of increased mortality were the following: sepsis (OR: 9.95, $p < 0.0001$, 95% CI: 2.95 - 16.95), acute kidney injury (AKI) (OR 5.63, $p < 0.0001$, CI 4.64 - 6.82), malnutrition (OR 3.28, $p < 0.0001$, CI 2.66 - 4.04), post-procedural bleeding (OR 2.85, $p < 0.0069$, CI 1.95 - 3.70), aspiration (OR 4.94, $p < 0.0001$, CI 2.59 - 6.80), congestive heart failure (CHF) (OR 1.48, $p < 0.001$, CI 1.19 - 1.86).

LOS was increased if patients had any of the following complications: sepsis (+2.86 days, $p < 0.0001$, 95% CI: 2.59 - 3.13), AKI (+3.44 days, $p < 0.0001$, 95% CI: 3.16 - 3.73), malnutrition (+6.44 days, $p < 0.0001$, CI 5.89 - 6.99), post-procedural bleeding (+4.99 days, $p < 0.0001$, CI 3.29 - 6.68), aspiration (+9.87 days, $p < 0.0001$, 95% CI 7.48 - 12.27), or CHF (+1.87 days, $p < 0.0001$, CI 1.53 - 2.22).

TOTHC were increased in patients who had the following complications: sepsis (\$46,978, $p < 0.0001$, CI \$41,364 - \$52,593), AKI (\$53,007, $p < 0.0001$, CI \$44,221 - \$61,793), malnutrition (\$85,454, $p < 0.0001$, \$64,515 - \$106,393), post-procedural bleeding (\$114,168, $p < 0.0001$, \$61,465 - \$166,871), aspiration (\$198,071, $p < 0.0001$, \$113,911 - \$282,230) or CHF (\$20,191, $p < 0.0001$, \$12,983 - \$27,398).

Conclusion: Based on our study results, those with ERCP who had a co-morbidity of frailty had increased mortality, LOS, and TOTHC with the following complications: sepsis, AKI, malnutrition, post-procedural bleeding, aspiration, and CHF. While frailty is not a contraindication to doing an ERCP, our study demonstrates that there must be close monitoring and preparation of these patients before ERCP to avoid complications because many complications significantly increase mortality. This is a high-risk patient population. Randomized trials will be required to further study the impact of frailty on ERCP.

Disclosure: Nothing to disclose.

MP535

INTEROBSERVER VARIABILITY IN LYMPH NODE EVALUATION WITH ENDOSCOPIC ULTRASONOGRAPHY IN PERIHILAR AND INTRAHEPATIC CHOLANGIOCARCINOMA

D.M. de Jong¹, D. Roosterman¹, M.J. Bruno¹, L.M. van Driel¹, W.J. Lammers¹

¹Erasmus MC University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: d.m.dejong@erasmusmc.nl

Introduction: Surgery is the only curative treatment option for patients with intrahepatic and perihilar cholangiocarcinoma (CCA) without metastatic disease in lymph nodes (LNs) and beyond. Therefore, pre-operative staging is crucial for appropriate treatment decision-making [1]. Endoscopic ultrasound (EUS) is a promising technique to assess LN preoperatively to find proof of metastatic disease in addition to regular scans [2-5]. Although specific LN characteristics have been recognized as important predictive factors for metastatic disease in hepatobiliary disease in general, inter-observer agreement is suggested to be poor. This study aims to assess interobserver agreement among endosonographers evaluating LN characteristics specifically in intrahepatic cholangiocarcinoma (iCCA) and perihilar cholangiocarcinoma (pCCA).

Aims & Methods: A cross-sectional survey study involving 145 endosonographers from the Netherlands as well as the POELH-trial (NCT05678218) was conducted. Participants reviewed 42 randomly selected de-identified EUS images of LNs in a web-based survey. The primary outcome of this study was to assess the interobserver agreement of LN characteristics among endosonographers. In addition, it was evaluated how concordant endosonographers judged LNs to be malignant. Interobserver agreement was evaluated using Light's kappa for the following LN characteristics: demarcation, shape, echogenicity, homogeneity, suspicion of malignancy and retrieving tissue. Subgroup analyses were performed for experts vs. non-experts (>1000 vs. <1000 EUS procedures), and experienced vs. non-experienced (15-30 years vs. 0-15 years). Diagnostic accuracy, sensitivity and specificity were determined based on a 2x2 table where presumed suspicious/not suspicious (based on EUS characteristics) was plotted against definite benign/malignant (EUS-fine needle aspiration/biopsy or surgical specimen pathology).

Results: Twenty-four endosonographers (16.6%) completed the survey. Participants showed fair to moderate agreement on EUS features with Light's kappa values of 0.24 for demarcation, 0.45 for shape, 0.38 for echogenicity, 0.52 for homogeneity, 0.36 for suspiciousness and 0.27 for performing FNA/B. Subgroup analyses suggest that experts and experienced endosonographers showed higher agreement on LN characteristics compared to non-experts and non-experienced endosonographers. The overall visual diagnostic accuracy for suspecting malignancy in LNs was 64%, ranging from 45 to 76%.

Conclusion: This study shows a fair to moderate inter-observer agreement of LN characteristics as well as a moderate rate of correct assessment of malignant LNs. among both expert and non-expert endosonographers. These findings support the justification to biopsy all LNs as carried out in the POELH trial (NCT05678218).

References: 1. Schulick RD. Criteria of unresectability and the decision-making process. HPB (Oxford). 2008;10(2):122-125.

2. Gleeson FC, Rajan E, Levy MJ, et al. EUS-guided FNA of regional lymph nodes in patients with unresectable hilar cholangiocarcinoma. Gastrointest Endosc. 2008;67(3):438-443.

3. Malikowski T, Levy MJ, Gleeson FC, et al. Endoscopic Ultrasound/Fine Needle Aspiration Is Effective for Lymph Node Staging in Patients With Cholangiocarcinoma. Hepatology. 2019;10.1002/hep.31077.

4. de Jong DM, den Hoed CM, Willemsen FEJA, et al. Impact of EUS in liver

transplantation workup for patients with unresectable perihilar cholangiocarcinoma. *Gastrointestinal Endoscopy*. 2024;99(4):548-556.

5. de Jong DM, van de Vondervoort S, Dwarkasing RS, et al. Endoscopic ultrasound in patients with resectable perihilar cholangiocarcinoma: impact on clinical decision-making. *Endosc Int Open*. 2023;11(2):E162-E168.

Disclosure: M.J. Bruno serves as a consultant and receives support for industry and investigator-initiated studies from Boston Scientific and Cook Medical and receives support for investigator-initiated studies from Pentax Medical, 3M, Interscope, and Mylan. The other authors declare that they have no conflicts of interest.

MP536

EUS-CHOLEDOCHODUODENOSTOMY VERSUS HEPATICOGASTROSTOMY COMBINED WITH EUS-GASTROENTEROSTOMY IN MALIGNANT DOUBLE OBSTRUCTION (CABRIOLET_PRO): A PROSPECTIVE COMPARATIVE STUDY

G. Vanella^{1,2}, R. Leone^{1,2}, F. Frigo^{1,2}, G. Dell'Anna^{1,2}, M. Reni^{2,3}, L. Aldrighetti^{2,4}, M. Falconi^{2,5}, G. Capurso^{1,2}, P.G. Arcidiacono^{1,2}

¹IRCCS San Raffaele Scientific Institute, Pancreatobiliary Endoscopy and Endosonography Division, Milan, Italy, ²Vita-Salute San Raffaele University, Milan, Italy, ³IRCCS San Raffaele Scientific Institute, Medical Oncology Department, Milan, Italy, ⁴IRCCS San Raffaele Scientific Institute, Hepatobiliary Surgery Unit, Milan, Italy, ⁵IRCCS San Raffaele Scientific Institute, Pancreatic Surgery Unit, Milan, Italy

Contact E-Mail Address: g.e.vanella@gmail.com

Introduction: Combined Biliary (BO) and Gastric Outlet Obstruction (GOO) represent a challenging clinical scenario. Previous retrospective experiences have demonstrated shorter Dysfunction-Free survival (DFS) of EUS-guided Choledochoduodenostomy (EUS-CDS) versus EUS-Hepatogastrostomy (EUS-HGS) in this scenario, but no prospective evidence is available.

Aims & Methods: All consecutive patients treated for double obstruction between 2021-2023 were eligible for inclusion upon receiving EUS-guided Gastroenterostomy (EUS-GE) for GOO and either EUS-CDS or EUS-HGS for BO according to endoscopist preference. DFS prospective surveillance started from the day the 2 procedures coexisted. Efficacy and safety were evaluated, with biliary dysfunctions as primary outcome and DFS using Kaplan-Meier estimates (with log-rank test) as primary measure.

Results: Twenty patients (75% with pancreatic cancer, 50% with metastatic disease) with EUS-GE were included (7 EUS-CDS and 13 EUS-HGS). No significant difference was detected at baseline. Technical success was 100% in both groups. EUS-CDS versus EUS-HGS showed similar clinical success (100% vs. 92.3%, $p=0.5$), a higher rate of post-procedural adverse events (42.9% vs. 7.7%, $p=0.067$, mostly related to severe/fatal cholangitis in the EUS-CDS group) and a higher rate of biliary dysfunctions during follow-up (57.1% vs. 16.7%, $p=0.074$).

DFS was significantly shorter in the EUS-CDS group (39 [12-66] vs. 267 [192-344] days, $p=0.0043$), with a 30-days probability of DFS of 53.6% vs. 100%, $HR=7.4$ [1.1-52.3].

Conclusion: In this prospective comparison of patients with malignant double obstruction undergoing EUS-GE, treating jaundice with EUS-CDS versus EUS-HGS resulted in reduced probability of survival without biliary events, with detection of severe/fatal cholangitis.

Disclosure: GV reports travel grants from Pentax Medical, Boston Scientific and Euromedical, and lecture fees by Boston Scientific.

All the other authors declare no conflict of interest.

MP537

ENDOSCOPIC ULTRASOUND (EUS)-GUIDED GALLBLADDER DRAINAGE VS CHOLEDOCODUODENOSTOMY IN DISTAL MALIGNANT BILIARY OBSTRUCTION

J. Lariño-Noia^{1,2}, Y. Dominguez-Novoa^{1,2}, M. Otero_iglesias^{1,2}, A. Rama-Fernandez^{1,2}, M. Loureiro-Veira^{1,2}, I. Meijide-Fernandez^{1,2}, M. Galego-Fernández^{1,2}, L. Diaz-Argüeso^{1,2}, R. Montoto-Meijide^{1,2}, X. Martinez-Seara³, J. Iglesias-García^{1,2}, J.E. Domínguez Muñoz^{2,1}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: joselarnoi@outlook.es

Introduction: EUS-guided biliary drainage, including choledoco-duodenostomy (EUS-CD) and transmural gallbladder drainage (EUS-GD), is an emerging alternative to ERCP for the treatment of malignant distal biliary obstruction (MBO).

Aims & Methods: The aim of our study was to compare the efficacy of EUS-CD and EUS-GD in the treatment of MBO. **METHODS:** We identified patients with MBO who underwent either EUS-CD or EUS-GD using a prospective EUS registry. The procedures were performed using Pentax linear echoendoscopes attached to a HITACHI system. Lumen Apposing Metal Stents (LAMS) of 6x8 mm or 8x8 mm were used for EUS-CD and 10x10 mm for EUS-GD. The primary outcome was clinical success, defined as at least a 50% reduction in serum bilirubin levels at 2 weeks. Secondary outcomes included adverse events (AE) and stent occlusion (SO) rates. Data are presented as median (range), frequencies and percentages. Statistical analysis was performed using chi-squared or Fisher's test and Student t test or U-Mann-Whitney test as appropriate.

Results: A total of 42 patients were included in the study (mean age 73.5 years [range 50-90 years], 24 males). Pancreatic adenocarcinoma was diagnosed in 81% of patients, of which 78.6% were unresectable. The clinical characteristics of the patients were similar between the two groups. The common bile duct (CBD) size was 16.7 mm (11.5-25 mm) in the EUS-CD group and 10.3 mm (6-13 mm) in the EUS-GD group. The clinical success rate was 92.6% for EUS-CD and 86.7% for EUS-GD ($p=0.06$). In five cases (four EUS-CD and one EUS-GD) a plastic pigtail stent (PPS) was initially placed through the LAMS. There were 6 AEs in the EUS-CD group (21.8%) (2 bleeding, 2 infections) and 5 in the EUS-GD group (33.4%) (1 perforation, 4 infections) ($p=0.45$). Two of the AEs resulted in death. The percentage of SO was 11.1% vs. 40% for EUS-CD and EUS-GD ($p=0.04$).

Conclusion: EUS-CD and EUS-GD are effective techniques for the treatment of MBO. Clinical success and SO rate tend to support EUS-CD over EUS-GD. However, it is important to note that the rate of severe AEs is not negligible. Prospective, comparative, randomised studies comparing these two techniques are needed.

Disclosure: Julio Iglesias-García: Advisor Fujifilm.

MP538

FEASIBILITY, CLINICAL SUCCESS AND SAFETY PROFILE OF INTRADUCTAL RADIOFREQUENCY ABLATION IN THE MANAGEMENT OF INOPERABLE PERIHILAR CHOLANGIOCARCINOMA PATIENTS - INTERIM ANALYSIS OF THE COMBO-RFA RANDOMIZED CLINICAL TRIAL

M. Birligea^{1,2}, C. Diaconu¹, A.M. Voiosu^{1,2}, A. Bengus¹, C. Popp¹, E. Dumea^{1,2}, B. Galateanu³, O. Ginghina^{4,2}, B.R. Mateescu^{1,2}, T.A. Voiosu^{1,2}

¹Colentina Clinical Hospital, Gastroenterology, Bucharest, Romania, ²"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, ³University of Bucharest, Faculty of biochemistry, Bucharest, Romania, ⁴Oncologic Institute of Bucharest, General Surgery, Bucharest, Romania

Contact E-Mail Address: mbirligea@gmail.com

Introduction: Intraductal radiofrequency ablation (RFA) has been proposed as an adjunctive therapeutic method for patients with inoperable perihilar cholangiocarcinoma (pCCA). Because there is limited data regarding the benefits of RFA, we aimed to evaluate the feasibility, efficacy and safety of a RFA based endoscopic palliation protocol.

Aims & Methods: Consecutive inoperable patients presenting biliary obstruction secondary to pCCA were evaluated according to the ongoing, single center, randomized clinical trial (NCT05563870). Native-papilla patients were randomized 1:1 to biliary drainage of the viable liver territories with plastic stents (control) or drainage plus RFA of the entire length of the tumor (active arm). Following index procedure, patients were scheduled for stent exchange and additional RFA treatment (active arm only) at 8-10 weeks intervals. Primary outcome was clinical efficacy defined as bilirubin levels < 3mg/dL at 4 weeks after index ERCP; secondary outcomes included overall survival and safety outcomes.

Results: Heretofore we included 25 patients (13 active arm) undergoing 72 procedures (37 with RFA) for a median follow-up of 3 months (range 2-15). Most patients received either 2 (10/25) or 3 (3/25) plastic stents at index ERCP and 23/25 of the patients reached effective drainage at 4 weeks, only 7 patients receiving undelayed oncologic treatment. There were 11 deaths during follow-up - 6 unrelated to the cholangiocarcinoma, 3 from therapy-related complications and 2 from cancer progression. 20/25 patients experienced at least 1 adverse event - including 15 severe biliary events with no significant differences between the study groups.

Conclusion: Extensive liver drainage followed by iterative stent exchange with intraductal RFA applications seems feasible and effective in the palliation of biliary obstruction in pCCA patients, with no additional risk related to RFA applications. However, adverse events related to biliary infection remain a frequent and life-threatening occurrence during follow-up in this patient population. Further data on the optimal timing and RFA application protocol is required.

Disclosure: No conflict of interest.

MP539

EVOLUTION OF ENDOSCOPIC MANAGEMENT FOR ANASTOMOTIC BILIARY STRICTURES AFTER LIVER TRANSPLANTATION: A TWO-DECADE RETROSPECTIVE STUDY

S.S. De Lucia¹, M. Birligea², T. Schepis³, V. Perri³, P. Familiari³, I. Boskoski³, R. Landi¹, V. Bove¹, M. Montalbano⁴, G.M. Ettorre⁵, N. Guglielmo⁵, A.W. Avolio⁶, S. Agnes⁶, G. Costamagna¹, C. Spada³, A. Tringali³

¹Catholic University, Centre for Endoscopic Research Therapeutics and Training (CERTT), Rome, Italy, ²Colentina Clinical Hospital and "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, ³Fondazione Policlinico Gemelli IRCCS, Digestive Endoscopy Unit, Rome, Italy, ⁴INMI L. Spallanzani, Department of Hepatology and Infective Diseases, Rome, Italy, ⁵Polo Ospedaliero Interaziendale Trapianti Azienda San Camillo and INMI L. Spallanzani, General Surgery and Transplantation Unit, Rome, Italy, ⁶Fondazione Policlinico Gemelli IRCCS, Transplantation Unit, Rome, Italy

Contact E-Mail Address: saras.delucia@gmail.com

Introduction: Biliary adverse events manifest in approximately 25% of liver transplant recipients. Among these, anastomotic biliary strictures (ABS) are the most prevalent, occurring in approximately 6%-12% of cases and can be successfully managed endoscopically.

Aims & Methods: Our study aims to present the evolution of method and long-term results of placing multiple plastic stents to treat ABS after orthotopic liver transplantation (OLT). All consecutive patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) for liver transplantation-related biliary complications at our Endoscopy Unit between July 1994 and September 2022 were retrospectively identified. The analysis focused only on the patients diagnosed with ABS undergoing dilatation by a progressively increasing number of plastic stents. Follow-up after stent removal was obtained by office visit, telephone contact with the patient or referring physician and extended to this year or until patient succumbed.

Results: Two hundred and ninety-five patients referred by 4 Liver Transplant Units underwent ERCP in need of endoscopic treatment for biliary complications after liver transplantation. However only 151 represented our intention-to-treat group with ABS. Out of these, 21 patients were excluded because of split liver transplantation, the use of metallic stents or incomplete endoscopic treatment. The mean age of the remaining 130 patients was 56 ± 9 years old and included 107 males and 23 females. We divided these patients in 2 groups according to similar timeframes, 28 ABS patients being treated before 2008 and 102 patients after 2008. In the first group the median number of stents was 4 (range 2-7), with a median of 3 ERCPs (range 2-5) per patient. Patients treated after 2008 received a median number of 6 stents (range 3-9) (p = .000, Mann-Whitney U), with a median of 4 ERCPs (range 3-7) (p = .002, Mann-Whitney U). The mean treatment duration was 15.3 ± 16.7 months in the first group and 14 ± 10 months in the second. Stricture recurrence was noted in 14.2% of patients treated before 2008 versus 4.9% after 2008. Nevertheless, the follow-up period was 10.6 ± 7.5 years for the first group and 4.7 ± 4 years in the second group.

Conclusion: The endoscopic treatment with multiple plastic stents proved to be effective for the majority of patients with ABS after OLT. In the last decade, the endoscopists shifted towards a more aggressive treatment strategy, with an increased number of stents and a reduced period between stent replacement procedures. This intensive approach seems also to underline a lower stricture recurrence rate however a longer follow-up period needs to be considered for the patients treated after 2008.

Disclosure: Nothing to disclose.

A. Mauro¹, G. Vanella², V.G. Mirante³, A. Fugazza⁴, M. Spadaccini⁵, C. Binda⁶, E. Forti⁷, R. Di Mitri⁸, D. Berretti⁹, H. Bertani¹⁰, P. Cantù¹¹, F. Desideri¹², L. Elli¹³, R. Grassia¹⁴, R. Leone¹⁵, A. Lisotti¹⁶, M. Manno¹⁷, S. Mazza¹⁸, A. Mussetto¹⁹, I.M. Parisi²⁰, A. Parodi²¹, E. Troncone²², G. Venezia²³, M. Delliponti²⁴, V. Ferretti²⁴, G. Gambini²⁴, P.G. Arcidiacono²⁵, M. Mutignani²⁶, R. Sassatelli²⁷, I. Tarantino²⁸, C. Fabbri²⁹, A. Anderloni³⁰

¹Fondazione IRCCS Ospedale San Matteo, Gastroenterology and Digestive Endoscopy Unit, Milano, Italy, ²IRCCS San Raffaele Institute, Pancreatobiliary Endoscopy and Endosonography Division, Milan, Italy, ³Azienda USL-IRCCS Di Reggio Emilia, Unit of Gastroenterology and Digestive Endoscopy, Reggio Emilia, Italy, ⁴Humanitas Research Hospital, Rozzano, Milan, Italy, ⁵Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano, Italy, ⁶Humanitas University, Biomedical Science, Rozzano, Italy, ⁷AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena Hospitals, Forlì, Italy, ⁸ASST Grande Ospedale Metropolitano Niguarda, Interventional Digestive Endoscopy, Milan, Italy, ⁹ARNAS Civico-Di Cristina-Benfratelli, Gastroenterology and Endoscopy Unit, Palermo, Italy, ¹⁰Academic Center of Udine, Department for Gastroenterology and Digestive Endoscopy, Udine, Italy, ¹¹Endoscopy Unit AOU di Modena, Modena, Italy, ¹²Fondazione IRCCS Istituto Nazionale Tumori, Diagnostic and Therapeutic Endoscopy Unit, Milan, Italy, ¹³Ospedale Di Bolzano, Gastroenterology, Bolzano, Italy, ¹⁴Fondazione IRCCS Ca' Granda Policlinico di Milano, Gastroenterologia ed Endoscopia Digestiva, Milano, Italy, ¹⁵A.O. "Istituti Ospitalieri Di Cremona", Digestive Endoscopy And Gastroenterology Unit, Cremona, Italy, ¹⁶IRCCS San Raffaele Institute, Milan, Italy, ¹⁷Hospital of Imola, University of Bologna, Gastroenterology Unit, Bologna, Italy, ¹⁸Azienda USL Hospital Carpi, Digestive Endoscopy, Carpi, Italy, ¹⁹San Matteo Hospital Foundation, University of Pavia, Gastroenterology and Digestive Endoscopy Unit, Milano, Italy, ²⁰Azienda AUSL Ravenna Dept. of Gastroenterology, Ravenna, Italy, ²¹San Matteo Hospital Foundation, University of Pavia, Gastroenterology and Digestive Endoscopy Unit, Pavia, Italy, ²²Lavagna Hospital, Gastroenterology and Digestive Endoscopy Unit, Lavagna, Italy, ²³Campus Biomedico, Roma, Italy, ²⁴Azienda Ospedaliera S.Croce e Carle, Gastroenterology Unit, Cuneo, Italy, ²⁵San Matteo Hospital Foundation, University of Pavia, Pavia, Italy, ²⁶Ospedale San Raffaele, PancreatoBiliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Center, Milan, Italy, ²⁷Ospedale Niguarda, Endoscopy, Milano, Italy, ²⁸Arcispedale Santa Maria Nuova, Reggio Emilia, Italy, ²⁹ISMETT, Gastroenterology, Palermo, Italy, ³⁰AUSL Romagna, Forlì-Cesena gastroenterology, Gastroenterology, Bologna, Italy, ³⁰Fondazione IRCCS Policlinico San Matteo, Gastroenterology and Digestive Endoscopy Unit, Pavia, Italy

Contact E-Mail Address: aurelio.mauro88@gmail.com

Introduction: Endoscopic biliary drainage (BD) in patients with altered anatomy is a challenging scenario reducing the chance of clinical success compared to standard anatomy. The choice between different BD approaches is still not standardized and relies on local availability and expertise.

Aims & Methods: Aim of this study was to explore the type and the number of endoscopic BD approach in patients with altered anatomy in different Italian centers. This was a retrospective multicenter cohort study

within the i-EUS network of biliopancreatic endoscopy. All adult patients with upper GI surgical altered anatomy who underwent endoscopic BD for any indication in the last 5 years were enrolled. Patients with Billroth-I or sleeve gastrectomy were excluded. Patients with duodenopancreasectomy were grouped with patients with BillrothII reconstruction for the statistical analysis. Fisher's exact test and Mann-Whitney test were used when appropriate.

Results:

		Billroth II (263)	Roux-en-Y (165)	p value
Age, years old		81 (72-87)	72 (57-78)	<0.001
Sex	Male	68.2%	57.9%	0.035
	Female	31.8%	42.1%	
Comorbidities	ASA I	4.8%	3.7%	ns
	ASA II	43.2%	43.5%	
	ASA III	46%	47.2%	
	ASA IV	6%	5.6%	
Surgery Indication	Gastric cancer	14.8%	39.6%	0.001
	Pancreatic cancer	14.8%	6.3%	
	Bariatric surgery	0.4%	9.4%	
	Peptic or other benign diseases	60.2%	15.7%	
	OLTx	0%	8.8%	
	Others	9.8%	20.1%	
BD Indication	Benign	75.2%	73.3%	ns
	Malignant	24.8%	26.7%	
Any previous attempt	No	83.1%	82%	ns
	Yes	16.9%	18%	
Endoscopic technique	Device-assisted enteroscopy ERCP	6%	38.8%	<0.001
	Duodenoscope or colonoscope/gastroscope	84.9%	28.7%	
	EUS-BD	7.5%	30.6%	
	Laparoscopic-assisted ERCP	1.6%	1.9%	
Clinical success	No	16.1%	21.1%	ns
	Yes	83.9%	78.9%	
Technical success	No	15.2%	20.5%	ns
	Yes	84.8%	79.5%	

21 centers participated in the study. All centers were equipped for interventional endoscopic ultrasound (EUS) whereas only 7 centers had also the availability of device-assisted enteroscopy (DAE). 428 patients were enrolled. Clinical and BD techniques characteristics of patients are described in table 1. Indication to BD was not different between patients with Billroth-II (B-II, N=263) or Roux-en-Y (RY, N=165) reconstructions. 16% of patients had at least one previous failed BD attempt. B-II anatomies were more frequently managed transpapillary with a duodenoscope or a forward viewing scope (85%), whereas in case of RY reconstruction BD approach was more heterogeneous. In 68% of RY cases endoscopic BD was performed with a luminal approach (in 43% of cases with standard scopes). In patients who underwent to EUS-BD, hepaticogastrostomy or antegrade stenting were performed in 74% of cases mostly for malignant indications (90%). Type of surgical reconstruction did not affect the clinical success (84% in BII and 79% in RY, p=ns). Interventional EUS demonstrated a higher clinical success compared to DAE (94% vs 73%, p=0.004). The total number of procedures to achieve clinical success was similar between B-II and RY patients. Patients who failed endoscopic BD for whom follow-up was available were managed by PTBD or surgery in 71% and 15% of cases respectively.

Conclusion: Endoscopic BD in altered anatomy has a sub-optimal clinical success compared to standard anatomy. A relevant proportion of patients requires more than one endoscopic attempt to achieve the clinical success. Despite the recent advent, interventional EUS is optioned in a significant proportion of patients and demonstrated a high efficacy in patients with surgically altered anatomy.

Disclosure: Nothing to disclose.

MP541

PREDICTORS OF REINTERVENTION AFTER ENDOSCOPIC
ULTRASOUND-GUIDED CHOLEDOCHODUODENOSTOMY FOR DISTAL
MALIGNANT BILIARY OBSTRUCTION

S. Giri¹, B. Shah², J. Narayan³, S. Sundaram⁴, R. Chavan⁵, V.R. Donapati⁶, S. Khare⁷, J. Varghese⁸, B. Mallick¹, A. Kale⁴
¹Kalinga Institute of Medical Sciences, Department of Gastroenterology and Hepatology, Bhubaneswar, India, ²Shree Narayana Hospital, Department of Gastroenterology, Raipur, India, ³IMS and SUM Hospital, Department of Gastroenterology, Bhubaneswar, India, ⁴Tata Memorial Hospital, Department of Gastroenterology, Mumbai, India, ⁵Ansh Clinic, Department of Gastroenterology, Ahmedabad, India, ⁶Yashoda Hospital, Department of Gastroenterology, Hyderabad, India, ⁷Sir Ganga Ram Hospital, Department of Gastroenterology and Hepatology, New Delhi, India, ⁸NS Hospital, Department of Gastroenterology and Hepatology, Kollam, India

Contact E-Mail Address: supg19167@gmail.com

Introduction: Endoscopic ultrasound (EUS)-guided choledochoduodenostomy (CDS) is primarily used for biliary drainage in patients with malignant distal biliary obstruction. A recent meta-analysis reported a reintervention rate of 15.8% with EUS-CDS. However, studies analyzing the factors associated with reintervention on follow-up after EUS-CDS are limited.

Aims & Methods: The study aimed to analyze the incidence and predictors of reintervention in patients with malignant biliary obstruction undergoing EUS-CDS. The present study is a retrospective analysis of data from eight tertiary care centers in India from January 2022 to January 2024. Patients aged 18-70 years with malignant distal biliary obstruction undergoing EUS-CDS, with a follow-up duration of more than eight weeks, were included. The study's primary outcome was reintervention, which was required in patients with failure of jaundice to improve due to stent migration or stent blockage during the follow-up, presenting as the worsening of jaundice, with or without cholangitis. The secondary outcomes included clinical success and adverse events. Multivariate analysis using the logistic regression model was used to identify the independent predictors of reintervention.

Results: A total of 140 patients underwent EUS-CDS, out of which 134 patients completed the 8-week follow-up. The median age of the patients was 54.5 (range: 22-90) years, with 53% (71/134) being male. The most common indication for EUS-CDS was inaccessible papilla (59/134, 44.0%), followed by failed cannulation (57/134, 42.5%). The technical success rate was 97.8% (131/134), with placement of self-expanding metal stent (SEMS) in 86.6% (116/134) and lumen-apposing metal stent in 11.2% (15/134). Coaxial double pigtail plastic stent was placed in 19.4% (26/134) cases. Periprocedural adverse events (AE) were seen in 6% (8/134) cases, with severe AE in 0.7% (1/134) cases. Clinical success was achieved in 93.9% (123/131) of the cases with successful stent placement. Over a median follow-up of 20 weeks, reintervention was required in 8.4% of the cases after a median interval of 11 weeks. All patients requiring reintervention could be managed successfully with endoscopic or percutaneous techniques. On multivariate analysis (Table 1), cholangitis at presentation [Odd ratio (OR) 6.26, 95% confidence interval (CI) 1.03-38.09; p =.046] and the absence of coaxial stent with concomitant duodenal stent (OR 7.41, 95% CI: 1.44-38.05; p=.016) were independent predictors of reintervention in the overall cohort. On subgroup analysis of patients undergoing EUS-CDS with SEMS, the absence of coaxial stent with concomitant duodenal stent (OR 10.15, 95% CI: 1.80-57.29; p=.009) was an independent predictor of reintervention.

Parameters	All patients (N = 131)		Only SEMS (N = 116)	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Inaccessible papilla	0.85 (0.21 – 3.50)	0.817	0.818 (0.19 – 3.41)	0.782
Cholangitis at presentation	6.26 (1.03 – 38.09)	0.046	5.71 (0.88 – 37.19)	0.068
Baseline bilirubin	1.05 (0.94 – 1.17)	0.386	1.07 (0.94 – 1.21)	0.287
CBD size > 15 mm	3.63 (0.36 – 36.26)	0.273	4.31 (0.37 – 49.82)	0.243
Absence of coaxial stent with concomitant duodenal stent	7.41 (1.44 – 38.05)	0.016	10.15 (1.80 – 57.29)	0.009

Conclusion: Reintervention on follow-up after EUS-CDS is required in around 8.4% of cases, with all cases being managed successfully. The absence of coaxial stent with concomitant duodenal stent was an independent predictor of reintervention in the overall cohort as well as in those undergoing EUS-CDS with SEMS.

Disclosure: Nothing to disclose.

MP542

DRAINAGE TECHNIQUES FOR DISTAL MALIGNANT BILIARY
OBSTRUCTION: A NETWORK META-ANALYSIS OF RANDOMIZED
CONTROLLED TRIALS

G. Lauri¹, L. Archibugi¹, P.G. Arcidiacono¹, A. Repici², C. Hassan², G. Capurso¹, A. Facciorusso³
¹San Raffaele Hospital, Pancreatico-Biliary Endoscopy and Endosonography Division, Milan, Italy, ²Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Pieve Emanuele MI, Italy, ³University of Foggia, Gastroenterology, Foggia, Italy

Contact E-Mail Address: gaetanolauri.94@gmail.com

Introduction: Distal malignant biliary obstruction (dMBO) presents a significant clinical challenge, necessitating effective drainage strategies to improve patient outcomes. Various drainage procedures have been utilized, encompassing percutaneous transhepatic biliary drainage (PTBD), endoscopic retrograde cholangiopancreatography (ERCP), or Endoscopic ultrasound-guided biliary drainage (EUS-BD) including EUS choledochoduodenostomy (EUS-CDS). However, the first-line optimal drainage approach remains debated. This network meta-analysis aims to compare the efficacy and safety of different drainage techniques for distal malignant biliary obstruction.

Aims & Methods: We conducted a systematic literature search of randomized control trials (RCTs) comparing different drainage methods as first-line treatment for distal malignant biliary obstruction. MEDLINE database was searched for relevant studies. Studies reporting outcomes such as technical success, clinical success, adverse events, and stent patency were included. Data were extracted, and a network meta-analysis was performed to compare the efficacy and safety of PTBD, ERCP and EUS-BD.

Results: Review of 649 studies yielded 7 RCTs meeting inclusion criteria for quantitative synthesis. These studies were published between 1987 and 2023, with 3 conducted in single centers and 4 at multiple centers, spanning all continents worldwide. They collectively involved 653 patients with distal malignant biliary obstruction. In terms of technical success, EUS-CDS demonstrates a significant superiority over ERCP (risk ratio [RR] 1.17, 95% CI 1.01–1.35), while no significant differences were observed in other comparisons. Furthermore, for clinical success, EUS-CDS outperforms alternative interventions (RR 1.12, 95% 1.02-1.24). Both in terms of technical and clinical success, EUS-CDS ranked the highest (surface under the cumulative ranking [SUCRA] score, respectively 0.90 and 0.86). Conse-

quently, EUS-CDS emerges as the premier treatment modality. Regarding adverse events, PTBD exhibits a pronounced inferiority compared to all other interventions (RR 2.74, 95% CI 1.25–6.02), whereas no statistically significant distinctions were noted among the remaining treatments.

Conclusion: In conclusion, our network meta-analysis suggests that EUS-CDS emerges as the most effective first-line intervention for distal malignant biliary obstruction, demonstrating superior technical and clinical success rates compared to ERCP. Furthermore, PTBD appears to carry a higher risk of adverse events compared to alternative treatments. These results underscore the importance of considering EUS-CDS as the preferred initial drainage approach in clinical practice, with potential implications for improving patient outcomes in this challenging condition.

Disclosure: Nothing to disclose.

H.pylori treatment: Part 2

10:00-11:00 / Poster Stage 5

MP543

USE OF FOURIER-TRANSFORM INFRARED SPECTROSCOPY (FT-IR) FOR MONITORING AN EXPERIMENTAL *HELICOBACTER PYLORI* INFECTION AND RELATED INFLAMMATORY RESPONSE IN GUINEA PIG MODEL

W. Gonciarz¹, P. Płoszaj¹, Ł. Lechowicz², M. Urbaniak³, W. Kaca², M. Chmiela¹

¹University of Lodz, Institute of Microbiology, Biotechnology and Immunology, Faculty of Biology and Environmental Protection, Department of Immunology and Infectious Biology, Łódź, Poland,

²Jan Kochanowski University, Institute of Biology, Faculty of Natural Sciences, Department of Mikcobiology, Kielce, Poland,

³Jan Kochanowski University, Institute of Chemistry, Faculty of Natural Sciences, Kielce, Poland

Contact E-Mail Address: weronika.gonciarz@biol.uni.lodz.pl

Introduction: Infections due to Gram-negative bacteria *Helicobacter pylori* (Hp) may result in humans in the development of-gastritis, gastric or duodenal ulcer, and even gastric cancer. Investigation of soluble biomarkers, correlating with Hp infection quantitatively is a promising tool for monitoring the course of infection and related inflammatory response.

Aims & Methods: Aim: The aim of this study was to determine, using an experimental model of Hp infection in guinea pigs, the specific characteristics of infrared spectra (IR) of sera from Hp infected (40) vs. uninfected (20) animals

Material and methods: We employed an *in vivo* guinea pig model after 28 days from inoculation with Hp, corresponding with chronic stage of infection. All animal experiments were carried out according to the agreement with the Local Ethics Committee for Anima Experiments, Medical University of Lodz Poland (Decision 58/ŁB45/2016).

Results: The Hp status in animals was confirmed by histological (the presence of Helicobacter-like organisms, inflammatory response) and molecular (detection of *ureC* and *cagA* sequences by polymerase chain reaction – PCR) examination of gastric tissue and by serological testing of Hp stool antigens and anti-Hp serum antibodies. The IR spectra were measured using a Fourier-transform (FT)-IR spectrometer Spectrum 400 (PerkinElmer) within the range of wavenumbers 3000–750 cm⁻¹ and converted to first derivative spectra. Ten wavenumbers correlated with Hp infection, based on the chi-square test, which were selected for a K-nearest neighbors (k-NN) algorithm. The wavenumbers correlating with infection were identified in the W2 and W3 windows associated mainly with proteins and in the W4 window related to nucleic acids and hydrocarbons. The k-NN for detection of Hp infection has been developed based on chemometric data. Using this model, animals were classified as infected with Hp with 100% specificity and 97% sensitivity.

Conclusion: To summarize, the IR spectroscopy and k-NN algorithm are useful for monitoring experimental Hp infection and related inflammatory response in guinea pig model and may be considered for application in humans.

Financing: The research was financially supported the National Science Center by the grant SONATA 18 “Assessment of the ability of *Mycobacterium bovis* BCG-onco bacilli to control the development of *Helicobacter pylori* infection”, UMO-2022/47/D/NZ7/01097.

Disclosure: Nothing to disclose.

MP544

THE ROLE OF *HELICOBACTER PYLORI* IN GASTRIC PATHOGENESIS IN COLOMBIA

K. Guzman¹, V. Pabon², A. Hidalgo^{3,4}, A. Pazos^{5,4}

¹Kevin Guzman, Centro de Estudios en Salud Universidad de Nariño (CESUN), San Juan de Pasto, Colombia, ²SENA, Regional Nariño, Semillero de investigación Ciencia para la Vida de Tecnoacademia Túquerres, Túquerres, Colombia, ³Universidad de Nariño, Departamento de Matemáticas, San Juan de Pasto, Colombia, ⁴Universidad de Nariño, Centro de Estudios en Salud Universidad de Nariño (CESUN), San Juan de Pasto, Colombia, ⁵Universidad de Nariño, Departamento de Biología, San Juan de Pasto, Colombia

Contact E-Mail Address: keving346@gmail.com

Introduction: In Colombia, the severity of lesions in gastric cancer pathogenesis varies depending on geographical location (Pacific coast: Low risk; Andean region: High risk), human ancestry, and *Helicobacter pylori* strain. *Helicobacter pylori*, the main causative agent of gastric adenocarcinoma, triggers a proinflammatory Th1 immune response and dysbiosis of the gastric microbiota upon infection by this microorganism.

Aims & Methods: Our research focuses on understanding how the ancestral origins of both *Helicobacter pylori* and humans in Colombia influence the composition and behavior of the gastric microbiota, particularly in relation to the immune response and genetic polymorphisms associated with gastric cancer pathogenesis. Through comprehensive genomic, microbiome, and immunological analyses in individuals with high and low risk of gastric cancer in Colombia.

Results: It was observed that in Colombian Pacific coast reveal a predominant presence of *Helicobacter pylori* strains hspWAfrica and hpAfrica1, aligning closely with the African ancestry of the human population. However, a new strain, hspColombia, is notably present among human individuals of European and Native American descent in the Andean region. Immune responses differ between these regions, with an anti-inflammatory Th2 response prevalent on the Pacific coast, contrasting with a Th1 response observed in the Andean region, linked to specific human polymorphisms such as Mutations *IL-1B-511TT* (72%) and *IL-10-1082AG* (79%). These mutations elevate the risk of developing precursor lesions of gastric cancer by 5.45 times (OR: 5.45; CI: 95%). Comparative analysis of the microbiota indicates a decline in species diversity with increasing severity of gastric lesions due to *Helicobacter pylori* infection. Among the most representative genera of the gastric microbiota were *Helicobacter*, *Pseudomonas*, *Methylobacterium*, *Streptococcus*, *Corynebacterium*, and *Staphylococcus*, as determined by U test (p < 0.001).

Conclusion: The interplay between geographical and genomic variations of *Helicobacter pylori* and humans in Colombia is pivotal in driving the progression of lesions in gastric pathogenesis. The immune response, marked by Th1 and Th2 profiles, exhibits regional disparities and is closely tied to human polymorphisms, notably mutations in the *IL-1B-511TT* and *IL-10-1082AG* genes, which heighten the risk of gastric cancer. *Helico-*

bacter pylori infection modulates the diversity of the gastric microbiota, culminating in a reduction in species diversity as gastric lesion severity escalates. This underscores the significance of maintaining the coevolutionary equilibrium between *Helicobacter pylori* and humans, as its disruption critically impacts dysbiosis in the gastric microbiota, exacerbates proinflammatory immune responses, and contributes to the progression of lesions in the pathogenesis of gastric cancer in Colombia.

References: Malfertheiner, P., Camargo, M. C., El-Omar, E., Liou, J. M., Peek, R., Schulz, C., & Suerbaum, S. (2023). *Helicobacter pylori* infection. *Nature reviews Disease primers*, 9(1), 19.

Disclosure: Nothing to disclose.

MP545

SEROPREVALENCE OF *HELICOBACTER PYLORI* IN 25-64 YRS AGED ADULT POPULATION IN LITHUANIA

L. Kupcinskas¹, V. Šaltenienė², J. Petkevicienė³, E. Ciupkeviciene³, L.V. Jonaitis¹, J. Kupcinskas¹

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³Lithuanian University of Health Sciences, Department of Preventive Medicine, Kaunas, Lithuania

Contact E-Mail Address: l.kupcinskas@gmail.com

Introduction: *Helicobacter pylori* (*H. pylori*) infection is the most prevalent type of bacterial infection in the world. Despite significant reduction of prevalence of infection globally, *H. pylori* remains the main cause of chronic gastritis and gastric cancer. Previous studies on *H. pylori* prevalence in Lithuania was performed on small size selective population groups.

Aims & Methods: The aim of the current study was to investigate *H. pylori* seroprevalence in general adult population. The study “Chronic Diseases and their Risk Factors in the Adult Population” involved Kaunas city residents aged 25-64 years, who were randomly selected from the Lithuanian population register lists. The study started in 2020, but was terminated after a quarantine due to COVID-19 infection. It was resumed in 2023. Invitations were sent by post to the selected population to come for a health check-up at Kaunas Clinics, Lithuanian University of Health Sciences Hospital. By 23 June 2023, 1074 people had taken part in the study. An ELISA (SERION ELISA® Classic *H. pylori* IgG, Serion, Germany) was used for the detection of human IgG antibodies to *H. pylori* in blood serum. All subjects were administered a questionnaire that included questions about factors possibly associated with the prevalence of *H. pylori* infection.

Results: *H. pylori* antibodies were tested in the blood serum of 1046 participants, representing 97.4% of the total population. The mean age was 47.2 ± 11.5 years. Standardization of the prevalence of *H. pylori* antibodies according to the age structure of the population of Kaunas city showed that the seroprevalence of *H. pylori* antibodies in males was 66.0%, in females - 59.3%, and in all the subjects - 61.8%. Seroprevalence increased with age in groups of 25-34, 35-44, 45-54, 55-64 yrs and was 49.2%, 62.5%, 71.1%; 67.5%, and 64%, respectively. *H. pylori* antibodies were significantly ($p < 0.05$) more common in subjects with secondary and lower education compared to those with higher and university education. Place of residence during childhood did not influence the prevalence of *H. pylori* infection. Subjects who consumed drinking tap water during childhood were less likely to be infected with *H. pylori*. The prevalence of *H. pylori* antibodies was found to be higher in homes without hot water when growing up. A survey of the participants revealed that previously 17.6 % of them were tested for *H. pylori*, infection was detected in 56.5 %. Medication to eradicate *H. pylori* was used by 132 (84.6%) subjects with a history of infection. In the current study, *H. pylori* antibodies were found in 58.3% of subjects

who had previously taken medication to eradicate the infection, but seroprevalence significantly ($p < 0.05$) decreased with increasing the time since eradication, especially in women.

Conclusion: *H. pylori* IgG antibodies have been detected in a large proportion of adult Kaunas residents aged 25-64 years. High seroprevalence of *H. pylori* in Lithuania (a country with moderate incidence of gastric cancer) raise a question on possible introducing of screen-and-test strategies for *H. pylori* to diminish gastric cancer incidence and mortality.

References:

Disclosure: Nothing to disclose.

MP546

IMMUNOHISTOLOGICAL ALTERATIONS POST *HELICOBACTER PYLORI* ERADICATION AND THEIR CONNECTION TO METACHRONOUS RECURRENCE IN GASTRIC CANCER

M.-J. Kim¹, J. Chun¹, Y.H. Youn¹, H. Park¹, J.H. Nahm², J.-H. Kim¹
¹Yonsei University College of Medicine, Internal medicine, Seoul, South Korea, ²Yonsei University College of Medicine, Pathology, Seoul, South Korea

Contact E-Mail Address: kmj0630@yuhs.ac

Introduction: *Helicobacter pylori* (*H. pylori*) infection is a significant contributing factor of gastric cancer. Despite advances in early detection and endoscopic resection, metachronous neoplasms still pose a risk. The impact of *H. pylori* eradication on preventing metachronous gastric cancer remains debated, with its underlying mechanisms unclear. This study aimed to investigate immunohistological changes in gastric mucosa after *H. pylori* eradication and identify mechanisms preventing metachronous recurrence.

Aims & Methods: Patients diagnosed with early gastric cancer and *H. pylori* infection, who underwent endoscopic resection, were included. 36 cases of metachronous neoplasms occurring after eradication (metachronous group) were compared to an equal number of controls matched for age, sex, atrophy, and metaplasia (control group). Histological features and immunohistochemical staining for T cell markers (CD3, CD4, CD8), and immune exhaustion markers (Foxp3, PD-L1) were evaluated.

Results: In the control group, chronic inflammation, neutrophil infiltration, glandular atrophy, and intestinal metaplasia in the gastric mucosa significantly improved following *H. pylori* eradication. However, in the metachronous recurrence group, improvement was observed only in chronic inflammation and neutrophil infiltration. CD3 cell counts increased in both groups after eradication, but CD8 and CD8/CD3 ratios saw an increase only in the control group. Additionally, the CD4/CD3 ratio and PD-L1/CD4 expression significantly decreased after *H. pylori* eradication in the control group but not in the metachronous group.

In the subgroup analysis of the metachronous cancer group, which consists of cases with recurrent lesion cancer, CD8, PD-L1, and PD-L1/CD4 ratios showed significant differences when compared to the control group.

Conclusion: *H. pylori* eradication may prevent metachronous recurrence in early gastric cancer by improving histologic inflammation and recovering immune system.

Disclosure: Nothing to disclose.

TRENDS IN THE PRESCRIPTION OF ERADICATION TREATMENTS AND THEIR EFFECTIVENESS IN NAÏVE PATIENTS OVER 11 YEARS (2013-2023) IN EUROPE: DATA FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, L. Jonaitis², Á. Pérez-Aísa³, B. Tepeš⁴, U. Mahmudov⁵, I. Voynovan⁶, S.J. Martínez-Domínguez⁷, L. Bujanda⁸, A.J. Lucendo⁹, L. Rodrigo¹⁰, L. Vologzanina¹¹, E. Mammadov¹², F. Lerang¹³, R. Bumane¹⁴, M. Denkovski¹⁵, G. Fadieienko¹⁶, I. Tatiana¹⁷, J. Tejedor-Tejada¹⁸, A. Garre¹, G. Babayeva¹², A. S. Sarsenbaeva¹⁹, J.M. Huguet²⁰, O. Zaytsev²¹, Q. Færid Vidadi Oğlu²², M. Pabón-Carrasco²³, M. Perona²⁴, S. Alekseenko²⁵, M. Castro-Fernández²³, Ó. Núñez²⁶, I. Bakulin²⁷, M. Areia²⁸, P. Bogomolov²⁹, J. Barrio³⁰, N. Brglez Jurecic¹⁵, A. Moreno Loro³¹, B.J. Gómez Rodríguez³², R. Abdulkhakov³³, J. Kupcinskas², A. Gasbarrini³⁴, L. Hernández³⁵, D.S. Bordin³⁶, M. Leja¹⁴, O. Gridnyev¹⁶, R. Marcos-Pinto³⁷, A. Cano-Català³⁸, P. Parra¹, L. Moreira³⁹, F. Megraud⁴⁰, C. O'Morain⁴¹, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania, ³Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ⁴Department of Gastroenterology, DC Rogaska, Rogaska Slatina, Slovenia, ⁵Modern Hospital, Baku, Azerbaijan, ⁶A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ⁷Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁸Department of Gastroenterology, Biodonostia Health Research Institute, Department of Medicine, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ⁹Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ¹⁰Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ¹¹Gastrocentr, Perm, Russian Federation, ¹²Department of Internal Medicine and Gastroenterology, Azerbaijan State Advanced Training Institute for Doctors named by A. Aliyev, Baku, Azerbaijan, ¹³Østfold Hospital Trust, Grålum, Norway, ¹⁴Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia, ¹⁵Interni oddelek, Diagnostic Centre, Bled, Slovenia, ¹⁶Departments the Division for the Study of the Digestive diseases and its Comorbidity with Noncommunicable Diseases, Government Institution L.T. Malaya Therapy National Institute of NAMS of Ukraine, Kharkiv, Ukraine, ¹⁷Department of Gastroenterology, SM-clinic, Saint-Petersburg, Russian Federation, ¹⁸Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ¹⁹Department of Gastroenterology, Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁰Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ²¹First Clinical Medical Centre, Kovrov, Russian Federation, ²²National Oncology Centre, Baku, Azerbaijan, ²³Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ²⁴Department of

Gastroenterology, Hospital Quirón Marbella, Marbella, Spain, ²⁵Far Eastern State Medical University, Khabarovsk, Russian Federation, ²⁶Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ²⁷I. I. Mechnikov North-Western State Medical University, Saint-Petersburg, Russian Federation, ²⁸Department of Gastroenterology, Portuguese Oncology Institute of Coimbra, Faculty of Medicine of the University of Porto (FMUP), Center for Health Technology and Services Research (CINTESIS), Coimbra, Portugal, ²⁹Universal Clinic Private Medical Center, Moscow, Russian Federation, ³⁰Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ³¹Department of Gastroenterology, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ³²Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ³³Department of Hospital Medicine, Kazan State Medical University, Kazan, Russian Federation, ³⁴Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ³⁵Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁶Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow clinical scientific center, Department of outpatient therapy and family medicine, Tver State Medical University, Department of propaedeutic of internal diseases and gastroenterology, Russian University of Medicine, Moscow, Russian Federation, ³⁷Gastroenterology Department, Centro Hospitalar do Porto, Universidade do Porto, Instituto De Ciências Biomédicas de Abel Salazar, Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal, ³⁸Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ³⁹Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ⁴⁰INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴¹School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: The infection by *H. pylori* can be successfully treated and eradicated if the recommendations from consensus documents are followed correctly. It is essential to continuously assess the applicability of these recommendations to confirm what happens in clinical practice.

Aims & Methods: Multicentre, prospective registry evaluating the decisions and outcomes of *Helicobacter pylori* management by European gastroenterologists. Data were registered at AEG-REDCap e-CRF until December 2023. Modified intention-to-treat (mITT), and time trend analyses were performed.

Results: Overall, 58,334 (82%) were first-line empirical prescriptions. The total number of different therapeutic regimens prescribed exceeded 100. Triple therapy prescriptions decreased from approximately 60% during 2013/15 to 30% in 2023; likewise, non-bismuth concomitant therapy use decreased from 21% in 2013/15 to 15% in 2021/23, while three-in-one single-capsule increased from 0.3% in 2013/2015 to 20% in 2021/23. An increase in the average duration of treatments (from 9.8 days to 12.4 days) in 2013-2023 was identified, as well as in the use of standard/high-dose of PPIs (increasing from 36% to 60%) in 2013-2023. There was a ~10% overall improvement in first-line mITT overall effectiveness from 86% to 94% in 11 years of evolution, both globally and in each geographic region (Table).

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Treatment											
Quadruple-C+A+B	2.3%	3.2%	6.2%	18.5%	11.8%	24.8%	10.9%	13.1%	15.1%	14.0%	15.3%
Single-capsule*	0.2%	0.2%	0.5%	14.2%	21.0%	16.7%	20.7%	19.2%	18.6%	20.9%	20.4%
Quadruple-M+Tc+B	1.9%	1.7%	0.4%	0.2%	0.3%	0.6%	1.2%	1.3%	1.2%	3.1%	2.1%
Concomitant-C+A+M/T	19.4%	18.8%	23.9%	19.5%	17.8%	8.6%	11.8%	13.9%	14.6%	13.6%	16.6%
Sequential-C+A+M/T	15.3%	9.1%	6.8%	1.8%	7.6%	7.1%	5.7%	3.5%	3.3%	3.5%	1.4%
Triple-A+L	2.1%	2.1%	2.9%	1.7%	0.6%	0.6%	1.2%	1.2%	1.4%	2.4%	3.4%
Triple-A+M	4.9%	4.3%	3.2%	2.9%	2.8%	0.5%	1.6%	1.0%	1.5%	2.6%	1.6%
Triple-C+M	3.2%	5.5%	7.2%	5.4%	1.2%	0.8%	1.1%	6.2%	3.8%	3.8%	2.9%
Triple-C+A	45.9%	50.3%	41.6%	29.0%	30.3%	30.3%	35.8%	31.9%	32.0%	26.4%	23.1%
Therapy length											
7 days	27.6%	26.0%	22.0%	15.4%	7.2%	2.0%	2.7%	3.2%	2.8%	8.9%	3.6%
10 days	56.8%	55.8%	59.7%	50.0%	53.1%	46.4%	41.0%	38.2%	42.6%	43.7%	35.1%
14 days	15.7%	18.2%	18.3%	34.5%	39.7%	51.6%	56.3%	58.6%	54.6%	47.5%	61.3%
PPI doses**											
Low	64.4%	54.6%	45.6%	39.1%	43.8%	30.9%	34.6%	44.7%	41.5%	33.7%	40.4%
Standard	15.8%	22.9%	24.3%	22.6%	22.7%	37.0%	27.9%	23.5%	26.2%	36.0%	32.3%
High	19.9%	22.5%	30.1%	38.3%	33.5%	32.1%	37.5%	31.7%	32.3%	30.3%	27.3%
Overall effectiveness											
Eradication rate (mITT)	86.0%	85.9%	86.3%	87.7%	88.2%	90.3%	89.0%	89.6%	90.9%	91.9%	93.9%
Effectiveness depending on geographical region											
East	91.5%	80.5%	85.2%	82.9%	81.4%	91.3%	89.5%	92.0%	92.9%	91.5%	93.1%
East-Centre	87.4%	84.9%	85.2%	84.7%	86.1%	88.2%	89.6%	93.1%	91.5%	91.7%	95.4%
South-West	84.2%	86.8%	86.0%	89.8%	91.3%	90.6%	88.4%	86.1%	91.0%	93.5%	95.3%
West-Centre	88.7%	92.1%	92.9%	94.3%	89.1%	92.4%	91.4%	89.9%	88.3%	93.8%	92.5%
North	83.8%	84.4%	85.6%	86.5%	86.6%	77.5%	83.0%	82.5%	82.1%	83.7%	81.9%

PPI: proton pump inhibitor; mITT: modified intention-to-treat; A – amoxicillin; C – clarithromycin; M – metronidazole; T – tinidazole; L – levofloxacin B; – bismuth salts; Tc – tetracycline; East – Ukraine, Serbia, Bulgaria, Turkey, Russia, Romania, Albania, North Macedonia; East-Centre – Croatia, Poland, Hungary, Latvia, Lithuania, Greece, Slovenia, Czech Rep, Azerbaijan, Slovakia, Malta; South-West – Portugal, Spain; West-Centre – France, Austria, Belgium, Germany, Italy; North – United Kingdom, Finland, The Netherlands, Ireland, Israel, Norway, Switzerland, Sweden, Denmark; *Three-in-one single-capsule containing metronidazole, tetracycline and bismuth; **Low dose PPI – 4.5 to 27 mg omeprazole equivalents. b.i.d.; standard dose PPI – 32 to 40 mg omeprazole equivalents. b.i.d.; high dose PPI – 54 to 128 mg omeprazole equivalents. b.i.d.

Table. Prescriptions and effectiveness trends of first-line empirical treatments in Europe in the period 2013–2023.

Conclusion: European gastroenterological practice is constantly adapting to the newest published evidence and recommendations (reducing the use of triple therapies and increasing both the duration of treatment and the dose of PPIs), with a subsequent progressive improvement in overall effectiveness.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

MP548

EFFICACY OF TEGOPRAZAN-CONTAINING SEQUENTIAL THERAPY COMPARED TO PROTON PUMP INHIBITOR-BASED ERADICATION - IN A REGION WITH HIGH ANTIMICROBIAL RESISTANCE

N. Kim^{1,2}, J.W. Lee³, S. Kim¹, Y. Choi¹, D.-H. Lee^{1,2}

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea, ³Samsung Changwon Hospital, Department of Internal Medicine, Changwon-si, South Korea

Contact E-Mail Address: nakim@snubh.org

Introduction: Eradication treatment containing potassium-competitive acid blocker has shown acceptable eradication efficacy. In regions such as Korea, where the prevalence of antimicrobial resistance is high, alternative combinations of antibiotics such as sequential or concomitant therapy are needed.

Aims & Methods: This study compared the outcome of sequential therapy containing tegoprazan, a new potassium-competitive acid blocker, with the conventional esomeprazole-containing sequential therapy. Patients with *H. pylori* infection were consecutively recruited. Patients were allocated to esomeprazole-containing sequential therapy group, as conventional proton pump inhibitor, or tegoprazan-containing sequential therapy. Sequential therapy consisted of esomeprazole (40 mg) or tegoprazan

(50 mg) plus amoxicillin (1000 mg) twice a day for initial 5 days, and then esomeprazole (40 mg) or tegoprazan (50 mg) with clarithromycin (500 mg) and metronidazole (500 mg) twice a day for the remaining 5 days. Eradication rate, medication compliance, and adverse events were gathered.

Results: A total of 406 patients with *H. pylori* were receive treatment and 406 patients analyzed by per-protocol (Table). The eradication rate by intention-to-treat and per-protocol was 83.8% (95% CI 78.7 – 88.9) for esomeprazole-containing sequential, and 87.1% (95% CI 82.5 – 91.8) for tegoprazan-containing sequential, with no statistical significance ($p = 0.399$). There was also no statistical difference in treatment compliance between the two groups. In tegoprazan-containing sequential, nausea was more prevalent (23.3%, 27/202), which was statistically higher than esomeprazole-containing sequential (14.2%, 29/204) ($p = 0.022$).

	Esomeprazole-containing sequential (n=204) (%)	Tegoprazan-containing sequential (n=202) (%)	p
Age (mean±SD)	61.7±11.6	61.3±11.6	0.731
Sex	Male	94 (46.1)	0.160
	Female	110 (53.9)	
BMI (kg/m ²) (mean±SD)	23.7±3.7	23.6±3.3	0.849
Diagnosis	Gastritis	144 (70.6)	0.080
	Peptic ulcer disease	5 (2.5)	
	Benign neoplasm of UGI tract	33 (16.2)	
	Malignant neoplasm of UGI tract	22 (10.8)	
		15 (7.4)	

SD, standard deviation; BMI, body mass index; UGI, upper gastrointestinal.

Conclusion: Tegoprazan-containing 10-day sequential eradication therapy seems to provide adequate eradication efficacy compared to conventional proton pump inhibitor-containing treatment, even in a region with high antimicrobial resistance like Korea.

Disclosure: Nothing to disclose.

MP549

EFFECTIVENESS OF SINGLE-CAPSULE BISMUTH QUADRUPLE RE-TREATMENT AFTER PREVIOUS FAILURE WITH THE SAME THERAPY: RESULTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, M. Pabón-Carrasco², M. Castro-Fernández², S.J. Martínez-Domínguez³, A. Keco-Huerga², A.J. Lucendo⁴, E. Iyo⁵, G. Kamto⁶, T. Matysiak-Budnik⁷, I. Ortiz-Polo⁸, L. Rodrigo⁹, B.J. Gómez Rodríguez¹⁰, S. Montori¹¹, E. Alfaro³, K. Priadko⁷, M. Suárez Matías¹², S. Gil Rojas¹², M. Pavoni¹³, G. Fiorini¹⁴, R. Rosania¹⁵, R. Vasapolli¹⁶, A. Garre¹, Á. Pérez-Aísa¹⁷, J. Barrio¹⁸, M. Soledad Marcos¹⁹, R. Pajares Villarroya²⁰, J.X. Segarra Ortega²¹, A. Moreno Loro²², G.O. Patrón Román²³, D. Burgos-Santamaría²⁴, V. Flores²⁵, A. Gasbarrini²⁶, M. Romano²⁷, A. G. Gravina²⁸, P. Szredzki²⁹, M. Doulberis³⁰, M. Sánchez Alonso³¹, J.M. Huguet³², J. Tejedor-Tejada³³, E. Albéniz¹¹, M. Jiménez-Moreno³⁴, L. Hernández³⁴, W. Marlicz³⁵, M. Venerito¹⁵, A. Cano-Català³⁶, P. Parra¹, L. Moreira³⁷, F. Megraud³⁸, C. O'Morain³⁹, J. P. Gisbert¹, on behalf of the Hp-EuReg Investigators

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ³Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁴Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ⁵Department of Gastroenterology, Hospital Comarcal de Inca, Inca, Spain, ⁶Hepatic Medical, Private Medical Center, Krakow, Poland, ⁷Hepato-Gastroenterology & Digestive Oncology Unit, University Hospital of Nantes, Nantes, France, ⁸Department of Gastroenterology, Hospital Universitario y Politécnico La Fe, Valencia, Spain, ⁹Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ¹⁰Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ¹¹Department of Gastroenterology, Hospital Universitario de Navarra, Navarrabiomed, Universidad Pública de Navarra, Pamplona, Spain, ¹²Department of Gastroenterology, Hospital Virgen de la Luz, Cuenca, Spain, ¹³Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ¹⁴IRCCS Azienda Ospedaliero-Universitaria di Bologna, Hypertension and Cardiovascular Risk Research Center, Medical and Surgical Sciences Department, Alma Mater Studiorum University of Bologna, Cardiovascular Medicine Unit, Heart, Chest and Vascular Department, Bologna, Italy, ¹⁵Department of Gastroenterology, Hepatology and Infectious Diseases, Otto von Guericke University Hospital, Magdeburg, Germany, ¹⁶Medical Department 2, University Hospital LMU Munich, Munich, Germany, ¹⁷Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ¹⁸Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ¹⁹Department of Gastroenterology, Hospital 12 de Octubre, Madrid, Spain, ²⁰Department of Gastroenterology, Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain, ²¹Department of

Gastroenterology, Hospital Universitario de Salamanca, Grupo de Investigación Salmantino en Aparato Digestivo (GISAD), Instituto de Investigación Biomédica de Salamanca, Salamanca, Spain, ²²Department of Gastroenterology, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ²³Department of Gastroenterology, Hospital Parque Llevant, Manacor, Spain, ²⁴Department of Gastroenterology and Hepatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, ²⁵Department of Gastroenterology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ²⁶Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ²⁷Department of Gastroenterology and Endoscopy, Department of Precision Medicine, Università Vanvitelli, Napoli, Italy, ²⁸Department of Hepato-Gastroenterology, University of study of Campania "L. Vanvitelli", Napoli, Italy, ²⁹Department of Gastroenterology, Hospital John Paul II City Hospital, Rzeszow, Poland, ³⁰Department of Gastroenterology, Kantonsspital Aarau, Aarau, Switzerland, ³¹Department of Gastroenterology, Hospital Universitario Santa Bárbara, Puertollano, Spain, ³²Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ³³Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ³⁴Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁵Department of Gastroenterology, Pomeranian Medical University in Szczecin, The Centre for Digestive Diseases, Endoklinika, Szczecin, Poland, ³⁶Gastrointestinal Oncology, Endoscopy and Surgery (GOES) Research Group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ³⁷Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ³⁸INSERM U 1312, Université de Bordeaux, Bordeaux, France, ³⁹School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: The effectiveness of *H. pylori* treatment decreases as eradication failures accumulate; however, bismuth quadruple therapy with the single-capsule has shown optimal results not only in first but also in second and subsequent lines of treatment, even in patients with dual clarithromycin and metronidazole resistant strains.

Aims & Methods: To evaluate the use and effectiveness of the single-capsule bismuth quadruple therapy when empirically prescribed as retreatment, despite one or multiple previous eradication failures with the same treatment.

All patients registered at e-CRF AEG-REDCap as part of the European Registry on *H. pylori* management (Hp-EuReg) from 2013 to 2023, who had received single-capsule therapy in at least 2 different treatment lines (not necessarily consecutive), were analyzed.

Results: Out of 2,579 patients treated with the single-capsule from 2nd to 6th rescue treatment line, 101 cases received again the same single-capsule therapy at least in 2 different treatment lines: 67 re-treatments in 2nd line having previously failed in 1st line with the single-capsule; 16 re-treatments in 3rd line (of which 12 had previously received this same therapy in 2nd line); 11 in 4th line (previously having failed the same therapy in either 1st, 2nd or 3rd line); 4 in 5th line; and further 3 in 6th line (Table). The effectiveness of bismuth quadruple therapy as single-capsule when empirically prescribed repeatedly in 2nd line was over 90%, and achieved almost 80% in all cases retreated in 3rd line.

Previous failed line, N	2 nd line	3 rd line	4 th line	5 th line	6 th line
1 st line	67	4	3	0	0
2 nd line	0	12	5	1	1
3 rd line	0	0	3	1	0
4 th line	0	0	0	2	2
Total number of cases re-treated	67	16	11	4	3

Effectiveness by modified intention-to-treat of bismuth quadruple rescue therapy as single-capsule when prescribed empirically after previous failure(s) with the same therapy.

Previous failed line, %, (n/N)	2 nd line	3 rd line	4 th line	5 th line	6 th line
1 st line	94%	75% (3/4)	100% (2/2)		
2 nd line	(62/66)	80% (8/10)	75% (3/4)	100% (1/1)	
3 rd line			67% (2/3)	100% (1/1)	
4 th line	94%	79%		50% (1/2)	100% (2/2)
Overall	(62/66)	(11/14)	78% (7/9)	75% (3/4)	100% (2/2)

N: total number of patients analysed; n/N: patients with a successful eradication/total number of patients analysed.

Table. Use of bismuth quadruple rescue therapy as single-capsule when prescribed empirically after previous failure(s) with the same therapy.

Conclusion: The empirical administration of bismuth quadruple therapy as single-capsule when prescribed as re-treatment in 2nd line after previous failure with the same therapy achieves optimal effectiveness (>90%).

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

MP550

THE EFFECT OF SACCHAROMYCES BOULARDII SUPPLEMENTATION TO BISMUTH QUADRUPLE THERAPY ON *HELICOBACTER PYLORI* ERADICATION

X. Wang¹, Y. Jiang²

¹The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Gastroenterology, Changzhou, China, ²The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Changzhou, China

Contact E-Mail Address: wxy20009@126.com

Introduction: It is still controversial whether the supplementation of *Saccharomyces boulardii* to bismuth quadruple therapy is beneficial for *Helicobacter pylori* eradication. The aim of the study was to determine the effects of *S. boulardii* supplementation on *H. pylori* eradication.

Aims & Methods: We performed a systematic literature search across PubMed, Embase, Web of Science, and China National Knowledge Infrastructure for articles published up to October 2023. We calculated the pooled relative risk (RR) with the 95% confidence interval (CI). Subgroup analyses were also performed. Statistical analyses were conducted using Stata/SE 15.1 software.

Results: Ten randomized controlled trials were included. Notably, *S. boulardii* supplementation to bismuth quadruple therapy significantly improved *H. pylori* eradication rates (RR = 1.08, 95% CI: 1.04–1.12, $P < 0.0001$) and reduced the incidence of total adverse effects (RR = 0.53, 95% CI: 0.45–0.62, $P < 0.0001$).

Furthermore, it reduced the incidence of some gastrointestinal adverse effects and nonspecific adverse effects, including diarrhea (RR = 0.28, 95% CI: 0.22–0.36, $P < 0.0001$), constipation (RR = 0.32, 95% CI: 0.18–0.55, $P < 0.0001$), abdominal distention (RR = 0.39, 95% CI: 0.26–0.59, $P < 0.0001$), nausea (RR = 0.59, 95% CI: 0.36–0.97, $P = 0.039$), and rash (RR = 0.49, 95% CI: 0.28–0.86, $P = 0.013$). In the subgroup analysis, long-term eradication duration (>10 days; RR = 1.08, 95% CI: 1.04–1.13, $P < 0.0001$) and *S. boulardii* supplementation to be started and stopped at the same time

as bismuth quadruple therapy (RR = 1.09, 95% CI: 1.04–1.14, $P < 0.0001$) were found to significantly improve the eradication rate regardless of the *S. boulardii* dose (500 mg/day, RR = 1.10, 95% CI: 1.03–1.17, $P = 0.003$; 1000 mg/day, RR = 1.08, 95% CI: 1.03–1.12, $P < 0.0001$).

Conclusion: The addition of *S. boulardii* to bismuth quadruple therapy significantly increased *H. pylori* eradication rates and decreased the adverse effects. We recommend adding 500 mg/day *S. boulardii* concurrently with bismuth quadruple therapy and continuing this therapy for >10 days for optimal *H. pylori* eradication efficacy.

Disclosure: Nothing to disclose.

MP551

RISK OF DEVELOPING OSTEOPOROSIS AFTER *HELICOBACTER PYLORI* ERADICATION; A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Y. Kim¹, N. Kim^{1,2}, E.-b. Jeon¹, J. Lee¹, Y. Choi¹, H.-k. Lee¹, Y.K. Jun¹, H. Yoon¹, C.-M. Shin¹, Y.-S. Park¹, D.-H. Lee^{1,2}

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea

Contact E-Mail Address: yjwhite07@gmail.com

Introduction: Previous studies have suggested an association between *Helicobacter pylori* (HP) infection and osteoporosis. However, the influence of HP eradication on osteoporosis has not been established.

Aims & Methods: The objective of this study was to evaluate whether the risk of developing osteoporosis could be decreased by HP eradication. So, we conducted an observational study of prospectively enrolled cohort. All participants received esophagogastroduodenoscopy with HP tests at the Seoul National University Bundang Hospital from May 2003 to February 2023. HP infection was defined if any one of the following tests was positive: urea breath test, rapid urease test, or histology. Osteoporosis was diagnosed using dual-energy X-ray absorptiometry. The risk of osteoporosis was analyzed using Cox proportional hazard regression analyses.

Results: A total of 8,025 patients were included in the study, and patients under the age of 20, with unknown HP infection status, having a prior history of HP eradication, gastric cancer, or osteoporosis were excluded. Finally, there were 730 patients in the eradicated group and 116 patients in the non-eradicated group. In Cox proportional hazard analyses, the hazard ratio (HR) for osteoporosis in the eradicated group was 0.588 (95% confidence interval [CI] 0.41–0.84, $p=0.003$) referring the non-eradicated group as reference. In addition, multivariate analyses showed that advanced age (HR 1.05, 95% CI 1.03–1.06, $p<0.001$), menopause (HR 3.46, 95% CI 2.25–5.32, $p<0.001$), and history of medicine use (HR 2.86, 95% CI 2.13–3.84, $p<0.001$) were risk factors for osteoporosis (Table).

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
HP non-eradicated	Ref.		Ref.	
HP eradicated	0.564 (0.399 – 0.795)	<.001	0.588 (0.413 – 0.836)	0.003
Sex (female)	2.983 (2.018 – 4.411)	<.001		
Age, per year	1.076 (1.061 – 1.091)	<.001	1.046 (1.029 – 1.063)	<.001
BMI, per kg/m ²	0.952 (0.912 – 0.993)	0.023		
Menopause	4.703 (3.387 – 6.532)	<.001	3.457 (2.245 – 5.322)	<.001
*History of medicine use	5.220 (3.966 – 6.871)	<.001	2.861 (2.132 – 3.838)	<.001

Table. Univariate and multivariate analysis of incidence of osteoporosis with *Helicobacter pylori*.

Abbreviations: HR, hazard ratio; CI, confidence interval; HP, *Helicobacter pylori*; BMI, body mass index.

*History of medicine use, patients who have taken any one of denosumab, bisphosphonate, selective estrogen-receptor modulator (SERMs), or hormone replacement therapy (HRT).

Conclusion: The beneficial effect of HP eradication on preventing osteoporosis was observed in this study, even after the adjustment of other confounding factors.

Disclosure: Nothing to disclose.

MP552

EVALUATION OF PCR-TAILORED THERAPY EFFECTIVENESS IN THE ERADICATION OF *HELICOBACTER PYLORI*: RESULTS OF THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

V. Milivojevic¹, D. Kekic², T. Milosavljevic³, I. Babic⁴, G. Losurdo⁵, J. Tejedor-Tejeda⁶, T. Matysiak-Budnik⁷, L. Vologzanina⁸, T. Ilchishina⁹, I. Linas¹⁰, I. Voinovan¹¹, L. Rodrigo¹², N. Bakulina¹³, I. Bakulin¹⁴, M. Romano¹⁵, M. Pavoni¹⁶, B.J. Gómez Rodríguez¹⁷, G.M. Buzás¹⁸, M. Ražov-Radas¹⁹, A.G. Gravina²⁰, N.V. Baryshnikova²¹, G. Fiorini²², M. Nikolic²³, L. Belousova²⁴, K. Jankovic²⁵, K. Priadko²⁶, I. Hasukic²⁷, A. Di Leo²⁸, A. Osmanovic²⁹, C.I. Paez Cumpa³⁰, D. Vaira³¹, A. Sushilova³², S. Hodzic²⁹, A. Perelló Juan³³, A. Gasbarrini³⁴, L. Hernández Villalba³⁵, D.S. Bordin³⁶, M. Doulberis³⁷, A. Mestrovic³⁸, V. Papp³⁹, A. Cano-Catala⁴⁰, P. Parra⁴¹, L. Moreira Ruiz⁴², O. P. Nyssen⁴¹, F. Megraud⁴³, C. O'Morain⁴⁴, J. P. Gisbert⁴¹

¹University Clinical Centre of Serbia, Belgrade University, Gastroenterology and Hepatology, Belgrade, Serbia, ²Medical Faculty University of Belgrade, Institute of Microbiology and Immunology, Belgrade, Serbia, ³General hospital Euromedic, Belgrade, Serbia, ⁴Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia, ⁵University of Bari, Section of Gastroenterology, Dept. Emergency and organ transplantation, Bari, Italy, ⁶Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ⁷CHU de Nantes IMAD, Institut des maladies de l'appareil digestif, Nantes, France, ⁸Gastrocentr, Perm, Russian Federation, ⁹Department of Gastroenterology, SM-clinic, Saint-Petersburg, Russian Federation, ¹⁰Gastroenterologische Gruppenpraxis / Hirslanden Clinic Beau-Site, Gastroenterology, Münsingen, Switzerland, ¹¹A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ¹²Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ¹³North-Western State Medical University n. a. I. I. Mechnikov, St. Petersburg, Russian Federation, ¹⁴North-Western State Medical University n. a. I. I. Mechnikov, Propedeutics of Internal Diseases, Gastroenterology and Dietology n. a. S. M. Riss, Moscow, Russian Federation, ¹⁵Department of Gastroenterology and Endoscopy, Department of Precision Medicine, Università Vanvitelli, Napoli, Italy, ¹⁶Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ¹⁷Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ¹⁸Ferencvaros Health Centre, Dr., Budapest, Hungary, ¹⁹Department of Gastroenterology and Hepatology, General Hospital Zadar, Health Studies, University of Zadar, Zadar, Croatia, ²⁰Division of Hepatogastroenterology, University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy, ²¹Pavlov First Saint Petersburg State Medical University, Saint-Petersburg, Russian Federation, ²²Sant'Orsola Hospital Dept. of Internal Medicine, Dept. of Medical and Surgical sciences, Bologna, Italy, ²³University Hospital Center Sestre Milosrdnice, Gastroenterology And Hepatology, Zagreb, Croatia, ²⁴University Hospital Peter The Great, St. Petersburg, Russian Federation, ²⁵Clinic for Gastroenterohepatology, University Clinical Centre of Serbia, Sabac, Stitar, Serbia, ²⁶Hepato-

Gastroenterology & Digestive Oncology Unit, University Hospital of Nantes, Gastroenterology, Nantes, France, ²⁷UKC Tuzla, Tuzla, Bosnia and Herzegovina, ²⁸Section of gastroenterology, DETO, University of Bari, Dr., Bari, Italy, ²⁹Department of Gastroenterology and Hepatology, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina, ³⁰Hospital Cruz Roja Palma de Mallorca, Palma de Mallorca, Spain, ³¹Cardiovascular Medicine Unit, Heart, Chest and Vascular Dept., IRCCS Azienda Ospedaliero-Universitaria di Bologna, Hypertension and Cardiovascular Risk Research Center, Medical and Surgical Sciences, Bologna, Italy, ³²University Hospital Peter The Great, Saint-Petersburg, Russian Federation, ³³Department of Gastroenterology, Hospital Universitario Son Espases, Palma de Mallorca, Spain, ³⁴Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ³⁵Santos Reyes, Gastroenterology, Aranda de Duero, Spain, ³⁶A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ³⁷Kantonsspital Aarau, Gastroenterology & Hepatology, Dietikon, Switzerland, ³⁸KBC SPLIT, Split, Croatia, ³⁹Semmelweis University, II. departement of internal medicine, Budapest, Hungary, ⁴⁰Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ⁴¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology, Madrid, Spain, ⁴²Hospital Clinic de Barcelona, Gastroenterology, Gava, Spain, ⁴³Hopital Pellegrin, Laboratoire de Bacteriologie, Bordeaux, France, ⁴⁴Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: dotorevlada@gmail.com

Introduction: Antibiotic resistance is the leading cause of failure in the eradication of *Helicobacter pylori* (*H. pylori*) infection. In addition to general overuse and misuse of antibiotics, the repetition of the same therapy regimen further promotes the prevalence of resistant *H. pylori* strains. Molecular PCR techniques have enabled clinicians to tailor the treatment according to the antibiotic sensitivity of specific *H. pylori*. For the first time, the Maastricht VI Consensus has made a statement regarding the implementation of PCR.

Aims & Methods: Our aim was to assess the effectiveness of tailored therapy implementation in eradicating *H. pylori* infection evaluating the data from a multicentric, prospective registry of the clinical practice of European gastroenterologists in the management of *H. pylori* infection (Hp-EuReg). All *H. pylori*-infected and PCR-diagnosed patients registered until December 2023 at e-CRF AEG-REDCap were included. Treatment effectiveness was analysed per protocol (accounting only those adherent cases and those with a result either as success or failure to treatment). Effectiveness >85% was considered as satisfactory and >90% as optimal.

Results: A total of 265 patients from XX European countries were tested using the molecular PCR method, 203 (77%) cases on gastric tissue and 62 (23%) on stools. The effectiveness of tailored therapy in treatment-naïve patients was 95%, while the eradication rate in the rescue (from 2nd to 6th) line was 86%. In the first line, the most common prescribed regimens were quadruple-clarithromycin+amoxicillin+metronidazole (C+A+M) therapy, followed by single-capsule quadruple therapy with metronidazole+tetracycline+bismuth (M+T+B), with an eradication rate of 95% and 97%, respectively. In the rescue line, the most common prescribed regimen was

single-capsule quadruple therapy with M+T+B (achieving 87% effectiveness by PP), followed by quadruple C+A+M therapy (94%), triple-amoxicillin+metronidazole (A+M) (93%), and triple levofloxacin+amoxicillin (L+A) therapy (91%) (Table). Clarithromycin and fluoroquinolone resistance rates in the first line were 31% and 33%, respectively; while in rescue line, they were reported higher, that is 63% and 52%; respectively. Table. Most frequent PCR-guided treatments prescriptions and per protocol effectiveness in Europe.

Treatment lines	Patients prescribed (n, %)	Effectiveness (N, %)
First Line		
Quadruple-C+A+M	62, 48%	59, 95%
Single capsule M+T+B	39, 30%	38, 97%
Triple-C+A	7, 5%	7, 100%
Triple-M+A	5, 4%	5, 100%
Rescue line		
Single capsule M+T+B	58, 45%	50, 87%
Quadruple-C+A+M	36, 28%	34, 94%
Triple-M+A	15, 11%	14, 93%
Triple-L+A	11, 8%	10, 91%
C-clarithromycin, A-amoxicillin, M-metronidazole, L-levofloxacin, T-tetracycline, B- bismuth		

Conclusion: PCR-guided tailored therapy showed a consistent optimal (>90%) effectiveness in all therapy lines and prescriptions. This indicates that clarithromycin-based therapy can still be a reasonable treatment choice even in regions with high clarithromycin resistance rate, provided that pretreatment *H. pylori* antibiotic sensitivity is assessed.

Disclosure: Olga P. Nyssen received research funding from Mayoly and Allergan. Javier P. Gisbert served as speaker, consultant, and advisory member for or received research funding from Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

Endoscopy: Upper GI

10:00-11:00 / Poster Stage 6

MP553

PERFORMANCE OF ENDOSCOPIC APPROACHES FOR ZENKER DIVERTICULUM MANAGEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Papaefthymioy¹, B. Norton¹, A. Telese¹, K. Siggers¹, M. Duku², A. Murino², G. Johnson², C. Murray², B. Mohammadi², M. Mughal², R. Bisschops³, P. Bhandari⁴, M. Birchall⁵, R.J. Haidry²
¹Cleveland Clinic London, Gastroenterology, London, United Kingdom, ²Portsmouth University Hospitals, Department of Gastroenterology, Portsmouth, United Kingdom, ³Katholieke Universiteit Leuven, Gastroenterology, Leuven, Belgium, ⁴Portsmouth University Hospital, Dept. of Gastroenterology, Portsmouth, United Kingdom, ⁵University College London Hospital, Department of Otolaryngology, London, United Kingdom

Contact E-Mail Address: Andrea.Telese@nhs.net

Introduction: Zenker's diverticulum is associated with a significant burden on quality of life and morbidity, predisposing to dysphagia, regurgitation and aspiration pneumonia. This is often a condition that affects senior patients and access to interventions is limited. Surgery has been the preferred option historically due to a lack of alternative options but remains invasive with major potential complications in an already high-risk patient group. Endoscopic approaches offer a minimally invasive alternative treatment option including rigid and flexible diverticulotomy, and the emerging Zenker per-oral endoscopic myotomy (Z-POEM), albeit no superiority has been demonstrated among these techniques.

Aims & Methods: This systematic review and meta-analysis aimed to summarize the efficacy and safety of these endoscopic techniques. A systematic search in Medline, Cochrane and Scopus databases was performed until November 2023. The primary outcome was technical success, defined as the completion of diverticulotomy/myotomy in one session. Secondary outcomes included clinical success which corresponded to the complete resolution of dysphagia or a post-procedure Dakkak and Bennett score ≤ 1. Moreover, the recurrence rates and the overall adverse events were recorded. Subgroup analyses per outcome were performed to discriminate the results depending on the endoscopic approach (Rigid, flexible diverticulotomy and Z-POEM), whereas the comparative studies were meta-analyzed to compare Z-POEM with alternatives. We used a random effects model and the results were reported as percentages for pooled rates and odds ratios (OR) for comparative data with 95% Confidence Intervals (95%CI).

Results: From 2004 to 2023 twenty-three studies (1357 patients; 40% female; mean age 43-80) were included in our analysis. The cumulative technical success rate was 97.7% (95%CI: 96.9-98.5) with null heterogeneity (I²=0%), and this outcome was preserved in all subgroups. Considering clinical success, the overall pooled rate was 84.8% (95%CI: 80.8-88.8; I²=79.15%) with Z-POEM yielding higher rate [90.4% (95%CI: 87.8-93.1)] with low heterogeneity (I²=11%), in contrast to the alternatives. 8.6% (95%CI: 6.0-11.3; I²: 63.6%) of cases experienced recurrence, with those post-Z-POEM having the lowest rates [5.7% (95%CI: 2.3-9.1; I²:55.68%)] and post-flexible myotomy the highest ones [12.1% (95%CI: 8.0-16.2; I²=36.09%)]. Finally, complications occurred in 8.7% (95%CI: 6.0-11.4; I²=78.08%) with no changes in subgroup analysis. Five studies (759 patients) provided comparative data for Z-POEM and alternatives. Technical success and recurrence rates were similar between comparators [OR:1.38 (95%CI: 0.59-3.23, p=0.5; I²=0%) and OR:0.69 (95%CI: 0.29-1.51, p=0.39; I²=48.71%), respectively], whereas Z-POEM achieved higher clinical success rates [OR:2.38 (95%CI: 1.54-3.68, p<0.001; I²=0%)]

Conclusion: Endoscopic treatment offers high technical success and symptom resolution in patients with Zenker diverticulum, with relatively low prevalence of adverse events and recurrence. Z-POEM offers higher clinical success rates compared to alternatives with optimal homogeneity.

Disclosure: Nothing to disclose.

MP554

COMPARATIVE EVALUATION OF ARTIFICIAL INTELLIGENCE AND ENDOSCOPISTS ACCURACY IN ENDOSCOPIC ULTRASOUND FOR IDENTIFYING NORMAL ANATOMICAL STRUCTURES: A MULTI-INSTITUTIONAL, CROSS-SECTIONAL STUDY

C. Robles-Medranda¹, J. Baquerizo-Burgos^{1,2}, M. Puga-Tejada¹, I. Rajjman^{3,4}, T. Berzin⁵, J. Autran Nebel⁶, J. Iglesias⁷, R. Kunda⁸, R. Del Valle Zavala¹, J. Alcivar-Vasquez¹, J.C. Mendez², A. Chilan-Puley², M. Sanchez-Cepeda², G. Lara¹, V. Oregel-Aguilar⁹, I. Boston⁵, C. Pattni⁵, M. Egas-Izquierdo¹, D. Cunto¹, M. Arevalo-Mora^{1,10}, H. Pitanga-Lukashok¹, D. Tabacelia^{11,12}

¹Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Mdconsgroup, Research & Development, Guayaquil, Ecuador, ³Houston Methodist Hospital, Gastroenterology, Houston, United States of America, ⁴Baylor Saint Luke's Medical Center, Gastroenterology, Houston, United States of America, ⁵Beth Israel Deaconess Medical Center, Boston, United States of America, ⁶Barralife Medical Center, Rio de Janeiro, Brazil, ⁷Universidad de Santiago de Compostela (USC), Coruña, Spain, ⁸Aarhus University Hospital, Surgical Gastroenterology, Aarhus, Denmark, ⁹Hospital Civil Morelia, Michoacan, Mexico, ¹⁰Larkin Community Hospital, South Miami, United States of America, ¹¹Elias Emergency University Hospital, Bucharest, Romania, ¹²Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Endoscopic ultrasound (EUS) has emerged as a powerful diagnostic and therapeutic tool in gastroenterology, providing detailed images of the structure's layers, as well as nearby structures. However, EUS is operator-dependent and variability in operator proficiency results in discrepancies in diagnostic accuracy. Artificial intelligence (AI) can be trained to process and interpret EUS images in real-time, potentially mitigating the operator-dependent variability and improving diagnostic accuracy. Moreover, AI can analyze vast datasets offering a level of consistency and efficiency that is challenging for human operators to match.

Aims & Methods: The aim of this study is to compare the diagnostic accuracy of an AI-based model (AIWorks-EUS, mdconsgroup, Guayaquil, Ecuador) against that of expert and nonexpert gastrointestinal endoscopists visual impression in the identification of normal anatomical structures during EUS procedures.

A multi-institutional, cross-sectional, comparative study designed to assess the diagnostic accuracy of the AIWorks-EUS (mdconsgroup, Guayaquil, Ecuador), in identifying normal anatomical structures during EUS procedures compared to that of endoscopists of different expertise. Consecutive patient videos of linear-array EUS were included for analysis. Then, the video dataset was reviewed by 9 endoscopists (5 expert endoscopists and 4 nonexpert endoscopists (<250 EUS procedures), who were blinded to the AI model interpretations. Finally, their visual impression was compared to the observation outputs provided by the AI models.

Results: A total of 29 normal anatomic structures were evaluated by the endoscopists and the AIWorks-EUS software in 39 videos of linear-array EUS. The software reported an observed agreement (OA) of 100% in 15/29 structures (4/9 mediastinal window, 6/12 in gastric window, 5/8 in duode-

nal window). Subcarinal space and portal vein (gastric window) obtained the lowest OA (92.35%). The AIWorks-EUS software obtained a pooled sensitivity, specificity, positive (PPV) and negative predictive value (NPV), and OA for anatomical structure recognition of 95.2%, 99.3%, 97.9%, 98.4%, and 98.2%, respectively. Additionally, the software obtained higher diagnostic accuracy than expert and nonexpert endoscopists ($P < 0.05$). Agreement between endoscopists and the AI per organ evaluated was obtained, with a difference of 18% between the organ with the higher agreement (Aorta) and the lower agreement (Ampulla).

Conclusion: The EUS-based AI model achieved higher diagnostic accuracy than both expert and nonexpert endoscopists in the identification of normal anatomical structures. This model can provide assistance to both groups during live procedures, and studies evaluating its use for training should be conducted to evaluate its application in EUS training programs.

Disclosure: Carlos Robles-Medranda is a key opinion leader and consultant for Pentax Medical, Steris, Medtronic, Motus, Micro-tech, G-Tech Medical Supply, CREO Medical, and mdconsgroup.

Issac Rajjman is a speaker for Boston Scientific, ConMed, Medtronic, and GI Supplies; advisory board member for Micro-Tech; co-owner of EndoRx. Tyler M. Berzin is a consultant for Medtronic, Boston Scientific, Wision, A.I., Magentiq Eye, and RSIP Vision. The other authors declare no conflicts of interest.

MP555

LINKED COLOUR IMAGING (LCI) AND BLUE LIGHT IMAGING (BLI) ROLE IN ASSESSING CHRONIC GASTRITIS STIGMATA: A PROSPECTIVE STUDY

C. Borges Chaves¹, M. Costa¹, D. Feijó¹, A. Trigo¹, L. Santos¹, M. Cristiano¹, P. Rocha¹, A.L. Alves², J. Madeira², B. Sepodes², J. Pimentel², F. Ramalhosa², M. Meruje², V. Almeida², M.R. Silva², M.A. Cipriano², M. Ferreira¹, E. Gravito-Soares^{1,3}, M. Gravito-Soares^{1,3}, P. Souto¹, M. Marques da Silva Sant'Anna¹, P. Amaro¹, R. Pimentel¹, D. Perdigoto^{1,3}, P. Narra Figueiredo^{1,3}

¹Unidade Local de Saúde de Coimbra, Gastroenterology Department, Coimbra, Portugal, ²Unidade Local de Saúde de Coimbra, Anatomical Pathology Department, Coimbra, Portugal, ³Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal

Contact E-Mail Address: carlosbchaves123@gmail.com

Introduction: Atrophy and intestinal metaplasia (IM) are well-defined preneoplastic conditions and their endoscopic appearance may be subtle. The importance of their identification lies in the fact that it allows the recognition of a high-risk population, enabling an appropriate follow-up.¹ The stigmata of chronic gastritis have been extensively studied and validated with Narrow Band Imaging (NBI) worldwide, while European studies with Blue Light Imaging (BLI) are still limited.^{2,3}

Aims & Methods: The primary aim of this study is to evaluate the applicability of BLI in characterizing chronic gastritis (CG), atrophy and IM comparing it to the gold-standard histology.

All patients undergoing upper digestive endoscopy requiring gastric biopsies, between November 2023 and March 2024, who agreed to participate after written informed consent, were prospectively included. Gastric mucosa was endoscopically evaluated using white light (WL), Linked Colour Imaging (LCI) and BLI, documenting findings and performing biopsies for mapping. Patients with history of gastric surgery were excluded. Statistical analysis was performed using IBM SPSS Statistics version 26®.

Results: A total of 169 patients were included, 55.6% female, with a mean age of 60.2±15.2 years. At the time of the endoscopy, most of the patients had never been tested for *Helicobacter pylori* (74.0%), 12.4% had con-

firmed eradication, 7.1% had previous negative tests and 6.5% had active infection. There was a family history of gastric cancer in 14.2% of patients. Of all endoscopies, 53.8% were performed without any type of sedation. For the evaluation of CG, BLI, LCI and WL were similar (sensitivity = 91.8% vs 92.6% vs 90.2%; specificity = 16.3% vs 14.0% vs 18.6%; positive predictive value (PPV) = 75.7% vs 75.3% vs 75.9%; negative predictive value (NPV) = 41.2% vs 40.0% vs 40.0%; area under ROC curve (AUROC) = 0.54 vs 0.53 vs 0.54, respectively; BLI vs WL *p*-value 0.87; LCI vs WL *p*-value 0.54; BLI vs LCI *p*-value 0.54), as well as for atrophy (sensitivity = 85.9% vs 85.9% vs 84.4%; specificity = 25.7% vs 25.7% vs 31.7%; PPV = 42.3% vs 42.3% vs 43.9%; NPV = 74.3% vs 74.3% vs 76.2%; AUROC = 0.56 vs 0.56 vs 0.58, respectively; BLI vs WL *p*-value 0.17; LCI vs WL *p*-value 0.12; BLI vs LCI *p*-value 1.0). On the other hand, the diagnostic accuracy of BLI was superior to LCI, and both were superior to WL for IM, although at the expense of a higher rate of false positives (sensitivity = 65.9% vs 50.5% vs 34.1%; specificity = 77.2% vs 82.2% vs 85.6%; PPV = 39.5% vs 39.0% vs 34.8%; NPV = 91.0% vs 88.1% vs 85.2%; AUROC = 0.72 vs 0.66 vs 0.60, respectively; BLI vs WL *p*-value <0.001; LCI vs WL *p*-value 0.01; BLI vs LCI *p*-value 0.009). Considering those who underwent endoscopy without any type of sedation, only BLI showed superiority when compared to WL (*p*-value 0.045) but not to LCI (*p*-value 0.41). Also, in this subgroup, LCI was not superior to WL. However, in the subgroup who underwent sedation, the diagnostic accuracy of BLI was even better than the global results (AUROC = 0.79; BLI vs WL *p*-value <0.001; BLI vs LCI *p*-value 0.006). There were eleven visible lesions identified, three of which were detected only with BLI assessment (two with low-grade and one with high-grade dysplasia).

Conclusion: BLI appears to increase the diagnostic accuracy of IM when compared to LCI and WL, and LCI when compared to WL. Regarding the assessment of CG and atrophy, there seems to be an overestimation of findings due to the high rate of false positives. Given the focal nature of IM, sedation is vital for adequate identification and targeted tissue sampling.

References: 1. Pimentel-Nunes P, et al.; Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy*. 2019 Apr;51(4):365-388.

2. Jochen Weigt, et al.; Blue Light Imaging and Linked Color Imaging for the Characterization of Mucosal Changes in Chronic Gastritis: A Clinicians View and Brief Technical Report. *Dig Dis* 8 January 2020; 38 (1): 9–14.

3. Castro, R., et al.; Reliability and accuracy of blue light imaging for staging of intestinal metaplasia in the stomach. *Scandinavian Journal of Gastroenterology*, 54(11), 1301–1305.

Disclosure: Nothing to disclose.

MP556

ASSESSING THE BENEFIT OF ENDOSCOPIC FOLLOW-UP FOR GASTRIC ULCER AND ASSESSMENT OF A SCORING SYSTEM FOR BENIGN GASTRIC ULCERS

A. Srinivasa¹, S. Wallis¹, S. Booth¹, S. Abdelbadiee¹, N. Yemula¹, A. Subramanian¹, D. Soni¹, E. Plant¹, C. Brew¹, N. Trudgill¹

¹Sandwell and West Birmingham NHS Trust, Gastroenterology, West Bromwich, United Kingdom

Contact E-Mail Address: amarsrinivasa@nhs.net

Introduction: All patients in the UK with a diagnosis of gastric ulcer are recommended to have a follow-up endoscopy within 12 weeks. However, in a low-risk population, such measures may not be necessary. We have assessed a recently developed risk stratification model for gastric ulcers (Brindle Frontline 2022) in a single provider.

Aims & Methods: The aim of this study was to assess the pick up rate of gastric cancer on follow-up endoscopy for patients diagnosed with gastric ulcers and validate a risk stratification model.

A retrospective service evaluation was performed between June 2019 to June 2023 at Sandwell and West Birmingham NHS trust of all patients with an endoscopic diagnosis of gastric ulcer. Patients were followed up until ulcer healing, cancer diagnosis or no further planned follow-up.

Results: 461 patients were studied: median age 63 [interquartile range (IQR) 52-72]; 74% male; and median Charlson comorbidity index 3 (IQR 2-5).

The majority of ulcer diagnoses came from outpatient endoscopy - 69.6%. The ulcer biopsy rate was 64.4% and lower biopsy rates were seen in those who had inpatient endoscopy (41.4%) and therapy (12.1%). The median number of biopsies taken was 4 (IQR 2-5). Additional diagnoses were as follows; gastritis 77%, no additional diagnosis 8%, premalignant lesions 4% (e.g. chronic gastric atrophy) and lymphoma 3%.

Cancer was suspected in 8.7% of ulcers at the initial endoscopy and confirmed histologically in 7%. Cancer diagnoses were in older patients - median age 67 (IQR 59-76) - and all met the urgent two week wait referral criteria for suspected cancer.

Repeat endoscopy for ulcer healing was not done in 32% (reasons included frailty, non-attendance or cancer diagnosis). Two cancers were diagnosed on follow-up endoscopy but both were suspected on index endoscopy - in one the index biopsies did not confirm cancer and in the second no biopsies were taken due to GI bleeding.

Using the risk stratification model proposed by Khalla and Masterton, which required 6 biopsies taken at index endoscopy along with a risk score of less than 3 (consisting of age, ulcer site and ulcer size), 15.6% met the low-risk criteria, where repeat endoscopy may not be required. In that group there were no cancers diagnosed on the second endoscopy.

Conclusion: The risk stratification model appears to perform well suggesting that at least 15.6% of our current endoscopies for gastric ulcer follow-up may not be necessary. Further multi-centre validation of the model is needed.

References: Brindle WM, Grant RK, Smith M, Suddaby M, Wallace A, Gillespie SL, Church NI, Noble CL, Penman ID, Plevris JN, Robertson AR, Watson EF, Selinger CP, Kalla R, Masterton GSM; EGAR (Edinburgh GI Audit and Research) Collaborative. Risk stratifying gastric ulcers: development and validation of a scoring system. *Frontline Gastroenterol*. 2021 Feb 26;13(2):111-118. doi: 10.1136/flgastro-2020-101759. PMID: 35295750; PMCID: PMC8862450.

Disclosure: Nothing to disclose.

MP557

POST-ENDOSCOPY CARE IN OESOPHAGEAL FOOD BOLUS IMPACTION: INSIGHTS FROM A TERTIARY CENTRE COHORT STUDY

C. Borges Chaves¹, M. Cristiano¹, P. Rocha¹, D. Feijó¹, P. Souto¹, N.P. Almeida^{1,2}, P. Narra Figueiredo^{2,1}

¹Unidade Local de Saúde de Coimbra, Gastroenterology Department, Coimbra, Portugal, ²Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal

Contact E-Mail Address: carlosbchaves123@gmail.com

Introduction: Oesophageal food bolus impaction (FBI) is a frequent emergency in Gastroenterology. Appropriate management involves not only the index endoscopy to resolve the impaction, but also accurate diagnosis and treatment of the underlying oesophageal pathology. If the latter is not achievable during the initial endoscopy, comprehensive follow-up care should be provided. Several recent studies have shown that patients

often do not receive adequate post-endoscopic care after an FBI episode, potentially leading to missed diagnoses of eosinophilic esophagitis and malignancies^{1,2}.

Aims & Methods: The aim of this study was to evaluate the management of patients with FBI and their subsequent follow-up.

A retrospective evaluation of all emergent upper gastrointestinal endoscopies (UGE) conducted at a tertiary centre between November 2019 and December 2023 was performed, including only those with FBI as the indication. Subsequently, follow-up care was assessed. Statistical analysis was conducted using IBM SPSS Statistics version 26®.

Results: A total of 794 patients with FBI were included, with a mean age of 60.3±20.7 years and 41.6% were female. In 19.8% of patients there were previous episodes of FBI, 59.2% of which with a known cause. The majority of food boluses consisted of meat (44.1%), followed by a mixture of foods (26.0%). Most of the times, the FBI episode was solved by carefully pushing the food bolus into the stomach (47.9%). During the index UGE, a probable structural aetiological factor was identified in 38.6% of cases, with Schatzki's ring being the most frequent (19.6%).

However, only 4.4% received appropriate treatment directed toward the cause during the index UGE. Classic findings of eosinophilic oesophagitis were identified in 8.3% of patients, but biopsies were performed in only 30.3% of these cases. Among all patients, only 17.9% underwent endoscopic reevaluation, 5.2±5.6 months after the index UGE, with the aetiology being identified in 77.5% of these.

Globally, the cause of FBI was identified in 42% of cases, known either before, during, or after the index UGE, and only 38.4% of these received treatment. There were 51 cases (6.4%) of diagnosed neoplasia, all known previously or at the index procedure, except for 1 case in a patient not endoscopically reevaluated, and 2 cases reevaluated endoscopically but late (6 and 14 months after FBI).

Conclusion: Most patients did not receive an adequate follow-up plan after index UGE for FBI, albeit a follow-up endoscopy in primary care was proposed in the report. A detailed protocol must be implemented in each endoscopic unit to maintain adequate follow-up and care for patients with FBI.

References: 1. Guo H, Hamilton P, Enns E, Gupta M, Andrews CN, Nasser Y, Bredenoord AJ, Dellon ES, Ma C. Postendoscopy Care for Patients Presenting With Esophageal Food Bolus Impaction: A Population-Based Multicenter Cohort Study. *Am J Gastroenterol*. 2023 Oct 1;118(10):1787-1796. 2. Terkelsen, J.H., Holl  nder, M., Bredal, K. *et al*. A retrospective cohort study on oesophageal food bolus obstruction in the North Denmark region in 2021—two thirds were never diagnosed with a cause. *BMC Gastroenterol* 24, 3 (2024).

Disclosure: Nothing to disclose.

MP558

EFFECT OF BINAURAL BEATS ON ANXIETY AND TOLERANCE IN PATIENTS UNDERGOING UPPER GASTROINTESTINAL ENDOSCOPY WITHOUT SEDATION

F. Sapmaz¹, S. Demirci², S. Sezer²

¹G  lhane Faculty of Medicine, Gastroenterology, Ankara, Turkey, ²Ankara Onkoloji Education and Training Hospital, Gastroenterology, Ankara, Turkey

Contact E-Mail Address: ferda-sapmaz@hotmail.com

Introduction: Binaural beats are perceptual auditory illusions occurring when presenting two similar frequencies to each ear separately, and have been used to reduce anxiety in some procedures. There have been no prior studies involving preprocedure binaural music exposure in patients undergoing upper gastrointestinal endoscopy.

The purpose of this study was to investigate the effect of binaural beats on anxiety and tolerance in patients undergoing sedation-free upper gastrointestinal endoscopy.

Aims & Methods: This prospective randomized controlled trial included 96 Turkish patients aged 18-70 years old scheduled for upper gastrointestinal endoscopy regardless of sex or underlying disease. The patients were randomly divided into two groups: the binaural beat music group (n=48) and the control group (n=48). Those in the binaural music group listened to music using earphones for 15 minutes before endoscopy. No special treatment was given to the control group. The level of anxiety was measured using the State-Trait Anxiety Inventory questionnaire. Hemodynamic changes before and after endoscopy, patient satisfaction based on the number of retches recorded by the physician and tolerance were recorded and compared between the two groups.

Results: STAI state scores were significantly lower after the procedure than before the procedure in the music group, compared to the control group (p=0.016). There were no significant differences between the two groups in terms of systolic and diastolic blood pressure or heart rate changes (p>0.05). Procedure tolerance scores and procedure satisfaction were significantly higher in the music group than in the control group (p>0.05).

Conclusion: In patients undergoing upper gastrointestinal endoscopy, music containing binaural beats was shown to reduce anxiety levels and improve patient tolerance. Music containing binaural beats may be a suitable alternative to sedative medications in patients undergoing gastrointestinal interventions.

References: 1. Salmore, R.G. and J.P. Nelson, The effect of preprocedure teaching, relaxation instruction, and music on anxiety as measured by blood pressures in an outpatient gastrointestinal endoscopy laboratory. *Gastroenterol Nurs*, 2000. 23(3): p. 102-10.

2. Shafiee, H., et al., Comparison of the Sedative Effect of Ketamine, Magnesium Sulfate, and Propofol in Patients Undergoing Upper Gastrointestinal Endoscopy: Double-Blinded Randomized Clinical Trial. *CNS Neurol Disord Drug Targets*, 2022.

3. Trimble, M. and D. Hesdorffer, Music and the brain: the neuroscience of music and musical appreciation. *BJPsych Int*, 2017. 14(2): p. 28-31.

4. K  hlmann, A.Y.R., et al., Meta-analysis evaluating music interventions for anxiety and pain in surgery. *Br J Surg*, 2018. 105(7): p. 773-783.

5. Nilsson, U., The anxiety- and pain-reducing effects of music interventions: a systematic review. *Aorn J*, 2008. 87(4): p. 780-807.

6. HW., D.,   ber die Combination der Eindr  cke beider Ohren und beider Augen zu einem Eindruck. *Verhandlungen der K  niglich Preussischen Akademie der Wissenschaften zu Berlin*.

7. Opartpunyasarn, P., P. Vichitvejpaisal, and N. Oer-Areemit, The effect of binaural beat audio on anxiety in patients undergoing fiberoptic bronchoscopy: A prospective randomized controlled trial. *Medicine (Baltimore)*, 2022. 101(24): p. e29392.

Disclosure: Nothing to disclose.

MP559

CHARACTERISTICS AND FEATURES OF UPPER GASTRO INTESTINAL BLEEDING IN PATIENTS ON ANTITHROMBOTIC DRUGS: A PROSPECTIVE STUDY

R. Chaibi¹, S. Hdiye¹, I. Mouslim¹, F. Aitiken¹, A. Benhamdane¹, T. Addajou¹, S. Mrabti¹, R. Berraida¹, E. Ilham², F. Rouibaa³, H. Seddik⁴

¹Mohamed V Military Instruction Hospital, Gastroenterology II, Rabat, Morocco, ²Faculte De Medecine Et De Pharmacie De Rabat, Gastroenterology, Rabat, Morocco, ³Military hospital Mohamed V-Souissi University, Hay Ryad - 10100, Rabat, Morocco, ⁴Mohammed V Military Teaching Hospital. Mohammed V – Souissi University. Rabat. Morocco, Hepato-Gastro-Enterology II, Rabat, Morocco

Contact E-Mail Address: reemchaibi46@gmail.com

Introduction: Upper gastrointestinal bleeding (UGIB) is the most common diagnostic and therapeutic emergency in hepato-gastroenterology, potentially life-threatening and requiring multidisciplinary management. Anti-thrombotic (AT) drugs commonly prescribed for cardiovascular diseases are considered a recognised risk factor for UGIB. However, few studies have evaluated their effect on endoscopic outcomes in patients admitted for UGIB, and have concluded that the results remain controversial.

Aims & Methods: Aims: Evaluate the effect of AT use on endoscopic outcomes in patients admitted for UGIB.

Methods: This is a prospective monocentric cross-sectional study of 332 patients conducted between June 2020 and August 2021. We considered as users of AT drugs all patients on antiplatelet agents (low-dose aspirin, thienopyrimidines) and/or anticoagulants (vitamin K antagonists, direct-acting anticoagulants, heparin).

Results: The average age was 59+/-16.7 years. Our series was characterised by a clear male predominance of 77.1%. 63 patients (19%) were taking AT drugs (41 antiplatelet, 39 anticoagulant). The two groups differed in age (68 vs 57; p<0.001), comorbidities (75.8% vs 16.7%; p<0.001), however there was no statistically significant difference in active bleeding at endoscopy (12.7% vs 16.8%; p=0.425), and the need for endoscopic haemostasis (7.9% vs 16%; p=0.1). In multivariate analysis and adjusting for age, sex, comorbidities, presence of active bleeding and use of anti-thrombotics, only the presence of active bleeding could predict the need for endoscopic haemostasis. Indeed, the presence of active bleeding at the time of endoscopy multiplies by 26 the risk of recourse to endoscopic haemostasis (OR: 26, CI: 12.9–62.15, p<0.001), whereas the use of AT drugs does not influence the need for endoscopic haemostasis (OR: 0.386, CI: 0.105–1.42, p=0.154).

Conclusion: Older patients using AT admitted for UGIB do not appear to have an increased risk of active bleeding at endoscopy or needing endoscopic haemostasis.

Disclosure: Nothing to disclose.

MP560

BLEEDING SEVERITY AND TIMING TO ENDOSCOPY: IS THERE ANY EFFECT FOR THE DEATH RISK? A PROSPECTIVE MULTICENTRE COHORT STUDY

C. Marmo¹, C. Buccì², M. Soncini¹, R. Marmo¹, GISED, Gruppo Italiano Studio Emorragia Digestiva

¹Gruppo Italiano Studio Emorragia Digestiva, Rome, Italy, ²Cristina Buccì, Gruppo Italiano Studio Emorragia Digestiva, Rome, Italy

Contact E-Mail Address: clelia.marmo@outlook.it

Introduction: The severity of bleeding and the time-to-endoscopy are generally recognised as risk factors for mortality in patients with GI bleeding. However, how to grade the bleeding severity (BS) is not clearly defined and it is not clear its relationship with the time-to-endoscopy. We found that the bleeding severity correlates with 5 clinical items: altered mental status, systolic blood pressure ≤100 mmHg, blood ureic nitrogen ≥130 mg/dl, haemoglobin ≤8 gr/dl and clinical presentation with hematemesis.

Aims & Methods: The aim of the study is to evaluate if the interaction between bleeding severity and timing-to-endoscopy could impact on the death risk. A prospective multicentre cohort study, including all consecutive patients with upper gastrointestinal bleeding admitted to 50 Italian hospitals was conducted. Charlson's *comorbidity index* and ASA scores were used to define the patients' performance status. According to the previously cited clinical items, we defined bleeding severity (BS) and graded it in low, intermediate, and high-risk classes depending on the presence and the number of items at the time of admission. Timing to endoscopy was defined according to ESGE* guidelines and was divided into 4 time-frames (<6h; 6/12h; 12/24h; >24h).

Weight of risk factors for bleeding severity

Bleeding Severity	Weight
Altered Mental Status	3
Systolic blood pressure ≤100	2
Blood Ureic Nitrogen ≥130 mg/dl	2
Haemoglobin ≤8 gr/dl	2
Hematemesis	1
Max total	10

Results: 2,525 patients were included (mean age 68 [±15.8], male 67.3%); the bleeding was non-variceal in 82.3%. Overall, 176 patients died (6.9%); 28 (1.9%) in the low BS group (1,463 patients), 28 (8.6%) in the intermediate BS group (606 pts) and 96 (21%) in the high BS group (p<0.000). In our population, the 4-time frames do not impact on the mortality in the low and intermediate classes of risk. In the high BS class, there is an interaction between the time to endoscopy and the mortality, with the lower mortality observed in the 6/12 hrs frame.

Conclusion: In our population, the death risk gradually rises as the bleeding severity increases. Bleeding severity identifies 3 different classes of death risk and the time to endoscopy seems unrelated to mortality in low and intermediate BS classes. In the high BS patients, the lower mortality was observed in the timing to endoscopy 6-12 hrs.

References: * Ian M. Gralnek et al. Endoscopy 2021; 53: 300–332

Disclosure: nothing to disclose.

MP561

SEDATION PRACTICES AND PARADOXICAL REACTIONS IN UPPER GASTROINTESTINAL ENDOSCOPY: AN ONLINE NATIONWIDE SURVEY IN JAPAN

T. Watanabe¹, T. Hirasawa², A. Inaba¹, H. Sunakawa¹, K. Nakajo¹, T. Kadota¹, K. Shinmura¹, T. Yano¹

¹Japan National Cancer Center Hospital East, Gastroenterology and Endoscopy, Kashiwa, Japan, ²Cancer Institute Hospital, Japanese Foundation of Cancer Research., Gastroenterology, Tokyo, Japan

Contact E-Mail Address: takaswat@east.ncc.go.jp

Introduction: Globally, there is no standardized approach to sedation during endoscopic procedures, leading to variability in practices both regionally and across institutions. Sedation plays a crucial role in alleviating patient discomfort and ensuring the safety of endoscopic examinations and treatments.

However, it occasionally leads to paradoxical reaction, which can adversely affect the outcomes of these procedures. As of 2023, in Japan, choice of sedatives and frequency of their use, and the incidence and management of paradoxical reaction during upper gastrointestinal endoscopy remain unclear.

Aims & Methods: This study is aimed to delineate the frequency and types of sedatives used in upper gastrointestinal endoscopy across different medical facilities in Japan and to investigate the extent of anesthesiologist involvement and the incidence and handling of paradoxical reactions. An anonymous online survey was distributed from November 28 to December 13, 2023, through mailing lists reaching about 2,500 gastroenterologists and endoscopists.

Results: The survey received responses from 635 participants including 418 hospital-based endoscopists, 118 clinic-based endoscopists, and screening 29 facility-based endoscopists. Sedation performed by anesthesiologists was found to be rare, with only 3.5% of examinations and 7.1% of treatments being managed by anesthesiologists once a week or more. 87% of respondents reported not using anesthesiologists managed sedation at all for examinations, and 61% reported the same for treatments.

Regarding the frequency of sedation use during examinations, 9.8% of respondents reported using sedation in over 95% of cases, and 53% reported using it in more than half of the cases. 6.6%, reported not using sedation at all. In treatments, 86% of respondents used sedation in over 95% of cases, and 96% used it in more than half of their cases.

Midazolam was the most common sedative for examinations (n=593), chosen in over 80% of cases by 54% of respondents, while only 9.9% never selected it. Meperidine was frequently used by 10% of respondents in similar proportions. Other sedatives like flunitrazepam, diazepam, and propofol were selected by 5.0%, 3.5%, and 2.5% of respondents, respectively.

For treatments (n=401), midazolam was again the most frequently chosen, selected in over 80% of cases by 72% of respondents. Other commonly used sedatives were meperidine and pentazocine, selected in over 80% of cases by 29% of respondents, with propofol and dexmedetomidine each chosen by 12%.

64% of endoscopists who use sedative drugs experienced difficult cases to continue procedures due to paradoxical reactions, with a median incidence of 5% of cases and median of two cases are required to discontinue procedures. Midazolam was the most common cause, reported by 91% of respondents, followed by flunitrazepam (13%), diazepam (8.8%), and propofol (8.3%). The typical response involved physically restraining the patient with multiple staff members' assistance. Eighteen percent of respondents did not use antagonist drugs for examinations, and 22% for treatments.

Conclusion: In Japan, over half of upper gastrointestinal procedures used sedation, with 53% in diagnostics and 96% in treatments predominantly using midazolam. Additionally, 64% of physicians experience difficulties with paradoxical reactions during procedures under sedation by themselves.. These reactions are recognized as significant challenges that must be addressed in the management of sedation for upper gastrointestinal endoscopy.

Disclosure: Nothing to disclose.

MP562

THE ROLE OF NURSE IN HIGH QUALITY GASTROSCOPY

M. Lupo¹, G.C. Fernicola¹, F. Pigò¹, I. Lolli¹, G.M. De Franco¹

¹Azienda Ospedaliera universitaria di Modena, Gastroenterology and Digestive Endoscopy, Modena, Italy

Contact E-Mail Address: marinella.lupo@gmail.com

Introduction: Digestive Endoscopy services are at third place among hospital services in terms of CO₂ production. In this regard, the European Commission requires a complete reduction of CO₂ emissions by 2050 1-3 . According to the International Agency for cancer research (AIRC) stomach cancer is at 5 th place for incidence and 4th place for mortality 4,5 and these ones have not changed on national scale and they have remained stable since about twenty years. Therefore is necessary an improvement of the endoscopy procedure, that can recognize the risk factors in real time and guarantee more accurate patient care.

Aims & Methods: From April to July 2023 we realized a retrospective control trial enrolling all patients undergoing a gastroscopy added with Endofaster for the evaluation of gastric ph and the presence of H. Pylori.

Results: In a sample of 158 enrolled patients the Endofaster system has demonstrated an accuracy of 79% with a negative predictive value (NPV) of 95%, According to main scientific studies for the diagnosis of atrophic gastritis (AG) and the H. Pylori urease test.

Conclusion: The Endofaster system allows to recognize in real time the alert situations, leading the medical- nursing equipe to the evaluation of the highlighted risk picture, for a best and personalize planning of the diagnostic and therapeutic iter. Furthermore the reduction in biopsy samples leads to a decrease of about 48% in CO₂ emissions per year. 6 Nurses have the opportunity to work alongside and in support of the specialist during an high quality gastroscopy.

References: 1. E. Rodriguez de Santiago, M. Dinis- Riberio et al. Reducing the environmental footprint of gastrointestinal endoscopy: European society of Gastrointestinal endoscopy (ESGE) and European society of gastroenterology and endoscopy nurses and associates (ESGENA) positions Statement. Thieme, 2022:54:797-826.

2. F. Bortoluzzi, L. Lelli et al Sustainability in gastroenterology and digestive endoscopy: position paper from the Italian association of hospital gastroenterology and digestive endoscopy (AIGO). Digestive and liver disease, may 2022.

3. Comune Reggio Emilia. Progetto Carbon Zero. Metodologia di calcolo delle emissioni di CO₂ nel rispetto dei requisiti della norma UNI ISO 14064-1, applicabile alle nuove urbanizzazioni. Febbraio 2020.

4. Globoscan 2020 – The Global Cancer Observatory - World Health Organization

5. AIOM (2021) I numeri del cancro.

6. Esposito, D.Libanio,I.Ligato, D.Ramos Silva, E. Dilaghi, R.Ortigao, J.Chaves, B. Annibale, M. DinisRibeiro. Endofaster and eggim for the diagnosis of Helicobacter pylori infection and advanced stages of gastric intestinal metaplasia. Poster session - UEGW 2022.

Disclosure: Nothing to disclose.

Identifying drug targets in IBD: Part 2

11:30-12:30 / Poster Stage 1

MP563

GUSELKUMAB DECREASES KEY CELLULAR INFLAMMATORY PROCESSES ACROSS ILEUM AND COLON TISSUE IN CROHN'S DISEASE

D. Richards¹, S. Venkat¹, D. Ruane¹, M. Zeeman¹, N.A. Terry¹, M. Vetter¹, M.A. Gomez Camacho¹, D. Cua¹, T.C. Freeman¹, B. McRae², B.G. Feagan³, W. Reinisch⁴, P. Branigan¹

¹Janssen Research & Development, LLC, Spring House, PA, United States of America, ²Janssen Research & Development, LLC, Cambridge, MA, United States of America, ³Alimentiv, Inc, Western University, London, Ontario, Canada, ⁴Division Gastroenterology & Hepatology, Medical University of Vienna, Vienna, Austria

Contact E-Mail Address: DRicha14@ITS.JNJ.com

Introduction: Crohn's disease (CD) is characterized by significant heterogeneity in phenotypic disease expression, making it challenging to define molecular mechanisms associated with disease and response to therapy. Here we provide a detailed evaluation of the cellular and molecular mode of action of guselkumab (GUS), an IL-23p19 subunit antagonist, in participants with moderately to severely active Crohn's disease (CD) from the GALAXI Phase 2b induction study (NCT03466411).

Aims & Methods: Serum samples were evaluated at baseline, Week (WK) 4 and WK12 for proinflammatory and effector cytokines (serum amyloid A [SAA], CRP, IL-6, IFN γ , IL-22 and IL-17A) from participants treated with intravenous (IV) GUS 200 mg, 600 mg or 1,200 mg induction therapy (n=131 combined) or placebo (PBO) (n=44) who had at least one paired sample at WK0 with WK4 or WK12. A subset of participants from the combined GUS IV induction treatment and PBO groups with a history of stricture or current ileal narrowing were evaluated for collagen-formation (PRO-C3) and degradation (C3M, C4M) serum biomarkers. Baseline biopsies from 241 participants were obtained from rectum (R), splenic flexure (SF), and terminal ileum (TI). Transcriptional profiling was performed with bulk RNA sequencing (RNAseq). An objective tissue-based Molecular Activity Score (MAS) was used to identify inflamed biopsy samples. Inflamed tissue was used to assess regional molecular profiles which were correlated with paired regional histology scores defined by Global Histologic Activity Score (GHAS) and endoscopic severity defined by Simple Endoscopic Score for CD (SES-CD).¹ Transcriptional modules developed using publicly available single cell RNAseq data were then used to assess changes in baseline inflamed tissue associated with specific cellular and immune processes at WK12. Paired biopsies were assessed from the combined GUS IV induction treatment (n=140) and PBO groups (n=51).

Results: Local MAS per region showed highest correlations with paired GHAS from adjacent biopsies (Spearman R 0.72; SF 0.63 and TI 0.70), followed by SES-CD in local segments (R 0.69; TI 0.58). Compared with placebo at WK12, GUS reduced ileum and colon RNA expression levels of IL-17A, IL-22, and IFN γ at Week 12 ($P \leq 0.05$). GUS also significantly decreased cellular processes associated with epithelial inflammation, inflammatory fibroblast and myeloid biology, interferon response and the IL-23 pathway. Regional molecular change was greatest in colon, followed by rectum and ileum. Serum collagen degradation biomarker C4M and the C3M/PRO-C3 ratio demonstrated an association with ileal narrowing and history of stricture at baseline ($P \leq 0.001$). GUS IV induction treatment reduced serum SAA, CRP, and IL-22 as early as WK4 ($P \leq 0.01$) which further declined through WK12 (SAA, CRP, IL-6, IFN γ , IL-22 and IL-17A [$P \leq 0.001$]).

Conclusion: Induction treatment with GUS attenuated key proinflammatory and effector cytokines associated with the IL-23 pathway in CD. Tissue transcriptomics demonstrated attenuation of key immune and inflammatory related processes across all tissue regions compared with PBO. Association of serum collagen degradation biomarkers with ileal

narrowing at baseline provides rationale to further explore the association of differentially expressed genes and transcriptional processes with stricture, fibrosis, and response to treatment.

References: 1. Richards D, et al. P006 Development of a Crohn's disease molecular activity score to identify region-specific chronically inflamed and non-inflamed processes. *J Crohns Colitis*. 2024;18 (S1):i251-i252. <https://doi.org/10.1093/ecco-jcc/jjad212.0136>

Disclosure: DR, SV, DR, MZ, NAT, MV, MG, DC, TCF, BM, and PB are current or former employees of Janssen and may hold stock in Johnson & Johnson.

BF received consulting fees from AbbVie, AbolentIS, AgomAB, Alliantera, Amgen, AnaptysBio, Applied Molecular Transport Inc, Arena, Avaro Capital Advisors, Atomwise, BioJump, Biora, Boehringer-Ingelheim, Boxer, Celsius, Celgene/Bristol Myers Squibb, Connect BioPharma, Cytokine, Disc Medicine, Duality, EcoR1, Eli Lilly, Equillum, Ermium,, First Wave, First Word Group, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, Gossamer, GlaxoSmithKline, Hinge Bio, Hot Spot, Index, Imhotex, Immunic, JAKAcademy, Janssen, Japan Tobacco Inc., Kaleido, Landos, Leadiant, L.E.K. Consulting, LifeSci Capital, Lument AB, Millennium, MiroBio, Morphic, Mylan, OM Pharma, Origo, Orphagen, Pandion, Pendopharm, Pfizer, Prometheus, Play to Know AG, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Sandoz, Sanofi, Seres, Silverback, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared Ltd., Viatrix, Ysios, Ysopia, Zealand Pharma; a member of the speakers bureau for AbbVie, Janssen, Takeda, BI; payment for expert testimony from Morgan Lewis and Lenczner Slaght; support for attending meetings and/or travel from AbbVie, Janssen, Pfizer, Takeda, BI; participation on a Data Safety Monitoring Board or Advisory Board from AbbVie, Amgen, AMT, AnaptysBio, Boehringer-Ingelheim, Celgene/Bristol Myers Squibb, Eli Lilly, Genentech/Roche, Janssen, MiroBio, Origo BioPharma, Pfizer, Prometheus, RedX, Sanofi, Takeda, Tillotts, Teva, Progenity, Index, Ecor1Capital, Morphic, GlaxoSmithKline, Axio; stock or stock options in Gossamer.

WR has served as a speaker for AbbVie, Celltrion, Ferring, Janssen, Galapagos Medice, MSD, Roche, Pfizer, Sobi, Takeda, as a consultant for AbbVie, Amgen, AOP Orphan, Boehringer Ingelheim, Bristol Myers Squibb, Calyx, Celltrion, Eli Lilly, Galapagos, Gilead, Index Pharma, Janssen, Medahead, Microbiotica, Pfizer, Takeda; as an advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Galapagos, Janssen, Pfizer, and has received research funding from AbbVie, Janssen, Sandoz, Sanofi, Takeda.

MP564

ACUTE EXPOSURE OF EX VIVO INFLAMED UC AND CD BIOPSIES TO THE SELECTIVE SIK2/SIK3 INHIBITOR GLPG3970 RESULTS IN A STRONG REDUCTION OF PRO-INFLAMMATORY RESPONSES

L. Giorio¹, K. Arnauts¹, M. Colli², E. Vissers¹, B. Verstockt^{1,3}, S. Vermeire^{1,3}, S. De Vos²

¹KU Leuven, Department of Chronic Diseases and Metabolism (CHROMETA), Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ²Galapagos NV, Mechelen, Belgium, ³KU Leuven, University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium

Contact E-Mail Address: lorenzo.giorio@kuleuven.be

Introduction: GLPG3970, a potent and selective salt-inducible kinase (SIK) 2/3 inhibitor, exerts a dual mechanism combining anti-inflammatory and immunoregulatory activity.¹ In chronic inflammatory diseases, such as inflammatory bowel disease (IBD), GLPG3970 has the potential to restore immune balance and homeostasis.^{2,3} In a 6-week signal-detection phase 2a study in patients with ulcerative colitis (UC),⁴ GLPG3970 showed

positive effects in histology, endoscopy and faecal calprotectin versus placebo, despite no differentiation from placebo on change from baseline on total Mayo Clinic Score at week 6.^{4,5}

Aims & Methods: We investigated the dual mechanism of GLPG3970 in severely inflamed *ex vivo* treated IBD tissue biopsies. Inflamed intestinal biopsies (most affected segment; n = 9 per patient) were obtained from patients with UC (n = 10) and Crohn's disease (CD; n = 10) with active endoscopic disease (UC: Mayo endoscopic subscore ≥ 2 ; CD: SES-CD of ≥ 4). Patients were biologic-naïve (UC: n = 5; CD: n = 5) or biologic-experienced (UC: n = 5; CD: n = 5). Three individual biopsies per condition were exposed *ex vivo* for 24 hours to vehicle control (DMSO), tofacitinib (10 μ M, positive control) or GLPG3970 (60 μ M). Protein secretion in supernatant was analysed by V-PLEX Human Biomarker 54-Plex (two-way ANOVA, Dunnett's multiple comparison). RNA sequencing of biopsies was performed on Illumina NovaSeq 6000. Gene expression was quantified using Salmon (v1.5.2) and differential expression analysis was performed with DESeq2 (v1.28.0; criteria: $|\log_2FC| > 0.58$, FDR < 0.05, baseMean > 32).

Results: High levels of inflammatory cytokines and chemokines were observed in the supernatant after *ex vivo* culturing. Exposure to GLPG3970 resulted in a significant decrease of pro-inflammatory cytokines (e.g. TNF α , GM-CSF, IFN- γ , IL-2) and chemokines (e.g. MCP-1, MIP1 α , MIP1 β) in both UC and CD biopsies, relative to vehicle control. GLPG3970 activity was statistically stronger than tofacitinib for most evaluated proteins (*p* value), except for IL-1RA, IL-3, IL-9, IL-22, IL-23, among others. RNAseq analysis showed a clear signature of differentially expressed genes (DEGs) for GLPG3970 versus vehicle control (UC: 549 DEGs, with 288 downregulated, including pro-inflammatory genes *CSF2*, *MMP9* and *CCL4*; CD: 673 DEGs, with 238 downregulated, including *CSF2*, *CXCL10* and *CXCL11*). Tofacitinib versus vehicle resulted in 582 (UC) and 681 (CD) DEGs including JAK/STAT dependent genes, such as *MX1*, *SOCS3* and *IFITM1*. Direct comparison of GLPG3970 versus tofacitinib highlighted the impact of GLPG3970 on pathways involved in 'TGF- β signalling', indicative of enhancing immunoregulatory mechanisms, 'TNF α signalling via NF- κ B' and 'glycolysis', whereas tofacitinib mainly affected 'IFN- α response' and 'IFN- γ response' in both UC and CD biopsies. In addition, GLPG3970 exposure to *ex vivo* biopsies resulted in a partial reversion of UC and CD transcriptome signatures (Spearman correlation: -0.25 [UC], -0.22 [CD]).⁶

Conclusion: Acute exposure of GLPG3970 to *ex vivo* inflamed tissue biopsies from patients with UC and CD showed a strong reduction in the release of pro-inflammatory mediators. Transcriptomic analysis further confirmed GLPG3970's robust activity in reducing inflammatory NF- κ B-mediated pathways while modulating TGF- β -related immunoregulatory pathways versus tofacitinib. Our findings support the dual mechanism of GLPG3970 in relevant pathogenic pathways in IBD and confirm the therapeutic potential of SIK2/3 inhibition in treating patients with either UC or CD.

References: 1. Peixoto C *et al.* *J Med Chem* 2024;67:5233–58.

2. Pereira-Fernandes A *et al.* [abstract] *United European Gastroenterol J* 2021;9:S8.

3. Lavazais S *et al.* [abstract] *United European Gastroenterol J* 2021;9:S8.

4. ClinicalTrials.gov. A Study Evaluating the Effects of GLPG3970 Given as an Oral Treatment for 6 Weeks in Adults With Ulcerative Colitis (SEA TURTLE). 2020. Available from: <https://clinicaltrials.gov/study/NCT04577794> (Accessed 8 April 2024).

5. Galapagos. Galapagos demonstrates early clinical activity with SIK2/3 inhibition in inflammation. 2021. Available from: <https://www.glp.com/press-releases/galapagos-demonstrates-early-clinical-activity-with-sik2-3-inhibition-in-inflammation/> (Accessed 8 April 2024).

6. Massimo L *et al.* *Nat Comput Sci* 2021;1:511–15.

Disclosure: This study was funded by Galapagos NV (Mechelen, Belgium). Editorial and publications management support was provided by PharmaGenesis London, London, UK, and was funded by Galapagos NV.

LG and KA are joint first authors.

LG, KA and EV report no disclosures.

MC and SDV are employees of Galapagos.

BV reports research support from AbbVie, Biora Therapeutics (formerly Progenity), Landos Biopharma, Pfizer, Sosei Heptares and Takeda; speaker fees from AbbVie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, Lilly, MSD, Pfizer, R-Biopharm, Sandoz, Takeda, Tillots Pharma, Truvion Healthcare and Viartis; consultancy fees from AbbVie, Alfasigma, Alimentiv, Applied Strategic, AstraZeneca, Atheneum, BenevolentAI, Biora Therapeutics (formerly Progenity), Boxer Capital, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Lilly, Mylan, Inotrem, Ipsos, Janssen Pharmaceuticals, Pfizer, Sandoz, Sanofi, Santa Ana Bio, Sapphire Therapeutics, Sosei Heptares, Takeda, Tillots Pharma and Viartis; and stock options from Vagustim.

SV reports speaker and/or consultancy fees from AbbVie, Abivax, AbolentS Pharma, AgomAb Therapeutics, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Biora Therapeutics (formerly Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, Gilead Sciences, GSK, Hospira, IMIDomics, Janssen Pharmaceuticals, Johnson & Johnson, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic Therapeutic, MRM Health, MSD, Mundipharma, Pfizer, ProDigest, Prometheus Biosciences, Roberts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillots Pharma, VectivBio, Ventyx Biosciences and Zealand Pharma; grants from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; and participation on a data safety monitoring board for Sanofi.

MP565

ACTIVATED MACROPHAGE-CONDITIONED MEDIA INDUCES FIBROGENESIS IN A GASTROINTESTINAL SCAR-IN-A-JAR MODEL THAT IS QUANTIFIABLE WITH SEROLOGICAL BIOMARKERS OF COLLAGEN FORMATION

M. Pehrsson¹, F. Gillesberg², Y. Luo³, T. Tsapanou Katranara¹, E.M. Hur³, A.-C. Bay-Jensen¹, S.H. Nielsen¹, S. Khan², M. Sorokina Alexdóttir¹, H.S. Hector¹, J.H. Mortensen¹

¹Nordic Bioscience A/S, Immunoscience, Herlev, Denmark,

²University of Copenhagen, Copenhagen, Denmark, ³BMS, Lawrenceville, United States of America

Contact E-Mail Address: mpe@nordicbio.com

Introduction: Chronic inflammation in inflammatory bowel disease can lead to the development of intestinal fibrosis, exacerbating the disease. The activation of immune cells results in the release of pro-inflammatory cytokines suspected to drive the activation of fibroblasts and excessive formation of extracellular matrix proteins. While anti-inflammatory therapies exist, their direct effects on fibrogenesis are limited, and model systems for evaluating inflammation-dependent fibrosis are warranted.

Aims & Methods: We aimed to evaluate the profibrotic effects of activated macrophages in a gastrointestinal scar-in-a-jar model by quantifying type I, III, and type VI collagen and fibronectin formation biomarkers.

Macrophages (M ϕ) were isolated from buffy coats from healthy donors and polarized to TNF- α producing M1-like macrophages (M1-M ϕ) using 25 ng/mL IFN- γ and M-CSF over two rounds from days 0 to 6 and from days 7 to 12. The M1-conditioned media was collected on days 6 and 12 (experimental groups: days 0-6 and days 7-12). Colonic fibroblasts (CCD18-Co) were cultured in a crowded pseudo-3D environment using Ficoll (75 mg/mL Ficoll 400 and 112.5 mg/mL Ficoll 70) and supplemented with 50 μ g/mL ascorbic acid to support collagen synthesis. Starting on day 0, exchanging the media every fourth day, the cells were stimulated with 0.3, 3, and 30% of M1 conditioned media, 50 pM TGF- β , or 25 ng/mL IFN- γ and

M-CSF for 12 days, using 3% FBS as the control. The biomarkers PRO-C1, PRO-C3, PRO-C6, and FBN-C, quantifying type I, III, and VI collagen formation and fibronectin, were measured in the supernatants on days 0, 4, 8, and 12. The metabolic activity of the cells was assessed on days 0 and 12 using an Alamar Blue assay. The statistical differences in biomarker levels were calculated using the area under the curve (AUC) compared with the unstimulated FBS control applying Brown-Forsythe and Welch or one-way ANOVA tests.

Results: Quantified using the PRO-C1, PRO-C3, PRO-C6, and FBN-C biomarkers stimulation with 30% M1-Mφ media from days 0-6 and 7-12 resulted in a switch in collagen formation compared to the FBS control, reducing type I collagen and fibronectin and increasing type III and VI collagen formation (Table 1). A similar response was observed using 3% of 0.3% M1-Mφ media, though to a lesser degree (Table 1). The data suggest increased pathological fibroblast activity and fibrotic deposition of type III and VI collagen formation driven by Mφ-derived cytokines. TGF-β, a known profibrotic cytokine, induced a significant formation of type I, III, VI, and fibronectin compared to the FBS control (Table 1), demonstrating a different fibrotic biomarker profile than Mφ induced fibrosis. IFN-γ+M-CSF stimulation, used for Mφ activation, inhibited the formation of type III collagen (Table 1).

Stimulation	PRO-C1 (p-value)	PRO-C3 (p-value)	PRO-C6 (p-value)	FBN-C (p-value)
30% M1-Mφ (days 0-6/days 7-12)	Decreased: p<0.05 / p<0.05	Increased: p<0.01 / p<0.0001	Increased: p<0.01 / p<0.0001	Increased: ns / p<0.01
3% M1-Mφ (days 0-6/days 7-12)	Decreased: p<0.05 / ns	Increased: ns / p<0.01	Increased: ns / p<0.001	Increased: ns / p<0.05
0.3% M1-Mφ (days 0-6/days 7-12)	ns	Increased: ns / p<0.05	ns	Increased: ns / p<0.05
TGF-β	Increased: p<0.0001	Increased: p<0.01	Increased: p<0.0001	Increased: p<0.0001
IFN-γ+M-CSF	ns	Decreased: p<0.0001	ns	ns

Calculation of statistical differences was done between the specific stimulation and the unstimulated FBS control applying Brown-Forsythe and Welch or one-way ANOVA tests. For each biomarker a notation of „Increased or Decreased“ is applied to indicate the numerical change compared to the FBS control. P-values < 0.05 was deemed a significant change. Abbreviations: ns, non-significant

Table 1: Overview of the statistical differences in the PRO-C1, PRO-C3, PRO-C6, and FBN-C biomarkers between the stimulated and unstimulated FBS control.

Conclusion: Stimulating colonic fibroblasts with conditioned media from activated macrophages induced a profibrotic response with increased type III and type VI collagen formation. The applied serological biomarkers enabled the objective quantification of collagen and fibronectin formation to assess fibrogenesis in the model and their potential use for investigating macrophage induced fibrosis.

Disclosure: Martin Pehrsson, Marta Alexdottir, Helene Hector, Morten Karsdal, and Joachim Mortensen are employed at Nordic Bioscience Yi Luo and Eun Mi Hur are employed at Bristol-Meyers Squibb. The remaining authors have no declaration of conflict.

MP566

A NEW APPROACH TO MOLECULAR DIAGNOSTICS AND STAGING OF ULCERATIVE COLITIS

A. Iakovlev¹, G. Tarasova¹, A. Volkov¹, O. Bastovaya¹, A. Zubova¹, V. Piscovets¹
¹Rostov State Medical University, Gastroenterology, Rostov-on-Don, Russian Federation

Contact E-Mail Address: gastroklinika@yandex.ru

Introduction: The molecular pathways for the development of ulcerative colitis (UC) are unclear. The purpose of the work is to study the molecular interactions of the apoptotic pathway in patients with UC.

Aims & Methods: The study was prospective comparative cohort with parallel design and included 65 patients (range from 22 to 35 years, 24 men and 41 women) with left-sided UC, mild and moderate activity (True-love - Witts' criteria, Mayo score). The induction of UC remission assumed the acceptance of mesalazine 3 to 4 g/day p.o. and rectally 1 to 2 g/day, the duration of therapy was 4.6 years. The control group included 30 healthy individuals. The separation of individual proteins of colon mucosa was based on technologies of IEF, SDS-PAGE, 2DPAGE, by standard sets (MB-HIC C8 Kit, MB-IMAC Cu, MB-Wax Kit, «Bruker», USA). Automated mass spectrometry imaging was performed by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF-MS/MS, Ultraflex II, «Bruker», USA). The partially identified sequences were then submitted to “BLAST protein-protein” and screened against the Homo sapiens Swissprot database to check if this identification matched the MASCOT-identification (Matrix Science, UK). The data of the molecular interactions and functional features of proteins were received with STRING 10.0 database. Based on the data of standard methods of identification of UC and molecular phenotyping of colon mucosa we conducted new prognostic markers, molecular pathways of UC and diagnostic tests in patients with UC. Statistical analysis of the survey data was performed using the software “Statistica 12.0” (Statsoft).

Results: Bioinformatics analysis revealed the presence of molecules that are the participants in the universal pathways of UC in the active stage, and the molecular interactions involved. We identified following functional groups of peptides and proteins in molecular patterns of biotates of colon mucosa in UC patients: peptides and proteins regulating the barrier function of colon mucosa; proteins-participants of specific metabolism in epitheliocytes and endocrinocytes; proteins of the fibrosis in colon mucosa; proteins regulating cell cycle, oncogenesis, proteolysis in cell, hormones processing, angiogenesis, coagulation factors; proteins of free radical oxidation and antioxidant system; proteins regulating the receptor activity of epitheliocytes and immune cells; structural proteins of colon mucosa; transcription and translation factors regulating the activity of cell nucleus, regulators of protein folding; transport proteins; proteins-enzymes of detoxification. Significant decrease of the PPARγ expression promotes the activation of STAT and AP-1 signaling pathways, which promotes an increase in the synthesis of IL-2,6,8,12, TNFα, matrix metalloproteinases, the activity of immune and inflammation processes in colon mucosa. A significant increase in the NF-κB expression in colon mucosa is associated with the activation of TNFα and IL-1, which promotes the increase of immune processes in colon mucosa. The molecular interactions of β-defensin-1: the reduction of the β-defensin-1 expression in cells of colon mucosa is accompanied by increased expression of CCR6, which promotes the formation of inflammatory infiltrates in colon submucosa in UC.

Conclusion: Identification of potential new molecular markers for UC development may provide opportunities for the development of diagnostic tests to evaluate the disease.

Disclosure: Nothing to disclose.

MP567

WITHDRAWN

MP568

DISCOVERY AND CHARACTERIZATION OF A NOVEL HIGH-AFFINITY ANTI-TL1A MONOCLONAL ANTIBODY WITH EXTENDED HALF-LIFE FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

J. Ernst¹, K. Avery¹, V. Davra¹, M. Faber¹, J. Qi¹, T. Truong¹, S. Hao¹, C. Nguyen¹, K. Balcazar¹, C. Weeramange¹, H. Nguyen¹, T. Anzelon¹, E.F. Cardozo-Ojeda¹, R. Rashid¹, J. Diaz¹, J. Wieler¹, S. Karki¹, S. Belouski¹, S. Chu¹, J. Kanodia¹, R. Bahjat¹, D. Szymkowski¹, N. Barlow¹, K. Hung¹, B. Dahiyat¹, S. Gujrathi¹, J. Desjarlais¹

¹Xencor, Inc, Pasadena, United States of America

Contact E-Mail Address: jernst@xencor.com

Introduction: Tumor necrosis factor (TNF)-like ligand 1A (TL1A) mediates a broad spectrum of pro-inflammatory and fibrotic effects and has been genetically linked to multiple immunologic disorders. In clinical trials, antagonist antibodies that interfere with the interaction between TL1A and Death Receptor 3 (DR3) reduce disease activity in ulcerative colitis (UC) and Crohn's disease (CD).

Here, we provide data on a novel human IgG1 effector-less monoclonal antibody (mAb) that incorporates the Xtend™ half-life extension technology. This antibody binds soluble and cell surface-expressed TL1A with high affinity and selectivity and potently inhibits TL1A-DR3 mediated signaling.

Aims & Methods: Over 1000 anti-TL1A antibodies were screened in binding and/or functional assays. Select clinical candidate antibodies were further compared to clinical-stage anti-TL1A mAbs PRA023/MK-7240/tulisokibart, RVT-3101/RG6631, and TEV-48574. Binding affinity of the lead antibodies to soluble TL1A was determined by surface plasmon resonance (SPR). Binding to cell plasma membrane-expressed TL1A was confirmed by flow cytometry (FACS). Competitive inhibition of TL1A binding to DR3 and its decoy receptor DcR3 was determined by ELISA and biolayer interferometry. Inhibition of TL1A binding to plasma membrane-expressed DR3 was evaluated using FACS.

Antibody antagonism of cellular DR3 signaling by exogenous TL1A was evaluated through assessment of TF-1 cell apoptosis and interferon γ (IFN γ) secretion from CD4⁺ T cells. Lead antibodies incorporating the Xtend™ Fc domain (M428L/N434S substitutions) to improve half-life were evaluated in pharmacokinetic studies using human FcRn knock-in mice and non-human primates.

Results: The clinical candidate anti-TL1A antibodies bind with high affinity and specificity to trimeric TL1A and not to the related TNF ligand superfamily members LIGHT, TRAIL and FasL. The lead antibodies demonstrate an apparent K_D of less than 20 pM for soluble TL1A at 37°C and bind to TL1A over-expressed on the cell plasma membrane. Further, these antibodies potently inhibit TL1A-induced apoptosis of TF-1 cells, and IFN γ secretion from human CD4⁺ T cells - all with IC₅₀ values comparable to those of RG6631 and lower than those of tulisokibart. Lead antibodies demonstrate an improved serum half-life in human FcRn knock-in mice relative to the non-half-life extended RG6631.

In preliminary non-human primate studies, the clinical candidate antibodies demonstrate half-lives greater than 20 days, with the expected antibody-TL1A complex formation. Allometric scaling using parameters adjusted for half-life engineered antibodies predict human half-lives of 70 days or higher, potentially enabling dosing intervals of Q8wk or longer. Preliminary formulation development supports a high concentration, citrate-free formulation above 150 mg/mL, suitable for subcutaneous administration.

Conclusion: The clinical candidate antibodies bind with high affinity and specificity to TL1A and demonstrate potent blockade of TL1A-mediated DR3 receptor signaling. In human FcRn knock-in mice and in cynomolgus monkeys, these antibodies show an extended half-life consistent with FDA-approved antibodies using the Xtend™ technology. These data demonstrate the therapeutic potential of the clinical candidate antibodies in the treatment of TL1A-mediated diseases such as ulcerative colitis and Crohn's disease - with the advantage of infrequent subcutaneous dosing.

Disclosure: The authors are employees of Xencor, Inc.

MP569

BIFIDOBACTERIUM ANIMALIS INDUCES ANTIVIRAL RESPONSES IN HUMAN PRIMARY EPITHELIAL CELLS DERIVED FROM ILEAL AND COLONIC ORGANIDS

A. Stepanyan¹, M. Scarpa², G. Bernabè³, P. Brun³, V. Zatta³, M. Scarpa¹, I. Castagliuolo^{1,3}

¹Azienda Ospedaliera Universitaria di Padova, Padova, Italy,

²Veneto Institute of Oncology IOV-IRCCS, Padova, Italy, ³University

of Padova Dept. of Molecular Medicine, Dept. of Molecular Medicine, Padova, Italy

Contact E-Mail Address: stepanyan.astgh@gmail.com

Introduction: Viral infections targeting the intestinal epithelium are a significant cause of gastroenteritis, leading to decreased nutrient and electrolyte absorption. Despite supportive care, the lack of effective treatment options necessitates exploration of various alternatives, with probiotics being among them. Probiotics, live microorganisms with demonstrated health benefits, have emerged as a potential solution due to their ability to interfere with viral replication and modulate immune responses. The use of intestinal organoids in research has highlighted the advantages, particularly in mimicking the innate immune response and allowing for the study of host-specific interactions.

Aims & Methods: Building upon *in vivo* evidence of probiotics' antiviral activity, this study aims to investigate their immunomodulatory effects on primary human intestinal epithelial cells derived from organoids. Intestinal organoids were established from the non-inflamed ileal and colonic mucosa of Crohn's disease and Ulcerative colitis patients. Organoid-derived monolayers were generated and used to evaluate the anti-viral effect of *L. rhamnosus* GG® and *B. animalis* ssp. *lactis* BB-12. Differentiated intestinal epithelial monolayers were exposed to the probiotic strains with multiplicity of infection (MOI) 1:10 for 3 hours, and following extensive washing incubated for additional 24 hours in complete medium containing antibiotics. The expression of viral recognition genes (*IFIH1*, *TLR3*, *TLR7*, *TLR9*), antiviral response signaling pathway genes (*IRF3*, *IRF7*, *MAVS*), antiviral cytokines (Type I IFN) genes (*IFNA1*, *IFNB1*), Type I IFN signaling pathway genes (*STAT1*, *STAT2*) and Interferon Stimulated Genes (*EIF2AK2*, *IFITM1*, *IFITM2*, *IFITM3*, *OAS1*, *MX1*) was assessed by Real Time RT-PCR.

Results: Exposure to both *L. rhamnosus* GG® and *B. animalis* ssp. *lactis* BB-12 significantly increased the expression of the antiviral cytokine *IFNB* in ileum-derived monolayers but not in colon-derived monolayers compared to untreated controls. Moreover, *B. animalis* ssp. *lactis* BB-12, but not *L. rhamnosus* GG®, significantly induced the expression of *OAS1*, a gene involved in the inhibition of viral replication, in both ileum and colon-derived monolayers compared to untreated controls.

Conclusion: Preliminary findings suggest that certain probiotic strains may elicit robust antiviral responses, presenting a promising avenue for the prevention and management of viral gastroenteritis.

Disclosure: Nothing to disclose.

MP570

NATURAL COMPOUNDS IN ULCERATIVE COLITIS AND IRRITABLE BOWEL SYNDROME: INSIGHTS FROM IMMUNE-METABOLIC PROFILES

C. Mcshane¹, F. O'Connell², M. Piggott³, I. Obaidi³, D. Kevans¹, H. Sheridan³, J. O'Sullivan²

¹St James's Hospital Dublin, Gastroenterology, Dublin, Ireland, ²Trinity College Dublin, Department of Surgery, Trinity St. James's Cancer Institute and Trinity Translational Medicine Institute, Dublin, Ireland, ³Trinity College Dublin, NatPro Centre, School of Pharmacy and Pharmaceutical Sciences, Dublin, Ireland

Contact E-Mail Address: mcshanca@tcd.ie

Introduction: Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) represent chronic and occasionally disabling conditions, necessitating innovative treatment strategies. Covering 14% of Ireland's landscape, bogland ecosystems house unique plant biodiversity, yielding biologically active secondary metabolites.

Informed by traditional medicinal knowledge and in vitro screening for immunomodulatory potential, three plant extracts (NTP0226A, NTP0127B, NTP0206EA) were selected for exploration of their potential to treat IBD and IBS within the "Unlocking Nature's Pharmacy from Bogland Species" project.

Aims & Methods: Patients undergoing colonoscopy were prospectively recruited in three cohorts: healthy controls, IBS, and ulcerative colitis (UC). Recto-sigmoid biopsies were collected. Ex-vivo colonic tissue explants were generated and cultured for 24 hours with treatments (Infliximab, NTP0226A, NTP0127B, NTP0206EA). Real-time energy metabolism profiles and secretion of 10 inflammatory mediators were assessed using Seahorse Xfe24 analyser and multiplex ELISA, respectively. Levels of macrophage polarisation following exposure to treated explants were analysed by flow cytometry. Total protein content allowed result normalization, with significance set at $P < 0.05$.

Results: Twenty-seven patients were recruited (6 healthy controls, 6 IBS, and 15 UC). UC patient explants exhibited elevated glycolytic metabolism and increased IL-4, IL-6, and IL-12p70 secretion compared to non-UC patients. No differences were observed between healthy controls and IBS patients. Linear regression did not show difference between age and mitochondrial bioenergetics. There was no change in metabolism profiles of any cohort following treatment with Infliximab or the 3 novel extracts. In the UC tissue, treatment with Infliximab reduced IL-12p70 secretion ($p=0.0098$), this reduction was not seen in the other 2 cohorts. NTP0206EA reduced IL-10 secretion in the UC cohort ($p=0.0255$). In the IBS cohort; NTP0127B reduced IL-10 secretion ($p=0.0048$) and NTP0226A reduced IL-4 ($p=0.004$) and IL-6 ($p=0.0219$) secretion. Macrophages exposed to UC explants treated with infliximab showed a reduction in HLA-DR, CD54 and CD163 and an increase in TIM-3 and CD206 expression ($p<0.05$). Macrophages exposed to UC explants treated with NTP0206EA showed reduced CD163/CD206 expression ($p<0.05$). NTP0226A and NTP0127B did not alter macrophage polarisation. Principal components analysis demonstrated reduced separation between the immune-metabolic profiles of UC patients and healthy controls following treatment with NTP0226A.

Conclusion: Using an explant model, we have shown that UC patients have a distinct immune-metabolic profile modifiable by a standard IBD therapy and novel plant extracts. Blockade of IL-6 trans-signalling has recently shown promise as an effective treatment target in IBD. Our natural extract NTP0226A reduced IL-6 secretion in IBS patients and is a promising candidate for therapeutic exploration. These findings contribute to our understanding of the complex interplay in the colonic microenvironment and highlight potential avenues for novel therapeutic interventions.

References: <https://www.cso.ie/en/csolatestnews/pressreleases/2021pressreleases/pressstatementecosystemaccounts-peatlandsand-heathlands2018/>

Disclosure: Nothing to disclose.

MP571

LIPIDS DRIVE MYOFIBROBLAST ACTIVATION AND THE EPITHELIAL-MESENCHYMAL TRANSITION PROCESS IN CROHN'S DISEASE

G. Rizzo^{1,2}, A. Carriles Linares³, G. Mori¹, M. Wozny³, S.E. Pineda Chavez³, F. Hrvat³, L. Morosi^{4,5}, G. Martano^{4,6}, S.M.L. Ghisletti⁷, F. Gandolfi⁷, V. Valleslonga⁷, M. Paulis^{8,9}, L. Loy¹⁰, C. Bezzio¹⁰, P. Spaggiari¹¹, A. Dal Buono¹⁰, R. Gabbiadini¹⁰, M. Carvello¹², A. Spinelli^{3,12}, A. Repici^{3,13}, A. Armuzzi^{3,10}, S. Vetrano^{1,3}

¹IRCCS Humanitas Research Hospital, Department of Gastroenterology, Rozzano, Italy, ²University of Cagliari, Department of Medical Science and Public Health, Gastroenterology Unit, Cagliari, Italy, ³Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy, ⁴IRCCS Humanitas Research Hospital, Metabolomics Unit, Rozzano, Italy, ⁵IRCCS Humanitas Research Hospital, Laboratory of Cancer Pharmacology, Rozzano, Italy, ⁶CNR, Institute of Neuroscience, Milan, Italy, ⁷European Institute of Oncology (IEO) IRCCS, Department of Experimental Oncology, Milan, Italy, ⁸IRCCS Humanitas Research Hospital, Rozzano, Italy, ⁹National Research Council of Italy, Institute of Genetic and Biomedical Research, Milan, Italy, ¹⁰IRCCS Humanitas Research Hospital, IBD Unit, Department of Gastroenterology, Rozzano, Italy, ¹¹Humanitas Clinical and Research Center-IRCCS, Department of Pathology, Rozzano, Italy, ¹²IRCCS Humanitas Research Hospital, Colon and Rectal Surgery Unit, Rozzano, Italy, ¹³Humanitas Clinical and Research Center-IRCCS, Digestive Endoscopy Unit, Department of Gastroenterology, Rozzano, Italy

Contact E-Mail Address: alejandra.carrileslinares@humanitasresearch.it

Introduction: Fibrostenosis represents one of the major clinical complications of Crohn's Disease (CD). However, the molecular mechanisms underlying intestinal fibrogenesis remain poorly understood and anti-fibrotic therapy has not yet been developed. Growing evidence supports that oxidative stress and the epithelial-mesenchymal transition (EMT) process contribute to the development and progression of fibrosis.

Aims & Methods: Based on these evidences, we assessed the role of lipids in fibrogenesis and whether mitochondria dysfunction can support fibrosis formation.

Spatial metabolomics analysis and adipophilin (ADFP) staining were performed on surgical specimens from fibrotic ileum and the surrounding region (healthy) derived from CD patients. Fibroblasts isolated from fibrotic and healthy ileum and human induced pluripotent stem cell-derived intestinal organoids (iHOs) were treated for 1-3 weeks with lipid mix (2%) and analyzed by RNA sequencing. Pathways significantly modulated were validated by RT-PCR, WB, FACS analysis, and proliferative, migratory and contraction assays, and mitochondrial functions by Seahorse analyzer.

Results: Spatial metabolomics revealed a significant accumulation of lipids characterized by very long-chain fatty acids in the fibrotic area compared to surrounding healthy regions, which was further confirmed by ADFP staining. RNA-seq analysis showed overlapping dysregulated pathways between healthy fibroblasts stimulated with lipids and fibrotic fibroblasts, in particular genes related to cell cycle, cytoskeletal reorganization, migration, contractility and cell metabolism (oxidative stress) which were further confirmed by functional assays. Among the genes re-

lated to oxidative stress, lipid stimulation significantly decreased *NFE2L2* and promoted an increase in *CPT1A*, gene encoding for a fatty oxidation mediator.

Moreover, lipid-stimulated fibroblasts showed a reduction in mitochondrial respiration, particularly basal and maximal respiration, and spare respiratory capacity by Seahorse analysis. On the other hand, long exposure of iHOs to lipids promoted the EMT process through the upregulation of *TWIST*, *ZEB*, and *VIM*.

Conclusion: Lipid stimulation induced myofibroblast activation through oxidative stress and alteration of mitochondrial metabolism, and increased the expression of EMT transcription factors in intestinal epithelial cells (iHOs) that may support fibroblast-mediated pro-fibrotic activity. These data indicate that regulators of fatty acid oxidation involved in the fibrotic process may represent new potential targets for the treatment of fibrostenotic CD patients.

Disclosure: Nothing to disclose.

MP572

IDENTIFICATION OF IL36RN MISSENSE MUTATIONS IN CROHN'S DISEASE PATIENTS AS A POTENTIALLY NEW DRUG TARGET FOR TREATING RARE PATIENTS WITH OVER-ACTIVATION OF THE IL36 SIGNALING CASCADE

J. Hecker¹, J. Saurenbach¹, M. Letizia¹, B.-S. Löscher², A. Franke², K. Koop³, C. Neufert³, A. Schütz⁴, B. Siegmund¹, C. Weidinger¹, The TRR241 IBDome Consortium

¹Charité - Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany, ²University of Kiel, Institute of Clinical Molecular Biology, Kiel, Germany, ³Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Medicine 1, Erlangen, Germany, ⁴Max-Delbrück-Center for Molecular Medicine in the Helmholtz Association (MDC), Berlin, Germany

Contact E-Mail Address: Carl.weidinger@charite.de

Introduction: The interleukin 36 (IL-36) family includes the agonists IL-36 α , IL-36 β , IL-36 γ , which activate the NF- κ B pathway and the natural antagonist IL-36RA, which inhibits IL-36 signaling. While missense mutations in the gene encoding IL-36RA (*IL36RN*) are associated with severe skin inflammation, their role in Crohn's disease (CD) is currently unknown. Therefore, we here investigated if *IL36RN* mutations contribute to inflammation in CD and whether IL-36 signaling might represent a potential drug target for personalized therapy.

Aims & Methods: Mutations in *IL36RN* were identified by whole exome sequencing (WES) followed by targeted Sanger sequencing. Peripheral blood mononuclear cells (PBMCs) of affected patients were analyzed by mass cytometry and serum cytokines were measured by ELISA. Identified *IL36RN* mutations were characterized by overexpression experiments and functional assays. Clinical and molecular responses of one *IL-36RN* mutant patient to combined treatment with spesolimab and certolizumab pegol was assessed by fecal calprotectin, endoscopy and mass cytometry at week 0 and 12 of treatment.

Results: In a cohort of 86 ulcerative colitis patients, 244 CD patients and 45 healthy controls, we identified 4 CD patients with heterozygous missense mutations in *IL36RN* (IL-36RA S113L, IL-36RA P76L and IL-36RA L133I). In the patient carrying the IL-36RA S113L variant, we detected elevated serum levels of IL-18 and IL-23, as well as an increased frequency of TH17 cells in PBMCs, suggesting an overactivation of the IL-36 pathway. Overexpression experiments showed that IL-36RA S113L causes decreased expression of IL-36RA, resulting in increased IL-36 signaling. The patient was therefore treated with 1200 mg of the IL-36R blocking antibody spe-

solimab every 4 weeks and 200 mg of certolizumab pegol biweekly on the basis of an Out Of Scope request. This approach resulted in reduced intestinal inflammation and a reduction in the frequency of pro-inflammatory myeloid cells in PBMCs.

Conclusion: In this study, we show that pathogenic *IL36RN* mutations are present in a subset of CD patients and that blocking IL-36 signaling may represent a personalized therapeutic approach for this rare subset of patients in whom conventional biologic therapies have failed.

Disclaimer: Boehringer Ingelheim was given the opportunity to review the abstract for medical and scientific accuracy as well as intellectual property considerations in relation to the potential mention of BI substances. Boehringer Ingelheim had no role in the design, analysis or interpretation of the results in this study.

Spesolimab was made available on the basis of an out of scope request. Boehringer Ingelheim was given the opportunity to review this abstract as a courtesy.

Disclosure: Britta Siegmund has served as consultant for Abbvie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forga Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; Speaker fees: Abbvie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer and grant support by Arena/Pfizer (served as representative of the Charité).

Microbiota as a diagnostic and therapeutic tool

11:30-12:30 / Poster Stage 2

MP573

PREDICTIVE VALUE AND FUNCTIONAL IMPLICATION OF TRYPTOPHAN METABOLITE INDOLE-3-ALDEHYDE PRIOR TO *E. COLI* LATE ONSET SEPSIS IN PRETERM INFANTS IN DUTCH MULTICENTRE COHORT

Y. van Schajik^{1,2}, A.J. Pieterse^{1,2}, G. Pitotti^{1,3,2}, T.B.M. Hakvoort^{1,2}, I. Admiraal - van den Berg^{1,2}, M. Davids⁴, A.H.L.C. van Kaam⁵, N.H. de Boer^{6,2}, H.J. Niemarkt⁷, J.P.M. Derikx³, G. Gross⁸, T.G.J. de Meij^{9,2}, W.J. de Jonge^{1,6,10,2}, B. Sovran^{1,3,11,2}

¹Amsterdam UMC, Tytgat Institute for Liver and Intestinal Disease, Amsterdam, Netherlands, ²Amsterdam UMC, Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³Amsterdam UMC, Paediatric Surgery, Amsterdam, Netherlands, ⁴Microbiota Center Amsterdam, Amsterdam, Netherlands, ⁵Amsterdam UMC, Neonatology, Amsterdam, Netherlands, ⁶Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁷Máxima Medical Centre, Neonatology, Veldhoven, Netherlands, ⁸Reckitt/Mead Johnson Nutrition Institute, Science Platforms, Nijmegen, Netherlands, ⁹Amsterdam UMC, Department of Paediatric Gastroenterology, Amsterdam, Netherlands, ¹⁰University of Bonn, Surgery, Bonn, Germany, ¹¹Amsterdam UMC, Emma Center for Personalized Medicine, Amsterdam, Netherlands

Contact E-Mail Address: y.vanschajik@amsterdamumc.nl

Introduction: Late onset neonatal sepsis (LOS) is a leading cause of mortality in preterm infants, affecting up to 15% of preterm neonates and a mortality rate of ~15%¹. Clinical symptoms of LOS are nonspecific and the diagnosis is therefore often established in an advanced stage of infection, negatively impacting prognosis, illustrating the need for novel preclinical biomarkers².

This study aimed to identify predictive biomarkers for LOS in preterm infants using faecal metagenomics and targeted metabolomics. Functional implication of identified biomarker on preterm neonatal barrier function was assessed in foetal intestinal organoid models.

Aims & Methods: In a Dutch multicentre study, including 9 neonatal intensive care units, faecal samples and clinical data were collected daily from birth to onset of *S. aureus* and *E. coli* LOS in preterm neonates (<30wks gestation) and matched to healthy controls by gestational and postnatal age, mode of birth, antibiotics exposure and birth centre (n=10 *E. coli*, n=10 *S. aureus*). 16S sequencing and shotgun metagenomics was performed to characterise fecal microbiota, as well as targeted HPLC MS/MS to determine tryptophan (Trp) metabolites of serotonin, kynurenine and indole pathway up to 7 days before LOS diagnosis.

In vitro effect of Indole-3-aldehyde (I3A) and heat inactivated culture medium (CDM) of *E. coli* clinical isolates was assessed human foetal intestinal organoid models. Tight junction and AhR expression was determined in 3D organoids by RTqPCR on TJP-2, CLDN-1,-4,-10, OCLN, AHR and CYP1A1. Exposed 2D organoid monolayers were assessed by longitudinal trans epithelial electrical resistance (TEER) and wound healing assay³. Consecutively, effect of I3A on intestinal barrier function during infection with *E. coli* clinical isolate was assessed by barrier translocation and longitudinal TEER⁴.

Results: The metagenomic faecal relative abundance of *E. coli* was significantly higher 4-5 days before onset of clinical symptoms of *E. coli* LOS, compared to matched controls (P=0.045, 95% CI cont. -0.47-1.72%, LOS = 17.21-101.3%). In contrast, no significant difference in abundance of faecal *S. aureus* was detected in neonates prior to *S. aureus* LOS. Further analysis indicated altered genetic abundance of Trp related genes in the *E. coli* LOS metagenome 4-5 days prior to LOS diagnosis. Of detected me-

tabolites, Tryptamine was significantly decreased (adj.P=0.03), Indole (adj.P=0.002), Indole-3-sulfate (adj.P=0.02) and I3A (adj.P <0.0001) were significantly elevated prior to *E. coli* LOS.

3D fetal intestinal organoid experiments showed significantly increased CYP1A1 expression in organoids exposed to I3A at concentration measured in faeces (100µM). A trend of increased tight junction expression was observed, indicating potential effect of I3A on intestinal barrier prior to LOS. TEER measurements showed increased barrier resistance and decreased proliferation of I3A exposed 2D organoids.

Additionally, infection of I3A exposed organoid monolayers with clinically isolated *E. coli* showed indication of more rapid and increased barrier disruption.

Conclusion: This research indicates an increase in faecal relative abundance of *E. coli*, but not of *S. aureus* prior to LOS onset, and a functional difference mediated by Trp metabolism and microbially produced I3A. *In vitro* analysis of I3A effect on barrier integrity, proliferation and *E. coli* infection suggest altered barrier function preceding LOS. These results indicate relevance of I3A as novel preclinical biomarker as well as a functional metabolite potentially influencing the preterm intestinal barrier.

References: 1. Granger C, Dermyshe E, Roberts E, Beck LC, Embleton N, Berrington J. Necrotising enterocolitis, late-onset sepsis and mortality after routine probiotic introduction in the UK. Arch Dis Child Fetal Neonatal Ed. 2022 Jul;107(4):352-358. doi: 10.1136/archdischild-2021-322252. Epub 2021 Aug 25. PMID: 34433587.

2. Kurul S, Fiebig K, Flint RB, Reiss IKM, Küster H, Simons SHP, Voller S, Taal HR. Knowledge gaps in late-onset neonatal sepsis in preterm neonates: a roadmap for future research. Pediatr Res. 2022 Jan;91(2):368-379. doi: 10.1038/s41390-021-01721-1. Epub 2021 Sep 8. PMID: 34497356.

3. Ouahoud S, Giugliano FP, Muncan V. Monitoring Intestinal Organoid-Derived Monolayer Barrier Functions with Electric Cell-Substrate Impedance Sensing (ECIS). Bio Protoc. 2024 Mar 5;14(5):e4947. doi: 10.21769/BioProtoc.4947. PMID: 38464939; PMCID: PMC10917696.

4. Zhu Z, Schnell L, Müller B, Müller M, Papatheodorou P, Barth H. The Antibiotic Bacitracin Protects Human Intestinal Epithelial Cells and Stem Cell-Derived Intestinal Organoids from *Clostridium difficile* Toxin TcdB. Stem Cells Int. 2019 Aug 5;2019:4149762. doi: 10.1155/2019/4149762. PMID: 31467562; PMCID: PMC6701344.

Disclosure: Nothing to disclose.

MP574

HOST AND MICROBIAL TRYPTOPHAN METABOLISM IN IRRITABLE BOWEL SYNDROME: RELATION TO ORO-ANAL TRANSIT TIME AND SYMPTOMS

C. Moretti¹, K. Sjöberg Jabbar¹, H. Törnblom¹, T. van Gils¹, W. Sjöland¹, J. Algera¹, V. Tremaroli¹, F. Bäckhed¹, M. Simrén¹

¹University of Gothenburg, Institute of Medicine, Department of Molecular and Clinical Medicine, Sahlgrenska Academy, Gothenburg, Sweden

Contact E-Mail Address: chiara.mo91@gmail.com

Introduction: The pathophysiology of irritable bowel syndrome (IBS) includes alterations in gut-brain communication, gastrointestinal (GI) physiology and gut microbiota. The essential amino acid tryptophan (Trp) is metabolized in the gut to different classes of metabolites, including serotonin, kynurenine and indoles which have been implicated in the modulation of intestinal motility, immune function and pain sensation.

Balanced Trp metabolism requires a complex host-microbiota interplay, which might be dysregulated in IBS. However, Trp metabolism is incompletely understood, and studies are needed to clarify its link with IBS and gastrointestinal physiology.

Aims & Methods: Aim: To profile fecal and circulating levels of Trp metabolites in IBS and explore relationships with oro-anal transit time (OATT) and symptoms.

Methods: We combined targeted and untargeted metabolomics to determine fecal and serum Trp metabolites in a cohort of healthy controls (HC; n=29) and IBS patients with predominant constipation (IBS-C; n=59), diarrhea (IBS-D; n=53) or mixed bowel habits (IBS-M; n=55). OATT was measured using radiopaque markers and participants completed questionnaires to assess GI symptom severity (GSRS-IBS), stool frequency and consistency (Bristol Stool Form Scale), non-GI somatic symptoms (PHQ-12), and symptoms of anxiety and depression (HAD). For correlation analyses, Spearman's rho (r) was used.

Results: Levels of Trp did not differ significantly between HC and IBS subtypes. The Trp metabolite kynurenine, the microbially produced indole propionic acid (IPA) and the serotonin degradation metabolite 5-hydroxy-indoleacetic acid (5-HIAA) were lower in IBS-C compared to HC and IBS-D. There were inverse correlations between OATT and both fecal ($p < 0.0001$; $r = -0.40$) and circulating ($p = 0.021$; $r = -0.17$) Trp levels. Similarly, stool kynurenine and indoles were negatively correlated with OATT. Fecal but not circulating serotonin was positively correlated with OATT ($p = 0.041$; $r = 0.14$) while 5-HIAA showed a negative correlation ($p < 0.0001$; $r = -0.29$), suggesting potential serotonin accumulation due to deficient degradation. In IBS patients, fecal Trp, 5-HIAA, IPA and kynurenine, correlated negatively with the proportion of hard stools (BSF1-2) and positively with the proportion of loose stools (BSF6-7). Finally, serotonin catabolites and IPA were negatively correlated with the severity of constipation and positively correlated with diarrhea. No statistically significant correlations were noted between these metabolites and abdominal pain, abdominal distension, early satiety, or postprandial fullness while bloating was positively correlated with circulating IPA ($p = 0.018$; $r = 0.18$). Additionally, we report a negative correlation between circulating serotonin with symptoms of depression and anxiety, which was not found for fecal serotonin. No significant correlations were noted with non-GI somatic symptoms.

Conclusion: Our results suggest that slower transit time may favour increased intestinal catabolism of Trp, directly or indirectly through its effects on the gut environment and the microbiota. In addition, we report an association of fecal Trp metabolites with bowel habits, in line with their relations to OATT. On the other hand, these same fecal metabolites did not correlate with other GI (i.e., pain and bloating) or non-GI symptoms. This study underscores the link between intestinal transit time and the regulation of host and microbial metabolites important for intestinal homeostasis.

Disclosure: Nothing to disclose.

MP575

CROSS-ETHNIC MICROBIOME ANALYSES IDENTIFY SHARED AND SPECIFIC SIGNALS FOR INFLAMMATORY BOWEL DISEASE IN NORTHERN INDIA

R. Gacesa¹, A. Singh², G. Juyal³, M. Joshi⁴, V. Midha⁵, B.K. Thelma⁶, R.K. Weersma¹

¹University Medical Center Groningen (UMCG), Gastroenterology and Hepatology, Groningen, Netherlands, ²Dayanand Medical College & Hospital, Department of Gastroenterology, Ludhiana, India, ³School of Engineering and Applied Sciences, Bennett University, Department of Biotechnology, Greater Noida, India, ⁴Jamia Millia Islamia, Multidisciplinary Centre for Advance Research and Studies MCARS, New Delhi, India, ⁵Dayanand Medical College & Hospital, Department of Internal Medicine, Ludhiana, India, ⁶University of Delhi South Campus, Department of Genetics, New Delhi, India

Contact E-Mail Address: rgacesa@gmail.com

Introduction: Inflammatory bowel disease (IBD) shows significant variations in clinical presentation, prevalence, and epidemiology across the world. We hypothesized that these differences might be, in part, due to regional variations in gut microbiomes. To test this, we examined gut microbiota of IBD patients and healthy controls in Northern part of India, and compared our findings to Dutch patients and population.

Aims & Methods: We collected stool samples and clinical metadata from 226 IBD patients (198 ulcerative colitis, 28 Crohn's disease) and 66 controls in Northern India. Metagenomic shotgun sequencing was employed to assess gut microbiota diversity, composition, and function. Associations between microbiome profiles and IBD subtypes, along with clinical parameters like medication usage, drug response, and disease activity, were investigated. We compared our findings to a Dutch cohort comprising 436 IBD patients and 903 controls, using a consistent analytical approach. Finally, we used machine learning approaches to evaluate the generalizability of Indian IBD signals to the Dutch population.

Results: Indian IBD patients exhibited reduced microbiome diversity and alterations in beta diversity ($FDR < 0.05$, replicated in the Dutch cohort). We identified 319 taxa and 71 biochemical pathways significantly altered in Indian patients ($FDR < 0.05$), with 39% of these signals replicated in the Dutch cohort (at $FDR < 0.05$). Shared dysbiosis patterns across Indian and Dutch IBD patients included expansion of opportunistic pathogens (e.g., *Clostridium*, *Streptococcus*, *Lactobacilli* genera) and oral bacteria (e.g., *Streptococcus oralis*, *Bifidobacterium dentium*), alongside reduction in butyrate producers (e.g., *Faecalibacteria*, *Roseburia hominis*, *Blautia massiliensis*). Furthermore, we identified unique pathobionts specific to the Indian cohort, including *Scardovia* and *Oribacterium* genera, *Actinomyces dentalis* and *Klebsiella pneumoniae*. Machine learning models trained on the Indian cohort exhibited high predictive accuracy within the Indian test set (Sensitivity 0.84, Specificity 0.95) and demonstrated generalizability to the Dutch cohort (Sensitivity 0.77, Specificity 0.69). Additionally, we found associations between medication use and gut microbiota independent of disease activity: Tofacitinib usage (by 26 UC patients) correlated with decreased *Lactobacilliales* and increased *Clostridia*, while Prednisolone and Azathioprine usage associated with reduced *Roseburia* and increased *Streptococcus* and *Granulicatella*.

Conclusion: IBD patients from Northern India exhibit gut dysbiosis patterns similar to European patients, alongside enrichment in India-specific pathobionts. Microbiome-based diagnostic models show generalizability across populations, demonstrating the potential utility of microbiota-based approaches in IBD diagnosis and management across diverse populations.

Disclosure: Nothing to disclose.

MP576

AGE-DEPENDENT GUT MICROBIOTA PROFILES IN CYSTIC FIBROSIS: A META-ANALYSIS

B. Bódy^{2,1}, R. Molnár^{1,2}, B. Riba^{2,1}, R. Tóth³, T. Kói³, K. Ocskay¹, A. Párnitzky^{25,1}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Heim Pál National Pediatric Institute, Budapest, Hungary, ³Semmelweis University, Budapest, Hungary, ⁴University of Pécs, Institute for Translational Medicine, Pécs, Hungary

Contact E-Mail Address: blanka.rebeka.body@gmail.com

Introduction: Gut micorbiota in patients with cystic fibrosis (pwCF) is severely disrupted and a potential source of further complications. We aim to provide quantitative evidence of the differences in gut microbiota between pwCF and non-CF controls to understand CF gut flora composition and identify potential sites for microbiota modulation with special focus on time-dependent changes.

Aims & Methods: We conducted a systematic review and meta-analysis of PubMed, EMBASE, CENTRAL, Web of Science, and Scopus up to November 13, 2023 (CRD42023482792). Included were case-control studies assessing gut microbial alpha diversity or relative abundance in pwCF and controls without gut-affecting conditions or drugs. Standardized mean differences (SMD) with 95% confidence intervals (CI) were calculated using a random-effects model for both outcomes. We performed subgroup analysis for alpha diversity for infants, children, and adults. We used the Joanna Briggs Institute risk of bias tool.

Results: Among 2550 studies, 11 met inclusion criteria (enrolling 1174 subjects). Alpha diversity analysis showed age-specific changes. Observed OTUs were non-significantly decreased in adult pwCF compared to controls (SMD=-1.57; 95%CI -4.21 to 1.08, across 3 studies, 80 pwCF and 100 controls).

Children with CF displayed a significantly reduced Shannon index (SMD=-1.43; 95%CI -2.06 to -0.79, across 3 studies, 77 pwCF and 78 controls). However, in infants, no difference was detected in Shannon index between CF patients and controls (SMD=0.05; 95%CI -0.74 to 0.84, across 4 studies, 288 pwCF, 519 controls).

Analysis of follow-up data in infants revealed a decreasing tendency of Shannon index in pwCF compared to controls during the first year of life (SMD=0.67; 95%CI -1.20 to 2.54 at 4 months vs. SMD=0.45; 95%CI -1.81 to 2.71 at 6 months vs. SMD=-0.61; 95%CI -1.98 to 0.75 at 12 months).

A significant increase in the relative abundance of Veillonella and E.coli marked the CF group with a noticeable increase of Enterobacter and decrease of Bacteroides and Faecalibacterium compared to controls (see Table).

Taxon name	No of studies	No of pwCF and controls	Level of taxonomic order	Standardised mean difference	Confidence interval (95%)	Heterogeneity
Actinobacteria	4	219/93	Phylum	-0.12	-1.04 – 0.80	69%
Bacteroides	4	96/512	Genus	-0.53	-2.04 – 0.98	93%
Blautia	4	96/512	Genus	-0.14	-0.51 – 0.24	0%
Enterobacter	3	255/461	Genus	0.32	-0.11 – 0.76	0%
Enterococcus	4	96/512	Genus	0.07	-0.70 – 0.83	70%
Faecalibacterium	3	75/103	Genus	-0.32	-2.01 – 1.37	83%
Streptococcus	4	96/512	Genus	0.16	-0.79 – 1.11	79%
Veillonella	4	96/512	Genus	0.97	0.04 – 1.90	78%
E.coli	4	213/107	Species	0.65	0.10 – 1.20	33%

Conclusion: Gut microbial alpha diversity is reduced in adults and children with CF compared to controls, while infants with CF exhibit similar diversity, which continuously decreases during the first year of life. Perturbations in the intestinal microbial ecosystem are defined by a significant

increase in E.coli and Veillonella abundances within individuals with CF compared to controls enabling specifically targeted microbiota modulation.

Disclosure: Nothing to disclose.

MP577

CLINICAL RELEVANCE OF POSITIVE MOLECULAR STOOL TESTING FOR INTESTINAL PATHOGENS IN DIFFERENT GASTROINTESTINAL DISORDERS

T. Rozera¹, P. Frasca¹, F. Kaitsas¹, R. Maresca¹, S. Porcari¹, M. Fiorani¹, A. Severino¹, W. Fusco¹, D. Rondinella¹, I. Venturini¹, G. Quaranta², L. Masucci², M. Sanguinetti², B. Posteraro², F. Scaldaferri³, G. Cammarota³, L. Laterza³, G. Ianiro³

¹Università Cattolica del Sacro Cuore, Digestive Disease Center, Roma, Italy, ²Università Cattolica del Sacro Cuore, Microbiology, Roma, Italy, ³Fondazione Policlinico Universitario A. Gemelli IRCCS, Digestive Disease Center, Rome, Italy

Contact E-Mail Address: tommaso.rozera@gmail.com

Introduction: Gut pathogens play a relevant role in shaping the natural history of noncommunicable chronic gastrointestinal (GI) disorders, as they are not only a risk factor for the development of irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD)^{1,2}, but can also trigger a clinical relapse of these conditions². Molecular testing for quick pathogen detection have been made available in recent years, but their sensitivity may result in clinically insignificant positive findings, as gut pathogens may be present, at low counts, also in clinically healthy individuals³. Their use is also recommended in stool donor screening flowchart to minimize the risk of transmission of infectious diseases during fecal microbiota transplantation (FMT).

Aims & Methods: Our aim was to evaluate whether the presence of gut pathogens, assessed by a direct molecular stool testing, differs in different GI disorders and healthy individuals. In this retrospective study, we evaluated the results of a commercially available, RT-PCR-based molecular stool testing for the detection and identification of 25 common gut pathogens (RT-PCR Allplex™ Gastrointestinal Panel Assays, Seegene, Seoul, Korea) in three different cohorts, including: patients with IBD; patients with IBS; candidate stool donors of our FMT centre. Testing were required when common microbiological stool testing (i.e. stool culture, C. difficile toxin, parasitological assays) were negative. We collected the following data of recruited individuals: age, gender, presence of GI symptoms (assessed with the GSRS) and disease activity (assessed with PMS, HBI).

Results: Overall, 403 stool tests were retrospectively analyzed. Of them, 177 came from 46 healthy donors (n= 89 tests of females, mean age 44; range: 21-69; SD 12.5); 183 from 146 patients with IBD (n=100 tests of females, mean age 40.4; range: 16-82; SD 16.2), and 27 from 26 patients with IBS (n= 12 tests of females, mean age 39; range: 16-68; SD 17.1). Among healthy donors, 60 (34%) tests were positive, 15 (8%) for multiple species. Enteropathogenic Escherichia coli (EPEC) was the most frequently isolated strain (n=23; 13%). In the IBD cohort, 155 tests were collected in patients with active disease, and among them 59 (38%) tests turned out to be positive, 18 (12%) for multiple species, with EPEC being the most common strain (n=15; 10%), followed by Aeromonas spp (n=13; 8%), Blastocystis hominis (n=11; 7%) and Clostridium difficile (n= 10; 6%). In this cohort, 28 tests were also requested to patients under quiescent disease, and 10 (36%) were positive. In patients with IBS, all tests were conducted during active, symptomatic phases of disease (IBS-D: n=19, 68%; IBS-C: n=8; 30%), with 13 (48%) positive testing, mainly due to Blastocystis hominis (n=5; 19%), followed by Dientamoeba (n=3; 11%), and by multiple species in 11% of patients (n=3).

Conclusion: In our cohort, the positivity rates of gut pathogens at direct molecular stool testing were similar among healthy donors (34%), patients with active (38%) and quiescent (36%) IBD, being slightly higher in patients with active IBS (48%). Based on these preliminary finding, direct molecular stool testing, in absence of positive stool cultures, is associated with asymptomatic colonization from gut pathogens, rather than with clinically relevant infections, both in healthy controls and in patients with noncommunicable chronic GI disorders.

References: (1) Lupu, V. V.; Ghiciuc, C. M.; Stefanescu, G.; Mihai, C. M.; Popp, A.; Sasaran, M. O.; Bozomitu, L.; Starcea, I. M.; Adam Raileanu, A.; Lupu, A. Emerging Role of the Gut Microbiome in Post-Infectious Irritable Bowel Syndrome: A Literature Review. *World J Gastroenterol* 2023, 29 (21), 3241–3256. <https://doi.org/10.3748/wjg.v29.i21.3241>.

(2) Axelrad, J. E.; Joelson, A.; Green, P. H. R.; Lawlor, G.; Lichtiger, S.; Cadwell, K.; Lebowitz, B. Enteric Infections Are Common in Patients with Flares of Inflammatory Bowel Disease. *Am J Gastroenterol* 2018, 113 (10), 1530–1539. <https://doi.org/10.1038/s41395-018-0211-8>.

(3) Rondinella, D.; Quaranta, G.; Rozera, T.; Dargenio, P.; Fancello, G.; Venturini, I.; Guarnaccia, A.; Porcari, S.; Bibbò, S.; Sanguinetti, M.; Gasbarrini, A.; Masucci, L.; Cammarota, G.; Ianiro, G. Donor Screening for Fecal Microbiota Transplantation with a Direct Stool Testing-Based Strategy: A Prospective Cohort Study. *Microbes and Infection* 2024, 105341. <https://doi.org/10.1016/j.micinf.2024.105341>.

Disclosure: G.I. has received personal fees for acting as speaker for Biocodex, Danone, Sofar, Malesci, Metagenics and Tillotts Pharma, and for acting as consultant and/or advisor for Ferring Therapeutics, Giuliani, Malesci and Tillotts Pharma. A.G. reports personal fees for consultancy from Eisai Srl, 3PSolutions, Real Time Meeting, Fondazione Istituto Danone, SinergieSrl, Board MRGE and Sanofi SpA personal fees for acting as a speaker for Takeda SpA, AbbVie and Sandoz SpA and personal fees for acting on advisory boards for VSL3 and Eisai. G.C. has received personal fees for acting as advisor for Ferring Therapeutics. All other authors have no conflicts of interest to disclose.

MP578

BUTYRIC ACID MITIGATES GUT MICROBIOTA ALTERATIONS INDUCED BY H. PYLORI ERADICATION

S. Abdulkhakov^{1,2}, M. Markelova², D. Safina^{2,3}, M. Siniagina², D. Khusnutdinova², R.A Abdulkhakov¹, T.V Grigoryeva²

¹Kazan State Medical University, Kazan, Russian Federation,

²Kazan Federal University, Kazan, Russian Federation, ³IQVIA, Moscow, Russian Federation

Contact E-Mail Address: sayarabdul@yandex.ru

Introduction: H. pylori eradication therapy induces significant alterations in the gut microbiome. While probiotics have been extensively studied as a potential strategy to mitigate microbiota-related consequences of antibiotics, their efficacy remains a subject of debate.

Aims & Methods: The aim of our study was to evaluate the influence of butyric acid+inulin supplements on gut microbiota changes (including gut microbiota taxonomic composition, functional potential, and gut resitome) induced by H.pylori eradication therapy.

A total of 22 H. pylori-positive patients aged 19 to 64 years were enrolled in the study. Patients were randomized into two H. pylori eradication regimens: 1) ECAB-14: esomeprazole 20 mg, clarithromycin 500 mg, amoxicillin 1000 mg, and bismuthate tripotassium dicitrate 240 mg, twice daily, orally, for 14 days. 2) ECAB-Z-14: esomeprazole 20 mg, clarithromycin 500 mg, amoxicillin 1000 mg, and bismuthate tripotassium dicitrate 240 mg, twice daily, along with butyric acid+inulin (Zacofalk) supplementation (two tablets daily, each containing 250 mg of butyric acid and 250 mg of

inulin), orally, for 14 days. Stool samples were collected from each subject at three time points: prior to eradication therapy (I), after therapy completion (II), and one month post-therapy (III). Total DNA from fecal samples was isolated for whole genome sequencing using the Illumina NextSeq 500 platform.

Results: Gut Microbiota Alpha Diversity (Shannon Index): Immediately after eradication therapy, both the ECAB-14 and ECAB-Z-14 groups experienced a significant decrease in gut microbiota alpha diversity compared to the initial level: (2.46 ± 1.06) vs. (3.75 ± 0.342), p = 0.0029, and (3.22 ± 0.73) vs. (3.82 ± 0.30), p = 0.037, respectively. After one month, the Shannon index was restored to the baseline level in the ECAB-Z-14 treatment group: no statistically significant differences were identified between time points III and I [(3.71 ± 0.33) vs. (3.82 ± 0.30), p = 0.206]. However, even a month after therapy, the ECAB-14 treatment group still exhibited a lower Shannon index than the baseline level [(3.27 ± 0.39) vs. (3.75 ± 0.342), p = 0.019].

Functional Potential Alterations: In the ECAB-Z-14 treatment group, less pronounced alterations in gut microbiota functional potential were observed. Specifically, 72 metabolic pathways changed immediately after eradication therapy. In contrast, the ECAB-14 group showed impact on 112 signaling pathways.

Butyrate Production Genes: The abundance of genes associated with butyrate production decreased only in the ECAB-14 treatment group. However, in the ECAB-Z-14 treatment group, the abundance of genes responsible for butyrate production remained stable.

Antibiotic Resistance Genes: The prevalence of gut microbiota antibiotic resistance genes increased significantly in both treatment groups immediately after eradication. Notably, more severe alterations were observed in the ECAB-14 treatment group, where the abundance of 73 antibiotic resistance genes significantly increased. Meanwhile, the ECAB-Z-14 group showed an increase in only 50 antibiotic resistance genes immediately after eradication therapy.

Conclusion: H. pylori eradication therapy significantly affects gut microbiota composition, functional potential, and increases the abundance of antibiotic resistance genes. However, the addition of butyric acid+inulin supplements to the H. pylori eradication regime may mitigate these effects.

Disclosure: Nothing to disclose.

MP579

ANTIDEPRESSANT TREATMENT OF IBS: ACTION OF A HERBAL ANTIDEPRESSANT, ST. JOHN'S WORT EXTRACT, ON GUT MICROBIOTA

M.E. Grafakou¹, E.-M. Pferschy-Wenzig¹, H. Aziz-Kalbhenn², O. Kelber², R. Bauer¹

¹University of Graz, Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Graz, Graz, Austria., Graz, Austria, ²Steigerwald Arzneimittelwerk GmbH, Phytomedicines Supply and Development Center, Bayer Consumer Health, Darmstadt, Germany

Contact E-Mail Address: maria.grafakou@uni-graz.at

Introduction: Antidepressants are an integral part of the treatment of IBS as a disorder of gut-brain interaction (DGBI). Accordingly also a direct interaction with the gut microbiota might be relevant as an additional mode of action. With its high content of flavonoids, a substance group for which beneficial neuromodulatory effects, mediated by the microbiota, are known. St. John's wort extract, an antidepressant with clinically proven therapeutic equivalence to TCAs and SSRIs, could be a promising candidate for such an additional action, also as there is a history of use also in GI complaints.

Aims & Methods: Aim was to follow the test substance, a St. John's wort extract (STW 3-VI), with clinically proven anti-depressant activity [1] and standardized flavonoid content [2], through the GI tract. According to the Infogest protocol [3,4], first the influence of the upper GI digestion on the extract was modelled by subsequent incubation with respective enzymes and buffer mixes. The predigested extract was subsequently incubated with fecal samples from ten healthy donors (24h, anoxic, 37°C). The metabolism of the flavonoids by the gut microbiota was captured by UHPLC-HRMS, and also proteolytic markers (BCFA and ammonium) were measured by GC-FID and IPB colorimetric analysis. 16S rRNA gene sequencing was used to assess shifts in microbial community composition, followed by functional analysis via ATLAS, using KEGG, Cazy and Pfam for annotations.

Results: All major extract constituents were stable towards upper intestinal tract digestion. They were, however, readily catabolized by the gut microbiota. Metabolites of the flavonoids included taxifolin, hydroxy-phenylpropionic acids and protocatechuic acid. Proteolytic markers were significantly decreased. Differential abundance analysis of the microbial communities showed that several taxa were significantly modulated by the extract, with e.g. Bacteroides ($p=0.005$) Marinifilaceae ($p=0.0007$) and Prevotellaceae ($p=0.035$) decreasing. Functional analysis revealed 540 differently expressed genes ($p<0.01$), some involved in flavonoid metabolism.

Conclusion: Beyond the known antidepressant activity of St. John's wort extract, its components are also prodrugs for substances with potential therapeutic benefits in IBS as well as in psychic depression [5]. This is in accordance to the results of the functional analysis of the gut microbiota, given that changes of abundance of bacterial taxa by the treatment antagonize abundance shifts described in depressive as well as IBS patients [6]. The decrease of proteolytic markers is also in line with a beneficial action in IBS [7]. In conclusion, St. John's wort might, beyond its known efficacy in mild to moderate depression, also be a promising therapeutic option in IBS patients, especially with co-occurring depressive symptoms.

References: 1. Gastpar M, Singer A, Zeller K. Efficacy and tolerability of hypericum extract STW3 in long-term treatment with a once-daily dosage in comparison with sertraline. *Pharmacopsychiatry*. 2005;38:78-86.
2. www.ema.europa.eu/en/medicines/herbal/hyperici-herba
3. Brodkorb A, Egger L, Alminger M, et al. INFOGEST static in vitro simulation of gastrointestinal food digestion. *Nat Protoc* 2019; 14: 991-1014.
4. Pérez-Burillo S, Molino S, Navajas-Porras B. et al. An in vitro batch fermentation protocol for studying the contribution of food to gut microbiota composition and functionality. *Nat Protoc* 2021; 16: 3186-3209.
5. Vissienon C, Nieber K, Kelber O, Butterweck V. Route of administration determines the anxiolytic activity of the flavonols kaempferol, quercetin and myricetin -- are they prodrugs? *J Nutr Biochem*. 2012; 23: 733-740
6. Duan R, Zhu S, Wang B, Duan L. Alterations of gut microbiota in patients with irritable bowel syndrome based on 16S rRNA-targeted sequencing: A Systematic Review. *Clin Transl Gastroenterol*. 2019; 10:e00012.
7. Hou JJ, Wang X, Li Y, Su S, Wang YM, Wang BM. The relationship between gut microbiota and proteolytic activity in irritable bowel syndrome. *Microb Pathog*. 2021; 157:104995.

Disclosure: MEG, EMPF and RB have received fees from Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany, HEK and OK are employees of the same company.

MP580

ASSESSING AWARENESS AND ATTITUDES TOWARDS FECAL MICROBIOTA TRANSPLANTATION (FMT) IN ARMENIA: A STUDY AMONG MEDICAL STUDENTS, HEALTHCARE PROFESSIONALS, AND PATIENTS

S. Grigoryan¹, I. Navoyan¹, A. Hazoyan¹, A. Gabrielyan¹, M. Grigoryan¹, G. Matsakyan¹, A. Khalatyan², M. Gemilyan¹

¹Yerevan State medical University, Gastroenterology and Hepatology, Yerevan, Armenia, ²Mikayelyan Institute of Surgery, GI Endoscopy, Yerevan, Armenia

Contact E-Mail Address: Sofyagrigoryan13@gmail.com

Introduction: Fecal Microbiota Transplantation (FMT) stands as a promising therapeutic approach for gastrointestinal disorders, notably recurrent *Clostridioides difficile* infection. Despite its potential, the awareness and perceptions surrounding FMT among stakeholders in low and middle-income countries, such as Armenia, remain relatively unexplored.

Aims & Methods: This study aimed to assess awareness and attitudes towards FMT among 4th to 6th-year medical students of Yerevan State Medical University (YSMU), healthcare professionals at Mikayelyan University Hospital, and patients of the same hospital in Armenia. The primary aim is to evaluate awareness and attitudes towards FMT among these groups and, as a conclusion, to increase awareness among the Armenian population, both patients and physicians, and to promote the integration of microbiota-based researches and therapeutic methods in Armenia. **Methods:** A questionnaire-based study was conducted among 143 medical students from YSMU (Yerevan State Medical University), 56 healthcare professionals (including gastroenterologists, infectious disease specialists, internists, and endoscopists) at Mikayelyan University Hospital, and 82 patients undergoing outpatient and inpatient treatment at the same hospital. Participants were surveyed to gauge their awareness level, perceptions, and willingness regarding FMT.

Results: This study explores the intricate landscape of awareness and attitudes towards Fecal Microbiota Transplantation (FMT) among medical students, healthcare professionals, and hospital patients in Armenia. Delving into their perspectives, this research offers nuanced insights into the reception and readiness for FMT adoption. Among surveyed medical students, university education emerged as the predominant source of knowledge (47.5%), while 43.4% recognized FMT's efficacy in treating *Clostridium difficile* infection, with notable percentages acknowledging its potential for inflammatory bowel disease (37.3%) and irritable bowel syndrome (12.0%). Among healthcare professionals, insights revealed that conferences/seminars (41.4%) and scientific journals/publications (37.5%) played pivotal roles in information dissemination, with a striking 72.1% recognizing FMT's effectiveness against *Clostridium difficile* infection. However, challenges such as the lack of clear guidelines (40.3%) and limited donor material availability (25.8%) underscored existing barriers to FMT application. Patient perspectives offered invaluable insights, with 12.5% exhibiting prior awareness of FMT, prompting further exploration into their readiness and reservations. Post-information dissemination, 33.8% expressed a newfound readiness for FMT application, highlighting the pivotal role of education in shaping patient attitudes. Noteworthy concerns among patients included apprehensions regarding the procedure's unpleasantness (52.2%) and the perceived lack of evidence (13.0%). Furthermore, preferred delivery methods, such as oral capsules (70.6%) and colonoscopy (23.5%), shed light on patient preferences and comfort levels.

Conclusion: The study highlights a significant knowledge gap regarding Fecal Microbiota Transplantation (FMT) among medical students, doctors, and patients in Armenia. Specifically, 44.1% of students, 21.4% of doctors, and 83.3% of patients had never heard of FMT. Despite this initial lack of awareness, 33.8% of patients expressed willingness to undergo FMT after

receiving explanations. This underscores the potential for education and awareness-raising initiatives to positively impact attitudes towards FMT adoption in Armenia.

Disclosure: Nothing to disclose.

MP581

STUDY OF THE EFFECT OF FECAL MICROBIOTA TRANSPLANT THAWING TIME ON THE TREATMENT EFFECT OF RECURRENT CLOSTRIDIODES DIFFICILE INFECTION

J.B. Shin¹, B. Cha¹, J. Hong¹, K.-S. Kwon¹

¹Inha University Hospital, Gastroenterology, Incheon, South Korea

Contact E-Mail Address: shinjongv@naver.com

Introduction: Fecal microbiota transplantation (FMT) is most effective treatment for recurrent *clostridioides difficile* infection (rCDI). Some factors associated with donor, recipients and FMT protocols (amount of feces, infusion route, number of infusion, time of thaw) affect FMT outcome. However, the appropriate FMT protocol is still being studied, and research on the most effective thawing time is lacking.

Aims & Methods: The purpose of this study was to optimize the effect of thawing time of frozen FMT stool on rCDI.

This prospective, single center and randomized controlled trial was performed from October 2022 to December 2023. Patients were randomly assigned to groups that received stool for FMT thawed 4 hours at room temperature (4HTG) or thawed 12 hours in a refrigerator (12HTG). Stools were donated from single healthy donor. Each donation was diluted in glycerol-saline solution (12.5% glycerol in 0.90% w/v NaCl in water) and thoroughly homogenized. A 250 mL formulation containing 60g of stool was stored at -80 °C and administered via colonoscopy within 4 months. The primary outcome was the cumulative recurrence rate of *Clostridioides difficile*-associated diarrhea (CDAD) at week 8. The CDAD resolution rate at 1 week, adverse events related to thawing time were also evaluated.

Results: Total of 22 patients were randomized into 4HTG (n=12) vs 12HTG (n=10). CDAD resolution was achieved in all patients regardless of thawing time (100% vs 100%, p<0.001). On the other hand, the cumulative recurrence rate was significantly lower in 4HTG compared to 12HTG. (0% vs 30%, p=0.045). The observed species, Chao1, and Shannon indices for alpha-diversity measures revealed that there was greater microbial richness among groups in the post FMT group than in the pre FMT group. (p<0.001) A comparison of gut microbiota composition was performed using PCoA based on beta diversity of unweighted UniFrac distances. The 4HT group was found to be more similar to the donor than the 12HT group.

Conclusion: This study demonstrated that thawing time did not affect CDAD resolution but did make a difference in recurrence rate. This is the first study to show that the thawing time of frozen stools affects the CDAD recurrence rate and that 4-hour room temperature thawing should be preferred.

Disclosure: Nothing to disclose.

MP582

MH002, AN OPTIMIZED LIVE BIOTHERAPEUTIC PRODUCT, FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASES, HAS MODE-OF-ACTIONS LINKED TO RESTORATION OF INTESTINAL DYSBIOSIS, MUCOSAL INTEGRITY, AND IMMUNE HOMEOSTASIS

S. Bolca¹, M. Doynova¹, M. de Leeuw¹, I. Pinheiro¹, K. Conrath¹, S. Possemiers¹, L. Haazen¹, S. Vermeire²

¹MRM Health NV, Zwijnaarde, Belgium, ²University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: selin.bolca@mrmhealth.com

Introduction: Treatment options for patients with mild-to-moderate ulcerative colitis (UC) failing 5-ASA are limited. MH002 is an optimized live biotherapeutic product consisting of 6 non-pathogenic, well-characterized commensal bacteria. Its anticipated mechanism in UC is reversion of dysregulated host inflammatory mechanisms and interactions with gut microbiota, and induction of mucosal healing.

Aims & Methods: In this 2:1-randomized, double-blind, placebo-controlled first-in-disease study (EudraCT 2020-001355-33), 45 patients with mild-to-moderate active UC (Modified Mayo Score [MMS] =4-8 and centrally assessed Mayo Endoscopic Sub-score [MES] ≥2) received treatment with 400mg MH002 or placebo (PBO) once daily for 8wks, followed by an 8-wk extension with MH002 (same dose) unless responding to PBO. All patients were on stable 5-ASA for ≥4wks prior and during the study. Full colonoscopies with biopsies were performed at baseline and wk8. The primary endpoint was the rate of treatment-emergent adverse events. Exploratory efficacy endpoints included clinical remission (MMS≤2 with all sub-scores ≤1 and rectal bleeding =0), endoscopic improvement (MES≤1), clinical response (reduction of MMS of ≥3 points or a reduction of ≥1 point of the Mayo sub-scores for stool frequency and rectal bleeding), biomarker normalisation, and mechanistic effects of MH002. Here, changes in faecal microbiome (shotgun metagenomics) and gene expression of colonic mucosal biopsies (whole transcriptome RNAseq) are reported.

Results: MH002 treatment was safe and well tolerated, and resulted in clinically meaningful improvements in disease activity and inflammatory parameters¹. At wk8, endoscopic improvement was achieved in 6/28 (21%) and 2/14 (14%) patients treated with MH002 and PBO, respectively. In this MH002-treated subgroup, α-diversity (Pielou evenness, Shannon diversity) increased significantly as compared to baseline whereas the relative abundance of Enterobacterales decreased significantly over time (1-sided Wilcoxon p<0.05). Similar but less pronounced changes were observed in MH002-treated patients achieving clinical response or even no response. Furthermore, a total of 1496 significantly differentially expressed genes (DEGs) at wk8 vs. baseline were found in the MH002-treated patients with endoscopic improvement (p<0.05; lnFC>1.5). Among the most significantly downregulated DEGs are the regenerating islet-derived (REG) genes (REG1α, REG1β, REG3α) and serum amyloid A (SAA) genes (SAA1, SAA2, SAA4). Since REG proteins have bactericidal, anti-inflammatory, and tissue repair functions, and SAA are acute-phase proteins induced by inflammatory stimuli, this could result from a state of lower inflammation and activation by bacterial components, from the resolution of tissue injury, and from lower local gut inflammation following treatment. Lastly, when intersecting these DEGs with UC-associated DEGs reported in 3 independent studies^{2,3}, 16-21% of intersecting DEGs showed fold changes in opposite polarity to UC vs. healthy individuals whereas 0-3% showed similar fold changes.

Conclusion: These observations suggest that MH002-treated patients had positive changes in gut microbial diversity and overall microbiome composition, coinciding with clinical improvement and downregulation of genes involved in immune and inflammatory responses, antimicrobial defense mechanisms, and resulting in dampening of immune cells' activi-

ty, and associated with UC. MH002, therefore, represents a promising new treatment for mild-to-moderate UC patients insufficiently controlled with 5-ASA. These results warrant further development in a phase 2/3 study.

References: 1) Vermeire et al. JCC 2024 (S1)

2) Lloyd-Price et al. Nature 2019

3) Haberman et al. Nat Commun 2019

Disclosure: SB, MD, MdL, IP, KC, SP & LH: employee, paid consultant and/or shareholder of MRM Health

SV: financial support for research from AbbVie, J&J, Pfizer, Takeda and Galapagos; speakers' and/or consultancy fees from AbbVie, Abivax, AbolterISPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cytokine Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MRM Health, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Surrozen, Takeda, Theravance, Tillots Pharma AG, VectivBio, Ventyx, Zealand Pharma

Overview of pancreatic diseases

11:30-12:30 / Poster Stage 3

MP583

USE OF STATINS INCREASES OVERALL SURVIVAL IN PATIENTS AFFECTED BY PANCREATIC DUCTAL ADENOCARCINOMA

R. Ponz de Leon Pisani¹, L. Archibugi², C. Fortunato², G. Lauri², L. De Carolis², D. Tamburrino³, G. Orsi⁴, L. Apadula², M. Reni⁴, M. Falconi³, P.G. Arcidiacono², G. Capurso²
¹IRCCS San Raffaele Milan, Milan, Italy, ²Hospital San Raffaele, Pancreato-biliary Endoscopy And Endosonography Division, Milan, Italy, ³Hospital San Raffaele, Pancreatic Surgery Unit, Milan, Italy, ⁴Hospital San Raffaele, Oncology Unit, Milan, Italy

Contact E-Mail Address: gaetanolauri.94@gmail.com

Introduction: Statins and anti-inflammatory non-steroidal drugs (NSAIDs) like aspirin have already been demonstrated to reduce the risk of developing PDAC. Whether there is a beneficial effect of these drugs in patients with established PDAC is poorly investigated.

Aims & Methods: Our aim is to investigate the association between the use of aspirin, statins, angiotensin-converting-enzyme (ACE) inhibitors and sartans and the clinical outcome in a prospective cohort of PDAC patients.

Single-centre prospective cohort of consecutive PDAC patients, with baseline demographics, exposome and pharmacological data, details on tumour features, treatment (chemotherapy/surgery) and survival recorded. The effect of the investigated drugs on overall survival was investigated by Kaplan-Meier curves and multivariate analysis using a Cox proportional hazards regression model. Tests of statistical significance and confidence intervals were two-sided; a value of $p < 0.05$ was considered statistically significant.

Results: 419 patients with histologically diagnosed PDAC were included, mean age 67, 51.7% male; 50 (11.9%) stage I, 152 (36.2%) stage II, 110 (26.2%) stage III, 107 (25.5%) stage IV; 368 patients (87.8%) underwent chemotherapy as first treatment, of whom 304 (82.6%) polychemotherapy (PAXG, FOLFIRINOX or gemcitabine plus nab-paclitaxel); 129 patients (30.7%) underwent surgical resection, most after chemotherapy. Ninety-four patients (22.4%) aspirin users, 101 (24.1%) statin users, 72 (17.1%) ACE inhibitors users, 91 (21.7%) sartans users. Median estimated OS was 20 months with 228 patients (54.4%) dead at last follow-up. In the whole cohort Kaplan Meier survival analysis showed a longer OS in statin users vs non users (21 vs 18 months). At Cox regression use of statins (HR 0.69; $p=0.02$ (0.506-0.952 95% CI)), age (HR 1.046 (1.030-1.062 95% CI), $p<0.0001$) and stage (HR 1.466 (1.280-1.679 95% CI), $p<0.0001$) had a significant impact on OS. In subgroup analyses of patients with resectable patients (stage I and II) and advanced stages (III and IV) there was no significant effect. All the other investigated drugs were not significantly associated with OS.

Conclusion: The present results suggest that chronic use of statins is significantly associated with increased OS in patients affected by PDAC at Cox proportional hazard regression. Whether this beneficial effect is due to less indolent tumours or better response to treatments require further investigation.

Disclosure: Nothing to disclose.

MP584

EARLY ONSET PANCREATIC CANCER: PRELIMINARY DATA FROM A THIRD LEVEL CENTRE

M. Andreozzi¹, A. Dal Buono², M. Terrin³, V. Poletti³, P. Spaggiari⁴, C. Bonifacio⁵, S. Bozzarelli⁶, M. Colombo⁷, M. Spadaccini⁸, A. Fugazza¹, A. Zerbi⁹, S. Carrara¹⁰
¹Humanitas Research Hospital, Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano, Italy, ²Humanitas University, Gastroenterology, Milan, Italy, ³Humanitas University, Rozzano, Italy, ⁴Humanitas Research Hospital, Pathology Department, Rozzano, Italy, ⁵Humanitas Research Hospital, Radiology, Rozzano, Italy, ⁶Humanitas Research Hospital, Oncology, Rozzano, Italy, ⁷Humanitas Research Hospital, Rozzano, Italy, ⁸Humanitas University, Biomedical Science, Rozzano, Italy, ⁹Humanitas Research Hospital, Pancreatic Surgery, Rozzano, Italy, ¹⁰Istituto Clinico Humanitas, Digestive Endoscopy Unit, Division of Gastroenterology, Milano, Italy

Contact E-Mail Address: marta.snpp@gmail.com

Introduction: The incidence of Early Onset Pancreatic Cancer (EOPC), which is defined as PC diagnosed before the age of 50 years, seems to be rising in recent years. It has been suggested that EOPC may differ from Late Onset Pancreatic Cancer (LOPC) in terms of biology, genetic expression, and tumour behaviour. Our aim was to retrospectively analyze EOPC cases diagnosed at our institute to have a better insight into the PC disease when it affects young patients.

Aims & Methods: This is a retrospective cohort study: pathological reports from pancreatic EUS-biopsy or transabdominal liver biopsies were collected. Demographic data, risk factors exposure (smoke, alcohol intake, BMI), oncologic familiar history as well as genetic tests, stage at diagnosis and follow-up data were collected.

Results: We found 49 cases of EOPC diagnosed at our institute since 2015. Twenty-seven on 49 patients were male (55%); mean age at diagnosis was 45.9 years old; mean BMI was 22.37. Sixteen on 49 (32 %) patients were metastatic at the diagnosis. Twenty-two patients were tested on a genetic panel of 26 genes (18 genes before 2023) associated with PC and 9 (18%) patients had a positive test for a high penetrance pathogenetic variant (PGVs). Eighteen on 49 (37 %) patients had positive familiar oncologic history (mostly pancreatic, breast, and ovarian cancers).

Conclusion: Based on our data, we would conclude that there is a significant association between EOPC and high penetrance PGVs. A consistent number of cases are diagnosed in metastatic stage, which means we should invest on prevention and early diagnosis, especially for high-risk population such as for patients with positive familiar oncologic history. Our aim for the future is to create a prospectively maintained and multi-centre registry of EOPC.

Disclosure: Nothing to disclose.

MP585

SHOULD RISK VARIANTS AT THE *RIPPLY1-CLDN2-MORC4* AND *TRPV6* LOCI BE TESTED IN NON-ALCOHOLIC CHRONIC PANCREATITIS?

K. Ocskay¹, P. Mátrai², M.F. Juhász¹, M. Sahin-Toth³, A. Párnicky^{1,2,4}

¹Heim Pál National Pediatric Institute, Budapest, Hungary, ²Institute for Translational Medicine, University of Pécs, Pécs, Hungary, ³Department of Surgery, University of California Los Angeles, Los Angeles, United States of America, ⁴Centre for Translational Medicine, Semmelweis University, Budapest, Hungary

Contact E-Mail Address: ocskay.klementina@gmail.com

Introduction: Chronic pancreatitis (CP), influenced by both genetic and environmental factors, poses a significant health burden with its progressive nature. While excessive alcohol consumption is a prominent risk factor, non-alcoholic chronic pancreatitis (NACP) presents challenges due to less overt precipitating factors.

Aims & Methods: We aimed to assess the impact of rs7057398 and rs12688220 variants at the *RIPPLY1-CLDN2-MORC4* locus and rare functionally deficient *TRPV6* variants in NACP susceptibility.

Systematic search was conducted on PubMed, Embase, and Web of Science databases on November 2, 2023, aiming to assess non-alcoholic acute recurrent pancreatitis (ARP) and CP cases, excluding conference abstracts and preprints. The protocol was prospectively registered (CRD42023438777). Utilizing a random-effect model with REML estimation, odds ratios (OR) with 95% confidence intervals (CI) were computed using the allelic model (rs7057398: C vs T; rs12688220: T vs C) for the total population and hemizygotes as well, the homozygote (rs7057398: CC vs TT; rs12688220: TT vs CC) and heterozygote model (rs7057398: CT vs TT; rs12688220: TC vs CC). Minor allele frequency (MAF) was calculated for both variants. In the analysis of functionally deficient rare *TRPV6* variants were collectively pooled and compared to cases without mutations affecting *TRPV6* function, calculating OR with 95% CI. Subgroup analysis, stratified by age, set the threshold for early-onset CP at 30 years in all cases. Statistical heterogeneity was evaluated using Chi² tests and I² values. Due to limited study numbers, funnel plots and Egger's test were deemed inappropriate. Risk of bias was assessed using the Joanna Briggs Institute's tool.

Results: Six studies were included in the quantitative analyses for SNPs rs7057398 and rs12688220. MAF for rs7057398 was 0.49 (CI 0.31 to 0.67) in cases and 0.38 (CI 0.27 to 0.50) in controls. For rs12688220, MAF was 0.46 (CI 0.27 to 0.67) in cases compared to 0.35 (CI 0.24 to 0.47) in controls. MAF was notably higher in Indian and Asian studies compared to European cohorts. Both risk alleles were significantly associated with NACP in homozygotes, heterozygotes and hemizygotes, respectively (see Table).

SNP	Model	Cohorts	Cases	Controls	OR	95% CI	I ² [95% CI]
rs7057398	Allelic	6	1424 / 3049	2884 / 8803	1.54	1.17; 2.01	75% [44;89]
	Homozygote	6	200 / 506	361 / 1830	2.22	1.12; 4.42	63% [10;85]
	Hemizygote	6	577 / 1153	935 / 2689	1.52	1.14; 2.03	51% [0;80]
	Heterozygote	6	447 / 753	1227 / 2696	1.64	1.36; 1.98	0% [0;75]
rs12688220	Allelic	6	1589 / 3396	3418 / 10405	1.64	1.10; 2.45	92% [85;96]
	Homozygote	5	146 / 502**	287 / 1834**	1.87	1.31; 2.66	30% [0;71]
	Hemizygote	5	497 / 1333**	807 / 3275**	1.53	1.07; 2.17	69% [28;87]
	Heterozygote	5	367 / 723	1131 / 1678	1.36	1.07; 1.73	0% [0;79]

In the allelic model, minor allele carriers displayed significantly increased odds for NACP for rs7057398 (OR 1.54, CI 1.17 to 2.01, p=0.009) and rs12688220 (OR 1.64, CI: 1.10 to 2.45, p=0.025). Limited data was available on early-onset cases, therefore definitive conclusions cannot be drawn. Functionally deficient *TRPV6* variants were associated with a 35-fold increased odds of developing NACP compared to individuals without these

variants (OR = 35.32, CI 20.72 to 60.22, across 4 cohorts, 2236 cases and 2748 controls). Risk of bias was generally judged to be high in the included studies.

Conclusion: Our meta-analysis highlights the significant association of variants rs7057398 and rs12688220 of the *RIPPLY1-CLDN2-MORC4* locus, along with functionally deficient *TRPV6* variants, with NACP. These findings emphasize the importance of genetic screening for identifying individuals at risk of NACP and inform personalized intervention strategies.

Disclosure: Nothing to disclose.

MP586

PANCREATIC CANCER ASSOCIATED WITH ACUTE PANCREATITIS – A COHORT ANALYSIS

S. Bunduc^{1,2}, B. Varzaru², A. Marinescu¹, I. Parola¹, R. Panait², C. Gheorghe^{1,2}

¹Fundeni Clinical Institute, Digestive Disease and Liver Transplant Center, Bucharest, Romania, ²Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Contact E-Mail Address: stfnbndc@gmail.com

Introduction: Pancreatic cancer (PC) diagnosis may be preceded by acute pancreatitis (AP) in up to 14% of cases. Although follow-up imaging is recommended in AP with unclear etiology, the particularities of the PC cases associated with AP are still to be defined.

Aims & Methods: The aim of our study was to characterize the subgroup of PC cases preceded by AP.

We included in the analysis all patients referred to our tertiary center for endoscopic ultrasound guided tissue acquisition and subsequently confirmed diagnosis of pancreatic adenocarcinoma (PAC) between January 2019 and December 2023. We cases with and without AP prior to PAC diagnosis. Continuous variables are reported as mean ± standard deviation (SD) or median and range. Categorical variables are reported as rates (%). To compare the groups, we used 2 tailed Fisher's exact and independent samples t test. Subsequent multivariate analysis was to identify the characteristics of the AP prior PAC subgroup.

Results: Our cohort comprised 144 patients, aged 68 (40-86), with almost equal sex distribution (55% males). 48% were metastatic at diagnosis, and there was a slight predominance of proximal tumor location (57% - head/uncinate process lesions). AP preceded PAC in 9% of cases. These patients were younger (61.54±10.45 vs. 67.08±8.19, P=.035), more frequently smokers (84 vs. 44%, P=.007), had mostly proximal lesions (84 vs. 55% - head/uncinate process located tumors, P=.015) and pain at diagnosis (100 vs. 73%, P=.044). There was no association between AP prior PC and sex, alcohol consumption, diabetes, obesity, tumor size, vascular invasion or metastatic stage. Smoking (OR 5.92; 95%CI 1.18-29.59) and proximal tumor location (OR 5.57; 95%CI 1.13-27.58) were independently associated with AP prior PAC.

Conclusion: Although small, our cohort study revealed that AP precedes PAC in younger patients and smokers. The increased inflammatory response occurring at younger age may favor the carcinogenesis while smoking is a risk factor for recurrent AP and chronic pancreatitis. Association with proximal tumor location probably results from the obstructive AP pathomechanism in these cases.

Disclosure: Nothing to disclose.

MP587

ASSOCIATION OF PANCREATIC CANCER AND DIABETES MELLITUS IN THE CZECH REPUBLIC WITHIN THE PERIOD 2017 - 2021

J. Bures¹, O. Ngo², M. Zavoral¹, K. Hejcmanova², L. Dusek², D. Kohoutova³, S. Suchanek¹, J. Skrha⁴, O. Majek²

¹Charles University First Faculty of Medicine and Military University Hospital Prague, Institute of Gastrointestinal Oncology, Prague, Czech Republic, ²Institute of Health Information and Statistics of the Czech Republic, Prague, Czech Republic, ³The Royal Marsden NHS Foundation Trust, London, United Kingdom, ⁴Charles University First Faculty of Medicine, 3rd Department of Internal Medicine, Prague, Czech Republic

Contact E-Mail Address: bures.jan@uvn.cz

Introduction: Pancreatic cancer has remained one of the most serious malignancies and is still a leading cause of cancer-related deaths worldwide. Great attention has been paid to the relationship between diabetes mellitus and pancreatic cancer. At the time of diagnosis of pancreatic cancer, impaired glucose metabolism has been reported to be present in variable rates according to particular studies (ref.).

Aims & Methods: Aims: The aim of our study was to analyse mutual association of pancreatic cancer and diabetes mellitus in the whole population of the Czech Republic within a 5-year period.

Methods: Based on the individual population data from the Czech National Cancer Registry, the incidence of pancreatic cancer in 2017-2021 was estimated. Another data source, the National Registry of Reimbursed Health Services that collects data from health insurance companies, was used to estimate people recently diagnosed with diabetes mellitus. For the purpose of this study, diagnosis of new-onset of diabetes mellitus was defined as the time of the first prescription of any antidiabetic drug (subgroup of patients with prediabetes treated with metformin was included). Patients with diabetes treated with diet only were not included. Subsequently, people diagnosed with pancreatic cancer in 2021 were retrospectively followed up to see if they had been diagnosed with diabetes mellitus in the last 5 years (or earlier) before diagnosis of pancreatic cancer.

Time of diagnosis of diabetes mellitus (DM)	Age: 39 years and younger	Age: 40-59-year old	Age: 60-74-year old	Age: 75 years and older	TOTAL
DM diagnosed within 1 year prior to cancer diagnosis	0 (0.0%)	29 (9.4%)	82 (7.1%)	54 (5.9%)	165 (6.9%)
DM diagnosed within 2 years prior to cancer diagnosis	1 (5.6%)	5 (1.6%)	44 (3.8%)	11 (1.2%)	61 (2.6%)
DM diagnosed within 3 years prior to cancer diagnosis	1 (5.6%)	5 (1.6%)	33 (2.9%)	27 (3.0%)	66 (2.8%)
DM diagnosed within 4 years prior to cancer diagnosis	0 (0.0%)	5 (1.6%)	29 (2.5%)	18 (2.0%)	52 (2.2%)
DM diagnosed within 5 years prior to cancer diagnosis	0 (0.0%)	7 (2.3%)	38 (3.3%)	22 (2.4%)	67 (2.8%)
DM diagnosed 6 or more years prior to cancer diagnosis	2 (11.1%)	47 (15.2%)	389 (33.7%)	392 (43.1%)	830 (34.7%)
DM diagnosed after the cancer diagnosis	0 (0.0%)	9 (2.9%)	40 (3.5%)	17 (1.9%)	66 (2.8%)
DM not diagnosed	14 (77.8%)	203 (65.5%)	500 (43.3%)	368 (40.5%)	1,085 (45.4%)
TOTAL NUMBER OF PATIENTS DIAGNOSED WITH PANCREATIC CANCER (2021)	18 (100.0%)	310 (100.0%)	1,155 (100.0%)	909 (100.0%)	2,392 (100.0%)

Table 1. Mutual association of diabetes mellitus and pancreatic cancer within the period 2017-2021.

Results: There were 310,427 new cases of diabetes mellitus identified within the period 2017 - 2021. Over this period, an average of 2,448 people were diagnosed with pancreatic cancer per year (23.1 / 100,000 popula-

tion). In 2021, 2,064 patients > 60 years were diagnosed with pancreatic cancer. New onset of diabetes mellitus was recorded in 12.2% three years before the diagnosis of pancreatic cancer and four or five years before this diagnosis in another 5.2%. If we focus only on the 60-74 age group, the proportion was 13.8% and 5.8 %, respectively. Mutual association of diabetes mellitus and pancreatic cancer is displayed in Table 1.

Conclusion: Incidence of pancreatic cancer in the Czech Republic belongs to the highest ones in Europe. New-onset of diabetes mellitus precedes the diagnosis of pancreatic cancer in nearly 20 % of cases within a 5-year period. These findings lead to considerations of the introduction of an early detection programme for pancreatic cancer in the Czech Republic based on new-onset of diabetes mellitus and possible other risk factors.

References: Cancers (Basel) 2023; 15(14): 3669

Disclosure: Nothing to disclose.

MP588

ROLE OF ADIPOSE-DERIVED FACTORS IN PREDICTING CACHEXIA IN PANCREATIC CANCER PATIENTS

A. Saray¹, N. Zubcevic¹, N. Custovic¹, A. Mehmedovic¹, S. Glavaš¹, V. Papovic¹, A. Valjevac²

¹Clinical Center University of Sarajevo, Clinic for Gastroenterology and Hepatology, Sarajevo, Bosnia and Herzegovina, ²Faculty of Medicine University of Sarajevo, Department of Physiology, Sarajevo, Bosnia and Herzegovina

Contact E-Mail Address: sarayaida19@gmail.com

Introduction: Due to the role of adipose tissue in mediating human metabolism, identification of prognostic biomarkers of fat loss in cancer cachexia are crucial to achieve better outcomes for cancer patients.

Aims & Methods: The aim of the study was to analyze the role of adipose-tissue derived adipokines in predicting cachexia in pancreatic cancer patients. We evaluated 71 patients with newly diagnosed pancreatic cancer. Serum adiponectin (ADP), leptin (L), ghrelin, tumor necrosis factor- α (TNF- α), and interleukin 6 (IL 6) were tested at baseline and after a follow-up period of 6 months. Our primary endpoint was 10% weight loss within 6 months. Receiver operating characteristics (ROC) analysis was employed to calculate the area under the curve (AUC). Survival analysis used the Kaplan-Meier curve and the Cox proportional hazards model.

Results: 53 of 71 patients met the primary endpoint. ADP levels were inversely correlated with leptin levels ($\rho = -0.433, P < 0.01$) in patients showing weight loss (WL). Thus, ADP concentration were corrected by leptin values (A/L ratio). Ghrelin, TNF- α and IL-6 levels showed an overall increase in the WL group, but the difference was statistically not significant. High A/L ratio was the only independent predictor of cachexia ($\beta = 0.655, P < 0.001$). At ROC analysis the diagnostic profile of A/L (AUC 0.932; sensitivity 82%; specificity 97%) in detecting cachexia was superior to that of leptin alone (AUC 0.698; sensitivity 70%; specificity 74%). Kaplan-Meier global survival analysis revealed a low A/L ratio was associated with an increased survival compared to patients with high A/L ratio (Cox F test = 2.260, $P < 0.05$).

Conclusion: Our results support the hypothesis that the combined measurement of adiponectin and leptin (A/L ratio) might provide prognostic information in predicting cachexia and survival in pancreatic cancer patients.

Disclosure: Nothing to disclose.

MP589

THE IMPACT OF COMBINED CHEMOTHERAPY AND INTRA-TUMORAL INJECTION OF PHOSPHORUS-32 MICROPARTICLES ON VASCULARITY IN LOCALLY ADVANCED PANCREATIC CARCINOMA

A. Lim^{1,2}, J. Zobel², M. Bills³, W. Hsieh³, B. Crouch³, R. Joshi⁴, J.-E. Thomson⁵, E. Neo⁵, L. Kuan⁶, R. Safaeian², E. Tse^{2,1}, C.K. Rayner^{1,2}, A. Ruszkiewicz^{7,8}, N. Singhal⁹, D. Bartholomeusz^{2,1}, N.Q. Nguyen^{2,1}

¹University of Adelaide, Adelaide, Australia, ²Royal Adelaide Hospital, Department of Gastroenterology, Adelaide, Australia, ³Royal Adelaide Hospital, Department of Nuclear Medicine, Adelaide, Australia, ⁴Lyell McEwin Hospital, Department of Oncology, Elizabeth Vale, Australia, ⁵Royal Adelaide Hospital, Department of Hepatobiliary Surgery, Adelaide, Australia, ⁶Queen Elizabeth Hospital, Department of Upper Gastrointestinal Surgery, Woodville, Australia, ⁷SA Pathology, Surgical Pathology, Adelaide, Australia, ⁸University of South Australia, Centre of Cancer Biology, Adelaide, Australia, ⁹Royal Adelaide Hospital, Department of Oncology, Adelaide, Australia

Contact E-Mail Address: amanda.hw.lim@gmail.com

Introduction: Despite advances in treatment, overall survival for pancreatic cancer has not improved beyond a 5-year survival of 10%. Reasons for resistance to chemotherapy include a dense stroma, immunosuppressive environment, and poor vascularity within the primary pancreatic tumors. Vascularity within pancreatic tumors has been shown not to increase on contrast-enhanced harmonic EUS (CH-EUS) following 2 months of chemotherapy (Gemcitabine/Nab-Paclitaxel).

Preliminary data has suggested that endoscopic ultrasound (EUS) guided intra-tumoral injection of phosphorus-32 (³²P) microparticles in addition to standard chemotherapy is potentially beneficial in locally advanced pancreatic cancer (LAPC).

We aimed to assess vascularity changes within pancreatic tumors (via CH-EUS) following implantation of ³²P microparticles in combination with standard chemotherapy.

Aims & Methods: We performed a prospective single-center trial of patients with unresectable, non-metastatic locally advanced pancreatic cancer (LAPC) undergoing standard chemotherapy (FOLFIRINOX) and ³²P implantation after 2 or 3 cycles of chemotherapy. We perform EUS with contrast-enhanced harmonic EUS (CH-EUS) after 2 cycles of chemotherapy and at 4 weeks and 12 weeks after implantation of ³²P microparticles. Time intensity curve (TIC) analysis was performed over 90 seconds from IV contrast bolus with baseline intensity (prior to contrast bolus) and peak intensity obtained. Intensity gain was defined as median peak intensity – median baseline intensity.

Results: Twenty patients (45% male, median age: 65) have been enrolled in the trial with 15 patients completing 12-week follow-up (3 withdrawals, 1 death, 1 proceeded to surgery prior). Technical success of ³²P implantation was 100% with no procedural complications. Median longest primary tumor size reduced from 32mm (IQR 27.5-38.75) pre-implantation to 24mm (IQR 16-26) 12 weeks post-implantation ($p < 0.001$). Five patients (25%) thus far, have had tumor downstaging, with 3 resections (R1) and one pending.

One patient refused surgical treatment. All tumors demonstrated hypoenhancement (lower intensity of enhancement relative to surrounding normal pancreatic tissue suggestive of hypovascularity) at baseline. Median intensity gain of contrast enhancement within the tumor pre-implantation post median 2 cycles of chemotherapy, was 32.15 (IQR 18.08-54.35). Median intensity gain increased to 46.85 (IQR 35.05-76.6; $p = 0.007$) and 66.3 (IQR 54.7-76.3; $p = 0.001$) at 4 weeks and 12 weeks post implantation respectively. Over a median follow-up period of 7.4 months (IQR 5.1-14.6),

16/20 (80%) remain alive (estimated median survival time of 16.0 months) with 3/20 (15%) demonstrating both local and distant disease progression, whilst 3/20 (15%) have had distant progression only.

Conclusion: This is the first study to demonstrate increased vascularity within pancreatic primary tumors in response to ³²P implantation in addition to standard chemotherapy with FOLFIRINOX, whilst historical data has not supported vascularity changes in response to chemotherapy alone. The result of this current study forms a platform to understand further, the potential benefits of chemoradiotherapy over chemotherapy alone in patients with LAPC. Larger comparative trials are warranted.

Disclosure: 32P provided by OncoSil Medical

MP590

HIGH PREVALENCE OF PANCREATIC STEATOSIS IN PANCREATIC CANCER PATIENTS: A META-ANALYSIS AND SYSTEMATIC REVIEW

C. Vlăduț^{1,2}, C. Steiner³, D. Turan Gökçe⁴, P. Maisonneuve⁵, T. Hank⁶, M. Löhr^{7,8}, D. Öhlund⁹, M. Sund^{10,11}, S. Hoogenboom¹², Pancreas 2000 Study Group

¹Clinical Emergency Hospital "Prof Dr Agrippa Ionescu", Department of Gastroenterology, Bucharest, Romania, ²Carol Davila University of Medicine and Pharmacy, Faculty of Medicine, Bucharest, Romania, ³Capio Stockholm Gastro Center, Stockholm, Sweden, ⁴Ankara Bilkent City Hospital, Ankara, Turkey, Department of Gastroenterology, Ankara, Turkey, ⁵IEO European Institute of Oncology IRCCS, Division of Epidemiology and Biostatistics, Milan, Italy, ⁶Heidelberg University Hospital, Department of General, Visceral and Transplantation Surgery, Heidelberg, Germany, ⁷Karolinska Institutet, Department of Upper Abdominal Diseases, Stockholm, Sweden, ⁸Karolinska Institute, Department of Clinical Science, Intervention, and Technology (CLINTEC), Stockholm, Sweden, ⁹Umeå University, Department of Diagnostics and Intervention (oncology) and Wallenberg Centre of Molecular Medicine (WCMM), Umeå, Sweden, ¹⁰Umeå University, Department of Diagnostics and Intervention (surgery), Umeå, Sweden, ¹¹University of Helsinki and Helsinki University Hospital, Department of Surgery, Helsinki, Finland, ¹²HagaZiekenhuis Hospital, Department of Gastroenterology, Hague, Netherlands

Contact E-Mail Address: drcatalinavladut@gmail.com

Introduction: Defining pancreatic steatosis (PS) and establishing its association with pancreatic cancer has been a discussed theme in the last decade. However, no consensus guidelines have yet been published on the clinical relevance and management of PS. In this systematic review and meta-analysis, we investigated the association between PS and pancreatic ductal adenocarcinoma (PDAC).

Aims & Methods: Medical literature between 2007 and 2023 was reviewed for eligible trials investigating the prevalence of PS in patients with PDAC. Eligible studies reporting on PS, assessed via imaging or histology, were included. Our primary objective was to determine the association between PDAC and PS by comparing the prevalence of PS in individuals with- and without PDAC. Subsequently, an evaluation was conducted to determine whether the method of assessment (CT, MRI, EUS or histology) and study country was correlated with the association between PS and PDAC. Measures of effect size were determined using odds ratios (ORs) and corresponding 95% confidence intervals (95% CI).

Results: The systematic review identified a total of 23 studies, of which seventeen studies examined PS prevalence among PDAC patients. Overall, the pooled prevalence of PS in patients with PDAC was 53.6% (95% CI 40.9-66.2). No significant difference in PS prevalence was observed across various diagnostic methods or geographical regions ($p = 0.71$ and $p = 0.50$,

respectively). Overall, the pooled OR for PS in patients with PDAC compared to controls was 3.23 (95% CI 1.86-5.60, Figure 1). Subgroup analysis did not reveal any difference according to country ($p = 0.52$), but higher OR was observed in studies using EUS for the assessment of PS (pooled OR=6.26, 95% CI 1.23-31.8) compared to studies using CT (pooled OR=3.31, 95% CI 1.93-5.68), histology (pooled OR=1.76, 95% CI 1.22-2.54) or MRI (pooled OR=1.19, 95% CI 1.06-1.33).

Conclusion: Patients with PDAC have notable prevalence of pancreatic steatosis (53.6%). Furthermore, PDAC patients are significantly more likely to have PS (OR 3.23). These findings underscore the importance of prioritizing a standardized approach to the diagnosis, follow-up, and treatment of PS. Future studies should prioritize the identification of patients with PS who will benefit from PDAC surveillance programs.

Disclosure: Nothing to disclose.

MP591

CHANGES OF CFDNA LEVELS IN PATIENTS WITH PANCREATIC CANCER

R. Riauka^{1,2}, R. Kupcinskaite-Noreikiene³, I. Grabauskys⁴, G. Barauskas¹, A. Gulbinas^{1,2}, A. Jasukaitiene², P. Ignatavicius¹

¹Lithuanian University of Health Sciences, Department of Surgery, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Laboratory of Surgical Gastroenterology, Institute for Digestive Research, Kaunas, Lithuania, ³Lithuanian University of Health Sciences, Institute of Oncology, Kaunas, Lithuania, ⁴Lithuanian University of Health Sciences, Department of Physics, Mathematics and Biophysics, Kaunas, Lithuania

Contact E-Mail Address: romualdasriauka@gmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains a challenge in oncology with an overall survival rate remaining about 10%. Surgery and adjuvant chemotherapy stands as only curative treatment options. Only a minority of patients are diagnosed with resectable disease. While traditional diagnostic modalities show limitations in detecting and monitoring pancreatic cancer, liquid biopsies is a relatively new, non-invasive and promising diagnostic method for early detection, molecular profiling, and observation.

Despite previous published or ongoing research projects and studies, liquid biopsies and specifically cell-free DNA (cfDNA) alterations role in management of pancreatic cancer remains unverified.

Aims & Methods: The aim of our study was to evaluate the diagnostic value of liquid biopsies and alterations in cfDNA levels in patients with pancreatic cancer. This study was approved by the Kaunas Regional Bioethics Committee (Approval ID: BE-2-31). Patients with newly diagnosed and histologically confirmed pancreatic cancer and patients with chronic pancreatitis, admitted to the Department of Surgery at Lithuanian University of Health Sciences Hospital, Kaunas Clinics, between September 2022 and December 2023, and healthy volunteers (control group) were included. Blood samples were obtained from the patients before any treatment procedures commenced. cfDNA was extracted from the collected blood using the QIAmp Circulating Nucleic Acid Kit (Qiagen).

The concentration and quality of the extracted cfDNA were determined using the Qubit™ 1X dsDNA High Sensitivity (HS) and Broad Range (BR) Assay Kits (ThermoFisher Scientific, Inc., Waltham, MA, USA). Mann-Whitney U-test and Kruskal-Wallis H-test were used to determine the differences in quantitative traits between the comparison groups, with results being presented in median (min – max). The predictive capability (diagnostic performance) of cfDNA to distinguish PDAC and chronic pancreatitis/healthy controls was investigated by means of the area under the ROC (Receiver-Operating Characteristics) curve (AUC).

Results: Sixty-five patients were included (47 patients with PDAC, 10 patients with chronic pancreatitis and 8 healthy controls). Levels of cfDNA were statistically significantly higher in PDAC patients (46.5 (4 - 768) ng/ml) compared to patients with chronic pancreatitis (23.4 (8.56 - 138.4) ng/ml) ($p = 0.032$) and healthy controls (19.75 (17.6 - 22.8) ng/ml) ($p < 0.001$). The cfDNA cut-off value distinguishing PDAC from chronic pancreatitis and healthy controls were determined to be 23,65 ng/ml (AUC = 0.716) and 22.9 ng/ml (AUC = 0.915), respectively. There were no differences in cfDNA levels concerning tumor localization, size, differentiation, spread, or survival rates (all $p > 0.05$).

Conclusion: Liquid biopsies and cfDNA level alterations offer promising opportunities for distinguishing pancreatic cancer from benign inflammatory diseases, such as chronic pancreatitis. However, additional experiments and studies are necessary for more comprehensive validation and clinical use.

Disclosure: This study was partially funded by Lithuanian University of Health Sciences Scientific fund and Lithuanian Future Biomedicine foundation.

MP592

SERUM MATRIX METALLOPROTEINASE-7, SYNDECAN-1 AND CA 19-9 AS A BIOMARKER PANEL FOR DIAGNOSIS OF PANCREATIC DUCTAL ADENOCARCINOMA

D. Yablecovitch^{1,2}, M. Nadler^{1,2}, S. Ben-Horin^{1,2}, O. Picard^{1,2}, M. Yavzori^{1,2}, E. Fudim^{1,2}, M. Tardio Duchan^{1,2}, E. Sakhnini^{1,2}, A. Lang^{1,2}, M. Lahav^{1,2}, T. Saker^{3,2}, S. Neuman^{1,2}, L. Selinger Feigin^{1,2}, B. Freitz^{1,2}, R. Dvir^{1,2}, M. Raites - Gurevich^{4,2}, T. Golan^{4,2}, I. Levy^{1,2}, I. Laish^{1,2}

¹Chaim Sheba Medical Center Dept. of Gastroenterology, Ramat Gan, Israel, ²School of Medicine, Faculty of Medical and Health Science, Tel Aviv University, Tel Aviv, Israel, ³Shalvata Mental Health Center, Hod Hasharon, Israel, ⁴Chaim Sheba Medical Center Dept. of Oncology, Ramat Gan, Israel

Contact E-Mail Address: doronyab@gmail.com

Introduction: Matrix metalloproteinase-7 (MMP-7) and Syndecan-1 (SDC1) are involved in multiple functions during tumorigenesis. While most pancreatic ductal adenocarcinoma (PDAC) develop from Pancreatic Intraepithelial Neoplasia (PanIN), about 15-20% grows from well-defined pre-malignant cystic lesions. The presence of worrisome features in imaging cannot reliably differentiate cysts with neoplastic progression from those without. Therefore, implementation of new biomarkers is needed. MMP-7 has been shown to be overexpressed in both tissue and serum of patients with PDAC, but was never evaluated in pre-malignant cystic lesions. Similarly, SDC1, which has been linked to mutated overexpressed KRAS (the initiating step in most PDACs) and was recently shown by our lab to be elevated in PDAC, was not evaluated in cystic lesions yet.

Aims & Methods: To evaluate the diagnostic and prognostic performance of these serum proteins as potential panel biomarkers, in patients with PDAC and benign pancreatic cysts. In this, case-control study, patients with newly diagnosed PDAC (N= 121) were compared with benign cyst (N= 66) and healthy control (N=48) groups. Serum MMP-7 and SDC1 were measured by ELISA. The diagnostic accuracy of their levels for diagnosing PDAC and pancreatic cysts was computed, and their association with survival outcomes was evaluated.

Results: MMP-7 median serum levels were significantly elevated in PDAC (7.3 ng/ml) and cyst groups (3.7 ng/ml) compared with controls (2.9 ng/ml) ($p < 0.001$ and 0.02, respectively), and also between PDAC and cyst groups ($p < 0.001$), while SDC-1 median serum levels were significantly elevated in PDAC (43.3 ng/ml) compared with either cysts (30.1 ng/ml, $p <$

0.001) or controls (31.2 ng/ml, $P < 0.001$). The ROC analysis area under the curve (AUC) in PDAC vs. controls was 0.90 and 0.78 for MMP-7 and SDC-1, respectively, while it was 1.0 for the combination of the two and CA 19-9 ($p < 0.001$). Negative and positive predictive values of the 3 biomarkers panel were 100% and 79%, respectively. For patients with baseline serum MMP-7 ≤ 10 ng/ml vs. > 10 ng/ml, there was a trend for survival benefit after 1 year (50% vs. 36%, respectively; $p = 0.095$) and a significant benefit after 3 years (14% vs. 7%, respectively; $p = 0.016$). For patients with baseline serum SDC-1 < 35 ng/ml vs. ≥ 35 ng/ml, there was a trend for survival benefit after 1 year (52% vs 40%, respectively; $p = 0.06$) and no benefit after 3 years (19% vs. 20%, respectively; $p = 0.193$).

Conclusion: Despite a limited diagnostic utility as a biomarker for early detection of PDAC, this biomarker panel can safely rule out PDAC in healthy population

References:

Disclosure: Nothing to disclose.

MP593

GENETIC RISK FACTORS FOR STEATOTIC LIVER DISEASE AFTER LIVER TRANSPLANTATION

V. Liukkonen^{1,2}, M. Semenova³, K. Hyvärinen³, J. Lauronen³, J. Partanen³, A. Nordin⁴, J. Arola^{1,5}, M.A. Färkkilä⁶, F. Åberg⁴
¹University of Helsinki, Faculty of Medicine, Helsinki, Finland, ²North Carelia Central Hospital, Gastroenterology, Joensuu, Finland, ³Finnish Red Cross Blood Service, Helsinki, Finland, ⁴Helsinki University Hospital, Transplantation and Liver Surgery, Helsinki, Finland, ⁵Helsinki University Hospital, Diagnostic Center, Department of Pathology, Helsinki, Finland, ⁶Helsinki University Hospital, Dept. of Gastroenterology, Helsinki, Finland

Contact E-Mail Address: vliukkonn@outlook.com

Introduction: Steatotic liver disease (SLD) is a common problem after liver transplantation (LT). Previous studies have confirmed the role of donor PNPLA3 rs738409 G allele as a risk factor for post-LT SLD, but the role of other recipient and donor genetic risk variants is largely unknown.

Aims & Methods: Aims: To study the prevalence of genetic risk variants for SLD in LT recipients and donors and their impact on development of post-LT SLD.

Methods: Of 807 adult patients undergoing LT in Finland between 2000–2019, 56 SLD-associated genetic risk variants were extracted from genotype data for 666 donor-recipient-pairs. Recipient genotypes were compared with ~10 000 Finnish population controls from gnomAD database. Incident post-LT SLD was assessed from protocol liver biopsies. The impact of donor and recipient genetic variants was studied in multivariate Cox regression analysis adjusted for phenotype factors.

Risk allele	Adjusted hazard ratio / number of risk alleles			p-values		
	0	1	2			p
Recipient PSD3 rs71519934-G	indicator	0.80	0.66	0.11	0.15	0.04
Recipient FADS1 rs174556-T	indicator	1.01	1.63	0.03	0.94	0.02
Recipient UCP2 rs695366-G	indicator	0.63	0.50	0.003	0.002	0.04
Donor MERTK rs4374383-A	indicator	1.51	1.46	0.02	0.007	0.10
Donor HSD17B13 rs6834314-G	indicator	0.68	0.46	0.02	0.02	0.07
Donor TM6SF2 rs58542926-T	indicator	1.61	1.71	0.08	0.03	0.46
Donor PNPLA3 rs738409-G	indicator	1.39	2.51	0.002	0.03	0.001

Table 1. Genetic variants significantly associated with post-LT SLD.

Results: Of 56 risk variants, the minor allele frequencies (MAFs) of 17 variants were significantly different between LT recipients and population controls. The greatest MAF differences were observed for PNP-LA3 rs738409-G (0.33 vs 0.22, $p = 2.56 \times 10^{-20}$), TNF rs1800629-A (0.19 vs 0.12, $p = 1.48 \times 10^{-12}$), IFNL4 rs12979860-T (0.29 vs 0.24, $p = 7 \times 10^{-6}$), CD14 rs2569190-A (0.41 vs 0.37, $p = 0.005$) and MERTK rs4374383-A (0.36 vs 0.33, $p = 0.014$).

Patients transplanted for metabolic dysfunction-associated steatohepatitis (MASH) ($n = 42$) exhibited high prevalence of PNPLA3 rs738409-G (0.63 vs 0.22, $p = 1.47 \times 10^{-19}$) and low prevalence of the protective HSD17B13 rs6834314-G (0.07 vs 0.21, $p = 0.001$) and MARC1 rs2642438-A (0.14 vs 0.29, $p = 0.002$).

Incidence of post-LT SLD was 29.1% in median follow-up time of 7.6 years. The lowest incidence (14.8%) was observed among patients transplanted for acute liver failure, and the highest (52.9%) in patients transplanted for MASH.

Final multivariate regression model to predict post-LT SLD included high SLD-risk indication (HR 2.03, $p < 0.001$), BMI (HR 1.10, $p < 0.001$), diabetes (HR 1.37, $p = 0.016$) and alcohol consumption (HR 2.01, $p < 0.001$). Table 1 shows the hazard ratios of the donor and recipient genetic variants most strongly predicting post-LT SLD after adjusting for recipient phenotype factors (high-SLD risk indication, BMI, diabetes, and alcohol consumption).

Conclusion: SLD-associated risk alleles were common in LT recipients, especially in MASH. Post-LT SLD incidence was high (29.1%), but with large variation across transplantation indications. Donor, but not recipient, PNPLA3 allele was most strongly associated with post-LT SLD. Several other donor and recipient genetic variants also contributed to post-LT SLD. Both LT recipient and donor genotypes provide novel insights into the genetic determinants of SLD after LT, providing help in future individual risk assessment.

Disclosure: Nothing to disclose.

MP594

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) AND PANCREATIC DISEASES - A POPULATION-BASED NATIONWIDE COHORT AND SIBLING-CONTROLLED STUDY

M. Vujasinovic^{1,2}, F. Ebrahimi^{3,4}, B. Roelstraete⁴, M. Löhr^{1,5}, J.F Ludvigsson^{6,4,7}

¹Karolinska University Hospital, Department of Upper Abdominal Diseases, Stockholm, Sweden, ²Karolinska Institutet, Department of Medicine Huddinge, Stockholm, Sweden, ³University Digestive Health Care Center Basel, Department of Gastroenterology and Hepatology, Basel, Switzerland, ⁴Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, ⁵Karolinska Institutet, CLINTEC, Stockholm, Sweden, ⁶Columbia University Medical Center, Celiac Disease Center, Department of Medicine, New York, United States of America, ⁷Örebro University Hospital, Department of Pediatrics, Örebro, Sweden

Contact E-Mail Address: mvujas@gmail.com

Introduction: Some data suggest a possible association between metabolic dysfunction-associated steatotic liver disease (MASLD) and pancreatic disorders. However, evidence from population-based studies taking advantage of liver histology is lacking.

Aims & Methods: In this population-based cohort including all Swedish adults with biopsy-proven MASLD (1965-2017), we aimed to investigate the overall incidence of pancreatic diseases including acute and chronic pancreatitis, pancreatic cancer as well as pancreas-related mortality. Individuals with MASLD were matched to up to 5 individuals from the general population by age, sex, calendar year and county. Using the unique Swedish personal identity number, several validated nationwide registers were linked to obtain data on demographics, in- and outpatient diagnoses, prescribed medications, incident cancers, and causes of death. The primary endpoint of adverse pancreatic outcome was a composite of acute non-biliary pancreatitis, chronic pancreatitis, and pancreatic cancer. Secondary outcomes included each of the single outcomes as well as acute biliary pancreatitis and pancreas-related mortality. Using Cox proportional hazards modelling, we calculated multivariable adjusted HRs (aHRs). Sibling-controlled analyses were additionally performed to account for familial susceptibilities.

Results: In total, 8563 patients with biopsy-proven MASLD and 38,858 matched reference individuals were included. Among MASLD patients, the average age at index biopsy was 54.5 years, and 56.9% were male.

Overall, we documented 359 incident adverse pancreatic outcomes in MASLD patients (2.74/1,000 person-years (PYs)) and 880 events in matched reference individuals (1.19/1000 PYs), resulting in one extra case of adverse pancreatic outcome in 65 MASLD patients followed-up for ten years (incidence rate difference: 1.54/1000 PYs).

After multivariable adjustment, the aHR for incident adverse pancreatic outcomes was 2.19 (95%CI=1.92-2.50).

Compared with reference individuals, the incidence rate differences and corresponding aHRs increased with worsening histologic MASLD severity with 2.46 /1,000 PYs (aHR, 2.07 [95%CI=1.77-2.43]) in simple steatosis, 3.39 /1,000 PYs (aHR, 2.69 [95%CI=1.83-3.96]) in non-fibrotic MASH, and 3.56 /1,000 PYs (aHR, 2.53 [95%CI=1.87-3.43]) in patients with MASLD-associated fibrosis or cirrhosis, respectively.

Compared to reference individuals, the most common adverse pancreatic outcome in individuals with biopsy-proven MASLD was acute non-biliary pancreatitis with 1.44 vs. 0.44/1,000 PYs, resulting in an aHR of 2.24 (95%CI=1.83-2.75).

Consistent with the results on acute pancreatitis, individuals with MASLD had significantly higher rates of developing chronic pancreatitis (0.54 vs. 0.12/1,000 PYs; aHR 3.78, 95% CI 2.70-5.29).

In addition, MASLD patients had significantly higher rates of incident pancreatic cancer (0.88 vs. 0.47 per 1000 PY), resulting in an absolute rate difference of 0.41/1,000 PYs.

We documented 130 vs. 344 pancreas-related deaths among individuals with MASLD and their matched comparators (0.97 vs. 0.46/1,000 PY), yielding an absolute risk difference of 0.51/1,000 PY and an aHR of 2.41 (95%CI=1.95-2.97).

Conclusion: In this nationwide histology cohort, MASLD was associated with significantly higher rates of acute non-biliary pancreatitis, chronic pancreatitis, and pancreatic cancer, all of which led to a higher risk of pancreas-related mortality. In contrast, the risk of biliary pancreatitis was only slightly increased. Excess risk was evident across all stages of NAFLD and increased with worsening disease severity.

Disclosure: Dr Ludvigsson is coordinating a study on behalf of the Swedish IBD quality register (SWIBREG). This study has received funding from the Janssen corporation. Dr Ludvigsson has also received financial support from MSD to develop a paper reviewing national healthcare registers in China and has an ongoing collaboration about celiac disease with Takeda. Dr Vujasinovic and Dr L  hr have received lecture fees from Abbott and Viatri. Dr Ebrahimi has served on an advisory board for Boehringer Ingelheim. All other authors declare that they have no conflicts of interest and nothing to declare.

Grants and financial support: Swedish Magtarmfondens stipendium for research and Ruth and Richard Julin Foundation for research (Dr Vujasinovic). The Swedish Cancer Foundation (Dr Ludvigsson). Swiss National Science Foundation P500PM_210866 (Dr Ebrahimi).

MP595

E2F1-HDAC1 COMPLEX TARGETS PIWIL1 TO REGULATE PANCREATIC STELLATE CELL ACTIVATION

R. Xue¹

¹Peking University Cancer Hospital and Institute, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: xueran2@sina.com

Introduction: Pancreatic fibrosis is the main pathological feature of chronic pancreatitis. Activated pancreatic stellate cells (PSCs) are the main effector cells of pancreatic fibrosis.

The purpose of this study was to investigate the function of E2F1-HDAC1 complex in the activation of PSCs, evaluate the role of HDAC1 inhibitor Ce-

daramine during pancreatic fibrosis, and explore the molecular regulated mechanism between E2F1-HDAC1 complex and PIWIL1/mTOR signaling pathway.

Aims & Methods: When inducing pancreatic fibrosis in C57BL/6 mice, 20% L-arginine (250 mg/100g) was injected intraperitoneally twice a week, with an interval of 1 hour, lasting for 8 weeks, and then PSCs were isolated. Use RNA interference (RNAi) constructed by lentivirus and vectors constructed based on over-expression vectors to knock out and over-express E2F1 and HDAC1 Protein. In order to explore the effects of E2F1-HDAC1 complex on PSC activation and EMC secretion, western blotting and IHC staining were used respectively.

To explore transcriptional molecular mechanism between E2F1-HDAC1 complex and PIWIL1, luciferase reporter assay, chromatin immunoprecipitation (ChIP) and electrophoretic mobility shift assay (EMSA) were applied. Hematoxylin-eosin, Masson and Sirius red staining were used to analyze the effect of E2F1-HDAC1 complex and HDAC1 inhibitor Cedaramine on histological changes and collagen deposition.

Results: In LV-E2F1 and LV-HDAC1 group, the level of α -SMA, Col I and Col III were significantly increased compared with si-E2F1 and si-HDAC1 group. However, the expression of PIWIL1, desmin and p-mTOR were reduced in LV-E2F1 and LV-HDAC1 group. Meanwhile, E2F1-HDAC1 complex directly binded to the PIWIL1 promoter and then activated its transcription. In addition, as fibrosis aggravated over time, the levels of E2F1 and HDAC1 significantly increased. HDAC1 inhibitor Cedaramine can significantly improve collagen deposition in pancreatic fibrosis.

Conclusion: Our findings suggest that E2F1-HDAC1 complex targets PIWIL1 to regulate pancreatic stellate cell activation. HDAC1 inhibitor Cedaramine could become a potential drug in the treatment of pancreatic fibrosis.

Disclosure: This work was supported by grants from the Fund for Fostering Young Scholars of Peking University Health Science Center (BMU2021PY010), National Natural Science Foundation of China (No. 82002461), Beijing Municipal Hospital Management Center "Youth" Talent Plan (QML20231104) and Medjaden Academy and Research Foundation for Young Scientists (MJR20211110).

MP596

MAS-DEPENDENT MACROPHAGE EFFEROCYTOSIS MAINTAINS IMMUNE HOMEOSTASIS IN ISCHEMIA-STRESSED MOUSE AND HUMAN LIVER

S. Chen¹, Z. Lu², S. Li¹, C. Yang¹

¹Tongji Hospital, School Of Medicine, Tongji University, Shanghai, China, ²Department of Automation, Tsinghua University, Beijing, China

Contact E-Mail Address: shuai_chenrj@163.com

Introduction: Liver ischemia-reperfusion injury (LIRI) is an inevitable detrimental event following liver transplantation, significantly impacting clinical outcomes. Novel therapeutic approaches are urgently needed to ameliorate recipient injury.

We recently has revealed the beneficial role of Mas receptor in drug-induced liver injury^[1, 2], which is also highlighted by the editorial of *Journal of Hepatology*^[3]. However, its specific roles in myeloid cell innate immunity and the maintenance of hepatic tissue homeostasis remain unclear.

Aims & Methods: The hepatic expression of Mas was investigated in ischemia-stressed mouse and human livers. Multiple cell-specific knockout mice were used to clarify the effector cells of Mas. Single-cell RNA sequencing (scRNA-seq), spatial transcriptomics (ST), multiplex Immunohistochemistry (mIHC), flow cytometry and subcellular intravital imaging were used to analyze macrophage efferocytosis and pathological interaction. RNA-seq, CUT&Tag and luciferase reporter assay were used for mo-

lecular studies. Adenovirus, mouse primary cells, Adeno-associated virus, *LysM^{cre}Klf4^{fl/fl}* mice and human liver samples were used to validate the discoveries of bioinformatics analysis.

Results: Long-term subcellular intravital imaging showed that macrophage efferocytosis occurs frequently during the early stage of LIRI and is crucial for the resolution of inflammation. Mice with systemic or myeloid cell-specific *Mas1* deficiency were vulnerable to LIRI. DAOSLIMIT, a novel intravital microscopy that fulfills the unmet requirement for hour-long, high-speed subcellular observations *in vivo*^[4]. scRNA-seq, ST, and intravital imaging collectively revealed that myeloid deficiency of *Mas1* results in impaired macrophage efferocytosis by downregulating MerTK, leading to the accumulation of aged neutrophils and exacerbating inflammation. Molecular studies demonstrate that Mas receptors regulate the transcription factor KLF4 via the PKA/CREB signaling pathway, thereby directly promoting the expression of macrophage MerTK. CUT&Tag, ChIP-qPCR and luciferase reporter assay revealed that the transcription factor KLF4 can directly bind to the promoter region of MerTK. Macrophage-specific knockout of KLF4 significantly exacerbated LIRI, and macrophage-specific overexpression of KLF4 *in vivo* effectively reversed the exacerbated phenotype caused by myeloid *Mas1* deficiency. mIHC also revealed that Mas⁺MerTK⁺ macrophages actively migrate towards aged neutrophils in ischemia-stressed human livers, thereby promptly clearing aged neutrophils.

Conclusion: In summary, our study documents a novel regulatory function of the Mas/KLF4/MerTK axis via PKA/CREB signaling in macrophage efferocytosis. It may serve as a therapeutic target and as a checkpoint regulator of homeostasis in response to LIRI. By combining scRNA-seq, ST and intravital imaging, this work provides a comprehensive paradigm for studying mammalian cellular interactions in complex pathophysiological microenvironments.

References: [1] Chen S, Lu Z, Jia H, et al. Hepatocyte-specific Mas activation enhances lipophagy and fatty acid oxidation to protect against acetaminophen-induced hepatotoxicity in mice. *Journal of Hepatology*, 2023, 78(3): 543-557.

[2] Chen S, Lu Z, Zhao Y, et al. Myeloid-Mas Signaling Modulates Pathogenic Crosstalk among MYC⁺CD63⁺ Endothelial Cells, MMP12⁺ Macrophages, and Monocytes in Acetaminophen-Induced Liver Injury. *Advanced Science*, 2024: 2306066.

[3] Nogueiras R, Aspichueta P. Expanding the roles of the renin-angiotensin system: drug-induced liver injury. *Journal of Hepatology*, 2023, 78(3): 457-459.

[4] Wu J, Lu Z, Jiang D, et al. Iterative tomography with digital adaptive optics permits hour-long intravital observation of 3D subcellular dynamics at millisecond scale. *Cell*, 2021, 184(12): 3318-3332. e17.

Disclosure: Nothing to disclose.

MP597

NEW INSIGHT OF LIVER FIBROSIS: ALTERED CHROMATIN ACCESSIBILITY IN HEPATIC STELLATE CELLS

T. Jia¹, Y. Shen¹, L. Yang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology and Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, Chengdu, China

Contact E-Mail Address: 2018151621145@stu.scu.edu.cn

Introduction: The treatments for liver fibrosis are still in need so far. As the crucial initiators, activated hepatic stellate cells (aHSCs) undergo a series of epigenetic changes.

The study intends to explore transcription factors (TFs) that facilitate HSCs activation and provide novel therapeutic targets for liver fibrosis.

Aims & Methods: Three distinct HSCs activation models were established in present study.

Firstly, *in vitro* activation involved isolating primary HSCs from normal Sprague-Dawley rats and culturing them for two days (n=5) and seven days (n=5), namely natural activation model.

Secondly, *in vivo* activation entailed isolating primary HSCs from bile duct ligated rats (n=4) and normal controls (n=4), followed by culturing until the next day. Lastly, transforming growth factor- β (TGF- β , 2.5ng/ml) (n=10) or control buffer (n=10) were added to the human HSCs cell line LX2 and cultured for 24 hours. Subsequently, assay for transposase-accessible chromatin using sequencing (ATAC-seq) was conducted on the abovementioned cells, along with motif enrichment and footprint analysis.

Pathway enrichment analysis was performed on differentially accessible genes (DAGs). RNA sequencing (RNA-seq) was employed to analyze gene expression profiles of primary HSCs in the natural activation model (n=4).

The integration of ATAC-seq and RNA-seq further identified potential key TFs. RT-qPCR and differential expression analysis of public datasets was utilized to confirm the dysregulation of TFs in primary HSCs, fibrotic liver and fibrotic model of induced pluripotent stem cells.

Finally, enrichment at enhancers and promoters of these genes was validated by H3K27Ac and H3K4me3 chromatin immunoprecipitation followed by sequencing (ChIP-seq) of human HSCs.

Results: For ATAC-seq, primary HSCs exhibited higher chromatin accessibility after activation compared with the controls. After peak annotation, the up-regulated peaks were mainly located in the promoter region in all comparison groups, uncovering the dynamic transcriptional regulation during HSC activation. In the motif enrichment analysis, 150 aHSCs related TFs and 54 quiescent HSCs (qHSCs) related TFs were identified in the *in vitro* activation model.

The three models shared 12 aHSCs related TFs, namely *Runx-aml*, *Runx1*, *Runx2*, *Runx*, *Ets:Runx*, *Atf2*, *Atf4*, *Atf7*, *c-Jun-Cre*, *Creb5*, *Smad3* and *CArG*; and 19 qHSCs related TFs, including *Foxf1*, *Foxo3*, *Foxk1*, *Foxp1*, *Hoxa1*, *Hoxa2*, *Stat3*, *Hnf4a*, *Hnf6*, *Elk1*, *Elk4*, *Cux1*, *Crx*, *Duxbl*, *Vdr*, *Tr4*, *Ebf2*, *Gata2*, *Gata6*. Footprint analysis validated the alteration of accessibility in *Atf2*, *Atf4*, *Atf7*, *Creb5*, *Hnf6* and *Gata2*.

Actin filament organization, Ras protein signal transduction and intrinsic apoptotic signal pathways were enriched in DAGs. Integration of ATAC-seq and RNA-seq showed that gene expression was significantly correlated with chromatin accessibility, among which *Runx2*, *Creb5*, and *Smad3* were significantly upregulated in aHSCs at transcription level. The dysregulation of these three genes was verified in primary HSCs, fibrotic liver and fibrotic model of human induced pluripotent stem cells.

Finally, enrichment at active enhancers and promoters of these TFs was validated by H3K27Ac and H3K4me3 ChIP-seq of human HSCs, revealing the crucial role of genes in the transcription.

Conclusion: We generated chromatin accessibility profiles of different HSCs activation models, highlighting the significance of *Runx2*, *Creb5*, and *Smad3* as key TFs mediating HSCs activation. These findings proposed these TFs as promising targets for future liver fibrosis treatment.

Disclosure: The author declare no competing interests and financial relationships with commercial interests.

MP598

JUND-REGULATED GLUTAMINE METABOLISM IN PANCREATIC STELLATE CELLS PROMOTES PANCREATIC FIBROSIS VIA PIWIL1/MTOR SIGNALING PATHWAY

R. Xue¹

¹Peking University Cancer Hospital and Institute, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: xueran2@sina.com

Introduction: Pancreatic fibrosis is the main pathological feature of chronic pancreatitis and stroma of pancreatic cancer, which is the result of excessive deposition of extracellular matrix of collagen fibers. Activated pancreatic stellate cells (PSCs) are the main effector cells of pancreatic fibrosis. The characteristics of heterogeneity and subgroup of PSCs may help to determine the therapeutic target of pancreatic fibrosis. The purpose of this study was to investigate the function of JUND in the activation of PSCs, evaluate the role of JUND in glutamine metabolism during pancreatic fibrosis, and explore the molecular regulated mechanism between JUND and PIWIL1/mTOR signaling pathway.

Aims & Methods: When inducing pancreatic fibrosis in C57BL/6 mice, 20% L-arginine (250 mg/100g) was injected intraperitoneally twice a week, with an interval of 1 hour, lasting for 8 weeks, and then PSCs were isolated. Use RNA interference (RNAi) constructed by lentivirus and vectors constructed based on over-expression vectors to knock out and over-express JUND and PIWIL1 Protein. In order to explore the effects of JUND on PSC activation, EMC secretion, actin cytoskeleton, invasion and migration ability, as well as glutamine metabolism, ELISA, western blotting, wound healing test, transwell and phalloidin staining were used respectively. To explore transcriptional molecular mechanism between JUND and PIWIL1, luciferase reporter assay, chromatin immunoprecipitation (ChIP) and electrophoretic mobility shift assay (EMSA) were applied. Hematoxylin-eosin, Masson and Sirius red staining were used to analyze the effect of JUND on histological changes and collagen deposition.

Results: In LV-JUND group, the level of α -SMA, Col I and Col III were significantly increased compared with si-JUND group. However, the expression of PIWIL1, desmin and p-mTOR were reduced in LV-JUND group. Meanwhile, the synthesis and metabolism of glutamine decreased significantly under the LV-JUND treatment. Wound healing test, transwell indicated that JUND promoted the migration and invasion ability of PSCs. Furthermore, JUND directly binded to the PIWIL1 promoter and then activated its transcription. In addition, as fibrosis aggravated over time, the levels of JUND significantly increased.

Conclusion: Our findings suggest that JUND-regulated glutamine metabolism in PSCs promotes pancreatic fibrosis via PIWIL1/mTOR signaling pathway. JUND could become a potential target for the treatment of pancreatic fibrosis.

Disclosure: This work was supported by grants from the Fund for Fostering Young Scholars of Peking University Health Science Center (BMU2021PY010), National Natural Science Foundation of China (No. 82002461), Beijing Municipal Hospital Management Center "Youth" Talent Plan (QML20231104) and Medjaden Academy and Research Foundation for Young Scientists (MJR20211110).

MP599

PROGNOSTIC VALUE OF THE TP53 MUTATION IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA RECEIVING FOLFIRINOX

Y. Song¹, S.H. Lee¹, I.R. Cho¹, J.H. Choi¹, M.K. Kim², Y. Kim³, J. Kim⁴, S. Kim⁵, H. Yun⁵, J. Yoon¹, D.-Y. Oh¹, K. Kim⁶

¹Seoul National University Hospital, Internal Medicine, Seoul, South Korea, ²Asan Medical Center, Department of Gastroenterology, Seoul, South Korea, ³Seoul National University, Bioinformatics, Seoul, South Korea, ⁴Seoul National University Bundang Hospital, Internal Medicine, Division Of Gastroenterology, Seongnam, South Korea, ⁵Seoul National University Hospital, Genomic Medicine, Seoul, South Korea, ⁶Seoul National University Hospital, Transdisciplinary Medicine, Seoul, South Korea

Contact E-Mail Address: yongsoono1@naver.com

Introduction: *KRAS*, *TP53*, *CDKN2A*, and *SMAD4* have been the main driver mutations in pancreatic ductal adenocarcinoma (PDAC). Studies on the clinical significance and treatment response to 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) regimen in terms of the presence of these mutations remain inconclusive.

Aims & Methods: This study analyzed patients diagnosed with pancreatic adenocarcinoma using a targeted next-generation sequencing platform at two tertiary referral hospitals from January 2016 to March 2022. Patients receiving FOLFIRINOX chemotherapy as the initial treatment were retrospectively investigated.

Results: The analysis included 100 patients. *KRAS* mutation was identified in 92 (92.0%) patients, followed by *TP53*, *CDKN2A*, and *SMAD4* in 63 (63.0%), 18 (18.0%), and 17 (17.0%) patients, respectively. The *TP53* wild type group demonstrated longer overall survival (OS) than the *TP53* mutated group (median OS: 29 months vs. 19 months, $p = 0.03$), and *TP53* served as a prognostic factor for survival (hazard ratio = 1.74, 95% confidence interval: 1.00–3.00, $p = 0.048$). The difference in OS according to *TP53* mutation was intensified in localized pancreatic adenocarcinoma (37 months vs. 19 months, $p = 0.01$). The *TP53* wild type group demonstrated a higher objective response rate to FOLFIRINOX chemotherapy than the *TP53* mutation group in localized pancreatic adenocarcinoma (50.0% vs. 17.6%, $p = 0.024$).

Conclusion: PDAC patients with wild type *TP53* demonstrated longer OS than those with *TP53* mutation, and this trend was intensified in patients with localized disease. This result may be due to an impaired response to FOLFIRINOX chemotherapy in patients with *TP53* mutation.

Disclosure: Nothing to disclose.

MP600

GENOME-WIDE META-ANALYSIS ASSOCIATES DONOR-RECIPIENT NON-HLA GENETIC MISMATCH WITH ACUTE CELLULAR REJECTION AFTER LIVER TRANSPLANTATION

L. Nieuwenhuis^{1,2}, Y. Li², B.-L. Loza³, A.J. Lambeck⁴, S. Hu², R. Gacesa², M. Voskuil², B.G. Hepkema⁴, B.H. Jansen², H. Blokzijl², H.J. Verkade², M.C. van den Heuvel⁵, S. Asrani⁶, G. Testa⁶, G. Klintmalm⁶, J. Trotter⁶, K.M. Olthoff³, A. Shaked³, B.J. Keating³, R.K. Weersma², E.A. Festen², V.E. de Meijer¹

¹University Medical Center Groningen, Department of Surgery, Groningen, Netherlands, ²University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ³Penn Transplant Institute, Department of Surgery, Philadelphia, United States of America, ⁴University Medical Center Groningen, Department of Laboratory Medicine, Groningen, Netherlands, ⁵University Medical Center Groningen, Department of Pathology, Groningen, Netherlands, ⁶Baylor University Medical Center, Dallas, United States of America

Contact E-Mail Address: l.m.nieuwenhuis@umcg.nl

Introduction: Acute cellular rejection (ACR) remains a common complication causing significant morbidity after liver transplantation.^{1,2}

Recent studies suggest that the proportion of non-HLA mismatched SNPs, referring to all SNPs outside the HLA region, also known as major histocompatibility complex (MHC), was associated with increased rejection risk after kidney transplantation.³⁻⁶

This is currently unexplored in liver transplantation.

Aims & Methods: We aimed to investigate whether donor-recipient non-HLA genetic mismatch is associated with increased incidence of biopsy-proven grade 2/3 ACR, hereafter referred to solely as ACR, within 1-year after liver transplantation. We conducted an international multicenter case-control genome-wide association study of donor and liver transplant recipient pairs in three independent cohorts, totaling 1846 pairs. To assess the burden of donor-recipient genetic incompatibility, we calculated sum scores for single nucleotide polymorphism (SNP) mismatch based on all non-HLA functional SNPs.

Additionally, we performed an analysis specifically including only SNPs coding for transmembrane or secreted proteins, which are more likely to affect the immune system.

We analyzed the association between the log-normalized non-HLA mismatch scores and ACR in a multivariable cox regression model per cohort, followed by a weighted meta-analysis.

Results: During the first-year post-transplantation, 90 of 689 (13%), 161 of 720 (22%) and 48 of 437 (11%) recipients experienced ACR in cohorts 1-3, respectively. After correcting for potential confounders using multivariable cox regression analysis, our weighted meta-analyses showed that higher mismatch in functional non-HLA SNPs was associated with increased incidence of 1-year ACR (HR 5.31; 95%CI 1.39-20.08; $P=0.015$). Moreover, we also confirmed the effect of mismatch in the subset of SNPs coding only for transmembrane or secreted proteins on 1-year ACR (HR 6.69; 95%CI 1.82-24.78; $P=0.004$).

Conclusion: In this multi-center genome-wide meta-analysis we show that genetic non-HLA incompatibility between donors and recipients is an important independent predictor of ACR after liver transplantation. Donor-recipient mismatch of functional non-HLA SNPs overall and, especially, of SNPs coding for transmembrane or secreted proteins correlated with ACR developed within the first year after liver transplantation. Identifying high-risk immunological burden between donor-recipient pairs may potentially prevent early graft rejection and help future efforts to personalize immuno-suppressive medication. This is important as immune suppressive medication causes significant morbidity and mortality.

References:

1. Burra P. The adolescent and liver transplantation. *J Hepatol.* 2012; doi:10.1016/j.jhep.2011.07.032
2. Choudhary NS, Saigal S, Bansal RK, et al. Acute and Chronic Rejection After Liver Transplantation: What A Clinician Needs to Know. *J Clin Exp Hepatol.* 2017; doi:10.1016/j.jceh.2017.10.003
3. Reindl-Schwaighofer R, Heinzel A, Kainz A, et al. Contribution of non-HLA incompatibility between donor and recipient to kidney allograft survival: genome-wide analysis in a prospective cohort. *Lancet.* 2019; doi:10.1016/S0140-6736(18)32473-5
4. Pineda S, Sigdel TK, Chen J, et al. Novel non-histocompatibility antigen mismatched variants improve the ability to predict antibody-mediated rejection risk in kidney transplant. *Front Immunol.* 2017; doi:10.3389/fimmu.2017.01687
5. Steers NJ, Li Y, Drace Z, et al. Genomic Mismatch at LIMS1 Locus and Kidney Allograft Rejection. *N Engl J Med.* 2019; 380(20):1918-1928. doi: 10.1056/NEJMoa1803731. PMID: 31091373; PMCID: PMC6589355.
6. Markkinen S, Helanterä I, Lauronen J, et al. Mismatches in Gene Deletions and Kidney-related Proteins as Candidates for Histocompatibility Factors in Kidney Transplantation. *Kidney Int Rep.* 2022; 7(11):2484-2494. doi: 10.1016/j.ekir.2022.08.032. PMID: 36531875; PMCID:

Disclosure: Nothing to disclose.

MP602

IDENTIFYING DRIVERS OF PATIENT PREFERENCE IN THE TREATMENT OF PRURITUS IN PRIMARY BILIARY CHOLANGITIS

A. Halliday¹, H.T. Smith¹, D. Szinay², A. Walker¹, P.J.F. Troke¹, K. Meginnis³, S. Heidenreich², J. Seo⁴

¹GSK, London, United Kingdom, ²Evidera, London, United Kingdom, ³Evidera, Glasgow, United Kingdom, ⁴Evidera, Bethesda, United States of America

Contact E-Mail Address: phil.j.troke@gsk.com

Introduction: Pruritus is common in primary biliary cholangitis (PBC) and can significantly impact patients' quality of life (QoL). Cholestyramine is recommended as the first-line treatment option for pruritus in PBC, but tolerability, inconvenient administration, and limited efficacy data restrict its use. Patient-focused drug development can help address this unmet need, but an understanding of patients' perspectives on pruritus and treatments is required. This study conducted semi-structured qualitative patient interviews to explore patients' experiences, expectations, and concerns with regards to pruritus and treatments.

Aims & Methods: Semi-structured virtual interviews were designed following a literature review and conducted with patients from the USA, Germany, UK, and Italy. Eligible patients self-reported a PBC diagnosis and had a worst itch score of ≥ 4 on a 0-10 numerical rating scale (NRS) in the past 2 months. Interviews had four parts:

- 1) pruritus experience,
- 2) treatment desires and concerns,
- 3) treatment experience,
- 4) hypothetical choice questions that required patients to make trade-offs between two options.

Responses were used in an inductive thematic analysis and visually summarized.

Results: Ten patients per country were interviewed (N=40); most were female (78%) and mean (standard deviation) age was 52.5 (15.2) years. For 53% (n=21), pruritus had started within the last 3 years. On the NRS, patients rated their pruritus over the last 2 months on average as mean 5.4 (range 2-10), and worst itch as mean 7.1 (range 4-10). Key themes that emerged from patient discussions were visualized with a concept map.

Pruritus was widespread over patients' bodies, persistent despite scratching, and described as 'crawling', 'burning' and 'nettles'. Pruritus impacted social interactions, sleep quality, appearance, emotional stability, and work productivity. Many patients wished for complete resolution, but primarily wanted treatment to reduce pruritus severity (60%; n=23). Of those who had ever received cholestyramine (n=12), 62% reported a repulsive taste and texture; 50% mentioned concerns about interactions between cholestyramine and PBC medication. From five potential pruritus medication side effects, diarrhea and nausea were of greatest concern.

Conclusion: Pruritus impacts QoL in PBC in several ways and the limitations of existing treatments mean patients would welcome alternative options. Future research will establish the relative importance to patients of treatment aspects such as administration, benefits, and tolerability.

Funding: GSK (218705).

Encore statement: This abstract was originally presented as poster 4550-C at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting on November 13, 2023, this encore is presented on behalf of the original authors with their permission.

Disclosure: HTS, AW and PJFT are employees of, and hold stocks/shares in, GSK. AH is an employee of, and holds stocks/shares in, GSK and is a former employee of, and holds stocks/shares in, Novartis. DS and KM are employees of Evidera who were funded by GSK to carry out this study. JS and SH are employees of Evidera who were funded by GSK to carry out this study and are minority stockholders in Thermofisher Scientific as part of their employment with Evidera.

The varied spectrum of malnutrition

11:30-12:30 / Poster Stage 5

MP603

PREDIABETES, DIABETES AND GASTROINTESTINAL CANCER RISK IN KOREAN ADULTS: RESULTS FROM THE INTEGRATED DATA OF NATIONAL HEALTH INSURANCE SERVICE AND KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

H. Jo¹, E. Ji², C.M. Shin¹, S. Ahn², J.H. Ohn¹, Y. Choi¹, Y.K. Jun¹, H. Yoon¹, Y.S. Park¹, N. Kim¹, D.H. Lee¹

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, South Korea, ²Seoul National University Bundang Hospital, Medical Research Collaborating Center, Seongnam, South Korea

Contact E-Mail Address: hyemin135@naver.com

Introduction: The worldwide prevalence of diabetes is increasing and while there are numerous studies on the impact of prediabetes and diabetes on cancer incidence, research focusing on the Korean population is scarce.

Aims & Methods: This study aimed to evaluate whether prediabetes, diabetes, and poorly controlled diabetes in the Korean population affect the risk of the incidence of various types of gastrointestinal cancers using integrated data of two public datasets. Combining data from the National Health Insurance Service (NHIS) and Korean National Health and Nutrition Examination Survey (KNHANES) from 2013 to 2021, we generated integrated datasets using 3 key identifiers: name, gender, and date of birth. Subsequently, a retrospective cohort study was performed using the combined cohort to enroll subjects aged 20 years or older from 2014 to 2019 (N = 30,684) and followed up until 2021. The 4 groups were defined as follows: group 1 (non-diabetic individuals): hemoglobin A1c (HbA1c) < 5.7% and fasting glucose level (FBS) < 100 mg/dL, group 2 (prediabetes): no diabetes and 5.7% ≤ HbA1c < 6.5% or 100 ≤ FBS < 125 mg/dL, group 3 (controlled diabetes): diagnosed as diabetes and HbA1c < 8.0%, and group 4 (uncontrolled diabetes): diagnosed as diabetes and HbA1c ≥ 8.0%. Covariates including age, sex, alcohol consumption, smoking status, body mass index, total cholesterol, hypertension, income level were adjusted for, and cancer diagnoses were determined using both claim ICD-10 C codes and cancer-specified diagnosis code (V193). We evaluated the risk of overall cancer and gastrointestinal cancers including stomach, colorectal, pancreatic, bile duct, and liver cancers in the 4 groups.

Results: In the final dataset, 24,058 individuals were included, and 675 subjects (2.8 %) developed any cancers during the follow-up. Compared to group 1 (reference), overall cancer risk was significantly increased in the groups 2-4 (adjusted hazard ratio [95% confidence interval]; 1.249 [1.05-1.487], 1.990 [1.511-2.613], and 2.435 [1.305-4.544] in the groups 2, 3, and 4, respectively; $p_{\text{trend}} < 0.001$.) Among gastrointestinal cancers, the risk of pancreatic cancer was significantly increased in group 2 as well as group 3 (1.249 [1.050-1.487] and 6.412 [1.870 – 21.983], respectively.); the risk of liver cancer was increased in the groups 3 and 4 (2.407 [1.095 – 5.291] and 5.483 [1.413-21.28], respectively). For stomach and bile duct cancers, the risk was significantly increased only in group 4 (6.349 [2.296-17.557] and 8.676 [1.339-56.228], respectively.) Colorectal cancer risk also showed a positive correlation with diabetes, which did not reach a statistical significance ($p > 0.05$).

Conclusion: We conducted a novel retrospective cohort study using the integrated dataset of NHIS and KNHANES. Diabetes and prediabetes are risk factors for various types of cancer. The impact of diabetes on gastrointestinal cancers varies possibly depending on the mechanism specific to each cancer type, including the presence or absence of glycemic control, the presence of diabetes, and the prediabetes status.

Disclosure: Nothing to disclose.

MP604

EVALUATING THE ALLURION ELIPSE® GASTRIC BALLOON: A NON-INVASIVE AND RESOURCE-EFFICIENT WEIGHT LOSS SOLUTION DURING THE COVID-19 PANDEMIC

C. Simeth¹, M. Campigotto¹, M. Giuffrè^{2,3}, I.V. Albergati³, F. Monica¹
¹Azienda Sanitaria Universitaria Giuliano Isontina, Gastroenterologia ed Endoscopia Digestiva, Trieste, Italy, ²Yale School of Medicine, Department of Internal Medicine (Digestive Diseases), New Haven, United States of America, ³Università degli Studi di Trieste, Dipartimento universitario clinico di scienze mediche, chirurgiche e della salute, Trieste, Italy

Contact E-Mail Address: i.albergati91@gmail.com

Introduction: Since the global emergence of the COVID-19 pandemic in Spring 2020, numerous bariatric units worldwide have indefinitely postponed elective weight loss procedures, responding to the heightened risk profile associated with obesity during viral infections. Concomitantly, lockdown measures have led to significant lifestyle changes, notably reductions in physical activity and increases in food consumption, collectively contributing to weight gain in various populations. Intra-gastric balloons, recognized as effective means for initiating weight loss or serving as an interim solution before bariatric surgery, require upper endoscopy for insertion and removal. These procedures have faced significant disruptions due to the pandemic-driven reallocation of medical resources, including anesthesiologists and endoscopic services.

Aims & Methods: This study aims to evaluate the feasibility and safety of employing the Allurion Elipse® gastric balloon, an innovative device designed for administration without anesthesia or endoscopic guidance. This device could potentially reduce patient risk and conserve valuable hospital resources in times of medical crisis. A selected group of obese patients, as determined by our multidisciplinary bariatric team, were administered an encapsulated pill balloon, which, once ingested, expands with 550mL of fluid under the direct supervision of a gastroenterologist. Placement accuracy was confirmed through X-ray imaging. Alongside the physical intervention, patients received comprehensive support, including a customized diet plan, access to a digital health application connected to a weighing scale for remote monitoring, and regular virtual follow-ups. The primary measure of clinical efficacy was the percentage of total body weight loss (%TBWL).

Results: The study included seventeen consecutive patients (11 females, 6 males) with a mean age of 43.7 ± 9.9 years. These individuals had a mean weight of 104.21 ± 21.72 kilograms and a mean BMI of 36.11 ± 4.7 kg/m2. The balloon positioning procedures were efficiently completed in 20 to 30 minutes without technical complications. Most patients reported transient nausea and vomiting. However, these symptoms were manageable and did not lead to any severe adverse events. Only one patient required early balloon removal due to intolerance.

After eight months of the procedure, with the balloon passing naturally four months prior, two patients reported a %TBWL of 19.8. The average %TBWL recorded at the four-month mark was 13%, and the weekly check-in compliance rate was 62%.

Conclusion: The COVID-19 pandemic has drastically impacted the availability and functionality of bariatric and endoscopic services, prompting the need for alternative methods that simplify and expedite the weight loss process. Although limited, the available data support the Allurion Program with the Elipse Balloon as a non-invasive, secure, and effective method to manage obesity. It facilitates rapid and sustainable weight loss, enables continuous remote support, and minimizes the impact on patients and the already strained health systems. This method represents a valuable alternative to traditional approaches, particularly during health-care resource constraints.

References: Tønnesen CJ, et al. A novel intra-gastric balloon for treatment of obesity and type 2 diabetes. A two-center pilot trial. *Scand J Gastroenterol.* 2022

Mauro A., et al. A Comprehensive Review on Bariatric Endoscopy: Where We Are Now and Where We Are Going. *Medicina (Kaunas).* 2023

Navarra, G, et al. Bariatric surgery and the COVID-19 pandemic: SICOB recommendations on how to perform surgery during the outbreak and when to resume the activities in phase 2 of lockdown. *Updates Surg.* 2020

Vargas EJ, et al. Single Fluid-Filled Intra-gastric Balloon Safe and Effective for Inducing Weight Loss in a Real-World Population. *Clin Gastroenterol Hepatol.* 2018

Kumar N, et al. The Influence of the Orbera Intra-gastric Balloon Filling Volumes on Weight Loss, Tolerability, and Adverse Events: a Systematic Review and Meta-Analysis. *Obes Surg.* 2017

Disclosure: Nothing to disclose.

MP605

THE IMPACT OF RE-DO ENDOSCOPIC SLEEVE GASTROPLASTY FOR INSUFFICIENT WEIGHT LOSS, WEIGHT PLATEAU AND WEIGHT REGAIN

G. Carlino¹, L. Gualtieri¹, M.V. Matteo¹, V. Pontecorvi¹, M. De Siena², C. Spada¹, I. Boskoski¹, V. Bove¹

¹Fondazione Policlinico Universitario A. Gemelli, Roma, Italia - IRCCS, Digestive Endoscopy Unit, Roma, Italy, ²POLICLINICO A. GEMELLI, Roma, Italy

Contact E-Mail Address: giorgio.carlino1996@gmail.com

Introduction: Endoscopic Sleeve Gastroplasty (ESG) is one of the main interventions of primary minimally invasive bariatric surgery, especially for subjects suffering from I and II class obesity^{1,2}. However, since obesity is a chronic, relapsing, and multifactorial disease, a second intervention may be necessary. The purpose of this study is to assess the effectiveness of endoscopic revision (Re-ESG) versus primary intervention (P-ESG).

Aims & Methods: A prospective dataset enrolling all subjects undergone ESG in a tertiary center from May 2017 to December 2023 was retrospectively analyzed. All subjects undergone Re-ESG for weight regain (WR), weight plateau (WP) or weight loss failure (WF), as defined by Lopez Nava et al.³, were enrolled. Weight loss outcomes [Absolute Weight Loss (AWL), Excess Weight Loss (EWL), Total Body Weight Loss (TBWL), Body Mass Index Loss (BMIL)] at 6-,12-,18- and 24-months after P-ESG and Re-ESG were collected and compared.

Results: Out of a total of 578 patients, 53 patients (9.2%) underwent Re-ESG: 24 for WR, 18 for WP and 12 for WF, after a mean time of 25.4 ± 11.4 months from P-ESG (35 subjects underwent revision in the first 24 months, whereas other 18 between 30 and 66 months). One subject underwent a second revision, for a total of 54 revisions.

Both P-ESG and Re-ESG were associated with significant total body weight loss and excess body weight loss up to 24 months and when compared, endoscopic revision were proven to be as effective as primary intervention, at least in the short and medium term, as showed in Table 1.

	6-months				12-months				18-months				24-months			
	AWL (kg)	EWL (%)	TBWL (%)	p	AWL (kg)	EWL (%)	TBWL (%)	p	AWL (kg)	EWL (%)	TBWL (%)	p	AWL (kg)	EWL (%)	TBWL (%)	p
P-ESG	18.4 (7.9)	55.2 (24.5)	17.3 (6.7)	<0.01	17.9 (9.7)	52.9 (27.7)	16.7 (8.2)	<0.01	18.1 (10.5)	50.0 (22.7)	16.6 (8.3)	<0.01	16.3 (11.9)	45.7 (32.7)	15.1 (10.6)	<0.01
Re-ESG	15.0 (7.7)	52.9 (23.5)	14.7 (6.1)	<0.01	17.0 (8.0)	55.7 (21.8)	16.5 (7.2)	<0.01	11.9 (10.9)	41.4 (44.2)	11.4 (11.0)	<0.01	7.3 (11.8)	25.4 (25.9)	7.0 (9.2)	0.937
P	0.32	0.571	0.434		0.712	0.684	0.924		0.121	0.569	0.128		0.122	0.183	0.109	

Table 1. Comparison of weight loss outcomes between primary ESG and endoscopic revision (Re-ESG) at 6-,12-,18- and 24-months follow-up. Data are reported as mean value (standard deviation). A two sample T-Test was used to compare baseline weight and weight loss outcomes. ESG=Endoscopic Sleeve Gastroplasty; P-ESG= Primary ESG; Re-ESG= Revision of ESG; AWL=Absolute weight loss; EWL=Excess weight loss; TBWL=Total body weight loss.

Conclusion: Our study, despite the limit of a low sample, highlights how the endoscopic revision of a previous ESG is as effective as the primary intervention in the short and medium term.

These results may pave the way for an exclusively minimal-invasive multi-step treatment of chronic obesity.

References: 1. Abu Dayyeh BK, Bazerbach F, Vargas EJ, et al. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. *The Lancet*. 2022;400(10350):441-451. doi:10.1016/S0140-6736(22)01280-6

2. Saumoy M, Gandhi D, Buller S, et al. Cost-effectiveness of endoscopic, surgical and pharmacological obesity therapies: a microsimulation and threshold analyses. *Gut*. Published online August 8, 2023;gut-jnl-2023-330437. doi:10.1136/GUTJNL-2023-330437

3. Lopez-Nava G, Sharaiha RZ, Vargas EJ, et al. Endoscopic Sleeve Gastroplasty for Obesity: a Multicenter Study of 248 Patients with 24 Months Follow-Up. *Obesity Surgery*. 2017;27(10):2649-2655. doi:10.1007/s11695-017-2693-7

Disclosure: Nothing to disclose.

MP606

FLUID-FILLED INTRAGASTRIC BALLOON'S FILLING VOLUME AT 500, 600, OR 700 ML: WHICH IS THE MAGIC NUMBER?

S.F. Vadalà di Prampero¹, I. Bassu², V. Cosseddu³, A. Zuddas², K. Jankovic⁴, F. Di Maio⁵, P. Bazzu⁶, J. Formichetti³, C. Rocchi², M. Massidda², S. Masia³, G. Faleschini⁷, N. Panic⁸, G. Manzoni⁹, G. Costamagna¹, **M. Bulajic**¹

¹Isola Tiberina - Gemelli Isola Hospital, Digestive Endoscopy Unit, Center of Excellence for Gastrointestinal and Metabolic Disorders, Rome, Italy, ²Mater Olbia Hospital, Gastroenterology and Digestive Endoscopy Department, Olbia, Italy, ³Mater Olbia Hospital, Department of Nutrition and Dietetics, Olbia, Italy, ⁴Clinic for Gastroenterohepatology, University Clinical Centre of Serbia, Belgrade, Serbia, ⁵Mater Olbia Hospital, Department of Internal Medicine, Olbia, Italy, ⁶Mater Olbia Hospital, Department of Psychology, Olbia, Italy, ⁷Spital STS, Department of Gastroenterology, Thun, Switzerland, ⁸CHC Dr Dragisa Misovic-Dedinje, Digestive endoscopy unit, Belgrade, Serbia, ⁹Mater Olbia Hospital, Department of Radiology, Olbia, Italy

Contact E-Mail Address: bulajic.milutin@gmail.com

Introduction: Obesity awareness has recently increased following its pandemic evolution. Besides nutritional and lifestyle modifications and pharmacological therapy, many other therapeutic strategies have been evaluated, with fluid-filled intragastric balloon (FF-IB) being the most prevalent. There is still no consensus around which is the best filling volume for FF-IB, that is usually filled according to the physician's expertise, with the purpose to tailor the filling on patient's BMI and stomach shape.

This study aimed to find out any differences in terms of outcomes of different FF-IB's filling volume.

Aims & Methods: This was a single-center, observational prospective study of obese patients undergoing FF-IB (Medsil, Orbera) for 6 months, with a random filling volume of 500, 600, or 700 ml of saline and Methylene Blue (fig.1). The outcomes were evaluation of early post-procedural complications (pain, nausea and/or vomiting in the first 24 hours), percentage of early removal for intolerance, percentage of Total Body Weight Loss (TBWL%) and percentage of Excess Weight Loss (EWL%) at 6 months follow-up, quality of Life (QoL, measured by EQ-5D test) at 1, 3, and 6 months follow-up and modifications of blood tests and blood pressure at 6 months.

Results: Between July 2020 and May 2023, 180 obese patients (41.7±9.02 kg/m², 46.2±14 years, 70% female, 53% obesity class III, Fatty Liver Disease as the main comorbidity; other baseline characteristics in table 1) underwent a FF-IB placement, that was removed after 180±12 days. Pain was the most frequent complication in the first 24 hours, being encountered in 77.5 % of patients, while nausea and/or vomiting were detected in 50.7 % of cases; no differences were observed among the three groups with different filling volume (pain p=0.180, nausea p=0.718, and vomiting p=0.480). Early removal was detected at a mean time of 75±43 days in 19 patients (10.6 %), with no differences among the 3 groups (p=0.870). At 6 months follow-up the mean TBWL% was 14.6±7.14, EWL% was 30.8±23.30, with no differences among the three groups (p=0.882 and p=0.733, respectively). QoL at 1, 3, and 6 months follow-up significantly improved from the baseline in each time frame (p<0.001) and this improvement was the same among the three groups (p=0.819, p=0.822, p=0.849). Mean levels of cholesterol, triglycerides, low-density lipoprotein, and HbA1c, as well as systolic and diastolic blood pressure, were significantly improved at 6 months after FF-IB placement (P<0.05), and no differences among the three groups of filling volume were detected.

Conclusion: An IB's filling volume of 500, 600, or 700 ml seems to give the same outcomes in terms of post-procedural complications, percentage of early removal, TBWL%, EWL%, QoL, and improvement of blood tests and blood pressure, regardless of the baseline characteristics of patients.

Disclosure: The following authors have completed their 2024 DDW disclosure: Salvatore Vadalà di Prampero: Disclosure completed | Ica Bassu: No Answer. | Valentina Cosseddu: No Answer. | Alessandro Zuddas: No Answer. | Federica Di Maio: No Answer. | Paola Bazzu: No Answer. | Jessica Formichetti: No Answer. | Chiara Rocchi: No Answer. | Marco Massidda: No Answer. | Simona Masia: No Answer. | Giacomo Faleschini: No Answer. | Nikola Panic: No Answer. | Gabriella Manzoni: No Answer. | Guido Costamagna: No Answer. | Milutin Bulajic: No Answer.

MP607

CLINICAL EVALUATION AND INTESTINAL MICROBIOTA COMPOSITION PRE- AND POST ENDOSCOPIC SLEEVE GASTROPLASTY: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

N. Citterio¹, M. Martino², A. Altomare^{3,1}, C. Di Rosa³, T. Mancuso¹, A. Falcone³, D. Biasutto², G. De Carlo^{1,4}, B. Neri⁵, M. Pandolfi², F. Di Matteo², M. Cicala^{1,4}, M.P.L. Guarino^{4,1}

¹Campus Bio Medico University, Gastroenterology Unit, Rome, Italy,

²Fondazione Policlinico Campus Bio-Medico di Roma, Therapeutic

GI Endoscopy Unit, Rome, Italy, ³Campus Bio-medico University,

Departmental Faculty of Sciences and Technology for Sustainable

Development and Human Health, Rome, Italy, ⁴Fondazione

Policlinico Campus Biomedico di Roma, Gastroenterology and

Endoscopy Unit, Rome, Italy, ⁵Università degli studi di Roma Tor

Vergata, Medicina dei sistemi, Rome, Italy

Contact E-Mail Address: citterion@gmail.com

Introduction: Obesity is associated with gut dysbiosis, partially restored after a nutritional or surgical intervention. In the latter, the anatomical modification due to bariatric surgery, together with multiple antibiotic therapies, could be responsible for heterogeneous reported results. Endoscopic Sleeve Gastroplasty (ESG) is a new effective and minimally invasive treatment for patients with obesity (PWO).

Aims & Methods: This prospective observational study aimed to assess the effects of the ESG treatment on weight loss and gut microbiota. Adult PWOs were consecutively enrolled and underwent ESG at the Endoscopy Unit of Fondazione Policlinico Campus Bio-medico of Rome. At the baseline (T0) and at four (T1) and eight (T2) months (T1) after ESG,

anthropometric parameters (body weight, BMI, waist (WC), hip (HC), neck (NC) circumferences), blood pressure and heart rate measurement, and the food frequencies questionnaire (FFQ) were collected. Moreover, stool samples were collected at each visit, then analyzed using Next Generation Sequencing techniques (NGS). Significance was assessed for a p -value < 0.05.

Results: A total of 29 patients were enrolled in this study; at present, 15 patients completed the T1 and 10 the T2. No procedural complications were observed; none of the patients required antibiotic therapy after the endoscopic procedure. Body weight and BMI significantly decreased at T1 ($p=0.0358$ and $p=0.0263$, respectively) and T2 ($p=0.0297$ and $p=0.0080$, respectively) compared to the baseline. HC significantly decreased between T0 and T2 ($p=0.0057$) while WC and NC showed a decreasing trend. Maximum blood pressure decreased from T0 to T1 ($p=0.0125$). Regarding FFQ no statistical changes were observed in their food habits at each visit.

After 4 months participants reduced the consumption of semi – skimmed milk, aged cheeses, red meat, eggs, vegetables, fruit, pasta, rice, bread and burger in the bun and increased the consumption of fresh cheeses, white meat, fish, coffee, alcoholic beverages, soft drinks and sugar. The consumption of semi – skimmed milk, fresh cheeses, red meat, eggs, pasta, rice, bread, vegetables and fruits and coffee increased again at t2. The consumption of fruit was almost of 1 fruit per day while the consumption of red meat after 8 months was 2 times/week, more than what is reported in nutritional recommendations.

Regarding microbiota composition, the mean value of richness, biodiversity index and dysbiosis index at T0 were 167.13 ± 41.22 , 8.71 ± 1.97 and 1.15 ± 1.83 , respectively. After 4 and 8 months an increasing trend in richness (174.71 ± 38.56 and 207 ± 22.87 , respectively) and biodiversity (8.93 ± 2.25 and 10.75 ± 2.1 , respectively) was observed even if not statistically significant. Dysbiosis decreased significantly at T2 (0.027 ± 0.03) compared to baseline ($p=0.0419$).

No significant differences were found at phyla and family levels at each time compared to baseline: an interesting increasing trend of Akkermansia Muciniphila was observed at T1 (2.08 ± 6.62) compared to T0 (0.53 ± 1.1) values. This result was maintained until T2 without significant changes.

Conclusion: Preliminary results of the present study confirm the effectiveness of ESG in reducing body weight without significant post-operative complications. It seems to positively modulate the intestinal microbiota, partially increasing some beneficial species such as A. Muciniphila.

Disclosure: Nothing to disclose.

MP608

BREATH-BASED MONITORING OF MICROBIOME METABOLIC RESPONSES BEFORE AND AFTER INGESTION OF NUTRIENTS

A. Tawfike¹, A. Murgia¹, I. Banda¹, Y. Ahmed¹, M. Manhota¹, D. Fonseca¹, F. Ricciardi¹, K. Sweeney¹, L. Nicholson-Scott¹, L. McConville¹, E. Crone¹, E. Piscitelli¹, O. Gandelman¹, M. Allsworth¹, B. Boyle¹, G. Ferrandino¹

¹Owlstone Medical Limited, Cambridge, United Kingdom

Contact E-Mail Address: Elizabeth.Crone@owlstone.co.uk

Introduction: The nutrients we ingest also feed the microbiome that lives in our digestive system. The resulting metabolic products may have beneficial or deleterious effects on our health. For example, ethanol and 2-3-butanediol, produced by carbohydrate fermentation, were found to be associated with non-alcoholic steatohepatitis (NASH).

Interestingly, several microbiome-derived metabolites are volatile organic compounds (VOCs) that can be measured in breath. In this ongoing study, we explored the feasibility of microbiome metabolic characterization before and after carbohydrate or amino acid ingestion.

Aims & Methods: A total of 13 healthy subjects were recruited with age ≥ 18 years and body weight ≥ 50 Kg. Subjects were instructed to fast overnight and to not drink alcoholic beverages the day before the experiments. Breath samples were collected before, and up to 90 minutes after ingestion of 75 g of glucose, cysteine, or tryptophan, with a time resolution of 5 minutes. Compounds of interest were measured using Soft Ionization Flow Tube Mass Spectrometry (SIFT-MS) with direct sampling. Results were expressed as part per billion (PPB v) as a function of time post-glucose ingestion.

Results: Intraoral swishing of 250 mg/mL glucose in water for 30 seconds, followed by spitting, elicits a peak of ethanol within 10-15 minutes that disappears after 25-30 minutes. However, ingestion of 300 mL of the same solution showed a variable response among different subjects. Some individuals showed a peak after 15 minutes, others, after 30-50 minutes (Fig. 1). Median (M) and interquartile range (IQR) baselines levels (before glucose administration) of ethanol, were 99.4 [71.6-182.4] PPB. Post glucose ingestion, breath peak levels ranged between 130, and 1600 PPB. Similarly, glucose administration induced spikes of acetoin, and propanoic acid, with ranges of 7-20 PPB and 18-160 PPB, respectively. Administration of tryptophan and cysteine elicits spikes of p-cresol, phenol, and hydrogen sulfide. Additional compounds were also detected, such as trimethylamine (M: 42.3, IQR: 33.6-54.3 PPB), methanol (M: 443, IQR: 199-531.4 PPB), and methane (M: 26988, IQR: 10100-76213 PPB).

Conclusion: Breath analysis is suitable for the clinical characterization of microbiome metabolism in the digestive system in healthy and disease populations to establish correlations between metabolites and disease severity and progression, as well as investigate the interaction of gut microbiota in response to therapeutic interventions. We aim to expand this approach to carbohydrates of different complexity, other amino acids, and nutrients (Table 1). This non-invasive method can replace the current need for blood collection enabling easier scaling to large cohort populations.

Disclosure: Tawfike A. Murgia A. Banda I. Ahmed Y. Manhota M. Fonseca D. Ricciardi F. Sweeney K. Nicholson-Scott L. McConville L. Gandelman O. Allsworth, M. Boyle B. Ferrandino G. are employees of Owlstone Medical Limited

MP609

STOOL MICROBIOME CHARACTERISTICS DIFFER BETWEEN ADULTS WITH IBS AND HEALTHY CONTROLS AND CORRELATE TO USUAL AND 24-HOUR RECALL DIETARY INTAKE

K. Duncanson¹, E. Hoedt¹, G. Williams¹, S. Keely¹, N.J. Talley¹

¹The University of Newcastle, College of Health, Medicine and Wellbeing, New Lambton Heights, Australia

Contact E-Mail Address: kerith.duncanson@newcastle.edu.au

Introduction: Limiting fermentable carbohydrates (FODMAPs) is an evidence-based irritable bowel syndrome (IBS) management approach and food antigen avoidance is common in IBS (1). The gut microbiota degrades undigested food and specific microbes may produce antigens that trigger IBS symptoms (2). Correlations between the gut microbiota and whole-of-diet intakes of specific microbiota-degradable food compounds and food antigens by people with IBS have not been elucidated.

Aims & Methods: The aim of this study was to compare dietary intakes and the gut microbiota of adults with IBS to healthy controls to inform personalised diet intervention-based research. This cross-sectional study used data and samples from a digestive health biobank. Demographic, psychological and symptom data were analysed against dietary data from a food frequency questionnaire (FFQ) and 24-hour diet recall (24-HR) aligned with biobanked stool samples. Dietary data were compared using

independent and paired t-tests. Stool sample gDNA was extracted using the Promega Maxwell DNA recovery system and shotgun metagenomic sequencing performed to a depth of 3Gb. Taxonomic profiling was completed with MetaPhlan4 and results analysed using R packages phyloseq, MicroEco and Maaslin2.

Results: Thirty-four adults with IBS (23 IBS-D, 11 IBS-C) and 39 healthy controls were included. Demographic and clinical characteristics were not significantly different between IBS and controls except for psychological distress ($p<0.001$), anxiety and depression ($p<0.05$) and gastrointestinal symptom burden ($p<0.001$). Usual dietary intake of participants with IBS was significantly lower than controls for total FODMAPs ($p<0.05$) and lactose (both $p<0.05$). In the 24-48 hours prior to stool sampling, participants with IBS consumed significantly lower total fibre ($p<0.01$), fruit serves ($p<0.01$) and gluten ($0<0.05$).

Energy, macro- and micronutrients did not differ between groups (FFQ or 24-HR) and were consistent between FFQ and 24-HR for most dietary variables. Microbial beta diversity differed between IBS and controls ($p<0.01$ PERMANOVA) and IBS-C and IBS-D subtypes ($p<0.001$). Microbiota profiles differed between IBS and controls. Two microbial species (sp.) were positively associated with gluten (24-HR) intake (1 unclassified Clostridia sp., 1 unclassified sp. from Actinomycetaceae family, both $p<0.01$) in the IBS cohort. Strong positive correlations were evident in controls for saturated fat (12 bacterial species, all $p<0.001$) and total energy (15 species, all $p<0.05$), with strong negative correlations evident between *Akkermansia muciniphila* and saturated fat ($p<0.001$), total energy ($p<0.01$), total fat, and caffeine (both $p<0.05$). Bacterial species with significant correlations to dietary variables across both usual and 24-HR dietary data were *Akkermansia muciniphila* and unclassified Firmicutes GGB14025.

Dietary intake	IBS (n=23) (past 12 months)	Controls (n=18) (past 12 months)	p-value	IBS (n = 30) (24 hour recall)	Control (n = 31) (24 hour recall)	p-value
Dietary fibre (grams/day)	32.0± 14.0	32.1±6.3	0.997	20.6±8.9	28.8±12.3	0.015*
Gluten (grams/day)	NA	NA	NA	10.94 (6.15)	7.5±4.5	0.030*
Total FODMAPs (grams/day)	22.8±14.3	33.6±18.9	0.049*	NA	NA	NA
Lactose (grams/day)	11.2±12.9	21.7±13.8	0.017*	14.3±13.9	17.4±9.6	0.311
Fruit (serves/day)	NA	NA	NA	0.87±0.7	1.6±1.2	0.009**

Conclusion: Microbiota differences between adults with IBS and controls were associated with diet and clinical characteristics. Differences in relationships between specific FODMAPs (lactose) and food antigens (gluten) and microbiota associations has clinical relevance for IBS dietary management.

Future translation-focussed research investigating personalisation of dietary intervention for microbiota-targeted symptom management in IBS is warranted.

References: 1. Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. *Gut*. 2022;71(6):1117-26.
2. Wang Y, Ma W, Mehta R, Nguyen LH, Song M, Drew DA, et al. Diet and gut microbial associations in irritable bowel syndrome according to disease subtype. *Gut Microbes*. 2023;15(2):2262130.

Disclosure: Nicholas J Talley's disclosures include Intrinsic Medicine (2022) (human milk oligosaccharide), Alimentary (2023) (gastric mapping), Agency for Health Care Research and Quality (fiber and laxation) (2024), outside the submitted work. In addition, Dr. Talley has a patent Nepean Dyspepsia Index (NDI) 1998, a patent Licensing Questionnaires Talley Bowel Disease Questionnaire licensed to Mayo/Talley, "Diagnostic marker for functional gastrointestinal disorders" Australian Provisional Patent

Application 2021901692, "Methods and compositions for treating age-related neurodegenerative disease associated with dysbiosis" US Patent Application No. 63/537,725.

MP610

RETHINKING THE REROUTING OF NASOJEJUNAL TUBE INSERTION: CONSIDERING PATIENT AND ENVIRONMENTAL FACTORS

S. Dimitriadis¹, P. Dahiya², K. Hamesch³, O. Cahyadi⁴

¹University Hospital Coventry and Warwickshire, Gastroenterology, Coventry, United Kingdom, ²University of Birmingham, Birmingham, United Kingdom, ³University Hospital Aachen, Gastroenterology, Aachen, Germany, ⁴St. Josef-Hospital, Hospital of the Ruhr-University-Bochum, Gastroenterology, Essen, Germany

Contact E-Mail Address: dimitriadis.stavros@yahoo.com

Introduction: Nasojejunal tubes (NJT) are usually inserted into the small intestine with the help of an endoscope, after which they need to be redirected through the nose. The current method of redirection involves using a rerouting tube, a laryngoscope, and forceps, which can be uncomfortable for patients due to the sensitivity of the throat. Besides, this method is resource-intensive and creates sustainability issues, as the instruments are mostly single-use and contain batteries. The National Health Service (NHS) accounts for 5.4% of UK carbon dioxide emissions, one which, in 2015, amounted to 26.6 million tonnes of carbon dioxide equivalent—equating to 39% of all public sector emissions in England. Endoscopy appears to be a significant contributor to health care's environmental footprint, generating about 3.09 kg of waste per bed per day (the third highest emitting hospital department).¹

Aims & Methods: We aimed to gather information on the standard practices related to NJT placement and understand the challenges faced by endoscopists and patients as perceived by practitioners such as nurses and endoscopists. For this purpose, we designed a short survey consisting of 16 questions on Survey Monkey. We shared the survey through various channels such as WhatsApp groups, X, and emails from gastroenterologists, endoscopists, and nurse groups. The survey remained open for 30 days and was shared globally.

Results: A total of 146 participants responded to the survey. The majority (73.9%) were from the UK, 13 % from Europe and the remaining from the rest of the world. The majority (88.4%) were medical endoscopists, with a median experience of 6 (1-30) years in NJT placement. The standard "through the scope" method was the preferred technique for NJT insertion (78.8%) of participants. Some (10.9%) preferred a slim scope through the nose and then placing NJT over a wire; others reported mixed methods, including under fluoroscopy guidance. Most respondents used midazolam and an opiate for the procedure (67.1%), only midazolam (13.7%), propofol (16.4%), and only a handful did it without sedation. The most challenging step reported by participants was the NJ tube rerouting from the mouth to the nose (41.7%), followed by avoiding displacement of the NJ tube during scope removal (27.4%). Redirection from the mouth to the nose was also considered the most uncomfortable step for patients, with 71.2% of participants, followed by oesophageal intubation (15.1%). Laryngoscopes were used as a light source during rerouting by 74.7%, out of which 45.9% used disposable laryngoscopes. Similarly, 80% of respondents used Magill's forceps, half of which were single-use. Notably, 80.8% of participants expressed concern about the environmental impact of single-use instruments in endoscopy.

Conclusion: This study highlights endoscopy practitioners' primary difficulties when performing NJ tube placement. Rerouting the tube from the mouth to the nose is considered the most challenging and uncomfortable

step for patients. The findings emphasise the urgency for improved techniques or equipment to address this challenge, reduce patient discomfort, and consider environmental sustainability in endoscopy.

References:

1. Siau, Keith, Bu'Hussain Hayee, and Swapna Gayam. "Endoscopy's current carbon footprint." *Techniques and Innovations in Gastrointestinal Endoscopy* 23, no. 4 (2021): 344-352.

Disclosure: Nothing to disclose.

MP611

BURIED BUMPER SYNDROME: A RETROSPECTIVE STUDY OF INTERVENTION SUCCESS

L. Herlihy¹, S. Taylor¹, C. Neelankavil¹, Z. Zeino²

¹North Bristol NHS Trust, Bristol, United Kingdom, ²North Bristol NHS Trust, Gastroenterology, Bristol, United Kingdom

Contact E-Mail Address: laura.herlihy@nbt.nhs.uk

Introduction: Buried bumper syndrome (BBS) is a complication of a percutaneous endoscopic gastrostomy (PEG) which occurs when the internal bumper migrates into the gastric wall. There are several techniques used to manage BBS. The Flamingo is a novel device specifically developed to release buried bumpers and was first used at North Bristol Trust (NBT) in 2018. This study compared the effectiveness of methods used to free buried bumpers before and after the introduction of this device.

Aims & Methods: The primary endpoint was to determine the success of the Flamingo device in resolving BBS compared to balloon dilatation, needle knife and surgical removal. Data was obtained retrospectively from single endoscopy unit study between January 2010 to July 2023. Due to low numbers, balloon dilatation and needle knife were grouped together for analysis. Additional outcome parameters were complication rate, site change and sedation. Baseline patient demographic and clinical parameters were compared between groups.

Results: Forty-three cases of BBS were identified where balloon/knife, Flamingo or surgery was used to free the buried bumper (median age, 59; 31 males (72.15%)). 20 BBS cases attended endoscopy prior to January 2018 with balloon/knife intervention successful in 11/16 patients (68.75%) and 4 successful surgical removals. After January 2018, balloon/knife interventions succeeded in 2/5 (40%), with subsequent successful surgical (n=1) or flamingo (n=2) interventions. Flamingo alone succeeded in 17/18 patients (94.4%). Combining all BBS cases, the overall success rate of Flamingo was 95% compared to 61.9% for balloon/knife ($P = .02$). Surgical removal success rate was 100%. Complication rate was highest post-surgical removal (60%) compared to Flamingo (20%) and balloon/knife (4.76%).

	Balloon/knife	Flamingo	Surgical
Initial intervention	21	18	4
Rescue intervention used	0	2	1
Success rate	61.9% (13/21)	95% (19/20)	100% (5/5)
Complication rate	4.76% (1/21)	20% (4/20)	60% (3/5)
New site	4	2	1
Same site, new tract	5	1	0
Sedation	1 GA	1 GA	5 GA

Conclusion: Removal of buried bumpers using the Flamingo device was significantly more successful than using the balloon/knife. All surgical procedures were prior to Flamingo or required to rescue balloon/knife. This means there needs to be investigations to determine whether the flamingo can obviate need for surgery and whether these two procedures cause an overall excess of complications.

Disclosure: No Conflict of Interest.

MP612

EARLY VERSUS DELAYED NUTRITION IN PATIENTS AFTER UPPER GASTROINTESTINAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

M. Obeidat¹, B. Teutsch^{1,2,3}, D.-E. Floria^{1,4}, D.S. Veres^{1,5}, P. Hegyi^{1,6,2}, B. Eröss^{1,6,2}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ³Semmelweis University, Department of Radiology, Medical Imaging Centre, Budapest, Hungary, ⁴Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania, ⁵Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁶Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary

Contact E-Mail Address: dr.mahmoud.obeidat@gmail.com

Introduction: Despite a lack of evidence, patients are often not fed for 48 to 96 hours after upper gastrointestinal bleeding (UGIB); however, many trials have demonstrated the benefits of early nutrition (EN). We conducted a meta-analysis of randomized controlled trials (RCTs) to evaluate the outcomes of EN compared to delayed nutrition (DN) after UGIB.

Aims & Methods: The protocol was registered on PROSPERO (CRD42022372306). PubMed, Embase, CENTRAL, Scopus, and Web of Science were searched on the 27th of August 2023 to identify eligible RCTs. The primary outcomes were early (within 7 days) and late (within 30-42 days) mortality and rebleeding. Pooled risk ratios (RR), mean differences (MD), and corresponding 95% confidence intervals (CI) were calculated using a random-effects model.

Results: A total of 10 trials with 1,051 patients were included in the analysis. Early mortality was not significantly different between the two groups (RR: 1.20, CI: 0.85 – 1.71, $P = 0\%$), whereas late mortality was reduced to a clinically relevant extent in the EN group (RR: 0.61, CI: 0.35 – 1.06, $P = 0\%$). When comparing the two groups, we found no significant difference in terms of early and late rebleeding (RR: 1.04, CI: 0.66 – 1.63, $P = 0\%$ and RR: 1.16, CI: 0.63 – 2.13, $P = 0\%$, respectively). Our analysis also showed that the length of hospital stay was reduced in the EN group compared to the DN group (MD: - 1.22 days, CI: - 2.43 to - 0.01, $P = 94\%$).

Conclusion: Compared with DN, EN (within 24 hours) appears to be a safe intervention and could reduce the length of hospital stay without increasing the risk of complications after UGIB.

Disclosure: None to declare.

IL-23 inhibitor in UC and Crohn's disease: Part 1

13:00-14:00 / Poster Stage 1

MP613

MIRIKIZUMAB IMPROVED BOWEL URGENCY, ABDOMINAL PAIN, AND FATIGUE IN PEDIATRIC PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 2 SHINE-1 STUDY

M.C. Dubinsky¹, J.L. Kaplan², A. Bousvaros³, D. Turner⁴, T. Hunter Gibble⁵, W. Komocsar⁶, A. Larkin⁷, J. Johns⁷, X. Zhang⁷, W. Crandall⁷, J. Hyams⁸

¹Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ²Massachusetts General for Children, Boston, United States of America, ³Boston Children's Hospital, Boston, United States of America, ⁴Shaare Zedek Medical Center, Pediatric GI, Jerusalem, Israel, ⁵Eli Lilly and Company, Global Patient Outcomes and Real World Evidence, Indianapolis, United States of America, ⁶Eli Lilly and Company, BioMedicines, Indianapolis, United States of America, ⁷Eli Lilly and Company, Indianapolis, United States of America, ⁸Connecticut Children's Medical Center, GI, Hartford, United States of America

Contact E-Mail Address: marla.dubinsky@mssm.edu

Introduction: Mirikizumab is a humanized immunoglobulin G4 monoclonal antibody against the p19 subunit of interleukin-23, a key inflammatory mediator in ulcerative colitis (UC). Mirikizumab demonstrated an acceptable safety profile, clinical response, clinical remission, and endoscopic remission in the pediatric SHINE-1 study.

Here we describe patient-reported outcomes in pediatric patients with moderate to severe UC from the phase 2 SHINE-1 study (NCT04004611) following 52 weeks of mirikizumab treatment.

Aims & Methods: Patients aged 2 to <18 years with active UC who had an inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressants, or biologic therapies, or had corticosteroid-dependent colitis, were included in the study. Patients weighing >40 kg received an induction dose of mirikizumab 300 mg via intravenous infusion; patients weighing ≤40 kg received mirikizumab 5 or 10 mg/kg via intravenous infusion at weeks 0, 4, and 8. At week 12, patients were assessed for clinical response using the Modified Mayo Score. Responders entered a maintenance period and received subcutaneous doses of mirikizumab at 200 mg (>40 kg), 100 mg (>20 kg to ≤40 kg), or 50 mg (≤20 kg) once every 4 weeks, with the last patient visit at week 52. Abdominal Pain Numeric Rating Scale (NRS), Urgency NRS, and Fatigue NRS scores were assessed through 52 weeks.

Age Range, n	Change from Baseline at Week 52 (Responder population) (N=18) ^a		
	Abdominal Pain NRS Score ^b Mean (SD)	Urgency NRS Score ^c Mean (SD)	Fatigue NRS Score ^d Mean (SD)
2 to <8 years, n=2	-4 (2.8)	-4 (4.2)	-3 (2.8)
8 to <12 years, n=3	-2 (1.0)	-2 (1.5)	-2 (1.0)
12 to <18 years, n=11	-4 (2.5)	-5 (2.1)	-3 (2.0)

Abbreviations: n = sample population; NRS = numeric rating scale; SD = standard deviation.

aTwo patients did not have baseline data and were not included in this analysis.

bThe Abdominal Pain NRS measures the „worst abdominal pain in the past 24 hours“ using an NRS ranging from 0 to 5 (8 to 11 years old) and 0 to 10 (12 to 17 years old). For children less than 8 years old, caregivers completed an observer-reported instrument ranging from 0 to 10.

cThe Urgency NRS measures the severity of the urgency (sudden or immediate need) to have a bowel movement in the past 24 hours using an NRS ranging from 0 to 5 (8 to 11 years old) and 0 to 10 (12 to 17 years old). For children less than 8 years old, caregivers completed an observer-reported instrument ranging from 0 to 10.

dThe Fatigue NRS is a single item that measures the „worst fatigue“ (weariness, tiredness) in the past 24 hours using an NRS ranging from 0 to 5 (8 to 11 years old) and 0 to 10 (12 to 17 years old). For children less than 8 years old, caregivers completed an observer-reported instrument ranging from 0 to 10.

Table 1.

Results: Responders (69.2%, n=18/26) reported improvements in Abdominal Pain NRS, Urgency NRS, and Fatigue NRS scores through all age groups compared to baseline at week 52 (Table 1). A ≥30% improvement in the Abdominal Pain NRS was observed in 50% (n=7) of patients aged 12 to <18 years who scored ≥3 at baseline (N=14).

Conclusion: Mirikizumab demonstrated improvements in abdominal pain, bowel urgency, and fatigue following induction and maintenance treatment. These results provide supporting evidence for the pivotal phase 3 pediatric study SHINE-2 and suggest important improvements in quality of life.

Disclosure: M. Dubinsky has received honoraria as a consultant for: AbbVie, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, F. Hoffmann-La Roche, Genentech, Gilead Sciences, Janssen, Pfizer, Prometheus Therapeutics and Diagnostics, Takeda, and UCB Pharma; has been contracted for research by: AbbVie, Janssen, Pfizer, and Prometheus Biosciences; has stock interest in: Trelus Health; and has received licensing fees from: Takeda; J. L. Kaplan has nothing to disclose; A. Bousvaros has received research support from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, BUHLMANN Diagnostics, Eli Lilly and Company, Janssen, ProCiseDx, and Takeda; was a consultant for: Best Doctors, Eli Lilly and Company, Fresenius Kabi, and Takeda; and has received honoraria and royalties from: Boston University and UpToDate; D. Turner has received consultation fees, research grants, royalties, and/or honoraria from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Pfizer, Prometheus Biosciences, Roche, Shaare Zedek Medical Center, Shire, Sorriso Pharmaceuticals, Takeda, The Hospital for Sick Children, and Thermo Fisher Scientific; T. Hunter Gibble, W. J. Komocsar, A. Larkin, J. Johns, X. Zhang, and W. Crandall are employees and shareholders of: Eli Lilly and Company; J. Hyams is on the advisory board for: Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, and Janssen; and was a consultant for: AbbVie, Pfizer, and Takeda.

MP614

CORTICOSTEROID-FREE CLINICAL AND ENDOSCOPIC OUTCOMES OF RISANKIZUMAB THROUGH WEEK 144 IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: A POST HOC ANALYSIS FROM THE FORTIFY LONG-TERM EXTENSION SUBSTUDY

I. Dotan¹, S. Schreiber², G.R. D'Haens³, M. Dubinsky⁴, J. Lasa⁵, J.C. Chapman⁶, S.M. Ford⁷, Y. Zhang⁷, K. Kligys⁷, J. Zambrano⁷, A. Song⁷, P. Bossuyt⁸

¹Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ²Kiel University, Department of Internal Medicine, Kiel, Germany, ³Amsterdam University Medical Center, Department of Gastroenterology, Amsterdam, Netherlands, ⁴Icahn School of Medicine at Mt Sinai, Department of Pediatrics, New York, United States of America, ⁵Centro de Educación Médica e Investigaciones Clínicas, Buenos Aires, Argentina, ⁶Crohn's and Colitis Center and Inflammatory Bowel Disease, Baton Rouge, United States of America, ⁷AbbVie Inc., North Chicago, United States of America, ⁸Imelda General Hospital, Department of Gastroenterology, Bonheiden, Belgium

Contact E-Mail Address: irisdotan31@gmail.com

Introduction: Corticosteroid (CS) chronic overuse is a concern in the treatment of Crohn's disease (CD), with adverse events and toxicities seen with the long-term use of CS resulting in increased follow-up morbidity and economic burden.^{1,2} Risankizumab (RZB) is an interleukin 23 p19 inhibitor that demonstrated efficacy for the treatment of moderately to severely active CD in phase 3 trials. Here, we report the results of a post

hoc analysis evaluating the ability of RZB to achieve corticosteroid-free outcomes in patients with CD enrolled in the FORTIFY open-label, long-term extension (LTE) substudy.

Aims & Methods: This analysis was designed to understand how effectively RZB can manage CD without the use of CS. The ongoing FORTIFY (NCT03105102) open-label, LTE substudy enrolled patients who entered the open-label extension trial after 52 weeks of RZB maintenance dosing. Patients received RZB 180 mg every 8 weeks, except for patients who had prior rescue therapy, who continued RZB 360 mg. Changes to CD-related CS dose were made at investigators' discretion. Prescheduled visits occurred every 24 weeks and endoscopies every 96 weeks. Baseline CS use was per induction baseline. Outcomes assessed among the overall population and patients with baseline CS use included mean time of CS use, median CS dose, and proportion of patients who achieved CS-free (ie, no CS use at evaluation) clinical remission, assessed by average daily stool frequency and abdominal pain score (SF/APS) and Crohn's Disease Activity Index (CDAI), endoscopic response, and endoscopic remission. Data are presented as observed for all patients and by nonresponder imputation for patients with 2 years of complete (matured) data.

Results: Of 1147 patients enrolled in the LTE study, 325 (28.3%) patients had baseline CS use. Overall, 143 of 1147 (12.5%) of patients received CS at any time during the LTE; median (IQR) time of CS use was 0.0 (0.0) days and median (IQR) CS dose was 0.0 (0.0) mg through data cutoff. Among 325 patients with baseline CS use, 79 received CS during the LTE for a median (IQR) of 138.0 (452.0) days. Among the 754 patients with 2-year matured data, 206 (27.3%) received baseline CS. For patients with 2-year matured data, CS-free clinical remission was demonstrated at week 48 and week 96 per SF/APS (overall, 50.1%, 43.9%; with baseline CS use, 39.8%, 38.3%) and CDAI (overall, 52.5%, 45.4%; with baseline CS use, 45.1%, 40.8%). At week 96 for patients with 2-year matured data, CS-free endoscopic response was achieved by 49.5% overall and 46.6% of patients with baseline CS use; 39.7% and 32.5% achieved CS-free endoscopic remission, respectively. As observed data are also presented (Table). Overall, CS-free clinical remission and CS-free endoscopic remission were maintained from week 0 to week 96 in 62.3% and 72.2% of patients with 2-year matured data.

Endpoint	NRI ^a									AO								
	Overall									Baseline corticoste-roid use								
	Pooled, n/N (%)			180mg, n/N (%)			360mg, n/N (%)			Pooled, n/N (%)			180mg, n/N (%)			360mg, n/N (%)		
	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]	[95% CI]
Corticoste-roid-free	331/754	281/577	50/177	79/206	64/156	15/50	334/493	283/400	51/93	79/135	64/109	15/26						
SF/APS	(43.9)	(48.7)	(28.2)	(38.3)	(41.0)	(30.0)	(67.7)	(70.8)	(54.8)	(58.5)	(58.7)	(57.7)						
clinical	[40.4,	[44.6,	[21.6,	[31.7,	[33.3,	[17.3,	[63.6,	[66.3,	[44.7,	[50.2,	[49.5,	[28.4,						
remission	47.4]	52.8]	34.9]	45.0]	48.7]	42.7]	71.9]	75.2]	65.0]	66.8]	68.0]	76.7]						
Corticoste-roid-free	342/754	285/577	57/177	84/206	72/156	12/50	343/460	285/369	58/91	84/129	72/104	12/25						
CDAI	(45.4)	(49.4)	(32.2)	(40.8)	(46.2)	(24.0)	(74.6)	(77.2)	(63.7)	(65.1)	(69.2)	(48.0)						
clinical	[41.8,	[45.3,	[25.3,	[34.1,	[38.3,	[12.2,	[70.6,	[73.0,	[53.9,	[56.9,	[60.4,	[28.4,						
remission	48.9]	53.5]	39.1]	47.5]	54.0]	35.8]	78.5]	81.5]	73.6]	73.3]	78.1]	67.6]						
Corticoste-roid-free	373/754	303/577	70/177	96/206	74/156	22/50	374/535	303/425	71/110	96/143	74/114	22/29						
endo-	(49.5)	(52.5)	(39.5)	(46.6)	(47.4)	(44.0)	(69.9)	(71.3)	(64.5)	(57.1)	(64.9)	(75.9)						
scopic	[45.9,	[48.4,	[32.3,	[39.8,	[39.6,	[30.2,	[66.0,	[67.0,	[55.6,	[59.4,	[56.2,	[60.3,						
response	53.0]	56.6]	46.8]	53.4]	55.3]	57.8]	73.8]	75.6]	73.5]	74.8]	73.7]	91.4]						
Corticoste-roid-free	299/754	251/577	48/177	67/206	55/156	12/50	299/535	251/425	48/110	67/143	55/114	12/29						
endo-	(39.7)	(43.5)	(27.1)	(32.5)	(35.3)	(24.0)	(55.9)	(59.1)	(43.6)	(46.9)	(48.2)	(41.4)						
scopic	[36.2,	[39.5,	[20.6,	[27.8,	[27.8,	[12.2,	[51.7,	[54.4,	[34.4,	[38.7,	[39.1,	[23.5,						
remission	43.1]	47.5]	33.7]	38.9]	42.8]	35.8]	60.1]	63.7]	52.9]	55.0]	57.4]	59.3]						

AO, as observed; CDAI, Crohn's Disease Activity Index; NRI, nonresponder imputation; SES-CD, Simple Endoscopic Score for Crohn's Disease; SF/APS, stool frequency/abdominal pain score.
*Only patients with 2-year matured data are included in NRI analysis.
SF/APS clinical remission: Average daily SF ≤ 2.8 and not worse than baseline value and average daily APS ≤ 1 and not worse than baseline value.
CDAI clinical remission: CDAI < 150.
Endoscopic response: Decrease in SES-CD > 50% from baseline as scored by a central reviewer.
Endoscopic remission: SES-CD ≤ 4 and at least a 2-point reduction vs baseline and no subscore greater than 1 in any individual variable, as scored by a central reviewer.

Table. Corticosteroid-free Clinical and Endoscopic Outcomes With Risankizumab at Week 96 in the Overall Population and in Patients With Baseline Corticosteroid Use.

Conclusion: Long-term use of RZB in patients with moderately to severely active CD may achieve CS-free clinical remission, endoscopic response, and endoscopic remission. Additionally, a majority of patients did not add CS during the LTE. Thus, RZB may be used to support the reduction of CS in patients with CD.

References:

1. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517.
2. Walter E, et al. *Bone*. 2018;108:44-54.

Disclosure: ID has received consultation fees, research grants, or honoraria from AbbVie, Altman, Arena Pharmaceuticals, Athos, Celgene/Bristol Myers Squibb, Celltrion, Dr Falk Pharma, Ferring, Galapagos, Genentech, Gilead, Iterative Scopes, Janssen, Lilly, Pfizer, Prometheus, Sandoz, Sangamo, Sublimity, Takeda. She is a shareholder in Gutreat and Harp Diagnostics.

SS has been a consultant for AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion Healthcare, Dr Falk Pharma, Ferring, Fresenius, Galapagos, Genentech, Gilead, GlaxoSmithKline, IMAB-Biopharma, Janssen, Lilly, Merck, Novartis/Sandoz, Pfizer, Protagonist, Takeda, Theravance, and Ventyx.

GD'H has served as a consultant and/or received speaker fees from AbbVie, Alimentiv, AstraZeneca, Biora (Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celltrion Healthcare, Cytokine Pharma, Ferring, Galapagos, GlaxoSmithKline, Gossamer Bio, Immunic, InDex Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Lilly, Pfizer, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Takeda, Tillotts, and Ventyx Biosciences.

MD has been a consultant for AbbVie, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Gilead, Janssen, Lilly, Merck, Pfizer, Prometheus, Takeda, and UCB. She has received research grants from AbbVie, Janssen, and Prometheus.

JL has received consulting fees from AbbVie, honoraria from Janssen, and served as a consultant for GlaxoSmithKline and Takeda.

JCC has been a consultant and advisor for AbbVie, Janssen, Medtronic, Pfizer, and Takeda.

SMF, YZ, KK, JZ, and AS are employees of AbbVie and may hold AbbVie stock or stock options.

PB has received research grants from AbbVie, Amgen, Celltrion, Mylan, Pfizer, and Takeda; lecture fees from AbbVie, Celltrion, Janssen, Lilly, and Takeda; and consulting fees from AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Celltrion, Dr Falk Pharma, Galapagos, Janssen, Lilly, Pentax, PSI-CRO, Roche, Takeda, and Tetrameros.

AbbVie funded this study and participated in the study design, study research, data collection, analysis, interpretation of data, reviewing, and approval of the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship.

AbbVie and authors thank all trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Jory Fleischauer, PharmD, of JB Ashtin, and funded by AbbVie.

MP615

THE IMPACT OF MIRIKIZUMAB INDUCTION, MAINTENANCE, AND LONG-TERM TREATMENT ON DISEASE CLEARANCE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: POST HOC ANALYSIS OF LUCENT TRIALS

J.-F. Colombel¹, T. Kobayashi², J. Wu³, B. Zhu³, V. Jairath⁴, I. Redondo³, R. Moses³, C. Siegel⁵, B. Siegmund⁶, F. Magro⁷

¹Icahn School of Medicine at Mount Sinai, Henry D. Janowitz Division of Gastroenterology, Department of Medicine, Usa, United States of America, ²Kitasato University Kitasato Institute Hospital, Center for Advanced IBD Research and Treatment, Tokyo, Japan, ³Eli Lilly and Company, Indianapolis, United States of America, ⁴Western University, London, Canada, ⁵Dartmouth Hitchcock Medical Center, Lebanon, United States of America, ⁶Charité - Universitätsmedizin Berlin, Department of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany, ⁷Centro Hospitalar São João, Gastroenterology, Porto, Portugal

Contact E-Mail Address: fm@med.up.pt

Introduction: Symptomatic, endoscopic, and histological remission simultaneously, known as disease clearance (DC), has been proposed as an aspirational target in ulcerative colitis (UC). [1, 2] Mirikizumab (miri), an anti-IL-23p19 antibody, has demonstrated strong efficacy as shown by single and combined clinical endpoints in LUCENT Phase 3 trials. [3-5] This analysis evaluated the impact of miri on DC during LUCENT-1 (NCT03518086), LUCENT-2 (NCT03524092) and long-term LUCENT-3 (NCT03519945) trials and the association between DC and other clinical and patient-reported outcomes (PROs).

Aims & Methods: DC is defined as symptomatic remission [Mayo stool frequency (SF)=0, 1 with a ≥ 1 point decrease from baseline + rectal bleeding (RB)=0], and histologic-endoscopic mucosal remission [HEMR: Mayo endoscopic remission (ER: endoscopy subscore of 0 or 1, excluding friability) + Geboes score ≤ 2 B.0]. PROs of interest included Fatigue NRS, IBDQ remission, SF-36, WPAI:UC, PGRS, and PGRC (see table footer). Clinical outcomes include clinical remission, corticosteroid-free remission, ER, HEMR, bowel urgency (BU) remission, SF remission, and RB remission. [2,5] The proportion of patients achieving DC was assessed at W12, W52, and W104. Treatment comparisons were made using a CMH test adjusting for randomization factors. Associations between the PROs and DC were evaluated at W12 and W52 in miri-treated patients.

The associations between clinical outcomes and early achievement of DC in miri-treated patients at W12 and W52 were evaluated at W52 and W104, respectively. Non-responder imputation was used for all analyses.

Results: A significantly higher proportion of miri-treated patients achieved DC vs PBO at W12 [N=868 miri, 294 PBO] (DC: 16.0% vs 7.1%, $p<0.0001$) and W52 [N=365 miri, 179 PBO] (DC: 36.4% vs 19.6%, $p=0.0002$). Similar trends were seen for biologic failure subgroups at W12 (bio/JA-Ki-failed: [n=361 miri, 118 PBO; DC: 9.1% vs 5.9%]; bio/JAKi-naïve: [n=492 miri, 171 PBO; DC: 20.9% vs 7.6%]) and W52 (bio/JAKi-failed: [n=128 miri, 64 PBO; DC: 31.3% vs 12.5%]; bio/JAKi-naïve: [n=229 miri, 114 PBO; DC: 39.3% vs 23.7%]). At W104 (N=239 miri), 40.6% of patients achieved DC with 2-year treatment with miri. Specifically, 38.4% of bio/JAKi-failed (n=73) and 40.9% of bio/JAKi-naïve (n=159) patients achieved DC. Significantly greater improvement in all PROs was seen at W12 for patients who achieved DC vs those who did not at W12 in miri-treated patients. Similar associations were observed at W52, except in WPAI:UC overall work productivity (Table 1A). Patients achieving DC at W12 were more likely to achieve all clinical outcomes, except BU remission, at W52 versus those who did not achieve DC at W12. This trend was repeated in patients who achieved DC at W52 and continued to W104 (Table 1B).

Conclusion: Miri consistently demonstrated DC across induction, maintenance, and long-term studies. Over 36% of patients achieved DC after one year of miri treatment. The attainment of DC was associated with improvement in PROs in LUCENT-1 and -2. Early achievement of DC was associated with better long-term clinical outcomes.

Table 1. A. Association Between Disease Clearance Achievement and Improvement in Patient-Reported Outcomes in Miri-treated Patients				Table 1. B. Association of Early Disease Clearance and Subsequent Achievement of Long-term Positive Clinical Outcomes in Miri-treated Patients			
W12	W12 DC: (Y/N) [N=139 vs 729]	W52	W52 DC: (Y/N) [N=133 vs 232]	W52	W12 DC: (Y/N) [N=93 vs 272]	W104	W52 DC: (Y/N) [N=111 vs 128]
Fatigue NRS change from baseline, LSM (std)	-2.5 (0.2) vs -1.8 (0.1)***	Fatigue NRS change from baseline, LSM (std)	-3.2 (0.2) vs -2.3 (0.2)**	Clinical Remission, n (%)	59 (63.4) vs. 123 (45.2)**	Clinical Remission, n (%)	73 (65.8) vs. 56 (43.8)***
IBDQ remission, n (%)	114 (82.0) vs. 385 (52.8)***	IBDQ remission, n (%)	116 (87.2) vs. 148 (63.8)***	CS-free Remission, n (%)	55 (59.1) vs. 109 (40.1)**	CS-free Remission, n (%)	71 (64.0) vs. 55 (43.0)**
SF-36 PCS change from baseline, LSM (std)	8.8 (0.6) vs. 5.4 (0.3)***	SF-36 PCS change from baseline, LSM (std)	10.7 (0.6) vs. 8.0 (0.5)***	Endoscopic Remission, n (%)	64 (68.8) vs. 150 (55.1)*	Endoscopic Remission, n (%)	87 (78.4) vs. 69 (53.9)***
SF-36 MCS change from baseline, LSM (std)	6.9 (0.7) vs. 4.7 (0.3)**	SF-36 MCS change from baseline, LSM (std)	8.0 (0.7) vs. 6.3 (0.6)*	HEMR, n (%)	55 (59.1) vs. 103 (37.9)**	HEMR, n (%)	68 (61.3) vs. 46 (35.9)***
WPAI:UC Overall Work Productivity change from baseline, LSM (std)	-29.0 (2.5) vs. -18.0 (1.3)***	WPAI Overall Work Productivity change from baseline, LSM (std)	-34.9 (2.4) vs. -29.0 (2.1)	BU Remission, n (%)	44 (47.3) vs. 114 (41.9)	BU Remission, n (%)	58 (52.3) vs. 62 (48.4)
PGRS change from baseline, LSM (std)	-1.9 (0.1) vs. -1.0 (0.04)***	PGRS change from baseline, LSM (std)	-2.3 (0.1) vs. -1.7 (0.1)***	SF Remission, n (%)	83 (89.2) vs. 203 (74.6)**	SF Remission, n (%)	103 (92.8) vs. 106 (82.8)*
PGRC, LSM (std)	1.7 (0.1) vs. 2.4 (0.05)***	PGRC, LSM (std)	1.5 (0.1) vs. 1.8 (0.1)**	RB Remission, n (%)	87 (93.5) vs. 224 (82.4)*	RB Remission, n (%)	106 (95.5) vs. 109 (85.2)**

Note: * $p<0.05$; ** $p<0.01$; *** $p<0.001$.

DC = Symptomatic Remission & HEMR.

Fatigue Numeric Rating Scale (NRS) is a single item patient-reported outcome measure that assesses fatigue on an 11-point NRS scale ranging from 0 (no fatigue) to 10 (fatigue as bad as you can imagine).

Inflammatory Bowel Disease Questionnaire (IBDQ) = A 32-item patient-completed questionnaire that assesses four domains of IBD-related quality of life: "Bowel Symptoms", "Systemic Symptoms", "Emotional Function", and "Social Function". A higher total score of all 32-items combined indicates better IBD-related quality of life. An IBDQ score equal or greater than 170 points has been suggested for disease remission.

Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard (SF-36) = a 36-item patient-reported outcome measure designed to assess health-related quality of life in eight domains: physical functioning, role-physical, role-emotional, bodily pain, vitality, social functioning, mental health, and general health. The mental and physical well-being domains ladder to the Mental Component Summary (MCS) score and the Physical Component Summary (PCS) score. The MCS and PCS summary scores range from 0 to 100, where higher scores indicate better levels of function and/or better health.

WPAI:UC = Work Productivity and Activity Impairment Questionnaire-Ulcerative Colitis (WPAI:UC) is a 6-item patient-reported outcome measure that assesses UC-related impairment of daily activity and work productivity over the past 7 days. Scores are represented as impairment percentages, with higher numbers indicating greater impairment and less productivity. (change from baseline)

PGRS = A 1-item patient-rated questionnaire designed to assess the patients' rating of their disease symptom severity over the past 24 hours. Responses are graded on a 6-point scale in which a score of 1 indicates the patient has no symptoms (that is, "none") and a score of 6 indicates that the patient's symptom(s) are "very severe."

PGRC = A patient-rated instrument designed to assess the patients' rating of change in their symptom(s). Responses are graded on a 7-point Likert scale in which a score of 1 indicates that the subject's symptom(s) is "very much better," a score of 4 indicates that the subject's symptom has experienced "no change," and a score of 7 indicates that the subject's symptom(s) is "very much worse."

Symptomatic remission = MMS SF=0 or SF = 1 with a ≥ 1 point decrease from baseline and RB = 0.

HEMR = endoscopic remission (MMS ES = 0 or 1 (excluding friability)) and a Geboes subscore of 0 for grades 2b (lamina propria neutrophils), 3 (neutrophils in epithelium), 4 (crypt destruction), and 5 (erosion or ulceration).

Clinical remission = MMS SF = 0 or 1 with a ≥ 1 point decrease from baseline, RB = 0, and ES = 0 or 1 (excluding friability).

CS-free remission = At LUCENT-2 W40 (W52 of continuous treatment), clinical remission at W40, symptomatic remission at W28, and no CS use for ≥ 12 weeks prior to W40. At LUCENT-3 W52 (W104 of continuous treatment), corticosteroid-free remission is defined as clinical remission at W52 and no corticosteroid use for at least 12 weeks prior to W52.

Endoscopic remission = MMS ES = 0 or 1 (excluding friability).

BU remission = Urgency NRS Score = 0 or 1.

SF remission = MMS SF=0, or SF=1 with a ≥ 1 -point decrease from induction baseline.

RB remission = MMS RB=0.

Associations between DC and categorical outcomes were analyzed using a CMH test adjusted for randomization factors, and corresponding odds ratios were determined. Non-responder imputation was used to impute missing values. For continuous outcomes, associations were analyzed using analysis of covariance with mBOCF using a model that included baseline outcome value and randomization factors. Relative effect sizes were determined.

Abbreviations:

BU = Bowel Urgency; CS = corticosteroid; CMH = Cochran-Mantel-Haenszel; HEMR = histologic-endoscopic mucosal remission; IBDQ = inflammatory bowel disease questionnaire; LSM = least squares mean; MCS = mental component score; MMS = modified Mayo score; N = number of patients in the analysis population; n = number of patients in the specified category; NRS = numeric rating scale; PCS = physical component score; PGRC = patient global rating of change; PGRS = patient global rating of severity; RB = Rectal Bleeding; SF = Stool Frequency; SF-36 = 36-item short-form health survey; std = standard error; UNRS = Urgency Numeric Rating Scale; W = week; mBOCF = modified baseline observation carried forward; WPAI = work productivity activity impairment questionnaire.

References: 1. D'Amico, F., et al., *Disease Clearance as a New Outcome in Ulcerative Colitis: a Systematic Review and Expert Consensus*. Inflammatory Bowel Diseases, 2023.

2. Ramos, L., J. Teo-Loy, and M. Barreiro-de Acosta, *Disease clearance in ulcerative colitis: Setting the therapeutic goals for future in the treatment of ulcerative colitis*. Front Med (Lausanne), 2022. 9: p. 1102420.

3. D'Haens, G., et al., *Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis*. N Engl J Med, 2023. 388(26): p. 2444-2455.

4. Sands, B.E., et al., *Two-Year Efficacy and Safety of Mirikizumab Following 104 Weeks of Continuous Treatment for Ulcerative Colitis: Results From the LUCENT-3 Open-Label Extension Study*. Inflamm Bowel Dis, 2024.

5. Magro, F., et al., *Resolving Histological Inflammation in Ulcerative Colitis With Mirikizumab in the LUCENT Induction and Maintenance Trial Programmes*. Journal of Crohn's and Colitis, 2023. 17(9): p. 1457-1470.

Disclosure: J-F. Colombel reports research grants from AbbVie, Janssen, and Takeda; payment for lectures from AbbVie, Allergan, Amgen, Ferring, Shire, and Takeda; consulting fees from AbbVie, Amgen, Anaptys Bio, Arena, BMS, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Ferring, Galmed, Genentech, GlaxoSmithKline, Janssen, Kaleido, Imdex, Immunic, Iterative Scopes, Landos, Merck, Microba, Novartis, Otsuka Pharmaceutical, PBM Capital, Pfizer, Protagonist Therapeutics, Sanofi, Takeda, TiGenix, and Vifor; and holds stock options in Intestinal Biotech Development.

T. Kobayashi served as an advisory board member, consultant, or speaker for AbbVie, Activaid, Alfresa Pharma, Alimentiv, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda and Zeria Pharmaceutical and has received research funding from AbbVie, Alfresa Pharma, EA Pharma, Kyorin Pharmaceutical, Mochida Pharmaceutical, Nippon Kayaku, Otsuka Holdings, Pfizer, Sekisui Medical, Takeda and Zeria Pharmaceutical. research grants from AbbVie GK, Activaid, Alfresa Pharma Corporation, Bristol-Myers Squibb Eli Lilly Ferring Pharmaceuticals Japan K.K., Gilead Sciences, Inc., JMDC Inc., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., received scholarship contributions from Mitsubishi Tanabe Pharma Corporation, Nippon Kayaku Co., Ltd Zeria Pharmaceutical Co., Ltd., EA Pharma Co., Ltd., and belonged to study group sponsorship by Alfresa Pharma Corporation, JIMRO Co., Ltd., Kyorin Pharmaceutical Co., Ltd., Mochida Pharmaceutical Co., Ltd. ZeriaPharmaceutical Co., Ltd. And received advisory/consultancy fees from AbbVie GK, Activaid, Celltrion Healthcare, EA Pharma Co., Ltd., Eli Lilly, Ferring Pharmaceuticals Japan K.K., Gilead Sciences, Janssen Pharmaceutical K.K., KISSEI Pharmaceutical Co., Ltd, itsubishi Tanabe Pharma Corporation, Pfizer Japan Inc, Takeda Pharmaceutical Co., Ltd.

J. Wu, B. Zhu, I. Redondo, and R. Moses are employees of Eli Lilly.

V. Jairath reports consulting / advisory board for AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; speaker for AbbVie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi.

C. Siegel reports consulting for AbbVie Inc, Bristol Myers Squibb, Fresenius Kabi, Eli Lilly and Company, Janssen Pharmaceuticals, Napo Pharmaceuticals Inc, Pfizer Inc, ProciseDx, Prometheus, Takeda Pharmaceutical Company, and Trellus Health Inc; being a speaker for continuing medical education activities for AbbVie Inc, Janssen Pharmaceuticals, Pfizer Inc,

and Takeda Pharmaceutical Company; and receiving grant support from AbbVie Inc, Janssen Pharmaceuticals, Pfizer Inc, and Takeda Pharmaceutical Company.

B. Siegmund received research grants from Pfizer and Arena; consulting fees from AbbVie, Abivax, Arena, Bristol Myers Squibb, Boehringer, CED Service, Celgene, CT Scout, Endpoint Health, Falk, Forga Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, and PsiCro; speaker honoraria from AbbVie, Bristol Myers Squibb, CED Service, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, and Pfizer; and is President of the European Crohn's and Colitis Organisation.

F. Magro has served as a speaker and received honoraria from: AbbVie, Biogen, Falk, Ferring, Hospira, Laboratórios Vitória, Merck Sharp & Dohme, and Vifor.

MP616

EFFECT OF MIRIKIZUMAB ON CLINICAL AND ENDOSCOPIC OUTCOMES AFTER 1 ANTI-TNF FAILURE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

A. Hart¹, M.D. Martín-Arranz², D. Laharie³, K. Matsuoka⁴, E. Dhesi⁵, I. Redondo⁵, S. Baygani⁵, L. Zaremba-Pechmann⁶, K. Samaan⁵, S. Navabi⁷

¹St Mark's Hospital & Imperial College London, London, United Kingdom, ²Gastroenterology Department. Hospital Universitario La Paz, Madrid, Spain, ³Centre Hospitalier Universitaire de Bordeaux, Hôpital Haut-Lévêque, Service d'Hépatogastroentérologie et Oncologie Digestive, Université de Bordeaux, Bordeaux, France, ⁴Toho University Sakura Medical Center, Sakura, Chiba, Japan, ⁵Eli Lilly and Company, Indianapolis, United States of America, ⁶HaaPACS GmbH, Schriesheim, Germany, ⁷United Medical Doctors, Long Beach, California, United States of America

Contact E-Mail Address: ailsa.hart@nhs.net

Introduction: Mirikizumab (miri), an anti-IL-23p19 antibody, has demonstrated efficacy and safety in moderately to severely active ulcerative colitis (UC) Phase 3 trials (LUCENT-1 and -2; NCT03518086, NCT03524092) among patients who had an inadequate response, loss of response, or intolerance to conventional or advanced therapy. At the LUCENT-1 induction baseline, 41% of the population had experienced a biologic/tofacitinib failure, and 36.3% experienced at least one anti-TNF failure. Among patients with one prior anti-TNF failure only, this analysis evaluated the clinical efficacy of miri compared to placebo (PBO) in induction and maintenance therapy and the efficacy of miri in extended induction.

Aims & Methods: In LUCENT-1, UC patients were randomized to receive 3 intravenous (IV) doses of 300mg miri or PBO every four weeks (Q4W) at W0, W4, and W8 (induction population). In LUCENT 2, responders to miri induction at W12 were re-randomized to subcutaneous (SC) 200mg miri or PBO Q4W through W52 of continuous therapy (maintenance population). Patients not achieving clinical response with miri 300mg IV at W12 received extended induction treatment with open-label 300mg miri IV at W12, W16, and W20 (extended induction population). Patients responding to extended induction at W24 entered open-label maintenance and received 200mg miri Q4W SC until W52 (extended induction responders). Endpoints evaluated were clinical response, clinical remission, symptomatic remission, endoscopic remission, corticosteroid (CS)-free remission, and histologic-endoscopic mucosal remission (HEMR). Efficacy in the subgroup of patients with failure of one anti-TNF only was assessed using Cochran-Mantel-Haenszel tests at W12 (induction population) and W52 (maintenance population).

Results: At LUCENT-1 baseline, of patients who experienced anti-TNF failure, 45% of patients (n=190) had one prior anti-TNF failure only. The one anti-TNF failure subgroup had a longer disease duration, higher rate of pancolitis, similar disease severity (MMS and ES) and slightly higher baseline CS and IMM use, compared to the overall LUCENT population. In the induction and maintenance population, a significantly greater proportion of miri-treated patients achieved the following efficacy endpoints compared with PBO [miri vs. PBO, p-value]: clinical response (W12: [64.4% vs. 34.1%, p=0.001]; W52: [67.2% vs. 44.8%, p=.03]), clinical remission (W52: [44.3% vs. 17.2%, p=.017]), symptomatic remission (W52: [63.9% vs. 34.5%, p=.005]) (Table). Among the extended induction population, 45.7% achieved clinical response at W24; 75% achieved clinical response, 30% achieved clinical remission and CS-free remission at W52 (Table).

	LUCENT-1 W12 (Induction Population)				LUCENT-2 W52 (Maintenance Population)			
	PBO IV n (%)	300mg Miri IV n (%)	p-value ^b	Risk Difference (95% CI) ^c	PBO SC n (%)	200mg miri SC n (%)	p-value ^b	Risk Difference (95% CI) ^d
Clinical Response	15 (34.1)	94 (64.4)	0.00148	27.4 (11.2, 43.5)	13 (44.8)	41 (67.2)	0.03	24.4 (3.1, 45.7)
Clinical Remission	6 (13.6)	27 (18.5)	0.66	2.9(-9.4, 15.2)	5 (17.2)	27 (44.3)	0.017	27.3 (8.3, 46.2)
Symptomatic Remission	12 (27.3)	64 (43.8)	0.109	13.5(-2.3, 29.4)	10(34.5)	39 (63.9)	0.005	32.6 (11.6, 53.6)
Endoscopic Remission	7 (15.9)	44 (30.1)	0.105		8 (27.6)	29 (47.5)	0.073	20.4 (-0.1, 40.9)
CS-Free Remission				12.8(-0.8, 26.5)	5 (17.2)	23 (37.7)	0.074	19.5 (0.7, 38.2)
HEMR					5 (17.2)	20 (32.8)	0.067	19.1 (1.3, 37.0)

	LUCENT-2 W24 (Extended Induction Population)	LUCENT-2 W52 (Extended Induction Responders)
	300mg miri IV, n (%)	200mg miri SC, n (%)
Clinical Response	21 (45.7)	15 (75)
Clinical Remission	2 (4.3)	6 (30)
Symptomatic Remission	13 (28.3)	11 (55)
Endoscopic Remission	5 (10.9)	8 (40)
CS-Free Remission		6 (30)
HEMR		6 (30)

[a] modified-Intent-To-Treat population, non-responder imputation.

[b] Cochran-Mantel-Haenszel (CMH) test adjusted by corticosteroid use (yes/no) at AMAN baseline, region (North America/Europe/Other), Clinical Remission status (yes/no) at AMAN Week 12. **Statistically significant p-values are bolded.**

[c] The common risk difference is the difference in proportions adjusted for the stratification factor(s): baseline corticosteroid use (yes/no), baseline disease activity (MMS: [4-6] or [7-9]), and region (North America/Europe/Other), where the confidence intervals are calculated using Mantel-Haenszel-Sato method.

[d] Risk difference based on difference in proportions adjusted for the stratification factor(s): corticosteroid use (yes/no) at LUCENT 1 baseline, region (North America/Europe/Other), Clinical Remission status (yes/no) at LUCENT 1 Week 12, where the confidence intervals are calculated using Mantel-Haenszel-Sato method.

IV = intravenous; miri = Mirikizumab, PBO = placebo; SC = subcutaneous; TNF = tumor necrosis factor; CS = corticosteroid. Clinical response = decrease in the modified Mayo score of ≥ 2 points and $\geq 30\%$ decrease from baseline (BL), and decrease of ≥ 1 point in the rectal bleeding (RB) subscore from BL or an RB score of 0 or 1. Clinical remission = Stool frequency (SF) = 0, or SF = 1 with a ≥ 1 -point decrease from baseline; rectal bleeding (RB) = 0; endoscopic subscore (ES) = 0 or 1 (excluding friability). Endoscopic remission = Mayo endoscopic subscore = 0 or 1 (excluding friability). Symptomatic Remission = stool frequency (SF) = 0, or SF = 1 with a ≥ 1 -point decrease from baseline and rectal bleeding = 0. CS Free Remission = Clinical remission at Week 40, symptomatic remission (SF = 0, or SF = 1 with a ≥ 1 -point decrease from induction baseline; and RB=0) at Week 28, and no corticosteroid use for ≥ 12 weeks prior to Week 40. HEMR = histologic-endoscopic mucosal remission, histologic remission with resolution of mucosal neutrophils, determined by Geboes $\leq 2B.0$ score.

Table: Efficacy of miri vs PBO for subjects with Only One Prior anti-TNF Failure^a

Conclusion: Mirikizumab is efficacious for induction and maintenance therapy in patients with moderately to severely active UC who have failed one prior anti-TNF.

Disclosure: A. Hart has served as a speaker, consultant, and advisory board member for: AbbVie, AstraZeneca, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Galapagos NV, Genentech, Janssen, Johnson & Johnson, Merck Sharp & Dohme, Pfizer, Pharmacosmos, Takeda, and Roche

M. D. Martín-Arranz has served as a speaker or has received research or educational funding or advisory fees from: AbbVie, Eli Lilly and Company, Faes Farma, Ferring Pharmaceuticals, Janssen, Merck Sharp & Dohme, Pfizer, Shire Pharmaceuticals, Takeda, and Tillots Pharma

D. Laharie has received consulting, boards, transports, or fees from: AbbVie, Amgen, Biogaran, Biogen, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Galapagos NV, Janssen, Merck Sharp & Dohme, Pfizer, Prometheus, Roche, Takeda, and Theradiag

K. Matsuoka has received fees for grants and/or contracts from: AbbVie, EA Pharma, JIMRO, Kissei, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, and Zeria Pharmaceutical; lecture fees from: AbbVie, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen, JIMRO, Kissei, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical; and manuscript preparation fees from: Eli Lilly and Company

E. Dhesi, I. Redondo, S. Baygani, and K. Samaan are employees and shareholders of: Eli Lilly and Company

L. Zaremba-Pechmann is a contractor for: Eli Lilly and Company through HaaPACS

S. Navabi has served as an advisor for: Eli Lilly and Company

Medical writing assistance was provided by Estelle Sontag, PhD, and Alice Carruthers, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

Previously presented at the European Crohn's and Colitis Organisation - 2024 Congress

MP617

LONG-TERM EFFICACY AND SAFETY OF MIRIKIZUMAB FOLLOWING 152 WEEKS OF CONTINUOUS TREATMENT: RESULTS FROM THE LUCENT-3 OPEN-LABEL EXTENSION STUDY

B.E. Sands¹, G.R. D'Haens², D. Clemow³, P. Irving⁴, J.T. Johns⁵, T. Hunter Gible⁶, M.T. Abreu⁷, S. Lee⁸, T. Hisamatsu⁹, T. Kobayashi¹⁰, M.C. Dubinsky¹¹, S. Vermeire¹², C.A. Siegel¹³, L. Peyrin-Biroulet¹⁴, R. Moses¹⁵, J. Milata⁵, V. Arora⁵, R. Panaccione¹⁶, A. Dignass¹⁷

¹Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America, ²AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands, ³Eli Lilly And Company Corporate Center, Indianapolis, United States of America, ⁴Guy's and St Thomas' Hospital, Dept. of Gastroenterology, London, United Kingdom, ⁵Eli Lilly and Company, Indianapolis, United States of America, ⁶Eli Lilly and Company, Global Patient Outcomes and Real World Evidence, Indianapolis, United States of America, ⁷University of Miami, Miller School of Medicine, Crohn's and Colitis Center, Coral Gables, United States of America, ⁸University of Washington Medical Center, Seattle, United States of America, ⁹Kyorin University School of Medicine, Tokyo, Japan, ¹⁰Kitasato University Kitasato Institute Hospital, Suginami-ku, Japan, ¹¹Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ¹²University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ¹³Dartmouth-Hitchcock Medical Center, Lebanon, United States of America, ¹⁴Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ¹⁵Eli Lilly and Company, Rydal, Pa, United States of America, ¹⁶University of Calgary, Medicine, Calgary, Canada, ¹⁷Agaplesion Markus Krankenhaus, Medizinische Klinik I, Frankfurt/Main, Germany

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: Mirikizumab, a p19-directed interleukin-23 monoclonal antibody, is efficacious in inducing clinical remission at Week (W) 12 and maintaining clinical remission through W52 and W104 in patients with moderately-to-severely active ulcerative colitis (UC) (LUCENT-1, NCT03518086; LUCENT-2, NCT03524092; LUCENT-3, NCT03519945).

Here we present efficacy and safety results through W152 of mirikizumab treatment from the open-label extension LUCENT-3 study.

Aims & Methods: Symptomatic, clinical, endoscopic, histologic, quality-of-life, and adverse event (AE) outcomes are reported for mirikizumab induction responders, including biologic failed patients, who entered the LUCENT-3 study, with data shown for W52 maintenance responders or remitters. Discontinuations or missing data were handled by nonresponder imputation (NRI), modified NRI (mNRI), and observed case (OC). mNRI uses multiple imputation for missing data and balances bias of NRI and OC. Table 1 provides endpoint and population definitions and abbreviations.

Results: Using mNRI, among W52 mirikizumab responders, 82% demonstrated clinical response at W152. Remission rates at W152 for W52 clinical responders were 56% clinical, 55% corticosteroid-free (CSF), 61% endoscopic, 53% histologic-endoscopic mucosal remission (HEMR), 75% symptomatic, and 59% bowel urgency.

Patients achieving histologic-endoscopic mucosal improvement (HEMI) and bowel urgency clinically meaningful improvement (CMI) at W152 were 53% and 74%, respectively. For W52 mirikizumab remitters, 85% demonstrated clinical response at W152. Remission rates at W152 for W52 clinical

remitters were 70% clinical, 69% CSF, 72% endoscopic, 63% HEMR, 81% symptomatic, and 61% bowel urgency. Patients achieving HEMI and bowel urgency CMI at W152 were 64% and 76%, respectively. Biologic Failed/Not Biologic Failed subgroup data demonstrate maintenance of efficacy (Table 1).

Endpoints at Week 152	In Week 52 Responders ¹ n=286 % All (95% CI) ³	In Week 52 Responders ¹ n=195 % Not Biologic Failed (95% CI) ³	In Week 52 Responders ¹ n=91 % Biologic Failed (95% CI) ³	In Week 52 Remitters ² n=179 % All (95% CI) ³	In Week 52 Remitters ² n=120 % Not Biologic Failed (95% CI) ³	In Week 52 Remitters ² n=59 % Biologic Failed (95% CI) ³
Clinical response ⁴	71.6 (66.1, 76.5)	76.4 (70.0, 81.8)	60.4 (50.2, 69.9)	72.6 (65.7, 78.6)	79.2 (71.1, 85.5)	59.3 (46.6, 70.9)
Clinical remission ⁵	49.5 (43.7, 55.2)	52.3 (45.3, 59.2)	42.9 (33.2, 53.1)	60.3 (53.0, 67.2)	65.8 (57.0, 73.7)	49.2 (36.8, 61.6)
Symptomatic remission ⁶	66.3 (60.6, 71.6)	71.3 (64.6, 77.2)	54.9 (44.7, 64.8)	69.8 (62.7, 76.1)	75.8 (67.4, 82.6)	57.6 (44.9, 69.4)
CSF remission ⁷	48.1 (42.3, 53.9)	50.8 (43.8, 57.7)	41.8 (32.2, 52.0)	59.2 (51.9, 66.1)	65.0 (56.1, 72.9)	47.5 (35.3, 60.0)
HEMR ⁸	49.3 (43.6, 55.1)	51.3 (44.3, 58.2)	45.1 (35.2, 55.3)	59.2 (51.9, 66.1)	63.3 (54.4, 71.4)	50.8 (38.4, 63.2)
Endoscopic remission ⁹	59.1 (53.3, 64.6)	59.5 (52.5, 66.1)	58.2 (48.0, 67.8)	69.8 (62.7, 76.1)	73.3 (64.8, 80.4)	62.7 (50.0, 73.9)
HEMI ¹⁰	50.3 (44.6, 56.1)	51.8 (44.8, 58.7)	47.3 (37.3, 57.4)	59.8 (52.5, 66.7)	64.2 (55.3, 72.2)	50.8 (38.4, 63.2)
Bowel urgency remission ¹¹	51.6 (45.8, 57.3)	55.4 (48.4, 62.2)	42.9 (33.2, 53.1)	52.5 (45.2, 59.7)	60.0 (51.1, 68.3)	37.3 (26.1, 50.0)
	n=266 ¹³ 65.4 (59.5, 70.9)	n=180 ¹³ 69.4 (62.4, 75.7)	n=87 ¹³ 56.3 (45.9, 66.3)	n=169 ¹³ 63.9 (56.4, 70.8)	n=112 ¹³ 68.8 (59.7, 76.6)	n=57 ¹³ 54.4 (41.6, 66.6)

Bowel urgency CMI¹²

Abbreviations: CI=confidence interval; CMI=clinically meaningful improvement; CSF=corticosteroid-free; ES=endoscopic subscore; HEMI=histologic-endoscopic mucosal improvement; HEMR=histologic-endoscopic mucosal remission; MMS= Mayo Modified Score; mNRI=modified NRI; n=number of participants in the specific category; N=number of participants in the analysis population; NRI=nonresponder imputation; NRS=numeric rating scale; OC=observed case; RB=rectal bleeding; SF=stool frequency; UC=ulcerative colitis; UNRS=Urgency Numeric Rating Scale.

Definitions: Biologic Failed: Inadequate response, loss of response, or intolerant to a biologic therapy or the Janus kinase inhibitors for UC. Cerebrocardiovascular events: atrial fibrillation (N=2), angina unstable (N=1), coronary arterial stent insertion (N=1), hypertensive crisis (N=1), ventricular tachycardia (N=1) – angina and stent were same patient. Not Biologic Failed: failed conventional treatments (i.e., immunomodulators/corticosteroids); may include some participants who were exposed to but did not fail biologic treatment. Malignancy: thyroid cancer metastatic (N=1). mNRI (text): patients who discontinue treatment treated as nonresponders and patients who are otherwise missing endpoint data imputed using multiple imputation. NRI (table): patients who discontinue treatment treated as nonresponders and patients who are otherwise missing endpoint data tagged as nonresponders. OC (referred to): patients who discontinue treatment or are otherwise missing data are excluded from analyses. Opportunistic infection: herpes zoster (N=4), candidiasis (N=3) – one patient had each. ¹Responders: ≥30% and 2-point decrease from baseline in the composite clinical endpoint of the summary of ES, SF, and RB subscores, and RB=0 or 1, or ≥1-point decrease from baseline.

²Remitters: (MMS SF=0 or SF=1 with ≥1-point decrease from baseline; RB=0; ES=0 or 1) cohort of LUCENT-2 at Week 52.

³Response confidence interval: constructed using Wilson method, without continuity correction.

⁴Clinical response: ≥2-point and ≥30% decrease in MMS from baseline; RB=0 or 1, or RB ≥1-point decrease from baseline.

⁵Clinical remission: SF=0 or SF=1 with ≥1-point decrease in MMS from baseline; RB=0; ES=0 or 1 (excluding friability).

⁶Symptomatic remission: SF=0 or SF=1 with ≥1-point decrease in MMS from baseline; RB=0.

⁷CSF remission: clinical remission, and no corticosteroid use for at least 12 weeks prior to Week 52; SF=0 or SF=1 with a ≥1-point decrease from induction baseline; RB=0; ES=0 or 1 (excluding friability).

⁸HEMR: ES=0 or 1 (excluding friability) + Geboes ≤2.0.

⁹Endoscopic remission: ES=0 or 1 (excluding friability); score ranges 0 to 4; a lower score indicates less mucosal damage.

¹⁰HEMI: ES=0 or 1 (excluding friability) + Geboes ≤3.1.

¹¹Bowel urgency remission: UNRS=0 or 1 (Dubinsky MC, et al. J Patient Reported Outcomes 2022;6(1):1–15).

¹²Bowel urgency CMI: change from baseline in UNRS ≥3 in patients with UNRS ≥3 at induction baseline (Dubinsky MC, et al. J Patient Reported Outcomes 2022;6(1):1–15).

¹³In patients who had UNRS ≥3 at induction baseline.

Stool frequency, rectal bleeding, bowel urgency, and abdominal pain symptom score reductions from induction baseline at W52 were sustained through W152. Severe AEs were reported in 7.4% of patients, while 5.3% discontinued treatment due to an AE. AEs of special interest included opportunistic infection (1.8%), cerebrocardiovascular events (1.5%), and malignancy (0.3%). Elevated liver enzymes ≥3 upper limit of normal (ULN)

included alanine aminotransferase (0.9%), aspartate aminotransferase (1.2%); 2xULN total bilirubin (1.8%), alkaline phosphatase (0.6%), gamma-glutamyltransferase (2.9%); ≥ 5 ULN: AST (0.3%).

Conclusion: Symptomatic, clinical, endoscopic, histologic, and quality-of-life outcomes support the long-term sustained benefit of mirikizumab treatment up to 152 Wks in patients with UC, including biologic failed patients, with no new safety concerns.

References: Dubinsky MC, et al. J Patient Reported Outcomes 2022;6(1):1-15

Disclosure: Abbreviated disclosures below to accommodate wordcount. Full disclosures available upon request.

Bruce Sands reports consulting fees from Abbvie, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphic Therapeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Ventyx Biosciences. Geert D'Haens reports advisor fees from AbbVie, Alimentiv, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli Lilly and Company, Galapagos, GlaxoSmithKline, Gossamerbio, Pfizer, Immunicon, Johnson and Johnson, Takeda, Prometheus Biosciences, Prometheus Laboratories, Protagonist, Samsung, Seres, Tillotts, Ventyx.

Peter Irving reports research grants from Celltrion, Pfizer, Takeda, Galapagos, consulting fees from AbbVie, Arena, Boehringer-Ingelheim, BMS, Celltrion, Elasmogen, Gilead, Janssen, Eli Lilly and Company, Pfizer, Prometheus, Sandoz

David Clemow, Jordan Johns, Theresa Hunter Gible, Richard Moses, Joe Milata, and Vipin Arora report being Eli Lilly and Company employees and stockholders.

Maria Abreu reports consulting and/or served on an advisory board for AbbVie Inc, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celsius Therapeutics, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceuticals, Pfizer Pharmaceutical, Prometheus Biosciences, UCB Biopharma SRL

Scott Lee reports grants and research support from AbbVie Pharmaceuticals, Takeda Pharmaceuticals Inc, Pfizer Pharmaceuticals Inc, Atlantic Pharmaceuticals Ltd., Cornerstones, Johnson and Johnson Pharmaceuticals Inc, Takeda Pharmaceuticals Inc, Eli Lilly and Company, Celltrion Healthcare Co, Protagonist, Altrubio.

Tadakazu Hisamatsu reports advisory/consultancy fees from Janssen Pharmaceutical K.K., EA pharma Co. Ltd., AbbVie GK, Pfizer Inc., Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Co. Ltd., GILEAD, Eli Lilly and Company

Taku Kobayashi reports has serving as a speaker, a consultant, or an advisory board member for AbbVie, Alfresa Pharma, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eiken chemical, Eli Lilly and Company, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen, JIMRO, Kissei, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Sekisui Medical, Takeda Pharmaceutical, Zeria Pharmaceutical

Marla Dubinsky reports consulting fees from Abbvie, Arena Pharmaceuticals, Astra Zeneca, Boehringer Ingelheim International GmbH, Bristol-Meyer Squibb, Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Genentech Inc, Gilead, Janssen Pharmaceuticals, Pfizer Inc, Prometheus Biosciences, Takeda Pharmaceuticals, UCB SA

Severine Vermeire reports consulting and/or speaking fees from AbbVie, Abivax, Aboleris Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Cytokine Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead,

GSK, Hospira, Imidomics, Janssen, Johnson and Johnson, Lilly, Materia Prima, Mestag Therapeutics and others.

Corey Siegel reports being a consultant for Abbvie, BMS, Fresenius, Eli Lilly and Company, Janssen, Napo Pharmaceuticals, Pfizer, ProCiseDx, Prometheus, Takeda, Trellus Health

Laurent Peyrin-Biroulet reports personal fees from AbbVie, Adaclyte, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytokine Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Eli Lilly and Company, Medac, Mopac, Morphic, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics and others.

Remo Panaccione reports being a consultant for Abbott, AbbVie, Abbivax, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly and Company, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz and others.

Axel Dignass reports consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, Celltrion, Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Janssen, Eli Lilly and Company, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada; Takeda, Tillotts, and Vifor Pharma

MP618

EARLY SYMPTOMATIC IMPROVEMENT WITH MIRIKIZUMAB INDUCTION THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM THE PHASE 3 VIVID-1 STUDY

B.E. Sands¹, M. Chen², S. Danese³, M. Fischer⁴, T. Hisamatsu⁵, S. Hoque⁶, L. Peyrin-Biroulet⁷, F. Seibold⁸, F. Durand⁹, Z. Lin⁹, M. Ugolini Lopes⁹, N. Morris⁹, E. Hon⁹, G.R. D'Haens¹⁰
¹Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ²The First Affiliated Hospital of Sun Yat-sen University, Division of Gastroenterology, Guangzhou, China, ³Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁴IUPUI, Gastroenterology, Indianapolis, United States of America, ⁵Kyorin University School of Medicine, Tokyo, Japan, ⁶Barts Health NHS Trust, London, United Kingdom, ⁷Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ⁸Crohn-Colitis Zentrum, Bern, Switzerland, ⁹Eli Lilly and Company, Indianapolis, United States of America, ¹⁰AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: Mirikizumab (miri), an anti-IL-23p19 antibody, demonstrated robust efficacy in improving clinical, endoscopic, and inflammatory biomarker endpoints, and an acceptable safety profile for patients with moderately to severely active Crohn's disease (CD) in the Phase 3 VIVID-1 study. Here, we investigate the onset of symptomatic improvement and the safety of miri as induction therapy through Week 12 (W12) for patients with moderately to severely active CD.

Aims & Methods: In VIVID-1 (NCT03926130), patients (N=1065) had moderately to severely active CD (unweighted daily average stool frequency (SF) ≥ 4 [loose and watery stools defined as Bristol Stool Scale Category 6 or 7] AND/OR unweighted daily average abdominal pain (AP) ≥ 2 at baseline) and had prior failure to biologic and/or conventional therapy. Patients were randomized in a 6:3:2 ratio to receive miri (a single 900mg intravenous (IV) dose at W0, W4, and W8 followed by a subcutaneous (SC) dose of 300mg at W12 and then every 4 weeks), ustekinumab (uste) (6mg/kg IV at W0 and SC dose of 90mg at W8 and then every 8 weeks), or placebo (PBO). Results for the co-primary endpoints and major secondary endpoints versus PBO, as well as for the 2 major secondary endpoints versus uste, have been reported previously^{1,2}. This analysis focuses on comparisons of clinical response by Patient Reported Outcome (PRO) (defined as at least a 30% decrease in SF and/or AP with neither score worse than baseline), clinical remission by PRO (defined as SF ≤ 3 and not worse than baseline [as per Bristol Stool Scale Category 6 or 7] and AP ≤ 1 and no worse than baseline), change from baseline (CFB) in SF, and CFB in AP up to W12 in patients who were randomized to miri or PBO.

Results: Baseline characteristics were balanced across the miri (N=579) and PBO (n=199) treatment groups¹. Compared to PBO, a greater proportion of patients on miri achieved clinical response by PRO at W4, 6, 8, and 12, and clinical remission by PRO at W6, 8, and 12. Treatment with miri resulted in significant improvements in SF at W6, 8, and 12, and in AP at W4, 6, 8, and 12 when compared to PBO (Table 1). The overall safety was consistent with the known safety profile of miri. The most common treatment-emergent adverse events (TEAEs) during induction period in miri-treated patients were COVID-19, anaemia and headache. There were lower frequencies of SAEs (miri: 5.9%, PBO: 9.0%) and discontinuations due to adverse events (miri: 2.4%, PBO: 4.7%) in miri-treated patients versus PBO. There were no malignancies, no MACes, no Hy's law cases or deaths in the miri arm up to W12. One death was reported in the induction period in the PBO group.

	Clinical response by PRO ^a n (%)		Clinical remission by PRO ^a n (%)		Stool Frequency (CFB) ^b LSM (SE)		Abdominal Pain (CFB) ^b LSM (SE)	
	Miri N=579	PBO N=199	Miri N=579	PBO N=199	Miri N=579	PBO N=199	Miri N=579	PBO N=199
Week 2	224 (38.7)	75 (37.7)	41 (7.1)	10 (5.0)	-1.24 (0.076)	-1.24 (0.129)	-0.38 (0.022)	-0.31 (0.036)
Week 4	308 (53.2)*	87 (43.7)	90 (15.5)	27 (13.6)	-1.74 (0.087)	-1.42 (0.146)	-0.55 (0.026)*	-0.43 (0.043)
Week 6	376 (64.9)***	100 (50.3)	150 (25.9)*	36 (18.1)	-2.20 (0.091)*	-1.81 (0.153)	-0.72 (0.028)***	-0.52 (0.047)
Week 8	404 (69.8)****	101 (50.8)	175 (30.2)**	37 (18.6)	-2.43 (0.096)**	-1.85 (0.162)	-0.80 (0.029)****	-0.56 (0.049)
Week 12	409 (70.6)****	103 (51.8)	216 (37.3)****	44 (22.1)	-2.65 (0.101)****	-1.86 (0.171)	-0.90 (0.031)****	-0.61 (0.052)

Footnotes: ^aNonresponder imputation was used. ^bModified baseline observation carried forward was used.
* refers to $p < 0.05$ significance; ** refers to $p < 0.01$ significance; *** refers to $p < 0.001$ significance; **** refers to $p < 0.0001$ significance
Abbreviations: AP=abdominal pain; CDAI= Crohn's Disease Activity Index; CFB=change from baseline;
PRO=Patient Reported Outcome (2 of the patient-reported items of the CDAI, AP and SF); LSM=least square mean; SE=standard error; SF=stool frequency; miri=mirikizumab; PBO=placebo

Conclusion: In patients with moderately to severely active CD, miri induction was associated with higher rates of clinical response and greater improvement in AP as early as W4, and higher rates of clinical remission and greater improvement in SF as early as W6 versus PBO. Increasing treatment effect was observed through W12. The safety of miri induction therapy was consistent with its known favourable safety profile.

References:

1. M Ferrante, S Danese, M Chen, G D'Haens, S Ghosh, T Hisamatsu, V Jairath, J Kierkus, L Peyrin-Biroulet, B Siegmund, S M Bragg, W Crandall, T Hunter Gible, Z Lin, M Ugolini Lopes, N Morris, H Carlier, B Sands, VIVID Study Group, OP05 Primary efficacy and safety of mirikizumab in moderate to severe Crohn's Disease: results of the treat-through VIVID 1 study, *Journal of Crohn's and Colitis*, Volume 18, Issue Supplement_1, January

2024, Pages i7–i9, <https://doi.org/10.1093/ecco-jcc/jjad212.0005>

2. V Jairath, B E Sands, P Bossuyt, F Farraye, M Ferrante, T Hisamatsu, A Kaser, J Kierkus, D Laharie, W Reinisch, B Siegmund, S M Bragg, E Hon, Z Lin, M Ugolini Lopes, N Morris, M Protic, S Danese, VIVID Study Group, OP35 Efficacy of mirikizumab in comparison to ustekinumab in patients with moderate to severe Crohn's disease: Results from the phase 3 VIVID 1 study, *Journal of Crohn's and Colitis*, Volume 18, Issue Supplement_1, January 2024, Pages i62–i64, <https://doi.org/10.1093/ecco-jcc/jjad212.0035>

Disclosure: Bruce E Sands: reports consulting fees from Abbvie, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphic Therapeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock options from Ventyx Biopharma.

Minhu Chen: provided educational activities for AbbVie, China Medical System, IPSEN, Janssen, and Takeda; served on an advisory board for Boehringer Ingelheim and Janssen; and has support for clinical research from Janssen and Takeda.

Silvio Danese: has consulting fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, and Vifor; has lecture fees from Abbvie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, and Takeda.

Monika Fischer: has served as an Advisor, Review Panel Member, Speakers Bureau, or DSMB for AbbVie, BMS, Lilly, Ferring, Janssen, Pfizer, Rebiotix, Scioto, Seres

Tadakazu Hisamatsu: has joint research agreement from Kissei Pharmaceutical and EA Pharma; has received research grants from AbbVie, Daiichi Sankyo, EA Pharma, JIMRO, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, Boston Scientific, and Zeria Pharmaceutical; and has received consulting and lecture fees from AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical, Pfizer, Kissei Pharmaceutical, and Takeda.

Sami Hoque: Reports advisory to Eli Lilly and Company and advisory and lecture fees to Tillots.

Laurent Peyrin-Biroulet: Reports the following: personal fees from Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillots, Pharmacosmos, Celltrion, Takeda, Boehringer Ingelheim, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Alma, Sterna, Nestle, Inotrem, Enterome, Allergan, MSD, Roche, Arena, Gilead, Hikma, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius Kabi, Oppilan Pharma, Sublimity Therapeutics, Applied Molecular Transport, OSE Immunotherapeutics, Entera, and Theravance; grants from Abbvie, MSD, and Takeda; and stock options from CTMA

Frank Siebold: has consulting fees from Abbvie, Amgen, BMS, Dr. Falk, Eli Lilly, Geilead, Janssen, Pfizer, Takeda.

Geert D'Haens: has served as adviser and/or speaker for Abbvie, Alimentiv, Amgen, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Ferring, Eli

Lilly, Engene, Galapagos, Glaxo Smith Kline, Immunic, Index Pharmaceuticals, Johnson and Johnson, Merck, Polpharm, Prometheus biosciences, Prometheus Laboratories, Proctise diagnostics, Protagonist, Sandoz, Takeda, Tillotts, and Ventyx.

Frederick Durand, Emily Hon, Zhantao Lin, Nathan Morris, and Michelle Ugolini Lopes are all Eli Lilly and Company employees and stockholders.

MP619

ACHIEVEMENT OF NORMALISED HEALTH-RELATED QUALITY OF LIFE OUTCOMES WITH RISANKIZUMAB TREATMENT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: A POST-HOC ANALYSIS OF PHASE 3 INSPIRE & COMMAND STUDIES

J. Panés¹, P.S. Dulai², J. Torres³, S. Tanida⁴, I. Blumenstein⁵, P.M. Hecht⁶, N. Shukla⁶, J. Kalabic⁷, V. Remple⁶, Y. Sanchez Gonzalez⁶, D. Sharma⁶, R. Panaccione⁸
¹Hospital Clínic Barcelona, Dept. of Gastroenterology, Barcelona, Spain, ²Northwestern University, Division of Gastroenterology and Hepatology, Chicago, United States of America, ³Gastroenterology Division, Hospital Beatriz Ângelo; Gastroenterology Division, Hospital da Luz, Lisbon, Portugal, ⁴Gamagori City Hospital, Gamagori, Japan, ⁵Goethe University Hospital, Frankfurt, Germany, ⁶AbbVie Inc., North Chicago, United States of America, ⁷AbbVie Deutschland GmbH Co. KG, Ludwigshafen am Rhein, Germany, ⁸University of Calgary, Department of Gastroenterology and Hepatology, Calgary, Canada

Contact E-Mail Address: julian.panes@gmail.com

Introduction: Ulcerative colitis (UC) is associated with symptoms that may considerably impair patients' health-related quality of life (HRQoL). Long-term treatment goals established in STRIDE-II include the recuperation of HRQoL in patients with active UC.¹

This post-hoc analysis evaluated the impact of Risankizumab (RZB) as induction and maintenance therapy on normalisation of HRQoL in patients with moderate to severe UC.

Aims & Methods: This study evaluated data from two double-blind, Phase 3 trials, INSPIRE (induction: NCT03398148) and COMMAND (maintenance: NCT03398135). During induction, patients were randomised 2:1 to receive intravenous (IV) RZB 1200 mg or placebo (PBO) at Weeks 0, 4, and 8. Those with a clinical response based on Adapted Mayo score were randomised 1:1:1 to subcutaneous (SC) RZB 180 mg, RZB 360 mg, or PBO (RZB withdrawal) every 8 weeks for 52 weeks of maintenance. The proportion of patients achieving normalisation of individual HRQoL outcomes, per literature-based normative value threshold, was assessed at baseline and Weeks 12 and 52: FACIT-Fatigue score; IBDQ score; WPAI-UC (overall work impairment, work time missed, impairment while working, activity impairment); SF-36 PCS; SF-36 MCS; EQ-5D-5L VAS; and EQ-5D-5L index. A composite endpoint was determined to evaluate patients achieving normalisation of all HRQoL outcomes. Adjusted treatment differences between RZB and PBO were analysed using Mantel-Haenszel common rate difference. P values were calculated using Cochran-Mantel-Haenszel test and adjusted for strata.

Results: At Week 12, for RZB 1200 mg IV (n=650) vs PBO (n=325), more patients achieved normalisation of each individual HRQoL outcome (p<0.01) (Table 1). For RZB SC 180 mg (n=179) and 360 mg (n=186), more patients achieved normalisation of FACIT-fatigue, IBDQ, and SF-36 PCS vs PBO at Week 52 (p<0.05). More patients also achieved normalisation of all WPAI-UC scores with RZB 180 mg SC vs PBO (p<0.05), excluding overall work impairment. For SF-36 MCS and both EQ-5D-5L scores, more patients achieved normalisation with RZB 180 mg SC vs PBO (p<0.05), but not with RZB 360 mg SC. Normalisation of the composite HRQoL score

was achieved by more patients with all doses of RZB vs PBO at Weeks 12 (RZB 1200 mg: 12.5%; PBO: 4.9%) and 52 (RZB 360 mg: 20.4%; RZB 180 mg: 21.2%; PBO: 10.9%) (p<0.05).

HRQoL endpoints at Weeks 12 and 52, n (%)	Induction (Week 12) PBO IV N=325	Induction (Week 12) RZB 1200 mg IV N=650	Between group diff. (RZB 1200 mg IV vs PBO) % [95% CI]	Maintenance (Week 52) PBO (withdrawal) SC N=183	Maintenance (Week 52) RZB 180 mg SC N=179	Maintenance (Week 52) RZB 360 mg SC N=186	Between group diff. (RZB 180 mg SC vs PBO) % [95% CI]	Between group diff. (RZB 360 mg SC vs PBO) % [95% CI]
FACIT-F score ≥40.1	103 (31.7)	268 (41.3)	9.7 ** [3.4, 16.0]	52 (28.4)	89 (49.7)	81 (43.6)	21.3 *** [11.9, 30.7]	15.1 ** [5.7, 24.4]
IBDQ score ≥170	115 (35.4)	347 (53.3)	18.1 *** [11.7, 24.4]	78 (42.6)	107 (59.8)	101 (54.1)	17.2 *** [7.5, 27.0]	12.1 * [2.3, 22.0]
WPAI-UC 0% Overall work imp. ^{a,b}	22 (10.9)	90 (21.7)	10.9 *** [5.2, 16.7]	25 (21.9)	35 (30.7)	32 (28.6)	9.6 [-0.8, 20.1]	8.6 [-2.4, 19.6]
Work time missed ^{a,b}	86 (42.6)	237 (57.1)	14.6 *** [6.4, 22.7]	47 (41.2)	65 (57.0)	52 (46.4)	14.6 * [2.5, 26.7]	7.3 [-5.1, 19.6]
Imp. while working ^{a,b}	24 (11.9)	92 (22.2)	10.4 *** [4.5, 16.3]	27 (23.7)	40 (35.1)	34 (30.4)	12.1 * [1.2, 22.9]	9.0 [-2.1, 20.2]
Daily activity imp.	35 (10.8)	148 (22.8)	11.9 *** [7.3, 16.6]	44 (24.0)	63 (35.2)	56 (30.1)	12.0 ** [3.1, 21.0]	6.0 [-2.8, 14.8]
SF-36 PCS ≥50	108 (33.2)	308 (47.4)	14.4 *** [8.2, 20.7]	72 (39.3)	105 (58.7)	98 (52.6)	19.9 *** [10.2, 29.6]	14.0 ** [4.2, 23.9]
SF-36 MCS ≥50	94 (28.9)	245 (37.8)	8.9 ** [2.8, 15.1]	55 (30.1)	79 (44.1)	70 (37.9)	14.3 ** [4.8, 23.8]	8.3 [-1.0, 17.7]
EQ-5D-5L VAS ≥80	91 (28.0)	273 (42.1)	14.1 *** [8.0, 20.2]	61 (33.3)	80 (44.7)	73 (39.4)	12.0 * [2.5, 21.5]	6.2 [-3.3, 15.7]
EQ-5D-5L Index ≥0.825	105 (32.3)	297 (45.6)	13.5 *** [7.3, 19.8]	65 (35.5)	91 (50.8)	74 (40.0)	16.0 ** [6.1, 25.8]	4.6 [-5.0, 14.3]
Composite HRQoL endpoint ^c	16 (4.9)	81 (12.5)	7.5 *** [4.1, 11.0]	20 (10.9)	38 (21.2)	38 (20.4)	10.1 ** [2.7, 17.5]	9.3 * [2.1, 16.5]

*p<0.05. **p<0.01. ***p<0.001. ^aInduction: PBO IV, N=202; RZB 1200 mg IV, N=415. ^bMaintenance: PBO (withdrawal) SC, N=114; RZB 180 mg SC, N=114; RZB 360 mg SC, N=112. ^cProportion of patients achieving FACIT-F score ≥40.1, IBDQ score ≥170, 0% for WPAI-UC Daily Activity Impairment, SF-36 PCS ≥50 and MCS ≥50, EQ-5D-5L VAS ≥80.0 and EQ-5D-5L Index ≥0.825; employment-related scores were excluded.

For induction data, the Cochran-Mantel-Haenszel test was used to calculate p values and was adjusted for strata: Advanced Therapy-IR status (yes vs no), baseline steroid use (yes vs no), and baseline Adapted Mayo score (<=7 vs >7).

For maintenance data, the Cochran-Mantel-Haenszel test was used to calculate p values and was adjusted for strata: induction baseline Advanced Therapy-IR status (yes vs no), clinical remission status per Adapted Mayo score at Week 0 (per central read) (yes vs no) and last IV RZB induction dose (600 mg vs 1200 mg vs 1800 mg).

For induction and maintenance data, Mantel-Haenszel common rate difference was used to calculate adjusted treatment differences and 95% CIs.

CI, confidence interval; diff., difference; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Levels; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HRQoL, health-related quality of life; IBDQ, Inflammatory Bowel Disease Questionnaire; imp., impairment; IR, inadequate response; IV, intravenous; MCS, Mental Component Summary; PBO, placebo; PCS, Physical Component Summary; RZB, risankizumab; SC, subcutaneous; SF-36, Short Form 36; UC, ulcerative colitis; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment Questionnaire. <=

Table 1. Proportion of patients with UC achieving normalisation of HRQoL outcomes after treatment.

Conclusion: RZB shows greater normalisation of HRQoL compared to PBO, with results seen early during induction and subsequently continued through maintenance. These results indicate that the long-term treatment goal of HRQoL normalisation in patients with moderately to severely active UC may be achievable with RZB.

References:

1. Turner D, et al. *Gastroenterology*. 2021;160:1570–83.

Disclosure: Julian Panés received consultancy fees/honorarium from AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman, and has served on a data safety monitoring board for Alimentiv, Mirum, Sorriso, Sanofi, and Surrozen.

Parambir Dulai received research support and/or consulting for AbbVie, Abivax, Adiso, Alimentiv, Bristol Meyer Squibb, Celltrion, Genentech/Roche, Geneoscopy, Janssen, Pfizer, Takeda.

Joana Torres has received grant funding/speaker fees from and/or has participated in advisory boards for AbbVie, Galapagos, Janssen, and Pfizer.

Satoshi Tanida received speaker fees from Kissei, Mitsubishi Tanabe Pharma, Jimro, AbbVie, and Janssen.

Irina Blumenstein has received consultancy honoraria from AbbVie Deutschland, Amgen GmbH, Bristol Myers Squibb, Janssen Cilag GmbH, Fresenius Kabi Deutschland, Pharmacosmos GmbH, Pfizer GmbH, Shire

Deutschland GmbH, and Takeda Pharma GmbH; and received honoraria from AbbVie Deutschland, Biogen GmbH, DGVS, Dr. Falk Pharma GmbH, Endoakademie, Ferring Arzneimittel, Fraunhofer, Fresenius Kabi Deutschland, Kompetenznetz Darmerkrankungen, MSD Sharp Dome, Mylan GmbH, Pfizer GmbH, Janssen Cilag GmbH, Shire Deutschland GmbH, and Takeda Pharma GmbH.

Remo Panaccione has received consulting fees, speaker fees, research/educational support from, and/or advisory board member for AbbVie, Abbott, Alimentiv (formerly Robarts), Amgen, Arena, AZ, BI, BMS, Celgene, Celltrion, Cosmos, Eisai, Elan, Ferring, Galapagos, Genentech, Gilead, GSK, Janssen, Lilly, Merck, Mylan, Oppilan, Pandion, Pfizer, Progenity, Protagonist, Roche, Satisfai, Sandoz, Schering-Plough, Shire, Sublimity, Theravance, Takeda, and UCB.

Yuri Sanchez Gonzalez, Dolly Sharma, Nidhi Shukla, Valencia Remple, Jasmina Kalabic, and Patrick M Hecht are full-time employees of AbbVie and may hold AbbVie stock and/or stock options.

Funding statement: Financial support for the study was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. No honoraria or payments were made for authorship. Medical writing services provided by Kay Hallam, MSc, of Fishawack Facilitate, Ltd, part of Avalere Health and funded by AbbVie.

MP620
CLINICAL OUTCOMES OF RISANKIZUMAB THERAPY IN PATIENTS WITH ULCERATIVE COLITIS BY BASELINE DISEASE CHARACTERISTICS: RESULTS FROM THE PHASE 3 INSPIRE AND COMMAND STUDIES

C. Ha¹, M. Long², S.R. Fernandes³, T. Fujii⁴, Z. Ran⁵, J. Kalabic⁶, P. Levine⁷, S. Chen⁸, L. Cheng⁸, R. Vladea⁸, P.M Hecht⁸, F. Argüelles-Arias⁹, R. Atreya¹⁰
¹Mayo Clinic, Division of Gastroenterology and Hepatology, Scottsdale, United States of America, ²University of North Carolina, Chapel Hill, Center for Gastrointestinal Biology and Disease,, Chapel Hill, United States of America, ³Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Gastroenterology and Hepatology Department, Lisboa, Portugal, ⁴Tokyo Medical and Dental University, Department of Gastroenterology and Hepatology, Tokyo, Japan, ⁵Shanghai Jiaotong University School of Medicine, Division of Gastroenterology and Hepatology, Shanghai, China, ⁶AbbVie Deutschland GmbH Co. KG, Ludwigshafen am Rhein, Germany, ⁷Former employee of AbbVie Inc., North Chicago, United States of America, ⁸AbbVie Inc., North Chicago, United States of America, ⁹University Hospital Virgen Macarena and Seville University, Sevilla, Spain, ¹⁰Erlangen University Hospital, Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Medicine 1, Erlangen, Germany

Contact E-Mail Address: jasmina.kalabic@abbvie.com

Introduction: The efficacy and safety of risankizumab (RZB), an anti-interleukin 23p19 monoclonal antibody, as induction and maintenance therapy for adults with moderately to severely active ulcerative colitis (UC) was recently reported.^{1,2} Influences of baseline disease characteristics on clinical outcomes are important to consider when optimizing UC treatment. Herein we analyze the efficacy of RZB stratified by baseline UC disease characteristics.

Aims & Methods: In the 12-week phase 3 INSPIRE induction study (NCT03398148) patients with moderately to severely active UC were randomized 2:1 to receive intravenous (IV) RZB 1200 mg or placebo (PBO) at weeks 0, 4, and 8. Patients with clinical response to RZB IV induction at

week 12 or 24 in the phase 2b/3 induction studies were randomized 1:1:1 to receive subcutaneous (SC) RZB 180 mg, RZB 360 mg, or PBO (RZB withdrawal) every 8 weeks in the 52-week phase 3 COMMAND maintenance study (NCT03398135). This post hoc analysis evaluates clinical response, clinical remission, endoscopic remission, endoscopic improvement, and histological-endoscopic mucosal improvement (HEMI) at week 12 and 52 in subgroups stratified by baseline disease characteristics (Adapted Mayo score, pancolitis, high-sensitivity C-reactive protein [hs-CRP], Mayo endoscopic subscore [ES], and disease duration).

Subgroup	Induction Week 12		Maintenance Week 52	
	Clinical Response	Clinical Remission	Clinical Response	Clinical Remission
Patients, % (95% CI)				
AMS	PBO	31.1 (24.5, 37.6)	PBO	57.6 (47.5, 67.7)
	RZB 1200 mg IV	63.8 (59.4, 70.7)	RZB 180 mg SC	66.7 (57.5, 75.8)
			RZB 360 mg SC	63.3 (54.3, 72.4)
> 7	PBO	42.2 (33.9, 50.6)	PBO	42.6 (35.9, 56.4)
	RZB 1200 mg IV	65.1 (59.4, 70.7)	RZB 180 mg SC	70.1 (59.9, 80.4)
			RZB 360 mg SC	61.0 (50.1, 71.9)
Pancolitis	PBO	32.8 (25.8, 39.7)	PBO	44.9 (35.1, 54.7)
	RZB 1200 mg IV	58.4 (53.1, 63.7)	RZB 180 mg SC	64.9 (55.2, 74.5)
			RZB 360 mg SC	62.8 (53.0, 72.5)
No	PBO	39.1 (31.3, 46.9)	PBO	60.0 (49.3, 70.4)
	RZB 1200 mg IV	70.5 (65.4, 75.5)	RZB 180 mg SC	71.8 (62.2, 81.3)
			RZB 360 mg SC	61.9 (52.0, 71.9)
hs-CRP, mg/L	PBO	39.0 (31.8, 46.2)	PBO	58.5 (48.6, 68.5)
	RZB 1200 mg IV	68.9 (64.3, 73.5)	RZB 180 mg SC	62.2 (52.2, 72.2)
			RZB 360 mg SC	67.5 (59.0, 76.0)
> 5	PBO	30.5 (22.9, 38.1)	PBO	47.1 (36.4, 57.7)
	RZB 1200 mg IV	57.3 (51.1, 63.5)	RZB 180 mg SC	73.6 (64.3, 82.8)
			RZB 360 mg SC	53.7 (41.8, 65.7)
Mayo ES	PBO	38.3 (28.5, 48.1)	PBO	59.6 (46.3, 73.0)
	RZB 1200 mg IV	75.5 (69.6, 81.3)	RZB 180 mg SC	80.9 (69.6, 92.1)
			RZB 360 mg SC	66.7 (55.0, 78.3)
3	PBO	34.6 (28.5, 40.8)	PBO	48.9 (40.3, 57.4)
	RZB 1200 mg IV	59.0 (54.4, 63.6)	RZB 180 mg SC	63.6 (55.4, 71.8)
			RZB 360 mg SC	60.1 (51.5, 68.8)
Duration, years	PBO	42.9 (29.9, 55.8)	PBO	60.9 (40.9, 80.8)
	RZB 1200 mg IV	66.0 (57.0, 75.1)	RZB 180 mg SC	70.4 (53.1, 87.6)
			RZB 360 mg SC	75.0 (53.8, 96.2)
< 2	PBO	32.5 (22.0, 42.9)	PBO	35.3 (22.2, 48.4)
	RZB 1200 mg IV	63.4 (56.5, 70.4)	RZB 180 mg SC	59.1 (44.6, 73.6)
			RZB 360 mg SC	66.6 (54.0, 79.2)
2-5	PBO	32.3 (23.1, 41.5)	PBO	60.0 (47.6, 72.4)
	RZB 1200 mg IV	64.9 (58.0, 71.8)	RZB 180 mg SC	76.5 (64.8, 88.1)
			RZB 360 mg SC	50.0 (34.9, 65.1)
5-10	PBO	37.6 (27.8, 47.5)	PBO	55.1 (41.2, 69.0)
	RZB 1200 mg IV	63.4 (56.2, 70.6)	RZB 180 mg SC	66.7 (54.4, 78.9)
			RZB 360 mg SC	63.5 (52.5, 74.5)
> 10	PBO			
	RZB 1200 mg IV			

AMS, Adapted Mayo score; ES, endoscopic subscore; hs-CRP, high-sensitivity C-reactive protein; IV, intravenous; PBO, placebo; RBS, rectal bleeding subscore; RZB, risankizumab; SC, subcutaneous; SFS, stool frequency subscore. Data are reported using nonresponder imputation while incorporating multiple imputation to handle missing data due to COVID-19 or the geo-political conflict in Ukraine and surrounding impacted regions. Clinical response is defined as a decrease in AMS that is ≥ 2 points and $\geq 30\%$ from baseline plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 . Clinical remission is defined as SFS ≤ 1 (and not greater than baseline), RBS = 0, and endoscopic subscore ≤ 1 without evidence of friability.

Table. Clinical Response and Clinical Remission by Baseline Disease Characteristics.

Results: The induction analysis included 650 and 325 patients who received RZB 1200 mg IV and PBO IV, respectively. The maintenance analysis included 179, 186, and 183 patients who received RZB 180 mg SC, RZB

360 mg SC, and PBO (RZB withdrawal) SC, respectively. At induction week 12, the proportions of patients receiving RZB 1200 mg IV who achieved clinical response were numerically higher for the following baseline characteristic subgroups: pancolitis absence (70.5%) vs pancolitis presence (58.4%), Mayo ES of 2 (75.5%) vs Mayo ES of 3 (59.0%), and hs-CRP ≤ 5 mg/mL (68.9%) vs hs-CRP > 5 mg/mL (57.3%); the proportions of patients receiving RZB 1200 mg IV who achieved clinical remission at induction week 12 were also numerically higher for subgroups with pancolitis absence (25.3%) vs pancolitis presence (15.6%), Mayo ES of 2 (31.7%) vs Mayo ES of 3 (14.9%), and hs-CRP ≤ 5 mg/mL (23.7%) vs hs-CRP > 5 mg/mL (14.5%; Table). Differences in outcomes were not observed between subgroups stratified by Adapted Mayo score or disease duration. At week 52 of the maintenance study, there was no impact of baseline disease characteristics on achievement of clinical response and clinical remission with RZB (Table).

Conclusion: RZB induction and maintenance therapy improved clinical outcomes, regardless of baseline disease characteristics. Numerically higher RZB induction efficacy was observed for patients with no baseline pancolitis, Mayo ES of 2, and hs-CRP ≤ 5 mg/L. These trends are consistent with prior observations that patients with milder UC disease phenotypes tend to be more responsive to therapy.

References:

1. Louis E, et al. *United Eur Gastroenterol J*. 2023;11(S8):26–28. Abstract OP021.
2. Louis E, et al. *J Crohns Colitis*. 2024;18(S1):i10–12. Abstract OP06.

Disclosure: CH has served as a consultant, advisor, and/or has received education funds from AbbVie, Bausch Health, BMS, the Helmsley Charitable Trust, Janssen, Pfizer, Roivant, and Takeda.

MDL has received consulting fees and/or research grants from AbbVie, BMS, Intercept, Janssen, Lilly, Pfizer, Prometheus, Takeda, and Target RWE.

SRF has served as a consultant or advisor for AbbVie, Janssen, MSD, Takeda, Tillots, and Vitoria.

TF has received research grants and/or speaking honoraria from AbbVie, Ajinomoto, Alfresa, BI, BMS, Celgene, Celltrion, Daiichi Sankyo, EA Pharma, Eisai, Gilead, Janssen, Kissei, Kyorin, Kyowa Hakko Kirin, Lilly, Mebix, Mitsubishi Tanabe, Mochida, Nichiiko, Nippon Kayaku, Pfizer, Sanofi, Taiho, Takeda, and Zeria.

ZR has no disclosures to report.

JK, PL, SC, LC, RV, and PMH are employees of AbbVie and may hold AbbVie stock and/or stock options.

FA-A has served as a consultant and/or has received grants and speaker fees from AbbVie, Celltrion, Kern, MSD, and Takeda.

RA has served as a consultant or advisor for AbbVie, AstraZeneca, BI, Biogen, BMS, CED-Service GmbH, Celltrion, Falk Foundation, Galapagos, Gilead, InDex, Janssen-Cilag, Lilly, MSD, Roche, and Takeda.

Funding: AbbVie funded this study and participated in the study design, research, data collection, analysis, interpretation of data, reviewing, and approval of the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship. AbbVie and the authors thank all trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Morgan A Gingerich, PhD, of JB Ashtin, and funded by AbbVie, and Karen Chien, PhD, of AbbVie.

MP621

EFFECTIVENESS AND SAFETY OF RISANKIZUMAB IN PATIENTS WITH CROHN'S DISEASE: ONE-YEAR FOLLOW-UP DATA FROM A LARGE TERTIARY CENTER

A. Zinger¹, D. Choi¹, N. Choi¹, E. Fear¹, Z. Fine¹, R.D. Cohen¹, D.T. Rubin¹

¹University of Chicago Medicine, Inflammatory Bowel Disease center, Chicago, United States of America

Contact E-Mail Address: adar.zinger@mail.huji.ac.il

Introduction: Risankizumab is a selective IL23 inhibitor that was approved by the FDA for the treatment of moderately to severely active Crohn's disease (CD) in June 2022. The effectiveness of risankizumab in ustekinumab-experienced patients is of particular interest due to a similar mechanism of action. Here, we present our one-year experience of risankizumab treatment in CD patients, with a focus on the comparison between ustekinumab-naïve and ustekinumab-experienced patients.

Aims & Methods: We prospectively followed patients with CD treated with risankizumab in our center and documented their clinical disease activity using Harvey-Bradshaw Index (HBI) score at baseline and at weeks 12, 26, and 52 after treatment initiation. We included patients who were treated for active luminal disease, defined as HBI ≥ 5, fecal calprotectin (FCP) ≥ 250, steroid dependence or who had evidence of active disease per ileocolonoscopy or imaging in the effectiveness analysis. We excluded from the effectiveness cohort patients with ileostomy, J-pouch or surgery within the 6 months prior to risankizumab commencement. We recorded adverse events in all patients. Patients who stopped treatment due to ineffectiveness or intolerance were counted as non-responders for the purpose of remission-rate calculations at each time point.

Characteristic	All patients (n=253)	Patients in the effectiveness cohort (n=153)
Age, y, median (IQR)	42 (30-54)	41.5 (30.25-54)
Disease duration y, median (IQR)	14 (9-22)	12 (8-22.75)
Female sex, n (%)	151 (60.9)	89 (58.2)
White race	198 (80.2)	116 (75.8)
Smoking history, n (%)		
current	13 (5.3) 56 (23)	10 (6.6) 38 (25)
former		
Baseline HBI, median (IQR)	5 (2-8)	5.5 (3-9)
Advanced therapy naïve n (%)	28 (11)	14 (9.1)
History of bowel resection, n (%)	158 (65)	89 (59.3)
Steroid treatment at baseline, n (%)	61 (29)	48 (33.6)

Results: 253 patients were treated with risankizumab and had at least 12 weeks of follow up. 153 patients were included in the effectiveness cohort. Demographics and patient characteristics are detailed in Table 1. At week 12, 71.3% (92/129) achieved clinical remission (CR), and 63.6% (82/129) achieved steroid-free clinical remission (SFCR). At week 26, 64.5% (60/93) and 62.4% (58/93) achieved CR and SFCR respectively. At 1 year, CR rate was 53.3% (40/75), and SFCR rate was 48% (36/75). Median FCP was 385.5µg/g (IQR 168.25-905, n=33) at baseline, 102.5µg/g (IQR 39-354, n=20) at week 12, 118µg/g (IQR 40-183, n=24) at week 26, and 63µg/g (IQR 19-122, n=16) at 1 year. 79.6% (74/93) remained on risankizumab 6 months after treatment initiation, and 64.3% (52/75) of patients remained on treatment at one year. In the effectiveness cohort, 47.7% (73/153) of patients were ustekinumab-naïve, and 53.3% (80/153) were ustekinumab-experienced. SFCR rates in ustekinumab-naïve and ustekinumab-experienced patients were 73.8% (45/61) vs. 54.4% (37/68) at week 12 (p=0.0282), 67.4% (31/46) vs. 57.4% (27/47) at week 26 (p=0.3936), and 54.1 (20/37) vs. 42.1% (16/38) at one year (p=0.3588), respectively.

Minor adverse events were documented in 12.6% (32/253) of patients, including fatigue, pruritus, nausea, joint pain, and upper-respiratory tract infection. One patient had a suspected allergic reaction to the first infusion and treatment was not continued. In 1.9% (5/253) of patients, treatment was discontinued d/t adverse events. No serious adverse events were observed.

Conclusion: In this large real-world experience in patients with CD, we found that risankizumab has excellent efficacy and safety, with notable effectiveness in ustekinumab-experienced patients.

Disclosure: Nothing to disclose.

MP622

RISANKIZUMAB IS ASSOCIATED WITH GREATER IMPROVEMENTS IN SIMPLE ENDOSCOPIC SCORE FOR CROHN’S DISEASE VS USTEKINUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN’S DISEASE: POST HOC RESULTS FROM THE PHASE 3B SEQUENCE TRIAL

P. Irving¹, J.-F. Colombel², G.R. D’Haens³, M. Ferrante⁴, F. Caprioli⁵, B. Siegmund⁶, S. Van Haaren⁷, B. Kim⁷, T. Anschutz⁷, A. Garrison⁷, L. Peyrin-Biroulet⁸

¹Guy’s and St Thomas’ NHS Foundation Trust, School of Immunology and Microbial Sciences, King’s College London, Department of Gastroenterology, London, United Kingdom, ²Icahn School of Medicine at Mount Sinai, Usa, United States of America, ³Amsterdam University Medical Centers, Department of Gastroenterology, Amsterdam, Netherlands, ⁴University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁵Università degli Studi di Milano; Unit of Gastroenterology and Endoscopy, Fondazione IRCCS Ca Granda Ospedale Policlinico di Milano, Department of Pathophysiology and Transplantation, Milano, Italy, ⁶Charité-Universitätsmedizin Berlin, Medical Department, Division of Gastroenterology, Infectiology, Rheumatology, Berlin, Germany, ⁷AbbVie Inc., Chicago, United States of America, ⁸Nancy University Hospital, Department of Gastroenterology, Vandoeuvre-les-Nancy, France

Contact E-Mail Address: Peter.Irving@gstt.nhs.uk

Introduction: Risankizumab (RZB) is an interleukin [IL]-23 p19 inhibitor approved for the treatment of Crohn’s disease (CD). In the SEQUENCE head-to-head trial in patients with moderately to severely active CD, RZB was more effective in achieving endoscopic outcomes over ustekinumab (UST; IL-12/IL-23 p40 inhibitor),¹ with higher rates of endoscopic remission, regardless of CD location, observed in post hoc analyses.²⁻³ Here, we evaluate the changes from baseline in Simple Endoscopic Score for Crohn’s Disease (SES-CD) total score and SES-CD components at weeks 24 and 48.

Aims & Methods: SEQUENCE was an open-label, multicenter, randomized, efficacy assessment-blinded study in adults with moderately to severely active CD who had experienced inadequate response to ≥ 1 anti-tumor necrosis factor (TNF) therapy. Patients in the primary efficacy analysis set were randomized 1:1 to receive RZB (intravenous [IV] 600 mg induction dose at weeks 0, 4, and 8, followed by a subcutaneous [SC] 360 mg maintenance dose every 8 weeks starting at week 12) or UST (single weight-based IV induction dose, followed by a SC 90 mg maintenance dose every 8 weeks starting at week 8) up to week 48. A mandatory corticosteroid taper started at week 2. In this post hoc analysis, the mean changes from baseline in total SES-CD score and individual SES-CD components (affected surface, ulcerated surface, size of ulcers, and presence of narrowing) at weeks 24 and 48 were evaluated. Data include patients with nonmissing values at both baseline and the corresponding visit; all P values are nominal.

Results: Of 520 enrolled patients (RZB, 255; UST, 265), evaluable endoscopy data were available at week 24 for 461 patients (RZB, 238; UST, 223) and at week 48 for 379 patients (RZB, 210; UST, 169). Baseline SES-CD scores were generally similar between treatment groups (Table). At week 24, treatment with RZB resulted in greater improvement in total SES-CD from baseline compared with UST (–6.6 vs –3.9; nominal P < .0001), and similarly, improvements at week 48 were greater with RZB vs UST (–7.3 vs –4.8; nominal P = .0006).

Further, numerically greater improvements were observed with RZB vs UST across all individual SES-CD components at weeks 24 and 48, with notable differences between RZB and UST seen in the individual SES-CD components of affected surface, ulcerated surface, and size of ulcers (nominal P < .01).

Parameter, mean (SD)	Baseline ^a		Change From Baseline at Week 24 ^a		Change From Baseline at Week 48 ^a	
	RZB (n = 238)	UST (n = 223)	RZB (n = 238)	UST (n = 223)	RZB (n = 210)	UST (n = 169)
Total SES-CD	13.4 (7.1)	13.8 (7.2)	–6.6 (7.4)***	–3.9 (6.4)	–7.3 (7.4)***	–4.8 (6.8)
SES-CD components						
Affected surface	4.7 (2.9)	5.0 (3.3)	–2.5 (2.9)***	–1.5 (3.0)	–2.6 (3.0)**	–1.8 (3.1)
Ulcerated surface	3.6 (2.4)	3.7 (2.3)	–1.9 (2.4)***	–1.2 (2.0)	–2.1 (2.4)**	–1.4 (2.2)
Size of ulcers	4.3 (2.5)	4.4 (2.5)	–2.2 (2.7)***	–1.4 (2.2)	–2.5 (2.7)***	–1.7 (2.1)
Presence of narrowing	0.8 (1.3)	0.7 (1.2)	–0.1 (1.3)	0.1 (1.1)	–0.1 (1.2)	0.1 (1.1)

RZB, risankizumab; SES-CD, Simple Endoscopic Score for Crohn’s Disease; UST, ustekinumab.
Nominal P < .01; *nominal P < .001 vs UST based on Student’s t test.
^aValues only include patients with nonmissing values at both baseline and week 24.
^bValues only include patients with nonmissing values at both baseline and week 48. Patients discontinuing the study before week 24 or 48 were not included in the analysis for that respective timepoint.

Table. Total SES-CD and Individual SES-CD Components Over Time.

Conclusion: In this head-to-head study, RZB was more effective than UST in improving endoscopic disease activity per SES-CD scores in patients with CD who had experienced inadequate response to anti-TNF therapy. Differences were observed both at weeks 24 and 48 and were driven by SES-CD components of the size of ulcers, ulcerated surface, and affected surface.

References:

1. Peyrin-Biroulet L, et al. *United European Gastroenterol J*. 2023;11: 919–922. Abstract LB01.
2. Peyrin-Biroulet L, et al. *J Crohns Colitis*. 2024;18:i90–i91. Abstract DOP10.
3. Peyrin-Biroulet L, et al. *J Crohns Colitis*. 2024;18:i104–i105. Abstract DOP18.

Disclosure: PMI has received speaking fees, research grants, and/or advisory fees from AbbVie, Arena, Boehringer Ingelheim, BMS, Celgene, Celltrion, Dr Falk, Ferring, Galapagos, Genentech, Gilead, Hospira, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Samsung Bioepis, Sandoz, Sapphire, Shire, Takeda, Tillotts, Topivert, VH2, Vifor, and Warner Chilcott.

J-FC has been a consultant or advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Arena, Celgene, Celltrion, Enterome, Ferring, Genentech, Gilead, J&J, Lilly, Medimmune, Merck, Nextbiotix, Novartis, Otsuka, Pfizer, Protagonist, Second Genome, Seres, Shire, Takeda, and Theradiag. He is a speaker for AbbVie, Celgene, Ferring, and Takeda; holds stock options for Intestinal Biotech Development, and GENFIT; and has received research grants from AbbVie, J&J, and Takeda.

GD’H has been an advisor for AbbVie, Ablynx, Active Biotech AB, Agomab, Alimentiv, Allergan, Alphabio, Amakem, Amgen, AM, Applied Molecular Therapeutics, Arena, AstraZeneca, Biogen, BMS, Boehringer Ingelheim, Celltrion, DSM, Echo, Engene, Exeliom, Dr Falk, Ferring, Galapagos, Genentech/Roche, Gilead, GSK, Gossamerbio, Immunic, J&J, Kintai, Lilly, Lument, Lycera, Medtronic, MSD, Mitsubishi Tanabe, Novo Nordisk, Otsuka, Pfizer, Photopill, ProciseDx, Prodigest, Progenity, Prometheus laboratories/Nestlé, Protagonist, RedHill, Samsung Bioepis, Sandoz, Seres, Setpoint, Shire, Takeda, Teva, Tillotts, Topivert, Versant, and Vifor.

MF has received research grants from AbbVie, Biogen, EG, Janssen, Pfizer, Takeda, and Viartis; consultancy fees from AbbVie, AgomAb, Boehringer Ingelheim, Celgene, Celltrion, Janssen-Cilag, Lilly, MRM Health, MSD, Pfizer, Takeda, and ThermoFisher; and speakers' fees from AbbVie, Biogen, Boehringer Ingelheim, Dr Falk, Ferring, Janssen-Cilag, MSD, Pfizer, Takeda, Truvion, and Viartis.

FC has received consulting fees from AbbVie, Biogen, BMS, Celgene, Ferring, Galapagos, Gilead, Janssen, Lilly, Lionhealth, MSD, Mundipharma, Pfizer, Roche, and Takeda; lecture fees from AbbVie, Allergy Therapeutics, Biogen, Ferring, Janssen, Pfizer, and Takeda; and unrestricted research grants from AbbVie, Giuliani, MSD, Sofar, and Takeda.

BS has received consulting fees from AbbVie, Abivax, Arena, Boehringer Ingelheim, BMS, Celgene, Dr Falk, Endpoint Health, Galapagos, Gilead, Janssen, Lilly, Pfizer, Prometheus, and Takeda, and speaker's fees from AbbVie, BMS, CED Service, Dr Falk, Ferring, Galapagos, Janssen, Lilly, Novartis, Pfizer, and Takeda.

SvH, BK, TA, and AG are full-time employees of AbbVie and may own AbbVie stock or stock options.

LP-B has received personal fees from AbbVie, Abivax, Adacyte, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytoki, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Norgine, Nordic, Novartis, OM, ONO, OSE Immunotherapeutics, Pandion, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, VectivBio, Ventyx, Viartis, Vifor, and Ysopia.

Biomarkers and prediction of treatment responses in IBD

13:00-14:00 / Poster Stage 2

MP623

ASSOCIATION OF FAECAL CALPROTECTIN WITH SYMPTOMATIC, ENDOSCOPIC, AND CLINICAL REMISSION IN PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH MIRIKIZUMAB

S. Vermeire¹, M. Long², P.S. Dulai³, C. Ma⁴, F. Chan-Diehl⁵, R. Moses⁵, B. Zhu⁵, J. Paulissen⁶, S. Travis⁷, R. Panaccione⁴

¹University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ²University of North Carolina at Chapel Hill, Chapel Hill, United States of America, ³Northwestern University, Division of Gastroenterology and Hepatology, Chicago, United States of America, ⁴University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada, ⁵Eli Lilly and Company, Indianapolis, United States of America, ⁶Syneos Health, Morrisville, United States of America, ⁷University of Oxford, Kennedy Institute and Biomedical Research Centre, Oxford, United Kingdom

Contact E-Mail Address: severine.vermeire@uzleuven.be

Introduction: Mirikizumab (miri), a p19-directed IL-23 antibody, has been shown to be effective in patients with moderately-to-severely active ulcerative colitis (UC) in Phase 3 trials (LUCENT-1 NCT03518086; LUCENT-2 NCT03524092).¹

The relationship between symptomatic, endoscopic, and clinical remission and levels of the inflammatory biomarker faecal calprotectin (fCAL) was studied for miri-treated patients enrolled in the trials.

Aims & Methods: This post hoc analysis evaluated patients treated with intravenous (IV) miri 300mg every 4 weeks (Q4W) until week (W)12 in induction (n=868) followed by subcutaneous miri (n=365) Q4W up to W52 (miri induction responders at W12 who were rerandomized for the maintenance period) or placebo.

The improvement in fCAL at W12 and W52 between miri and placebo were compared using Cochran Mantel Haenszel, adjusting for randomization stratification factors. Missing data were imputed as nonresponse.

The relationship between achieving symptomatic, endoscopic, or clinical remission (defined in Table) and fCAL levels at W4, W12 and W52 was assessed using receiver operating characteristic (ROC) approaches. Predictability was measured by area under the ROC curve (AUC), and AUC≤0.5 indicates no predictability. Optimal fCAL threshold was obtained based on Youden Index.

Results: Greater proportions of miri-treated patients compared to placebo achieved fCAL≤250 ug/g at W4, W12, and W52. A total of 19.0% vs. 12.5%, 34.3% vs. 20.1%, 50.7% vs 19.3% patients achieved fCAL≤250 ug/g at W4, W12, and W52 miri vs. placebo, respectively. Greater proportions of patients achieving symptomatic, endoscopic, and clinical remission reached the predefined threshold of fCAL≤250 ug/g or the optimum fCAL threshold obtained from the ROC (see Table footnote) in this study compared with those not achieving the endpoints (Table).

W4 fCAL levels had 70.5% predictability for W12 endoscopic remission and 64.9% for clinical remission, but lower predictability for symptomatic remission (59.1%). W12 fCAL levels had 83.0% predictability for W12 endoscopic remission, 78.5% for clinical remission, and 67.4% for symptomatic remission.

W52 fCAL levels had higher predictability for W52 endoscopic (76.6%) and clinical remission (72.7%) than for symptomatic remission (62.3%).

Week	Symptomatic Remission		Endoscopic Remission		Clinical Remission	
	Achieving (N=360)	Not Achieving (N=406)	Achieving (N=290)	Not Achieving (N=478)	Achieving (N=193)	Not Achieving (N=571)
Week 4						
fCAL ≤ 250 ug/g	109 (30.3)	79 (19.5) [†]	122 (42.1)	65 (13.6) [†]	77 (39.9)	110 (19.3) [†]
Optimum fCAL threshold	193 (53.6)	159 (39.2) [†]	158 (54.5)	106 (22.2) [†]	103 (53.4)	168 (29.4) [†]
Week 12						
fCAL ≤ 250 ug/g	200 (55.0)	116 (29.2) [†]	216 (73.7)	100 (21.2) [†]	151 (75.9)	164 (29.2) [†]
Optimum fCAL threshold	237 (65.1)	149 (37.4) [†]	216 (73.7)	93 (19.7) [†]	151 (75.9)	157 (27.9) [†]
Week 52						
fCAL ≤ 250 ug/g	161 (70.0)	22 (50.0) [*]	151 (80.3)	38 (40.9) [†]	133 (80.1)	49 (45.8) [†]
Optimum fCAL threshold	161 (70.0)	21 (47.7) [*]	134 (71.3)	24 (25.8) [†]	129 (77.7)	42 (39.3) [†]

Table. Faecal Calprotectin Normalization at Week 12 in LUCENT-1 and Week 52 in LUCENT-2 per achievement of efficacy outcomes.

ES=Endoscopic Subscore; fCAL=Faecal Calprotectin; RB = Rectal Bleeding; SF=Stool Frequency.

Data shown as n(%). * $p < 0.05$ and $^{\dagger}p < 0.001$ from Fisher's exact test. Symptomatic remission: SF=0 or 1 with a ≥ 1 -point decrease from baseline, RB=0. Endoscopic remission: ES=0 or 1 (excluding friability). Clinical remission: SF=0 or 1 with a ≥ 1 -point decrease from baseline, RB=0, and ES=0 or 1 (excluding friability). Optimal fCAL for symptomatic/endoscopic/clinical remission: $\leq 585/\leq 390/\leq 415$ ug/g at Week 4; $\leq 365/\leq 230/\leq 230$ ug/g at Week 12; $\leq 230/\leq 150/\leq 205$ ug/g at Week 52.

Conclusion: These results support the use of fCAL as an early predictor of clinical outcomes and as a non-invasive biomarker for predicting clinical outcomes.

References: 1. D'Haens G, et al. *NEJM* 2023;388(26):2444-2455. DOI: 10.1056/NEJMoa2207940

Disclosure: SV has received research support from AbbVie, Johnson & Johnson, Pfizer, Galapagos, and Takeda; lecture fees from AbbVie, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Ferring, Galapagos, Genentech-Roche, Gilead, Janssen, Johnson & Johnson, Lilly, Materia Prima, Merck Sharp & Dohme, Pfizer, Takeda, Tillotts Pharma, and Zealand Pharma; and consulting fees from AbbVie, AbolerIS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, Johnson & Johnson, Lilly, Materia Prima, MiroBio, Morphic, MrMHealth, Mundipharma Merck, Pfizer, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance, Tillotts Pharma, and Zealand Pharma.

ML has served as a Consultant for AbbVie, Pfizer, Takeda, Lilly, Bristol-Meyers Squibb, Target RWE, and Prometheus and has received research support from Pfizer, Takeda, and Janssen.

PD has consulted for Abbvie, Abivax, Adiso, Bristol Myers Squibb, GSK, Janssen, Lilly, Pfizer, and Takeda; grant support from Bristol-Myers Squibb, Janssen, Pfizer, and Takeda; Licensing royalties from PreciDiag.

CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Pendopharm, Pfizer, Prometheus Biosciences Inc., Roche, Sanofi, Takeda, Tillotts Pharma; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Eli Lilly, Ferring, Fresenius Kabi, Janssen, Organon, Pendopharm, Pfizer, Sanofi, Takeda, Tillotts Pharma; royalties from Springer Publishing; research support from AbbVie, Ferring, Pfizer.

F C-D, RM, and BZ are employees and minor shareholders of Eli Lilly and Company.

JP is an employee of Syneos Health.

ST has served as a paid consultant to AbbVie, Allergan, Amgen, Asahi,

Bioclinica, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, ChemoCentryx, Cosmo, Enterome, Equillum, Ferring, GSK, Genentech, Genzyme, Giuliani SpA, Immunocore, Immunometabolism, Janssen, Lilly, MSD, Merck, Mestag, Neovacs, Novo Nordisk, NPS Pharmaceuticals, Pfizer, Proximagen, Receptos, Roche, Satisfai Health, Sensyne Health, Shire, Sigmoid Pharma, Sorriso, Takeda, Topivert, UCB, VHSquared, Vifor, and Zeria; he has received grants and/or has grants pending from AbbVie, ECCO, Helmsley Trust, IOIBD, Janssen, Lilly, Norman Collisson Foundation, Pfizer, UCB, UKIERI, and Vifor; he has received honoraria from AbbVie, Amgen, Biogen, Ferring, Lilly, Pfizer, and Takeda; and he has had travel/accommodation expenses covered or reimbursed by AbbVie, Amgen, Biogen, Ferring, Lilly, Johnson & Johnson, Pfizer, and Takeda.

RP reports personal fees from Abbott, AbbVie, Alimentiv [formerly Robarts], Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, HC3 Communications, Janssen, Meducom, Merck, Mylan, Oppilan, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Receptos, Roche, Sandoz, Satisfai Health, Schering-Plough, Shire, Sublimity Therapeutics, Takeda, Theravance Biopharma, Trellus Health, and UCB.

MP624

HUMAN EXTRACHROMOSOMAL CIRCULAR DNA (ECCDNA) IS A NOVEL BIOMARKER IN INFLAMMATORY BOWEL DISEASE

F. Di Vincenzo¹, V. Petito², D. Gervoska³, A. Piazzesi⁴, A. Russo⁵, L. Turchini¹, L. Masi¹, L.R. Lopetuso⁶, B. Regenber⁷, A. Gasbarrini⁸, L. Putignani⁵, M.J. Arauzo-Bravo^{9,3,10}, F. Scalfaferr¹
¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS, IBD Unit-UOS Malattie Infiammatorie Croniche Intestinali, CEMAD, Digestive Diseases Center, Roma, Italy, ²Catholic University of Sacred Heart, Department of Internal Medicine, Gastroenterology Division, Roma, Italy, ³Biogipuzkoa Health Research Institute, Computational Biology and Systems Biomedicine, San Sebastian, Spain, ⁴Bambino Gesù Children's Hospital, IRCCS, Multimodal Laboratory Medicine Research Area, Unit of Human Microbiome, Rome, Italy, ⁵Bambino Gesù Children's Hospital, IRCCS, Department of Diagnostic and Laboratory Medicine, Unit of Microbiology and Diagnostic Immunology, Unit of Microbiomics, Rome, Italy, ⁶Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Surgical and Medical Sciences Department, Roma, Italy, ⁷University of Copenhagen, Department of Biology, SECTION FOR ECOLOGY AND EVOLUTION, Copenhagen, Denmark, ⁸Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁹University of Basque Country (UPV/EHU), Department of Cell Biology and Histology, Faculty of Medicine and Nursing, Leioa, Spain, ¹⁰IKERBASQUE, Calle María Díaz Harokoa 3, Basque Foundation for Science, Bilbao, Spain

Contact E-Mail Address: federica.divincenzo30@gmail.com

Introduction: Inflammatory Bowel Diseases (IBD) are chronic inflammatory disorders of the gastrointestinal tract, characterized by a relapsing-remitting course, primarily comprising Ulcerative Colitis (UC) and Crohn's Disease (CD). These conditions, which lack a clearly defined cause, pose significant interest to the medical community for identifying reliable predictors of disease progression and treatment response.

The specific profile of extrachromosomal circular DNA fragments (eccDNA) has emerged as a promising diagnostic and prognostic biomarker for

various types of cancer. However, their role in IBD patients, including the specific gene fragments they carry, has not been thoroughly investigated so far.

Aims & Methods: This monocentric, observational, case-controlled study enrolled consecutive patients diagnosed with IBD and non-IBD healthy controls undergoing colonoscopy for colorectal cancer screening at Fondazione Policlinico Universitario “A: Gemelli”. Disease activity in IBD patients was assessed using different scoring systems: the Partial Mayo Score (PMS) and Mayo Endoscopic Subscore (MES) for UC, and the Harvey-Bradshaw Index (HBI) and Simple Endoscopic Score for CD (SES-CD) for CD. Colonic biopsies were obtained from both inflamed and healthy mucosa of IBD patients and from non-IBD controls. Purification of human eccDNA was optimized according to the Circle-Seq method, including eccDNA enrichment, removal of linear and mitochondrial DNA, rolling-circle amplification and sequencing; subsequently, eccDNAs were identified using Circle Finder software. The study compared the relative abundances of genes within eccDNAs between IBD patients and non-IBD controls, focusing on those that were differentially abundant, defined as *Differentially Produced per Gene eccDNAs (DPpGCs)*.

Results: 133 patients with IBD (69 with CD, 64 with UC) and 17 healthy controls (HC) were included in the study. Colonic mucosal samples from IBD patients revealed a higher average abundance of eccDNAs compared to samples from HC. This increase was consistent across all chromosomes, suggesting a global upregulation of eccDNA production throughout the human genome. Furthermore, there was a slight yet statistically significant trend towards larger eccDNAs sizes in IBD patients compared to HC. Even when considering only eccDNA derived from genic elements (“genic eccDNAs”), IBD patients exhibited a significantly higher abundance of eccDNA in the gut compared to non-IBD controls.

Further analysis focused on DPpGCs with a fold change $>1 \log_2$ between IBD patients and HC, with a significance threshold of $p < 0.01$. Forty-nine genes were found to be enriched in IBD patients, including GRID2 and NRG3. Similarly, in CD patients, 176 genes, such as FGF14, SOX5, and ZBTB20, were significantly enriched compared to HC. In UC patients, 31 genes, including NRG1, SPOCK3, and ATP13A4, showed enrichment compared to HC. Moreover, IBD patients in endoscopic remission (SES-CD < 3 , EMS of 0-1) tended to have fewer eccDNAs in their intestines compared to those with active disease, although this difference did not reach statistical significance. Five DPpGCs, including FARS2, HERC3, and PNK2, were identified when applying the aforementioned criteria.

Conclusion: In conclusion, our study unveils a distinct pattern of eccDNA production specific to IBD. We showed that circles harboring specific genes can distinguish UC and CD from healthy controls with statistical significance ($p < 0.01$). We suggest that eccDNA identification may serve as a novel diagnostic biomarker for IBD patients.

Disclosure: Nothing to disclose.

MP625

ANALYSIS OF IMMUNOLOGICAL VARIABLES IN EX VIVO TOFACITINIB-TREATED HUMAN BIOPSIES FROM ACTIVE ULCERATIVE COLITIS PATIENTS TO PREDICT CLINICAL RESPONSE (THE AVATAR STUDY)

S. Onali¹, A. Di Petrillo¹, P. Soddu², A. Favale¹, I. Ibba², M. Demurtas², N. Raho¹, E. Marrocchi³, D. Amodio³, P. Palma³, S. Milenkovic¹, M. Ceccarelli¹, M.C. Fantini¹

¹Università degli Studi di Cagliari, Monserrato, Italy, ²Azienda Ospedaliera Universitaria di Monserrato, Monserrato, Italy,

³Università di Tor Vergata, Roma, Italy

Contact E-Mail Address: massimoc.fantini@unica.it

Introduction: Ulcerative colitis (UC) is characterized by chronically relapsing inflammation of the colonic mucosa. Tofacitinib (TOFA) is a pan-inhibitor of the JAK kinases, a family of intracellular kinases involved in the signal transduction pathway of multiple inflammatory signals. Despite the efficacy shown by TOFA in inducing and maintaining remission in moderately-to-severely active UC, rates of primary non response remains high. We propose a new method to identify predictors of responsiveness to TOFA based on “ex-vivo” challenge of organ cultures from biopsies collected from candidate patients.

Aims & Methods: Baseline biopsies from inflamed areas of UC patients with active disease and candidate to receive TOFA 10mg b.i.d. for 8 weeks, were used for “ex-vivo” organ culture and stimulated with TOFA 20 μ M and 200nM or left untreated. After 24 hours, proteomic analysis was performed and quantitative expression of 92 inflammation-related human proteins (Olink® Human Inflammation panel) was correlated with week 8 clinical response defined by Modified Mayo Score (MMS). Intestinal biopsies were also collected at baseline and at 8 weeks for proteomic analysis. To decipher the nature of TOFA's effects, both unsupervised and supervised machine learning (ML) methods were employed (sklearn module, Python). The K-means method was used for unsupervised learning followed by a supervised ML approach to classify week 8 responders and non-responders. Data were transformed in into a second-order polynomial format and logistic regression was used for modelling.

Results: Between January 2022 and January 2023, 17 UC patients were enrolled. At week 8, 13/17 (76.5%) patients treated with TOFA showed clinical response. Unsupervised ML, utilizing proteomic data from organ cultures stimulated with TOFA 200nM, achieved a 90% success rate in predicting a positive clinical response. This prediction was based on forming two distinct clusters, with significant contributions from key variables such as CASP-8, CCL19, CCL20, CD5, CXCL9, EN-RAGE, GDNF, HGF, IL-18R1, MCP-1, MCP-2, MCP-4, MMP-10, OPG, PD-L1, STAMBP, TNFRSF9, TRANCE, TWEAK, and VEGFA. In our supervised ML approach, logistic regression was employed with 30 shuffle splits to refine the predictive model. The mean precision value for the best profile, logistic regression with Ridge regularization, was 0.73. We also discovered that transforming the dataset into second-order polynomial format significantly enhanced the model's performance. In this case, the most effective logistic regression model achieved a mean precision score of 0.82.

Conclusion: Our predictive model demonstrates a high level of precision in identifying positive treatment responses, emphasizing the potential of further dataset expansion and the use of advanced machine-learning to predict response in TOFA-treated UC patients.

Disclosure: This study is supported by Pfizer.

MP626

WITHDRAWN

MP627

THE PREDICTIVE VALUE OF IRON DEFICIENCY ANAEMIA ON THE ONE-YEAR DISEASE COURSE IN INFLAMMATORY BOWEL DISEASE PATIENTS BEING IN CLINICAL AND BIOCHEMICAL REMISSION

T. Resál¹, P. Bacsur¹, B. Farkas², A. Balint¹, K. Farkas¹, R. Bor¹, A. Fabian³, E. Ivány¹, S. Zoltán¹, T. Tóth¹, D. Lupas⁴, M.M. Hajdune Dr. Varga⁴, K. Csefko⁵, T. Molnár⁶
¹University of Szeged, Department of Medicine, Szeged, Hungary, ²SZTE SZAKK Center for Gastroenterology, Department of Internal Medicine, Szeged, Hungary, ³University of Szeged, First Department of Medicine, Szeged, Hungary, ⁴Réthy Pál Kórház, Békéscsaba, Hungary, ⁵Réthy Pál Hospital, Gastroenterology, Békéscsaba, Hungary, ⁶University Of Szeged, Department of Internal Medicine, Szeged, Hungary

Contact E-Mail Address: resal.tamas@med.u-szeged.hu

Introduction: Iron deficiency anaemia (IDA) is a common comorbidity in inflammatory bowel diseases (IBD). Previous studies have already showed the predictive value of anaemia on hospitalization and mortality rates, however, these studies did not focus on the effect of IDA on patients with clinical and biochemical remission, however, due to the ethiopathology, certain effects are hypothesized.

Aims & Methods: This was a multicenter retrospective real-life cohort study assessing the effect of IDA on clinically and biochemically inactive IBD patients. We included patients from the outpatient setting who has been followed-up for a year. Patients with need of blood transfusion at baseline were excluded. IDA was defined as no clinical and biochemical activity, ferritin <30 µg/mL and transferrin saturation <20% with the presence of anemia. Primary outcome was disease aggravation, defined as need of change in the current treatment/hospitalization/abdominal surgery. Secondary outcome was proportion of major complications, defined as need of hospitalization/abdominal surgery. Pearson’s chi squared sample size calculation (n=720) was performed on our pilot results based on 200 IBD patients.

Results: In total, 711 patients (median age: 43.1 years [IQR: 32.3 - 49.6]; male/female ratio: 332/379; CD: 397, UC: 311; IDA/non-IDA 85/623) were enrolled. Mean follow-up period was 1.1±0.28 years. The presence of IDA increased the risk of disease aggravation (OR: 1.7) and major complications (OR: 2.8). Furthermore, male sex (OR: 0.6) and older age (OR: 0.8) were protective, and ileocecal resection (OR: 2.0) and higher C-reactive protein levels (OR: 1.5) increased the disease aggravation.

Conclusion: IDA predicts the risk of relapse at some degree in patients with clinical and biochemical remission in the outpatient setting. IDA may help to identify underlying disease activity in patients with clinical and biochemical remission in time, therefore, we recommend to be implemented in the treat-to-target approach.

Disclosure: Nothing to disclose.

MP628

PROGNOSTIC VALUE OF THE VEDOLIZUMAB CROHN’S DISEASE CLINICAL DECISION SUPPORT TOOL IN A REAL-WORLD COHORT

X.Y. Choon¹, C. White¹, E. Sharma¹, R. Dart¹, K.B. Gecse¹, J. Mawdsley¹, S.H. Anderson¹, S. Ray¹, P. Irving¹, M.A. Samaan¹
¹Guy’s and St Thomas’ NHS Foundation Trust, Gastroenterology, London, United Kingdom

Contact E-Mail Address: xin.choon@gstt.nhs.uk

Introduction: The vedolizumab clinical decision support tool (VDZ-CDST) was developed and validated as a clinical prediction tool for vedolizumab (VDZ) use in Crohn’s disease (CD). It has demonstrated prognostic value

with the ability to stratify patients by probability of clinical and endoscopic response to VDZ at week 26. We examined the applicability of the tool in a real-world dataset of VDZ treated CD patients.

Aims & Methods: We performed a retrospective data collection and analysis at a single tertiary centre on patients who had started VDZ between January 2015 to February 2022. We collected baseline data to calculate the CDST: prior exposure to tumour necrosis factor (TNF) antagonists, prior surgery for CD, prior fistulating disease, baseline albumin and C reactive protein (CRP). Our main endpoints were treatment persistence at 12 and 24 months. We also retrieved the following parameters of disease activity at 12 month follow up: CRP, faecal calprotectin (FCP), mucosal healing (defined as ulcer free endoscopy) and progression to surgery. Chi square for trend was used for 12 month persistence and Kaplan-Meier curves with log rank test for trend was used for 24 month persistence. ANOVA was used for comparing continuous variables.

Results: 130 patients were included. 74.6% had prior TNF antagonist exposure, median baseline CRP was 4 mg/L, and median albumin was 43 g/L. Using the CDST at baseline, 3 groups were defined – 9 (7%) were low, 51 (39%) were intermediate, and 70 (54%) had a high probability of treatment response. One year treatment persistence rates were 56%, 69%, and 80% in the low, intermediate and high probability groups respectively (p=0.048). Kaplan-Meier analysis demonstrate increasing rates of persistence at 24 months in keeping with CDST-defined probability of response (p=0.035). There were also statistically significant differences in outcomes across the 3 groups, with lower CRP at 12 months, higher rates of mucosal healing and lower rates of progression to surgery in the high probability group versus the low and intermediate groups.

	Low probability group n = 9 (%)	Intermediate probability group n = 51 (%)	High probability group n = 70 (%)	p value
Treatment persistence at 12 months	5 (56)	35 (69)	56 (80)	0.048
CRP at 12 months, median (mg/L)	10	3	2	0.015
FCP at 12 months, median (µg/g)	223	209	92	0.59
Mucosal healing	1/5 (20)	13/28 (46)	28/37 (76)	0.0023
Surgery for CD	3 (33)	16 (31)	11 (16)	0.042

Conclusion: The prognostic value of the VDZ-CDST appears valid in a real-world CD cohort with high rates of prior TNF antagonist exposure. The tool has demonstrated predictive ability for long-term treatment persistence as well as measures of biochemical and endoscopic activity. Our study is consistent with a growing body of published evidence on the applicability of CDST and suggests a role for CDST in guiding therapeutic decision making in routine clinical practice.

References: 1. Dulai PS, Boland BS, Singh S, Chaudrey K, Koliani-Pace JL, Kochhar G, Parikh MP, Shmidt E, Hartke J, Chilukuri P, Meserve J. Development and validation of a scoring system to predict outcomes of vedolizumab treatment in patients with Crohn’s disease. Gastroenterology. 2018 Sep 1;155(3):687-95.
2. Dulai PS, Amiot A, Peyrin-Biroulet L, Jairath V, Serrero M, Filippi J, Singh S, Pariente B, Loftus EV Jr, Roblin X, Kane S, Buisson A, Siegel CA, Bouhnik Y, Sandborn WJ, Lasch K, Rosario M, Feagan BG, Bojic D, Trang-Poisson C, Shen B, Altwegg R, Sands BE, Colombel JF, Carbonnel F; GETAID OBSERV-IBD, VICTORY Cohorts Collaboration*. A clinical decision support tool may help to optimise vedolizumab therapy in Crohn’s disease. Aliment Pharmacol Ther. 2020 Mar;51(5):553-564. doi: 10.1111/apt.15609. Epub 2019 Dec 22. Erratum in: Aliment Pharmacol Ther. 2021 Apr;53(8):963. PMID: 31867766; PMCID: PMC7028036.

Disclosure: Nothing to disclose.

MP629

PREDICTING RESPONSE TO ANTI-TNF THERAPY USING THE BLOOD TRANSCRIPTOME IN CROHN'S DISEASE PATIENTS

F. Mol¹, S. van Zon², V. Joutstra², A.Y. Li Yim^{3,1}, P. Henneman³, I. Hageman¹, A. te Velde¹, T. de Waard⁴, E. Levin⁴, A. Noble⁵, T. Chapman^{6,5}, C. McGregor⁵, A. Adams⁵, J. Satsangi⁵, G.R. D'Haens², W.J. de Jonge^{1,7}

¹Amsterdam UMC, Tytgat Institute for Liver and Intestinal Research, Amsterdam, Netherlands, ²Amsterdam UMC, Gastroenterology and hepatology, Amsterdam, Netherlands, ³Amsterdam UMC, Clinical Genetics, Amsterdam, Netherlands, ⁴Horizon BV, Delft, Netherlands, ⁵Gastrointestinal Unit, Translational Gastroenterology Unit, Nuffield Department of Medicine, John Radcliffe Hospital, University of OXFORD, Oxford, United Kingdom, ⁶St Richard's and Worthing Hospitals, Gastroenterology,, West Sussex, United Kingdom, ⁷University of Bonn, Department of Surgery, Bonn, Germany

Contact E-Mail Address: femke.mol@amsterdamumc.nl

Introduction: Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract. Current therapies include monoclonal antibodies, such as adalimumab (ADA) and infliximab (IFX), that target the inflammatory cytokine tumor necrosis factor alpha, collectively known as anti-TNF. While it has been shown that anti-TNF is effective at inducing and maintaining remission in patients with CD, this treatment fails in up to 40% of CD patients. Ineffective treatment results in disease progression and complications, emphasizing the need to understand mechanisms behind non-response and to define prognostic biomarkers. We previously identified differences in the peripheral blood DNA methylome associated with response and non-response. However, it is unclear how differential methylation can affect the transcriptome.

Aims & Methods: In this study, we assembled a cohort of 58 adult CD patients that were scheduled to start ADA or IFX treatment. Response to treatment was assessed after 6-9 months based on strict combination of endoscopic ($\geq 50\%$ reduction SES-CD), biochemical (CRP reduction $\geq 50\%$ or CRP ≤ 5 mg/L and FCP reduction $\geq 50\%$ or FCP ≤ 250 $\mu\text{g/g}$) and clinical criteria (≥ 3 point drop in HBI or HBI ≤ 4 without corticosteroids). Whole peripheral blood leukocytes (PBL) were collected from patients before baseline endoscopy or at first infusion/injection, and 6-9 months later. mRNA was extracted using QIAasympyphony system, converted into cDNA and sequenced in a paired-end format on the Illumina NovaSeq at the Amsterdam UMC Core Facility Genomics. Differential expression (DE) analysis was carried out within the R statistical environment (v 4.3.1) using the Bioconductor package DESeq2 (v 1.40.2).

Results: Prior to the start of treatment, we identified 504 and 750 differentially expressed genes (DEGs) distinguishing responders from non-responders in ADA and IFX cohorts, respectively. While 13 genes presented response-associated differential expression for both ADA and IFX, no overall correlation was observed between response-associated differential expression profiles. However, based on canonical pathway analysis, we found that expression differed in both ADA and IFX responders and non-responders at the level of neutrophil degranulation, B-cell receptor regulation, and cell growth and differentiation.

Conclusion: Our data suggest that response to ADA and IFX can be associated to the PBL transcriptome prior to treatment. Furthermore, while the differences between responders and non-responders to ADA and IFX display limited overlap in DEGs, we observe that response-associated pathways are shared.

Disclosure: Nothing to disclose.

MP630

ANALYSIS OF CLINICAL PREDICTORS OF EARLY POSTOPERATIVE ENDOSCOPIC RECURRENCE REVEALS THE IMPACT OF EXPOSURE TO BIOLOGICS BEFORE SURGERY IN CROHN'S DISEASE

M. Allez¹, N. Hammoudi¹, S. Brand², S. Nancey³, P. Wils⁴, X. Treton⁵, A. Buisson⁶, F. Carbonnel⁷, M. Fumery⁸, A. Bourreille⁹, E. Louis¹⁰, L. Peyrin-Biroulet¹¹, X. Hebuterne¹², M. Serrero¹³, G. Pineton de Chambrun¹⁴, M. Bezault¹⁵, J. Lambert², P. Seksik¹⁶

¹Hopital Saint-Louis APHP, Université Paris Cité, Gastroenterology, Paris, France, ²Hopital Saint-Louis APHP, Université Paris Cité, Statistics, Paris, France, ³CHU Lyon, Dept. de Gastroenterologie, Pierre Benite, France, ⁴CHRU Lille, Gastroenterology, Lille, France, ⁵Hopital Beaujon, Asnieres, France, ⁶CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France, ⁷CHU Bicetre - Dept. de Hepato-Gastroenterologie, CHU Bicetre; Le Kremlin Bicetre/FR - Dept. de Hepat, Dept. de Hepato-Gastroenterologie, Le Kremlin Bicetre, France, ⁸Amiens University Hospital, Gastroenterology department, Amiens, France, ⁹Hopital Hotel Dieu Et Hme - Hge Aile Sud, Gastroenterologie, Nantes Cedex 1, France, ¹⁰CHU Liège and Liège University, Gastroenterology, Liège, Belgium, ¹¹Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ¹²Hospital Archet 2, Nice, Department of gastroenterology and clinical nutrition, Nice, France, ¹³Hopital Nord, Gastroenterology, Marseille, France, ¹⁴Montpellier University Hospital, Department of Gastroenterology, Montpellier, France, ¹⁵REMIND, Paris, France, ¹⁶Gastroenterology & Nutrition Department, Gastroenterology and Nutrition Unit, Paris, France

Contact E-Mail Address: matthieu.allez@aphp.fr

Introduction: Patients with ileocolonic Crohn's disease are often treated with biologics. However, many patients develop complications and need surgery. Ileocolonic resection (ICR) is associated with a very high risk of postoperative recurrence.

Aims & Methods: The aim of this study was to identify predictors of early postoperative endoscopic recurrence. This is a prospective multicentre international study. All patients who had ICR for CD were eligible. Demographic and clinical data, as well as past-medical history, including prior exposure to immunosuppressant and biologics (anti-TNFs, ustekinumab, vedolizumab, others), number of lines of biologics used before surgery, were recorded. A prophylactic treatment was discussed according to a pre-established algorithm, based on the following risk factors: current smoking, previous ICR, penetrating phenotype and active perianal disease. Endoscopic recurrence was defined as a Rutgeerts score $\geq 2b$. The identification of factors associated with the endoscopic recurrence was performed by logistic regression model.

Results: 874 patients have been included between 2010 and December 2023 patients; 625 CD patients who had a colonoscopy performed within the year after surgery were included in the analysis. The median [IQR] age at surgery was 34 years [26.00, 45.00], 308 (49.3%) patients were male. Median disease duration was 7.70 years [2.90, 14.10].

At time of surgery, 202 patients (32.3%) were active smokers and 167 (26.7%) were ex-smokers. Three quarters of the patients (n=461, 74%) had been exposed to at least one biologic therapy before surgery. In most cases, only one anti-TNF agent was used before surgery (n=334); 136 patients (21%) received two biologics or more.

Half of the patients (n=311) received a prophylaxis after surgery, with thiopurines alone (n=68) or a biologic therapy [n=254: Anti-TNF (n= 158), ustekinumab (n=76), vedolizumab (n=20)]. The median time between

surgery and colonoscopy was 6.40 months [6.00, 7.40]. Endoscopic recurrence (modified Rutgeerts score ≥ 2), occurred in 235 patients (37.6%). In multivariate analysis, active smoking [OR 2.74 (95%CI: 1.73, 4.37), $p < 0.001$], exposure to biologics before surgery [OR 2.66 (95%CI: 1.51, 4.78), $p < 0.001$], prior ICR [OR 1.69 (95%CI: 1.03, 2.77) $p = 0.038$], male gender [OR 1.79 (95%CI: 1.2, 2.63), $p = 0.004$], and a temporary stoma [OR 2.97 (95%CI: 1.40, 6.59), $p = 0.004$] were associated with an increased risk of postoperative endoscopic recurrence; while prophylaxis by biologics was protective [OR 0.44 (95%CI: 0.25, 0.78), $p < 0.001$].

Conclusion: In this large multicentre prospective study of CD patients included at time of an ileocolonic resection, we show that smoking and prior exposure to biologics are the strongest predictors of early postoperative recurrence. To our knowledge, this is the first study demonstrating the impact of prior exposure to biologics on the risk of postoperative recurrence in CD.

Disclosure: Nothing to disclose.

MP631

UNMASKING CROHN’S DISEASE: NOVEL ANTI-GLYCAN ANTIBODIES MAY IMPROVE DIAGNOSTIC ACCURACY WHILE PROVIDING PROGNOSTIC VALUE, ESPECIALLY IN ASCA-SERONEGATIVE PATIENTS

J. Yang¹, A. Aikins², D. Alfego², K.Y. Chun¹
¹Labcorp, Specialty Medicine, Calabasas, United States of America, ²Labcorp, Center for Excellence in Data Science, Artificial Intelligence and Bioinformatics, Burlington, United States of America

Contact E-Mail Address: yangj5@labcorp.com

Introduction: Anti-Glycan Antibodies (AGA), gASCA (Anti-*Saccharomyces cerevisiae*) together with the more novel ACCA (Anti-chitobioside), ALCA (Anti-laminaribioside), and AMCA (Anti-mannobioside) are antibodies specific to Crohn’s Disease (CD) that target glycans (polysaccharides) found in microorganisms, such as *C. albicans* and *S. cerevisiae* and may alter the immune response to fungal dysbiosis. The presence of AGA in patient serum differentiates CD from ulcerative colitis (UC) and non-IBD with about 85% specificity. Moreover, concomitant positivity of 2 or more AGA increases CD specificity (>95%) and predicts faster progression to more severe disease with strictures and fistulae.

This diagnostic accuracy of AGA has been validated by more than a dozen independent, peer-reviewed studies in over 4000 IBD patients.¹ More recent utilization and real-life performance of AGA in clinical practice have yet to be characterized.

Aims & Methods: We assessed the utilization and positivity of 4 AGA in 163,364 patient samples when ordered as the IBD Expanded Profile from January 2012 through March 2024. The antibodies, gASCA, ACCA, ALCA and AMCA, are detected in serum, quantitated by enzyme-linked immunosorbent assays (ELISA) using phophomannan, chitobioside, laminaribioside, and mannobioside, and reported in units where >50, >90, >60, and >100, respectively, are positive. gASCA utilizes an improved purified form of mannan and is comparable to conventional ASCA.

Results: Of a total of 163,394 patient samples, one quarter (25.2%) were positive for at least one AGA. Isolated positivity of only one AGA was found in 18.3% where gASCA alone was the most common (7.0%) followed by AMCA (6.1%).

Concomitant positivity of 2 or more AGA occurred in only 7.0% of all samples with the most frequent co-occurrences, ALCA + AMCA and AMCA + gASCA. Individual AGA frequencies were gASCA (11.3%), AMCA (11.3%), ALCA (7.2%), and ACCA (4.3%). Median antibody levels (interquartile range) for positive samples were: gASCA 66.0 (57.0-84.0), ACCA 124.0 (104.0-167.0), ALCA 76.0 (67.0-92.0) and AMCA 147.0 (118.0-205.0).

Isolated Positivity of 1 AGA	n (% of total)	Concomitant Positivity of 2 AGA	n (% of total)	Concomitant Positivity of 3 or 4 AGA	n (% of total)
ACCA only	3623 (2.2%)	ALCA + gASCA only	1,567 (1.0%)	ALCA + gASCA + AMCA only	1,257 (0.8%)
ALCA only	4832 (3.0%)	ALCA + AMCA only	2,609 (1.6%)	ALCA + gASCA + ACCA only	185 (0.1%)
AMCA only	9888 (6.1%)	ACCA + ALCA only	300 (0.2%)	ALCA + AMCA + ACCA only	546 (0.3%)
gASCA only	11,508 (7.0%)	AMCA + gASCA only	2,466 (1.5%)	gASCA + AMCA + ACCA only	370 (0.2%)
		ACCA + gASCA only	743 (0.5%)	gASCA + AMCA + ACCA + ALCA	437 (0.3%)
		ACCA + AMCA only	891 (0.5%)		

Table 1. Anti-Glycan Antibodies in 163,394 Patient Serum Samples.

Conclusion: Serum AGA were frequently positive in over 160,000 patient samples. One quarter (25.2%) of all samples were positive for at least one AGA supporting their potential usefulness in differentiating CD from UC and non-IBD. Most positivity (18.3%) occurred as one isolated positive AGA (~85% specific for CD). A smaller subset, 7.0%, had 2 or more AGA and as such, are associated with a very high specificity (>95%) for CD as well as an odds ratio of 3 for severe disease and need for abdominal surgery.^{1,2} Of note, most samples (88.7%) were seronegative for gASCA, reiterating the limited sensitivity of conventional IBD serology (only pANCA and ASCA). Of 144,864 gASCA-seronegative samples, a substantial number, 18,533 (13.9%), were positive for one or more of the novel AGA (ACCA, ALCA or AMCA). This result substantiates the potential incremental benefit of these novel Anti-Glycan Antibodies in identifying those patients more likely to have CD and its disease complications.

References: 1. Bonneau J, et al. Systematic review: New serological markers (anti-glycan, anti-GP2, anti-GM-CSF Ab) in the prediction of IBD patient outcomes. *Autoimmunity Reviews* 2015;14:231-245.
2. Kaul A, et al. Serum Anti-glycan Antibody Biomarkers for Inflammatory Bowel Disease Diagnosis and Progression: A Systematic Review and Meta-analysis. *Inflamm Bowel Dis* 2012;18(10):1872-1884.

Disclosure: Nothing to disclose.

Clinical features and outcomes in liver disease

13:00-14:00 / Poster Stage 3

MP632

RED CELL DISTRIBUTION WIDTH (RDW) TO PLATELET RATIO (RPR): A ROUTINELY PERFORMABLE TOOL TO PREDICT 7-YEAR RISK AND MODALITIES OF DECOMPENSATION IN ADVANCED CHRONIC LIVER DISEASE (ACLD). A PRELIMINARY OBSERVATION

M. Romeo¹, F. Di Nardo¹, P. Vaia¹, C. Napolitano¹, S. Auletta¹, M. Cipullo¹, G. Zagaria¹, M. Niosi¹, M. Dallio¹, A. Federico¹
¹University of Campania Luigi Vanvitelli, Department of Precision Medicine, Hepatogastroenterology Division, Naples, Italy

Contact E-Mail Address: marioromeo@virgilio.it

Introduction: The decompensation occurrence constitutes the main factor affecting survival for compensated advanced chronic liver disease (cACLD) patients. Based on the type of first decompensation event (DE), two distinct modalities of progression, with relatively different prognostic implications, have been described: "Non-Acute" (NAD) [slow ascites onset, mild hepatic encephalopathy (HE), or progressive jaundice] or "Acute" (AD) [grade 2/3 ascites within 2 weeks, severe HE, or acute bleeding]. Clinically significant portal hypertension (CSPH), defined by Hepatic Venous Pressure Gradient (HVPG) values ≥ 10 mmHg, represents the best predictor for decompensation. However, it's affected by the invasiveness, the general availability, and the relative strict operator dependence. Alternatively, various noninvasive tools (NITs), usually adopted to estimate liver function and hepatic fibrosis, have been proposed to predict decompensation.

Red cell distribution width (RDW)/Platelet ratio (RPR) has recently been suggested as a routinely assessable NIT predicting fibrosis severity in chronic hepatopathies. However, its predictive role in ACLD patients has never been explored.

Aims & Methods: We aimed to evaluate the accuracy of the RPR in predicting the occurrence and modalities (NAD or AD) of the first DE in cACLD patients.

In this observational study, 140 controls and 680 cACLD patients of various etiologies were prospectively enrolled and followed up (FU) semiannually for 7 years. At baseline, biochemical, clinical, and Liver Stiffness Measurement (LSM) data were collected, as well as the Child-Pugh (CP), MELD, AST/Platelet Ratio Index (APRI), Fibrosis-4 score (FIB-4), Albumin-Bilirubin (ALBI), ALBI-FIB-4, and RPR were calculated. CSPH was defined by the presence of endoscopic esophageal varices and/or assumed for LSM values > 25 kPa. During FU the DEs were recorded.

Results: 208 (30.5%) cACLD patients progressed to decompensated ACLD (dACLD): 141 (67.8%) presented NAD and 67 AD (32.2%) as first DE. Baseline RPR resulted significantly higher in dACLD patients compared to cACLD and controls, as well as in AD patients compared to NAD (all $p < 0.0001$). RPR positively correlated with APRI, FIB-4, ALBI, ALBI-FIB-4, MELD, CP, and LSM [R:0.88, R:0.81, R:0.61, R:0.74, R:0.68, R:0.75, R:0.74, R:0.94; all $p < 0.0001$]. ROC analysis revealed RPR ≥ 0.472 and ≥ 0.894 as the best cut-offs [AUC: 0.95; AUC: 0.94] in the prediction respectively of 7-year first DE and relative modality (AD), as well as better predictive performance if compared to APRI [AUC:0.87; AUC:0.90], FIB-4 [AUC: 0.71; AUC:0.80], ALBI [AUC:0.90; AUC:0.77], ALBI-FIB-4 [AUC: 0.93; AUC:0.79], MELD [AUC:0.78; AUC:0.89], CP [AUC:0.77; AUC:0.71], and LSM [AUC:0.87; AUC:0.94] for both first DE and AD occurrence (all $p < 0.0001$). Multivariable analysis revealed the RPR [adjusted hazard ratio (aHR): 2.24[MD1] [MR2]] and the presence of baseline CSPH (aHR:1.84) as the variables independently and significantly influencing both outcomes (all $p < 0.0001$). The Kaplan-Meier Log-Rank Test analysis on DE occurrence showed HR:4.62 [C.I. 95% 3.110-5.810] for baseline RPR ≥ 0.472 and HR: 5.10 [C.I. 95% 3.481-6.125] for patients presenting simultaneously baseline RPR ≥ 0.472 and CSPH.

Conclusion: The availability of a non-invasive tool predicting the decompensation is an unmet need. RPR non-invasively predicts the timing and modalities of decompensation in cACLD patients representing a potential clinically useful biomarker in this context.

References:

1. Taefi, Amir, et al. "Red cell distribution width to platelet ratio, a useful indicator of liver fibrosis in chronic hepatitis patients." *Hepatology international* vol. 9,3 (2015): 454-60. doi:10.1007/s12072-015-9638-9
2. Abalde, Juan G, and Guadalupe Garcia-Tsao. "Simple Clinical Tools to Predict Decompensation in Patients With Compensated Cirrhosis: An Unmet Need." *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association* vol. 17,11 (2019): 2179-2181. doi:10.1016/j.cgh.2019.04.026
3. D'Amico, Gennaro et al. "Towards a new definition of decompensated cirrhosis." *Journal of hepatology* vol. 76,1 (2022): 202-207. doi:10.1016/j.jhep.2021.06.018

Disclosure: Nothing to disclose.

MP633

NATURAL HISTORY AND RENAL INVOLVEMENT OF CONGENITAL HEPATIC FIBROSIS AND CAROLI DISEASE - A SINGLE CENTER EXPERIENCE

D. Janakiraman¹, N. Dheivamani¹, S. T A¹, S.K. R¹, W. Thomas¹
¹Institute Of Child Health/Madras Medical College, Paediatric Gastroenterology, Chennai, India

Contact E-Mail Address: rdherdhe9@gmail.com

Introduction: Congenital hepatic fibrosis (CHF) is a rare autosomal recessive disease derived from biliary dysgenesis secondary to ductal plate malformation; it often coexists with Caroli's disease, von Meyenburg complexes, autosomal dominant polycystic kidney disease (ADPKD), and autosomal recessive polycystic kidney disease (ARPKD). Congenital hepatic fibrosis (CHF) and Caroli syndrome has varied clinical presentations with or without renal involvement.

Aims & Methods: Our study aimed to describe the clinical manifestations and natural history of children with CHF and Caroli with or without renal involvement. Retrospective data from January 2022 to January 2024 was collected and analyzed.

Results: Twenty-three children (Caroli=7, CHF=16) were enrolled male predominance (76%) was noted. Consanguinity was noted in 76% and 23% had affected siblings. Median age at initial presentation was two years and abdominal distension was the most common presentation (47.6%) followed by variceal bleeding (23.8%), cholangitis (14.2%), incidental diagnosis (9.5%) and pancytopenia (4.76%). Median age at presentation and diagnosis was later with variceal bleeding at 5.6 years compared with children with abdominal distension who presented at 18 months respectively ($p=0.0001$). Renal involvement was present in 76% of the children. Autosomal Recessive Polycystic Kidney Disease (ARPKD) was the most common renal manifestation noted. Of them, 18% had developed Chronic Kidney Disease (CKD). All Caroli cases (100%) had renal involvement. There was no statistical difference in the age of presentation of CHF with or without renal involvement ($p=0.5998$). Growth faltering was noted in 52% of children. Statistical analysis revealed no significant difference in the likelihood of developing portal hypertension among children with either congenital hepatic fibrosis (CHF) or Caroli disease, regardless of renal involvement. Portal hypertension was seen in 76%. Only one child had variceal bleeding on follow up.

Conclusion: Abdominal distension, organomegaly, variceal bleeding, and cholangitis are frequently observed clinical manifestations in both congenital hepatic fibrosis (CHF) and Caroli disease. Interestingly, while renal involvement is more prevalent in Caroli disease compared to CHF, there

doesn't appear to be a direct correlation between renal involvement and the severity of hepatic manifestations or growth faltering in affected children. This underscores the complexity of these conditions and the need for tailored management approaches that address both hepatic and renal complications.

References: 1. Srinath, Arvind, and Benjamin L Shneider. "Congenital hepatic fibrosis and autosomal recessive polycystic kidney disease." *Journal of pediatric gastroenterology and nutrition* vol. 54,5 (2012): 580-7. doi:10.1097/MPG.0b013e31824711b7

2. Gunay-Aygun M, Font-Montgomery E, Lukose L, Tuchman Gerstein M, Piwnica-Worms K, Choyke P, Daryanani KT, Turkbey B, Fischer R, Bernardini I, Sincan M, Zhao X, Sandler NG, Roque A, Douek DC, Graf J, Huizing M, Bryant JC, Mohan P, Gahl WA, Heller T. Characteristics of congenital hepatic fibrosis in a large cohort of patients with autosomal recessive polycystic kidney disease. *Gastroenterology*. 2013 Jan;144(1):112-121.e2. doi: 10.1053/j.gastro.2012.09.056. Epub 2012 Oct 3. PMID: 23041322; PMCID: PMC4162098.

Disclosure: Nothing to disclose.

MP634

CURRENT MANAGEMENT OF ACUTE ALCOHOLIC HEPATITIS IN FRANCE: RESULTS OF A NATIONAL SURVEY

J.-F.D. Cadranel¹, T. Thevenot², H. Zougmore³, T. Dao⁴, J.-B. Noursbaum⁵, M. Rudler⁶, N. Carbonell⁷, A. Coilly⁸, K. Bideau⁹, P. Mathurin¹⁰, A. Abergel¹¹, E. Nguyen-Khac¹², C. Barrault¹³, T. Paupard¹⁴, P. Sogni¹⁵, F. Durand¹⁶, L. Caroline¹⁷, V. De Ledinghen¹⁸, F. Heluwaert¹⁹, J.-P. Richardet²⁰, G.P. Pageaux²¹, M. Medmoun²², G. Fantognon²², P. Pulwermacher²², T. Le Magoarou²³

¹Ghpso Creil, Department Of Liver And Igestive Diseases, Creil, France, ²CHU Besançon, Department of liver and digestive Diseases, Besancon, France, ³GHPSO Creil, Nogent Sur Oise, France, ⁴CHU Caen, Caen, France, ⁵CHU Brest, Brest, France, ⁶Pitié-Salpêtrière Hospital - Hépatogastro-entérologie, Pitié-Salpêtrière Hospital; Paris/FR, Paris, France, ⁷Hôpital Saint-Antoine, Paris, France, ⁸Hôpital Paul Brousse, Centre Hépatogastro-Biliaire, Villejuif, France, ⁹CH QUIMPER, Quimper, France, ¹⁰CHRU Lille Service MADN Hopital Huriez, Lille, France, ¹¹CHU de Clermont-Ferrand, Medecine Digestive, Clermont-Ferrand, France, ¹²CHU Amiens, Amiens, France, ¹³Centre hospitalier intercommunal de Créteil, Liver and Addiction Unit, Creteil, France, ¹⁴CH de Dunkerque Gastroenterologie, Dunkerque Cedex 1, France, ¹⁵Hôpital Cochin, Paris, France, ¹⁶Hospital Beaujon, Hepatology Unit, Clichy, France, ¹⁷Caroline Lemaitre, 76000, Rouen, France, ¹⁸CHU BORDEAUX, Bordeaux, France, ¹⁹CH Annecy, Annecy, France, ²⁰Hôpital Henri Mondor, Creteil, France, ²¹CHU Montpellier, Montpellier, France, ²²GHPSO Creil, Creil, France, ²³GHPSO Creil, DIM, Creil, France

Contact E-Mail Address: honoretz87@gmail.com

Introduction: Since 2010 (1), little data has been available in France on the management of severe acute alcoholic hepatitis (SAH). In order to obtain a current "mapping" of the management of severe HAS in France, a practice survey was conducted from 04/2022 to 07/2023.

Aims & Methods: A Google questionnaire pre-established by a working group was sent to all the hepatogastroenterology departments of general hospitals (nUH), the hepatology departments of university hospitals (UH). The results are expressed as means $\pm$ SD. Data analysed: demographics, type of practice (university hospital, general hospital), predominant speciality, experience, number of AA treated per centre with corticosteroids (C) or N-acetylcysteine corticosteroids (NAC). Existence of an AA treatment

protocol. Systematic use of transjugular liver biopsy (LB), on-site LB, time taken to obtain results. Treatment: use of C alone or C-NAC. Screening for bacterial infections, use of antibiotic therapy (ATB) in the event of infection, time taken to start treatment for AA. Whether or not to use C in antigen-positive HBs patients (with or without pre-emptive treatment). Interruption of C in the event of an intermediate Lille score at D7. Indication for transfer to a liver transplant centre.

Results: 465 respondents (R): 40 years (12.5); 50% M, 50% F, UH 53.3%, nUH 46.7%, hepatologists 57%, gastroenterologists 39%, juniors 21%. Number of AA treated with CS or CS NAC 25 (0 to 300); the number of AA treated in UH was higher than in non UH: 34 (29), nUH 15.4 (13.4), $p < 0.001$. Treatment protocol for AA, 62% (University Hospital) vs 42% (Hospital), $p < 0.001$. LB systematically performed: 98% AA vs 50% other, $p < 0.001$. Time taken to obtain LB (days): 3.4 (UH) vs 4.9 (nUH), $p < 0.001$. Nutritional status was assessed by 98% of patients. A systematic chest CT scan was routinely requested by 34% of patients in the event of suspected pulmonary infection (UH versus nUH ns); 83% of patients waited 4 days (2-6) before starting treatment in the event of documented infection. Treatment: C alone 70% of patients (UH vs nUH ns), NAC use: UH 40% vs nUH 47.3% (ns). Treatment protocol for alcohol withdrawal syndrome: 86.3% nUH vs 76.3% UH ($p < 0.01$). CS stopped in the event of an intermediate Lille score at D7: 80% nUH vs 77% UH; ns. 69% of R's were responsible for initiating treatment. 68.2% of R were responsible for initiating treatment; 64.7% in UH vs 72.3% (NS); 80.6% senior doctors vs 20.4% junior doctors ($p < 0.001$). 62% of R used pre-emptive treatment before CS in the case of a positive HBs antigen; 59.4% in UH vs 65% in nUH ($p = 0.004$) and 76% used upper gastrointestinal endoscopy if there had been none previously, 77% in UH vs 75% nUH ($p = 0.782$).

Conclusion: The results of this study of national practice carried out in a large sample of doctors practising in or outside university hospitals show a disparity in the use of LB in cases of suspected severe AA, since 50% of R outside university hospitals do not use LB, mainly because of the absence of local possibilities. Dual C-NAC therapy is used fairly frequently. There is a disparity between university hospitals and general hospitals in the management of alcohol withdrawal syndrome and pre-emptive treatment in cases of positive HBs antigen. This study provides an update on the management of severe AA in France.

References: E.Nguyen-Khac et al J Hepatol 2010 (abstract)

Disclosure: Nothing to disclose.

MP635

CLINICAL FEATURES AND TREATMENT OUTCOMES OF HEPATOBILIARY TUBERCULOSIS: A CASE SERIES AND LITERATURE REVIEW

T.P. Madrigal¹, C.J. David², A.M. Valle³, M.T. Panlilio¹

¹University of the Philippines - Philippine General Hospital, Division of Gastroenterology, Manila, Philippines, ²University of the Philippines - Philippine General Hospital, Department of Radiology, Manila, Philippines, ³University of the Philippines - Philippine General Hospital, Department of Laboratories, Manila, Philippines

Contact E-Mail Address: madrigalt21@gmail.com

Introduction: Hepatobiliary tuberculosis (HBTB) is an uncommon manifestation of *Mycobacterium tuberculosis* infection. It can present as an isolated involvement of the liver, bile duct, gallbladder, or, more commonly, as part of a disseminated process. HBTB poses a diagnostic challenge due to its varied clinical manifestations and potential for mimicking other hepatic disorders, particularly malignancies. Despite advancements in diagnostic techniques, no finding is considered pathognomonic, making the definitive diagnosis of HBTB reliant on histologic or microbiologic confirmation.

Aims & Methods: The records of patients with bacteriologically confirmed or biopsy-proven HBTB were reviewed for the following data: demographic features, clinical manifestations, laboratory and imaging results, and clinical follow-up. The histologic findings of granulomatous inflammation and Langhan's type giant cells, identification of acid-fast bacilli, or a positive PCR test result were used to diagnose HBTB.

Age/ Sex	Site/s of Involvement	Other Organ Involvement	History of Prior PTB Treatment	Duration from onset of symptoms to presentation	Imaging Findings	Diagnosis of HBTB	Treatment Outcome
32/M	Liver	Lungs	Yes	2 months	Multiple, hypodense nodular densities with internal calcifications	Biopsy of liver nodule Sputum MTB PCR	Improved
36/F	Gallbladder Bile ducts	CNS Lymph nodes	None	8 months	Gallbladder hydrops Intrahepatic and extrahepatic bile duct ectasia secondary to stricture formation. Retropertitoneal lymphadenopathies	Biopsy of brain mass Bile TB PCR	Improved
39/M	Bile ducts Liver	Lungs Lymph nodes	None	2 months	Multiple, hypodense nodular densities with internal calcifications and hepatic abscess Intrahepatic and extrahepatic bile duct ectasia secondary to stricture formation.	Hepatic abscess AFB staining Sputum AFB staining	Improved
31/F	Liver	Duodenum Lymph nodes Lungs	None	5 months	Intra-abdominal and retroperitoneal lymphadenopathies Multiple, hypodense nodular densities with internal calcifications	Biopsy of liver nodule	Improved
39/M	Liver Bile ducts	Lungs Lymph nodes	Yes	3 months	Intra-abdominal lymphadenopathies Intrahepatic and extrahepatic bile duct ectasia secondary to stricture formation. Hepatic mass with associated capsular retraction	Biopsy of liver mass	Developed liver cirrhosis
39/M	Liver Bile Ducts	Lungs	None	12 months	Intra-abdominal lymphadenopathies Intrahepatic bile duct ectasia secondary to stricture formation. Hepatic mass with internal calcifications	Biopsy of liver mass Bile AFB staining	Developed liver cirrhosis
50/M	Liver Bile Ducts	Lungs Lymph nodes	None	3 months	Hepatic mass with internal calcifications Intrahepatic and extrahepatic bile duct ectasia secondary to stricture formation. Intra-abdominal lymphadenopathies	Biopsy of liver mass Bile AFB staining	Mortality
51/F	Liver	Lungs Lymph nodes	Yes	3 months	Intrahepatic bile duct ectasia secondary to stricture formation. Multiple, hypodense nodular densities with internal calcifications	Biopsy of liver mass	Mortality

Results: Eight patients were included; most were male (n = 5), with a mean age of 39.6 years. Three patients had a prior history of treatment for pulmonary TB. Among them, the most common site of hepatobiliary involvement was the liver (n=7), followed by bile ducts (n = 4) and gallbladder (n=1). All patients exhibited extrahepatic involvement, primarily pulmonary (n=7). Three patients had a prior history of treatment for

pulmonary TB. The average duration from the onset of symptoms to the initial presentation was 4.8 months. The most common symptoms were abdominal pain and jaundice, followed by weight loss, fever, and anorexia. Most patients presented with a cholestatic pattern of elevation of liver function tests. Other findings include hypoalbuminemia, anemia, and leukocytosis. The most common imaging findings were the presence of lymphadenopathies, followed by intrahepatic biliary dilation, extrahepatic biliary dilation, and hepatic nodules with internal calcifications. All patients were started on anti-tubercular therapy (ATT). Four patients improved with ATT. Two patients developed secondary biliary cirrhosis despite completing ATT. Two patients succumbed to complications, one due to pulmonary embolism and the other to bacterial peritonitis.

Conclusion: The cases presented shed light on the complexities of diagnosing HBTB, emphasizing the importance of histologic or microbiologic testing to ascertain a definitive diagnosis. The importance of a multidisciplinary approach cannot be underscored in these cases. As delineated in this series, HBTB usually presents with non-specific clinical features and often exhibits extra-hepatic involvement, more commonly in the lungs. Although the majority of patients demonstrated a favorable response to ATT, patients can develop complications such as secondary biliary cirrhosis and even fatal outcomes, highlighting the importance of a high index of suspicion, particularly in endemic regions, in avoiding treatment delays and potential complications. Further studies are warranted to better understand the clinical spectrum and optimal management strategies for this uncommon yet significant manifestation of tuberculosis.

References:

1. Sollano JD, Luspo-Quiblat MMB, Ismael AE. Epidemiology and clinical profile of gastrointestinal tuberculosis in the past 10 years. 2000. Philippine Journal of Internal Medicine, 38(2), 108
2. Chaudhary P. Hepatobiliary tuberculosis. Ann Gastroenterol. 2014;27(3):207-211. PMID: 24976240; PMCID: PMC4073015.
3. Chong VH. Hepatobiliary tuberculosis: a review of presentations and outcomes. South Med J. 2008 Apr;101(4):356-61. doi: 10.1097/SMJ.0b013e318164ddbb. PMID: 18360350.
4. Ch'ng LS, Amzar H, Ghazali KC, Siam F. Imaging appearances of hepatic tuberculosis: experience with 12 patients. Clin Radiol. 2018 Mar;73(3):321.e11-321.e16. doi: 10.1016/j.crad.2017.10.016. Epub 2017 Nov 22. PMID: 29174175.
5. Malikowski T, Mahmood M, Smyrk T, Raffals L, Nehra V. Tuberculosis of the gastrointestinal tract and associated viscera. J Clin Tuberc Other Mycobact Dis. 2018 Apr 14;12:1-8. doi: 10.1016/j.jctube.2018.04.003. Erratum in: J Clin Tuberc Other Mycobact Dis. 2020 Sep 09;21:100177. PMID: 31720391; PMCID: PMC6830173.

Disclosure: Nothing to disclose.

MP636

WITHDRAWN

MP637

MELD 3.0: IS THIS THE FUTURE OF MORTALITY PREDICTION IN DECOMPENSATED LIVER CIRRHOSIS?

M. Souto^{1,2,3}, A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, S. Leite^{1,2,3}, J. Berkeley Cotter^{1,2,3}
¹Hospital da Senhora da Oliveira, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga/Guimarães, Portugal, ³ICVS/3B's – PT Government Associated Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: mariana.souto9@gmail.com

Introduction: Patients with decompensated cirrhosis have high mortality rates. Several prognostic scores have been developed, based on clinical and laboratory parameters, to assess the prognosis of patients with cirrhosis. However, to date, there is no consensus on the best prognostic model. The MELD 3.0 score was recently published with the aim of refining the MELD score to contemporary data.

Aims & Methods: The objective of this study was to evaluate and compare models based on the hepatic severity index to investigate their predictive performance in mortality.

A retrospective cohort study was conducted, including consecutively admitted patients to a Gastroenterology Department for first admission due to decompensated cirrhosis. MELD, MELD-Na, MELD 3.0, and Child-Pugh scores were calculated upon admission. Mortality at 6 weeks and 180 days was the main outcome studied.

Results: 109 patients admitted for the first episode of decompensated cirrhosis were included, 82.6% with alcoholic aetiology. Mean age was 61.8 ±10.8 years, 73.4% were men and 26.6% were women. Of the included patients, 11% died within the first 6 weeks and 25.7% died within the first 180 days after admission.

All models showed good accuracy in predicting mortality at 6 weeks and 180 days, with slight superiority of the MELD 3.0 score (AUC 0.693, 95% CI 0.598-0.778 at 6 weeks; AUC 0.712, 95% CI 0.617-0.795 at 180 days), although statistically significant differences between the different prognostic models were not observed.

Conclusion: The use of models based on hepatic severity indices accurately predicts the risk of mortality at 6 weeks and 180 days in patients with decompensated cirrhosis. The new MELD 3.0 score showed superior predictive performance in mortality, although without statistically significant differences.

Disclosure: Nothing to disclose.

MP638

THE ELIMINATE PROJECT – A PCR-BASED SYSTEMATIC RECALL OF PEOPLE LIVING WITH HCV ENABLES RE-LINKAGE TO CARE AND HCV ELIMINATION IN AUSTRIA

M. Schwarz^{1,2}, L. Balcar¹, L. Dorn³, M. Jachs¹, L. Hartl¹, L. Weseslindtner⁴, N. Pfisterer^{1,5}, B. Hennlich⁵, A. Stücker⁵, R. Strassl⁶, A. Voill-Glaninger⁷, W. Hübl⁸, M. Willheim⁹, K. Köhrer¹⁰, S. Jansen-Skoupy¹¹, S. Tomez¹², W. Krugluger^{12,13}, C. Madl^{5,14}, L. Burghart^{1,2}, L. Antonitsch¹⁵, G. Weidinger¹⁵, F. Riedl³, H. Laferl¹⁶, J. Hind¹⁶, C. Wenisch¹⁶, C. Sebesta^{17,18}, J. Wachter-Welzl¹⁹, P. Watzl²⁰, M. Neuhauser²⁰, D. Chromy¹, M. Mandorfer¹, D. Schmid²¹, M. Gschwantler^{2,14}, T. Reiberger¹, A. Maieron³, D.J.M. Bauer^{1,2}, C. Schwarz^{1,2}

¹Medical University of Vienna, Department of Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria, ²Klinik Ottakring, Department of Internal Medicine IV, Vienna, Austria, ³Karl Landsteiner University of Health Sciences, University Hospital of St. Pölten, Internal Medicine II, Gastroenterology and Hepatology and Rheumatology, Sankt Pölten, Austria, ⁴Medical University of Vienna, Center for Virology, Vienna, Austria, ⁵Klinik Landstraße, Department of Internal Medicine IV, Vienna, Austria, ⁶Medical University of Vienna, Clinical Institute for Laboratory Medicine, Vienna, Austria, ⁷Klinik Landstraße, Central Laboratory and Blood Bank, Vienna, Austria, ⁸Klinik Ottakring, Central Laboratory, Vienna, Austria, ⁹Karl Landsteiner University of Health Sciences, University Hospital of St. Pölten, Clinical Institute of Laboratory Medicine, Sankt Pölten, Austria, ¹⁰Landeskrankenhaus Wiener Neustadt, Institute of Medical-Chemical and Molecularbiological Laboratory Diagnostics with Blood Depot, Wiener Neustadt, Austria, ¹¹Klinik Favoriten, Institute of Laboratory Diagnostics, Vienna, Austria, ¹²Klinik Donaustadt, Institute of Laboratory Medicine with Blood Depot, Vienna, Austria, ¹³Klinik Floridsdorf, Institute of Laboratory Medicine and Blood Depot, Vienna, Austria, ¹⁴Sigmund Freud University, Vienna, Austria, ¹⁵Landeskrankenhaus Wiener Neustadt, Department of Internal Medicine, Gastroenterology and Hepatology, Wiener Neustadt, Austria, ¹⁶Klinik Favoriten, Department of Internal Medicine IV, Vienna, Austria, ¹⁷Klinik Floridsdorf, Department of Internal Medicine and Gastroenterology, Vienna, Austria, ¹⁸Klinik Donaustadt, Department of Internal Medicine II, Vienna, Austria, ¹⁹Landeskrankenhaus Mistelbach, Department of Internal Medicine II, Mistelbach, Austria, ²⁰Barmherzige Schwestern Hospital, Department of Internal Medicine II, Vienna, Austria, ²¹Austrian Agency for Health and Food Safety (AGES), Vienna, Austria

Contact E-Mail Address: schwarz.medizin@gmail.com

Introduction: To achieve the WHO's goal of eliminating hepatitis C by 2030, higher rates of detection of people infected with the hepatitis C virus (HCV) and of treatment uptake are needed. The ELIMINATE (ELIMINATION of HCV in Austria East) project is an Austrian HCV macroelimination program that utilized readily available hospital laboratory data to identify patients with a "last positive" HCV RNA PCR, who are thus potentially still viremic, to contact them and to allow re-linkage to medical care.

Aims & Methods: Ten major liver centers in Eastern Austria participated. A systemic readout of HCV RNA PCR tests obtained between 2008 and 2020 from the respective hospital's database was conducted and between 2020 and 2023 identified people living with HCV were contacted by phone and, if unsuccessful, by letter. Patients were informed of the possibility of effective treatment via direct-acting antivirals (DAAs) and were offered a pre-treatment evaluation at the respective center.

Results: Overall, 5,695 individuals with “last positive” HCV RNA were identified (62.5% male, mean age 57.3±17.3 years). At the time of data acquisition, 1,931 (34%) had already died (33.8% liver-related deaths) and 759 (13%) had no valid contact information. At the time of recall, 1,171 (40.0%) of the 3,005 remaining patients had already achieved sustained virologic response (SVR). We successfully contacted 617 (20.5%) eligible patients, of whom 417 (67.6%) attended a pre-treatment evaluation visit. DAA therapy was started in 397 (64.3%) patients (median time from “last positive” PCR to initiation of DAA treatment: 59.8 months). As of now, SVR was confirmed in 258 patients (SVR rate 65.0%).

Conclusion: Through the ELIMINATE project we were able to identify 5,695 potentially still viremic individuals. Invalid contact information was a barrier to re-linkage to care and the amount of already diseased patients underlined the severity of the disease and the impact of potentially associated comorbidities. A systematic readout of hospitals’ HCV PCR records represents an effective macroelimination strategy to identify patients regardless of risk behavior.

Disclosure: L.D., M.J., L.H., L.W., N.P., B.H., A.S., R.S., A.V.-G., W.H., M.W., K.K., S.J.-S., S.T., W.K., C.M., L.A., L.Bu., G.W., F.R., H.L., J.H., C.W., J.W.-W., P.W., M.N., D.S., J.R. and S.R. have nothing to disclose outside of the submitted work.

L.B. received speaking honoraria from Chiesi, and Gilead.

M.S. received travel support from MSD, Sandoz, BMS, AbbVie and Gilead; and speaking honoraria from BMS and Gilead.

D.C. served as a speaker and/or advisory board member for Gilead, Viiv Healthcare and MSD and received travel support from MSD, Viiv Healthcare, and Gilead.

M.M. served as a speaker and/or consultant and/or advisory board member for AbbVie, Collective Acumen, Echosens, Gilead, Takeda, and W. L. Gore & Associates and received travel support from AbbVie and Gilead.

M.G. received grant support from Abbvie, Gilead, and MSD; speaking honoraria from Abbvie, Gilead, Janssen, Roche, Intercept, and MSD; consulting/advisory board fees from Abbvie, Gilead, Janssen, Roche, Intercept, Norgine, AstraZeneca, Falk, Shionogi, and MSD; and travel support from Abbvie and Gilead.

A.M. received grant support from Abbvie and Gilead; speaking honoraria from Abbvie, Gilead, Janssen, Roche, Intercept, and MSD; consulting/advisory board fees from Abbvie, Gilead, Janssen, Roche, Intercept, Norgine, and MSD; and travel support from Abbvie, Gilead and Roche.

T.R. served as a speaker and/or consultant and/or advisory board member speaking honoraria from AbbVie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Roche, Siemens, and W. L. Gore & Associates and received travel support from AbbVie, Boehringer-Ingelheim, Gilead, and Roche as well as grants/research support from AbbVie, Boehringer-Ingelheim, Gilead, Intercept, MSD, Myr Pharmaceuticals, Philips Healthcare, Pliant, Siemens, and W. L. Gore & Associates.

D.B. received travel support from Gilead and AbbVie; speaking honoraria from AbbVie and Siemens and grant support from Gilead and AbbVie.

C.S. received travel support from Gilead, Abbvie, Galápagos, and Gebro; speaking honoraria from Abbvie and Gilead; and payments for consulting from Gilead.

MP639

ENDOSCOPIC ULTRASOUND GUIDED FINE NEEDLE BIOPSY OF FOCAL LIVER LESIONS: AN EFFECTIVE MINI INVASIVE ALTERNATIVE TO PERCUTANEOUS APPROACH

G. Rancatore¹, D. Ligresti¹, G.E.M. Rizzo¹, L. Carrozza¹, M. Traina¹, I. Tarantino¹

¹IRCCS-ISMETT, Endoscopy Service, Department of Diagnostic and Therapeutic Services, Palermo, Italy

Contact E-Mail Address: gabriele.rancatore@gmail.com

Introduction: Despite the introduction into clinical practice of serological neoplastic biomarkers and typical radiological characteristics, useful for the differential diagnosis of focal liver lesions, liver biopsy (LB) is still often necessary, especially in unclear cases, to achieve histological diagnosis. Nowadays, LB via percutaneous approach (PC-LB), under computed tomography (CT) scan or ultrasonography (US) guidance, is the route of choice. However, there are focal liver lesions that are poorly reachable via percutaneous approach. In these cases endoscopic ultrasound (EUS) guided fine needle biopsy (FNB) may represent an attractive minimally invasive alternative.

Aims & Methods: Aim of this retrospective observational study was to evaluate the efficacy, diagnostic performances and safety of EUS-FNB of focal liver lesions. The indication to perform EUS-LB was the presence of a focal liver lesion poorly accessible via a percutaneous approach or incidentally found during an EUS examination

Results: 58 patients were included, 43 patients had a final diagnosis of malignancy. The localization of lesions was 72.4 % (42 cases) in the left lobe and 27.6 % (16 cases) in the right lobe. The focal liver lesions localizations were summarized in Table 2. The median number of needle passes was 2 (IQR: 3–4). Only in 3 cases (5 %) the specimen was suboptimal for histological evaluation and in all of these, the focal liver lesions were located in right lobe. The overall sensitivity and specificity were 95% and 100% respectively while overall adequacy and accuracy were 95 % and 96% respectively. Subgroup analysis, conducted for different gauge FNB needles used, showed different diagnostic yield. In particular, adequacy and accuracy for 19-gauge FNB needle were 100% and 95%, adequacy and accuracy were both 100 % for 20-gauge FNB needle and were 90% and 96% for 22-gauge FNB needle. Of note, all three inadequate biopsies were performed with a 22-gauge needle. On the other hand, subgroup analysis for different FNB needle type used, showed adequacy and accuracy of 94 % and 95% respectively for Acquire needle (Boston Scientific, Natick, MA, United States) and, adequacy and accuracy of both 100% for ProCore needle (Cook Medical Inc., Winston-Salem, North Carolina, United States). Technical success was 100% both for right and left liver lobe. Adequacy for focal liver lesion located in left and right lobe was 100 % and 81.2 % respectively and the difference was statistically significant [p= 0.001]. We also compared the diagnostic yield of EUS-LB between the right lobe and left lobe mass. Median size of lesions on EUS and median number of needle passes did not differ significantly between the left and right lobes. Sensitivity for lesions located in left liver lobe and right liver lobe were 96 % and 91% respectively [p=0.001]. Specificity was 100% for lesions located in left and right liver lobe. Predictive positive value (PPV) was 100% for lesions located in both liver lobe. Predictive negative value (PPV) for lesions located in left liver lobe and right liver lobe were 90% and 50% respectively [p= 0.001]. No intra/postprocedural adverse events were recorded according to AGREE classification.

Conclusion: EUS-guided focal liver lesions biopsy using FNB is effective in achieving accurate diagnosis with an excellent safety profile. The main indication for EUS-FNB of focal liver lesions could be to obtain a specimen from the lesions located in the left liver lobe, close to big vessels or in obese patients which are more difficult to obtain by other techniques.

Disclosure: Nothing to disclose.

Chronic pancreatitis

13:00-14:00 / Poster Stage 4

MP640

LONG-TERM BEHAVIOUR OF EARLY CHRONIC PANCREATITIS AND FACTORS ASSOCIATED WITH MORPHOLOGICAL AND FUNCTIONAL DISEASE PROGRESSION

Y. Dominguez-Novoa^{1,2}, J. Iglesias-Garcia^{1,2}, J. Lariño-Noia^{1,2}, X. Martinez-Seara³, P. Miguez-Sanchez^{1,2}, L. Nieto-Garcia³, M.d.S. Porto-Silva³, J.E. Domínguez Muñoz^{1,2}
¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: yessica.dominguez.novoa@sergas.es
Introduction: Diagnosis of early chronic pancreatitis (CP) is challenging due to the limited accuracy of the available diagnostic methods. Endoscopic ultrasound (EUS) is the most sensitive method in this setting, but the specificity of mild EUS findings of CP is limited. No factor has been described to predict the progression of mild EUS changes to definite CP.
Aims & Methods: Aim of our study was to evaluate the long-term morphological and functional behavior of mild EUS changes of CP and factors associated with progression to definite CP.
Methods: A prospective longitudinal cohort study was designed. Patients with suspected early CP based on the presence of epigastric pain, toxic habits (alcohol and/or smoking) and mild changes of CP on initial EUS (3 or 4 minor criteria) with a minimum clinical and EUS follow-up of 5 years were included. Morphological progression was defined as the development of suggestive or definite EUS criteria of CP (≥5 criteria) during follow-up. Faecal elastase (FE-1) and HbA1C were measured annually for exocrine and endocrine function, respectively. Data are presented as percentages, mean±SD and OR (95%CI) and analysed by chi-squared test and logistic regression.
Results: 136 patients were included (mean age 56.5±13.3 years, 64.7% male). EUS changes progressed in 84 patients (61.8%) (group A) over a median follow-up of 8.7 years (range 5.1-14.8 years), whereas the remaining 52 patients (group B) (38.2%) did not progress. Age, sex and BMI were similar between the two groups (p=0.716). The association between toxic habits during follow-up and progression of EUS findings in the multivariate analysis is shown in the table.

Toxic habits during follow-up	Risk (OR) of morphological progression	Risk (OR) of exocrine pancreatic dysfunction
Smoking, No Alcohol	86.36 (16.74-445.50) p<0.001	5.33 (1.67-17.03) p=0.005
Alcohol, No Smoking	10.59 (3.49-32.14) p<0.001	3.12 (0.91-10.74) p=0.071
Smoking and Alcohol	150.43 (17.49-1293.97) p<0.001	5.31 (1.60-17.60) p=0.006

Smoking cessation (OR 0.24, 0.07-0.86, p=0.028) and alcohol cessation (OR 0.21, 0.06-0.82, p=0.024) were associated with lack of morphological progression of EUS changes in CP. Smoking, but not alcohol consumption during follow-up, was associated with persistent abdominal pain (OR 5.30, 2.02-13.9, p=0.001). FE-1 was normal at baseline in all patients. Impaired pancreatic secretion (FE-1 <200µg/g) was present at the end of follow-up in 32 patients in group A (38.1%) and 5 (9.6%) in group B (p<0.001). Six patients in group A required enzyme replacement therapy. The percentage of patients with diabetes at baseline (10.7% and 5.8%) and at the end of follow-up (17.9% and 9.8%) was similar in groups A and B (ns). Four patients in group A required insulin therapy.

Ongoing smoking, either as a single toxic habit or in combination with alcohol consumption, was associated with impairment of exocrine pancreatic function during follow-up (Table).
Conclusion: In patients with suspected early CP based on symptoms, toxic habits and the presence of mild EUS changes of CP, continued smoking and alcohol consumption are associated with morphological progression to definite CP and a higher risk of impaired exocrine pancreatic secretion, whereas cessation of toxic habits is protective against progression. Smoking during follow-up is associated with persistent epigastric pain.
Disclosure: Julio Iglesias Garcia: Advisor Fujii.

MP641

SIRTUIN 3 ALLEVIATES THE PROGRESSION OF CHRONIC PANCREATITIS BY DEACETYLATING PYRUVATE DEHYDROGENASE COMPLEX IN PANCREATIC STELLATE CELLS

W. Li¹, J. Li¹, D. Zhang¹, Z. Jin¹, H. Huang¹
¹Changhai Hospital, Department of Gastroenterology, Shanghai, China

Contact E-Mail Address: 2239568754@qq.com
Introduction: Chronic pancreatitis (CP) is a progressive inflammatory disease of the pancreas, characterized by persistent pain and irreversible fibrosis, leading to significant morbidity[1]. The disease's progression is closely linked with the activation of pancreatic stellate cells (PSC), which are instrumental in the fibrotic remodeling of the pancreatic architecture[2]. Acetylation, a key post-translational modification, plays a crucial role in regulating cellular functions and fibrosis[3]. Sirtuin 3 (SIRT3), a mitochondrial deacetylase, plays a key role in a variety of metabolic and inflammatory diseases[4]. Preliminary evidence suggests that SIRT3 might counteract fibrosis by modulating the acetylation status of key metabolic enzymes. Among these, the pyruvate dehydrogenase (PDH) emerges as a critical target[5]. However, whether the conditioning of SIRT3 on PDH plays a role in CP progression remains unknown.
Aims & Methods: In our study, we confirmed that SIRT3 may play a key role in the course of chronic pancreatitis through immunohistochemical staining and Western Blot experiments. Subsequently, acetylation sequencing was performed on the pancreatic tissue of CP mice with normal C57 and SIRT3 knockout to target the specific action of SIRT3. We aimed to elucidate the elevated degree of acetylation and the loss of SIRT3 during CP, and to explore the potential role of the SIRT3, acetylation, and pyruvate dehydrogenase complex in the development of fibrosis.

Results: The results of WB and immunohistochemical staining of pancreatic tissue showed that SIRT3 was significantly reduced and the level of acetylation was significantly increased in CP. We subsequently treated human pancreatic stellate cells (HPSCs) with either HKL or plasmid to overexpress SIRT3, or we used 3-TYP or siRNA to knock down SIRT3. The results showed that SIRT3 in HPSC was inversely proportional to the level of acetylation and the degree of fibrosis. In order to seek specific targets of SIRT3, we performed acetylation sequencing on pancreatic tissues of SIRT3 knockout and normal CP mice. Based on the sequencing results, the pyruvate dehydrogenase complex(pdhx) was identified and deacetylated at lysine 189. Convincingly, we also confirmed the above results by co-immunoprecipitation and immunofluorescence double-label staining. Finally, we generated pdhx knock-in mice carrying an acetylation-defective lysine to arginine K194R mutation (pdhx^{K194R}), which showed reduced pancreatic inflammation and suppressed pancreatic fibrosis.
Conclusion: In conclusion, our study revealed the role of SIRT3 and acetylation in CP, and identified specific targets for interactions between SIRT3 and pyruvate dehydrogenase complex.

- References:** 1. Sarles, H., *Etiopathogenesis and definition of chronic pancreatitis*. Dig Dis Sci, 1986. 31(9 Suppl): p. 91s-107s.
2. Apte, M.V., et al., *Periacinar stellate shaped cells in rat pancreas: identification, isolation, and culture*. Gut, 1998. 43(1): p. 128-33.
3. Shvedunova, M. and A. Akhtar, *Modulation of cellular processes by histone and non-histone protein acetylation*. Nat Rev Mol Cell Biol, 2022. 23(5): p. 329-349.
4. Mishra, Y. and R.K. Kaundal, *Role of SIRT3 in mitochondrial biology and its therapeutic implications in neurodegenerative disorders*. Drug Discov Today, 2023. 28(6): p. 103583.
5. Zhang, Y., et al., *Sirtuin 3 regulates mitochondrial protein acetylation and metabolism in tubular epithelial cells during renal fibrosis*. Cell Death Dis, 2021. 12(9): p. 847.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

MP642

SARCOPENIA IN EXPERIMENTAL CHRONIC PANCREATITIS: UNVEILING THE ROLE OF TGF- β SUPERFAMILY MEMBERS AND THEIR ACTIVATION AND IMPACT ON MYOGENESIS AND PROTEASOME ACTIVITY

M. Gischke¹, J. Doller¹, S. Schmidt¹, L. Zierke¹, M.L. Wiese¹, M. Sendler¹, F.U. Weiss¹, A. Geisz², M.M. Lerch^{3,1}, A.A. Aghdassi¹
¹Medizin, Universität Greifswald, Inst. für Medizin A, Greifswald, Germany, ²Boston University Chobanian & Avedisian School of Medicine, Department of Surgery, Boston, United States of America, ³LMU-Klinikum, Ärztliche Direktion, Campus Großhadern/Innenstadt, Medical Director, CEO, München, Germany

Contact E-Mail Address: sebastianschmidt2001@online.de

Introduction: Sarcopenia, characterized by reduced skeletal muscle mass and function, is a significant complication in patients with chronic pancreatitis (CP) and associated with a poor clinical outcome. CP is a progressive fibro-inflammatory disorder of the pancreas that affects both endocrine and exocrine pancreas.

While mechanisms underlying sarcopenia have been explored in elderly and cancer patients, understanding remains limited in chronic inflammatory disorders.

Aims & Methods: Our study aims to close this knowledge gap by comprehensively investigating the extent of sarcopenia in different experimental CP models, while elucidating the cellular mechanisms involved.

CP was induced in male C57BL/6 mice using three strategies: 1) by repetitive injections of caerulein over a period of 10 weeks, 2) ligation of the pancreatic duct, or 3) utilizing a knock-in mouse model carrying a heterozygous mutation in the cationic trypsinogen (T7D23A) which induces endogenous trypsinogen activation. PBS injected or sham operated mice served as controls.

To assess changes, we measured muscle diameter via HE-stained sections and MR-imaging, and evaluated muscle strength using grip force measurements.

In muscle lysates, we analyzed the expression levels of TGF- β superfamily members such as activin A, myostatin, and follistatin, along with E3 ubiquitin ligase RING-finger protein-1 (MuRF1), using both, qRT-PCR and immunoblotting techniques. Additionally, myogenesis factors in muscles as well as in vitro in C2C12 myotubes treated with activin A were investigated using qRT-PCR. Myotube diameters were measured after immunofluorescence staining of myosins. Moreover, activin A treated C2C12 myotubes, were assessed on proteasome expression analyzing α 4, rpt6 and LMP7 subunits and chymotrypsin-like activity via native PAGE and fluorogenic substrate activity assay.

Results: Reduced skeletal muscle size and strength were observed in the caerulein injection and pancreatic duct ligation model, while no reduction was determined in T7D23A mutant mice.

A decline in muscle diameter and force coincided with elevated levels of activin A, myostatin and MuRF1, accompanied by a simultaneous reduction in follistatin expression. In contrast, the expression levels of activin A, follistatin, myostatin, and MuRF1 remained unaltered in the muscle tissue of T7D23A mutant mice.

Stimulation of C2C12 myotubes with activin A for 48 h led to a significant reduction in muscle diameter compared to untreated cells and mRNA expression of key myogenesis factors such as myocyte-specific enhancer factor 2c (MEF2C), myogenic factor 3 (MyoD), and myosin heavy chains of fast muscle fiber type (MYH 1 and MYH 2) significantly decreased in vitro and in vivo.

Additionally, activin A increases the chymotrypsin-like activity and abundance of proteasomal subunits α 4 and rpt6 in a concentration dependent manner. Stimulation kinetics over 24 h revealed a dip after 4 h and significantly increased peak activity after 8 h und 12 h. Moreover, LMP7 was elevated, suggesting the formation of the immunoproteasome in vitro.

Conclusion: Signs of sarcopenia emerge in experimental CP models. Their onset appears to be associated with an activation of the activin receptor signaling pathways. These findings improve our mechanistic understanding and suggest potential biomarkers for sarcopenia. Furthermore targeting the TGF- β signaling cascade may be a promising therapeutic approach for sarcopenia in CP.

Disclosure: Nothing to disclose.

MP643

IDENTIFICATION OF SPECIFIC BIOMARKERS IN THE PANCREATIC JUICE OF PATIENTS WITH EARLY CHRONIC PANCREATITIS USING PROTEOMIC TECHNIQUES: A PILOT STUDY

S. Leal.Lopez¹, J. Iglesias-Garcia^{2,3}, J. Lariño-Noia^{2,3}, M.J. Otero-Fraga¹, S. Bravo-Lopez⁴, Y. Pazos-Randulfe¹, J.E. Domínguez Muñoz^{2,3}

¹Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain,

²University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain,

⁴Health Research Institute of Santiago de Compostela (IDIS), Proteomic, Santiago de Compostela, Spain

Contact E-Mail Address: web.icedig@gmail.com

Introduction: Diagnosis of early chronic pancreatitis remains a challenge due to the limitations of current diagnostic techniques. Therefore, finding biomarkers that allow detection of the disease in early stages is necessary. In this regard, pancreatic juice is the ideal source of information and together with high-throughput techniques such as proteomics makes it possible to identify specific diagnostic candidates of early chronic pancreatitis.

Aims & Methods: The aim of the present study is to identify specific biomarkers for the diagnosis of ECP in PJ using proteomic techniques.

Exploratory, prospective, observational and descriptive study. A total of 32 patients were included: 11 healthy controls, 12 early chronic pancreatitis and nine chronic pancreatitis, according to Rosemont criteria (0-2, 3-4 or ≥ 5 , respectively; CAEIG 2018/537). Endoscopic pancreatic function test was performed by intravenous administration of 0.2 μ g/kg secretin, obtaining pancreatic juice samples at 15, 30 and 45 minutes.

Qualitative proteomic analysis was performed using a data-dependent acquisition (DDA) and quantitative analysis was carried out by sequential

window acquisition of all theoretical fragment ion mass spectra (SWATH-MS, DIA). For statistical analysis, log2FC was calculated with the mean or median. Significant differences between groups were assessed using the Mann-Whitney U-test or Student's t-test. Proteins with p-values <0.05 and log2FC $\geq$ +0.585 and $\leq$ -0.585 were selected.

Results: Twenty-three proteins were identified exclusively in patients with early chronic pancreatitis. In addition, quantitative analysis revealed 27 downregulated and 83 upregulated proteins compared to the other groups. These proteins are involved in nucleic acid regulation, signal transduction, cell communication, metabolism and energy pathways. Moreover, analyzing early chronic pancreatitis and chronic pancreatitis together, 54 unique proteins were observed. When comparing early chronic pancreatitis and chronic pancreatitis to healthy controls, 72 downregulated and 38 upregulated proteins were identified. Signal transduction, cell communication, metabolism, energy pathways, acid nucleic regulation, cell growth and/or maintenance and protein metabolism are the most related biological processes.

Conclusion: Proteomic characterization of pancreatic juice detected qualitative and quantitative differences both in chronic pancreatitis and early chronic pancreatitis, and also specifically in early chronic pancreatitis patients compared to healthy controls. These proteins might be potential biomarker candidates of early-stage disease. Moreover, these chronic pancreatitis-specific biomarkers could be potentially detected in more easily accessible human biofluids.

Disclosure: Julio Iglesias-Garcia. Advisor Fujifilm.

MP644

NLRP3 INFLAMMASOME ACTIVATION-INDUCED ACUTE PAPILLITIS AS A TRIGGER OF ACUTE PANCREATITIS - A NOVEL MECHANISM OF MICROLITHIASIS-INDUCED ACUTE PANCREATITIS

S. Sirtl¹, M. Ahmad¹, P. Allawadhi¹, S. Ormanns², G. Beyer¹, L. Krupa³, R. Staron³, C. Schulz¹, L. Fahr¹, C. Schulz⁴, O. Buchstab⁵, A. Sendelhofert⁵, K. Steiger⁶, I. Regel¹, M. Zorniak⁷, U.M. Mahajan¹, J. Mayerle¹

¹LMU University Hospital, Department of Medicine II, Munich, Germany, ²Institute of Pathology GmbH, Tirolkliniken, Innsbruck, Austria, ³University of Rzeszów, Department of Gastroenterology and Hepatology with Internal Disease Unit, Medical Department, Rzeszów, Poland, ⁴Medical Faculty Mannheim, Heidelberg University, Department of Immunopharmacology, Mannheim Institute for Innate Immunoscience (MI3), Mannheim, Germany, ⁵LMU, Institute of Pathology, Faculty of Medicine, Munich, Germany, ⁶Technical University of Munich, Institute of Pathology, School of Medicine and Health, Munich, Germany, ⁷The Maria Skłodowska-Curie National Research Institute of Oncology (MSCNRIO), Endoscopy Unit, Gliwice, Poland

Contact E-Mail Address: simon.sirtl@med.uni-muenchen.de

Introduction: The incidence of acute pancreatitis is rising globally and current studies show that around one in four acute pancreatitis cases labelled as idiopathic are of biliary etiology¹. As a cause of biliary pancreatitis, microlithiasis and sludge play a decisive role alongside classic gallstones².

However, the pathomechanism of microlithiasis and sludge, in contrast to classic gallstones, causing acute pancreatitis is not yet understood. Gallstone-induced duct obstruction is mimicked in many animal models via duct ligation and is considered to be a critical trigger of pancreatitis. Nonetheless, biliary microlithiasis does not lead to bile duct obstruction, and thus the trigger of biliary pancreatitis remains elusive.

Aims & Methods: The aim of this study was to identify the mechanism of microlithiasis-induced acute pancreatitis. Assuming that biliary microlithiasis induces mechanical damage while passing through the papilla, human papilla biopsies were studied (acute pancreatitis (n = 4) and control patients without any pancreatobiliary pathology (n = 4)). Papilla biopsies were stained for CD45 and NLRP3. *In vitro*, bone marrow-derived and yolk-sac-derived macrophages were treated with cholesterol monohydrate and calcium bilirubinate crystals and the NLRP3 inflammasome activation was quantified. *In vivo*, microlithiasis formation was induced and sonographically monitored over 6-8 weeks in 8-10 weeks-old female mice using a lithogenic high-fat diet and twice daily i.p. devazepide injections. After caerulein-induced acute pancreatitis, low-dose CCK i.p. injections (40 ng/kg; 8 x) induced microlithiasis ejection from the gallbladder and the pancreatitis phenotype was compared with caerulein-induced pancreatitis and control mice.

Results: Significantly higher CD45 and NLRP3 expression levels were found in the papilla biopsies of microlithiasis-induced acute pancreatitis patients. In line with this, significantly higher IL-1 β secretion and caspase-1 activation were observed *in vitro* in bone marrow-derived macrophages stimulated with cholesterol monohydrate and calcium bilirubinate crystal, but not in yolk-sac-derived macrophages. Likewise, crystal-induced increased NLRP3 inflammasome recruitment was shown. *In vivo* microlithiasis formation and sonographic monitoring was achieved in all mice with high fat diet and devazepide injections. Compared to the caerulein-induced pancreatitis group, the caerulein + microlithiasis pancreatitis group showed higher LDH, GPT and ALP levels in serum but without a correlating microlithiasis-aggravated pancreatitis phenotype in HE damage scoring or CD45 staining.

Conclusion: We describe for the first time a mechanism in which biliary microlithiasis leads to a local inflammatory reaction at the papilla (acute papillitis) via NLRP3 inflammasome activation driven by bone marrow-derived macrophages. Secondly, this may lead to pancreatic duct obstruction and acute pancreatitis through papillary edema.

References: 1. Umans DS et al. Prospective multicentre study of indications for surgery in patients with idiopathic acute pancreatitis following endoscopic ultrasonography (PICUS). Br J Surg. 2023 Nov 9;110(12):1877-1882.

2. Żorniak M, Sirtl S et al. Consensus definition of sludge and microlithiasis as a possible cause of pancreatitis. Gut. 2023 Oct;72(10):1919-1926.

Disclosure: Nothing to disclose.

MP645

SARCOPENIA IN PATIENTS WITH CHRONIC PANCREATITIS: SARCOPAN STUDY PRELIMINARY RESULTS

F. Vitale¹, M. Paratore², A. Nicoletti¹, M. Negri¹, M.E. Ainora², G. Pulcini³, M. Cintoni³, E. Rinninella³, E. Genco⁴, M.G. Brizi⁴, M.C. Mele³, E.C. Nista², A. Gasbarrini¹, L. Zileri Dal Verme¹, M.A. Zocco²

¹UCSC - Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Internal Medicine and Gastroenterology, Rome, Italy, ²UCSC - Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD, Rome, Italy, ³UCSC - Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Clinical Nutrition, Rome, Italy, ⁴UCSC - Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Radiology, Rome, Italy

Contact E-Mail Address: mattia.paratore01@gmail.com

Introduction: Chronic pancreatitis is a fibro-inflammatory syndrome of the pancreas with mixed etiology, multifactorial pathogenesis and persistent pathological response to parenchymal damage, characterized by chronic inflammation, endocrine dysregulation, malnutrition and mal-

absorption. These factors represent secondary causes of sarcopenia, a progressive and generalized skeletal muscle disease associated with an increased risk of adverse events including falls, fractures, physical disabilities and death.

Aims & Methods: This study aimed to evaluate the prevalence of sarcopenia in patients affected by chronic pancreatitis (eventually complicated by exocrine pancreatic insufficiency), to compare parameters of body composition, muscular strength and ultrasound muscle thickness between sarcopenic and non-sarcopenic patients, and to clarify the role of ultrasound in the diagnosis of sarcopenia compared to gold standard imaging (CT or MRI). 29 patients with diagnosis of chronic pancreatitis (according to the UEG criteria) were prospectively enrolled between February 2023 and September 2023. Data about anthropometric parameters, blood chemistry tests, fecal elastase, Body Independence Assessment (BIA), Hand Grip Strength and Sit To Stand test were collected. The presence of sarcopenia was assessed by CT or MRI at the third level lumbar vertebra, through the quantitative analysis of various muscles. Patients underwent muscle ultrasound to evaluate the echogenicity, thickness and length of different muscular fibers.

Results: The prevalence of radiologically defined sarcopenia was 34.5% (10/29). Among patients without exocrine pancreatic insufficiency, the prevalence of sarcopenia was 28.6%, resulting lower than the prevalence of sarcopenia among patients with exocrine pancreatic insufficiency treated with pancreatic enzyme replacement therapy (PERT) (37.5%) and without exocrine pancreatic insufficiency treated with PERT (40%). Evaluation of BMI did not show significant differences in the sarcopenic group compared to the non-sarcopenic group (21.5 vs 23.4 – $p = 0.08$). Sarcopenic patients showed significantly lower values of phase angle (4.85° vs 6.4° , $p = 0.004$), free fat mass (46.3 kg vs 56.6 kg, $p = 0.02$), body cell mass (22.9 kg vs 30.4 kg, $p = 0.001$), body cell mass index (7.8 vs 10.7, $p = 0.004$), total body water (32.2 L vs 41.4 L, $p = 0.03$) and a lower performance both in terms of strength at HGS (24.7 kg vs 38.4 kg, $p = 0.003$) and average power at STS test (33.3 W vs 102.2 W, $p = 0.002$). The rectus abdominis muscle and the left radial muscular compartment showed a statistically significant difference in terms of thickness between non-sarcopenic and sarcopenic patients (8.4 mm vs 6.9 mm – $p = 0.003$; 18.5 mm vs 15.7 mm – $p = 0.004$), with high accuracy in distinguishing the two groups (respectively AUC of 84% and 83%).

Conclusion: Sarcopenia is a highly prevalent comorbidity in patients suffering from chronic pancreatitis with or without exocrine pancreatic insufficiency, with an increasing prevalence of this condition along with the progression of the pancreatic disease. BMI does not represent a valid tool for assessing and monitoring the nutritional state. Muscle ultrasound has shown good diagnostic accuracy in diagnosis of sarcopenia compared with the radiological gold standard, when specific muscle groups are considered.

Disclosure: Nothing to disclose.

MP646

A 10-YEAR FOLLOW-UP OF CHRONIC PANCREATITIS: WITH DATA ON MORTALITY, DISEASE DEVELOPMENT, AND RISK EXPOSURE

I.K. Nordaas¹, E. Tjora², D.A. Sangnes¹, F.G. Erchinger³, G.G. Dimcevski³, T. Engjom¹

¹Haukeland University Hospital, Department of Medicine, Bergen, Norway, ²Haukeland University Hospital, Pediatric department, Bergen, Norway, ³Kanalspesialistene, Bergen, Norway

Contact E-Mail Address: ingridnordaas@hotmail.com

Introduction: The clinical presentation of chronic pancreatitis (CP) varies between patients, and can include pain, diabetes, exocrine insufficiency, and malnutrition. Studies describing the course of the disease are lacking. The Bergen Pancreatic club collects data from patients with CP in Western Norway, and we present results from the first patients reaching 10-year follow-up.

Aims & Methods: We aimed to describe the disease development of patients with CP in our prospective observational study. Patients with CP were included during the period 2009 to 2021. We used M-ANNHEIM diagnostic criteria for diagnosing CP. The collected data included sex, age, aetiology, bodyweight, smoking status, alcohol use, and data on treatment and complications from CP. Exocrine pancreatic dysfunction (EPD) was defined as faecal elastase $<200\mu\text{g/g}$.

Results: Upon data extraction in February 2024, 55 patients had reached 10 years after inclusion. Seven patients were lost for follow-up. The remaining 48 patients (30 males) were included for analysis. At time of inclusion, the mean age (SD) was 58 (13) years, 52% had EPD, and 33% had diabetes. Forty-one (85%) were former or active smokers, and 16 (33%) had a daily alcohol intake. Reported aetiologies were alcohol (46%), smoke (66%), efferent duct factors (32%), immunological (7%), hereditary (9%), metabolic (2%), and idiopathic (21%).

Seventeen patients (39%, 11 males) deceased during follow-up. Median age for the deceased where 66 years (range 55-85 years) for females and 73 years (range 44-88 years) for males. The deceased patients had a higher age at inclusion compared to patients alive after 10 years. There were no significant differences in aetiologies or baseline frequencies of current drinkers, smokers, EPD or diabetes between the deceased and surviving patients.

Disease development and treatment during follow-up:

Exocrine function: 20 patients (42%) remained exocrine pancreatic sufficient (EPS), 23 patients (48%) remained EPD, 3 patients (6%) developed EPD, and 2 (4%) regained EPS. Eleven (23%) remained without pancreatic enzyme replacement therapy (PERT), 6 (13%) started PERT, 2 (4%) stopped PERT and 29 (60%) were stable on PERT.

Diabetes: 27 (56%) remained endocrine sufficient, and 5 (10%) developed diabetes. Among the 21 patients who had or developed diabetes, 5 patients used insulin upon inclusion, and 6 started using insulin during the follow-up period.

Pain: Thirty-seven patients (83%) reported pain at one or more follow-up visits, and 17 patients (35%) used opioids intermittently or regularly during the 10-year follow-up.

Conclusion: There was a high mortality among the CP patients during the 10-year follow-up. A significant portion of subjects continued risk exposures during the whole follow up period. Complications were present in the majority of patients.

Disclosure: Nothing to disclose.

MP647

METABOLOMIC PROFILE ANALYSIS OF THE PANCREATIC JUICE AND SERUM OF PATIENTS WITH EARLY CHRONIC PANCREATITIS

S. Leal-López¹, J. Iglesias-García^{2,3}, J. Lariño-Noia^{2,3}, M.J. Otero-Fraga¹, Y. Pazos-Randulfe¹, J.E. Domínguez Muñoz^{2,3}
¹Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain,
²University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Contact E-Mail Address: web.icedig@gmail.com

Introduction: Chronic pancreatitis (CP) is a progressive inflammatory disorder currently diagnosed by morphologic features. In contrast, an accurate diagnosis of early CP (ECP) is not possible using imaging criteria alone. Therefore, specific biomarkers are needed to assist ECP diagnosis. Metabolomics and its branch lipidomics are 'omic' disciplines that present a close association between metabolites and phenotype.

Aims & Methods: The aim of this study is to evaluate potential metabolic differences between patients with ECP and two control groups, CP and healthy controls (HC), determining the metabolome of human serum and PJ in ECP, as well as possible phenotypical biomarkers of these ECP patients using UHPLC-MS.

Thirty-three patients were included: 11 healthy controls (HC), 12 ECP and 10 CP, according to Rosemont criteria (0-2, 3-4 or ≥ 5 , respectively; CAEIG 2018/537). PJ samples were obtained through endoscopic pancreatic function test and serum samples were obtained just before the previously mentioned test. Separate UHPLC-MS platforms were used:

- 1) fatty acyls, bile acids, steroids and lysoglycerophospholipids;
- 2) glycerolipids, glycerophospholipids, sterol lipids and sphingolipids, and
- 3) amino acids. Multivariate (principal components analysis, PCA) and univariate (log₂FC) data analysis were performed. Significant differences were assessed using the Student's t-test or Wilcoxon-Mann-Whitney test. Three levels of significance were considered ($p < 0.05$, 0.01, and 0.001).

Results: The most remarkable differences in PJ samples were found in several oxidized fatty acids (oxFA), which were increased in ECP. Besides, the analysis of serum samples showed:

- 1) levels of several amino acids were increased in ECP/CP when compared to HC;
- 2) oxFA were increased in ECP when compared to HC; and
- 3) levels of several ether-linked lysophosphatidylcholines (ether-LPC) and ether-linked lysophosphatidylethanolamines (ether-LPE) were reduced in ECP.

Conclusion: Our results showed alterations in circulating levels of some amino acids in ECP/CP; indeed, these alterations are known to modulate pancreatic function. Lipid metabolism dysregulation in cells with CP suggests that changes in blood lipidome could contribute to the development of pancreatic cancer. In line with this, circulating levels of some ether-LPC were significantly decreased in ECP. Oxidative stress is intimately related to the pathogenesis of CP. The increment in circulating levels of oxFA in ECP was also confirmed in PJ. Subsequently, measuring the levels of oxidized fatty acids could be a useful biomarker for the disease in both serum and PJ samples.

Disclosure: Julio Iglesias-García. Advisor Fujifilm.

MP648

TIME COURSE DEVELOPMENT OF DIABETES MELLITUS FOLLOWING ACUTE PANCREATITIS: INTERIM ANALYSIS OF THE GOULASH PLUS TRIAL

M. Lipp^{1,2}, A. Szentesi^{3,1}, Z. Abonyi-Tóth¹, V. Vass³, K. Márta^{2,1}, F. Izbéki⁴, L. Gajdán⁴, B. Erőss^{2,1,3}, P. Hegyi^{2,1,3,5}, A. Mikó^{3,6,1}, Hungarian Pancreatic Study Group

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary, ³Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁴Szent György Teaching Hospital of Fejér County, Szekesfehérvár, Hungary, ⁵Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, University of Szeged, Szeged, Hungary, ⁶Department of Medical Genetics, Medical School, University of Pécs, Pécs, Hungary

Contact E-Mail Address: lipp.monika@gmail.com

Introduction: 96-98% of patients survive acute pancreatitis (AP), but in the post-AP phase, patients are at high risk of morbidity and mortality. One of the objectives of the GOULASH PLUS (ISRCTN63396106) longitudinal, observational multicentre study is to investigate the development of diabetes mellitus (DM) following AP. The GOULASH PLUS trial reached 50% of the planned patient enrolment. This interim data analysis aims to understand the time course evolution of DM after AP. The last two authors contributed equally.

Aims & Methods: Data from 349 patients were collected on DM using HbA1c and oral glucose tolerance tests (OGTT). We formed four groups according to the baseline morphology status of the exocrine pancreas: 1) AP with one episode, 2) Recurrent acute pancreatitis (RAP) with two episodes, 3) Early chronic pancreatitis (ECP) with characteristic signs on imaging or three or more episodes of AP and 4) Chronic pancreatitis (CP). Abdominal ultrasonography in the first and third years and endoscopic ultrasound or magnetic-resonance-cholangiopancreatography in the second and fourth years were conducted.

Results: Out of the 349 patients monitored following AP, 261 (74.8%) were grouped into AP, 40 (11.5%) into RAP, 26 (7.4%) into ECP, and 22 (6.3%) in the CP groups. Before the initial AP episode, in the AP group, 14.6% of patients had DM, whereas, 27.6% had prediabetes (preDM). In the RAP group 12.5% had DM and 20% preDM, in the ECP group 3.8% had DM and 38.5% preDM, whereas in the CP group, 18.2% had DM and 36.4% preDM. The following data represent the results at 1, 2, 3, and 4 years after AP. In the AP group, 23.3%, 28.1%, 31.3%, and 33.7% presented with DM, and 35.4%, 39.1%, 38.2%, and 40.6% with preDM. In the RAP group 33.3%, 36.8%, 38.1%, 42.9% presented with DM, and 36.1%, 47.4%, 42.9%, and 42.9% with preDM. In the ECP cohort, 28.6%, 38.5%, 58.3%, and 28.6% presented with DM, while 38.1%, 30.8%, 16.7%, and 42.9% with preDM. Among patients with CP, 38.1%, 66.7%, 50.0%, and 58.3% presented with DM, and 42.9%, 25.0%, 50.0%, and 25.0% with preDM.

Conclusion: AP patients with advanced morphological changes in the pancreas face a heightened risk of developing DM or preDM within the first four years after their episode.

Disclosure: Nothing to disclose.

MP649

PANCREATIC MORPHOLOGICAL AND FUNCTIONAL CHANGES IN TYPE II DIABETES MELLITUS (DM): A PROSPECTIVE, SINGLE-CENTRE, CASE-CONTROL STUDY

B. Cigarrán Vicente^{1,2}, L. Nieto-García², J. Iglesias-García^{3,4}, J. Lariño-Noia^{3,4}, Y. Dominguez-Novoa^{3,4}, M.d.S. Porto-Silva², X. Martinez-Seara², D. De la Iglesia-García⁵, J.E. Domínguez Muñoz^{3,4}

¹Hospital Virxe da Xunqueira, Internal Medicine, Cee, Spain,

²Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain,

³University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ⁴Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain,

⁵Hospital Universitario Puerta de Hierro, Gastroenterology, Majadahonda, Spain

Contact E-Mail Address: web.icedig@gmail.com

Introduction: Pancreatic fibrosis and exocrine pancreatic insufficiency have been described in patients with type II DM.

Aims & Methods: Aim of our study was to evaluate the degree of pancreatic fibrosis and exocrine pancreatic secretion in patients with type II DM. Methods: A prospective, single-centre, age- and sex-matched case-control study was performed. Diabetic (cases) and non-diabetic (controls) patients undergoing endoscopic ultrasound (EUS) for a non-pancreatic indication were invited to participate in the study. Linear echoendoscopes (Pentax 34J10, 38J10, and Fujifilm 740UT) and the Arietta-850 ultrasound system were used. The number of EUS criteria described for CP by the Rosemont classification was calculated. Pancreatic fibrosis was assessed in the head, body, and tail of the pancreas by EUS elastography and expressed as strain ratio (SR). Faecal elastase was quantified to assess pancreatic secretion. Data are presented as percentages, mean $\pm$ standard deviation or [95% confidence interval]. Results in cases and controls were compared using Fisher's exact test and Student-t test or U-Mann-Whitney test, as appropriate.

Results: Based on previous sample size calculation, 57 cases (age 66.6 $\pm$ 9.3 years, 31 males) and 54 controls (age 65.9 $\pm$ 9.5 years, 30 males) were included. Body mass index was 29.2 $\pm$ 5 in diabetic patients and 27.5 $\pm$ 4.7 in controls (p=0.087). The number of EUS criteria was 2.2 [1.6-2.7] in diabetics and 1.8 [1.2-2.3] in controls (p=0.34). The degree of fibrosis in the head of the pancreas was higher in diabetics (SR=2.82 [2.53-3.11]) than in controls (SR=2.44 [2.25-2.63]) (p=0.031), but not in the body and tail. Faecal elastase was similar in diabetic patients (516.9 [454.6-579.2] mcg/g) and controls (475.8 [408.3-543.3] mcg/g) (p=0.371). Six cases and nine controls had faecal elastase less than 200 mcg/g (p=0.32). Morphological and functional changes of the exocrine pancreas were not associated with the time since the onset of DM.

Conclusion: Type II DM is not associated with significant morphological, fibrotic, and functional changes in the exocrine pancreas as assessed by EUS, EUS-elastography and faecal elastase. EUS elastography shows a higher degree of pancreatic fibrosis in the head in patients with DM compared to non-diabetic subjects. This study challenges previous studies of exocrine pancreatic changes in type II DM.

Disclosure: Julio Iglesias-García: Advisor Fujii.

Coeliac disease: Part 3

13:00-14:00 / Poster Stage 5

MP650

CONFOCAL ENDOMICROSCOPY FOR THE VISUALIZATION OF DUODENAL EPITHELIAL BARRIER DEFECTS IN CELIAC DISEASE AFTER GLUTEN EXPOSURE

F. Branchi¹, J.J. Wiese¹, R. Ullrich¹, C. Bojarski¹, M. Schumann¹

¹Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Medizinische Klinik für Gastroenterologie, Infektiologie und Rheumatologie - Campus Benjamin Franklin, Berlin, Germany

Contact E-Mail Address: michael.schumann@charite.de

Introduction: In celiac disease (CeD), it is known that damage to the duodenal mucosa occurs as a consequence of a T-lymphocyte-triggered immune reaction, leading to epithelial barrier defects^{1,2}.

In addition to this adaptive immune response, intraepithelial lymphocytes are known to play a role in generating the epithelial lesion in CeD as their Natural Killer (NK) receptors are able to recognize atypical MHC-expressing enterocytes².

However, the timing of onset of epithelial barrier defects is still far from clearly understood^{3,4}.

Aims & Methods: The aim of the study was to observe if, in CeD, gluten exposure of the duodenal mucosa generates rapid epithelial barrier changes. Confocal laser endomicroscopy (CLE) allows the observation of the mucosal epithelia *in vivo*⁵.

CeD patients and controls undergoing gastroscopy were examined with CLE before and after exposing the duodenal mucosa to a gluten-containing solution applied with a spraying catheter. All CeD patients were on a long-term gluten-free diet and had negative transglutaminase antibodies at the time of the CLE examination.

Fluorescein, which has molecular size of 330 Dalton, was administered intravenously at the beginning of the examination. The presence of an epithelial barrier defect was defined if fluorescein passed from the mucosal capillaries to the lumen.

Results: Eight CeD patients and seven controls were included. In none of the 15 subjects a barrier defect was observed at the CLE after administration of fluorescein and before duodenal exposure to gluten. After gluten exposure, signs of a barrier defect, such as a fluorescein in the lumen or transepithelial fluorescein leaks, were observed in seven out of eight CeD patients (88%). The median time from gluten exposure to the detection of the barrier defect was 20 minutes (range 15-30 minutes). No signs of fluorescein leak were detected after gluten exposure of the eight controls after a median observation of 30 minutes.

Conclusion: A rapid occurrence of a gluten-induced barrier defect, as early as within 15 minutes after gluten exposure, was observed *in vivo* in CD patients.

This observation suggest the possibility that innate immune mechanisms, rather than the activation of gluten-specific T-cells, might play a role in such a rapid onset of this barrier leak.

References: 1. Jabri B, Sollid LM. T Cells in Celiac Disease. *The Journal of Immunology*. 2017;198(8):3005-3014. doi:10.4049/jimmunol.1601693

2. Hüb S, Menten JJ, Monteiro RC, et al. A Direct Role for NKG2D/MICA Interaction in Villous Atrophy during Celiac Disease. *Immunity*. 2004;21(3):367-377. doi:10.1016/j.immuni.2004.06.018

3. Schumann M, Günzel D, Buergel N, et al. Cell polarity-determining proteins Par-3 and PP-1 are involved in epithelial tight junction defects in coeliac disease. *Gut*. 2012;61(2):220-228. doi:10.1136/gutjnl-2011-300123

4. Schumann M, Siegmund B, Schulzke JD, Fromm M. Celiac Disease: Role of the Epithelial Barrier. *Cell Mol Gastroenterol Hepatol*. 2017;3(2):150-162. doi:10.1016/j.jcmgh.2016.12.006

5. Günther U, Daum S, Heller F, et al. Diagnostic value of confocal endomicroscopy in celiac disease. *Endoscopy*. 2010;42(03):197-202. doi:10.1055/s-0029-1243937

Disclosure: Nothing to disclose.

MP651

ABERRANT AND CLONAL VARIATIONS IN REFRACTORY COELIAC DISEASE TYPE II

C. Walker¹, A. Hayat², M. O'Donnell², V. Byrnes¹

¹University Hospital Galway, Gastroenterology Department, Galway, Ireland, ²University Hospital Galway, Haematology Department, Galway, Ireland

Contact E-Mail Address: walkerca@tcd.ie

Introduction: The presence of an aberrant clonal IEL population is the hallmark of RCDII. We have observed patients who have clinical features of RCDII but do not fit the classical immunophenotypic or molecular features of same.

Aims & Methods: Our aim was to describe the profile of RCDII patients who present with classical aberrancy in the absence of clonality or atypical aberrancy +/- clonality.

We conducted a retrospective review of flow cytometry and TCR-GR analysis of RCDII patients in University Hospital Galway over a 14 year period.

Results: We included 13 RCDII patients, 5 males and 7 females, with a median age of 62 years at RCDII diagnosis. 6 patients had classical RCDII, median 80% aberrant IELs (cytoCD3+/sCD3-/sCD8-) and had a clonal TCR-GR. Of the remaining 7 patients, 4 had classical aberrancy (median 52%) without clonality, including 1 who lost the TCR-GR clone 1 year post autologous stem cell transplant but whose aberrancy persisted (43%) 10 years later, and 1 who subsequently developed a clonal TCR-GR on follow up. 2 patients had an atypical aberrant IEL population without clonal TCR-GRs; one of whom developed lymphoma 3 years post RCDII diagnosis and the other remains under surveillance (16% classical aberrancy, 41%NK cells). The remaining patient has a mixed aberrant IEL population (71% cytoCD3+/sCD3-/sCD8+, 19% cytoCD3+/sCD3-/sCD8-) but has a clonal TCR-GR. Mortality rate for the classical RCD II was 66% compared to 14% in variant RCD II.

Conclusion: The heterogeneity of RCDII poses many diagnostic challenges. Newer sequencing technologies will likely aid the expansion of the diagnostic criteria to include variant RCDII. While follow up is ongoing, variant RCDII maybe associated with a lower mortality.

Disclosure: Nothing to disclose.

MP652

EFFECT OF COMMERCIAL ENZYME SUPPLEMENTS ON DEGRADATION OF GLUTEN IMMUNOGENIC PEPTIDES IN PIZZA

G. Mazzarella¹, A. Camarca¹, G. D'Auria², D.A. Leffler³, C. Nitride², N. Giardullo¹, P. Ferranti², V. Rotondi Aufiero²

¹Institute of Food Sciences-CNR, ImmunoMorphology, Avellino, Italy, ²University of Naples Federico II, Department of Agricultural Sciences, Naples, Italy, ³Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School, Boston, MA, USA., Celiac Center, Boston, United States of America, ⁴San G. Moscati Hospital, Gastroenterology, Avellino, Italy

Contact E-Mail Address: Daniel.leffler@takeda.com

Introduction: Very few studies have addressed the effect of digestive supplements on gluten hydrolysis, particularly in a complex food matrix.

Aims & Methods: Here, we investigated the effect of such supplements on gluten immunogenic peptides digestion in a standardized pizza.

Pizza samples were digested using the harmonized INFOGEST *in vitro* digestion method, in absence (CTR) or in the presence of 3 different commercial supplements (*i.e.*, S1, S2 and S3). Gluten content after gastric (G, T120min) or gastro-duodenal (GD, T240min) digestion, was evaluated by RIDASCREEN® Gliadin competitive R5-ELISA and immunogenicity of resistant, deamidated peptides, was assayed on celiac disease derived intestinal-T cell lines (iTCLs).

Results: Supplemental enzymes reduced the R5-specific peptide amount, both at the end of G stage (decrease vs CTR_G: S1 76%, S2 96.5%, S3 98.5%) and after GD digestion (decrease vs CTR_GD: S1 52%, S2 52%, S3 85%). iTCLs activation assays showed a consistent IFN- γ reduction by S3-treatment, both for G (55 % decrease vs CTR_G, $p=0.027$) and GD peptides (93 % decrease vs CTR_GD, $p=0.016$). Regarding S1, a significant reduction was obtained only at the end of GD digestion (87 % decrease vs CTR_GD, $p=0.024$) while for S2 reduction did not reach statistical significance (25% decrease vs CTR_G, 69% decrease vs CTR_GD).

Conclusion: In a complex food matrix, different rates of gluten degradation were seen depending on enzyme supplements composition. The highest protease activity was observed for S3. Notably, the R5-ELISA results were not consistent with iTCLs activation assays, suggesting that iTCLs are mandatory to exclude significant residual immunoreactivity of digested products.

Disclosure: This study was supported by an unrestricted grant from Takeda Pharmaceuticals.

MP653

THE ROLE OF HIGHLY PROCESSED FOODS AND MEDITERRANEAN DIET ON GASTROINTESTINAL SYMPTOMS, METABOLIC PROFILE AND QUALITY OF LIFE IN ADULT COELIAC PATIENTS ON A GLUTEN-FREE DIET: A MULTICENTRE PROSPECTIVE STUDY

D. Scalvini¹, B. Bongiovanni², A. Schieppati³, S. Maimaris², G. Mantica², C. Scarcella², F. Zingone⁴, F. Marta⁵, D. Maniero⁴, L. Roncoroni⁶, A. Costantino⁷, A. Mussetto⁸, L. Elli⁷, F. Biagi³

¹University of Pavia, PhD in experimental Medicine, Pavia, Italy, ²UNIVERSITY OF PAVIA, Pavia, Italy, ³University of Pavia; Istituti Clinici Scientifici Maugeri IRCCS, Gastroenterology Unit of Pavia Institute, Pavia, Italy, ⁴University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ⁵University of Padua, Department of Surgery, Oncology, Gastroenterology, Padua, Italy, ⁶Center for Prevention and Diagnosis of Celiac Disease-Gastroenterology and Endoscopy Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy, ⁷Center for Prevention and Diagnosis of Celiac Disease-Gastroenterology and Endoscopy Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, ⁸Gastroenterology Unit, Santa Maria delle Croci Hospital, Ravenna, Italy

Contact E-Mail Address: davidescalvini.med@gmail.com

Introduction: A strict lifelong gluten-free diet (GFD) is the mainstay of treatment for coeliac disease (CD). However, persistence of gastrointestinal symptoms in coeliac patients despite a GFD is a relevant clinical scenario. The impact of highly processed foods (HPF) intake and the adherence to a correct Mediterranean diet (MD) on these symptoms, the quality of life (QOL), and the metabolic profile of coeliac patients on a GFD is not well understood. This study aimed to investigate the influence of HPF and MD on gastrointestinal symptoms, QOL, and metabolic profile in coeliac patients on a GFD.

We hereby present partial data of this ongoing study.

Aims & Methods: Adult CD patients were prospectively enrolled between November-2023 and March-2024 at four Italian referral centers. For each enrolled patient, the following data were recorded: persistent symptoms over the previous 12 months and in the 7 days prior to enrolment by using the GRS-CeD, adherence to a GFD, adherence to a MD evaluated by means of the Pyramid-based Mediterranean Diet Score (PyrMDS), the consumption of highly processed food evaluated by means of the sQ-HPF, the Celiac Disease-specific Quality of Life Scale (CD-QoL) and metabolic profile. These data were subsequently statistically analyzed.

Results: A total of 121 patients (83F, mean age 44±15 years) were enrolled. Overall, 61% of patients reported persistent gastrointestinal symptoms despite a GFD. Patients with persistent symptoms were more likely to be female (78% vs 53%, $p<0.01$), to have a lower HPF intake (26% vs 30%, $p=0.02$), a higher GRS-CeD score (median 3 vs 18.5, $p<0.001$), and lower CD-QoL scores (mean CD-QoL 80 vs 88, $p<0.001$), but did not have higher PyrMDS scores ($p=0.21$). PyrMDS was inversely correlated with HPF intake ($r=-0.20$, $p=0.03$) and serum triglycerides ($r=-0.22$, $p=0.05$), and positively correlated with HDL cholesterol ($r=0.20$, $p=0.08$). At multivariate logistic regression adjusted for age and sex, persistence of gastrointestinal symptoms despite a GFD was associated with female sex ($p<0.01$), lower HPF intake ($p=0.04$), but not adherence to MD ($p=0.31$).

Conclusion: Persistence of gastrointestinal symptoms in coeliac patients despite a GFD is common, but unrelated to the adherence to a MD. Female sex and lower intake of HPF were associated with persistence on gastro-

intestinal symptoms despite a GFD despite a better metabolic profile. Optimising dietary treatment of coeliac patients with persistent gastrointestinal symptoms despite a GFD requires expert nutritional counselling.

Disclosure: Nothing to disclose.

MP654

ENDOMYSIAL ANTIBODY DETECTION FOR COELIAC DISEASE ON ENGINEERED CELL EXTRACELLULAR MATRIX

I. Korponay-Szabo^{1,2}, R. Király³, J. Gyimesi², M. Mäki⁴

¹University of Debrecen, Paediatrics, Debrecen, Hungary, ²Heim Pál National Paediatric Institute, Coeliac Disease Centre, Budapest, Hungary, ³University of Debrecen, Biochemistry and Molecular Cell Biology, Debrecen, Hungary, ⁴Tampere University Faculty of Medicine and Health Technology, Paediatric gastroenterology, Tampere, Finland

Contact E-Mail Address: ilma.korponay-szabo@tuni.fi

Introduction: Serum endomysial antibody (EMA) detection is still an important verification tool with high positive predictive value for coeliac disease (CeD) in patients positive with anti-transglutaminase antibody IgA (TGA) result or in seronegative cases with small intestinal villous atrophy. Moreover, EMA positivity is part of the non-invasive diagnostic criteria of CeD in children and adolescents with TGA+ results above 10 times of the upper limit of normal ($>10\times\text{ULN}$). EMA detections on the classical substrates, monkey oesophagus or human umbilical cord are less sensitive than TGA and both the preparation of the tissue slides and the reading are time-consuming and need expertise. Moreover, it is getting difficult to get commercial slides for the testing. Human umbilical cord vein-derived endothelial cells (HUVECs) produce in cell culture a regular extracellular matrix (ECM) resembling endomysial network with similar exposure of celiac-relevant transglutaminase epitopes as in tissue sections.

Aims & Methods: The aim of this study was to evaluate the diagnostic performance of EMA testing on HUVEC-ECM. Ninety new patients consecutively referred to our center between May–September 2023 in reason of positive coeliac antibody results in outside laboratories or by various rapid tests were prospectively tested for EMA-IgA on HUVEC-ECM prepared on 18-well plastic slides. Results were compared with those of our hospital's TGA-IgA ELISA and EMA-IgA performed in 1:2.5 dilutions on a composite substrate containing monkey oesophagus, human umbilical cord and gut wall tissues.

Results: TGA-IgA, EMA-IgA on tissues and EMA-IgA on HUVEC-ECM were positive in 73, 62 and 67 samples with 94.4%, 92.9% and 95.7% accuracies for the final CeD diagnosis (non-invasive + biopsy-based), respectively. In 17 samples all three antibodies were negative; most of these patients had only TGA-IgG or DGP earlier.

	TGA	EMA+ on tissues	EMA+ on HUVEC-ECM
$>10\times\text{ULN}$	51	51	51
2-10xULN	16	11	14
1-1.9xULN	6	0	2

Conclusion: The easily available novel HUVEC-ECM substrate provided high sensitivity and specificity for EMA-IgA detection and also may improve the evaluation of coeliac autoimmunity when TGA is low positive or borderline.

Disclosure: Nothing to disclose.

MP655

COMPARISON OF INTER-READER AGREEMENT FOR COMPOSITE CELIAC HISTOLOGY ENDPOINTS AND CONTRAST WITH TRADITIONAL HISTOLOGY ENDPOINTS

J.R. Maxwell¹, D. Raunig¹, M. Zarei¹, Q. Lei¹, V. Gupta¹, J. Isola^{2,3}, J. Laatta³, K. Salonoja³, T.-T. Wu⁴, J. Murray⁵, M.E. Robert⁶, D.A. Leffler¹, G. Smithson¹

¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²University of Tampere, Tampere, Finland, ³Jilab Inc., Tampere, Finland, ⁴Mayo Clinic, Department of Laboratory Medicine and Pathology, Rochester, United States of America, ⁵Mayo Clinic, Division of Gastroenterology and Hepatology, Rochester, United States of America, ⁶Yale University School of Medicine, Department of Pathology, New Haven, United States of America

Contact E-Mail Address: daniel.leffler@takeda.com

Introduction: Measuring changes in mucosal damage and inflammation is important for assessing efficacy of experimental therapeutics in celiac disease clinical trials; however, there is no consensus on the optimal histologic endpoints. We previously demonstrated that quantitative endpoints (villous height to crypt depth ratio [Vh:Cd] and intraepithelial lymphocyte [IEL] counts), have better concordance among readers than qualitative measurement of pathology (Marsh-Oberhuber) when using a digital microscopy platform (SlideVantage, Jilab Inc.). The aim of this study was to further compare reader agreement when using composite and multiple component celiac pathology measures.

Aims & Methods: We compared reader agreement with three composite endpoints that combine Vh:Cd and IEL measurements into one score: Quantitative Mucosal Algorithmic Rules for Scoring Histology (Q-MARSH), Vh:Cd IEL (VCIEL), and multiparametric VCIEL (mpVCIEL), using duodenal biopsies from a phase 2 trial in patients with celiac disease (NCT03738475).

Results: We observed a kappa statistic for Q-MARSH of 0.35 and concordance correlation coefficient (CCC) of 0.86 for VCIEL and 0.60 for mpVCIEL. Compared to previous measurements with IEL (CCC = 0.85) or Vh:Cd (CCC = 0.80), VCIEL and mpVCIEL performed comparably and had better reader agreement than the categorical scoring systems, Q-MARSH and Marsh-Oberhuber (kappa = 0.42). We further examined reader agreement when measuring a change from baseline after gluten challenge or after therapeutic treatment and graphically contrasted how changes in each composite endpoint associated with traditional endpoints.

Conclusion: The composite measures assessed in this study capture changes in both architectural (Vh:Cd) and inflammatory (IEL) components of intestinal pathology in celiac disease. Quantitative endpoints, measuring single components or combined into a composite quantitative endpoint, provide the best interobserver agreement and appear most appropriate for assessment of celiac histology in clinical trials.

Disclosure: JM, DR, MZ, QL, VG, DL and GS are employees and shareholders of Takeda. JI is the founder and owner of Jilab, Inc.; is a Full Professor at Tampere University, Medical Faculty; and has a consulting agreement with Takeda. JL and KS are full-time employees of Jilab, Inc. TTW has nothing to disclose. JAM holds grants (to institution) from National Institutes of Health, Immunogenix, Takeda Pharmaceutical, Allakos, ProventionBio, Oberkotter Foundation, and 9Meters, Inc.; contract (to institution) from Kanyos Bio (a wholly owned subsidiary of Anokion); and consultancy fees from Johnson and Johnson, Bristol Myers Squibb, Intrexon Corporation, Dren Bio, Neoleukin, Reistone pharma, GSK, Immunic Therapeutics, Brightseed Bio, Chugai Pharma, Alimentiv, Equillium, Ukko, Medibeacon, Israel Biotech Fund, Precigen, triangle insights group, Sanofi, Zag Bio, Loop bio, and Orbimed and has received royalties from Evelo. MER is a consultant for Takeda, Perspectum and Alimentiv.

MP656

INCREASED FAECAL CALPROTECTIN MEASUREMENT AS A PREDICTOR OF SEVERE DISEASE PHENOTYPE AND PROGNOSIS IN COELIAC DISEASE AND NON-COELIAC ENTEROPATHIES

A. Cappellini¹, A. Schieppatti^{1,2}, S. Maimaris¹, P. Minerba¹, G. Mantica¹, M. Retrosi¹, C. Scarcella², G. Arpa^{3,4}, P.I. Bianchi⁵, A. Di Sabatino^{1,5}, F. Biagi^{1,2}

¹University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy, ²Istituto Clinici Scientifici Maugeri, IRCCS, Gastroenterology Unit of Pavia Institute, Pavia, Italy, ³Department of Molecular Medicine, Unit of Anatomic Pathology, University of Pavia, Pavia, Italy, ⁴Unit of Anatomic Pathology, ICS Maugeri, Pavia, Italy, ⁵First Department of Internal Medicine, San Matteo Hospital Foundation, Pavia, Italy

Contact E-Mail Address: alessandro.cappellini9@gmail.com

Introduction: Faecal calprotectin (FC) is a non-invasive biomarker of gut inflammation widely used in the diagnosis and follow-up of inflammatory bowel disease. Coeliac disease (CeD) is a gluten dependent disorder characterised by an increased mortality than in the general population mainly due to the development of complications (CCeD) [1,2]. Non-coeliac enteropathies (NCEs) are a group of rare conditions that can pose problems of differential diagnosis with CCeD and are characterised by poor prognosis [3]. The role of FC in monitoring disease activity in CeD and NCEs is currently undefined.

Aims & Methods: We aimed to retrospectively evaluate FC as a tool for assessing clinical and histological disease activity and prognosis in patients with CeD and NCEs.

Patients with uncomplicated and complicated CeD and NCEs with available data on FC at baseline and/or during follow-up, evaluated at our centre between June-2008 and December-2023, were enrolled. We retrospectively collected data on FC levels, clinical and histological response to therapies, and long-term outcomes, including complications and mortality. Values of FC > 50mg/kg were considered elevated. The relationship between elevated FC and disease activity was statistically analysed and Cox regression adjusted for age and sex was used to compare development of complications and mortality in patients with elevated/normal FC.

Results: 177 patients (109F, mean age at diagnosis 39±20 years, 132 uncomplicated CeD, 17 CCeD, 28 NCEs) were enrolled. 55 patients (31.1%) had elevated FC (median value 250 mg/kg), which was significantly associated with lack of clinical response to therapy and persistence of small bowel villous atrophy (both p<0.001). During a median follow-up of 103 months (IQR 54-176), 22 (12.4%) patients developed complications and 21 (11.9%) died. Elevated FC was significantly more common in CCeD (70.6%) and NCEs (67.9%) than in uncomplicated CeD (18.2%), p<0.001. On a multivariate analysis elevated FC was an independent predictor of complications (HR 4.8, 95%CI 1.4-16.7, p=0.01) and mortality (HR 4.8, 95%CI 1.6-14.3, p<0.01).

Conclusion: Increased FC levels were associated with lack of clinical and histological response to therapy, development of complications and increased mortality in patients with CeD and NCEs. FC may be a useful non-invasive biomarker to help identify patients with CeD and NCEs with a severe disease phenotype at high risk of poor long-term outcomes and should be included in the diagnostic work-up for these conditions.

References:

- [1] Ludvigsson JF et al. Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology. Gut. 2014; 63(8):1210-28
- [2] Biagi F et al. Risk of complications in coeliac patients depends on age at diagnosis and type of clinical presentation. Dig Liver Dis. 2018; 50(6):549-552

[3] Schieppatti A et al. Nomenclature and diagnosis of seronegative coeliac disease and chronic non-coeliac enteropathies in adults: the Paris consensus. *Gut*. 2022; 71(11):2218-2225

Disclosure: Nothing to disclose.

MP657

ENDOSCOPIC FINDINGS IN COELIAC DISEASE IDENTIFIED THROUGH POPULATION-BASED SCREENING, THE TRØNDELAG HEALTH STUDY, NORWAY

S. Bostrøm¹, L. Uthaug¹, R. Hjort^{1,2,3}, I.L. Andersen^{1,3}, P. Lukina^{1,3}, L.M. Sollid^{4,5}, K.E. Lundin^{4,6}, E. Ness-Jensen^{2,1,3,7}

¹NTNU, Norwegian University of Science and Technology, HUNT Research Centre, Department of Public Health and Nursing, Levanger, Norway, ²NTNU, Norwegian University of Science and Technology, HUNT Centre for Molecular and Clinical Epidemiology, Department of Public Health and Nursing, Trondheim, Norway, ³Nord-Trøndelag Hospital Trust, Department of Medicine, Levanger Hospital, Levanger, Norway, ⁴University of Oslo, Norwegian Coeliac Disease Research Centre, Institute of Clinical Medicine, Oslo, Norway, ⁵Oslo University Hospital, Department of Immunology, Oslo, Norway, ⁶Oslo University Hospital, Department of Gastroenterology, Rikshospitalet, Oslo, Norway, ⁷Karolinska Institutet & Karolinska University Hospital, Department of Molecular Medicine and Surgery, Stockholm, Sweden

Contact E-Mail Address: eivind.ness-jensen@ntnu.no

Introduction: Coeliac disease (CD) is a chronic small intestinal immune-mediated enteropathy which occurs in genetically predisposed individuals by exposure to ingested gluten, globally about 1% of the world's population. CD mainly affects the gastrointestinal tract but may also affect other organs. CD may therefore present with a wide range of symptoms and signs. Diagnosing CD involves assessment of symptoms, clinical findings, serology, and endoscopy with duodenal biopsies.

In children and adolescents, endoscopy with biopsies can be omitted if serology is conclusive, but this is controversial in adults. Endoscopy can have an additional yield by diagnosing other non-CD related findings, including premalignant and malignant lesions of the upper gastrointestinal tract.

Aims & Methods: The aim of this study was to assess the additional non-CD related findings at the diagnostic endoscopy for CD in an adult population screened for CD. The study was based on the fourth Trøndelag Health Study (HUNT4), a population-based study of adults above 20 years of age in Norway (1).

Serum samples of 54,505 participants were analysed using a dual anti-transglutaminase 2 immunoglobulin A and G assay, and the 1107 seropositive individuals were invited to upper gastrointestinal endoscopy with duodenal biopsies. CD was confirmed if histological findings corresponding to Marsh grade 3 were found. At the diagnostic investigation performed by specialists in gastroenterology, additional endoscopic findings were recorded systematically.

Multivariable logistic regression analysis was used to estimate the risk of additional findings at the diagnostic endoscopy for CD. The risk was adjusted for sex, age, and use of medications (non-steroid anti-inflammatory drugs/acetysalicylic acid and proton pump inhibitors/histamine-2 receptor antagonists).

Results: In the present study, 476 individuals with confirmed CD were included. Median age was 55 years and 54.6% were women. The proportion of additional non-CD related endoscopic findings increased with increasing age, especially above 50 years of age. Seven Barrett's oesophagus and one duodenal adenoma with low grade dysplasia were found, all among

participants above 50 years of age. No malignant lesions were found. The risk of additional endoscopic findings increased with advancing age and was higher among men and those using proton pump inhibitors or histamine-2 receptor antagonists.

Conclusion: This study suggests that diagnosing CD without endoscopy will not result in missing clinically significant additional findings in the younger adult population below 50 years of age. However, with advancing age above 50 years, the risk of non-CD related premalignant lesions increases. These lesions can be detected at the diagnostic endoscopy for CD and treated or included in surveillance programs to prevent sinister outcomes.

References: 1. Lukina P, Andersen IL, Eggen PT, Mjones PG, Ronne E, Bolstad N, et al. Coeliac disease in the Trondelag Health Study (HUNT), Norway, a population-based cohort of coeliac disease patients. *BMJ Open*. 2024;14(1):e077131.

Disclosure: Nothing to disclose.

MP658

MAPPING OF HLA-DQ HAPLOTYPES IN ADULTS WITH COELIAC DISEASE IN A LARGE, SCREENED POPULATION – RESULTS FROM THE NORWEGIAN HUNT STUDY

R. Hjort^{1,2,3}, I.L. Andersen^{1,3}, P. Lukina^{1,3}, K. Hveem^{1,2}, K.E. Lundin^{4,5}, L.M. Sollid^{4,6}, E. Ness-Jensen^{1,2,3,7}

¹HUNT Research Centre, NTNU, Norwegian University of Science and Technology, Levanger, Norway, ²HUNT Center for Molecular and Clinical Epidemiology, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, ³Department of Medicine, Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway, ⁴Norwegian Coeliac Disease Research Centre, Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ⁵Department of Gastroenterology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, ⁶Department of Immunology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, ⁷Department of Molecular Medicine and Surgery, Karolinska Institutet & Karolinska University Hospital, Stockholm, Sweden

Contact E-Mail Address: rebecka.hjort@ntnu.no

Introduction: The HLA-DQ2.5, -DQ2.2 or -DQ8 haplotypes are necessary for coeliac disease development with homozygotes of DQ2.5 carrying the highest disease risk. However, with only 1:4-1:7 of true patients usually diagnosed, the true haplotype distribution is unknown.

It can be hypothesized that the distribution differs in the large group of undiagnosed individuals who likely present with less distinct symptoms and older age.

Aims & Methods: The aim of this study was therefore to investigate the HLA-DQ haplotype distribution including both known and new, previously undiagnosed patients. A population-based study of 52,588 adults was screened for coeliac disease by serology, identifying 470 new cases (Marsh 3) in addition to 376 known cases identified via registries. All cases and a random sample of 1412 controls underwent HLA-DQA1- and HLA-DQB1-sequencing to infer relevant HLA-DQ haplotype combinations (DQ2.5/DQ2.5, DQ2.5/DQ2.2, DQ2.2/DQ7.5 [DQ2.5trans], DQ8/DQ8, DQ2.5/DQ8, DQ2.5/DQ7.5, DQ2.5/DQX, DQ2.2/DQ2.2, DQ2.2/DQ8, DQ2.2/DQX, DQ8/DQX, DQX/DQX [neither DQ2 nor DQ8]). Odds ratios (OR) with 95% confidence intervals (CI) for risk assessment were calculated.

Results: Haplotype frequencies in cases vs. controls were 85.2% vs. 22.3% (DQ2.5cis), 8.3% vs. 21.6% (DQ8), and 1.2% vs. 8.2% (DQ2.2). DQ2.5 homozygosity carried the highest risk: OR 16.6 (CI 9.6-31.1), while DQ2.5/DQX had an OR of 6.3 (5.2-7.7). DQ2.5trans, although rare, still conferred a high risk (OR 10.6, 3.8-30.8). DQ8 homozygosity also posed a high risk (OR 7.5,

3.9-14.2) while DQ8/DQX had an OR of 2.1 (1.4-3.0). ORs for DQ2.2/DQ2.2 and DQ2.2/DQX were 3.0 (0.4-13.0) and 0.7 (0.3-1.3), respectively. No clear risk differences were observed between new and known cases, however, none of the new cases carried DQX/DQX in contrast to 5.6% of the known cases.

Conclusion: We found a gene-dose effect linked to DQ2.5 and DQ8 in both known and new cases, with a surprisingly high proportion of DQ8 for a Nordic population. Conversely, the large proportion of DQX/DQX in known cases compared to the absence in new cases, suggests a high prevalence of historically misdiagnosed patients.

References: 1. Sollid LM (2017) The roles of MHC class II genes and post-translational modification in celiac disease. *Immunogenetics* 69: 605-616

2. Lukina P, Andersen IL, Eggen PT, Mjones PG, Ronne E, Bolstad N, et al. Coeliac disease in the Trondelag Health Study (HUNT), Norway, a population-based cohort of coeliac disease patients. *BMJ Open*. 2024;14(1):e077131.

Disclosure: Nothing to disclose.

MP659

UNNECESSARY GLUTEN-FREE DIET IMPACTS GUT MICROBIOTA IN HEALTHY SUBJECTS: UNSUPERVISED GLUTEN RESTRICTION VS A NUTRITIONAL FOLLOW-UP

F. Manza¹, A. Costanzini¹, L. Lungaro¹, M. Puncochár², N. Segata², F. Pinto², F. Asnicar², F. Armanini², A. Carroccio³, P. Mansueto³, A. Seidita³, A. Calabrò⁴, D. Cavalieri⁵, G. Barbara^{6,7}, V. Stanghellini^{6,7}, U. Volta⁶, R. De Giorgio¹, G. Caio^{1,8}

¹University of Ferrara, Ferrara, Italy, ²University of Trento, Cellular, Computational and Integrative Biology, Trento, Italy, ³University of Palermo, Internal Medicine and Medical Specialties (DIMIS), Palermo, Italy, ⁴University of Florence, Florence, Italy, ⁵University of Florence, Biology, Florence, Italy, ⁶University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁷IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ⁸Massachusetts General Hospital-Harvard Medical School, Mucosal Immunology and Biology Research Center, Boston, United States of America

Contact E-Mail Address: mnzfn@unife.it

Introduction: Nowadays the use of a gluten-free diet (GFD) is erroneously considered a healthy life choice worldwide, despite evidence supports its beneficial effect only in the treatment of celiac disease and, possibly, gluten sensitivity. GFD can modify microbiota composition, decreasing specifically bacterial species involved in polysaccharides metabolism and short chain fatty acids (SCFAs) production.

In fact, a GFD usually show a lower carbohydrate composition with an increase of dietary fats, and a fiber intake significantly below the recommended range.

In this study, we investigated whether the amount of daily intake complex carbohydrates during GFD was associated with the reduction of microbial richness and species' relative abundance.

Aims & Methods: We enrolled 36 healthy subjects and randomly assigned to a self-made GFD (SGFD) regimen (n=23, yrs=35±14) or to a GFD under nutritional supervision (NGFD) that ensured 60% of daily dietary carbohydrates intake (n=13; 29±12 yrs). A total of 144 fecal samples were collected at day 0, and 3, 7, 30 days during GFD, sequenced via shotgun metagenomic and profiled via bioBAkery 3. Data were analyzed on MetaPhlAn 4.0 and HUMAnN 3.0 for taxonomic and functional profiling. Alpha-diversity (Shannon index, SI) and relative abundances were computed. Only species detectable in at least 5 subjects were considered (600 species). Statis-

tical analysis was performed using a linear mixed model and Friedman's ANOVA. P-values were combined and corrected for multiple hypothesis testing (q-value).

Results: Alpha-diversity did not significantly change during 30 days of GFD in both groups.

However, 14 and 10 species significantly changed in their relative abundance in the SGFD and NGFD groups, respectively. We observed a decrease of *Bifidobacterium longum* (SGB17248) and *Candidatus Cibionibacter quicibialis* (SGB15286) (q<0.05) with no intergroup differences. SGFD showed a decrease of butyrate producing species, i.e. *Dorea longicatena* and *Anaerobutyricum hallii*.

Conclusion: During GFD, microbial alpha-diversity preservation is independent from the daily carbohydrate intake. However, we identified consistent modifications in microbial relative abundances that partially differ in the two groups. The NGFD group showed a significant decrease in five *Bifidobacterium* species' bacteria. *Bifidobacteria* are functionally linked to complex carbohydrate metabolism and associated with immunomodulatory properties. Despite we cannot point out specific role for gluten or carbohydrate intake in the microbiota's richness variation, healthy subjects should not be encouraged to follow a GFD for its negative effects on gut health.

References: Melini, Valentina; Melini, Francesca (2019). Gluten-Free Diet: Gaps and Needs for a Healthier Diet. *Nutrients*, 11(1), 170-. doi:10.3390/nu11010170

Jones AL. The Gluten-Free Diet: Fad or Necessity? *Diabetes Spectr*. 2017 May;30(2):118-123. doi: 10.2337/ds16-0022. PMID: 28588378; PMCID: PMC5439366.

Gessaroli M, Frazzoni L, Sikandar U, Bronzetti G, Pession A, Zagari RM, Fucio L, Forchielli ML. Nutrient intakes in adult and pediatric coeliac disease patients on gluten-free diet: a systematic review and meta-analysis. *Eur J Clin Nutr*. 2023 Aug;77(8):784-793. doi: 10.1038/s41430-023-01280-0. Epub 2023 Mar 1. PMID: 36859658.

Hansen, L.B.S., Roager, H.M., Søndergaard, N.B. et al. A low-gluten diet induces changes in the intestinal microbiome of healthy Danish adults. *Nat Commun* 9, 4630 (2018). <https://doi.org/10.1038/s41467-018-07019-x>

Disclosure: Nothing to disclose.

Eosinophilic oesophagitis: Mechanisms

13:00-14:00 / Poster Stage 6

MP660

DUPILUMAB IMPROVES ESOPHAGEAL INFLAMMATORY FEATURES AS MEASURED BY ENDOSCOPIC REFERENCE SCORE IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS: 52-WEEK RESULTS FROM THE PHASE 3 EOE KIDS TRIAL

I. Hirano¹, S. Schroeder², M. Chehade³, C. Menard-Katcher⁴, N. Virk Hundal⁵, R. Liu⁶, R. Abdulai⁷, J. Maloney⁶, M. Louisias⁷, A. Radin⁶

¹Northwestern University, Division of Gastroenterology, Chicago, United States of America, ²Division of Gastroenterology, Hepatology, and Nutrition, Phoenix Children's, Phoenix, United States of America, ³Mount Sinai Center for Eosinophilic Disorders, Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁴GI Digestive Health Institute, Children's Hospital Colorado, Aurora, United States of America, ⁵Food Allergy Center, Massachusetts General Hospital, Boston, United States of America, ⁶Regeneron Pharmaceuticals Inc., Tarrytown, United States of America, ⁷Sanofi, Bridgewater, United States of America

Contact E-Mail Address: mirna.chehade@mssm.edu

Introduction: Eosinophilic esophagitis (EoE) is a chronic, progressive, type 2 inflammatory disease. Dupilumab is a fully human monoclonal antibody that blocks interleukin (IL)-4 and IL-13, key drivers of type 2 inflammation. The EoE-Endoscopic Reference Score (EREFS) is validated for assessment of esophageal features of EoE and includes subscores for inflammation and remodeling. This study assessed the impact of dupilumab on EREFS in children aged 1 to <12 years with active EoE in the Phase 3 EoE KIDS trial.

Aims & Methods: In Part A, patients were randomized 2:2:1:1 to receive dupilumab higher-exposure (HE) or lower-exposure (LE), or placebo (2 groups) for 16 weeks. Patients who completed Part A could enter Part B, where those on dupilumab continued the same regimen and those on placebo switched to their preassigned dupilumab regimen (dupilumab HE or LE) for a further 36 weeks. EREFS total score was calculated as the sum of edema (score range 0–1), rings (0–3), exudates (0–2), furrows (0–2), and strictures (0–1) in the distal and proximal (0–9 each) regions. Absolute change from baseline in centralized EREFS total score (0–18), EREFS inflammation (0–10) and remodeling (0–8) subscores, and proportion of patients achieving endoscopic remission, defined by EREFS total score ≤4, was assessed at Week (W) 16 and W52. This evaluation focused on patients who received dupilumab HE or placebo.

Results: 102 patients were enrolled (37 HE dupilumab, 31 LE dupilumab, and 34 placebo); baseline EREFS scores were similar across treatment groups with EREFS inflammation subscores higher than remodeling subscores (6.0 vs 0.9 in the total population). EREFS total score was significantly reduced at W16 with dupilumab HE vs placebo (least squares mean change from baseline [95% confidence interval (CI)] -3.5 [-4.3, -2.6] vs 0.3 [-0.6, 1.2]; least squares mean difference [95% CI] -3.8 [-4.9, -2.6], p<0.0001). Improvement observed in the dupilumab HE group was sustained through W52 (mean change from Part A baseline [standard deviation (SD)] -4.8 [3.1] and patients switching from placebo to dupilumab HE in Part B saw improvement at W52 (-3.6 [3.3]). At W16, a significantly greater proportion of dupilumab HE- vs placebo-treated patients achieved an EREFS total score ≤4 (mean difference [95% CI] 75.1% [60.3–90.0], nominal p<0.0001). At W52, EREFS total score ≤4 was achieved by 87.9% of patients receiving dupilumab for the duration of the study, and 58.8% of patients switching from placebo to dupilumab HE. EREFS inflammation subscore was reduced at W16 with dupilumab HE vs placebo (mean change from baseline [SD] -3.5 [2.2] vs 0.1 [2.2], nominal p<0.0001). Improvement was

sustained through W52 in the continuous dupilumab HE group (mean change from Part A baseline [SD] -4.2 [2.5]) and patients switching from placebo to dupilumab HE in Part B improved at W52 (-3.2 [2.4]). As expected, assessment of changes in remodeling (W16: -0.2 [1.1] vs -0.2 [1.2]) was limited by low prevalence of fibrostenotic features in young children.

Conclusion: Dupilumab HE led to significant improvement in EREFS total score at W16 vs placebo, which was sustained through W52. This change was mainly driven by improvement in EREFS inflammation subscore. A significantly greater proportion of patients treated with dupilumab HE achieved endoscopic remission at W16 compared with placebo, which was sustained through W52.

Disclosure: Hirano I: Adare Pharmaceuticals/Ellodi Pharmaceuticals, Allakos, Aslan Pharmaceuticals, AstraZeneca, Calyx/Parexel, Celldex Therapeutics, Inc., Eli Lilly, EsoCap Biotech, Gossamer Bio, Meritage Pharma Inc., Nexstone Immunology, Pfizer/Arena Pharmaceuticals, Phathom Pharmaceuticals, Receptos/Celgene/Bristol Myers Squibb, Sanofi/Regeneron Pharmaceuticals Inc., Shire/Takeda – consultant; Adare Pharmaceuticals/Ellodi Pharmaceuticals, Allakos, AstraZeneca, Meritage Pharma, Inc., Pfizer/Arena Pharmaceuticals, Receptos/Celgene/Bristol Myers Squibb, Regeneron Pharmaceuticals Inc., Shire/Takeda – research funding; Sanofi/Regeneron Pharmaceuticals Inc. – speaker fees. Schroeder S: EvoEndo, Regeneron Pharmaceuticals Inc., Sanofi – consultant; Allakos, AstraZeneca, Celgene, Regeneron Pharmaceuticals Inc. – research funding. Chehade M: Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, BMS, Nexstone Immunology, Phathom, Recludix Pharma, Regeneron Pharmaceuticals Inc., Sanofi, Shire/Takeda – consultant; Adare Pharma Solutions/Ellodi, Allakos, AstraZeneca, Celgene/BMS, Danone, Regeneron Pharmaceuticals Inc., Shire/Takeda – research funding. Menard-Katcher C: No disclosures to report. Virk Hundal N: AstraZeneca, Celgene/BMS, Regeneron Pharmaceuticals Inc. – research funding. Liu R, Maloney J, and Radin A: Regeneron Pharmaceuticals Inc. – employees and shareholders. Abdulai R and Glotfelty L: Sanofi – employees, may hold stock and/or stock options in the company.

MP661

WITHDRAWN

MP662

BLOOD EOSINOPHILS ACCURATELY PREDICT A DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS AMONG PATIENTS REPORTING DYSPHAGIA AND TREATMENT RESPONSE IN EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE MULTI-CENTER STUDY

D. Stefani Donati¹, P. Visaggi¹, G. Pellegatta², I. Solinas¹, M. Ghisa³, F. Ovidi¹, G. Adamo¹, G. Scaramuzza¹, G. Del Corso⁴, F.P. Giugliano², M.E. Filice⁵, E. Marciano⁶, A. Repici², E.V. Savarino³, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²IRCCS Humanitas Research Hospital, Endoscopic Unit, Department of Gastroenterology, Milan, Italy, ³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁴Institute of Information Science and Technologies “A. Faedo”, National Research Council of Italy (CNR), Pisa, Italy, ⁵Azienda Ospedaliero Universitaria Pisana, Department of Pathology, Pisa, Italy, ⁶Azienda Ospedaliero Universitaria Pisana, Endoscopy Unit, Pisa, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Upper endoscopy (EGD) with esophageal biopsies is required to rule out eosinophilic esophagitis (EoE) in patients reporting dysphagia. Moreover, EoE monitoring currently requires esophageal biopsies to assess treatment response based on eosinophil counts on histology. Non-invasive screening and monitoring strategies are needed to reduce the diagnostic delay and streamline the follow-up of patients with EoE.

Aims & Methods: In this prospective cross-sectional multicenter study conducted at three EoE-referral centers in Italy, we investigated whether absolute eosinophil count (AEC) and eosinophil percentage (EosPercent) could a) predict a diagnosis of EoE among patients referred for dysphagia, b) serve as a marker of histological remission in treated EoE patients. We enrolled consecutive patients undergoing EGD with six esophageal biopsies for suspected or known EoE. For all patients, a full blood count was obtained prior to the EGD. A diagnosis of active EoE or histological remission was performed based on current guidelines. Non-EoE dysphagia (NED) patients were identified based on the presence of <15 eosinophils/high-power field in all six esophageal biopsies while off eosinophil-depleting treatments. Demographic, clinical, AEC, and EosPercent data were collected. Kruskal-Wallis Rank Sum Test and Pearson’s Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to assess the diagnostic accuracy (AUC) of AEC and EosPercent. Significance threshold was p<0.05.

Results: Of the 92 included patients, 33 had active EoE, 18 had EoE in histological remission while on budesonide orodispersible tablets (BOT) or proton pump inhibitors (PPI), and 41 had NED. Patients with EoE were younger and more frequently male and atopic compared to NED (p<0.01 for all). Overall, 98% (50/51) of EoE had AEC, and 84.3% (43/51) had EosPercent within the normal range. Similarly, 100% (41/41) of NED had AEC, and 90.2% (37/41) had EosPercent within the normal range. There were no differences between EoE and NED in terms of proportion of patients with AEC or EosPercent above the upper limit of normal (p>0.4 for all) (Table 1). Median AEC [380 (210, 460)/mm3 vs 120 (70, 220)/mm3; p<0.001] and EosPercent [5.40 (3.60, 7.05)% vs 1.80 (0.8, 3.0)%; p<0.01] were significantly higher in active EoE compared to NED. Based on ROC curve analysis, a cut-off of 155 eosinophils/mm3 segregated active EoE from NED with AUC of 0.82, specificity of 91.0%, and sensitivity of 65.8%, while a cut off value of 2.5% of EosPercent had AUC of 0.83 with 68.2% specificity and 93.5% sensitivity for the identification of EoE among patients with dysphagia. In terms of prediction of BOT or PPI response, median AEC [380 (210, 460)/mm3 vs 150 (98, 268)/mm3; p<0.01] and EosPercent [5.40 (3.60, 7.05)%

vs 1.85 (1.55, 4.47)%; p<0.01] were significantly higher in active EoE compared to EoE in histological remission. Based on ROC curve analysis, a cut-off of 375 eosinophils/mm3 had AUC of 0.75 with 94.1% specificity and 54.5% sensitivity, while a cut off value of 2.25% of EosPercent had AUC of 0.79 with 93.5% specificity and 60.0% sensitivity for the identification of histological remission among EoE patients (Table 1).

	EoE, n=51	NED, n=41	p value
AEC within normal range	50/51 (98%)	41/41 (100%)	0.72
Eos Percent within normal range	43/51 (84.3%)	37/41 (90.2%)	0.41
Table 2) Biomarker	AUC	Specificity	Sensitivity
AEC in the diagnosis / monitoring of response in EoE	0.82 / 0.75	91% / 94.1%	65.8% / 54.5%
EosPercent in the diagnosis / monitoring of response in EoE	0.83 / 0.79	68.2% / 93.5%	93.5% / 60.0%

Table 1. Circulating eosinophil.

Conclusion: AEC and EosPercent are within the normal range in most EoE patients regardless of histological disease activity. Nevertheless, AEC and EosPercent values accurately predict a diagnosis of EoE among patients reporting dysphagia, as well as histological remission among BOT- or PPI-treated EoE patients. If these findings are replicated on a larger scale, AEC and EosPercent could be used as biomarkers in clinical practice.

Disclosure: Nothing to disclose.

MP663

SERUM EOTAXIN-3 AND IL-10 ARE USEFUL NON-INVASIVE BIOMARKERS FOR THE DIAGNOSIS AND MONITORING OF EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE, LONGITUDINAL STUDY

P. Visaggi¹, F. Pisani², G. Adamo¹, I. Solinas¹, F. Ovidi¹, D. Stefani Donati¹, G. Scaramuzza¹, G. Del Corso³, A. Bottari¹, M. Bellini¹, S.S. Zeki⁴, E.V. Savarino⁵, I. Puxeddu², N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²University of Pisa, Allergology and Clinical Immunology Unit, University of Pisa, Italy, Pisa, Italy, ³Institute of Information Science and Technologies “A. Faedo”, National Research Council of Italy (CNR), Pisa, Italy, ⁴St Thomas’ Hospital, Gastroenterology, London, United Kingdom, ⁵University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: The diagnosis and follow-up of eosinophilic esophagitis (EoE) currently requires an esophagogastroduodenoscopy (EGD) with multiple esophageal biopsies. Since the follow-up of the disease is highly demanding in terms of healthcare resources, non-invasive biomarkers are needed to make the management of EoE less cumbersome.

Aims & Methods: We investigated the utility of serum Eotaxin-1, Eotaxin-2, Eotaxin-3, Interleukin (IL)-4, IL-5, and IL-10 as biomarkers for the diagnosis and monitoring of EoE in a prospective, longitudinal fashion. Consecutive adults (age>18 years) with a new diagnosis of EoE [i.e., esophageal eosinophil counts per high-power field ≥15] were prospectively enrolled. At baseline (T0), patients underwent EGD with six esophageal biopsies to diagnose active EoE, as well as blood sampling immediately after the confirmed histological diagnosis of EoE (within one week from the EGD) while off EoE-directed treatments. Following the diagnosis, EoE-directed treatment was started, and histological response was assessed after 12 weeks of treatment (T1). Serum levels of Eotaxin-1, Eotaxin-2, Eotaxin-3, IL-4, IL-5, and IL-10 were assessed at T0 and at T1. Baseline clinical data were recorded for each EoE patient. Age-, Sex-, and atopy-matched sub-

jects were used as healthy controls (HC). Kruskal-Wallis Rank Sum Test and Pearson's Chi-squared were used for comparisons as appropriate. ROC curve analysis was used to calculate the diagnostic accuracy (AUC) of the biomarkers. Significance threshold was p<0.05.

Results: We enrolled 25 patients with active EoE and 14 HC, which were comparable in terms of age, sex, and atopy. At baseline (T0), patients with active EoE had significantly higher serum levels of eotaxin-3 compared to HC (501 pg/mL vs 224 pg/mL; p=0.002) and of IL-10 (100 pg/mL vs 56 pg/mL; p=0.01), while other biomarkers were not statistically different between active EoE and HC. Based on ROC curve analysis, a value of 389 pg/mL of etaxin-3 had AUC of 0.80 for the diagnosis of EoE with 93% specificity. A value of 168 pg/mL of IL-10 had AUC of 0.74 for the diagnosis of EoE with 100% specificity. Following treatment (T1), remission of EoE was achieved by 18/25 (72%) of EoE patients taking budesonide orodispersible tablets or PPIs. At T1, patients with EoE in histological remission had significantly lower serum levels of eotaxin-3 (252 pg/mL vs 501 pg/mL; p=0.02) and of IL-10 (67 pg/mL vs 100 pg/mL; p<0.05) compared to T0. A cut-off value of 241 pg/mL of eotaxin-3 had AUC of 0.7, and a cut-off value of 199.5 of IL-10 had AUC of 0.68 for the identification of histological remission at T1 (Table 1).

Biomarker (pg/mL)	Active EoE, N = 25 (64%)	Healthy Controls, N = 14 (36%)	p-value	Cut off value	AUC	Specificity	Sensitivity
Eotaxin-3 (median, IQR)	501 (276, 1,857)	224 (74, 321)	0.002	389 pg/mL	0.80	93%	68%
IL-10 (median, IQR)	100 (51, 247)	56 (12, 90)	0.01	168 pg/mL	0.74	100%	44%
Biomarker (pg/mL)	Active EoE, N = 25	EoE in remission, N = 18	p-value	Cut off value	AUC	Specificity	Sensitivity
Eotaxin-3 (median, IQR)	501 (276, 1,857)	252 (91, 434)	0.02	241 pg/mL	0.7	84%	50%
IL-10 (median, IQR)	100 (51, 247)	67 (29, 97)	0.04	199.5 pg/mL	0.68	40%	94%

Table 1.

Conclusion: Serum Eotaxin-3 and IL-10 are promising non-invasive biomarkers for the diagnosis of EoE with high specificity. In addition, Eotaxin-3 and IL-10 can monitor therapeutic response in patients with EoE.

Disclosure: Nothing to disclose.

MP664

INFLUENCE OF PHARMACOGENETICS ON RESPONSE TO PROTON PUMP INHIBITORS IN EOSINOPHILIC ESOPHAGITIS: RESULTS FROM A LARGE RETROSPECTIVE COHORT FROM FOUR SPANISH HOSPITALS

L. Rodríguez-Alcalado^{1,2,3}, M. Navares-Gómez^{4,5}, S. Casabona-Francés^{5,6}, J. Molina-Infante^{7,8}, D. Guagnozzi⁹, MP. Navarro Sánchez^{3,7,5,1}, P. Soria-Chacartegui^{4,5}, S. Feo Ortega^{10,1}, L. Arias-González^{7,3,5,1}, M. Torres-Larrubia⁸, R. Llerena Castro⁹, V. Martín Domínguez^{6,5}, J. Zamorano¹¹, F. Molina-Jiménez^{6,5}, P.L Majano^{7,6,5,12}, J. Fernández-Pacheco^{6,5}, D. Rivas¹¹, E. Grueso-Navarro^{3,1}, P. Zubiaur^{4,5}, F. Abad-Santos^{4,5,7}, C. Santander Vaquero^{7,5,6}, A.J. Lucendo^{7,5,13,1}, E.J. Laserna-Mendieta^{3,5,1,7}

¹Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain, ²Universidad de Alcalá, Surgery, Medical and Social Sciences, Alcalá de Henares (Madrid), Spain, ³Hospital General de Tomelloso, Gastroenterology Research Unit, Tomelloso, Spain, ⁴Hospital Universitario de La Princesa, Clinical Pharmacology, Madrid, Spain, ⁵Instituto de Investigación Sanitaria de La Princesa, Madrid, Spain, ⁶Hospital Universitario de La Princesa, Gastroenterology, Madrid, Spain, ⁷Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ⁸Hospital San Pedro de Alcantara, Gastroenterology, Cáceres, Spain, ⁹Hospital Universitario Vall d'Hebron, Gastroenterology, Barcelona, Spain, ¹⁰Hospital General de Tomelloso, Pediatrics, Tomelloso (Ciudad Real), Spain, ¹¹Hospital San Pedro de Alcantara, Research Unit, Cáceres, Spain, ¹²Universidad Complutense de Madrid, Cellular Biology, Faculty of Biology, Madrid, Spain, ¹³Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain

Contact E-Mail Address: leticia3r@gmail.com

Introduction: Proton-pump inhibitors (PPIs) are the most prescribed first-line treatment for eosinophilic esophagitis (EoE). However, only around half of patients respond histologically to a double dosage of PPI (1). Pharmacogenetics of PPIs is largely known to depend on CYP2C19 haplotypes (2).

Previous studies in EoE have shown promising results to predict PPI response by analyzing genetic variations in CYP2C19 and STAT6 genes, while other single nucleotide variations (SNPs) could play also a role (3).

Aims & Methods: The study aims to analyze the effect of 60 previously described SNPs associated with the response to PPIs in EoE or other diseases, or related to EoE genetics. Those SNPs were genotyped using an Open Array platform on DNA obtained from peripheral blood. Inclusion criteria were patients diagnosed with EoE according to clinical guidelines and treated with PPIs. Exclusion criteria were: response not evaluated under double or higher PPI doses, lack of histopathologic response assessment or unresponsiveness to PPIs before 8 weeks of treatment length. Patients were recruited in 4 Spanish referral hospitals and demographical and clinical data were obtained retrospectively. Patients were classified as non-responders (peak of eosinophils ≥15 per high power field, hpf) or responders (<15 eos/hpf). Chi-square or Fisher's exact test were used for statistical comparisons. Statistical significance was established for p<0.05.

Results: Overall, 505 patients (75% male and 15% <18 years-old at PPI onset, mean age 34.5 ± 14.9 years) were included; 48% responded to double o higher PPI doses. Omeprazole was the most common PPI (57%). Seventeen percent of patients presented mixed or stricturing EoE phenotypes. Regarding clinical variables, sex and age did not influence PPI effectiveness. In concordance with previous studies, a lower response rate was found in patients with mixed/structuring compared with inflammatory phenotypes (27% vs 52%, p<0.001). Treatments length over 10 weeks

achieved higher effectiveness ($p=0.028$). Using omeprazole and rabeprazole trended to produce higher effectiveness ($p=0.067$).

Two SNPs were found to be associated with response to double or higher PPI doses: *CYP3A5* rs776746 ($p=0.013$, intermediate phenotype associating to a lower response rate of 35%, and being present in 14% of patients) and *KCNJ2* rs312691 (recessive model, $p=0.006$, this variant increasing response up to 69%, and being present in 8% of patients).

Since phenotype had a great influence in response to PPIs, patients' genotypes were analyzed according to this variable. The 2 aforementioned variants had no effect on mixed/stricturing phenotypes, while statistical significance was kept for *CYP3A5* rs776746 and *KCNJ2* rs312691 in patients with inflammatory phenotypes ($p=0.007$ and $p=0.005$, respectively). For patients with mixed/stricturing phenotypes, the presence of variants in *chr14* rs7144958 (dominant model), *STAT6* rs3024974 (recessive model) or being a *CYP2C19* rapid/ultrarapid metabolizer (frequency of 18%, 19% and 28% in this type of patients, respectively) produced a trend to unresponsiveness to PPI (93%, $p=0.097$; 92% $p=0.100$; and 86%, $p=0.094$, respectively).

On the other hand, when sub-groups were created according to PPI drug, the use of esomeprazole in patients carrying the *CYP3A5* rs776746 variant further reduced the response rate to only 19% ($p=0.072$).

Conclusion: We have identified two SNPs affecting the response to double or higher doses of PPI in EoE patients with inflammatory phenotype and three SNPs that may decrease PPI effectiveness in patients with mixed or stricturing phenotypes.

References: 1. Laserna-Mendieta EJ, Casabona S, Guagnozzi D, et al. Efficacy of Proton Pump Inhibitor Therapy for Eosinophilic Oesophagitis in 630 Patients: Results from the EoE Connect Registry. *Aliment Pharmacol Ther* 2020, 52:798–807.

2. Lima JJ, Thomas CD, Barbarino J, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for *CYP2C19* and Proton Pump Inhibitor Dosing. *Clin Pharmacol Ther* 2021, 109:1417–1423.

3. Rodríguez-Alcolado L, Navarro P, Arias-Gonzalez L, et al. Proton-Pump Inhibitors in Eosinophilic Esophagitis: A Review Focused on the Role of Pharmacogenetics. *Pharmaceutics* 2024, 16:487.

Disclosure: Nothing to disclose.

MP665

CENDAKIMAB EXHIBITS ROBUST ANTI-FIBROTIC EFFECTS BY INHIBITING IL-13RA2 SIGNALING

J. Koenitzer¹, G. Fernando-Mehta¹, S. Kumar¹, J. Li¹, P. Schafer¹, S. Harris¹

¹Bristol Myers Squibb, Immunology, Cardiovascular, & Neuroscience Translational Medicine Disease Team, Princeton, United States of America

Contact E-Mail Address: jennifer.koenitzer@bms.com

Introduction: Cendakimab is a recombinant, humanized IgG1 monoclonal antibody with high affinity and selectivity for IL-13. IL-13 is a key mediator of type 2 inflammation and contributes to eosinophil recruitment, epithelial barrier dysfunction, tissue remodeling, and fibrosis. Cendakimab prevents IL-13 from interacting with its two cognate receptors, IL-13Rα1 and IL-13Rα2, and is under clinical investigation for eosinophilic esophagitis (EoE), eosinophilic gastritis (EoG), and eosinophilic duodenitis (EoD) which are marked by elevated levels of IL-13. [1, 2]

Aims & Methods: Our primary objective was to investigate the role of IL-13Rα2, which has thus far primarily been considered to be a decoy receptor that lacks signaling ability [3–6], in fibroblast function. Further, we wanted to understand cendakimab's mechanism of action as it relates to human fibroblasts.

A human melanoma cell line model (A375) and cultures of primary human esophageal and dermal fibroblasts were stimulated with recombinant IL-13 in the presence or absence of cendakimab before assessing the induction of the Activator Protein-1 (AP-1) transcription factor, which has been described as a master regulator of fibrotic disease [7]. AP-1 was measured using a colorimetric enzyme-linked immunosorbent assay (ELISA). Flow cytometry was employed to determine the cell surface expression of IL-13Rα1 and IL-13Rα2. To assess the functional response in IL-13 stimulated fibroblasts, secreted proteins were quantified by mesoscale discovery (MSD) immunoassays and gene expression changes were investigated using quantitative PCR (qPCR).

Results: Results show that IL-13Rα2 is not a decoy but a signaling cytokine receptor whose stimulation with IL-13 leads to the induction of AP-1 in A375 cells which natively express IL-13Rα2. This signaling is specific to IL-13Rα2 as AP-1 induction was not observed using A375 cells in which the parental gene IL13RA2 has been knocked-out and which also lack expression of IL-13Rα1. Cendakimab blocks IL-13 induced AP-1 production in A375 cells.

Similar results were also noted in primary human esophageal and dermal fibroblasts. Cendakimab inhibits IL-13 induced AP-1 signaling with a potency of 2.9nM (A375) and 1.7nM or 2.7nM in esophageal or dermal fibroblasts, respectively.

IL-13 stimulation of primary human esophageal and dermal fibroblasts led to the production of the cytokine IL-6, the monocyte chemoattractant protein-1 (MCP-1, also known as CCL2), hepatocyte growth factor (HGF), as well as extracellular matrix proteins periostin and tenascin C, suggesting these factors may be controlled by AP-1. IL-6 and MCP-1 have both been described as pro-fibrotic mediators under chronic inflammatory conditions [8, 9], HGF is a known regulator of epithelial-mesenchymal transition (EMT) driving tissue fibrosis [10], and periostin and its interacting partner tenascin C have been shown to mark areas of fibrosis as well as being directly involved in eosinophil infiltration [11]. Cendakimab treatment inhibited the production of all these proteins in primary human esophageal and dermal fibroblasts.

Conclusion: These experiments confirm that IL-13Rα2 is a signaling cytokine receptor whose engagement leads to the pro-fibrotic activation of primary human fibroblasts. Cendakimab's potent ability to attenuate this behavior has important implications for its potential value in targeting the fibrostenotic aspects of esophageal dysfunction in EoE [12] and addressing the unmet need of patients suffering from this chronic and progressive disease.

References:

- [1] Tripp CS, et al. *Adv Ther*. 2017;34:1364–1381.
- [2] Hirano I, et al. *Gastroenterology*. 2019;156:592–603.
- [3] Donaldson DD et al. *J Immunol*. 1998;161(5):2317–24.
- [4] Bernard J et al. *Lab Invest*. 2001;81:1223–1231.
- [5] Wynn TA et al. *Lab Invest*. 1998;78:591–602.
- [6] Wood N et al. *J Exp Med*. 2003;197:703–709.
- [7] Werning G et al. *PNAS*. 2017;114(18):4757–4762.
- [8] Li Y et al. *Int J Biol Sci*. 2022; 18(4):5405–5414.
- [9] Gharaee-Kermani M et al. *J Biol Chem*. 1996; 271(30):17779–84.
- [10] Zavadil J et al. *Oncogene*. 24:5764–5774.
- [11] Blanchard C et al. *Mucosal Immunol*. 2008; 1(4):289–296.
- [12] Armbruster-Lee J et al. *JLB*. 2018;104(1):31–40.

Disclosure: The authors are employees and shareholders of Bristol Myers Squibb. Bristol Myers Squibb provided the funding for this work.

MP666

USEFULNESS OF IGG4 DETERMINATION IN ESOPHAGEAL TISSUE FOR EOSINOPHILIC ESOPHAGITIS AND ITS CORRELATION WITH ALLERGIC SENSITIZATION

A. Menéndez Ramos¹, J.A. Muñoz León¹, L. Tejerizo García¹, R. Domínguez Gómez¹, J.X. Segarra Ortega¹, E.M. Macías Iglesias¹, A.J. Velasco Guardado¹

¹Hospital Universitario de Salamanca, Salamanca, Spain

Contact E-Mail Address: ana.menendez94@gmail.com

Introduction: Eosinophilic esophagitis (EE) is an immunoallergic disorder with multifactorial genetic and environmental etiology which affects both children and adults (1,2,3). It is more common in men, with a male/female ratio of 3:1 (4,5,6). Its symptoms include gastric acid reflux, regurgitation and dysphagia. The diagnosis requires histological confirmation with the presence of over 15 eosinophils/HPF.

Treatment includes proton-pump inhibitors, corticoids, empirical and elimination diets based on allergy tests and endoscopic dilation in cases of esophageal stricture (7). The role that IgG4 plays in EE is still unclear, we want to determine the presence of IgG4 via immunohistochemical staining in the esophageal epithelium.

The purpose of this research is to analyze the role of IgG4 in EE and to study whether there are differences in IgG4 between patients diagnosed with EE with or without concomitant food allergies and establish whether there is a correlation between esophageal IgG4, total IgE, and IgG4 specific for the 6 foods more commonly associated with EE.

Aims & Methods: A retrospective study from 2017 to 2023 analyzed immunohistochemical IgG4 staining in esophageal biopsies of 78 adult patients with an EE diagnosis

Results: Out of the 78 patients included in the study, 74.4% were men. The median age at diagnosis was 35 years. Patients with positive interstitial staining for IgG4 had a significantly higher concentration of specific serum IgG4 to: milk casein and lactoglobulin ($p=0.017$) and ($p=0.018$), respectively and peanut-specific IgG4 ($p=0.023$) (Table 1). Patients with positive results for IgG4 in more than 10% of their plasma cells also presented a significantly higher concentration of serum IgG4 that was specific for the following food groups: soy ($p=0.003$), peanut ($p=0.001$) and seafood ($p=0.001$). With regard to their clinical evolution, patients with positive results for IgG4 in more than 10% of their plasma cells required a second therapeutic step more often ($p=0.04$). They also presented a more delayed diagnosis, with an average span from the appearance of symptoms to diagnosis compared with patients with negative staining ($p=0.039$). With regard to the correlation between food-specific IgE and food-specific IgG4, a significant positive correlation was observed for all food groups: milk-specific IgE presented a positive correlation with IgG4 to casein with a correlation coefficient of 0.44 ($p<0.001$), and with lactoglobulin with a correlation coefficient of 0.52 ($p<0.001$), for wheat 0.40 ($p<0.001$), for egg 0.41 ($p<0.001$), for soy 0.31 ($p=0.006$), for peanut 0.35 ($p=0.002$), for fish 0.45 ($p<0.01$), and for seafood 0.25 ($p=0.03$).

	Interstitial staining + (mean)	Interstitial staining - (mean)	p
Milk IgE	0.62	0.38	0.38
IgG4 milk casein	82	10,36	0,017
IgG4 milk lactoglobulin	31,84	5,65	0,018
Peanut IgE	0.65	1.24	0.40
Peanut IgG4	1.08	0.82	0.023

Conclusion: Positive IgG4 staining in EE indicates the need for second-step therapy and longer symptom evolution. Patients with interstitial IgG4 staining correlate with higher serum IgG4 levels for cow milk and peanut. A positive correlation exists between specific IgE and IgG4

for foods commonly linked to EE. These findings impact patient follow-up and treatment options. Larger prospective studies are needed to understand IgG4 behavior.

References: 1. Landres RT, Kuster GG, Strum WB. Eosinophilic esophagitis in a patient with vigorous achalasia. *Gastroenterology* 1978; 74: 1298-1301
2. Attwood SE, Smyrk TC, Demeester TR, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci* 1993; 38: 109-116
3. Straumann A, Spichtin HP, Bernoulli R, Loosli J, Vögtlin J. Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings. *Schweiz Med Wochenschr* 1994; 124: 1419-1429
4. Navarro P, Arias Á, Arias-González L, Laserna-Mendieta EJ, Ruiz-Ponce M, Lucendo AJ. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. *Aliment Pharmacol Ther* 2019; 49: 1116-1125
5. Kapel RC, Miller JK, Torres C, Aksoy S, Lash R, Katzka DA. Eosinophilic esophagitis: a prevalent disease in the United States that affects all age groups. *Gastroenterology* 2008; 134: 1316-1321.
6. Dellon ES, Hirano I. Epidemiology and Natural History of Eosinophilic Esophagitis. *Gastroenterology* 2018; 154: 319-332
7. Gómez-Aldana A, Jaramillo-Santos M, Delgado A, Jaramillo C, Lúquez-Mindiola A. Eosinophilic esophagitis: Current concepts in diagnosis and treatment. *World J Gastroenterol*. 2019; 28; 25(32): 4598-4613

Disclosure: Nothing to disclose.

MP667

PATHOGENIC HELPER TH2 CELLS REMAIN WITHIN THE ESOPHAGEAL MUCOSA OF EOE IN EVEN REMISSION PHASE

A. Kurosugi¹, C. Iwamura², T. Kaneko¹, K. Okimoto¹, T. Matsumura¹, J. Kato¹, K. Hirahara², N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Chiba, Japan, ²Chiba University, Department of Immunology, Chiba, Japan

Contact E-Mail Address: akanekurosugi1125@chiba-u.jp

Introduction: Eosinophilic esophagitis (EoE) is treated with oral antacids, steroid-swallowing therapy, and antigen elimination diet. Despite treatment, EoE often recurs, and the mechanism has not been elucidated. Recently, pathogenic helper Th2 (Tpath2) cell was reported to be responsible for chronic eosinophilic inflammation, for example asthma and eosinophilic chronic rhinosinusitis, by producing large amount of Th2 cytokine [1].

Our previous research has identified the presence of Tpath2 cells in the esophageal mucosa of patients with EoE [2].

However, there has been no previous report whether Tpath2 remains in the tissues during remission or after treatment.

Aims & Methods: The aim of this study was to examine the association between the progression of EoE and Tpath2 cells in the esophageal mucosa. We collected esophageal mucosa biopsies regardless of the endoscopic findings from 11 patients (generally 2 specimens from 5cm and 15cm oral side of esophagogastric junction respectively) previously diagnosed as EoE. Flow cytometry was utilized to quantify the frequency of eosinophils and Tpath2 cells in these samples. Each patient's medical history or disease course were also reviewed.

Results: Of the 11 patients, 6 (54.5%) were in remission from EoE and 5 (45.5%) had active disease. Notably, abnormal frequency of Tpath2 cells within the esophageal mucosa of the patients in remission (median 1.41%, range 0.31 - 2.85%) were observed to the same levels in those with active disease (median 2.48%, range 1.02 - 4.18%) ($P=0.33$. Mann-Whitney

test.). In remission cases, the median period from confirmation of remission to this biopsy was 38 months (range 24 - 49) , meaning T path2 cells still remained at least for that period after remission. Among patients in remission at the time of biopsy, two patients who were absence of treatment relapsed EoE during subsequent disease course.

Conclusion: Tpath2 cells remain within the esophageal mucosa of patients with EoE for a relatively long time regardless of eosinophil control. Although further investigation is needed, some cases of EoE recurred during remission phase, suggesting that Tpath2 cells may also be involved in the recurrence.

References: 1. Nakayama T et al. Th2 cells in health and disease. *Annu Rev Immunol.* 2017; 35:53-84.
2. Kaneko T et al. Amphiregulin-producing T helper 2 cells facilitate esophageal fibrosis of eosinophilic esophagitis. *J Allergy Clin Immunol Global.* 2024; Epub ahead of print
Disclosure: Nothing to disclose.

MP668
ROLE OF TSLP IN AN EXPERIMENTAL MOUSE MODEL OF EOSINOPHILIC ESOPHAGITIS

K. Komori¹, L. Wittmer², H. Ortega¹
¹Uniquity Bio, R&D, San Diego, United States of America, ²Uniquity Bio, R&D, Malvern, United States of America

Contact E-Mail Address: kiyomi.komori@uniquity.com
Introduction: Eosinophilic esophagitis (EoE) is an inflammatory disease that is the leading cause of food impaction in children and young adults. EoE is thought to be a food antigen-driven allergic disease, best characterized by eosinophil-predominant inflammation, esophageal dysfunction, and expression of Th2 cytokines. Thymic stromal lymphopoietin (TSLP) is a cytokine primarily secreted by epithelial cells in barrier tissues in response to danger signals, infectious agents, Th2 cytokines and environmental antigens. TSLP is a master regulator of Th2 inflammation. Genetic studies have linked single nucleotide polymorphisms in TSLP to Th2 driven diseases, including eosinophilic esophagitis. Recent single-cell sequencing studies demonstrated memory CD4 T cells expressing TSLP receptor correlated with esophageal eosinophil counts. While some data suggest a key role of TSLP in the pathogenesis of EoE, its relative contribution has not been established in *in vivo* models.
Aims & Methods: Experimental EoE was induced in male wild type mice by an initial skin-sensitization using oxazolone (OXA, 17 days) followed by intraesophageal challenge with oxazolone or vehicle control (19 days, total duration 36 days). TSLP expression in the esophagus was measured during the sensitization and challenge periods. To determine the role of TSLP in EoE, treatment with a TSLP neutralizing antibody or isotype control began prior to esophageal challenge. Eosinophil counts, epithelial and lamina propria thickening, epithelial cell proliferation and esophageal vascularization were assessed in esophageal tissue on day 36.
Results: Intraesophageal challenge with OXA induced a transient upregulation of TSLP in the esophagus at day 29, with TSLP being expressed primarily in esophageal epithelial cells. Inhibition of TSLP activity with a blocking antibody in OXA sensitized mice resulted in 60% fewer eosinophils compared to isotype treated controls (p<0.001). Additionally, anti-TSLP treatment also induced statistically significant reductions in epithelial and lamina propria thickness and basal cell zone proliferation (Table 1).
When assessed by region, TSLP neutralization statistically significantly reduced esophageal vascularization in regions with the highest degree of eosinophil infiltration.

	Eosinophils per section			Epithelial thickness (mM)			Lamina propria thickness (mM)			Basal cell zone proliferation (Ki-67 cells/mm)			CD31+ blood vessels		
	Vehicle	OXA	Anti-TSLP	Vehicle	OXA	Anti-TSLP	Vehicle	OXA	Anti-TSLP	Vehicle	OXA	Anti-TSLP	Vehicle	OXA	Anti-TSLP
Eso-phageal challenge															
Treatment group	Isotype	Isotype	Anti-TSLP	Isotype	Isotype	Anti-TSLP	Isotype	Isotype	Anti-TSLP	Isotype	Isotype	Anti-TSLP	Isotype	Isotype	Anti-TSLP
n	10	11	10	10	11	10	10	11	10	10	11	10	7	9	8
Mean (SD)	1.2 (0.52)	353.4 (183.5)	141.5 (62.4)	51.9 (5.5)	86.1 (13.4)	76.4 (8.8)	28.3 (3.65)	73.1 (12.1)	62.6 (12.7)	129.1 (12.5)	207.5 (36.8)	167.0 (32.0)	4.6 (1.1)	24.3 (3.9)	20.5 (3.5)
OXA anti-TSLP vs OXA isotype			p= 0.0001			p= 0.0323			p= 0.0252			p= 0.0055			p= 0.0521

Conclusion: This is the first time neutralization of TSLP in an experimental mouse model of EoE is reported, demonstrating a key role of TSLP in EoE disease pathogenesis. Inhibition of TSLP markedly decreased esophageal eosinophilia, a key diagnostic criterion for EoE. Other histologic features of EoE were also reduced upon TSLP neutralization. Together with genetic and mechanistic studies associating TSLP with EoE pathogenesis, this data suggests TSLP may serve as a treatment target for patients with EoE.
Disclosure: KK, LW, and HO are employees of Uniquity Bio.

MP669
WITHDRAWN

MP670

THE EFFICACY AND SAFETY OF GUSELKUMAB AS MAINTENANCE THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 QUASAR MAINTENANCE STUDY

D.T. Rubin¹, J. Allegretti², J. Panés³, N. Shipitofsky⁴, S. Yarandi⁴, K.-H. Huang⁴, M. Germinaro⁴, R. Wilson⁴, H. Zhang⁴, B.G. Feagan⁵, T. Hisamatsu⁶, G. Lichtenstein⁷, B. Bressler⁸, L. Peyrin-Biroulet⁹, B.E. Sands¹⁰, A. Dignass¹¹

¹University of Chicago Medicine, Inflammatory Bowel Disease Center, Chicago, United States of America, ²Brigham and Women's Hospital Crohn's and Colitis Center, Dept. of Gastroenterology, Boston, United States of America, ³Hospital Clínic Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain, ⁴Janssen Research & Development, LLC, Spring House, United States of America, ⁵Alimentiv Inc, London, Canada, ⁶Kyorin University School of Medicine, Tokyo, Japan, ⁷University of Pennsylvania School of Medicine, Merion Station, United States of America, ⁸University of British Columbia, Medicine, Vancouver, Canada, ⁹Nancy University Hospital, Université de Lorraine, Nancy, France, ¹⁰Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ¹¹Agaplesion Markus Krankenhaus, Medizinische Klinik I, Frankfurt/Main, Germany

Contact E-Mail Address: axel.dignass@agaplesion.de

Introduction: The Phase 3 QUASAR Maintenance Study is a randomized-withdrawal, double-blind, placebo (PBO)-controlled, study that evaluated the efficacy and safety of maintenance treatment with subcutaneous (SC) guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor that binds to CD64, in patients (pts) with moderately to severely active ulcerative colitis (UC) who had prior inadequate response or intolerance to conventional or advanced therapy (ADT) and demonstrated a clinical response to GUS IV induction.

Aims & Methods: At maintenance baseline, clinical responders to 12 weeks of GUS IV induction from QUASAR Phase 2b and Phase 3 induction studies (NCT04033445) were randomized 1:1:1 to SC GUS 200mg q4w, GUS 100mg q8w, or PBO (GUS withdrawal).

The primary endpoint was clinical remission at Week (Wk) 44.

Major secondary endpoints included corticosteroid-free clinical remission, maintenance of clinical remission, maintenance of clinical response, symptomatic remission, endoscopic improvement, histo-endoscopic mucosal improvement, and endoscopic normalization (remission) at Wk44.

Results: The primary analysis population included 568 pts (mean age, 40.7yr; mean UC duration, 7.8yr; mean modified Mayo score, 6.9 [63.9% with severe disease]; Mayo endoscopy subscore of 3, 66.4%; baseline oral corticosteroid use, 40.0%).

Approximately 42% had prior inadequate response or intolerance to ADT (TNF antagonists, vedolizumab, or tofacitinib), and 48.3% of these pts failed ≥2 ADT. Disease characteristics were similar across treatment groups at induction and maintenance baseline.

With both GUS SC maintenance regimens, a significantly higher proportion of pts achieved the primary endpoint and all the major secondary endpoints at Wk44 compared with GUS withdrawal (Table 1).

The proportion of pts with ≥1 adverse events (AEs) was similar across treatment groups: GUS 200mg q4w, 70.0%; GUS 100mg q8w, 64.5%, and GUS withdrawal, 68.2%. The most common AEs in the combined GUS group vs withdrawal group were COVID-19 (11.2% vs 14.1%), UC (11.2% vs 29.7%), and arthralgia (6.1% vs 6.8%), respectively.

No cases of death, active tuberculosis, opportunistic infection, anaphylaxis, serum sickness, Hy's Law, or serious hepatic AEs were reported. Two cases of malignancy (clear cell renal carcinoma, rectal adenocarcinoma) and 1 major adverse cardiovascular event (hemorrhagic stroke) were reported among GUS-treated pts (primary safety population).

	GUS Withdrawal (Placebo) (N=190)	GUS 100 mg q8w (N=188)	GUS 200 mg q4w (N=190)
Clinical remission (primary endpoint), n (%) ^a	36 (18.9%)	85 (45.2%)	95 (50.0%)
Adjusted treatment difference (95% CI)		25.2 (16.4, 33.9), P<0.001	29.5 (20.9, 38.1), P<0.001
Corticosteroid-free clinical remission, n (%) ^b	35 (18.4%)	85 (45.2%)	93 (48.9%)
Adjusted treatment difference (95% CI)		25.7 (17.0, 34.5), P<0.001	29.0 (20.5, 37.6), P<0.001
Maintenance of clinical remission, n/N (%) ^c	20/59 (33.9%)	40/66 (60.6%)	50/69 (72.5%)
Adjusted treatment difference (95% CI)		25.9 (9.2, 42.5), P=0.004	38.4 (22.7, 54.1), P<0.001
Maintenance of clinical response, n (%) ^d	82 (43.2%)	146 (77.7%)	142 (74.7%)
Adjusted treatment difference (95% CI)		33.6 (24.5, 42.7), P<0.001	30.7 (21.5, 40.0), P<0.001
Symptomatic remission, n (%) ^e	71 (37.4%)	132 (70.2%)	131 (68.9%)
Adjusted treatment difference (95% CI)		31.9 (22.5, 41.2), P<0.001	30.5 (21.2, 39.9), P<0.001
Endoscopic improvement, n (%) ^f	36 (18.9%)	93 (49.5%)	98 (51.6%)
Adjusted treatment difference (95% CI)		29.5 (20.7, 38.3), P<0.001	31.1 (22.5, 39.8), P<0.001
Histo-endoscopic mucosal improvement ^g	32 (16.8%)	82 (43.6%)	91 (47.9%)
Adjusted treatment difference (95% CI)		25.7 (17.1, 34.3), P<0.001	29.6 (21.1, 38.0), P<0.001
Endoscopic normalization (remission), n (%) ^h	29 (15.3%)	65 (34.6%)	64 (33.7%)
Adjusted treatment difference (95% CI)		18.5 (10.2, 26.8), P<0.001	16.8 (9.0, 24.7), P<0.001

Primary Analysis Population included randomized patients with a modified Mayo score of 5-9 at induction baseline who received at least 1 maintenance study treatment dose. Adjusted treatment difference (Δ) was based on the Wald statistic with Cochran-Mantel-Haenszel (CMH) weight. P-values were based on the CMH test, stratified by clinical remission status at maintenance baseline and induction treatment, except for the maintenance of clinical remission, which was based on the CMH test stratified by induction treatment. ^a Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability. ^b Corticosteroid-free clinical remission: Not requiring any treatment with corticosteroids for at least 8 weeks prior to Week 44 and also meeting the criteria for clinical remission (98.9% of guselkumab-treated patients who achieved clinical remission at Week 44 were not taking corticosteroids for at least 8 weeks prior to Week 44). ^c Maintenance of clinical remission: Clinical remission at Week 44 among patients in clinical remission at maintenance baseline. ^d Clinical response: A decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from induction baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1. ^e Symptomatic remission: A stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0. ^f Endoscopic improvement: An endoscopy subscore of 0 or 1 with no friability present on the endoscopy. ^g Histo-endoscopic mucosal improvement: Achieving a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue per Geboes grading system) and endoscopic improvement. ^h Endoscopic normalization (remission): An endoscopy subscore of 0.

Table 1. Primary and major secondary endpoints at Week 44: Primary analysis population.

Conclusion: Among pts with moderately to severely active UC who responded to GUS IV induction, maintenance therapy with both GUS SC regimens was safe and efficacious. The primary endpoint of clinical remission and all secondary endpoints across clinical, symptomatic, endoscopic, and histologic measures were met with statistical significance by both GUS SC maintenance regimens. Safety results through maintenance Wk44 were consistent with the known and favorable safety profile of GUS in approved indications.

Disclosure: DTR: AbbVie, Altrubio, Allergan, Inc., Arena Pharmaceuticals, Aslan Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Ltd., Bristol Myers Squibb, Celgene Corp/Syneos, Connect BioPharma, GalenPharma/Atlantica, Genentech/Roche, InDex Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Eli Lilly, Materia Prima, Pfizer, Prometheus Biosciences, Reistone, Takeda, Techlab, Inc and is a co-founder of Cornerstones Health, Inc.

JRA: Finch Therapeutics, Artugen, Pfizer, Takeda, Janssen, and Iterative Scopes, Merck and BMS.

JP: AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman.

NS, SY, KGH, MG, RW, and HZ: Employees of Johnson & Johnson.

BGF: AbbVie Inc., Amgen Inc., AdMIRx Inc., Akebia Therapeutics, Allergan, AstraZeneca/MedImmune Ltd., Applied Molecular Transport, Aptevio Therapeutics, Asta Pharma, Atlantic Pharmaceuticals Ltd., Avaxia Biologics Inc., Avir Pharma, Biogen Idec, BioMx Isreal, Boehringer -Ingelheim, Boston Pharmaceuticals, Bristol-Myers Squibb, Calypso Biotech, Celgene Corporation, Celltech, Centocor Inc, Elan/Biogen, Ferring Pharma, Genentech Inc/Hoffmann-La Roche Ltd., Galapagos, Galen/Atlantica, GiCare Pharma, Gilead Sciences Inc., Gossamer Pharma, GlaxoSmithKline (GSK), Inception IBD Inc, Intact Therapeutics, Janssen Research & Development LLC., Kyo-wa Kakko Kirin Co Ltd., Lexicon, Lilly, Lycera BioTech, merck, Mesoblast Pharma, Millennium, Nestles, Nextbiotix, Novonordisk, ParImmune, Parvus Therapeutics, Pfizer Inc., Prometheus Therapeutics and Diagnostics, Progenity, Protagonist, Qu Biologics, Rebiotix, Receptos Inc. / Celgene International, Salix Pharma, Sanofi, Santarus Inc., Shire, Sienna Biologics, Sihmoid Pharma, Sterna Biologics, Synergy Pharma Inc., Takeda Development Center Americas Inc., Teva Pharam, TiGenix, Tillotts Pharma AG, UCB, Vertex Pharma, Vivelix Pharma, VHSquared Ltd., Zyngenia and Senior Scientific Officer – Robarts Clinical Trials Inc.

TH: AbbVie, Daiichi-Sankyo, EA Pharma Co, Ltd. Janssen Research & Development LLC., JIMRO, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Inc., and Takeda Pharmaceutical Co., Ltd.,

GRL: Abbvie, Allergan, American College of Gastroenterology, American Gastroenterological Association, American Regent, Celgene, Chemed, Eli Lilly, Endo Pharmaceuticals, Ferring, Gastroenterology and Hepatology, Gilead, IMEDEX, Ironwood, Janssen/ Janssen Orthobiotech, MedEd Consultants, Merck, Morpich Therapeutics, Pfizer Pharmaceuticals, Professional Communications, Inc., Prometheus Laboratories, Inc, Romark, Sandoz, Salix Pharmaceuticals/Valeant, Shire Pharmaceuticals, SLACK, Inc, Springer Science and Business Media, Takeda, University of Kentucky, UCB, Up-To-Date, Vindico, and Virgo.

BB: Abbvie, Amgen, BI, BMS, Ferring, Janssen, Merck, Novartis, Organon, Pfizer, Sandoz, Takeda, Alimentiv, Allergan, AMT, Bausch Health, Celgene, Celltrion Healthcare, Eupraxia, Fresenius Kabi, Genentech, GSK, Gilead, Iterative Scopes, Jamp Pharma, Merck Amgen, Microbiome Insights, Mylan, Pendopharm, Protagonist, Qu Biologic, and Viatrisgen.

LPB: AbbVie, Allergan, Alma, Amgen, Applied Molecular Transport, Arena, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, CTMA, Enterome, Enthera, Ferring, Fresenius, Genentech, Gilead, Hikma, Index Pharmaceuticals, Janssen, Lilly, MSD, Mylan, Nestlé, Norgine, Opiphan Pharma, OSE Immunotherapeutics, Pfizer, Pharmacosmos, Roche, Samsung Bioepis, Sandoz, Sterna, Sublimity Therapeutics, Takeda, Tillots and Vifor; grants from AbbVie, MSD and Takeda.

BES: Abbvie, Abbivax, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Janssen, Kaleido, Kallyope, Lilly, Merck, Morpich Therapeutics, MRM Health, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Takeda, Target RWE, Teva, Theravance Biopharma, TLL Pharmaceutical, and Ventyx Biosciences.

AD: Abivax, AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, CED Service GmbH, Celltrion,

Dr Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Gilead, High5MD, Janssen, Lilly, Materia Prima, MedToday, MSD, Pfizer, Pharmacosmos, Roche/Genentech, Sandoz/Hexal, Takeda, Thieme, Tillotts, UniMed Verlag, and Vifor Pharma.

MP671

EFFICACY OF GUSELKUMAB IN MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE ACCORDING TO INDUCTION CLINICAL RESPONSE STATUS: WEEK 48 RESULTS FROM THE GALAXI 2 & 3 PHASE 3 TRIALS

A. Afzali¹, J. Panés², B.E. Sands³, D.T. Rubin⁴, R. Panaccione⁵, N.A. Terry⁶, L. Salese⁶, R. Van Rampelbergh⁷, Z. Yang⁶, M.E. Frustaci⁶, D. Tarabar⁸, M. Chen⁹, E. Mihály¹⁰, D. Wolf¹¹, G. D'Haens¹²

¹Division of Digestive Diseases, University of Cincinnati, College of Medicine, Cincinnati, United States of America, ²Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain, ³Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁴University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States of America, ⁵Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Canada, ⁶Janssen Research & Development, LLC, Spring House, United States of America, ⁷Janssen Research & Development, Antwerp, Belgium, ⁸University Hospital Center Dr Dragiša Mišović, Belgrade, Serbia, ⁹The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, ¹⁰Semmelweis University, Department of Internal Medicine, Budapest, Hungary, ¹¹Atlanta Gastroenterology Associates, Atlanta, United States of America, ¹²Department of Gastroenterology, Amsterdam University Medical Centers, Amsterdam, Netherlands

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: GALAXI 2 & 3 (G2/3) (NCT03466411) are identical 48-week (wk), randomized, double-blind, double-dummy, placebo (PBO)- and active-comparator-controlled registrational trials assessing the efficacy and safety of guselkumab (GUS), a dual-acting IL-23p19 subunit inhibitor, in participants (pts) with moderately to severely active Crohn's disease. G2/3 used a treat-through design, where GUS pts were assigned to 1 of 2 IV induction→SC maintenance regimens at Wk0, and maintenance treatment was not influenced by their clinical response status after induction (Wk12). We report pooled exploratory analyses of clinical and endoscopic endpoints at Wk48 among pts with and without a Wk12 clinical response to GUS induction therapy.

Aims & Methods: Pts were randomized 2:2:2:1 to the following induction→maintenance regimens: GUS 200mg IV q4w (x3)→100mg SC q8w, GUS 200mg IV q4w (x3)→200mg SC q4w, ustekinumab ~6mg/kg IV→90mg SC q8w, or PBO. These analyses of pooled G2/3 data for GUS recipients were conducted post hoc; comparable analyses of the individual trials were prespecified. Clinical response was defined as a ≥100-point reduction from baseline in CDAI score or CDAI≤150. Wk48 endpoints included clinical remission (CDAI≤150), endoscopic response (≥50% improvement in SES-CD or SES-CD≤2) and PRO-2 remission (patient-reported CDAI components of abdominal pain and stool frequency [mean daily scores ≤1 and ≤3, respectively] with no worsening from baseline).

Results: The pooled analyses included 268 pts who received GUS 200mg IV→100mg SC q8w and 278 who received GUS 200mg IV→200mg SC q4w. Combined, approximately 66% were in clinical response to GUS induction at Wk12. Clinical remission rates at Wk48 were 77.0–83.5% among Wk12 GUS induction clinical responders and 55.6–58.3% among pts not in clinical response at Wk12, and PRO-2 remission rates were 71.3–75.8% and

46.7–49.0%, respectively (Table). Endoscopic response rates at Wk48 were 58.4–60.4% and 36.7–47.9% among induction responders and non-responders, respectively (Table).

Week 48 Endpoint, n (%) ^a	GUS Induction Responders ^b		GUS Induction Non-responders ^b	
	GUS 200mg IV→ 100mg SC q8w (N=178)	GUS 200mg IV→ 200mg SC q4w (N=182)	GUS 200mg IV→ 100mg SC q8w (N=90)	GUS 200mg IV→ 200mg SC q4w (N=96)
Clinical Remission ^d	137 (77.0%)	152 (83.5%)	50 (55.6%)	56 (58.3%)
Endoscopic Response ^e	104 (58.4%)	110 (60.4%)	33 (36.7%)	46 (47.9%)
PRO-2 Remission ^f	127 (71.3%)	138 (75.8%)	42 (46.7%)	47 (49.0%)

AE=adverse event; AP=abdominal pain; CD=Crohn's disease; CDAI=Crohn's disease activity index; COVID-19=coronavirus disease 2019; GUS=guselkumab; IV=intravenous; PRO-2=patient-reported CDAI components of abdominal pain and stool frequency; pts=participants; q4w=every 4 weeks; q8w=every 8 weeks; SC=subcutaneous; SES-CD=Simple Endoscopic Score for Crohn's Disease; SF=stool frequency.

^aIncludes pts from the primary analysis set, defined as all randomized pts who received ≥1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for pts with isolated ileal disease), who were treated at Week 12 and did not have a CD-related surgery; prohibited change in concomitant CD medication; or discontinued study agent due to lack of efficacy, an AE of worsening CD, or for any other reason other than COVID-19-related reasons or regional crisis in Ukraine and Russia prior to Week 12.

^bResponder and non-responder to GUS induction treatment defined as achieving a clinical response at Week 12 (≥100-point reduction from baseline in CDAI or CDAI<150) or not, respectively.

^cPts with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Pts who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. Missing data imputation: After accounting for these scenarios, pts with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

^dCDAI remission defined as CDAI score <150.

^eEndoscopic response defined as ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2.

^fPRO-2 remission is defined as AP mean daily score ≤1 and SF mean daily score ≤3, and no worsening of AP or SF from baseline.

Table. Efficacy Outcomes at Week 48 in GALAXI 2 & 3 Participants with and without a Clinical Response to 12-Week Induction Treatment with Guselkumab (Week 12 Treated Primary Analysis Set^a).

Conclusion: Among the subset who achieved clinical response at Wk12, most pts in both GUS maintenance dose groups went on to achieve clinical remission, PRO-2 remission, or endoscopic response at Wk48. Moreover, efficacy at Wk48 with both GUS maintenance doses was also observed in pts not in clinical response at Wk12, suggesting a benefit of continued treatment with GUS even if clinical response is not achieved at Wk12.

Disclosure: Anita Afzali reports potential conflicts of interest with AbbVie, Bristol Myers Squibb, DiaSorin, Eli Lilly, Gilead, IBD Horizons, Janssen, Pfizer, Takeda, and TLL Pharmaceuticals.

Julian Panés reports potential conflicts of interest with AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman.

Bruce E. Sands reports potential conflicts of interest with AbbVie, Abivax, Adiso Therapeutics, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, AstraZeneca, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Janssen, Kaleido, Kallyope, Lilly, Merck, Microbiotica, Mobius Care, Morphic Therapeutics, MRM Health, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sun Pharma, Surrozen, Target RWE, Takeda, Teva, Theravance Biopharma, TLL Pharmaceutical, TRIX, Union Therapeutics and Ventyx Biosciences.

David T. Rubin reports potential conflicts of interest with AbbVie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. Remo Panaccione reports potential conflicts of interest with Abbivax, Abbott, AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceu-

ticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatrix, Ventyx, and UCB.

Natalie A. Terry, Leonardo Salese, Rian Van Rampelbergh, Zijiang Yang, and Mary Ellen Frustaci are employees of Janssen Research & Development (a Johnson & Johnson Company) and may own company stock/stock options.

Dino Tarabar reports potential conflicts of interest with AbbVie, Ferring, Janssen, Pfizer, and Takeda.

Minhu Chen reports potential conflicts of interest with Janssen.

Emese Mihaly reports potential conflicts of interest with Janssen.

Douglas Wolf reports potential conflicts of interest with AbbVie, Bristol Myers Squibb, Janssen, Lilly, Pfizer, and Takeda.

Geert D'Haens reports potential conflicts of interest with AbbVie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exelion, Galapagos, GlaxoSmithKline, Gossamerbio, Immunic, Index, Johnson & Johnson, Kaleido, Origo, Pfizer, Polpharma, Procise Diagnostics, Prometheus Laboratories, Prometheus Biosciences, Progenity, and Protagonist Therapeutics Inc., Seres Health, and Takeda.

MP672

WEEK 48 EFFICACY OF GUSELKUMAB AND USTEKINUMAB IN CROHN'S DISEASE BASED ON PRIOR RESPONSE/EXPOSURE TO BIOLOGIC THERAPY: RESULTS FROM THE GALAXI 2 & 3 PHASE 3 STUDIES

S. Danese¹, A. Afzali², R. Panaccione³, J. Panés⁴, W. Reinisch⁵, N.A. Terry⁶, L. Salese⁶, R. Van Rampelbergh⁷, K.Y.Y. Wan⁸, Z. Yang⁶, J. Johanns⁶, M. Zmudzinski⁹, E. Zittan¹⁰, K. Matsuoka¹¹, V. Jairath¹², D.T. Rubin¹³

¹Gastroenterology and Endoscopy, IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Milan, Italy, ²Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, United States of America, ³Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Canada, ⁴Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain, ⁵Division of Gastroenterology & Hepatology, Medical University of Vienna, Vienna, Austria, ⁶Janssen Research & Development, LLC, Spring House, United States of America, ⁷Janssen Research & Development, Antwerp, Belgium, ⁸Janssen Research & Development, Basel, Switzerland, ⁹Gastromed, Gastrology and Endoscopy Center, Toruń, Poland, ¹⁰The Abraham and Sonia Rochlin IBD Unit, Department of Gastroenterology and Liver Diseases, Emek Medical Center, Afula, Israel, ¹¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Sakura Medical Center, Chiba, Japan, ¹²Schulich School of Medicine & Dentistry, Western University, London, Canada, ¹³University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States of America

Contact E-Mail Address: sdanese@hotmail.com

Introduction: GALAXI 2 & 3 (NCT03466411) are identically designed 48-week (Wk), randomized, double-blind, double-dummy, placebo (PBO)- and ustekinumab (UST)-comparator, treat-through registrational trials assessing the efficacy and safety of therapy with guselkumab (GUS), a du-

al-acting IL-23p19 subunit inhibitor, in participants (pts) with moderately to severely active Crohn's disease (CD). Wk48 comparisons of GUS and UST in the pooled GALAXI 2 & 3 dataset were previously reported. Here we explore the impact of biologic therapy exposure on GUS and UST efficacy for these same endpoints.

Aims & Methods: Pts with inadequate response or intolerance to conventional therapies or biologic therapies (BIO-ir), active CD (CDAI 220–450 + mean daily SF>3 or AP>1), and SES-CD≥6 (≥4 for isolated ileal disease) were eligible. Randomization was stratified by CDAI score, SES-CD score, BIO-ir status, and corticosteroid use with pts assigned 2:2:2:1 to GUS 200mg IV q4w (x3)→100mg SC q8w, GUS 200mg IV q4w (x3)→200mg SC q4w, UST ~6mg/kg IV (x1)→90mg SC q8w, or PBO. Pooled Wk48 analyses comparing GUS and UST (active comparator) in all pts were prespecified major secondary, multiplicity-controlled endpoints. Pooled analyses in the BIO-ir and BIO-naïve subgroups were prespecified but not controlled for multiple comparisons.

Results: Across the pooled GALAXI 2 & 3 dataset, 52% (456/873) of pts randomly assigned to GUS or UST had prior history of BIO-ir and 42% (365/873) were BIO-naïve (6% [52/873] had prior exposure to biologics but no documented failure). At Wk48, in both the BIO-ir and BIO-naïve subgroups, both GUS dose groups demonstrated greater rates of endoscopic response, endoscopic remission, and the composite endpoints of clinical remission + endoscopic response and clinical remission + endoscopic remission (deep remission) compared with the UST group (*Table*). Rates of clinical remission at Wk48 in the BIO-ir subgroup were greater in both GUS dose groups compared to UST and similar in the BIO-naïve subgroup.

	Overall population ^a			Participants with a history of inadequate response or intolerance to at least 1 prior biologic ^b (BIO-ir) ^a			Participants with no history of exposure to biologics ^c (BIO-naïve) ^a		
	GUS 100mg ^b N=286	GUS 200mg ^b N=296	UST ^d N=291	GUS 100mg ^b N=153	GUS 200mg ^b N=147	UST ^d N=128	GUS 100mg ^b N=116	GUS 200mg ^b N=128	UST ^d N=121
Endoscopic response at Wk48	137 (47.9%) Δ 10.6% P=.009	156 (52.7%) Δ 15.6% P<.001	108 (37.1%) P<.001	66 (43.1%) Δ 11.2% P=.039	69 (46.9%) Δ 15.4% P=.005	49 (31.4%) P=.005	68 (58.6%) Δ 15.4% P=.018	76 (59.4%) Δ 16.8% P=.007	52 (43.0%) P=.007
Endoscopic remission at Wk48	95 (33.2%) Δ 8.5% P=.024	110 (37.2%) Δ 12.3% P=.001	72 (24.7%) P=.001	43 (28.1%) Δ 7.8% P=.111	42 (28.6%) Δ 8.3% P=.092	32 (20.5%) P=.092	51 (44.0%) Δ 13.8% P=.027	59 (46.1%) Δ 16.5% P=.007	36 (29.8%) P=.007
Deep remission at Wk48 (composite endpoint)	85 (29.7%) Δ 7.4% P=.040	100 (33.8%) Δ 11.3% P=.002	65 (22.3%) P=.002	39 (25.5%) Δ 8.4% P=.072	36 (24.5%) Δ 7.3% P=.115	27 (17.3%) P=.115	45 (38.8%) Δ 9.5% P=.123	56 (43.8%) Δ 15.0% P=.013	35 (28.9%) P=.013
Clinical remission at Wk48 + endoscopic response at Wk48 (composite endpoint)	119 (41.6%) Δ 7.8% P=.049	140 (47.3%) Δ 13.6% P<.001	98 (33.7%) P<.001	57 (37.3%) Δ 11.3% P=.032	60 (40.8%) Δ 15.1% P=.005	40 (25.6%) P=.005	59 (50.9%) Δ 7.7% P=.239	70 (54.7%) Δ 12.0% P=.055	52 (43.0%) P=.055
Clinical remission at Wk48	187 (65.4%) Δ 2.6% P=.512	208 (70.3%) Δ 7.3% P=.058	183 (62.9%) P=.058	93 (60.8%) Δ 8.4% P=.132	94 (63.9%) Δ 11.5% P=.043	82 (52.6%) P=.043	85 (73.3%) Δ -1.8% P=.755	98 (76.6%) Δ 1.5% P=.784	91 (75.2%) P=.784

Data are presented as n (%); Δ (adjusted treatment difference) vs UST; p-value vs UST.
Adjusted treatment differences and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used are baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-ir status (Yes or No; this variable used only in analyses of the overall population), and baseline corticosteroid use (Yes or No). Population N values reflect the primary analysis set, defined as all randomized participants who received at least 1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for participants with isolated ileal disease).

Endpoint definitions: endoscopic response, ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2; endoscopic remission, SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component; deep remission, clinical remission (CDAI < 150) + endoscopic remission (SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component). Participants with treatment failure or missing data were considered to not have met the endpoint.

a. Anti-TNF agents or vedolizumab
b. Participants assigned to GUS 200mg IV every 4 weeks (q4w) (x3)→100mg SC q8w
c. Participants assigned to GUS 200mg IV q4w (x3)→200mg SC q4w
d. Participants assigned to UST ~6mg/kg IV (x1)→90mg SC q8w. Placebo participants who switched to UST at Wk12 are not included.
* Analyses in this population were prespecified major secondary endpoints; p-values are multiplicity controlled
† Analyses in this population were prespecified but not controlled for multiple comparisons; p-values are nominal

Table. Comparison of guselkumab (GUS) and ustekinumab (UST) for long-term clinical and endoscopic endpoints in all participants and BIO-ir and BIO-naïve subgroups in the pooled GALAXI 2 & 3 dataset.

Conclusion: Guselkumab was efficacious in pts with CD regardless of prior biologic exposure. In pooled analyses of the double-blind GALAXI 2 & 3 trials, both GUS doses demonstrated greater rates of efficacy versus UST across multiple endpoints in the BIO-naïve subgroup and the more refractory BIO-ir subgroup.

Disclosure: Silvio Danese reports potential conflicts of interest with AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity, Takeda, TiGenix, UCB, and Vifor. Anita Afzali reports potential conflicts of interest with AbbVie, Bristol Myers Squibb/Celgene, DiaSorin, Eli Lilly, Gilead, IBD Horizons, Janssen, Pfizer, Takeda, and TLL Pharmaceuticals.

Remo Panaccione reports potential conflicts of interest with Abbivax, Abbott, AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatrix, Ventyx, and UCB.

Julián Panés reports potential conflicts of interest with AbbVie, Alimentiv, Athos, Atomwise, Boehringer Ingelheim, Celsius, Ferring, Galapagos, Genentech/Roche, GlaxoSmithKline, Janssen, Mirum, Nimbus, Pfizer, Progenity, Prometheus, Protagonist, Revolo, Sanofi, Sorriso, Surrozen, Takeda, and Wasserman.

Walter Reinisch reports potential conflicts of interest with AbbVie, Aesca, Agomab, Algenon, AltruBio, Amgen, AM, AMT, AOP Orphan, Aptalis, Arena, Astellas, Astra Zeneca, Avaxia, Roland Berger, Bioclinica, Biogen, Boehringer-Ingelheim, Bristol Myers Squibb, Calyx, Cellerix, Chemocentryx, Celgene, Celltrion, Covance, Danone Austria, DSM, Elan, Eli Lilly, Ernest & Young, Falk, Ferring, Fresenius, Galapagos, Gatehouse, Genentech, Gilead, Grünenthal, ICON, Immundiagnostik, Index, Inova, Intrinsic Imaging, Janssen, Johnson & Johnson, Kyowa Hakko Kirin, Landos, Lipid, LivaNova, Mallinckrodt, Medahead, Medice, MedImmune, Millenium, Mitsubishi Tanabe, MSD, Nash, Nestle, Nippon Kayaku, Novartis, Ocera, OMass, Otsuma, Parexel, PDL, Periconsulting, Pfizer, Pharmacosmos, PLS Education, Procter & Gamble, Prometheus, Protagonist, Provention, Quell, Robarts Clinical Trial, Sandoz, Schering-Plough, Second Genome, Seres, Setpoint-medical, Sigmoid, Sublimity, Takeda, Teva, Therakos, Theravance, Tigene, UCB, Vifor, Yakult, Zealand, Zyngenia, and 4SC.

Natalie A. Terry, Leonardo Salese, Rian Van Rampelbergh, Kitty Yuen Yi Wan, Zijiang Yang, and Jewel Johanns are employees of Janssen Research & Development (a Johnson & Johnson Company) and may own company stock/stock options.

Marcin Zmudziński reports potential conflicts of interest with AbbVie, Alimentiv, Allergan, AstraZeneca, Celgene, Celltrion, Eli Lilly, Gilead, Janssen, Johnson & Johnson, Index, Pfizer, Polpharma, Prometheus, Protagonist Therapeutics, Rejston, Roche, Takeda, Teva, and Theravance Biopharma. Eran Zittan reports potential conflicts of interest with Janssen, AbbVie, Takeda, Neopharm, Celgene and Pfizer.

Katsuyoshi Matsuoka reports potential conflicts of interest with Janssen, Abbvie, Takeda, Pfizer, Gilead, Eli Lilly, Mitsubishi Tanabe Pharma, EA Pharma, Mochida, Kyorin, Zeria, Nippon Kayaku, JIMRO, and Celltrion Healthcare.

Vipul Jairath reports potential conflicts of interest with AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, AstraZeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck,

Metacrine, Mylan, MRM Health, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reystone Biopharma, Roche, Roivant, Sandoz, Second Genome, Shire, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, and Vividion.

David T. Rubin reports potential conflicts of interest with AbbVie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda.

MP673

ANALYSIS OF THE EFFICACY OF INTRAVENOUS USTEKINUMAB MAINTENANCE TREATMENT IN PATIENTS WITH REFRACTORY INFLAMMATORY BOWEL DISEASE

B. López Sáez¹, E. Brunet Mas^{1,2}, L. Melcarne¹, A. Villoria Ferrer^{1,2}, A. Puy Guillén¹, S. Lario¹, M.J. Ramírez-Lázaro¹, L.P. Llovet Soto¹, B. García Sague¹, L.E. Frisancho Morales¹, A. Altadill¹, X. Calvet Calvo^{1,2,3}

¹Parc Taulí Hospital Universitari. Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Gastroenterology, Sabadell, Spain, ²CIBERehd. Instituto de Salud Carlos III, Madrid., Madrid, Spain, ³Universitat Autònoma de Barcelona, Bellaterra.; Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Sabadell, Spain

Contact E-Mail Address: blopezs@tauli.cat

Introduction: Ustekinumab (UST) is a monoclonal antibody that inhibits the p40 subunit of IL-12 and IL-23, approved for the treatment of Crohn's Disease (CD) and Ulcerative Colitis (UC). Its administration is intravenous during induction and subcutaneous during maintenance.

Several studies have assessed the efficacy of reinduction and intensification of this treatment in patients with loss of response. However, there are few studies evaluating the effectiveness of intravenous UST for maintenance.

Aims & Methods: The aim of the study is to evaluate the efficacy and safety of maintenance with intravenous UST in patients with Inflammatory Bowel Disease (IBD).

Observational, retrospective, and single-center study. All patients receiving maintenance with intravenous UST until June 2023 were reviewed. Clinical response was evaluated with Harvey-Bradshaw Index for CD and partial Mayo for UC. Biochemical response was evaluated with calprotectin and C-reactive protein.

Results: A total of 29 patients with IBD (24 CD and 5 UC) were included. The mean follow-up of patients was 449 days (74-948). The cohort's characteristics are summarized in Table 1.

In all cases, intravenous maintenance was performed with UST 130mg/4 weeks. In 4 cases (13.8%), maintenance was initiated directly with intravenous UST. In 9 (31%) patients due to primary failure to UST and in 16 (55.2%) patients due to secondary failure.

The clinical response to intravenous UST maintenance in patients with CD at week 8 and 16 and at one year of follow-up was 87.5% (n=21/24), 83.3% (n=20/24), 73.3% (n=11/15) respectively. For UC, the response was 60% (n=3/5) at week 8 and 16 and at one year. The drug survival was 723 days (± 74) (Figure 1).

No predictive variable for treatment response was identified. Two patients (both with CD) experienced recurrent respiratory infections as an adverse effect, without the need to discontinue UST.

	n = 29
Gender (% women)	15 (51.7%)
Smokers (%)	11 (37.9%)
Type of disease (%)	
Crohn's Disease	24 (82.8%)
Ulcerative Colitis	5 (17.2%)
Extension of the disease:	L1 6 (25%),
Crohn's Disease (L1-L2-L3-L4)	L2 4 (16.7%),
	L3 13 (54.2%),
	L4 1 (4.2%),
	p 10 (34.5%)
Ulcerative Colitis (E2-E3)	E1 0
	E2 0
	E3 5 (100%)
Behaviour Crohn's Disease (B1-B2-B3)	B1 7 (29.2%)
	B2 7 (29.2%)
	B3 3 (12.5%)
	B2+3 7 (29.2%)
Disease severity at diagnosis:	Mild-Moderate 15(62.5%)
Crohn's Disease	Moderate-Severe 9 (37.5%)
Ulcerative Colitis	Mild 1 (20%)
	Moderate 2 (40%)
	Severe 2 (40%)
Surgical history (%)	11 (37.9%)
Ileal resection	2 (6.9%)
Right hemicolectomy + ileal resection	4 (13.8%)
Other procedures	5 (17%)
Extraintestinal manifestations (%)	8 (27.6%)
Previous treatments (%)	
Naive	2 (6.9%)
Mesalazine	9 (31%)
Immunosuppression	23 (79.3%)
Biologic	
Anti-TNF	26 (89.7%)
Vedolizumab	3 (10.3%)
Tofacitinib	1 (3.4%)
Previous treatment with anti-TNF (%)	
Number of anti-TNF	1 - 21 (72.4%)
	2 - 5 (17.2%)
Types of failure	Primary 3 (11.1%)
	Secondary 23 (85.2%)
Reason for intravenous intensification	
Initial IV maintenance	4 (13.8%)
Primary failure to Ustekinumab	9 (31%)
Secondary failure to Ustekinumab	16 (55.2%)
Side effects (%)	
Recurrent respiratory infections	2 (6.9%)

Table 1.

Conclusion: Maintenance treatment with intravenous UST can be useful and safe in patients with severe IBD and/or failure of subcutaneous UST maintenance.

Disclosure: Nothing to disclose.

SHORT AND LONG-TERM EFFECTIVENESS AND SAFETY OF USTEKINUMAB IN ULCERATIVE COLITIS IN REAL LIFE: THE ULISES STUDY

M. Chaparro¹, S. Hermida¹, D. Acosta¹, A. Fernández-Clotet², M. Barreiro-de Acosta³, A. Hernández Martínez⁴, M. Arroyo⁵, M.M. Bosca-Watt⁶, M.T. Diz-Lois Palomares⁷, L. Menchén⁸, J. Martínez-Cadilla⁹, E. Leo-Carnerero¹⁰, C. Muñoz Villafranca¹¹, M. Sierra-Ausín¹², Y. González¹³, S. Riestra¹⁴, P. Sendra Rumbeu¹⁵, M.J. Cabello Tapia¹⁶, I. García de la Filia¹⁷, E. Montil Miguel¹⁸, D. Ceballos¹⁹, R. Pajares Villarroja²⁰, P. Ramírez de la Piscina²¹, M.D. Martín-Arranz²², L. Ramos²³, A. Ruiz-Cerulla²⁴, T.d.J. Martínez-Pérez²⁵, E. San Miguel²⁶, X. Calvet²⁷, J.M. Huguet²⁸, A. Keco-Huerta²⁹, R. Lorente Poyatos³⁰, J.F. Muñoz³¹, Á. Ponferrada³², B. Sicilia Aladrén³³, P. Delgado-Guillena³⁴, E. Gómez Delgado³⁵, F.J. Rancel-Medina³⁶, H. Alonso-Galán³⁷, B. Herreros³⁸, M. Rivero Tirado³⁹, P. Varela⁴⁰, F. Bermejo⁴¹, M. García Sepulcre⁴², L. Gimeno-Pitarch⁴³, L. Kolle-Casso⁴⁴, L. Márquez-Mosquera⁴⁵, P. Martínez Tirado⁴⁶, C. Ramírez⁴⁷, J.P. Gisbert¹, on behalf of the ULISES Study Group

¹Hospital Universitario de La Princesa, IIS-Princesa, UAM and CIBEREHD, Gastroenterology Unit, Madrid, Spain, ²Hospital Clinic of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and CIBERehd, Gastroenterology Unit, Barcelona, Spain, ³Complejo Hospitalario Universitario de Santiago, Gastroenterology Unit, Santiago de Compostela, Spain, ⁴Hospital Universitario Torrecárdenas, Gastroenterology Unit, Almería, Spain, ⁵Hospital Clínico Universitario Lozano Blesa, IIS Aragón and CIBEREHD, Gastroenterology Unit, Zaragoza, Spain, ⁶Hospital Clínico Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ⁷Complejo Hospitalario Universitario A Coruña, Gastroenterology Unit, A Coruña, Spain, ⁸Hospital General Universitario Gregorio Marañón, Gastroenterology Unit, Madrid, Spain, ⁹Hospital Álvaro Cunqueiro, Gastroenterology Unit, Vigo, Spain, ¹⁰Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ¹¹Hospital Universitario de Basurto, Gastroenterology Unit, Basurto, Spain, ¹²Complejo Asistencial Universitario de León, Gastroenterology Unit, León, Spain, ¹³Hospital Universitario Puerta de Hierro Majadahonda, Gastroenterology Unit, Madrid, Spain, ¹⁴Hospital Universitario Central de Asturias and ISPA, Gastroenterology Unit, Oviedo, Spain, ¹⁵Hospital Universitario Son Espases, Gastroenterology Unit, Palma de Mallorca, Spain, ¹⁶Hospital Universitario Virgen de las Nieves, Gastroenterology Unit, Granada, Spain, ¹⁷Hospital Universitario Ramón y Cajal, Gastroenterology Unit, Madrid, Spain, ¹⁸Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain, ¹⁹Hospital Universitario de Gran Canaria Dr. Negrín, Gastroenterology Unit, Las Palmas de Gran Canaria, Spain, ²⁰Hospital Universitario Infanta Sofía, Gastroenterology Unit, Madrid, Spain, ²¹Hospital Universitario de Araba, Gastroenterology Unit, Vitoria, Spain, ²²Hospital Universitario La Paz, Universidad Autónoma de Madrid and IdiPAZ, Gastroenterology Unit, Madrid, Spain, ²³Complejo Hospitalario Universitario de Canarias, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ²⁴Hospital Universitario de Bellvitge, Gastroenterology Unit, L'Hospitalet de Llobregat, Spain, ²⁵Hospital Virgen de la Luz, Gastroenterology Unit, Cuenca, Spain, ²⁶Hospital Universitario de Getafe, Gastroenterology Unit, Getafe, Spain, ²⁷Hospital Universitari Parc Taulí, I3PT-CERCA, Universitat Autònoma de Barcelona. Sabadell and CIBERehd, Gastroenterology Unit, Sabadell, Spain, ²⁸Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia,

Spain, ²⁹Hospital de Valme, Gastroenterology Unit, Sevilla, Spain, ³⁰Hospital General Universitario de Ciudad Real, Gastroenterology Unit, Ciudad real, Spain, ³¹Hospital Universitario de Salamanca, Gastroenterology Unit, Salamanca, Spain, ³²Hospital Universitario Infanta Leonor, Gastroenterology Unit, Madrid, Spain, ³³Hospital Universitario de Burgos, Gastroenterology Unit, Burgos, Spain, ³⁴Hospital de Mérida, Gastroenterology Unit, Mérida, Spain, ³⁵Hospital Universitario Juan Ramón Jiménez, Gastroenterology Unit, Huelva, Spain, ³⁶Hospital Río Carrión, Complejo Asistencial de Palencia (CAUPA), Gastroenterology Unit, Palencia, Spain, ³⁷Hospital Universitario Donostia and Instituto Instituto Biogipuzkoa, Gastroenterology Unit, San Sebastián, Spain, ³⁸Hospital Marina Baixa, Gastroenterology Unit, Alicante, Spain, ³⁹Hospital Universitario de Valdecilla and IDIVAL, Gastroenterology Unit, Santander, Spain, ⁴⁰Hospital Universitario de Cabueñes, Gastroenterology Unit, Gijón, Spain, ⁴¹Hospital Universitario de Fuenlabrada, Gastroenterology Unit, Fuenlabrada, Spain, ⁴²Hospital General Universitario de Elche, Gastroenterology Unit, Elche, Spain, ⁴³Hospital General Universitario de Castellón, Gastroenterology Unit, Castellón, Spain, ⁴⁴Hospital Universitario de La Palma, Gastroenterology Unit, La Palma, Spain, ⁴⁵Hospital del Mar and IMIM, Gastroenterology Unit, Barcelona, Spain, ⁴⁶Hospital Universitario San Cecilio and PTS, Gastroenterology Unit, Granada, Spain, ⁴⁷Hospital Universitario Galdakao-Usansolo, Gastroenterology Unit, Galdakao, Spain

Contact E-Mail Address: mariachs2005@gmail.com

Introduction: Ustekinumab has been shown to be effective in the treatment of UC. Data on its effectiveness in clinical practice are needed both in the short and long term.

Aims & Methods: Primary aim: To assess the durability of ustekinumab treatment in patients with ulcerative colitis (UC).

Secondary aims: To assess the short-term effectiveness, the durability of response, and the tolerability of ustekinumab in clinical practice.

Methods: Retrospective, multicenter study including UC patients who had received the 1st ustekinumab dose at least 16 weeks before inclusion. Patients were followed-up from the 1st ustekinumab dose to treatment discontinuation or last visit. Only patients with active disease [Partial Mayo Score (PMS)>2] at ustekinumab start were considered in the effectiveness analysis. Clinical effectiveness was based on PMS. Patients who stopped ustekinumab before their last visit were considered not in remission at subsequent time points (negative imputation).

Results: 620 patients with UC were included, 57% with extensive colitis, 95% exposed to biologics (mean number of biologics 2), and 25% to tofacitinib. 78% of patients who started ustekinumab maintenance treatment, did it with 90 mg every-8-weeks dose. 155 patients (25%) withdrew ustekinumab during follow-up [median=12 months (m)]. Incidence rate of ustekinumab discontinuation was 20% per patient-year of follow-up. The probability of maintaining ustekinumab was 78% at 1 year and 68% at 2 years. Among patients who withdrew ustekinumab, the main reasons were primary non-response (39%) and loss of response (35%). Anaemia at baseline (HR=1.5, 95%CI=1.1-2.1), steroids at baseline (HR=1.5; 95%CI=1.06-2.08), and more severe clinical activity at baseline (HR=1.5; 95%CI=1.09-2.06) were associated with higher risk of ustekinumab discontinuation. At the end of the induction (week 16), 226 (40%) patients were in steroid-free remission; 11 (20%) patients were in steroid-free remission at week 4, and 191 (34%) at week 8. In the long-term, the proportion of patients in steroid-free remission was 50% at 1 year, 49% at 2 years and 49% at 3 years. Moderate-severe vs. mild disease activity at baseline (OR=0.3, 95%CI=0.2-0.5), male sex (OR=0.5; 95%CI=0.4-0.8), and increased number of previous biologics (OR=0.6, 95%CI=0.6-0.8) were associated with lower likelihood of steroid-free remission at week 16. A to-

tal of 57 (25%) patients among those with active disease at baseline and with steroid-free remission at week 16, lost response during a median follow-up of 8 m (IQR=3-16 m); 75% of patients maintained effectiveness at 1 year, and 57% at 2 years.

The dose was escalated in 72% of patients with loss of response, and 80% improved (67% remission); an intravenous reinduction was given in 3 patients, and none of them improved. A total of 176 patients (28%) had at least one adverse event, with infections being the most frequent (11%). No negative impact on extraintestinal manifestations and/or immunome-mediated diseases was seen.

Conclusion: Ustekinumab was effective in inducing remission even in highly refractory UC patients. A proportion of patients discontinued the treatment, mostly due to primary failure and loss of response. Dose escalation may be effective to regain response after loss of effectiveness. The safety profile was consistent with previous studies.

Disclosure: This is an investigator-initiated study with financial support from Janssen (CNT01275UC04008).

MP675

THE EFFICACY OF KEVERPRAZAN BASED QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN CHINESE PATIENTS: A DOUBLE BLIND, RANDOMIZED, PHASE III STUDY

N. Tan¹, H. Wu², C. Lan³, C. Liu⁴, A. Liao⁵, Z. Jiao⁶, D. Su⁷, X. Zhang⁸, Z. Zhang⁹, W. Xiao¹⁰, F. Li¹¹, X. Li¹², M. Xia¹³, R. Qiu¹⁴, H. Chen¹⁵, Y. Liu¹⁶, M. Su¹⁷, M. Chen¹, Y. Xiao¹

¹The First Affiliated Hospital of Sun Yat-Sen University, Department of Gastroenterology, Guangzhou, China, ²The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Department of Gastroenterology, Wenzhou, China, ³Hainan General Hospital, Department of Gastroenterology, Haikou, China, ⁴Binzhou Medical University Hospital, Department of Gastroenterology, Binzhou, China, ⁵The First Affiliated Hospital, Hengyang Medical School, University of South China, Department of Gastroenterology, Hengyang, China, ⁶Yuebei People's Hospital, Department of Gastroenterology, Shaoguan, China, ⁷The Second Nanning People's Hospital, Department of Gastroenterology, Nanning, China, ⁸Xiangya Hoapital Central South University, Department of Gastroenterology, Changsha, China, ⁹Shengjing Hospital of China Medical University, The Second Department of Gastroenterology, Shenyang, China, ¹⁰Affiliated Hospital of Yangzhou University, Department of Gastroenterology, Yangzhou, China, ¹¹The First People's Hospital of Chenzhou, Department of Gastroenterology, Chenzhou, China, ¹²Pingxiang People's Hospital, Department of Gastroenterology, Pingxiang, China, ¹³The Affiliated Wuxi People's Hospital of Nanjing Medical University, Wuxi Medical Center, Nanjing Medical University, Department of Gastroenterology, Wuxi, China, ¹⁴Yueyang People's Hospital, Department of Gastroenterology, Yueyang, China, ¹⁵Huizhou Central People's Hospital, Department of Gastroenterology, Huizhou, China, ¹⁶Xuancheng People's Hospital, Department of Gastroenterology, Xuancheng, China, ¹⁷Jiangsu Carephar Pharmaceutical Co., Ltd, Nanjing, China

Contact E-Mail Address: tannd3@mail.sysu.edu.cn

Introduction: Keverprazan, a novel potassium-competitive acid blocker, was approved in 2023 for the treatment of duodenal ulcer and reflux oesophagitis in China. Its advantages as a potent antacid in *Helicobacter pylori* (*H. pylori*) eradication still aren't demonstrated. This study aims to evaluate the efficacy of Keverprazan as a component of bismuth quadruple therapy in *Helicobacter pylori* treatment.

Aims & Methods: This randomized, positive drug controlled study was conducted in non-inferior design and enrolled Chinese *H. pylori* positive patients aged 18-90 years to randomly (1:1) take keverprazan (Kev group) or esomeprazole (PPI group)-quadruple therapy (regimen contains keverprazan 20 mg or esomeprazole 20 mg, clarithromycin 500 mg, amoxicillin 1000 mg, bismuth potassium citrate 240 mg) twice daily (BID) for 14 days. The primary endpoint was the *H. pylori* eradication rate at 4 weeks after quadruple therapy. The Clopper Pearson method and the Miettinen & Nurminen method were respectively used to calculate the primary endpoint in each group and the treatment difference between groups. The missing data of primary endpoints was imputed as "not eradicated".

Results: In full analysis set, 252 of 287 (87.8%) patients in Kev group and 236 of 286 (82.52%) patients in PPI group eradicated the *H. pylori* successfully at 4 weeks after treatment, the difference of eradication rate: 5.29% ([95%CI: -0.55%, 11.18%], $P=0.0750$). The superiority of keverprazan compared with esomeprazole on eradication rate was observed in per protocol set ($P=0.0382$). The eradication rates were also numerically higher in Kev group than PPI group across the subgroups including sex, age, the resistance of clarithromycin, gene polymorphism of CYP2C19 and areas. The incidence of adverse events was similar in Kev and PPI group (76.31% vs. 77.62%), most adverse events (>90%) were mild in severity and no lead to death adverse events happened.

Conclusion: Keverprazan 20 mg BID as a component of bismuth quadruple therapy provided effective *H. pylori* eradication and non-inferior to PPI based regimen (Trial registration number: ChiCTR2200058521).

Disclosure: Mei Su is the employee of Jiangsu Carephar Pharmaceutical Co., Ltd. The other authors have no conflicts of interest to declare. This study was funded by Jiangsu Carephar Pharmaceutical Co., Ltd. We thank all participants and investigators for supporting this study. Editorial support for this abstract was provided by Liangjie Zhong (the employee of Shanghai Fosun Pharmaceutical Development Co., Ltd.).

MP676

PERSISTENCE TO USTEKINUMAB IN PATIENTS WITH CROHN'S DISEASE TREATED IN REAL-LIFE CARE SETTING IN GREECE: FINAL RESULTS FROM THE PROSPECTIVE 'REASSURE' STUDY

G.J. Mantzaris^{1,2}, S. Michopoulos³, C. Gkamaloutsos⁴, K. Thomopoulos⁵, M. Tzouvala⁶, I. Koutroubakis⁷, C. Liatsos⁸, S. Vradelis⁹, T. Sdonas¹⁰, G. Papatheodoridis¹¹, D.K. Christodoulou¹², K.D. Paraskeva¹³, I. Goulis¹⁴, E. Zampeli¹⁵, K.H. Katsanos¹⁶, G. Germanidis¹⁷, A. Protopapas¹⁸, K. Soufleris¹⁹, I. Pachiadakis²⁰, V. Ntelis²¹, E. Papanthanasios³, M.L. Chatzinikolaou²², K. Chalakatevaki²², G. Theocharis⁵, A. Trikola²³, E. Beka²⁴, G. Tribonias², M. Palatianou⁶, K. Foteinogiannopoulou⁷, A. Machaira⁷, N. Kyriakos²⁵, M. Giakoumis⁹, E. Giannakouloupoulou⁷, A. Tassovassili¹⁰, P. Karatzas²⁶, N. Mathou¹³, G. Kokkonis²⁷, G. Kalopitas¹⁷, G. Michalopoulos²¹, P. Giannelis²⁸, A. Protopapas¹⁸, K. Fasoulas¹⁹, A. Boubonaris²⁰, A. Nakos²⁰, C. Taloumtzis²⁰, E. Orfanoudaki⁷, C. Lamouri¹², A. Mpartsea⁴, I. Kanistras⁴, G. Bamias²²

¹Hygeia General Hospital, Dept. of Gastroenterology, Athens, Greece, ²White Cross Clinic, Dept. of Gastroenterology, Athens, Greece, ³Alexandra General Hospital, Dept of Gastroenterology, Athens, Greece, ⁴Janssen-Cilag, Athens, Greece, ⁵University Regional Hospital of Patras, Gastroenterology Clinic, Patras, Greece, ⁶General Hospital of Nikaia, Dept of Gastroenterology, Nikaia, Greece, ⁷University General Hospital of Heraklion, Gastroenterology Clinic, Heraklion, Greece, ⁸401 Army General Hospital of Athens, Dept. of Gastroenterology, Athens, Greece, ⁹Democritus University Hospital, Dept of Endoscopy,

Alexandroupolis, Greece, ¹⁰General Oncology Hospital “Agiol Anargyroi”, Dept of Gastroenterology, Kifissia, Greece, ¹¹Univ. Medical School Hippokration Hospital - Academic Dept. of Gastroenterology, Univ. Medical School, Academic Dept. of Gastroenterology, Athens, Greece, ¹²Gastroenterology Unit University Hospital, 1st Division Of Internal Medicine And Hepato-Gastroenterology Unit, Ioannina, Greece, ¹³General Hospital “Agia Olga”, Gastroenterology, Athens, Greece, ¹⁴Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece, ¹⁵Alexandra General Hospital, Dept. of Gastroenterology, Athens, Greece, ¹⁶Medical School of Ioannina, Division of Internal Medicine, 45333 Ioannina, Greece, ¹⁷AHEPA University General Hospital, A' University Internal Medicine Clinic, Thessaloniki, Greece, ¹⁸AHEPA University General Hospital, 1st Propaedeutic Internal Medicine Clinic, Thessaloniki, Greece, ¹⁹Theagenion Anticancer Hospital of Thessaloniki, Dept of Gastroenterology, Thessaloniki, Greece, ²⁰424 Military General Hospital of Thessaloniki, Gastroenterology and Hepatology, Thessaloniki, Greece, ²¹“G. Genimatas” General Hospital, Dept of Gastroenterology, Athens, Greece, ²²National and Kapodistrian University of Athens, GI-Unit, 3rd Academic Dpt. of Internal Medicine, Athens, Greece, ²³Naval Hospital of Athens, Gastrointestinal Department, Athens, Greece, ²⁴Evangelismos Hospital, Gastroenterology and Hepatology, Athens, Greece, ²⁵401 Army General Hospital of Athens, Athens, Greece, ²⁶Hygeia Hospital, Gastroenterology Clinic, Athens, Greece, ²⁷Bioclinic Hospital, Dept of Gastroenterology, Thessaloniki, Greece, ²⁸“Tzaneio” General Hospital, Gastroenterology Clinic, Piraeus, Greece

Contact E-Mail Address: gjmantzaris@gmail.com

Introduction: There is currently lack of published data on the use of ustekinumab (UST) in routine care setting in Greece. REASSURE study aimed to generate real-world evidence (RWE) on treatment persistence, and patient-reported outcomes (PROs) in patients with Crohn’s Disease (CD).

Aims & Methods: This was an observational, prospective study of adult (18-80 years old) patients with confirmed diagnosis of CD, who commenced therapy with UST as 1st, 2nd, or 3rd line biologic treatment, according to physician’s decision, local standards of clinical practice and as per label indication. Data were collected by routine assessments, including Harvey-Bradshaw Index (HBI), and PROs at baseline (start of UST) and follow-up visits every 6-months. Last visit was done at month 24 (±2 months) or at treatment discontinuation (whichever occurred first). Drug persistence, disease activity and safety outcomes over the 24-month observation period are presented herein.

Results: A total of 169 eligible patients were enrolled in 19 Gastroenterology Clinics in Greece between April 2019 and February 2021. At baseline, median age was 45.0 years, 50.9% (86/169) of patients were females, 43.4% (72/166) were employed, and 68.5% (113/165) were former or current smokers. UST was the 1st, 2nd, and 3rd biologic treatment in 35.5% (60/169), 35.5% (60/169), and 29.0% (49/169) of patients, respectively. The median duration of study participation was 23.9 months (median number of injections received: 13.0). At 24 months, 21.9% (37/169) of patients had discontinued UST after a mean of 10.2 months due to lack/loss of response (15/37), safety issues (10/37), lost at follow-up (6/37), patient’s wish (2/37), death (2/37; both unrelated to UST), pregnancy (1/37) and patient issues (1/37).

The Kaplan-Meier (KM)-estimated median drug survival (i.e., time to treatment discontinuation) was not reached in the overall population or subgroups by treatment line, with no statistically significant differences in the risk of UST discontinuation between subgroups of interest [2L vs

1L: hazard ratio (HR)=1.07, 95% confidence interval (CI)=0.48-2.39; 3L vs 1L: HR=1.54, 95% CI=0.70-3.40; 3L vs 2L: HR=1.42, 95% CI=0.65-3.11). The KM-estimated UST treatment-persistence rates for the overall population were 86.7%, 80.5%, and 78.0%, at 12-, 18-, and 24-months, respectively. The baseline median total HBI (8.0) significantly improved ($P<0.001$) at 12, 18, and 24 months, with a median 4-point reduction at each timepoint, among paired observations.

Significant improvements were also noted based on imputed data and in the subgroups per treatment line. The adverse event (AE), serious AE, and UST-related AE rates were 63.9% (108/169), 18.9% (32/169), and 19.5% (33/169), respectively. Each UST-related AE was reported in <4.0% of the patients. Further details on baseline characteristics, 12/18/24-month outcomes, and UST-related AEs are presented in Table 1.

	Overall (N=169)		Bio-naïve (1L) (N=60)		UST as 2LT (N=60)		UST as 3LT (N=49)	
Time from CD diagnosis to UST initiation, median (IQR), years	7.0 (1.8 – 13.0)		1.3 (0.3 – 6.2)		8.2 (3.8 – 11.7)		12.9 (9.0 – 22.1)	
Baseline characteristics								
Age ≤50 years	N	n _a (%)	N	n _a (%)	N	n _a (%)	N	n _a (%)
Females	169	106 (62.7)	60	31 (51.7)	60	45 (75.0)	49	30 (61.2)
At least 1 comorbidity	169	86 (50.9)	60	25 (41.7)	60	30 (50.0)	49	31 (63.3)
Prior CD-related surgery	169	93 (55.0)	60	33 (55.0)	60	35 (58.3)	49	25 (51.0)
Prior systemic treatment for CD	169	54 (32.0)	60	3 (5.0)	60	24 (40.0)	49	27 (55.1)
Strictureing and/or penetrating disease	169	158 (93.5)	60	49 (81.7)	60	60 (100.0)	49	49 (100.0)
Extraintestinal manifestations	162	70 (43.2)	57	19 (33.3)	57	27 (47.4)	48	24 (50.0)
Steroid-dependent/refractory disease	167	61 (36.5)	60	19 (31.7)	59	23 (39.0)	48	19 (39.6)
Starting UST maintenance dosage: 90 mg SC Q8W	149	24 (16.1)	55	10 (18.2)	52	5 (9.6)	42	9 (21.4)
UST initiated as monotherapy	169	152 (89.9)	60	50 (83.3)	60	56 (93.3)	49	46 (93.9)
	169	99 (58.6)	60	37 (61.7)	60	32 (53.3)	49	30 (61.2)
No disease activity based on HBI (i.e., score of 0-4 points)								
	N	n _a (%)	N	n _a (%)	N	n _a (%)	N	n _a (%)
At Month 12	131	102 (77.9)	49	42 (85.7)	49	37 (75.5)	33	23 (69.7)
At Month 18	117	90 (76.9)	43	37 (86.0)	42	33 (78.6)	32	20 (62.5)
At Month 24	114	100 (87.7)	43	39 (90.7)	40	36 (90.0)	31	25 (80.6)
Kaplan-Meier-estimated persistence to UST treatment								
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
12-month rate	86.7	80.6 – 91.1	89.9	78.8 – 95.3	88.3	77.1 – 94.3	80.9	66.5 – 89.6
18-month rate	80.5	73.6 – 85.8	82.9	70.6 – 90.4	83.1	70.9 – 90.6	74.3	59.2 – 84.6
24-month rate	78.0	70.8 – 83.6	81.2	68.6 – 89.1	79.4	66.5 – 87.8	72.2	56.9 – 82.8
Safety*								
	N	n _a (%)	N	n _a (%)	N	n _a (%)	N	n _a (%)
UST-related AEs	169	33 (19.5)	60	6 (10.0)	60	14 (23.3)	49	13 (26.5)
UST-related AEs leading to withdrawal	169	8 (4.7)	60	1 (1.7)	60	3 (5.0)	49	4 (8.2)
UST-related AEs leading to interruption/dose delay	169	3 (1.8)	60		60	3 (5.0)	49	

*Excluding drug ineffective/loss of therapeutic response/off-label use. Abbreviations: 1/2/3L: First/Second/Third Line; AE: Adverse Event; CD: Crohn’s Disease; CI: Confidence Interval; HBI: Harvey-Bradshaw Index; IQR: Interquartile Range; IV: intravenous; N: number of patients with available data; n_a: number of patients with variable; Q8W: every 8 weeks; SC: subcutaneous; UST: ustekinumab.

Table 1: Baseline characteristics, 12/18/24-month outcomes, and UST-related adverse events.

Conclusion: Our data provide RWE for high persistence rate of treatment with UST in our series with Greek patients with CD. Treatment with UST demonstrated a highly favorable effect on disease activity, in combination with a predictable safety profile.

Disclosure: This study was sponsored by Janssen - Cilag, Greece. Giorgos Bamias Advisor/lecturer for Janssen, Pfizer, Takeda, Abbvie, MSD, Mylan, Genesis Pharma, Adacety Therapeutics, Amgen, Ferring, Cooper, BMS; Funding (Grants/Honoraria): Pfizer, Takeda, Abbvie, Aenorasis; Research/Clinical Trials: Abbvie, Takeda, Janssen.

Gerassimos J. Mantzaris has received consultant and/or speaker fees from AbbVie, MSD, Celtrion, Ferring, Aenorasis, Janssen, Pfizer, Takeda, Falk Pharma, and Vianex and research support from AbbVie, Ferring, MSD, and Vianex

Maria Tzouvala has received clinical research funding from Janssen-Cilag Pharmaceuticals SACI, Takeda HELLAS SA, AbbVie Pharmaceuticals S.A. Consulting and/or speaking fees MSD Sharp & Dohme, Janssen-Cilag Pharmaceuticals SACI, Takeda, AbbVie Pharmaceuticals S.A, Pfizer, Amgen. Advisory boards: Janssen-Cilag Pharmaceuticals SACI, Takeda, AbbVie Pharmaceuticals S.A, Pfizer, Amgen

Dimitrios Christodoulou has received consulting and speaking fees for Janssen, MSD, Galenica. Advisory Board for Galenica

Ioannis Koutroubakis has received clinical research funding: Abbvie, Faran, Ferring, Pfizer, Viatrix, Vianex, Vifor, Unipharm. Consulting and/or speaking fees Abbvie, Genesis, Janssen, MSD, Takeda, Vianex. Advisory boards: Abbvie, Janssen, MSD, Pfizer, Takeda, Vianex

Christos Liatsos has received clinical research funding from: Janssen, and consulting and/or speaking fees from: MSD, Pfizer, Boston SCI, Amgen, Galenica.

Georgios Papatheodoridis Clinical research funding: Abbvie, Gilead, Takeda, Vianex. Consulting and/or speaking fees: Abbvie, Astra-Zeneca, BioARS Therapeutics, Elpen, Genesis, Gilead, GlaxoSmithKline, Ipsen, Novo Nordisk, Roche, Sobi. Advisory boards: Abbvie, Astra-Zeneca, Albireo, Amgen, Galenica, Genesis, Gilead, GlaxoSmithKline, Ipsen, Janssen, Novo Nordisk, Roche, Takeda

Dr Katsanos Konstantinos received honoraria for consulting services (educational services, scientific articles, participation in Advisory Boards, clinical trials, lecture fees, other) from the companies as follows:AbbVie, AMGEN, ENORASIS, Epsilon Health, Ferring, Genesis, Grifols S.A., JANSSEN, MSD, Mylan, Shire and Takeda.

Evanthia Zampeli has received clinical research funding: Janssen, TAKE-DA, ABBVIE. Consulting and/or speaking fees: Janssen, TAKEDA, BMS, AMGEN, MYLAN. Advisory boards: BMS, GALENICA

Georgios Germanidis has received clinical research funding from Janssen. Konstantinos Soufleris Consulting and/or speaking fees: AbbVie, Janssen, MSD, Pfizer, Takeda. Clinical research funding:Pfizer. Advisory board: BMS, Galenica.

Matina-Lydia Chatzinikolaou has received consulting fees from Abbvie, Takeda, Amgen, Ferring, Janssen

George Kokkonis has received clinical Research funding from Janssen and speaking fees from Janssen and Amgen

Alexandros Boubonaris has served as advisory board member for Amgen, Takeda

Marios Giakoumis has received clinical research funding from Janssen

Artemis Trikola has received clinical research funding from Janssen

George Michalopoulos has received speaker fees : Takeda, MSD, , Abbvie, Janssen, Pfizer, Amgen

Vasileios Delis, Konstantina Paraskeva, Theodosios Sdonas, Athanasia Tasovasilis, Evgenia Papathanasiou, Maria Palatianou, Andreaddis Nakos, Nikolett Mathou, George Kalopitas, Panagiotis Giannelis, Kalliopi Fotinogiannopoulou, Konstantina Chalakevaki, Eleni Beka, Chara Lamouri, Eleftheria Giannakouloupoulou have no conflicts to disclose.

Konstantinos Thomopoulos, Stergios Vradelis, Andreas Protopapas, Ioannis Pachiadakis, Ioannis Goulis, Pantelis Karatzas, George Theocharis, George Tribonias, Angeliki Machaira, Nikolaos Kyriakos, Adonis Protopapas, Konstantinos Fasoulas, Eleni Orfanoudaki and Charilaos Talountzis have not disclosed any conflicts.

Spyridon Michopoulos has received clinical research funding from Janssen, Takeda, BMS, consulting and/or speaking fees from Takeda, and has served as advisory board member for Takeda.

Christos Gkamaloutsos, Ioannis Kanistras and Aikaterini Mpartsea are employees of Janssen - Cilag, Greece.

MP677

IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE TREATED WITH RISANKIZUMAB VERSUS USTEKINUMAB IN THE PHASE 3 SEQUENCE STUDY

E.V. Loftus, Jr.¹, B.E. Sands², V. Jairath³, I. Blumenstein⁴, N. Joshi⁵, N. Shukla^{5,5}, K. Kligys⁵, T. Anschutz⁵, J. Griffith⁵, J. Zambrano⁵, E. Louis⁶

¹Mayo Clinic College of Medicine, Division of Gastroenterology and Hepatology, Rochester, United States of America, ²Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ³Western University, Department of Medicine Schulich School of Medicine & Dentistry, London, Canada, ⁴University Clinic Frankfurt, Department of Gastroenterology, Hepatology and Nutrition, Frankfurt, Germany, ⁵AbbVie, North Chicago, United States of America, ⁶CHU Liège and Liège University, Gastroenterology, Liège, Belgium

Contact E-Mail Address: loftus.edward@mayo.edu

Introduction: Crohn's disease (CD) is a chronic progressive inflammatory bowel disease (IBD) that can substantially impact one's health-related quality of life (HRQoL). The treatment effect of risankizumab (RZB) vs ustekinumab (UST) on achieving clinically meaningful within-person changes (MWPCs) in patient (pt) reported outcomes (PROs) as measured by Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-item Short-Form Health Survey (SF-36 v.2) scores, as well as on select individual items (symptoms) of the IBDQ, were evaluated using data from the phase 3 SEQUENCE (NCT04524611) study.

Aims & Methods: The SEQUENCE open-label, multicenter, randomized, efficacy assessor-blinded study directly compared the efficacy and safety of RZB vs UST in pts with moderate to severe CD with prior anti-TNF failure. Pts were randomized 1:1 to receive recommended induction and maintenance doses of RZB (N=255) or UST (N=265)¹. The proportion of pts who achieved MWPCs as measured by IBDQ response (≥ 16 point increase in total score), IBDQ remission (total score ≥ 170 points), and improvement in the SF-36 physical (PCS) and mental (MCS) component scores (≥ 4.1 and ≥ 3.9 points, respectively) between baseline (BL) and weeks 24 and 48 of maintenance were compared between pts who received RZB vs UST. In addition, the proportion of pts who reported all/most/a good bit/some of the time ("all-some of the time") for the fatigue, depression, anxiety, and bowel urgency items on the IBDQ were compared for RZB vs UST. Chi-square *P* values are reported.

Results: A significantly greater proportion of RZB- vs UST-treated pts demonstrated clinically meaningful improvements in IBDQ response (week 24, 75.3% vs 64.2%; week 48, 68.6% vs 50.9%), IBDQ remission (week 24, 52.5% vs 30.9%; week 48, 49.8% vs 33.2%), and improvement from BL in SF-36v2 PCS (week 24, 65.9% vs 53.2%; week 48, 63.9% vs 46.0%) (all comparisons *P* < 0.01). In addition, a significantly greater proportion of RZB-treated pts vs UST demonstrated a MWPC from BL at week 48 in SF-36 MCS (54.1% vs 40.0%; *P* < 0.01) (Table).

At BL, a similar proportion of pts with RZB vs UST, reported fatigue (92.2% vs 92.8%), depression (66.7% vs 70.9%), anxiety (71.4% vs 75.5%), or bowel urgency (69.8% vs 73.2%) "all-some of the time" on the IBDQ (Table).

At both weeks 24 and 48, a significantly lower proportion of pts with RZB vs UST reported experiencing fatigue (week 24, 51.4% vs 69.1% [*P* < .0001]; week 48, 54.9% vs 72.1% [*P* < .0001]), depression (week 24, 34.1% vs 42.6% [*P* = .05]; week 48, 35.7% vs 58.1% [*P* < .0001]), anxiety (week 24, 34.1% vs 49.8% [*P* < .001]; week 48, 35.3% vs 58.5% [*P* < .0001]) or bowel urgency (week 24, 27.1% vs 40.0% [*P* < .01]; week 48, 27.1% vs 50.6% [*P* < .0001]) "all-some of the time" (Table).

Outcomes	Proportion of Patients Who Achieved Meaningful Within-Person Change (MWPC) ^a					
	From Baseline to Week 24			From Baseline to Week 48		
	Risankizumab N=255 n (%)	Ustekinumab N=265 n (%)	Chi-square P-value	Risankizumab N=255 n (%)	Ustekinumab N=265 n (%)	Chi-square P-value
IBDQ ^b total score (≥ 16-point increase)	192 (75.3%)	170 (64.2%)	<.01	175 (68.6%)	135 (50.9%)	<.0001
IBDQ ^b remission (IBDQ ≥ 170 points)	134 (52.5%)	82 (30.9%)	<.0001	127 (49.8%)	88 (33.2%)	.0001
SF-36 ^c Physical Component Score (PCS) (≥ 4.1-point increase)	168 (65.9%)	141 (53.2%)	<.01	163 (63.9%)	122 (46.0%)	<.0001
SF-36 ^c Mental Component Score (MCS) (≥ 3.9-point increase)	141 (55.3%)	133 (50.2%)	.2	138 (54.1%)	106 (40.0%)	<.01
IBDQ Items (Symptoms)	Proportion of Patients Who Reported IBDQ Items/Symptoms „All/Most/A Good Bit/Some of the Time ^b					
	Week 24			Week 48		
	Risankizumab N=255 n (%)	Ustekinumab N=265 n (%)	Chi-square P-value	Risankizumab N=255 n (%)	Ustekinumab N=265 n (%)	Chi-square P-value
Fatigue ^d	131 (51.4%)	183 (69.1%)	<.0001	140 (54.9%)	191 (72.1%)	<.0001
Depression ^e	87 (34.1%)	113 (42.6%)	.05	91 (35.7%)	154 (58.1%)	<.0001
Anxiety ^f	87 (34.1%)	132 (49.8%)	<.001	90 (35.3%)	155 (58.5%)	<.0001
Bowel urgency ^g	69 (27.1%)	106 (40.0%)	<.01	69 (27.1%)	134 (50.6%)	<.0001

IBDQ, inflammatory bowel disease questionnaire; MWPC, meaningful within-person change; SF-36, 36-item Short-Form Health Survey.

^aMWPC is the point at which an individual patient experiences clinically meaningful within-person benefit/improvement in quality of life.

^bThe IBDQ includes 32 items that represent 4 domains (physical, social, emotional, and systemic). Items are rated on a 7-point scale (1 = all of the time; 2 = most of the time; 3 = a good bit of the time; 4 = some of the time; 5 = a little bit of the time; 6 = hardly any of the time; 7 = none of the time), providing a total score ranging from 32 to 224; higher scores indicate better HRQoL. For IBDQ items assessed, the proportion of patients providing scores of 1 to 4 were combined, and the proportion of patients providing scores of 5 to 7 were combined; categories 1 to 4 are displayed here.

^cThe SF-36 includes 36 items are summarized in two components, the physical component summary (PCS) and mental component summary (MCS). The PCS comprises four subscales: physical function (PF), role limitations owing to physical health (RP), bodily pain (BP), and general health perceptions (GH). The MCS also comprises four subscales: vitality (VT), social functioning (SF), role limitations owing to emotional problems (RE), and mental health (MH). Scores range from 0 to 100 for each subscale in both components, with higher scores indicating better health.

^dThe amount of time one feels fatigued, tired, and worn out.

^eThe amount of time one felt depressed or discouraged.

^fThe amount of time one felt worried and anxious about never feeling any better and having a relapse.

^gThe amount of time one felt troubled by a feeling of having to go to the bathroom even with empty bowels. Patients with missing observations at any time point were considered as reporting the symptoms „all/most/a good bit/some of the time“.

Conclusion: RZB was more effective than UST in delivering clinically meaningful improvements in PROs in pts with moderate to severe CD who failed anti-TNF therapy. A significantly lower proportion of patients who received RZB vs UST reported symptoms of fatigue, depression, anxiety, and bowel urgency at weeks 24 and 48.

References: 1 Peyrin-Biroulet, L. et al. UEG Journal. 2023; 11, 919–940.

Disclosure: Edward V. Loftus, Jr. has received consulting fees from AbbVie, Alvotect, Amgen, Arena, Avalo Therapeutics, BMS, Boehringer Ingelheim, Calibr, Celgene, Celltrion Healthcare, Eli Lilly, Fresenius Kabi, Genentech, Gilead, GlaxoSmithKline, Gossamer Bio, Iota Biosciences, Iterative Scopes, Janssen, KLS Diagnostics, Morphic Therapeutics, Ono Pharma, Pfizer, Protagonist, Scipher Medicine, Sun Pharma, Surrozen, Takeda, and UCB; has served as an advisory board participant for Eli Lilly and Morphic; has received research support from AbbVie, BMS, Celgene/Receptos, Genentech, Gilead, Gossamer Bio, Janssen, Pfizer, Takeda, Theravance, and UCB; and holds stock in Exact Sciences.

Bruce Sands has received consulting fees from Abbvie, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biologic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Entera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus

Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma.

Vipul Jairath has received consulting/advisory board fees from AbbVie, Alimentiv, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; speaker's fees from, Abbvie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi

Irina Blumenstein has no competing interests to declare.

Edouard Louis received educational and research grants from Takeda, Pfizer, Janssen, AbbVie, and Fresenius-Kabi; speaker fees from AbbVie, Ferring, Falk, Takeda, Janssen, Pfizer, Celgene, Galapagos, and BMS; and consultancy fees from AbbVie, Ferring, MSD, Takeda, Celgene, Janssen, Gilead-Galapagos, Arena, Pfizer, Eli Lilly, and BMS.

Namita Joshi, Nidhi Shukla, Kristina Kligys, Toni Anschutz, Jenny Griffith, and Javier Zambrano are full-time employees/contractor of AbbVie and may own AbbVie stock or options.

Funding and Acknowledgments:

AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship. AbbVie and authors thank all the trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Stephanie Parsons, PhD, and copy editing support was provided by Angela Hadsell, BS, both employees of AbbVie.

MP678

EFFECTIVENESS AND SAFETY OF MONOCLONAL ANTIBODIES AGAINST IL23 SUBUNIT P19 FOR TREATING PATIENTS WITH ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

S. Khalil¹, M. Souza², K. Eskandar³, M. Meine³, G. Meine⁴

¹University de Buenos Aires, Buenos Aires, Argentina, ²Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, ³Pontifical Catholic University of Parana, Curitiba, Brazil, ⁴Feevale University, Novo Hamburgo, Brazil

Contact E-Mail Address: samiramohamad96@gmail.com

Introduction: The efficacy of IL-23 blockade has been established in the treatment of patients with ulcerative colitis (UC). While studies in psoriasis have indicated that selectively targeting the IL-23 subunit p19 is more effective than general IL-23 blockade, it remains unclear whether a similar response can be expected in UC.

Aims & Methods: This study aimed to assess the efficacy and safety of monoclonal antibodies against the interleukin-23 subunit p19 (IL-23 p19 monoclonal antibodies) vs. placebo for induction therapy of patients with

moderate to severely active UC who had failure to conventional treatment. We searched PubMed, Embase, and Cochrane databases. The primary outcomes were clinical remission and clinical response. The secondary outcomes were endoscopy remission, symptomatic remission, and adverse events (AEs). We pooled the risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes and used the DerSimonian-Laird random-effects model. P-values inferior to 0.05 were deemed indicative of statistical significance. Heterogeneity was assessed with I^2 statistics.

Results: We included 3 RCTs (1,716 patients) conducted on several continents. A total of 1,227 patients (70.9%) received IL23 p19 monoclonal antibodies (Mirikizumab, 1019 patients [59.4%]; Guselkumab, 208 patients [12.1%]) and 489 patients (28.5%) received placebo. The mean disease duration was ≥ 6 years, and the follow-up period was 12 weeks. Patients in both the intervention and placebo groups concomitantly received aminosalicylates, glucocorticoids, or immunomodulators. The results of the pooled analyses are shown in Table 1. The IL-23 p19 monoclonal antibodies group had a significantly higher probability of clinical remission (RR 1.91; 95% CI 1.46-2.49), clinical response (RR 1.88; 95% CI 1.36-2.61), endoscopic remission (RR 1.76; 95% CI 1.40-2.21) and symptomatic remission (RR 1.94; 95% CI 1.46-2.56) compared to the placebo group. Additionally, the IL-23 p19 monoclonal antibodies group presented a lower risk of serious AEs (RR 0.54; 95% CI 0.32-0.90) and discontinuation of treatment due to AEs (RR 0.24; 95% CI 0.14-0.43) than the placebo group. However, there was no significant difference between the groups in terms of overall AEs (RR 0.94; 95% CI 0.84-1.05).

Outcome	RR [95% CI]	I^2 (%)	P value
Clinical remission	1.91 [1.46, 2.49]	0	<0.00001
Clinical response	1.88 [1.36, 2.61]	69	0.0001
Endoscopy remission	1.76 [1.40, 2.21]	0	<0.00001
Symptomatic remission	1.94 [1.46, 2.56]	44	<0.00001
Serious adverse events	0.54 [0.32, 0.90]	0	0.02
Discontinuation due to adverse events	0.24 [0.14, 0.43]	0	<0.00001
Overall adverse events	0.94 [0.84, 1.05]	0	0.26

Table 1. Results from the pooled analyses.

CI, confidence interval; RR, risk ratio

Conclusion: This analysis supports the use of IL-23 p19 monoclonal antibodies as a safe and effective option for induction therapy in patients with moderate to severely active UC who had failure to conventional treatment. However, new large RCTs are required to confirm these findings.

References:

1. D'Haens G, Dubinsky M, Kobayashi T, et al. Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med*. 2023;388(26):2444-2455.
2. Peyrin-Biroulet L, Allegretti JR, Rubin DT, et al. Guselkumab in Patients With Moderately to Severely Active Ulcerative Colitis: QUASAR Phase 2b Induction Study. *Gastroenterology*. 2023 Dec;165(6):1443-1457.
3. Sandborn WJ, Ferrante M, Bhandari BR, et al. Efficacy and Safety of Mirikizumab in a Randomized Phase 2 Study of Patients With Ulcerative Colitis. *Gastroenterology*. 2020;158(3):537-549.e10.

Disclosure: Nothing to disclose.

MP679

VEDOLIZUMAB VERSUS USTEKINUMAB IN CROHN'S DISEASE WITH PRIOR ANTI-TNF FAILURE: A SYSTEMATIC REVIEW AND UPDATE META-ANALYSIS

N.J. Milioli¹, V. Antunes², T. Correa³, O. Martins⁴, A.A. Prata⁵, A.M. Reis⁶, A.C. Coan⁵, E. Bulhões⁷, P. Romeiro⁸, M.V. Fernandes²

¹Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ²Federal University of Health Science of Porto Alegre, Porto Alegre, Brazil, ³Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁴Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁵Federal University of Espírito Santo, Vitória, Brazil, ⁶State University of Campinas, Campinas, Brazil, ⁷College of Higher Education of the United Amazon, Redenção, Brazil, ⁸Department of Medicine, University Center of Maceió, Maceió, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction:

Anti-TNF plays a mean role in induction and maintenance therapy of moderate to severe Crohn's disease. However, approximately 30% of patients lose response to treatment after the first year of therapy.

Aims & Methods: This study aims to compare Vedolizumab vs Ustekinumab in the setting of anti-TNF failure. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for randomized and non-randomized studies comparing Vedolizumab vs. Ustekinumab in patients with Crohn's disease with previous anti-TNF failure or intolerance. The primary outcome was steroid-free clinical remission (SFR) at the pos-induction and maintenance period. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I^2 statistics.

Results: The meta-analyses included 10 studies and 2,514 patients. There was a significant difference favoring Ustekinumab in SFR at pos-induction period (OR 1.44; 95% CI 1.11 to 1.88, $p=0.006$; $I^2=27\%$), in SFR at the maintenance period (OR 1.74; 95% CI 1.12 to 2.70, $p=0.014$; $I^2=80\%$), in clinical remission at pos-induction period (OR 2.04; 95% CI 1.58 to 2.63, $p<0.001$; $I^2=3\%$) and in treatment discontinuation due to adverse events (OR 0.48; 95% CI 0.26 to 0.88; $p=0.018$; $I^2=0\%$).

Conclusion: In patients with Crohn's disease with prior anti-TNF failure, ustekinumab showed higher SFR during both the post induction and maintenance period and lower rate of treatment discontinuation due to adverse events.

References:

1. Alrashed F, Abdullah I, Alfadhli A, Shehab M. Effectiveness of vedolizumab and ustekinumab as second biologic agent in achieving target outcomes in tumor necrosis factor antagonists experienced patients with inflammatory bowel disease (enroll-ex study). *Front Pharmacol*. 2023;14:1243080.
2. Alric H, Amiot A, Kirchgesner J, Tréton X, Allez M, Bouhnik Y, et al. The effectiveness of either ustekinumab or vedolizumab in 239 patients with Crohn's disease refractory to anti-tumour necrosis factor. *Aliment Pharmacol Ther*. 2020 May;51(10):948-57.
3. Onali S, Pugliese D, Caprioli FA, Orlando A, Biancone L, Nardone OM, et al. An Objective Comparison of Vedolizumab and Ustekinumab Effectiveness in Crohn's Disease Patients' Failure to TNF-Alpha Inhibitors. *Am J Gastroenterol*. 2022 Aug 1;117(8):1279-87.
4. Townsend T, Razanskaite V, Michail S, Morgan J, Davies M, Storey D, et al. Comparative effectiveness of vedolizumab and ustekinumab in anti-tnf refractory Crohn's disease: Multi-centre retrospective cohort study. *Gut*. 2021;70(SUPPL 1):A127.

5. Yang H, Huang Z, Li M, Zhang H, Fu L, Wang X, et al. Comparative effectiveness of ustekinumab vs. vedolizumab for anti-TNF-naïve or anti-TNF-exposed Crohn's disease: a multicenter cohort study. *eClinicalMedicine*. 2023 Dec;66:102337.

Disclosure: Nothing to disclose.

Small molecules in the treatment of IBD

14:30-15:30 / Poster Stage 2

MP680

DELAYED RESPONSE TO OZANIMOD IN PATIENTS WITH MODERATE VS. SEVERE ENDOSCOPIC DISEASE: 4-YEAR INTERIM ANALYSIS OF THE TRUE NORTH OPEN-LABEL EXTENSION STUDY

P. Irving¹, R.K. Cross², T. Ritter³, A. Stallmach⁴, P. Hindryckx⁵, S. Chang⁶, S. Tharmarajah⁷, H. Wu⁷, M.T. Osterman⁷, A. Jain⁷, D.C. Wolf⁸

¹IBD Centre, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, ²Division of Gastroenterology and Hepatology, University of Maryland School of Medicine, Baltimore, United States of America, ³Texas Digestive Disease Consultants Research Gastroenterology, Southlake, United States of America, ⁴Jena University Hospital, Jena, Germany, ⁵Department of Gastroenterology, University Hospital Ghent, Ghent, Belgium, ⁶Division of Gastroenterology, New York University Langone Health, New York, United States of America, ⁷Bristol Myers Squibb, Princeton, United States of America, ⁸Center for Crohn's Disease & Ulcerative Colitis, Atlanta Gastroenterology Associates, Atlanta, United States of America

Contact E-Mail Address: Peter.Irving@gstt.nhs.uk

Introduction: Ozanimod (OZA) is approved for the treatment of moderately to severely active ulcerative colitis (UC). Approximately 30% of patients (pts) were clinical nonresponders after 10 wk of OZA treatment in the phase 3 True North (TN) study (NCT02435992), but ~50% of these OZA nonresponders achieved symptomatic response after 5–10 wk of additional OZA treatment during the open-label extension (OLE) study (NCT02531126).

Aims & Methods: This analysis evaluated the impact of TN baseline (BL) endoscopic disease activity on the durability of OZA response in Week (W) 10 OZA clinical nonresponders after extended induction during the OLE up to 4 years (OLE W190).

Pts were categorized by BL Mayo endoscopy subscore (MES) as moderate (MES=2) or severe (MES=3). Symptomatic, clinical, and mucosal efficacy were assessed through OLE W190 using observed case (OC) and non-responder imputation (NRI) analyses.

Results: Of the 226 W10 OZA clinical nonresponders who entered the OLE, 67 had moderate and 159 had severe endoscopic disease at BL. Pt characteristics were generally similar between groups, but more pts with severe vs moderate endoscopic activity had prior immunomodulator (52.8% vs 34.3%), anti-tumor necrosis factor (TNF; 45.9% vs 25.4%), or non-anti-TNF biologic (36.5% vs 19.4%) exposure.

Some symptomatic response was observed in OZA W10 clinical nonresponders from BL to W10/OLE entry, which was greater in pts with moderate disease and further improved with extended OZA exposure by OLE W5 (moderate: 36.9% at W10 and 66.2% by OLE W5; severe: 23.8% at W10 and 47.9% by OLE W5). Similar patterns were observed with symptomatic remission but overall rates were lower (moderate: 6.2% at W10 and 26.2% by OLE W5; severe: 1.3% at W10 and 13.0% by OLE W5).

Symptomatic response and remission rates after OLE W5 were generally similar in moderate and severe endoscopic activity groups, and rates were maintained throughout the OLE. Likewise, clinical and mucosal efficacy were durable and rates were generally similar between subgroups through OLE W190 (*Table*).

Notably, higher endoscopic improvement rates were achieved through OLE W190 in pts with BL moderate endoscopic activity despite ~50% of these pts progressing to severe by TN W10. Similar data trends were observed in the NRI analysis.

Parameters	Moderate UC (MES=2) (n=67)				Severe UC (MES=3) (n=159)			
	OLE W46	OLE W94	OLE W142	OLE W190	OLE W46	OLE W94	OLE W142	OLE W190
Clinical remission ^a % (n/N)	25.6 (10/39)	52.4 (11/21)	63.2 (12/19)	38.9 (7/18)	26.1 (23/88)	29.7 (19/64)	39.6 (21/53)	43.5 (20/46)
Clinical response ^b % (n/N)	48.7 (19/39)	71.4 (15/21)	84.2 (16/19)	61.1 (11/18)	68.6 (59/86)	74.6 (47/63)	77.4 (41/53)	78.3 (36/46)
Endoscopic improvement ^c % (n/N)	30.0 (12/40)	59.1 (13/22)	75.0 (15/20)	52.6 (10/19)	29.9 (29/97)	43.9 (29/66)	49.2 (29/59)	53.8 (28/52)
CS-free remission ^d % (n/N)	23.1 (9/39)	47.6 (10/21)	52.6 (10/19)	27.8 (5/18)	23.9 (21/88)	28.1 (18/64)	37.7 (20/53)	41.3 (19/46)
Histologic remission ^e % (n/N)	42.9 (15/35)	50.0 (10/20)	66.7 (12/18)	41.2 (7/17)	41.9 (39/93)	45.8 (27/59)	52.7 (29/55)	53.2 (25/47)
Mucosal healing ^f % (n/N)	22.9 (8/35)	45.0 (9/20)	55.6 (10/18)	41.2 (7/17)	24.7 (23/93)	35.6 (21/59)	32.7 (18/55)	42.6 (20/47)

Denominators were based on the number of pts who completed OLE W46, W94, W142, or W190 and had data available for the endpoints in question. ^aClinical remission: RBS=0, SFS ≤1 point (and a decrease of ≥1 point from BL SFS), and MES ≤1 point. ^bClinical response: decrease from BL in the 3-component Mayo score (sum of RBS, SFS, and MES) of ≥2 points and ≥35% and a reduction of ≥1 point in RBS or absolute RBS of ≤1 point. ^cEndoscopic improvement: MES ≤1 point without friability. ^dCS-free remission: clinical remission while off CS for ≥12 wk. ^eHistologic remission: Geboes score <2.0. ^fMucosal healing: MES ≤1 point and Geboes score <2.0. CS, corticosteroid; RBS, rectal bleeding subscore; SFS, stool frequency subscore.

Table. OZA clinical and mucosal efficacy rates through OLE W190 by BL endoscopic disease activity in TN W10 clinical nonresponders (OC analysis).

Conclusion: Delayed response to OZA was observed in pts who did not achieve clinical response after 10 wk of OZA therapy, regardless of BL endoscopic activity. W10 nonresponders with moderate endoscopic activity responded faster with additional OZA exposure, whereas those with severe endoscopic activity needed longer exposure to OZA to achieve similar efficacy rates that were durable with continuous OZA exposure. These results suggest that some pts may require a longer induction on OZA but ultimately maintain durable OZA response.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Traci Stuve, MA, and Julie Ko, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

PI: received lecture fees from AbbVie, Bristol Myers Squibb, Celgene, Celltrion, Dr. Falk Pharma, Ferring, Galapagos, Gilead, Janssen, MSD, Pfizer, Sandoz, Sapphire Medical, Shire, Takeda, Tillotts, and Warner Chilcott; received financial support for research from Celltrion, MSD, Pfizer, and Takeda; received advisory fees from AbbVie, Arena, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Genentech, Gilead, Hospira, Janssen, MSD, Pfizer, Pharmacosmos, Prometheus Biosciences, Roche, Samsung Bioepis, Sandoz, Takeda, TopiVert, VH2, Vifor, and Warner Chilcott.

RKC: consulted for AbbVie, Bristol Myers Squibb, Fresenius Kabi, Fzata, Janssen, Magellan Health, Option Care, Pfizer, Pharmacosmos, Samsung Bioepis, Sandoz, Sebela, and Takeda; scientific co-director of the CorEvitas Registry and executive committee member of the IBD Education Group; received financial support for research from Janssen.

TR: served on advisory boards for AbbVie, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Genentech, Intercept Health, Janssen, Merck, Pfizer, and Takeda; speaker for AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Pfizer, and Takeda.

AS: declares no competing financial or nonfinancial interests.

PH: consultant and speaker for Boston Scientific, FujiFilm, MedWork, and Viatrix.

SC: consultant for AbbVie, Bristol Myers Squibb, Janssen, and Pfizer.

ST, HW, MTO, and AJ: employees and/or shareholders of Bristol Myers Squibb.

DCW: received research funding from AbbVie, Amgen, Arena/Pfizer, Celgene/Bristol Myers Squibb, Genentech, and Janssen; lectured for AbbVie, Bristol Myers Squibb, Janssen, and Takeda; consulted for AbbVie, Arena/Pfizer, Celgene/Bristol Myers Squibb, Eli Lilly, Janssen, and Takeda.

MP681

IMPACT OF BASELINE DISEASE DURATION ON OZANIMOD EFFICACY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: A POST HOC ANALYSIS OF THE PHASE 3 TRUE NORTH STUDY

A. Hart¹, G. D'Haens², A. Walsh³, S.C. Glover⁴, D.J. Lukin⁵, B.L. Cohen⁶, G. Lawlor⁷, M. Rosen⁷, H. Wu⁷, M.T. Osterman⁷, A. Jain⁷, G.R. Lichtenstein⁸

¹St Mark's Hospital and Imperial College, London, United Kingdom,

²Amsterdam University Medical Center, Amsterdam, Netherlands,

³Oxford University Hospitals NHS Foundation Trust, Oxford,

United Kingdom, ⁴Tulane University School of Medicine, New Orleans, United States of America, ⁵Jill Roberts Center for

Inflammatory Bowel Disease, New York Presbyterian Hospital-Weill

Cornell Medicine, New York, United States of America, ⁶Cleveland

Clinic, Cleveland, United States of America, ⁷Bristol Myers Squibb,

Princeton, United States of America, ⁸Perelman Center for

Advanced Medicine, University of Pennsylvania, Philadelphia,

United States of America

Contact E-Mail Address: ailsa.hart@nhs.net

Introduction: Ozanimod (OZA) is approved for patients with moderately to severely active ulcerative colitis (UC) based on results from the pivotal phase 3 True North (TN) trial.

Aims & Methods: This analysis evaluated the impact of disease duration at TN baseline (BL) on OZA efficacy during the TN induction period (IP). In the 10-week TN IP, patients were randomized to receive in a double-blind fashion either placebo (PBO) or OZA in Cohort 1 or open-label OZA in Cohort 2. All patients in Cohort 1 of the TN IP were included in this analysis and stratified by disease duration at TN BL; subgroups included patients with <2 years, 2 to <5 years, 5 to <10 years, or ≥10 years since UC diagnosis. Symptomatic remission and response were assessed through W10 within these subgroups using PBO-adjusted difference in proportions; treatment differences and *P*-values for comparisons between OZA and PBO were based on the Cochran-Mantel-Haenszel test, stratified by corticosteroid use at screening and prior anti-tumor necrosis factor (TNF) use.

Clinical response and clinical remission at W10 were also analyzed. A step-wise logistic regression model was used to adjust for potential BL patient characteristic confounders.

Results: A total of 645 patients were included in Cohort 1 of the TN IP (PBO, N=216; OZA, N=429). At TN BL, 158 patients had a disease duration of <2 years (PBO, n=55; OZA, n=103), 178 had 2 to <5 years (PBO, n=64; OZA, n=114), 163 had 5 to <10 years (PBO, n=52; OZA, n=111), and 146 had ≥10 years (PBO, n=45; OZA, n=101). BL patient characteristics were generally similar in all subgroups of the OZA and PBO treatment arms.

As expected, more patients with longer disease duration had prior exposure to biologic therapies. In Cohort 1, prior anti-TNF use and prior biologic use, except anti-TNF, was reported in 5.1% and 3.2% of patients, respectively, in the <2 years duration group, 32.6% and 19.7% in the 2 to <5 years group, 38.7% and 27.6% in the 5 to <10 years group, and 43.8% and 26.7% in the ≥10 years group.

Patients with disease duration <2 years achieved greater symptomatic clinical response by W4 (*P*<0.001) compared to other subgroups, but differences were similar across other subgroups by W10; symptomatic remission rates were also generally similar across subgroups by W10. The proportions of patients achieving clinical remission and clinical response

after 10 weeks of OZA treatment were comparable, regardless of TN BL disease duration (Table). Finally, a logistic regression model demonstrated that BL disease duration did not affect OZA efficacy.

Clinical efficacy	<2 years			2 to <5 years			5 to <10 years			≥10 years		
	PBO (n=55)	OZA (n=103)	Nominal P-value	PBO (n=64)	OZA (n=114)	Nominal P-value	PBO (n=52)	OZA (n=111)	Nominal P-value	PBO (n=45)	OZA (n=101)	Nominal P-value
Clinical remission, ^a % (n)	3.6 (2)	20.4 (21)	0.005	6.3 (4)	16.7 (19)	0.08	3.8 (2)	17.1 (19)	0.016	11.1 (5)	19.8 (20)	0.139
Clinical response, ^b % (n)	21.8 (12)	47.6 (49)	0.002	21.9 (14)	46.5 (53)	0.001	28.8 (15)	45.0 (50)	0.033	33.3 (15)	52.5 (53)	0.025

^aClinical remission: RBS = 0, SFS ≤1 point (and a decrease of ≥1 point from BL SFS), and MES ≤1 point. ^bClinical response: decrease from BL in the 3-component Mayo score (sum of RBS, SFS, and MES) of ≥2 points and ≥35% and a reduction of ≥1 point in RBS or absolute RBS of ≤1 point.
MES, Mayo endoscopy subscore; RBS, rectal bleeding subscore; SFS, stool frequency subscore.

Table. Clinical efficacy at W10 in all patients in Cohort 1 of the TN IP by BL disease duration.

Conclusion: OZA efficacy at the end of induction was not affected by duration of disease in patients with UC. These results suggest that OZA is an optimal oral therapeutic option for newly diagnosed patients and for those with long-standing UC disease.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb, Princeton, NJ, USA. Professional medical writing assistance was provided by Anny Wu, PharmD, and Julie Ko, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

AH: consultant, advisory board member, or speaker for AbbVie, Atlantic, Bristol Myers Squibb, Celltrion, Dr. Falk Pharma, Ferring, Janssen, MSD, Napp Pharmaceuticals, Pfizer, Pharmacosmos, Shire, and Takeda; served on the Global Steering Committee for Genentech.

GD: served as an advisor for AbbVie, Agomab Therapeutics, Alimientiv, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Exelium Biosciences, Ferring, Galapagos, GlaxoSmithKline, Immunic, Johnson & Johnson, Pfizer, Polpharma, ProCiseDx, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Seres, Takeda, Tillotts, and Ventyx; received speaker fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Galapagos, Johnson & Johnson, Pfizer, Takeda, and Tillotts.

AW: received research grants or consulting fees from AbbVie, Bühlmann Laboratories, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Pfizer, Takeda, and Vifor.

SCG: declared no competing interests.

DJL: received consulting fees from AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Fresenius Kabi, Janssen, Magellan Health, Palatin Technologies, Pfizer, Prometheus Laboratories, PSI, and Takeda; received research funding from AbbVie, Boehringer Ingelheim, Janssen, and Takeda; served on speaker bureaus for AbbVie and Janssen.

BLC: received consultancy or speaker fees from AbbVie, Emmes, Janssen, Takeda, and Target RWE; received support and/or funding from AbbVie, Bristol Myers Squibb, Celgene, Janssen, and Pfizer.

GL, MR, HW, MTO, and AJ: employees and/or shareholders of Bristol Myers Squibb.

GRL: received research support and/or funding from Celgene, Janssen, Ortho Biotech, Pfizer, Shire, Takeda, and UCB; received consultancy fees from AbbVie, American Regent, Cellceptix, Celgene, Eli Lilly, Endo, Ferring, Gilead, Janssen, Merck, Morphic Therapeutic, Ortho Biotech, Pfizer, Prometheus Laboratories, Romark, Salix/Valeant, Shire, Takeda, and UCB; received honoraria from American College of Gastroenterology, American Regent, Gastroenterology & Hepatology journal, Merck, Romark, Springer Science and Business Media, and UpToDate; received royalties from Professional Communications Inc. and SLACK Inc.

MP682

OZANIMOD IN ROUTINE CLINICAL CARE OF ULCERATIVE COLITIS: AN INTERIM ANALYSIS OF THE MULTICENTRE, PROSPECTIVE, NONINTERVENTIONAL STUDY COLIBRI (NIS COLIBRI) EVALUATING EFFECTIVENESS AND SAFETY IN GERMANY

S. Zeißig¹, J. Stein², P. Effen³, U. Helwig⁴, T. Hellms⁵, E. Jörgensen⁶, J.R. Müller⁷, J. Müller-Ziehm⁸, A.-M. Pöhler⁹, M. Makki⁹, G. Emanuel¹⁰, S. Schubert¹¹

¹University Medical Center Dresden, Dresden, Germany, ²CED Studien UG, Frankfurt, Germany, ³Gastroenterologische Gemeinschaftspraxis Minden, Minden, Germany, ⁴Internistische Praxengemeinschaft Oldenburg, Oldenburg, Germany, ⁵Hannover Medical School, Hannover, Germany, ⁶Magen-Darm-Zentrum Remscheid, Remscheid, Germany, ⁷Gastroenterologische Praxis Heil und Müller, Andernach, Germany, ⁸Gastroenterologische Schwerpunktpraxis, Hannover, Germany, ⁹Bristol Myers Squibb GmbH & Co KGaA, München, Germany, ¹⁰Bristol Myers Squibb, Uxbridge, United Kingdom, ¹¹VZ für Gastroenterologie am Bayerischen Platz, Berlin, Germany

Contact E-Mail Address: sebastian.zeissig1@tu-dresden.de

Introduction: Real-world data are needed to confirm clinical trial results and determine treatment effects in a more diverse population. The NIS COLIBRI (NCT05382715) assesses the use, effectiveness, and safety of ozanimod (OZA) and quality of life in patients (pts) with moderate-to-severe (MOD/SEV) active ulcerative colitis (UC) in routine clinical practice in Germany. This interim analysis (IA) reports baseline (BL) characteristics, safety information, and effectiveness of OZA until Week (W) 10.

Aims & Methods: Up to 380 adults with UC eligible for OZA treatment will be enrolled and observed over 52 or 104 weeks with visits and diagnostic and therapeutic measures corresponding to routine practices of the respective sites. In this IA, the partial Mayo score (pMS; sum of stool frequency subscore [SFS], rectal bleeding subscore [RBS], and Physician Global Assessment subscore [PGA]), RBS, SFS, and clinical response (defined as reduction by ≥ 2 points in pMS + a reduction of ≥ 35% in pMS & RBS reduction of ≥ 1 point or an absolute RBS of ≤1 or pMS of ≤1 + RBS=0) were assessed at W4 and W10. Data are collected by electronic case report forms and the study-specific interface of the MyTARGET app (Kiel, Germany) for pt-reported outcomes, which are evaluated throughout the study.

Pt characteristics		Pts enrolled in COLIBRI (N=109)
Montreal Classification	E1 - Ulcerative proctitis	6 (5.5)
	E2 - Left sided UC (distal UC)	51 (46.8)
Extensivity, n (%)	E3 - Extensive UC (pancolitis)	52 (47.7)
Years since UC diagnosis, ^a y, mean (SD)		11.4 (8.9)
Prior use of ≥1 ATs (biologics & small molecules), ^b n (%)		87 (83.7)
pMS category, ^c n (%)	Remission	6 (5.7)
	Mild	30 (28.3)
	Moderate	37 (34.9)
	Severe	31 (29.3)
SFS category, ^d n (%)	Normal	12 (11.3)
	1–2 stools more than normal	18 (17.0)
	3–4 stools more than normal	31 (29.3)
	≥5 stools more than normal	45 (42.5)
RBS category, ^d n (%)	No blood	39 (36.8)
	Streaks of blood with stool less than half the time	29 (27.4)
	Obvious blood with stool most of the time	22 (20.8)
	Blood alone passed	16 (15.1)

Table. BL demographics, clinical characteristics, and disease activity of pts enrolled in COLIBRI as of 4 January 2024

^aN=100 as 6 pts were missing data and 3pts were excluded due to limited window for BL. ^bN=104 as 5 pts were missing data. ^cpMS: Sum of SFS, RBS, and PGA subscore. N=104 as 2 pts had missing pMS data and 3pts were excluded due to limited window for BL. ^dN=106 due to 3pts were excluded due to limited window for BL.

Results: Of 109 pts included in the IA, the median (interquartile range) age of pts was 41 (29.0–53.0) years, 55 (50.5%) were female, 51.4% had prior exposure to ≥ 3 advanced therapies (ATs). Additional BL pt and clinical characteristics are shown in the *Table*.

104 pts had pMS data at BL, 79 pts at W4 and 54 pts at W10. Mean [SD] pMS decreased from BL (5.2 [2.1]) to 4.0 [2.5] at W4 (mean change from BL (CBL): -1.31 [2.2]) and to 3.48 [2.2] at W10 (CBL: -1.69 [2.3]). All mean [SD] disease activity subscores showed a numerical improvement from BL to W4 and W10: SFS at BL (2.0 [1.0]), W4 (1.6 [1.2; CBL: -0.48 [1.2]), and W10 (1.45 [1.1]; CBL: -0.51 [1.0]); RBS at BL (1.1 [1.1]), W4 (0.74 [1.0]; CBL: -0.38 [0.9]), and W10 (0.58 [0.9]; -0.55 [1.0]). Clinical response was achieved in 36.3% (29/80) of pts at W4 and 42.9% (24/56) at W10. The most common reasons for dropping out were adverse events (AEs) (n=14; 13.2%), insufficient effectiveness (n=10; 9.4%) and patient request (n=4; 3.8%). The most frequently reported AEs (non-UC associated; $\geq 1.5\%$, n, %) were lymphopenia (n=2, 1.8%), headache (n=2, 1.8%), and rash (n=3, 2.8%).

Conclusion: This first IA of the German COLIBRI study showed that highly refractory pts with MOD/SEV UC on OZA achieved clinical response and improvement in disease activity subscores at W4 and W10, indicating that OZA is effective in real-world clinical practice.

Disclosure: SZ: consulted for AbbVie Deutschland GmbH, Amgen GmbH, Biogen GmbH, Bristol Myers Squibb GmbH, Celgene GmbH, Celltrion, Ferring Arzneimittel GmbH, Galapagos Biopharma Germany GmbH, Hogg Robinson GmbH, Janssen Pharmaceutica NV, Janssen Cilag GmbH, MICE Service GmbH, Mylan, Pfizer Pharma GmbH, and Takeda Pharma GmbH; speaker for AbbVie Deutschland GmbH, Amgen GmbH, Biogen GmbH, Bristol Myers Squibb GmbH, CED Service GmbH, Falk Foundation, Ferring Arzneimittel GmbH, FORGA Solutions GmbH, GWT-TUD GmbH, Janssen Cilag GmbH, Janssen Pharmaceutica NV, Merck Sharp & Dohme, Pfizer Pharma GmbH, Pharma-Zentrale GmbH, Roche, Takeda Pharma GmbH, and WebMD Global.

JSt: received consultancy fees from AbbVie, Fresenius Kabi, GI Dynamics, Immundiagnostik, MSD, Pharmacosmos, Takeda, and Vifor; received payment for lectures from AbbVie, Falk Foundation, Ferring, GI Dynamics, Immundiagnostik, MSD, Pharmacosmos, Takeda, ThermoFisher, and Vifor; received payment for manuscript preparation from AbbVie, Falk Foundation, and MSD.

PE: consulted for AbbVie, Galapagos, and Janssen.

UH: received lecture and/or consulting fees from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Falk Foundation, Ferring, Janssen, MSD, Mundipharma, Mylan Pharma, Pfizer, Sandoz, Shield Therapeutics, Takeda, and Vifor.

TH: consulted for and received speaker fees from Bristol Myers Squibb GmbH and Galapagos Biopharma Germany GmbH, and Pfizer Pharma GmbH.

EJ: conducted research studies for, served as an advisor for, or received travel grants from AbbVie, Arena, AstraZeneca, Bausch Health, Galapagos, Janssen, Pfizer, SymBio Pharma, and Takeda.

JRM: nothing to declare.

JMZ: Received lecture and/or consulting fees or speaker from AbbVie, Bristol Myers Squibb GmbH, Ferring Arzneimittel GmbH, Galapagos Biopharma Germany GmbH, Janssen Cilag GmbH, Mylan, Pfizer Pharma GmbH, Takeda Pharma GmbH, and Falk Foundation.

AMP, MM, and GE: employees and/or shareholders of Bristol Myers Squibb. SS: consulted for AbbVie Deutschland GmbH, Bristol Myers Squibb GmbH, Celltrion, Galapagos Biopharma Germany GmbH, Janssen Pharmaceutica NV, Pfizer Pharma GmbH, and Takeda Pharma GmbH; speaker for AbbVie Deutschland GmbH, Amgen GmbH, Bristol Myers Squibb GmbH, CED Service GmbH, Falk Foundation, Galapagos Biopharma Germany GmbH, Janssen Cilag GmbH, Lilly Pharma Germany, Pfizer Pharma GmbH, and Takeda Pharma GmbH.

MP683

IMPACT OF OZANIMOD ON TYPE III COLLAGEN TURNOVER BIOMARKERS AND THE ASSOCIATION WITH OZANIMOD EFFICACY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 TRUE NORTH STUDY

G. D'Haens¹, R. Maddux², C. Wu², Y. Hu², B.E. Sands³, J.H. Mortensen⁴, J. Zhang², A. Petersen², S. Harris²

¹Amsterdam University Medical Center, Amsterdam, Netherlands,

²Bristol Myers Squibb, Princeton, United States of America, ³Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁴Nordic Bioscience, Herlev, Denmark

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Ozanimod, an oral sphingosine 1-phosphate 1 and 5 receptor modulator, was efficacious and well tolerated for up to 52 weeks in adults with moderately to severely active ulcerative colitis (UC) in the phase 3 True North study (NCT02435992).

Alterations in the degradation and formation of type III collagens, a major component of the extracellular matrix of the intestinal wall, may play a role in the pathogenesis of UC.

Aims & Methods: The objective of this analysis was to assess the effect of ozanimod on type III collagen levels and turnover and the association of type III collagen levels and turnover with ozanimod efficacy in the True North study. In a 10-week induction period, patients in Cohort 1 were randomized to receive oral ozanimod 0.92 mg (n=429) or placebo once daily (n=216) in a double-blind manner and patients in Cohort 2 received open-label ozanimod at the same daily dose (n=367). At Week 10, patients with a clinical response to ozanimod in either cohort underwent rerandomization to receive double-blind ozanimod (n=230) or placebo (n=227) for 52 weeks (maintenance period). Type III collagen biomarker plasma levels were assessed at baseline, Week 10, and Week 52. Associations between type III collagen biomarker levels and disease activity or efficacy outcomes were assessed using Spearman's *rho* correlation and logistic regression, respectively.

Results: At Week 10, treatment with ozanimod resulted in significantly decreased type III collagen degradation (C3M), increased type III collagen formation (PRO-C3), and decreased type III collagen turnover (C3M/PRO-C3) vs placebo (*Table*).

	Induction (Week 10)			Maintenance (Week 52)	
	Placebo: Cohort 1	Ozanimod: Cohort 1	Ozanimod: Cohort 2	Ozanimod/ placebo	Ozanimod/ ozanimod
C3M	-0.3 (-4.2, 3.8) n=165	-10.6*** (-13.1, -8.0) n=346	-11.5*** (-14.1, -8.9) n=298	-16.4 (-20.1, -12.5) n=112	-20.8 (-23.8, -17.6) n=157
PRO-C3	-2.1 (-5.9, 1.8) n=164	5.0** (2.1, 7.9) n=343	8.4*** (5.3, 11.6) n=293	-1.1 (-6.1, 4.1) n=108	8.9** (4.2, 13.8) n=155
C3M/PRO-C3	1.5 (-4.1, 7.5) n=163	-14.6*** (-18.0, -11.1) n=343	-17.7*** (-21.1, -14.1) n=292	-14.8 (-20.3, -8.9) n=108	-27.3*** (-31.4, -23.1) n=155

** $P < 0.01$, *** $P < 0.001$ vs placebo: Cohort 1 for induction or ozanimod/placebo for maintenance.

Table. Adjusted mean percent change from baseline in type III collagen biomarker levels (95% CI).

Significant reductions in C3M and C3M/PRO-C3 were observed in patients with vs without a clinical response in all treatment groups ($P < 0.001$), while significant increases in PRO-C3 were observed in responders vs nonresponders ($P < 0.001$; Cohort 1 only). The significantly greater reductions in C3M/PRO-C3 were observed with ozanimod vs placebo regardless of prior exposure to biologics or tumor necrosis factor inhibitors. Changes in C3M, PRO-C3, and C3M/PRO-C3 levels from baseline to Week 10 were significantly correlated with improvements in all disease activity scores from baseline to Week 10 with ozanimod and placebo.

These changes in C3M, PRO-C3, and C3M/PRO-C3 continued through Week 52 (Table) in patients who continued ozanimod. At Week 52, significantly greater reductions in C3M/PRO-C3 ratios were observed in responders vs nonresponders in patients who continued ozanimod.

Conclusion: These data show that patients with UC who were treated with ozanimod had decreased plasma type III collagen degradation and turnover, with greater reductions in ozanimod responders than nonresponders. This further supports the evaluation of type III collagen fragments as potential markers of treatment response in patients with UC.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Traci Stuve, MA, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

GD: served as an advisor for AbbVie, Agomab Therapeutics, Alimentiv, Applied Molecular Therapeutics, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Cytoki, Eli Lilly, Exeliom Biosciences, Ferring, Galapagos, GlaxoSmithKline, Gossamer Bio, Immunic, Johnson & Johnson, Pfizer, Polpharma, ProciseDx, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Seres, Takeda, Tillotts, and Versant; received speaker fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Galapagos, Johnson & Johnson, Pfizer, Takeda, and Tillotts.

RM, CW, YH, JZ, AP, and SH: employees and/or shareholders of Bristol Myers Squibb.

BES: received speaker fees from and consulted for Abivax, Bristol Myers Squibb, Eli Lilly, Janssen, Pfizer, and Takeda; received consulting fees from AbbVie, Adiso Therapeutics, Alimentiv, Amgen, Arena, Artizan Biosciences, Artugen, AstraZeneca, Bacinn Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celltrion, ClostraBio, Cytoki Pharma, Connect Biopharma, Entera, Evommune, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Therapeutics, Inotrem, Ironwood Pharmaceuticals, Kaleido Biosciences, Kallyope, MiroBio, Morphic Therapeutics, MRM Health, OSE Immunotherapeutics, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma, Surrozen, Synlogic, Target RWE, Teva, Theravance, TLL Pharmaceutical, USWM Enterprises, Viela Bio, and VTA Labs; received personal fees and stock options for consulting from Thelium Therapeutics and Ventyx.

JHM: employed at Nordic Bioscience A/S, a company involved in the discovery and development of biochemical biomarkers.

MP684

EFFICACY AND SAFETY OF 5 YEARS OF CONTINUOUS OZANIMOD TREATMENT: AN INTERIM ANALYSIS OF THE TRUE NORTH OPEN-LABEL EXTENSION STUDY

J.O. Lindsay¹, S. Danese², D.C. Wolf³, K. Matsuoka⁴, I. Dotan⁵, B.S. Boland⁶, L.E. Raffals⁷, D. Mehra⁸, N.R. Santiago⁸, A. Petersen⁸, M. Desai⁸, H. Wu⁸, D. Wang⁹, M.T. Osterman⁸, A. Jain⁸, R.K. Cross¹⁰

¹Barts and the London School of Medicine and Dentistry, London, United Kingdom, ²Department of Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milan, Italy, ³Center for Crohn's Disease & Ulcerative Colitis, Atlanta Gastroenterology Associates, Atlanta, United States of America, ⁴Toho University Sakura Medical Center, Sakura, Chiba, China, ⁵The Division of Gastroenterology, Rabin Medical Center, Petah-Tikva, Israel; Faculty of Medical and Health Sciences, Tel-Aviv University, Tel Aviv, Israel, ⁶Department of Medicine, University of California San Diego, La Jolla, United States of America, ⁷Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, United States of America, ⁸Bristol Myers Squibb, Princeton, United States of America, ⁹Bristol Myers Squibb K. K., Tokyo, Japan, ¹⁰Division of Gastroenterology and Hepatology, University of Maryland School of Medicine, Baltimore, United States of America

Contact E-Mail Address: James.Lindsay@bartshealth.nhs.uk

Introduction: Ozanimod (OZA) was efficacious and well tolerated over 52 wk in pts with moderately to severely active ulcerative colitis (UC) in the phase 3 True North (TN) study (NCT02435992). Previous interim analyses of the ongoing TN open-label extension (OLE; NCT02531126) through OLE Week (W) 142 demonstrated long-term efficacy and safety of ~4 y of continuous OZA treatment.

Aims & Methods: The efficacy and safety of OZA were assessed for an additional year in pts who completed OLE W190 (~5 y of continuous OZA) or discontinued the OLE by data cutoff (January 10, 2024). Clinical responders after 52 wk of continuous OZA treatment (0.92 mg/d) who subsequently entered the OLE were included. Symptomatic response and symptomatic remission were evaluated from OLE W5 through OLE W190. Clinical remission, clinical response, endoscopic improvement, and corticosteroid (CS)-free remission were evaluated at OLE W46, W94, W142, and W190. Treatment-emergent adverse events (TEAEs) were monitored during TN and the OLE through data cutoff. Laboratory abnormalities, including absolute lymphocyte count (ALC) reductions, were repeatedly assessed during the OLE through data cutoff.

Results: In all, 131 W52 clinical responders entered the OLE. At data cutoff, 75/131 pts (57.3%) had completed OLE W190; the most common reasons for discontinuation up to OLE W190 included withdrawal by pt (19/131 pts, 14.5%) and lack of efficacy (15/131 pts, 11.5%). Symptomatic response was maintained in the OLE, with 76/77 pts (98.7%) and 62/63 pts (98.4%) achieving the endpoint at OLE W142 and OLE W190, respectively, in the observed case (OC) analysis (76/131 pts [58.0%] and 62/131 pts [47.3%], respectively, in the nonresponder imputation [NRI] analysis). Similar patterns were observed for symptomatic remission, with 68/77 pts (88.3%) and 54/63 pts (85.7%) achieving the endpoint at OLE W142 and OLE W190, respectively, in the OC analysis (68/131 pts [51.9%] and 54/131 pts [41.2%], respectively, in the NRI analysis). Clinical remission, clinical response, endoscopic improvement, and CS-free remission were also maintained over an additional year in the OLE (Table). There were no new cases of bradycardia, third-degree atrioventricular block, infection (including serious infection and herpes zoster), macular edema, or malignancy, and no new discontinuations due to TEAEs with an additional year

in the OLE. ALC <200 cells/μl was observed in 8/131 pts (6.1%); however, none of these pts developed serious or opportunistic infections during the OLE. No serious hepatic events occurred.

		OLE W142	OLE W190
Clinical remission, ^a	OC	65.3 (47/72)	69.5 (41/59)
% (n/N)	NRI	35.9 (47/131)	31.3 (41/131)
Clinical response, ^b	OC	97.2 (70/72)	94.9 (56/59)
% (n/N)	NRI	53.4 (70/131)	42.7 (56/131)
Endoscopic improvement, ^c	OC	72.0 (54/75)	80.0 (56/70)
% (n/N)	NRI	41.2 (54/131)	42.7 (56/131)
CS-free remission, ^d	OC	65.3 (47/72)	69.5 (41/59)
% (n/N)	NRI	35.9 (47/131)	31.3 (41/131)

^aRBS=0, SFS ≤1 (and ≥1-point decrease from baseline SFS), and MES ≤1. ^b≥2-point and ≥35% decrease from baseline in the 3-component Mayo score (sum of RBS, SFS, and MES) and ≥1-point decrease in RBS or absolute RBS of ≤1. ^cMES ≤1. ^dClinical remission while off CS for ≥12 wk.

MES, Mayo endoscopy subscore; RBS, rectal bleeding subscore; SFS, stool frequency subscore.

Table. OZA efficacy at TN OLE W142 and W190 (194 and 242 wk of continuous treatment, respectively).

Conclusion: OZA efficacy was sustained for a total of ~5 y of continuous treatment in TN and the OLE. No new safety concerns were observed. These findings suggest that OZA is a durable, safe, and tolerable therapy for pts with UC for up to 5 y.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Traci Stuve, MA, and Alexandra Stafford, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

JOL: received consulting and/or speaker fees from AbbVie, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Engitix, Ferring, Galapagos, Gilead, GlaxoSmithKline, Janssen, MSD, Napp, Orchard Therapeutics, Pfizer, Shire, and Takeda; received investigator-led research grants from AbbVie, Gilead, and Takeda.

SD: received honoraria as a speaker, consultant, and/or advisory board member from AbbVie, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB, and Vifor.

DCW: received honoraria as a speaker, consultant, and/or advisory board member from AbbVie, Arena, Celgene/Bristol Myers Squibb, Janssen, Pfizer, and Takeda.

KM: received speaker fees from AbbVie, EA Pharma, Eli Lilly, Gilead, Janssen, Kissei, Mitsubishi Tanabe, Mochida, Pfizer, and Takeda; received research grants from AbbVie, JIMRO, Mochida, Nippon Kayaku, and Zeria.

ID: served as a speaker, consultant, and advisory board member for AbbVie, Altman, Athos, Celltrion, Celgene/Bristol Myers Squibb, Eli Lilly, Ferring, Gilead, Galapagos, Iterative Scopes, Janssen, Pfizer, Roche/Genentech, Sangamo, Sublimity, Sandoz, Takeda, and Prometheus; shareholder of Gutreat and Harp Diagnostics.

BSB: consultant for Bristol Myers Squibb and Pfizer; received grant support from Merck and Gilead.

LER: consultant and/or advisory board member for Bristol Myers Squibb, Fresenius Kabi USA, Geneoscopy, Janssen, Roivant Sciences, and Takeda. DM, NRS, AP, MD, HW, DW, MTO, and AJ: employees and/or shareholders of Bristol Myers Squibb

RKC: consulted for AbbVie, Adiso, Bristol Myers Squibb, Fresenius Kabi, Fzata, Janssen, Magellan Health, Option Care Health, Pfizer, Pharmacosmos, Samsung Bioepis, Sandoz, Sebel, and Takeda; received grant support from Janssen; scientific co-director of the CorEvitas Registry; executive committee member of the IBD Education Group.

MP685

SIMILAR EFFICACY OF MESALAZINE (ASACOL) AND OZANIMOD (ZEPOSIA) FOLLOWING INDUCTION TREATMENT IN 5-ASA-EXPOSED ADVANCED THERAPY-NAÏVE ULCERATIVE COLITIS PATIENTS

E. Safroneeva^{1,2}, H. Wüthrich¹, R. Laoun¹

¹Tillotts Pharma AG, Medical Affairs, Rheinfelden, Switzerland,

²Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

Contact E-Mail Address: raphaellaoun@yahoo.fr

Introduction: Ozanimod, a sphingosine-1-phosphate receptor modulator approved for the treatment of adults with moderately-to-severe ulcerative colitis (UC), ameliorates local inflammation, most likely, by reducing lymphocyte homing to the colon.¹ Mesalazine acts locally in colonic mucosa and reduces inflammation through numerous anti-inflammatory, not entirely understood, processes.² We compared the efficacy of oral Mesalazine (Asacol) and Ozanimod, without concomitant corticosteroids, following induction treatment in 5-ASA-exposed, advanced therapy-naïve, immunomodulator-naïve UC patients.

Aims & Methods: This was a *post-hoc* analysis of True North (10-wk induction study with 1 mg/day Ozanimod [n=1012]) and an 8-wk non-inferiority induction study with 3.2 g/day Mesalazine (n=817) in UC patients.^{3,4} Endpoints from the non-inferiority study were calculated using the definitions from the True North study: 1) clinical response defined as reduction from baseline in the 3-component modified Mayo score (sum of rectal bleeding subscore (RBS), stool frequency subscore (SFS), and Mayo endoscopic score (MES) ≥2 points and ≥35%, and a reduction from baseline in RBS ≥1 point or an absolute RBS ≤1; 2) clinical remission defined as RBS =0, SFS ≤1 (and decrease of ≥1 point from baseline SFS), and MES ≤1; and 3) endoscopic improvement defined as MES ≤1 without friability. Cochran's Q test was used to assess the consistency of proportions across the studies.

Results: Similar baseline characteristics were observed between the Mesalazine and Ozanimod populations (Table 1).

	Total (n=538)	Mesalazine Moderate UC (n=388)	Severe UC (n=150)	Total (n=281)	Ozanimod Moderate UC (n=150)	Severe UC (n=131)
Age, mean (SD)	44 (15)	43 (14)	48 (15)	44 (13.5)	44 (13.4)	44 (13.7)
Male, n (%)	313 (58%)	223 (57%)	90 (60%)	156 (56%)	79 (53%)	77 (59%)
Years since UC diagnosis, mean (SD)	6.3 (7.2)	5.8 (7.0)	7.5 (7.5)	5.5 (6.7)	5.5 (6.7)	5.5 (6.6)
Extensive UC, n (%)	85 (16%)	61 (16%)	24 (16%)	76 (27%)	36 (24%)	40 (31%)
Prior corticosteroid use, n (%)	45 (8%)	32 (8%)	13 (9%)	125 (44%)	74 (49%)	51 (39%)
Total Mayo score, mean (SD)	7.6 (1.3)	7.2 (1.2)	8.7 (1.1)	8.6 (1.1)	7.8 (1.2)	9.6 (1.1)
Partial Mayo score, mean (SD)	5.4 (1.2)	5.2 (1.2)	5.7 (1.1)	6.2 (1.1)	5.8 (1.2)	6.6 (1.1)
Modified Mayo score, mean (SD)	5.8 (1.2)	5.4 (1.0)	6.7 (1.0)	6.4 (1.0)	5.8 (1.1)	7.2 (0.9)
Faecal calprotectin in mg/g, mean (SD)	1032 (1471)	936 (1401)	1285 (1622)	2211 (4606)	1946 (4325)	2515 (4906)

Table 1. Baseline Characteristics.

Mesalazine-treated subjects had numerically lower total Mayo score, lower prior use of corticosteroids and less extensive disease but longer disease duration compared to Ozanimod-treated subjects.

Post-induction, no differences in efficacy were observed in overall population; clinical response was 59% and 58% in Mesalazine and Ozanimod group, respectively (p=0.837). Clinical remission was 24% and 28% in Mesalazine and Ozanimod group, respectively (p=0.168). MES ≤1 was observed in 35% and 38% of Mesalazine and Ozanimod-treated subjects, respectively (p=0.434).

In subjects with MES=2 at baseline, there were no differences in both clinical response (61% and 67% in Mesalazine and Ozanimod group, respectively; $p=0.189$) and MES ≤ 1 (43% and 51% in Mesalazine and Ozanimod group, respectively; $p=0.066$) rates. However, clinical remission rates were lower in Mesalazine (29%) compared to Ozanimod-treated (39%) subjects ($p=0.027$).

In subjects with MES=3 at baseline, clinical response was 53% and 48% in Mesalazine and Ozanimod group, respectively ($p=0.380$), clinical remission was 11% and 16% in Mesalazine and Ozanimod group, respectively ($p=0.188$), and MES ≤ 1 was observed in 15% and 22% in Mesalazine and Ozanimod group, respectively ($p=0.145$).

Conclusion: Similar efficacy was observed between Mesalazine and Ozanimod in moderate to severe UC, most likely due to impact of these drugs on reducing local inflammation. This highlights the importance of considering dose optimisation of mesalazine before escalating to other agents.

References:

1. Sands BE, Schreiber S, Blumenstein I, et al. Clinician's Guide to Using Ozanimod for the Treatment of Ulcerative Colitis. *J Crohns Colitis*. 2023;17:2012-2025.
2. Lacucci M, de Silva S, Ghosh S. Mesalazine in inflammatory bowel disease: a trendy topic once again? *Can J Gastroenterol*. 2010;24:127-33.
3. Sandborn WJ, Feagan BG, D'Haens G, et al. Ozanimod as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med*. 2021;385:1280-1291.
4. D'Haens GR, Sandborn WJ, Zou G, et al. Randomised non-inferiority trial: 1600 mg versus 400 mg tablets of mesalazine for the treatment of mild-to-moderate ulcerative colitis. *Aliment Pharmacol Ther*. 2017;46:292-302.

Disclosure: ES, HW and RL are employees of Tillotts Pharma AG.

MP686

EFFICACY AND SAFETY PROFILE OF ETASIMOD WAS NOT IMPACTED BY BASELINE DISEASE ACTIVITY: A POST HOC ANALYSIS OF THE ELEVATE UC PROGRAMME

B.E. Sands¹, M.C. Dubinsky², P.G. Kotze³, S. Vermeire⁴, R. Panaccione⁵, M. Long⁶, J.C. Woolcott⁷, J. Wu⁸, A. McDonnell⁹, M. Goetsch¹⁰, E. Bananis⁷, A.J Yauru¹¹

¹Icahn School of Medicine at Mount Sinai, Dr. Henry D.

Janowitz Division of Gastroenterology, New York, United States

of America, ²Icahn School of Medicine at Mount Sinai, Susan

and Leonard Feinstein IBD Center, New York City, United

States of America, ³Pontifícia Universidade Católica do Paraná

(PUCPR), IBD Outpatient Clinics, Colorectal Surgery Unit,

Curitiba, Brazil, ⁴University Hospitals Leuven, Department of

Gastroenterology and Hepatology, Leuven, Belgium,

⁵University of Calgary, Division of Gastroenterology and

Hepatology, Department of Medicine, Calgary, Canada,

⁶University of North Carolina, Center for Gastrointestinal

Biology and Disease, Chapel Hill, United States of America,

⁷Pfizer Inc, Collegeville, United States of America, ⁸Pfizer Inc,

Cambridge, United States of America, ⁹Pfizer Ltd, Sandwich,

United Kingdom, ¹⁰Pfizer AG, Zürich, Switzerland, ¹¹Cedars-Sinai

Medical Center, Inflammatory Bowel Disease Center and Division

of Gastroenterology and Hepatology, Los Angeles, United

States of America

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: Etasimod is an oral, once-daily, selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC).

Aims & Methods: This post hoc analysis of ELEVATE UC 52 and ELEVATE UC 12 describes etasimod efficacy and safety in patients stratified according to baseline disease activity. In ELEVATE UC 52 (NCT03945188) and ELEVATE UC 12 (NCT03996369), patients aged 16–80 years with moderately to severely active UC were randomised 2:1 to etasimod 2 mg once daily or placebo.¹ ELEVATE UC 52 had a treat-through design comprising a 12-week (wk) induction period followed by a 40-wk maintenance period. ELEVATE UC 12 comprised a 12-wk induction period. In this analysis, data were pooled from both trials and patients' baseline UC activity was stratified as moderately or severely active based on a Modified Mayo score (MMS) of 5–7 or 8–9, respectively. Efficacy endpoints were measured at Wk 12 and included mean percentage change from baseline in MMS and clinical response/remission according to MMS category. Efficacy data were analysed descriptively, and 95% confidence intervals (CIs) were calculated for all means or proportions using normal approximation or simultaneous estimation method, respectively. Safety was assessed up to Wk 52 in the pooled safety analysis set.

Results: Of the 743 patients in this analysis, 525 (70.7%) had a baseline MMS 5–7 and 218 (29.3%) had a baseline MMS 8–9. Baseline characteristics were broadly similar between subgroups, with the exception of lower rates of proctitis in patients with MMS 8–9 vs 5–7 (3.3% and 3.0% vs 9.3% and 9.4% in etasimod and placebo groups, respectively). At Wk 12, patients treated with etasimod showed larger mean percentage reductions (95% CI) in MMS, vs placebo, regardless of baseline disease activity (48.4% [52.3, 44.4] vs 27.0% [32.2, 21.7] for baseline MMS 5–7, and 46.4% [51.2, 41.5] vs 29.8% [37.2, 22.3] for baseline MMS 8–9). At Wk 12, more patients treated with etasimod achieved clinical response, vs placebo, regardless of baseline disease activity, with an overall reduction from baseline disease activity as measured by MMS categorisation in both baseline MMS subgroups (Table). Generally, rates of treatment-emergent adverse events (TEAEs) were similar across treatment and baseline disease activity subgroups (proportion of patients with any TEAE: 59.0% vs 50.8% and 65.1% vs 56.1% for etasimod vs placebo, in baseline MMS 5–7 and 8–9 groups, respectively).

	Baseline MMS 5–7 (moderate)		Baseline MMS 8–9 (severe)	
	Placebo QD (N=181)	Etasimod 2 mg QD (N=344)	Placebo QD (N=66)	Etasimod 2 mg QD (N=152)
Clinical response, ^a % (95% CI) ^b	39.8 (32.6, 46.9)	61.3 (56.2, 66.5)	30.3 (19.2, 41.4)	64.5 (56.9, 72.1)
MMS category, % (95% CI) ^c				
Remission (MMS 0–2)	17.1 (11.1, 25.5)	38.4 (31.9, 45.3)	10.6 (4.2, 24.2)	21.7 (14.4, 31.4)
Mild (MMS 3–4)	26.0 (18.5, 35.1)	24.4 (19.0, 30.8)	15.2 (7.0, 29.6)	25.7 (17.7, 35.7)
Moderate (MMS 5–7)	35.4 (26.9, 44.9)	23.0 (17.7, 29.3)	37.9 (24.3, 53.7)	30.3 (21.7, 40.5)
Severe (MMS 8–9)	8.3 (4.4, 15.2)	2.6 (1.1, 5.9)	24.2 (13.4, 39.8)	13.2 (7.6, 21.8)
MMS not available ^d	13.3 (8.1, 21.1)	11.6 (7.9, 16.8)	12.1 (5.1, 26.0)	9.2 (4.8, 17.1)

^aClinical response was defined as a ≥ 2 -point and $\geq 30\%$ decrease from baseline in MMS, and a ≥ 1 -point decrease from baseline in RBS or an absolute RBS ≤ 1 .

^b95% CI is based on normal approximation to binomial proportion.

^c95% CI was calculated using the Goodman method of simultaneous CI estimation.

^dMMS was not available for some patients at Wk 12 for various reasons, including discontinuation prior to Wk 12.

CI, confidence interval; MMS, Modified Mayo score; N, number of patients in the baseline disease activity subgroup by treatment; QD, once daily; RBS, rectal bleeding subscore; UC, ulcerative colitis.

Table. Proportion of patients achieving clinical response and each MMS category at Wk 12 stratified according to baseline disease activity (pooled data from ELEVATE UC 52 and ELEVATE UC 12).

Conclusion: Etasimod showed greater reductions in disease severity and higher rates of clinical response, vs placebo, regardless of baseline disease activity. The safety profile of etasimod was consistent with the overall trial population¹ and was not impacted by baseline disease activity.

References: 1. Sandborn WJ et al. *Lancet* 2023; 401: 1159–1171

Disclosure: BES has received consulting fees from AbbVie, Abivax, Alimentiv, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Boston Pharmaceuticals,

Calibr, Celgene, Celltrion, ClostraBio, Equillum, Entera, Evomune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmith-Kline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Janssen, Kaleido, Kallyope, Lilly, Merck, Morphee Therapeutics, MRM Health, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Takeda, Target RWE, Teva, Theravance Biopharma, TLL Pharmaceutical, Ventyx Biosciences; speaker fees from Abivax, Bristol Myers Squibb, Janssen, Lilly, Pfizer, Takeda; research grants from Bristol Myers Squibb, Janssen, Pfizer, Takeda, Theravance Biopharma; stock options from Ventyx Biopharma; and other support from Bristol Myers Squibb, Lilly, Janssen, Pfizer and Takeda. MCD is a consultant for AbbVie, Abivax, AstraZeneca, Bristol Myers Squibb, Janssen, Lilly, Merck, Pfizer Inc, Prometheus Labs, Spyre and Takeda. PGK has received consulting and speaker fees from AbbVie, Janssen, Pfizer Inc, and Takeda and has received scientific grants from Pfizer Inc and Takeda. SV has received speaker fees from AbbVie, Dr. Falk Pharma, Ferring, Galapagos, Hospira, Janssen, MSD, Takeda, and Tillotts; consultancy/advisory fees from AbbVie, Abolentis Pharma, Alimentiv, Arena, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Dr Falk Pharma, Lilly, Ferring, Galapagos, Genentech/Roche, Gilead, Hospira, Imidomics, Janssen, Johnson and Johnson, Materia Prima, MiroBio, Morphee, MrMHealth, MSD, Mundipharma, Pfizer Inc, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma AG and Zealand Pharma; and grant/research support from AbbVie, MSD, Pfizer Inc, Galapagos, Janssen and Takeda. RP has received consulting fees from Abbott, AbbVie, Abivax, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda, Theravance Biopharma, Trellus, Viatrix, Ventyx, UCB; speaker fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, Takeda; an advisory board member for AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda, Ventyx; and received research support from AbbVie, Janssen, Takeda and Pfizer. MDL is a consultant for AbbVie, Janssen, Pfizer Inc, Takeda, BMS, Target PharmaSolutions, Prometheus, Lilly, Salix, Valeant, Genentech, Roche, Calibr, Theravance; and has received research support from Pfizer Inc and Takeda. JCW, JW and EB are employees and shareholders of Pfizer Inc. AM is an employee of Pfizer Ltd and shareholder of Pfizer Inc. MG is an employee and shareholder of Pfizer AG. AJY has received consultancy fees from AbbVie, Pfizer Inc, Arena, Takeda, Bristol Myers Squibb; and speaker fees from Bristol Myers Squibb.

MP687

EFFICACY AND SAFETY OF ETASIMOD INDUCTION THERAPY IN ASIA PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE 12-WEEK INDUCTION PERIOD OF A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, MULTICENTER, CHINA REGISTRATIONAL STUDY (ES101002)

K. Wu¹, Z. Zhang², Y. Ding³, Q. Cao⁴, X. Gao⁵, J. Zhong⁶, H. Zhang⁷, X. Wang⁸, X. Liu⁹, C.-T. Chiu¹⁰, J.-W. Chou¹¹, T.-O. Kim¹², Y. Lin¹³, L. Ying¹⁴, Z. Zhu¹³, X. Chen¹³

¹Xijing Hospital, Xi'an, China, ²Shengjing Hospital of China Medical University, Shenyang, China, ³Renmin Hospital of Wuhan University, Wuhan, China, ⁴Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China, ⁵The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, ⁶Ruijing Hospital Affiliated to the Shanghai Jiaotong University Medical School, Shanghai, China, ⁷West China Hospital, Sichuan University, Chengdu, China, ⁸Tangdu Hospital of Air Force Medical University, Xi'an, China, ⁹Xiangya Hospital, Central South University, Changsha, China, ¹⁰Chang Gung Memorial Hospital, Linkou, Taiwan, ¹¹China Medical University Hospital, Taichung, Taiwan, ¹²Inje University Haeundae Paik Hospital, Busan, South Korea, ¹³Everest Medicines Limited, Shanghai, China, ¹⁴Everest Medicines Limited, New Jersey, United States of America

Contact E-Mail Address: xia.chen@everestmedicines.com

Introduction: Etrasimod is an oral, selective, synthetic sphingosine 1-phosphate receptor 1, 4, 5 modulator being developed for immune-mediated inflammatory disorders including ulcerative colitis (UC). Below are efficacy and safety results from the 12-week induction period of Study ES101002.

Aims & Methods: ES101002 (NCT04176588) is an ongoing Phase 3, randomized, placebo (PBO) -controlled, double-blind, multicenter, China registrational study aiming to evaluate efficacy and safety of etrasimod 2 mg in patients (pts) with moderately to severely active UC (modified Mayo score 4-9 points, centrally read endoscopic subscore ≥ 2 , and rectal bleeding subscore ≥ 1) and documented history of inadequate response to, loss of response to, or intolerance to ≥ 1 UC treatment. The study (re-randomization design) includes a 12-week Induction (2:1 ratio etrasimod: PBO), a 40-week maintenance period (1:1), and an optional open label period. Permitted concomitant medications include oral 5-aminosalicylic acid compounds and corticosteroids (prednisone ≤ 20 mg/day or equivalent). The primary efficacy endpoint is clinical remission; key secondary efficacy endpoints are endoscopic improvement and clinical response. Safety is evaluated throughout the study.

Results: ES101002 is being conducted in mainland China, Taiwan, and South Korea. A total of 340 pts were randomized and dosed for Induction. Baseline demographics and disease characteristics were balanced between groups. All primary and key secondary efficacy objectives were achieved with etrasimod and met statistical significance ($P < 0.0001$) at Week 12 (Table). Moreover, the significant difference in the proportion of etrasimod treated pts achieving symptomatic remission, endoscopic normalization and mucosal healing objectives compared with PBO (Table) demonstrates that treatment with etrasimod results in a concurrent improvement in symptoms of active UC and in the endoscopic and histologic improvement of the mucosa. The percentage of pts reporting ≥ 1 treatment-emergent adverse event (TEAE) was 67.1% in the etrasimod group and 54.5% in the PBO group. Compared to those taking PBO, a smaller percentage of pts taking etrasimod reported Grade 3 TEAEs, serious TEAEs, and TEAEs leading to study drug discontinuation. The most common TEAE leading to study drug discontinuation was UC worsening (2 pts [0.9%] in the etrasimod group and 2 pts [1.8%] in the PBO group). The

most common Grade 3 TEAEs were alanine aminotransferase increased (2 pts [0.9%] in the etrasimod group; no pts in the PBO group) and UC worsening (2 pts [0.9%] in the etrasimod group and 5 pts [4.5%] in the PBO group). No Grade 4 TEAEs or deaths were reported.

Efficacy Endpoints at Induction (Week 12) in Study ES101002 (Full Analysis Set)	Etrasimod 2mg (N=228)	Placebo (N=112)	Difference in proportion (Etrasimod – Placebo), % (95% CI)	P value
Clinical remission ^a , n (%)	57 (25.0%)	6 (5.4%)	20.4% (13.4, 27.4)	<0.0001
Endoscopic improvement ^b , n (%)	85 (37.3%)	11 (9.8%)	28.6% (20.5, 36.7)	<0.0001
Clinical response ^c , n (%)	133 (58.3%)	31 (27.7%)	32.0% (21.8, 42.2)	<0.0001
Endoscopic Normalization ^d , n (%)	35 (15.4%)	3 (2.7%)	13.2% (7.6, 18.8)	0.0003
Mucosal Healing ^e , n (%)	59 (25.9%)	5 (4.5%)	22.3% (15.5, 29.1)	<0.0001
Symptomatic Remission ^f , n (%)	91 (39.9%)	20 (17.9%)	23.1% (13.6, 32.6)	<0.0001

^a SF = 0 (or = 1 with ≥1-point decrease from BL), RB = 0, and ES ≤ 1 (excluding friability); ^b ES ≤ 1 (excluding friability); ^c ≥2-point decrease and ≥30% decrease from baseline in MMS, and ≥1-point decrease from BL in RB or RB ≤ 1; ^d ES = 0 + ES ≤ 1 (excluding friability) with Geboes Index score < 2.0; ^e SF = 0 (or = 1 with ≥1-point decrease from BL) and RB = 0. BL = baseline; CI = confidence interval; ES = endoscopy; MMS = modified Mayo score; RB = rectal bleeding; SF = stool frequency.

Conclusion: Compared to PBO, etrasimod 2 mg treatment showed greater improvement, resulting in clinically meaningful and statistically significant improvement in the primary endpoint and all key secondary endpoints post-Induction. Treatment with etrasimod was safe and well tolerated. The safety profile was consistent with previous studies; no new safety findings were observed.

Disclosure: Nothing to disclose.

MP688

IMPACT OF OBEFAZIMOD INDUCTION THERAPY ON HISTOLOGIC AND COMBINED HISTOLOGIC AND ENDOSCOPIC OUTCOMES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: WEEK 8 RESULTS FROM THE PHASE 2B INDUCTION TRIAL

L. Peyrin-Biroulet¹, B.E. Sands², S. Danese³, P.S. Dulai⁴, H. Tilg⁵, B. Siegmund⁶, S. Sloan⁷, C. Rabbat⁸, S. Vermeire⁹

¹University of Lorraine, Gastroenterology, Vandoeuvre-les-Nancy, France, ²Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ³Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁴Feinberg School of Medicine Northwestern University, Chicago, United States of America, ⁵Innsbruck Medical University - Department of Medicine, Innsbruck Medical University; Innsbruck/AT, Department of Medicine, Innsbruck, Austria, ⁶Charité - Universitätsmedizin Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ⁷Abivax, Paris, France, ⁸Abivax, Medical Affairs, Paris, France, ⁹University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: britta.siegmund@charite.de

Introduction: Obefazimod is an investigational, oral, once-daily (od), small molecule which enhances expression of microRNA-124 and is currently in phase 3 clinical trials for the treatment of patients with moderately to severely active ulcerative colitis (UC) [1].

Obefazimod demonstrated efficacy and safety in patients with UC at week-8 in a placebo-controlled, Phase 2b induction trial and in the subsequent open-label maintenance (OLM) study [2].

Here we present results for effects of obefazimod induction on histologic and combined histologic and endoscopic outcomes at week 8.

Aims & Methods: Patients with a modified Mayo score of 5-9 and a centrally read Mayo endoscopy subscore ≥ 2 at induction baseline were randomized 1:1:1 to receive either obefazimod 25mg, 50mg or 100mg od or placebo. Rectal or sigmoidal biopsies were collected during endoscopy at baseline and week 8 to evaluate treatment effect on histopathology

scores utilizing the Geboes Index. Histologic improvement (Geboes histologic score ≤ 3.1), and histo-endoscopic mucosal improvement (Geboes histologic score ≤ 3.1 + Mayo endoscopy subscore of 0 or 1 with no friability; HEMI) were evaluated at week 8.

Results: Of the 252 patients randomized (with a mean age of 41.2 years; 41.3% female; mean UC disease duration of 8.05 years), 188 received obefazimod treatment, and 64 were administered a placebo. Baseline demographics, disease characteristics and histologic activity were consistent across treatment groups. The proportion of patients with histologic improvement at week 8 was 43% among obefazimod-treated patients (all doses) and 31% among those receiving placebo (Table 1). The proportion of patients with endoscopic improvement at week 8 was 35% among obefazimod-treated patients (all doses) and 13% among those receiving placebo. The proportion of obefazimod-treated patients who achieved HEMI at week 8 was greater than placebo-treated patients (27% vs 13%, respectively). Consistently positive histological outcomes were observed when evaluating all three obefazimod induction doses individually compared to placebo (Table 1).

Efficacy Endpoint, % (n)	Placebo (n=64)	Obefazimod 25 mg (n=61)	Obefazimod 50 mg (n=63)	Obefazimod 100 mg (n=64)	Obefazimod All doses (n=188)
Histologic improvement ¹	31.3 (20)	50.8 (31)	36.5 (23)	42.2 (27)	43.1 (81)
Endoscopic improvement ²	12.5 (8)	32.8 (20)	33.3 (21)	37.5 (24)	34.6 (65)
Histo-endoscopic mucosal improvement (HEMI) ³	12.5 (8)	26.2 (16)	23.8 (15)	31.3 (20)	27.1 (51)

Table 1: Histologic and combined histologic and endoscopic outcomes at week 8.

1: Histological improvement: Neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤ 3.1); 2: Endoscopic improvement: endoscopic sub-score ≤ 1; 3: Histo-endoscopic mucosal improvement: A combination of histologic improvement (ie, Geboes histologic score ≤ 3.1) and endoscopic improvement (Mayo endoscopy subscore of 0 or 1 with no friability).

Conclusion: In this Phase 2b induction trial, patients with moderately to severely active UC treated with obefazimod experienced clinically meaningful improvements in histologic and combined histologic and endoscopic outcomes at week 8.

References:

- Vermeire S, et al. J Crohns Colitis. 2023; 17: 1689-1697
- Vermeire S, et al. The Lancet Gastroenterology & Hepatology. 2022; 7: 1024-1035.

Disclosure: Bruce E Sands has served as a consultant or received speaker's fees from AbbVie, Abivax, Adiso Therapeutics, AgomAb, Alimentiv, Amgen, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytokine Pharma, Eli Lilly and Company, Entera, Evomune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morphic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio, and stock options from Ventyx Biosciences.

S  verine Vermeire has received grants from AbbVie, J&J, Pfizer, Takeda and Galapagos; SV has received consulting and/or speaking fees from: AbbVie, Abivax, AbolerIS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance, Tillots Pharma AG, Zealand Pharma. Laurent Peyrin-Biroulet has received grants from Celltrion, Fresenius Kabi, Takeda; LPB has served as a consultant or received speaker's fees from Abbvie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, Connect Biopharm, Cytoki Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, Hac Pharm, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopa, Morphic, MSD, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par' Immune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance, Thermo Fischer, Tigenix, Tillots, Viatrix, Vifor, Vectivbio, Ventyx, Ysopia.

Silvio Danese has served as consultant or received speaker's fees from AbbVie, Ferring, Hospira, Johnson & Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim.

Parambir Dulai received speaker's fees from Abbvie, Abivax, Adiso, Bristol Meyer Squibb, Geneoscopy, GSK, Janssen, Lilly, Pfizer, Takeda.

Herbert Tilg has served as a consultant or received speaker's fees from Abbvie, Abivax, Dr Falk Pharma, ferring, Galapagos, Microbiotica, MSD, Pfizer, Takeda.

Britta Siegmund has served as consultant for Abbvie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forge Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; Speaker fees: AbbVie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer and grant support by Arena/Pfizer (served as representative of the Charit  ).

MP689

CORTICOSTEROID-FREE EFFICACY AND SAFETY OF UC PATIENTS RECEIVING ONCE DAILY OBEFAZIMOD IN AN OPEN LABEL, 96-WEEK MAINTENANCE STUDY AMONG PATIENTS WHO WERE RECEIVING CONCOMITANT CORTICOSTEROIDS AT INDUCTION BASELINE

S. Vermeire¹, L. Peyrin-Biroulet², S. Danese³, P.S. Dulai⁴, H. Tilg⁵, B. Siegmund⁶, J. Nitcher⁷, S. Sloan⁷, C. Rabbat⁸, B.E. Sands⁹

¹University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ²University of Lorraine, Gastroenterology, Vandoeuvre-Nancy, France, ³Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ⁴Feinberg School of Medicine Northwestern University, Chicago, United States of America, ⁵Innsbruck Medical University - Department of Medicine, Innsbruck Medical University; Innsbruck/AT, Department of Medicine, Innsbruck, Austria, ⁶Charit   - Universit  tsmedizin Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ⁷Abivax, Paris, France, ⁸Abivax, Medical Affairs, Paris, France, ⁹Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America

Contact E-Mail Address: severine.vermeire@uzleuven.be

Introduction: Obefazimod (Obe) is an investigational, oral, once-daily (od), small molecule which enhances expression of microRNA-124 and is currently in phase 3 clinical trials for the treatment of patients (pts) with moderately to severely active ulcerative colitis (UC) [1]. Obe demonstrated efficacy and safety in pts with UC at week (wk)-8 in a placebo-controlled, Phase 2b induction trial and in the subsequent open-label maintenance (OLM) study [2]. This *post hoc* analysis reports corticosteroid (CS)-free efficacy and safety at wks 48 and 96 in pts receiving concomitant CS at induction baseline.

Aims & Methods: Pts received placebo or Obe 25mg, 50mg or 100mg od during the Phase 2b, induction trial and, irrespective of their clinical response, could enter the optional 96-wk OLM study with Obe 50mg od. Pts were followed monthly for safety and efficacy. At entry of the induction trial, pts could receive concomitant CS (prednisone or equivalent [≤ 20 mg/day], budesonide [≤ 9 mg/day], beclomethasone [≤ 5 mg/day]) if on a stable dose ≥ 2 wks immediately before screening; beginning at baseline of the OLM study, CS tapering was recommended but not required. CS-free was defined as withdrawal of CS ≥ 12 wks prior to assessment timepoint. CS-free outcomes were assessed at wks 48 and 96 of the OLM and included CS-free clinical remission (CR), CS-free endoscopic improvement (EI), and CS-free endoscopic remission (ER). Safety among this subgroup was also assessed.

Results: At induction baseline, 115 pts (out of 252, 46%) received CS. Among pts with CS at induction baseline, CR rates were 56% (64/115) at wk 48 and 52% (60/115) at wk 96. CS-free CR was attained by 37% (43/115) at wk 48 and maintained at 35% (43/115) at wk 96 within the same cohort. Among the 21 pts that were in CR but did not meet the definition of CS-free at wk 48, the Principal Investigator (PI) did not attempt the optional CS tapering for 13 pts (13/21, 62%). An additional 4 pts (4/21, 19%) were CS free, but for less than 12wks before the wk 48 endpoint. Among the 20 pts that were in CR but did not meet the definition of CS-free at wk 96, the PI did not attempt the optional CS tapering for 8 pts (8/20, 62%). An additional 7 pts (7/20, 35%) were CS free, but for less than 12wks before the wk 96 endpoint. EI was achieved by 64% (73/115) at wk 48 and 58% (67/115) at wk 96, with CS-free EI achieved by 44% (50/115) of pts at wk 48 and 39% (45/115) at wk 96. ER was achieved by 33% (38/115) at wk 48 and 31% (36/115) at wk 96, with CS-free ER achieved by 24% (27/115) of pts at wk 48 and 21% (24/115) at wk 96 (Table 1).

Overall, the safety profile within this cohort was consistent with the overall study population.

Efficacy Endpoint, % (n)	Patients with CS at induction baseline (N=115)	
	Week 48 % (n)	Week 96 % (n)
Clinical remission	55.7 (64)	52.2 (60)
CS-free clinical remission	37.4 (43)	34.8 (40)
Endoscopic improvement	63.5 (73)	58.3 (67)
CS-free endoscopic improvement	43.5 (50)	39.1 (45)
Endoscopic remission	33.0 (38)	31.3 (36)
CS-free endoscopic remission	23.5 (27)	20.9 (24)

Non-responder imputation (NRI) was used for missing efficacy data; clinical remission: stool frequency sub-score ≤ 1 , RBS = 0 and endoscopic sub-score ≤ 1 ; clinical response: decrease from baseline in the Modified Mayo score (MMS) ≥ 2 points and $\geq 30\%$ from baseline, plus a decrease in rectal bleeding sub-score (RBS) ≥ 1 or an absolute RBS ≤ 1 ; endoscopic improvement: endoscopic sub-score ≤ 1 ; endoscopic remission: endoscopic sub-score = 0 CS: corticosteroids; CS-free: withdrawal of CS ≥ 12 weeks prior to assessment timepoint. Concomitant CS at induction baseline is defined by ADSL.CORT=Y (ie, there exists on-treatment concomitant medications with CM.CMCAT is missing and CMINDC='STUDY INDICATION' and SUPPCM.QVAL in (A07EA, H02, D07BA, H02AB) when SUPPCM.QNAM='ATCCD') in study ABX464-103 and ADSL.ENRFL=Y in study ABX464-104

Table 1: Efficacy and CS-free efficacy at wks 48 and 96 of OLM study in patients with CS at induction baseline.

Conclusion: Among pts receiving concomitant CS at induction baseline, meaningful proportions achieved CR, EI, and ER at both wks 48 and 96 in the OLM. Notably, a substantial proportion of pts met CS-free efficacy endpoints despite CS tapering not being required in this OLM study. Concomitant use of CS at induction baseline had no notable effect on the safety profile of Obe.

References:

1. Vermeire S, et al. J Crohns Colitis. 2023; 17: 1689-1697
2. Vermeire S, et al. The Lancet Gastroenterology & Hepatology. 2022; 7: 1024-1035.

Disclosure: Bruce E Sands has served as a consultant or received speaker's fees from AbbVie, Abivax, Adiso Therapeutics, AgomAb, Alimentiv, Amgen, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytoki Pharma, Eli Lilly and Company, Entera, Evommune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morpnic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio, and stock options from Ventyx Biosciences. Séverine Vermeire has received grants from AbbVie, J&J, Pfizer, Takeda and Galapagos; SV has received consulting and/or speaking fees from: AbbVie, Abivax, AbolerIS Pharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Cytoki Pharma, Dr Falk Pharma, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Lilly, Materia Prima, MiroBio, Morpnic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance, Tillots Pharma AG, Zealand Pharma. Laurent Peyrin-Biroulet has received grants from Celltrion, Fresenius Kabi, Takeda; LPB has served as a consultant or received speaker's fees from Abbvie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, Connect Biopharm, Cytoki Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead,

Gossamer Bio, GSK, Hac Pharm, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopa, Morpnic, MSD, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par' Immune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance, Thermo Fischer, Tigenix, Tillots, Viatris, Vifor, Vectivbio, Ventyx, Ysopia. Silvio Danese has served as consultant or received speaker's fees from AbbVie, Ferring, Hospira, Johnson & Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim. Parambir Dulai received speaker's fees from Abbvie, Abivax, Adiso, Bristol Meyer Squibb, Geneoscopy, GSK, Janssen, Lilly, Pfizer, Takeda. Herbert Tilg has served as a consultant or received speaker's fees from Abbvie, Abivax, Dr Falk Pharma, ferring, Galapagos, Microbiotica, MSD, Pfizer, Takeda. Britta Siegmund has served as consultant for Abbvie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forga Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; Speaker fees: AbbVie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer and grant support by Arena/Pfizer (served as representative of the Charité).

Molecular and clinical therapies in HPB

14:30-15:30 / Poster Stage 3

MP690

**LIQUID BIOPSIES IN PANCREATIC DUCTAL ADENOCARCINOMA:
A NOVEL APPROACH FOR DETECTING KRAS MUTATIONS THAT CAN
TURN THIS VISION INTO REALITY**

A.C. Bravo¹, B. Morão¹, A. Luz^{2,3}, B. Oliveira^{2,3}, R. Dourado^{2,3},
B. Costa^{2,3}, S. Saraiva¹, C. Fidalgo¹, L. Mascarenhas Lemos^{4,5,6},
M.P. Costa-Santos⁷, R. Maio⁴, P. Viana Baptista^{2,3},
A. R. Fernandes^{2,3}, M. Cravo⁴

¹Hospital Beatriz Ângelo, Loures, Portugal, ²Associate Laboratory
i4HB - Institute for Health and Bioeconomy, NOVA School of Science
and Technology, NOVA University Lisbon, Caparica, Portugal,
³UCIBIO - Applied Molecular Biosciences Unit, Department of Life
Sciences, NOVA School of Science and Technology, NOVA University
Lisbon, Caparica, Portugal, ⁴Hospital da Luz, Lisbon, Portugal,
⁵NOVA Medical School, Universidade de Lisboa, Lisboa, Portugal,
⁶Faculdade de Medicina da Universidade Católica Portuguesa,
Lisboa, Portugal, ⁷Hospital do Divino Espírito Santo, Ponta
Delgada, Portugal

Contact E-Mail Address: catarina.bravoo@gmail.com

Introduction: Although circulating tumor DNA (ctDNA) has shown promising results in monitoring response/relapse in pancreatic cancer patients, the limited availability of sensitive, cost-effective, and efficient molecular technologies for their detection has restricted its use.

Here, we present a fast single-step methodology utilizing the amplification-refractory mutation system (ARMS) coupled with high-resolution melting analysis (HRMA) as a new method to evaluate KRAS mutations in tumor samples and ctDNA.

Aims & Methods: This is a prospective bicentric cohort study including pancreatic ductal adenocarcinoma cancer patients with tumor samples and liquid biopsies collected at diagnosis. Codon-12 KRAS mutations were tested by Sanger-Sequencing (SS) and G12D, G12V, G12R, G12C mutations were tested by ARMS/HRMA. The frequency of KRAS mutations by both techniques was evaluated. Progression-free survival and overall survival were also calculated.

Results: 41 patients, 61% male, with median-age at diagnosis of 69 (IQR 62-76) years-old, 40% with metastatic disease at diagnosis were included. SS detected KRAS mutations in 23 (56%) tumor samples (G12D=12, G12V=7, G12R=2, G12C=2) and ARMS/HRMA in 33 (81%) (G12D=18, G12V=9, G12R=2, G12C=1, G12V/G12D=2, G12D/G12C=1), with a moderate concordance in mutation detection ($\kappa=0.48$, $p<0.001$). Regarding liquid biopsies, no mutations were detected with SS technique, but ARMS/HRMA detected KRAS mutations in 7 patients (G12D=4, G12V=2, G12V/G12D=1), all of which were in agreement with mutations found in primary tumor. In non-operated patients, those with KRAS mutations detected in liquid biopsies showed a trend towards lower OS compared to patients with wildtype tumors (2 vs 10 months, HR 3.143, $p=0.133$).

Conclusion: The ARMS/HRMA method is a more effective means of detecting KRAS mutations in both PDAC tumor samples and liquid biopsies compared to SS, although its accuracy in liquid biopsies can be optimized. It might become a cost-effective tool to assess response to medical or surgical therapy as well as to detect early relapse. Further studies are required to validate these findings.

Disclosure: Nothing to disclose.

MP691

**ASSESSMENT OF INTESTINAL BARRIER DYSFUNCTION IN PATIENTS
WITH LIVER CIRRHOSIS USING CONFOCAL LASER ENDOMICROSCOPY
(CLE)**

J. Hammer¹, B. Simbrunner¹, D. Steinacher¹, A. Frick¹,
T. Reiberger¹, M. Trauner¹

¹Medical University of Vienna, Vienna, Austria

Contact E-Mail Address: johann.hammer@meduniwien.ac.at

Introduction: Increased intestinal permeability, or leaky gut, is a condition where the gut's epithelial barrier is compromised, allowing bacteria and toxins to enter the blood stream. In liver cirrhosis, this can exacerbate liver damage and accelerate disease progression by perpetuating inflammation and immune system activation. Accurate assessment of this dysfunction is critical to the management of cirrhotic patients, but traditional methods such as serum markers and indirect assays often lack specificity and sensitivity.

Confocal laser endomicroscopy (CLE) is an advanced imaging technique that provides real-time, high-resolution visualisation of the gastrointestinal tract at the cellular and subcellular levels. CLE is used to diagnose leaky gut by directly observing disruptions in the intestinal mucosa. It integrates a confocal microscope within an endoscope, enabling in vivo histology-like imaging during routine endoscopic examinations.

Aims & Methods: We aimed to use confocal laser microendoscopy (CLE) in the diagnosis of intestinal barrier dysfunction by direct observation of the intestinal mucosa, in patients with liver cirrhosis. CLE (Cellvizio, Mauna Kea Technologies) was performed in the second part of the duodenum following intravenous administration of 2.5 – 5 mg of fluorescein in 58 patients with liver cirrhosis of various aetiologies. These patients were undergoing routine endoscopic surveillance or therapeutic intervention for oesophageal varices. The study cohort consisted of 39 men (61.9%) and 19 women (30.2%), with a mean age of 53.9 ± 14.0 years. We collected and analysed the most recent results of hepatic venous pressure gradient (HVPG), liver stiffness measurement (LSM), and fibrosis index for liver fibrosis (Fib-4). A Watson score of 1 indicates normal barrier function, while a Watson score of 2 indicates impaired barrier function. Data are given as mean $\pm$ standard deviation, statistical analysis included Chi-square tests and Student's t-tests, with a significance level set at $p<0.05$. NS=not significant.

Results: We observed a gradation of intestinal barrier dysfunction that correlated with the severity of liver cirrhosis. Specifically, of the 35 patients with Child-Pugh A cirrhosis, 18 (51.4%) had a Watson score of 2. In the group of 14 patients with Child-Pugh B cirrhosis, 9 (64.3%) had a Watson score of 2 and of the 9 patients with Child-Pugh C cirrhosis, 8 (88.9%) had a Watson score of 2, further underscoring the trend of increasing intestinal barrier dysfunction with increasing liver disease severity ($p<0.05$). In contrast, no significant differences in hepatic venous pressure gradient (HVPG) were observed between patients with Watson score 1 (16.8 ± 6.2 mmHg) and Watson score 2 (17.2 ± 6.2 mmHg, p NS). Similarly, liver stiffness measurements (LSM) showed no statistical difference between patients with Watson score 1 (39.0 ± 23.7 kPa) and those with score 2 (40.2 ± 22.9 kPa) (p NS). Similarly, Fib-4 was 4.5 ± 3.1 in patients with Watson score 1 and 5.7 ± 3.6 in patients with Watson 2 (p NS).

Conclusion: The findings suggest an association between the severity of liver cirrhosis and impaired intestinal barrier function as assessed by CLE. This impairment does not correlate with changes in haemodynamic parameters or liver fibrosis. The CLE promises to provide accurate and immediate diagnostic data and to improve our understanding of the pathophysiological changes in the gut associated with liver cirrhosis. Further research is needed to explore the mechanisms linking the severity of cirrhosis to intestinal barrier dysfunction and its clinical implications.

Disclosure: No conflict of interest to declare.

MP692

ACCURACY AND OPTIMAL THRESHOLDS OF CONTROLLED ATTENUATION PARAMETER (CAP) FOR MASLD DIAGNOSIS USING MAGNETIC RESONANCE IMAGING PROTON DENSITY FAT FRACTION (MRI-PDFF) AS THE REFERENCE STANDARD. A DIAGNOSTIC ACCURACY STUDY

K. Malandris^{1,2}, D. Daravigas³, A. Sarakapina⁴, E. Korakas⁵, A. Liakos^{1,2}, T. Glykeria⁴, P. Paschos⁴, E. Gigi¹, E. Theocharidou¹, G. Kalopitas⁶, O. Gioulema⁷, A. Katsoula⁷, E. Bekiari^{1,2}, V. Lambadiari⁵, E. Sinakos⁸, A. Tsapas^{1,2,9}

¹Aristotle University of Thessaloniki, Second Medical Department, Thessaloniki, Greece, ²Aristotle University of Thessaloniki, Clinical research and Evidence-Based Medicine, Thessaloniki, Greece, ³Affidea Diagnostic Center, Thessaloniki, Greece, ⁴Papageorgiou Hospital, First Medical Department, Thessaloniki, Greece, ⁵National and Kapodistrian University of Athens, Research Institute and Diabetes Center, Second Department of Internal Medicine, Athens, Greece, ⁶Aristotle University of Thessaloniki, First Medical Department, Thessaloniki, Greece, ⁷Aristotle University of Thessaloniki, Second Propaedeutic Medical Department, Thessaloniki, Greece, ⁸Aristotle University of Thessaloniki, Fourth Medical Department, Thessaloniki, Greece, ⁹University of Oxford, Harris Manchester College, Oxford, United Kingdom

Contact E-Mail Address: kostas_malandris@yahoo.gr

Introduction: Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD) is the most prevalent hepatic disorder worldwide. While histology remains the gold standard, a shift is evident in emerging studies favoring Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF) over biopsy as a reliable alternative for steatosis assessment. Similarly, Controlled Attenuation Parameter (CAP) enables the noninvasive assessment of liver steatosis.

Aims & Methods: To assess the accuracy of CAP for MASLD diagnosis as defined by MRI-PDFF. We performed a cross-sectional, diagnostic accuracy study with prospectively collected data. We included consecutive adult participants with type 2 diabetes (T2D) and increased body mass index (BMI ≥ 25 kg/m²). We used receiver operating characteristic (ROC) curve analyses to assess the accuracy of CAP for diagnosing MASLD (MRI-PDFF $\geq 5\%$), and hepatic fat content (HFC) $\geq 10\%$. For each ROC analysis, we calculated the area under the ROC (AUROC) alongside 95% Confidence Intervals (CIs), and cutoffs for ruling out (sensitivity $>90\%$) and ruling in (specificity $>90\%$) the target condition. For each cutoff, we calculated the negative (NPV) and positive predictive values (PPV), as well as negative (LRn) and positive (LRp) likelihood ratios with their 95% CIs.

Results: We included 113 participants (58.4% males, mean age 59.6 years). Most participants (95.6%) had a BMI ≥ 30 kg/m². CAP measurements were performed with the M probe in 36.3% of the participants, and the remaining (63.7%) were scanned with the XL probe. MRI-PDFF values ranged from 1.9% to 37.8% covering the whole spectrum of steatosis. The prevalence of MASLD was 72.6%. The AUROC of CAP for MASLD diagnosis was 0.82 (0.74 to 0.89). The threshold for ruling out MASLD was 249 dB/m yielding a sensitivity (Sens) of 90.2% (81.7 to 95.7), specificity (Sp) 35.5% (19.2 to 54.6), LRp 1.40 (1.07 to 1.83), LRn 0.27 (0.12 to 0.62), PPV 78.7% (73.8 to 82.9) and NPV 57.9% (37.9 to 75.6). Similarly, the threshold for ruling in MASLD was 328 dB/m yielding a Sens, Sp, LRp, LRn, PPV and NPV of 47.6% (36.4 to 58.9), 90.3% (74.2 to 98.0), 4.91 (1.64 to 14.75) and 0.58 (0.46 to 0.74), 92.9% (81.2 to 97.5) and 39.4% (34.0 to 45.2), respectively. The AUROC of CAP for detecting HFC $\geq 10\%$ was 0.81 (0.73 to 0.88). CAP thresholds for ruling out/in HFC $\geq 10\%$ were 271 dB/m and 345 dB/m respectively. CAP measurements with IQR < 30 dB/ did not improve the accuracy of CAP for MASLD diagnosis.

Conclusion: CAP has acceptable diagnostic accuracy in identifying patients with MRI-PDFF defined MASLD. Thresholds below 249 and 271 dB/m can be used to exclude MASLD and HFC $\geq 10\%$ with adequate sensitivity. Similarly, CAP values over 328 and 345 dB/m can rule in MASLD and HFC $\geq 10\%$ respectively.

Disclosure: This study was supported by the Hellenic Association for the Study and Education of Diabetes Mellitus.

MP693

TIME COURSE OF COMPUTED TOMOGRAPHY FINDINGS OF PANCREATIC DUCTAL ADENOCARCINOMA UNTIL DIAGNOSIS: A LARGE-SCALE MULTICENTER STUDY

M. Gonda¹, A. Masuda¹, T. Kobayashi¹, T. Iemoto², S. Kakuyama³, T. Ezaki⁴, T. Ikegawa⁵, Y. Hirata⁶, H. Tsumura⁷, K. Ogisu⁸, R. Nakano⁹, S. Fujigaki¹⁰, T. Nakagawa¹¹, M. Takagi¹², K. Yamanaka¹³, Y. Sato¹⁴, K. Fujita¹⁵, K. Furumatsu¹², T. Kato¹⁶, A. Sakai¹, H. Shiomi⁹, T. Sanuki¹⁷, Y. Arisaka⁸, Y. Okabe⁶, H. Toyama¹⁸, K. Sofue¹⁹, Y. Kodama¹

¹Kobe University Graduate School of Medicine, Division of Gastroenterology, Department of Internal Medicine, Kobe, Japan, ²Kitaharima medical center, Department of Gastroenterology, Ono, Japan, ³Takatsuki General Hospital, Department of Gastroenterology, Takatsuki, Japan, ⁴National Hospital Organization Kobe Medical Center, Department of Gastroenterology, Kobe, Japan, ⁵Japanese Red Cross Kobe Hospital, Department of Gastroenterology, Kobe, Japan, ⁶Kakogawa Central City Hospital, Department of Gastroenterology, Kakogawa, Japan, ⁷Hyogo Cancer Center, Department of Gastroenterology, Akashi, Japan, ⁸Nippon Life Hospital, Department of Gastroenterology, Osaka, Japan, ⁹Hyogo Medical University, Division of Gastroenterology and Hepatobiliary and Pancreatic Diseases, Department of Internal Medicine, Nishinomiya, Japan, ¹⁰Hyogo Prefectural Harima-Himeji General Medical Center, Department of Gastroenterology, Himeji, Japan, ¹¹Chibune General Hospital, Department of Gastroenterology, Osaka, Japan, ¹²Osaka Saiseikai Nakatsu Hospital, Department of Gastroenterology, Osaka, Japan, ¹³Konan Medical Center, Department of Gastroenterology, Kobe, Japan, ¹⁴Hyogo Prefectural Tamba Medical Center, Department of Internal Medicine, Tamba, Japan, ¹⁵Yodogawa Christian Hospital, Department of Gastroenterology, Osaka, Japan, ¹⁶Hyogo Prefectural Awaji Medical Center, Department of Gastroenterology, Sumoto, Japan, ¹⁷Hyogo Prefectural Harima-Himeji General Medical Center, Department of Gastroenterology, Himeji, Japan, ¹⁸Kobe University Graduate School of Medicine, Department of Hepato-Biliary-Pancreatic Surgery, Kobe, Japan, ¹⁹Kobe University Graduate School of Medicine and Kobe University Hospital, Department of Radiology, Kobe, Japan

Contact E-Mail Address: mgonda@med.kobe-u.ac.jp

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers, but diagnosis at an early stage can improve the prognosis. Focal parenchymal atrophy and main pancreatic duct (MPD) dilatation have been identified as early signs of PDAC through imaging studies. However, limited evidence exists regarding their temporal progression due to previous study limitations with restricted case numbers.

Aims & Methods: We aimed to ascertain a more precise frequency assessment of suspicious PDAC findings as well as delineate the temporal progression of them. A multicenter retrospective study was conducted on patients diagnosed with PDAC between 2015 and 2021.

We included patients who had undergone at least one computed tomography (CT) scan ≥ 6 months before diagnosing PDAC. The temporal progression of suspicious PDAC findings on CT was investigated. As an additional relatively small control group analysis, we reviewed the CT findings of each 30 consecutive patients with chronic pancreatitis and autoimmune pancreatitis at our hospital between 2022 and 2023.

Results: Out of 1832 patients diagnosed with PDAC at 17 facilities, 320 had a previous CT before their diagnosis. Suspicious PDAC findings were detected in 153 cases (47.8%), with focal parenchymal atrophy being the most common (26.6%), followed by MPD dilatation (11.3%), pancreatic swelling or mass (6.9%), retention cysts (5.0%), pancreatic inflammation (3.8%), and MPD stricture (1.9%). Focal parenchymal atrophy was the earliest detectable sign among all suspicious findings and became visible on average 2.7 years before diagnosis, and the next most common, MPD dilatation, 1.1 years before diagnosis. Other findings were less frequent and appeared around 1 year before diagnosis. Focal parenchymal atrophy followed by MPD dilatation was observed in 10 patients but not in reverse order. Focal parenchymal atrophy was more frequently detected in the pancreatic body/tail. No significant relationship was found between the pathological PDAC differentiation or tumor stage and the time course of the CT findings. All cases of focal parenchymal atrophy progressed just prior to diagnosis, and the atrophic area was occupied by tumor at diagnosis. Main pancreatic duct dilatation continued to progress until diagnosis. In the study of the control group, among the patients with chronic pancreatitis, 96.7% (29/30) exhibited diffuse pancreatic atrophy, while focal pancreatic atrophy was observed in 3.3% (1/30) in the body of the pancreas. There was no significant progression of focal pancreatic atrophy observed in chronic pancreatitis patient. Among the patients with autoimmune pancreatitis, pancreatic atrophy was identified in 90% (27/30), and all instances of atrophy observed in diffuse pancreatic parenchyma.

Conclusion: This large-scale study revealed that the temporal progression of focal parenchymal atrophy is the earliest detectable sign indicating PDAC. The morphology of the atrophy and whether it is progressive or not are important factors in distinguishing pancreatic atrophy with malignancy from that with benign lesion. These results provide crucial insights for early PDAC detection.

Disclosure: Nothing to disclose.

MP694

ONE-YEAR UPDATE ON: DYNAMIC CONTRAST ENHANCED HARMONIC ENDOSCOPIC ULTRASOUND (CEH-EUS) AND INFLOW-TIME MAPPING: DIFFERENTIAL DIAGNOSIS AND PROGNOSIS OF FOCAL PANCREATIC LESIONS WITH COLOR PARAMETRIC IMAGING

S. Badiu¹, A. Săftoiu¹, A. Cazimirovitz¹, S. Adriana¹

¹Elias Emergency University Hospital, Bucharest, Romania

Contact E-Mail Address: simona.badiu@yahoo.com

Introduction: Contrast-enhanced endoscopic ultrasound (CEH-EUS) is a crucial imaging modality for evaluating focal pancreatic lesions. However, its interpretation often relies on subjective judgment and operator proficiency. Computer-aided color parametric imaging is a novel technique for contrast-enhanced endoscopic ultrasound that can highlight hemodynamic features of focal pancreatic lesions enabling a more objective assessment.

Aims & Methods: To explore the utility of ITM (Inflow-time Mapping)- a computer-aided color parametric imaging technique- in characterizing pancreatic focal lesions, identifying prognostic factors, and facilitating targeted management strategies in conjunction with CEH-EUS.

50 patients including 20 cases of pancreatic ductal adenocarcinomas (PDAC), 15 cases of chronic pancreatitis, 4 cases of pancreatic neuroen-

docrine tumors (NETs), 1 renal cell carcinoma metastasis, and 10 cystic lesions which include 2 mucinous cystadenomas (MCA), 2 serous cystadenomas (SCA), 4 pseudocysts and 2 intraductal papillary neoplasms were enrolled. All patients underwent CEH-EUS and ITM examinations of the frames obtained during the arterial phase. Before establishing the optimal starting frame for the ITM examination, a quantitative analysis was conducted on each CEH-EUS recording. Regions of interest (ROIs) were strategically positioned in either adjacent parenchyma or vascular structures. Subsequently, parameters derived from time-intensity curve (TIC) analysis, notably arrival time (AT), were estimated.

A retrospective review of CEH-EUS and ITM images involved assigning two criteria sets: (1) Routine CEH-EUS, focusing on enhancement degree and pattern, and (2) Combined CEH-EUS and ITM, emphasizing differentiation of pancreatic lesions based on contrast agent uptake speed compared to adjacent tissue. The final diagnosis was based on EUS-guided tissue acquisition.

Results: 31 pancreatic lesions were initially considered PDAC based on their hypoenhanced appearance on CEH-EUS. ITM analysis could not provide additional information in 17 patients due to insufficient vascularization, while in 3 cases, ITM showed large intralesional vessels suggesting vascular invasion, supporting the PDAC diagnosis. In 11 patients, by showing no difference in the speed of UCA uptake in the enhanced regions of the lesion compared to the surrounding parenchyma, ITM analysis was able to correctly identify chronic pancreatitis, as proven by histology. In 4 patients, both CEH-EUS and ITM were consistent regarding the diagnosis of chronic pancreatitis. ITM analysis was able to provide an extensive characterization of the 4 pancreatic NETs by showing a greater speed of UCA uptake in the lesion and a centrifugal pattern of the parametric map for well-differentiated NETs. A centripetal, faster uptake of the UCA was noted in the case of pancreatic metastasis. ITM analysis also proved useful in objectively highlighting the speed and pattern of enhancement (septal/mural) of the cystic lesions included, particularly for SCAs.

Conclusion: In patients with chronic pancreatitis, where parenchymal inhomogeneity and altered local perfusion might influence the purely visual assessment, ITM complements CEH-EUS, potentially reducing unnecessary biopsies and enabling follow-up care. Additionally, for hypervascular pancreatic lesions, ITM aids in both differential diagnosis and prognostic assessment. Intralesional vessels noted on ITM images should be carefully assessed since vascular invasion can serve as an indirect marker for malignancy, particularly in hypoenhanced lesions.

Disclosure: Nothing to disclose.

MP695

ACCURACY OF FIBROSCAN-ASPARTATE AMINOTRANSFERASE (FAST) SCORE FOR RULING OUT/IN FIBROTIC MASH. SYSTEMATIC REVIEW AND DIAGNOSTIC ACCURACY META-ANALYSIS

K. Malandris^{1,2}, M. Mainou^{1,2}, N. Papadopoulos³, A. Liakos^{1,2}, T. Karagiannis^{1,2}, P. Paschos^{2,4}, A. Katsoula^{2,5}, E. Theocharidou¹, M. Touloumtzi¹, E. Gigi¹, G. Kalopitas⁶, E. Bekiari^{1,2}, E. Sinakos⁷, A. Tsapas^{1,2,8}

¹Aristotle University of Thessaloniki, Second Medical Department, Thessaloniki, Greece, ²Aristotle University of Thessaloniki, Clinical research and Evidence-Based Medicine, Thessaloniki, Greece, ³Aristotle University of Thessaloniki, School of Medicine, Faculty of Health Science, Thessaloniki, Greece, ⁴Papageorgiou Hospital, First Medical Department, Thessaloniki, Greece, ⁵Aristotle University of Thessaloniki, Second Propaedeutic Medical Department, Thessaloniki, Greece, ⁶Aristotle University of Thessaloniki, First Medical Department, Thessaloniki, Greece, ⁷Aristotle University of Thessaloniki, Fourth Medical Department, Thessaloniki, Greece, ⁸University of Oxford, Harris Manchester College, Oxford, United Kingdom

Contact E-Mail Address: kostas_malandris@yahoo.gr

Introduction: Patients with metabolic-dysfunction associated steato-hepatitis (NAFLD activity score ≥ 4) and significant fibrosis ($\geq F2$) (fibrotic MASH) are at increased risk for disease progression and development of cirrhosis. Following the recent approval of the first agent for the management of noncirrhotic MASH, timely identification of these patients is of major importance. Fibroscan-aspartate aminotransferase (FAST™) score enables the noninvasive diagnosis of fibrotic MASH, and has been assessed in several studies.

Aims & Methods: To assess the overall performance of FAST™ score for diagnosing fibrotic MASH. We searched Medline, Cochrane library, Web of science and Scopus up to January 2024. We included diagnostic accuracy studies assessing the performance of FAST™ score for ruling out (FAST™ score ≤ 0.35) and ruling in (FAST™ score ≥ 0.67) fibrotic MASH using liver biopsy as the reference standard. We calculated pooled diagnostic accuracy estimates using bivariate random-effects models, and assessed risk of bias using the Quality Assessment of Diagnostic Accuracy Studies 2 tool.

Results: We included 16 studies with 8838 participants. Most studies (87.5%) were at high or unclear risk of bias due to concerns regarding patient selection, interpretation of FAST score without knowledge of biopsy results, and length of biopsy specimens for fibrotic MASH diagnosis. Across all participants, 54.8% were females and 31% had type 2 diabetes. Mean age and body mass index (BMI) were 52.4 years and 32.4 kg/m². Mean aspartate aminotransferase and alanine aminotransferase were 45.0 IU and 57.6 IU, respectively. The prevalence of fibrotic MASH across studies was 32.9% ranging from 14% to 55%. Using the rule out cut off (≤ 0.35), FAST™ yielded a pooled sensitivity of 0.88 (95 % CI; 0.83, 0.91), specificity 0.52 (0.45, 0.60), positive likelihood ratio (LRp) 1.8 (1.6, 2.1) and negative likelihood ratio (LRn) 0.23 (0.18, 0.30). By applying the rule in cut off (≥ 0.67), pooled sensitivity, specificity, LRp, and LRn were 0.45 (0.39, 0.52), 0.87 (0.82, 0.90), 3.4 (2.8, 4.1) and 0.63 (0.58, 0.69) respectively. Assuming a pre-test probability (prevalence) of 30% for fibrotic MASH, a FAST™ score ≥ 0.67 resulted in a positive predictive value of 60%, while with a FAST™ score ≤ 0.35 the negative predictive value was 91%.

Conclusion: FAST™ score has acceptable accuracy for the diagnosis of fibrotic MASH. Proposed thresholds of ≤ 0.35 and ≥ 0.67 might be useful for ruling out/in fibrotic MASH respectively.

Disclosure: Nothing to disclose.

MP696

DEVELOPMENT OF AN AI MODEL FOR EARLY DETECTION OF SMALL PANCREATIC CANCER USING INDIRECT IMAGE FINDINGS

H. Takahashi^{1,2,3}, K. Yamao^{1,3}, H. Yokota², S. Takemoto², J. Nakahodo^{4,3}, R. Minami^{5,3}, R. Sagami^{6,3}, T. Ishikawa^{1,3}, Y. Mizutani¹, T. Iida¹, K. Uetsuki¹, H. Kawashima¹

¹Nagoya University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Nagoya, Japan, ²RIKEN, Center for Advanced Photonics, Image Processing Research Team, Wako, Japan, ³Pancreatic Cancer Research for Secure Salvage Young Investigators (PASSYON), Osaka-Sayama, Japan, ⁴Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Department of Gastroenterology, Tokyo, Japan, ⁵Tenri Hospital, Department of Gastroenterology, Tenri, Japan, ⁶Oita University, Faculty of Medicine, Department of Gastroenterology,, Oita, Japan

Contact E-Mail Address: htaka@med.nagoya-u.ac.jp

Introduction: Pancreatic cancer, known for its poor prognosis, can potentially be cured if diagnosed early, specifically when the tumor is 10 mm or less in diameter, referred to as Small Pancreatic Cancer (SPC).¹ Despite recent advancements of AI diagnostic models for various diseases, detecting SPC remains a significant challenge.^{2,3,4} This difficulty arises because the detection rate decreases as SPC tumors diminish in size, necessitating an imaging interpretation approach different from that used for general pancreatic cancer. SPC complicates direct identification through imaging, necessitating reliance on indirect image findings such as partial pancreatic parenchymal atrophy and abnormalities in the main pancreatic duct.^{5,6,7} These subtle findings demand advanced interpretive skills. Furthermore, the rarity of SPC complicates the collection of a sufficient dataset for research and diagnosis.

Aims & Methods: This study aims to construct an SPC-specific AI-based diagnostic model by incorporating indirect image findings, achieved through collaboration with multiple institutions that specialize in SPC diagnosis to ensure a sufficient number of cases. We first analyzed portal phase CT scans of 30 SPC cases and 30 normal pancreas (NP) cases from our institution. Two specialists annotated the abnormal areas, including indirect image findings of SPC, and the entire pancreas for NP, from which small region images, each measuring 28×28 pixels, were randomly extracted. These images were converted into feature vectors using a pre-trained deep learning model (ResNet-50), and the feature distribution of each small region was compared and classified using a machine learning model. Following this initial experiment, we conducted external validation using SPC cases collected from three other institutions.

Results: In our institution's SPC cases, abnormalities in the main pancreatic duct were seen in 77%, partial pancreatic parenchymal atrophy in 40%, and upstream pancreatic parenchymal atrophy in 16%. In cases from the other institutions, these figures were 71%, 46%, and 13%, respectively. t-SNE plotting of feature vectors indicated a trend of separation between small regions of SPC and NP, with SPC displaying varied features among cases, while NP exhibited similar features. Classification using the LightGBM model, a type of decision tree-based learning algorithm, achieved an average accuracy of 0.944 through 5-fold cross-validation, and an accuracy of 0.919 for cases from other institutions.

Conclusion: Using the indirect image findings of SPC enabled good classification performance for small regions of NP. A slight decrease in accuracy was observed in cases from the other institutions, suggesting the influence of imaging conditions and equipment. Through multi-institutional collaboration, we have amassed a dataset of over 100 SPC cases, which we will utilize to further refine and enhance our model. Our future work will focus on improving preprocessing methods and expanding the data-

set with additional multi-institutional data. Achieving these goals will enable AI to support clinicians in the reliable diagnosis of SPC, potentially leading to an increase in the number of pancreatic cancer patients who can undergo curative surgical treatments.

- References:** 1. Kanno A, et al. *Pancreatology* 2018; 18(1): 61-7.
 2. Chu LC, et al. *AJR Am J Roentgenol* 2019; 213(2): 349-57.
 3. Kenner BJ, et al. *Pancreas* 2021; 50(7): 916-22.
 4. Chen PT, et al. *Radiology* 2023; 306(1): 172-82.
 5. Yamao K, et al. *Diagnostics* 2020; 10(7): 445.
 6. Sagami R, et al. *Cancers* 2021; 13(5): 945.
 7. Nakahodo J, et al. *Pancreatology* 2022; 22(8): 1148-58.

Disclosure: Nothing to disclose.

MP697

CHANGES IN BODY COMPOSITION ARE ASSOCIATED WITH POOR OVERALL SURVIVAL IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

K. Wijsman^{1,2}, D. Klatte^{1,2}, A. Bogdanski^{1,2}, A. Weston³, J. van Hooft¹, M. van Leerdam^{1,4}, M. Wallace², Y. Bi²
¹Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²Mayo Clinic, Department of Gastroenterology and Hepatology, Jacksonville, United States of America, ³Mayo Clinic, Department of Quantitative Health Sciences, Jacksonville, United States of America, ⁴Netherlands Cancer Institute, Department of Gastrointestinal Oncology, Amsterdam, Netherlands

Contact E-Mail Address: koen.wijsman@hotmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest malignancies. Even in patients undergoing curative resection, prognosis is poor. In this setting, gaining a better understanding of factors influencing survival of patients with PDAC is urgently needed in order to tailor treatment. Previous research suggests that abdominal body composition at diagnosis – particularly the distribution of skeletal muscle, adipose tissue, and bone area – may have prognostic value. Therefore, this study aims to investigate the association of various CT-based body composition parameters with survival in PDAC patients with resectable and irresectable disease.

Aims & Methods: Patients diagnosed with PDAC between 2000 and 2020 were identified using the Mayo Clinic Cancer Registry, and diagnostic CT scans were retrieved. Body composition was evaluated using an automated abdominal segmentation algorithm that three-dimensionally measured tissue volume and density in a 20 cm section surrounding vertebral L3. Multivariable Cox regression analyses were conducted to evaluate the association of body composition parameters with survival.

Results: A total of 1666 patients were included, 56.3% male, median age 69 (IQR 61 – 76) years old. Median follow-up was 9.5 months (IQR 3.7 – 20.8). Median survival was 28.3 months for patients undergoing resection (n = 509), against 6.7 months for patients with irresectable disease (n = 1157). Table 1 displays the association between various body composition parameters and overall survival, after adjustment for age, sex, race, tumor localization, tumor stage, BMI, and comorbidities. Myosteatosi (defined as the infiltration of fat in skeletal muscle) was independently associated with worse overall survival (HR 1.20, 95% CI 1.06 – 1.36, p = 0.004). Subgroup analysis in patients undergoing resection revealed that lower subcutaneous adipose tissue was independently associated with worse survival. In patients with irresectable disease, lower skeletal muscle density, the presence of myosteatosi, lower subcutaneous adipose tissue, lower visceral adipose tissue, and higher vertebral bone area were independently associated with worse survival.

Body composition parameters	Resectable PDAC (n = 509)	Irresectable PDAC (n = 1157)
	Hazard ratio (95% CI)	Hazard ratio (95% CI)
Body mass index	1.01 (0.99 – 1.03)	1.01 (1.00 – 1.02)
Skeletal muscle area (cm ²)	0.99 (0.94 – 1.03)	1.03 (1.00 – 1.06)
Sarcopenia	1.00 (0.80 – 1.25)	0.93 (0.81 – 1.07)
Skeletal muscle density (Hounsfield Units)	0.94 (0.84 – 1.06)	0.86 (0.80 – 0.92)*
Myosteatosi	1.10 (0.88 – 1.39)	1.24 (1.06 – 1.44)*
Subcutaneous adipose tissue area (cm ²)	0.98 (0.96 – 1.00)*	0.99 (0.98 – 1.00)*
Visceral adipose tissue area (cm ²)	1.00 (0.98 – 1.01)	0.99 (0.98 – 1.00)*
Vertebral bone area (cm ²)	1.07 (0.94 – 1.21)	1.12 (1.05 – 1.21)*
Vertebral bone density (Hounsfield Units)	0.99 (0.97 – 1.01)	1.00 (0.98 – 1.01)

Table 1: hazard ratios (95% CI) for mortality.

Hazard ratios for mortality in patients with pancreatic ductal adenocarcinoma (PDAC) based on various body composition parameters. Hazard ratios for variables in cm² and Hounsfield Units are per 10 units increase. Determined using multivariable Cox regression analysis and adjusted for age, sex, race, tumor localization, tumor stage, BMI, and comorbidities. Asterisks indicate p-values <0.05.

Conclusion: Lower subcutaneous adipose tissue (in patients undergoing curative resection) and lower skeletal muscle density, lower subcutaneous and visceral adipose tissue, and higher vertebral bone area (in patients with irresectable disease) are independently associated with worse overall survival in patients with PDAC. This highlights the significance of body composition, which can be evaluated through routinely performed diagnostic CT scans, in enabling a more patient-specific treatment approach.

Disclosure: Michael B. Wallace, MD, MPH

Consulting: Verily, Boston Scientific, Endiatrix, Fujifilm, Medtronic, Surgical Automations.

Research grants: Fujifilm, Boston Scientific, Olympus, Medtronic, Ninepoint Medical, Cosmo/Aries Pharmaceuticals.

Stock/Stock Options: Virgo Inc., Surgical Automations.

Consulting on behalf of Mayo Clinic: Boston Scientific, Microtek.

General payments/Minor Food and Beverage: Synergy Pharmaceuticals, Boston Scientific, Cook Medical.

Jeanin E. van Hooft, MD, PhD, MBA

Consulting fees: Olympus.

Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events: Cook Medical, Boston Scientific, Falk.

Participation on a Data Safety Monitoring Board or Advisory Board: Olympus.

All other authors

No potential conflicts of interest to disclose.

MP698

A NEW TOOL FOR MOLECULAR PROFILING OF KRAS MUTATIONS IN TUMOR SAMPLES FROM PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA – BRINGING HOPE TO ENHANCE TREATMENT STRATEGIES

A.C. Bravo¹, B. Morão¹, A. Luz^{2,3}, B. Oliveira^{2,3}, R. Dourado^{2,3}, B. Costa^{2,3}, S. Saraiva¹, C. Fidalgo¹, L. Mascarenhas Lemos^{4,5,6}, M.P. Costa-Santos⁷, R. Maio^{1,4}, P. Viana Baptista^{2,3}, A. R. Fernandes^{2,3}, M. Cravo⁴

¹Hospital Beatriz Ângelo, Loures, Portugal, ²Associate Laboratory i4HB - Institute for Health and Bioeconomy, NOVA School of Science and Technology, NOVA University Lisbon, Caparica, Portugal, ³UCIBIO – Applied Molecular Biosciences Unit, Department of Life Sciences, NOVA School of Science and Technology, NOVA University Lisbon, Caparica, Portugal, ⁴Hospital da Luz, Lisbon, Portugal, ⁵NOVA Medical School, Universidade de Lisboa, Lisboa, Portugal, ⁶Faculdade de Medicina da Universidade Católica Portuguesa, Lisboa, Portugal, ⁷Hospital do Divino Espírito Santo, Ponta Delgada, Portugal

Contact E-Mail Address: catarina.bravoo@gmail.com

Introduction: Although there is growing interest on prognostic and therapeutic value of KRAS mutations detection in pancreatic ductal adenocarcinoma (PDAC) patients, the limited availability of sensitive, cost-effective and efficient molecular technologies has restricted its use. We present the fast single-step methodology utilizing amplification refractory mutation system (ARMS) coupled with high-resolution melting analysis (HRMA) to evaluate KRAS mutations and their prognostic value.

Aims & Methods: This is a prospective bicentric cohort study including PDAC patients with tumor samples collected at diagnosis. Codon-12/13 KRAS mutations were tested by Sanger Sequencing (SS) and the most frequent mutations were tested by ARMS/HRMA (G12D, G12V, G12R and G12C). Primary endpoint was the frequency of KRAS mutations by both techniques and their concordance. Secondary endpoints were the association of KRAS mutations and progression free survival (PFS) and overall survival (OS).

Results: 83 patients, 57% male, with median-age at diagnosis of 70 (IQR 63-75) years-old, 55% submitted to upfront-surgery, 45% to palliative-chemotherapy or best-supportive care were included. SS detected KRAS mutations in 67% of tumor samples (G12D=47%, G12V=30%, G12R=13%, G12C=4%, G13V=4%, G12A=2%) and ARMS/HRMA in 82% (G12D=48%, G12V=35%, G12R=10%, G12C=2%, G12V/G12D=3%, G12D/G12C=2%) with a moderate concordance in mutation detection ($\kappa=0.517$, $p<0.001$). Operated patients with G12C-mutated tumors had lower PFS (0 vs 8.5 months, HR=14.08 95%CI 1.435-138.207, $p=0.023$) and OS (0 vs 10 months, HR=11.49 95%CI 1.190-110.988, $p=0.035$) compared with wildtype tumors. No other differences were found in PFS and OS between KRAS-mutated and wildtype patients.

Conclusion: ARMS/HRMA appears to offer greater accuracy than SS in evaluating KRAS mutations in PDAC tumor samples, with the added benefits of speed and reduced costs. The presence of the G12C mutation was associated to lower OS and PFS, with early relapse after surgery. As such and with the recent emergence of drugs targeting G12C mutation (adagrasib), even resectable tumors might have indication for medical therapy, opening new avenues for personalized therapy in PDAC patients.

Disclosure: Nothing to disclose.

MP699

DETECTION OF PANCREATIC DUCTAL ADENOCARCINOMA FROM COMPUTED TOMOGRAPHY USING A CONVOLUTIONAL NEURAL NETWORK-BASED DEEP LEARNING MODEL

HS. Ahmed¹

¹Bangalore Medical College and Research Institute, Bangalore, India

Contact E-Mail Address: shafeeqahmed2002@gmail.com

Introduction: Pancreatic Ductal Adenocarcinoma (PDAC) is a highly aggressive and lethal malignancy of the pancreas due to limited treatment response and lack of early diagnosis. PDAC accounts for more than 90% of all pancreatic neoplasms and early PDAC may be missed on Computed Tomography (CT) scan due to similar attenuation as healthy pancreas, small size and hidden location.

Aims & Methods: The current study aims at improving detection of PDAC with CT scans using a deep learning model. It uses three different Convolutional Neural Network (CNN) models namely, Visual Geometry Group 19 (VGG19), Residual Neural Network 50 (ResNet-50) and Inception-v3. A compendium of 129,910 abdomen CT images (107 patients) of PDAC patients and 18,942 abdomen CT images (80 patients) of healthy controls were considered from The Cancer Imaging Archive. Additionally, several pre-processing and image augmentation methods were used to prevent overfitting and improve accuracies.

Results: The current model showed high construct validity with markedly lowered computational power. The Inception-v3 model showed the highest accuracy in the detection of PDAC with an accuracy of 97.93%. Specificity of the VGG-19 model was the highest at 98.77 whereas sensitivity was the highest for the Inception-v3 model at 98.75%. Data on the CNN models' Performance Metrics (accuracy, sensitivity, specificity and area under ROC) were all compared.

Conclusion: The deep learning enabled tool accurately detected PDAC on CT scans versus healthy controls. The models were also reasonably sensitive for tumours below 2 cm.

References: 1. Ushio J, Kanno A, Ikeda E, et al. Pancreatic Ductal Adenocarcinoma: Epidemiology and Risk Factors. *Diagnostics (Basel)*. 2021;11(3):562. doi:10.3390/diagnostics11030562

2. Qureshi TA, Gaddam S, Wachsman AM, et al. Predicting pancreatic ductal adenocarcinoma using artificial intelligence analysis of pre-diagnostic computed tomography images. *Cancer Biomark*. 2022;33(2):211-217. doi:10.3233/CBM-210273

3. Ahmed HS. BEYOND TRADITIONAL TOOLS: EXPLORING CONVOLUTIONAL NEURAL NETWORKS AS INNOVATIVE PROGNOSTIC MODELS IN PANCREATIC DUCTAL ADENOCARCINOMA. *Arq Gastroenterol*. 2024;61:e23107. doi:10.1590/S0004-2803.24612023-117

Disclosure: Nothing to disclose.

MP700

WITHDRAWN

Cholangitis and cholecystitis

14:30-15:30 / Poster Stage 4

MP701

TITLE: EOSINOPHILIC CHOLANGITIS: A SHEEP IN WOLF'S CLOTHING?

T. Ye¹

¹Colchester Hospital, Gastroenterology, Colchester, United Kingdom

Contact E-Mail Address: yetianren@gmail.com

Introduction: Eosinophilic cholangitis is a rarely-described cause of cholestasis whose cause, clinical features, natural history and prognosis is unclear. It is clinically important not least because it can be difficult to distinguish from serious pathologies, including cholangiocarcinoma, primary sclerosing cholangitis and IgG4-related cholangitis.

Aims & Methods: We describe the case of a patient who developed jaundice whilst awaiting surgery for Crohn's disease. Primary sclerosing cholangitis was suspected given the underlying inflammatory bowel disease, however the history was atypically short with recent normal liver blood tests. Despite an abnormal cholangiogram we proceeded to liver biopsy which showed eosinophilic cholangitis. The jaundice resolved rapidly on corticosteroid treatment. He was able to proceed to surgery and the disease has not recurred three years after cessation of corticosteroid treatment. We have reviewed the literature of this condition.

Results: 40 cases have now been described in the literature. Pain (24 cases), jaundice (18), fever (8) and weight loss (7) are the commonest presenting symptoms. The condition affects the intrahepatic ducts (17 cases), the extrahepatic ducts (31) and the gallbladder (18), with approximately equal frequency. Almost all cases follow a benign course, although many have undergone surgery. Most non-surgical cases have responded to corticosteroids. A few cases have received no treatment and have followed a benign course.

Conclusion: This is a rare condition which appears to be benign and may require no treatment. Its main clinical significance lies in its ability to mimic more serious conditions. Liver biopsy or cholangioscopy could be considered in cases of jaundice presenting with an abnormal history, peripheral eosinophilia, fever or diffuse gallbladder involvement. In some cases this will prevent unnecessary surgery.

Disclosure: Nothing to disclose.

MP702

OUTCOME OF A 'STEP-UP APPROACH' FOR RECURRENT CHOLANGITIS IN PATIENTS WITH A NON-STENOTIC HEPATICOJEJUNOSTOMY AFTER HEPATO-PANCREATO-BILIARY SURGERY: SINGLE CENTER SERIES

A.M. Bonomi¹, A. Overdevest², J.A. Fritzsche², O.R. Busch³, F. Daams⁴, G. Kazemier⁵, R.-J. Swijnenburg³, U. Beuers⁶, B.M. Zonderhuis⁴, R.L. van Wanrooij⁷, J.I. Erdmann³, R.P. Voermans⁸, M.G. Besselink³

¹University of Milan, Department of Surgery, Milan, Italy,

²Amsterdam UMC, location University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ³Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands, ⁴Amsterdam UMC, location Vrije Universiteit, Surgery, Amsterdam, Netherlands, ⁵Amsterdam UMC, location Vrije Universiteit, Amsterdam, Netherlands, ⁶Amsterdam UMC, location AMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁷Amsterdam UMC, location Vrije Universiteit, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁸Amsterdam UMC, location University of Amsterdam, Gastroenterology and hepatology, Amsterdam, Netherlands

Contact E-Mail Address: a.overdevest@amsterdamumc.nl

Introduction: Recurrent non-stenotic cholangitis (NSC) is a challenging and poorly understood complication of a surgical hepaticojejunostomy (HJ).¹ Optimal treatment remains unclear as etiology of NSC is unknown and large series are lacking.^{2,3,4}

Aims & Methods: This study aims to analyze a tertiary single center's experience in managing patients diagnosed with recurrent NSC in preparation for a future multicenter prospective study. A retrospective single center series including patients with recurrent NSC after surgery with HJ (2015-2022) was conducted. Patients with HJ stenosis were excluded. Primary outcome was resolution of NSC (i.e. free of NSC during six months). Secondary outcomes included reduction of NSC monthly episode frequency and secondary sclerosing cholangitis.

	Description	Patients (n)	Treatment options (n)	NSC resolution	Reduction in NSC frequency	Complications
First step	Short-course antibiotic therapy	50 (100%)	Empiric or targeted, less than two weeks	8 (16%)	9 (18%)	multidrug resistance 1 (2%)
Second step	Prolonged antibiotic therapy	26 (52%)	1. Rotating 6 - 8 weeks (n=21) 2. Continuous prophylaxis (n=3)	7 (14%)	6 (10%)	multidrug resistance 6 (33.3%) chronic kidney injury 2 (11.1%)
Third step	Surgery	7 (16%)	1. Conversion of Billroth 2 to Roux-en-Y (n=6)* 2. Lengthening of Roux-en-Y biliary loop (n=1)*	0	7 (14%)#	anastomotic leak 1 (14.3%)

*additional maneuvers were deemed necessary in three cases, namely revision of HJ (n=1) and resection of blind limb of the HJ (n=1)

#in three patients prolonged antibiotic therapy was maintained after surgery.

Results: Overall, 50 of 1179 (4.2%) patients with HJ developed NSC. Index surgery was mostly pancreatoduodenectomy (n=35, 70%). Treatment included a 'step-up approach' with short-course antibiotics (n=50, 100%), prolonged antibiotics (n=26, 52%), and revisional surgery (n=7, 14%). During a median follow-up of 42.5 months (IQR 23.5-60), patients experienced a median of 7 (IQR 4-9.2) recurrent NSC episodes, requiring hospitalization in 29 patients (58%). Resolution of NSC was achieved in

15 patients (30%) and reduction of NSC frequency in an additional 21 patients (42%). Concomitant ursodeoxycholic acid use and discontinuation of proton pump inhibitors was the only predictor for resolution (OR 4.229, $p=0.035$). Secondary sclerosing cholangitis occurred in 12 patients (24%) and was associated with the number of NSC episodes (OR 1.2, $p=0.050$).

Conclusion: A 'step-up approach' to recurrent NSC after HJ resulted in 30% resolution and further 42% reduced frequency of NSC although still a quarter of patients developed secondary sclerosing cholangitis. Future prospective studies should assess whether a protocolized approach could improve outcomes.

References: 1. Birgin E, Téoule P, Galata C, Rahbari NN, Reissfelder C. Cholangitis following biliary-enteric anastomosis: A systematic review and meta-analysis. *Pancreatology*. 2020 Jun;20(4):736-745. doi: 10.1016/j.pan.2020.04.017. Epub 2020 Apr 30. PMID: 32386969.

2. Overdevest AG, Fritzsche JA, Smit MAD, Besselink MG, Bonomi AM, Busch OR, Daams F, van Delden OM, Kazemier G, Langver J, Ponsioen CY, Swijnenburg RJ, van Wanrooij RLJ, Wielenga MCB, Zonderhuis BM, Zijlstra IAJ, Erdmann JI, Voermans RP. Recurrent cholangitis in patients with a non-stenotic hepaticojejunostomy: incidence and risk factors. *HPB (Oxford)*. 2024 Jan 7:S1365-182X(24)00003-0. doi: 10.1016/j.hpb.2024.01.003. PMID: 38245491.

3. van den Hazel SJ, Speelman P, Tytgat GN, van Leeuwen DJ. Successful treatment of recurrent cholangitis with antibiotic maintenance therapy. *Eur J Clin Microbiol Infect Dis*. 1994 Aug;13(8):662-5. doi: 10.1007/BF01973995. PMID: 7813499.

4. Matthews JB, Baer HU, Schweizer WP, Gertsch P, Carrel T, Blumgart LH. Recurrent cholangitis with and without anastomotic stricture after biliary-enteric bypass. *Arch Surg*. 1993 Mar;128(3):269-72. doi: 10.1001/archsurg.1993.01420150023004. PMID: 8442681.

Disclosure: Alessandro M. Bonomi, Anouk G. Overdevest, Jeska A. Fritzsche, Olivier R. Busch, Rutger-Jan Swijnenburg, Babs M. Zonderhuis, Ulrich Beuers and Joris I. Erdmann have no conflicts of interest or financial ties to disclose.

Freek Daams reports speaker fees, consultancy fees and research support from Medtronic, research support from Hak foundation outside of the current project.

Marc G. Besselink has received research support from Intuitive Surgery, Medtronic, Ethicon and acted as proctor for Intuitive Surgical.

Geert Kazemier reports research support and travel fees from SAS Analytics and research grants from KWF, ZonMw, Cancer Center Amsterdam Foundation, and Bennink Foundation outside the submitted research.

Roy L.J. van Wanrooij performed as a consultant for Boston Scientific.

Rogier P. Voermans reports research grants from Boston Scientific and Prion Medical, performed as a consultant for Boston Scientific and Cook Medical, and received speaker's fee from Mylan and Zambon.

All outside the submitted work.

MP703

DEVELOPMENT OF PREOPERATIVE ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE KIT FOR ACUTE CHOLECYSTITIS

T. Okuzono¹, S. Ito¹

¹Sendai Kousei Hospital, Department of Gastroenterology, Sendai, Japan

Contact E-Mail Address: okuzonotoru@gmail.com

Introduction: Laparoscopic cholecystectomy (LC) remains the standard treatment for acute cholecystitis; however, it is not always suitable for patients who are poor candidates for surgery. Moreover, the rate of complications is approximately 10-30% and the mortality rate is approximately 1-2 %, which is not low. Percutaneous transhepatic gallbladder drainage

(PTGBD) is recommended as conservative treatment, but the average hospital stay for PTGBD is considerably longer than that for LC especially in Japan. Recently, endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) has been reported as an alternative treatment for inoperable cholecystitis.

However, it has rarely been reported as a preoperative gallbladder drainage because the stent is commonly placed between the gallbladder and duodenum. We have developed an EUS-GBD kit for preoperative gallbladder drainage and have verified the function of it in live pigs for clinical introduction. This kit consists of anchors to fix between the gallbladder and stomach walls and the drainage tube.

Aims & Methods: The purpose of this study is to investigate the feasibility of LC after EUS-GBD with our novel drainage kit. Between May 2019 and March 2024, EUS-GBD with the novel drainage kit was performed on 52 live pigs. In twelve of them, LC was performed 2-9 weeks after EUS-GBD. We investigated the feasibility of LC, the rate of conversion to open cholecystectomy, and the complications.

Results: LC was successfully performed in all cases. In seven cases, the anchors and drainage tube were endoscopically removed just before LC. In five cases, they were not removed before LC, and the gallbladder was removed along with the fistula including a part of the stomach. In all cases, there were no conversion to open cholecystectomy and no complications.

Conclusion: Laparoscopic cholecystectomy after EUS-GBD using our novel drainage kit is feasible in live pigs, and we are currently verifying it through clinical trials involving humans.

Disclosure: I hold a 71% ownership stake in KOEDA Inc.

MP704

THE PRESENCE OF PULMONARY HYPERTENSION, OR COPD, INCREASES MORTALITY IN PATIENTS UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

J. John¹, C.J. Foster¹, L. Joo³, B. Blair³, N. Dasu², H. Suga³, Y. Khalid⁴, K. Dasu²

¹Jefferson Health NJ, Internal Medicine, Cherry Hill, United States of America,

²Jefferson Health NJ, Interventional Gastroenterology, Cherry Hill, United States of America,

³Jefferson Health NJ, Gastroenterology, Cherry Hill, United States of America, ⁴Beth Israel Lahey Hospital and Medical Center, Interventional Endoscopy/Gastroenterology, Burlington, United States of America, ⁵Geisinger Health System/ Wright Center for GME, Scranton, United States of America, ⁶Drexel University, Philadelphia, United States of America

Contact E-Mail Address: nrdsu4@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is a universally established therapeutic modality used by endoscopists to evaluate and treat numerous pancreato-biliary diseases. Few large-scale database studies evaluate risk factors that worsen outcomes in patients undergoing ERCP. In this study, we aim to estimate in-hospital outcomes of ERCP in patients from a nationally representative database.

Aims & Methods: We retrospectively analyzed the Nationwide Inpatient Sample (NIS) database for 2015-2019. Patients with a principal diagnosis of ERCP and a secondary diagnosis of certain cardiac or pulmonary diseases [non-ST-elevation myocardial infarction (NSTEMI), pulmonary hypertension (pulmonary HTN), COPD, lung cancer, and asthma] were identified using the ICD-10 codes. The NIS, a large publicly available all-payer inpatient care database in the USA, was queried from 2015 to 2019. Multivariate regression analysis was used to calculate the odds ratios of in-hospital mortality, the average length of hospital stay (LOS), and hospital charges (TOTHC) using STATA 17 MP.

Results: Our study identified approximately 1,088,175 patients undergoing ERCP. Of these patients, 15,950 patients died (1.47%). We identified certain risk factors causing worsened in-hospital outcomes in this patient population.

On multivariate analysis, in patients undergoing ERCP, a positive predictor of increased mortality was the presence NSTEMI (OR: 4.54, $p < 0.0001$, 95% CI: 2.64 - 7.80), pulmonary HTN (OR: 3.84, $p < 0.023$, 95% CI: 1.42 - 5.87), or COPD (OR: 1.32, $p < 0.024$, 95% CI: 1.04 - 1.67).

LOS was increased if patients had any of the following comorbidities: NSTEMI (+5.19 days, $p < 0.0001$, 95% CI: 3.39- 6.99), COPD (+1.75 days, $p < 0.0001$, 95% CI: 1.50-2.00), or lung cancer (+2.29 days, $p < 0.004$, 95% CI: 1.40 - 3.18).

TOTHC were increased in patients who had NSTEMI (\$92,791.01, $p < 0.0001$, 95% CI: \$60,523.12 - \$125,058.90), COPD (\$11,276.42, $p < 0.001$, 95% CI: \$6,687.48 - \$15,865.37) or asthma (\$9,619.18, $p < 0.010$, 95% CI: \$2,257.79 - \$16,980.58).

Conclusion: We found that mortality in patients undergoing ERCP is extremely low (1.47%). Positive predictors of mortality for those undergoing ERCP were NSTEMI, pulmonary HTN, and COPD. These comorbidities are essential as early identification and treatment before ERCP can lead to improved hospital outcomes. Future prospective and randomized controlled studies are required to reduce complications and improve outcomes of ERCP in these patient populations.

Disclosure: Nothing to disclose.

MP705

DEVELOPMENT AND VALIDATION OF A CLINICAL DECISION TOOL FOR PREDICTING LONG-TERM PAIN REDUCTION FOLLOWING CHOLECYSTECTOMY IN PATIENTS WITH SYMPTOMATIC CHOLECYSTOLITHIASIS

D.J. Comes¹, C.S. Latenstein¹, S. Bluiminck¹, J.D. van der Bilt², S.C. Donkervoort³, J. Heisterkamp⁴, V.B. Nieuwenhuijs⁵, J.M. Schreinemakers⁶, H.B. Stockmann⁷, B. Wiering⁸, J.P. Drenth⁹, C.J. Van Laarhoven¹, G. Hannink¹⁰, P. de Reuver¹

¹Radboud University Medical Centre, Surgery, Nijmegen, Netherlands, ²Flevoziekenhuis, Surgery, Almere, Netherlands, ³Onze Lieve Vrouwe Gasthuis, Surgery, Amsterdam, Netherlands, ⁴Elisabeth-Tweesteden Ziekenhuis, Surgery, Tilburg, Netherlands, ⁵Isala, Surgery, Zwolle, Netherlands, ⁶Amphia, Surgery, Breda, Netherlands, ⁷Spaarnse Gasthuis, Surgery, Hoofddorp, Netherlands, ⁸Slingeland, Surgery, Doetinchem, Netherlands, ⁹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁰Radboud University Medical Centre, Medical Imaging, Nijmegen, Netherlands

Contact E-Mail Address: stijn.bluiminck1@radboudumc.nl

Introduction: Laparoscopic cholecystectomy (LC) for symptomatic cholecystolithiasis is one of the most performed abdominal surgeries worldwide, with 700,000 procedures performed in the United States of America annually. (1)

However, postoperative outcomes are often mediocre, with 20-40% of patients experiencing persistent pain. (2-3)

This is primarily due to the absence of selection criteria for surgery. Internationally, the ROME III criteria are used; however, they are developed as a diagnostic measure for symptomatic cholecystolithiasis rather than a tool to predict surgical outcomes. (4)

A randomized trial comparing usual care with a restrictive, criteria-based strategy, utilizing the ROME III criteria, showed that abdominal pain persists in 40% of patients regardless of the study arm. (5) That the ROME criteria are insufficient to predict a pain-free state is at least partly attrib-

utable to the sole focus on pain characteristics with inattention to accompanying functional gastrointestinal disease (FGID). Coexistence of FGID is important to consider, as a recent trial showed that 30% of patients with symptomatic cholecystolithiasis meet the criteria for FGID, which is associated with a 2.5-fold increased risk of persistent pain post-cholecystectomy. (6) The poor outcome of LC, accompanying FGID, and the limited predictive value of the ROME criteria to reach a pain-free state, underline the need to develop a tool that aids the surgeon and gastroenterologist in deciding if a patient will benefit from surgery. (7) Therefore, this study presents the development and validation of a clinical decision tool to predict short- and long-term surgical outcomes and to select patients for cholecystectomy.

Aims & Methods: This study evaluates five-year follow-up data of 2 multicentre prospective trials. These studies included a total of 1561 patients diagnosed with symptomatic cholecystolithiasis in 25 hospitals. The primary aim was to develop a predictive model to predict clinically relevant pain reduction five years after cholecystectomy. The model development process included multivariable regression analysis, internal and external validation. Model performance on external validation was assessed through flexible calibration plots, C statistic and decision curve analysis. The TRIPOD guideline were followed.

Results: A total of 1240 of 1561 patients (79.4%) had undergone cholecystectomy at five-year follow-up. After surgery, 746 of 1240 patients (70.2%) reported a clinically relevant pain reduction. A multivariable model showed that male sex, increased VAS pain score at baseline, pain radiating to the back, nausea, and absence of obstipation, diarrhoea and postprandial bloating were independent predictors of clinical pain reduction after cholecystectomy. External validation indicated a good discrimination and calibration between patients with and without clinically relevant pain reduction (C statistic of 0.75; 95% CI, 0.70-0.79).

Conclusion: We developed and validated a model to predict the long-term clinical pain reduction following LC in patients with abdominal pain and gallstones. By adapting the SUCCESS criteria to predict the outcome of surgery, we can enhance the shared decision-making process, allow more tailored care to patients with FGID, reduce ineffective operations, and improve surgical outcomes. Based on our results we advocate for utilizing the ROME III criteria for diagnosing symptomatic cholecystolithiasis, while adopting the SUCCESS criteria for selecting patients for treatment.

References: 1. Lammert F, et al. Gallstones. *Nat Rev Dis Primers* 2016; 2:16024.

2. Wennmacker S, et al. Consistency of patient-reported outcomes after cholecystectomy and their implications on current surgical practice: a prospective multicenter cohort study. *Surg Endosc* 2017; 31: 215-24.

3. Thistle JL, et al. Factors that predict relief from upper abdominal pain after cholecystectomy. *Clin Gastroenterol Hepatol* 2011; 9: 891-96.

4. Thunnissen FM, et al. Patients with Clinically Suspected Gallstone Disease: A More Selective Ultrasound May Improve Treatment Related Outcomes. *J Clin Med*. 2023 Jun 20;12(12):4162.

5. van Dijk AH, et al. Restrictive strategy versus usual care for cholecystectomy in patients with gallstones and abdominal pain (SECURE): a multicentre, randomised, parallel-arm, non-inferiority trial. *Lancet* 2019; 393(10188):2322-2330.

6. de Jong JJ, et al. Functional Dyspepsia and Irritable Bowel Syndrome are Highly Prevalent in Patients With Gallstones and Are Negatively Associated With Outcomes After Cholecystectomy: A Prospective, Multicenter, Observational Study (PERFECT - Trial). *Ann Surg*. 2022 Jun 1;275(6):e766-e772.

7. Latenstein CSS, et al. SECURE trial collaborators. A Clinical Decision Tool for Selection of Patients With Symptomatic Cholelithiasis for Cholecystectomy Based on Reduction of Pain and a Pain-Free State Following Surgery. *JAMA Surg*. 2021 Oct 1;156(10):e213706.

Disclosure: Nothing to disclose.

MP707

CIRCULATING THROMBOSPONDIN-2 (TSP2): A SUPERIOR SERUM MARKER OF LIVER FIBROSIS AND PROGNOSIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

R. Surabattula^{1,2}, L.J Horst³, K. Füssel³, M. Sebode³, S.R. Myneni^{1,2}, A.W. Lohse³, C. Schramm^{3,4}, D. Schuppan^{1,2,5}
¹University Medical Center Mainz, Institute of Translational Immunology, Mainz, Germany, ²European Union Innovative Medicines Initiative 2 (IMI2) Joint Undertaking under grant agreement 777377, LITMUS (Liver Investigation: Testing Biomarker Utility in Steatohepatitis), Mainz, Germany, ³University Medical Centre Hamburg-Eppendorf, Department of Medicine, Hamburg, Germany, ⁴University Medical-Center Hamburg-Eppendorf, Martin-Zeit Center for Rare Diseases, Hamburg, Germany, ⁵Beth Israel Deaconess Medical Center, Harvard Medical School, Division of Gastroenterology, Boston, United States of America

Contact E-Mail Address: rasuraba@uni-mainz.de

Introduction: Primary sclerosing cholangitis (PSC) is still one of the most complex and least understood liver diseases. In contrast to other autoimmune diseases of the liver, no effective therapy is yet available. Furthermore, there is a lack of good biomarkers for the objective assessment of disease severity and fibrosis stage. Thrombospondin-2 (TSP2) is a matricellular protein with multiple functions in organ fibrosis, including TGFβ1 activation and angiogenesis. TSP2 expression is highly upregulated in active fibrogenesis, as shown in patients with fibrotic fatty liver disease, lung fibrosis and in a pilot intervention study in patients with primary sclerosing cholangitis (PSC). We therefore hypothesised that TSP2 may serve as a novel direct serum marker of fibrosis dynamics in PSC.

Aims & Methods: A sandwich ELISA assay measuring the C-terminal domain of TSP2 was established using the combination of recombinantly expressed protein, monoclonal and polyclonal antibodies. Sensitivity and specificity were optimized, with intra- and inter assay variations for serum or plasma below 10% and 15%, respectively. 142 subjects with PSC were selected from the biobank of the University Medical Centre Hamburg-Eppendorf and included in the study. Liver stiffness was measured by transient elastography (TE). In addition, parameters of disease activity and patient outcome were assessed.

Results: Baseline patient characteristics are displayed in Table 1. Serum TSP2 levels showed a strong positive correlation with stages of liver fibrosis, as determined by TE ($r=0.631$, $p<0.001$). Patients with F2-4 fibrosis displayed significantly higher levels of TSP2 compared with fibrosis F0-1 (144 vs 62.4 ng/ml). These differences were more pronounced comparing fibrosis F3-4 with F0-1 and F3-4 from F0-2 was 0.78 and 0.83, respectively, significantly superior to FIB-4 index (0.76) and APRI (0.77). Over a median follow-up of 70 months, 12.2% of patients underwent liver transplantation. In a Cox model adjusted for age, sex, PSC-associated colitis, ALT, ALP and BMI, TSP2 remained independently associated with transplant-free survival. Patients with baseline serum TSP2 levels indicating advanced fibrosis (≥ 73.1 ng/ml) had significantly reduced transplant-free survival (Log Rank $p<0.001$).

Conclusion: The matricellular fibrosis marker TSP2 was highly associated with the presence of advanced fibrosis and predicted transplant-free survival, suggesting its potential as a dynamic prognostic fibrosis marker and to monitor the effect of antifibrotic interventions for PSC. Confirmation of these findings in larger, prospective cohorts is on the way.

Disclosure: Nothing to disclose.

M. Hlavatý¹, O. Fabian², J. Brezina³, P. Wohl³, M. Cahova⁴, P. Drastich³, L. Bajer³
¹Ikem, Department of Hepatogastroenterology, Prague, Czech Republic, ²IKEM, Clinical and Transplant Pathology Centre, Prague, Czech Republic, ³IKEM, Department of Hepatogastroenterology, Prague, Czech Republic, ⁴IKEM, Experimental Medicine Centre, Prague, Czech Republic

Contact E-Mail Address: hltn@ikem.cz

Introduction: Recurrence of primary sclerosing cholangitis (rPSC) is a common long-term complication after liver transplantation (LT), which affect graft survival and overall patient survival. There are several lines of evidence indicating that dysregulation of the microbiome and intestinal barrier dysfunction are key etiologic factors in the pathogenesis of PSC.

Aims & Methods: The aim of this cross-sectional study was to evaluate serological markers of intestinal barrier permeability in patients with PSC after LT and in control group, to determine potential biomarkers for rPSC. The control group consisted of LT recipients for alcohol-related liver disease and/or hepatocellular carcinoma. The rPSC was assessed by MRCP and/or biopsies, all patients underwent colonoscopy. Serum levels of iFABP, Zonulin and Reg3a were evaluated. Non-parametric tests were used to for initial assessment. We further built generalized linear models for the prediction of PSC diagnosis independent of recurrence (Model_1), for the prediction of non-rPSC (Model_2) and for the prediction of rPSC (Model_3) using all three permeability markers, BMI and faecal calprotectin as predictors.

Results: A total of 113 patients were included in the study after LT for PSC and 69 controls. The clinical characteristics of the study participants are listed in Table 1. No significant difference in median of concentrations of Reg3a was found between the PSC group and control group ($p=0.01$). Interestingly, medians of concentrations of iFABP ($p<0.01$) and ($p<0.0001$) Zonulin were significantly higher in the control group in comparison with PSC group. The ROC AUC for Model_1 for prediction of PSC diagnosis per se was 0.79. The increased probability of PSC occurrence was associated with higher Reg3a serum concentration, while a negative relationship was found between the probability of PSC occurrence and BMI, zonulin and iFABP. Model_2, prediction of PSC without recurrence (non-rPSC), achieved slightly better performance, ROC AUC = 0.83, but the predictors and their coefficients and OR were close to Model_1. The ROC AUC for Model_3 predicting rPSC was 0.73. In contrast to previous models, BMI, Reg3A and iFABP were not significantly associated with rPSC, while both higher serum concentrations of zonulin and calprotectin increased the probability of PSC recurrence.

	control	PSC	p-value
n	69	113	
age (years)	61 (56; 65)	50 (44; 62)	< 0.0001
sex F/M	26/43	30/83	
BMI (kg.m ²)	27.5 (24.6; 30.9)	24.6 (22.3; 26.9)	< 0.0001
rPSC (n)	N/A	26	
DM (n)	28	22	n.s.
IBD (n)	0	100	
Retransplantation (n)	1	9	

Table 1. - Cohort characteristics.

Conclusion: Recurrence of PSC was positively associated with the intestinal permeability marker zonulin and the inflammatory marker calprotectin, while it was independent of BMI, iFABP and Reg3a.

Disclosure: Nothing to disclose.

MP709

IMPACT OF DOMINANT STRICTURE ON PROGNOSIS OF PAEDIATRIC-ONSET PRIMARY SCLEROSING CHOLANGITIS

A. Tenca¹, K.-L. Kolho², D. Consonni³, K. Jokelainen¹, M.A. Färkkilä¹

¹Helsinki University and Helsinki University Hospital HUS, Abdominal Center, Helsinki, Finland, ²Helsinki University and Children's Hospital, Department of Paediatric Gastroenterology, Helsinki University Hospital HUS, Helsinki, Finland, ³Epidemiology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Contact E-Mail Address: ante14@hotmail.it

Introduction: In adults with primary sclerosing cholangitis (PSC), dominant stricture (DS) develops in up to 50% of the patients (1) and is associated with an impaired long-term prognosis (2).

The impact of dominant stricture (DS) on the outcomes of paediatric-onset primary sclerosing cholangitis (PSC) is unknown.

Aims & Methods: This study was aimed at investigating the impact of DS on the clinical course and prognosis of patients with paediatric-onset PSC. We identified patients with paediatric-onset PSC diagnosed between January 1993 and May 2017 from Helsinki University Hospital records or our PSC registry. The diagnosis of PSC was made according to the EASL Clinical Practice Guidelines (3). DS was defined as a stricture with a diameter less than 1.5 mm in the common bile duct or less than 1 mm in the hepatic duct within 2 cm from the bifurcation (4).

Data including clinical (i.e., presence of inflammatory bowel disease (IBD), autoimmune hepatitis (AIH) and other autoimmune diseases), laboratory markers (i.e., bilirubin, alanine aminotransferase (ALT), gamma glutamyl-transferase (GGT), carbohydrate antigen 19-9, Ca 19-9) were collected. Endoscopic retrograde-cholangiography (ERC) images were scored for severity with the modified Amsterdam PSC-score). Therapeutic interventions (i.e., need of dilatation and stenting), and cytology (i.e., biliary dysplasia and aneuploidy) were collected.

The following outcomes were evaluated: biliary dysplasia, cirrhosis, liver transplantation (LT) (for all indications: decompensated cirrhosis, repeatedly confirmed biliary dysplasia and hepatocellular carcinoma), cholangiocarcinoma (CC), and/or PSC-related-death. Fisher's exact, Wilcoxon (Mann-Whitney) tests and the fitted univariate or multiple Cox regression models to calculate hazard ratios (HR) and 95% confidence intervals (CI), for selected variables were used. In these analyses, DS was treated as a time-varying variable.

Results: We traced 68 patients (42 males) with paediatric-onset PSC (median age at diagnosis 15 years). The median follow-up was 13 years and the median age at the last follow-up was 27 years. In total 35 (51%) had concomitant AIH. DS was diagnosed in 33 patients (48%): in eight at the time of PSC diagnosis (12%) and in 25 (37%) by the end of follow-up. DS appeared on a median of 3 years after PSC diagnosis; 20/33 patients (61%) were still ≤ 18 years at the last follow-up.

Out of 33 patients with DS, 21 (64%) needed dilatations and 11 (33%) stenting. In patients with DS, two developed cirrhosis, seven were transplanted and one patient was operated on for a biliary mass with low-grade dysplasia. In patients without a DS, two developed cirrhosis, and four were transplanted; one female was excluded from survival analysis because she already had cirrhosis at the time of PSC diagnosis.

Cirrhosis or biliary dysplasia or needing LT for these indications were more frequent after the development of DS (10/33, adjusted HR 4.26, 95%CI: 1.26-14.4). Also, one unit increase of log-GGT at the time of PSC diagnosis was associated with these outcomes (13/54 adjusted HR 1.78 for one unit increase of log-GGT, 95%CI: 1.04-3.05). Sex or age at PSC diagnosis, overlap with AIH, association with another autoimmune disease or IBD,

bilirubin, ALT, Ca 19-9, and modified Amsterdam PSC-score at PSC diagnosis were not associated with outcomes. No CC or death occurred during the follow-up.

Conclusion: DS was present at diagnosis or developed during follow-up in about half of the patients with paediatric-onset PSC and was associated with impaired outcomes.

References: 1. Björnsson E, Olsson R. Dominant strictures in patients with primary sclerosing cholangitis-revisited. *Am J Gastroenterol*. 2004;99(11):2281.

2. Stiehl A, Rudolph G, Klöters-Plachky P, Sauer P, Walker S. Development of dominant bile duct stenoses in patients with primary sclerosing cholangitis treated with ursodeoxycholic acid: outcome after endoscopic treatment. *J Hepatol*. 2002;36(2):151-6.

3. easloffice@easloffice.eu EAftSotLEa, Liver EAftSot. EASL Clinical Practice Guidelines on sclerosing cholangitis. *J Hepatol*. 2022;77(3):761-806.

4. Chapman MH, Webster GJ, Bannoo S, Johnson GJ, Wittmann J, Pereira SP. Cholangiocarcinoma and dominant strictures in patients with primary sclerosing cholangitis: a 25-year single-centre experience. *Eur J Gastroenterol Hepatol*. 2012;24(9):1051-8.

Disclosure: Nothing to disclose.

Barrett's oesophagus

14:30-15:30 / Poster Stage 5

MP710

L1 CAPSID PROTEIN EXPRESSION IN HUMAN PAPILLOMAVIRUS POSITIVE BARRETT'S METAPLASIA-DYSPLASIA-ADENOCARCINOMA LESIONS

D.I Vythilingam^{1,2}, S. Gautam¹, L.D Santos³, W. Xuan⁴, M. Rabiei^{1,5}, S. Rajendra^{1,5,6}

¹Ingham Institute for Applied Medical Research,

Gastro-Intestinal Viral Oncology Group, Sydney, Australia,

²St. Mary's Hospital, NHS England, Isle of Wight, United Kingdom,

³Liverpool Hospital, Anatomical Pathology, Sydney, Australia,

⁴Ingham Institute for Applied Medical Research, Department of

Medical Statistics, Sydney, Australia, ⁵University of New South

Wales, South Western Sydney Clinical School, Sydney, Australia,

⁶Bankstown-Lidcombe Hospital, Gastroenterology & Hepatology, Sydney, Australia

Contact E-Mail Address: divya.vythilingam@gmail.com

Introduction: High-risk human papillomavirus (hr-HPV) has been associated with a subset of Barrett's dysplasia (BD) and oesophageal adenocarcinoma (OAC).^{1,2,3,4} The L1 major capsid protein has been closely linked to disease regression and is a prognostic factor in HPV driven cancers of the cervix and anus.^{5,6} The progression of cervical intraepithelial neoplasia to invasive cancer is accompanied by a loss of viral L1 capsid protein expression.

Aims & Methods: Thus, in a retrospective, cross-sectional study, we investigated L1 protein expression in HPV-positive patients representing the oesophageal squamous (controls) [Group 1]-Barrett's metaplasia [Group 2]-low-grade dysplasia [Group 3]-high-grade dysplasia [Group 4]-adenocarcinoma [Group 5] sequence. L1 protein immuno-histochemical staining was correlated with p16 overexpression and E6/E7 mRNA in-situ hybridization. The association between the 5 patient groupings and L1 expression was analysed using the Chi-square test. Multivariable logistic regression was undertaken to investigate the above association with adjustment of potential confounders (age, gender, BMI, ever smoked and excess alcohol). Adjusted odds ratio (95% CI) was calculated.

Results: Of 116 HPV DNA-positive patients [(age range: 19-90, mean (SD), 63.2 (13.5)], 88 males and 28 females), 73 (62.9%) were genotype 16, 37 (31.9%) genotype 18 and 6 (5.2%) were genotype 6. L1 nuclear staining was observed in 64 individuals. L1 expression was detected in 84.9% (28/33) of controls; 94.1% (16/17) of BO patients; 50% (7/14) of LGD subjects; 38.1% (8/21) of HGD individuals and 16.1% (5/31) of OAC patients; [adjusted P < 0.0001]. Conversely, p16 was present in 9.1% (3/33) of controls, 17.7% of BO (3/17), 57.1% (8/14) in LGD individuals, 61.9% (13/21) of HGD patients and 64.5% (20/31) of OAC subjects [p<0.0001]. Corresponding figures for E6/E7 mRNA positivity was 6.1% (2/33), 23.5% (4/17), 28.6% (4/14), 38.1% (8/21) and 45.2% (14/31) respectively [p=0.008]. Expression of HPV-L1 and p16 or L1 and E6/E7 mRNA was largely mutually exclusive.

Conclusion: HPV L1 capsid expression is incrementally lost with increasing oesophageal disease severity as in viral driven anal and cervical lesions. Utility of L1 alone or in combination with p16/E6/E7 mRNA in stratifying HPV-positive oesophageal lesions for treatment should be further explored.

References: 1. Rajendra S, Wang B, Snow ET, et al. Transcriptionally active human papillomavirus is strongly associated with Barrett's dysplasia and esophageal adenocarcinoma. *Am J Gastroenterol* 2013;108:1082-1093. 2. Rajendra S, Yang T, Xuan W, et al. Active human papillomavirus involvement in Barrett's dysplasia and oesophageal adenocarcinoma is characterized by wild-type p53 and aberrations of the retinoblastoma protein pathway. *Int J Cancer*. 2017;141(10):2037-2049.

3. Li X, Gao C, Yang Y, et al. Systematic review with meta-analysis: the association between human papillomavirus infection and oesophageal cancer. *Aliment Pharmacol Ther*. 2014;39(3):270-281.

4. Rajendra, S., W. Xuan, N. Merrett, et al. Survival Rates for Patients With Barrett High-grade Dysplasia and Esophageal Adenocarcinoma With or Without Human Papillomavirus Infection. *JAMA Netw Open*. 2018; 1: e181054.

5. Choi YS, Kang WD, Kim SM, et al. Human papillomavirus L1 capsid protein and human papillomavirus type 16 as prognostic markers in cervical intraepithelial neoplasia 1. *Int J Gynecol Cancer* 2010;20(2):288-293.

6. Hernandez J, Elahi A, Siegel E, Coppola D, Riggs B, Shibata D. HPV L1 capsid protein detection and progression of anal squamous neoplasia *Am J Clin Pathol* 2011; 135: 436-41.

Disclosure: None.

MP711

THE ASSOCIATION BETWEEN OBESITY AND MALIGNANT PROGRESSION OF BARRETT'S OESOPHAGUS: A SYSTEMATIC REVIEW AND DOSE-RESPONSE META-ANALYSIS

M.T. Ko¹, T. Thomas², E. Holden¹, I. Beales³, L. Alexandre⁴

¹University Of East Anglia, Norwich, United Kingdom, ²Kennedy Institute of Rheumatology, University of Oxford, Oxford,

United Kingdom, ³Norfolk & Norwich University Hospital,

Gastroenterology, Norwich, United Kingdom, ⁴Norfolk and Norwich

University Hospital, Department of Gastroenterology, Norwich, United Kingdom

Contact E-Mail Address: miethuko3@gmail.com

Introduction: Barrett's oesophagus (BO) is the precursor to oesophageal adenocarcinoma (OAC), a malignancy with a poor overall prognosis. Endoscopic surveillance of patients with BO aims to detect dysplasia and OAC to improve long-term outcomes. However, the majority of patients with BO do not progress to cancer.^{1,2}

It is therefore important to establish the relevant clinical risk factors for malignant progression in this cohort to enable risk stratification and facilitate a personalised approach to management. While obesity is an independent risk factor for both BO and OAC,³⁻⁵ the role of obesity in the malignant progression of BO is unclear.

We undertook a systematic review and dose-response meta-analysis to estimate the association between obesity and malignant progression in patients with BO.

Aims & Methods: We searched MEDLINE and EMBASE databases via the OVID interface to December 2023. Studies which reported the effect of body mass index (BMI) on the progression of BO (no dysplasia or low-grade dysplasia [LGD] at baseline) to HGD or OAC were included. Two-stage dose-response meta-analysis was performed to estimate the association between BMI and malignant progression. Study quality was appraised using a modified Newcastle-Ottawa scale. The review was registered on PROSPERO (CRD42017051046).

Results: Twenty studies reported data on 38565 patients in total, of whom 1684 patients were diagnosed with HGD/OAC/OC. Each 5kg/m² increase in BMI was associated with a 4% increase in malignant progression to HGD or OAC (unadjusted OR 1.04; 95% CI 1.00 to 1.07; p<0.001; I² 57.2%). The association remained consistent after adjusting for potential confounders (adjusted OR 1.06; 95% CI 1.02 to 1.10; p<0.001; I² 0%). Nineteen studies were considered moderate to high quality.

Conclusion: Our meta-analysis suggests that obesity as measured by BMI is associated with malignant progression of BO with a dose-response relationship. The findings from our study are consistent with mechanistic evidence for the role of obesity in the pathogenesis of OAC. Future risk

prediction models could incorporate measures of obesity to potentially improve risk stratification in patients with BO. Weight loss might reduce the risk of malignant progression in patients with BO.

- References:** 1. Bhat S, Coleman HG, Yousef F, et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. *J Natl Cancer Inst* 2011;103:1049-57.
2. Hvid-Jensen F, Pedersen L, Drewes AM, et al. Incidence of adenocarcinoma among patients with Barrett's esophagus. *N Engl J Med* 2011;365:1375-83.
3. Kubo A, Cook MB, Shaheen NJ, et al. Sex-specific associations between body mass index, waist circumference and the risk of Barrett's esophagus: a pooled analysis from the international BEACON consortium. *Gut* 2013;62:1684-91.
4. Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet* 2008;371:569-78.
5. Corley DA, Kubo A, Zhao W. Abdominal obesity and the risk of esophageal and gastric cardia carcinomas. *Cancer Epidemiol Biomarkers Prev* 2008;17:352-8

Disclosure: Nothing to disclose.

MP712

EARLY DETECTION OF BARRETT'S OESOPHAGUS USING A SECRETORY PROTEIN BIOMARKER PANEL FROM A CAPSULE SPONGE

A. Ustaoglu¹, S. Pavagada¹, A. Bartram¹, M. di Pietro¹, R. Fitzgerald¹

¹Early Cancer Institute, University of Cambridge, Cambridge, United Kingdom

Contact E-Mail Address: au280@cam.ac.uk

Introduction: Early detection of oesophageal adenocarcinoma (OAC) will facilitate preventive treatment for a major public health priority. There are major efforts to devise better non-invasive tests for the precursor lesion of OAC which is defined by metaplastic transformation from the squamous oesophageal epithelium to intestinal metaplasia known as Barrett's esophagus (BO).

The minimally invasive non-endoscopic capsule sponge test collects cells from the lining of the oesophagus. The current laboratory assays rely on processing the cells retrieved from the device for pathology, immunohistochemistry or sequencing.

Aims & Methods: In this proof-of-concept study, we investigated the possibility of using the acellular portion of the sponge sampling to test for secretory protein biomarkers. These proteins are released from the cells collected by the sponge into the preservative fluid and we hypothesised they could be used for a more rapid diagnostic that does not rely on cytological pathology reports.

Biomarker candidates were selected from previously published bulk and single cell-RNA-sequencing (scRNA-seq) data^{1,2} based on their differential expression in BO compared to normal oesophagus and gastric cardia, and subsequent validation at protein level with immunohistochemical staining. Enzyme-linked immunosorbent assays (ELISA) were used to quantitatively detect trefoil factor-3 (TFF3) (Bio-Techne, #SPCKB-PS-000530, USA), regenerating family member 4 (REG4) (Biorbyt, orb180655, UK), Meprin A subunit alpha (MEP1a) (Abcam, ab26727), and serine peptidase inhibitor kazal type-4 (SPINK4) (Abxexa, abx528747) using manual sandwich-ELISA from capsule sponge supernatant samples.

Six different classification algorithms were tested to distinguish between BO and heartburn controls based on the cell-free protein quantification of protein biomarkers either used singly or in combination to maximise performance.

Results: Data from scRNA-seq analysis highlighted REG4, TFF3, SPINK4, and MEP1a as strong candidate biomarkers related to the characteristic BO goblet cells which are secretory in nature. TFF3 and REG4 were individually detected at a significantly higher concentration in BO sponge supernatants (n=56) compared to controls (n=53) ($p = <0.0001$, Mann-Whitney test). While the average TFF3 concentration for BO samples was 1.2 times higher (62.5ng/ml) compared to controls (33.1 ng/ml), the average concentration of REG4 in BO samples was 5.9 times higher (2.1 ng/ml) compared to heartburn (0.36 ng/ml). REG4 protein concentration positively correlated with Barrett's segment length ($p < 0.0001$, Spearman's correlation). A significant difference was also observed with SPINK4 in BO (n=34) compared to controls (n=38) ($p = 0.01$). Gaussian NB emerged as the best performing prediction model with a specificity of 0.94, sensitivity of 0.70 and area under the curve (AUC) of 0.86 when testing TFF3 and REG4 combined. Although MEP1a concentration could not significantly differentiate between BO and heartburn alone ($p = ns$), adding MEP1a as an additional marker to the TFF3/REG4 prediction model reached a AUROC of 0.85 ($p < 0.0001$, logistic regression).

Conclusion: A panel of secreted proteins in the Cytosponge supernatant has potential to serve as non-invasive biomarkers for earlier detection and risk stratification of patients with BO. Our initial findings warrant further validation studies to investigate the clinical utility of the capsule sponge supernatant.

References: 1 Jammula S, Katz-Summercorn A, Li X, et al. *Gastroenterology* (2020) 158(6):1682-1697

2 Nowicki-Osuch K, Zhuang L, Cheung TS, et al. *Cancer Discovery* (2023) 13(6):1346-1363

Disclosure: RCF is named on patents related to the Cytosponge-trefoil factor 3 test. Covidien GI Solutions (now Medtronic) licensed the Cytosponge from the Medical Research Council, and the device has now received the CE mark and is cleared by the US Food and Drug Administration. RCF is a shareholder in Cyted, a company working on early detection technology. MDP reports personal consultant fees from Medtronic, outside of the submitted work. The remaining authors have no conflicts of interest to declare.

MP713

CURRENT PREVALENCE AND RISK FACTORS OF BARRETT'S ESOPHAGUS IN TAIWAN- A PROSPECTIVE MULTICENTER STUDY

E.-J. Lee¹, C.-Y. Chang¹, M.-C. Tsai², M.-W. Wong³, C.-S. Chung⁴, P.-H. Tseng⁵, J.-Y. Wu⁶, H.-H. Yen⁷, Y.-N. Tsai⁸, M.-T. Hsieh⁹, J.-T. Lin¹⁰

¹Fu Jen Catholic University Hospital, Gastroenterology and Hepatology, New Taipei City, Taiwan, ²Chung Shan Medical University Hospital, Gastroenterology and Hepatology, Taichung, Taiwan, ³Hualien Tzu Chi Hospital, Division of Gastroenterology, Department of Internal Medicine, Hualien, Taiwan, ⁴Far Eastern Memorial Hospital, Division of Gastroenterology and Hepatology, Department of Internal Medicine, New Taipei City, Taiwan, ⁵National Taiwan University Hospital, Dept. of Internal Medicine, Taipei, Taiwan, ⁶Kaohsiung Medical University Chung-Ho Memorial Hospital, Gastroenterology, Kaohsiung, Taiwan, ⁷Changhua Christian Hospital, Gastroenterology, Changhua, Taiwan, ⁸E-Da Cancer Hospital, Gastroenterology and Hepatology, Kaohsiung, Taiwan, ⁹National Cheng Kung University Hospital, Department of Internal Medicine, Tainan, Taiwan, ¹⁰E-Da Hospital, Digestive Medicine Center, Kaohsiung City, Taiwan

Contact E-Mail Address: paul6130@gmail.com

Introduction: With the recent rise in the occurrence of esophageal adenocarcinoma (EAC) in Western nations, there is an escalating worry regarding Barrett's esophagus (BE). In contrast, Asian countries exhibit a low-

er prevalence of BE compared to their Western counterparts. Given the annual increase in chronic gastroesophageal reflux disease (GERD) cases, there is an expectation of a concurrent rise in the prevalence of BE. Consequently, we are embarking on a multicenter prospective study to assess the current prevalence of BE and pinpoint its risk factors in Taiwan.

Aims & Methods: Aim: to evaluate current prevalence and risk factors of Barrett's esophagus in Taiwan.

Methods: We carried out a prospective multicenter study involving consecutive outpatients who underwent upper gastrointestinal endoscopy for various upper gastrointestinal symptoms. Biopsies were taken from endoscopically suspected esophageal metaplasia (ESEM), clearly visible at least 1 cm above the gastroesophageal junction during endoscopy. The biopsy procedure involved obtaining standardized random samples, with four pieces taken every 2 cm from the four quarters of the esophagus exhibiting the ESEM lesion. BE was defined based on the histological confirmation of specialized intestinal metaplasia in the metaplastic esophageal epithelium.

Results: A total of 8925 subjects were enrolled in this study. The prevalence of BE was 2.6%. A total of 228 subjects with BE were detected among 751 ESEM subjects. Short segment BE (78.1 % , n = 178) was more prevalent than long segment BE (22.9 % , n = 50). The prevalence of GERD symptoms, erosive esophagitis (EE), and hiatal hernia (HH) was 52.5%, 27.3% and 7.85%, respectively. Multivariate analysis disclosed that old age [odds ratio (OR) = 1.59; 95% CI, 1.20-2.11; P < 0.01], male gender (OR = 2.27; 95%CI, 1.65-3.11; P < 0.01), alcohol consumption (OR = 1.70, 95%CI, 1.19-2.44; P< 0.01), GERD symptoms (OR = 1.45, 95%CI, 1.10-1.92; P< 0.01), EE (OR = 1.94, 95%CI, 1.47-2.56; P< 0.01) and presence of hiatal hernia (OR = 2.49; 95%CI, 1.78-3.47; P < 0.001) were significant risk factors predicting BE.

Risk factors for Barrett esophagus: multivariable analysis.

Characteristics	Odd ratio	95% CI	P
Male	2.27	1.65-3.11	< 0.01
Old Age (50y/o)	1.59	1.20-2.11	< 0.01
Body mass index			
<25	1	-	-
25-30	1.21	0.91-1.62	0.19
>30	1.30	0.84-2.01	0.24
Smoking_Ever	1.19	0.86-1.63	0.30
Alcohol	1.70	1.19-2.44	< 0.01
GERD symptoms	1.45	1.10-1.92	< 0.01
Reflux esophagitis	1.94	1.47-2.56	< 0.01
Hiatal hernia	2.49	1.78-3.47	< 0.01

Conclusion: The prevalence of BE was identified as 2.6%. Notably, advanced age (>50), male gender, alcohol consumption, symptoms of gastroesophageal reflux disease (GERD), erosive esophagitis, and the presence of hiatal hernia emerged as independently significant risk factors for Barrett's esophagus.

References: 1. Sharma P. Barrett Esophagus: A Review. *Jama*. 2022;328(7):663-71.
2. Marques de Sá I, et al. The global prevalence of Barrett's esophagus: A systematic review of the published literature. *United European Gastroenterol J*. 2020;8(9):1086-105.
3. Chang CY, et al. Current status of Barrett's esophagus research in Asia. *J Gastroenterol Hepatol*. 2011;26(2):240-6.
4. Shiota S, et al. Prevalence of Barrett's Esophagus in Asian Countries: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol*. 2015;13(11):1907-18.
5. Chang CY, et al. The application of Prague C and M criteria in the diagnosis of Barrett's esophagus in an ethnic Chinese population. *Am J Gastroenterol*. 2009;104(1):13-20.
6. Fock KM, et al. Asia-Pacific consensus on the management of gastro-oesophageal reflux disease: an update focusing on refractory reflux disease and Barrett's oesophagus. *Gut*. 2016;65(9):1402-15.

7. Eusebi LH, et al. Global prevalence of Barrett's oesophagus and oesophageal cancer in individuals with gastro-oesophageal reflux: a systematic review and meta-analysis. *Gut*. 2021;70(3):456-63.
8. Akiyama T, et al. Alcohol consumption is associated with an increased risk of erosive esophagitis and Barrett's epithelium in Japanese men. *BMC Gastroenterol*. 2008;8:58.
9. Andrici J, et al. Hiatal hernia and the risk of Barrett's esophagus. *J Gastroenterol Hepatol*. 2013;28(3):415-31.

Disclosure: Nothing to disclose.

MP714

EFFICACY AND SAFETY OF HYBRID ARGON PLASMA COAGULATION TECHNIQUE IN PATIENTS WITH BARRETT'S ESOPHAGUS-RELATED DYSPHASIA: A MULTICENTER ITALIAN PROSPECTIVE STUDY

R. Maselli¹, D. Massimi¹, M. Menini¹, A. Capogreco¹, A. D'Aprano^{1,1}, R. De Sire¹, R. Nicoletti¹, F. Coppola², M.A. La Terra², G. Andrisani³, F.M. Di Matteo³, S. Pecere⁴, C. Spada⁵, P.A. Galtieri⁶, C. Hassan¹, A. Repici¹
¹IRCCS Humanitas Research Hospital, Dept. of Gastroenterology, Rozzano, Italy, ²San Giovanni Bosco ASL TO2, Dipt. of Gastroenterology, Torino, Italy, ³Complesso Integrato Columbus, Catholic University, Dept. of Gastroenterology, Rome, Italy, ⁴Catholic University of Rome, Gemelli Hospital, Gastroenterology and Digestive Endoscopy Unit, Roma, Italy, ⁵Catholic University Rome - Digestive Endoscopy unit, Catholic University Rome; Rome/IT, Digestive Endoscopy unit, Rome, Italy, ⁶IRCCS humanitas Research Hospital, Dept. of Gastroenterology, Rozzano, Italy

Contact E-Mail Address: roberta.maselli@hunimed.eu

Introduction: Radiofrequency Ablation is the gold standard for ablating neoplastic Barrett Esophagus (BE). Hybrid argon plasma coagulation (H-APC) is a novel technique involving submucosal fluid injection before Argon Plasma Coagulation. We aim to assess its efficacy, safety, and tolerability.

Aims & Methods: We prospectively enrolled patients undergoing H-APC ablation at 4 Italian Hospitals in a multicenter observational study. Included were patients with histopathologically confirmed LGD, HGD, or residual BE after endoscopic resection of visible lesions, and who had not undergone previous ablative treatment. Complete eradication of intestinal metaplasia (CE-IM) and dysplasia (CE-D) were confirmed by biopsy samples from the neo-epithelium. Pain and dysphagia scores within 7 days post-ablation were evaluated by phone by the local investigator.

Results: Among the 61 enrolled patients (mean age 61.05 years, 85.3% males, mean C length 0.52 cm, mean M length 2.36 cm), 45.9% (28/61) had prior endoscopic resection of visible lesions, with adenocarcinoma being the most common worst histology (48.3%). Of the 51 patients who completed treatment sessions until April 2024, all of them achieved complete eradication of intestinal metaplasia by April 2024, with an average of 1.51 (S.D 0.83) sessions. 92 hybrid-APC sessions were performed without major complications, except for one case of post-ablation electrocoagulation syndrome. Mean pain score was 1.38/10 (S.D 2.1), mean dysphagia score was 1.3/5 (S.D. 0.6).

Conclusion: The Hybrid-APC technique shows robust efficacy and safety, with good tolerability in achieving initial CE-D and CE-IM. Definitive evidence of its effectiveness awaits prospective randomized comparative trials.

Disclosure: Nothing to disclose.

MP715

OVERCOMING IMAGE QUALITY HETEROGENEITY FOR COMPUTER AIDED DETECTION OF BARRETT'S NEOPLASIA

M.R. Jong¹, T. Jaspers², C. Kusters², J. Jukema¹, R. van Eijck van Heslinga¹, K. Fockens¹, T. Boers², J. van der Putten², F. van der Sommen², P. de With², J. de Groof¹, J.J. Bergman¹, BONSAI-Consortium
¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Technische Universiteit Eindhoven, Electrical Engineering, Eindhoven, Netherlands

Contact E-Mail Address: r.a.h.vaneijckvanheslinga@amsterdamumc.nl

Introduction: Artificial intelligence (AI) systems in endoscopy are predominantly developed in expert centers using high-quality images and may not perform as expected in community hospitals due to the heterogeneity of image quality. This can be attributed to the tendency of AI systems to perform well on familiar data but deteriorate quickly on data that slightly deviates from the training set. This phenomenon can be referred to as 'domain shift'.

Aims & Methods: This study aimed to evaluate the performance drop of a computer-aided detection (CADE) system for Barrett's neoplasia when exposed to the diverse imaging conditions found in community hospitals and assess various training strategies to mitigate this decline of performance. First, a CADE system was developed using a high-quality training set collected by experts, consisting of 437 images from 173 neoplastic Barrett's patients and 574 images from 200 non-dysplastic Barrett's esophagus patients. Classification performance was tested on three test sets comprising different levels of image quality (high, moderate, and low). These quality levels represented the image quality heterogeneity of community hospitals. Each test set included 120 images from a the same cohort of 65 neoplastic and 55 non-dysplastic Barrett's patients. We then applied three training strategies to improve the CADE systems robustness to image quality variability: 1) additional training data comprising lower quality images; 2) domain-specific pretraining; and 3) adjustments to the architecture of the CADE system.

Results: The CADE system trained solely on high-quality data scored an AUC of 83% on the high-quality test set, which significantly decreased to 80% (p=0.0039) and 71% (p=0.0001) on the moderate and low-quality sets, respectively. Implementation of the robustness-enhancing strategies significantly improved AUC scores on all test sets to 92% for high-quality (p=0.0039), 93% for moderate-quality (p=0.0006), and 85% for low-quality images (p=0.0001). These methods also significantly reduced the performance decline on moderate (+1% vs -3%; p=0.0043) and low-quality test sets (-7% vs -12%; p=0.0163).

Test Set	Metric	Conventional CADE system	Robust CADE system	P-value
High-Quality	AUC	83%	92%	0.0039
Moderate-Quality	AUC	80%	93%	0.0006
	AUC loss	-3%	+1%	0.0043
Low-Quality	AUC	71%	85%	0.0001
	AUC loss	-12%	-7%	0.0163

Conclusion: CADE systems developed solely on high-quality training images acquired by experts may not be as effective when deployed in community hospitals due to image quality heterogeneity. Adopting robustness enhancing techniques can limit performance loss caused by this domain shift.

References: 1. Finlayson SG, Subbaswamy A, Singh K, Bowers J, Kupke A, Zittrain J, et al. The Clinician and Dataset Shift in Artificial Intelligence. *New England Journal of Medicine*. 2021.

Disclosure: Nothing to disclose.

MP716

THE ADDED DIAGNOSTIC VALUE OF AN ON-THERAPY 24H PH-IMPEDANCE MONITORING IN ASYMPTOMATIC PATIENTS WITH BARRETT ESOPHAGUS.

M. Pesce¹, A. Cefaliello¹, M.M. Sannino¹, M. Pagliaro¹, M. Ricchiuti¹, F. Maione¹, R. Maione¹, A. Chini¹, G.D. De Palma¹, G. Sarnelli¹
¹Univers. of Naples "Federico II", Dept. Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: mapesc@hotmail.com

Introduction: Barrett Esophagus (BE) is a pre-cancerous esophageal condition caused by chronic uncontrolled gastro-esophageal reflux disease (GERD). The goal of Proton Pump Inhibitors (PPIs) therapy in BE patients is to effectively achieve symptoms control. However, BE patient tend to be asymptomatic or to under-report acid-related symptoms. Furthermore, previous evidence in Literature showed that optimal control of esophageal acid exposure, as objectively assessed by an on-therapy 24h pH-impedance monitoring (24h MII-pH) is able to decrease COX-2 expression in esophageal biopsy of BE patients [1].

In spite of that, to date, current guidelines [2] suggest the use of a standard dose once daily PPI for chemoprevention in BE patients and do not advise for evaluating the effectiveness of therapy, by means of an on-therapy 24h MII-pH.

Aims & Methods: This is a prospective study involving consecutive BE patients referred to our tertiary center. The diagnosis of non-dysplastic BE was confirmed in all patients through endoscopic and histological assessment by a single experienced endoscopist. After the endoscopy, patients were prescribed therapy with full dose PPIs (either esomeprazole or pantoprazole 40 mg b.i.d.). After one month of PPI therapy, a high-resolution manometry (HRM) and on-therapy 24h MII-pH were performed. GERD refractory patients without BE matched for age, gender and therapy (drug and dose) were used as controls. Data are expressed as mean±SD.

Results: Twenty-five BE patients (16 M, 49±18 years) were enrolled. Fourteen BE patients showed a pathological 24h MII-pH compared to only 4 patients with refractory GERD (56 vs 16%; p=0.001). In both populations, the gastric acid exposure time was sub-optimally controlled by PPI therapy (44±24% vs 50±26% in BE and GERD patients; p=NS).

In BE patients, however, total and upright esophageal Acid Exposure Time (AET) were significantly higher and reached pathological values as compared to refractory GERD patients (8.4±11.1% vs 2±3% and 6±6.5% vs 1.7±2.1%, both p<0.01). Total distal and acid refluxes were not significantly different between the two groups (52±30 vs 38±22 and 32±29 vs 21±16, p=NS).

Nonetheless, when comparing the duration of the longest reflux episode, BE patients showed significantly longer reflux episodes compared to refractory GERD (33.7±41.4 vs 8.3±12.4 minutes, p=0.02) and more ineffective esophageal swallows at HRM (49±42% vs 18±25%; p=0.006).

Conclusion: In our hands, more than half of asymptomatic BE patients show persistently abnormal AET despite PPI therapy. This could be explained by prolonged reflux episodes and a worsened esophageal clearance and motility compared to GERD patients, despite the similar gastric acid exposure time and number of acid refluxes.

In BE patients, we found a consistent risk of underestimating the esophageal acid burden by simply relying on patients' symptoms. Although, further larger studies are needed to validate our results, an on-therapy 24h MII-pH could guide the choice of the most adequate acid-suppressive therapy, by objectively measuring AET values.

References: 1- de Bortoli N, Martinucci I, Piaggi P, et al. Randomised clinical trial: twice daily esomeprazole 40 mg vs. pantoprazole 40 mg in Barrett's oesophagus for 1 year. *Aliment Pharmacol Ther*. 2011;33(9):1019-1027. doi:10.1111/j.1365-2036.2011.04616.x

2- Weusten BLAM, Bisschops R, Dinis-Ribeiro M, et al. Diagnosis and management of Barrett esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2023;55(12):1124-1146. doi:10.1055/a-2176-2440

Disclosure: Nothing to disclose.

MP717

EVALUATION OF AN IMPROVED COMPUTER AIDED DETECTION SYSTEM FOR BARRETT’S NEOPLASIA ON REAL-WORLD IMAGING CONDITIONS

R. van Eijck van Heslinga¹, M.R. Jong¹, C. Kusters², T. Boers², J. van der Putten², L. Duits¹, R.E. Pouw¹, B.L. Weusten³, M. Houben⁴, A. Alkhalaf⁵, F. van der Sommen², P. de With², J. de Groof¹, J.J. Bergman¹, Bonsai Consortium

¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Technische Universiteit Eindhoven, Electrical Engineering, Eindhoven, Netherlands, ³St Antonius Hospital, Departement of Gastroenterology and Hepatology, Nieuwegein, Netherlands, ⁴HagaTeaching Hospital, Gastroenterology, The Hague, Netherlands, ⁵Isala Dept. of Gastroenterology, Dept. of Gastroenterology, Groningen, Netherlands

Contact E-Mail Address: r.a.h.vaneijckvanheslinga@amsterdamumc.nl

Introduction: Computer Aided Detection (CAdE) systems may improve detection of (pre-)malignant lesions by endoscopists. Most CAdE systems are developed using homogeneous datasets collected by experts, which do not represent the heterogeneous imaging conditions of daily clinical practice. Such heterogeneity is caused by endoscopist-dependent variation (e.g. skill and experience) as well as endoscopist-independent variation (e.g. endoscopy equipment). Recently, we presented a CAdE system for Barrett’s neoplasia¹. However, all training and test data originated from expert centers.

Aims & Methods: We aimed to develop an updated CAdE system (CAdE 2.0) demonstrating more robustness to the varied imaging conditions found in routine patient care. Our previously published CAdE system (CAdE 1.0) was trained and internally validated on a high-quality dataset originating from 15 expert centers. The dataset included 6.337 neoplastic (1.362 patients) and 7.695 non-dysplastic images (1.139 patients). The updated CAdE system (CAdE 2.0) underwent four improvements. First, we included more heterogeneous training data from our training set patient population. We extracted video frames from videos comprising various quality artefacts (e.g. blurred lenses or insufficient mucosal cleaning). Second, we applied advanced data augmentation methods to address the diversity of post-processing enhancement settings used by modern endoscopy systems. Third, we updated the CAdE system with a Vision Transformer architecture², which has shown to improve performance on lower quality endoscopic images³. Finally, we transitioned our pretraining approach from semi-supervised to a self-supervised learning framework⁴. Both CAdE systems were evaluated using three prospectively collected, independent test sets. The first test set represented the true diversity and complexity encountered in daily clinical practice. This dataset comprised all videos captured from all included patients in five referral centers between April 2022 and January 2024 (431 ten-second BE videos from 115 patients). The second test set focused on endoscopist-dependent variation. It included three paired subsets with high, moderate and low-quality images from 122 patients. Quality was determined by factors such as esophageal expansion and mucosal cleaning. The third test set addressed endoscopist-independent variation. It contained 16 paired subsets of 396 images (122 patients). Every subset was based on a different post-processing enhancement setting of the endoscopy system.

Results: For test set 1, CAdE 1.0 reached a sensitivity and specificity of 84% and 73%. CAdE 2.0 scored 93% and 76%. For test set 2, CAdE 2.0 reached higher sensitivity and specificity scores on high-quality images compared to CAdE 1.0. In addition, CAdE 2.0 performance loss on moderate and low-quality images was smaller. On test set 3 CAdE 1.0 scores substantially varied depending on the test sets enhancement setting (82-94% sensitivity, 52-83% specificity). Variation of CAdE 2.0 was limited to 91-95% and 81-88%.

Test Set	Metric	CAdE 1.0	CAdE 2.0
Test set 1: Video Performance	Sensitivity	84%	93%
	Specificity	73%	76%
Test set 2: High Quality Images	Sensitivity	93%	96%
	Specificity	68%	85%
Test set 2: Moderate Quality Images	Sensitivity (loss)	76% (-17%)	85% (-11%)
	Specificity (loss)	69% (+1%)	87% (+2%)
Test set 2: Low Quality Images	Sensitivity (loss)	61% (-32%)	72% (-24%)
	Specificity (loss)	76% (+8%)	90% (+5%)
Test set 3: Enhancement Setting	Sensitivity range (min-max)	12% (82-94)	4% (91-95)
	Specificity range (min-max)	31% (52-83)	8% (81-88)

Table 1. Results of CAdE 1.0 and CAdE 2.0

Conclusion: The updated CAdE system displayed improved performance for detection of Barrett’s neoplasia in videos. More importantly, this CAdE system also displayed less performance loss when exposed to lower image quality and less performance variability when confronted with differing post-processing enhancement settings.

References: 1. Fockens N, Jong MR, Jukema JB, Pouw RE, Duits LC, Van Munster SN, et al. A deep learning system for detection of early Barrett’s neoplasia: a model development and validation study. *The Lancet Digit Health*. 2023;5:905-21.

2. Yu W, Si C, Zhou P, Luo M, Zhou Y, Feng J, et al. MetaFormer Baselines for Vision2022 October 01, 2022:[arXiv:2210.13452 p.]. Available from: <https://ui.adsabs.harvard.edu/abs/2022arXiv221013452Y>.

3. Kusters CHJ, Boers TGW, Jaspers TJM, Jukema JB, Jong MR, Fockens KN, et al., editors. CNNs vs. Transformers: Performance and Robustness in Endoscopic Image Analysis. *Applications of Medical Artificial Intelligence*; 2024 2024//; Cham: Springer Nature Switzerland.

4. Caron M, Touvron H, Misra I, Jégou H, Mairal J, Bojanowski P, et al. Emerging Properties in Self-Supervised Vision Transformers2021 April 01, 2021:[arXiv:2104.14294 p.]. Available from: <https://ui.adsabs.harvard.edu/abs/2021arXiv210414294C>.

Disclosure: Nothing to disclose.

MP718

IMPACT OF COVID-19 ON ADHERENCE TO BARRETT'S ESOPHAGUS ENDOSCOPIC SURVEILLANCE INTERVALS AND OUTCOMES IN A DISTRICT GENERAL HOSPITAL

I.M. Gianfrancesco¹, A.A. Schumacher¹, M. di Pietro², T. Das³, I. Amin³, A.V. Hadjinicolaou², W.K. Tan²

¹University of Cambridge, School of Clinical Medicine, Cambridge, United Kingdom, ²University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom, ³Peterborough City Hospital, North West Anglia Foundation Trust, Department of Gastroenterology, Peterborough, United Kingdom

Contact E-Mail Address: img31@cam.ac.uk

Introduction: Barrett's esophagus (BE) is a known precursor to esophageal adenocarcinoma (EAC). As such, endoscopic surveillance of non-dysplastic BE (NDBE) is recommended for the detection of dysplastic disease. COVID-19 significantly impacted endoscopic services in the UK, including the surveillance of patients with BE.

Here, we aim to investigate the impact of COVID-19 on adherence to recommended endoscopic surveillance intervals and outcomes associated with BE.

Aims & Methods: We performed a retrospective analysis of all patients undergoing BE surveillance between January 2012 and March 2024 at a district general hospital in the UK. Patients were eligible if they had NDBE with at least 2 pre-COVID-19 endoscopies (i.e. both endoscopies pre-2020) and 1 post-pandemic endoscopy (i.e., 2020 onwards).

The primary outcome was the proportion of participants who experienced a delay between surveillance endoscopies comparing pre-COVID endoscopies (pre-2020) versus endoscopies affected by COVID (i.e., 1 pre-2020 and 1 post-2020 endoscopy).

Delayed endoscopy was defined as an endoscopy outside of recommended intervals (>3 years + 3 months for BE maximum (M) length ≥3cm and >5 years + 3 months for M<3cm). Secondary outcomes were:

- 1) progression rates of NDBE to high-grade dysplasia (HGD)/cancer,
- 2) progression of NDBE to any dysplasia, and;
- 3) factors predictive of dysplastic progression.

Progressors were defined as progression >12 months from baseline endoscopy. Invasive cancer was defined as cancer stage ≥T2.

Results: 453 patients were included in the analyses. 8.61% (21/244) of pre-COVID-19 endoscopies (i.e., both endoscopies pre-2020) were outside surveillance intervals, compared to 20.6% (89/432) of endoscopies affected by COVID (Chi-square p<0.0001). 61 patients progressed: 67.2% low-grade dysplasia (LGD) (41/61), 21.3% HGD (13/61), 3.28% intramucosal carcinoma (IMC) (2/61), and 8.2% invasive cancer (5/61).

Among progressors, 29.5% (18/61) had an surveillance endoscopy outside surveillance intervals, compared to 19.1% (71/371) of non-progressors, though this did not reach significance (Chi-square p=0.06). Of the 5 invasive cancer cases, there were 3 deaths, with one linked to a C9M10 BE with a 4.1-year interval between pre- and post-COVID endoscopies.

The other EAC patients, T3N2M1 (palliative treatment) and T2N0M0 (scheduled for esophagectomy), remain alive at last follow-up. The proportion of EAC-related deaths among all EAC diagnoses (including IMC) was 42.9% (3/7).

Progression rates for NDBE to HGD/cancer, and to any dysplasia were 0.90% per-patient year, and 2.74% per-patient year, respectively. Factors predictive of NDBE progression included age (per 1-year increase; OR 1.03, 95% CI 1.01-1.06), male sex (OR 2.03, 95% CI 1.08-4.13), BE circumferential (C) length (OR 1.17, 95% CI 1.07-1.27) and M length (OR 1.20, 95% CI 1.09-1.31) (Table 1).

Patient characteristics	Progressors (n=61)	Non-progressors (n=392)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p-value	OR (95% CI)	p-value
Age; mean (SD)	71.6 (8.7)	67.5 (12.0)	1.03 (1.01 - 1.06)	0.012	1.03 (1.00 - 1.05)	0.051
Sex; n (%)				0.037		0.034
Females	12 (19.7)	130 (33.2)	Ref		Ref	
Males	49 (80.3)	262 (66.8)	2.03 (1.08 - 4.13)		2.06 (1.10 - 4.30)	
C length (cm); median (IQR)	3.0 (5.0)	1.0 (3.0)	1.17 (1.07 - 1.27)	0.0005	1.03 (0.85 - 1.26)	0.73
M length (cm); median (IQR)	5.0 (5.0)	3.0 (3.0)	1.20 (1.09 - 1.31)	<0.0001	1.15 (0.93 - 1.40)	0.23
Number with delayed post-COVID endoscopy; n (%)	18 (29.5)	74 (19.8)	1.76 (0.94 - 3.20)	0.068	1.67 (0.87 - 3.10)	0.12

Table 1: Demographics of patients undergoing BE surveillance and factors predictive of progression.

Conclusion: The COVID-19 pandemic significantly curtailed endoscopic surveillance of patients with BE where 21% of endoscopies were delayed, compared to 9% pre-COVID. Such delays may have contributed to the increased rates of progression to dysplasia, as well as the EAC-related deaths reported in our cohort.

Disclosure: Nothing to disclose.

MP719

PATHWAY-SPECIFIC PERSULFIDATION OF PROTEINS AND GASEOUS MEDIATORS-SIGNALING CONTRIBUTE TO THE PATHOGENESIS AND PREVENTION OF BARRETT'S ESOPHAGUS

E. Korbut¹, M. Wierdak², T. Vignane³, K. Magierowska¹, V.T. Janmaat⁴, D. Bakalarz^{1,5}, M. Whiteman⁶, M. Kukla⁷, R. Smits⁴, R. Souza⁸, M. Filipovic³, M. Magierowski¹

¹Jagiellonian University Medical College, Department of Physiology, Cracow, Poland, ²Jagiellonian University of Cracow, 2nd Department of Surgery, Cracow, Poland, ³Leibniz-Institut für Analytische Wissenschaften-ISAS e.V. Dortmund, Dortmund, Germany, ⁴Erasmus MC, Gastroenterology & Hepatology, Rotterdam, Netherlands, ⁵Institute of Forensic Research, Department of Forensic Toxicology, Cracow, Poland, ⁶University of Exeter, Exeter, United Kingdom, ⁷Jagiellonian University Medical College, Department of Internal Medicine and Geriatrics, Kraków, Poland, ⁸Baylor University Medical Center, Center for Esophageal Research, Dallas, United States of America

Contact E-Mail Address: edyta.korbut@uj.edu.pl

Introduction: Persulfidation of proteins (PSSH) appears functionally significant, e.g. in aging, preventing cellular oxidation, but its role in GI diseases remains clinically elusive. This posttranslational proteins modification relies on endogenous hydrogen sulfide (H₂S) signaling. GERD induces oxidation in esophageal squamous cells. However, the contribution of persulfidation and H₂S bioavailability in etiology, diagnosis or treatment of Barrett's esophagus (BE) is unknown. We hypothesized that GERD-induced pathway-specific PSSH impairments underlie BE pathogenesis. We explored whether restoration/depletion of esophageal H₂S impacts persulfidation-sensitive, BE-associated targets and BE development.

Aims & Methods: We clinically performed a wide-scale analysis of persulfidated proteins (normalized to total proteins levels) in three-sets of endoscopic biopsies representing BE or squamous segments +/- GERD (n=4-5 each), using the recent chemoproteomic method. We used the microsurgical rat model of GERD/BE (esophago-gastroduodenal anastomosis) +/- i.g. pharmacological treatments to up-/downregulate esophageal H₂S levels over 10 weeks. In parallel, we employed in vitro model of chronic GERD +/- H₂S donors using human esophageal squamous cell lines with (NES-G2T) or without (EPC2) clinical GERD and a Barrett's cells (BAR-T). CRISPR-Cas9 was used to knockout H₂S-producing enzymes.

Results: Global persulfidation level (reflecting H₂S bioavailability) was decreased in clinical BE vs GERD-exposed squamous biopsies. GERD induced statistically significant pathway-specific PSSH changes of ≈90 proteins in squamous segments compared to patients w/o GERD. These persulfidomic alterations further increased in BE where >900 targets were deregulated. IL-1b, prostaglandin (PG)E₂ pathways or mTOR-associated proteins, but not exclusively, showed persulfidation shift (e.g. PSSH fall of IL-1b-receptor antagonist (IL-1RA)). H₂S-decrease was noted in vitro or in vivo after long-term GERD in rats with chronic esophageal lesions and in human squamous, but not BAR-T cells. In cells and/or rats, treatment with NaSH or GYY4137 to restore H₂S induced IL-1RA and inhibited IL-1b/PGE₂/mTOR signaling, RNA oxidation, limiting molecular or morphological BE development. H₂S-enzymes inactivation promoted BE-related events in both models.

Conclusion: BE is preceded by GERD-induced, pathway-specific persulfidation shifts, initiated early in squamous epithelium and enhanced in metaplasia. Decreased but stable biosynthesis of H₂S reflects the adaptive resistance of the metaplastic cells to GERD. Restored H₂S signaling counteracts BE development by interfering in oxidative balance and BE-associated IL-1β, PGE₂ and mTOR pathways activation. These findings suggest that BE is a mechanistic outcome of reduced esophageal H₂S caused by GERD. [Funding: National Science Centre (Poland): 2016/23/D/NZ4/01913, 2019/33/B/NZ4/00616, 2023/07/X/NZ4/01052]

Disclosure: Nothing to disclose.

Upper functional GI disorders: From basic to clinical

14:30-15:30 / Poster Stage 6

MP720

IN VIVO IMAGING OF THE ENTERIC NERVOUS SYSTEM USING PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY IN PARKINSON'S DISEASE

S. Schoch¹, A. Mittelstädt¹, A. Kluge², E. Schäffer³, D. Berg³, F. Cossais², M. Ellrichmann¹

¹University Hospital Schleswig-Holstein, Interdisciplinary Endoscopy, Medical Department 1, Kiel, Germany, ²Christian-Albrechts-University Kiel, Institute of Anatomy, Kiel, Germany, ³University Hospital Schleswig-Holstein, Department of Neurology, Kiel, Germany

Contact E-Mail Address: stephan.schoch@uksh.de

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder. Prior to the manifestation of the motor-symptom of bradykinesia, non-motor symptoms like constipation frequently occur in the prodromal stadium (pPD). Therefore, involvement of the gastrointestinal (GI) tract, especially alterations of the enteric nervous system (ENS), in the pathogenesis can be assumed. Studying the GI tract with its ENS became the focus of research due to its good accessibility. Probe-based confocal laser-endomicroscopy (pCLE) allows to visualize structures of the GI tract in 1000-fold magnification. Therefore, pCLE seems to be a promising approach in the visualization of the ENS in vivo.

Aims & Methods: Aim: Visualization of the ENS by pCLE to create an imaging biomarker for the severity of PD in vivo compared to healthy controls (HC).

Patients with manifest PD and HC undergoing screening colonoscopy were included in this prospective trial. After removal of the mucosal surface with large biopsy forceps, label-free in vivo pCLE (Coloflex, Cellvizio) was performed in the rectum to visualize the ENS in vivo. Observation of neuronal structures in the submucosal plexus was performed with the help of tissue specific autofluorescence (AF). The specific AF was quantified per field of view and assigned to corresponding neuronal structures - small nerve fibre strands, big nerve fibre strands (NFS) and nerve cell bodies (NCB) (impressing as "cotton-balls"). To reliably compare our findings, we performed a direct comparison between conventional immunohistology and ex vivo pCLE. The results of in vivo pCLE were finally correlated to the severity of clinical symptoms.

Results: 28 patients with PD and 15 healthy controls were included in this prospective trial. Age and sex distribution did not exhibit statistical differences. In PD we could observe a higher tissue AF in images with small NFS (AF_{PD}=2848±1889; AF_{HC}=972±811; p=0.007), with big NFS (AF_{PD}=22217±1940; AF_{HC}=687±702; p=0.008) and a larger diameter of nerve cell bodies ("cotton balls") in PD patients (Diameter_{PD}=8.2±1.9µm; Diameter_{HC}=6.7±0.6µm; p=0.04). The total number of small nerves and ganglions in both groups did not differ (ns). Of note, a strong positive correlation of age and increasing accumulation of AF was observed in both groups (p=0.02). Specific morphological distinctions were not noticed. ENS phenotypes showed a strong correlation with clinical manifestation of symptoms (p=0.002).

Conclusion: Label-free pCLE allows reliable in vivo imaging of the ENS in vivo and differentiate between NFS and NCB. Patients with PD have increased AF of submucosal nerve components in comparison to HC. Furthermore, the severity of PD symptoms significantly correlates with increasing AF of ENS in the rectum and can therefore be used as an imaging biomarker for PD that potentially allows for diagnosis of pPD.

Disclosure: Nothing to disclose.

MP721

STRETCH-INDUCED REGULATION OF CXCL-1 EXPRESSION

J. Kola¹, K. Uray², T. Docsa²

¹University of Debrecen, Molecular Medicine, Debrecen, Hungary,

²University of Debrecen, Medical Chemistry, Debrecen, Hungary

Contact E-Mail Address: baffin.kola@med.unideb.hu

Introduction: Ileus, a slowing or halting of intestinal motility, develops in trauma, critically ill, and surgical patients, resulting in prolonged hospital and ICU stays, increased infectious complications, and more hospital readmissions. Inflammatory insult to the gastrointestinal smooth muscle is frequently brought on by direct manipulation of the intestines during surgery, but can also be caused by systemic inflammation, which activates mast cells and macrophages and increases the production of inflammatory cytokines. We have demonstrated that the chemokine (C-X-C motif) ligand 1 (CXCL1), which inhibits intestinal motility, is enhanced in rodent ileus models and in the blood of trauma patients who develop ileus. P21-activated kinase (PAK) 1, which is elevated in response to mechanical stretch, has also been connected to the emergence of ileus.

Aims & Methods: In this study, we focused on the relationship between mechanotransduction, CXCL1, and PAK1. We utilized both an organ bath system and cyclical stretch of cell models via a Flex cell apparatus to study the role of mechanotransduction. Both human intestinal smooth muscle cells (hiSMCs) and macrophages were subjected to physiological (control cyclical stretch, CCS) and pathological (edema cyclical stretch, ECS, as experienced during edema development or ileus) stretch. The role of NF- κ B, which has been shown to regulate CXCL1 expression, was investigated. Intestinal tissue samples from wildtype and PAK1 knockout mice were also stretched in the presence or absence of IPA-3, a PAK1 inhibitor, and IMD-5304, an NF- κ B inhibitor. The expression and secretion of CXCL-1 in intestinal smooth muscle cells and macrophages were determined by ELISA and RT-qPCR.

Results: In response to the induction of ileus (via gut manipulation), CXCL1 expression was increased in wild-type mice but not PAK1 knockout mice. PAK1 inhibition did not attenuate the inhibitory effects of CXCL1 on intestinal motility; however, the inhibitory effects of CXCL1 were partially inhibited in PAK1 knockout mice. Mechanical stretch increased CXCL1 in the media of macrophages and human intestinal smooth muscle cells. PAK1 inhibition did not prevent the increased CXCL1 secretion in human intestinal smooth muscle cells. NF- κ B activation was increased in response to increased stretch, and NF- κ B inhibition prevented stretch-induced increase in CXCL1 secretion.

Conclusion: We conclude that during the development of edema and/or ileus, pathological strain can stimulate CXCL1 release from both intestinal smooth muscle cells and macrophages. However, inhibition of NF- κ B, but not PAK1, prevents stretch-induced CXCL1 secretion.

References: Asgeirsson, T., El-Badawi, K. I., Mahmood, A., Barletta, J., Luchtefeld, M., & Senagore, A. J. (2010). Postoperative Ileus: It Costs More Than You Expect. *Journal of the American College of Surgeons*, 210(2), 228–231. <https://doi.org/10.1016/j.jamcollsurg.2009.09.028>

Chu, J., Pham, N. T., Olate, N., Kisilitsyna, K., Day, M. C., LeTourneau, P. A., Kotss, A., Stewart, R. H., Laine, G. A., Cox, C. S., & Uray, K. (2013). Biphasic regulation of myosin light chain phosphorylation by p21-activated kinase modulates intestinal smooth muscle contractility. *Journal of Biological Chemistry*, 288(2), 1200–1213. <https://doi.org/10.1074/JBC.M112.370718>

Docsa, T., Bhattarai, D., Sipos, A., Wade, C. E., Cox, C. S., & Uray, K. (2020). CXCL1 is upregulated during the development of ileus resulting in decreased intestinal contractile activity. *Neurogastroenterology & Motility*, 32(3), e13757. <https://doi.org/10.1111/NMO.13757>

Joshi, V., Strege, P. R., Farrugia, G., & Beyder, A. (2021). Mechanotransduction in gastrointestinal smooth muscle cells: Role of mechanosensitive ion

channels. *American Journal of Physiology - Gastrointestinal and Liver Physiology*, 320(5), G897–G906. <https://doi.org/10.1152/AJPGI.00481.2020/ASSET/IMAGES/MEDIUM/GI-00481-2020R01.PNG>

Rychter, J., & Clavé, P. (2013). Intestinal inflammation in postoperative ileus: pathogenesis and therapeutic targets. *Gut*, 62(11), 1534–1535. <https://doi.org/10.1136/gutjnl-2012-304176>

Disclosure: Nothing to disclose.

MP722

ENDOSCOPIC MANAGEMENT OF DELAYED GASTRIC CONDUIT EMPTYING AFTER ESOPHAGECTOMY IN A TERTIARY REFERRAL CENTER: COMPARISON BETWEEN DIFFERENT ENDOSCOPIC PROCEDURES

G. Dell'Anna^{1,2}, F.V. Mandarino¹, J. Fanizza¹, E. Fasulo¹, A. Barchi¹, F. Azzolini¹, L. Fanti¹, E. Viale¹, D. Esposito¹, M.C. Verga¹, M. Napolitano¹, S. Battaglia³, F. Puccetti³, U. Elmore³, L. Fuccio⁴, V. Annesse², R. Rosati³, S. Danese¹

¹IRCCS San Raffaele Scientific Institute and University, Gastroenterology and Gastrointestinal Endoscopy Unit, Milan, Italy, ²IRCCS Policlinico San Donato, Gastroenterology and Gastrointestinal Endoscopy Unit, San Donato Milanese, Italy, ³IRCCS San Raffaele Scientific Institute and University, Gastrointestinal Surgery Unit, Milan, Italy, ⁴S.Orsola-Malpighi University Hospital, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: g.dellanna93@gmail.com

Introduction: Delayed Gastric Conduit Emptying (DGCE) after Esophagectomy with a gastric conduit is a complication that occurs in 15-39% of patients. It is associated with short and long-term complications and with a poor quality of life. Intra-Pyloric Injection of Botulinum Toxin (BT), Pyloric Pneumatic Dilation (PD), and a combination of these two techniques (BTPD) in the same session, represent the main endoscopic procedures, but comparative data are currently unavailable.

Aims & Methods: Retrospectively analyzed prospectively collected data on all consecutive patients with DGCE after esophagectomy, refractory to prokinetics drugs and treated endoscopically. with BT, PD, or BTPD from January 2014 to November 2023 in San Raffaele Hospital (Milan). International Society Disease of the Esophagus (ISDE) Diagnostic Criteria were used for DGCE diagnosis and classification. Gastric Outlet Obstruction Score (GOOS) was used for clinical staging at diagnosis and at discharge. All patients undergoing BT received 100 UI of toxin, while those undergoing PD were dilated with the same model of pneumatic balloon, progressively inflated from 18 to 20mm, and left in site for one minute for every different size. BTPD underwent BT and BD during the same procedure. Technical success (TS) was defined as the completion of the procedure, clinical success (CS) as the resolution of symptoms/resumption of feeding (soft solid, GOOS 2) at discharge or expanding dietary intake at any rate, without the need to replace the nasogastric tube. Recurrence was defined as symptom relapse after more than 15 days of well-being requiring endoscopic or surgical intervention. Adverse events (AEs) were classified using the AGREE classification.

Results: 64 patients (81.2% male, ASA II 54.7%, 90.6% Ivor-Lewis esophagectomy, 77.4% adenocarcinoma), median age 62 years (IR 55-70), were enrolled: 18 (28.1%) in the BT group, 24 (37.5%) in the PD group and 22 (34.4%) in the BTPD group. No statistically significant differences were found in the baseline characteristics among the three groups and in indication, disease stage, neoadjuvant treatments, type of surgery with/without intraoperative pyloric surgical procedures, other surgical complications, and median follow-up. Despite identical TS success (100%), BTPD group exhibited a higher CS rate (100%) compared to the PD and BTPD

groups (p=0.02). Among patients who achieved CS, BT group showed a higher recurrence rate (23.1%) compared to the other two groups but not statistically different (p=0.41). Kaplan-Meier dysfunction analysis revealed that the BTPD group was characterized by both a significantly shorter median time to refeeding of 1 day (IR 1-1) compared to the other two groups (log-rank test p=0.0049), and a shorter median time to discharge of 1 day (IR 1-4) (log-rank test p=0.02). No AEs procedures related were recorded.

Conclusion: Endoscopic management of DGCE is challenging and BT and PD represent the main available treatments. Our study shows that the same session combination approach (BTPD) could offer patients a higher rate of clinical efficacy and a shorter time to refeed and to be discharged, maintaining an equivalent safety profile. Further prospective studies are needed to validate these findings.

Disclosure: Nothing to disclose.

MP723

THE DIFFICULT-TO-DIGEST DILEMMA OF CATEGORIZING POSTPRANDIAL EPIGASTRIC PAIN

C. Van de Bruaene¹, F. Carbone², K. Van den Houte², B. Broeders¹, E. Colomier², M.P. Jones³, T. Vanuytsel¹, J. Tack¹
¹Katholieke Universiteit Leuven / Universitaire Ziekenhuizen Leuven Campus Gasthuisberg, Translational Research Center for Gastrointestinal Disorders, Department of Neurogastroenterology and Motility, Leuven, Belgium, ²Katholieke Universiteit Leuven, Translational Research Center for Gastrointestinal Disorders, Department of Neurogastroenterology and Motility, Leuven, Belgium, ³Macquarie University, Psychology, North Ryde, Australia

Contact E-Mail Address: cedric.vandebuaene@kuleuven.be

Introduction: According to the Rome criteria, functional dyspepsia (FD) is subdivided into postprandial distress syndrome (PDS), with meal-related symptoms (i.e. early satiation or postprandial fullness) and epigastric pain syndrome (EPS), with meal-unrelated symptoms (i.e. epigastric pain and/or burning). However, currently available research has not addressed to what extent epigastric pain is truly meal-unrelated.

Aims & Methods: Aim: To assess the relationship of epigastric pain to ingestion of a meal, using a systematic approach in four independent, prospectively collected FD databases.

Methods: For this purpose both secondary & tertiary care Rome IV positive FD patients were included, originating from an open-access endoscopy cohort of 223 FD patients, an outpatient clinic cohort of 265 FD patients, and an international dataset consisting of 1080 DGBI patients (of which 483 FD) from 16 centers (9 European/7 Asian). All patients completed an extended Rome questionnaire, based on recall data, including questions on meal-related symptom occurrence. Furthermore 498 tertiary care patients, who underwent a standard gastric emptying breath test (GEBT) meal with simultaneous registration of perceived symptoms were evaluated for FD symptoms, based on a Likert score of 0-4 (with 0=absent, 4=unbearable and 2=bothersome/clinically relevant threshold), identifying 366 FD patients. In total, 1337 FD patients were included. Questions regarding the relationship of epigastric pain to meal intake allowed categorizing patients as having postprandial epigastric pain (pEPS), meal-unrelated epigastric pain (murEPS), and PDS symptoms with or without postprandial epigastric pain. The different cohorts were compared with respect to demographics and symptom profile, using Chi-square and Mann-Whitney U tests. P-value <0.05 is considered significant.

Results: Distribution for PDS/EPS/overlap was 896/252/186. Postprandial epigastric pain in the absence of PDS symptoms, i.e. pEPS, was present in about 40% of EPS patients, while 60% had murEPS. Postprandial epi-

gastric pain was present in about 50% of PDS patients. The proportion of patients with overlapping PDS and murEPS accounted for about 14% of patients. Patient demographics (age, sex and BMI) were similar for pEPS, murEPS, and PDS patients with and without postprandial pain. In two datasets, pEPS was associated with significantly higher heartburn scores, as compared to PDS without postprandial pain. However, PDS patients with postprandial pain had more associated symptoms compared to pEPS, murEPS, or PDS without postprandial epigastric pain (table). They also scored significantly higher for epigastric pain during the GEBT, when compared to murEPS or pEPS (p<0.05).

	pEPS	murEPS	PDS without postprandial pain	PDS with postprandial pain	P
1: Endoscopy cohort					
# patients, N	17	28	80	71	
Bloating, N/total (%)	11/16 (68.8) ^a	10/26 (38.5) ^{b,c}	56/75 (74.7) ^{b,d}	64/70 (91.4) ^{b,c,d}	<0.001
Heartburn, N/total (%) [*]	8/11 (72.7) ^a	11/21 (52.4)	23/62 (37.1) ^{a,b}	35/64 (54.7) ^b	0.075
2: Outpatient clinic cohort					
# patients, N	9	16	82	118	
Bloating, N/total (%)	5/9 (55.6) ^a	8/15 (53.3) ^b	61/79 (77.2)	102/117 (87.2) ^{a,b}	0.003
Heartburn, N/total (%)	6/9 (66.7) ^a	8/16 (50.0)	20/77 (26.0) ^{a,b}	48/113 (42.5) ^b	0.020
3: International cohort					
# patients, N	44	89	181	106	
Bloating, N/total (%)	14/44 (31.8)	27/89 (30.3)	70/181 (38.7)	39/106 (36.8)	0.541
Heartburn, N/total (%)	13/44 (29.5)	32/89 (36.0) ^a	34/181 (18.8) ^{a,b}	43/106 (40.6) ^b	<0.001
4: GEBT cohort					
# patients, N	29	20	117	141	
Bloating, N/total (%)	3/28 (10.7) ^{a,b}	4/20 (20.0) ^{c,d}	73/117 (62.4) ^{b,c,e}	116/141 (82.3) ^{b,d,e}	<0.001

Table. Symptom patterns across newly defined functional dyspepsia categories
PDS, postprandial distress syndrome; pEPS, postprandial epigastric pain syndrome; murEPS, meal-unrelated epigastric pain syndrome; GEBT, gastric emptying breath test. ^{*}Missing data in symptom reporting. Values with a same superscript highlighting statistically significant differences per row.

Conclusion: In contrast to earlier characterisation of EPS symptoms as being purely meal-unrelated, four large, independent datasets identified the existence of a relevant patient cohort with postprandial epigastric pain in the absence of PDS symptoms. Further research is needed to better understand the underlying pathophysiology, and the response to treatment compared to meal-unrelated epigastric pain.

Disclosure: Speaker fee from the Rome Foundation
Speaker fee from Mayo.

MP724

FRUCTOSE MALABSORPTION IN PATIENTS WITH FUNCTIONAL BLOATING: FREQUENCY AND PREDICTORS

K. Mehta¹, A. Ahuja¹, S. Sachdeva², A. Kulandaivelu², A. Dalal², A. Kumar², A. Puri²
¹Maulana Azad Medical College, New Delhi, India, ²GB pant Hospital, Gastroenterology, New Delhi, India

Contact E-Mail Address: kartikmht0@gmail.com

Introduction: Functional bloating, a common gastrointestinal symptom marked by stomach discomfort and excessive gas production, presents a substantial problem for patients and healthcare practitioners. Fructose malabsorption is one of the main causes of functional bloating among the many other variables. When fructose is not well absorbed, it ferments in the colon, causing bloating and discomfort. The study examines the relationship between functional bloating and fructose malabsorption, emphasizing the significance of this relationship for diagnosis and treatment. Comprehending this correlation is crucial for executing focused measures to mitigate symptoms and enhance the well-being of impacted persons.

Aims & Methods: Aim: To study the frequency of fructose malabsorption in patients with functional bloating and its comparison to that in healthy controls.

Methods: We included 70 patients with functional bloating satisfying ROME III criteria and 35 healthy controls. Both the groups initially underwent a Glucose Hydrogen breath test (GHBT) to exclude Small intestinal bacterial overgrowth (SIBO). Subsequently, both groups underwent a fructose hydrogen breath test (FHBT) to assess for fructose malabsorption. 25 g of fructose in 250 ml of water was used. Breath hydrogen & methane concentrations were noted at baseline & every 15 min after administration of fructose for a total of 3 h. Persistent rise in breath hydrogen or methane > 20 ppm above basal was considered diagnostic of fructose malabsorption. Symptoms experienced during the test were noted.

Results: In our study, 20/70 (29%) patients with functional bloating had evidence of fructose malabsorption compared to 1/35 (3%) healthy controls ($P=0.01$). 51/105 (48%) participants in our study had symptoms during FHBT. 16/21 (76%) participants with positive FHBT had concomitant symptoms. Symptoms (suggestive of fructose intolerance) without the presence of malabsorption, occurred in 42% (35/84) of participants in our study. In univariate analysis, predictors of fructose malabsorption in patients with functional bloating were younger age, female gender, Bristol score >4, symptoms of epigastric discomfort, and mucus in stools ($P<0.05$). There was no

significant difference among patients with FM and those without FM for diet, duration of symptoms, severity of bloating, recent PPI usage, use of promotility drugs, or BMI ($P=0.26$, $P=0.69$, $P=0.20$, $P=0.07$, $P=0.24$ and $P=0.25$ respectively). However, in the multivariate analysis, only female gender was significantly associated with a positive FHBT ($P=0.02$).

Conclusion: More than 1/4th of patients with functional bloating in our study had evidence of fructose malabsorption compared to healthy controls and this subset of patients with functional bloating might benefit from dietary restriction of fructose.

Disclosure: Nothing to disclose.

MP725

CYCLICAL VOMITING SYNDROME: OPIOIDS OUT, TRICYCLIC ANTIDEPRESSANTS IN

M. Butt¹, F. Cefalo¹, C. Sbarigia¹, M. Corsetti¹

¹University of Nottingham, Nottinghamshire, United Kingdom

Contact E-Mail Address: cate.sbarigia@gmail.com

Introduction: The proportion of patients who take opioid based analgesics and cannabis has not been studied in a large cohort of patients with cyclical vomiting syndrome (CVS) in the UK. It is also unclear whether the efficacy of prophylactic tricyclic antidepressants (TCAs) is impacted by ongoing opioid or cannabis use.

Aims & Methods: (A) To study the burden of opioid and cannabis use in patients with CVS.

(B) To study the clinical response to prophylactic TCA and whether this was augmented by opioid/cannabis intake.

Clinical characteristics and healthcare outcomes of patients diagnosed with ROME IV CVS in a single neurogastroenterology clinic between January 2016 to December 2023 were retrospectively collected. A standardised clinic template was used to collect data relating to age, sex, gastrointestinal symptoms, medication usage, and patient-reported response to TCA. Patients commenced 10mg TCA for 60 days which was up titrated by 10 mg at each routine outpatient consultation (unless poorly tolerated) until clinical remission was achieved or the maximum dose (50 mg daily) was prescribed. Clinical remission was defined as the absence of stereotypical episodes of vomiting for at least 6 months prior to the last clinic consultation.

Results: 95 patients (male 21%, mean age 30.8 ± 11.8 years) were identified and 84 (88%) were seen on at least two or more occasions with a median duration of follow-up of 22 (IQR: 5, 39) months. The treatment outcomes for all patients treated with TCA are outlined in Table 1. At the initial consultation, 35 (37%) and 16 (17%) patients took prescribed opioid analgesics and cannabis, respectively. All were provided with drug cessation advice and were prescribed a TCA: only 12/35 (34%) and 11/16 (69%) of patients adhered to drug cessation advice. On follow-up, 100% of patients who adhered to recommendations to stop opioids and cannabis responded to TCA whilst 0% of patients who continued to take opioids/cannabis responded to TCA. Illicit drugs were found at urine drug screening in 5 patients who failed to respond to TCA (cocaine $n=2$ and heroin $n=3$).

Tricyclic antidepressant	n (%)	Final dose	Clinical response	Other comments
Amitriptyline	65 (68.4%)	20 (IQR 10, 30) mg	28 (43%)	Not tolerated at lowest dose in 10/65 (15.3%)
Nortriptyline	26 (27.3%)	30 (IQR 10, 40) mg	9 (34.6%)	Not tolerated at lowest dose in 3/26 (11.5%)

Table 1. Response to tricyclic antidepressants.

Conclusion: This is the first UK study reporting the impact of opioid usage and illicit drugs in patients with CVS. TCAs are useful in treating CVS patients providing they do not consume prescribed opioids or illicit drugs.

Disclosure: Nothing to disclose.

MP726

WITHDRAWN

MP727

PREDICTORS OF EOSINOPHILIC ESOPHAGITIS IN PATIENTS WITH DYSPHAGIA AND NORMAL ENDOSCOPY

F. Ovidi¹, P. Visaggi¹, I. Solinas¹, E. Marciano², J.M. Dunn³, T. Wong³, E.V. Savarino⁴, N. de Bortoli¹, S.S. Zeki³

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²Azienda Ospedaliero Universitaria Pisana, Endoscopy Unit, Pisa, Italy, ³St Thomas' Hospital, Gastroenterology, London, United Kingdom, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Endoscopy abnormalities of eosinophilic esophagitis (EoE) are currently graded based on the EoE endoscopic reference score (EREFS) ranging 0 to 9. Research has shown that esophageal biopsies are often omitted in Europe in patients reporting dysphagia when the upper endoscopy (EGD) shows no abnormalities [1].

However, a proportion of patients with eosinophilic esophagitis (EoE) may have normal endoscopy (i.e., EREFS=0), making the diagnosis more difficult and increasing the risk of diagnostic delay.

Aims & Methods: We investigated predictors of a diagnosis of EoE when the EGD is unremarkable (i.e., EREFS=0). Consecutive adult patients (≥ 18 years) with dysphagia who had EREFS=0 at an EGD with six esophageal biopsies were prospectively enrolled. All patients underwent EGD while off any eosinophil-depleting treatment. EoE with EREFS=0 was diagnosed based on the presence of at least 15 eosinophils/high-power field in at least one of six esophageal biopsies. When all six esophageal biopsies showed <15 eosinophils/high-power field, patients were diagnosed with non-EoE dysphagia (NED). Demographics, diagnostic delay (i.e., interval

time between symptoms onset and diagnosis), esophageal symptoms, and atopic comorbidities (i.e., allergic rhinitis, asthma, eczema) were collected for all patients. Pearson's Chi-squared test and Fisher's exact test were used for comparisons. Odds ratios (ORs) were calculated to quantify associations between disease states. Significance threshold was set at $p<0.05$.

Results: Of 133 included patients, 51 (38%) had NED, while 82 (62%) had EoE with EREFS=0. Patients with EoE were more commonly males (67% vs 35%; $p<0.001$) and younger (37 vs 46 years; $p=0.005$) compared to patients with NED. Patients with EoE were diagnosed with a significantly longer diagnostic delay than NED (28 vs 4 months; $p<0.001$). Heartburn, regurgitation, chest pain and dyspepsia had similar prevalence in the two groups. In contrast, patients with EoE had a significantly higher prevalence of atopic comorbidities compared to NED (83% vs 39%; $p<0.001$). The presence of rhinitis, diagnostic delay longer than 12 months, any atopic comorbidity, age younger than 37 years, and male sex were associated with an increased risk of EoE with OR of 47.0, 11.6, 7.4, 3.8, and 3.7, respectively ($p<0.01$ for all).

Conclusion: EoE remains a possible diagnosis in patients reporting dysphagia even when endoscopy is normal. The presence of rhinitis and longer diagnostic delay, the presence of any atopic comorbidity, and younger age are associated with a diagnosis of EoE and are helpful to raise the suspicion of EoE and prompt endoscopists to collect esophageal biopsies.

Characteristic	NED (Non-EoE dysphagia) with EREFS 0 N = 51 (38%)	EoE with EREFS 0 N = 82 (62%)	p-value	Odds Ratio
Sex (Male/total)	18 / 51 (35%)	55 / 82 (67%)	<0.001	3.7 (IQR, 1.6 - 8.3)
Age at diagnosis	46 (40, 58)	37 (28, 50)	<0.01	3.8 (IQR, 1.4 - 10.8)
Diagnostic delay(months)	4 (1, 10)	28 (10, 90)	<0.001	11.6 (IQR, 3.8 - 40.8)
Atopy	20 / 51 (39%)	68 / 82 (83%)	<0.001	7.4 (IQR, 3.1 - 18.2)
Rhinitis	3 / 51 (5.9%)	62 / 82 (76%)	<0.001	47.6 (IQR, 13.2-264.1)

References: [1] Tourlaimain, G., Garcia-Puig, R., Gutiérrez-Junquera, C., Papadopoulou, A., Roma, E., Kalach, N., Oudshoorn, J., Sokollik, C., Karolewska-Bochenek, K., Oliva, S., Strisciuglio, C., Bauraind, O., Auth, M. K., Thomson, M., Otte, S., Rok, O., Dias, J. A., Tzivinikos, C., Urbonas, V., Kostovski, A., ... ESPGHAN EGID Working group (2020). Differences in Management of Eosinophilic Esophagitis in Europe: An Assessment of Current Practice. *Journal of pediatric gastroenterology and nutrition*, 71(1), 83–90. <https://doi.org/10.1097/MPG.0000000000002672>

Disclosure: Nothing to disclose.

MP728

EMERGENCY FOOD IMPACTION VS NON-EMERGENCY ONSET OF EOSINOPHILIC OESOPHAGITIS: A CROSS-SECTIONAL SINGLE-CENTER STUDY

E. Dilaghi¹, C. Sbarigia¹, C. Ritieni¹, G. Amici¹, M. Carabotti¹, G. Esposito¹, E. Lahner¹, B. Annibale¹

¹Department of Medical-Surgical Sciences and Translational Medicine, Sapienza University of Rome, Sant'Andrea University Hospital, Gastroenterology Unit, Rome, Italy, Rome, Italy

Contact E-Mail Address: emanuele.dilaghi@uniroma1.it

Introduction: Eosinophilic oesophagitis (EoE) is a chronic, T-helper type 2 immune-mediated oesophageal disease, characterized by symptoms of oesophageal dysfunction and eosinophil-predominant inflammation. In adults, the main clinical presentation associated with EoE is dysphagia and/or food impaction (FI); gastroesophageal reflux-like (GER-like) symptoms are less common but may also be the presenting symptoms.

Aims & Methods: We aimed to assess and compare the clinical, endoscopic, and histological characteristics of adult EoE patients presenting with FI or with no FI (NFI).

A single-center cross-sectional study was conducted on consecutive adult EoE patients (April 2023-April 2024). Based on presenting symptoms, patients were grouped into:

- I) FI patients, diagnosed following an emergency endoscopy, and;
- II) NFI patients, diagnosed due to the presence of dysphagia or GER-like symptoms (i.e. heartburn, regurgitation, retrosternal-pain) in an outpatient setting.

Symptoms were evaluated according to a structured questionnaire. All patients underwent gastroscopy with at least 6 biopsies from distal and medium/proximal oesophageal third. EoE was diagnosed if eosinophils were ≥ 15 /high power field, in any biopsy specimen.

The main features were compared between FI and NFI patients by Chi-square and/or Student's t test for dicotomic or continuous variables.

Results: Thirty-one EoE patients were included [males 74.2%, median-age 34 (19-57) years, BMI ≥ 25 Kg/ m² 61.3%]. FI patients (13; 41.9%) [males 76.9%, median-age 39 (20-57) years] and NFI patients (18; 58.1%) [males 72.2%, median-age 33 (19-57) years] did not differ in terms of age, gender, and BMI ($p=0.33$, $p=1.00$, $p=0.71$, respectively). Moreover, no differences were observed in the occurrence of atopy and the use of proton pump inhibitors (before EoE diagnosis) between FI and NFI groups [30.1% vs 50% ($p=0.46$) and 46.1% vs 66.6% ($p=0.29$), respectively].

Before EoE diagnosis, dysphagia and heartburn were less frequently reported in FI patients compared to NFI patients [38.5% vs 83.3% ($p=0.02$) and 23.1% vs 72.2% ($p=0.01$)]. Furthermore, 84.6% of FI, compared to 5.5% of NFI patients, showed a diagnostic delay of more than 5 years ($p<0.005$). The mean EREFS score was significantly higher in FI patients than in NFI patients [5.3 ± 1.8 vs 3.3 ± 2.1 ($p=0.005$)]. According to the EREFS score, inflammatory (based on Edema, Exudates, and Furrows scores) and fibrostenotic (based on the Rings and Strictures scores) phenotypes were both higher in FI patients than in NFI patients [3.2 ± 1.3 vs 2.1 ± 1.7 ($p=0.03$) and 2.2 ± 0.8 vs 1.3 ± 0.8 ($p=0.005$), respectively].

Conclusion: EoE patients presenting with food impaction seem to be paucisymptomatic before the EoE diagnosis compared to those without food impaction. This may explain the delay of EoE diagnosis often requiring emergency gastroscopy.

Disclosure: Nothing to disclose.

MP729

EOSINOPHILIC ESOPHAGITIS PATIENTS RETAIN ALTERED EATING BEHAVIORS EVEN AFTER HISTOLOGICAL REMISSION AND DYSPHAGIA IMPROVEMENT

A. Cefaliello¹, M. Pesce¹, M. Ricchiuti¹, G. Di Girolamo¹, P. Senneca¹, P. Di Pierro¹, C. Mormone¹, M. Napolitano¹, A. Detoraki¹, M. Maniscalco¹, E. Cantone¹, G. Sarnelli¹

¹University of Naples Federico II, Department of Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: antonio.cefaliello@outlook.com

Introduction: Controversy still remains regarding the appropriate tools to investigate symptoms' severity in Eosinophilic esophagitis (EoE). It is, indeed, recognized that the behavioral adaptation strategies implemented by EoE patients may overshadow the effective burden of dysphagia at presentation. On the other hand, it has also been reported that EoE patients are at higher risk of developing Avoidant restrictive food intake disorder (ARFID) in both pediatric and adult settings, calling for the need of assessing their eating patterns [1]. Given this background, the Eosinophilic Esophagitis Score Activity Index (EESAI) has been specifically developed

to evaluate the severity of dysphagia and eating behaviors in EoE patients [2]. To date, this standardized tool has never been explored in an Italian EoE population.

Aims & Methods: This was a prospective study involving consecutive EoE patients referred to our tertiary center from March 2022. The EEsAI was translated and adapted to an Italian cultural context by replacing “grits” with “porridge”, “dry rice” with “boiled rice” and “omelet and mash” instead of “pudding and jelly”. All patients underwent the EEsAI questionnaire at baseline and after each therapy modification, independently from histological remission.

The EEsAI score ranges between 0-100 and consists of two domains:

1. The Visual Dysphagia Question (VDQ) that explores the difficulty in swallowing 8 different food consistencies [meat, mashed potato, boiled rice, hamburger, soft bread, porridge, raw vegetables, fries; range 0-3 for each food] and;

2. The Avoidance, Modification and Slowly eating (AMS) score, which measures the behavioral modifications implemented in a 7-day recall period.

Data are presented as mean±SD.

Results: 40 EoE patients (32M, 31±11 ys) were studied. 26 patients (65% of the population, 23M; 30±12 ys) achieved histological remission: 7 patients (27%; 24±11ys) on proton pump inhibitors, 14 (54%; 31.5±15ys) on topical steroids and 5 patients (19%; 21±11ys) with Interleukin 4 receptor α antibody. The total VDQ questionnaire subscores significantly differ between active and inactive esophagitis (2.6 ± 2.3 vs 1.2 ± 1.4 $p=0.01$), with a significant difference in the difficulty to swallow boiled rice and hamburger (0.7 ± 1 vs 0.1 ± 0.3 ; $p=0.01$ and 0.9 ± 0.9 vs 0.3 ± 0.7 ; $p=0.005$, respectively). On the other hand, no difference was observed for all the other food consistencies. Mirroring this, the pre-post treatment total EEsAI scores significantly differ (30 ± 24 vs 16 ± 19 $p=0.01$). Interestingly, despite the improved severity of dysphagia, no significant differences were observed in Avoidance behavior (0.4 ± 1.1 vs 0.4 ± 0.8), Modification (0.3 ± 1 vs 0.4 ± 1.3), Slow eating (0.8 ± 2 vs 0.6 ± 1.9) and total AMS subscore (2.3 ± 2.3 vs 2 ± 2 ; all $p=NS$). Overall, avoidance behaviors were retained in 27% of EoE patients who achieved clinical and histological remission.

Conclusion: EoE patients show a significant improvement in dysphagia severity after histological remission, as measured by the VDQ item. However, this is not paralleled by an improvement in eating behaviors and avoidance strategies. This implies that patients, once established an abnormal eating pattern, avoid to adjust these behaviors, even following resolution of symptoms and histological activity. Properly evaluating eating patterns in EoE patients in clinical practice, through the standardized EEsAI questionnaire is crucial to promptly identify and correct abnormal eating patterns in EoE patients.

References:

1. Ketchem CJ, Dellon ES. Avoidant Restrictive Food Intake Disorder in Adults With Eosinophilic Esophagitis. *Gastro Hep Adv.* 2022;1(1):52-54. doi:10.1016/j.gastha.2021.09.004
2. Schoepfer AM, Straumann A, Panczak R, et al. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. *Gastroenterology.* 2014;147(6):1255-66.e21. doi:10.1053/j.gastro.2014.08.028

Disclosure: Nothing to disclose.

Poster
Oesophageal, gastric and duodenal disorders

Oesophageal, gastric and duodenal disorders

09:00-18:00 / Poster Exhibition

PP0001

THE LIQUID-LIQUID PHASE SEPARATION OF PACSIN1 MAY CAUSE POOR PROGNOSIS IN GASTRIC CANCER PATIENTS

W. Jing^{1,2}, J. Yang³, K. Deng^{1,2}, J. Yang^{1,2}, H. Jiang³

¹West China Hospital, Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China, ²Sichuan University-Oxford University Huaxi Gastrointestinal Cancer Centre, Department of Gastroenterology & Hepatology, Chengdu, China, ³West China Hospital, Sichuan University, Laboratory for Aging and Cancer Research, Frontiers Science Center Disease-related Molecular Network State Key Laboratory of Respiratory Health and Multimorbidity and National Clinical Research Center for Geriatrics, Chengdu, China

Contact E-Mail Address: daisyjingwn@163.com

Introduction: Recently, liquid-liquid phase separation (LLPS) of membrane protein has been found to play a critical role in the development of tumors [1-3]. Meanwhile, Protein Kinase C and Casein Kinase Substrate in Neurons 1 (PACSIN1), a peripheral membrane protein with intrinsically disordered regions (IDRs), is associated with the prognosis of gastric cancer patients [4].

However, whether PACSIN1 could undergo LLPS and whether PACSIN1 involved in the development of gastric have not been studied until now.

Aims & Methods: Here, we aimed to investigate whether PACSIN1 could undergo LLPS and the potential role of PACSIN1 in gastric cancer. We analyzed disease free survival of gastric cancer samples from The Cancer Genome Atlas dataset. The protein sequence prediction website (Disprot - Database of Protein Disorder) was used to predict the IDRs of PACSIN1. Besides, droplet formation experiments, fluorescence recovery after photobleaching (FRAP) and cellular immunofluorescence were used to explore whether PACSIN1 could undergo LLPS. What's more, cell proliferation assay and cell migration assay were utilized to investigate the potential role of PACSIN1 in gastric cancer.

Results: In the prognosis analysis of the TCGA database, it was found that the disease-free survival rate of gastric cancer patients with high expression of PACSIN1 was significantly lower than that of patients with low expression of PACSIN1 (Figure 1).

Overexpression of PACSIN1 in gastric cancer cell resulted in decreased proliferation (Figure 2A-B) and increased migration (Figure 2C-D) of gastric cancer cells. In the prediction of protein structure, it could be found that the IDRs region of PACSIN1 accounted for more than 50% (Figure 3). When fully mixed with 5% Polyethylene glycol (PEG), one of the characteristics of LLPS- droplet formation - could be observed under the microscope (Figure 4B). After the fluorescence bleaching of the droplet formed by PACSIN1 with mCherry, the fluorescence gradually recovered within a few minutes (Figure 4C). What's more, PACSIN1 formed puncta with irregular distribution in cytoplasm (Figure 4D), which also proved that PACSIN1 could undergo LLPS.

Conclusion: Overall, high expression of PACSIN1 is associated with poor prognosis of patients, and overexpression of PACSIN1 in gastric cancer cell can promote the proliferation and migration. PACSIN1 can also undergo LLPS in vitro and in vivo. Therefore, we speculate that PACSIN1 may promote the development of gastric cancer through LLPS.

References: [1] Beutel O, Maraschini R, Pombo-García K, et al. Phase Separation of Zonula Occludens Proteins Drives Formation of Tight Junctions. *Cell*. 2019 Oct 31;179(4):923-936.e11. doi: 10.1016/j.cell.2019.10.011. PMID: 31675499.

[2] Boeynaems S, Alberti S, Fawzi NL, et al, Polymenidou M, Rousseau F, Schymkowitz J, Shorter J, Wolozin B, Van Den Bosch L, Tompa P, Fuxreiter M. Protein Phase Separation: A New Phase in Cell Biology. *Trends Cell Biol*. 2018 Jun;28(6):420-435. doi: 10.1016/j.tcb.2018.02.004. Epub 2018 Mar 27. PMID: 29602697; PMCID: PMC6034118.

[3] Peng Q, Tan S, Xia L, et al. Phase separation in Cancer: From the Impacts and Mechanisms to Treatment potentials. *Int J Biol Sci*. 2022 Aug 1;18(13):5103-5122. doi: 10.7150/ijbs.75410. PMID: 35982902; PMCID: PMC9379413. Liu Z, Li L, Li X, Hua M,

[4] Sun H, Zhang S. Prediction and prognostic significance of ALOX12B and PACSIN1 expression in gastric cancer by genome-wide RNA expression and methylation analysis. *J Gastrointest Oncol*. 2021 Oct;12(5):2082-2092. doi: 10.21037/jgo-21-508. PMID: 34790376; PMCID: PMC8576218.

Disclosure: The authors declare that there are no competing interests.

PP0002

AUTOMATIC DEEP LEARNING MODELS FOR GASTROINTESTINAL TUMOR DIAGNOSIS AND PROGNOSIS USING HEMATOXYLIN AND EOSIN SLIDES

J. Wang¹, S. Zhang¹, L. Wu^{2,1}, H. Yu¹

¹Renmin Hospital of Wuhan University, Wuhan, China, ²Cambridge University, Cambridge, China

Contact E-Mail Address: wang102581@163.com

Introduction: Immunohistochemistry (IHC) is a critical tool for tumor diagnosis and treatment. However, IHC is time consuming and costly, relies on the pathologists' subjective interpretation. Deep learning has gained ground for predicting the biomarker expression on hematoxylin and eosin (H&E) staining images.

In this study, we aim to create an automatic pipeline for the construction of deep learning models to generate virtual IHC output using H&E whole slide images and validate its clinical applicability by reader study.

Aims & Methods: We obtained 134 whole-slide images (WSIs) from 73 patients at Renmin Hospital of Wuhan University and extracted 415,463 patches from H&E-stained WSIs.

Our study focused on five widely used biomarkers in pathology reports, namely anti-P40, CK-pan, Desmin, P53, and Ki-67, as recommended by the NCCN guidelines. We validated these models by using independent whole-slide images (WSIs). The number of WSIs used for each model were as follows: model-P40 (6 WSIs, 38389 Patches), model-PCK (9 WSIs, 72443 Patches), model-Ki67 (7 WSIs, 53162 Patches), model-Desmin (5 WSIs, 23974 Patches), and model-P53 (5 WSIs, 36822 Patches).

We aimed to predict these biomarkers expression in H&E WSIs and quantify the percentage of Ki-67. There are three main steps: Firstly, we employed HEMnet neural network to align the corresponding IHC and H&E WSIs, transferring the molecular labels from IHC to H&E images. Secondly, pathologists reviewed the annotations made by HEMnet and corrected HE-IHC mismatched tiles using VIA labelling platform. Lastly, the deep learning models were trained to predict positive tiles. The performance of models was assessed by sensitivity, specificity, accuracy, and the area under the receiver operating characteristic curve (AUC). To assess the ap-

plicability of models, we randomly selected 30 cases including H&E and IHC WSIs for three pathologists to write the reports in the reader study by reading the interpretation of real IHC and AI-generated IHC.

Results: The sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve (AUC) of the models for classifying positive pixels of each biomarker was: P40 (91.64%, 87.39%, 88.66%, AUC: 0.95), PAN-CK (92.40%, 89.35%, 90.81%, AUC: 0.96), Ki67 (89.63%, 86.04%, 86.77%, AUC: 0.95), Desmin (91.44%, 88.11%, 89.17%, AUC: 0.96), and P53 (75.44%,86.52%,83.04%, AUC: 0.90). The predicted Ki-67 percentage was comparable to the assessments made by expert pathologists, with a difference ranging from 7.00%±3.69%. In the reader study, compared with real-IHC pathology report, the accuracy of AI-IHC pathology report of each biomarker was: Desmin(100%,66/66), Pan-CK(98.3% , 59/60), P53(98.3% ,59/60), T-stage(84.8% .56/66), P40(96.7% ,29/30). and there is no significant difference between the quatification of Ki-67 score($t=0.253$, $P=0.800$).

Items	Pathology report's accuracy of AI-IHC compared with Real-IHC					T test of Ki-67
	Desmin	Pan-CK	P53	T-stage	P40	
Pathologist 1	100.0% (22/22)	100.0% (20/20)	70.0% (21/30)	68.2% (15/22)	100.0% (10/10)	t= 0.475 (P= 0.637)
Pathologist 2	100.0% (22/22)	95.0% (19/20)	66.7% (20/30)	95.5% (21/22)	100.0% (10/10)	t= - 0.775 (P= 0.443)
Pathologist 3	100.0% (22/22)	100.0% (20/20)	60.0% (18/30)	90.9% (20/22)	90.0% (9/10)	t= - 0.510 (P= 0.613)
Average	100.0% (66/66)	98.3% (59/60)	98.3% (59/60)	84.8% (56/66)	96.7% (29/30)	t= 0.253 (P= 0.800)

Table. Result of Reader Study.

Conclusion: Our deep learning models have demonstrated promising performance in predicting gastrointestinal tumor biomarkers based on H&E slides. The utilization of these models can alleviate the burden of IHC staining and clinicopathological assessments. Furthermore, these models have the potential to aid in patient grading, facilitate informed treatment decisions, and provide valuable prognostic assessments.

Disclosure: There is no conflict of interest in this abstract.

PP0003

LOSS OF STROMAL BMP ACTIVITY DRIVES GASTRIC PATHOLOGY IN MICE

J. Wizeny¹, M. Sigal¹

¹Charité - Universitätsmedizin Berlin, Division of Gastroenterology and Hepatology, Medical Department, Berlin, Germany

Contact E-Mail Address: jonas.wizeny@charite.de

Introduction: The gastric epithelial gland homeostasis is driven by insufficiently characterized sub-epithelial stromal signals. Gastric stem cells in the gland base are fueled by a Wnt/Rspo^{high} niche where Bmp activity is suppressed, while terminally differentiated mucous pit cells are maintained by a BMP^{high} niche, that suppresses Wnt/Rspo activity. Infection with *Helicobacter pylori* reduces stromal and epithelial Bmp activity driving stem cell expansion. In line with this, genetic knockout of BMP activity in the epithelium leads to epithelial hyperplasia. The consequences of loss of BMP activity in the stroma on epithelial homeostasis and proliferative, regenerative, and inflammatory pathways in the interplay between stroma and epithelium are unknown.

Aims & Methods: The objective of this study was to analyze the epithelial pathology and epithelial-stromal interplay in the context of loss of BMP activity in the gastric stroma by using an inducible knockout of the BMP type 1 receptor in the stroma in mice.

Results: After two months of knockout of the BMP receptor in the gastric stroma, mice display drastic hyperplasia via stem cell expansion in the antrum and the corpus. Loss of stromal BMP signaling causes the occurrence of a bulky stroma with expanded fibroblasts and aberrant glands within the pit area, that resemble the gland base with expression of stem cell factors, high proliferation, enhanced epithelial inflammation (marked by NF-κB p65) and expression of metaplasia markers (CD44v9, Aqp5). Using scRNAseq as well as organoid and assembloid technologies we now study the mechanisms by which loss of stromal BMP affects epithelial homeostasis.

Conclusion: Collectively, our data demonstrate that alterations in stromal BMP activity can promote premalignant lesions. This model will allow us to study the underlying principles of stromal-epithelial interplay in the stomach and explore mechanistically the consequences of stromal responses observed upon *H. pylori* infection in detail.

Disclosure: Nothing to disclose.

PP0004

THE OCCURANCE OF GENES OF THE HLA SYSTEM IN PATIENTS WITH ACHALASIA AND HEALTHY VOLUNTEERS IN RUSSIAN FEDERATION

E. Valitova^{1,2}, A. Chegodar³, D.S. Bordin^{4,5,6}, M. Chanyshev⁷, N. Vlasenko⁷, A. Glushchenko^{8,7}, K. Khafizov⁷, O. Berezina¹, N. Bodunova³

¹A.S. Loginov Moscow Clinical Scientific Center, Laboratory of functional diagnostics of diseases of esophagus and stomach, Moscow, Russian Federation, ²Organizational and Methodological Department on Gastroenterology of Moscow Department of Health, 111111, Russian Federation, ³A.S. Loginov Moscow Clinical Scientific Center, Center of personalized Medicine, Moscow, Russian Federation, ⁴A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ⁵Russian University of Medicine, Moscow, Russian Federation, ⁶Tver State Medical University, Tver, Russian Federation, ⁷Central Research Institute for Epidemiology of the Federal Service for Surveillance of Consumer Rights Protection and Human Wellbeing, Moscow, Russian Federation, ⁸Moscow Institute of Physics and Technology, National Research University, Dolgoprudny, Russian Federation

Contact E-Mail Address: dbordin@mail.ru

Introduction: Human leucocyte antigen (HLA) strongly associated with autoimmune diseases. In some studies it was demonstrated, that achalasia is an autoimmune disease and associated with genetic factors.

Aims & Methods: The aim of our study was to investigate the association of genes of the HLA system in patients with achalasia and in healthy citizens of Russian Federation.

Material and methods: 140 patients with achalasia were included in this study: 75 females (55%), age from 18 to 75. The diagnosis of idiopathic achalasia was established by upper endoscopy and high resolution water-perfused manometry (MMS, Netherland). Healthy 332 volunteers from 21 to 74 y.o. (asymptomatic) were included in this study: there were 305 females.The DNA from blood samples was isolated using QIAamp DNA Blood Mini Kit (Qiagen, Germany) according to the manufacturer’s recommendations. The concentration of DNA samples was measured by fluorimetric method on a Qubit 4 fluorimeter using the Qubit dsDNA BS Assay Kit (Thermo Fisher Scientific, USA). All patients underwent HLA typing by massively parallel sequencing (NGS): *HLA-A*, *HLA-B*, *HLA-C*, *HLA-DQB1*, *HLA-DRB1*, *HLA-DPB1*, on the platform MiSeq (Illumina, USA) v.2, Omixon. The analysis of the HLA gene sequences obtained as a result of sequencing was carried out using a computer program TypeStream Visual Software (TSV) (One Lambda, USA), and database IPD-IMGT/HLA.

Results: The allelic variants *HLA-A*02*, *HLA-B*37*, *HLA-B*39*, *HLA-C*5*, *HLA-C*7*, *HLA-C*14*, *HLA-C*15*, *HLA-DRβ1*01*, *HLA-DRβ1*03*, *HLA-DRβ*08*, *HLA-DRβ1*13*, *HLA-DPβ1*06*, *HLA-DPβ1*11*, *HLA-DPβ1*05*, *HLA-DPβ1*15* and *HLA-DQβ1*04* were evaluated equally in healthy volunteers and achalasia patients. The allelic variants *HLA-A*66*, *HLA-B*15*, *HLA-B*44*, *HLA-B*52*, *HLA-C*12*, *HLA-C*16*, *HLA-DPβ1*01*, *HLA-DPβ1*02*, *HLA-DPβ1*23*, *DRβ1*11*, *HLA-DRβ1*14*, *DQβ1*06* were found statistically more frequently in patients with achalasia than in healthy volunteers. The allelic variants *HLA-A*11*, *HLA-A*23*, *HLA-A*25*, *HLA-A*26*, *HLA-B*7*, *HLA-B*57*, *HLA-C*3*, *HLA-C*06*, *HLA-DPβ1*03*, *HLA-DPβ1*13*, *HLA-DPβ1*17*, *DRβ1*13*, *HLA-DRβ1*15* were insignificantly evaluated more frequently in group with achalasia than in healthy volunteers.

Conclusion: The absence of differences in some allelic variants of genes of HLA in patients with achalasia and healthy volunteers confirm that they are not specific for achalasia in Russian Federation. The statistical difference in predominance of some allelic variants of HLA system indicates, that these findings should be compare with medical history and symptoms. After that these allelic variants of genes of HLA can be consider as a prognostic factor.

Disclosure: Nothing to disclose.

PP0005

WITHDRAWN

PP0006

ASSOCIATION BETWEEN ACID-SUPPRESSIVE DRUGS AND RISK OF PSORIASIS: RETROSPECTIVE STUDY USING KOREAN NATIONAL HEALTH INSURANCE SERVICE-NATIONAL SAMPLE COHORT

S. Kim¹, S.C. Park², Y.W. Jo³, Y. Her³, J.W. Kwon⁴, J.H. Kim²
¹Kangwon National University Hospital, Gastroenterology and hepatology, Chuncheon City, South Korea, ²Kangwon National University/Kangwon National University Hospital, Gastroenterology and Hepatology, Chuncheon City, South Korea, ³Kangwon National University/Kangwon National University Hospital, Dermatology, Chuncheon City, South Korea, ⁴Kangwon National University/Kangwon National University Hospital, Allergy and clinical immunology, Chuncheon City, South Korea

Contact E-Mail Address: kimjihyun81@naver.com

Introduction: Psoriasis is a common inflammatory skin disorder following non-specific triggers such as scratching, piercing, sunburn, and chemical irritants. Involvement of immune system is widely accepted for pathogenesis studies have demonstrated importance of gut microbiota in pathogenesis of inflammatory skin diseases. Proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RA) are acid suppressing drugs widely used for gastrointestinal diseases, and long-term use has been reported to be associated with altered gut microbiota. This study aimed to investigate association between psoriasis and acid suppressing drugs in Korean population.

Aims & Methods: We used Korean National Health Insurance Service-National Sample Cohort (NHIS-NSC) data of 746,816 patients with upper gastrointestinal (GI) diseases between 2002 and 2013. Duration of acid suppressing drug exposure and other socio-demographic characteristics were compared between patients with and without psoriasis, and hazard ratios were estimated.

Results: Significantly larger number of patients with exposure to acid suppressing drugs had developed psoriasis compared to control cohort (46.3% vs. 33.7% respectively, $P < 0.001$). In the multivariate analysis, lon-

ger use of acid suppressing drugs and greater Charlson comorbidity index score were significantly associated with increased risk of psoriasis with an adjusted odds ratio, 1.89 (95% confidence interval, 1.66-2.17, $P < 0.001$) and 1.33 (1.17-1.51, $P = < 0.001$), respectively.

Conclusion: Results from our study indicate that prolonged use of H2RA or PPI is associated with the risk of psoriasis among patients with GI diseases in Korean population. The risk was increased in dose-response trend, even after adjusting for confounding variables. Clinicians should be aware of risks associated with prolonged use of acid suppressing drugs.

References: 1. Buhas MC, Gavrila LI, Candrea R, Catinean A, Mocan A, Miere D, et al. Gut Microbiota in Psoriasis. *Nutrients* 2022;14(14).
 2. Schon MP, Boehncke WH. Psoriasis. *N Engl J Med* 2005;352(18):1899-912.
 3. Boehncke WH, Schon MP. Psoriasis. *Lancet* 2015;386(9997):983-94.
 4. Nickoloff BJ, Qin JZ, Nestle FO. Immunopathogenesis of psoriasis. *Clin Rev Allergy Immunol* 2007;33(1-2):45-56.
 5. Sabat R, Philipp S, Hoflich C, Kreutzer S, Wallace E, Asadullah K, et al. Immunopathogenesis of psoriasis. *Exp Dermatol* 2007;16(10):779-98.

Disclosure: Nothing to disclose.

PP0007

CYANOCOBALAMIN INTRAMUSCULAR TREATMENT IN PATIENTS WITH CORPUS ATROPHIC GASTRITIS AND VITAMIN B12 DEFICIENCY: EFFICACY AND PREDICTORS OF INCREASED REQUIREMENT

C. Palumbo¹, F.P. Schiavone¹, L. Dottori¹, G. Cozza¹, I. Ligato¹, G. Pivetta¹, S. Scalamenti¹, E. Dilaghi¹, B. Annibale², E. Lahner¹
¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea University Hospital, Gastroenterology Unit, Rome, Italy, Rome, Italy, ²University Hospital S. Andrea, Rome, Medical and Surgical sciences, Rome, Italy

Contact E-Mail Address: carlapal94@gmail.com

Introduction: Corpus atrophic gastritis (CAG) is associated with vitamin B12 deficiency. Untreated vitamin B12 deficiency can lead to megaloblastic anaemia (also known as Pernicious Anaemia) and other potential serious clinical manifestations such as acute cardiocerebral events and severe neurological consequences, thus timely B12 supplementation is relevant. To date, the dosage of intramuscular B12 supplementation in CAG patients with vitamin B12 deficiency is not standardized.

Aims & Methods: The aim was to assess the efficacy of cyanocobalamin treatment (Tx) at long term follow-up and predictors of increased cyanocobalamin requirement.

A monocentric retrospective longitudinal cohort study was conducted on 190 pts (62.1% F, age 63±1 yrs) consecutively diagnosed (2007-2021) with CAG and vitamin B12 deficiency. Inclusion criteria were age >18 years, histological diagnosis of CAG (updated Sydney System), serum B12 <250 pg/ml, intramuscular cyanocobalamin supplementation, and follow-up of at least 12 mos. Demographic, clinical, biochemical, and histological data were retrospectively collected. After the diagnosis of vitamin B12 deficiency pts were first treated with TxA schedule (5000µg intramuscular cyanocobalamin every 5 days for 3 times, followed by 5000µg intramuscular every 3 mos (20000µg/yr)), and reevaluated at follow up. If TxA was not sufficient to restore B12 levels, TxB was prescribed (5000µg intramuscular cyanocobalamin every 5 days for 3 times, followed by 5000µg intramuscular cyanocobalamin every 2 mos (30000µg/yr)). Primary Tx endpoint was B12 normalization. Baseline and follow-up data of pts on TxA and TxB were compared by Student's t-test. Logistic regression was performed to find out predictors of increased B12 need.

Results: Macrocytic anaemia was mild, moderate and severe in 60, 17, 14 out of 190 pts, while 94 pts had vitamin B12 deficiency without anaemia.

TxA efficaciously corrected vitamin B12 deficiency in 130 (68.4%) pts and was maintained until longest available follow-up (41±2.4 mos). The remaining 60 (31.6%) pts, due to persistent vitamin B12 deficiency observed at 12 (6-48) mos, were switched to TxB which was then maintained until longest available follow-up (49.9±4.1 mos). At longest available follow-up, a significant increase of Hb (TxA: 12±0.2 vs 13.1±0.2; TxB: 12.1±0.4 vs 13.8±0.2, $p<0.0001$) and B12 (TxA: 162.9±8.6 vs 400±22.2; TxB: 142.3±11.2 vs 323.4±22.3, $p<0.001$) was shown in both schedules. A significant decrease of MCV was shown in TxB only (96.4± 2.1 vs 88.1±0.9, $p<0.0001$). At logistic regression, switch to TxB was associated with severe intestinal metaplasia (OR10.6, IC 95% 2.6-43.0, $p=0.0009$) and macrocytosis at diagnosis (OR2.8, IC95% 1.1-6.9, $p=0.0231$), and male gender (OR 2.5, IC95% 1.1-5.7, $p=0.0213$), while other features such as age, severity of vitamin B12 deficiency, previous vitamin B12 therapy, concomitant iron deficiency were not significantly associated with increased need of intramuscular cyanocobalamin.

Conclusion: At long term follow-up, about 70% of pts restore vitamin B12 deficiency with 5000µg intramuscular cyanocobalamin every 3 mos, while only 30% require an increased dosage of 5000µg intramuscular cyanocobalamin every 2 mos. In particular, male pts with severe intestinal metaplasia and macrocytosis at diagnosis require a higher dosage of cyanocobalamin to obtain B12 normalization. In CAG pts with vitamin B12 deficiency regular clinical-biochemical follow-up is important to monitor efficacy of B12 treatment to restore B12 levels and to treat and prevent clinical manifestations of vitamin B12 deficiency.

References: Lenti MV, Rugge M, Lahner E, Miceli E, Toh B-H, Genta RM, et al. Autoimmune gastritis. *Nat Rev Dis Primers*. (2020);

Green R, Allen L, Bjørke-Monsen A et al. Vitamin B 12 deficiency. *Nature reviews | Disease primers* (2017);

Devalia V, Hamilton MS et al. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *British Journal of Haematology* (2014);

Disclosure: Nothing to disclose.

PP0008

CLINICAL AND EPIDEMIOLOGICAL CHANGES IN CAUSTIC INGESTION OVER THE LAST DECADES

J. Tosca Cuquerella¹, P. Poyatos García¹, A. Sanahuja Martínez¹, A.M. Sánchez Pardo¹, R. Villagrasa Manzano¹, T. García Ballester¹, I. Lorca Antón¹, M. Brosel Martínez¹, P. Mas Mercader¹, P. Lluch García¹, R. Antón Ausejo¹, M. Ponce Romero¹, C. Gálvez Castillo¹, A. Peña Aldea¹, V. Sánchez Soler¹, B. Herreros Martínez², M. Mínguez Pérez¹, I. Pascual Moreno¹

¹Hospital Clinic Universitari de Valencia, *Digestive Medicine, Valencia, Spain*, ²Hospital de la Marina Baixa, *Digestive Medicine, Vila Joiosa, Spain*

Contact E-Mail Address: paloma.poyatos@alu.umh.es

Introduction: The incidence of caustic ingestion has remained stable in recent years due to its difficult prevention and limited changes in its management.

Aims & Methods: Aims:

1. To explore changes in the epidemiological and clinical characteristics of caustic ingestion over the last decades
2. To identify epidemiological risk factors of adverse outcomes.

Methods: We present data from an observational study that prospectively collected caustic ingestions in our centre since 1995 and included all adult patients whose acute episode was evaluated in the emergency department. Epidemiological data and variables related to the type of ingestion, prognostic risk factors and the adverse outcomes, defined as the need for admission to the intensive care unit, emergency surgery, patient death

and oesophageal or gastric stricture development, were analysed; the results were compared for the periods 1995-2009 and 2010-2024.

Results: A total of 582 episodes of caustic ingestion were included, 305 during the first period and 277 during the second.

Epidemiological characteristics and type of ingestion were overall similar in both periods, as were the clinical, analytical, endoscopic and radiologic indicators of severity.

Adverse outcomes were also similar in the two time periods, both in the short term (comparable frequency of intensive care unit admission, need for surgery and death) and in the long term (stricture development).

The main risk groups for severe ingestions were patients older than 45 years (OR 4.3; 95%CI: 2.3-7.9) and psychiatric comorbidity (OR 5.2; 95%CI: 3.0-9.1), especially depressive syndrome (OR 7.2; 95%CI: 4.2-12.4).

Recurrent ingestions were more frequent in men (OR 1.9; 95%CI: 1.0-3.5) and psychiatric illness (OR 7.6; 95%CI: 3.5-16.5), mainly personality disorder (OR 11.0; 95%CI: 5.5-21.9).

	1995-2009	2010-2024	p value
Women	164 (53,8)	133 (48,0)	0,192
Age	44 (30)	50 (30)	0,193
Voluntary intake	154 (50,5)	121 (44,0)	0,139
pH of caustic			
Strong acid	50 (16,9)	40 (14,7)	0,318
Weak acid	17 (5,8)	25 (9,2)	
Weak alkali	215 (72,9)	200 (73,3)	
Strong alkali	13 (4,4)	8 (2,9)	
Psychiatric illness	155 (50,8)	119 (43,0)	0,007
Depression	112 (36,7)	75 (27,1)	0,016
Bipolar disorder	5 (1,6)	11 (4,0)	0,143
Personality disorder	28 (9,2)	20 (7,2)	0,479
Psychotic disorder	16 (5,2)	13 (4,7)	0,908
Alcohol/toxic substances consumption	23 (7,5)	26 (9,4)	0,515
Intensive care unit admission	40 (13,1)	29 (10,5)	0,391
Emergency surgery	8 (2,6)	10 (3,6)	0,655
Death	15 (4,9)	19 (6,9)	0,412
Stricture formation	11 (5,1)	8 (3,7)	0,624

Qualitative variables: absolute (relative) value, Chi-squared +/- continuity correction.

Quantitative variables: median (interquartile range), Mann-Whitney U test

Conclusion: No relevant changes were identified in the epidemiological and clinical characteristics of caustic ingestions over the last decades, nor in their evolution. The most vulnerable groups to prioritise prevention measures would be patients with psychiatric comorbidity.

Disclosure: Nothing to disclose.

PP0009

ANTI-INFLAMMATORY ACTION OF A MUCOSA PROTECTIVE AGENT, MARSHMALLOW ROOT EXTRACT, IN ENDOTHELIAL CELLS, FIBROBLASTS AND MACROPHAGES IN VITRO

G. Bonaterra¹, J. Schmitt¹, N. Seller¹, O. Kelber², H. Aziz-Kalbhenn², K. Bedal², R. Kinscherf¹

¹Philipps-University, *Institute for Anatomy and Cell Biology, Dept. of Medical Cell Biology, Marburg, Germany*, ²Steigerwald Arzneimittelwerk GmbH, *Phytomedicines Supply and Development Center, Bayer Consumer Health, Darmstadt, Germany*

Contact E-Mail Address: olaf.kelber@bayer.com

Introduction: Mucosa protective effects can be mediated by physical as well as by anti-inflammatory mechanisms of action. For the root extract of marshmallow (*Althaea officinalis* L., REAo), known to cure mild irritation of stomach/gut mucosa [1], only a physical action had been considered. Recent studies have shown that it also induces regeneration of irritated mucosa [2,3].

Mucosal wound healing depends on the recruitment of several cell types, e.g., endothelial cells, fibroblasts, and macrophages (MΦ). Reactive oxygen species (ROS)-induced damage is associated with mucosal infiltration of activated leukocytes, such as MΦ, which produce excessive ROS and pro-inflammatory cytokines that may overwhelm the antioxidant and immune defenses of the cells and exacerbate mucosal inflammation. Additionally, fibroblasts exhibit a metabolic adaptation to control inflammation-related oxidative stress.

Aims & Methods: We aimed to investigate whether REAo has, on top of its physical effects, also anti-inflammatory/-oxidative properties in human dermal fibroblasts (NHDF), human umbilical vein endothelial cells (HUVEC), and human acute monocytic leukemia (THP-1) differentiated MΦ, critical cellular components of the gastrointestinal and oral mucosa.

The cells were pre-treated with REAo or its final formulation STW 42, containing REAo and selected excipients, followed by incubation with H₂O (pro-oxidative) or lipopolysaccharide (LPS, pro-inflammatory). Intracellular ROS were quantified with DCFDA. The releases of IL-6 and TNF-α were determined by ELISA. THP-1 cells were differentiated into MΦ with 0.1 µg/ml phorbol-12-myristate-13-acetate for 3–5 days.

Results: Pre-treatment (24 h) of HUVEC, NHDF or THP-1-MΦ with STW 42 or REAo (100–1000 µg/ml) significantly inhibited the H₂O-induced intracellular ROS production by 30.0% to 58.7%. Whereas 24h(HUVEC, NHDF) or 48 h (THP-1-MΦ) pre-treatment with STW 42 or REAo (100–1000 µg/ml) inhibited the LPS-activated IL6 release by 25.0–67.0%. Additionally, 48 h pre-treatment of THP-1-MΦ with 50–500 µg/ml STW 42 or REAo significantly inhibited LPS-induced TNF-α release by 21.5% (50 µg/ml) to 52.0% (500 µg/ml), in comparison with LPS-treated MΦ. The observed effects of STW 42 or REAo were similar to 25–100 µM Diclofenac, which was used as an anti-inflammatory control.

Conclusion: These anti-inflammatory and antioxidant properties may support the benefit of STW 42 and its constituent REAo in patients with mucosal irritation with subsequent irritative cough or gastric complaints due to its protective/repairative effects on the mucosa.

References:

1. HMPC of EMA 2016. European Union herbal monograph on *Althaea officinalis* L., radix. EMA/HMPC/436679/2015
2. Deters A, Zippel J, Hellenbrand N, Pappai D, Possemeyer C, Hensel A. 2010. Aqueous extracts and polysaccharides from Marshmallow roots (*Althaea officinalis* L.): Cellular internalisation and stimulation of cell physiology of human epithelial cells *in vitro*. *J Ethnopharmacol*. 127: 62–9. doi: 10.1016/j.jep.2009.09.050.
3. Bonaterra GA, Schmitt J, Schneider K, Schwarzbach H, Aziz-Kalbhen H, Kelber O, Müller J, Kinscherf R. Phytostil and root extract of *Althaea officinalis* L. exert anti-inflammatory and anti-oxidative properties and improve the migratory capacity of endothelial cells *in vitro*. *Front Pharmacol*. 2022 Dec 8;13:948248.

Disclosure: JS and NS have nothing to disclose. GAB and RK received project support from Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany. OK, HAK and KB are employees of Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany.

PP0010

ATHEROSCLEROSIS AND THE MICROBIOME: A NEW MICROBIOME BIOMARKER THAT PROTECTS AGAINST ATHEROSCLEROSIS?

N. Boyko¹, A. Dorofeyev², S. Burmei¹, O. Pallah¹, L. Yusko¹, T. Meleshko¹, T. Chendey³

¹*Uzhhorod National University, Uzhhorod, Ukraine,* ²*Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine,*

³*Transcarpathian regional clinical center of cardiology and cardiosurgery, Uzhhorod, Ukraine*

Contact E-Mail Address: nadiya.boyko@uzhnu.edu.ua

Introduction: The relationship between disruptions in the intestinal microbiome, psychological well-being, and modern lifestyle factors in individuals with prevalent non-communicable diseases, such as atherosclerosis, has been partially elucidated but remains inadequately investigated. This raises the inquiry into the feasibility of diagnosing, preventing, and treating atherosclerosis through the measurement and adjustment of disease markers associated with intestinal microbiome, psychological state, and lifestyle indicators.

Aims & Methods: This study aims to broaden the spectrum of these markers to a degree adequate for establishing models to diagnose atherosclerosis within the alternative categories of “no atherosclerosis,” “asymptomatic atherosclerosis,” and “symptomatic atherosclerosis,” as well as by the level of associated health risks (non-significant, significant, and high). Our cohort study data were employed to fulfill this goal.

Results: We identified microbial markers from 955 gut microbiome species and other markers from 52 indicators of psychological state and lifestyle among participants. Marker properties were assessed based on their ability to distinguish between “no atherosclerosis,” “asymptomatic atherosclerosis,” and “symptomatic atherosclerosis” groups, as well as “not significant risk,” “significant risk,” and “high risk” groups. We measured their correlation with each participant’s group membership using the p-level parameter to prioritize markers, resulting in a rating for each. Eleven microbial species (including *Oxalobacter aliiformigenes*, *Lactobacillus acidophilus*, and *Bifidobacterium longum*) and six other indicators (including “feeling of slowness” and “duration of physical activity”) showed the highest scores. Cluster-type models based on these markers accurately predict group membership, with predictive accuracies ranging from 93.7% to 97.1%. This study provides novel insights into atherosclerosis-associated markers, laying a foundation for future research in this field.

Conclusion: The inclusion of microbial, psychological state, and lifestyle indicators has significantly enhanced the existing markers for atherosclerosis. These new markers have facilitated the development of models that, for the first time, enable the diagnosis of atherosclerosis within the categories of “no atherosclerosis,” “asymptomatic atherosclerosis,” and “symptomatic atherosclerosis,” as well as by the associated health risks (non-significant, significant, and high). In addition to microbial markers, these models also incorporate an individual’s psychological state and lifestyle indicators.

References:

1. Meleshko T. V., Pallah O. V., Rukavchuk R. O., Yusko L. S., & Boyko N. V. (2020). Edible Fruits Extracts Affect Intestinal Microbiota Isolated from Patients with Noncommunicable Diseases Associated With Chronic Inflammation. *Biotechnologia Acta*, 13 (5), 87–100.
2. Toth, S., Boyko, N., & Sihotsky, V. (2021). Hypothesis of “stroke-stop” formula: a tool for risk index determination in development of acute cerebrovascular disease in asymptomatic individuals with carotid stenosis.
3. Bubnov, R. V., Spivak, M. Y., Lazarenko, L. M., Bomba, A., & Boyko, N. V. (2015). Probiotics and immunity: provisional role for personalized diets and disease prevention. *EPMA Journal*, 6, 1–11.

4. Kopolovets, I., Berek, P., Stefanic, P., Lotnyk, D., Mucha, R., Hertelyova, Z., ... & Sihotsky, V. (2020). Relevance of Lp-PLA2 blood concentration for morphological structure of atherosclerotic plaque: a shift from reactive to predictive, preventive and personalized medicine to predict stroke in patients with asymptomatic internal carotid artery stenosis.

Disclosure: Nothing to disclose.

PP0011

ESOPHAGEAL AND SALIVARY MICROBIOME RELATED WITH EOSINOPHILIC ESOPHAGITIS

M. Sasahira¹, H. Matsumoto¹, O. Handa¹, E. Umegaki¹, A. Shiotani¹, R. Inoue²

¹Kawasaki Medical School hospital, Gastroenterology, Kurashiki, Japan, ²Setsunan university, Animal Science, Neyagawa, Japan

Contact E-Mail Address: momomo0318@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic, food and/or aeroallergen-mediated inflammatory disease, characterized by esophageal dysfunction and eosinophil inflammation of the esophageal mucosa. The incidence of EoE has increased in recent years, including Japan. Pathogenesis of EoE is incomplete, and the data on microbiome related with EoE are limited. The aim of this study was to identify the esophageal and salivary microbiome in patients with EoE.

Aims & Methods: Patients either with EoE or non-EoE patients with symptoms of esophageal dysfunction who underwent esophagogastroduodenoscopy (EGD) at Kawasaki Medical School hospital between April 2021 and April 2023 were enrolled. The endoscopic reference score (EREFs) is used to determine severity of endoscopic findings. EoE patients were classified as the active group, if the presence of esophageal eosinophilia greater than or equal to 15 eosinophils per high-power field were detected during the endoscopy. Saliva and Esophageal mucous taken from esophagus using brushing samples and saliva were used to investigate microbiome in EoE patients and controls. The microbiota of samples was profiled using the Illumina MiSeq platform.

Results: Total 24 patients were enrolled including 8 active EoE patients, 5 inactive EoE patients, and 11 controls.

There were no significant differences in age, PPI use, history of gastro-esophageal reflux disease and *H. pylori* infection among the three groups. The comparative analysis of the taxonomic composition at the genus level among esophageal mucous samples indicated that *Streptococcus* were less abundant in the active EoE group compared to the other groups, and *Stomatobaculum* were more abundant in the inactive EoE group than in the controls. On salivary, The abundance of the genera *Megasphaera* were significantly more prevalent in the inactive EoE group than in the other groups. The abundance of the genera *Streptococcus* was negatively correlated with ERFs scores.

Conclusion: *Streptococcus* might be involved in the pathogenesis of EoE.

Disclosure: Nothing to disclose.

PP0012

THE ANALYSIS OF THE MICROBIOME COMPOSITION OF THE GASTRIC MUCOSA PROVIDES REPRODUCIBLE RESULTS EVEN IF DIFFERENT ANALYSIS PIPELINES ARE APPLIED

K. Lehr^{*1}, B. Oosterlinck^{*2}, C.K. Then^{*3,4}, M.R. Gemmell^{*5}, R. Gedgudas^{*6}, J. Bornschein⁷, J. Kupcinkas⁵, A. Smet², G. Hold⁸, A. Link¹, on behalf of ENIGMA: European Network for the Investigation of Gastrointestinal Mucosal Alterations *authors contributed equally

¹Otto-von-Guericke University, Gastroenterology, Hepatology and Infectious Diseases, Magdeburg, Germany, ²University of Antwerp, Laboratorium Experimental Medicine and Pediatrics, Wilrijk (Antwerp), Belgium, ³University of Oxford, MRC Oxford Institute for Radiation Oncology, Oxford, United Kingdom, ⁴Taipei Medical University, Radiation Oncology, New Taipei City, Taiwan, ⁵University of Liverpool, Centre for Genomic Research, Liverpool, United Kingdom, ⁶University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ⁷University of Oxford, MRC Translational Immune Discovery Unit, John Radcliffe Hospital, Oxford, United Kingdom, ⁸University of New South Wales, UNSW Microbiome Research Centre, Sydney, Australia

Contact E-Mail Address: konrad.lehr@med.ovgu.de

Introduction: Microbiome analysis is a promising approach for the application of findings from basic research in the clinical field. However, there is an ongoing debate about the consistency of different bioinformatics analysis platforms. The lack of established standards affects the implementation of research findings.

Aims & Methods: In our study, we demonstrated that the results on the microbial composition of gastric mucosal biopsies are only slightly influenced by the efficacy of different microbiome analysis platforms. Furthermore, we investigated whether recent revisions to the International Code of Nomenclature for Prokaryotes and consequent alterations in taxonomic classification influenced the findings.

Gastric biopsy specimens were obtained from gastric cancer patients with well-defined clinical profiles (n=40), including individuals with and without *Helicobacter pylori* (*H. pylori*) infection, and from control subjects (n=39) with and without *H. pylori* infection. DNA extraction and 16S rRNA gene sequencing (V1-V2) was performed at one site, and the resulting fastQ files were distributed to five expert teams for independent analysis. Three widely used bioinformatics pipelines for microbiome analysis, namely DADA2, MOTHUR and QIIME2, were used for the analysis.

Results: The generated fastQ files exhibited no platform-dependent clustering, indicating the comparability of the sequences. Microbial diversity was slightly reduced in both GC groups and significantly reduced in the *H. pylori* positive controls. This is due to an extreme increase in the relative abundance of *H. pylori* in this group. It also follows that the samples of the *H. pylori* positive control group have a very high similarity and form the clearest cluster in the corresponding analysis. Regardless of the protocol used, *H. pylori* status, microbial diversity and relative bacterial abundance were reproducible on all platforms. Although minor differences in performance were detected and assessed, similarity analysis and bacterial enrichment assessment also yielded consistent results. The introduction of the new taxonomy only had a major impact on the *Proteobacteria* phylum, as it originally also included *H. pylori* according to the old taxonomy, but this is now assigned to the new *Campilobacterota* phylum.

Conclusion: In summary, our findings demonstrate that disparate microbiome analysis methodologies employed by independent research teams can yield comparable results from identical datasets.

Disclosure: Nothing to disclose.

PP0013

GUT MICROBIOTA AND AUTOIMMUNE ATROPHIC GASTRITIS

M. Palo¹, F. Pelizzaro², G. Corra^{1,2}, S. Facchin³, E.V. Savarino⁴, F. Zingone⁵

¹University of Padua, Potenza, Italy, ²University of Padua, Padua, Italy, ³University of Padua, Surgical, Oncology and Gastroenterology, Padova, Italy, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁵University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy

Contact E-Mail Address: fabiana.zingone@unipd.it

Introduction: Autoimmune Atrophic Gastritis (AAG) is a chronic immune-mediated condition that mainly affects the body and fundus of the stomach. AAG is often under-diagnosed due to the slow progression of the disease and a variable spectrum of symptoms. Recent data suggests a potential role of altered gastric microbiota in the natural history of AAG, due to the potential overgrowth of bacteria linked to the development of neoplastic complications (neuroendocrine tumors- NETs and gastric cancer) (1,2). Moreover, the same data hypothesizes the use of fecal microbiota as a possible non-invasive marker to diagnose and monitor AAG. Thus, we aimed to prospectively characterize the salivary and fecal microbiota of patients with AAG to provide further insights in this field.

Aims & Methods: We collected salivary and fecal samples from consecutive patients with an established diagnosis of AAG, enrolled at the Gastroenterology Unit of Azienda Ospedale Università Padova from March to June 2023 at the time of endoscopic follow-up examination. All patients needed to be off Proton-Pump Inhibitors, antibiotics, and probiotics for at least one month before enrolment. Stool samples were collected by the patients on the day of the endoscopy, transferred in a buffer solution, and stored at -20°C. Oral samples were collected through salivary commercial kits and frozen at -20°C. Both salivary and faecal samples were analyzed by BMR Genomic (Padua, Italy) that amplified the V3-V4 hypervariable ribosomal RNA region. Sequencing of the 16S rRNA gene V3- V4 region was performed using the Illumina MiSeq. Preliminary analyses were conducted on individual fecal samples compared to an internal population of healthy subjects (provided by BMR genomics) using Qiime2 tools. Shannon-Wiener index was used to calculate α -diversity and then the microbial biodiversity index (MBI) and Dysbiosis Index (DI). Mann-Whitney tests were performed to verify statistical differences in the α -diversity across AAG patients and healthy subjects.

Results: We enrolled 15 AAG patients with a mean age of $\pm 63 \pm 11$ years (9/15 females). OLGA 2 stage was reported in 10/15 patients. Sixty percent of the patients showed a MBI between 7.11 and 12.45, indicating that each sample contained phylogenetically similar species. The remaining patients have an index greater than 12.45 compared to the healthy population. More than half of the patients had dysbiosis (>0.082). The highest indices of dysbiosis were found in patients with a history of NET (n=3), gastric cancer (n=1), and previous HP- infection and OLGA 3 stage (n=1). Firmicutes, Bacteroidetes, and Proteobacteria were more frequent phyla found in the fecal samples, whereas Enterobacteriaceae and Streptococcaceae were the most common bacterial families (13/15, 87%). In particular, Klebsiella and Campylobacter pathogens genera were found in some samples. Streptococcus and Prevotella were the most abundant genera found in the salivary samples.

Conclusion: Patients with AAG were found to have a great proportion of Firmicutes and Bacteroidetes, which aligns with the literature (3,4). Moreover, a dominant of Proteobacteria, especially Enterobacteriaceae commonly associated with proinflammatory states, was found. (5) Our preliminary data showed a possible positive association between higher degrees of dysbiosis and a previous history of NET or gastric cancer.

References:

1. Parsons BN, Ijaz UZ, D'Amore R, Burkitt MD, Eccles R, Lenzi L, Duckworth CA, Moore AR, Tiszlavicz L, Varro A, Hall N, Pritchard DM. Comparison of the human gastric microbiota in hypochlorhydric states arising as a result of Helicobacter pylori-induced atrophic gastritis, autoimmune atrophic gastritis and proton pump inhibitor use. *PLoS Pathog.* 2017 Nov 2;13(11):e1006653.
2. Conti L, Annibale B, Lahner E. Autoimmune Gastritis and Gastric Microbiota. *Microorganisms.* 2020 Nov 19;8(11):1827.
3. Castaño-Rodríguez N, Goh KL, Fock KM, et al. Dysbiosis of the microbiome in gastric carcinogenesis. *Sci Rep.* 2017;7(1):15957.
4. Conti L, Borro M, Milani C, Simmaco M, Esposito G, Canali G, Pilozi E, Ventura M, Annibale B, Lahner E. Gastric microbiota composition in patients with corpus atrophic gastritis. *Dig Liver Dis.* 2021 Dec;53(12):1580-1587.
5. Rizzatti G, Lopetuso LR, Gibiino G, Binda C, Gasbarrini A. Proteobacteria: A Common Factor in Human Diseases. *Biomed Res Int.* 2017;2017:9351507.

Disclosure: Nothing to disclose.

PP0014

REVIEW OF CONSECUTIVE CASES OF CLOSTRIDIODES DIFFICILE INFECTION AND ASYMPTOMATIC CARRIAGE OF TOXIGENIC C. DIFFICILE IN CHILDREN, OVER A 7-YEAR PERIOD

A. Desai^{1,2,3}, Y. Mahida^{1,2,3}

¹NIHR Nottingham Biomedical Research Centre, School of Medicine, University of Nottingham, Nottingham, United Kingdom, ²Nottingham Digestive Diseases Centre, University of Nottingham, Nottingham, United Kingdom, ³Translational Medical Sciences, School of Medicine, University of Nottingham, Nottingham, United Kingdom

Contact E-Mail Address: avnidesai31@gmail.com

Introduction: *C. difficile* infection (CDI) remains a significant clinical problem and has been extensively investigated in adults but by comparison is much less studied in children. Following colonisation with toxigenic *C. difficile*, clinical presentation may range from asymptomatic carriage to pseudomembranous colitis. Diagnosis of CDI can be challenging, with toxin-positive stool test (in the presence of diarrhoea) believed to reflect infection.

Aims & Methods: Our aim was to study children diagnosed with CDI and asymptomatic carriage of the organism. From 2015 - 2022, details of relevant stool test results were collected prospectively and clinical information was reviewed retrospectively. Detection of stool *C. difficile* toxin (toxin +ve) was used to imply CDI and its absence (toxin -ve), together with positive polymerase chain reaction (PCR) test for toxigenic *C. difficile* (PCR +ve) deemed to reflect asymptomatic carriage. Hospital-association was based on stool test undertaken >48 hours post-admission or within 4 weeks of discharge.

Results: Of total 113 patients, 57 [50.4%, median 11.0 (range 1-17) yrs, 31 male] were toxin +ve and were treated for CDI; 26 (45.6%) had co-existing cancer (80.8% on chemotherapy), 9 patients (15.8%) suffered from inflammatory bowel disease (IBD, 5 Crohn's disease and 3 unclassified) and 5 patients (8.77%) had had a transplant. Of the 57 CDI patients, 11 (19.3%) previously had a toxin-negative stool test result and 14 (24.6%) had a subsequent recurrence of CDI [of the latter subgroup, 7 (50%) were on chemotherapy for cancer and 2 (14.3%) had a prior transplant]. Of the 113 patients studied 48 [42.5%, 11.5 (1-18) yrs, 21 male] were PCR +ve but toxin -ve and were deemed asymptomatic carriers as they did not require treatment for CDI; 22 patients (45.8%) had co-existing cancer (all

on chemotherapy), 11 (23%) suffered from IBD (9 Crohn's disease) and 3 patients (6.25%) had had a transplant. There were no significant differences between the above 2 groups (CDI and asymptomatic carriers) in age, male:female ratio, co-existing cancer, IBD, current / recent antibiotics or chemotherapy. Eight [7.1%, 13.5 (9-17) yrs, 5 male] of the 113 patients studied were PCR +ve and toxin -ve but were deemed to require treatment for CDI. For all 3 groups, >84% were hospital-associated episodes and >71% were associated with the use of antibiotics.

Conclusion: A significant proportion of children with CDI and asymptomatic carriage of toxigenic *C. difficile* had co-existing cancer (majority on chemotherapy) and IBD and were predominantly hospital-associated. Some asymptomatic carriers may subsequently develop CDI and require measures to reduce this risk. Stool *C. difficile* toxin test may be <100% sensitive for diagnosis of CDI. Following initial episode of CDI, antibiotic use and chemotherapy for cancer represent significant risk factors for recurrence for CDI in children. Further research is needed to identify risk factors for CDI in children with asymptomatic carriage of toxigenic *C. difficile*.

Disclosure: Nothing to disclose.

PP0015

MULTIDRUG RESISTANT ORGANISMS IN GASTROENTEROLOGIC PATIENTS: PREVALENCE AND RISK FACTORS

R. Galli¹, A. Toppeta¹, P. Molteni², S. Ardizzone², G. Maconi^{2,1}, A. Dell'Era^{2,1}
¹Università degli Studi di Milano, Department of Biomedical and Clinical Sciences 'Luigi Sacco', Milano, Italy, ²ASST Fatebenefratelli Sacco, UOC Gastroenterologia ed Endoscopia Digestiva, Milano, Italy

Contact E-Mail Address: angelica.toppeta@unimi.it

Introduction: Colonization/infection with multidrug-resistant organisms (MDROs) such as methicillin-susceptible staphylococcus aureus (MSSA), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase (ESBL) producing Enterobacterales and carbapenem resistant *P. aeruginosa*, is an increasing problem being reported worldwide. Rectal, cutaneous and nasal swab screening allows for the detection of MDROs in asymptomatic individuals, enabling early identification and subsequent implementation of infection control measures to prevent transmission.

Aims & Methods: The aim of this study was to determine the prevalence as well as the risk factors of colonization/infection with MSSA, MRSA, VRE, ESBL producing Enterobacterales and carbapenemase producing *P. aeruginosa*, in patients hospitalized in gastroenterologic and oncologic and surgical unit for gastroenterologic diseases. Methods: all the consecutive patients hospitalized from May 2023 to March 2024 in the abovementioned units at admission underwent rectal swabs to identify the presence of MDROs, primarily methicillin-susceptible staphylococcus aureus (MSSA), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase (ESBL) producing Enterobacterales and carbapenemase producing *P. aeruginosa*. Demographic, clinical and therapeutic variables were evaluated.

Results: 242 patients were hospitalized (mean age 65,6 ± 17,8 years; 56% males). MDRO were present in 17,36% of patients (n.42). 7 % of patient tested positive for *Escherichia coli* ESBL+, 3.7% for *Klebsiella pneumoniae* ESBL+ and 2.5% for *Enterococcus faecium* VRE at rectal swab. 2.1% of patient tested positive at nasal swabs for MSSA, 2.1% for MRSA, 0.4% for *E. coli* ESBL and 0.4% for *K. pneumoniae* ESBL. 0.4% of patient were positive at cutaneous swab for *E. faecium* VRE and 0.4% for *K. pneumoniae* ESBL. At univariate analysis hospitalization within 1 year, ongoing treatment with PPI, ongoing steroid treatment and chronic renal failure were asso-

ciated to the risk of a positive surveillance swab. At multivariate analysis only hospitalization, ongoing steroid treatment and chronic renal failure were independent predictors of colonization (table).

	Univariate	Multivariate
	OR (95% C.I.)	OR (95% C.I.)
Hospitalization within 1 year	2.4 (1.2 - 4.6)	2.2 (1.1 - 4.4)
PPI treatment	2.2 (1.1 - 4.4)	
Ongoing steroid treatment	3.7 (1.4 - 9.7)	2.9 (1.1 - 8.2)
Chronic Renal Failure	6.5 (1.9 - 22.4)	6.6 (1.8 - 24.5)

Conclusion: This research offers information on how common MDROs are among gastroenterology patients. It contributes to the existing knowledge and aids in addressing the spread of MDROs by customizing screening methods based on individual patient factors, like past hospital stay, ongoing steroid treatment and chronic renal failure.

Disclosure: Nothing to disclose.

PP0016

IMPACT OF NSAIDS ON OUTCOMES OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

R. Fernandez¹, M. López-Vico², A. Lanco Muñoz¹, J.M. Lopez Tobaruela³, C. Tintero-Peinado¹, E.J. Ortega-Suazo⁴, R. Jiménez-Rosales⁵, J.G. Martínez-Cara⁶, E. Redondo-Cerezo²
¹Hospital Universitario Virgen de las Nieves, Granada, Spain, ²Hospital Universitario Virgen de las Nieves, Gastroenterology, Granada, Spain, ³Hospital Virgen de las Nieves, Department of Gastroenterology and Hepatology, Granada, Spain, ⁴Hospital Universitario Virgen de las Nieves, Aparato Digestivo, Granada, Spain, ⁵Hospital Universitario Virgen de Las Nieves, Gastroenterology, Granada, Spain, ⁶Hospital virgen de las nieves, Endoscopy Unit, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: Non-variceal upper gastrointestinal bleeding (NVUGI) represents a significant gastrointestinal disorder with elevated mortality rates (1).

Non-steroidal anti-inflammatory drugs (NSAIDs) have been firmly established as a risk factor for NVUGI, yet their precise impact on clinical outcomes remains insufficiently defined (2,3).

Conversely, proton pump inhibitors (PPIs) have shown efficacy in reducing the incidence of NVUGI associated with NSAIDs. However, the extent of their influence on the clinical outcomes of NVUGI remains inadequately substantiated. Therefore, it is necessary to study the impact of these drugs on the clinical outcomes of patients with NVUGI.

Aims & Methods: The primary objective of our study is to compare the outcomes of NVUGI patients using NSAIDs with or without PPIs against those who did not use either medication. We conducted a retrospective analysis at a Spanish tertiary hospital, encompassing NVUGI cases from 2013 to 2022. NVUGI was defined as hematemesis or melena accompanied by a two-point decrease in hemoglobin or hemodynamic instability. Key clinical outcomes included the necessity for intervention (endoscopic, radiological, or surgical) and in-hospital mortality.

Additionally, we compared baseline characteristics and pertinent clinical results such as rebleeding and delayed cardiovascular events. Statistical analysis was performed using SPSS.

Results: A total of 1200 cases were included, with 6.6% undergoing concomitant treatment with PPIs and NSAIDs, and 15.7% utilizing NSAIDs alone. Patients who took NSAIDs alone were younger (57 years vs. 66 in both other groups) and had a lower rate of comorbidities. Table 1 presents risk scores and outcome comparisons among the three groups. Statisti-

cal differences were observed, revealing lower acute mortality (9.6% vs. 7 vs. 2.8%, $p=0.011$) and reduced need for intervention (74% vs. 69.6 vs. 57.8%, $p<0.001$) in the group using NSAIDs alone. In multivariate analysis, MAP(ASH) > 2 (OR: 8, CI: 3-21, $p<0.001$) and ASA > 2 (OR: 4.4, CI: 1.7-11.4, $p:0.002$) emerged as independent risk factors for acute mortality, with an elevated MAP(ASH) score (OR: 8.8, CI: 5.9-13, $p<0.001$) being the sole independent factor explaining the need for intervention.

	Naive	NSAIDs and PPIs	NSAIDs without PPIs	P
ASA 3-4	596 (64,3%)	50 (63,3%)	63 (33,7%)	<0,001
MAPASH>2	448 (59,3%)	39 (65%)	52 (34,4)	<0,001
Need for intervention	691 (74%)	55 (69,6%)	108 (57,8%)	<0,001
Rebleeding	96 (10,3%)	9 (11,4%)	6 (3,2%)	0,008
Acute mortality	86 (9,6%)	5 (7%)	5 (2,8%)	0,011
Mortality at 6 months	77 (8,8%)	7 (9,3%)	7 (3,8%)	0,075
Delayed Cardiovascular event	77 (8,7%)	3 (3,9%)	4 (2,2%)	0,004
Delayed rebleeding	145 (16,4%)	15 (19,5%)	6 (3,3%)	<0,001

Conclusion: Patients abstaining from NSAIDs or those concurrently undergoing PPI therapy exhibited a higher incidence of intervention or acute mortality compared to those solely using NSAIDs. Through multivariate analysis, our study indicates that bleeding severity and baseline comorbidities, expressed by elevated MAP(ASH) scores and ASA classification, are pivotal factors influencing the clinical outcomes of NVUGI. In summary, the use of NSAIDs or PPIs to safeguard against gastrointestinal lesions induced by these drugs did not demonstrate a discernible impact on the short-term outcomes of patients with non-variceal upper gastrointestinal bleeding.

References:

1. Lakatos L, Gonczi L, Lontai L, Izbeki F, Patai A, Racz I, et al. Incidence, predictive factors, clinical characteristics and outcome of non-variceal upper gastrointestinal bleeding – a prospective population-based study from hungary. *Journal of Gastrointestinal and Liver Diseases*. 2021 Sep 1;30(3):327–33.

2. Durak MB, Şimşek C, Yüksel İ. Clinical Outcomes of Older Patients with Non-Variceal Upper Gastrointestinal Bleeding Taking Anti-Thrombotic or Non-Steroidal Anti-Inflammatory Agents. *Turkish Journal of Gastroenterology*. 2023 Sep 1;34(9):918–24.

3. Åhsberg K, Höglund P, Kim WH, Von Holstein CS. Impact of aspirin, NSAIDs, warfarin, corticosteroids and SSRIs on the site and outcome of non-variceal upper and lower gastrointestinal bleeding. *Scand J Gastroenterol*. 2010 Dec;45(12):1404–15.

Disclosure: Nothing to disclose.

PP0017

FACTORS ASSOCIATED WITH EARLY VARICEAL ERADICATION AFTER ENDOSCOPIC LIGATION

M. Piazzolla¹, N. Favia¹, A. Iannone¹, S. Rizzi¹, A. Di Leo¹, G. Losurdo¹
¹University of Bari, Section of Gastroenterology, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy

Contact E-Mail Address: nicolasfavia96@gmail.com

Introduction: Esophageal varices are present in up to 40% and 85% of patients with compensated and decompensated cirrhosis, **respectively**. Endoscopic treatment of esophageal varices is used for the prevention of first variceal bleeding, treatment of active variceal bleeding, and prevention of rebleeding. Endoscopic variceal ligation (EVL) is the most common treatment. Multiple EVL sessions are often required to eradicate them. We aimed to detect factors predicting lower number of endoscopic treatments.

Aims & Methods: The study recruited all cirrhotic patients admitted to the hospital within the last two years, who have been treated for esophageal varices by EVL and achieved eradication through this endoscopic treatment. For each patient, main demographical and clinical characteristics were collected, including, etiology of cirrhosis, severity of liver disease according to Child-Pugh and MELD score and main laboratory tests. Varices were described according to the Japanese classification, and for each EVL session number of placed bands was recorded. Binomial logistic regression was used for univariate and multivariate analysis and odds ratios (OR) were calculated.

Results: A total of 31 patients (71% males, mean age 62.7±9.2) with liver cirrhosis and esophageal variceal (F2 41.9% and F3 58.1%) were included. The most frequent etiologies were alcoholic cirrhosis, non-alcoholic steatohepatitis and cryptogenic cirrhosis, in 8 (25.8%), 9 (29%) and 4 (12.9%), respectively. Esophageal Varices with Red Color Sign on Endoscopy, Cherry Red Spot (CRS), Red Wale Markings (RWM) and Hematocystic Spots (HCS), were detected in 19 (61.3%) 23 (74.2%) 5 (16.1%) patients. Only 8 patients (25.8 %) had gastroesophageal varices (GOV) while 30 subjects (96,8%) had congestive gastropathy. Concerning severity of cirrhosis, there were 13 (41,9%), 17 (54,8%), 1(3,2%) patients in Child Pugh's class A, B and C, respectively. In 14 subjects, a single session was sufficient to eradicate varices, while 9 patients required ≥3 sessions. At multivariate analysis, higher platelet count (OR=0.98, $p=0.15$), higher number of rubber bands (OR=0.67 $p=0.16$) and female sex (OR= 0.24, $p=0.11$) predicted the fewer number of endoscopic sessions required for eradication of varices, while at multivariate analysis, only higher platelet count demonstrated a non significant trend (OR= 0.98, $p=0,07$).

Conclusion: When performing endoscopic ligation of esophageal varices, the number of platelets could influence the number of endoscopic sessions to eradicate esophageal varices.

Disclosure: Nothing to disclose.

PP0018

ALCOHOL ABUSE DOES NOT IMPACT IN OUTCOMES OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

R. Fernandez¹, J.M. Lopez Tobaruela², C. Tendaro-Peinado¹, R. Jiménez-Rosales³, A. Lancho Munoz⁴, M. López-Vico⁴, E.J. Ortega-Suazo⁵, J.G. Martínez-Cara⁶, E. Redondo-Cerezo⁴
¹Hospital Universitario Virgen de las Nieves, Granada, Spain, ²Hospital Virgen de las Nieves, Department of Gastroenterology and Hepatology, Granada, Spain, ³Hospital Universitario Virgen de Las Nieves, Gastroenterology, Granada, Spain, ⁴Hospital Universitario Virgen de las Nieves, Gastroenterology, Granada, Spain, ⁵Hospital Universitario Virgen de las Nieves, Aparato Digestivo, Granada, Spain, ⁶Hospital virgen de las nieves, Endoscopy Unit, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: Alcohol abuse is a significant risk factor for the development of hepatic cirrhosis, which can lead to upper gastrointestinal bleeding. In non-cirrhotic patients, alcohol has been studied as a risk factor for non-variceal upper gastrointestinal bleeding (NVUGI), particularly in cases of peptic ulcer bleeding (1). However, the clinical impact of alcohol abuse on outcomes remains unclear. Only one retrospective study has analyzed this, finding an increased risk of rebleeding and non-significant increased mortality among alcohol consumers (2). Nevertheless, this study included cirrhotic patients, who accounted for most of the mortality. There is currently no available data on the impact of alcohol on NVUGI outcomes in non-cirrhotic patients.

Aims & Methods: This study aims to determine the impact of alcohol consumption on clinical outcomes in NVUGI.

We conducted a retrospective analysis at a Spanish tertiary hospital, encompassing NVUGI cases from 2013 to 2022. Alcohol abuse was defined as daily alcohol intake exceeding 20g. Key clinical outcomes included the need for intervention (transfusion, endoscopic, radiological, or surgical) and in-hospital mortality. In addition, we compared baseline characteristics and assessed both acute and delayed 6 months outcomes, including rebleeding and delayed cardiovascular events. Statistical analysis was performed using SPSS.

Results: A total of 892 cases were included. The alcohol abuse group had a higher proportion of men (95.6% vs. 64.1%, $p < 0.001$) and were younger (median age of 56 years vs. 66 years, $p < 0.001$). Non-alcohol consumers had more comorbidities and a higher ASA comorbidity risk score (58% had ASA 3 or 4 vs. 46% in the other group, $p = 0.015$). Additionally, the MAP(ASH) score was higher in the first group (>2 in 54.5% vs. 46.3%, $p = 0.030$). We did not find any other differences between groups, neither in key outcomes nor in the remaining comparisons for the acute episode. However, delayed mortality (8.2% in group 1 vs 3.1% in group 2, $p=0.046$) and six months cardiovascular events (8.9% vs 2.3%, $p=0.011$) were more frequent in the non-alcohol group. In multivariate analysis, only ASA 3-4 (OR: 4.17, CI: 1.49-11.68, $p = 0.006$) and MAP(ASH) (OR: 7.61, CI: 2.54-22.8, $p < 0.001$) were found to be independent risk factors for acute mortality.

	No Alcohol	Alcohol	p
Age	66,75	56,88	<0,001
Sex	Men 464 (61,4%)	Men 130 (95,6%)	<0,001
Chronic obstructive pulmonary disease	75 (9,9%)	13 (9,6%)	0,896
Chronic renal disease	126 (16,7%)	6 (4,4%)	<0,001
Heart failure	91 (12%)	6(4,4%)	0,009
High blood pressure	368(48,7%)	52 (38,2%)	0,071
Diabetes mellitus	182 (24,1%)	19 (14%)	0,009
Smoking	95 (12,6%)	69 (50,7%)	<0,001
MAPASH >2	334 (54,5%)	49 (43,4%)	0,030

Conclusion: Alcohol abuse is more common among younger individuals with fewer comorbidities. This consumption does not worsen clinical outcomes in non-cirrhotic NVUGI patients, with similar rates of need for intervention or mortality. Our results indicate that only comorbidities and bleeding severity (summarized as high ASA score and MAP(ASH)) score influence the outcomes. In summary, while alcohol consumption may increase the risk of NVUGI incidence, it does not impact acute outcomes.

References:

1. Kelly JP, Kaufman DW, Koff RS, Laszlo A, Wiholm BE, Shapiro S. Alcohol consumption and the risk of major upper gastrointestinal bleeding. *Am J Gastroenterol*. 1995 Jul;90(7):1058-64.
2. Kärkkäinen JM, Mäilunpohja S, Rantanen T, Koskela JM, Jyrkkä J, Hartikainen J, Paajanen H. Alcohol Abuse Increases Rebleeding Risk and Mortality in Patients with Non-variceal Upper Gastrointestinal Bleeding. *Dig Dis Sci*. 2015 Dec;60(12):3707-15

Disclosure: Nothing to disclose.

PP0019

ACUTE UPPER GI BLEEDING – IMPROVING INITIAL MANAGEMENT IN 2 DGHS

R. Bragg¹, M. Mohamed², A. Hutchings², E. Brown², Z. Courtoux², W. Mulvaney², I. Malik², F. Kelly², H.M. Amin², S. Ullah², M. Javaid², M. Butt², L.J. Neilson³

¹South Tyneside and Sunderland NHS Foundation Trust, South Shields, United Kingdom, ²South Tyneside and Sunderland NHS Foundation trust, South Shields, United Kingdom, ³South Tyneside and Sunderland NHS Foundation Trust, Gastroenterology, South Shields, United Kingdom

Contact E-Mail Address: rebecca.bragg@nhs.net

Introduction: Acute Upper GI bleeds (AUGIB) are common and are associated with significant mortality (1). Quick recognition, resuscitation and endoscopy improves patient outcomes (2).

Care bundles are known to improve care. The BSG 2018 AUGIB bundle was designed to standardise care. We aimed to audit management of AUGIB in two sites in North East England.

Aims & Methods: We retrospectively analysed patients who underwent endoscopy for AUGIB from May-October 2023. We surveyed junior doctors to assess knowledge and confidence in managing AUGIB.

Results: 98 patients were identified across 2 sites, the mean age was 66, and 58% were male. The AUGIB bundle was used in 10% cases.

Recognition: 83% presented to A+E with AUGIB with the remainder already inpatients. 78% presented with melaena, and 24% were suspected variceal bleeds.

Resuscitation: 100% had EWS scores, 87% received IV fluids, and 93% patients with Hb<70 received RBC transfusion.

Risk Assessment: Mean Glasgow-Blatchford score (GBS) was 9 for both sites. Site 1 had calculated a GBS in 65% cases, and site 2 in 88%.

	Site 1	Site 2	Overall
Variceal bleeds receiving antibiotics and terlipressin	50% (n=5)	69% (n=9)	61% (n=14)
Aspirin continued	60% (n=3)	66% (n=6)	64% (n=9)
Other antithrombotics held	100% (n=17)	91% (n=20)	95% (n=37)

Table 1: Summary of treatment

Refer: of the 98 patients 70% discussed with endoscopist within 24hours, 47% had an OGD within 24 hours, and 30% required endoscopic intervention.

Review: 84% (site1) and 63% (site 2) had PPI plan, 50% (site 1) and 36% (site 2) had antithrombotic plan.

Of the small number of patients in which the bundle was used, all received appropriate resuscitation, all had GBS completed and all had OGD within 24hours of presentation.

200 surveys were sent across sites, 61 junior doctors responded. 73% felt confident in recognising AUGIB, and 65% felt confident in management. Only 32% knew appropriate initial variceal management. 40% were unsure when to call OOH endoscopist, and only 36% knew aspirin should continue.

Conclusion: Whilst recognition of AUGIB and fluid resuscitation is good, improvement is needed for risk assessment with GBS, management of suspected variceal bleeds, and timely referral for endoscopy. More detailed endoscopy reports are needed regarding PPI and antithrombotic plans.

More education with junior doctors is needed regarding management of AUGIB, and particularly when to call endoscopist and antithrombotic decisions. It would be helpful to educate staff to improve management. A reaudit of clinical management and the junior doctor survey is planned.

References: (1) Button LA, Roberts SE, Evans PA, Goldacre MJ, Akbari A, et al. (2011) Hospitalized incidence and case fatality for upper gastrointestinal bleeding from 1999 to 2007: a record linkage study. *Aliment Pharmacol Ther* 33: 64–76.

(2) McPherson SJ et al, National confidential enquiry into patient outcomes and deaths, Gastrointestinal haemorrhage, time to get control? 2015

Disclosure: Abstract submitted to BSG Live 24.

PP0020

AN IN-DEPTH ANALYSIS OF MORTALITY OF HOSPITALIZED PATIENTS WITH SUSPECTED NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING – DATA FROM A PROSPECTIVE REGISTRY

D. Venturi^{1,2}, M. Birk^{1,2}, S. Bernhofer^{1,2}, A. Maieron^{1,2,3}, J. Prosenz^{1,2,3}

¹Karl Landsteiner University of Health Sciences, GI Endoscopy Quality Matters working group (GIEQM), Krems, Austria,

²University Hospital St. Pölten, Department of Internal Medicine 2 Gastroenterology & Hepatology, St. Pölten, Austria, ³Paracelsus Medical University, Salzburg, Austria

Contact E-Mail Address: David.Venturi@stpoelten.lknoe.at

Introduction: Non-variceal upper gastrointestinal bleeding (nvUGIB) mortality has improved but remains high. Guidelines on nvUGIB often focusing on pre- and endoscopic management. However, more data on causes of death are needed, because non-bleeding specific mortality is unlikely to be improved by interventional advances.

Aims & Methods: The aims of this retrospective analysis of a single tertiary center registry of patients with nvUGIB were to assess causes of death in patients with nvUGIB and characterize this cohort. All hospitalized patients evaluated for suspected non-variceal UGIB (i.e., patients undergoing endoscopy) at our endoscopy unit between January 2018 and October 2020, either due to presentation for nvUGIB or with a suspected bleeding episode during hospitalization for any reason, were included in a prospective registry.

Data on pre-endoscopic signs/symptoms of UGIB, epidemiological data, laboratory values, and medications were extracted from the electronic health record. Endoscopy reports were individually searched and relevant data including the most likely culprit lesion in the opinion of the endoscopist as well as respective hemostatic treatment extracted.

Results: Among 1135 patients – 41.7% women, mean age 70.4 (±15.7) years, median length of stay 8 (IQR 4;16) days – 92 (8.1%) died during hospitalization and were further analyzed. Mean age was 73.2 (±12.9) years, 44.5% were women, 36% of patients were on anticoagulation, 27% on antiplatelet therapy, and 9% on both. The median Charlson comorbidity index was 5 (IQR 3;6.8), the CHA₂DS₂-VASc-Score 3 (IQR 2;5).

However, the median AIMS65 score was only 2 (IQR 1;2). Median time from admission to death was 17 (IQR 6.5;30) and from endoscopy to death 11 (IQR 4;21.5) days. The most common sources of bleeding as determined by endoscopy reports were: uncertain (24%), peptic ulcer (21%), esophagitis (14%), and non-peptic ulcers (9%). Adherence to guideline-based endoscopic peptic ulcer management recommendations was 70%. Radiological intervention for bleeding was performed in 1%, surgical intervention in 8.7%. Patients who died were older (73.2 vs. 70 years, $p=0.0336$), had lower hemoglobin nadirs (7.1 vs. 7.8 g/dL, $p<0.0001$), high c-reactive protein levels ($p<0.0001$) and creatinine ($p<0.01$), had longer lengths of stay (LOS) (median LOS 17 vs. 8 days, $p<0.0001$), and longer times from admission to endoscopy (median 3 days vs. 1 day, $p<0.0001$). However, sex was not associated with mortality ($p=0.58$). Looking at bleeding in association with causes of death, mostly ($n=55$, 59.8%), bleeding was cat-

egorized as a bystander. Only 32.6% of causes of death were judged as directly due to or likely associated with the bleeding episode, and these patients had a higher AIMS65 ($p=0.0301$). Only 12% died due to an unmanageable bleeding (or change to best supportive care). Overall, the following major groups of causes of death were identified: malignancy (18.5%), multi-organ failure (17.4%), infection/sepsis (15.2%), bleeding-associated (15.2%), cardiovascular (13.0%), and others (23.9%).

Conclusion: UGIB mortality remains relatively high despite management advances. However, only a minority of patients die due to UGIB and even among those most deaths are related to sequelae of the bleeding instead of unmanageable bleeding. Patients who die are older, likely sicker, and suffer from many comorbidities. Based on these data, it is uncertain whether focusing on endoscopic management improvements will significantly change UGIB-related mortality. Possibly, the focus should be shifted to improving general/internal medicine or geriatric care.

Disclosure: Nothing to disclose.

PP0021

TIMING OF ANTICOAGULATION RESUMPTION AFTER GASTROINTESTINAL BLEEDING: A COHORT STUDY OF 218 PATIENTS

D. Palinkas^{1,2}, B. Teutsch^{2,3}, N. Vörhendi³, O.A. Simon^{3,4}, E. Boros^{5,3}, L. Frim³, P. Hegyi^{2,6}, T.Z. Gyökeres¹, B. Eross^{2,6}

¹Central Hospital of Northern Pest – Military Hospital, Department of Gastroenterology, Budapest, Hungary,

²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³University of Pécs, Institute for

Translational Medicine, Pécs, Hungary, ⁴University of Pécs, First Department of Medicine, Pécs, Hungary, ⁵Fejér County Szent György University Teaching Hospital, First Department of Internal Medicine, Székesfehérvár, Hungary, ⁶Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary

Contact E-Mail Address: dr.d.palinkas@gmail.com

Introduction: Restarting anticoagulation (AC) therapy following acute gastrointestinal bleeding (GIB) is a multidisciplinary, personalized decision. Current guidelines recommend resuming AC, though data on the optimal timing is limited.

Aims & Methods: Our aim is to assess the short-term effect of early and delayed AC therapy resumption.

We analyzed the data of the Hungarian GIB Registry (a multicenter, prospective database) between 2019-2022. Patients were included after successful management of AC-related GIB. Detailed medical and drug history, demographics, and data on the index bleeding and management (bleeding source, endoscopic, and medical therapy) were collected. 30 and 90-day rebleeding, thromboembolic (TE) complications, all-cause, and 30-day recurrent GIB or TE-related mortality were assessed in the early (≤ 7 days) and delayed (>7 days) AC resumption groups.

Results: 218 cases were analyzed. Except for the CHA₂DS₂-VASc score (mean (SD) 5.19 (1.65) vs 4.37 (1.549); $p=0.02$), the main characteristics (e.g., age, Charlson comorbidity index, active malignancy, anamnestic previous GIB, co-medications, HAS-BLED score, hemodynamic instability, high-risk bleeding site, endoscopic intervention) were similar between the two groups. Delayed AC therapy resumption was not associated with decreased 30-day rebleeding risk (5.3% vs. 6.7%; HR = 1.26, 95%CI 0.27-5.77, $p=0.76$). Delayed resumption was not associated with a higher 90-day TE complications rate (2.1% vs. 6.6%; HR = 3.17, 95%CI 0.58-17.33, $p=0.18$). Recurrent GIB-related 30-day mortality occurred only in one case (early resumption group, 12 days after admission with index bleeding). TE-related mortality was not observed during the follow-up.

Conclusion: Anticoagulation resumption in the first seven days after GIB was proven to be safe, which supports the suggestion of the actual European guidelines. Further research on separated bleeding sources and types of anticoagulants is needed.

Disclosure: Authors do not have any conflict of interest to disclose.

PP0022

EXPERIENCE IN THE MEDICAL TREATMENT (THALIDOMIDE, LAR OCTREOTIDE) OF PATIENTS WITH BLEEDING FROM UPPER GASTROINTESTINAL (GI) VASCULAR MALFORMATIONS RESISTANT TO ENDOSCOPIC THERAPY

B. Németh¹, G. Kiss¹, G. Pécsi¹

¹Petz Aladár University Teaching Hospital, Department of Internal Medicine-Gastroenterology, Győr, Hungary

Contact E-Mail Address: nemethbence92@gmail.com

Introduction: In the treatment of bleeding from GI vascular malformations, the priority of endoscopic hemostasis methods, particularly argon plasma coagulation (APC), is unquestionable. Until now, no effective medication-based therapy has been available as an alternative or supplemental method. Previous studies have reported on the ineffectiveness of steroids, estrogens, and progestogens. In the past decade, several promising clinical trials have been conducted regarding the use of thalidomide and long-acting-release (LAR) octreotide to reduce bleeding from vascular malformations.

Aims & Methods: At the Department of Internal Medicine-Gastroenterology of the Petz Aladár University Teaching Hospital in Győr-Ménfőcsanak, in patients who did not respond to endoscopic treatment, either.

1. Investigate the efficacy and side effects of thalidomide,
2. Investigate the efficacy and side effects of LAR octreotide in patients resistant to thalidomide treatment.

From July 2021 to February 2024, 25 patients were treated for bleeding and anemia from GI vascular malformations. In 20 patients, bleeding was stopped with 35 (1-2) APC treatments. 5 polymorbid patients (male:female= 1:4, average age ~64.6 years) required regular transfusions despite previous ~7.2 APC treatments. Their predominant underlying diseases included Banti's syndrome, autoimmune hemolytic anemia, ischemic cardiomyopathy, atrial fibrillation, Osler's disease, and autoimmune hepatitis. These 5 patients underwent a 3-month course of 100mg thalidomide per day. In patients where thalidomide was ineffective or caused side effects, LAR octreotide intramuscular injections were indicated once every four weeks at a 30mg dose. Visits, blood counts, and lab tests were conducted monthly.

Results: With thalidomide treatment, the transfusion requirement ceased in 2/5 patients. In 2/5 patients, the treatment was suspended due to ineffectiveness and side effects (deep vein thrombosis, emesis). Treatment was ineffective in 1/5 patients. In the last 3 patients, LAR octreotide treatment was also ineffective. Mild side effects (meteorism, nausea, exanthemas) were observed in these patients.

Conclusion: In the care of patients bleeding from vascular malformations resistant to endoscopic therapy,

1. Thalidomide may be an effective medication,
2. Close patient monitoring is important to filter out side effects,
3. The effectiveness of LAR octreotide cannot be determined based on the study,
4. Further follow-up studies are necessary.

Disclosure: Nothing to disclose.

PP0023

ENDOSCOPIC MANAGEMENT OF NON VARICEAL UPPER GI HEMORRAGES: OUR EXPERIENCE AS A TYPE 1 DEPARTMENT

F. Frattaroli¹, M. Varanese¹, G. Burrelli Scotti¹, M. Marchese¹, A. Antoniozzi¹, S. Pontone¹, A. Pronio¹, S. Frattaroli¹, E. Fiori¹, A. Lamazza¹

¹University of Rome La Sapienza, Roma, Italy

Contact E-Mail Address: flaminia.frattaroli@uniroma1.it

Introduction: This study aims at evaluating the appropriate timing of endoscopic intervention in patients with non-variceal upper GI hemorrhages upon admission in the emergency department and treated while on call during night shifts and public holidays. The need for blood transfusion, effectiveness of treatment, safety and reliability of endoscopic management were taken into account. We analyzed the results obtained after endoscopic treatment in terms of bleeding control, procedure-related complications, average days of hospital stay, need for second endoscopic look, surgical intervention or interventional radiology, and mortality.

Aims & Methods: From January 2019 to January 2024, 1215 patients admitted in the emergency department of Policlinico Umberto I in Rome with signs of digestive bleeding, underwent an esophagogastroduodenoscopy which demonstrated that the cause of bleeding was a non-variceal lesion of the upper digestive tract. Only adult patients aged 20 to 95 (33.3% between 60 and 80), who underwent operative endoscopic procedure were included in the study. Four hundred ninety-two patients were female (40.5%). Nine hundred sixty-three (79.3%) (963) did not undergo endoscopic therapy due to spontaneous or pharmacological resolution of the cause of bleeding while in 161 patients (16.7%) endoscopic therapy was not possible due to death caused by hemodynamic instability and underlying comorbidities. Two hundred fifty-two patients (20.7%) presented, during the endoscopic examination, signs of recent or ongoing bleeding, requiring endoscopic therapy. Eleven patients who underwent treatment (4.4%) died from complications unrelated to the procedure.

Results: Urgent EGDS, within 12 hours, was performed in 78.6% (198) of cases who presented signs of persistent hemodynamic instability, with definitive endoscopic success in 51.2% (111). Fifty-four patients (21.4%) underwent emergency intervention within 24 hours once hemodynamic stability was achieved with an endoscopic success in thirty one patients (59.1%). The average duration of the endoscopic procedure was 17 minutes. The post-procedure hospital stay was 6.5 days in 79.7% (201) of patients. All procedures were performed under deep sedation, in a dedicated operating room in the presence of the anesthesiologist. Patients who underwent a very early EGDS (<12h) had an average hospital stay, need for second look and mortality similar to that of patients treated between 12 and 24h. The single endoscopic intervention was successful in 56.4% of patients (142); 26.2% (66) underwent an endoscopic second look, 5.2% (13) a surgical procedure and 3.6% (9) interventional radiology. The overall mortality was 8.8% (22 patients).

Conclusion: In our experience, the endoscopic procedure was performed in most cases within 6-12 hours of admission in the emergency room. In light of our data and the heterogeneity of the population in urgent/emergency conditions, we can state that acting within 12-24 hours has proven to be an adequate timing for the management of non-variceal upper digestive hemorrhage, with good results in terms of haemostasis and the need for an endoscopic, surgical or radiological second look. The average hospital stay and the operating time is short and the mortality rate linked to the procedure is low. In accordance with the recommendations of the European Society of Gastrointestinal Endoscopy we believe that this timing is adequate to guarantee good long-term results. A very early EGDS <12h can be considered in patients who present signs of hemodynamic instability.

Disclosure: Nothing to disclose.

PP0024

OVER-THE-SCOPE CLIP (OTSC) VS STANDARD ENDOSCOPIC APPROACH FOR PRIMARY TREATMENT OF NONVARICEAL GASTROINTESTINAL BLEEDING: SYSTEMATIC REVIEW AND METANALYSIS

Y. Dominguez-Novoa^{1,2}, J. Iglesias-Garcia^{1,2}, F. Challoukh¹, J. Lopez-Diaz^{1,2}, J.E. Domínguez Muñoz^{1,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Contact E-Mail Address: yessica.dominguez.novoa@sergas.es

Introduction: Non-variceal gastrointestinal bleeding is a common condition associated with significant morbidity and mortality. Several approaches are available for primary endoscopic treatment. The standard endoscopic approach uses contact thermal methods or hemoclips with or without pre-injection of diluted epinephrine. A newer alternative is the use of an over-the-scope clip (OTSC).

Aims & Methods: The aim of our study was to evaluate the efficacy of these two modalities in the treatment of non-variceal gastrointestinal bleeding. Methods: PubMed, EMBASSE and the Cochrane Library databases were searched for multicentre randomised controlled trials comparing the efficacy of OTSC with standard endoscopic procedures for the primary treatment of non-variceal gastrointestinal bleeding published up to January 2024. The primary outcome measure was the 7-day re-bleeding rate. We also assessed the presence of persistent bleeding, 30-day rebleeding rate, length of hospital stay and mortality. A systematic review and network meta-analysis was performed for both treatments.

Results: Four trials met the inclusion criteria and were included. Regarding the 7-day rebleeding rate, OTSC showed superior efficacy compared to standard endoscopic therapy in the treatment of non-variceal gastrointestinal bleeding (RR 0.29, 95%CI 0.14-0.62). OTSC was also superior to standard endoscopic therapy in terms of re-bleeding within 30 days (RR 0.43, 95%CI 0.24-0.78). In terms of failure to achieve primary haemostasis, results were similar between the two methods, with a trend in favour of OTSC (RR 0.37, 95%CI 0.37-1.02). Finally, no differences were found in mortality (RR 0.61, 95%CI 0.25-1.51) and length of hospital stay (SMD -0.01, 95%CI -0.20-0.17).

Conclusion: OTSC significantly reduced the 7-day and 30-day re-bleeding rate compared to standard endoscopic therapy. There were no differences in mortality and length of hospital stay.

Disclosure: Julio Iglesias-Garcia: Advisor Fuji.

PP0025

EFFICACY OF DANIS-ELLA ESOPHAGEAL STENT FOR POST-EVL ULCER BLEEDING: A SINGLE-CENTER STUDY

N.S. Malhi¹, R. Grover¹, J.S. Dhingra¹

¹Advanced Gastroenterology Institute (A.G.I.)-The GASTROCITI, Ludhiana, India

Contact E-Mail Address: doctorjasmeet@gmail.com

Introduction: Post-esophageal variceal ligation (EVL) ulcer bleeding poses a significant challenge in clinical practice, with various management modalities employed. However, there is a lack of established guidelines for effective management. This study aims to evaluate the effectiveness and safety of self-expandable metal SX-DANIS-ELLA (DE) stents in controlling post-EVL ulcer bleeding.

Aims & Methods: This retrospective audit focused on cirrhotic patients who underwent SEMS placement for post-EVL ulcer bleed. The study assessed bleeding control rates within 48 hours post-treatment and mortality rates within 6 weeks post-treatment

Results: Among 1025 endoscopic procedures for variceal ligation over 40 months, 1.4% (15 patients) presented with post-EVL ulcer bleed, all managed with DE stents. SEMS successfully controlled bleeding in 100% of cases at 48 hours post-procedure without the need for alternative rescue strategies. Median SEMS placement duration was eight days, with complete ulcer healing observed in 14 patients upon stent removal. However, one patient passed away within 72 hours due to decompensation. Early rebleeding within 6 weeks occurred in two (13.3%) patients which was managed with EVL. The 6-week mortality rate was notable at 20% (3 out of 15 patients). Adverse events included superficial esophageal ulcers at upper end of stent mesh in 9 patients out of 15 (60%), SEMS dislocations in 3 out of 15 patients (20%) and one very deep esophageal tear with ulcer at the upper end of the stent mesh (6.6%). Two patients also had aspiration pneumonia post procedure which was managed conservatively

Conclusion: SX-ELLA esophageal stents effectively controlled post-EVL ulcer bleeding. Despite successful bleeding control, the high mortality rate underscores the need for further strategies. SEMS dislocations highlight the complexity of this intervention and the importance of expertise in stent placement. Future research should explore the role of early transplant referral in reducing mortality following SEMS placement and improving patient outcomes

Disclosure: Nothing to disclose.

PP0026

UPPER GASTROINTESTINAL BLEEDING: RECURRENCE AND IMPACT ON MORTALITY

M. Cherkaoui Malki¹, I. Errabih², S. Mechhor¹, F.Z. Mghyly¹, N. Benzoubeir¹, H. El Bacha³

¹Ibn Sina Hospital- Université Mohamed V of Rabat, Gastroenterology "Médecine B", Rabat, Morocco, ²Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco, ³Ibn Sina Hospital / Université Mohamed V / Faculté de Médecine, Gastroenterologie et Hépatologie, Rabat, Morocco

Contact E-Mail Address: cherkaoui.manal23@gmail.com

Introduction: Upper gastrointestinal bleeding is a common reason for emergency department visits. Thanks to advancements in new hemostasis techniques, morbidity and mortality rates have decreased but remain significant in most studies reported in the literature. The aim of our study is to investigate the epidemiological and evolutionary profiles of upper gastrointestinal bleeding.

Aims & Methods: This is a prospective, descriptive, and analytical study conducted over a period of 4 years from April 2020 to February 2024. Patients presenting with gastrointestinal bleeding who underwent a complete clinical examination, comprehensive laboratory tests, esophagogastroduodenal endoscopy, and immediate and follow-up care were included in our study. Patients who did not undergo esophagogastroduodenal endoscopy and those with incomplete medical records were excluded.

Results: 282 patients with gastrointestinal bleeding were included in our study. The mean age was 56.1 years (range: 20 to 90 years). The male-to-female ratio was 1.26. A history of upper gastrointestinal bleeding was noted in 41 patients (14.5%).

The presentation of upper gastrointestinal bleeding included melena with hematemesis in 93 patients (32%), melena in 68 patients (24.1%), hematemesis in 50 patients (17.7%), and rectal bleeding in 20 patients (7%). 150 patients received blood transfusions (53%), and 38 patients required admission to the intensive care unit (13% of cases). Peptic ulcer disease was the most common cause of bleeding encountered in 136 patients (48% of cases). 70 patients (24%) underwent hemostatic procedures. Total recurrence of bleeding was noted in 35 patients (12.3%); 12 patients

had esophageal variceal rupture (34.28%), and 8 patients had peptic ulcer disease (22%). The mean time to recurrence was 25.51 days. Ten of these patients were on anticoagulants and/or antiplatelet therapy before the bleeding episode (43%). There were 6 cases of death (2.59% of cases): 2 cases of peptic ulcer disease and 4 cases of esophageal variceal rupture. All deceased patients had experienced recurrent bleeding (100%).

Conclusion: The total recurrence rate of bleeding in our series was 2.59%. The presence of esophageal varices, the use of anticoagulant and/or antiplatelet therapy, and the absence of endoscopic treatment appear to be factors associated with recurrent bleeding. All deceased patients had experienced recurrent bleeding.

Disclosure: Nothing to disclose.

PP0027

CLINICAL PRESENTATIONS, ENDOSCOPIC FINDINGS, AND OUTCOMES OF ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING IN ELDERLY PEOPLE

K.B. Pegatraju¹, E.G. Simon¹, A. Joseph¹, A.K. Dutta¹, S.D. Chowdhury¹, R.T. Kurien¹, R. Jaleel¹, A. John¹, A. Thomas¹

¹Christian Medical College, Dept. of Gastroenterology, Vellore, India

Contact E-Mail Address: Krishnabharadwaj004@gmail.com

Introduction: Acute upper gastrointestinal (UGI) bleeding is a common medical emergency among the elderly. There is limited data on the management and outcomes of non-variceal UGI bleeding in the elderly in India.

Aims & Methods: We aimed to study clinical presentation, endoscopic findings, and outcomes in elderly patients with acute non-variceal UGI bleeding. All elderly patients (≥ 60 years of age) who presented with acute UGI bleed and were admitted for the same from 2021 to 2022 were retrospectively analysed. Baseline characteristics, blood transfusions before and after endoscopy, endoscopic diagnosis and therapy, AIMS65 score, complete Rockall score, and outcomes such as in-hospital re-bleeding and mortality were recorded.

Results: Of the 399 patients who had acute non-variceal UGI bleed, 309 patients aged <60 years were excluded. Of the 90 patients studied, the mean age of presentation was 69.8 ± 7.35 years, with 81.1% males. The most common presentation was melena (30%). Forty-one (45.5%) patients had a history of antiplatelet and anticoagulant use. The most common endoscopic finding was gastric ulcer (54.4%), followed by duodenal ulcer (22.2%), gastroesophageal junction ulcer (7.7%), Mallory-Weiss tear (6.6%), duodenal diverticular bleed (2.2%). The majority of ulcers were Forrest III (43.3%), followed by Forrest IIa (23.3%) and IIc (18.3%). Around 65% of patients with non-variceal UGI bleeds did not require endotherapy. Dual endotherapy was done in 25.5% of patients. Triple endotherapy was done in two patients. AIMS65 score was 1 in 50% of patients and 2 in 24.5% of patients. The majority (81.1%) of patients had a complete Rockall score of 3-7, indicating a moderate risk of re-bleeding and mortality. All the 90 patients were discharged without any mortality.

Conclusion: Our study showed that gastric ulcer was the most common cause of acute non-variceal UGI bleeding in the elderly, and melena was the most common presentation. Early endoscopic therapy may reduce blood transfusion requirements, in-hospital re-bleeding, and mortality.

Disclosure: Nothing to disclose.

PP0028

RECURRENCE RATE OF DIGESTIVE BLEEDING DUE TO RUPTURE OF ESOPHAGEAL VARICES

A.A.T. Alraeeini¹, H. El Bacha², M. Cherkaoui Malki³, S. Mechhor⁴, N. Benzoubeir¹, I. Errabih⁵

¹Faculty Of Medicine And Pharmacy - Mohammed V University, Hepato-gastro-enterology and proctology department (medicine B) - Ibn Sina university hospital center, Rabat, Morocco, ²Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ³University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ⁴Ibn Sina Hospital, Medecine B, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: arafat4h@gmail.com

Introduction: Upper gastrointestinal bleeding is a frequent reason for consultation in the emergency room, and digestive bleeding due to rupture of esophageal varices represents the second cause in terms of frequency and can cause serious and recurrent bleeding. Recurrence of digestive bleeding due to rupture of esophageal varices (OV) is a major concern in gastroenterology and hepatology. Due to the evolution of hemostasis techniques and management strategies, the rates of recurrence, morbidity and mortality have decreased but remain significant in most studies reported in the literature.

Aims & Methods: The aim of our work is to study the epidemiological profile of hemorrhagic recurrence of esophageal varices.

This is a prospective, descriptive and analytical study, carried out over a period of 24 months from January 2022 to December 2023. we included in our study patients who had consulted for digestive bleeding due to rupture of esophageal varices and who had benefited from a complete clinical examination, a complete biological assessment, an Esophago-gastro-duodenoscopy and immediate and remote monitoring. Patients who did not benefit from an esophago-gastro-duodenoscopy and those whose files were incomplete were excluded.

Results: 90 patients presenting with digestive bleeding due to rupture of esophageal varices were included in our study. The average age is 55 years (extremes: 17 and 89 years). The M/F sex ratio is 0.8. The mode of revelation of upper digestive bleeding was melena associated with hematemesis in 10 patients (11.1%), melena in 30 patients (33.3%), hematemesis in 50 patients (55.5%).

12 (13.3%) patients required intensive care. Hemorrhagic recurrence was noted in 30 (33.3%) patients, including 11 (12.2%) early recurrence < 06 weeks, and 19 (21.1%) late recurrence after 06 weeks. For patients who had presented a recurrence, we found 18 (60%) patients with an age > 60 years, 16 (53.3%) patients with a history of ascitic decompensation, 10 (33.3%) patients with an initial large-scale digestive hemorrhage.

Conclusion: Hemorrhagic recurrence in our series was 33.3%. More frequent in elderly subjects, and with ascitic decompensation, and severe initial hemorrhage.

Disclosure: Nothing to disclose.

PP0029

RISK FACTORS OF IN-HOSPITAL MORTALITY AMONG PATIENTS WITH GASTROINTESTINAL BLEEDING AND ISCHEMIC HEART DISEASE

H. Yan¹, L. Ma¹, J. Yang¹

¹West China Hospital, Sichuan University, Chengdu, China

Contact E-Mail Address: hailin_yan@163.com

Introduction: Gastrointestinal bleeding (GIB) and Ischemic heart disease (IHD) both remain the important causes of morbidity and mortality. Patients with IHD are more likely to suffer from GIB due to the characteristics of the population, heart disease, stress state and long-term use of anti-thrombotic drugs^[1-3].

Previous studies have found that patients with simultaneous GIB and IHD have higher mortality than that of each individual disease^[4-5].

Treatment for those patients is a challenge for both the cardiologists and gastroenterologists. In order to assess the frequency of in-hospital mortality in patients with GIB and IHD, and determine the potential risk factors for this condition, we designed and conducted this single center study.

Aims & Methods: Our study assessed the hospitalized outcomes of patients with simultaneous GIB and IHD. Moreover, we explored the risk factors of in-hospital mortality in those patients.

We performed a retrospective study in West China hospital between January 2014 and December 2018. Patients diagnosed with GIB and IHD were included. The primary outcome was in-hospital mortality for all causes. Clinical and laboratory data were collected and analyzed for clinical characteristics and potential risk factors of in-hospital mortality.

Results: 574 GIB patients with IHD were enrolled in the current study, and among them 107 in-hospital deaths were observed (in-hospital mortality rate of 18.64%). The causes of death included cardiovascular death (46, 42.99%), hemorrhagic shock (10, 9.35%), severe infection (33, 30.84%), and other causes (18, 16.82%).

Patients who died were older than survivors [78 (68, 82) vs. 74 (65, 80), $P = 0.008$], with a higher incidence of COPD (27.10% vs. 13.70%, $P = 0.001$) and chronic renal failure (47.66% vs. 27.19%, $P < 0.001$). Patients with a higher heart rate at admission (90 vs. 81, $P = 0.006$), or with a course of CHD less than 3 months (53.27% vs. 32.76%, $P < 0.001$) were more likely to die. More patients in death group received plasma infusion (24.30% vs. 7.92%, $P < 0.001$), and present with acute coronary syndrome (53.27% vs. 38.97%, $P = 0.007$).

Compared with survivors, patients who died showed increased peak white blood cell (WBC) count [18.75(14.35, 24.9) vs. 9.79 (7.19, 13.82) $\times 10^9/L$, $P < 0.001$], increased peak INR [1.51 (1.21, 2.58) vs. 1.13 (1.05, 1.31), $P < 0.001$], and lower minimum platelet counts [94 (52, 147) vs. 128 (83, 180) $\times 10^9/L$, $p < 0.001$]. In multivariable logistic analysis, age [OR (95% CI) = 1.032 (1.006-1.058), $P = 0.014$], peak WBC count [OR (95% CI) = 1.123 (1.085-1.163), $P < 0.001$], peak INR levels [OR (95%CI) = 1.220(1.061-1.402), $P = 0.005$], and heart rate at admission [OR (95%CI) = 1.015(1.002-1.028), $P = 0.026$] were independent predictors of in-hospital mortality.

Conclusion: Patients with simultaneous GIB and IHD had a high in-hospital mortality. Age, peak WBC count, peak INR levels, and heart rate at admission were independent risk factors for in-hospital death.

References:

- [1]. Steg PG, Huber K, Andreotti F, Arnesen H, Atar D, Badimon L, Bassand JP, De Caterina R, Eikelboom JA, Gulba D, Hamon M, Helft G, Fox KA, Kristensen SD, Rao SV, Verheugt FW, Widimsky P, Zeymer U, Collet JP. Bleeding in acute coronary syndromes and percutaneous coronary interventions: position paper by the Working Group on Thrombosis of the European Society of Cardiology. *Eur Heart J*. 2011 Aug;32(15):1854-64.
- [2]. Cea Soriano L, Lanás A, Soriano-Gabarró M, García Rodríguez LA. Incidence of Upper and Lower Gastrointestinal Bleeding in New Users of Low-Dose Aspirin. *Clin Gastroenterol Hepatol*. 2019 Apr;17(5):887-895.e6.

[3]. Kawasaki K, Kurahara K, Yanai S, Kochi S, Fuchigami T, Matsumoto T. Low-Dose Aspirin and Non-steroidal Anti-inflammatory Drugs Increase the Risk of Bleeding in Patients with Gastroduodenal Ulcer. *Dig Dis Sci*. 2015 Apr;60(4):1010-5.

[4]. Manoukian SV, Feit F, Mehran R, et al. Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY trial. *J Am Coll Cardiol* 2007;49:1362-8

[5]. Rao SV, O'Grady K, Pieper KS, et al. Impact of bleeding severity on clinical outcomes among patients with acute coronary syndromes. *Am J Cardiol* 2005;96:1200-6.

Disclosure: Nothing to disclose.

PP0030

UTILIZATION OF HEMOSTATIC POWDER SPRAY VERSUS STANDARD ENDOSCOPIC TREATMENT IN THE MANAGEMENT OF MALIGNANCY-RELATED GASTROINTESTINAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS

L. Laurel¹, Z.R. Amores¹, R.L. Galang¹

¹St. Luke's Medical Center- Global City, Institute of Digestive and Liver Diseases, Taguig, Philippines

Contact E-Mail Address: laurenceelaurel@gmail.com

Introduction: Managing tumoral bleeding poses a significant challenge for endoscopists. Traditional tools such as clips and heat-probes frequently prove inadequate in controlling stubborn bleeding caused by mucosal invasion from these tumors. Hemostatic powder sprays provide a novel solution by applying a combination of minerals and polymers directly onto the tumor surface, forming a mechanical barrier to seal the bleeding site. However, there is a scarcity of data regarding their effectiveness in treating hemorrhagic gastrointestinal neoplasms.

This study seeks to evaluate the efficacy of Hemostatic powder spray in patients suffering from gastrointestinal bleeding related to malignancies.

Aims & Methods: This study aimed to evaluate the effectiveness of Hemostatic powder spray compared to standard clinical treatment in controlling gastrointestinal bleeding originating from malignant lesions. The primary outcome measures included the combined rates of rebleeding within 30 days, while secondary outcomes encompassed the combined rates of mortality over any time period.

We gathered relevant data, an extensive search of electronic databases was conducted up to April 2024. Only randomized controlled trials (RCTs) were included in the study, focusing specifically on cases where Hemostatic powder spray was pitted against conventional endoscopic techniques for managing bleeding caused by gastrointestinal tumors.

Results: Three studies involving a total of 162 patients were included in this meta-analysis. Among them, 83 patients underwent treatment with Hemostatic spray powder alone, while 79 patients received conventional hemostatic techniques.

The pooled results of the analysis revealed that Hemostatic powder spray was associated with a lower incidence of re-bleeding beyond 30 days from the onset of treatment (odds ratio [OR] 0.36, 95% confidence interval [CI] 0.15-0.84), demonstrating a significant advantage over standard endoscopy in the management of gastrointestinal tumor bleeding (p-value 0.01).

Additionally, there was no significant difference observed in all-time mortality between the two treatment groups (OR 0.40, 95% CI 0.19-0.83, p-value 0.09).

Conclusion: Hemostatic spray powders demonstrate significant efficacy in achieving hemostasis for gastrointestinal bleeding associated with malignancies. They should be regarded as a viable alternative to conventional endoscopic methods in such cases. Subsequent research should be

structured to assess both the effectiveness and safety of hemostatic spray powders as a primary hemostatic approach compared to traditional endoscopic techniques.

References:

1. Pittayanon, Rapat et al. "The efficacy of Hemospray in patients with upper gastrointestinal bleeding from tumor." *Endoscopy international open* vol. 4,9 (2016): E933-6. doi:10.1055/s-0042-109863
2. Chen YI, Wyse J, Lu Y, et al. TC-325 hemostatic powder versus current standard of care in managing malignant GI bleeding: a pilot randomized clinical trial. *Gastrointest Endosc* 2020;91:321–328.
3. Bruno da Costa Martins, et al. Mo1140. Preliminary results of a randomized controlled trial comparing hemostatic powder versus optimal clinical treatment in the management of gastrointestinal bleeding from malignancy, *Gastrointestinal Endoscopy*, Volume 87, Issue 6, Supplement, 2018, Pages AB415-AB416, ISSN 0016-5107.
4. Martins BC, Abnader Machado A, Scomparin RC, et al. TC-325 hemostatic powder in the management of upper gastrointestinal malignant bleeding: a randomized controlled trial. *Endosc Int Open* 2022;10:E1350–E1357.
5. Minhem MA, Nakshabandi A, Mirza R, et al. Gastrointestinal hemorrhage in the setting of gastrointestinal cancer: anatomical prevalence, predictors, and interventions. *World J Gastrointest Endosc* 2021; 13:391–406.
6. Hussein, Mohamed et al. "Hemostatic powder TC-325 treatment of malignancy-related upper gastrointestinal bleeds: International registry outcomes." *Journal of gastroenterology and hepatology* vol. 36,11 (2021): 3027-3032. doi:10.1111/jgh.15579

Disclosure: Nothing to disclose.

PP0031

IMPROVING DOCUMENTED ADVICE REGARDING ANTICOAGULANTS AND ANTIPLATELETS IN ACUTE UPPER GASTROINTESTINAL BLEEDS

E. Creed¹, V. Theis¹, K. Clark¹, S. Gurung¹, A. Motam¹, G. FarrellBinns¹

¹*Mersey and West Lancashire Teaching Hospitals NHS Trust, Gastroenterology, Liverpool, United Kingdom*

Contact E-Mail Address: emily_creed@hotmail.co.uk

Introduction: Systemic anticoagulants are often prescribed to prevent and treat thromboembolism among other indications, yet presentations with Acute Upper Gastrointestinal Bleeds (AUGIB) in this cohort are common. Medical care bundles have been shown to improve both standards of care and patient outcomes. As a result, the British Society for Gastroenterology (BSG) created an AUGIB care bundle in 2019, and guidelines for endoscopy in patients on antiplatelets and anticoagulants in 2021. However, the former lacks definitive statements regarding resumption of antiplatelet/anticoagulant therapy, while the latter is not routinely referred to by non-Gastrointestinal specialists. It is recognised however, that resumption of antiplatelets and anticoagulants is associated with improved survival and reduced incidence of thrombotic complications. Thus, all patients should have a clear plan.

Aims & Methods: Admissions with AUGIB proceeding to endoscopy over a 6 month period were analysed. Of the 319 patients, 72 (22.5%) were taking either an antiplatelet, warfarin or a Direct Oral Anticoagulant (DOAC). Medical records were reviewed in relation to pre-procedure management of these medications, advice from the endoscopist regarding resumption (or not) of antithrombotic therapy and whether these medicines were managed appropriately thereafter.

Several interventions were then made; a change to the reporting software led to a prompt relating to antiplatelet/anticoagulant medications (though the template remains non-specific), an education campaign for

post graduate doctors in training and medication guidance summaries visible in the endoscopy department.

A second 6-month review was then undertaken to evaluate if there had been any improvement in outcomes. In this time frame, 283 patients underwent endoscopic evaluation for suspected AUGIB of whom 83 (29.3%) were taking antithrombotic therapy.

Results: Results can be found in Table 1:

	Pre-Intervention	Post Intervention
Pre-procedure appropriate management	76%	81%
Documented advice on endoscopy report	35%	65%
Post procedure appropriate prescribing	68%	75%

Table 1.

A recurring theme was the discontinuation of aspirin in low-risk bleeds, and low quality medication advice given at the time of endoscopy with almost 4 in 10 reports simply stating 'continue medication'. Those without documentation resulted in further advice being sought (12.9% of cases) Further subanalysis of the data revealed that advice was almost always documented in those presenting with major upper gastrointestinal bleeds (defined as patients presenting with haemodynamic instability). In this cohort 87.5% of patients had clearly documented advice regarding their anticoagulation or antiplatelet medication.

Conclusion: Further education to junior staff around utility of the BSG AUGIB bundle, as well as the anticoagulation guidelines is needed to improve pre and post procedure care. Further upgrades to the templates on the reporting software will also serve as prompts to the endoscopist to provide more specific advice. Human factors also need to be considered; limited advice is likely related to the high endoscopy workload pressures. Sub-analysis of the data suggests that we are better at providing more specific advice in high-risk bleeds/where endotherapy is required, reflecting that antithrombotic therapy decisions are considered by the endoscopist. Improved documentation at procedure, should translate into improved post procedure management and reduce further demands on the service.

References: BSG AUGIB bundle : Siau K, Hearnshaw S, Stanley AJ, et al. *Frontline Gastroenterology* 27/03/2020. doi:10.1136/flgastro-2019-101395
Endoscopy in patients on antiplatelet or anticoagulant therapy: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guideline update Veitch AM, Radaelli F, Alikhan R, et al. *Gut* 2021;70:1611–1628

Disclosure: Nothing to disclose.

PP0032

SAFETY AND EFFICACY OF PROTON PUMP INHIBITORS IN CRITICALLY ILL PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

N. Mostafa Al-dardery¹, M. Mohamed El-sayed¹, A. Khaled Madeeh¹, D. Osama Yehia Ibrahim¹, M. Salah mahklouf¹, N. Ahmed Kamel Ahmed¹, M. El-Samahy², A. Khaity³

¹Fayoum University, Faculty of medicine, Fayoum, Egypt, ²Zagazig University, Faculty of medicine, Zagazig, Egypt, ³Elrazi University, Faculty of medicine, Khartoum, Sudan

Contact E-Mail Address: ndardery449@gmail.com

Introduction: Critically ill patients are at high risk for upper gastrointestinal (GI) bleeding.¹ Proton pump inhibitors (PPIs) are commonly used for prophylaxis, but their safety and efficacy compared to histamine-2 receptor antagonists (H2 blockers) and placebo remain unclear.¹⁻⁴

Aims & Methods: Our systematic review and meta-analysis aims to assess the safety and efficacy of PPIs for preventing upper GI bleeding in critically ill adults. We conducted a comprehensive search of Scopus, Web of Science, PubMed, and Cochrane Central for relevant randomized controlled trials (RCTs) from inception until March 2024. Data were extracted from eligible studies and pooled as mean difference (MD) for continuous outcomes and Odds ratio (OR) for dichotomous data in a random-effect model meta-analysis, using R software.

Results: Nineteen RCTs were included in this meta-analysis with a total of 62221 patients. Our study showed that PPI was superior to control in terms of GI bleeding [RR 0.55, (95% CI, 0.42 to 0.72); P = <0.01]. However, the overall effect did not favor either of the two groups in terms of ICU, mortality rate, and nosocomial infection [MD -1.45, (95% CI, -5.31 to 2.42); P = 0.4], [RR 1.04, (95% CI, 1.00 to 1.09); P = 0.07], and [RR 1.27, (95% CI, 0.98 to 1.65); P = 0.07], respectively.

Conclusion: In conclusion, our findings demonstrated a significant reduction in GI bleeding risk associated with PPI use. At the same time, we did not find a statistically significant difference between PPI and control groups regarding ICU mortality rate, overall mortality rate, or nosocomial infection rates. These findings suggest that PPIs may be effective in reducing upper GI bleeding in critically ill patients. However, further research might be necessary to definitively determine the impact of PPIs on mortality and infection risks in this population.

References: 1. Wang Y, Ye Z, Ge L, et al. Efficacy and safety of gastrointestinal bleeding prophylaxis in critically ill patients: Systematic review and network meta-analysis. *The BMJ*. 2020;368. doi:10.1136/bmj.l6744

2. Kondo Y, Ohbe H, Matsui H, Fushimi K, Tanaka H, Yasunaga H. Proton pump inhibitors versus histamine-2 receptor antagonists for stress ulcer prophylaxis during extracorporeal membrane oxygenation: a propensity score-matched analysis. *BMJ Open*. 2020;10(9):e037534. doi:10.1136/bmjopen-2020-037534

3. Alshamsi F, Belley-Cote E, Cook D, et al. Efficacy and safety of proton pump inhibitors for stress ulcer prophylaxis in critically ill patients: A systematic review and meta-analysis of randomized trials. *Crit Care*. 2016;20(1). doi:10.1186/S13054-016-1305-6

4. Jung YS, Park JH, Park CH. Impact of proton pump inhibitors on the risk of small bowel or colorectal bleeding: A systematic review and meta-analysis. *United European Gastroenterol J*. 2023;11(9):861-873. doi:10.1002/ueg2.12448

Disclosure: Nothing to disclose.

PP0033

UPPER GASTROINTESTINAL BLEEDING IN THE PORTUGUESE POPULATION: A MULTICENTRIC STUDY

E. Vara Luiz^{1,2}, I. Mendes¹, C. Palma¹, D. Simas³, P. Gomes³, A. Gonçalves³, I. Simao⁴, M. Teixeira⁵, S. Ramos Lopes⁵, F. Côrte-Real⁶, M.A. Duarte⁶, A.C. Bravo⁷, M. Patita¹, G. Nunes¹, P. Pinto Marques¹, J. Fonseca^{1,2}

¹Hospital Garcia de Orta, Gastroenterology, Almada, Portugal, ²Egas Moniz School of Health and Science, Aging Lab, Almada, Portugal, ³Unidade Local de Saúde da Região de Leiria, Gastroenterology, Leiria, Portugal, ⁴Unidade Local de Saúde Lisboa Ocidental, Gastroenterology, Lisboa, Portugal, ⁵Unidade Local de Saúde da Arrábida, Gastroenterology, Setúbal, Portugal, ⁶Hospital do Divino Espírito Santo de Ponta Delgada, EPER, Lagoa, São Miguel, Portugal, ⁷Unidade Local de Saúde de Loures-Odivelas, Gastroenterology, Lisboa, Portugal

Contact E-Mail Address: franciscovaraluz@gmail.com

Introduction: Upper gastrointestinal bleeding (UGIB) is one of the most common medical emergencies managed by gastroenterologists. Despite advances in pharmacological/endoscopic therapy, this condition is still associated with considerable morbidity/mortality.

Aims & Methods: We aimed to characterize Portuguese patients and clinical approaches in UGIB, as well as factors associated with adverse outcomes. We conducted a retrospective multicentric cohort study which included adult patients consecutively presenting UGIB at 6 participating centers over a 6-month period. Data relevant to the initial UGIB episode and for up to 30 days afterwards were collected from patient medical records. Patients' clinical information was presented using descriptive statistics. Continuous variables were described by mean ± standard deviation. Categorical data were presented as absolute numbers and percentages. Qualitative variables were compared with Chi-square and Fisher's tests. Non-normal distribution quantitative variables were compared with Mann-Whitney test. A p value < 0,05 was considered statistically significant.

Results: 600 patients presenting with UGIB were included, mostly men (58,2%, n=349) with a mean age of 71 (18-100), with multiple comorbidities and a mean Charlson comorbidity index of 5 (0-16). Antiplatelet/Anticoagulant/NSAID consumption was present in 53,5% (n=321). The primary symptoms were melena (47,2%, n=283) and hematemesis (27,3%, n=164). The median Rockall score (RS) and Glasgow-Blatchford score were 5 (0-10) and 12 (0-21), respectively. A higher RS was associated with prolonged hospitalization (p=0,03). At least one cause for UGIB was documented in 499 patients (83%). Peptic ulcer disease (PUD, 37,8%, n=192), erosive gastroduodenitis (10,0%, n=51) and gastric/duodenal angiodysplasia (6,7%, n=34) were the main bleeding causes of nonvariceal UGIB (n=507). In patients with chronic liver disease (n=93), variceal bleeding (46,2%, n=43) was the main bleeding cause, followed by PUD (19,4%, n=18). Endoscopic hemostasis was performed in 257 patients (42,8%). Combination therapy (injection therapy + thermal/mechanical therapy) was used in 122 cases. Median hospitalization time was 11 days (0-168) and admission in intensive care unit (ICU) was needed in 9,8% (n=59). Surgery for severe UGIB was performed in 2% (n=12). In-hospital rebleeding occurred in 13,3%, more frequently in chronic liver disease (p=0,02). Death occurred in 90 patients (15%), 73 from a non-bleeding related cause. Logistic regression showed that age ≥ 65 years (p=0,02), chronic liver disease (p=0,049) and ICU admission (p=0,045) were associated with in-hospital mortality.

Conclusion: This study contributed to characterization of Portuguese patients admitted with UGIB in real clinical setting. Gastroenterologists are facing a progressively older population, with multiple comorbidities and on therapies potentially causing UGIB. Although PUD still remains the

most common cause of UGIB, other conditions such as angiodysplasia are becoming more frequent in clinical practice. Chronic liver disease is a risk factor for rebleeding and in-hospital mortality. The high mortality observed in this research was mainly due to decompensation of comorbid conditions rather than exsanguination, which reflects the complexity of the elderly. These patients require early risk assessment, adequate resuscitation and an attempt to identify and treat the bleeding source, which might help us to improve the management of UGIB in Portugal.

References:

1. Lanás A, Aabakken L, Fonseca J, et al. Variability in the management of nonvariceal upper gastrointestinal bleeding in Europe: an observational study. *Adv Ther.* 2012 Dec;29(12):1026-36.
2. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy.* 2021 Mar;53(3):300-332.
3. Mathialagan R, Illangantilaka A, Radhakrishnan H. "Gastroenterology in the elderly." *Medicine* 47.7 (2019): 466-469.
4. Triantafyllou K, Vlachogiannakos J, Ladas SD. Gastrointestinal and liver side effects of drugs in elderly patients. *Best Pract Res Clin Gastroenterol.* 2010 Apr;24(2):203-15.
5. Cremers I, Ribeiro S. Management of variceal and nonvariceal upper gastrointestinal bleeding in patients with cirrhosis. *Therap Adv Gastroenterol.* 2014 Sep;7(5):206-16.
6. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet.* 2000 Oct 14;356(9238):1318-21.
7. Rockall TA, Logan RF, Devlin HB, et al. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut.* 1996 Mar;38(3):316-21.
8. Forrest JA, Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. *Lancet.* 1974 Aug 17;2(7877):394-7.
9. Stolor E, Moreau C, Sayana H, Patel S. Management of Non-Variceal Upper GI Bleeding in the Geriatric Population: An Update. *Curr Gastroenterol Rep.* 2021 Mar 25;23(4):5.

Disclosure: Nothing to disclose.

PP0034

ENDOSCOPIC HEMOSTASIS DURING UPPER GASTROINTESTINAL BLEEDING OF NON-VARICEAL ORIGIN

A. Asmaa¹, S. Mechhor², M. Cherkaoui Malki³, H. El Bacha⁴, N. Benzoubeir¹, I. Errabih⁵

¹Mohammed V, Rabat, Morocco, ²Ibn Sina Hospital, Medecine B, Rabat, Morocco, ³University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ⁴Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: asmaa.aboullait@gmail.com

Introduction: Upper digestive hemorrhage (HDH) is a frequent reason for hospitalization in the emergency department. Schematically, they are divided into HDH of varicose origin and HDH of non-varicose origin. Upper GI endoscopy must be performed as quickly as possible, under the best possible technical conditions.

The objective of our study is to evaluate the hemostatic endoscopic management of these hemorrhages in the emergency department.

Aims & Methods: This is a retrospective descriptive study covering a period of 26 months, from January 2022 to March 2024, and including all patients admitted in an emergency for upper digestive haemorrhage of non-variceal origin, identified during the endoscopy on-call duty at the "Médecine B" Hepato-gastroenterology and Proctology Department, CHU Ibn Sina.

All patients underwent clinical examination, blood count and oeso-gastro-duodenal fibroscopy (FOGD).

Patients admitted for HDH of varicose origin or with normal FOGD were excluded from our study.

Results: 91 cases of HDH of non-varicose origin were diagnosed out of a total of 225 cases of HDH consulting the emergency department, with a prevalence of 40.44%.

The mean age of our patients was 54.8 years (20-84 years), with a male predominance of 70.3% and a sex ratio of M/F : 2.3.

11 patients (12.08%) had a history of smoking, 11 (12.08%) had heart disease on anticoagulants, 10 (11%) had taken NSAIDs, 8 (8.79%) had nephropathy at the hemodialysis stage, and 7 (8%) were hypertensive.

The mode of externalization of HDH was melena associated with hematemesis in 26 patients (28.6%), isolated melena in 44 (48.4%), hematemesis in 16 (17.6%) and rectal discharge in 5 (5.5%).

The main etiologies of HDH of non-varicose origin revealed by FOGD were: gastro-duodenal ulcer in 73 patients (80.2%), with Forrest Ib ulcer in 9 (12.3%), Forrest IIa in 4(5.4%), Forrest IIb in 4(5.4%), Forrest IIc in 13(17.8%) and Forrest III in 43(59%).

Of the 91 patients, 15(16.48%) had esophagitis, 5(5.5%) had gastric process, 1(1.09%) had duodenal process and 8 patients (8.8%) had angiodysplasia lesions.

All patients were treated with a loading dose of injectable PPI, followed by a maintenance dose.

Endoscopic haemostasis was required in 19 patients (20.8%), of whom 8 (8.7%) benefited from injection of adrenaline serum and placement of haemostatic clips, 2 patients (2.2%) from exclusive injection of adrenaline serum, 8 patients (8.7%) from exclusive placement of haemostatic clips and one patient (1.09%) benefited from per-endoscopic surgical suturing. The mortality rate in our study was 3.2%.

Conclusion: HDH of non-varicose origin remains dominated by ulcerative origin. Impregnation with PPIs prior to FOGD and the possibility of endoscopic haemostasis reduce the mortality rate.

Disclosure: Nothing to disclose.

PP0035

PATIENTS WITH IRON DEFICIENCY ANAEMIA BENEFIT FROM A SPECIALIZED GASTROINTESTINAL EVALUATION

L. Gonzalez Gonzalez¹, M. Puig¹, S. Dall'Oglio¹, M. Calafat Sard², J. Llaó Guàrdia¹, M. Mañosa Ciria³, E. Domenech Morral⁴

¹Hospital Universitari Germans Trias i Pujol, Badalona, Spain, ²Hospital Universitari Germans Trias i Pujol, Gastroenterology, Barcelona, Spain, ³Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ⁴Hospital Germans Trias i Pujol, Gastroenterology Unit, Badalona, Barcelona, Spain

Contact E-Mail Address: mariapugo93@gmail.com

Introduction: Iron deficiency anaemia (IDA) is a frequent reason for consultation with a high consumption of health resources both for its diagnosis and for its treatment.

Aims & Methods: To evaluate the characteristics of patients referred to a specialized gastrointestinal (GI) consultation for IDA without macroscopic haemorrhage and the impact of this specialized evaluation on the consumption of health resources. We performed a retrospective observational study of patients evaluated in a specialized gastrointestinal hospital consultation for IDA from January 2021 to October 2023.

Results: We evaluated 218 patients where 134 were excluded due to macroscopic haemorrhage. Finally, 84 patients were analysed, 63% were men with a median age of 73 years (range 39-93) and a median Charlson index of 6 (range 0-15). The median time from the diagnosis of IDA to the first

gastrointestinal visit was 46 months (range 1-161). 74% of the patients had been evaluated by another specialty previously. 43% were on antiplatelet treatment and 31% on anticoagulant treatment. The aetiology of anaemia was multifactorial in 24% (n=20) and in those with iron deficiency the most frequent cause was angiodysplasias (42%) but in up to 19% of cases the aetiology was not found despite a complete evaluation.

During follow-up, 58% required an anticoagulation switch, requiring definitive withdrawal of anticoagulation in 8% of patients. Prior to the GI consultation, only one patient was under somatostatin analogues treatment, which was subsequently started in 17 new patients. During follow-up, 12% (n=10) were included in a special management group with parallel blood test monitoring by the primary care physician for a more thoroughly monitoring of the haemoglobin levels.

When comparing the consumption of health resources in the year before and after the GI assessment, a non-significant trend was observed towards a lower need for gastroscopies [0.87 vs. 0.65, p=0.07], but we found an statistically significant reduction in the number of colonoscopies [0.88 vs. 0.40, p<0.001].

We also observed a significant increase in the mean haemoglobin [10.6 g/dL vs. 12.1 g/dL, p<0.001] without statistically significant differences in the number of blood transfusion [2.82 units vs. 2.30 units, p=0.21] or intravenous iron therapy [1.44 g vs. 1.50 g, p=0.74] before and after the GI assessment respectively. A significant reduction in emergency department visits was also observed [0.79 vs. 0.43, p=0.002] as in hospital admissions [0.46 vs. 0.23, p=0.004] related to anaemia or its complications.

During follow-up, 12 patients died (none due to haemorrhage or anaemia), resulting in a cumulative mortality incidence of 6.7 deaths per 100 patients/year.

Conclusion: Multimorbid patients with iron deficiency anaemia benefit from the care of a specialized digestive consultation which is associated with a decrease in the use of health resources.

Disclosure: Nothing to disclose.

PP0036

WITHDRAWN

PP0037

VARIATION IN GASTRODUODENAL FUNCTION TESTING IN CLINICAL PRACTICE: RESULTS FROM AN INTERNATIONAL SURVEY

S. Kindt¹, A. Fikree², M. Fox³

¹UZ Brussels, Gastro-enterology and Hepatology, Brussel, Belgium, ²University College Hospital NHS Trust, Dept. of Gastroenterology, London, United Kingdom, ³Klinik Arlesheim & Zürich University, Center for integrative Gastroenterology, Arlesheim, Switzerland

Contact E-Mail Address: sebastien.kindt@uzbrussel.be

Introduction: Gastric emptying scintigraphy (GES) is an accepted standard for gastroduodenal function (GDF) testing, while various other investigations are available for the assessment of dyspeptic symptoms. However, in the absence of guidelines, it remains uncertain which test one should favour.

Aims & Methods: This study examined variation in GDF testing between centres to establish the status of current practice. A web-based questionnaire assessing availability, standard operating procedures and interpretation of 15 different GDF testing techniques was distributed among specialist practitioners via professional organizations. Availability, indication, meal-related characteristics and standard operating procedures (SOP) were compared.

Results: Fifty-nine complete responses (57 clinical practice, 86% tertiary care) were included from 28 countries. Eleven (19%) respondents referred more than 10 patients for further testing monthly. Accessibility for clinical practice were as follows: 100% gastroscopy, 91% measurement of gastric emptying (79% by GES; 19% gastric emptying breath testing (GEBT); 5% SPECT), 39% intragastric pressure measurements (IGP), 33% pyloric Endo-flip (PE), 30% gastric MRI, 19% nutrient drinking challenge (NDC), 18% gastric ultrasound (US), 18% motility capsule (MC) and 16% antroduodenal manometry (AM). Other techniques were available to less than 15% of the respondents. In clinical practice, meal-related dyspeptic symptoms and chronic unexplained nausea and vomiting (CUNV) represented the main indications for GE studies as compared to epigastric pain, burning or discomfort (GES: 70% and 94% vs. 20%, p<0.0001; GEBT: 100% and 100% vs. 0%, p<0.001). Similar results were present for PE (73% and 93% vs. 33%, p=0.002), NDC (100 and 82 vs. 27%, p=0.006). MC (33% and 67% vs. 0%, p=0.05), AM (28% and 75% vs. 25%, p=0.11), MRI (75% and 88% vs. 38%, p=0.09) and IGP (33% and 33% vs. 0%, p=0.15). By contrast, US was indiscriminately performed (57% and 71% vs. 57%, p=0.82).

There was a large heterogeneity in the type of meal and meal quantity used for each test as well as between tests. Symptoms were recorded by only half the respondents during GES and MRI, with higher percentages for other testing modalities. Variation in the specific symptoms included in questionnaires was present.

Conclusion: GES is widely available in clinical practice. Meal-related symptoms and CUNV represent the main indications for GDF testing in clinical practice. A large variation in the availability of GDF testing and SOPs exists between centres. This hampers clinical interpretation, data transfer between centres and research collaboration. These findings emphasise the need for an international co-operation effort at standardisation.

Disclosure: Nothing to disclose.

PP0038

BREAKING BARRIERS IN FUNCTIONAL DYSPESIA – A SYSTEMATIC REVIEW AND META-ANALYSIS ON DUODENAL TIGHT JUNCTION PROTEIN EXPRESSION

R. Farcas¹, S. Grad¹, A. Ismaiel¹, D.-C. Leucuta¹, P. Stefan-Lucian¹, D.L. Dumitrascu¹

¹Iuliu Hatieganu University of Medicine and Pharmacy, 1 2nd Department of Internal Medicine, Cluj-Napoca, Romania

Contact E-Mail Address: radufr@gmail.com

Introduction: Disruptions in tight junction (TJ) protein expression leading to duodenal epithelial barrier impairment may contribute to increased intestinal permeability, potentially playing a role in functional dyspepsia (FD) pathophysiology. Currently published studies evaluated the role of several TJ proteins in FD patients with inconsistent results. Therefore, we conducted this systematic review and meta-analysis to evaluate the duodenal mucosal expression of several TJ proteins in FD.

Aims & Methods: We performed a systematic electronic search on PubMed, EMBASE, and Scopus using predefined keywords. Diagnosis of FD by ROME III or ROME IV criteria was considered acceptable. Full articles satisfying our inclusion and exclusion criteria were included. The principal summary outcome was the mean difference (MD) of several TJ proteins in FD patients and control subjects. The study aimed to find if patients diagnosed with functional dyspepsia have lower gene expression of intestinal TJ proteins compared to healthy subjects.

Results: A total of 8 and 5 studies were included in our qualitative and quantitative synthesis, respectively, with a total population of 666 participants, out of which 420 were FD patients. No significant differences were observed between FD patients and controls in the expression of claudin-1

(-0.102 [CI 95% -0.303,0.099]), claudin-2 (0.161 [CI 95% -0.134,0.456]), claudin-3 (0.278 [CI 95% -0.280,0.837]), claudin-4 (0.045 [CI 95% -0.264,0.354]), ZO-1 (-0.221 [CI 95% -0.683, 0.241]), ZO-2 (-0.070 [CI 95% -0.147,0.007]), ZO-3 (-0.129 [CI 95% -0.376, 0.118]), B-catenin (-0.135 [CI 95% -0.484,0.214]), E-cadherin (-0.083 [CI 95% -0.229,0.063]), and occludin (-0.158 [CI 95% -0.409, 0.093]).

Conclusion: The expressions of all evaluated proteins including claudin-1, claudin-2, claudin-3, claudin-4, ZO-1, ZO-2, ZO-3, B-catenin, E-cadherin, and occludin did not significantly differ between FD patients and controls. However, due to the limited number of included studies, results should be interpreted with caution.

Disclosure: Nothing to disclose.

PP0039

DUODENAL FOOD ADMINISTRATION IN FUNCTIONAL DYSPESIA LEADS TO MUCOSAL REACTIONS, OBSERVED ON CONFOCAL LASER ENDOMICROSCOPY, WITHOUT ALTERATIONS IN PERMEABILITY OR MAST CELL ACTIVATION EX VIVO

C. Van de Bruaene¹, J. Schol¹, L. Balsiger¹, K. Raymenants¹, J. Toth², R. Farré², K. Routhiaux², K. Van den Houte², F. Carbone², T. Vanuytsel¹, J. Tack¹

¹Katholieke Universiteit Leuven / Universitaire Ziekenhuizen Leuven Campus Gasthuisberg, Translational Research Center for Gastrointestinal Disorders, Department of Neurogastroenterology and Motility, Leuven, Belgium, ²Katholieke Universiteit Leuven, Translational Research Center for Gastrointestinal Disorders, Department of Neurogastroenterology and Motility, Leuven, Belgium

Contact E-Mail Address: cedric.vandebruaene@kuleuven.be

Introduction: Functional dyspepsia (FD) is a common gastrointestinal disorder, comprising postprandial distress syndrome, PDS, with meal-related symptoms, and epigastric pain syndrome, EPS, with meal-unrelated symptoms. In a pilot study in PDS patients, the 6-food elimination diet was able to provide symptom relief (1). Using confocal laser endomicroscopy (CLE), acute disruption of the duodenal epithelium in response to food protein administration can be observed (2). This assessment may have the potential to identify food components that should be the target of an elimination diet treatment approach.

Aims & Methods: **Aim:** To evaluate the acute effect of food administration on duodenal mucosal integrity in FD patients and to determine whether visualized alterations are associated with changes in mucosal permeability or markers of mast cell activation ex-vivo.

Methods: In 17 Rome IV FD patients (8 PDS, 1 EPS, 8 overlap PDS/EPS), classic allergy to nutrients was excluded by specific serum IgE tests. Index upper GI endoscopy (EGD) was followed at least 2 weeks later by a second EGD with CLE. Duodenal mucosa was visualized at baseline and after consecutive administration of egg white, soy, milk, wheat, lyophilized fish and shellfish and nuts solutions through the working channel in a randomized order. In those with reaction to one of the first 2 administered food solutions, an additional CLE was scheduled. Serum was obtained at baseline and 30 minutes after occurrence of acute mucosal alterations. Biopsies were obtained at index EGD and after acute alterations to measure transepithelial electrical resistance (TEER) in Ussing chambers. Tryptase levels in biopsy supernatants after 1h and following 24h incubation were assessed. Data are reported as mean ± SEM. Comparisons were done using two-sided t-tests. P-value <0.05 is considered significant.

Results: 29 CLE exams were carried out in 17 patients (age 35±3.7y, f16, BMI 22±0.7 kg/m²). In 90% of exams (n=26), acute alterations were visible only after food exposure, while in 10% (n=3), these were already present

at baseline. Twelve patients (71%) showed alterations on CLE after exposure to one of the first 2 food components and underwent a second CLE procedure. Highest percentage of acute alterations was observed after soy administration (6/11 exposed). In the table, distribution of reactions per food is presented. After acute alterations, there was no difference in serum tryptase compared to baseline (4.52µg/L±0.6 vs. 4.72µg/L±0.6, p=0.21), nor did TEER change compared to baseline (28±0.9 Ωxcm² vs 28±1.6 Ωxcm², p=0.25), nor did tryptase content alter in biopsy supernatants, both after 1h and 24h compared to baseline (0.23µg/g±0.04 vs. 0.28µg/g±0.07, p=0.15 and 1.66µg/g±0.44 vs. 1.06µg/g±0.33, p=0.60).

Observations	Number of exams with exposure	Number of acute alterations	% of acute alterations per food item
Baseline	29	3	10
Milk	8	2	25
Nuts	12	4	33
Soy	11	6	55
Wheat	7	3	43
Fish	10	2	20
Egg white	8	3	38

Table. Number of examinations with exposure and alterations per specific food components.

All patients had a baseline visualization during CLE examination.

Conclusion: In FD patients without IgE mediated classical allergies, CLE visualized a high rate of acute food induced mucosal alterations. These acute responses were not associated with altered permeability, a rise in systemic tryptase, or release of tryptase from biopsy supernatants. Mechanisms underlying acute mucosal alterations and its impact on elimination diet efficacy needs further investigation.

References: 1. Schol J, Routhiaux K, Van den Houte K, Huang I, Tóth J, Balsiger L, et al., editors. The six-food elimination diet improves symptoms of functional dyspepsia. DDW; 2023.

2. Fritscher-Ravens A, Schuppan D, Ellrichmann M, Schoch S, Rocken C, Brasch J, et al. Confocal endomicroscopy shows food-associated changes in the intestinal mucosa of patients with irritable bowel syndrome. Gastroenterology. 2014;147(5):1012-20 e4.

Disclosure: Speaker fee from the Rome Foundation
Speaker fee from Mayoly.

PP0040

WITHDRAWN

PP0041

GENDER GAP IN THE TREATMENT OF FUNCTIONAL DYSPESIA? DATA FROM THE GERIATRIC POPULATION

J. Worbs¹, E. Complido¹, O. Kelber¹, K. Nieber², K. Kraft³
¹Steigerwald Arzneimittelwerk GmbH, Phytomedicines Supply and Development Center, Bayer Consumer Health, Darmstadt, Germany, ²Leipzig University, Institute for Pharmacy, Leipzig, Germany, ³University Medicine Rostock, Chair for Naturopathy, Rostock, Germany

Contact E-Mail Address: olaf.kelber@bayer.com

Introduction: Functional gastrointestinal disorders (FGIDs) are more prevalent in female than in male patients [1,2]. This triggers the question whether this is also reflected in medical care, especially also in self-medication, where often botanicals are used. A potential source of data to address this question is the PhytoVIS study, a pharmacoepidemiological study conducted in Germany in more than 20,000 patients taking herbal medicinal products.

Aims & Methods: To have a large and homogenous data base for a gender-related evaluation, records for a clinically proven herbal medicinal product (HMP) often used in FGIDs, STW 5 [3,4], were evaluated to uncover potential gender-related differences in the pharmacotherapy of FGIDs.

Results: 1513 records were evaluated, 71 % of them from females and 29 % from males, i.e. a 4 % higher proportion of females compared to the overall population of the PhytoVIS study. Main criterium for the evaluation was the Clinical Global Impression Scale – Efficacy (CGI-E). No major differences between females and males were found, apart that women perceived a minimally better effect of the therapy. The reported symptoms were differentiated into symptoms associated with functional dyspepsia (FD), irritable bowel syndrome (IBS), or symptoms that can be associated with both. As far as the records allow a differentiation, no gender differences could be observed. This applies also to the perceived efficacy, the tolerability and the onset of action.

Conclusion: So, while there are differences in the prevalence of FGIDs in women and men, there are no therapeutically relevant pharmacoepidemiological differences in patients with functional gastrointestinal diseases treated with a medicinal product indicated in these diseases, so suggesting that there is no gender gap in this highly relevant therapeutic field.

References:

1. Kim YS, Kim N. Sex-Gender Differences in Irritable Bowel Syndrome. *J Neurogastroenterol Motil.* 2018;24:544-558
2. Houghton LA, Heitkemper M, Crowell M, Emmanuel A, Halpert A, McRoberts JA, Toner B. Age, Gender and Women's Health and the Patient. *Gastroenterology.* 2016; S0016-5085(16)00183-9;
3. Malfertheiner P. STW 5 (Iberogast) Therapy in Gastrointestinal Functional Disorders. *Dig Dis.* 2017;35 Suppl 1:25-29
4. Madisch A, Vinson BR, Abdel-Aziz H, Kelber O, Nieber K, Kraft K, Storr M. Modulation of gastrointestinal motility beyond metoclopramide and domperidone : Pharmacological and clinical evidence for phytotherapy in functional gastrointestinal disorders. *Wien Med Wochenschr.* 2017;167:160-168

Disclosure: JW and EC were interns, OK, is employee of Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany, KN und KK have received fees from the same company.

PP0042

ACTIVATING TRANSCRIPTION FACTOR 3 ASSOCIATED WITH NAUSEA IN GASTROPARESIS PATIENTS - A WHOLE GENOME SEQUENCING STUDY

H. Bai¹, S. Smieszek¹, J.L. Carlin¹, C. Xiao¹, G. Birznieks¹, C. Polymeropoulos¹, M.H. Polymeropoulos¹
¹Vanda Pharmaceuticals Inc., Washington, United States of America

Contact E-Mail Address: baihm_steven@hotmail.com

Introduction: Gastroparesis is a severe medical condition characterized by delayed gastric emptying and symptoms of nausea, vomiting, bloating, fullness after meals, and abdominal pain. Thus far, little is known about the underlying genetic risk factors for nausea in gastroparesis patients. We explored the association of genetic variants with nausea severity in a set of WGS data from a clinical gastroparesis study.

Aims & Methods: Blood samples were obtained from adults with a diagnosis of diabetic or idiopathic gastroparesis, having evidence of delayed gastric emptying, and moderate to severe nausea, daily average nausea score of >2.5, at least one episode of vomiting, PAGI-SYM nausea score of ≥2 at screening, and controlled blood glucose levels. WGS was conducted with 30x read depth using whole blood samples. Nausea score was assessed from a daily symptom diary with a range from 0 mild to 5 severe. GWAS using linear model was conducted on variants with MAF ≥0.01 with adjustment of the subject's age, sex, BMI, etiology, and the first 3 PCs.

Results: Variant clusters from multiple genes are significantly associated with baseline nausea score at p=1e-5 level. Among the top scoring variants are loci within ATF3, PP2D1, CNTN4, BMP2, ABL1, CTNNA3 and KIF6. Interestingly, upon comparing our results with a published transcriptomic analysis that included both diabetic and idiopathic gastroparesis subjects, we found that ATF3 and BMP2 were overlapping with genes differentially expressed in both diabetic and idiopathic gastroparesis when compared with controls. ABL1 was however differentially expressed in diabetic cases whereas CNTN4 was differentially expressed in idiopathic controls. We expanded the analysis with single gene tests which shows that ATF3 is significant especially for MAF>0.05 variants (SKAT p=0.02). The top variant in ATF3 is rs79151334 (beta= 0.68, p=5.76e-6), whose minor allele associates with higher nausea score.

Conclusion: Additionally, we report new potential associations CTNNA3, PP2D1, and KIF6 as well as a cluster of variants between CDH2 and MIR302F, that associated with baseline nausea score. Among those, both CTNNA3 and CDH2 encode cadherin related proteins, suggesting this type of junction could play a role in the underlying mechanism.

Disclosure: I am an employee at Vanda Pharmaceuticals Inc.

PP0043

HOW MANY SUBJECTS WITH SEVERE DISORDERS OF GUT-BRAIN INTERACTION HAVE AN INTOLERANCE OF GLUTEN WHEN A DOUBLE-BLIND GLUTEN EXPOSURE IS PERFORMED?

N. Smith¹, A. Do¹, B. McKillen¹, T. Fairlie¹, N.A. Koloski¹, K. Duncanson², N.J. Talley³, A. Shah¹, G.J. Holtmann¹

¹Princess Alexandra Hospital, Gastroenterology & Hepatology, Brisbane, Australia, ²University of Newcastle, School of Medicine and Public Health, Callaghan, Australia, ³University of Newcastle, Faculty of Health & Medicine, New Lambton Heights, Australia

Contact E-Mail Address: nxsmith@gmail.com

Introduction: Approximately 50% of patients with disorders of gut-brain interaction (DGBI) report intolerance of wheat products [2]. While dietary gluten restrictions would be a feasible approach to managing gastrointestinal symptoms, in DGBI patients with gluten-related symptoms, there are challenges in relation to compliance and even adverse long-term effects of a gluten and wheat-free diet.

Aims & Methods: This study aims to test the feasibility of a double-blind gluten exposure test and determine the rate of patients with DGBI who respond with a change of symptom severity after exposure to gluten.

From a cohort of 70 consecutive patients referred to our Integrated Care Clinic for patients with complex DGBI, 35 agreed to participate in a double-blind gluten exposure test. This test was aligned with the gluten exposure test outlined in the Salerno criteria [1].

After exclusion of coeliac disease (endoscopy and serology), a seven-week gluten-free run-in, patients received one week of encapsulated gluten (8 g per day) or identical placebo. Each week with daily gluten exposure or placebo exposure was separated by one week of washout. Gluten and placebo were administered in a double-blind randomised fashion. The Structured Assessment of Gastrointestinal Symptoms (SAGIS) score was used at baseline before commencing the gluten exposure test and at the end of every week to assess changes of gastrointestinal symptoms.

Results: 34 patients completed the challenge test, of whom seven initially had self-reported symptoms associated with gluten or wheat consumption. Only one of these seven patients responded to gluten exposure with a >25% increase of the SAGIS score. 16 out of 34 patients (47 %, 95% CI 30-65) reported improved gastrointestinal symptoms while on a gluten-free diet.

Overall, 2 of the 34 patients (5.9%, 95% CI 0.7-20.0) showed a deterioration of symptoms during the gluten challenge week, while 8 patients (23.5%, 95% CI 10.8-41.2) reported a reduction of the symptoms while exposed to placebo. No effects of gluten exposure on extraintestinal symptoms were observed.

Conclusion: A standardised, double-blind gluten exposure test is suitable in the routine clinical setting to rule out gluten intolerance in patients with self-reported gluten sensitivity. Overall, gluten exposure is rarely associated with an increase of gastrointestinal symptoms in patients with DGBI. Self-reported non-celiac wheat sensitivity is a poor predictor for developing symptoms during double-blind gluten exposure.

References: [1] Catassi C, Elli L, Bonaz B, et al. Diagnosis of Non-Celiac Gluten Sensitivity (NCGS): The Salerno Experts' Criteria. *Nutrients* 2015;7:4966-77.

[2] Shah A, Talley NJ, Kang S, et al. Self-reported non-celiac wheat sensitivity in patients with chronic unexplained (functional) gastrointestinal symptoms: gut function, immune activation and duodenal mucosa associated microbiome. *Gastroenterology* 2020;158:S-488

Disclosure: Nothing to disclose.

PP0044

EFFECTS OF DA-9701 (MOTILITONE) ON GASTRIC EMPTYING, BLOOD GLUCOSE REGULATION, AND OXIDATIVE STRESS IN DIABETIC RATS

M. Kim¹, C.I. Sohn², Y.m. Song³

¹Asan Medical Center, Ulsan University School of Medicine, Department of Gastroenterology, Seoul, South Korea, ²Department of Internal Medicine, Sungkyunkwan University Gangbuk Samsung Hospital, Seoul, South Korea, ³Sungkyunkwan University Gangbuk Samsung Hospital, Institute of Medical Research, Seoul, South Korea

Contact E-Mail Address: daneel0717@naver.com

Introduction: Diabetes is associated with a variety of gastrointestinal disorders, including altered gastric emptying, which can be rapid, slow, or transient.

These changes can significantly influence gastrointestinal symptoms and potentially impact blood glucose levels. DA-9701 (motilitone), a known prokinetic agent derived from *Corydalis tuber* and *Pharbitis* seed, is employed in Korea to manage functional dyspepsia due to its noted anti-inflammatory and gastrointestinal motility-enhancing effects. This study aims to investigate the potential of DA-9701 in addressing altered gastric emptying and glycemic control in diabetic rats, thereby validating its broader clinical utility.

Aims & Methods: Diabetes mellitus was induced in rats by streptozotocin injection. Post-diabetes development, rats received oral administration of DA-9701 daily for two weeks. Evaluations included serum glucose levels, gastric emptying rates for liquids and solids, plasma insulin levels, and serum malondialdehyde concentration. Immunoblot assays assessed the expression of c-Kit, the *Ogg1* gene, and phosphorylated extracellular signal-regulated kinase (p-ERK).

Results: Diabetic rats exhibited blood glucose levels three to four times higher than nondiabetic control rats at weeks 3 and 4. Gastric emptying, initially accelerated by week 2 and persisting until week 4, was linked to increased interstitial cells of Cajal (ICC) activity driven by hyperglycemia-induced oxidative stress. The expression of c-Kit, an ICC marker, was elevated in the gastric tissues of diabetic rats by weeks 3 and 4 but reduced following two weeks of DA-9701 administration. Oral administration of DA-9701 (6 mg/kg) not only normalized gastric emptying but also improved blood glucose levels through increased serum insulin concentrations by weeks 3 and 4. Oxidative stress markers, including *Ogg1*, p-ERK, and serum malondialdehyde concentrations, initially upregulated, were reduced post-treatment.

Conclusion: Two weeks of DA-9701 treatment attenuated accelerated gastric emptying and reduced elevated blood glucose levels in diabetic rats. Normalized gastric emptying contributed to improved glucose homeostasis by reducing oxidative stress. Additionally, an unexpected increase in serum insulin levels post-treatment suggests that DA-9701's regulatory effects extend beyond gastric dynamics to direct modulation of blood glucose. These findings underscore DA-9701's significant potential in managing both gastrointestinal dysfunction and glucose control in diabetes mellitus.

References: 1. Goyal RK. Gastric Emptying Abnormalities in Diabetes Mellitus. *N Engl J Med*. 2021;384(18):1742-51.

2. Goyal RK, Cristofaro V, Sullivan MP. Rapid gastric emptying in diabetes mellitus: Pathophysiology and clinical importance. *J Diabetes Complications*. 2019;33(11):107414.

3. Oh JH, Pasricha PJ. Recent advances in the pathophysiology and treatment of gastroparesis. *J Neurogastroenterol Motil*. 2013;19(1):18-24.

4. Hayashi Y, Toyomasu Y, Saravanaperumal SA, Bardsley MR, Smestad JA, Lorincz A, et al. Hyperglycemia Increases Interstitial Cells of Cajal via MAPK1 and MAPK3 Signaling to ETV1 and KIT, Leading to Rapid Gastric Emptying. *Gastroenterology*. 2017;153(2):521-35.e20.

5. Kishi K, Kaji N, Kurosawa T, Aikiyo S, Hori M. Hyperglycemia in the early stages of type 1 diabetes accelerates gastric emptying through increased networks of interstitial cells of Cajal. *PLoS One*. 2019;14(10):e0222961. E
6. Jin M, Son M. DA-9701 (Motilitone): A Multi-Targeting Botanical Drug for the Treatment of Functional Dyspepsia. *Int J Mol Sci*. 2018;19(12). Epub 20181213.
7. Jung HK, Lee KJ, Choi MG, Park H, Lee JS, Rhee PL, et al. Efficacy of DA-9701 (Motilitone) in Functional Dyspepsia Compared to Pantoprazole: A Multicenter, Randomized, Double-blind, Non-inferiority Study. *J Neurogastroenterol Motil*. 2016;22(2):254-63.

Disclosure: Nothing to disclose.

PP0045

ASSESSMENT OF VAGAL NERVE INJURY THROUGH SHAM FEEDING

T. Li¹, S. Billings¹, T.A. Woodward¹, B. Lacy¹

¹Mayo Clinic Florida, Gastroenterology, Jacksonville, United States of America

Contact E-Mail Address: li.tian@mayo.edu

Introduction: Vagal nerve injury may lead to symptoms of nausea, vomiting, abdominal discomfort, and bloating. Be it by injury or an infiltrative process, vagal nerve function is difficult to assess. Measuring pancreatic polypeptide (PP) following a sham meal may serve as a reasonable surrogate marker of vagal nerve function. PP is released in response to eating and may correlate with slow gastric emptying.

Our aim is to assess vagal nerve integrity using sham feeding with measurement of PP, in addition to evaluating the relationship of symptoms with PP levels and gastric emptying.

Aims & Methods: This was a retrospective study of patients who underwent a sham feeding study at Mayo Clinic Florida from 2018 to 2023. We collected demographic and clinical data, sham feeding results, the indication for the study, and gastric emptying data. A 50 % increase in PP level within 30 mins compared to baseline after sham feeding was considered normal. A gastric emptying scan was classified as delayed if <75% of the material emptied at 4 hours.

Results: 29 patients were included (58.6% women) with a mean age of 57.3 years. Most patients were white (n=24), and the mean BMI was 27.9 kg/m². The most common reason to request a sham feeding study was abdominal pain (7, 24.1%), gastroesophageal reflux (GER) (6, 20.7%) and chronic nausea and vomiting (6, 20.7%). The main GI symptoms were nausea and vomiting (13, 44.8%) and diarrhea (11, 37.9%). The average weight loss from the onset of symptoms was 31 lb. 24 of 29 included patients had a history of abdominal surgery, with hiatal hernia repair (HHR) and HHR with Nissen fundoplication being the two most common surgeries (5, 17.2%). 20 of 29 studied patients (69.0%) had an abnormal sham feeding study and 48.1% of the patients who underwent gastric empty studies were found to have delayed gastric emptying. The mean baseline PP level of normal vs abnormal was 102.88 pg/mL and 226.4 pg/mL, respectively (p=0.21). The mean peak PP level of normal vs abnormal was 195.22 pg/mL and 245 pg/mL, respectively (p=0.68). Among the 20 patients with an abnormal sham feeding study, ten had delayed gastric emptying. Symptoms of nausea and vomiting were found to have a robust correlation with a positive sham feeding result (12, 92%), compared with gastric emptying scintigraphy (8, 61.5%). There was no correlation between sham feeding result with symptoms of abdominal pain and GER. The care after apparent vagus nerve injury required significant medical resources, including an average of 3.5 visits and 5.7 tests per patient to evaluate key GI symptoms.

Conclusion: Sham feeding is an underused method to measure vagus nerve injury. It is safe and easy to perform. PP levels measured during sham feeding were consistently abnormal in patients with predominant

symptoms of nausea and vomiting after foregut surgery while the correlation between gastric emptying measured using scintigraphy and gastroparesis symptoms was not significant. Interestingly, there was limited correlation between scintigraphy gastric emptying results and outcomes of sham feeding. Our research highlights the significant medical and financial burden evaluating patients with symptoms after foregut surgery. Larger prospective studies are needed to better quantify the relationship between PP levels and gastric emptying in patients with prior foregut surgery who remain symptomatic.

Disclosure: Nothing to disclose.

PP0046

ASSOCIATIONS BETWEEN GASTROINTESTINAL SYMPTOMS, MOTILITY, AND EXTRAGASTROINTESTINAL AUTONOMIC MEASURES IN DIABETIC GASTROENTEROPATHY: A CROSS-SECTIONAL STUDY

D. Smed Kornum¹, C. Brock², T. Okdahl³, D. Bertoli³, H. Kufaiishi⁴, A.-M. Wegeberg⁵, K. Lundby Høyer¹, E.B. Mark⁵, B. Brock⁴, C. Stevns Hansen⁴, F.K. Knop⁶, A.M. Drewes⁵, K. Krogh¹
¹Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus N, Denmark, ²Aalborg University Hospital, Aalborg, Denmark, ³Aalborg University Hospital, Mech-Sense, Department of Hepatology and Gastroenterology, Aalborg, Denmark, ⁴Steno Diabetes Center Copenhagen, Herlev, Denmark, ⁵Aalborg University Hospital, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ⁶Clinical Metabolic Research at Gentofte Hospital, Copenhagen, Denmark

Contact E-Mail Address: Dittiver@rm.dk

Introduction: Autonomic neuropathy affecting multiple organs is a common and severe complication of diabetes¹. Neuropathy of the enteric nervous system and the regulatory autonomic nerve fibers can affect the entire gastrointestinal tract, causing mild to severe gastrointestinal symptoms². The correlation between gastrointestinal symptoms and underlying pathophysiology is generally weak, so objective assessment is important to guide treatment³⁻⁵. Methods for direct evaluation of enteric neuropathy are not yet available in clinical practice. Hence, gastrointestinal transit times and contractile activity are used as proxies for enteric autonomic dysfunction^{6,7}. Panenteric gastrointestinal assessment is considered essential, yet suitable methods are generally inaccessible, and diagnosing diabetic gastroenteropathy often causes significant challenges^{4,8}. It is unknown whether measures of extraintestinal autonomic function can reflect diabetic gastroenteropathy and whether these measures could serve as supplementary diagnostic tools.

Aims & Methods: We aimed to assess 1) whether gastrointestinal symptoms are associated with motility measures and 2) whether gastrointestinal symptoms/motility measures are associated with extraintestinal autonomic markers. We included 81 persons with type 1 or type 2 diabetes (65% female, mean age 54) with gastrointestinal symptoms and either symptoms or signs of autonomic neuropathy. The Gastroparesis Cardinal Symptom Index (GCSI) and the Gastrointestinal Symptom Rating Scale (GSRS) were used to assess gastrointestinal symptoms. The wireless motility capsule assessed panenteric transit times and motility indices. Cardiovascular reflex tests performed with the VAGUS device and the cardiac vagal tone assessed with the eMotion Faros device estimated cardiovascular autonomic neuropathy, while the SUDOSCAN evaluated sudomotor function.

Results: Proximal gastrointestinal symptoms were positively associated with the gastric motility index (GCSI: 1.18 (1.04 - 1.35), p=0.01; GSRS: 1.15 (1.03 - 1.29), p=0.02; median ratio (95%CI)), while only satiety reflected gastric emptying time (1.24 (1.03 - 1.49), p=0.02). Diarrhea was associat-

ed with decreased small bowel transit time (0.93 (0.89 - 0.98), $p=0.005$), while constipation was associated with prolonged colonic transit time (1.16 (1.03 - 1.31), $p=0.02$). Gastrointestinal symptoms increased with the degree of abnormal cardiovascular reflex tests (GCSI: 0.67 (0.16 - 1.19), $p=0.03$; GSRS: 0.87 (0.30 - 1.45), $p=0.01$; mean difference (95%CI)) but not with motility measures. Cardiac vagal tone and sudomotor function were not associated with gastrointestinal markers.

Conclusion: Gastrointestinal and extraintestinal autonomic measures were not associated. However, proximal gastrointestinal symptoms were associated with the gastric motility index and cardiovascular reflex tests. Hence, the latter may contribute to evaluating whether proximal gastrointestinal symptoms are autonomically derived.

References: 1. Verrotti A, Prezioso G, Scattoni R, Chiarelli F. Autonomic neuropathy in diabetes mellitus. *Front Endocrinol (Lausanne)*. 2014;5:205.
2. Azpiroz F, Malagelada C. Diabetic neuropathy in the gut: pathogenesis and diagnosis. *Diabetologia*. 2016;59(3):404-408.
3. Arora Z, Parungao JM, Lopez R, Heinlein C, Santisi J, Birgisson S. Clinical utility of wireless motility capsule in patients with suspected multiregional gastrointestinal dysmotility. *Dig Dis Sci*. 2015;60(5):1350-1357.
4. Kuo B, Maneerattanaporn M, Lee AA, et al. Generalized transit delay on wireless motility capsule testing in patients with clinical suspicion of gastroparesis, small intestinal dysmotility, or slow transit constipation. *Dig Dis Sci*. 2011;56(10):2928-2938.
5. Roupheal C, Arora Z, Thota PN, et al. Role of wireless motility capsule in the assessment and management of gastrointestinal dysmotility in patients with diabetes mellitus. *Neurogastroenterol Motil*. 2017;29(9).
6. Kempler P, Amarenco G, Freeman R, et al. Management strategies for gastrointestinal, erectile, bladder, and sudomotor dysfunction in patients with diabetes. *Diabetes Metab Res Rev*. 2011;27(7):665-677.
7. Camilleri M, Chedid V, Ford AC, et al. Gastroparesis. *Nat Rev Dis Primers*. 2018;4(1):41.
8. Bertoli D, Mark EB, Liao D, et al. MRI-Based Quantification of Pan-Alimentary Function and Motility in Subjects with Diabetes and Gastrointestinal Symptoms. *J Clin Med*. 2023;12(18).

Disclosure: Nothing to disclose.

PP0047

PHARMACOLOGICAL ACTIVITY OF A HERBAL PREPARATION AND ITS INDIVIDUAL HERBAL EXTRACTS ON GASTRIC MOTILITY IN FUNCTIONAL DYSPESIA

M.-R. Piqué-Borràs¹, J. Röhrli¹, M. Mennet-von Eiff², G. Künstle¹

¹Weleda AG, Preclinical Research and Development, Arlesheim, Switzerland, ²Weleda AG, Research and Development Pharma, Arlesheim, Switzerland

Contact E-Mail Address: mpiqueborras@weleda.ch

Introduction: This study investigates the pharmacological activity of Amara-Drops, a traditional herbal remedy used for gastrointestinal dysmotility, and its nine individual herbal extracts on fundus accommodation, a characteristic aspect of functional dyspepsia. Impaired fundus accommodation after food intake can lead to symptoms such as epigastric pain and vomiting, yet its etiology remains poorly understood. Previous studies have demonstrated that the extract of Amara-Drops relaxes guinea-pig fundus stomach, potentially mediated by M2 muscarinic receptor inhibition, though the exact mechanism and responsible individual extracts were not investigated.

Aims & Methods: Our study aimed to explore the mechanisms of action of Amara whole extract and its constituent extracts (*Artemisia absinthium* Herba, *Centaurium erythraea* Herba, *Cichorium intybus* Planta tota, *Gentiana lutea* Rhizoma, *Juniperus communis* Summitates, *Achillea millefoli-*

um Herba, *Peucedanum ostruthium* Rhizoma, *Salvia officinalis* Folium and *Taraxacum Planta tota*) on fundus accommodation, both *ex vivo* and *in vitro*.

Dry extracts were obtained from the commercial product Amara-Drops or from the individual ethanolic tinctures. Guinea-pig fundus muscle strips were prepared and set up in organ baths in a circular orientation to study the relaxation effect of the whole extract (94.4–1,000 µg/mL) or vehicle, with or without Carbachol-induced contraction. To elucidate whether M2 or M3 muscarinic receptors were involved in the relaxation effect, guinea-pig fundus was pretreated with J-014129, an antagonist of M3, followed by addition of whole extract or three selected individual extracts. Furthermore, binding and antagonist activities on muscarinic M3 and M2, and opioid µ (OP1) receptors expressed in CHO-K1 cell line were assessed for the whole extract and/or individual extracts.

Results: Exposure of the whole extract to guinea-pig fundus muscle strips induced significant relaxation at the highest concentrations tested ($p<0.001$). Significant relaxation was observed in Carbachol-contracted muscle strips ($p<0.05$), regardless of J-014129 pretreatment, suggesting potential modulation of the M2 receptor.

In vitro studies revealed the whole extract bound to M3, M2 and OP1 receptors (IC_{50} : 380, 294 and 55 µg/mL, respectively), with selective M2 and OP1 receptor activity impairment (IC_{50} : 219 and 304 µg/mL, respectively) via inhibition of their respective reference agonist activity.

M3 receptor activity was not affected. *Juniperus communis*, *Salvia officinalis*, and *Peucedanum ostruthium* extracts showed M2 receptor inhibition (IC_{50} : 32, 20, and 21 µg/mL, respectively), with only *Peucedanum ostruthium* extract binding to M2 receptor (IC_{50} : 137 µg/mL) and significantly relaxing Carbachol-contracted muscle strips, irrespective of J-014129 pretreatment ($p<0.001$).

However, *Juniperus communis* and *Salvia officinalis* did not show M2 receptor binding nor relaxation effects. Furthermore, *Gentiana lutea*, *Juniperus communis*, *Artemisia absinthium*, and *Centaurium erythraea* extracts inhibited OP1 receptor activity (IC_{50} : 42, 25, 22 and 104 µg/mL, respectively).

Conclusion: These data highlight the potential of the medicinal product Amara-Drops, particularly its *Peucedanum ostruthium* extract, in modulating fundus accommodation by inhibiting M2 receptor activity.

Further investigations are needed to elucidate relaxation mechanisms through OP1 receptor inhibition. Nevertheless, this study provides a promising molecular basis for the efficacy of Amara-Drops in improving impaired fundus accommodation in functional dyspepsia.

Disclosure: All authors are employees of Weleda AG.

PP0048

EPIDEMIOLOGY OF MAJOR ESOPHAGEAL MOTILITY DISORDERS AMONG PATIENTS WITH TYPICAL VERSUS NON-TYPICAL SYMPTOMS OF ESOPHAGEAL MOTILITY DISORDERS

T. Voulgaris¹, T. Alexopoulos¹, D. Kamberoglou¹, J. Vlachogiannakos¹, G. Papatheodoridis¹, G. Karamanolis¹

¹National and Kapodistrian University, Laiko General Hospital, Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: georgekaramanolis@yahoo.co.uk

Introduction: Esophageal dysphagia and retrosternal chest pain are considered the typical manifestations of major esophageal motility disorders (mEMD). High Resolution Manometry (HRM) is the gold standard for the diagnosis of mEMD.

However, in real clinical practice patients are referred for HRM due to several non-typical esophageal symptoms and the rate of EMD among those patients is largely unknown.

Aims & Methods: Aim of our study was to search for mEMDs prevalence among patients with typical symptoms and compare them with patients referred for non-typical symptoms.

We retrospectively collected epidemiological, endoscopic (available in 263/302), barium swallow (available in 176/302) and manometric data from consecutive patients referred for HRM in our center from 1/2020 to 12/2023. Atypical symptoms for which patient were referred for HRM included; heartburn, regurgitation, globus, oropharyngeal dysphagia and epigastric pain.

Patients with a previous diagnosis of mEMDs/scleroderma/EoE, referred for pre-surgical evaluation for Gastroesophageal Reflux Disease (GERD) or submitted to gastro-esophageal surgery were excluded. Endoscopic data suggestive of an mEMD were considered esophageal dilation, solids/liquids/saliva in the lumen and difficulty to pass the scope through the Lower Esophageal Sphincter (LES), while delay in barium transit from Esophagus to the stomach, esophageal dilation and bird-like LES appearance as barium swallow were considered findings compatible to mEMD.

Results: We included 302 patients (M/F: 147/155, mean age: 56±17 years). Typical symptoms were reported by 234 (77.2%) patients, while only atypical in 68 (22.8%). Main referral symptom was; esophageal dysphagia: 176 (58.3%), chest pain: 42 (13.7%), heartburn: 27 (8.9%), regurgitation: 25 (8.3%), globus/oropharyngeal dysphagia/epigastric pain: 32 (10.8%). Diagnosis of mEMDs in HRM was set in 175/302 (57.9%) and was statistically more common when typical symptoms existed (163/233, 69.9% vs 12/78, 15.4%, p<0.001).

HRM diagnosis among patients with mEMDs are given in table 1. Among patients with a diagnosis of mEMD in HRM, endoscopic data compatible to mEMDs were statistically more common among patients with typical symptoms, though barium swallow data were not (103/149, 69.1% vs. 4/10, 40%, p=0.037 and 110/116, 94.8% vs. 9/9, 100%, p=0.633 respectively).

HRM diagnosis of mEMD among patients with compatible either barium swallow or endoscopic findings was found in a statistically increased rate among patients with typical symptoms (134/145, 92.4% vs. 10/19, 52.6%, p<0.001). We should point that among 43 patients with non-typical symptoms and normal endoscopy and barium swallow study only 1 (2.3%) had a mEMD diagnosis by HRM.

HRM diagnosis	Total cohort (n=175)	Typical symptoms (dysphagia-chest pain) (n=163)	Non-typical symptoms (n=12)
Achalasia	143 (81.7%)	135(82.8%)	8 (66.7%)
Type I	6/143 (4.2%)	5/135 (3.7%)	1/8 (12.5%)
Type II	134/143 (93.7%)	127/135 (94.8%)	7/8 (87.5%)
Type III	3/143 (2.1%)	3/135 (2.2%)	0
Esophago-Gastric Junction Outflow Obstruction	21 (11.4%)	18 (11.0%)	2 (16.6%)
Diffuse Esophageal Spasm (DES)	3 (1.7%)	3 (1.8%)	0
Hypercontractile Esophagus	1 (0.6%)	1 (0.6%)	0
Absent peristalsis	8 (4.6%)	6 (3.7%)	2 (16.6%)

Conclusion: More than half of patients referred for HRM will be diagnosed with mEMD, rate significantly increased when typical symptoms, as dysphagia or chest pain, are reported. Achalasia, more specifically type II, is in general the most commonly diagnosed mEMD. Absence of compatible endoscopic or barium swallow findings make mEMDs diagnosis, in the absence of typical symptoms, almost impossible.

Disclosure: Nothing to disclose.

PP0049

THE EFFECT OF BOLUS VOLUME, VISCOSITY AND SENSORY TRP STIMULANTS ON THE UPPER ESOPHAGEAL SPHINCTER AND PHARYNGEAL MOTILITY IN HEALTHY [JL1] ADULTS MEASURED WITH HIGH-RESOLUTION IMPEDANCE MANOMETRY

M. Martínez-Guillén^{1,2}, P. Clavé^{1,2}, M. Bolívar-Prados^{1,2}, E. Palomera¹, N. Tomsen^{1,2}, D. España^{1,2}, A. Raventós^{1,2}, L. Mundet^{1,2}, T.B Karunaratne^{1,2}, S. Carrion^{1,2}
¹Hospital de Mataró, Gastrointestinal Physiology Laboratory, Mataró, Spain, ²Centro de Investigación Biomédica en Red de enfermedades hepáticas y digestivas (CIBEREHD), Instituto de Salud Carlos III, Barcelona, Spain

Contact E-Mail Address: martinezguillenmiguel@gmail.com
Introduction: Introduction: High-resolution impedance manometry (HRIM) is now an important tool in the study of upper esophageal sphincter (UES) function and pharynx propulsion in patients with oropharyngeal dysphagia. Our aim was to study the effect of volume, viscosity and sensory TRP stimulants using HRIM in healthy adults.

Aims & Methods: Methods: We present a cross-sectional, controlled, quasi-experimental study in 14 healthy volunteers (median age 33 years) studied by high-resolution solid-state probe manometry of 30 unidirectional pressure channels and 6 circumferential channels at the UES with 16 impedance channels. Duplicate boluses of 5, 10 and 20 mL of 4 viscosities (50, 250, 800 and 2,000 mPa-s) and a duplicate bolus of 5 mL of TRP stimulants with the same 4 viscosities were administered. UES relaxation (UES-IRP), UES opening (UES Max Admittance), flow resistance (hypopharyngeal pressure at nadir impedance (PNadImp) and pharyngeal propulsive forces (peak pharyngeal pressure (PeakP) and pharyngeal contraction integral (PhCI) were assessed. The analysis was performed using Swallow-Gateway® software.

Results: Results: Bolus volume increase at different viscosities caused a) increase in UES integrated relaxation pressure (UES-IRP p < 0.05), b) increase in UES opening (UES Max Admittance p < 0.05), c) increase in flow resistance (PNadImp) at 800 and 2,000 mPa-s (p < 0.005) and d) increase in pharyngeal propulsion at 2,000 mPa-s (PhCI (p < 0.05) with no significant increase with other viscosities or at the PeakP level in all of them.

Viscosity increase at different volumes showed:
a) Increase in UES integrated relaxation pressure (UES-IRP p = 0.004) majority at higher volume boluses (10 and 20 mL),
b) increase in UES opening (UES Max Admittance p < 0.05 at 5 and 10 mL),
c) no changes in bolus resistance (PNadImp (20 ml) p > 0.05) and;
d) no changes in pharyngeal forces (PeakP p > 0.05 and PhCI p > 0.05).
TRP stimulants increased the UES-IRP (p < 0.011) and UES Adm (p < 0.001) and had no effect on pharyngeal contraction forces or bolus flow resistance.

Conclusion: Conclusions: In healthy adults without dysphagia, increasing volume has a significant effect on UES with an improvement on opening with less relaxation, increased flow resistance and increased pharyngeal propulsive forces. In contrast, increasing bolus viscosity and adding TRP stimulants impairs relaxation with improvement on the aperture of the UES with no effect on pharyngeal propulsive forces and flow resistance.

Disclosure: Nothing to disclose.

PP0050

REAL-LIFE TREATMENT IN NON-OBSTRUCTIVE ESOPHAGEAL DYSPHAGIA: ANALYSIS OF A PROSPECTIVE DATABASE

R.R. Mendes¹, J. Azevedo Rodrigues^{1,2}, A. Mascarenhas¹, H.C. Lima³, T. Guedes⁴, S.M. Barrias⁴, M. Costa⁵, P. Souto⁵, J.C. Silva⁶, J.P. Laranjeira Correia⁶, B. Morão⁷, J. Revés⁷, C. Leal⁸, R.T. Marinho^{9,2}, M. Mascarenhas Saraiva³

¹Unidade Local de Saúde de Lisboa Ocidental, Gastroenterology Department, Lisbon, Portugal, ²Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, ³ManopH, Laboratório de Endoscopia e Motilidade Digestiva, Porto, Portugal, ⁴Centro Hospitalar Universitário de Santo António, Gastroenterology Department, Porto, Portugal, ⁵Unidade Local de Saúde de Coimbra, Gastroenterology Department, Coimbra, Portugal, ⁶Unidade Local de Saúde Gaia e Espinho, Gastroenterology Department, Vila Nova de Gaia, Portugal, ⁷Hospital Beatriz Ângelo, Gastroenterology Department, Lisbon, Portugal, ⁸Unidade Local de Saúde de Leiria, Gastroenterology Department, Leiria, Portugal, ⁹Unidade Local de Saúde de Santa Maria, Gastroenterology and Hepatology Department, Lisbon, Portugal

Contact E-Mail Address: andremascarenhasmd@gmail.com

Introduction: Treatment of non-obstructive esophageal dysphagia (NOD) should consider not only the primary condition, but also its impact on patients' daily function, their perception and surgical risk. Between surgical, endoscopic, and medical therapies, there is a wide range of choices, most without well-established indications or outcomes.

Aims & Methods: This is an ongoing prospective multicentric study to evaluate the real-life approach to NOD in 7 centers, by comparing the efficacy of different treatments [per-oral endoscopic myotomy (POEM), botulinic toxin (BT), pneumatic dilation (PD), optimization of proton-pump inhibitors (PPI) and expectant], through the Eckardt, EuroQol-5D (TTO and VAS) and PROMIS GI Disrupted Swallowing (PDS) scores.

Results: According to Chicago V4, it included 97 esophagogastric junction (EGJ) outflow disorders, 24 spastic motility disorders, 38 hypomotile disorders and 91 dysphagia with normal manometry. Fifty-seven (22.8%) patients were submitted to therapy.

Forty-three (44.3%) patients with EGJ outflow disorders were treated (31 POEM, 5 BT, 2 PD, 1 surgical and 4 medical). In contrast to untreated, treated patients showed better differences in Eckardt, PDS and EuroQol-5D VAS scores (p-values <0.005) after 6 months.

PPI was introduced and/or optimized in five (13.2%) patients with hypomotile disorders. There were no differences in Eckardt, EuroQol-5D and PDS at 6-months in treated or untreated patients.

Three (12.5%) patients with spastic motility disorders were treated (2 BT and 1 calcium-channel blocker). Both treated and untreated showed no differences in Eckardt or EuroQol-5D scores at 6 months.

Regarding dysphagic patients with normal manometry, medical treatments were optimized in 6 patients (6.6%), without any differences in Eckardt and EuroQol-5D scores at 6-months. Interestingly, the PDS showed a better difference at 6 months in untreated patients (p-value <0.001).

Conclusion: Apart from EGD outflow disorders, which have well-established treatment options, real-life approach of NOD is heterogeneous and showed no clear benefit. To improve clinical results, specialized clinics must be created.

Disclosure: Nothing to disclose.

PP0051

IMPACT OF NON-OBSTRUCTIVE ESOPHAGEAL DYSPHAGIA ON QUALITY OF LIFE: A PORTUGUESE MULTICENTRIC PROSPECTIVE STUDY

A. Mascarenhas¹, J. Azevedo Rodrigues^{1,2}, R.R. Mendes¹, H.C. Lima³, T. Guedes⁴, S.M. Barrias⁴, M. Costa⁵, P. Souto⁵, J.C. Silva⁶, J.P. Laranjeira Correia⁶, B. Morão⁷, J. Revés⁷, C. Leal⁸, R.T. Marinho^{2,9}, M. Mascarenhas Saraiva³

¹Unidade Local de Saúde de Lisboa Ocidental, Gastroenterology, Lisboa, Portugal, ²Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, ³ManopH, Porto, Portugal, ⁴Centro Hospitalar Universitário de Santo António, Gastroenterology, Porto, Portugal, ⁵Unidade Local de Saúde de Coimbra, Gastroenterology, Coimbra, Portugal, ⁶Unidade Local de Saúde Gaia e Espinho, Gastroenterology, Vila Nova de Gaia, Portugal, ⁷Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal, ⁸Unidade Local de Saúde de Leiria, Gastroenterology, Leiria, Portugal, ⁹Unidade Local de Saúde de Santa Maria, Gastroenterology and Hepatology, Lisboa, Portugal

Contact E-Mail Address: andremascarenhasmd@gmail.com

Introduction: Dysphagia is a common condition with consequences surpassing the physical dimension and extending to the patient's psychological, personal, and professional life. However, when referring to non-obstructive esophageal dysphagia (NOD) and motility disorders, data is still scarce.

Aims & Methods: Our study consists in a prospective and multicentric evaluation of the severity of dysphagia and its impact on quality of life, that was measured with the Eckardt, EuroQol-5D (TTO and VAS) and PROMIS GI Disrupted Swallowing (PDS) scores, in patients with NOD and underlying motility disorders. We included 373 individuals (250 with NOD and 123 without dysphagia).

Results: Among patients with NOD, 97 had esophagogastric junction (EGJ) outflow disorders on manometry according to Chicago V4.0, 24 spastic motility disorders, 38 hypomotile disorders and 91 normal motility. Compared with non-dysphagic individuals, dysphagic patients had significantly worse scores of both EuroQol-5D and PDS (p-values <0.001). Among esophageal motility disorders, Eckardt score was significantly different between groups (p-value <0.001) as determined by ANOVA. Specifically, it was significantly higher in EGJ outflow disorders (mean of 5.2), when compared to spastic motility disorders (mean of 3.3) or dysphagic patients with normal motility (mean of 3.2).

With respect to Patient-reported outcomes, PDS score was statistically different between groups (p-value 0.003), being higher in the EGJ outflow disorders (mean T-score of 64.1) when compared to hypomotility disorders (mean of 60.2) and dysphagic patients with normal motility (mean of 60.3).

Regarding patient-reported quality of life, there were no differences between groups in terms of EuroQol-5D TTO or VAS score (p-value of 0.156 and 0.368, respectively).

Conclusion: Our findings highlights the impact of NOD on the quality-of-life of patients. Although physician and patient reported symptoms' severity were worse on EGJ outflow disorders, overall quality of life seems equally affected among all esophageal motility profiles.

Disclosure: Nothing to disclose.

PP0052

ASSESSING ANTRO-DUODENAL MANOMETRY PATTERNS IN PATIENTS WITH HYPERMOBILE EHLERS-DANLOS SYNDROME WITH GASTROINTESTINAL SYMPTOMS

K. Sweerts¹, Z. Mujagic², D. Keszthelyi², J.M. Conchillo³
¹Maastricht University, Gastroenterology & Hepatology, Maastricht, Netherlands, ²Maastricht University Medical Center, Gastroenterology & Hepatology, Maastricht, Netherlands, ³Maastricht UMC, Gastroenterology, Maastricht, Netherlands

Contact E-Mail Address: daniel.keszthelyi@maastrichtuniversity.nl
Introduction: Hypermobile Ehlers-Danlos syndrome (hEDS) is a hereditary non-inflammatory disorder of connective tissue laxity characterized by joint hyperextensibility in association with musculoskeletal symptoms. The prevalence of gastrointestinal (GI) symptoms, such as abdominal pain, nausea, and constipation is high in hEDS. Research on the relationship between EDS and GI symptoms has mostly been restricted to disorders of the gut-brain axis, whereas the relationship between hEDS and GI dysmotility remains to be clarified.

Aims & Methods: This study aimed to explore antro-duodenal manometry (ADM) patterns in patients with hEDS presenting with GI symptoms. In a prospective open-label study, patients with hEDS and GI symptoms presumed to be the results of GI dysmotility underwent a 6-hour high resolution ADM. The manometry tracings were analyzed by two investigators (KS and JC) independently. Antral contraction frequency (contractions per minute) < 1.0 was considered as antral hypomotility. Pylorospasm was defined as isolated pyloric pressure waves within 60 minutes postprandial. The following neuropathic enteric patterns were scored: presence of retrograde peristalsis, bursts, clustered contractions, and absence of phase III contractions. Abnormal ADM was defined as having antral hypomotility and/ or pylorospasm and/ or neuropathic enteric patterns.

Results: Fifty patients (48 women, mean age 30.4 ± 11.1 yrs.) were included. At baseline, 74% of patients were dependent on enteral feeding and the mean BMI was 20.4 ± 4.4 kg/m². Overall, ADM tracings with one or more abnormal patterns were identified in 53% of patients. Antral hypomotility and pylorospasm were detected in 29% and 15% of patients, respectively. Neuropathic enteric patterns were only seen in 17% of patients. In all cases, no more than one neuropathic pattern was identified. Among the observed neuropathic enteric patterns, 15% of patients showed retrograde peristalsis, 13% absence of phase III contractions, and 2% bursts. Clustered contractions were not identified in this cohort.

Conclusion: Hypermobile Ehlers-Danlos patients presenting with gastrointestinal symptoms showed low numbers of abnormal ADM patterns. In particular, enteric dysmotility was observed in only a small minority of cases. Antroduodenal dysmotility therefore does not appear to be a principle pathomechanism in the majority of hEDS cases studied. Further research is needed to understand the mechanisms that underlie GI symptom generation in this population.

Disclosure: Nothing to disclose.

PP0053

PERSISTENT NAUSEA AND VOMITING IN GASTROPARESIS (PNVGP): REAL-WORLD EVIDENCE FROM A LARGE US DATABASE

H. Ferdosi^{1,2}, Y.J. Chen³, Z. Huang¹, N. Stylopoulos¹, J. Williams¹, J. Tack⁴, H.P. Parkman⁵
¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²The George Washington University School of Public Health, Washington DC, United States of America, ³Takeda Development Center Americas, Inc. (affiliation at the time analysis was conducted), Cambridge, United States of America, ⁴University Hospital Leuven, Department of Gastroenterology, Leuven, Belgium, ⁵Temple University School of Medicine, Philadelphia, United States of America

Contact E-Mail Address: jan.tack@kuleuven.be
Introduction: Nausea and vomiting are prevalent in gastroparesis (GP) and may persist in some patients with GP (pNVGP) despite treatment with prokinetics/antiemetics. There is scarce evidence at the population level on the demographic and clinical characteristics and disease experience of patients with pNVGP.

Aims & Methods: A retrospective study was conducted using Optum Market Clarity, a large US database comprised of claims and electronic health records (EHR) that is linked at the patient level and has customised fields developed by Natural Language Processing from unstructured clinical notes (e.g., GP-specific symptoms, gastric emptying testing). The pNVGP cohort was defined as: all GP diagnoses from claims/EHR during the study period (01Jan2008–30Sep2020, 1st documented GP Dx date in EHR/claims as the index date), with encounters for ≥5 years pre- and ≥1 year post-index in study period; received ≥14 cumulative days' supply of prokinetics and/or antiemetics pre- and/or post-index; and still reported nausea/vomiting ≥28 days after treatment at encounters.

Results: Of 207,704 patients identified with GP (45% diabetic [DG], 45% idiopathic [IG], 10% other causes), 25,654 met the criteria for pNVGP (57% DG, 31% IG, 12% other; mean±SD age at index 51.3±16.6 years; 75% female; 80% Caucasian; mean Charlson Comorbidity Index score 2.6). Prior to index, abdominal pain (61%), nausea (50%), nausea and vomiting (42%) and vomiting (39%) were the most commonly reported symptoms for pNVGP patients. Prokinetic/antiemetic use was frequent during 1-year pre-index (71% of pNVGP patients) and increased during 1-year post-index (85%). Ondansetron (53% of pNVGP patients pre-index, 66% post-index) and metoclopramide (13% pre-index, 32% post-index) were the most frequently used.

% Patients who received prokinetics*antiemetics**	Diabetic GP (n=14,509)	Idiopathic GP (n=7962)	Other GP (n=3183)	Total pNVGP (n=25,654)
1 yr pre-index, 1 yr post-index	73%, 87%	66%, 82%	76%, 84%	71%, 85%

*e.g., metoclopramide, azithromycin; **e.g. ondansetron, diphenhydramine, lorazepam

Conclusion: In this study, a sizable subcohort of patients with GP had pNVGP despite the use of prokinetics/antiemetics. pNVGP occurs more often in diabetic GP, and often with abdominal pain. Patients with pNVGP had persistent unmet needs.

Disclosure: HF, ZH, NS and JW: Employees of Takeda and hold stock/stock options in Takeda. YJC: Employee of Takeda at the time this analysis was conducted. JT: Advisor: Adare Pharmaceuticals, Alfa Wassermann Pharma, Allergan (AbbVie), Arena Pharmaceuticals, Bayer, Chr. Hansen, Clasa-do Biosciences, Danone, Devintec Pharma, Dr Falk Pharma, Grünenthal, Ironwood Pharmaceuticals, Janssen, Kyowa Kirin, Menarini Group, Mylan (Viatris), Neurogastrx, NeuTec Pharma, Novartis, Noventure, Nutricia, Shanghai Tsumura Pharmaceuticals, Shionogi, Shire (Takeda), Takeda, Theravance Biopharma, Tramedico, Truvion Healthcare, Zealand Pharma and Zeria Pharmaceutical; Research support: Shanghai Tsumura Pharma-

ceuticals, Shire (Takeda), Sofar S.p.A and Takeda; Speaker fees: Abbott, Allergan (AbbVie), AstraZeneca, Janssen, Kyowa Kirin, Menarini Group, Mylan (Viatris), Novartis, Shire (Takeda), Takeda, Truvion Healthcare and Zeria Pharmaceutical. HPP: Consultancy fees: AEON Biopharma, Evoke Pharma, Medtronic, Renexion and Takeda.

Funding: This study was sponsored by Takeda.

PP0054

THE EFFICACY OF THE FUNCTIONAL LUMEN IMAGING PROBE (FLIP) PROCEDURE IN A COHORT OF PATIENTS WITH DYSPHAGIA

C. Maradey-Romero^{1,2}, A. Albshesh^{1,2}, O. Saukhat^{2,3}, D. Carter^{1,2}

¹Department of Gastroenterology, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel, ²School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel, ³Department of Radiology, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel

Contact E-Mail Address: Carlucha239@yahoo.com

Introduction: Functional lumen imaging probe (FLIP) is an adjunctive test indicated in the evaluation of the esophagogastric junction and esophageal motility, especially in those with an inconclusive diagnosis during esophageal high-resolution manometry (HRM) such as esophagogastric junction outflow obstruction (EGJOO) or absent contractility per Chicago Classification v4.0 (CCv4.0), and in patients that are unable to perform a HRM.

Aims & Methods: Our study aimed to evaluate the efficacy of the FLIP procedure in establishing diagnosis in a cohort of patients who underwent assessment due to dysphagia, who were either diagnosed with EGJOO or absent contractility according to CCv4.0, or were unable to perform HRM. Our study population consisted of patients who were evaluated by FLIP due to dysphagia between March 2023 and April 2024. All patients had completed an upper gastrointestinal endoscopy and HRM per CCv4.0. Additionally, most patients underwent further evaluation with a timed barium esophagram (TBE).

Results: We included 58 patients (52% female, median age 62.5 years) in the study cohort. Most patients (67.24%) referred to the FLIP procedure had a prior failed attempt to perform a HRM or had an inadequate test. 46.5 % of all patients had an abnormal FLIP procedure. Of those, 15 patients had EGJOO with absent contractile response compatible with achalasia (55.5 %) and another 5 patients had a confirmed diagnosis of EGJOO on FLIP (18.5 %). Of those patients who had a FLIP procedure performed due to abnormal esophageal manometry findings per CCv4.0 (n=19), 8 patients were diagnosed with EGJOO (42.1%), 5 had absent contractility (26.3 %), 4 had a hypercontractile esophagus (21 %) and 2 had ineffective esophageal motility (10.5 %). 60 % of the patients diagnosed with EGJOO by FLIP were offered an achalasia-targeted treatment (pneumatic dilation (6), POEM (4), Heller myotomy (1) and Botox injection (1)), while the rest were treated conservatively.

Additionally, TBE was performed in 55% of patients with an abnormal FLIP procedure and the result was pathological in about half of them. Furthermore, in 70% of patients the diagnosis of EGJOO during FLIP was correlated to a delayed esophageal clearance on TBE.

Conclusion: FLIP is a useful tool in the assessment of dysphagia in patients who have an inconclusive diagnosis per CCv4.0, either EGJOO or absent contractility, as well as in patients who are unable to perform a HRM.

Disclosure: Nothing to disclose.

PP0055

PREDICTING OUTCOMES OF G-POEM USING BODY SURFACE GASTRIC MAPPING: EARLY RESULTS FROM A TERTIARY CENTRE

H. Ayubi¹, C. Varghese², S. Thrumurthy³, A. Haji³, B.H. Hayee¹

¹King's College Hospital, Endoscopy and Gastroenterology, London, United Kingdom, ²University of Auckland, Department of Surgery, Auckland, New Zealand, ³King's College Hospital, London, United Kingdom

Contact E-Mail Address: homira.ayubi@gmail.com

Introduction: Gastroparesis (GP) is a poorly understood condition with current diagnostic tests lacking disease specificity. Gastric per oral endoscopic myotomy (G-POEM) has emerged as a promising treatment for refractory gastroparesis, however up to a third of patients fail to have an improvement in their symptoms.

Aims & Methods: We assessed the ability of Gastric Alimetry®, a new, non-invasive test of gastroduodenal function to enhance patient selection for G-POEM. Data was collected from patients with suspected GP (based on symptoms and scintigraphy), being worked up for G-POEM at Kings College Hospital between November 2022 and September 2023 (REC: 22/LO/0802). G-POEM success was defined as <1 point reduction in GCSI score. Descriptive comparisons were used to explore predictors of improvements in gastroparesis cardinal symptom index (GCSI).

Results: 11 patients were assessed (8F, median age 40 interquartile range 32.5-49.5). GCSI scores significantly improved after G-POEM (median difference -1.03, IQR 0.50). Aetiologies of gastroparesis included 5 (45.5%) diabetic, 4 (36.4%) idiopathic, and 2 other aetiologies. Gastric Alimetry spectral analysis showed 2 (18.2%) with high frequencies, 2 (18.2%) with neuromuscular dysfunction (low rhythm stability and/or low amplitude), and 7 (63.6%) with normal spectral metrics. Symptom profiles followed a continuous pattern in 4 (36.4%), sensorimotor in 2 (18.2%), post-gastric in 1 (9.1%) and meal-induced in the remainder (36.4%). High frequency phenotype was associated with treatment failure (2/2, 100%), and neuromuscular phenotype was associated with success (2/2, 100%). The change in GCSI score after G-POEM was significantly lower in the high frequency group compared to the group average (median difference -0.18, IQR 0.18; p = 0.03). The average frequency and rhythm index was 2.9 (0.1) cycles per minute (cpm) and 0.4 (0.2) respectively among responders vs 3.2 (0.4) cpm 0.6 among non-responders.

Conclusion: Gastric Alimetry® is a new, non-invasive test of gastric function with provisional utility in differentiating disease mechanisms in patients with suspected GP. Early data suggests biomarkers for gastric autonomic dysregulation (high slow wave frequencies) were associated with reduced response to G-POEM. Further data are eagerly anticipated to validate these findings and develop more sophisticated predictive models for G-POEM outcomes.

Disclosure: Nothing to disclose.

PP0056

ROUTINE X-RAY CONTRAST STUDY FOLLOWING PERORAL ENDOSCOPIC MYOTOMY (POEM) DOES NOT PREVENT POSTPROCEDURAL COMPLICATIONS – SINGLE CENTER RETROSPECTIVE ANALYSIS

M. Vojtko¹, M. Ďuriček², M. Demeter², P. Banovcin³, J. Vnučáková¹¹Jessenius Faculty of Medicine, Comenius University, Clinic of Internal Medicine-Gastroenterology, Martin, Slovakia, ²Jessenius Faculty of Medicine, University Hospital in Martin, Clinic of Internal Medicine - Gastroenterology, Martin, Slovakia, ³Jessenius Faculty of Medicine, Comenius University, Department of Gastroenterology, Martin, Slovakia**Contact E-Mail Address:** marek.vojtko98@gmail.com

Introduction: Peroral endoscopic myotomy has become the mainstay of treatment of achalasia. Oral feeding has been initiated if no submucosal leak of the contrast fluid was detected on the X-ray contrast study which was performed the following day after the procedure. However, as major adverse events are rare, and in case of their occurrence, are rarely asymptomatic, it has become unclear whether routine X-ray contrast study is necessary. In our center we have been performing POEM procedures since 2015 and initially routinely performed X-ray contrast study. However, during the course of time it has become unavailable and we were forced to initiate oral feeding diet based on our clinical decision. We adopted a protocol of the initiation of oral liquids on the 2nd postoperative day (or later in case of suspected complication). We therefore compared these two strategies in terms of periprocedural and postprocedural complications rate and the length of the hospital stay.

Aims & Methods: This is a retrospective analysis of the single high-volume center. We evaluated (1) the rate of peri- and postprocedural complications and (2) length of the hospital stay in patients hospitalized for POEM for esophageal achalasia in 2015-2023. We separately evaluated the “X-ray subgroup” (oral feeding was initiated after X-ray that was performed the day after the procedure) and the “clinical decision subgroup” (oral feeding was initiated on the 2nd postoperative day).

Results: We analyzed a total number of 274 POEM procedures (129 males, 145 females), mean age was 52.3±16 years. 102 patients (37.2%) received X-ray contrast study after the procedure, in 169 patients (62.8%) the initiation of oral feeding was based on clinical decision. The mean time of the hospital stay was 7.2±2.9 vs. 6.5±1.4 days in the X-ray group and in the clinical decision group, resp. (p<0.004).

In the X-ray group we detected complications in 8 patients (7.7%). 5 were periprocedural (mucosal perforation or aspiration during intubation), were solved during the procedure and did not lead to the extension of the hospital stay. There were postprocedural complications in 3 patients. In one case submucosal leak was detected on X-ray contrast study the following day after the procedure due to loosened clip in the mucosal entry and was solved by placing additional clips. In one case patient presented with bleeding from the mucosal entry after discharge. In one case the patient developed mediastinitis that led to the extension of the hospital stay. In the clinical decision group we detected complications in 10 patients (5.9%), 9 of them were periprocedural (mucosal perforation or aspiration during intubation), 8 of which were solved during the procedure by endoscopic clipping and did not lead to the extension of the hospital stay, 1 required surgery. In one case of postprocedural complication perforation with pleural effusion was detected on CT scan and required surgical intervention that led to the extension of the hospital stay.

Conclusion: Our analysis shows that severe complications after POEM are rare. In the X-ray subgroup there was only single postprocedural event in which X-ray was helpful in its early detection (1%). In the clinical decision subgroup there was also only single event that could have been identified on the X-ray (0.6%). The length of the hospital stay in the clinical judge-

ment group was significantly shorter than in the X-ray group. This can be attributed to the improvement of overall experience with the management of the POEM patients as X-ray contrast has become unavailable after performing c.a. 100 POEM procedures.

References: Weusten, Bas L A M et al. “Endoscopic management of gastrointestinal motility disorders - part 1: European Society of Gastrointestinal Endoscopy (ESGE) Guideline.” *Endoscopy* vol. 52,6 (2020): 498-515. doi:10.1055/a-1160-5549

Disclosure: Nothing to disclose.

PP0057

OPEN LABEL EFFICACY ANALYSIS OF TRADIPITANT IN IDIOPATHIC AND DIABETIC GASTROPARESIS

J.L. Carlin¹, C. Polymeropoulos¹, M. Fisher¹, P. Moszczynski¹, G. Johannsen¹, C. Xiao¹, G. Birznieks¹, M.H. Polymeropoulos¹¹Vanda Pharmaceuticals, Inc., Research & Development, Washington, United States of America**Contact E-Mail Address:** Jesse.Carlin@vandapharma.com

Introduction: Tradipitant is a novel NK1R antagonist studied in diabetic and idiopathic gastroparesis. This report presents the analysis from the open-label arm of a multicenter, randomized, double-blind, placebo-controlled study (VP-VLY-686-3301) assessing the efficacy of tradipitant in relieving symptoms of gastroparesis.

Aims & Methods: N=531 idiopathic and diabetic gastroparesis patients with delayed gastric emptying received open label 85mg tradipitant BID for 12 Weeks. Nausea was assessed using the 5-point Gastroparesis Core Symptom Daily Diary. An exposure response analysis was performed to control for low drug exposure. We used a threshold of ≤140ng/ml tradipitant blood concentration at any visit to classify participants in the High (n=309) and Low (n=218) PK Populations.

Results: Patients improved the average nausea score significantly from baseline after 12 weeks tradipitant (improvement of -1.01 vs 2.14 at baseline, p<0.0001). A significant improvement was also seen in the percent of nausea free days (an addition of 51.76% of days for tradipitant vs. 19.62% at baseline, p<0.0001).

Patients in the High PK group significantly improved average nausea score compared to the Low PK group at Week 12 (improvement of -1.19 vs -0.78, p<0.0001). A significant improvement was also seen in the percent of nausea free days (an addition of 35.6% of days for High PK versus 22.6% for Low PK, p=0.0002).

Conclusion: Tradipitant demonstrated statistically significant improvement from baseline in average nausea severity and percentage of nausea-free days in this 12 week open label study in both idiopathic and diabetic gastroparesis subjects. Additionally, a strong exposure response in nausea improvement was observed when comparing subjects with high drug exposure vs low drug exposure.

Disclosure: Study was sponsored by Vanda Pharmaceuticals, Inc. Authors are employees of Vanda Pharmaceuticals, Inc.

PP0058

EXPOSURE-RESPONSE ANALYSIS OF OPEN LABEL TRADIPITANT IN IDIOPATHIC GASTROPAIRESIS IN STUDY VP-VLY-686-3301

J.L. Carlin¹, C. Polymeropoulos¹, M. Fisher¹, P. Moszczynski¹, G. Johannsen¹, C. Xiao¹, G. Birznieks¹, M.H. Polymeropoulos¹
¹Vanda Pharmaceuticals, Inc., Research & Development, Washington, United States of America

Contact E-Mail Address: Jesse.Carlin@vandapharma.com

Introduction: To assess the exposure response of NK-1 receptor antagonist tradipitant in the reduction of gastroparesis symptoms in patients with idiopathic gastroparesis in the open label arm of phase 3 study (VP-VLY-686-3301).

The four etiologies of gastroparesis are diabetic, post-surgical, drug-induced, and idiopathic. The idiopathic etiology of gastroparesis is least common, presenting in about 11.3% of patients, which amounts to about 90,000 patients in the United States. Standards set by the FDA define a rare disease or condition as one that affects less than 200,000 people in the United States. This establishes idiopathic gastroparesis as a rare condition, as well as one with a high unmet need for treatment. Patients with gastroparesis have decreased quality of life associated with severe and chronic symptoms and no treatment is currently approved for idiopathic gastroparesis specifically. Tradipitant previously demonstrated efficacy in idiopathic gastroparesis in reducing gastroparesis symptoms in a phase 2 study (VP-VLY-686-2301).

Aims & Methods: The open label arm of Study 3301 enrolled n=531 idiopathic and diabetic gastroparesis patients with delayed gastric emptying, moderate to severe nausea, and at least 1 vomiting episode. Patients received 85 mg tradipitant twice a day for 12 weeks. Nausea was assessed daily using the 5-point Gastroparesis Core Symptom Daily Diary (GCSDD). Overall gastroparesis symptoms were assessed every 2 weeks in clinic using the Gastroparesis Cardinal Symptom Index (GCSI).

An exposure response analysis was performed on a subgroup of patients to control for low drug exposure. We used a threshold of ≤ 140 ng/ml tradipitant blood concentration at any visit to classify participants in the High (n=309) and Low (n=218) PK Populations. Results were further stratified to compare average nausea severity and gastroparesis symptoms at baseline nausea severity scores of ≥ 2 and ≥ 2.5 for Low (n=129 and n=89, respectively) and High (n=170 and n=110, respectively) PK subgroups.

Results: Patients in the High PK subgroup had statistically improved nausea severity at Week 12 compared to the Low PK subgroup (-1.19 vs. -0.78, respectively; $p < 0.0001$), including at baseline nausea severity scores of ≥ 2 (-1.61 vs. -0.98, respectively; $p < 0.0001$) and ≥ 2.5 (-1.77 vs. -1.03, respectively; $p < 0.0001$). The High PK subgroup also had statistically significant improvement in nausea-free days at Week 12 compared to Low PK (+35.65% vs. +22.56%, respectively; $p = 0.0002$), including at baseline nausea scores of ≥ 2 (+36.36% vs. 18.15%, respectively; $p = 0.0002$) and ≥ 2.5 (+33.44% vs. 14.11%, respectively; $p = 0.0009$).

Conclusion: A significant exposure response was seen in idiopathic gastroparesis patients receiving open label tradipitant for 12 weeks. Patients with higher blood levels of tradipitant significantly improved in average nausea severity and in endpoints measuring overall gastroparesis symptoms compared to subjects with low drug blood levels.

Disclosure: Study was sponsored by Vanda Pharmaceuticals, Inc. Authors are employees of Vanda Pharmaceuticals, Inc.

PP0059

SOLID AND LIQUID GASTRIC EMPTYING SCINTIGRAPHY WITH GASTRIC ALIMETRY ADDS DIAGNOSTIC VALUE IN ASSESSING CHRONIC GASTRODUODENAL SYMPTOMS

W.J. Wang^{1,2}, D. Foong², S. Calder³, V. Fernandes⁴, V. Ho^{2,5}, G. O'Grady^{3,6,7}, G.J. Holtmann^{1,8,9,10}

¹Princess Alexandra Hospital, Department of Gastroenterology and Hepatology, Brisbane, Australia, ²Western Sydney University, School of Medicine, Sydney, Australia, ³Alimetry Ltd, Auckland, New Zealand, ⁴Lumus Imaging, Sydney, Australia, ⁵Campbelltown Hospital, Department of Gastroenterology and Hepatology, Sydney, Australia, ⁶The University Of Auckland, Department of Surgery, Auckland, New Zealand, ⁷The University Of Auckland, Auckland Bioengineering Institute, Auckland, New Zealand, ⁸The University of Queensland, Faculty of Medicine, Brisbane, Australia, ⁹Translational Research Institute, Brisbane, Australia, ¹⁰AGIRA (Australian Gastrointestinal Research Alliance) and the NHMRC Centre of Research Excellence in Digestive Health, Brisbane, Australia

Contact E-Mail Address: william.wang3@health.qld.gov.au

Introduction: Solid gastric emptying scintigraphy (GES) is used to assess gastric motility by measuring the transit of a radioactively labelled solid meal, however it can be non-specific and insensitive by itself. Liquid gastric emptying scintigraphy provides an additional modality of motility testing using a similar process with a liquid meal. Gastric Alimetry is a non-invasive test that measures gastric electrophysiological activity through body surface gastric mapping (BSGM) and validated symptom profiling¹.

Aims & Methods: This study aimed to assess the additional diagnostic value of performing liquid GES and Gastric Alimetry in addition to solid GES alone.

Patients with chronic gastroduodenal symptoms underwent simultaneous solid GES and Gastric Alimetry, comprising of a 30-minute baseline recording followed by a 99mTc-labelled egg meal, and 4-hour postprandial recording. Patients would also have a glucose liquid GES study on a different date. Delayed emptying was defined as greater than 10% retention at 4 hours for solid GES and more than 50% retention at 2 hours for liquid GES^{2,3}.

Gastric Alimetry spectral metrics were referenced to normative ranges that included principal gastric frequency (cpm), Gastric Alimetry Rhythm Index (GA-RI) and BMI-adjusted amplitude⁴.

Results: 36 patients with chronic gastroduodenal symptoms were prospectively recruited (30 female, median age 38.0 years, median BMI 24.6 kg/m²). 10 (27.8%) patients had delayed solid GES whilst 7 (19.4%) patients had delayed liquid GES. 9 (25.0%) patients had abnormal Gastric Alimetry spectral metrics.

Combining solid and liquid GES detected an abnormality in 13 (36.1%) patients which was further enhanced when combined with Gastric Alimetry, detecting an abnormality in 17 (47.2%) of patients.

Of those 13 patients with either a delayed solid or liquid GES, 38.5% of them had abnormal Gastric Alimetry spectral metrics (3 High Frequency, 1 Low Rhythm Stability, 1 High Amplitude) while those with a normal solid and liquid GES had abnormal spectral metrics in 17.4%.

Conclusion: Combining solid and liquid GES with Gastric Alimetry detected a higher yield of motility abnormalities than solid GES alone. GES and Gastric Alimetry assess different aspects of gastric function with further studies required to understand their complementary roles as biomarkers in clinical practice to help tailor therapy.

References:

1. Sebaratnam G, Karulkar N, Calder S, et al. Standardized system and app for continuous patient symptom logging in gastroduodenal disorders: Design, implementation, and validation. *Neurogastroenterology & Motility* 2022; 34.
2. Abell TL, Camilleri M, Donohoe K, et al. Consensus recommendations for Gastric Emptying Scintigraphy: A joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Journal of Nuclear Medicine Technology*; 36: 44–54.
3. Phillips WT, McMahan CA, Lasher JC, et al. Anterior, posterior, left anterior oblique, and geometric mean views in gastric emptying studies using a glucose solution. *European Journal of Nuclear Medicine*; 22: 154–157.
4. Varghese C, Schamberg G, Calder S, et al. Normative values for body surface gastric mapping evaluations of gastric motility using gastric alimetry: Spectral analysis. *American Journal of Gastroenterology*; 118: 1047–1057.

Disclosure: Greg O'Grady holds intellectual property and grants in gastric electrophysiology and is a Director of the University of Auckland spin-out companies Alimetry and Insides Company. Stefan Calder is a member of Alimetry. The remaining authors have no relevant conflicts of interest to declare.

PP0060

COMPREHENSIVE ASSESSMENT OF GASTROINTESTINAL SYMPTOMS IN PEDIATRIC PATIENTS: INSIGHTS FROM INITIAL OUTPATIENT CONSULTATIONS USING THE PSAGIS

K. Hammer¹, B. Majcher¹, U. Anwar², J. Hammer²

¹St. Anna Kinderspital, Abt. für Gastroenterologie, Wien, Austria,

²Medical University Vienna, Vienna, Austria

Contact E-Mail Address: johann.hammer@meduniwien.ac.at

Introduction: Exploring paediatric gastrointestinal (GI) diseases is a dynamic medical challenge. Children and adolescents present with unique symptoms that require careful assessment. These can range from mild discomfort to indicators of serious disease. The initial outpatient visit is crucial for diagnosis and treatment planning.

Understanding the nature and spectrum of these symptoms is crucial for improving paediatric care.

Aims & Methods: We aimed to improve the understanding of GI disorders in paediatric patients, utilising the recently validated paediatric (p)SAGIS questionnaire, which provides an unbiased assessment of symptoms. From February 2016 to January 2023, all consecutive patients attending the outpatient GI clinic at St. Anna Kinderspital, Vienna, Austria, underwent a standard work-up to arrive at a final diagnosis.

In addition, and independently, the patients and/or their caregivers completed the pSAGIS for standardised symptom assessment on the day of their appointment before meeting the paediatrician. pSAGIS consists of 21 GI-related questions (assessment of type and 5 severity grades within the previous week) to arrive at five symptom groups (abdominal pain, diarrhea, constipation, dysphagia, and dyspepsia).

Pain was considered clinically relevant if the score was at least 1 (moderate pain) and severe if the score was ≥ 2 . Data were analyzed for functional bowel disorder (FBD) versus organic GI disease (OD), with a p-value < 0.05 considered significant.

Results: 1481 outpatients completed the pSAGIS questionnaire at their initial consultation. Patients were then followed up to establish a final diagnosis. 775 patients were diagnosed with organic disease, 441 patients were diagnosed with functional bowel disease, and 265 subjects were healthy or had a non-GI diagnosis or could not be definitively diagnosed. In the whole group, abdominal pain was reported by 405 patients (27.3%)

and severe pain by 140 patients (9.5%). 185 patients with organic disease (23.9%) but 199 patients with FBD (45.1%) reported abdominal pain ($p > 0.001$), severe pain was reported by 42 (5.4%; OD) and 54 (12.2%; FBD) patients, respectively ($p < 0.001$). Pain was reported as the main symptom by 105 OD patients (13.5%) vs. 113 FBD patients (25.6%) ($p < 0.001$). Pain was present but not the main symptom in 64 (8.3%; OD) and 65 (14.7%; FBD) patients, respectively ($p > 0.01$). Of the latter, 14 (1.8%; OD) and 18 (4.1%; FBD) patients reported severe pain.

Conclusion: Our study provides a comprehensive insight into paediatric gastrointestinal symptoms using the paediatric SAGIS questionnaire. The stark contrast in the prevalence of abdominal pain between patients with organic disease and functional bowel disorders underscores the complex landscape of paediatric GI problems. In particular, the high incidence of severe pain in functional bowel disorders challenges conventional perceptions of these disorders. Recognising pain as a prominent symptom in both organic and functional cases is critical for effective management. The findings underscore the critical role of standardised assessment tools, such as the pSAGIS questionnaire, in delineating the nuanced spectrum of paediatric GI symptoms and ultimately informing more targeted and comprehensive care strategies.

Disclosure: Nothing to disclose.

PP0061

DIFFERENCES IN GASTRIC FLUID MICROBIOTA BETWEEN POSTPRANDIAL DISTRESS SYNDROME AND EPIGASTRIC PAIN SYNDROME

K.J. Lee¹, G.H. Lee¹

¹Ajou University Hospital, Gastroenterology, Suwon, South Korea

Contact E-Mail Address: kjl@ajou.ac.kr

Introduction: Dysbiosis of gut microbiota has recently been suggested to be implicated in the pathophysiology of functional dyspepsia (FD). However, qualified studies on the gastric microbiota in FD patients are lacking, and it is unclear whether there are differences in gastric microbiota between the subgroups of FD.

Aims & Methods: Our aim of the present study was to compare the diversity and composition of gastric fluid microbiota between postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS) in patients with FD. Eighteen patients with FD who met the Rome IV criteria and 12 age- and gender-matched healthy controls who had no chronically recurrent abdominal symptoms with absence of past or present *Helicobacter pylori* (HP) infection participated in the study. Gastric fluid was obtained from the subjects after an overnight fast, using a sterilized tube inserted into the stomach through the working channel of the endoscope. DNA was extracted and quantified from the samples. Samples from 15 FD patients (83.3%) and 6 healthy controls (50%) were adequate for analysis. The V3 and V4 region of 16S rRNA gene was amplified and sequenced using the MiSeq™ platform (Illumina, San Diego, USA).

Results: The microbiota diversity indices did not significantly differ in FD patients without HP infection, compared with healthy controls. There were no significant differences in the microbiota diversity and composition at the phylum level between PDS patients and healthy controls, and between EPS patients and healthy controls. At the genus level, the relative abundance of *Centipeda* was significantly increased in patients with PDS, whereas that of *Massilia*, *Acinetobacter*, *Enterococcus*, *Bacteroides*, and *Blautia* was significantly decreased in patients with PDS. In patients with EPS, the relative abundance of *Collinsella*, *Holdemanella* and *Paraprevotella* was significantly increased, whereas that of *Massilia* was significantly decreased. At the species level, the relative abundance of *Prevotella intermedia*, *Veillonella tobetsuensis*, *Neisseria subflava*, and *Centipeda*

periodontii was significantly increased in patients with PDS. The relative abundance of *Clostridium leptum*, *Clostridium perfringens*, *Alistipes ihumii*, *Collinsella aerofaciens*, *Eubacterium ventriosum*, *Holdemanella bififormis*, *Klebsiella aerogenes*, *Paraprevotella clara*, *Sphingomonas olei*, and *Sutterella wadsworthensis* was significantly increased in patients with EPS.

Conclusion: Although the diversity of gastric fluid microbiota is not different between PDS and EPS subgroups, there are differences in their composition between PDS and EPS. Further investigation is needed to determine whether those differences in the composition of gastric fluid microbiota are cause or effect.

References: 1. Nakae H, et al. Gastric microbiota in the functional dyspepsia patients treated with probiotic yogurt. *BMJ Open Gastroenterol.* 2016 Sep 16;3(1):e000109.

2. Igarashi M, et al. Alteration in the gastric microbiota and its restoration by probiotics in patients with functional dyspepsia. *BMJ Open Gastroenterol.* 2017 May 1;4(1):e000144.

3. Tziatzios G, Gkolfakis P, Papanikolaou IS, et al. Gut microbiota dysbiosis in functional dyspepsia. *Microorganisms* 2020;8:691.

Disclosure: Nothing to disclose.

PP0062

REACHING THE END OF THE LINE: CHARACTERIZATION OF NON-OBSTRUCTIVE DYSPHAGIA WITH NORMAL ESOPHAGEAL MOTILITY

R.R. Mendes¹, J. Azevedo Rodrigues^{1,2}, A. Mascarenhas¹, H.C. Lima³, T. Guedes⁴, S.M. Barrias⁴, M. Costa⁵, P. Souto⁵, J.C. Silva⁶, J.P. Laranjeira Correia⁶, B. Morão⁷, J. Revés⁷, C. Leal⁸, R.T. Marinho^{9,2}, M. Mascarenhas Saraiva³

¹Unidade Local de Saúde de Lisboa Ocidental, Gastroenterology Department, Lisbon, Portugal, ²Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, ³ManopH, Laboratório de Endoscopia e Motilidade Digestiva, Porto, Portugal, ⁴Centro Hospitalar Universitário de Santo António, Gastroenterology Department, Porto, Portugal, ⁵Unidade Local de Saúde de Coimbra, Gastroenterology Department, Coimbra, Portugal, ⁶Unidade Local de Saúde Gaia e Espinho, Gastroenterology Department, Vila Nova de Gaia, Portugal, ⁷Hospital Beatriz Ângelo, Gastroenterology Department, Lisbon, Portugal, ⁸Unidade Local de Saúde de Leiria, Gastroenterology Department, Leiria, Portugal, ⁹Unidade Local de Saúde de Santa Maria, Gastroenterology and Hepatology Department, Lisbon, Portugal

Contact E-Mail Address: andremascarenhasmd@gmail.com

Introduction: Esophageal dysphagia is a common complaint in daily clinical practice. After excluding structural and motility disorders, it may be related to functional disorders, which are challenging to diagnose and manage, leading to high health care utilization and both patient and physician dissatisfaction.

Aims & Methods: This is a prospective multicentric 6-months follow-up study to characterize dysphagic patients with normal esophageal motility, in terms of epidemiology and clinical aspects, focusing on patient-reported outcome measures, and evaluate their evolution at 6-months.

Results: From 2021-2024, 91 patients were recruited, 78.0% female, with a median age of 65 years [22-88]. Of these, 27.5% (n = 25) suffered from rheumatologic or endocrinologic disorders, and 56.0% were previously exposed to medical therapies.

Dysphagic symptoms had a median duration of 3 years [1-31], with a median Eckardt of 3 [0-9], PROMIS GI Disrupted Swallowing (PDS) of 60.4 [40.3-84.1], EuroQol-5D TTO of 0.592 [-0.055-1] and VAS of 70 [0-100].

Compared to non-dysphagic participants (n=123), these patients had significantly worse Eckardt, EuroQol-5D and PDS scores (p-values <0.001).

Compared to esophageal motility disorders (Chicago V4.0), the Eckardt and PDS scores in this group were significantly lower when compared to EGJ outflow disorders (p-value <0.001 and 0.003), without differences regarding EuroQol-5D.

Regarding gastroesophageal reflux, 24 (26.4%) patients had a positive GERD-Q questionnaire and 3 had an objective GERD diagnosis. Even though, compared to motility disorders, this score was significantly lower in this group when compared to EGJ outflow disorders (p-value 0.001).

Medical treatments (PPI, amitriptyline) were optimized in 6 patients (6.6%), without any differences in Eckardt or EuroQol-5D scores at 6-months. However, at 6-months, the PDS improved in untreated patients (p-value <0.001).

Conclusion: Non-obstructive dysphagia with normal esophageal motility has a negative impact on quality of life. However, symptoms tend to have a favorable course independently of treatment, therefore mandating a holistic management.

Disclosure: Nothing to disclose.

PP0063

THE PREVALENCE OF NAUSEA IN EASTERN AND WESTERN SECONDARY AND TERTIARY CARE FUNCTIONAL DYSPESIA

B. Broeders¹, F. Carbone², C. Van de Bruaene³, T. Vanuytsel⁴, J. Tack⁵, AEGIS working group

¹KU Leuven, Chronic diseases and metabolism, Ku Leuven, Belgium, ²UZ Leuven, TARGID, Leuven, Belgium, ³Van de Bruaene Cedric, Gastroenterology, Leuven, Belgium, ⁴KU Leuven, Department of Gastroenterology, Leuven, Belgium, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: bert.broeders@kuleuven.be

Introduction: According to the ROME IV criteria, functional dyspepsia (FD) can be subdivided into PDS (postprandial distress syndrome) with meal-related symptoms such as early satiation and postprandial fullness and EPS (epigastric pain syndrome) with meal-unrelated complaints such as epigastric pain or burning. Nausea can also co-exist in FD but the literature is poor in reporting whether this symptom is mainly triggered by meal ingestion.

A recent global epidemiology study of gastroparesis-like symptoms showed that the prevalence of nausea or vomiting, in combination with postprandial fullness or early satiation varies between continents.¹

Aims & Methods: This study aims to compare the difference in prevalence rates of nausea within each FD subgroup between western and eastern secondary and tertiary care centers. Adult patients with disorders of gut-brain interaction (DGBI) recruited in 9 western and 7 eastern secondary and tertiary care facilities between the ages of 18 and 70 years completed the Enhanced Asian Rome IV questionnaire (Asian European Gastrointestinal Symptoms cohort or AEGIS). The western centers were located in Belgium, Bulgaria, France, Israel, Italy (2x), Slovakia, Sweden and The United Kingdom while the eastern centers were located in Australia, China, Iran, Japan, Malaysia and Singapore (2x).

FD patients were divided into PDS, EPS and PDS-EPS overlap (OVP) subgroups. Patients were furthermore classified as having nausea when this symptom was reported at least once per week. The questionnaire EARQ4 questionnaire was also used to address the relationship between nausea and food intake.

Patients were asked how often they experienced nausea, whether nausea was triggered or worsened by meal intake, how often nausea occurred after a meal and if so, how soon after a meal nausea started. A comparison of the prevalence of nausea and meal-related nausea was made between

eastern and western patients and among FD subgroups. Continuous variables are reported as median (IQR) and compared with a Kruskal-Wallis test. Categorical variables were compared using a Pearson Chi-square test.

Results: Of the 1074 DGBI patients that completed the survey, 483 were classified as having FD (59.4% PDS, 27.5% EPS, 13.0% PDS-EPS overlap). FD patients from eastern (N=202) and western sites (N=281) had a similar body mass index (22.5 (19.6-25.7) vs. 21.3 (19.7-25.4) kg/m²) and age (39.0 (29.0-55.0) vs. 38.0 (26.0-54.0) years). Eastern sites included significantly more female patients than western sites (43 % vs. 17.5%, p<0.001). PDS and EPS patients from eastern sites had significantly less nausea than PDS and EPS patients from western sites (17.9% vs. 46.3% and 6.8% vs. 40.5% respectively, both p<0.001). The majority of FD patients with nausea experienced meal-related nausea with no difference between eastern and western sites (63.9% vs. 73.7%). In PDS patients with nausea, nausea was significantly more triggered or worsened by a meal (72.4%) than in PDS-EPS overlap and EPS (48.6% and 35.3% respectively; p<0.001). All groups reported that meal-related nausea started mostly (> 85%) within 60 minutes after the meal.

Conclusion: In contrast to previous literature, we found that western PDS and EPS patients report nausea more frequently than eastern PDS and EPS patients. In both eastern and western patients nausea was mostly meal-related. Meal-related nausea is more common in PDS than in PDS-EPS overlap and EPS patients. Further research is needed to investigate the role of ethnic factors in the pathophysiology of nausea in functional dyspepsia.

References: Huang IH, Schol J, Khatun R, et al. Worldwide prevalence and burden of gastroparesis-like symptoms as defined by the United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on gastroparesis. *United Eur Gastroenterol J.* 2022;10(8):888-897.

Disclosure: Bert Broeders received lecture fees from the Rome Foundation.

PP0064

UNFOLDING THE MYTHS OF PEDIATRICS FUNCTIONAL ABDOMINAL PAIN DISORDERS (FAPDS)

I. Mushtaq¹, A. Saeed¹, W. Zahra²

¹The Children's Hospital, University of Child Health Sciences, Pediatric Gastroenterology & Hepatology, Lahore, Pakistan,

²The Children's Hospital, University of Child Health Sciences, Department of Development & behavioural Pediatrics, Lahore, Pakistan

Contact E-Mail Address: driqrakhawaja@gmail.com

Introduction: Functional abdominal pain disorders (FAPDs), linked to brain-gut interaction disturbances, are common in childhood, with a prevalence of 3-16%. They are classified based on the Rome IV criteria, involving persistent gastrointestinal symptoms due to abnormal enteric system functioning without organic issues. Childhood stress and anxiety are linked to FAPDs. Psychotherapy aims to educate patients and families about pain triggers and uses cognitive-behavioral therapy extensively.

Aims & Methods: To discuss different characteristics of patients with FAPDs and identify triggering factors for stress/anxiety. Moreover, to analyze the role of various treatment options, including mind-targeted therapies as a treatment.

This prospective cohort study included all patients who were referred to the Pediatric Gastroenterology and Hepatology Outdoor Department at Children's Hospital Lahore due to chronic abdominal pain and subsequently diagnosed with FAPDs based on Rome IV criteria after excluding

organic causes over a period of 18 months. Patients were screened for stress by the clinical psychologist using perceived stress scores after excluding organic causes. The role of various treatment options, including mind-targeted therapies, was studied in patients with different FAPDs. They were reassessed for symptom improvement or resolution at a 4-week follow-up by both gastroenterologists and clinical psychologists.

Results: This study included 300 patients aged 4-16 years, of any gender and economic background, using consecutive non-probability sampling. The overall mean age was 9.848 ± 2.6879 years, with 171 female (57%) & 129 male (43%) patients. 245 patients (81.7%) were diagnosed with an organic cause for chronic abdominal pain based on various clinical and biochemical parameters. Commonest cause was gastritis 83 (27.7%) followed by celiac 59 (19.7%), chronic pancreatitis 32 (10.7%), Abdominal TB 22 (7.3%), UTI 17 (5.7%), IBD 16 (5.3%), Choledochal cyst 9 (3%), Cholelithiasis 5 (1.7%), Hydatid cyst 2 (0.7%). In total 55 (18.3%) were diagnosed with functional GI disorders based on Rome IV criteria. Among them, Functional Abdominal Pain, not otherwise specified accounted for 21 cases (38.18%), followed by functional dyspepsia 19 (34.54%), irritable bowel syndrome 10 (18.18%), and abdominal migraine with 5 cases (9.09%). The age range of patients diagnosed with FAPDs spanned from 7.5 to 15 years, with a median age of 12 years. There were 34 females (61.8%) compared to 21 males (38.2%). 60% of them were from urban areas. Various triggers for stress were identified: financial issues (69.1%), followed by family conflict (58.2%), family member illness (18.2%), single parents/broken families (16.4%), exam failure (16.4%), abuse/bullying (12.7%), family member death (9.1%), frequent punishment at home (5.5%), sibling rivalry (3.6%), and frequent punishment at school (1.8%). The perceived stress scores were categorized as low (0-13) for 7 (12.7%), moderate (14-26) for 45 (81.8%), and high (27-40) for 3 (5.5%) patients before treatment. Among them, 43.3% received psychotherapy, followed by 25.5% receiving psychotherapy along with symptomatic treatment, 16.4% symptomatic treatment, 9.1% psychotherapy along with antidepressant, and 5.5% receiving only antidepressant. Patients with a moderate stress score were given psychotherapy alone in 48.9% of cases. Post-treatment perceived stress scores improved to low in 40 patients (72.7%) (p<0.001).

Conclusion: Functional GI disorders, with stress or masked depression, need assessment for better child welfare, as healthy psyche fosters resilience.

References:

1. Robin SG, et al. Prevalence of pediatric functional gastrointestinal disorders utilizing the Rome IV criteria. *J Pediatr.* 2018;195:134-139.
2. Hyams JS, et al. Functional disorders: children and adolescents. *Gastroenterology.* 2016. <https://doi.org/10.1053/j.gastro.2016.02.015>.
3. Newton E, Schosheim A, Patel S, Chitkara DK, van Tilburg MAL. The role of psychological factors in pediatric functional abdominal pain disorders. *Neurogastroenterol Motil.* 2019;31:e13538.

Disclosure: Nothing to disclose.

PP0065

3-YEAR PROSPECTIVE OBSERVATIONAL COHORT STUDY ON PREVALENCE OF SYMPTOMS OF FUNCTIONAL DYSPESIA, ANXIETY AND DEPRESSION

B. Maly¹, P. Liptak², I. Tonhajzerova³, Z. Visnovcova⁴, N. Ferencova⁴, N. Visnovcova⁵, M. Schnierer², I. Liptak Ziacikova⁶, O. Osina⁷, J. Jurica⁸, P. Banovcin²

¹Jessenius Faculty of Medicine in Martin, Comenius University, Department of Nursing, Martin, Slovakia, ²University Hospital in Martin, Clinic of Internal Medicine-Gastroenterology, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia, ³Jessenius Faculty of Medicine in Martin, Comenius University, Department of Physiology, Martin, Slovakia, ⁴Jessenius Faculty of Medicine in Martin, Comenius University, Biomedical Centre Martin, Martin, Slovakia, ⁵Jessenius Faculty of Medicine in Martin, Comenius University, Department of Medical Biophysics, Martin, Slovakia, ⁶University Hospital in Martin, Clinic of Pneumology and Phthisiology, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia, ⁷University Hospital in Martin, Clinic of Occupational Medicine and Toxicology, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia, ⁸University Hospital in Martin, Clinic of Internal Medicine, Jessenius Faculty of Medicine in Martin, Comenius University, Martin, Slovakia

Contact E-Mail Address: branomaly17@gmail.com

Introduction: Disorders of gut brain interaction (DGBIs) is a group of diseases with relatively high prevalence. One of the most common is functional dyspepsia. It has been repeatedly reported that university students tend to have higher prevalence of this disease than general population. Study at medical school is associated with high degree of stress and this could be accumulated during the passing years. As many other factors could affect the symptomatology, the best way to test this hypothesis is to perform a prospective cohort study following one particular group of students over the years.

Aims & Methods: The aim of this study is to evaluate the prevalence of symptoms of functional dyspepsia in selected cohort overtime. This is a prospective, observational study. The observed group were students of medicine from their 1st to 3rd year of study. Acquisition of the data was performed by questionnaires. The diagnosis was made by using ROME IV criteria for DGBI. Additional information was obtained from STAX1 and STAX2 validated questionnaires (STAI-X1 shows how the patient feel while answering the questionnaire (anxiety as a state) and STAI-X2 is based on how the patient feel overall (anxiety as a personality trait)) and Beck depression inventory. The measurement was performed in the middle of the school year, every October (2021 to 2023).

Results: Initially 121 students from first year agreed to participate in the study and filled out the questionnaire. Subsequently the response rate for 2nd year was 67.8 % and for 3rd 73%. The symptoms of Functional Dyspepsia were present in 14.9% of participants from 1st year, 13.4% from 2nd year and 14.6% from 3rd year. The cumulative cohort average of STAX 1 was 45.5 points for 1st year, 46.5 points for 2nd year and 46.2 points for 3rd year. The cumulative cohort average of STAX 2 was 47.7 points for 1st year, 46.2 points for 2nd year and 46.8 points for 3rd year. The cumulative cohort average of Beck depression inventory was 8.7 points for 1st year, 8.8 points for 2nd year and 8.4 points for 3rd year. The rate of smoking was 7.4 % of participants from 1st year, 13.4% participants from 2nd year and 14.6% from 3rd year.

Conclusion: The results of this prospective cohort observational study shows that the symptoms of Functional Dyspepsia are highly prevalent among medical students and this varies only insignificantly over time.

The probands in average showed no signs of depression however the average levels of anxiety and stress were high during all 3 years. This could be associated with significant rise of smokers within the cohort during the observation period.

Disclosure: Nothing to disclose.

PP0066

PREVALENCE AND BURDEN OF FUNCTIONAL DYSPESIA AND “GASTROPARESIS LIKE SYMPTOMS” IN A PRIMARY CARE DIABETIC POPULATION

H. Soliman^{1,2}, I-H. Huang², H. Ferdosi³, L. Balsiger², B. Broeders², D. Salvi^{2,4}, C. Van de Bruaene², K. Van den Houte², F. Carbone², J. Tack⁵

¹Hôpital Louis Mourier - AP-HP, Gastro-enterology Department, Colombes, France, ²KULeuven, TARGID, Leuven, Belgium, ³Global Evidence and Outcomes, Takeda Development Center Americas, Cambridge, United States of America, ⁴Fondazione Poliambulanza, Brescia, Italy, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: heithemsoliman90@hotmail.com

Introduction: The prevalence of functional dyspepsia (FD) and gastroparesis in diabetic patients remains unknown. A high prevalence of gastroparesis has been reported in diabetic patients reaching up to 5%.¹ However, recent consensus specified the symptom pattern for gastroparesis, with nausea and/or vomiting as predominant symptoms, now defined as “gastroparesis-like symptoms” (GPLS).² The global prevalence of GPLS has been estimated to reach only 1.2% in diabetic patients, but type 1 and type 2 diabetes were not assessed separately.²

Aims & Methods: We aimed to assess the prevalence and burden of FD and GPLS in primary care patients with diabetes, comparing patients with type 1 and type 2 diabetes. An online survey was addressed to diabetic patients through general practitioners and diabetic patient associations. The survey included the Rome IV questionnaire and the Patient Assessment of Gastro-Intestinal Disorders-Symptom Severity Index (PAGI-SYM) for upper gastro-intestinal symptoms. Anxiety, depression, somatization, and quality of life were also assessed by specific questionnaires (Generalized Anxiety Disorder GAD-7, Patient Health Questionnaire PHQ-9, PHQ-15, and PAGI-QoL questionnaires respectively).

	Type 1 diabetes (n=146)	Type 2 diabetes (n=68)	p value
Age	39 (29–51)	60 (50–67)	<0.001
Sex (female)	99 (67.8%)	35 (51.4%)	0.02
Functional dyspepsia	18 (12.3%)	10 (14.7%)	0.66
PDS	17 (11.6%)	10 (14.7%)	0.52
EPS	3 (2.1%)	3 (4.4%)	0.38
Gastroparesis-like symptoms	3 (2.1%)	6 (8.9%)	0.03
GAD-7 (Anxiety)	4 (1–6)	3 (0–7)	0.80
PHQ-9 (Depression)	3 (1–7)	3 (1–10)	0.05
PHQ-15 (Somatization)	7 (3.3–10)	8 (4–13)	0.10
PAGI-SYM	6.5 (1–8.8)	9.5 (2–35.5)	0.009
PAGI-QoL	6 (0–15.3)	10 (3–38)	0.003

Results: A total of 216 patients completed the questionnaires, among which 146 had type 1 diabetes, and 68 had type 2 diabetes, (2 patients did not know their type of diabetes). The median age of the population was 56 (50–61) years old, with 134 female patients (61.8%). The prevalence of FD was 13.0% with no difference between the 2 groups. The prevalence of GPLS reached 4.2% and was significantly higher in patients with type 2 diabetes (8.9% vs 2.1%; p=0.03). The burden of upper gastro-intestinal symptoms and their impact on quality of life was higher in type 2 dia-

betes patients with higher PAGI-SYM and PAGI-QoL scores while anxiety and somatization were not different between type 1 and type 2 diabetes patients (see Table). Overall, patients with GPLS had higher anxiety (9 vs 3; $p=0.003$), depression (12 vs 7; $p=0.001$) and somatization scores (16 vs 6; $p<0.001$) than patients without. Compared to patients with FD without GPLS, GPLS patients had numerically higher but not statistically different scores for symptom severity (51 vs 28; $p=0.46$), anxiety (9 vs 7; $p=0.29$), depression (12 vs 7; $p=0.07$), somatization (16 vs 11.5; $p=0.16$) and quality of life scores (52 vs 24; $p=0.16$).

Conclusion: This study confirms that the prevalence of GPLS seems to be higher in diabetic patients compared to available population data, especially in patients with type 2 diabetes. The impact of the symptoms was similar to the impact of FD in this population. Further studies are required to assess the prevalence of delayed gastric emptying in diabetic type 1 and 2 patients with GPLS.

References: 1. Choung RS, Locke GR, Schleck CD, et al. Risk of Gastroparesis in Subjects with Type 1 and 2 Diabetes in the General Population. *Am J Gastroenterol* 2012;107:82-88.

2. Huang I-H, Schol J, Khatun R, et al. Worldwide prevalence and burden of gastroparesis-like symptoms as defined by the United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on gastroparesis. *United European Gastroenterol J* 2022;10:888-897.

Disclosure: Nothing to disclose.

PP0067

GASTROESOPHAGEAL REFLUX DISEASE AND FUNCTIONAL DYSPESIA ARE ASSOCIATED WITH CAPSAICIN COUGH SENSITIVITY IN SEVERE ASTHMA

T. Kamiya¹, K. Ito², Y. Kanemitsu², M. Shikano³, E. Kubota³, A. Niimi²
¹Nagoya City University Graduate School of Medical Sciences, Department of Medical Innovation, Nagoya, Japan, ²Nagoya City University Graduate School of Medical Sciences, Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya, Japan, ³Nagoya City University Graduate School of Medical Sciences, Department of Gastroenterology and Metabolism, Nagoya, Japan

Contact E-Mail Address: kamitake@med.nagoya-cu.ac.jp
Introduction: Functional dyspepsia (FD) is one of the most prevalent functional gastrointestinal disorders. It is well known that asthma can complicate gastroesophageal reflux disease (GERD), and sensory nerve dysfunction is related to the pathophysiology of asthma and GERD. However, the relationship between FD and asthma has not been extensively examined yet. The capsaicin receptor transient receptor potential vanilloid 1 (TRPV1) is a non-selective ion channel, which can be activated capsaicin, acid (pH<6.5), and heat etc. TRPV1 channels are highly expressed in sensory nociceptive and visceral nerve fibers and are involved in inflammatory pain and hyperalgesia signaling. TRPV1 is found to be expressed in both airway epithelium and sensory neurons of the gastrointestinal tract, as previously reported. In addition, several studies have shown increased gastrointestinal sensory sensitivity to capsaicin in patients with FD.
Aims & Methods: The aim of this study was to clarify the physiological associations between GERD, FD, and asthma. Fifty-two patients with severe asthma who were performed capsaicin cough sensitivity (C-CS) test were analyzed. Clinical characteristics C-CS were compared between patients with and without comorbid GERD or FD. C-CS was evaluated by C5 (concentration of inhaled capsaicin that induced five or more coughs), and C5<2.44 uM was defined as heightened C-CS. GERD was diagnosed

based on the presence of the typical reflux symptoms of heartburn and/or acid regurgitation, which occurred more than twice a week prior to proton pump inhibitor (PPI) therapy. FD was diagnosed using the Rome IV criteria, which are defined as chronic and recurrent epigastric pain or postprandial distress, and no other organic disease that could have caused these symptoms.

Results: A total of 52 patients with severe asthma were eligible for this study. Twenty-two out of 52 patients had GERD comorbidity, and 15 out of them had FD comorbidity. Thirteen GERD patients showed heightened C-CS, while nine patients showed normal C-CS. Compared to the GERD (-) group, the GERD (+) group had a significantly lower threshold value of C5. Lower C2 and C5 thresholds were found in the FD (+) group than in the FD (-) group, and heightened C-CS was more prevalent in the FD (+) group than in the FD (-) group. Patients who had a heightened C-CS were more likely to experience GERD and FD than those who had a normal C-CS.

Effects of comorbidities on C-CS in patients with severe asthma				
		Heightened C-CS	Normal C-CS	p value
FD	n=15	11	4	0.003
GERD	n=22	13	9	0.04

Conclusion: These results suggest that FD, as well as GERD, and severe asthma are functionally linked by the interaction of sensory nerves between the airways and the upper gastrointestinal tract. TRPV1 may be involved in the pathophysiology of both GERD, FD, and asthma.

Disclosure: Nothing to disclose.

PP0068

REAL-WORLD EXPERIENCE OF USING PRUCALOPRIDE FOR THE TREATMENT OF DYSPHAGIA IN PATIENTS WITH NEGATIVE GASTROSCOPY AND CHICAGO III OESOPHAGEAL DYSMOTILITY IN CLINICAL PRACTICE

C. Lambiase^{1,2,3}, C. Sbarigia^{2,3,4}, J. Ortiz Fernàndez-Sordo^{2,3}, G.M. Villarejo^{2,3}, K. Kamaldeep⁵, L.A Houghton⁶, M. Corsetti^{2,3}
¹University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²University of Nottingham, NIHR Nottingham BRC, Nottingham University Hospitals NHS Trust and the University of Nottingham, Nottingham, United Kingdom, ³University of Nottingham, Nottingham Digestive Diseases Centre, Translational Medical Science, School of Medicine, Nottingham, United Kingdom, ⁴Sapienza University of Rome, Sant'Andrea University Hospital, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy, ⁵Nottingham University Hospitals NHS Trust, Department of Pharmacy, Nottingham, United Kingdom, ⁶University of Leeds, Division of Gastroenterology and Surgical Sciences, Leeds Institute of Medical Research, Leeds, United Kingdom

Contact E-Mail Address: cate.sbarigia@gmail.com
Introduction: Prucalopride, a 5-HT4 agonist approved for the treatment of refractory chronic constipation has been shown to reduce oesophageal acid exposure in healthy volunteers (Kessing BF, 2014) and improve oesophageal motility in gastroesophageal reflux (GER) patients with ineffective oesophageal motility (Lei W-Y, 2018). To date, no studies have evaluated its effect in patients with dysphagia and oesophageal dysmotility.
Aims & Methods: Our aim was therefore to evaluate the effect of prucalopride on dysphagia symptoms and to assess which, if any, motility or GERD diagnosis influenced outcome in patients with gastroscopy negative dysphagia. Clinical records, together with oesophageal high-resolution

manometry (HRM) and available 24hr pH-monitoring (pH-MII) reports of patients referred for dysphagia to a single Neurogastroenterology Clinic between April 2017 and March 2024 were retrospectively reviewed. All patients had a previous negative gastroscopy with oesophageal biopsies, were not responsive to PPIs and were prescribed prucalopride as an add-on treatment at the initial dosage of 1 mg/daily with the possibility to increase to 2 mg/daily after one week in case of no response. A standardized template was used to collect clinical data and patient-reported response to treatment. Clinical response was defined as a self-reported improvement in dysphagia symptoms associated with a reduction in Eckardt score of at least one point. Data are expressed as median (QR).

Results: Thirty-five patients [median age 62 (28) years; 19 (54%) female] were included. Mean duration of follow-up was 12 (19) months. Twenty-two (63%) patients responded to Prucalopride with a significant improvement in the Eckardt score before to after treatment [3.5 (2.3) vs 1 (1.8); $p < 0.001$]. Six patients (27.3% of responders) responded to 1 mg, with the rest increasing to 2mg/daily. Response was maintained for a median of 14.5 (16) months. Thirteen (37.1%) patients did not respond, of which four (11.4%) experienced adverse events (diarrhoea, headache, abdominal pain) leading to an early treatment discontinuation. In these patients the Eckardt score did not change before to after the treatment [3 (3) vs 3.5 (2.3), respectively; $p = 0.85$]. None of the clinical (data not shown) or key manometric parameters were associated with treatment response [median basal distal contractile integral 283 (425) vs 340 (470) mmHg/s/cm; $p = 0.71$ and median integrated relaxation pressure 6.2 (8) vs 8.4 (9.4) mmHg; $p = 0.13$ in responders and non-responders, respectively]. However, there were trends for more patients with absent contractility to be non-responders, and more patients with EGJOO to be responders to prucalopride. Normal acid exposure time and number of reflux events were associated with a positive response to treatment (Table 1).

Oesophageal Manometry	Non-Responders (n=13)	Responders (n=22)	p-value
Ineffective Oesophageal Motility (%)	7 (53.8%)	9 (40.9%)	0.46*
Oesophago-gastric junction outflow obstruction (%)	0 (0%)	5 (22.7%)	0.13*
Absent contractility (%)	5 (38.5%)	4 (18.2%)	0.24*
Other diagnoses (%)	1 (7.7%)	4 (18.2%)	0.63*
AET	14.2 [20.3]	1.4 [4.1]	0.06*
Mean number of acid refluxes	46 (107)	12 (15.5)	<0.01
Pathological AET (>6%)	11 (84.6%)	10 (45.4%)	0.03*

Table 1 – HRM and pH-monitoring characteristics of responder and non-responder patients at baseline.

*Mann-Whitney's U tests

*Fisher's Exact Test

Abbreviations: AET=acid exposure time

Conclusion: Our study suggests Prucalopride might be a well-tolerated and useful treatment for dysphagia in patients with dysmotility disorders, mainly in the absence of pathological reflux. However, prospective randomized controlled studies are needed to confirm these data.

Disclosure: Nothing to disclose.

PP0069

DIFFERENCES IN MEDICAL CARE SATISFACTION OF PATIENTS WITH “FUNCTIONAL” VS “ORGANIC” ESOPHAGEAL DISEASES: ITALIAN VALIDATION OF THE PPRS-SF QUESTIONNAIRE AND ITS APPLICATION IN CLINICAL ROUTINE PRACTICE

C. Soldaini¹, L. Ruggiero¹, A. Sellitti¹, A. Caloro¹, L. De Leo¹, A. Santonicola¹, P. Iovino¹

¹University of Salerno, Gastrointestinal Unit, Department of Medicine, Surgery and Dentistry “Scuola Medica Salernitana”, Baronissi, Italy

Contact E-Mail Address: carlo.soldaini@outlook.com

Introduction: Patient-physician relationship (PPR) plays a center role in modern health care, especially within gastrointestinal (GI) medical practice, where patients affected by non-structural disorders (better described as disorders of gut-brain interaction or DGBI) tend to report a low satisfaction towards their medical care. In 2017 Kurlander et al. developed and validated a Patient-Physician Relationship Scale (PPRS), a questionnaire used in patients affected by Irritable Bowel Syndrome (IBS) to assess their degree of medical care-satisfaction. The original PPRS was later shortened and simplified by Drossman et al. in 2021 by creating a PPRS-SF (short form), consisting in a 12-item questionnaire.

Aims & Methods: The aims of this study were to validate the PPRS-SF in Italian and to administer it to both patients with functional and organic esophageal diseases, in order to highlight the differences in patient-physician relationship between the two categories.

The process of validation to Italian language of the PPRS-SF questionnaire was carried out following a standardized forward-backward procedure and each step was overseen by an independent clinical monitor assigned by the Rome Foundation itself. The Italian version of the PPRS SF was successfully administered to 50 Eosinophilic Esophagitis (EoE), 53 Achalasia (Ach), 48 Gastroesophageal Reflux Disease (GERD) and 44 esophageal DGBI patients (affected by functional dysphagia or functional heartburn).

Results: In esophageal DGBI and GERD, the degree of patients' satisfaction was significantly lower, if calculated as a total summation, compared to that of EoE and Achalasia patients.. Between a minimum score of -36 and a maximum of +36, the mean PPRS-SF “Italian version” score for patients with EoE was 30.20 (± 9.78), for patients with Ach 23.78 (± 19.9); for patients with GERD 20.46 (± 16.03); for esophageal DGBI 17.91 (± 18.41). Moreover, there was a significant difference in PPR between younger patients (under 50 years old), who reported a score of 27.1 (± 12.29) and older patients (over 50 years old), reporting a score of 20.16 (± 19.72).

Conclusion: This study validated the Italian version of the PPRS-SF questionnaire and showed that the patients' diagnosis together with other factors such as their age, can affect the quality of the PPR. In particular, patients with DGBI and older patients reported lower scores than the ones with organic diseases and the younger ones, respectively. Further studies are necessary to confirm these results.

Disclosure: Nothing to disclose.

PP0070

INVESTIGATING INAPPROPRIATE PROTON PUMP INHIBITOR USE
IN PRIMARY CARE PATIENTS

J. Scheepers¹, F. Carbone^{1,2}, K. Van den Houte¹, J. Tack^{1,2}

¹KU Leuven, Translational Research Center for Gastrointestinal disorders, Leuven, Belgium, ²UZ Leuven, Department for Gastroenterology and Hepatology, Leuven, Belgium

Contact E-Mail Address: janne.scheepers@kuleuven.be

Introduction: Increasing concerns arise regarding inappropriate proton pump inhibitor (PPI) use in terms of indication and dosage, impacting healthcare budgets and posing possible risks and drug interactions. It was estimated that up to 70% of PPI use may not medically indicated, however, the characteristics of this population of patients have not been described (1,2).

Aims & Methods: We aim to describe demographic and clinical profiles of primary care PPI users who lack a strict medical indication. General practitioners included long-term PPI users without strict medical indication in the study. Demographic characteristics, duration and dosage of PPI use, and medical history (e.g. upper endoscopy findings, H. pylori status and previous attempts to stop PPI) were registered. Patients completed questionnaires assessing gastrointestinal symptoms (PAGI-SYM) and psychosocial co-morbidities (depression, somatization, and anxiety using respectively PHQ-9, PHQ-15, GAD-7). For this analysis, patients were categorized by: (I) initial indication for PPI therapy (GERD with low-grade esophagitis, dyspepsia, non-gastric symptoms) and (II) PPI dose (healing or maintenance). Statistical significance (p<0.05) was assessed using one-way ANOVA, student's T-test, and Fisher's exact test. Results are shown as mean±SD.

Results: Out of 482 recruited patients on long-term PPI therapy, 42% reported failed previous attempts to discontinue PPI therapy. Main indications for PPI initiation were low-grade reflux esophagitis (26%), functional dyspepsia (18%), uninvestigated reflux symptoms (13%), uninvestigated dyspepsia (10%), peptic ulcer (2%) and mixed causes (18%, e.g. polymedication, cough, hoarseness,...). A history of H. pylori infection was present in 9% of patients. Patients exhibited on average low somatization, no depression, and no anxiety (Table).

	Nausea/ vomiting (PAGI- SYM) mean score ± SD	Postprandial fullness/ early satiety (PAGI-SYM) mean score ± SD	Bloating (PAGI- SYM) mean score ± SD	Upper abdominal pain (PAGI-SYM) mean score ± SD	Lower abdominal pain (PAGI-SYM) mean score ± SD	Heartburn/ regurgitation (PAGI-SYM) mean score ± SD	Depression (PHQ-9) mean score ± SD	Somatization (PHQ-15) mean score ± SD	Anxiety (GAD-7) mean score ± SD
Total (n=482) Mean age 61 ± 14 y.o. 59% female BMI 27.9 ± 4.6 kg/m ²	0.4 ± 0.7	1.1 ± 1.1	1.7 ± 1.6	1.0 ± 1.2	0.7 ± 1.2	0.9 ± 1.0	4.6 ± 4.6	8.8 ± 5.1	5.0 ± 5.0
GERD (n=167) Mean age 60 ± 14 y.o. 59% female BMI 27.5 ± 4.7 kg/m ²	0.3 ± 0.7	1.1 ± 1.0	1.6 ± 1.5	0.8 ± 1.7	0.6 ± 1.1	0.9 ± 1.0	3.9 ± 3.9	8.2 ± 4.8	4.2 ± 4.7
Dyspepsia (n= 126) Mean age 60 ± 15 y.o. 63% female BMI 28.0 ± 4.6 kg/m ²	0.4 ± 0.6	1.3 ± 1.2	2.0 ± 1.6	1.1 ± 1.2	0.8 ± 1.2	0.9 ± 1.1	5.5 ± 5.0	9.8 ± 5.3	6.1 ± 5.1
Non-gastric (n=55) Mean age 64±11 y.o. 65% female BMI 27.8 ± 4.1 kg/m ²	0.4 ± 0.7	1.1 ± 1.2	1.3 ± 1.5	0.8 ± 1.4	0.5 ± 1.1	0.6 ± 0.9	4.5 ± 4.7	8.3 ± 4.6	3.9 ± 3.6

There were no differences in age and sex among cohorts on healing (n= 80, 62% female, mean age 61 ± 13 y.o.) or maintenance PPI dose (n=362, 58% female, mean age 61 ± 14 y.o.). However, those on healing doses had a significantly higher BMI (29.2 ± 4.9 vs 27.6 ± 4.4 kg/m², p=0.003) and reported higher scores on all PAGI-SYM subscales (NS), with a significantly higher score on the postprandial fullness & early satiety subscale (average score of 1.4 ± 1.3 vs. 1.1 ± 1.0, p=0.030). There were no significant differences in psychosocial co-morbidities between patients on healing or maintenance PPI doses (all p>0.05).

Sex, age, and BMI were similar among subgroups based on the initial reason for PPI therapy. Patients in whom PPI therapy was initiated for dyspepsia had significantly higher bloating scores than those with reflux or non-gastric symptoms (p=0.011). Furthermore, dyspepsia patients exhibited significantly higher somatization (p=0.015), depression (p=0.007), and anxiety (p=0.002) compared to reflux symptom patients.

Conclusion: A large subset of patients with prolonged PPI intake lacking a strict medical indication have unsuccessfully attempted to stop PPI usage. The patients who are long-term on healing doses have a significantly higher BMI and more severe postprandial distress syndrome symptoms. Psychosocial co-morbidity is significantly higher in patients in whom PPIs were started for dyspeptic symptoms. These characteristics are relevant when considering attempts to deprescribe PPIs in primary care.

References:

1. Boghossian TA, Rashid FJ, Thompson W, Welch V, Moayyedi P, Rojas-Fernandez C, et al. Deprescribing versus continuation of chronic proton pump inhibitor use in adults. *Cochrane Database Syst Rev.* 2017 Mar 16;3(3).
2. Consensusvergadering – Het rationeel gebruik van de protonpompinhibitoren (PPI's) bij nietulcereuze gastro-oesofageale pathologie. RIZIV. 2018; Available from: www.riziv.fgov.be

Disclosure: Nothing to disclose.

PP0071

HIGH-RESOLUTION VIDEO MANOMETRIC ASSESSMENT OF
DYSPHAGIA POST FUNDOPLICATION

V. Peranathan^{1,2}, M. Richards², R.E Burgell¹, G. Hebbard²

¹The Alfred Hospital, Gastroenterology and Hepatology, Melbourne, Australia, ²The Royal Melbourne Hospital, Melbourne, Australia

Contact E-Mail Address: varanp91@gmail.com

Introduction: Post-fundoplication dysphagia is common and can occur in up to 65% of patients¹. Following anti-reflux surgery, the oesophago-gastric junction (OGJ) is an anatomically complex and dynamic area which is subject to mechanical stress, herniation and slippage. Upper gastrointestinal endoscopy and barium oesophagrams are the most commonly utilised diagnostic modalities. High-resolution video manometry (HRVM) is an alternative and potentially superior technique as it allows for physiological assessment with high-resolution manometry (HRM) with simultaneous fluoroscopic views help delineate anatomy, location of the fundoplication and better appreciate hernias. We aimed to characterise modes of dysphagia post-fundoplication with HRVM.

Aims & Methods: We conducted a retrospective observational study over 62 months until March 2023. HRVM performed on patients with ongoing dysphagia post-fundoplication were selected from a HRVM database and modes of dysphagia were assessed.

Results: 501 patients had HRVM over 62 months of which 32 patients had dysphagia post-fundoplication. Median integrated relaxation pressure (IRP) was greater than 15mmHg in 9 patients (27.3%). HRVM was normal in 8 (25%), The causes of dysphagia post-fundoplication included pseudo-achalasia with oesophago-gastric junction outflow obstruction (OJ-GOO) due to a tight wrap in 9 (28.1%), ineffective oesophageal motility in 8 (25%), para-oesophageal hernia due to slippage of wrap in 3 (9.4%), non-achalasia oesophageal dysmotility disorders (i.e. hypercontractile oesophagus and distal oesophageal spasm) in 2 (6.3%) and new diagnosis of Type 2 achalasia in 2 (6.3%). Post fundoplication complications accounted for 12 (37.5%) and an underlying oesophageal motility disorder was diagnosed in 12 patients (37.5%).

Conclusion: Whilst iatrogenic causes of dysphagia due to fundoplication itself were commonly seen, underlying oesophageal motility disorders

were also identified in an equally large proportion of patients. Whether this reflects post-surgical motility disturbance or missed pre-morbid dysmotility is unclear. Nevertheless, these results highlight the importance of oesophageal manometry prior to anti-reflux surgery.

References:

1. Hasak S, Brunt LM, Wang D, Gyawali CP. Clinical characteristics and outcomes of patients with postfundoplication dysphagia. *Clinical Gastroenterology and Hepatology*. 2019 Sep 1;17(10):1982-90.

Disclosure: No conflicts of interest.

PP0072

COMPARISON OF ANXIETY AND DEPRESSION FREQUENCIES IN ROMA IV FUNCTIONAL DYSPESIA SUBGROUPS: A CROSS-SECTIONAL OBSERVATIONAL STUDY FROM TURKEY

S. Demirbaş Yücel¹, M. Sadeçolak², A. Bilgili², M. Tozlu², A.T. Eminler², M.I. Uslan²

¹Sakarya Training and Research Hospital, Gastroenterology, Sakarya, Turkey, ²Sakarya University Medical Faculty Hospital, Gastroenterology, Sakarya, Turkey

Contact E-Mail Address: selmademirbas@yahoo.com

Introduction: Different pathophysiological mechanisms are thought to play a role in functional dyspepsia (FD) subgroups defined by Rome IV criteria. However, many more studies are needed to determine whether a better separation of pathophysiological mechanisms, so a better therapy choice, can be obtained with the Rome IV subgrouping. This study aims to investigate the difference in psychopathological comorbidities between the FD subgroups defined by the Rome IV criteria. We hypothesized that anxiety and depression would be risk factors differently for each functional dyspepsia subgroup according to Roma IV criteria.

Aims & Methods: This is a cross-sectional observational study conducted at a tertiary gastroenterology center in Turkey between December 2022 and April 2023. Dyspeptic patients, aged over 18 years old referred for an upper gastrointestinal endoscopy were recruited. Participants were asked to fill out the Rome IV gastroduodenal questionnaire along with the Hospital Anxiety and Depression Scale. FD subgroups were defined using the Rome IV criteria. Hospital Anxiety and Depression Scale was used to assess the anxiety and depression of participants. All statistical analyses were conducted using SPSS version 23.0. The p-value of <0.05 was accepted as statistically significant.

Subgroups	PDS N:59	Overlapping N:37	EPS N:21	Total N:117
Depression n(%)	25 (37.9%) p>0.05	9 (30%) p>0.05	7 (33.3%) p>0.05	41 (35%)
Anxiety n (%)	26 (39.4%) *p<0.05	7 (23.3%) p>0.05	2 (9.5%) *p<0.05	35 (29.9%)

FD, functional dyspepsia; PDS, postprandial distress syndrome; EPS, epigastric pain syndrome

Table 1. Anxiety and depression frequencies among FD Rome IV subgroups.

Results: Of 424 dyspeptic participants, FD was identified in 117 (27.5%) patients. There were 66 (56.4%) PDS (postprandial distress syndrome), 21 (18%) EPS (epigastric pain syndrome), and 30 (25.6%) overlapping cases. Depression was detected in 35% of FD patients; in 37.9% of the PDS subgroup, 30% of the overlapping subgroup, and 33.3% of the EPS subgroup; There was no difference between the groups (p:0.622). Anxiety was detected in 29.9% of FD patients; in 39.4% of the PDS subgroup, 23.3% of the overlapping subgroup, and 9.5% of the EPS subgroup; detected more frequently in PDS subgroup than in EPS and overlapping subgroups (p:0.022) (Table 1). The frequency of anxiety was significantly higher in patients with postprandial fullness and early satiation symptoms according

to those without symptoms (35.8% vs. 15.6%, p:0.035; 44.7% vs. 23.9% p:0.027, respectively).

Conclusion: PDS subgroup, postprandial fullness, and early satiety symptoms were more associated with anxiety, according to the EPS subgroup undd epigastric pain symptom. Evaluating this patient groups in this respect and providing the necessary support can accelerate the recovery process of the patient. It seems reasonable to assume that anxiolytic drugs are of benefit in especially the PDS subgroup. Further studies assessing psychological factors and treatment strategies for FD Rome IV subgroups are required to confirm the relationship of subgroups with depression and anxiety.

References:

- Wauters L, Dickman R, Drug V, Mulak A, Serra J, Enck P, et al. United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on functional dyspepsia. *United European Gastroenterol J*. 2021 Apr;9(3):307-331. doi: 10.1002/ueg2.12061.
- Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of Functional Dyspepsia with Depression and Anxiety: A Systematic Review. *J Gastrointest Liver Dis*, June 2021 Vol. 30 No 2: 259-266. doi: 10.15403/jgld-3325.
- Van den Houte K, Carbone F, Goelen N, Schol J, Masuy I, Arts J, et al. Effects of Rome IV Definitions of Functional Dyspepsia Subgroups in Secondary Care. *Clinical Gastroenterology and Hepatology* 2021;19:1620–1626. doi: 10.1016/j.cgh.2020.06.043.
- Carbone F, Vanuytsel T, and Tack J. Analysis of Postprandial Symptom Patterns in Subgroups of Patients With Rome III or Rome IV Functional Dyspepsia. *Clinical Gastroenterology and Hepatology* 2020;18:838–846. doi:10.1016/j.cgh.2019.07.053.
- Aro P, Talley NJ, Johansson SE, Agréus L, Ronkainen J. Anxiety is linked to new-onset dyspepsia in the Swedish population: a 10-year follow-up study. *Gastroenterology* 2015;148(5):928-37. doi: 10.1053/j.gastro.2015.01.039.
- Adibi P, Keshteli AH, Daghighzadeh H, Roohafza H, Pournaghshband N, Afshar H. Association of anxiety, depression, and psychological distress in people with and without functional dyspepsia. *Adv Biomed Res* 2016;5:195. doi:10.4103/2277-9175.190936

Disclosure: None to declare.

PP0073

ESOPHAGEAL SAMPLING AFTER FOOD IMPACTION; PREJUDICE AFFECTS CLINICAL PRACTICE...

T. Voulgaris¹, T. Alexopoulos¹, J. Vlachogiannakos¹, D. Kamberoglou¹, A. Koutsoumpas¹, K. Papaxoinis¹, P. Fytily¹, G. Papatheodoridis¹, G. Karamanolis¹

¹National and Kapodistrian University, Laiko General Hospital, Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: georgekaramanolis@yahoo.co.uk

Introduction: Epidemiological studies have shown that Eosinophilic Esophagitis (EoE) is most commonly observed among young males with atopic background. Data have pointed out that approximately half of young patients presenting with bolus impaction will have EoE as a causative factor. According to guidelines, in patients with bolus impaction, EoE should be searched, by esophageal sampling, irrespective of patients age, sex or endoscopy findings.

Aims & Methods: Aim of our study was to elucidate if clinicians in an academic hospital in Greece cohere to guidelines or if epidemiological and endoscopic data precludes them from esophageal sampling.

We included 134 consecutive patients presented with bolus impaction

during a 6-year period (1/18-12/23). We excluded patients with a history of; esophageal stenosis, esophageal/gastric cancer esophageal motility disorders, metastatic disease, bone-foreign body ingestion, caustic agent ingestion, esophagogastric surgeries. We further excluded 34 patients with endoscopic evidence of another disease that could explain patients' symptoms. Epidemiological, endoscopic and histological data were collected and analyzed.

Results: We finally included 100 patients (M/F: 71/29, mean age 55±23 years old). A history of previous bolus impaction without biopsy sampling was reported by 35 (26.1%), while 12 (9%) reported history of dysphagia before the impaction episode. During the endoscopy 36 had endoscopic findings suggestive of EoE and 64 (47.8%) a normal Endoscopy. Biopsies were obtained by 47/100 (47%). In the univariate analysis, sampling was correlated, in a statistically significant way, with male sex, age <65 years old, endoscopic signs compatible to EoE and a history of previous bolus impaction or dysphagia. Though in the multivariate analysis only endoscopic findings and age were observed, in a statistically significant way, to affect clinicians decision to obtain biopsies. EoE was diagnosed in 33/47 (70.2%). In the univariate analysis EoE diagnosis was significantly correlated with age <65 years, male sex and the existence of compatible endoscopic findings but not with a history of previous bolus impaction or dysphagia. In the multivariate analysis only age <65 was independently correlated with EoE diagnosis. (Table)

Factor	Biopsy sampling among patients with Bolus impaction (patients without endoscopic findings other than EoE that could explain patients symptoms)			EoE diagnosis among patients with Bolus impaction		
	Univariate		Multivariate	Univariate		Multivariate
	p	p		p	p	
Younger than 65	44/71 62%	<0.001	0.002 OR: 0.951	33/44 75%	0.041	0.038 OR: 0.931
65 and older	3/29 10.3%		95% C.I.: 0.922-0.982	0/3 (0%)		95% C.I.: 0.870-0.996
Male	41/71 57.7%	0.001	0.231 OR: 0.441	31/41 76.5%	0.047	0.968 OR: 1.064
Female	6/29 20.7%		95% C.I.: 0.116-1.683	2/6 33.3%		95% C.I.: 0.052-21.887
Findings compatible to EoE	32/36 88.9%	<0.001	<0.001 OR: 21.836,	27/32 84.3%	0.031	0.062 OR: 7.536
Normal endoscopy/ other findings	15/64 23.4%		95% C.I.: 3.994-115.956	6/15 40.0%		95% C.I.: 0.900-63.101
History of previous bolus impaction or dysphagia	22/33 66.7%	0.010	0.493 OR: 1.690, 95% C.I.: 0.376-7.592	16/22 72.7%	0.555	
Yes	25/67 37.3%			19/25 76.0%		
No						

Conclusion: According to our study, esophageal biopsies are obtained in <50% of patients with a bolus impaction episode. Age and endoscopic evidence supportive of EoE seem to drive clinicians decision to obtain esophageal biopsies after a bolus impaction episode. EoE is more commonly observed in young male patients with bolus impaction.

Disclosure: Nothing to disclose.

PP0074

COHORT PROFILE UPDATE: THE SWISS EOSINOPHILIC ESOPHAGITIS COHORT STUDY (SEECs)

J. Wakim El-Khoury¹, E. Safroneeva², C. Saner³, J.-B. Rossel⁴, S. Trelle⁵, M. Zwahlen⁶, L. Biedermann⁶, A. Krienbühl⁷, T. Greuter⁷, P. Schreiner⁸, P. Netzer⁹, A. Franke¹⁰, S. Brand¹⁰, C. Hasler¹¹, P.R. Aepli¹¹, E. Burri¹², A. Weber¹³, C. Sempoux¹⁴, R. Biral¹⁵, W. Jochum¹⁶, J. Diebold¹⁷, N. Willi¹⁸, A. Straumann¹⁹, A.M. Schoepfer²⁰

¹Centre Hospitalier Universitaire Vaudois, Division of Gastroenterology and Hepatology, Lausanne, Switzerland, ²Tillotts Pharma, Inst. für Sozial- und Preventive Medizin, Rheinfelden, Switzerland, ³Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, ⁴University of Bern, 3. Department of Clinical Research, Bern, Switzerland, ⁵University of Bern, Institute of Social and Preventive Medicine, Bern, Switzerland, ⁶USZ Zürich, Gastroenterology & Hepatology, Zürich, Switzerland, ⁷University Hospital Zurich, Division of Gastroenterology and Hepatology, Zurich, Switzerland, ⁸University Hospital AKH Vienna, 6. Division of Gastroenterology and Hepatology, Vienna, Austria, ⁹GastroZentrum Netzer AG, Bern, Switzerland, ¹⁰Kantonsspital St. Gallen, Division of Gastroenterology and Hepatology, St. Gallen, Switzerland, ¹¹Kantonsspital Luzern, Division of Gastroenterology and Hepatology, Luzern, Switzerland, ¹²University Hospital Basel, Division of Gastroenterology and Hepatology, Basel, Switzerland, ¹³University Hospital Zurich, Division of Pathology, Zurich, Switzerland, ¹⁴Centre Hospitalier Universitaire Vaudois, Institute of Pathology, Lausanne, Switzerland, ¹⁵Pathologie Länggasse, Ittigen, Bern, Switzerland, ¹⁶Kantonsspital St. Gallen, Institute of Pathology, St. Gallen, Switzerland, ¹⁷Kantonsspital Luzern, Division of Pathology, Luzern, Switzerland, ¹⁸Kantonsspital Liestal, Division of Pathology, Liestal, Switzerland, ¹⁹University Hospital Zurich, Department of Gastroenterology, Kappel, Switzerland, ²⁰Lausanne University Hospital, Gastroenterology And Hepatology, Lausanne, Switzerland

Contact E-Mail Address: Jeanine.Wakim-El-Khoury@chuv.ch

Introduction: The Swiss Eosinophilic Esophagitis Cohort Study (SEECs) is a national prospective cohort for adults with eosinophilic esophagitis (EoE) that was established in 2015 with the aim of improving quality of care considering EoE's increased incidence. The SEECs allows for documentation of EoE's natural history, patients' quality of life (QoL) and monitoring of treatment efficacy and safety. It also aims to promote clinical and translational research projects with the availability of standard operating procedures (SOPs) for the submission of scientific protocols. The first cohort update was published in 2017.

Between 2020 and 2022, paper questionnaires were gradually replaced by fully electronic data capture using Research Electronic Data Capture (REDCap) software. We aim to provide a second update of the cohort, eight years after its launch.

Aims & Methods: The SEECs includes adult patients (age ≥18 years) with EoE, gastro-esophageal reflux (GERD) and healthy controls (HC) using strict eligibility criteria in line with the most recent guidelines. Upon inclusion and follow-up (typically once a year), patients and physicians complete questionnaires in REDCap which are available in German, French, and English.

Patients reported outcomes (PROs) and biologic activity are assessed all on the same day using validated instruments (EESAI PRO for symptoms; EoE-QoL-A for QoL; EREFS for endoscopic activity; modified EoE-HSS for histologic activity). The SEECs biobank includes biosamples (blood samples, esophageal biopsies) from patients with EoE, GERD, and HC.

Results: As of July 2023, the SEECS includes 778 patients [716 (92%) with EoE, 29 (3.8%) with GERD, and 33 (4.2%) HC; 559/778 (71.9%) are male]. Mean age $\pm$ SD (years) according to diagnosis is as follows: EoE 41.9 $\pm$ 12.9, GERD 53.6 $\pm$ 16.4, HC 51.7 $\pm$ 17.2. Mean diagnostic delay for the EoE group is 89.6 $\pm$ 96.2 months. Concomitant GERD is found in 200 patients (27.9%) of the EoE cohort. Concomitant allergic disorders (asthma, rhinoconjunctivitis, neurodermitis) are present in 500 patients (74.4%) with EoE. At inclusion, 694 (96.9%) of EoE patients have an ongoing treatment [oro-dispersible budesonide tablet: 290 patients (41.8%); budesonide/fluticasone syrup: 281 patients (40.5%); PPI: 162 patients (23.3%); elimination diets: 103 patients (14.8%); esophageal dilation at last visit: 166 patients (23.9%)]. Esophageal biopsies are available from 525/778 (67.5%) patients including 468 EoE patients (65.4%).

Conclusion: Our findings are in line with the available literature on EoE's natural history. To our knowledge, the SEECS is the only national cohort for EoE adult patients that includes both GERD and healthy controls with their biosamples. Data capture is based on validated instruments and is fully electronic using REDCap. The SEECS offers up-to-date epidemiologic data on EoE and promotes research projects.

Disclosure: Jeanine Wakim has no relevant financial, professional, or personal relationships to disclose. Ekaterina Safroneeva reports (i) consulting fees from Avir Pharma, Inc., Aptalis Pharma, Inc., Celgene Corp., Novartis, AG, and Regeneron Pharmaceuticals Inc; (ii) being an employee of Tillotts Pharma AG. Catherine Saner has no relevant financial, professional, or personal relationships to disclose. Jean-Benoit Rossel has no relevant financial, professional, or personal relationships to disclose. Sven Trelle has no relevant financial, professional, or personal relationships to disclose. Marcel Zwahlen has no relevant financial, professional, or personal relationships to disclose. Luc Biedermann received consulting fees and/or speaker fees and/or research grants from Adare/Ellodi Pharmaceuticals, Inc., AstraZeneca, AG, Switzerland, Receptos-Celgene-BMS, Dr. Falk Pharma, GmbH, Germany, Glaxo Smith Kline, AG, Nestlé S. A., Switzerland, Novartis, AG, Switzerland, and Regeneron-Sanofi Pharmaceuticals. Andrea Kreienbuehl has no relevant financial, professional, or personal relationships to disclose. Thomas Greuter received consulting fees and/or speaker fees and/or research grants from Adare/Ellodi Pharmaceuticals, Inc., AstraZeneca, AG, Switzerland, Receptos-Celgene-BMS, Dr. Falk Pharma, GmbH, Germany, Glaxo Smith Kline, AG, Nestlé S. A., Switzerland, Novartis, AG, Switzerland, and Regeneron-Sanofi Pharmaceuticals. Philipp Schreiner received consulting fees and/or speaker fees from Dr. Falk Pharma, GmbH, Takeda, Regeneron-Sanofi Pharmaceuticals, Abbvie, Janssen-Cilag, Receptos-Celgene-BMS. Peter Netzer has no relevant financial, professional, or personal relationships to disclose. Annett Franke has no relevant financial, professional, or personal relationships to disclose. Stephan Brand has no relevant financial, professional, or personal relationships to disclose. Chantal Hasler has no relevant financial, professional, or personal relationships to disclose. Patrick Aepli has no relevant financial, professional, or personal relationships to disclose. Emanuel Burri has no relevant financial, professional, or personal relationships to disclose. Achim Weber has no relevant financial, professional, or personal relationships to disclose. Christine Sempoux has no relevant financial, professional, or personal relationships to disclose. Ruggero Biral has no relevant financial, professional, or personal relationships to disclose. Wolfram Jochum has no relevant financial, professional, or personal relationships to disclose. Joachim Diebold has no relevant financial, professional, or personal relationships to disclose. Niels Willi has no relevant financial, professional, or personal relationships to disclose. Alex Straumann received consulting fees and/or speaker fees and/or research grants from Adare/Ellodi Pharmaceuticals, Inc., AstraZeneca, AG, Switzerland, Receptos-Celgene-BMS, Dr. Falk Pharma, GmbH, Germany, Glaxo Smith Kline, AG, Nestlé S. A., Switzerland, Novartis, AG, Switzerland, and Regeneron-Sanofi Pharmaceuticals. Alain Schoepfer received consulting fees and/or speaker fees and/or research grants from Adare/Ellodi Pharmaceuticals, Inc., Astra-

Zeneca, AG, Switzerland, Receptos-Celgene-BMS, Dr. Falk Pharma, GmbH, Germany, Glaxo Smith Kline, AG, Nestlé S. A., Switzerland, Novartis, AG, Switzerland, and Regeneron-Sanofi Pharmaceuticals.

PP0075

ENRICHMENT OF TSLP GENE SIGNATURES IN OESOPHAGEAL TISSUE OF PATIENTS WITH ACTIVE EOSINOPHILIC OESOPHAGITIS: POTENTIAL FOR TREATMENT WITH TEZEPELUMAB

J.D Sherrill¹, P.G Gavin¹, D. Ivanič², L. Öberg², T. Li³, A. Péterffy⁴, W. Rae⁵, S. Caveney⁶, R. Tsotsoros⁷, R. Trivedi⁸, K. Domek-Łopacińska⁹, C. Seminario¹⁰, A. Platt¹¹, D. Muthas²
¹AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology, BioPharmaceuticals R&D, Gaithersburg, United States of America, ²AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology, BioPharmaceuticals R&D, Gothenburg, Sweden, ³AstraZeneca, Biometrics, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Durham, United States of America, ⁴AstraZeneca, Clinical, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Gothenburg, Sweden, ⁵AstraZeneca, Clinical, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Cambridge, United Kingdom, ⁶Amgen, Global Development, Inflammation, R&D, Thousand Oaks, United States of America, ⁷AstraZeneca, Clinical Operations, Respiratory and Immunology, BioPharmaceuticals R&D, Gaithersburg, United States of America, ⁸AstraZeneca, Clinical, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Durham, United States of America, ⁹AstraZeneca, Clinical, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Warsaw, Poland, ¹⁰AstraZeneca, Clinical, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, Gaithersburg, United States of America, ¹¹AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology, BioPharmaceuticals R&D, Cambridge, United Kingdom

Contact E-Mail Address: joseph.sherrill@astrazeneca.com

Introduction: Eosinophilic oesophagitis (EoE) is a rare, chronic, inflammatory disorder with few approved treatments. Thymic stromal lymphopoietin (TSLP) is a pro-inflammatory epithelial cytokine. TSLP genetic variants are associated with EoE risk, and oesophageal TSLP mRNA and protein levels are elevated in patients with active EoE. Tezepelumab, a human monoclonal antibody approved for the treatment of severe asthma, specifically binds to and blocks the activity of TSLP.

Aims & Methods: This analysis aimed to determine whether TSLP-mediated gene expression changes are enriched in patients with EoE to understand whether tezepelumab could be a potential treatment for EoE. Gene signature analyses were performed to generate TSLP gene lists from two independent transcriptomic data sets obtained from: 1) bronchial brushings at week 28 from patients with moderate-to-severe, uncontrolled asthma, treated with tezepelumab in the phase 2 CASCADE study (NCT03688074); and 2) human myeloid dendritic cells (mDCs) treated *ex vivo* with recombinant TSLP for 24 hours. Using these TSLP gene lists, gene set variation analyses were performed on publicly available gene expression data from oesophageal biopsies in healthy individuals and patients with chronic oesophagitis, active untreated EoE, inactive treated EoE (responsive to swallowed topical corticosteroids [STCs]) and active treated EoE (unresponsive to STCs).

Results: The TSLP gene lists comprised 18 upregulated genes and 32 downregulated genes in bronchial brushings from CASCADE, and 183 upregulated and 161 downregulated genes in human mDCs. The TSLP gene scores from bronchial brushings were elevated in patients with active EoE, untreated and unresponsive to STCs, compared with healthy individuals (upregulated genes: $p \leq 0.05$ and $p \leq 0.001$, respectively; downregulated genes: $p > 0.05$ and $p \leq 0.01$, respectively). The TSLP gene scores from human mDCs were elevated in patients with active EoE, untreated and unresponsive to STCs, compared with healthy individuals (upregulated genes: $p \leq 0.05$ and $p \leq 0.01$, respectively; downregulated genes: $p \leq 0.05$ and $p \leq 0.001$, respectively). In both data sets, compared with patients who had inactive treated EoE, TSLP gene scores were elevated in patients with active treated EoE that was unresponsive to STCs (upregulated genes: $p < 0.001$; downregulated genes: $p \leq 0.05$ [bronchial brushings] and $p \leq 0.0001$ [human mDCs]). These data support clinical evaluation of tezepelumab in the treatment of EoE, which is being conducted in the ongoing phase 3 CROSSING study (NCT05583227). CROSSING is a double-blind, placebo-controlled study that will evaluate the efficacy and safety of tezepelumab in approximately 360 patients (12–80 years old) with symptomatic and histologically active EoE. Patients will be randomized (1:1:1) to receive one of two dose options for tezepelumab or placebo subcutaneously every 4 weeks for 52 weeks. The study includes an optional 24-week active treatment extension period in which patients previously receiving placebo will be re-randomized to receive one of the two tezepelumab doses. The co-primary endpoints are to assess the effect of tezepelumab on symptom improvement and histologic response.

Conclusion: Gene lists indicative of elevated TSLP activity were enriched in patients with active EoE (untreated or unresponsive). These data suggest that blocking TSLP with tezepelumab may be a therapeutic option for EoE. The efficacy and safety of tezepelumab in patients with symptomatic and histologically active EoE are being assessed in the ongoing CROSSING study.

Disclosure: J D Sherrill, P G Gavin, L Öberg, T Li, A Péterffy, W Rae, R Tstosoros, R Trivedi, K Domek-Lopacinska, C Seminario, A Platt and D Muthas are employees of AstraZeneca and may own stock or stock options in AstraZeneca. D Ivanič was an employee of AstraZeneca at the time of the study and may own stock options in AstraZeneca; he is a freelance data scientist at Kickresume. S Caveney is an employee of Amgen and owns stock in Amgen.

PP0076

SEX-RELATED DIFFERENCES IN THE PRESENTATION, PHENOTYPE AND COURSE OF EOSINOPHILIC ESOPHAGITIS IN THE EOE CONNECT REGISTRY: THE SEXEOE STUDY

E.J. Laserna-Mendieta^{1,2,3,4}, M.P. Navarro Sánchez^{2,3,4,1}, S. Casabona-Francés^{2,5}, E. Amorena Muro⁶, E. Savarino⁷, I. Pérez-Martínez^{8,9}, L. Blas-Jhon¹⁰, A. Guardiola Arévalo¹¹, M. Coletta¹², G. Pellegatta¹³, D. Guagnozzi¹⁴, J. Barrio¹⁵, M.A. Perelló¹⁶, E. Betoré¹⁷, A.L. Krarup¹⁸, M. Votto¹⁹, C. Gutiérrez-Junquera²⁰, J.E. Naves²¹, S. Oliva²², C. Teruel Sanchez - Vegazo²³, S. Carrión Bolorino^{24,4}, S. de la Riva²⁵, S. Espina²⁶, S. Fernandez-Fernandez²⁷, M. Llorente-Barrio²⁸, J.A. Rodríguez Oballe²⁹, M.L. Masiques-Mas³⁰, R. Honrubia-López³¹, R. Dainese Plichon³², N. Garcia Morales³³, J. Cobián³⁴, J.K. Bisso Zein³⁵, V. Roales³⁶, A. Juan-Juan³⁷, A. Rodríguez-Sánchez³⁸, S. Feo Ortega^{39,3}, V. Martín Domínguez^{2,5}, Ó. Nantes-Castillejo⁶, J. Nicolay Maneru⁶, M. Ghisa⁷, D. Maniero⁷, A. Suárez González^{8,9}, I. Maray Mateos^{9,40}, M. Álvarez-García¹⁰, A. Granja¹¹, F. Racca¹³, R. Llerena Castro¹⁴, C. Santander Vaquero^{4,5}, A.J. Lucendo^{4,2,41,3}, EUREOS and EoE CONNECT research group

¹Hospital General de Tomelloso, Gastroenterology Research Unit, Tomelloso, Spain, ²Instituto de Investigación Sanitaria de La Princesa, Madrid, Spain, ³Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain, ⁴Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ⁵Hospital Universitario de La Princesa, Gastroenterology, Madrid, Spain, ⁶Complejo Universitario de Navarra, Gastroenterology, Pamplona, Spain, ⁷Azienda Ospedaliera di Padova, Surgery, Oncology and Gastroenterology, Padova, Italy, ⁸Hospital Universitario Central de Asturias, Gastroenterology, Oviedo, Spain, ⁹Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Spain, ¹⁰Fundación Jiménez Díaz, Gastroenterology, Madrid, Spain, ¹¹Hospital Universitario de Fuenlabrada, Gastroenterology, Fuenlabrada (Madrid), Spain, ¹²Fondazione IRCCS Cà Granda & Ospedale Maggiore Policlinico, Milan, Italy, ¹³IRCCS Humanitas Research Hospital, Personalized Medicine Asthma and Allergy Clinic, Rozzano, Italy, ¹⁴Hospital Universitario Vall d'Hebron, Gastroenterology, Barcelona, Spain, ¹⁵Hospital Universitario Rio Hortega, Gastroenterology, Valladolid, Spain, ¹⁶Hospital de Viladecans, Gastroenterology, Viladecans (Barcelona), Spain, ¹⁷Hospital Universitario Miguel Servet, Gastroenterology, Zaragoza, Spain, ¹⁸The North Danish Regional Hospital, Hjoerring and Aalborg University, Gastroenterology, Aalborg, Denmark, ¹⁹Università di Pavia, Pediatrics, Pavia, Italy, ²⁰Hospital Universitario Puerta de Hierro & Universidad Autónoma de Madrid, Pediatric Gastroenterology, Majadahonda (Madrid), Spain, ²¹Parc de Salut Mar, Gastroenterology, Barcelona, Spain, ²²University Hospital Umberto I & Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Rome, Italy, ²³Hospital Ramón y Cajal, Gastroenterology, Madrid, Spain, ²⁴Hospital de Mataró, Gastroenterology, Mataró (Barcelona), Spain, ²⁵Clínica Universitaria de Navarra, Gastroenterology, Pamplona, Spain, ²⁶Hospital General de la Defensa, Gastroenterology, Zaragoza, Spain, ²⁷Hospital Universitario Severo Ochoa, Pediatric Gastroenterology, Leganés (Madrid), Spain, ²⁸Hospital de Santa Bárbara, Gastroenterology, Soria, Spain, ²⁹Hospital Universitario Arnau de Vilanova & Hospital Universitario Santa María, Gastroenterology, Lérida, Spain, ³⁰Hospital de Granollers, Pediatric Gastroenterology, Granollers (Barcelona), Spain, ³¹Hospital Universitario Infanta Sofía, Gastroenterology, San Sebastián de los Reyes (Madrid), Spain, ³²Centre Hospitalier d'Antibes Juan-les-Pins, Allergy, Antibes, France, ³³Hospital Universitario Álvaro Cunqueiro, Gastroenterology, Vigo, Spain, ³⁴Hospital Universitario de Donostia, Gastroenterology, San Sebastián, Spain, ³⁵Hospital Costa del Sol, Gastroenterology, Marbella (Málaga), Spain, ³⁶Hospital Clínico Universitario San Carlos, Gastroenterology, Madrid, Spain, ³⁷Hospital Sant Joan Despí Moisès Broggi, Gastroenterology, Sant Joan Despí (Barcelona), Spain, ³⁸Hospital Universitario Santa Lucía, Gastroenterology, Cartagena, Spain, ³⁹Hospital General de Tomelloso, Pediatrics, Tomelloso (Ciudad Real), Spain, ⁴⁰Hospital Universitario Central de Asturias, Pharmacy, Oviedo, Spain, ⁴¹Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain

Contact E-Mail Address: ajlucendo@hotmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder restricted to the esophagus that predominates in males (male:female ratio being around 3:1). The impact of patient sex on the onset, diagnosis and progression of EoE has been barely evaluated, with some reporting no or minor differences (1) while others discovered relevant changes between men and women regarding symptomatology, endoscopic findings and molecular signature (2,3).

Aims & Methods: The study aims to assess potential disparities in EoE presentation and phenotype at the moment of diagnosis, as well as to evaluate whether sex determines difference in disease progression and response to therapy. This is a cross-sectional, multicentre study that includes patients diagnosed with EoE from the EoE CONNECT registry. Demographical and clinical data were obtained from patients recruited at 37 hospitals in 4 European countries. Data extraction was conducted on March 21st, 2024.

Quantitative (age, diagnostic delay, dysphagia symptom score, EREFS endoscopic scale, peak of eosinophils per high power field, number of previous endoscopies, and number of endoscopic dilations) and qualitative (age by groups, phenotype, country, presence of fibro-stricturing findings, atopies, treatments and symptoms) variables were compared. Statistical significance was established for $p < 0.05$.

Results: Data from 2,976 patients (76% males) were retrieved, with no difference in female proportions among countries. Mean $\pm$ SD age at diagnosis was higher for females (34.8 $\pm$ 15.6 vs 32.7 $\pm$ 14.8 years, $p=0.007$), with no differences in diagnostic delay or number of previous endoscopies before diagnosis. Proportion of women diagnosed with EoE at 60 year or older age was twice compared to men (6.4% vs 3.1%, $p<0.001$). Abdominal (6.6% vs 4.4%, $p=0.023$) and epigastric (10.6% vs 8.1%, $p=0.047$) pains, heartburn (27.9% vs 22.0%, $p=0.003$) and dysphagia (79.7% vs 73.3%, $p=0.001$) were significantly more frequent in females; food bolus impaction predominated in males (59.5% vs 50.1%, $p<0.001$). Symptoms intensity measured with the Dysphagia Symptom Score was higher in female patients (6.9 $\pm$ 3.8 vs 6.3 $\pm$ 4.1, $p=0.003$).

Endoscopic features of fibrosis (rings and/or strictures) at baseline endoscopy predominated in males (61.0% vs 51.4%, $p<0.001$). Accordingly, overall EREFS score and its fibrotic sub-score (2.6 $\pm$ 1.7 vs 2.3 $\pm$ 1.6 and 1.0 $\pm$ 1.0 vs 0.8 $\pm$ 1.0, respectively, $p<0.001$), and mixed/stricturing phenotypes were more commonly found in male compared to female patients (25.0% vs 19.3%, $p=0.002$). Peak eosinophil count was higher in females (median 50 vs 42 cells/HPF, $p=0.005$).

No differences were found for first-line treatment choice and effectiveness of anti-inflammatory therapies between men and women. In addition, 126 patients underwent 215 endoscopic dilatation procedures overall, which were slightly more common among male patients (4.5% vs 3.4%, $p=0.187$). In contrast, the median number of dilation procedures was higher in female compared to male EoE patients (2 vs 1; $p=0.001$).

Regarding concomitant atopies, no differences were noted in the prevalence of rhinitis, conjunctivitis and asthma according to sex. However, atopic dermatitis was more common in women (21.7% vs 17.8%, $p=0.028$).

Conclusion: Sexual dimorphism exists in EoE, as observed in other immune-mediated diseases. Despite symptoms severity scored slightly higher in females, EoE in male patients appeared earlier, more commonly with food bolus impaction and with fibro-stricturing endoscopic features at diagnosis.

References: 1. Kozon I, Frandsen LT, Izgi B, et al. No gender differences in patients with eosinophilic oesophagitis. *Dan Med J* 2023;70(2):A06220393
2. Lynch KL, Dhalla S, Chedid V, et al. Gender is a determinative factor in the initial clinical presentation of eosinophilic esophagitis. *Dis Esophagus*. 2016;29(2):174-8.

3. Erwin EA, Jaramillo LM, Smith B, et al. Sex Differences in Blood Transcriptional Profiles and Clinical Phenotypes in Pediatric Patients with Eosinophilic Esophagitis. *J Allergy Clin Immunol Pract*. 2021;9:3350-3358.e8.

Disclosure: Nothing to disclose.

PP0077

RESULTS FROM DOSE ESCALATION IN RESOLVE, AN ONGOING PHASE 1B/2A DOSE-ESCALATION STUDY OF EP-104GI (EXTENDED-RELEASE FLUTICASONE PROPIONATE INTRA-ESOPHAGEAL INJECTION) FOR EOSINOPHILIC ESOPHAGITIS

J. Helliwell¹, A. Malone¹, M. Kowalski¹, A. Bredenoord², N.Q. Nguyen³, H.H. Ko⁴, C. Dobek¹, A. Litke¹, V. Peck¹, M. Webb¹, E.S. Dellon⁵

¹Eupraxia Pharmaceuticals Ltd., Victoria, Canada,

²Amsterdam UMC, Dept. of Gastroenterology, Amsterdam,

Netherlands, ³Royal Adelaide Hospital, Department of

Gastroenterology and Hepatology, Adelaide, Australia, ⁴GI

Research Institute (GIRI), Vancouver, Canada, ⁵University

of North Carolina School of Medicine, Chapel Hill, NC, United States of America

Contact E-Mail Address: amalone@eupraxiapharma.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by inflammation, influx of eosinophils and esophageal remodeling. Therapy for EoE includes swallowed/topical corticosteroids, dupilumab, proton pump inhibitors, and dietary elimination; but these are not always effective.

EP-104GI is an extended-release fluticasone propionate (FP) intra-esophageal injection being developed as a novel treatment for EoE. It consists of polymer-coated FP crystals that release drug locally via diffusion at a pre-defined rate to reduce peak concentrations and prolong the therapeutic window. Preclinical work in pigs has demonstrated that EP-104GI remains at injection sites for at least 6 weeks (duration of the study), with FP spreading 2-4 cm into the surrounding tissue.

Aims & Methods: RESOLVE (NCT05608681) is a Phase 1b, multicenter, open-label, 3+3 design dose-escalation study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of EP-104GI in patients with EoE.

The starting dose of EP-104GI consisted of 1 mg injected at each of 4 sites in 4 quadrants over 2 circumferential areas in the esophagus (4 mg total dose). Dose escalations increase the dose per site and/or number of sites; the second and third cohorts received 1 mg and 2.5 mg respectively at each of 8 sites; the fourth cohort received 2.5 mg at 12 sites (8, 20, and 30 mg total doses).

After a single administration of EP-104GI in these cohorts, participants are assessed for up to 24 weeks. Additional cohorts are planned to evaluate greater dose per injection site and/or increased number of injections with a longer duration of follow-up.

Assessments include Peak Eosinophil Count (PEC) from esophageal biopsies at 16 sites, patient-reported symptom outcomes including the Straumann Dysphagia Index (SDI) and Likert scales for dysphagia and odynophagia, and plasma concentrations of FP. Adverse events (AEs) and laboratory tests including serum glucose and cortisol are assessed.

Results: Cohort 1-3 safety observations include mild-moderate AEs; the majority not related to EP-104GI. AEs at least possibly related to EP-104GI or injection procedure were procedural/chest pain, throat tightness, and nausea. Glucose levels post-dose have remained stable. Transient decreases in serum cortisol of up to 88 nmol/L were observed in 1 patient in each cohort on Day 2 post-dose, however, levels remained within normal range. There have been no symptoms of adrenal insufficiency.

Response data from Cohorts 1 and 2 (Table 1) demonstrate a decrease from baseline in symptom scores at Weeks 12 and 24. Reduction in mean PEC has been observed in all patients in Cohort 2, with a trend indicating that increasing the total dose of EP-104GI results in a more consistent reduction in PEC at the 16 biopsy sites assessed.

	Cohort 1 (1 mg × 4 sites, total 4 mg)	Cohort 2 (1 mg × 8 sites, total 8 mg)
Mean change from baseline (CFB) in Straumann Dysphagia Index (0-9) at Weeks 12 and 24	-4.0, -4.0	-2.7, -3.3
Mean CFB in Dysphagia (0-10) at Weeks 12 and 24	-4.0, -5.0	-4.3, -4.0
Mean CFB in Odynophagia (0-10) at Weeks 12 and 24	-2.0, -3.0	-5.7, -4.3
Mean CFB in PEC at Weeks 4 and 12 (cells/hpf from 16 sites)	No reduction observed	-26%, -44%
Mean plasma concentration of FP at 2 hours post-dose (pg/mL)	4.3	11.2

Table 1: Patient-reported symptom outcomes, peak eosinophil count (PEC), and plasma fluticasone propionate (FP) after a single dose of EP-104GI.

Conclusion: A novel diffusion-based localized delivery of FP via EP-104GI injection into the esophagus is feasible and safe in patients with EoE in this initial escalating dose cohort study. Initial efficacy data show improvement in symptom outcomes and histological findings which may increase with dose. These findings support the potential for extended intervals of at least 6 months between injections. Recruitment is ongoing.

Disclosure: JH, AM, MMK, CD, AL, VP and MW: employees of Eupraxia Pharmaceuticals

ED: Research funding: Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Shire/Takeda Consultant: Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Apollo, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Upstream Bio Educational grant: Allakos, Aqilion, Holoclara, Invea
HHK: advisory board and speaker's bureau for Sanofi.

AJB: received research funding from Nutricia, Thelial, Sanofi/Regeneron, SST, and Dr. Falk Pharma and received speaker and/or consulting fees from Laborie, Medtronic, BMS, Dr. Falk Pharma, Calypso Biotech, Eupraxia, Aqilion, Alimentiv, Sanofi/Regeneron, Reckitt and AstraZeneca

NG: nothing to declare.

PP0078

PERSISTENT DYSPHAGIA IN STRICTURE-FREE EOSINOPHILIC ESOPHAGITIS IN HISTOLOGICAL REMISSION: EFFECTIVENESS OF EMPIRICAL DILATION

L. Cini¹, B. Marinoni², M. Coletta³, G. Aldinio¹, N. Siragusa¹, M. Vecchi⁴, R. Penagini⁵

¹Università degli studi di Milano / Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ²Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy,

³Università degli Studi di Milano Dept. of Gastroenterology, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico University of Milan, Milan, Italy, ⁵Università degli Studi di Milano, Department of pathophysiology and transplantation, Milan, Italy

Contact E-Mail Address: laura.cini@unimi.it

Introduction:

It is known that not all patients with eosinophilic esophagitis (EoE) in histological remission also achieve clinical remission. Several reasons have been postulated among which decreased esophageal compliance without apparent stricture at endoscopy is particularly appealing, but no data are so far available on effectiveness of empirical dilation.

Aims & Methods: Aim of our study was to investigate this topic. A retrospective analysis with prospectively collected data has been conducted on all EoE patients without stenotic features at endoscopy (i.e. no R3/S1 according to EREFS) in whom histological remission with drug and/or diet has been induced in a single referral Center from July 2018 to December 2023. All patients who had not achieved concurrent remission of dysphagia and/or bolus impaction were empirically dilated. At least 6 months of follow-up after remission was needed for inclusion. Demographic, clinical and endoscopic data were compared between patients who needed dilation and those who did not.

Results: A total of 33 patients aged 40; 30-51 yrs (median; IQR range), 23 men, were included. PPI was the main treatment (76% of pts). Nineteen of them (group 1) achieved clinico-histological whereas 14 (group 2) achieved histological remission only and underwent empirical dilation to 15-17 mm with no complications after which clinical remission was achieved in 13 of them. A second dilation was needed in 2 patients at 25 and 31 months respectively, in order to maintain remission. EREFS score at histological remission, but not at diagnosis, was higher in group 2 vs 1 (p=0.02, see table) and was accompanied by a higher % of patients with rings (R1 or R2), 78 vs 37 (p=0.04). A lower % of group 2 patients was treated with topical steroids, 7 vs 26 (p=NS).

	Group 1 (n=19)	Group 2 (n=14)
Age, yrs	37;28-46	44;22-55
Sex, male n (%)	12(63)	11(79)
Symptom duration, months (*)	46;23-102	36;19-77
I-SEE at diagnosis (**)	4;3-5	5;2-6
EREFS at diagnosis	2;1-2	2;0-3
EREFS at histological remission	1;0-2	2;1-2 #
Duration of follow-up, months	12;7-54	20;10-43

(*) up to histological remission, (**) I-SEE= Index of severity of EoE (1), # p=0.02 vs group 1

Conclusion: In our cohort of stricture free EoE patients achieving histological remission, over 40% still had residual obstructive symptoms which were relieved by empirical esophageal dilation in most, suggesting high relevance of decreased esophageal compliance. Prospective multicenter data with use of FLIP are warranted in order to assess if topical steroids are more effective than PPIs in reversing remodeling and avoiding dilation.

References: (1) Dellon ES, Khoury P, Muir AB, Liacouras CA, Safroneeva E, Atkins D, Collins MH, Gonsalves N, Falk GW, Spergel JM, Hirano I, Chehade M, Schoepfer AM, Menard-Katcher C, Katzka DA, Bonis PA, Bredenoord AJ, Geng B, Jensen ET, Pesek RD, Feuerstadt P, Gupta SK, Lucendo AJ, Genta RM, Hiremath G, McGowan EC, Moawad FJ, Peterson KA, Rothenberg ME, Straumann A, Furuta GT, Aceves SS. A Clinical Severity Index for Eosinophilic Esophagitis: Development, Consensus, and Future Directions. Gastroenterology. 2022 Jul;163(1):59-76. doi: 10.1053/j.gastro.2022.03.025. Epub 2022 May 20.

Disclosure: Nothing to disclose.

PP0079

PREDICTIVE HISTOLOGICAL FEATURES OF PROTON PUMP INHIBITOR RESPONSE IN UNTREATED EOSINOPHILIC ESOPHAGITIS PATIENTS

M. Machín Delgado¹, V. Roales Gómez¹, M.J. Fernández Aceñero¹, M. Suárez Solís¹, C. Rodríguez Carrillo¹, Y. Altuzarra Ranedo¹, J. Sánchez César¹, I. Cacho Soblechero¹, C. López Martínez¹, C. Ciriza de los Ríos¹, J.L. Mendoza Hernández¹

¹Hospital Clínico San Carlos, Madrid, Spain

Contact E-Mail Address: mariamacdel@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is an immunoallergic disease of increasing prevalence whose clinical manifestations are due to dysmotility resulting from eosinophil-mediated inflammation. The goal of treatment is the clinical, endoscopic and histological response, with discordant data on predictive criteria. Historically, histological response has been assessed with the intraepithelial eosinophil count until the validation of the Histological Score System (HSS), which includes microabscesses and eosinophilic degranulation, lamina propria fibrosis, intraepithelial lymphocytosis and spongiosis.

Aims & Methods: Our aim is to identify histological features in baseline esophageal biopsies at diagnosis that are predictive of response to proton pump inhibitors (PPI), first line treatment.

A retrospective cohort study, approved by the Ethics Committee of the Hospital Clínico San Carlos, was designed that included incident patients with diagnostic criteria for EoE evaluated between January and December 2022. They underwent a baseline gastroscopy and another after a cycle of PPIs at high doses. After 8-12 weeks induction, two cohorts were established: responders to PPI (PPI-REE) and non-responders (non PPI-REE). Clinical and endoscopic data were collected from reports, and biopsies were reviewed by expert pathologists after anonymisation of the patient cohort.

Histologic variable	Proximal esophagus			Distal esophagus		
	PPI-REE	Non PPI-REE	p value	PPI-REE	Non PPI-REE	p value
Predominance of eosinophils on epithelial surface	3 (6.4%)	2 (11.1%)	0.611	0	0	n. a.
Basal cell hyperplasia	36 (70.6%)	11 (61.1%)	0.458	50 (74.6%)	19 (73.1%)	0.878
Eosinophilic microabscesses	9 (17.3%)	7 (31.8%)	0.218	18 (27.3%)	12 (37.5%)	0.303
Eosinophil activation (degranulation)	16 (31.4%)	18 (81.8%)	<0.001	38 (56.7%)	25 (78.1%)	0.038
Submucosal lamina propria fibrosis	16 (76.2%)	9 (100%)	0.286	33 (97.1%)	11 (100%)	0.015
Intraepithelial lymphocytosis	10 (19.85%)	1 (4.8%)	0.158	13 (20%)	5 (15.6%)	0.602
Spongiosis	9 (17.6%)	17 (77.3%)	<0.001	25 (37.3%)	29 (93.5%)	<0.001
Papillary elongation	7 (53.8%)	1 (14.3%)	0.158	17 (77.3%)	5 (41.7%)	0.062

Results were analysed using IBM SPSS Statistics v.26, with χ^2 or Fisher's exact test for qualitative variables and Student's t-test or non-parametric Mann-Whitney U test for quantitative variables. A binary logistic regression model was used to analyse the association between cohorts and each individual variable, with a significant p-value of 0.005 accepted.

Results: 99 patients with EoE were included, 32 in the non-PPI-REE cohort (32.3%) and 67 in the PPI-REE cohort (67.7%), with no differences in baseline characteristics or endoscopic variables. Histological analysis (Table 1) shows that spongiosis, regardless of location, eosinophilic degranulation in the proximal esophagus and fibrosis of the lamina propria in the distal esophagus are predictive factors for non-response to PPI. However, in multivariate analysis, only the presence of spongiosis, regardless of location, was significant (p 0.021 proximal [95% CI 0.030-0.756] and 0.016 distal [95% CI 0.008-0.611]).

Conclusion: EoE is a growing entity. Being able to predict the response to PPIs at diagnosis would allow clinical improvement and early reduction of inflammation, reducing progression to the fibrostenotic phenotype.

According to our results, we consider it important to universalise the HSS, highlighting the importance of identifying spongiosis, easily identifiable histological changes with low interobserver variability and without additional cost, which could predict the absence of response to PPIs, with patients able to benefit from swallowed corticosteroids or exclusion diets from diagnosis. However, studies with greater power should confirm these data.

Disclosure: Nothing to disclose.

PP0080

PATIENT PREFERENCES REGARDING MEDICAL TREATMENT OPTIONS IN EOSINOPHILIC ESOPHAGITIS

P. Schreiner¹, B. Morell², H. Schlager³, H.P. Gröchenig⁴, K. Steidl⁴, F. Murray², L. Biedermann⁵

¹Medical University of Vienna, Vienna, Austria, ²Stadtspital Triemli, Abt. Gastroenterologie, Zürich, Switzerland, ³Medical University of Graz, Graz, Austria, ⁴Barmherzige Brüder St. Veit, Internal Medicine, St. Veit, Austria, ⁵USZ Zürich, Gastroenterology & Hepatology, Zürich, Switzerland

Contact E-Mail Address: philipp.schreiner@usz.ch

Introduction: Until a few years ago, there existed only off-label medical treatment options for eosinophilic esophagitis (EoE) such as proton pump inhibitors (PPI) or swallowed topical corticosteroids (STC) with various formulations and ingredients. Since the approval of a budesonide orodispersible tablet (BOT), the first biological agent (Dupilumab) has been approved by the EMA and FDA, and another budesonide oral suspension has been received approval by the FDA recently. Currently, many phase 3 trials with different drugs are running, resulting in various treatment options in the next years. However, data about patients' perspectives are lacking. We therefore aimed to assess patients' awareness, beliefs and restrictions to medical treatment options in EoE

Aims & Methods: We developed a web-based survey using SurveyMonkey and sent a questionnaire comprised of 47 questions about patients' preferences regarding medical treatment options to patients with established EoE in Switzerland, Austria and Germany.

Results: A total of 56 patients (64% male, 66% with other atopic diseases) from Switzerland (64%), Austria (34%) and Germany (2%) answered the questionnaire. A swallowed topical therapy was ranked first (71% of patients) in terms of patient's preference followed by a subcutaneous therapy every 4 weeks (21.4%) and by an oral therapy with systemic effect (7%). Although one third do not have reservations against long-term medical therapy, nearly half of patients (42%) are skeptical about long-term treatment and 65% are afraid of adverse events. However, a third of patients are not aware that STC are locally effective medications with nearly no systemic effect. Furthermore, 48% of patients believe that physicians underemphasize adverse events of medication. Nearly all patients understand the importance of not only treating symptoms but also inflammation (85%).

Conclusion: Patients with EoE prefer topical agents over other available routes of administration. Patient education should be carried out to address reservations about long-term treatment.

Disclosure: Falk Pharma, Sanofi (both consultancy meetings).

PP0081

WITHDRAWN

PP0082

RISK FACTORS FOR ORAL AND ESOPHAGEAL CANDIDIASIS DURING BUDESONIDE TREATMENT IN EOSINOPHILIC ESOPHAGITIS PATIENTS

L. Spinelli¹, M. Parmigiani¹, F. Fianchi¹, A. Aruanno¹, F. Castri¹, F.R. Ponziani¹, G. Ianiri¹, A. Gasbarrini¹

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Contact E-Mail Address: irenespinelli1@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic and progressive disease characterized by eosinophil-predominant inflammation of the esophagus. First-line therapy is represented by topical corticosteroids with anti-inflammatory effects, in particular budesonide orodispersible tablets (BOT). Their efficacy and safety are nowadays well established, but very low number of patients develop oral and esophageal candidiasis.

Aims & Methods: The aim of the study is to evaluate risk factors for the development of oral and esophageal candidiasis during budesonide therapy in eosinophilic esophagitis patients. To date, these data have not still been studied. A retrospective study was conducted to include all EoE patients in therapy with BOT referred to Fondazione Policlinico Universitario A. Gemelli IRCCS between March 2022 and November 2023. Prevalence, localization, and time of presentation of candidiasis were evaluated. Histological findings, in particular eosinophilic count in gastroscopy before BOT therapy were analyzed. Concomitant treatment with proton-pump inhibitors (PPI) and its dosage were reviewed. In addition, each case of discontinuation of BOT for disabling candidiasis was studied.

Results: A total of 52 EoE patients in BOT therapy, 44 males and 8 females, were included in the study. 7 patients (13%) developed oral and/or esophageal candidiasis, in particular 6 patients (85%) during induction phase (1 mg bid) and 1 patient (15%) during early maintenance phase (0.5 mg bid). All these 7 patients presented peak eosinophil count >35/HPF before corticosteroid treatment, with mean count of 46 eos/HPF. 4 patients (57%) of this group were in concomitant PPI therapy at 40 mg per day or more dosage. 3 patients (42%) presented recurrent and severe oral candidiasis inducing discontinuation of treatment.

Conclusion: Oral and esophageal candidiasis is a well-known side effect of budesonide orodispersible tablets in eosinophilic esophagitis. Our results suggest that consistent eosinophilic count (> 35/HPF) and concomitant PPI therapy could represent risk factors in developing mycosis in EoE patients. According to literature, major esophageal inflammation, PPI-induced elimination of the gastric acid barrier and corticosteroid immunosuppression are the main mechanisms leading to oral and esophageal candida colonization. Concomitant use of PPI during BOT treatment in eosinophilic esophagitis should be carefully evaluated, especially in patients with elevated eosinophilic count.

References: Lucendo AJ, Miehle K, Schlag C, Vieth M, von Arnim U, Molina-Infante J, Hartmann D, Bredenoord AJ, Ciriza de Los Rios C, Schubert S, Brückner S, Madisch A, Hayat J, Tack J, Attwood S, Mueller R, Greinwald R, Schoepfer A, Straumann A; International EOS-1 Study Group. Efficacy of Budesonide Orodispersible Tablets as Induction Therapy for Eosinophilic Esophagitis in a Randomized Placebo-Controlled Trial. *Gastroenterology*. 2019 Jul;157(1):74-86.e15. doi: 10.1053/j.gastro.2019.03.025. Epub 2019 Mar 26. PMID: 30922997.

Mohamed AA, Lu XL, Mounmin FA. Diagnosis and Treatment of Esophageal Candidiasis: Current Updates. *Can J Gastroenterol Hepatol*. 2019 Oct 20;2019:3585136. doi: 10.1155/2019/3585136. PMID: 31772927; PMCID: PMC6854261.

Daniell HW. Acid suppressing therapy as a risk factor for Candida esophagitis. *Dis Esophagus*. 2016 Jul;29(5):479-83. doi: 10.1111/dote.12354. Epub 2015 Apr 1. PMID: 25833302.

Disclosure: Nothing to disclose.

PP0083

COMPARATIVE PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF A SINGLE DOSE OF CENDAKIMAB IN HEALTHY CHINESE AND US PARTICIPANTS

Y. Chen¹, C. Xue², L. Liu², S. Peng¹, J. Rojo³, W. Kang², S. Basdeo³, B. Wang², Y. Qin², B. Yang², C. De Oliveira³, K. Yu³, M. Thomas³, B. Murthy³, P. Zhang³

¹The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China, ²Bristol Myers Squibb, Shanghai, China,

³Bristol Myers Squibb, Princeton, NJ, United States of America

Contact E-Mail Address: caifu.xue@bms.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic and progressive Type 2 inflammatory disease with a significant unmet need for effective and safe long-term targeted therapy. Cendakimab (CEN) is a recombinant, humanized, high-affinity, neutralizing monoclonal antibody that binds to interleukin 13 (IL-13) thereby blocking interaction with its receptors, IL-13Rα1 and IL-13Rα2. CEN is currently under clinical development for the treatment of EoE.

Here, we present the results of 2 phase 1, randomized, single-center, single-dose trials assessing the pharmacokinetics (PK), safety, and tolerability of CEN in healthy Chinese (NCT05638282) and US (NCT05337345) populations.

Aims & Methods: In the China study (NCT05638282), healthy participants (age, 18–55 years; body mass index [BMI], 18.0–28.0 kg/m²; weight, ≥50.0 kg) were sequentially assigned to 2 groups. Participants in each group were randomized 5:1 to receive: group 1, single-dose CEN 360 mg subcutaneous (SC) via 1 injection (n=10) or placebo (n=2), and group 2, single-dose CEN 720 mg SC via 2 injections (n=10) or placebo (n=2). All doses were administered in the abdomen using an autoinjector (AI). In 1 of 4 groups of the US study (NCT05337345), healthy participants (age, 18–55 years; BMI, 18.0–30.0 kg/m²; weight, ≥40.0 kg) received single-dose CEN 360 mg SC via 1 injection in the abdomen using an AI (n=32). Data from groups that received CEN via AI are presented here. The PK parameters assessed in both studies were maximum observed serum concentration (C_{max}), time of C_{max} (T_{max}), area under the concentration-time curve from time 0 to time of the last quantifiable concentration (AUC_{0-T}), AUC from time 0 to infinite time (AUC_∞), terminal elimination half-life (T_{1/2}), apparent total body clearance (CL/F), and apparent volume of distribution of terminal phase (Vz/F). Safety and tolerability were also evaluated.

Results: Demographic characteristics were generally similar in the China and US studies, eg. median BMI was 23 and 26 kg/m², respectively. In the China study, following SC doses of 360 and 720 mg, the absorption of CEN was slow, with a median T_{max} of 96 and 143 hours; mean T_{1/2} was 565 and 535 hours, and Vz/F was 11.8 and 10.7 liters, respectively (Table).

The geometric mean C_{max}, AUC_∞, and AUC_{0-T} increased in a dose-proportional manner between the 360 and 720 mg CEN doses. Antidrug antibodies (ADAs) were detected in 50% of participants in each of the 360 and 720 mg CEN groups, with a low titer in most of them.

Results for the 360 mg AI group from the China study were consistent with those of the 360 mg AI group in the US study. ADAs were detected in 16% of the participants in the US study. In both studies, the ADA response did not impact the safety or PK of CEN, and CEN (360 mg or 720 mg) was well tolerated with no deaths, serious adverse events (AEs), or discontinuations due to an AE.

Conclusion: Single-dose 360 mg or 720 mg SC CEN was safe and well tolerated in all healthy participants. CEN PK was generally dose-proportional for C_{max} and AUC from 360 mg to 720 mg. Overall, the PK, tolerability, and safety profiles of a single dose of 360 mg SC CEN in the China study were consistent with those observed in the US study, supporting the use of similar doses across both populations.

Study	Cendakimab dose ^a	AUC ₀₋₁₂ ^a , hours*µg/mL	AUC ₀₋₁₂ ^a , hours*µg/mL	C _{max} ^a , µg/mL	Median T _{max} ^a , hours (range)	Mean T _{1/2} ^a , hours (SD)	CL/F, L/h	Vz/F, L
China study	360 mg (n=10)	24,300 (22)	23,000 (23)	29.4 (38)	96 (72–312)	565 (116)	0.015 (22)	11.8 (30)
	720 mg (n=10)	51,200 (26)	49,300 (25)	66.5 (25)	143 (48–311)	535 (108)	0.014 (26)	10.7 (23)
US study	360 mg (n=32)	25,187 (35)	23,908 (34)	29.8 (34)	144 (8–314)	506 (114)	0.014 (36)	10.2 (33)

^aValues are geometric mean (% geometric coefficient of variation), except where otherwise noted.

^bAdministration in the abdomen using an AL.

SD, standard deviation.

Table. Summary of serum pharmacokinetic parameters^a

Disclosure: YC and SP have nothing to disclose; CX, SB, BW, YQ, KY, BM, and PZ are employees of Bristol Myers Squibb; LL, JR, WK, BY, CDO, MT, JM, PZ are employees and stockholders of Bristol Myers Squibb.

PP0084

ANALYSIS OF CLINICAL RESPONSE IN ADULTS WITH EOSINOPHILIC ESOPHAGITIS: PROSPECTIVE COHORT AT A UNIVERSITY HOSPITAL IN CHILE

C. von Muhlenbrock¹, J. Venegas¹, P. Nuñez¹, J. Achondo¹, N. Pacheco¹, K. Herrera¹, F. Castro¹, R. Quera¹

¹Universidad de los Andes, Gastroenterology, Santiago, Chile

Contact E-Mail Address: christianvon@uandes.cl

Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated inflammatory disease that affects the esophagus. In Chile and Latin America, its epidemiology is unknown.

Aims & Methods: The aim of this study is to describe the clinical, endoscopic, and histological characteristics of adult patients diagnosed with EoE. Prospective cohort of patients seen at the Digestive Diseases Center, diagnosed with eosinophilic esophagitis and undergoing one follow-up endoscopy. Endoscopic classification was performed using the Eosinophilic Esophagitis Endoscopic Reference Score (EERS), and histological response was defined as fewer than 15 eosinophils (Eos) per high-power field. Descriptive statistics (median and interquartile range) were used for sample characterization, considering the non-normal distribution of the sample evaluated by the Kolmogorov-Smirnov test. The Chi-square test was used for the analysis of nominal (categorical) or ordinal data. The Wilcoxon test was used for the comparison of histological and endoscopic results, while the Mann-Whitney U test was used for the analysis of medical treatment. Statistical software SPSS[®] v.29 and GraphPad Prism 8.3.0 were used. Values of $p < 0.05$ were considered statistically significant.

Results: Eighty-five patients aged between 17 and 77 years old (Median=36 years) were included, with 75.3% being male. The median age at symptom onset was 31 years and at diagnosis was 34 years. The most frequent reason for consultation was dysphagia (54%), and the most common concomitant immune-allergic diseases were allergic rhinitis (38%) and asthma (29%). Women had more frequent autoimmune comorbidity, peripheral eosinophilia, and food allergies but had a lower eosinophil count and endoscopic score. Regarding treatment, 55% were on PPI therapy and 40% on mixed treatment. In terms of clinical outcomes, patients at admission had a median score of 4 for EERS and 30 eosinophils/field on biopsy eosinophil count. At follow-up, a significant decrease was observed in both endoscopic and histological (biopsy) parameters ($p < 0.001$), with medians of 0 for each indicator, respectively. Moreover, regarding the influence of treatment type (PPI or mixed) on endoscopic or histological response, it was observed that both treatments are equally effective: patients on PPI therapy showed a 72% histological improvement and an 89% endoscopic response, while patients on mixed treatment showed a 77% and 85% improvement, respectively ($p=ns$).

Conclusion: This is the first patient cohort in Latin America to our knowledge with EoE. Characteristics are similar to those described in international groups. Women exhibited more frequent autoimmune comorbidity, peripheral eosinophilia, and food allergies but had a lower eosinophil count and endoscopic score. We did not observe differences among the various therapeutic regimens.

Disclosure: None.

PP0085

TREATMENT PATTERNS AND DISEASE PROGRESSION AMONG PATIENTS WITH EOSINOPHILIC ESOPHAGITIS IN EUROPE: A REAL-WORLD STUDY

U. von Arnim¹, F. Zerbib², T. Pela³, A. Radwan⁴, J.A Jacob-Nara³, B.P. Raphael⁴, R.C. Parikh⁵, F. Bello⁵, G. Le-Bagousse-Bego⁶, R.B. Thomas⁴, S.T. Tilton³

¹University Hospital, Department of Gastroenterology, Hepatology, and Infectious Diseases, Magdeburg, Germany, ²CHU de Bordeaux, Centre Médico-Chirurgical Magellan, Hôpital Haut-Levêque, Department of Gastroenterology, Université de Bordeaux, INSERM CIC 1401, Bordeaux, France, ³Sanofi, Cambridge, MA, United States of America, ⁴Regeneron Pharmaceuticals, Inc., Sleepy Hollow, NY, United States of America, ⁵RTI Health Solutions, Research Triangle Park, NC, United States of America, ⁶Sanofi, Chilly-Mazarin, France

Contact E-Mail Address: Ulrike.vonArnim@med.ovgu.de

Introduction: Eosinophilic oesophagitis (EoE) is a chronic, progressive type 2 inflammatory disease. Proton-pump inhibitors (PPIs), swallowed topical corticosteroids (STCs), and elimination diets have been used as standard treatments for EoE patients. However, the real-world evidence (RWE) highlighting disease burden in Europe are limited.

Aims & Methods: To assess disease burden and treatment patterns among adolescent and adult patients with EoE in real-world practice.

Medical records were retrospectively reviewed for patients (aged ≥ 12 years) who were newly diagnosed with EoE between 1 January 2009 and 31 December 2019 (index) in Germany, France, Spain, and the United Kingdom. Patients with a peak eosinophil (eos) count (PEC) of ≥ 15 eos/hpf within 90 days of the index date and ≥ 1 follow-up endoscopy within 24 months of the index date were included. Demographics, clinical features, treatment patterns, and health outcomes were assessed from the 12-month pre-index period to the last medical record entry or death. Disease progression was assessed via physician-defined (based on symptoms, endoscopy findings, histology, need for dilation, and food impaction) and proxy-reported outcomes (dilation performed, strictures, dysphagia, evidence of food impaction, treatment initiation in treatment-naïve patients and switching/augmentation).

Results: Overall, 385 patients were included, with 70.1%–78.1% being male; the mean age was 27.8 to 33.9 years. At EoE diagnosis, the PEC was 35.3–46.1 eos/hpf, the endoscopic appearance of the oesophagus was abnormal in 73.7%–85.6% of patients, and dysphagia was present in 59.8%–82.8% of patients. Most of the patients across all 4 countries were treated with PPIs (61.5%–91.8%), STCs (56.7%–82.3%) and elimination diets (41.4%–55.2%) after EoE diagnosis. Of the patients with available data, abnormal histology (≥ 15 eos/hpf) was reported in 44.8%–72.0% of patients during the first 5 years after EoE diagnosis. The abnormal endoscopic appearance of the oesophagus was observed in 34.6%–83.3% of patients after approximately 2 years of EoE diagnosis and dysphagia was present in 10.2%–25.0% of patients after 4 years of EoE diagnosis across all 4 countries. While physician-defined disease progression occurred in 6.1%–16.1% of patients, 19.4%–35.1% of patients experienced proxy-reported outcomes of potential disease progression (including oesophageal dilation performed in 10.8%–21.7% of patients) after EoE diagnosis. An

overview of patient and clinical characteristics at EoE diagnosis and treatment patterns and disease progression (physician-defined and proxy-reported) after EoE diagnosis across Germany, France, Spain, and the United Kingdom is provided in the *Table*.

Patient and clinical characteristics at eosinophilic oesophagitis diagnosis	Germany (N=96)	France (N=99)	Spain (N=97)	United Kingdom (N=93)
Male, n (%) / Age, years, mean (standard deviation)	78.1 / 32.0 (14.9)	72.7 / 27.8 (13.4)	70.1 / 32.2 (14.1)	72.0 / 33.9 (13.5)
Peak eosinophil count/ high-power field, mean (standard deviation)	35.3 (29.1)	39.5 (46.3)	46.1 (41.7)	43.3 (56.7)
Treatment patterns and disease progression (physician-defined and proxy-reported) after eosinophilic oesophagitis diagnosis				
Proton-pump inhibitors, n (%)	59 (61.5)	87 (87.9)	89 (91.8)	62 (66.7)
Swallowed topical corticosteroids (e.g., fluticasone budesonide), n (%) / Systemic (oral) corticosteroids, n (%)	79 (82.3) / 24 (25.0)	76 (76.8) / 7 (7.1)	55 (56.7) / 8 (8.3)	55 (59.1) / 4 (4.3)
Dietary modifications or eliminations, n (%)	53 (55.2)	41 (41.4)	46 (47.4)	41 (44.1)
Physician-defined disease progression, n (%)	12 (12.5)	6 (6.1)	7 (7.2)	15 (16.1)
Proxy-reported disease progression, n (%) / dilation performed, n (%)	26 (27.1) / 20 (20.8)	31 (31.3) / 16 (16.2)	34 (35.1) / 21 (21.7)	18 (19.4) / 10 (10.8)
Overall disease progression (Physician-defined OR Proxy-reported), n (%)	33 (34.4)	34 (34.3)	36 (37.1)	30 (32.3)

Table.

Conclusion: Adolescent and adult patients with EoE chronically experienced substantial disease burden. A subset demonstrated disease progression, perhaps underrecognised despite treatment with PPIs, STCs, and elimination diets. Hence, successful EoE management may include proactive disease monitoring, treating underlying pathophysiology and prescribing maintenance therapies to achieve long-term clinical remission.

References:

Disclosure: Ulrike von Arnim: Consulting and/or speaker fees from Dr. Falk Pharma, Sanofi, Astra Zeneca, EsoCap, Abbvie, Janssen, Takeda, Pfizer, Bristol Myers Squibb.
Frank Zerbib: Consulting and/or speaker fees from Sanofi, Dr Falk pharma, Bristol Myers Squibb, Bioprojet, AstraZeneca.
Tiffany Pela, Juby A. Jacob-Nara, Gaëlle Le-Bagousse-Bego, Sarette T. Tilton: Employees of Sanofi; may hold stocks and/or stock options in the company.
Bram P. Raphael, Amr Radwan, Ryan B. Thomas: Employees of Regeneron Pharmaceuticals, Inc.; may hold stocks and/or stock options in the company.
Rohan C. Parikh, Fareedat Bello: Employees of RTI Health Solutions, which received research funding from Sanofi to design and execute this study.
Funding: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.
Acknowledgement: Medical writing support was provided by Akshata Rao and Ali Nasir Siddiqui, PhD, of Sanofi.

PP0086

PATIENTS WITH SEVERE ATOPIC DERMATITIS CANDIDATES TO BIOLOGICAL THERAPY SHOW AN INCREASED PREVALENCE OF DYSPHAGIA: IMPLICATIONS FOR DIAGNOSIS AND MANAGEMENT OF COMORBID ATOPIC DISORDERS

M. Ricchiuti¹, M. Pesce¹, M. Napolitano¹, C. Patruno¹, M. Scalvenzi¹, A. Detoraki¹, I. Di Filippo¹, M. Maniscalco¹, E. Cantone¹, A. Cefaliello¹, G. Sarnelli¹
¹Univers. of Naples ‘‘Federico II’’, Dept. Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: mario.ricchiuti0411@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic Th-2 mediated inflammatory disease, closely associated with comorbid allergic disorders, including atopic dermatitis (AD). Studies show that EoE is associated with atopic conditions but the prevalence of EoE symptoms in patients with atopic conditions is unknown. To date, a single retrospective study involving 80 atopic patients has shown that the prevalence of dysphagia in atopic patients without a known history of EoE is higher than the control population, while it failed to find a significant association between dysphagia and atopic eczema [1].

Therefore, in our study we evaluated the prevalence of dysphagia in a population of patients severe with atopic dermatitis, candidates to biological therapy, in order to consider the possibility of screening these patients for comorbid EoE.

Aims & Methods: Consecutive patients with moderate to severe AD referred to our tertiary care center from January to October 2023 were prospectively screened. Based on AD severity and phenotypic manifestation and comorbidities, patients were referred to systemic therapy with cyclosporine (CsA), biological drugs (dupilumab, tralokinumab) or JAK inhibitors (upadacitinib, abrocitinib, baricitinib). The presence of dysphagia was evaluated by using the self-administered Eosinophilic Esophagitis Score Activity Index (EESAI). This score uses seven PRO (patient reported outcome) items that are used to assess characteristics of dysphagia, behavioral adaptations to living with dysphagia and pain while swallowing. The presence of other atopic disorders and esophageal symptoms was also recorded. Questionnaires were collected and analyzed at the gastroenterology department, while the dermatology consultant was blinded from the questionnaire results. Data are presented as mean±SD.

Results: 147 patients (85 M, 42.7±23) successfully completed the form. The prevalence of dysphagia in the population was low (7 patients, 4.7%). The prevalence of other atopic conditions was similar in dysphagia and non-dysphagia patients (42 vs 40%). Patients reporting dysphagia were more likely to have heartburn (28.5 vs 7.1%, p=0.043), while other esophageal symptoms did not differ. Based on clinical evaluation by a single experienced dermatology consultant (clinical phenotype of AD, AD severity and comorbidities), patients were assigned to either receive CsA (8 pts, 4 M, 41.7±18y), dupilumab (42 pts, 27 M, 39.6±21y), tralokinumab (21 pts, 11 M, 46.2±12.5y), or Jak inhibitors (76 pts, 43 M, 43±23y). The prevalence of dysphagia was significantly higher in the Dupilumab group as compared to other therapies (19 vs 1.9%, p=0.01), while other esophageal symptoms were comparable between the two groups.

Conclusion: We observed that the overall prevalence of dysphagia is relatively low in severe AD patients. However, we found a higher likelihood of complaining of dysphagia in the subset of patients who were candidate to treatment with Dupilumab. Due to the reported augmented risk for atopic patients to develop EoE, screening AD patients complaining of dysphagia before initiating biologic treatment is pivotal to prevent EoE under-diagnosis and under-treatment. Better characterizing the relationship between AD and EoE and a multidisciplinary approach to atopic patients will facilitate the optimal management to both conditions.

References: 1- Eid R, et al. The Prevalence of Dysphagia and Food Impactions is High in Atopic Patients Without a Known History of Eosinophilic Esophagitis (EoE), *Journal of Allergy and Clinical Immunology*, Volume 149, Issue 2, Supplement, 2022, <https://doi.org/10.1016/j.jaci.2021.12.689>.
Disclosure: Nothing to disclose.

PP0087

“THE PATH2 TASK FORCE”: REAL-LIFE EXPERIENCE FROM A MULTIDISCIPLINARY TEAM APPROACH FOR EOSINOPHILIC ESOPHAGITIS

M. Ricchiuti¹, M. Pesce¹, A. Cefaliello¹, V. Catapano¹, M. Falco¹, M. Flaminio¹, M. Napolitano¹, A. Detoraki¹, M. Maniscalco¹, E. Cantone¹, G. Sarnelli¹

¹Univers. of Naples ‘‘Federico II’’, Dept. Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: mario.ricchiuti0411@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a Th2-related disease characterized by dysphagia and food impaction. EoE has been associated with several other atopic disorders, supporting the knowledge that it may represent a late manifestation of the so-called “atopic march”. However; in everyday clinical practice, allergic comorbidities are rarely objectivized by means of specialist consultations and often rely on patients’ self-reporting. This bears the risk of not fully recognizing the burden of Th2-related pathology, since EoE patients may outgrow some of the allergic diseases presenting during childhood; or, conversely, they could underestimate the presence and severity of Th2-diseases. To this aim, a multidisciplinary task-force involving multiple specialists was established at our university hospital, in order to systematically investigate newly referred EoE patients.

Aims & Methods: This is a cross-sectional observational study, involving consecutive EoE patients that were referred to our tertiary center from January 2022. We prospectively collected data about patients’ clinical history, specifically recording the presence of Th2-related comorbidities. Each patient underwent an esophagogastroduodenoscopy with differential esophageal biopsies. After reaching a conclusive diagnosis of EoE, patients were referred to dermatology, ear, nose and throat specialist (ENT) for rhinofibroscopy, immunologist (performing prick test, as necessary) and respiratory consultant for spirometry.

Results: 40 EoE patients were included (34M, age 31±12 years), with a mean age of onset of 23±16 years. A clinical history of Th2-comorbidities was reported by 90% of the overall population with rhinitis being the most prevalent comorbidity (77.5%), while no patient reported Chronic Rhinosinusitis with Nasal Polyps (CRwNP). Asthma, food allergy and atopic dermatitis (AD) were reported in 15 (37.5%), 14 (35%) and 9 (22.5%) patients, respectively. Following the consultations, the presence of asthma, food allergy and AD did not significantly differ (37.5 vs 30%, 35 vs 45% and 22.5 vs 20%), since only 3 patients reporting a history of asthma did not confirm the diagnosis at spirometry and one patient with a history of AD had dermographic urticaria. On the contrary, following ENT consultation, 6 patients with rhinitis received the diagnosis of CRwNP (0 vs 15%, p=0.01). Overall, nearly 60% of patients had two comorbid Th2 disorders besides EoE and 25% of the whole population of EoE patients had 3 or more.

Conclusion: Our results clearly support the need for a multidisciplinary team approach to investigate the burden of Th2-related pathology in EoE patients. In our hands, the prevalence of Th2-related comorbidities was as high as 97.5% of EoE patients and up to 63% of our population had 2 or more allergic disorders. Furthermore, CRwNP is frequently under-reported and properly diagnosed only following rhinofibroscopy. This is further from being irrelevant when managing EoE patients. Indeed, it may guide

the most appropriate choice of therapy by targeting multiple atopic manifestations at the same time, since many Th2-related diseases share common pathophysiological mechanisms and treatment.

Disclosure: Nothing to disclose.

PP0088

RETROSPECTIVE ANALYSIS OF DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS IN A TERTIARY CENTRE

Y.J. Chew¹, K. Maqbool¹, A.M. Thant¹, A.K. Kurup¹

¹University Hospitals of North Midlands, Stoke-on-trent, United Kingdom, ²Royal Stoke University Hospital, Dept. of Gastroenterology, Stoke on Trent, United Kingdom

Contact E-Mail Address: khawaja.maqbool@uhnm.nhs.uk

Introduction: Eosinophilic Oesophagitis (EOE) has a mean estimate of 63 new cases per 100,000 in the Western World and is in increasing prevalence¹. It must be considered as a differential diagnosis amongst patients presented with dysphagia and food bolus obstruction. British Society of Gastroenterology (BSG) guideline recommends that patients undergoing endoscopy should have oesophageal biopsies taken if they have endoscopic signs associated with EOE or symptoms of dysphagia or food bolus obstruction with normal looking oesophagus. At least six biopsies should be taken from at least 2 different anatomical sites within the oesophagus for diagnosis of EOE². (GDG recommendation).

Aims & Methods: A single-centre, retrospective analysis of patients presenting for an oesophagogastroduodenoscopy (OGD) with an indication of dysphagia or food bolus obstruction and coded as oesophagitis over the past 5 years was performed. The study was undertaken at a tertiary NHS Hospital Trust in West Midlands which provides hospital services for approximately 900,000 people³.

Data was then collected for demographics, sedation, macroscopic findings, quality and location of biopsies as well as histology. This is measured against BSG recommendations.

Results: In total, 31 patients were included. 68% of patients were male and the mean age was 53 (range 14-90) 35% (n=11) had pharyngeal anaesthesia only, 16% (n=5) had midazolam and pharyngeal anaesthesia, 35% (n=11) had midazolam and fentanyl and 6% (n=2) had general anaesthesia (GA). Both patients who had GA were 14 and 15 years old. In terms of macroscopic findings, 61 % (n=19) had normal findings, 19% (n=6) had oesophagitis, 10 % (n=3) had EOE changes and 3% (n=1) had benign stricture with the same number for achalasia and tertiary contraction. 81% (n=25) had biopsies taken from at least 2 different anatomical sites and 32% (n=10) had more than 6 biopsies taken in total. There were 29 % (n=9) patients with a histological diagnosis of EOE, 29% was normal, 29% (n=9) had inflammation, 6% (n=2) had gastric metaplasia, 3% (n=1) had basal hyperplasia with 7-8 eosinophils per high-power field (HPF) and 3% (n=1) had basal hyperplasia with lymphocytic infiltration. In all patients with EOE, the histopathological report explicitly documented the presence of >15 eosinophils per HPF.

Conclusion: Our data suggest that our practice for diagnosis of EOE falls short of national recommendation, both in the number of anatomical sites and the number of biopsies taken. In terms of histopathology, we have adhered to the recommended diagnostic criteria of >15 eosinophils per HPF. Further work must be done to improve awareness and adherence to the guidelines for the diagnosis of this treatable condition.

References:

1. Navarro P, Arias Ángel, Arias-González L, et al. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. *Aliment Pharmacol Ther* 2019;49:1116–25.

2. Dhar A, Haboubi HN, Attwood SE, et al. British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. *Gut* 2022;71:1459-1487.

3. University Hospitals of North Midlands. *About us*. <https://uhnm-appointments.co.uk/about-us/> [Accessed 23rd November 2023]

Disclosure: Nothing to disclose.

PP0089

ESOPHAGEAL BIOPSY SAMPLING AMONG PATIENT WITH DYSPHAGIA. TO BITE OR NOT TO BITE?

T. Alexopoulos¹, T. Voulgaris¹, J. Vlachogiannakos¹, D. Kamberoglou¹, A. Koutsoumpas¹, K. Papaxoinis¹, P. Fytili¹, G. Papatheodoridis¹, G. Karamanolis¹
¹National and Kapodistrian University, Laiko General Hospital, Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: georgekaramanolis@yahoo.co.uk

Introduction: Dysphagia is a very common symptom and entities such as Eosinophilic Esophagitis (EoE) or an esophageal motility disorder can be its basis. A controversy among guidelines when approaching a patient with dysphagia exists, as it is mandated to obtain esophageal sampling when EoE is sought but is not a prerequisite for motility disorders diagnosis. Therefore, the necessity of esophageal sampling is based on endoscopists' assessment.

Aims & Methods: Aim of our study was to search for factors driving clinicians to obtain esophageal biopsies among patients with dysphagia. Secondary aim was to search for the incidence of EoE and factors correlated with EoE diagnosis among patients with dysphagia.

We included consecutive patients presented with dysphagia during a 6-year period (1/2018-12/2023). We excluded patients with a history of; esophageal stenosis, esophageal motility disorders, metastatic disease, EoE, esophageal/gastric cancer, carcinoma that could impair esophageal motility, bone/food impaction, caustic agent ingestion, esophagogastric surgeries as also severely immune-compromised patients (HIV, recently transplanted).

Furthermore, 58 patients were excluded as they showed endoscopic evidence of another disease that could explain patients' symptoms. Epidemiological, endoscopy and histological data were collected and analyzed.

Results: We included 63 patients (M/F: 29 (46.0%)/34 (54.0%), mean age 64±19 yrs). A history of dysphagia > 6 months was reported by 51 (80.9%), while <6 by 11 (19.1%). During the endoscopy; 7 (11.1%) had findings supportive of EoE, and 56 (89.9 %) had normal endoscopy. Biopsies were obtained by 30/63 (47.6%).

Significant higher rates of biopsy sampling were seen among patients <65 years old and with endoscopic EoE signs, while dysphagia duration and sex did not affect sampling. In the multivariate analysis only age, but not endoscopic findings compatible to EoE, drove clinician decision to obtain biopsies. (Table)

We were able to retrieve the histology report of 29/30 patients. EoE was diagnosed in 4/29 (13.8%). All patients with EoE were male (4/14, 28.6% vs female 0/15, 0% p=0.042). Existence of compatible endoscopic signs (3/6, 50% vs normal endoscopy 1/23, 4.3% p=0.020) was correlated with EoE diagnosis but age (<65 years old 4/22, 18.7% vs <65 year old 0/7, 0% p=0.307) and longstanding dysphagia (4/25, 16% vs female 0/4, 0% p=0.533) were not.

Factor	Biopsy sampling among patients with Dysphagia (patients without endoscopic findings other than EoE that could explain patients symptoms)	
	Univariate p	multivariate p
Younger than 65 years	25/35, 75.4%	<0.001
65 years and older	5/28 17.9%	OR: 0.092, 95% C.I.: 0.025-0.339
Male	12/29 41.4%	0.450
Female	18/34 52.9%	
Findings compatible to EoE	7/7 100%	0.004
Normal endoscopy/other findings	23/56 41.1%	0.099 OR: 21.327, 95% C.I.: 18,298-35.474
history of dysphagia <6 months	5/11 45.5%	0.989
history of dysphagia>6 months	25/52 48.1%	

Conclusion: Clinician obtain esophageal biopsies in less than 50% of patients with dysphagia. Endoscopic findings supportive of EoE and most importantly age seem to drive their decision. The rate of EoE among patients with dysphagia and esophageal sampling is not negligible and is more commonly observed in young males with longstanding dysphagia and compatible endoscopic findings.

Disclosure: Nothing to disclose.

PP0090

ENDOSCOPIC INDICATORS OF INSULIN RESISTANCE: ASSOCIATIONS WITH EROSIVE ESOPHAGITIS AND REGULAR ARRANGEMENT OF COLLECTING VENULES (RAC)

H. Hong¹, H.T. Lee¹, J.-y. Seo¹
¹Bundang Jesaeng General Hospital, Gastroenterology, Seongnam-si, South Korea

Contact E-Mail Address: whoim1020@nate.com

Introduction: With the increasing westernization of lifestyles, there has been a significant rise in obesity, leading to a growing interest in metabolic syndrome and insulin resistance. Identifying indicators of insulin resistance through endoscopic findings could be valuable in assessing a patient's systemic metabolic status. Thus, we conducted a retrospective study to explore the association between endoscopic findings and insulin resistance.

Aims & Methods: We retrospectively investigated the patients who underwent screening endoscopy at Bundang Jesaeng General Hospital between February and June 2023. We excluded patients who were not tested for insulin resistance. Insulin resistance was defined using Homeostatic Model Assessment for Insulin Resistance (HOMA_{IR}), with a value above 1.9. We also assessed the *Helicobacter pylori* (*H. pylori*) status using rapid urease test, and history of previous eradication into current infection, non-infection, and past infection. To ensure balanced variables between the two groups, we performed propensity score matching (1:2 ratio) based on age and *H. pylori* status. Multivariate analysis was performed to investigate the association between the endoscopic features and insulin resistance.

Results: Following propensity score matching, we selected 210 patients with insulin resistance and 420 patients without insulin resistance were selected. In baseline characteristics, age and *H. pylori* status were balanced between the two groups. Prior to propensity score matching, endoscopic findings including erosive esophagitis, RAC (regular arrangement of collecting venules), atrophy, and diffuse redness appeared to be significant associated with insulin resistance. However, after matching, only erosive esophagitis remained significantly associated with insulin resistance. Furthermore, the severity of erosive esophagitis showed positive correlation with the degree of insulin resistance, as indicated by increased HOMA_{IR}. Multivariate analysis demonstrated that erosive esophagitis (OR 1.81, *p* = 0.010) significantly raised the risk of insulin resistance while RAC was associated with a lower risk of insulin resistance (OR 0.68, *p* = 0.032).

Conclusion: Our study showed an obvious correlation between insulin resistance and erosive esophagitis, as well as RAC among the endoscopic findings.

Moreover, we observed a proportional relationship between the severity of erosive esophagitis and the degree of insulin resistance. Multivariate analysis showed that erosive esophagitis and RAC were significantly associated with the insulin resistance.

These findings suggest that individuals with erosive esophagitis and without RAC should undergo metabolic evaluation to assess their insulin resistance status. Further research is warranted to explore the underlying mechanisms and potential implications of these associations.

Disclosure: Nothing to disclose.

PP0091

THE EPIDEMIOLOGY AND SYMPTOMATIC CHARACTERISTICS OF REFLUX ESOPHAGITIS SUBGROUPS BASED ON THE LYON 2.0 CONSENSUS: A POPULATION-BASED STUDY

K. Wang¹, L. Duan², N. Hu², Z. Liu³

¹Peking University Third Hospital, Department of Gastroenterology, Beijing, China, ²Peking University Third Hospital, Beijing, China, ³Peking University Third Hospital, Gastroenterology, Beijing, China

Contact E-Mail Address: wangkun5555@sina.com

Introduction: Reflux esophagitis (RE) can present typical symptoms, atypical symptoms or asymptomatic. The proportions and epidemiology characteristics of these three symptomatic patterns of RE has not been clarified. The Lyon 2.0 consensus provides new conclusive criteria for RE diagnosis and adjusts the symptom spectrum. Thus, the RE subgroups were redefined.

Aims & Methods: The aim of this study was to clarify the prevalence and symptomatic characteristics of RE subgroups based on the update Lyon 2.0 consensus in a Chinese population. An Endoscopic Screening for Esophageal Cancer in China (ESECC) randomized controlled trial was initiated in Hua County in January 2012, a gastroesophageal reflux disease (GERD) database was constructed. This data was reviewed to analyze the subgroups of RE based on the Lyon 2.0 consensus. RE were divided into three subgroups: typical reflux symptoms (TSRE), atypical symptoms (ASRE) and asymptomatic RE (ARE). The rest esophagitis was inconclusive-GER esophagitis. Chi-square test was used for differences between groups.

Results: In this study, 2916 residents were enrolled. 271 (9.29%) participants had esophagitis, among them, 143 (4.87%) fulfilled the conclusive RE diagnosis based on the Lyon 2.0 consensus. In RE, 97 (67.83%) was TSRE, 11(7.69%) was ASRE and 35 (24.48%) was ARE. 115 esophagitis belonged to inconclusive-GER esophagitis group. The age (≥ 60 years), male sex, Body Mass Index (BMI) (≥ 24 kg/m²), and smoking were risk factors for TSRE. Smoking was also a risk factor for ARE (OR [95%CI]:4.521 (1.448, 14.113)).

Conclusion: This population-based study reported that 9.29% of residents had erosive esophagitis. The point prevalence rate of RE was 7.75%, according to the updated Lyon 2.0 consensus. ARE LA-B and non-RE EE are common. Smoking is a risk factor for ARE. The findings of this study can be beneficial in the diagnosis, prevention, and establishing the screening system for RE. A well-designed screening strategy and long-term follow-up study should be conducted for ARE and non-RE EE in the future.

References: 1.Vakil N, van Zanten SV, Kahrilas P et al.; Global Consensus Group. The Montreal definition and classification of gastro- esophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; 101:1900–20; quiz 1943.

2.Gyawali CP, Yadlapati R, Fass R, et al. Updateds to the modern diagnosis of GERD: Lyon consensus 2.0. *Gut*, 2023;0,1:1-11. Doi:10.1136/gut-jnl-2023-330616

Disclosure: All Authors declare that they have no conflict of interest.

PP0092

THE FREQUENCY OF GASTROESOPHAGEAL REFLUX AND RELATED FACTORS IN PERSIAN GUILAN COHORT STUDY (PGCS)

F. Joukar¹, S. Maroufizadeh², H. Olfati¹, F. Sheida¹, M. Naghipour¹, F. Mansour-Ghanaei¹

¹Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran, ²Department of Biostatistics, School of Health, Guilan University of Medical Sciences, Rasht, Iran

Contact E-Mail Address: fmansourghanaei@gmail.com

Introduction: Gastroesophageal reflux disease (GERD) is a prevalent digestive disorder characterized by the symptoms of heartburn and regurgitation. In recent years, the epidemiological characteristics of GERD have been studied due to its increasing prevalence and associated issues.

Aims & Methods: In the current study, we aimed to evaluate the prevalence of GERD among the Prospective Epidemiological Research Studies (PERSIAN) Guilan Cohort study (PGCS) population. This cross-sectional study was conducted on the PGCS population in Guilan, Iran. Demographical data and clinical characteristics of individuals were recorded, and a specialist applied the diagnosis of GERD. The association between variables and GERD was evaluated using SPSS version 17 based on a significant level <0.05.

Results: Out of 10520 participants, 5633 were female, and the mean age of individuals was 51.52 $\pm$ 8.9 years. The prevalence of GERD was 13.2% and it was most prevalent among females. The frequency of GERD was higher in unemployed individuals, individuals with a higher level of education, body mass index (BMI), higher waist-hip ratio (WHR), and a lower level of physical activity. In addition, patients with a higher number of underlying diseases, a history of hypertension, and the use of non-steroidal anti-inflammatory drugs (NSAIDs) had a higher prevalence of GERD (P<0.05). The multivariate analyses revealed that females, urban residents, and individuals with higher levels of education had greater odds of GERD (P<0.05). Moreover, with the increase in the number of underlying diseases, the odds of having GERD increased (P<0.001).

Conclusion: Our findings showed factors such as female gender, higher level of education, urban residency, and higher number of underlying diseases were associated with increased risk of GERD. Identifying the associated factors will allow specialists to better diagnose and control the GERD.

References: 1.Nocon M, Keil T, Willich SN. Prevalence and sociodemographics of reflux symptoms in Germany—results from a national survey. *Aliment Pharmacol Ther*. 2006;23(11):1601–5.

2.Çela L, Kraja B, Hoti K, Toçi E, Muja H, Roshi E, et al. Lifestyle characteristics and gastroesophageal reflux disease: a population-based study in Albania. *Gastroenterol Res Pract*. 2013;2013.

3.Sharma PK, Ahuja V, Madan K, Gupta S, Raizada A, Sharma MP. Prevalence, severity, and risk factors of symptomatic gastroesophageal reflux disease among employees of a large hospital in northern India. *Indian J Gastroenterol*. 2011;30:128–34.

4.Boltin D, Boaz M, Aizic S, Sperber A, Fass R, Niv Y, et al. Psychological distress is not associated with treatment failure in patients with gastroesophageal reflux disease. *J Psychosom Res*. 2013;75(5):462–6.

5.Chen T, Lu M, Wang X, Yang Y, Zhang J, Jin L, et al. Prevalence and risk factors of gastroesophageal reflux symptoms in a Chinese retiree cohort. *BMC Gastroenterol*. 2012;12(1):1–7.

Disclosure: Nothing to disclose.

PP0093

PREVALENCE OF REFLUX ESOPHAGITIS AND BARRETT'S ESOPHAGUS IN PORTUGAL: A MULTICENTER POPULATION-BASED ENDOSCOPIC STUDY

P. Pimentel-Nunes¹, R.P. Bastos¹, T. Moreira¹, M. Rocha², R.F. Veloso¹, I. Marques de Sá¹, C. Bernardes², M.T.d.A.P. Pais¹, M. Bento-Miranda¹, F. Barreto³, L. Prado Castro³, A. Maia-Gonçalves⁴, L. Rafael⁴, R. Panzeri-Rodrigues⁴

¹Unilabs Portugal, Gastroenterology Department, Porto, Portugal,

²Unilabs Portugal, Gastroenterology Department, Lisbon, Portugal, ³Unilabs Portugal, Pathology Department, Porto, Portugal, ⁴Unilabs Portugal, Porto, Portugal

Contact E-Mail Address: pedronunesml@gmail.com

Introduction: The incidence of esophageal adenocarcinoma has been increasing in Western countries, with gastroesophageal reflux (GERD) and Barrett's esophagus (BE) being important risk factors for such diagnosis. In Portugal, the current prevalence of reflux esophagitis and BE is unknown, and the aim of this study is to clarify these points.

Aims & Methods: A multicenter cross-sectional study including 13 national digestive endoscopy units, involving patients who underwent upper endoscopy from January to March 2024.

Results: 6320 patients were included (57% female, mean age 58). Reflux esophagitis was identified in 1105 patients (17% of the exams, 54% male, mean age 57) (Los Angeles Grade A 10.1%; B 5.6%; C 1.1%; D 0.4%) and 46 with BE (0.7% (95%CI 0.05-1%), 67.4% male, mean age 59 years), with only 4 (0.06% of the total) having 3 cm or more of extension.

The prevalence of BE was higher in the Lisbon region (1.35% vs 0.5%, $p<0.05$), with no difference in the prevalence of reflux esophagitis. Among patients who underwent endoscopy for GERD symptoms, 38% had erosive esophagitis ($p<0.05$ vs the rest of the population).

Among patients with esophagitis and BE, 27% and 39%, respectively, underwent endoscopy for symptoms and/or surveillance related to GERD (vs 11.6% of the rest of the population, $p<0.05$), with a prevalence of BE in patients with GERD of 2.3% (95%CI 2.1-2.5%, $p<0.05$ vs the rest of the population). Male gender was a risk factor for grade C/D esophagitis and BE ($p<0.05$).

Conclusion: Erosive esophagitis is common in Portugal, particularly in patients undergoing endoscopy for GERD symptoms. However, the prevalence of BE, particularly long segment BE, remains low compared to other Western countries, despite similar values of reflux esophagitis. This trend may be reversing in Lisbon with a higher prevalence of BE. Further studies are necessary to better understand these differences.

Disclosure: Nothing to disclose.

PP0094

HIGH-RESOLUTION MANOMETRY FEATURES CAN SEGREGATE NON-SEVERE FROM SEVERE GASTRO-ESOPHAGEAL REFLUX DISEASE

M. Sozzi¹, S. Siboni¹, P. Visaggi², B. Rogers³, A. Hobson⁴, B.E. Louie⁵, Y.Y. Lee⁶, S. Tolone⁷, I. Kristo⁸, E. Marabotto⁹, J. Haworth⁴, M.I. Ivy⁵, A. Lovece¹, D. Theodorou¹⁰, T. Triantafyllou¹⁰, C. Facchini⁹, V. Tee⁶, L. Cusmai¹, D. Bernardi¹, D. Kollmann⁸, T. Masuda¹¹, R. Penagini¹², M. Coletta¹³, S. Schoppmann⁸, N. De Bortoli², E.V. Savarino¹⁴, E. Asti^{1,15}, CP. Gyawali¹⁶

¹IRCCS Policlinico San Donato, General and Emergency Surgery, San Donato Milanese, Italy, ²Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ³Washington University in St. Louis, Gastroenterology, Louisville, United States of America, ⁴The Functional Gut Clinic, London, United Kingdom, ⁵Swedish Medical Center, Digestive Health Institute, Division of Thoracic Surgery, Seattle, United States of America, ⁶Universiti Sains Malaysia, Kota Bharu, Malaysia, ⁷Università degli Studi della Campania "Luigi Vanvitelli", Surgery, Naples, Italy, ⁸Medizinische Universität, Upper-GI-Service, Wien, Austria, ⁹POLICLINICO SAN MARTINO, Genova, Italy, ¹⁰University of Athens School of Medicine, Department of Surgery, Athens, Greece, ¹¹The Jikei University School of Medicine, Surgery, Tokyo, Japan, ¹²Università degli Studi di Milano, Department of pathophysiology and transplantation, Milan, Italy, ¹³Università degli Studi di Milano Dept. of Gastroenterology, Milan, Italy, ¹⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ¹⁵University of Milan, Milan, Italy, ¹⁶Washington University School Of Medicine, St Louis, Mo, Division Of Gastroenterology, St Louis, United States of America

Contact E-Mail Address: marco.sozzi@grupposandonato.it

Introduction: Gastro-esophageal reflux disease (GERD) is a multifactorial disease that manifests in patients with different degrees of anti-reflux barrier impairment. GERD significantly impacts quality of life despite the fact that symptom burden may not always correlate with disease severity. Precise pathophysiologic evaluation can identify patients with actionable GERD who may benefit from anti-reflux surgery or escalation of medical therapy.

The Milan Score, a novel high-resolution manometry (HRM) metric, numerically quantifies the degree of anti-reflux barrier disruption¹. While the Milan Score has been proven to predict pathologic GERD, its ability to distinguish non-severe from severe GERD and to identify patients with a higher grade of anti-reflux barrier disruption requires further study.

Aims & Methods: A database of prospectively collected data from a cohort of patients undergoing HRM and pH-study for persistent GERD symptoms was queried. Using Lyon 2.0 consensus, pathologic GERD was defined as AET >6%, grade B-C-D esophagitis or Barrett's esophagus on endoscopy. Severe reflux was defined as AET >12%, DeMeester score >50, grade C-D esophagitis or Barrett's esophagus².

Demographic, HRM and pH data were extracted, classified and compared between groups with varying GERD severity (no GERD, non-severe GERD, severe GERD). The Milan Score integrates the main manometric parameters related with the pathophysiology of GERD (ineffective esophageal motility, esophago-gastric junction (EGJ) contractile integral, EGJ morphology and straight leg raise maneuver response).

In order to simplify the use of the Milan Score, risk rates have been classified into six categories, from extremely unlikely to extremely likely. A cumulative odds ordinal logistic regression was run to determine the independent effect of HRM variables on reflux severity. The ability of the Milan Score to predict severe reflux was assessed, as well as its association

with the pH-study criteria proposed by Lyon 2.0 as adjunctive evidence for pathologic GERD (>80 reflux episodes, mean nocturnal baseline impedance (MNBI) <1500 W or positive reflux-symptom association).

Results: Among 603 patients enrolled (median age 49.9 years, median body mass index (BMI) 25.3 Kg/m², 50.5% males), 124 (20.6%) had non-severe and 142 (23.5%) had severe GERD. Non-severe and severe GERD patients had similar demographic and clinical characteristics, but were significantly different from the no-GERD group (Table). On univariate analysis, presence and size of hiatal hernia, Milan Score and Milan Score categories were significantly different among the groups ($p < 0.001$). On ordinal logistic regression, hiatal hernia size and Milan Score category were found to be independent predictors of GERD severity (OR 1.28, 95% CI, 1.04-1.57, $p = 0.018$ and OR 2.92, 95% CI, 2.47-4.45, $p < 0.001$ respectively). A significantly higher Milan Score ($p < 0.001$) was found in patients with >80 reflux episodes, MNBI <1500 W, positive reflux-symptom association and any criteria of severe GERD.

	Total (n=603)	No GERD (337)	Non severe GERD (n=124)	Severe GERD (n=142)	p-value
Female, n (%)	282 (49.5)	178 (56.2)a	54 (45.4)a,b	50 (37.3)b	<0.001
Age, (years)	49.9 (14.6)	48.6 ± 15.9 a	51.4 ± 13.5 a,b	52.0 ± 14.2 b	0.044
BMI, (Kg/m ²)	25.3 (5.8)	24.7 ± 23.8 a	25.9 ± 5.6 b	26.3 ± 5.1 b	<0.001
PPI use, n (%)	450 (79.8)	232 (73.9)a	105 (89.7)b	113 (85.0)b	<0.001
PPI non responders, n (%)	139 (30.6)	88 (37.4)a	31 (29.2)a,b	20 (17.7)b	0.002
EGD hiatal hernia, n (%)	327 (59.2)	145 (47.9)a	84 (71.8)b	98 (74.2)b	<0.001
EGD Esophagitis, n (%)	168 (30.6)	60 (19.9)a	42 (36.2)b	66 (50.0)b	<0.001

Conclusion: Hiatal hernia size and Milan Score assessed at HRM are independent factors associated with severe GERD. The Milan Score is significantly higher in patients with pathologic adjunctive pH-impedance metrics and in patients with severe GERD.

References: 1. Siboni S, Sozzi M, Kristo I et al. The Milan score: A novel manometric tool for a more efficient diagnosis of gastro-esophageal reflux disease. *United European Gastroenterol J*. 2024 Mar 27. doi: 10.1002/ueg2.12565. Epub ahead of print. PMID: 38536701.

2. Horvath KD, Jobe BA, Herron DM et al. Laparoscopic Toupet fundoplication is an inadequate procedure for patients with severe reflux disease. *J Gastrointest Surg*. 1999 Nov-Dec;3(6):583-91. doi: 10.1016/s1091-255x(99)80079-1. PMID: 10554364.

Disclosure: Nothing to disclose.

PP0095

PHYSIOLOGIC CHARACTERISTICS OF PATIENTS WITH ESOPHAGOGASTRIC JUNCTION TYPE 2 MORPHOLOGY ON HIGH-RESOLUTION MANOMETRY HELP IDENTIFY PATHOLOGIC GASTRO-ESOPHAGEAL REFLUX DISEASE

S. Siboni¹, D. Ferrari¹, M. Sozzi¹, P. Visaggi², I. Kristo³, S. Tolone⁴, E. Marabotto⁵, D. Bernardi¹, S. Schoppmann³, D. Kollmann³, B. Rogers⁶, A. Hobson⁷, J. Haworth⁷, Y.Y. Lee⁸, B.E. Louie⁹, T. Masuda¹⁰, M.I. Ivy⁹, P. Milito¹, D. Theodorou¹¹, T. Triantafyllou¹¹, C. Facchini⁵, V. Tee⁸, R. Penagini¹², M. Coletta¹², E.V. Savarino¹³, E. Asti^{1,14}, CP. Gyawali¹⁵, N. De Bortoli²

¹IRCCS Policlinico San Donato, General and Emergency Surgery, San Donato Milanese, Italy, ²Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ³Medizinische Universität, Upper GI service, Wien, Austria, ⁴Università degli Studi della Campania "Luigi Vanvitelli", Surgery, Naples, Italy, ⁵POLICLINICO SAN MARTINO, Genova, Italy, ⁶Washington University in St. Louis, Gastroenterology, Louisville, United States of America, ⁷The Functional Gut Clinic, London, United Kingdom, ⁸Universiti Sains Malaysia, Kota Bharu, Malaysia, ⁹Swedish Medical Center, Digestive Health Institute, Division of Thoracic Surgery, Seattle, United States of America, ¹⁰The Jikei University School of Medicine, Surgery, Tokyo, Japan, ¹¹University of Athens School of Medicine, Athens, Greece, ¹²Università degli Studi di Milano, Department of pathophysiology and transplantation, Milan, Italy, ¹³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ¹⁴Università degli Studi di Milano, Milan, Italy, ¹⁵Washington University School Of Medicine, St Louis, Mo, Division Of Gastroenterology, St Louis, United States of America

Contact E-Mail Address: stesibo@gmail.com

Introduction: Gastroesophageal Reflux Disease (GERD) is a common condition diagnosed by endoscopy and/or pH monitoring. However, only high-resolution manometry (HRM) provides detailed assessment of the pathophysiology underlying reflux mechanisms and GERD symptoms. While it is widely accepted that esophago-gastric junction (EGJ) type 3 is a strong predictor of GERD, EGJ type 2 is less clearly implicated in GERD pathogenesis¹. This study aimed to investigate the clinical and physiological characteristics of patients with EGJ type 2 and to identify HRM variables that predict GERD in this category of patients.

Aims & Methods: 535 patients with suspected GERD who underwent HRM and reflux monitoring were retrospectively analyzed. Patients were divided into three groups based on EGJ morphology (type 1, 2, or 3). Clinical data, HRM parameters, and reflux study results were compared among groups. The Milan Score², a novel metric that integrates ineffective esophageal motility (IEM), EGJ-contractile integral (EGJ-CI), EGJ morphology and straight leg raise (SLR) response, was applied to the EGJ type 2 group to identify patients at higher risk of developing GERD. Pathologic GERD was defined as AET >6% on pH-impedance monitoring and/or stricture, Barrett's esophagus or Los Angeles grade B, C or D, or at endoscopy. As previously demonstrated, a Milan Score of 137 (risk rate 50%) or higher was considered pathologic. Receiver operating characteristic (ROC) analysis was performed to determine Milan score prediction of GERD within patients with EGJ type 2 morphology.

Results: Patients with EGJ type 3 had the highest rate of GERD diagnosis, followed by EGJ type 2 and type 1 ($p < 0.001$). HRM showed differences in EGJ-CI, proportion of patients with IEM and positive SLR response among groups ($p < 0.001$). Reflux monitoring revealed a stepwise increase in AET from type 1 to 3 (5.1±7.3 vs. 8.3±11.1 vs. 12.2±11.3, $p < 0.001$). A pathologic

Milan Score identified two subgroups of patients within the EGJ type 2 group: patients with a score below 137 resembled type 1, while those with a score of 137 or higher resembled type 3 in terms of pH monitoring characteristics (Table). On ROC analysis the area under the curve was 0.858, and the optimal threshold to identify pathologic GERD in this group was 137 points (sensitivity 77.3%, specificity 87.7%).

	EGJ type 1 (n=277)	EGJ type 2 with MS<137 (n=93)	EGJ type 2 with MS≥137 (n=85)	EGJ type 3 (n=80)	P-value
AET (%), mean (SD)	5.1 (7.3) ^a	3.9 (5.8) ^a	13.2 (13.3) ^b	12.2 (11.1) ^b	<0.001
4%<AET<6%, n (%)	35 (12.6)	14 (15.1)	7 (8.2)	6 (7.5)	0.305
AET > 6%, n (%)	72 (26.0) ^a	12 (12.9) ^a	69 (81.2) ^b	62 (77.5) ^b	<0.001
DeMeester score, mean (SD)	21.7 (30.3) ^a	15.7 (23.2) ^a	55.0 (53.0) ^b	45.3 (39.5) ^b	<0.001
Total reflux ≥80, n (%)	37 (13.4) ^a	12 (12.9) ^a	24 (28.2) ^b	25 (31.3) ^b	<0.001
MNBI <1500 Ω, n (%) ^o	36 (21.8) ^a	11 (20.0) ^a	35 (66.0) ^b	39 (59.1) ^b	<0.001
PSPW <50%, n (%) ^o	54 (32.7) ^a	18 (32.3) ^a	39 (75.8) ^b	51 (77.2) ^b	<0.001

Conclusion: Our data suggests that EGJ type 2 encompasses a wide spectrum of disease severity. The Milan Score with a cut-off of 137 may help to identify patients with EGJ type 2 who are more likely to demonstrate pathologic GERD on reflux monitoring.

References: 1. Tolone S, de Cassan C, de Bortoli N, et al. Esophagogastric junction morphology is associated with a positive impedance-pH monitoring in patients with GERD. *Neurogastroenterol Motil.* 2015 Aug;27(8):1175-82. 2. Siboni S, Sozzi M, Kristo I et al. The Milan score: A novel manometric tool for a more efficient diagnosis of gastro-esophageal reflux disease. *United European Gastroenterol J.* 2024 Mar 27. doi: 10.1002/ueg2.12565. Epub ahead of print. PMID: 38536701.

Disclosure: Nothing to disclose.

PP0096

EVALUATION OF THE DECISION TREE CLASSIFICATION MODEL USING DIETARY AND LIFESTYLE FACTORS FOR PREDICTING GERD DIAGNOSIS IN GISTAR STUDY POPULATION

I. Birka¹, R. Amolins², D. Santare¹, M. Leja¹, I. Polaka²
¹University of Latvia, Institute of Clinical and Preventive Medicine, Riga, Latvia, ²Riga Technical University, Riga, Latvia

Contact E-Mail Address: ilzebirka@hotmail.com
Introduction: Dietary and lifestyle recommendations are the cornerstones of the treatment of GERD. However, the evidence of the efficacy of those recommendations is lacking. We performed a retrospective analysis of the GISTAR study¹ participants evaluating the symptoms of GERD and dietary and lifestyle parameters developing a tool for predicting GERD symptoms based on the aforementioned criteria.
Aims & Methods: The aim of the study was to analyse the factors pointing to GERD symptoms through the use of data mining and decision tree classifier.
Methods: GERD diagnosis was evaluated using a self-assessment questionnaire². Dietary, demographic and lifestyle data were collected within the GISTAR study protocol¹. 3340 40-64 year old participants from the GISTAR study were included in the analysis. 1670 of them did not have GERD symptoms. 41 attributes describing demographic, lifestyle, and dietary habits were used for these respondents to induce a decision tree classification model using Orange Data Mining software³.
Results: Fried potatoes including French fries were the most predictive factor of GERD symptoms (65.3% with symptoms; 1516 from 2321), especially for females (82.6%; 1048/1228). This was more pronounced in the group who consumed sweets once per week (87.2%, 950/1090). In males, who consumed fried potatoes, the next most important factor was the consumption of sweets (46.3%, 431/930).

For participants who didn't consume fried potatoes (14.6%; 147/1008), 1-3 cups of green tea (37.9%; 66/174) and male gender (71.4 % 20/28) were predictors of GERD symptoms.
The accuracy of the decision tree model was: sensitivity (74.8%), precision (75.6%), specificity (75.9%) and AUC (0.841%).
Conclusion: Fried potatoes, female gender and consumption of sweets are the risk factors predicting the diagnosis of GERD. None of the lifestyle factors were displayed as significant.
References: 1. Leja M, Park JY, Murillo R, et al. Multicentric randomised study of *Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality: the GISTAR study. *BMJ Open* 2017;7:e016999. doi: 10.1136/bmjopen-2017-016999 2. Jones R, Junghard O, Dent J, Vakil N, Halling K, Wernersson B, Lind T. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. *Aliment Pharmacol Ther.* 2009 Nov 15;30(10):1030-8. doi: 10.1111/j.1365-2036.2009.04142.x. Epub 2009 Sep 8. PMID: 19737151. 3. Demsar J, Curk T, Erjavec A, Gorup C, Hocevar T, Milutinovic M, Mozina M, Polajnar M, Toplak M, Staric A, Stajdohar M, Umek L, Zagar L, Zbontar J, Zitnik M, Zupan B (2013) Orange: Data Mining Toolbox in Python, *Journal of Machine Learning Research* 14(Aug): 2349–2353.
Disclosure: Nothing to disclose.

PP0097

IMPAIRED MUCOCILIARY CLEARANCE IN LARYNGOPHARYNGEAL REFLUX DOES NOT REFLECT THE AMOUNT OF GASTROESOPHAGEAL REFLUX

D. Vážanová¹, M. Ďuriček¹, P. Banovcin¹, P. Liptak¹, J. Kvaššayová², D. Oppová², P. Čelková²
¹Jessenius Faculty of Medicine in Martin (JFM CU), Comenius University in Bratislava, Clinic of Internal Medicine-Gastroenterology, Martin, Slovakia, ²Jessenius Faculty of Medicine in Martin (JFM CU), Comenius University in Bratislava, Department of Paediatrics, Martin, Slovakia

Contact E-Mail Address: diana.vazanova@gmail.com
Introduction: Gastroesophageal reflux is responsible for various extraesophageal symptoms that are commonly labelled as laryngopharyngeal reflux (LPR). These mostly include cough, throat clearing, globus sensation and hoarseness. The pathophysiological link between reflux and symptoms likely includes direct effect of the refluxate on the upper airways epithelium and reflex that is initiated by stimulation of the afferent nociceptive fibres in the distal esophagus by acidic gastroesophageal reflux.
Arguably, the relationship between reflux and laryngopharyngeal symptoms might involve other, yet not well explored mechanisms. In our previous research we found that LPR patients have impaired mucociliary clearance of the respiratory epithelium of the upper airways. This could contribute to the inflammation persistence and the presence of symptoms.
We therefore aimed to determine whether any parameter of the reflux burden as detected by 24-hour pH/impedance correlates with ciliary beat frequency (CBF), the major quantifiable aspect of mucociliary clearance.
Aims & Methods: Consecutive patients with LPR confirmed by off PPI 24-hour pH/impedance had a sample of the ciliated epithelium obtained from the nose using a cytology brush. Nasal CBF was analysed using a digital high-speed video microscope and the dedicated software application Ciliary Analysis (NI LabVIEW). Healthy volunteers without either esophageal or extraesophageal reflux symptoms served as a control group. Both patients' and healthy volunteers' group were without any airway inflam-

mation at least 3 months prior to the evaluation and were at least 10 days of PPI therapy. Maximal, minimal, and the median value of the CBF (Hz) was obtained. We performed correlation analyses between the acid exposure time (AET), number of reflux episodes, mean nocturnal baseline impedance (MNBI) in all impedance segments (Z1-Z6) and CBF values.

Results: 32 patients with LPR confirmed by 24-hour pH/impedance that had positive reflux symptom index (RSI>13) were included in the final analysis. Of them, 12 patients had confirmed by positive acid exposure time (AET>6%) and/or abnormal number of reflux episodes (>80). Firstly, we confirmed our previous observations that LPR patients had lower CB frequency (median value) compared to the healthy individuals (6,37±2,17 vs. 10,9±1,9; p<0.0001). Separate analysis of patients with proven GERD showed no CBF difference from the remaining (pH negative patients) (6,26±2,53 vs. 6,43±1,94; p=0,42). Secondly, we performed correlation analysis between AET/number of reflux episodes and CBF. We found no significant correlation between reflux burden and median value of CBF (N=32, R=-0.18, p=NS and R=0.05, p=NS for AET and number of refluxes, resp.). Thirdly, we performed correlation analyses between CBF and MNBI values of all impedance segments. Indeed, correlation analysis between median CBF and MNBI Z1-Z6 showed no significant correlations (N=32, R=-0.16, 0.09, 0.28, 0.01, 0.14 for Z1, Z2, Z3, Z4, Z5, Z6, resp., resulting in p=NS in all segments).

Conclusion: pH positive LPR patients had no difference in CBF values from the remaining (pH negative) patients. Reflux burden in the esophagus as determined by pH recording does not seem to be related to ciliary beat frequency. We observed no significant correlation between the MNBI values in any impedance segment and the median CBF value. Further research should be performed to determine the putative mechanism between the impairment of CBF and reflux.

Supported by: VEGA 1/0060/23

Disclosure: Nothing to disclose.

PP0098

EVALUATION OF THE SAFETY AND EFFICACY OF TRANSORAL INCISIONLESS FUNDOPLICATION (TIF2.0) FOR GASTRO-OESOPHAGEAL REFLUX DISEASE: A UK COHORT STUDY

B. Norton¹, N. Aslam², A. Papaefthymiou¹, A. Telese¹, M. Duku¹, A. Stevens¹, A. Murino¹, G. Johnson¹, C. Murray¹, B. Mohammadi¹, M. Mughal¹, R.J. Haidry¹

¹Cleveland Clinic London, Digestive Disease & Surgery Institute, London, United Kingdom, ²University College London Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: benjamin.norton@nhs.net

Introduction: Gastro-oesophageal reflux disease (GORD) is a common disorder with a prevalence of 10-20%. It occurs from disruption of the gastro-oesophageal flap valve (GFV) and/or a diaphragmatic abnormality causing a hiatus hernia (HH). Transoral incisionless fundoplication (TIF2.0) using the EsophyX device (Endogastric solutions) is an endoscopic treatment for GORD, which recreates the GFV through a partial 270° wrap. Prospective trials show the procedure is safe and effective and is recommended in North American guidelines, yet the experience of TIF is limited in Europe.

Aims & Methods: We conducted a UK-based, retrospective, cohort study to determine the safety and efficacy of TIF2.0. Patients undergoing TIF2.0 by a single operator were identified and analysed between 2019-2023. Patient demographics, reflux assessments (GERD-HRQL, endoscopy, pH testing), and procedural details were recorded. Primary outcomes were technical success and clinical response defined as complete (off regular anti-acid therapy) or partial (reduction from baseline in anti-acid therapy,

GERD-HRQL score, and/or physiological parameters) without the need for revision. Secondary outcomes were adverse events and changes in reflux parameters measured by Wilcoxon signed-rank test. A p-value <0.05 was significant.

Results: In total, 81 patients underwent TIF2.0 with 92.0% on oral anti-acid therapy. Median age was 51 (IQR 37-64), 23 (28.4%) were female, and the median ASA grade was 1 (IQR 1-2). A HH was present in 84.6% with an average size of 1.9cm (SD 0.5). The average acid exposure time (AET) was 8.9% (SD 4.1; n=61). The clinical outcomes are summarised in table 1. Technical success was 97.5% (n=79) with an average procedural time of 38.0 minutes (SD 10.3), and 1-day (IQR 1) inpatient stay. The device could not pass the cricopharynx in two patients despite routine balloon dilatation. Over 15.5 months of median follow-up (IQR 7-24), 55% had a complete response, and 71.7% partial response. On logistic regression analysis, no variables were predictive of response. Among those with paired pre-/post-testing, the average GERD-HRQL score reduced significantly (33.9 ±18.6 to 9.1 ±9.2; P<0.001) as well as the average AET (8.9 ±4.1 to 5.1 ±4.0; P=0.005) post-procedure. Procedure or device-related adverse events occurred in 12.2% (n=10), which were all managed conservatively. The single perforation was delayed and managed with intravenous antibiotics and endoscopic vacuum therapy. Seven patients underwent a revisional procedure, including two surgical funduplications, with 83.3% due to recurrent HH.

Procedure time in minutes (SD)	38.0 (7.2)
Technical success (%)	79 (97.5)
Inpatient stay (IQR)	1 (1)
Complete response*	33 (55.0)
Partial response†	43 (71.7)
Follow-up in months (IQR)	15.5 (7-24)
Repeat procedure (%)	7 (8.6)
Adverse events (%)‡	10 (12.2)

IQR – interquartile range; ; SD – standard deviation
* Off all regular anti-acid therapy (respondents during follow-up: n=60)
† Reduction from baseline in anti-acid therapy, symptomatology based on HRQL-GERD questionnaire, and/or physiological parameters (respondents during follow-up: n=60)
‡ Mucosal injury (n=1), chest infection (n=3), perforation (n=1), leak/collection (n=1), bleeding (n=1), dysphagia (n=2), admission for nausea and vomiting (n=1).

Table 1 - Clinical outcomes among patients undergoing Transoral Incisionless Fundoplication 2.0

Conclusion: TIF2.0 is associated with technical success in 97.5%, clinical response in 71.7%, and significant improvements in GERD-HRQL and AET. Recurrent HH is a frequent cause of failure showing the importance of patient selection and/or need for concomitant HH repair.

Disclosure: RH declares educational grants to support research infrastructure from Cook medical, Odin Vision, Pentax medical, Endogastric Solutions, Apollo Endosurgery, Medtronic, and Aqua Medical

PP0099

INDEPENDENT MEDICAL EDUCATION SIGNIFICANTLY IMPROVES PHYSICIANS KNOWLEDGE, CONFIDENCE AND COMPETENCE REGARDING THE LONG-TERM MANAGEMENT OF REFLUX AND DEPRESCRIBING PROTON PUMP INHIBITORS

J. Duffey¹, A. Piazza², K. Reid², G. Griffiths², P.J. Kahrilas³, A.P. Hungin⁴

¹Medscape Global Education, Clinical Strategy, London, United Kingdom, ²Medscape Global Education, London, United Kingdom, ³Northwestern University Feinberg School of Medicine, Chicago, IL, United States of America, ⁴Newcastle University, UK, Medicine, Stockton-on-Tees, United Kingdom

Contact E-Mail Address: kreid@webmd.net

Introduction: Proton pump inhibitors (PPIs) are widely prescribed open-ended fashion, but in an estimated 25-82% of patients this may be inappropriate.[1, 2] Chronic PPI use is associated with an increased risk of specific adverse events including pneumonia, dementia, and osteoporotic fractures although no causal relationships have been established.[3] However, recent surveys have found that among physicians who regularly prescribe PPIs, a considerable proportion were unfamiliar with deprescribing strategies.[2] Here, we assessed whether an 30-minute online independent medical education activity could improve primary care physicians' (PCPs) and gastroenterologists' knowledge, confidence and competence regarding the long-term management of reflux and PPI deprescribing.

Aims & Methods: Educational effect was assessed using a repeated-pairs design with pre-/post-assessment. Three multiple choice questions assessed knowledge, and one question assessed confidence. Statistical tests to assess significance included: Paired samples t-test for overall average number of correct responses and confidence. McNemar's test for individual questions and learning objectives ($P < .05$). Cohen's d estimated the effect size impact on number of correct responses ($< .20$ modest, $.20-.49$ small, $.50-.79$ moderate, $\geq .80$ large).

Results: From a total of 3422, there were 359 assessment completers. Overall, there were highly significant and impactful knowledge gains for both groups of physicians (PCPs $P < .001$, Cohen's $d = 0.87$; Gastroenterologists $P < .001$, Cohen's $d = 1.02$). For PCPs, the highest relative proportional change in knowledge was for the extent of PPI overuse and misuse at 161% with 38% of physicians improving their knowledge ($P < .001$). Whilst for gastroenterologists the highest relative proportional change was seen regarding the implications of PPI overuse at 277% with 37% of physicians improving knowledge following the activity ($P < .001$). Significant increases in physician competence in best practice in PPI deprescribing were found ($P < .001$ for both), despite high baseline levels of competence. A considerable proportion of PCPs (51%; confidence shift 69%; $P < .001$) and gastroenterologists (39%; confidence shift 52%; $P < .001$) increased their confidence regarding their ability to use appropriate management strategies to reduce or discontinue a patient's use of PPI therapy.

Conclusion: Online medical education significantly improved physicians' knowledge, confidence and competence regarding the extent and implications of PPI overuse and best practice in the long-term management of reflux and PPI deprescribing. As PPI prescribing is prevalent and long-term use is common, it is important that physicians understand appropriate indications and implications associated with over and long-term use and are also able to undertake clinically appropriate deprescribing approaches.

References:

1. Kurlander, J.E., et al., *Impact of large scale, multicomponent intervention to reduce proton pump inhibitor overuse in integrated healthcare system: difference-in-difference study*. *Bmj*, 2024. **385**: p. e076484.

2. Piñerúa-Gonsálvez, J.F., et al., *BEHIND THE PROTON PUMP INHIBITOR PRESCRIPTION: AN INTERNATIONAL SURVEY ON PHYSICIAN PRACTICES AND KNOWLEDGE*. *Arq Gastroenterol*, 2024. **61**: p. e23153.

3. Vaezi, M.F., Y.X. Yang, and C.W. Howden, *Complications of Proton Pump Inhibitor Therapy*. *Gastroenterology*, 2017. **153**(1): p. 35-48.

Disclosure: Nothing to disclose.

PP0100

PATIENT-REPORTED OUTCOMES OF VONOPRAZAN IN CHINESE REFLUX ESOPHAGITIS PATIENTS: A REAL-WORLD, OBSERVATIONAL STUDY

Y. Xiao¹, Z. Xue², X. Li³, Q. Song⁴, L. Xie⁵, M. Chen¹

¹The First Affiliated Hospital, Sun Yat-Sen University, Guang Zhou, China, ²The Second Affiliated Hospital of Wenzhou Medical University, Wen Zhou, China, ³Henan Provincial People's Hospital, Gastroenterology, Zheng Zhou, China, ⁴Takeda Pharmaceutical Company, Shang Hai, China, ⁵Takeda Pharmaceutical Company, BeiJing, China

Contact E-Mail Address: qi.song@takeda.com

Introduction: Reflux esophagitis (RE) is a common, chronic disorder characterised by the mucosal break with symptoms such as heartburn and/or acid regurgitation. Patient-reported outcomes (PROs) offer more comprehensive access to the symptoms and impact on RE, which is a widely used treatment option that is effective from the patient's perspective. Vonoprazan is a novel potassium competitive acid blocker, approved in China for treating RE since 2019. Here, we present the PROs of vonoprazan in Chinese RE patients.

Aims & Methods: VIEW (NCT04501627) is a multicenter, single-arm, prospective, observational, real-world study to evaluate the safety and effectiveness of Vonoprazan. The subgroup analysis of VIEW was designed to assess the effectiveness of vonoprazan in patients with endoscopically confirmed RE. All patients were treated with 20 mg vonoprazan orally q.d. for 4 weeks (continued for 8 weeks if the patient did not show any beneficial effects) followed by a safety follow-up for 2 weeks.

All the patients were assessed for symptomatic relief by PROs which included patient symptom diary (percentages of patients with complete relief of heartburn, nocturnal heartburn, regurgitation, and nocturnal regurgitation) and GERD questionnaire (GerdQ) scores.

Results: Out of 1040 endoscopy-confirmed RE patients, 935 (89.90%) patients were with mild RE (LA grade A/B) and 105 (10.09%) patients were with severe RE (LA grade C/D). For all RE patients with heartburn, night-time heartburn, regurgitation, and night-time regurgitation at enrollment, the percentages of patients with complete symptomatic relief during the first one-week of treatment were 35.1%, 47.2%, 29.5%, and 43.6% respectively; while during first two-weeks of treatment, the respective percentages were 60.7%, 71.3%, 52.3%, and 65.0%.

Higher percentages were observed in patients with complete night-time heartburn or night-time regurgitation. Among subgroups, severe RE patients exhibited marginally higher percentages than mild RE patients (severe RE: 44.9%, mild RE: 33.7%), (severe RE: 52.2%, mild RE: 46.5%), (severe RE: 39.7%, mild RE: 28%) (severe RE: 47.1%, mild RE: 43.1%) during first one-week of treatment. A similar trend of symptomatic relief in severe RE patients was observed during the first two-weeks of vonoprazan treatment compared to mild RE patients (Table 1).

The proportion of patients without typical GERD symptoms increased by 36.9% (95% CI: 32.79, 41.10), 36.7% (95% CI: 32.29, 41.09) and 39.3% (95% CI: 26.84, 51.78) for all RE, mild RE and severe RE patients, respectively, at week 4 compared to baseline. The total change in GerdQ scores from baseline to week 4 (mean (SD)) were -1.7 (2.76) (95% CI: -1.85, -1.48) in

all RE, -1.6 (2.72) (95% CI: -1.81, -1.42) in mild RE and -2.1 (3.05) (95% CI: -2.72, -1.42) in severe RE, where negative value represents improvement in the symptomatic relief.

GERD typical symptoms	Statistics	Percentage of patients with complete symptom relief					
		First one week*			First two weeks**		
		Overall	Mild RE	Severe RE	Overall	Mild RE	Severe RE
Heartburn	%	35.1	33.7	44.9	60.7	59.9	66.7
	(n/N)	(194/552)	(163/483)	(31/69)	(340/560)	(294/491)	(46/69)
	(95% CI)	(31.16, 39.29)	(29.54, 38.16)	(32.92, 57.38)	(56.53, 64.78)	(55.39, 64.24)	(54.29, 77.56)
Night-time heartburn	%	47.2	46.5	52.2	71.3	70.5	76.8
	(n/N)	(261/553)	(225/484)	(36/69)	(400/561)	(347/492)	(53/69)
	(95% CI)	(42.97, 51.45)	(41.97, 51.04)	(39.80, 64.35)	(67.36, 75.01)	(66.28, 74.52)	(65.09, 86.13)
Regurgitation	%	29.5	28.0	39.7	52.3	50.8	63.2
	(n/N)	(163/553)	(136/485)	(27/68)	(293/560)	(250/492)	(43/68)
	(95% CI)	(25.70, 33.47)	(24.08, 32.27)	(28.03, 52.30)	(48.09, 56.53)	(46.30, 55.32)	(50.67, 74.61)
Night-time Regurgitation	%	43.6	43.1	47.1	65.0	63.8	73.5
	(n/N)	(242/555)	(210/487)	(32/68)	(364/560)	(314/492)	(50/68)
	(95% CI)	(39.43, 47.84)	(38.67, 47.65)	(34.83, 59.55)	(60.89, 68.95)	(59.40, 68.07)	(61.43, 83.50)

Table 1. Percentage of complete symptom relief after treatment for RE patients with symptoms at baseline

* First one week was defined as Day 1 to Day 7.

**First two weeks were defined as ≥ 7 consecutive days between Day 1 and Day 14

Conclusion: Vonoprazan exhibited quick symptomatic relief for both mild and severe RE patients in the real-world setting.

Disclosure: Funding statement: This study was funded by Takeda (China) International Trading Co., Ltd.

Acknowledgements: Medical writing support for the development of this abstract, under the direction of the authors, was provided by Tanushree Goswami PhD, Cr Swathirajan PhD, and Ravi Kiran PhD of Indegene Private Limited, Bangalore, India, funded by Takeda Pharmaceuticals, and complied with the Good Publication Practice 2022.

Conflict of Interest: Yinglian Xiao, Zhanxiong Xue and Xiuling Li have no conflicts of interest. Li Xie and Qi Song are employees of Takeda, and they hold Takeda stock options. Minhu Chen received speaker honorariums from Takeda China, AstraZeneca China, Xian Janssen, and Eisai China.

PP0101

PHYSIOLOGICAL, SYMPTOMATIC AND NEUROCHEMICAL OUTCOMES AFTER STRETТА PROCEDURE

J. Cooney^{1,2}, T. Leech³, A. Henderson¹, A. Wolak¹, P. Appiahene¹, O. Khan^{4,2}, M. Reddy⁴, C. Lee³, P. Woodland³, J. Hayat^{1,2}

¹St George's University Hospitals NHS Foundation Trust, Gastroenterology, London, United Kingdom, ²St George's, University of London, London, United Kingdom, ³Queen Mary, University of London, Blizard Institute, London, United Kingdom, ⁴St George's University Hospitals NHS Foundation Trust, Upper Gastrointestinal Surgery, London, United Kingdom

Contact E-Mail Address: josephcooney@doctors.org.uk

Introduction: Gastro-oesophageal reflux disease (GORD) affects 25% of adults and impairs quality of life. Initial treatment is with lifestyle change and acid suppression however up to 1/3 will be refractory or intolerant to medical therapy. The Stretta procedure is an endoscopic treatment delivering radiofrequency energy around the gastro-oesophageal junction (GOJ). Whilst it can improve symptoms and reduce oesophageal acid exposure (AET) its mechanism of action is not fully understood. EndoFLIP is a device to measure GOJ distensibility (DI) and calcitonin gene related peptide (CGRP) is a neuropeptide marker for sensory afferents involved in GORD hypersensitivity - it is not known whether Stretta alters these factors and whether they are linked to normalisation of AET and symptoms.

Aims & Methods: This prospective study aimed to assess the effect of Stretta on UGI physiological parameters (LES pressure, IRP, DCI, AET, GOJ DI), mucosal CGRP presence, and symptom scores, by performing the following tests before and 6-months after Stretta:

Gastroscopy, EndoFLIP, HRM, ambulatory pH testing, oesophageal biopsies analysed using immunohistochemistry (IHC) for CGRP, and symptom questionnaires (Hull airway reflux, Reflux Symptom Index, Hospital Odynophagia Dysphagia, Reflux Disease, GERD-QOL).

Authors were blinded during analysis. Statistical analysis using SPSS with paired t-test for parametric data, Wilcoxon-signed rank test for non-parametric data, Pearson and Spearman tests for correlations. Ethical approval (IRAS 296193, NCT 05238636).

Results: 30 pts - 13F:17M, aged 22-71y (med. 55y).

		Pre-Stretta (Median, IQR)	Post-Stretta (Median, IQR)	Mean % delta (95% CI)	p value
EndoFLIP (40ml)	GOJ diameter (mm)	11.7 (8.4-13.5)	12.6 (10.4-14.8)	15.6 (3.7-27.5)	0.053
	Median pressure (mmHg)	34.9 (29.0-49.3)	37.3 (21.6-51.2)	1.3 (-9.7-12.3)	0.820
	GOJ distensibility index (mm2/mmHg)	3.1 (1.5-4.2)	4.5 (2.2-6.6)	71.1 (22.1-120.0)	0.014
HRM	Mean basal LES pressure (mmHg)	16.7 (7.8-28.6)	21.3 (9.3-33.3)	19.9 (-19.9-59.3)	0.758
	Median IRP (mmHg)	5.0 (3.1-10.0)	4.6 (2.5-7.9)	-16.5 (-51.0-18.0)	0.758
	Mean DCI (mmHg/s/cm)	1372.1 (306.0-2404.0)	1239.9 (369.8-2341.0)	3.4 (-29.5-36.2)	0.494
pH	Overall AET (%)	9.9 (6.4-14.8)	6.6 (3.0-14.3)	-19.2 (-44.3-5.8)	0.037
	DeMeester Score	43.3 (22.3-61.7)	27.4 (9.4-47.2)	-33.6 (-56.8 - -10.5)	0.012
	% papillae with CGRP (10µm)	5.7 (4.0-9.7)	9.3 (6.0-17.8)	73.0 (-6.9-152.8)	0.071

Tests before and 6 months after Stretta:

48.5% pts felt Stretta was "very" or "somewhat" helpful.

Statistically significant (SS) improvements were seen in Hull (p=0.029) and RSI (p=0.028) scores.

AET normalised for 31% however there were no SS correlations between symptom scores and AET (p>0.05).

SS negative correlation between GOJ DI and LES pressure both before (r =-0.5, p = 0.017) and after (r=-0.5, p=0.012) Stretta.

No SS correlations between GOJ DI, GOJ diameter, LES pressure, IRP vs AET (p>0.05).

SS positive correlation between the percent change in GOJ DI pre/post Stretta with the percent change in DeMeester score (r= 0.4, p=0.03).

CGRP was most prevalent in the lower oesophagus (mean 12.0% papillae), vs middle (6.8%) and upper (7.3%). There was a mean increase of 73% post stretta but this was not SS and did not correlate with symptom scores, GOJ DI nor AET.

Conclusion: The normalisation of AET in 31% is consistent with published meta-analysis (30%). There was a non-significant trend towards increased basal LES pressure without a reduction in GOJ DI. This suggests the mechanism of action of Stretta may not be related to changes in GOJ compliance. There was SS improvement in laryngopharyngeal symptoms (Hull, RSI) suggesting these pts may benefit most from Stretta, although this was not supported by concurrent improvement in AET. CGRP presence within mucosal papillae was not affected, suggesting that this neuropeptide is not involved and that Stretta may not alter oesophageal sensitivity.

References: Ford et al, *BMJ* (2009), Fass et al, *Surg Endosc* (2017), Lee et al, *Gut and Liver* (2021), Leech, *J Gastroenterol* (2024), Woodland et al, *Gastroenterology* (2017).

Disclosure: Nothing to disclose.

PP0102

KNOWLEDGE, ATTITUDES, AND PRACTICES AMONG DOCTORS MANAGING OF GASTROESOPHAGEAL REFLUX DISEASE IN A SRI LANKAN SETTING

N. Wickramasinghe¹, D.G. Wickramasinghe², A. Thuraisingham³,
N.M. Devanarayana⁴

¹Faculty of Medicine, University of Colombo, Physiology, Colombo,
Sri Lanka, ²Faculty of Medicine, University of Colombo, Surgery,
Colombo, Sri Lanka, ³Ministry of Health, Sri Lanka, Colombo,
Sri Lanka, ⁴Faculty of Medicine, University of Kelaniya, Physiology,
Kelaniya, Sri Lanka

Contact E-Mail Address: nilanka@physiol.cmb.ac.lk

Introduction: While the global prevalence of GERD ranges from 5% to 25%, in Sri Lanka, it is slightly higher at 25.3%. There are no Sri Lankan guidelines for management of GORD despite it been a relatively common condition.

However, there is a lack of studies in Sri Lanka documenting the current management practices for GERD among doctors both primary and specialized.

Aims & Methods: This study aims to give an insight about the Sri Lankan doctor's point of view in managing GERD.

A self-administered questionnaire designed to gather information on medication prescription, lifestyle advice given, investigations, and personal experiences and beliefs was used. MBBS doctors working as primary care doctors, consultant general physicians/ general surgeons/ gastroenterologists as well as trainees in the fields, attached to the National Hospital of Sri Lanka, Colombo South Teaching Hospital, Colombo North Teaching Hospital, and the College of General Practitioners, Sri Lanka were approached consecutively.

Data analysis was conducted using SPSS-28.

Results: Of the 100 participants recruited, 57 were male while the average age was 35 years. The average duration of practice as a doctor was 11 years, ranging from 1 to 50 years. A significant proportion of doctors reported personally experiencing reflux and regurgitation (n=62, 62.0%). In the first presentation of heartburn or reflux, the majority of doctors prescribed proton pump inhibitors (PPIs) (n=92, 92.0%), followed by domperidone (n=67, 67.0%), antacid syrups (n=42, 42.0%), H2 receptor blockers (n=37, 37.0%), antacid tablets (n=27, 27.0%), antidepressants and anxiolytics (n=11, 11.0%). Prescription at the second presentation showed a similar trend except for H2 receptor blockers taking precedence while only 3 doctors prescribed triple therapy. Only 46.0% advised the patients to come for a follow-up, and the mean follow-up period was 2 weeks, with n=88, 88.0% of the patients presenting.

Most doctors referred/ utilized upper gastrointestinal (GI) endoscopy (n=96, 96.0%), while upper GI manometry (n=13, 13%) and pH impedance studies (n=4, 4.0%) were referred at specialist level.

Most doctors reported advising their patients (n=88, 88.0%) on lifestyle changes, such as avoiding food that causes GERD symptoms (n=91, 91.0%), weight loss (n=71, 71.0%), reducing mental stress (n=70, 70.0%), and other lifestyle modifications. Spicy food (n=86, 86.0%), oily food (n=93, 93.0%), wheat-based food (n=50, 50.0%), and bread (n=52, 52.0%), were the types of food most commonly advised against.

The majority 73% of doctors co-prescribed PPIs for patients on multiple other medications and 36% co-prescribed PPIs when NSAIDs were prescribed (n=64, 64.0%).

Only 52.0% were satisfied with their management while 19% believed that anti-reflux surgery was a good option for managing GERD.

Conclusion: According to this study a majority of physicians prescribe proton pump inhibitors (PPIs) as the first-line treatment for GERD, followed by other medications such as domperidone and antacids. Lifestyle mod-

ifications, including dietary changes and stress reduction, are commonly advised. Upper GI endoscopy is the most preferred investigation method. Despite advising patients to avoid wheat and bread, many physicians report patients experiencing symptoms from these foods only sometimes or less. Overall, physicians are generally satisfied with their management of GERD and do not consider surgery as a treatment option.

Education programs and seminars on the management of GERD is recommended to ensure optimal patient care.

Disclosure: Nothing to disclose.

PP0103

DOES MUCIN EXPRESSION PHENOTYPE OF BARRETT'S ADENOCARCINOMA AFFECT THE RISK OF LYMPH NODE METASTASIS?

Y. Iwaya¹, T. Tomoaki¹, Y. Kou¹, H. Ikeuchi¹, H. Sawaguchi¹, S.
Kako¹, A. Hirayama¹, T. Okamura¹, T. Nagaya¹, M. Iwaya²

¹Shinshu University School of Medicine, Gastroenterology,
Matsumoto, Japan, ²Shinshu University Hospital, Laboratory
Medicine, Matsumoto, Japan

Contact E-Mail Address: yiwaya@shinshu-u.ac.jp

Introduction: Superficial Barrett's adenocarcinoma (BAC) is a rare disease in Japan, and its clinicopathological characteristics are not well-defined. As a result, indications for endoscopic treatment have not been determined.

Aims & Methods: A histopathological study was performed to investigate whether there is a relationship between risk factors for lymph node metastasis and the mucin expression phenotypes of BAC. We conducted a retrospective analysis of a database comprising consecutive patients with superficial BAC treated by endoscopic or surgical resection. Immunohistochemical analysis was performed using the antibodies of MUC5AC, MUC6, MUC2, and CD10 to determine the classification of mucin expression phenotype.

Results: A total of 74 BAC lesions in 68 patients (54 males, median age 69 years) were identified. Mucin expression classification showed gastric (64%, complete gastric 24%, predominantly gastric 39%), intestinal (34%, complete intestinal 14%, predominantly intestinal 20%) or null (3%) phenotypes. Surgical treatment was performed in 30 patients, including additional treatment after ESD, and lymph node metastasis was observed in 4 patients (13%). Compared to the intestinal phenotype group, patients with gastric phenotype BAC had an almost significantly higher rate of lymphovascular invasion (38% vs 16%, P=0.06) and poorly differentiated component (23% vs 4%, P=0.09). All 4 lymph node metastasis-positive cases were in the gastric phenotype group (P=0.28).

Conclusion: Although our study did not show a direct relationship between the risk of lymph node metastasis and mucin expression phenotype of BAC, it did suggest BAC with gastric phenotype may be more likely to have lymphovascular invasion and poorly differentiated component. The endoscopic-specific findings of BAC with gastric phenotype are unknown. However, some specific endoscopic findings of gastric phenotype in gastric cancer are well-known, such as intralobular loop pattern or vessels within epithelial circle pattern. If we see such findings in BAC, due to a possible higher risk of lymphovascular invasion or poorly differentiated components, we should perform ESD rather than piecemeal EMR to obtain en-bloc tissue specimens for detailed pathological evaluation.

Disclosure: Nothing to disclose.

PP0104

SAFETY AND EFFICACY OF CRYO-ABLATION ON BARRETT ESOPHAGUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Papaefthymiou¹, A. Telese¹, B. Norton¹, P. Gkolfakis², M. Duku¹, A. Murino¹, G. Johnson¹, C. Murray¹, R.J. Haidry¹
¹Cleveland Clinic London, Gastroenterology, London, United Kingdom, ²Konstantopouleion General Hospital of Nea Ionia, Hepatogastroenterology Unit, Second Department of Internal Medicine, Propaedeutic, Research Institute and Diabetes Center, Medical School, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece

Contact E-Mail Address: Andrea.Telese@nhs.net

Introduction: Barrett esophagus (BE) represents a pre-malignant condition of the esophagus and current guidelines favor endoscopic eradication therapy (EET). After endoscopic resection for visible neoplastic lesions, field ablation of the residual BE is advised to mitigate the risk of metachronous neoplasia. Cryoablation was introduced as an endoscopic ablative option for BE during the last decade with growing data on outcomes and interest in potential lower adverse events that established ablative techniques.

Aims & Methods: This systematic review and meta-analysis aimed to summarize the existing data regarding safety and efficacy of Cryoablation on BE treatment. A systematic literature search in Medline, Cochrane and Scopus databases was performed until November 2023 for full papers. Safety was considered as the primary outcome, interpreted as the overall rate of procedure related adverse events. Secondary outcomes included post-Cryoablation stricture development, and the complete eradication rates of intestinal metaplasia (CEIM) and dysplasia (CED). In case of heterogeneity, a sub-analysis based on the used device was performed for the primary outcome. Random effects model was used and the results were reported as percentages for pooled rates with 95% Confidence Intervals (95%CI).

Results: Ten full-paper studies (471 patients; 80.3% men; mean age 62.2-69) were eligible for analysis. The mean BE length, based on Prague classification, was C0-2M2-5. Regarding the primary outcome, the overall adverse events rate was 19.7% (95%CI: 14-25.4; I²=60.66%), although they were mild in the vast majority. Strictures warranting treatment were developed in 30 patients, representing 4.4% (95%CI: 1.8-7.1; I²=61.18%). Four studies provided results on CED, yielding a rate of 94.6% (95%CI: 90.1-99.1; I²=61.06%) whereas CEIM was assessed in six studies, reporting a rate of 90.1% (95%CI: 82.3-97.9; I²=87.92%). Given the high heterogeneity in all outcomes, a sub-analysis including studies on focal Cryoablation was performed, revealing a similar rate of adverse events [16.5% (95%CI: 11.1-21.8)] with lower heterogeneity and non-significant heterogeneity (I²=47.7%).

Conclusion: Cryoablation is a safe procedure with initial data showing a potentially low rate of esophageal strictures and comparable rates of dysplasia and BE eradication when compared to other ablative technologies. High-quality prospective studies including comparisons with established ablation techniques are warranted.

Disclosure: Nothing to disclose.

PP0105

BILE ACIDS IN SALIVA AS POSSIBLE NON-INVASIVE DIAGNOSTICS OF BARRETT'S ESOPHAGUS

S. Konecny^{1,2}, J. Dolina^{1,2}, V. Dosedelova³, M. Lastovickova⁴, P. Kuban³
¹University Hospital Brno, Department of Internal Medicine and Gastroenterology, Brno, Czech Republic, ²Masaryk University, Faculty of Medicine, Brno, Czech Republic, ³Institute of Analytical Chemistry of the Czech Academy of Sciences, Department of Bioanalytical Instrumentation, Brno, Czech Republic, ⁴Institute of Analytical Chemistry of the Czech Academy of Sciences, Department of Environmental Analytical Chemistry, Brno, Czech Republic

Contact E-Mail Address: stefankonecny@gmail.com

Introduction: Bile acids are a group of steroid compounds essential for lipid digestion. However, when bile acids are refluxed into the stomach and the esophagus during the so called duodenogastroesophageal reflux, they can have a detrimental effect on the esophageal epithelium and cause pathological changes of esophageal tissue, e.g., Barrett's esophagus (BE). The levels of bile acids in saliva could therefore serve as possible biomarkers for the diagnostics of BE.

Aims & Methods: We focused on optimization of saliva sampling methods for further analysis of bile acids. Three sampling methods were compared, i.e. sampling with Salivette sampler, Salivette Cortisol sampler and simple spitting. Then we performed quantification of 11 selected bile acids (un-conjugated, glycine-conjugated) in saliva from 10 healthy volunteers and 10 BE patients by ultra-high-performance liquid chromatography coupled to triple-quadrupole tandem mass spectrometry. Moreover, high resolution MS (Orbitrap-MS) was utilized for identification of new bile acids in saliva.

Results: The results showed a clear advantage of simple spitting compared to the Salivette samplers. The median concentration of bile acids in saliva from healthy volunteers was generally below 1 nmol L⁻¹ and approximately 2 nmol L⁻¹ in saliva from patients with BE. The determined concentrations of bile acids in saliva are in the same range as previously reported. Levels of most bile acid were significantly higher ($p < 0.05$) in saliva from patients than in saliva of healthy volunteers. The most distinctive differences were found in levels of glycolithocholic acid, chenodeoxycholic acid, hyocholic acid and the sum of bile acids. Taurocholic acid, taurochenodeoxycholic acid and taurodeoxycholic acid were identified in a pooled saliva sample. To the best of our knowledge, this is the first time taurine-conjugated bile acids were detected in saliva. Moreover, glycine-conjugated dihydroxy-bile acid sulfate was detected and identified. Sulfate-conjugated bile acid, specifically glycochenodeoxycholate-3-sulfate, was previously detected only in one metabolomic study.

Conclusion: Saliva from BE patients contained higher levels of almost all bile acids, and the patients with BE could be distinguished from healthy volunteers by principal component analysis. In untargeted analysis taurine-conjugated bile acids were identified in saliva for the first time. The number of subjects in this preliminary study is low as we wanted to pinpoint a possible application for the analysis of bile acids in saliva, but not to complete a large clinical study, that will be conducted in future research, also including the taurine-conjugated bile acids.

Disclosure: Nothing to disclose.

PP0106

CLINICAL EVALUATION OF CRYOBALLOON ABLATION FOR BARRETT'S OESOPHAGUS: A UK FIRST MULTI-CENTRE EXPERIENCE

N. Aslam¹, J. Gertner¹, M. Duku^{2,2}, J. Britton³, Y. Ang⁴, V. Sehgal¹

¹University College London Hospitals, London, United Kingdom,

²Cleveland Clinic London, London, United Kingdom, ³Northern Care

Alliance, Salford, United Kingdom, ⁴Salford Royal NHS Foundation,

Dept. of gastroenterology, Salford, United Kingdom

Contact E-Mail Address: n.s.aslam1@icloud.com

Introduction: The Cryoballoon Focal Ablation System (CbFAS) (Pentax Medical Inc) is an innovative device designed for the endoscopic ablation of Barrett's-related neoplasia. This system has been shown to provide advantages such as reduced stricture rates and improved patient tolerance compared to the conventional standard of care, radiofrequency ablation (RFA).

We report early outcomes from a prospective UK first multi-centre registry of consecutive patients who underwent Cryoablation for the endoscopic eradication (EET) of Barrett's-related neoplasia.

Aims & Methods: Patients were prospectively enrolled from two tertiary referral centres for Barrett's Oesophagus (BE). Inclusion criteria included patients with a BE segment no longer than 5cm with histologically-proven dysplasia on biopsy or endoscopic resection specimens suitable for EET of BE after MDT review. Cryoablation sessions were conducted at 3-month intervals until endoscopic eradication was complete. The standardised protocol involved administering 8 seconds per ablation for all enrolled patients with the CbFAS. Our primary outcome was complete eradication of BE. Secondary outcomes included the number of ablations performed, adverse events, device malfunction, stricture rate, patient tolerance, and endoscopist satisfaction which was evaluated using a 10-point Likert scale (1=poor, 10=excellent).

Results: Between January 2020 and December 2023, a total of 16 patients (35 treatment sessions) were treated. The median BE length was C0M2. Complete eradication of BE was achieved in 89% (8/9) of patients who had completed treatment. No instances of device malfunction or intraoperative adverse events were recorded. A stricture rate of 12.5% (2/16) was observed, both of which were successfully managed through endoscopic dilatation. All patients were recorded as tolerating the procedure well with sedation. The median endoscopist satisfaction score was 9 (+/- 2.4) with only one recorded instance of difficulty attributed to balloon positioning.

Conclusion: These preliminary results from the UK cryoablation registry suggest that cryoablation with the CbFAS is a safe and effective therapy for BE-related dysplasia. The stricture rate appears to be comparable to that observed with RFA and similar studies. With the planned enrolment of further centres and suitable patients, this registry will further enhance our understanding of the long-term efficacy and safety profile of cryoablation using the CbFAS.

Disclosure: Nothing to disclose.

PP0107

ORAL ADMINISTRATION OF BEVACIZUMAB-800CW AND CETUXIMAB-800CW FOR THE DETECTION OF EARLY ESOPHAGEAL NEOPLASTIC LESIONS BY QUANTITATIVE FLUORESCENCE MOLECULAR ENDOSCOPY

Y.J. van Ginkel¹, L.E. van Heijst¹, A.M. van der Waaij²,

G. Kats-Ugurlu³, D.J. Robinson⁴, D. Gorpas⁵, R.Y. Gabriëls¹,

W.B. Nagengast¹

¹University Medical Center Groningen, Gastroenterology,

Groningen, Netherlands, ²University Medical Center Groningen,

Groningen, Netherlands, ³University Medical Center

Groningen, Pathology, Groningen, Netherlands, ⁴Erasmus MC,

Otorhinolaryngology and Head and Neck surgery, Rotterdam,

Netherlands, ⁵Institute of Biological and Medical Imaging,

Helmholtz Zentrum München, Germany

Contact E-Mail Address: a.m.van.der.waaij@umcg.nl

Introduction: Patients with Barrett's esophagus (BE) have an increased risk of developing esophageal adenocarcinoma (EAC) and therefore surveillance is necessary. However, lesion detection with high-definition white light endoscopy (HD-WLE) and narrow-band imaging (NBI) is hampered by high miss rates. Previous phase II studies have confirmed the great potential of quantitative fluorescence molecular endoscopy (qFME) in combination with topically administered fluorescent tracers for lesion detection in BE.

However, incubation time after topical tracer administration prolongs the procedure time by five minutes. In this ongoing clinical study, oral administration of bevacizumab-800CW, targeting vascular endothelial growth factor A (VEGFA), and cetuximab-800CW, targeting epidermal growth factor receptor (EGFR), is evaluated to improve both lesion detection and the clinical implementation of qFME.

Aims & Methods: A total of 30 patients with BE scheduled for a diagnostic and/or therapeutic endoscopy will be included. First 5 – 10 patients receive 4.5 mg and/or 9 mg oral bevacizumab-800CW before qFME. Subsequently, five patients will be included who receive 4.5 mg cetuximab-800CW orally before the diagnostic endoscopy, before their therapeutic endoscopy they receive a dose of 9 mg.

The patients drink the tracer in two sips in an upright position ten minutes before qFME. qFME consisted of *in vivo* fluorescence signal visualization and quantification by multi-diameter single fiber reflectance / single fiber fluorescence (MDSFR/SFF) spectroscopy measurements on the mucosa. Additionally, biopsies are collected from non-dysplastic Barrett tissue and (suspected) dysplastic tissue and *ex vivo* analysis will be performed.

Results: Nine patients received 4.5 mg and/or 9 mg bevacizumab-800CW and five patients received 4.5 mg cetuximab-800CW. Oral administration of both tracers was well tolerated by all patients. No incubation time is needed after oral administration after the procedure. A higher fluorescence signal was seen in all visible lesions *in vivo*. 16 out of 17 endoscopically visible lesions were detected by qFME with bevacizumab-800CW or cetuximab-800CW and were pathologically confirmed to be dysplastic. We will conduct further analysis to evaluate target-to-background ratios and/or contrast-to-noise ratios *in vivo*. Additionally, quantitative *in vivo* fluorescence based on MDSFR/SFF spectroscopy will be assessed.

Conclusion: Our preliminary results show that qFME with oral administration of bevacizumab-800CW and cetuximab-800CW is feasible and, compared to topical administration, seems promising for shortening the procedure time, while remaining adequate in lesion detection.

After completion of the cetuximab-800CW cohort, the optimal dosis and tracer will be determined and compared to combined administration of both tracers. Lastly, depending on what achieves the best *in vivo* results,

either the optimal tracer or a combination of both tracers will be administered to five patients with non-dysplastic Barrett's esophagus to test the specificity of our tracers.

Disclosure: Nothing to disclose.

PP0108

HISTONE CHAPERONES IN ESOPHAGEAL CARCINOMA: CAUSAL INSIGHTS AND PROGNOSTIC BIOMARKERS THROUGH MULTI-DIMENSIONAL ANALYSIS

B. Xia¹, Y. Liu¹, J. Yang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: xbh0715@163.com

Introduction: Esophageal carcinoma (EC) is an aggressive cancer with poor outcomes, often stemming from disrupted cellular regulators that enhance malignancy¹. Although histone chaperones are crucial in maintaining genomic and cellular integrity and have been implicated in various solid tumors, their definitive causal roles and therapeutic potential in EC are yet to be fully determined².

Aims & Methods: Our study aims to elucidate the causal roles of Histone Chaperone-Related Genes (HCRGs) in EC and assess their potential as prognostic markers and therapeutic targets.

We utilized datasets from TCGA-Esophageal carcinoma, GSE53624, and genome-wide association study data from ebi-a-GCST90018841. We began our analysis by identifying HCRGs linked to EC prognosis through univariate Cox regression. We then used unsupervised cluster analysis on EC samples from the TCGA-EC dataset to identify distinct clusters and subsequently isolated differentially expressed genes (DEGs) within these clusters and compared to normal controls. This identified common DEGs, which were further analyzed using expression quantitative trait loci (eQTL) data to perform a two-sample Mendelian Randomization (MR) analysis, with EC as the outcome. This analysis, enhanced by sensitivity analysis and MR Steiger filtering, helped identify candidate genes whose expression patterns were consistent with their MR properties.

These candidate genes were used to classify EC samples into high and low expression groups, identifying genes with significant survival differences. A prognostic nomogram incorporating clinical features and these genes' expression levels was developed to predict three-year survival probabilities.

Additionally, we performed functional and pathway enrichment analyses to explore the biological processes these genes influence and assessed the immune microenvironment. Validation efforts included immunohistochemistry on EC patient tissues and molecular assays in EC cell lines, confirming the clinical relevance and biological impacts of our findings and highlighting potential diagnostic and therapeutic strategies.

Results: We identified eight key HCRGs in the TCGA-EC dataset, significant for predicting EC prognosis. Analysis revealed 1,742 common DEGs, categorized into 9 risk factors and 17 protective factors via two-sample MR. Among these, ADORA2B and SAPCD2 stood out as crucial hub genes, strongly influencing survival outcomes.

A developed nomogram incorporating pathological stage, nodal classification, and expression levels of these two genes demonstrated good predictive accuracy for three-year survival (AUC=0.749). Immunophenotyping linked ADORA2B with increased dendritic cells and decreased Tregs, while SAPCD2 was associated with higher M0 macrophages and lower Tregs, indicating their influence on the immune landscape in EC.

Clinically, increased expression of ADORA2B and SAPCD2 correlated with adverse outcomes, confirmed by qPCR and immunohistochemistry in paired EC tissues (n=63). Functional studies in cell lines (KYSE150, TE-9)

showed ADORA2B's overexpression enhanced cell proliferation, G1/S transition, and migration, altering key proteins like PCNA, CDK4, and cadherins, confirming its oncogenic role in EC.

Conclusion: This study elucidates the causal roles of histone chaperones in EC, identifying ADORA2B and SAPCD2 as risk factors and prognostic biomarkers based on the integrated analysis of transcriptome analysis, MR, clinical sample evaluation, and molecular experiments.

References: 1. Shah MA, Altorki N, Patel P, Harrison S, Bass A, Abrams JA. Improving outcomes in patients with esophageal cancer. *Nat Rev Clin Oncol.* 2023;20(6):390-407. doi:10.1038/s41571-023-00757-y

2. Ghiraldini FG, Filipescu D, Bernstein E. Solid tumours hijack the histone variant network. *Nat Rev Cancer.* 2021;21(4):257-275. doi:10.1038/s41568-020-00330-0

Disclosure: Nothing to disclose.

PP0109

ESOPHAGEAL SQUAMOUS CELL CANCER IN PLUMMER-VINSON SYNDROME

A. Lemrabott¹, M. Kadiri², N. Lagdali¹, F.-Z. Chabib³, C. Berhili¹, M. Borahma⁴, F.Z. Ajana⁵

¹University Mohammed V, Ibn Sina Hospital, Rabat,

Morocco, ²Ibn Sina Hospital, Rabat, Rabat, Morocco,

³Ibn Sina University Hospital, Rabat, Morocco, Medical Unit C, Seclin, France, ⁴Mohammed the Vth University, Ibn Sina

Hospital, Department of Gastroenterology C, Rabat, Morocco,

⁵CHU Ibn Sina, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: aichanelemrabott@gmail.com

Introduction: Plummer-Vinson syndrome is a rare entity that associates dysphagia, iron deficiency anemia, and cervical esophageal membrane. Our work aimed to describe the clinical profile and to specify the predictive factors of degeneration in patients with Plummer-Vinson syndrome associated with esophageal cancer and to show interest in endoscopic surveillance.

Aims & Methods: It was a retrospective descriptive and analytical study over 30 years (1993-2023) including all patients treated and followed up for Plummer-Vinson syndrome and who presented esophageal cancer. Data collection and statistical analysis were performed by SPSS version 20.0 software.

Results: Out of the 160 patients treated for Plummer-Vinson syndrome, 15 patients had associated esophageal cancer resulting in a prevalence of 9.37%. The median age was 50.6 years with extremes of 28 and 74 years, with a sex ratio of M/F = 2/13. The interval between the diagnosis of Plummer-Vinson syndrome and the appearance of cancer was 8 years +/- 7.4. All our patients with associated cancer had dysphagia with weight loss, odynophagia in 92.9% (n=13), clinical anemia syndrome in 59% (n=8), and upper gastrointestinal bleeding in 10% (n=1). All patients had hypoferritinemia with a median value of ferritin 6.2µg/L.

The location of the Plummer-Vinson ring was at the level of the Killian triangle at 46% (n=7) and the upper third of the esophagus at 54% (n=8).

The location of the cancerous process at the level of Killian's triangle was in 46% of cases (n=7), and the location at the level of the upper third of the esophagus was in 19.7% (n=3). In 33.3% of cases (n=5) in the middle third. It was squamous cell carcinoma in all cases.

Surgical treatment was initiated in 14% of cases (n=2), radio-chemotherapy in 72% (n=11) and refusal of treatment in 14% of cases (n=2). Two patients progressed well with the disappearance of dysphagia, 10 patients died between 5 months and 5 years of cancer progression, and the rest of the patients could not be followed up.

In multivariate analysis, the statistically significant predictive factors for the degeneration of Plummer-Vinson syndrome were: Age>50.6 years (OR= 2.37, p=0.003 CI=1.875-4.236), Ferritinemia <6.2 µg/l (OR=3.02, p=0.001 CI=0.977-12. 516) and location of the ring at the level of the Killian triangle (OR=1.140, p=0.001 CI=1.057-1.229). Gender and dysphagia did not appear to be associated with degeneration with (p=0.26) and (p=0.35) respectively.

Conclusion: Plummer-Vinson syndrome is a precancerous lesion requiring endoscopic surveillance. In our series, the prevalence was 9.37%. Malignant transformation of this ring at the level of the triangle of Killian was present in 46% of cases. The predictive factors of degeneration were advanced age, low ferritinemia, and the location of the ring in the mouth of Killian.

Disclosure: Nothing to disclose.

PP0110

PREDICTION OF ADDITIONAL TREATMENT AFTER ESD IN EARLY ESOPHAGEAL CANCER – ASSOCIATION WITH LESION SIZE

J.H. Yoon¹, G.H. Kim¹, D.H. Jung¹, J.C. Park¹, S.K. Lee¹, Y.C. Lee¹, S.K. Shin¹

¹Severance Hospital, Seoul, South Korea

Contact E-Mail Address: YJHOON89@yuhs.ac

Introduction: ESD is considered as a first-line treatment for early esophageal cancer. Although ESD is expanding its area and replacing surgery, it has complication risk that cannot be ignored and often lead to subsequent surgery or chemoradiation. Currently, in early esophageal cancer, ESD is indicated in the absence of definite SM invasion, but it is difficult to differentiate this by EGD or EUS at the time of diagnosis.

In this study, we aimed to determine the additional indications for selecting ESD candidates based on factors that can be easily identified at diagnosis.

Aims & Methods: We retrospectively analyzed the data of a total 244 cases of patients who underwent esophageal ESD or modified EMR (e.g. precutting EMR, cap-assisted EMR) for dysplasia of the esophagus from 1 center between January 2006 and October 2023 and were diagnosed with esophageal cancer at the final pathology report. Among them, the cases whose final pathology report suggested the need for additional treatment were further analyzed. The indication for additional treatment included SM invasion, vertical margin positive, lymphovascular invasion (LVI), and perineural invasion (PNI). To identify the risk factors associated with additional treatment, we performed multivariable analysis using the logistic regression model. Factors included in the analysis were baseline patient characteristics, endoscopic findings, and pathological findings of the endoscopic resection specimen.

The longest diameter in the final specimen was used as the size of the lesion, and the morphology of the lesion was referred to the gross endoscopic findings at the time of diagnosis.

Results: Of the 244 total cases, the mean age was 65.6 and 219 (89.75%) cases were male. There were 74 cases (30.33%) suggesting indications for additional treatment, which included SM invasion (65 case), vertical margin positive (10 case), LVI (23 case), PNI (0 case), respectively. Regarding lesion size, the number of cases exceeding 15mm, 20mm, 25mm, and 30mm were 98 (40.16%), 45 (18.44%), 27 (11.07%), and 22 (9.02%), respectively. On multivariable analysis, lesion size greater than 15mm was a significant independent risk factor for additional treatment (OR = 2.234, 95% CI 1.127–4.426, p=0.021). Additionally, cutoff sizes greater than 15mm (such as 20mm, 25mm, 30mm), elevated morphology, and moderate or poorly differentiated cell type were also independent risk factors for additional treatment.

Predicting factor	Univariable analysis			Multivariable analysis *		
	OR	[95% CI]	p-value	OR	[95% CI]	p-value
Size						
>=15mm	1.947	[1.123-3.376]	0.018	2.234	[1.127-4.426]	0.021
>=20mm	2.291	[1.181-4.446]	0.014	2.582	[1.145-5.823]	0.022
>=25mm	2.692	[1.197-6.054]	0.017	3.227	[1.225-8.498]	0.018
>=30mm	3.812	[1.551-9.373]	0.004	4.699	[1.604-13.762]	0.005

Table 1. Multivariable analysis of possible predictor for additional treatment*

adjusted for morphology, and cell type.

Conclusion: Our study suggests that lesion size can be used as an independent risk factor to predict the need for additional treatment after endoscopic resection of early esophageal cancer. However, when applying this size factor, there is a discrepancy between the microscopic size in the resection specimen analyzed in this study and the size measured during the endoscopic procedure. Nevertheless, assuming that the discrepancy is not significant, it seems that superficial esophageal cancer measuring 15mm or more on endoscopy may be recommended for surgery or chemoradiation rather than ESD. Future studies with larger numbers of patients and adjustment for this discrepancy are expected to provide more powerful results.

Disclosure: Nothing to disclose.

PP0111

CLINICAL OUTCOMES AND PROGNOSTIC FACTORS FOR 80 YEARS OR OLDER UNDERGOING ENDOSCOPIC RESECTION FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

W. Kurihara^{1,2}, Y. Horiuchi¹, Y. Yamamoto³, Y. Ikeda³, Y. Hiasa², J. Fujisaki⁴

¹Cancer Institute Hospital, Japanese Foundation for Cancer Research, Department of Gastroenterology, Tokyo, Japan,

²Ehime University Graduate School of Medicine, Department of Gastroenterology and Metabology, Ehime, Japan, ³Ehime University Hospital, Endoscopy Center, Ehime, Japan, ⁴Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Contact E-Mail Address: wataru.kurihara@jfcrr.or.jp

Introduction: Endoscopic resection (ER) is widely accepted as the standard treatment for superficial esophageal squamous cell carcinoma (ESCC). In contrast, many old patients, especially 80 years or older, may die as a result of other diseases soon after ER. Therefore, the investigation of clinical outcomes and identification of prognostic factors of patients 80 years or older undergoing ER are clinically important because these findings may inform decision-making regarding the suitability of ER.

Aims & Methods: This study aimed to identify such clinical outcomes and prognostic factors. We retrospectively evaluated the short and long-term outcomes and prognostic factors of 87 patients 80 years or older undergoing ER for ESCC at two cancers between April 2012 and March 2021. We also evaluated the relationships of patient characteristics (sex, age, Eastern Cooperative Oncology Group-performance status; ECOG-PS, American Society of Anesthesiologists physical status; ASA-PS, prognostic nutritional index; PNI, Charlson comorbidity index; CCI) and overall survival rate using the Kaplan-Meier method and a Cox proportional hazards regression model.

Results: The median age of the patients was 82 years, and male was 76 patients (87.4%). The background factors were ECOG-PS 0-1 in 81 patients (93.1%) and a median CCI of 3. As short-term outcomes, 79 patients (90.8%) were curative resections (pT1a-M, V0 and Ly0), 9 patients (10.3%) had adverse events occurred (pneumonia was the most common: 4.6%),

and no treatment-related deaths occurred. As long-term outcomes, 34 patients died; however, only two patients died due to ESCC. The 3-year overall survival rates and the 5-year overall survival rates were 81.4% and 71.6%, respectively. CCI $\geq$ 4 (hazard ratio 4.75, 95% CI: 2.03-11.10) was identified as an independent prognostic factor.

Conclusion: The short-term outcomes were good. In contrast, as the long-term outcomes, the overall survival rates of patients with CCI $\geq$ 4 were poor. The decision to perform ER for patients with CCI $\geq$ 4 should be carefully considered because follow-up without ER is possible.

Disclosure: Nothing to disclose.

PP0112

THE INCIDENCE AND PROGNOSIS OF RADIATION-INDUCED ESOPHAGEAL CANCER IN BREAST CANCER SURVIVORS: A NATIONWIDE REGISTRY-BASED STUDY

W. Januszewicz¹, K. Witczak², A. Balata³, K. Pawlewicz⁴, N. Pilonis¹, J. Didkowska⁵, U. Wojciechowska⁵, J. Regula⁶, M.F. Kaminski¹

¹National Institute of Oncology, Department of Gastroenterological Oncology, Warsaw, Poland, ²Ministry of Health of the Republic of Poland, Warsaw, Poland, ³Department of Analyses and Strategy, Warsaw, Poland, ⁴National Institute of Oncology, Breast Cancer and Reconstructive Surgery Department, Warsaw, Poland, ⁵National Institute of Oncology, Department of Radiotherapy, Warsaw, Poland, ⁶National Institute of Oncology, Department of Cancer Epidemiology and Primary Prevention, Warsaw, Poland, ⁶Maria Skłodowska-Curie National Research Institute of Oncology and Centre of Postgraduate Medical Ed, Department of Gastroenterology, Warsaw, Poland

Contact E-Mail Address: w.januszewicz@gmail.com

Introduction: Radiation therapy (Rth) remains an integral part of the multifactorial management of breast cancer (BC). Some reports suggest an increased risk of secondary esophageal cancer (SEC) following Rth for BC, but wide-ranged populational studies on this topic are scarce. We conducted this nationwide registry-based study to analyze the incidence, prognosis, and timing of SEC within BC survivors.

Aims & Methods: We used two high-volume national databases (the National Health Fund Registry and the National Cancer Registry) to identify adult patients with a confirmed diagnosis of primary BC who received oncological treatment either with or without Rth between 2009 and 2019. Those patients were followed-up for the diagnosis of SEC until December 2023. The Fine-Gray competing risk regression models were used to determine and compare the cumulative incidence of SECs in both groups. We applied the Kaplan-Meier method to calculate the 5-year overall survival rates (OS) for SECs in both subsets of BC patients.

Results: We screened 194,598 patients with primary BC, of which 128,625 (66.1%) with available treatment data were included in the final analysis (mean age 61 $\pm$ 13yrs.; 99% females). Of these, 89,078 (69%) received Rth within the treatment regime (post-Rth BC) and 39,547 (31%) did not receive Rth (no-Rth BC). The 10-year cumulative incidence of SEC within the post-Rth BC group was 0.06% (95%CI, 0.04%-0.09%), as compared to 0.02% (95%CI, 0.01%-0.04%) within the no-Rth group (Gray test $P=$.005). In a competing risk model, having received Rth was associated with a >2.5-fold increase in the risk of developing SEC relative to no-Rth BC patients (HR 2.67, 95%CI, 1.27-5.65, $P=$.010). The median time to SEC occurrence after Rth completion was 3.7 years (interquartile range [IQR], 1.3-6.6). Squamous cell cancers constituted 89% of SECs in the post-Rth BC group, which was higher than within the no-Rth BC group, of which 73% were

SCCs. The prognosis of post-Rth SECs was as poor as for no-Rth SECs, with 5-year OS of 23% (95%CI, 14%-37%) and 13% (95%CI, 4.4%-36%), respectively; $P=$ 0.3.

Conclusion: Radiotherapy significantly increases the risk of SECs in BC survivors, although the cumulative incidence of this unfavorable event is low. These results raise awareness of SEC after RTH for breast cancer.

Disclosure: Nothing to disclose.

PP0113

COMPARISON OF RESTAGING ACCURACY BETWEEN ENDOSCOPIC ULTRASOUND AND POSITRON EMISSION TOMOGRAPHY IN PATIENTS WITH ESOPHAGEAL CANCER ACHIEVING PATHOLOGICAL COMPLETE RESPONSE AFTER CONCURRENT CHEMORADIOTHERAPY

M.-L. Han¹, Y.-J. Kuo¹

¹National Taiwan University Hospital, Internal Medicine, Taipei, Taiwan

Contact E-Mail Address: minglun@ms18.hinet.net

Introduction: Endoscopic ultrasound (EUS) and positron emission tomography (PET) have been widely recognized as valuable imaging modalities for tumor-node-metastasis (TNM) staging and treatment decision-making in patients with esophageal cancer. However, the accuracy of EUS and PET in esophageal cancer patients following neoadjuvant concurrent chemoradiotherapy (CCRT) remains inconsistent. Our objective was to conduct a comparative study between EUS and PET to evaluate their accuracy in staging post-CCRT patients who underwent resection surgery and were diagnosed with tumor complete remission.

Aims & Methods: The subjects of this study comprised patients diagnosed with esophageal squamous cell carcinoma and treated with CCRT before surgery at National Taiwan University Hospital (NTUH). Data were collected from May 1, 2007, to May 31, 2022, from a database of 828 esophageal cancer patients who underwent both EUS and PET before and after CCRT, and subsequently underwent resection surgery with pathologically complete response, resulting in a total of 231 patients. After excluding 14 patients who did not receive CCRT, 217 patients were enrolled for further study. The analysis focused on the T and N stages of esophageal cancer as reported by EUS and PET before and after CCRT, correlating clinical stages with pathologic stages. Using pathological diagnosis as the criterion standard, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EUS and PET were calculated. Patients who did not receive EUS or PET before CCRT and those who did not receive EUS or PET after CCRT ($n=87$) were excluded, resulting in a final inclusion of 128 cases for analysis.

Results: Among the 128 recruited patients, the overall accuracy of EUS for T-stage was 6.3%, while PET exhibited an accuracy of 13.3%. For N-stage, the accuracy of EUS was 20.3%, whereas PET demonstrated an accuracy of 33.6%.

Conclusion: In post-CCRT esophageal patients who achieved complete pathological remission, PET exhibited superior accuracy compared to EUS for both T and N staging; however, neither modality attained satisfactory levels of accuracy.

References:

- Yen, T. J., et al. (2012). "Comparative study between endoscopic ultrasonography and positron emission tomography-computed tomography in staging patients with esophageal squamous cell carcinoma." *Dis Esophagus* 25(1): 40-47
- Ajani, J. A., et al. (2019). "Esophageal and Esophagogastric Junction Cancers, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology." *Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw* 17(7): 855-883.

3. Rice, T. W., et al. (2017). "8th edition AJCC/UICC staging of cancers of the esophagus and esophagogastric junction: application to clinical practice." *Ann Cardiothorac Surg* 6(2): 119-130.

Disclosure: Nothing to disclose.

PP0114

CLINICAL FEATURES AND SPECIFIC ENDOSCOPIC FINDINGS OF P16-POSITIVE OROPHARYNGEAL CANCER

D. Yoshimura¹, K. Fukaura¹, T. Sasaki¹, A. Ohkubo¹, S. Imamura¹, T. Takeuchi¹, A. Ogasawara¹

¹National Hospital Organization (NHO) Kyushu Medical Center, Gastroenterology, Fukuoka, Japan

Contact E-Mail Address: mdyoshimura@gmail.com

Introduction: Transnasal endoscopy by ultrathin endoscope with image-enhanced endoscopy and high image quality has contributed greatly to the diagnosis of superficial cancers of the pharynx due to its ease of use. Its role in the diagnosis of p16-positive pharyngeal carcinoma which is closely associated with HPV infection, and has been recently reported to be increasing, is not clear.

Aims & Methods: We retrospectively investigated the clinical, pathological and endoscopic features of the cases of oropharyngeal cancer at our hospital, who underwent upper gastrointestinal endoscopy in the period between January 2019 to December 2023. All pathological specimens were stained with p16 immunohistochemistry.

(Study 1) Patient background, age, history of alcohol consumption and smoking, and the presence of multiple primary cancers in other organs were compared between the p16-positive oropharyngeal squamous cell carcinoma (p16+OPSCC) group and the p16- negative squamous cell carcinoma (p16-OPSCC) group.

(Study 2) The endoscopic features of the p16+OPSCC lesions were compared with those of the p16-OPSCC lesions.

Results: Sixty patients were included in this study, with a male/female ratio of 48:12 and a mean age of 63.7 years. The mean age of the female patients was 58.5 years, which was significantly younger than that of the male patients (65.0 years).

(Study 1) The p16+OPSCC group consisted of 25 patients with a male/female ratio of 19:6 and a mean age of 58.3 years, and the proportion of female patients was higher than that of the p16-OPSCC group (35 patients, 29:6, 67.5 years). The number of patients without a history of alcohol consumption nor smoking was significantly higher in the p16-OPSCC group (11 and 6, respectively), and 6 patients (24%) had neither. Multiple primary cancers were more frequent in the p16-OPSCC group (17 cases, 49%) than in the p16+OPSCC group (3 cases, 12%), mainly found in the hypopharynx and the esophagus.

(Study 2) p16-OPSCC lesions showed brownish areas (BAs) with dotted vasodilatation under narrow band imaging, whereas p16+OPSCC lesions had a unique appearance of subepithelial mass-like, enlarged tonsil-like, or submucosal mass-like with ulceration or nodular elevation. These lesions were accompanied by BA in only 8 cases (32%), and in some cases, the lesions were difficult to even detect by transnasal endoscopic observation.

Conclusion: p16+OPSCC is a new clinical entity that may affect young patients who are not at risk for alcohol consumption and smoking. Our study showed that the endoscopic features of the tumor are not appropriate for BA-based diagnosis. Gastrointestinal endoscopists need to renew their awareness of the disease.

Disclosure: Nothing to disclose.

PP0115

THE USE OF PROTON PUMP INHIBITORS AMONG ADULTS IN NORWAY – A NATIONWIDE DRUG UTILIZATION STUDY

S. Molnes¹, O. Spigset^{2,3}, L. Sagatun^{1,2}, Ø. Salvesen⁴, R. Fossmark^{2,5}

¹St. Olavs Hospital, Department of Gastroenterology and Hepatology, Trondheim, Norway, ²Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ³St. Olavs Hospital, Department of Clinical Pharmacology, Trondheim, Norway, ⁴Norwegian University of Science and Technology, Unit of Applied Clinical Research, Department of Public Health and Nursing, Faculty of Medicine and Health Science, Trondheim, Norway, ⁵St. Olavs Hospital, Centre for Obesity Research, Clinic of Surgery, Trondheim, Norway

Contact E-Mail Address: sveinungm@gmail.com

Introduction: The use of proton pump inhibitors (PPIs) has increased in many Western countries over the past decades. This may reflect the increasing prevalence of symptoms of gastroesophageal reflux disease (GERD) and prophylactic PPI use against gastroduodenal ulcers and haemorrhage induced by non-steroid anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. However, increasing PPI use against functional or uninvestigated dyspepsia and other inappropriate prescription have previously been documented and may also have contributed to the observed increase in PPI use. In this study we describe the change in incident and prevalent PPI use over time and the indication for prescription.

Aims & Methods: Nationwide data were retrieved from the Norwegian Prescription Database (NorPD) and consisted of information about dispensed prescription drugs. The study population consisted of all adults with at least one PPI prescription during the study period from 2009 to 2022. PPIs were defined by their ATC codes A02BC01 – C05 in addition to M01AE52, which is an esomeprazole and naproxen combination product. Prevalent PPI use was defined as the period covered by the defined daily doses (DDD) in each prescription. The indications for prescription were defined by ICPC or ICD-10 codes depending on whether PPI was prescribed in primary care or secondary health care. National data from the Norwegian Patient Registry (NPR) on all upper endoscopies performed during the study period were combined with NorPD data and it was assessed whether incident PPI users, defined as no PPI dispensal for two years, had undergone an upper endoscopy 180 days before or after incident PPI use.

Results: The use of PPI increased from 58.1 mill DDD in 2009 to 166.9 mill DDD in 2022, i.e. 15700 DDD/1000 and 38700 DDD/1000 persons. The absolute increase in DDDs was driven by a 3.5-fold increase in esomeprazole and a 5-fold increase in the use of pantoprazole.

The prevalence of PPI use increased from 3.5% in 2009 to 9.9% in 2022. The incidence of PPI use increased from 2.85% in 2011 to 5.42% in 2022.

In 2009 the dominant indications in primary and secondary health care, respectively, were esophageal disease and GERD (72.5% and 10.7% of DDDs), gastric ulcer (3.3% and 0.46% of DDDs), duodenal ulcer (0.86% and 0.21% of DDDs), while prescriptions with no reimbursement diagnosis constituted 10.2% of DDDs. In 2022 the dominant indications were esophageal disease and GERD (57.6% and 4.7% of DDDs), musculoskeletal disorders and pain (7.1% and 0.39% of DDDs and in combination with naproxen), prophylaxis against gastroduodenal ulcer (4.8% and 0.95% DDDs), while prescriptions with no reimbursement diagnosis constituted 5.2% of the DDDs.

There were 2.27 mill cases of incident PPI use in the study period and the proportion of PPI users that underwent upper endoscopy around treatment start decreased from 25.3% in 2009 to 11.1% in 2022. In patients with esophageal disease or GERD combined the proportion examined by upper endoscopy fell from 41.4% to 27.1%, while in patients without a reimbursement diagnosis the proportion fell from 19.2% to 6.9%.

Conclusion: In this nationwide study a 2.8-fold increase in prevalent PPI use was observed during the 14-year study period. This was caused by an absolute increase in PPI use against esophageal disease and GERD as well as prophylaxis in patients given ulcerogenic comedication. The proportion of incident PPI use investigated by upper endoscopy was halved.

Disclosure: Nothing to disclose.

PP0116

EPIDEMIOLOGY OF PROTON PUMP INHIBITOR PRESCRIPTION IN THE CZECH REPUBLIC

J. Cyraný¹, M. Vysoudil², J. Jarkovsky^{2,3}, S. Sembera¹, P. Moravkova¹, S. Rejchrt¹, I. Tachecí¹

¹Charles University, Medical Faculty and University Hospital Hradec Kralove, 2nd Dept. of Internal Medicine - Gastroenterology, Hradec Kralove, Czech Republic, ²Institute of Health Information and Statistics of the Czech Republic, Praha, Czech Republic, ³Institute of Biostatistics and Analyses, Medical Faculty, Masaryk University, Brno, Czech Republic

Contact E-Mail Address: jiri.cyraný@fnhk.cz

Introduction: Proton pump inhibitors (PPIs) are one of the most frequently prescribed drugs with high risk of the over-prescription.

Aims & Methods: Objective: to find potential sources of the over-prescription by analysis of prescription policy and its evolution in time by means of descriptive statistics

Methods: Analysis from the National Registry of Reimbursed Health Services (2010-2022) was performed targeting reimbursed prescription of ATC group A02BC (PPIs) and A02BA (H2 receptor blockers) with respect to the age of patient and prescribing specialist.

Results: More than 300 million defined daily doses (DDD) of antisecretory drugs were prescribed in 2022; PPIs represent the vast majority (296.2 million, 99 %). This volume rose 2.6 times during the 13 years span, the speed of rise is slowing but still 2.4 % yearly.

PPI were prescribed to 1.314 million of patients in 2022 and this number also rose 1.5 times for 13 years. 48 % of PPI users in 2022 were seniors over 65 years, majority of patients treated by PPIs was in 7th decade of life (24 %), while it was 6th decade till 2018 - age of patients rose in the observed period. PPI was prescribed to more than 12 % of the overall population in 2022, but to 29 % of senior population over 65 years of age!

Vast majority of PPI prescription (in DDD) is realized by general practitioners (GP, 67.8 %). The highest proportion of non-GP prescription (95.5 million DDDs) is realized by: gastroenterology (26.9 %), internal medicine (19.2 %), cardiology (9 %), rheumatology (6.1 %) and ENT (ears-nose-throat, 5.4 %). While overall PPI prescription (in DDD) rose 2.6 times during the last 13 years; higher increment was reached by ENT (18.7 times), allergology/immunology (5.7 times), pneumology (4.4 times); cardiology (4 times) and rheumatology (3.1 times).

Conclusion: Global volume of PPI prescription is overwhelming and covers almost a third of senior population. The rise during 13 years was 2.6 times in DDD and 1.5 times in the number of patients; and probably approaches the plateau. GPs are responsible for longstanding maintenance prescription and realize more than 2/3 of the volume. Prescription by specialist probably mirrors rather introductions of prescription. Prophylactic co-prescription with antithrombotic agents and NSAIDs can be responsible for increase in cardiology and rheumatology. Excessive increase of prescription in ENT (and to less extent pneumology and allergology/immunology) is probably to the account of extraesophageal reflux (EER). Routine long-term prescription of PPI for EER (which has no unequivocal diagnostic criteria so far) is a matter of debate because profit was proven

dominantly in patients with simultaneous "classical" gastroesophageal reflux symptoms (1,2). EER can be a target population for de-prescribing strategies.

References: 1. Krause AJ. Review article: diagnosis and management of laryngopharyngeal reflux. *Aliment Pharmacol Ther.* 2024;00:1-16.

2. Raghu G. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults. An official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Resp Crit Care Medicine* 2022;9:e18-e47.

Disclosure: Nothing to disclose.

PP0117

EVALUATING GASTRIC FUNCTION AND ENDOSCOPIC CHARACTERISTICS IN CORONARY ARTERY DISEASE PATIENTS POST-PERCUTANEOUS CORONARY INTERVENTION

G. Sobirova¹, J. Uzokov², B. Alyavi², M. Karimov², A. Abdullaey²

¹Tashkent Medical Academy, Rehabilitation, Tashkent, Uzbekistan,

²Republican specialized scientific practical medical center of therapy and medical rehabilitation, Internal Medicine, Tashkent, Uzbekistan

Contact E-Mail Address: guzals@mail.ru

Introduction: The relationship between coronary artery disease (CAD) and gastrointestinal function post-percutaneous coronary intervention (PCI) is complex and multifaceted.

Aims & Methods: This study aims to investigate the implications of CAD on gastric function and endoscopic characteristics in patients following PCI, providing insight into potential clinical interventions that could improve outcomes. A longitudinal study encompassed 116 patients with CAD post-PCI, with a mean age of 62.4 ± 12.5 years and 55% male representation. These patients were observed over a mean duration of 2.3 ± 1.5 years. Comprehensive assessments included cardiac function evaluation via echocardiography and biomarker analysis, alongside detailed gastric function tests (gastric emptying studies, pH monitoring) and endoscopic examinations to identify morphological changes in the gastric lining. Statistical analysis involved the use of independent t-tests and chi-squared tests for baseline comparisons, with paired t-tests and the Wilcoxon signed-rank test applied to assess changes over time. The Cox regression model was employed to determine the impact of altered gastric function and endoscopic findings on the prognosis of CAD patients, adjusting for age, gender, and baseline cardiac function.

Results: Our study identified significant gastric functional impairments in patients post-PCI, including delayed gastric emptying and increased gastric acidity ($p < 0.01$). Endoscopic findings revealed a higher prevalence of gastritis and gastric erosions in this cohort compared to the general population ($p < 0.05$). These gastric alterations were associated with poorer cardiac function and increased incidence of adverse cardiac events. Cox regression analysis further highlighted that specific gastric dysfunctions, particularly delayed gastric emptying and severe gastritis, significantly predicted worse cardiac outcomes (HR=2.3, 95% CI: 1.4-3.8, $p = 0.001$), after controlling for conventional risk factors. This study sheds light on the notable impact of CAD and PCI on gastric function and morphology, underscoring the bidirectional relationship between heart disease and gastrointestinal health. The findings suggest that the stress and systemic inflammation associated with CAD and the intervention process itself may contribute to gastric dysfunction. Addressing these gastric issues through targeted therapies could potentially mitigate some of the adverse cardiac outcomes observed in this patient population.

Conclusion: The presence of impaired gastric function and specific endoscopic changes in CAD patients post-PCI underscores the need for a holistic approach to patient care, integrating cardiovascular and gastroin-

testinal management strategies. Early detection and treatment of gastric dysfunction in this cohort may offer a novel pathway to improving both gastrointestinal and cardiac outcomes, enhancing overall patient quality of life and reducing the burden of CAD.

Disclosure: Nothing to disclose.

PP0118

WITHDRAWN

PP0119

EARLY GASTRIC CANCER IN CENTRAL NORWAY 2001 TO 2016 – A POPULATION-BASED STUDY

K. Kvamme¹, T. Stillingen¹, A.D. Sandø^{2,1}, P. Mjones^{3,1}, E.A. Bringeland^{2,1}, R. Fossmark^{1,4}

¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²St. Olavs Hospital, Department of Gastrointestinal Surgery, Trondheim, Norway, ³St. Olavs Hospital, Department of Pathology, Trondheim, Norway, ⁴St. Olavs Hospital, Centre for Obesity Research, Clinic of Surgery, Trondheim, Norway

Contact E-Mail Address: reidar.fossmark@ntnu.no

Introduction: Early gastric cancers (EGC) are confined to the gastric mucosa and submucosa irrespective of lymph node metastases. The proportion of gastric cancers diagnosed at an early stage varies considerably between Western countries but is low compared to countries with a screening program for gastric cancer. The majority of EGC patients have been treated with surgical resection including standard lymphadenectomy in Western countries. In contrast, Asian countries have treated larger proportions of EGC with endoscopic submucosal dissection (ESD) followed by estimation of risk of lymph node metastases based on histopathological characteristics. The aim of the present study was to characterize EGCs in Central Norway before ESD was an available treatment option. Furthermore, we aimed to assess histopathological characteristics associated with lymph node metastases and long-term survival in our cohort of EGC patients.

Aims & Methods: The study was a retrospective population-based study using patients identified from the Norwegian Cancer Registry and Norwegian Patient Registry (NPR). The annual number of gastroscopies was retrieved from NPR. 1205 patients were diagnosed with gastric cancer from 2001 to 2016, a period when gastrectomy with a modified D2 resection was standard treatment. In accordance with Western diagnostic criteria, patients with carcinoma in situ were not included. Patients who received neoadjuvant chemotherapy and histologically ypT0 or ypT1 were excluded to study only chemo naïve (true) EGC. Histopathological specimens were re-examined and eCura score risk stratification was calculated. Finally, long-term survival and cause of death were assessed.

Results: Of the 1205 patients with gastric cancer 88 (7.3%) had EGC. The number of gastric cancers declined ($p=0.010$), but the relative proportion of EGC was unchanged during the study period despite a doubling of annual gastroscopies at a national level during the study period. Patients with EGC had median age 77 (43-91) years vs. 74 (21-99) years for non-EGC controls. EGCs were more often of the Lauren intestinal type ($p<0.001$) and were more often localized in the antrum or corpus. Eighty-three patients underwent surgical resection and eight (9.0%) of these had N+ disease. An eCura score could be calculated for 79 EGCs. A significant proportion (9.4%, $n=5$) of the patients with a low risk eCura had lymph node metastases, whereas further exclusion of tumours with histological ulceration or SM2 invasion in a post-hoc analysis identified a N0 cohort ($n=36$). Recurrence of cancer was diagnosed in seven (8.1%) patients after a median

time of 29 (14-124) months from the EGC diagnosis. Fifty-five (62.5%) EGC patients died during follow-up, whereof 43 (78.2%) deaths were unrelated to EGC, seven (12.7%) died of cancer recurrence and five (9.1%) died from postoperative complications. Median survival for EGC patients was 117.1 months (95% CI 99.8-134.3) and 5-year overall survival 75%. Approximately half of deaths related to cancer recurrence (3 of 7) occurred more than five years after the EGC diagnosis.

Conclusion: EGCs constituted a minor but constant proportion of gastric cancers despite a considerable increase in gastroscopies. In this historic cohort with formal gastric resection for EGC, 9.0% had pN+ disease. Low risk eCura score alone was insufficient to predict pN0 disease whereas additional exclusion of patients with histological ulceration or SM2 infiltration identified a pN0 cohort. Long-term follow-up of more than five years is needed to assess EGC related mortality.

Disclosure: Nothing to disclose.

PP0120

LONG-TERM PROGNOSIS OF PATIENTS WITH GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA HARBORING EXTRA COPIES OF THE MALT1 GENE

M. Yoshioka¹, M. Iwamuro², R. Takenaka³, K. Miyahara⁴, S. Okanou⁵, C. Sakaguchi⁶, K. Yamamoto⁷, Y. Kawai⁸, T. Toyokawa⁹, T. Tanaka¹⁰, M. Otsuka²

¹Okayama Saiseikai General Hospital, Department of Internal Medicine, Okayama, Japan, ²Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Department of Gastroenterology and Hepatology, Okayama, Japan, ³Tsuyama Chuo Hospital, Department of Internal Medicine, Tsuyama, Japan, ⁴Hiroshima City Hospital, Department of Internal Medicine, Hiroshima, Japan, ⁵Mitoyo General Hospital, Department of Gastroenterology, Mitoyo, Japan, ⁶Shikoku Cancer Center, Department of Gastroenterology, Matsuyama, Japan, ⁷Kagawa Prefectural Central Hospital, Department of Gastroenterology, Takamatsu, Japan, ⁸Onomichi Municipal Hospital, Department of Gastroenterology, Onomichi, Japan, ⁹Fukuyama Medical Center, Department of Gastroenterology, Fukuyama, Japan, ¹⁰Okayama University Hospital, Department of Pathology, Okayama, Japan

Contact E-Mail Address: masanga114@gmail.com

Introduction: Trisomy and tetrasomy 18 are genetic aberrations characterized by the presence of one or two additional copies of chromosome 18 within a subset or in the entirety of cellular components. This genomic anomaly is a prevalent karyotypic irregularity in extra nodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), which is a type of lymphoma that originates from mucosa-associated lymphoid tissue in various organs, including the stomach, lungs, eyes, and thyroid. In previous investigation, we examined 146 patients with MALT lymphoma of the stomach who underwent FISH analysis for t(11, 18) translocation¹. However, the importance of trisomy and tetrasomy 18 in gastric MALT lymphoma is not fully understood because of the lack of long-term patient monitoring focused on genetic abnormalities. Therefore, in this study, we extended our investigation by tracking the same cohort of patients for an additional period exceeding 5 years to analyze the long-term prognosis of patients with gastric MALT lymphoma harboring trisomy/tetrasomy 18.

Aims & Methods: The objective of this study was to clarify the long-term prognosis of patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma with additional copies of MALT1. In this multicenter retrospective study, we enrolled 145 patients with gastric MALT lymphoma who underwent fluorescence in situ hybridization (FISH) analysis to detect t(11;18) translocation.

Results: The patient cohort was divided into three groups: Group A (n=87), comprising individuals devoid of the t (11;18) translocation or extra *MALT1* copies; Group B (n=27), encompassing patients characterized by the presence of the t (11;18) translocation; and Group C (n=31), including patients with extra *MALT1* copies. The clinical outcomes in each cohort were collected. Over the course of a mean follow-up of 8.5±4.2 years, one patient died of progressive MALT lymphoma, while 15 patients died due to etiologies unrelated to lymphoma. The progression or relapse of MALT lymphoma was observed in 11 patients: three in Group A, two in Group B, and six in Group C. In Groups A, B, and C, the 10-year overall survival rates were 82.5%, 93.8%, and 86.4%, respectively, and the 10-year event-free survival rates were 96.1%, 96.0%, and 82.9%, respectively. The event-free survival rate in Group C was significantly lower than that in Group A. However, no differences were observed in the 10-year event-free survival rates among individuals limited to stage I or II₁ disease (equivalent to excluding patients with stage IV disease in this study, as there were no patients with stage II₂), with rates of 98.6%, 95.8%, and 92.3% for Groups A, B, and C, respectively.

Conclusion: The presence of extra copies of *MALT1* was identified as an inferior prognostic determinant of event-free survival.

References: 1.Iwamuro, M. *et al.* Management of gastric mucosa-associated lymphoid tissue lymphoma in patients with extra copies of the *MALT1* gene. *World J. Gastroenterol.* **23**, 6155–6163 (2017).

Disclosure: Nothing to disclose.

PP0121

EFFECT OF DIETARY ANIMAL PROTEIN ON DEVELOPING GASTRIC CANCER CONSIDERING *HELICOBACTER PYLORI*: MULTI-CENTER PROSPECTIVE STUDY

S.W. Jeon¹, S.Y. Nam¹

¹Kyungpook National University, Internal Medicine, Daegu, South Korea

Contact E-Mail Address: sw-jeon@hanmail.net

Introduction: Dietary animal protein effect on gastric cancer (GC) taking *Helicobacter pylori* status into account has rarely been reported and has therefore been investigated in this study.

Aims & Methods: GC patients and healthy subjects were prospectively registered by 6 hospitals from October 2016 to December 2018. Multivariate analysis adjusted for many epidemiological factors (Model I) and additionally *H. pylori* (Model II) was conducted to investigate dietary protein effect on GC. Dietary animal protein groups included red meat, processed meat, white meat, eggs, and fishes.

Results: A total of 5,535 subjects (1,629 GCs) were enrolled. In Model I, red meat, fish, and eggs showed non-linear associations. Two serving/week for red meat, 1 serving/week for fish, 2-3 serving /week for egg was associated with the lowest risk of GC. Both low (aOR, 1.33) and high intake (aOR, 1.49) of red meat were associated with increased risk of GC. Both low (aOR, 1.76) and high intake (aOR, 1.74) of fish were associated with increased risk of GC. Both low (aOR, 3.07) and high intake (aOR, 1.33) of egg were associated with increased risk of GC. High intake of processed meat was associated with GC (adjusted odd ratio [aOR], 1.78; 95% CI, 1.27-2.49). Frequent intake of white meat was associated with GC risk (aOR, 1.67 for 1 serving/week, 2.15 for 2 servings/week, and 4.16 for ≥3 servings/week). In model II, these non-linear or positive association were sustained. Sub-analysis by sex showed similar association in both men and women.

Conclusion: Dietary animal proteins had non-linear or positive association with GC after adjusted for *H. pylori*. Nonlinear relationships of some food groups with GC suggests modest intake of such foods may reduce GC risk.

Disclosure: No COI.

PP0122

SURVIVAL AMONG PATIENTS CURED FROM GASTRIC ADENOCARCINOMA COMPARED TO THE BACKGROUND POPULATION

W. Leijonmarck¹, F. Mattsson¹, J. Lagergren^{1,2}

¹Karolinska Institutet, Department of Molecular medicine and Surgery, Stockholm, Sweden, ²King's College London, School of Cancer and Pharmacological Sciences, London, United Kingdom

Contact E-Mail Address: wilhelm.leijonmarck@ki.se

Introduction: It is unknown if gastric adenocarcinoma survivors have longer, shorter, or similar survival compared to the background population. This knowledge could contribute to evidence-based monitoring strategies, healthcare recommendations, and information for patients and families.

Aims & Methods: We aimed to help clarify if the survival among survivors of gastric adenocarcinoma is different from the corresponding background population. This population-based cohort study included all patients who underwent gastrectomy for gastric adenocarcinoma between 2006-2015 in Sweden and survived ≥5 years after surgery who did not later die from tumour recurrence. They were followed up until death, postoperative year 10, or end of study period (31 December, 2020). The observed survival was divided by the expected survival, yielding relative survival rates with 95% confidence intervals (CIs) using the life table method. The expected survival was derived from the entire Swedish population of the corresponding age, sex, and calendar year. Data came from medical records and nationwide registers.

Results: The survival among all 733 gastric adenocarcinoma survivors was shorter than the expected. The reduction in relative survival increased for each follow-up year, from 98.7% (95% CI: 97.0-100.5%) year 6 to 90.9% (95% CI: 86.7-95.2%) year 10. The decline in relative survival was more pronounced among patients who had gastrectomy in earlier calendar years (88.4% [95% CI: 83.0-93.9%] year 10 for years 2011-2015), shorter education (87.9% [95% CI: 80.1-95.7%] year 10 for education ≤9 years), more comorbidities (82.5% [95% CI: 68.2-96.7%] year 10 for Charlson comorbidity score ≥2), and no neoadjuvant therapy (87.7% [95% CI: 81.9-93.5%] year 10).

Years after gastrectomy	Alive at the beginning of each year	Observed survival in % (95% CI)	Expected survival in %	Relative survival in % (95% CI)
6	733	94.5 (92.9-96.2)	95.7	98.7 (97.0-100.5)
7	625	89.0 (86.6-91.3)	92.0	96.7 (94.1-99.2)
8	537	85.1 (82.4-87.8)	88.9	95.8 (92.7-98.8)
9	444	80.3 (77.2-83.5)	86.0	93.4 (89.8-97.1)
10	350	75.8 (72.2-79.3)	83.3	90.9 (86.7-95.2)

Conclusion: Gastric adenocarcinoma survivors seem to have poorer survival than the corresponding background population, particularly in certain subgroups.

Disclosure: Nothing to disclose.

PP0123

WITHDRAWN

PP0124

KEY INDICATORS FOR GLOBAL GASTRIC CANCER ENDOSCOPIC SCREENING PROGRAMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

J. Wang¹, X. Zhou¹, Y. Du¹

¹Changhai Hospital, Naval Medical University, Department of Gastroenterology, Shanghai, China

Contact E-Mail Address: wangjiayue829@163.com

Introduction: Discrepancies in gastric cancer (GC) mortality reduction are evident across global GC screening programs. Specifically, the reduction brought by endoscopic screening nearly doubled in Japan and Korea compared with China.

Despite studies indicating that economic status, screening methods, and public health awareness may influence screening efficiency, there is no comprehensive study that has summarized and compared the outcomes of available screening programs and identified factors potentially influencing the cancer-preventive effects.

Aims & Methods: Here we present data, including response to invitation, uptake of endoscopy screening and cancer screening positivity, of global GC screening programs. By pooling three key indicators throughout screening process, including endoscopic compliance rate, GC detection rate and early diagnosis rate, we conducted a meta-analysis of global GC endoscopic screening programs, in order to compare the outcomes of available screening programs and identify possible influencing factors.

PubMed, Embase, Web of Science, and Scopus were searched for relevant articles published until September 20, 2023. Original articles providing enough information to calculate the indicators in the general screening population were included.

Pooled random effect estimates of the indicators were computed, and further subgroup analysis stratified according to study period, country or region, setting, screening interval, education level and socioeconomic status was conducted. This study was registered with PROSPERO (CRD42023464921).

Results: 90 studies (59 reported endoscopic compliance rate, 68 reported GC detection rate and 33 reported GC early diagnosis rate) were included. Overall, the rates of endoscopic compliance, GC detection, and early-cancer diagnosis were 46.94% (95%CI 41.35-52.53%), 0.62% (95%CI 0.46-0.80%), and 61.41% (95%CI 51.42-71.40%), respectively.

Subgroup analysis demonstrated a gradual increase in endoscopic compliance and a counterintuitive decline in GC detection rate over time. Stratified by countries, the three indicators in Japan (51.05% [37.06-65.05%] for endoscopic compliance rate, 0.89% [0.55-1.31%] for GC detection rate, and 78.98% [68.83-87.66%] for GC early diagnosis rate) and Korea (49.78% [38.77-60.80%] for endoscopic compliance rate, 1.07% [0.05-3.38%] for GC detection rate, and 69.84% [61.51-77.57%] for GC early diagnosis rate) were significantly higher in China (39.68% [31.84-47.52%] for endoscopic compliance rate, 0.51% [0.33-0.74%] for GC detection rate, and 51.35% [36.33-66.37%] for GC early diagnosis rate).

The highest endoscopic compliance and GC detection rate was reported in hospital, while GC early diagnosis rate was higher in community and health checkup. Screening programs with 2-3 years intervals, public health campaigns, higher education levels, and socioeconomic status showed higher compliance. Screening programs based on new endoscopic techniques generally reported higher GC detection and early diagnosis rates.

Conclusion: Among high-incidence countries for GC, China lags behind Japan and Korea regarding endoscopic compliance rate, GC detection rate and early diagnosis rate. Screening settings, intervals, campaigns, education and socioeconomic stratum may affect endoscopic compliance, while GC detection and early diagnosis rates are mainly influenced by screening settings and endoscopic techniques. In the future, continuous

monitoring of quality control indicators should be applied in GC screening programs and the screening strategy should be adjusted accordingly to improve screening effectiveness.

Disclosure: Nothing to disclose.

PP0125

A MATHEMATICAL SIMULATION MODEL DETERMINES THE OPTIMAL ENDOSCOPIC SCREENING STRATEGY FOR THE DETECTION OF *HELICOBACTER PYLORI*-NAÏVE GASTRIC NEOPLASM

Y. Yanai¹, F. Ishibashi², K. Okusa³, Y. Tokai⁴, T. Hirasawa⁴, T. Kawakami⁵, K. Mochida^{2,5}, C. Yokoi¹, Y. Hayashi⁶, S. Ozawa⁷, K. Uraushihara⁸, Y. Minato⁹, H. Nakanishi¹⁰, H. Ueyama¹¹, M. Kataoka¹², Y. Toyama¹³, Y. Mizokami¹⁴, S. Suzuki²

¹National Center for Global Health and Medicine, Gastroenterology, Tokyo, Japan, ²International University of Health and Welfare Ichikawa Hospital, Gastroenterology, Chiba, Japan, ³Chuo University, Faculty of Science and Engineering, Data Science for Business Innovation, Tokyo, Japan, ⁴Cancer Institute Hospital, Gastroenterology, Tokyo, Japan, ⁵Koganei Tsurukame Clinic, Endoscopy Center, Tokyo, Japan, ⁶National Center for Global Health and Medicine, Medical Examination Center, Tokyo, Japan, ⁷Japan Community Health Care Organization Yamanashi Hospital, Gastroenterology and Hepatology, Yamanashi, Japan, ⁸Showa General Hospital, Gastroenterology, Tokyo, Japan, ⁹NTT medical center Tokyo, Gastroenterology, Tokyo, Japan, ¹⁰Musashino Red Cross Hospital, Department of Gastroenterology and Hepatology, Tokyo, Japan, ¹¹Juntendo University School of Medicine, Department of Gastroenterology, Tokyo, Japan, ¹²International University of Health and Welfare Mita Hospital, Tokyo, Japan, ¹³New Tokyo Hospital, Department of Gastroenterology, Chiba, Japan, ¹⁴New Tokyo Hospital, Department of Medical Examination Center, Chiba, Japan

Contact E-Mail Address: getsudoku1112@gmail.com

Introduction: In recent years, as the rate of *Helicobacter pylori* (*H. pylori*) infection has declined, the number of *H. pylori*-related gastric neoplasms (HpRGNs) has decreased. Although the number of *H. pylori*-naïve gastric neoplasms (HpNGNs) is estimated to be small compared to that of HpRGNs, the exact prevalence has not been unknown. Therefore, the effectiveness of screening by esophagogastroduodenoscopy (EGD) in cohorts with low *H. pylori* infection rate has not been revealed.

Aims & Methods: The aim of this study is (1) to determine age-related HpNGN prevalence by using a large-scale Japanese cohort and (2) to develop the optimal EGD screening strategy to detect HpNGNs in terms of screening efficiency.

Database of EGD for health checkup from 12 institutions in Japan between 2016 and 2022 was retrospectively reviewed. Detailed information on identified HpNGNs was investigated; age, sex, pathological diagnosis (pure signet ring cell carcinoma (PSRCC), gastric adenocarcinomas of the fundic gland type (GA-FG), foveolar gastric adenoma-raspberry type (FGA-raspberry type), and undifferentiated type cancer), lesion size, lesion depth, lymphovascular invasion, and presence of lymph node metastasis, and EGD images. EGD images of patients who underwent multiple EGDs in the past were followed retrospectively for changes in tumor size. Tumor growth speed, missing rate, age-related HpNGNs prevalence, and detection threshold size were calculated from database.

A virtual cohort of 100,000 births in the first year and thereafter reflecting the Japanese fertility trend was constructed based on these parameters. In this virtual cohort for 70 years of follow-up, tumor detection rates and

number-needed-to-test (NNT) for PSRCC, GA-FG, and undifferentiated cancers at different EGD screening start ages (40, 45, and 50 years) and screening intervals (2, 5, and 10 years) were compared.

Results: A total of 519,368 EGD cases were initially screened and 113 HpNGN lesions were detected in 108 patients (0.021%). HpNGN was found in all generations from 20s to 80s (0.011-0.028%). The age-related prevalence varied widely by HPNGN type; the prevalence of PSRCC was highest (0.022%) in 60s, but the prevalence of GA-FG gradually increased after the age of 50 and was not detected in people under 40. Additionally, undifferentiated cancer was discovered in people in their 30s and 50s, but not in people over 60. Tumor characteristics were analyzed for the construction of the simulation model by investigating the 97 of those lesions (34 PSRCC cases, 26 GA-FG cases, 30 FGA-raspberry type cases, and 7 undifferentiated type cases). The tumor growth rate was 2.5 mm/year for PSRCC, 2.7 mm/year for GA-FG, 1.2 mm/year for FGA-raspberry type and 11.7 mm/year for undifferentiated carcinoma. The missed rate was 46.1% for PSRCC, 65.2% for GA-FG, 56.5% for FGA-raspberry type and 17.0% for undifferentiated type. Among the strategies with detection rates of 50% or higher in the virtual cohort, the NNT of the 5-year interval screening strategy starting at age 45 years was the lowest for all tumor types (PSRCC 4.89, GA-FG 9.92, undifferentiated cancer 4.69). By adopting this strategy, most of HpNGNs were detected in less than 20 mm in size and the deep submucosa invasion rate was less than 30%.

Conclusion: A large-scale Japanese cohort demonstrated that prevalence of HpNGN was very low (0.021%). Mathematical simulation modeling revealed that the strategy of screening every 5 years starting at age 45 was most efficient to detect HpNGN.

Disclosure: Nothing to disclose.

PP0126

DIFFERENT SURVIVAL RATES OF PATIENTS WITH GASTRIC CANCER DEPENDING ON AGE AND SEX: A LARGE-SCALE STUDY

Y. Choi¹, N. Kim^{1,2}, J.H. Lee¹, Y. Kim¹, J.-H. Kim¹, H.H. Jo¹, Y.K. Jun¹, H. Yoon¹, C.M. Shin¹, Y.S. Park¹, D.-H. Lee^{1,2}

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea

Contact E-Mail Address: moonsin12345@naver.com

Introduction: The sex differences in the incidence of gastric cancer have been well known. However, uncertainty still exists in terms of prognosis of GC. For example, the US SEER data reports a significantly better prognosis in females than in males, but the prognosis is better in males than in females in Korean Central Cancer Registry data. Roles of molecular markers and gut microbiota as new prognostic factor are emerging recently, but few studies seem to try to reveal sex differences.

Aims & Methods: In this background, we aimed to analyze the differences in GC characteristics according to sex in Korean patients, mainly focused on survival. This was a single-center retrospective study. A total of fifteen thousand patients diagnosed with GC at the Seoul National University Bundang Hospital between 2003 and 2023 were included. Clinicopathological characteristics, histologic types, survival rates with age- and stage-stratification, and associated risk factors were analyzed. Information related to death was cross-verified using medical record review and data from the National Statistical Office.

Results: The ratio of males and females was about 2:1, and there was no differences in stage between sexes. Female patients were significantly younger than males, had more gastric body cancers and tumors with diffuse type or poorly differentiated histology. Females underwent less

endoscopic treatment and more surgery, and tumors with microsatellite instability was more common in females, while mutation of p53 was less common. In histological types according to Lauren classification, diffuse type histology was more common in younger patients in both males and females. The proportion of intestinal type GC increased with age, but the proportion increased rapidly in males while increased gradually in females. In Cox multivariate regression analysis for GC-related death, older age, proximal tumor location, diffuse type histology and advanced tumor stage were risk factors. In terms of survival, overall and GC-specific survival did not show significant differences between sexes in the analysis of the total population. However, sex differences in survival reversed with age, that younger females under 50 showed survival disadvantages, but the survival became similar in 50s, and older females over 60 showed survival advantages in both overall and GC-specific survival. Furthermore, in the stratification analysis according to the stage, there were no significant differences in stages I to III. But, stage IV female patients showed significant survival disadvantages. In subgroup analysis of stage IV patients, the differences between males and females in median survival were two months, and female patients were significantly younger and had a higher proportion of diffuse type GC than male patients, which shows aggressive feature and is related to poorer survival.

		Total (N=1,924) (%)	Male (n=1,282) (%)	Female (n=642) (%)	P
Median survival (mo)		10	11	9	0.022
Age (mean±SD)		61.59±14.25	62.41±13.23	59.96±15.97	0.001
Age (in diffuse type patients, mean±SD)		54.55±14.71	56.43±14.29	52.26±14.91	0.001
Lauren classification	Intestinal	554 (48.0)	438 (56.7)	116 (30.4)	<0.001
	Diffuse	574 (49.7)	315 (40.7)	259 (68.0)	
	Mixed / Indeterminate	26 (2.3)	20 (2.6)	6 (1.6)	

Conclusion: Significant differences in survival between sexes were observed with stratification analysis, although sex itself was not an independent prognostic factor. These age-dependent changes are thought to suggest the effect of sex hormones. These differences should be considered in clinical practice and later research in terms of tailored medicine.

Disclosure: Nothing to disclose.

PP0127

VALIDATION OF SERUM PEPSINOGEN AND *HELICOBACTER PYLORI* TEST IN THE DETECTION OF DIFFUSE-TYPE GASTRIC CANCER AMONG 23,130 HEALTH CHECKUP SUBJECTS IN SOUTH KOREA

N. Kim^{1,2}, S.H. Lim¹, Y. Choi², D.-H. Lee^{2,3}

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea, ³Healthcare system Gangnam Center Seoul National University Hospital, and Healthcare Research Institute, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: nakim@snubh.org

Introduction: Serum pepsinogens (PGs) are the biomarkers for atrophic gastritis and severe gastric inflammation.

Aims & Methods: The aim of this study was to validate the role of PGs in gastric cancer (GC) screening. 1,705 gastric neoplasms (1,287 GC and 418 gastric adenoma (GA)) and 21,425 controls (total 23,130) were enrolled.

PGs and anti-*Helicobacter pylori* (HP) antibody were measured. Area under the curve and receiver operating characteristic curve were calculated to identify the optimal cutoff values for PGs. Multivariate logistic regression and risk stratification were conducted by combining each PG value and anti-HP antibody in GC subtypes.

Characteristics	Total (23,130) (%)	Control (21,425) (%)	Gastric Adenoma (418) (%)	GC (1,287) (%)	p	Intestinal- GC 762 (%)	Diffuse- GC (489) (%)	p
Sex	Female	8,897 (38.5)	8,358 (39.0)	134 (32.1)	405 (31.5)	175 (23.0)	219 (44.8)	<0.001
	Male	14,233 (61.5)	13,067 (61.0)	284 (67.9)	882 (68.5)	587 (77.0)	270 (55.2)	
Age (mean)	54	54	63	62	<0.001	64	55	<0.001
HP status	Negative	8,119 (35.1)	7,857 (36.7)	54 (12.9)	208 (16.2)	137 (18.0)	61 (12.5)	0.008
	Positive	15,009 (64.9)	13,566 (63.3)	364 (87.1)	1,079 (83.8)	625 (82.0)	428 (87.5)	
	Missing	2 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
PG series (ng/mL)	PGI	52.1 (28.8)	52.4 (27.9)	40.3 (38.85)	50.6 (50.2)	44 (42.65)	60.2 (56.75)	<0.001
	PGII	11.2 (10.8)	11.0 (10.3)	12.9 (11.7)	17.5 (19.2)	16 (16.63)	21.2 (21.0)	
	PGI/II ratio	4.6 (2.6)	4.8 (2.6)	3.0 (2.4)	2.9 (2.3)	2.9 (2.4)	2.9 (2.1)	0.328

GC, gastric cancer; HP, *Helicobacter pylori*; PG, pepsinogen.

Results: PGII ≥ 21 ng/ml was associated with the risk of GA (odds ratio (OR) 1.38, $p < 0.001$), GC (OR 2.77, $p < 0.001$), diffuse-type GC (DGC) (OR 4.26, $p < 0.001$), especially, early-stage DGC (OR 7.11, $p < 0.001$). When GC risk was assessed by combining each PG value and HP antibody, OR showed significance between categories, and even stepwise increment from HP negative to positive and from each PG value negative to positive after adjustment with other confounding GC risk factors.

Conclusion: Each PG value combining HP test can be used as a screening test for high risk subjects with GC, and especially the combination of PGII ≥ 21 ng/ml and positive HP status in young female was related to high risk of early-stage DGC.

Disclosure: Nothing to disclose.

PP0128

GASTRIC CANCER RISK AMONG IMMIGRANTS AND SOCIOECONOMIC GROUPS IN THE NETHERLANDS

D. Mülder¹, H.J. van de Schootbrugge-Vandermeer¹, J. F. O’Mahony², D. Sun¹, W. Han¹, R.H.A. Verhoeven^{3,4,5}, M. van Loo⁶, W. van de Veerdonk⁶, M.C. Spaander⁷, I. Lansdorp-Vogelaar¹
¹Erasmus MC, Public Health, Rotterdam, Netherlands, ²University College Dublin, Dublin, Ireland, ³Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands, ⁴Amsterdam UMC, Amsterdam, Netherlands, ⁵Cancer Center Amsterdam, Amsterdam, Netherlands, ⁶Thomas More University of Applied Sciences, Antwerp, Belgium, ⁷Erasmus Medical Center Rotterdam, Gastroenterology & Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: d.sun@erasmusmc.nl

Introduction: Gastric cancer (GC) often presents at advanced stages with high rates of metastasis and poor clinical outcomes. Identification of groups at a high-risk of GC could facilitate screening in countries with a low GC incidence. Current understanding of which groups in the Netherlands are at an elevated risk is limited.

Aims & Methods: Our aim was to identify such high-risk groups, based on individual-level population data on migration status and socioeconomic status (SES). Patient data from the Netherlands cancer registry were

linked to demographic data of Statistics Netherlands in the period 2010-2022. GC incidence rates in the 14 largest immigrant populations were compared to those born in the Netherlands. Odds ratios (ORs) were computed per birthplace and corrected for age, sex and SES. Additionally, we investigated GC risk among second-generation immigrants and by SES.

Results: A total of 21,299 GC patients were recorded in the Dutch cancer registry between 2010 and 2022. Immigrant populations at a significantly higher GC risk compared to the general population were identified (Table 1). These include people born in Bosnia-Herzegovina (OR: 2.42), Turkey (OR: 2.22), Afghanistan (1.92), China (OR: 1.92), Surinam (1.68), Morocco (1.63), and the Dutch Antilles (1.61). Low SES increased the odds of developing GC, with an OR of 1.48 in individuals with the lowest SES compared to those with the highest SES. Still, first-generation migrants remained at a higher risk when adjusting for SES. Second-generation migrants did not have a significantly higher risk of developing GC.

Birth place	All	Afghanistan	Turkey	Bosnia-Herzegovina	China	Morocco	Surinam	Iran	Poland	Netherlands	Iraq	Belgium	United Kingdom
Gastric Cancer (GC)	10.10	21.09	20.11	19.46	17.28	17.17	12.68	12.49	9.10	8.43	8.25	6.66	6.23
Non-cardia GC	4.87	13.1	12.28	13.51	11.95	10.87	8.86	8.11	5.64	3.89	4.99	4.15	2.62
cardia GC	3.10	5.16	3.20	2.99	2.64	3.14	1.27	2.01	0.40	2.76	1.87	2.00	1.72
Other GC	2.13	2.82	4.63	2.96	2.68	3.16	2.55	2.38	3.06	1.78	1.39	0.51	1.89

Table 1: Age-standardized incidence rates per 100,000 for immigrants from selected countries in the Netherlands in the period 2010-2021.

Conclusion: Individuals born in countries with a high GC incidence remain at an elevated risk despite migration to a low-risk region, likely due to prior infection of *H. pylori*. Potential benefits of targeted *H. pylori* test-and-treat in immigrant populations should be explored in clinical and modelling studies. Primary caregivers should be cognizant of high-risk immigrant and socio-economic groups, facilitating the early detection of cancer within these vulnerable populations.

Disclosure: Rob H.A. Verhoeven received research grant from Bristol Meyers Squibb and consultancy fee from Daiichi Sankyo, all paid to institution.

PP0129

OCCURRENCE AND CHARACTERISTICS OF ENDOSCOPIC GASTRIC POLYPS IN PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS: A MULTICENTRIC CROSS-SECTIONAL STUDY

S. Massironi¹, C. Gallo², E. Lahner³, V. Sciola⁴, F. Cavalcoti⁵, M.V. Lenti⁶, A. Zilli⁷, L. Dottori³, G. De Rossi³, E. Miceli⁸, B. Annibale³, M. Vecchi⁹, P. Cantù⁵, A. Di Sabatino⁶, P. Invernizzi¹⁰, S. Danese¹¹, ARIOSO

¹Fondazione IRCCS San Gerardo dei Tintori, Division of Gastroenterology, Monza, Italy, ²University of Milano-Bicocca, Department of Medicine and Surgery, Monza, Italy, ³Sapienza University of Rome, Medical-Surgical sciences and translational medicine, Rome, Italy, ⁴Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁵Fondazione IRCCS Istituto Nazionale dei Tumori, Gastroenterology and Digestive Endoscopy Unit, Milan, Italy, ⁶Fondazione IRCCS Policlinico San Matteo, University of Pavia, First Department of Internal Medicine, Pavia, Italy, ⁷IRCCS Ospedale San Raffaele, Gastroenterology and Endoscopy, Milan, Italy, ⁸Fondazione IRCCS Policlinico San Matteo, First Department of Internal Medicine, Pavia, Italy, ⁹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Gastroenterology and Endoscopy Unit, Milan, Italy, ¹⁰Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Division of Gastroenterology, Monza, Italy, ¹¹IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: sara.massironi@libero.it

Introduction: Autoimmune atrophic gastritis (AAG) leads to significant changes in the gastric mucosa, including hypo-achlorhydria and increased gastrin (G) levels, providing proliferative stimuli on the gastric mucosa (1-5).

Aims & Methods: The aim of our study is to evaluate the occurrence and characteristics of gastric polyps in AAG patients across six tertiary centers in Italy. We conducted a multicentric, cross-sectional study from January to June 2023, prospectively enrolling consecutive patients diagnosed with AAG, from January 2000 to June 2023, who underwent at least one endoscopy. Data on demographics, clinical history, biochemical profiles, serological data, and endoscopic and histopathological findings were collected.

	AAG overall population (#612)	AAG patients without lesions (#390)	AAG patients with non-NEN polyps (#162)	AAG patients with gNENs (#108)
Sex, female (%)	452 (73.9)	280 (71.6)	280 (71.6)	78 (72.2)
Age (years), median (IQR)	66 (54-74)	61.5 (51-70)	70 (58.7-76.2)	70 (58.7-76.2)
APCA positivity, n (%)	496 (81)	386 (99.1)	125 (77.2)	76 (70.4)
Current smokers, n/n available (%)	48/185 (21.8%)	13/96 (13.5%)	13/96 (13.5%)	13/96 (13.5%)
PPI treatment, n/n available (%)	48/137 (25.9%)	29/98 (29.6%)	7/41 (17.1%)	10/41 (24.4%)
OLGIM, n (%)	II: 245 (40)	II: 144 (37)	II: 63 (39)	II: 60 (56)
OLGA, n (%)	II: 325 (53)	II: 179 (46)	II: 92 (57)	II: 76 (70)
Chromogranin A (ng/mL), median (IQR)	153 (75.5-269.3)	139 (68-221)	139 (68-221)	160 (86.9-251.5)
Gastrin (pg/mL), median (IQR)	667 (336.5-1156.5)	589.0 (281.8-1071.5)	688 (425.8-1200)	874 (362.5-1335)

Conclusion: This study represents the largest multicentric cohort of AAG patients, highlighting the significant presence of gastric polyps, including gNENs and various non-endocrine types including a not negligible proportion of patients who showed gastric adenocarcinoma. These

results emphasize the importance of proactive endoscopic monitoring and comprehensive histopathological evaluation in patients with AAG, to effectively identify and manage these different gastric lesions.

References: 1. Zhang H, Jin Z, Cui R, Ding S, Huang Y, Zhou L. Autoimmune metaplastic atrophic gastritis in chinese: a study of 320 patients at a large tertiary medical center. *Scand J Gastroenterol.* 2017;52(2):150-6.
2. Krasinskas AM, Abraham SC, Metz DC, Furth EE. Oxyntic mucosa pseudopolyps: a presentation of atrophic autoimmune gastritis. *Am J Surg Pathol.* 2003;27(2):236-41.
3. Kishino M, Nonaka K. Endoscopic Features of Autoimmune Gastritis: Focus on Typical Images and Early Images. *J Clin Med.* 2022;11(12).
4. Park JY, Cornish TC, Lam-Himlin D, Shi C, Montgomery E. Gastric lesions in patients with autoimmune metaplastic atrophic gastritis (AMAG) in a tertiary care setting. *Am J Surg Pathol.* 2010;34(11):1591-8.
5. Massironi S, Elvevi A, Gallo C, Laffusa A, Tortorella A, Invernizzi P. Exploring the spectrum of incidental gastric polyps in autoimmune gastritis. *Dig Liver Dis.* 2023.

Disclosure: Nothing to disclose.

PP0130

ASSESSING THE FREQUENCY OF TYPE I GASTRIC NEUROENDOCRINE NEOPLASMS IN AUTOIMMUNE ATROPHIC GASTRITIS: A MULTI-CENTER STUDY IN ITALY

S. Massironi¹, C. Gallo², E. Lahner³, V. Sciola⁴, F. Cavalcoti⁵, M.V. Lenti⁶, A. Zilli⁷, L. Dottori³, G. De Rossi³, E. Miceli⁸, B. Annibale³, M. Vecchi⁹, P. Cantù⁵, A. Di Sabatino⁶, P. Invernizzi¹⁰, S. Danese¹¹, ARIOSO

¹Fondazione IRCCS San Gerardo dei Tintori, Gastroenterology and Endoscopy, Monza, Italy, ²University of Milano-Bicocca, Department of Medicine and Surgery, Monza, Italy, ³Sapienza University of Rome, Medical-Surgical sciences and translational medicine, Rome, Italy, ⁴Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁵Fondazione IRCCS Istituto Nazionale dei Tumori, Gastroenterology and Digestive Endoscopy Unit, Milan, Italy, ⁶Fondazione IRCCS Policlinico San Matteo, University of Pavia, First Department of Internal Medicine, Pavia, Italy, ⁷IRCCS Ospedale San Raffaele, Gastroenterology and Endoscopy, Milan, Italy, ⁸Fondazione IRCCS Policlinico San Matteo, First Department of Internal Medicine, Pavia, Italy, ⁹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Gastroenterology and Endoscopy Unit, Milan, Italy, ¹⁰Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Division of Gastroenterology, Monza, Italy, ¹¹IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: sara.massironi@libero.it

Introduction: In autoimmune atrophic gastritis (AAG), immune-mediated morpho-functional changes in gastric mucosa lead to hypo-achlorhydria and subsequent hypergastrinemia. This stimulates gastric enterochromaffin-like (ECL) cell proliferation, escalating the risk of type I gastric neuroendocrine neoplasms (gNENs). Yet, longitudinal studies on the AAG-type I gNENs association are still scanty.

Aims & Methods: Our study aims to assess in a multicentric cohort of AAG patients, the frequency and the characteristics of type I gNENs.

We conducted a multicentric, cross-sectional study from January to June 2023, prospectively enrolling consecutive patients diagnosed with AAG, from January 2000 to June 2023, who underwent at least one endoscopy. Data on demographics, clinical history, biochemical profiles, serological

data, and endoscopic and histopathological findings were collected.

Results: The study included 612 patients with AAG [444 (75.2%) female, median age 66 (IQR 54-73) years]. At enrollment, 355 (58.1%) patients had ECL cell hyperplasia. Over a median follow-up of 4 (IQR 2-7) years, and after a median number of two upper GI endoscopies per patient, and a median disease duration of 7 (IQR 3-8) years, 108 patients showed 125 gNENs, corresponding to an incidence rate of 0.051 person-years. All the gNENs were well-differentiated. In 22 (18%) cases Ki 67 was not available; of the remaining 103, 86 (68.8%) cases were G1, 17 (13.6%) were G2, all of which with a Ki-67 < 10%; no G3 lesions were observed. 119 (95.2%) gNENs were located in the body/fundus. The median size was 5 (IQR 3-10) mm. 79 (73.1%) patients underwent endoscopic removal, 10 (9.2%) gastrectomy, 12 (11.1%) somatostatin analog therapy due to multifocal/recurrent disease, and 7 (6.5%) were only monitored. Patients with AAG and gNENs had significantly higher gastrin levels compared to patients without gNENs [median 874 pg/mL (IQR 362.5-1335) vs 581.5 pg/mL (IQR 281.8-1071.5), $p=0.014$]. However, there were no significant differences in proton-pump inhibitor use, OLGa and OLGIM stages, H. pylori status, and notably, circulating chromogranin A levels.

AAG patients with gNENs (#108)	
Sex, female (%)	78 (72.2)
Age (years), median (IQR)	68 (57-75.8)
APCA positivity, n (%)	76 (70.4)
Current smokers, n/n available (%)	19/57 (33%)
PPI treatment, n/n available (%)	10/41 (24.4%)
OLGIM, n (%)	II: 60 (56)
OLGA, n (%)	II: 76 (70)
Chromogranin A (ng/mL), median (IQR)	160 (86.9-251.5)
Gastrin (pg/mL), median (IQR)	874 (362.5-1335)

Conclusion: Type I gNENs are a relevant complication in patients with AAG. Elevated circulating gastrin levels are linked to their occurrence, with hypergastrinemia acting as a driver for abnormal proliferation of gastric ECL cells. Regular endoscopic surveillance and thorough histopathological examination are crucial in patients with AAG, serving as a key strategy for early diagnosis and treatment of gNENs.

References: 1. Shah SC, Piazuelo MB, Kuipers EJ, Li D. AGA Clinical Practice Update on the Diagnosis and Management of Atrophic Gastritis: Expert Review. *Gastroenterology* 2021;161(4):1325-1332.e7.

2. Köseoğlu H, Düzenli T, Sezikli M. Gastric neuroendocrine neoplasms: A review. *World J Clin Cases* 2021;9(27):7973-85.

3. Sheikh-Ahmad M, Saiegh L, Shalata A, et al. Factors Predicting Type I Gastric Neuroendocrine Neoplasia Recurrence: A Single-Center Study. *Biomedicine* 2023;11(3):828.

4. Pachuaashvili NV, Nagornaya DP, Tertychnyi AS. [Metachronous tumors of the stomach in a patient with autoimmune gastritis]. *Arkh Patol* 2023;85(1):57-61.

Disclosure: Nothing to disclose.

PP0131

EBV, TUMOR LOCATION, AND HIGHER TNM STAGE AFFECTED PD-L1 EXPRESSION OF GASTRIC CANCER IN ONE TERTIARY HOSPITAL IN SOUTH KOREA

J.h. Lee¹, N. Kim^{1,2}, Y. Kim¹, Y. Choi¹, Y.K. Jun¹, H.-K. Lee¹, H. Yoon¹, C.-M. Shin¹, Y.-S. Park¹, D.-H. Lee^{1,2}

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, South Korea, ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, South Korea

Contact E-Mail Address: salmonhunter@naver.com

Introduction: Programmed cell death ligand-1 (PD-L1) is known to negatively regulate T-cell activation. Immune checkpoint inhibitors (ICIs) such as nivolumab and pembrolizumab have prolonged survival in gastric cancer (GC) as well as malignant melanoma and lung cancer.

Aims & Methods: The aim of this study was to investigate the affecting factors on the expression of PD-L1 in GC tissue in the Korean population in terms of clinicopathological variables.

Total 216 patients with GC who underwent PD-L1 immunohistochemistry (22C3) were prospectively enrolled at Seoul National University Bundang Hospital from March 2018 to February 2024. Positive PD-L1 expression was defined as a CPS score of 5 or higher. Univariate and multivariate analysis was performed.

Results:

		Univariate analysis		Multivariate analysis	
Variables		OR (95% CI)	p value	OR (95% CI)	p value
EBV infection	EBV negative	Ref.		Ref.	
	EBV positive	8.54 (1.59-158.42)	0.043	14.01 (2.23-278.16)	0.019
Tumor location	Non-cardia	Ref.		Ref.	
	Cardia	2.78 (1.18-7.35)	0.026	4.97 (1.17-16.08)	0.005
TNM stage	Stage I	Ref.		Ref.	
	Stage II,III, or IV	1.38 (1.00-1.92)	0.049	1.61 (1.09-2.42)	0.018

Table.Univariate and Multivariate analysis for affecting factors on PD-L1 expression.

Multivariate regression (Table) showed some few significant associations between PD-L1 expression and specific factors. EBV infection shows a strong effect in both univariate (odd ratio [OR] 8.54, 95% confidence interval [CI] 1.59-158.42, $p=0.043$) and multivariate analysis(OR 14.01, CI 2.23-278.16, $p=0.019$). Cardia portion involvement shows a significant correlation in both univariate (OR 2.78, CI 1.18-7.35, $p=0.026$) and multivariate analysis(OR 4.97, CI 1.71-16.08, $p=0.005$). And higher TNM stage also remains significant in both univariate (OR 1.38, CI 1.00-1.92, $p=0.049$) and multivariate analysis (OR 1.61, CI 1.09-2.42, $p=0.018$).

Conclusion: EBV infection, cardia involvement, and higher TNM stage were independent factors influencing PD-L1 expression.

Disclosure: Nothing to disclose.

PP0132

GENOTYPE-PHENOTYPE CORRELATION FOR GASTRIC AND DUODENAL NEOPLASTIC LESIONS IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

M. Granziera¹, A. Piruzza¹, P. Pelizzo², I. Albergati¹, F. Orbosuè¹, L. Ghelfi², M. Santarosa², S. Maiero², S.L. Crocè¹, A. Viel¹, R. Cannizzaro², S. Realdon³

¹Università di Trieste, Trieste, Italy, ²Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Oncological Gastroenterology, Aviano, Italy, ³Centro di Riferimento Oncologico (CRO) IRCCS, Aviano, Italy

Contact E-Mail Address: margherita.granziera@gmail.com

Introduction: FAP is a disorder characterized by an autosomal dominant mutation of the APC gene. Duodenal adenomas are indeed found in 60–90% of patients with FAP. Gastric polyps in FAP patients are found in 30–100% of cases and most of them are fundic gland polyps. Some patients have a neoplastic phenotype (low grade/high grade dysplasia or adenocarcinoma). Shimamoto et al. tried to explain this condition: they subdivided the APC gene into six groups (from A to F), each one corresponding to a codon range, and evaluated the phenotypic correlation for each of these regions. They found an association between APC variants in codons 1398–1580 (Region E) and neoplastic gastric and duodenal lesions.

Aims & Methods: The aim of our pilot study is to investigate the correlation between the different APC mutations and the presence of neoplastic gastric and duodenal phenotype in our case series of FAP patients.

We analysed 37 patients followed by our center for an average of 10 years: the APC gene was subdivided into six groups (from A to F) according to Shimamoto et al., each one corresponding to a codon range, and we studied the correlation between genotype and phenotypic manifestation of gastric and duodenal lesions according to their clinical history.

Results: We collected two patients with a mutation in region E: both developed gastric polyposis with low grade dysplasia (LGD) and high grade dysplasia (HGD) lesions of the duodenum. We also observed that two out of the three patients with mutation in region D (1250–1398) progressed to gastric cancer and duodenal cancer respectively. In Shimamoto's study region B (454–1020) appears to be associated with a low risk of developing gastric lesions and a moderate risk of duodenal polyposis (Spigelman ≥ III), while our analysis shows that two (out of 12) of the patients mutated in this region developed gastric cancer and two developed duodenal cancer. In our case series two patients had the mutation at the promoter level of the APC gene, and this correlates with GAPPs (Gastric Adenocarcinoma and Proximal Polyposis of the Stomach): a newly discovered disease that has a very high risk of gastric adenocarcinoma typically without duodenal polyps.

Region (tot pt)	Gastric LGD	Gastric HGD/AC	Spigelman ≥ 3	Duodenal HGD/AC
A (11)	4	0	4	0
B (12)	4	1	3	2
C (5)	4	0	2	0
D (3)	1	1	2	1
E (2)	2	0	2	2
F (2)	0	0	1	0
B1 APC promoter (2)	2	0	0	0

Conclusion: Currently there are no precise guidelines for upper gastrointestinal tract endoscopy based on genetic mutations. This pilot study highlights the need for further research to establish an evidence based consensus.

References: Shimamoto Y, Takeuchi Y, Ishiguro S, Nakatsuka SI, Yunokizaki H, Ezoe Y, Nakajima T, Tanaka K, Ishihara R, Takayama T, Yoshida T, Sugano

K, Mutoh M, Ishikawa H. Genotype-phenotype correlation for extracolonic aggressive phenotypes in patients with familial adenomatous polyposis. *Cancer Sci.* 2023 Dec;114(12):4596–4606.

Disclosure: Nothing to disclose.

PP0133

FEASIBILITY AND SAFETY OF ENDOSCOPIC RESECTION VIA SNARING FOR GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE

H. Yamazaki¹, Y. Kano¹, E. Yamabe¹, H. Eida¹, S. Kuwabara¹, M. Kanamori¹, I. Toshifumi¹, S. Banjoya¹, N. Tomita¹, T. Kimura¹, K. Furuta¹, S. Nagae¹, N. Takeuchi¹, Y. Kimoto¹, K. Ono¹, Y. Minato¹, K. Ohata¹

¹NTT Medical Center Tokyo, Department of Gastrointestinal Endoscopy, Tokyo, Japan

Contact E-Mail Address: hiroyama90@hotmail.com

Introduction: Gastric adenocarcinoma of the fundic gland type (GA-FG) originates from the deeper mucosal layer, and predominantly occurs in the upper gastric region. Endoscopic submucosal dissection (ESD) in the upper region often results in a perpendicular approach and can be technically challenging. On the other hand, most GA-FG are relatively small, and snaring resection such as hybrid ESD and endoscopic mucosal resection with a cap-fitted pan endoscope (EMRC) may offer efficacy. However, the safety and feasibility of snaring resection for GA-FG remain unclear.

Aims & Methods: We retrospectively analyzed 77 cases of GA-FG endoscopically resected between August 2013 and April 2024 at NTT Medical Center Tokyo. Cases were categorized into two groups: (i) ESD group (lesions resected by ESD, n=54) and (ii) Snaring group (lesions resected by hybrid ESD or EMRC, n=23), and treatment outcomes were compared between the two groups.

Results: There was no difference in gender between the two groups. Patients in the snaring group were significantly younger (median age 62.0 vs 56; p<0.05), and the lesions were significantly smaller (median tumor size 5.0 vs 4.0mm; p<0.05). The majority of lesions in both groups were located in the upper gastric region. The two groups had no significant differences in en bloc resection rate, rate of submucosal invasion, lymphovascular invasion, vertical/horizontal margin positivity rate, or R0 resection rate. However, the snaring group exhibited a shorter procedure duration (29.5 vs 12.0 minutes; p<0.05), and reduced hospital stay duration (7.0 vs 5.0 days; p<0.05) compared to the ESD group. Adverse event rates were not significantly different between the two groups. Submucosal tissue was present in 100% of snaring group specimens, with a median resected submucosal layer thickness of 667.0µm (IQR: 527.9–797.2).

	ESD group N=54 lesions	Hybrid ESD/EMRC group N=23 lesions	p
Procedure time, min, median (IQR)¶	29.5 (18.0–50.0)	12.0 (7.0–21.5)	<0.05
En-bloc resection, no. (%)	54 (100%)	23 (100%)	1
Tumor size, mm, median (IQR)¶	5.0 (3.0–8.0)	4.0 (2.9–5.0)	<0.05
Depth of Invasion, no. (%)			
M/SM1	48 (90.6%)	19 (95.0%)	
SM2	5 (9.4%)	1 (5.0%)	0.06
Lymphovascular invasion, no(%)	3 (5.7%)	1 (5%)	1
R0 resection (%)	46 (86.8%)	18 (90.0%)	1
Hospitalization period, day, median (IQR)¶	7.0 (5.3–7.0)	5.0 (5.0–5.5)	<0.05

Conclusion: Despite comparable rates of en bloc resection, positive vertical margin, and adverse events, the snaring group exhibited significantly shorter procedure time and hospital stay durations. All snaring group specimens contained submucosal tissue, with the resected submucosal layer thickness exceeding 500µm. Endoscopic resection by snaring might be a safe and feasible approach for resection of GA-FG.

References: 1. Iwamuro M, Kusumoto C, Nakagawa M, Matsueda K, Kobayashi S, Yoshioka M, et al. Endoscopic features of oxyntic gland adenoma and gastric adenocarcinoma of the fundic gland type differ between patients with and without *Helicobacter pylori* infection: a retrospective observational study. *BMC Gastroenterol.* 2022 Jun 12;22(1):294.

2. Ueyama H, Yao T, Nakashima Y, Hirakawa K, Oshiro Y, Hirahashi M, et al. Gastric adenocarcinoma of fundic gland type (chief cell predominant type): proposal for a new entity of gastric adenocarcinoma. *Am J Surg Pathol.* 2010 May;34(5):609–19.

Disclosure: Nothing to disclose.

PP0134

VALIDATION OF YPSTAGE AND CONSTRUCTION OF “YCSTAGE” AFTER PREOPERATIVE CHEMOTHERAPY IN GASTRIC CANCER

E. Bando¹, Y. Matsumoto¹, K. Takahashi¹, T. Hattori¹, S. Inoue¹, Y. Koseki¹, K.-i. Furukawa¹, K. Fujiya¹, Y. Tanizawa¹

¹Shizuoka Cancer Center, Division of Gastric Surgery, Suntogun, Japan

Contact E-Mail Address: e.bando@scchr.jp

Introduction: In the eighth edition of the TNM classification, clinical stage (cStage) and pathological stage after neoadjuvant chemotherapy (ypStage) were newly defined for gastric cancer. However, cStage after prior chemotherapy (ycStage) has not yet been defined.

Aims & Methods: This study aimed to validate ypStage and construct ycStage after preoperative chemotherapy in gastric cancer from the viewpoint of survival outcomes. One hundred-eighty-seven patients who planned to undergo gastrectomy with curative intention after preoperative chemotherapy were enrolled. Survival outcomes stratified by ypStage and ycStage was evaluated. ycStage was evaluated by extrapolating TNM cStage. In addition, macroscopic type, tumor size, histological type, and tumor marker (CEA/CA19-9) after chemotherapy were selected as other prognostic factors. These staging system and variables were evaluated by univariate and multivariable analysis. Harrell's concordance index (C-index: time dependent area under the curve) was used to evaluate predictive ability.

Results: Gastrectomy was not performed in 14 patients (7.5%) due to incurable factors during operation. Remaining 173 patients underwent surgery. Residual tumor was R0: 148 cases (85.5%), R1: 17 cases (9.8%), R2: 19 cases (4.6%), respectively. ypStage: The survival distribution of ypStage was assessed in 173 patients who underwent gastrectomy. The 5-year survival rates (ysr) for ypStage I (n = 36), II (n = 55), III (n = 60), and IV (n = 22) were 82.3%, 76.5%, 42.7%, and 14.1%, respectively. There were significant differences between II/III (P=0.001) and between III/IV (P=0.009), respectively. There was a tendency for there to be a difference in survival between I/II (P=0.087). The C-index of ypStage was 0.713 (standard error: se=0.027). ycStage constructed by ordinal TNM factor: The survival distribution of ycStage, ycT, and ycN was assessed in all 187 patients. The 5-ysr for ycStage I (n = 12), II (n = 39), III (n = 90), and IV (n = 46) were 54.7%, 57.5%, 61.0%, and 40.6%, respectively. The predictive ability was poor with C-index of 0.533 (se=0.031). The 5-ysr for ycT1 (N=9): 66.7%, ycT2 (N=16): 64.2%, ycT3 (N=27): 60.6%, ycT4 (N=135): 52.0%, respectively. There were no significant differences between ycT1/2 (P=0.734) and between ycT2/3 (P=0.872). The 5-ysr for ycN0 (N=55): 45.9%, ycN1 (N=55): 59.3%, ycN2 (N=54): 68.2%, ycN3 (N=23): 36.4%, respectively. The survival outcomes among cN0, cN1 and N2 are completely reversed. Other preoperative prognostic factors: In univariate analysis histological type (P=0.703), macroscopic type (P=0.125), and CA19-9 (P=0.296) were not significant prognostic factors, but tumor size (<80mm (n=117): 5-ysr; 64.6% vs. ≥80mm (n=70): 34.2%, P<0.001] and CEA [(negative (n=152): 5-ysr;

59.2% vs. positive (n=35): 33.0%, P<0.001]) were significant prognostic factors. Multivariate Cox proportional hazard model selected tumor size (P<0.001) and CEA (P=0.007) as independent prognostic variables. Construction of proposal ycStage: A new proposal stage was constructed from the results of multivariate analysis. ycStageI: size<80mm and CEA-negative, ycStageII: size<80mm and CEA-positive, ycStageIII: size≥80mm and CEA-negative, ycStageIV: size≥80mm and CEA-positive. The 5-ysr for new proposal ycStage I (n = 94), II (n = 26), III (n = 52), and IV (n = 15) were 71.3%, 54.0%, 37.0%, and 20.0%, respectively. The C-index of new proposal ycStage was 0.662 (se=0.029). It is significant higher value than that of ycStage constructed by ordinal TNM factor.

Conclusion: The predictive ability of the ypStage, on the basis of TNM factors, considered favorable. However, survival separation was poor for both ycT and ycN. Thus, ycStage based on ordinal TNM did not have the perspective of survival outcome prediction. Proposal ycStage constructed by tumor diameter and CEA may be recommended.

Disclosure: The first author (Etsuro Bando) received honorarium from Johnson & Johnson, Medtronic plc, Intuitive Surgical G.K., KAKEN PHARMACEUTICAL CO., LTD, and DAIICHI SANKYO COMPANY, LIMITED.

PP0135

RISK FACTORS AND CLINICAL CHARACTERISTICS OF EARLY-ONSET GASTRIC CANCER VS. LATE-ONSET GASTRIC CANCER: A CASE-CASE STUDY

M. Puzzono¹, A. Mannucci¹, C. Brombin², S. Balafas², C. Di Serio³, L. Iacopino³, L. Poliani¹, L. Albarello⁴, U. Elmore⁵, R. Rosati⁵, G.M. Cavestro¹

¹Gastroenterology and Gastrointestinal Endoscopy Unit, Vita-Salute San Raffaele University, IRCCS San Raffaele Scientific Institute, Milan, Italy, ²University Centre for Statistics in the Biomedical Sciences (CUSBS), Milan, Italy, ³Vita-Salute San Raffaele University, Milan, Italy, ⁴Pathology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, ⁵Department of Gastrointestinal Surgery, IRCCS San Raffaele Scientific Institute, Milan, Italy

Contact E-Mail Address: cavestro.giuliamartina@hsr.it

Introduction: Early-onset gastric cancer (eoGC), defined as GC before 50, accounts for about 5% of GC and 3% are part of a hereditary syndrome. Its incidence is rising. eoGC was reported to present at an advanced stage at diagnosis, with a poor differentiation and a worse prognosis than in the elderly (late-onset GC, loGC), even though eoGC risk factors and characteristics remain unclear.

Aims & Methods: Therefore, we compared eoGCs with loGCs in terms of clinicopathological characteristics and risk factors. We conducted a retrospective case-case study of patients with eoGC and loGC diagnosed from 2015 to December 2022 at IRCCS San Raffaele Scientific Institute (Milan, Italy). We collected clinical data, tumor characteristics (including *Helicobacter Pylori* status, HP), family history of GC, smoking habit, alcohol intake, and BMI. We performed multi-gene panel testing on all eoGC.

Results: 58 eoGC (51.7%M, 48.3%F; median age at diagnosis [IQR] 44.5y [39.00, 47.75]) and 290 loGCs (63.8%M, 36.2%F; median age at diagnosis [IQR] 70.33y [63.90, 75.00]) were enrolled. 19.2% eoGCs carried a germline pathogenic variant (4 CDH1; 2 TP53; 1 MMR; 1 ATM; 1 PTEN; 1 heterozygous MUTYH). Having a second-degree relative (SDR) with GC was significantly associated with eoGC (15.8% eoGCs vs. 4.6% loGCs, p = 0.015). eoGCs reported lower BMI (median 22 eoGC vs 24 loGC, p=0.016). We also found a statistically significant difference between groups in alcohol consumption (P = 0.042) and smoking status (P = 0.023). While eoGCs were mainly at

the cardia (29.3% eoGCs vs. 1.7 % loGCs; $p < 0.001$), loGCs were mostly at the antrum (19% eoGC vs. 36.9% oGCs; $p = 0.009$). eoGCs reported more dysphagia (30.9% eoGCs, compared to 4.9% loGCs, $p < 0.001$), while most patients in the loGC cohort had anemia (25.3% loGCs vs 7.3% eoGCs, $p = 0.002$) and asthenia (9.1% loGCs vs 0% eoGCs, $p = 0.012$). 48.3% eoGCs were diffuse-type adenocarcinoma ($p = 0.014$), while 51% loGCs were intestinal-type ($p < 0.001$). No significant differences were observed in terms of T and N status, while more eoGC were M1 (26.3% eoGCs vs. 9.7% loGCs, $p = 0.001$) and presented at stage III-IV (56.9% eoGCs vs. 41.7% loGCs, $p = 0.042$) at diagnosis.

Conclusion: 19.2% patients with eoGC carry a germline pathogenic variant, suggesting that patients with eoGC should be evaluated for germline testing at diagnosis. eoGC more often is localized at the cardia with dysphagia and presents as diffuse-type adenocarcinoma at an advanced stage (III-IV) at diagnosis. However, 35.6% patients with eoGC presents with early gastric cancer T1 (vs 24.1% loGCs), possibly implying that younger age does not entail worse outcomes.

Disclosure: Nothing to disclose.

PP0136

MICROBIOME COMPOSITION IN PATIENTS WITH UPPER GASTROINTESTINAL CANCER AND SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO).

R. Rosania¹, N. Hipler¹, K. Lehr¹, V. Keitel-Anselmino¹, A. Link¹, M. Venerito¹

¹Otto-von Guericke University Hospital, Gastroenterology, Hepatology, and Infectious Disease, Magdeburg, Germany

Contact E-Mail Address: rosa.rosania@med.ovgu.de

Introduction: Small intestinal bacterial overgrowth (SIBO) is frequent in patients with past or active upper GI cancer. SIBO is associated with clinical symptoms including, bloating and diarrhea that may impact negatively on quality of life. Current treatment of SIBO is empirical and relies on the cyclical use of antibiotics.

Aims & Methods: The aim of the present study was to characterize the microbiome composition of patient with upper GI cancer with or with no SIBO.

From April 2021 to May 2022, consecutive patients with past or active GI cancer attending our oncology outpatient department were enrolled in a prospective case control study. Treatment naïve patients with a first diagnosis of upper GI cancer but no SIBO-related symptoms served as controls. All included patients completed a standardised questionnaire about SIBO-related symptoms (bloating, diarrhoea), concomitant medications, and quality of life. They were offered upper endoscopy with duodenal aspirate, provided a 30-day period with no antibiotic intake. SIBO was defined as a bacterial count greater than 10^3 colony forming units per millilitre in the duodenal aspirate. Using optimized protocol, the DNA from duodenal aspirate was extracted and the V1-V2 region of the 16S rRNA gene was amplified by PCR and sequencing using the Illumina platform. Dedicated bioinformatical approach was used for the multifactorial sample analysis.

Results: The microbiome composition was analyzed in 7 controls, 17 patients with SIBO and 12 with no SIBO.

We detected 513 phylotypes from 71 genera belonging to 11 phyla in the duodenal aspirate. The most abundant genera were *Streptococcus*, *Veillonella* and *Prevotella*. All three groups differed significantly in terms of their microbiome at phylum level (PERMANOVA $p < 0.05$). Based on the analysis of the individual phyla, we were able to show that the abundance of *Proteobacteria* was significantly higher in the SIBO group (Kruskal-Wallis test $p < 0.05$). Correlation analyses revealed an association between

bacterial abundance and clinical phenotype. For instance, *Proteobacteria*, correlated positively with diarrhea intensity (Spearman $r = 0.35$, $p = 0.0362$), and that *Bacteroidetes* correlated negatively with the reduction in quality of life (Spearman $r = -0.4525$, $p = 0.0056$). Within the overall cohort, we were able to identify two clusters characterized by different microbial composition, underlying malignant diseases and clinical symptoms.

Conclusion: Among patients with upper GI cancer, the microbiome composition of the duodenal aspirate of patients with SIBO was different compared to patients with no SIBO and controls. Microbiome composition profiling may offer the opportunity for a personalized treatment in patients with SIBO.

Disclosure: Nothing to disclose.

PP0137

BIOLOGICAL CHARACTERISTICS OF OAS FAMILY AND REGULATION OF APOPTOSIS, NECROPTOSIS AND PYROPTOSIS IN GASTRIC CANCER

M. Zhang¹, T. Cai¹, J. Xie¹, X. Liu¹, F. Wang¹

¹The Third Xiangya Hospital, Central South University, Department of Gastroenterology, Changsha, China

Contact E-Mail Address: minglinzhang1993@163.com

Introduction: Gastric cancer (GC) is a common cancer and a leading cause of cancer-related death, with increasing morbidity and mortality in recent years. OAS gene family plays an important role in antiviral process, but its mechanism in gastric cancer is still unclear.

Aims & Methods: The biological function and prognosis of OAS gene family in human GC were analyzed by bioinformatics analysis and cell level verification. To explore the relationship of OAS3 and OASL with apoptosis, necroptosis and pyroptosis.

Results: We found through bioinformatics analysis, the expression of OAS family was up-regulated in GC, which was related to the prognosis of patients. OAS family is closely related to the immune infiltration and tumor burden mutation of GC. OAS family gene is positively correlated with the expression of apoptosis, necroptosis and pyroptosis molecules. OAS family genes were found to be up-regulated in GC by detection of clinical samples. *In vitro*, knockdown of OAS3 and OASL inhibited the proliferation and migration of GC cells, overexpression of OASL promoted the proliferation and migration of GC cells. *In vitro*, knockdown of OAS3 and OASL in AGS, up-regulated apoptotic molecules (cleaved Caspase 3, cleaved Caspase 9 and cleaved Caspase 8), necroptosis molecules (p-MLKL and p-RIPK3), pyroptotic molecules (cleaved Caspase 1, cleaved Caspase 4, GSDMD and PYCARD), and inflammatory factor IL-1 β . In addition, knockdown of OAS3 and OASL in MKN45, up-regulated the expression of apoptosis, necroptosis and pyroptosis mentioned above, as well as the expression of inflammatory factors. overexpression of OASL in HGC27 cells decreased the expression of apoptosis molecules cleaved Caspase 3, cleaved Caspase 9 and cleaved Caspase 8, and necroptosis molecules p-MLKL and p-RIPK3, the pyroptosis molecules cleaved Caspase 1, cleaved Caspase 4, GSDMD and PYCARD were down-regulated, the expression of inflammatory factor IL-1 β was down-regulated.

Conclusion: The high expression of OAS family genes is closely related to the prognosis of GC. OAS family is closely related to the immune infiltration and tumor burden mutation of GC. OAS3 and OASL may promote the progression of GC by inhibiting pan-apoptosis (apoptosis, necroptosis and pyroptosis). In summary, OAS3 and OASL may become biomarkers and therapeutic targets in GC.

Disclosure: The authors declare that they have no conflict of interest.

PP0138

EXPLORING THE PROGNOSTIC VALUE OF BLOOD CELL RATIOS AND C-REACTIVE PROTEIN IN GASTRIC CANCER: INSIGHTS INTO MOLECULAR SUBTYPES AND TUMOUR IMMUNE MICROENVIRONMENT

A.C. Bravo¹, J.C. Almeida^{2,3}, J.R. Silva⁴, D. Marques⁵, C. Nascimento¹, X. Wen^{6,4}, L. Mascarenhas-Lemos^{7,8,9}, F. Carneiro^{6,10,3}, I. Gullo^{6,2,3}, M. Lopes Cravo^{11,12}

¹Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal, ²Centro Hospitalar Universitário de São João, Pathology, Porto, Portugal, ³Faculty of Medicine of the University of Porto, Porto, Portugal, ⁴Centro Hospitalar Universitário do Porto, Porto, Portugal, ⁵Hospital Beatriz Ângelo, Loures, Portugal, ⁶i3S (Instituto de Investigação e Inovação em Saúde) and Ipatimup (Institute of Molecular Pathology and Immunology of the University of Porto), Porto, Portugal, ⁷Hospital da Luz, Pathology, Lisbon, Portugal, ⁸Faculty of Medicine, Catholic University of Portugal, Lisboa, Portugal, ⁹NOVA Medical School, Lisboa, Portugal, ¹⁰Centro Hospitalar Universitário de São João, Porto, Portugal, ¹¹Hospital da Luz, Gastroenterology, Lisbon, Portugal, ¹²Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Contact E-Mail Address: catarina.bravoo@gmail.com

Introduction: Lymphoplasmacytic-rich and neutrophilic-rich tumour immune microenvironment (TIM) have been described in Epstein-Barr-virus-associated (EBV+) and microsatellite-unstable (MSI-high) gastric cancer (GC), respectively. Aim: to explore associations between EBV+/MSI-high status, TIM, peripheral blood cell ratios, tumour serum biomarkers and prognostic outcomes in GC.

Aims & Methods: Lymphoplasmacytic-rich and neutrophilic-rich tumour immune microenvironment (TIM) have been described in Epstein-Barr-virus-associated (EBV+) and microsatellite-unstable (MSI-high) gastric cancer (GC), respectively. Aim: to explore associations between EBV+/MSI-high status, TIM, peripheral blood cell ratios, tumour serum biomarkers and prognostic outcomes in GC.

Results: The series encompassed 7/140 EBV+ (5.0%) and 38/140 MSI-high (27.1%) GCs, characterised by lymphoplasmacytic-rich (EBV+:71.4% vs EBV-:5.3%, p<0.001) and neutrophilic-rich (MSI-high:28.9% vs MSS:2.0%, p<0.001) TMI, respectively. Prior to surgery, patients who underwent NAC harboured lower NLR compared to those submitted to surgery alone (3.05 vs 2.53, p=0.021). Pre-operative NLR and post-operative CRP levels were lower in neutrophilic-rich TMI GC (p=0.015 and p=0.006, respectively). Serum tumour biomarkers (CA125, CA19.9, CEA) were not related to morphological features or molecular subgroups. Overall, GC patients with lower CRP after surgery (<1.1mg/dl) showed better overall survival (p=0.032), even when stratified by type of therapy (NAC versus surgery alone), MSI status and presence of neutrophilic-rich TMI.

Conclusion: This study contributes to the growing body of evidence of blood-based biomarkers as predictive markers of GC prognosis. A reduction of systemic pro-inflammatory status after surgery (e.g. CRP<1.1mg/dl) might contribute to better overall prognostic outcomes of GC patients. Moreover, we observed that GC patients with neutrophilic-rich TMI, a morphologic feature associated with MSI-high status, had lower levels of neutrophils in peripheral blood (low pre-operative NLR). Possible explanations include neutrophil sequestration within the tumour microenvironment and/or consumption by the tumour.

Disclosure: Nothing to disclose.

PP0139

RISK ASSESSMENT QUESTIONNAIRE IN A WESTERN COMMUNITY TO IDENTIFY A GASTRIC CANCER RISK POPULATION: THE GASTROSCREENING PROJECT

G.L. Baiocchi¹, R. Grassia², I. Benzoni¹, L. Martinelli³, A. Celotti¹, B. Elvo², A. Drago², C. Laurenza², I. Di Luna², L. Pignata², S. Soro², N.M. Cantisani⁴, L.M. Quarti¹, A. Tarasconi¹, G. Tanzi⁵, S. Garattini⁶, G. Verlato³

¹ASST Cremona, Department of Surgery, Cremona, Italy, ²ASST Cremona, Gastroenterology and Digestive Endoscopy Unit, Cremona, Italy, ³University of Verona, Department of Diagnostic and Public Health, Verona, Italy, ⁴Federico II University, Gastroenterology and Hepatology Unit, Napoli, Italy, ⁵ASST Cremona, Department of Pathology, Cremona, Italy, ⁶IRCCS "Mario Negri" Research Institute, Milano, Italy

Contact E-Mail Address: luca.pignata@hotmail.it

Introduction: Nowadays there is no screening test approved on large scale for gastric cancer even if this neoplasia represents one of the leading causes of cancer-related deaths globally^{1,2}. In Italy still remains one of the most frequent tumors, with incidence rates differing across geographical areas³.

Aims & Methods: This project aims to create an easily administrable tool to detect anamnestic gastric cancer risk factors together with alarm symptoms in an age-defined target population to identify patients in need of an esophagogastroduodenoscopy (EGD).

This paper describes the first study phase: the administration of the questionnaire to a first sample of 5000 people aged from 40 to 80 years and the preliminary results. GASTROFORM is an online questionnaire (<https://it.research.net/r/GASTROFORM>) collecting data about demographic and anthropometric features, physiological anamnesis, familial history, non-specific upper gastrointestinal symptomatology, alarm symptoms and recent EGD performance.

Results: 4426 valid questionnaires were submitted through the online form in November 2022, 612 of them (13,82%) reported at least one alarm symptom identifying patients in need to undergo an EGD as soon as possible. From an epidemiological point of view we expect to increase the rate of diagnosis in Barret esophagus (from 1,8% to 5-8%), atrophic gastritis (from 9% to 20-30%) and early gastric cancer (from 0,019% to 1-2 %).

Conclusion: The GASTROFORM questionnaire could provide useful informations to identify a population most likely to have significant endoscopic findings in early diagnosis during a screening EGD.

References: 1. Ilic M, Ilic I. Epidemiology of stomach cancer. *World J Gastroenterol.* 2022;28(12):1187-1203. doi:10.3748/wjg.v28.i12.1187

2. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Prz Gastroenterol.* 2019;14(1):26-38. doi:10.5114/pg.2018.80001

3. Donida BM, Tomasello G, Ghidini M, et al. Epidemiological, clinical and pathological characteristics of gastric neoplasms in the province of Cremona: the experience of the first population-based specialized gastric cancer registry in Italy. *BMC Cancer.* 2019;19(1):212. Published 2019 Mar 8. doi:10.1186/s12885-019-5366-1

Disclosure: Nothing to disclose.

PP0140

GLOBAL HEALTH INEQUALITY AND YOUNG-ONSET GASTRIC CANCER MORTALITY (1990 TO 2019): A SYSTEMATIC ANALYSIS OF GLOBAL BURDEN OF DISEASE

Y. Li¹, W.K. Leung²

¹Department of Medicine, LI Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China, ²University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong

Contact E-Mail Address: waikleung@hku.hk

Introduction: The temporal trend of mortality rates among young individuals with gastric cancer has sparked a contentious debate over the past few decades. Additionally, there remains an ambiguous distribution alteration of disease burden among different countries.

Aims & Methods: This population-based systematic analysis was conducted to investigate changes in health inequality related to mortality caused by young gastric cancer from 1990 to 2019. We performed a secondary analysis of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 by extracting cross-sectional data on young gastric cancer (<40 years). The age-specific mortality rate was used to determine deaths attributed to young gastric cancer. A prediction of young gastric cancer mortality rate and case number up to 2030 was performed using the Norpred APC model. The slope index of inequality (SII) and the health concentration index were used to quantitatively measure absolute and relative changes in health inequalities, taking into account the socio-demographic indexes (SDI) level. The data was further analysed across different GBD regions and sexes.

Results: The global mortality rate of young gastric cancer declined from 1.61 (95% Uncertainty interval [UI]: 1.49 to 1.72) per 100,000 in 1990 to 0.94 (95% UI: 0.87 to 1.02) per 100,000 in 2019, with an annual rate of change -0.42% (95% Confidence interval (CI): -0.47 to -0.35). The projected data suggests that the number of global mortality case and rate of young gastric cancer would decrease to 24,450 and 0.761 per 100,000 by 2030. Countries belong to the lower 50% of SDI accounted for 49.9% and 52.3% of the global young gastric cancer deaths in 1990 and 2019, respectively. Although the absolute cross-national inequality (SII) of mortality rate fell from 0.133 (95%CI: -0.533 to 0.416) in 1990 to -0.239 (95%CI: -0.432 to -0.046) in 2019, the relative inequality (concentration index) for global young gastric cancer mortality increased from 1990 (-0.058, 95%CI: -0.532 to 0.416) to 2019 (-0.104, 95%CI: -0.526 to 0.317). The observed rise in absolute health inequality was evident in both sexes, but relative health inequality increased in females only. The regions of Sub-Saharan Africa (including Western and Southern), Central Asia, and Central Europe exhibited an increase in both absolute and relative health disparities in young gastric cancer mortality.

Conclusion: Although there has been a decline in the global young gastric cancer mortality rate, health inequality has increased over the past three decades, especially in females and some low SDI countries. It is imperative to prioritize efforts in addressing inequality to further reduce the global burden of young gastric cancer mortality.

Disclosure: Nothing to disclose.

PP0141

COMPARATIVE STUDY OF STANDARDIZED (HIGH DEFINITION WHITE LIGHT ENDOSCOPY WITH IMAGE-ENHANCEMENT) VERSUS NON-STANDARDIZED (ROUTINE WHITE LIGHT ENDOSCOPY) FOR DETECTION OF UPPER GASTROINTESTINAL MUCOSAL LESIONS: A PROSPECTIVE ANALYSIS FROM NORTH INDIA

N.S. Malhi¹, R. Grover¹, J.S. Dhingra¹

¹Advanced Gastroenterology Institute (A.G.I.), The GASTROCITI, Ludhiana, India

Contact E-Mail Address: doctorjasmeet@gmail.com

Introduction: This study aims to compare the diagnostic efficacy and variables of standardized high definition white light endoscopy with image-enhancement versus non-standardized routine white light endoscopy in detecting upper gastrointestinal mucosal lesions.

Aims & Methods: A prospective analysis was conducted on 270 patients undergoing Upper Gastrointestinal Endoscopy at Advanced Gastroenterology Institute: AGI the GASTROCITI, Ludhiana located in Punjab region of North India between December 2023 and March 2024. Patients were randomly assigned (135 each) to undergo assessment using standardized versus non standardized format. Endoscopic findings were recorded and later analyzed by experienced gastroenterologists blinded to the endoscopic modality used.

Results: In the standardized group, the mean age was 47 years, with 63 % males and 37 % females. In the nonstandardized group, the mean age was 45 years, with 58 % males and 42 % females. The most common indications for endoscopy in both groups were dyspepsia and heartburn. Due to use of premedication preparation (Surfactant Simethicone + Mucolytic N acetyl-cysteine solution), the mucosal visibility score in the standardized group was significantly better at 76% versus 32% in the nonstandardized group. Also, the time taken to examine the complete mucosa (8 minutes versus 5 minutes) and corresponding Propofol anesthetic requirement dose (140 mg versus 120 mg) along with the lesion detection rate (68% versus 53%) was higher in the standardized group. Among the 135 patients, 43 were normal in the standardized group versus 64 in the non-standardized group. The diagnostic yield of standardized high-definition white light endoscopy with image enhancement was 68.1% versus 52.5 % in nonstandardized WLE. Specific lesions with higher rates of detection were Grade A Esophagitis, early short segment Barrett's Esophagus, gastric atrophy, and intestinal metaplasia. The relative risk and odds ratio to find an abnormality while doing a standardized procedure was 1.3 and 1.93 respectively which showed very high statistical significance (p Value 0.009).

Conclusion: Standardized (High Definition White Light Endoscopy with Image-Enhancement) demonstrates superior diagnostic efficacy compared to non standardized routine white light endoscopy in detecting upper gastrointestinal mucosal lesions. Further large-scale studies are warranted to validate these findings and determine the optimal use of standardized (High Definition White Light Endoscopy with Image-Enhancement) in clinical practice.

Disclosure: Nothing to disclose.

PP0142

WITHDRAWN

PP0143

EFFICACY AND SAFETY PROFILES OF GASTRIC ENDOSCOPIC RESECTION FOR TREATING EARLY GASTRIC NEOPLASMS IN EXTREMELY OLD ADULTS (>80 YEARS): DATA FROM SINGLE-CENTER 10-YEAR OF EXPERIENCE

Y.I. Choi¹, C.K. Lee¹, J.W. Choi¹, S.Y. Won¹, Y.S. Cho¹, B.K. Park¹

¹National Health Insurance Service Ilsan Hospital, Department of Gastroenterology and Hepatology, Goyang, South Korea

Contact E-Mail Address: cys7like@hanmail.net

Introduction: Even gastric endoscopic resection (ER) including endoscopic mucosal, and submucosal resection, has been an effective treatment method for treating gastric neoplasm in an early phase, there is limited data on the efficacy, and safety profiles of ER especially among extremely old age (>80year) patients.

Aims & Methods: To investigate the efficacy, and safety profiles of gastric ER among extremely old age patients, and to triage the high-risk groups for gastric ER related complication. We designed a retrospective study using data from electronic medical records in National Health Insurance Service Ilsan Hospital which performs ESD in recent 3 from January 2016 to June 2023. Among a total of 1663 gastric ESD cases, 173 cases were performed in patients aged over 76 years, and 45 cases in patients aged over 80 years. These patients were evaluated retrospectively short-term outcomes, and survival. The short-term efficacy profiles include curative resection rate, and safety profiles include perforation or bleeding risk after ESD, or ER visit or readmission rate in month after discharge.

Results: Average risk of perforation after ESD was 2.7%, and emergency room (ER) visit after discharge rate was 0.4% in this period. risk FOBT positive result patients (> 75year) at the time of health check-up, according to whether or not performed CFS within 2 years of positive results of stool occult blood, case (n=), and control(n=) groups were divided. The end point was defined as CRC diagnosis or mortality. After adjusting for confounding variables, multivariable analysis was performed to analyze the effect of colonoscopy on the risk of incidental CRC, and all-causes mortality.

Conclusion: For extremely old age patients (>80year), the efficacy, and safety profiles of gastric ER were generally acceptable for treating early gastric neoplasm. Even though still endoscopists careful to patient's medical history, life expectancy, and comparing risk/benefit from ER, clinicians might not be hesitate treating early neoplastic lesions in stomach just because of patients extremely old age

References: Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians 2021;71:209-249.

2. Morgan E, Arnold M, Camargo MC, et al. The current and future incidence and mortality of gastric cancer in 185 countries, 2020–40: A population-based modelling study. Eclinicalmedicine 2022;47.

3. Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Digestive Endoscopy 2021;33:4-20.

4. Pimentel-Nunes P, Libânio D, Bastiaansen BA, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline–Update 2022. Endoscopy 2022;54:591-622.

Disclosure: Nothing to disclose.

PP0144

FORCEPS BIOPSY FOR MICRO-PHARYNGEAL NEOPLASMS: A SINGLE-CENTER PROSPECTIVE STUDY

Y. Shimodate¹, M. Mizuno¹, R. Takezawa¹, T. Gotoda¹, N. Nishimura¹, K. Matsueda¹, H. Mouri¹

¹Kurashiki Central Hospital, Gastroenterology and Hepatology, Kurashiki, Japan

Contact E-Mail Address: kazukun26@hotmail.com

Introduction: We previously reported short-term outcomes at 3 months after cold forceps biopsy (CFB) using jumbo biopsy forceps (Boston Scientific or Olympus Medical Systems) for micro-pharyngeal neoplasms¹.

Aims & Methods: We extended the follow-up and present here outcomes at 12 months after the CFB (UMIN registry number: 000037980). One hundred twenty-five lesions in 101 patients endoscopically diagnosed with narrow-band imaging of dilated intrapapillary capillary loops with clear demarcation as micro-pharyngeal tumors of 3 mm or less and excised with CFB were prospectively registered. After excluding 28 lesions with benign pathology, 97 lesions (13 lesions of squamous cell carcinoma, 4 of high-grade dysplasia, and 80 of low-grade dysplasia) were endoscopically followed up 3 and 12 months after the first CFB. Additional CFB was performed if lesions with endoscopically determined local remnant/recurrence (ER, narrow-band imaging of dilated intrapapillary capillary loops with clear demarcation) were found. The primary outcome was ER rate. The secondary outcome was composite remnant/recurrence (CR) (ER with pathological recurrence, ER without pathological assessment, and non-ER scars but with pathological recurrence) rate.

Results: Endoscopy at 3 months after CFB was performed in 56 lesions in 47 patients, and CFB scars were identified in 25 lesions (44.6%). Additional CFB was performed in all scars judged as ER, and regular biopsy was obtained in some scars without ER. ER rate at 3 months was 23.2% (13/56, 95% confidence interval 13 - 36.4%), and CR rate was also 23.2% (13/56, 13 -36.4%) (one ER scar with negative pathology, and one non-ER scar with positive pathology). Endoscopy at 12 months was performed in 84 lesions in 71 patients. CFB scars were identified in 20 lesions (23.8%); ER rate at 12 months was 11.9% (10/84, 5.9 -20.8%), and CR rate was 8.3% (7/84, 3.4 -16.4%) (3 ER scars with negative pathology, no non-ER scar with positive pathology). Regarding safety of the procedure, no intraoperative or post-operative adverse event was observed in all the 125 lesions including 24 lesions excised under continued antithrombotic therapy.

Conclusion: About 10% remnant or recurrence rates at 12 months after the procedure suggest that CFB may be minimally invasive therapeutic option for micro-pharyngeal neoplasms of 3 mm or smaller. Further follow-up study is continuing.

References: 1: Shimodate Y et al. Efficacy and safety of cold forceps biopsy for diminutive pharyngeal neoplasms: Single-center, prospective pilot study. Dig Endosc 2021; 33: 761-769.

Disclosure: Nothing to disclose.

PP0145

UPPER-GASTROINTESTINAL ENDOSCOPY, OR OESOPHAGOGASTRODUODENOSCOPY (OGD), IS A PROCEDURE ROUTINELY PERFORMED IN SECONDARY CARE SETTINGS THROUGHOUT THE UK. LOCAL ANAESTHESIA, IN THE FORM OF THROAT SPRAY, AND INTRAVENOUS SEDATION ARE OFTEN USED TO MAKE THIS CLINICAL PROCEDURE MORE COMFORTABLE FOR THE PATIENT

E. Killan¹

¹Northumbria Healthcare NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom

Contact E-Mail Address: esther.killan@northumbria-healthcare.nhs.uk

Introduction: Upper-gastrointestinal endoscopy, or oesophagogastrroduodenoscopy (OGD), is a procedure routinely performed in secondary care settings throughout the UK. Local anaesthesia, in the form of throat spray, and intravenous sedation are often used to make this clinical procedure more comfortable for the patient.

Aims & Methods: This study focused primarily on the difference in administration of the local anaesthetic throat spray. The commonly used method was to spray the back of the patient's pharynx while their mouth was open: "mouth-open" technique. This study proposed a modified technique which involved spraying the pharynx with the mouth closed around the spray nozzle: "JASMEG" technique. This was a quality improvement study of 474 patients (male: female = 1.13) who were undergoing an OGD as part of routine care in a district general hospital in the United Kingdom. It was carried out to investigate whether this new method of spray administration would increase patient comfort and reduce patient anxiety, pulse rate and incidence of cough. Comfort and anxiety scores were scored on a 5-point Liker scale (1 = most comfortable/ least anxious, 5 = least comfortable/ most anxious). Outcomes were compared between the two groups using linear regression models controlling for sex. Incidence of cough was compared between groups using Fisher's exact test.

Results: A breakdown of the sample by treatment group and sex is shown in Table 1. As compared to the "mouth-open" group, the "JASMEG" group showed a smaller increase in pulse rates (group difference = -3.97, $p < 0.001$), lower anxiety scores (group difference = -1.31, $p < 0.001$), higher comfort scores (group difference = 1.07, $p < 0.001$) and lower incidence of cough (13 out of 252 vs 190 out of 222; $p < 0.001$). There were no significant differences in the results by sex.

Conclusion: The new "JASMEG" technique of local anaesthetic spray for patients undergoing OGD is superior in terms of patient comfort, anxiety levels, pulse rates and presence of cough. This is a low-cost alternative to reduce transmission of aerosol-transmitted infections, while also making it a more favourable procedure for patients.

References: 1, Department of Gastroenterology; Northumbria Healthcare, Newcastle Upon Tyne, 2, University College Institute of Child Health Great Ormond Street, London, UK; 2, Population, Policy & Practice, UCL Institute of Child Health, London, UK 3, Nobles Hospital, Strang, Isle of Man. 4, Department of Gastroenterology, Guy's and St Thomas' Hospital, London, UK 5, Faculty of Life Sciences and Medicine, King's College London, UK

Disclosure: Nothing to disclose.

PP0146

A PILOT STUDY ON THE UTILIZATION OF ENDOSCOPIC TWO-TOOTHED CLIPS FOR THE MANAGEMENT OF GASTROINTESTINAL DISEASES

Y. Liu¹, J. Chu¹, S. Hu¹, M. Min¹

¹The fifth medical center of Chinese PLA General Hospital, Gastroenterology, Beijing, China

Contact E-Mail Address: 13911798288@163.com

Introduction: With the progress made in the field of digestive endoscopy, a growing array of digestive disorders can now be effectively managed through endoscopic interventions. Notably, the utilization of clips for closure purposes has been documented in relation to several endoscopic procedures, including endoscopic submucosal dissection (ESD), endoscopic mucosal resection (EMR), and endoscopic full-thickness resection (EFTR). However, current clipping systems have demonstrated limitations in terms of dimensions, spacing between open arms, force exerted during closure, and adequate tissue compression. Emerging endoscopic suturing techniques are currently in the initial stage, with limited clinical investigation and insufficient reliable evidence. However, their reliance on an independent endoscopic apparatus results in elevated expenses related to equipment and treatment, and also calls for specialized clinical training. In order to tackle this concern, we have devised the two-toothed clip (TTC). Through a pilot study encompassing a cohort of 10 participants, our objective is to assess the safety, feasibility, and efficacy of the two-toothed clip.

Aims & Methods: The study employed a nitinol alloy-based two-toothed clip, where the teeth were affixed to the inner side of standard clip arms (ROCC-D-26-195-C, Micro-Tech, Nanjing, China) using plastic tubes and sutures. These teeth demonstrated enhanced length and sharpness compared to the standard clip arms. The technique used to advance the two-toothed clips towards the target lesions was the same as that employed for standard clips. Caution must be exercised while opening the arms to avoid unintentional harm to the normal mucosa due to the sharp teeth. With the aid of electrocautery snare, the TTCs were easy to be detached. Ten patients between the ages of 50 and 80 were included in this study. The treatment indications encompassed non-variceal bleeding, post-endoscopic submucosal dissection (ESD) lesions in the duodenum or colorectum, tracheoesophageal fistulas, duodenal or colorectal diverticulitis, as well as anchoring of self-expanding metal stents. Ethical approval was granted by the Institutional Review Board of our hospital, and written informed consent was obtained from all participants. The baseline characteristics of the patients were collected. The achievement of technical success was determined by the effective placement of the two-toothed clips at the designated location. Clinical success was defined as the successful resolution of the gastrointestinal issue for which the two-toothed clips were utilized. The patients were subjected to clinical and endoscopic follow-up for a duration ranging from 14 to 30 days.

Results: Ten patients meeting the eligibility criteria, with an age range of 41-80 years and consisting of 8 men and 2 women, received the TTC application. The treatment indications encompassed the closure of submucosal defects (n=2), diverticula (n=2), and non-variceal upper gastrointestinal bleeding (n=1). Additionally, the procedure involved anchoring fully covered self-expanding metal stents (n=4) and utilizing the clip-with-line traction method in endoscopic submucosal dissection (ESD) (n=1). The technical success rate and clinical success rate both reached 100%, and no adverse events related to the procedure were observed.

Conclusion: The utilization of endoscopic hemoclips for tissue compression using TTC technique has been shown to be both safe and effective. This study brings new treatment strategies for future clinical practice.

Disclosure: There are no conflicts to declare.

PP0147

OUTCOMES OF DELAYED ENDOSCOPIC MANAGEMENT FOR ESOPHAGEAL SOFT FOOD BOLUS IMPACTION: A MULTI-CENTRE RETROSPECTIVE STUDY

T. Hoang¹, A. Fetz¹, R.A. Singh²

¹University of British Columbia, Vancouver, Canada, ²University of British Columbia, Victoria, Canada

Contact E-Mail Address: thomash1@student.ubc.ca

Introduction: Esophageal food bolus impactions are a common reason for emergency room visits. Current guidelines recommend urgent endoscopy within 24 hours for incomplete obstructions, and emergent endoscopy within 6 hours for complete obstructions. While emergency endoscopy is required for sharp objects or disk batteries, data regarding soft food bolus impactions is more sparse. Recent retrospective evidence suggests that delaying endoscopy after twelve hours is not associated with an increase in morbidity or mortality.

Aims & Methods: This study expands on the existing literature to evaluate clinical outcomes associated with emergent (< 6 hours), urgent (6-12 hours), and delayed (>12 hours) endoscopy for patients presenting to emergency rooms with soft food bolus impaction.

This is a multicentre retrospective study involving two tertiary and one secondary care centre in British Columbia, Canada. All patients who presented with food bolus impaction between January 1, 2019 and Dec 31, 2022 were reviewed. The primary outcome was thirty-day mortality and repeat hospital presentation. Secondary outcomes included procedural morbidity (complications, procedural time, removal success) and length of stay. Endoscopic removal technique, optical diagnoses, and eosinophilic esophagitis incidence were also noted. Patients < 18 years old or those who had a non-food bolus impaction were excluded. Statistical analysis was performed using χ^2 /Fisher Exact test wherever applicable for categorical variables and Kruskal-Wallis one-way ANOVA for continuous variables.

Results: Of 416 patients identified with complete esophageal impaction, 77 met inclusion criteria and were stratified into three cohorts: emergent (<6 hours, n=47), urgent (6-12 hours n=17), and delayed (>12 hours, n=13) intervention. All groups displayed similar baseline demographics (Table 1). Primary outcomes are outlined in Table 2. We did not observe mortality by thirty days in any group. Two patients who underwent emergent endoscopy re-presented to ED with dysphagia-related complications (4.2%) within thirty days compared to one patient (7.7%) in the delayed intervention group (OR: 1.88, CI:0.17-22.7, p=0.53). Similar to the emergent group where two (4.3%) patients required hospitalization for at least one day, one patient respectively in the urgent (5.9%, OR: 0.71, CI:0.05-8.39, p=1.0) and delayed (7.7%, OR: 1.9, CI:0.16-22.5, p=0.53) groups required hospitalization for at least one day. There was no statistically significant difference in procedural time (p=0.62), and only one complication (mucosal tear) was noted in the urgent intervention group. Only one patient had unsuccessful removal on index endoscopy, again in the urgent intervention group. There was no statistically significant difference in removal techniques, optical diagnoses, and eosinophilic esophagitis incidence. There was no statistically significant difference in the rate of mucosal injury secondary to prolonged food bolus impaction in the urgent (p=0.17) and delayed (p=0.12) groups.

Conclusion: There is no significant difference in negative clinical outcomes, including thirty-day mortality, hospital readmission, and procedural morbidity, in patients who receive emergent, urgent, or delayed endoscopy for management of a soft food bolus esophageal impaction. These data add to the existing literature to assist endoscopists with risk stratification and timing of safe intervention for removal of food bolus causing complete esophageal obstruction.

References: 1. Krill T, Samuel R, Vela A, Marcondes F, Zaibaq J, Guturu P,

Parupudi S. Outcomes of delayed endoscopic management for esophageal soft food impactions. *Gastrointest Endosc.* 2020 Apr;91(4):806-812. doi: 10.1016/j.gie.2019.12.020. Epub 2019 Dec 24.

2. Ko HH, Enns R. Review of food bolus management. *Can J Gastroenterol.* 2008 Oct;22(10):805-8. doi: 10.1155/2008/682082.

Disclosure: Nothing to disclose.

PP0148

PREVENTION OF DELAYED BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION THROUGH CLIP CLOSURE WITH NOVEL ANCHOR-PRONGED CLIP

K. Okimoto¹, T. Matsumura¹, S. Mukai¹, A. Kurosugi¹, M. Sonoda¹, T. Ishikawa¹, T. Kaneko¹, Y. Ohta¹, T. Taida¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Department Of Gastroenterology, Graduate School Of Medicine,, Chiba, Japan

Contact E-Mail Address: kenrunaway@yahoo.co.jp

Introduction: Delayed bleeding (DB) after gastric endoscopic submucosal dissection (ESD) is major complication [1] that sometimes lead to shock vitals and the effect of mucosal defect closure for preventing DB was reported [2]. However, the thickness of the gastric mucosa and proper muscle layer makes suturing difficult [3].

Aims & Methods: The aim of this study was to investigate whether clip closure using novel anchor-pronged clip (MANTIS Clip; Boston Scientific) is effective in preventing DB after gastric ESD. Out of 70 cases (78 lesions) that underwent gastric ESD at our institution from August 2023 to February 2024, a retrospective analysis was conducted on 60 consecutive cases (65 lesions) where $\geq 50\%$ of the wound could be closed. If the wound was small, the closure method involved initially placing at least one MANTIS Clip to achieve mucosa-to-mucosa closure. If the wound was large, it was closed according to the method we previously reported [4]. In concrete terms, one side of the mucosa was grasped with MANTIS Clip, then move the clip to the opposite muscle layer, open the clip once, and after sufficient air aspiration, grasp the muscle layer. After shrinking mucosal defect enough, complete closure was achieved by adding mucosa-mucosa and mucosa-muscle closure similar to previous report of colonic closure [5] with normal clips (Sure Clip 16mm (Micro-Tech Co., Ltd, Nanjing, China) or EZ Clip (Olympus Medical Systems, Tokyo, Japan)). The primary outcome was the actual DB rate compared with the expected DB rate calculated from the BEST-J score [1]. Secondary outcomes included the technical success rate, complete closure rate (proportion of wounds with $\geq 90\%$ closure), and closure time.

Results: M/F=42/18. DB risk based on BEST-J score (low/intermediate/high/very high) = 46/7/6/1. The median tumor size (mm) was 10 (5-40). Adenoma/cancer = 10/55. The actual rate of DB was 0%, indicating lower tendency to the expected rate of 4.5% (p=0.244). The technical success rate was 85.7% (60/70), with a complete closure rate of 90.8% (59/65). The median closure time (min) was 9 (2-24), with a median of 1 MANTIS Clip used per lesion (range: 1-4).

Conclusion: Although further accumulation of cases is necessary, clip closure using the MANTIS Clip achieved low DB with rapid and high complete closure after gastric ESD.

References: Hatta W, Tsuji Y, Yoshio T et al. Prediction model of bleeding after endoscopic submucosal dissection for early gastric cancer: BEST-J score. *Gut.* 2021; 70: 476-484.

1. Maekawa S, Nomura R, Murase T et al. Complete closure of artificial gastric ulcer after endoscopic submucosal dissection by combined use of a single over-the-scope clip and through-the-scope clips (with videos). *Surg Endosc.* 2015; 29: 500-504.

2. Choi KD, Jung HY, Lee GH et al. Application of metal hemoclips for clo-

sure of endoscopic mucosal resection-induced ulcers of the stomach to prevent delayed bleeding. *Surg Endosc.* 2008; 22: 1882–1886.

3. Okimoto K, Matsumura T, Matsusaka K et al. Successful closure of large mucosal defect with novel anchor-pronged clip after gastric endoscopic submucosal dissection. *Endoscopy.* 2024. Epub ahead of print.
4. Nishizawa T, Banno S, Kinoshita S et al. Feasibility of endoscopic mucosa-submucosa clip closure method (with video). *Endosc Int Open.* 2018; 6: E1070–E1074.

Disclosure: Nothing to disclose.

PP0149

DEEP LEARNING BASED VIRTUAL LUGOL CHROMOENDOSCOPY FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA: A PRELIMINARY STUDY

Y. Toya¹, S. Suzuki², Y. Monno³, R. Arai³, M. Okutomi³, T. Matsumoto¹

¹Iwate Medical University, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Yahaba, Japan,

²International University of Health and Welfare Ichikawa Hospital, Division of Gastroenterology, Ichikawa, Japan, ³Tokyo Institute of Technology, Department of Systems and Control Engineering, Tokyo, Japan

Contact E-Mail Address: ytoya@iwate-med.ac.jp

Introduction: Lugol chromoendoscopy (LCE) has been established as a tool to increase the sensitivity for the detection of esophageal squamous cell carcinoma (ESCC). However, LCE has some disadvantages such as the time consumed for the technique, patients' discomfort, risk of aspiration and allergic reactions when compared to white light imaging (WLE) and image enhanced endoscopy (IEE).

Aims & Methods: We attempted to develop virtual lugol chromoendoscopy (V-LCE) images for ESCC using cycle-consistent generative adversarial network (CycleGAN) and to compare their diagnostic performance with that of WLE and real lugol chromoendoscopy (R-LCE). To obtain V-LCE images, we used 3425 images (1601 WLE and 1824 LCE) of superficial ESCC from 195 cases to train CycleGAN. For the test set to evaluate the usefulness of V-LCE images, other 25 WLE images from 25 patients with superficial ESCC were translated to 25 V-LCE images using trained CycleGAN. Six endoscopists (three experts and three non-experts) evaluated images obtained under WLE, V-LCE and R-LCE with respect to the detection and the margin of ESCC, using a five-point scale from 1 (poor) to 5 (excellent). We also calculated and compared the color difference (ΔE) between cancerous and non-cancerous areas each in WLE, V-LCE and R-LCE image.

Results: Comparison of WLE and V-LCE images showed a trend towards higher scores for V-LCE images (detection 3.3 vs 3.8, $p=0.089$, margin 2.7 vs 3.0, $p=0.13$). A comparison between V-LCE and R-LCE images revealed the scores in R-LCE were significantly higher than those in V-LCE (detection; 4.7 vs 3.8, $p<0.001$, margin; 4.3 vs 3.0, $p<0.001$). Among the experts, the score for margin in V-LCE tended to be higher than that in WLE (3.0 vs 2.7, $p=0.051$). Among the non-experts, the score for detection in V-LCE tended to be higher than that in WLE (4.0 vs. 3.3, $p=0.064$). ΔE in V-LCE was significantly higher than that in WLE (29.6 vs. 18.3, $p<0.001$), while it was significantly lower than in R-LCE (29.6 vs. 39.3, $p<0.001$).

Conclusion: Images in V-LCE have the potential for high sensitivity for the diagnosis of superficial ESCC, while the imaging quality need to be improved.

Disclosure: Nothing to disclose.

PP0150

MORPHOLOGY OF ULTRA-SHORT BARRETT'S ESOPHAGUS MAY BE INFLUENCED BY *HELICOBACTER PYLORI* INFECTION AND GASTRIC ATROPHY

S. Nakagome¹, O. Goto¹, M. Niikawa¹, K. Yoshikata¹, T. Habu¹, Y. Ishikawa¹, K. Kiritani¹, E. Koizumi¹, H. Noda¹, K. Higuchi¹, T. Onda¹, J. Omori¹, N. Akimoto¹, K. Iwakiri¹

¹Nippon Medical School, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: s13-076ns@nms.ac.jp

Introduction: Barrett's esophagus (BE) is known to be a precursor of esophageal and gastroesophageal junctional adenocarcinoma¹. Adenocarcinoma of the esophagus based on BE is still relatively rare in Japan, but the Westernization of dietary habits, the increase in obese patients, and the eradication of *Helicobacter pylori* (HP) infection may increase the number of cases in the future. In Japan, the prevalence of long-segmented BE (LSBE), which is common in the Western world, is relatively low, whereas SSBE is frequently observed². Atrophic gastritis (AG) caused by HP infection is also frequently observed in Japan, and the diagnosis of Japanese SSBE may be modulated by HP infection/AG. In this study, we retrospectively investigated whether the morphology of SSBE could be influenced by HP status.

Aims & Methods: In our institution, 60 patients who had endoscopic ultra-short segmented Barrett's esophagus (USBE; length of <1cm) were retrospectively collected and divided into two groups: 30 cases with AG caused by current HP infection (AG group) or without AG (non-AG group). As patient characteristics, we investigated age, sex, presence of reflux esophagitis (RE), presence of hiatus hernia, and use of proton pump inhibitor (PPI) therapy from the medical records. To objectively evaluate the roughness of the SCJ, we compared the morphology of USBE by measuring the respective perimeters of EGJ and SCJ, followed by the calculation of the SCJ/EGJ ratio. As a sub-analysis in the AG group, the SCJ/EGJ ratio was similarly compared in terms of the degree of AG (closed-type, $n = 3$; open-type, $n = 27$) according to the Kimura-Takemoto classification.

Results: In terms of patient characteristics, the median age was higher in the AG group than in the non-AG group (72 years old vs. 49 years old, $p<0.001$), and RE was less common in the AG group than in the non-AG group (3% vs. 36%, $p = 0.004$). There were no statistical differences between the two groups in sex, presence of hiatus hernia, and use of PPI. The mean SCJ/EGJ ratio was significantly higher in the AG group than in the non-AG group (2.26 vs. 1.43, $p<0.001$). In the sub-analysis, the mean SCJ/EGJ ratio was likely to be higher in open-type atrophy than in closed-type atrophy (2.33 vs. 1.58, $p = 0.092$).

Conclusion: In endoscopically diagnosed USBE, the circumference of SCJ appeared rough in the AG group, which suggested that the morphology of BE is influenced by HP infection and subsequent AG development. Particularly in Japan, simple rough margins of SCJ influenced by HP/AG may be estimated as USBE. In diagnosing BE, the morphological characteristics of SCJ and the HP/AG status should be taken into consideration.

References: 1. Haggitt RC et al. Barrett's esophagus, dysplasia, and adenocarcinoma. *Hum Pathol.* 1994; 25: 982-93.

2. Manabe N et al. Does short-segment columnar-lined esophagus elongate during a mean follow-up period of 5.7 years? *Dig Endosc.* 2011; 23: 166-72.

Disclosure: There is no conflict of interest in this study.

PP0151

INTRAOPERATIVE END-TIDAL CARBON DIOXIDE CONCENTRATION IS A POTENTIAL OBJECTIVE INDICATOR OF THE PNEUMOPERITONEUM MANAGEMENT DURING PERORAL ENDOSCOPIC MYOTOMY

T. Habu¹, O. Goto^{1,2}, S. Nakagome¹, M. Nikawa¹, K. Yoshikata¹, Y. Ishikawa¹, E. Koizumi¹, K. Kirita¹, K. Higuchi¹, H. Noda¹, T. Onda¹, J. Omori¹, N. Akimoto¹, K. Iwakiri¹

¹Nippon Medical School, Graduate School of Medicine, Department of Gastroenterology, Tokyo, Japan, ²Endoscopy Centre, Nippon Medical School Hospital, Tokyo, Japan

Contact E-Mail Address: thrush10ll@gmail.com

Introduction: Peroral endoscopic myotomy (POEM) is a less invasive endoscopic treatment for stenotic diseases caused by oesophageal motility dysfunction. During this procedure, the insufflation gas supplied from the endoscope migrates to the abdominal cavity, resulting in pneumoperitoneum. For excessive pneumoperitoneum, transabdominal puncture should be performed to rapidly decrease the intraabdominal pressure. However, the timing of puncture depends subjectively on the operator's decision.

Aims & Methods: In this study, we retrospectively analysed the factors leading to pneumoperitoneum and clarified the objective indicators to determine the timing of abdominocentesis. A total of 100 consecutive patients who underwent POEM at our hospital from October 2018 to December 2023 were included. In univariate analyses, patient-related (age, sex, body surface area [BSA], body mass index), disease-related (diagnosis, preoperative Eckardt score), and treatment-related factors (operator's POEM experience, myotomy length, peak end-tidal carbon dioxide concentration [ETCO₂]) were compared between Puncture and Nonpuncture groups. In these parameters, sex and BSA, which correlated with the intraabdominal space, and factors that were supposed to influence the severity of pneumoperitoneum and the need for subsequent abdominocentesis by showing p-values of less than 0.1 were enrolled for subsequent multivariate analyses.

Results: The mean age was 58 (standard deviation [SD], 19) and 51% of them were male. The mean Eckardt score was 6 (SD, 3). Most patients (n = 92, 92%) were diagnosed with oesophageal achalasia. The mean procedure time was 88 min (SD, 35 min). Abdominocentesis was performed in 65 patients (68%), who were allocated into the Puncture group. In the univariate analyses, the peak ETCO₂ was significantly higher in the Puncture group than in the Nonpuncture group (p < 0.01). In the multivariate analyses using sex, BSA, and the peak ETCO₂, high peak ETCO₂ was a single independent factor associated with abdominocentesis (odds ratio = 1.25, 95% confidence interval: 1.11–1.41, p < 0.01). The receiver operating characteristic curve indicated that the two groups were divided with a maximal area under the curve (0.76) when a cut-off value of the peak ETCO₂ was set at 44.5 mmHg (sensitivity, 0.79; specificity, 0.65).

Conclusion: This study demonstrated that the intraoperative ETCO₂ level was a significant independent factor related to severe pneumoperitoneum in POEM, and 45 mmHg of peak ETCO₂ was an optimal cut-off value to differentiate the Puncture group from the Nonpuncture group. This result should be clinically useful as an objective reference to determine abdominocentesis in patient with pneumoperitoneum due to CO₂ leakage to the abdominal space.

Disclosure: Nothing to disclose.

PP0152

CHARACTERISTICS OF WEB LIKE MUCUS AS AN ENDOSCOPIC FINDING OF PPI/P-CAB RELATED GASTROPATHY

Y. Shimada¹, Y. Kita¹, H. Nago¹, M. Yamaguchi¹, Y. Terai¹, R. Om¹, Y. Ikeda¹, S. Sato¹, A. Murata¹, S. Sato¹, A. Nagahara², T. Genda¹

¹Juntendo University Shizuoka Hospital, Gastroenterology and Hepatology, Izunokuni-city, Japan, ²Juntendo University School of Medicine, Gastroenterology, Tokyo, Japan

Contact E-Mail Address: yshimada@juntendo.ac.jp

Introduction: Due to the widely use of potassium competitive acid blocker (P-CAB) and proton pump inhibitor (PPI) for acid-related diseases, the incidence of PPI/P-CAB-related gastropathy become more common in Japan. In the revised 3rd. edition of the Kyoto Classification⁽¹⁾, web-like mucus (WLM) has been newly described as an endoscopic finding seen in PPI/P-CAB-related gastropathy. The mechanism of its formation has been speculated to be linked to the strong and sustained inhabitation of acid secretion⁽²⁾, however, the details of WLM are still unknown. We investigated the characteristics of WLM based on the database of upper gastrointestinal endoscopy performed at our department.

Aims & Methods: The aim of this study is to reveal the characteristics of subjects with WLM. This study is a retrospective cross-sectional study conducted in a single hospital. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2020 and December 2023. We examined subjects in which endoscopists recognized the presence of WLM. Statistical analyses were performed by Fisher's exact test.

Results: Out of a total of 3,564 subjects, WLM was observed in 14 cases (5 males and 9 females, mean age 72.4±16.3 years). All 14 patients were taking P-CAB. The duration of P-CAB administration varied from 8 days to 2 years. Interestingly, in some cases WLM was observed just a few days after starting oral administration of P-CAB. Regarding *Helicobacter pylori* infection, 10 cases were uninfected and 4 cases were past infected.

Conclusion: All subjects with WLM were taking P-CAB. All subjects with WLM were taking P-CAB. We found that WLM can be observed even just a few days after starting oral administration.

References: (1) Haruma K, Kato M, Inoue K, Murakami K, Kamada T. Kyoto Classification of Gastritis. 3rd. ed. Tokyo: Nihon Medical Center. 115-121. 2023

(2) Kudo K, Kimura N, Kato M. Potassium-competitive acid blocker-associated gastric mucosal lesions. Clin Endosc. 2024 Feb 29. Online ahead of print.

Disclosure: Nothing to disclose.

PP0153

EFFICACY OF A NOVEL THIN THERAPEUTIC ENDOSCOPE IN PERORAL ENDOSCOPIC MYOTOMY

H. Tomida^{1,2}, K. Tange³, Y. Ikeda¹, M. Hayashi⁴, K. Niida⁴, M. Okada⁴, Y. Yamamoto¹, E. Takeshita³, M. Kato⁵, N. Yahagi², Y. Hiasa⁴
¹Ehime University Hospital, Endoscopy Center, Ehime, Japan, ²Keio University School of Medicine, Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Tokyo, Japan, ³Ehime University Graduate School of Medicine, Department of Inflammatory Bowel Diseases and Therapeutics, Ehime, Japan, ⁴Ehime University Graduate School of Medicine, Department of Gastroenterology and Metabology, Ehime, Japan, ⁵Keio University Hospital, Center for Diagnostic and Therapeutic Endoscopy, Tokyo, Japan

Contact E-Mail Address: hideomi.tomida.epch@hotmail.com
Introduction: Per-oral endoscopic myotomy (POEM) is a leading therapeutic procedure for third space endoscopy (TSE) and has been the first choice for treatment of esophageal achalasia. TSE requires treatment in a narrow space. The recently launched thin therapeutic endoscope (EG-840TP, Fujifilm Medical) is expected to be useful for TSE including POEM.
Aims & Methods: To clarify the effectiveness of thin therapeutic endoscopy in POEM, we conducted a retrospective observational study of 66 patients who underwent POEM in our hospital between November 2019 and March 2024. Patient characteristics and outcomes were compared between 52 patients treated with a normal-diameter therapeutic endoscope (T group) and 14 patients treated with a thin therapeutic endoscope (TP group).
Results: The patients in T group were 26 males and 26 females, median age 61 years (18-88), 44 cases of esophageal achalasia (Type I/II/III: 28/15/1), 6 cases of EGJOO, and 2 cases of DES. The TP group included 7 men and 7 women, median age 60 years (13-81), 11 cases of esophageal achalasia type I, 2 cases of EGJOO, and 1 case of DES. Sigmoid type was 58% (n = 30) and 29% (n = 4) in the T/TP group, respectively, and was significantly more common in the T group. Treatment before POEM was balloon dilation 11/1, POEM1/1, and Heller-Dor5/0 in the T/TP group, all of which were not significantly different. There was no difference in the length of myotomy between the two groups in either the esophagus or stomach. The median treatment time in each group was 92 minutes in the T group and 107 minutes in the TP group, and there was no significant difference in the submucosal tunnel creation time. However, the myotomy time per cm was 2.5 min in the T group and 3.8 min in the TP group, which was significantly longer in the TP group (p<0.01). Clips required for entry closure were significantly less in the TP group (8 clips in the T group and 5 clips in the TP group) (p<0.01). Eckardt scores after POEM improved equally in the two groups, and the rates of adverse events and GERD after POEM did not differ between the two groups.

Conclusion: POEM using a thin therapeutic endoscope resulted in similar treatment outcome as conventional endoscopes. Although there was no difference in the treatment time, TP group required fewer clips to close the entry. The prolonged myotomy time in the TP group was considered to reflect the fact that the thin therapeutic endoscope made it easier to approach the muscle layer and more careful myotomy was performed. Although further investigation is needed, a thin therapeutic endoscope may be useful for TSE.
References: 1. Inoue, H., et al. (2010). "Peroral endoscopic myotomy (POEM) for esophageal achalasia." *Endoscopy* 42(4): 265-271.
2. Shimamura, Y., et al. (2023). "Evolving field of third-space endoscopy: Derivatives of peroral endoscopic myotomy." *Dig Endosc* 35(2): 162-172.
Disclosure: Nothing to disclose.

PP0154

A SINGLE-CENTRE RETROSPECTIVE STUDY OF ENDOSCOPY REFERRALS FOR ANAEMIA: INSIGHTS INTO CANCER AND NON-CANCER PATHOLOGIES

R. Al Saidi¹, C. Aydemir¹, L. Alhalabi¹, W. Taj-Aldeen²
¹University of Buckingham, Buckingham, United Kingdom, ²Milton Keynes University Hospital, Milton Keynes, United Kingdom

Contact E-Mail Address: raniahsarmad@gmail.com
Introduction: Anaemia is common and in some cases an indication for an urgent endoscopy via two week wait (2WW) pathway. This pathway allows patients with alarming symptoms to see a specialist within two weeks to exclude cancer. In this retrospective study, we assessed the clinical outcomes of such referrals, describing the types of cancer identified after full investigations in our centre.
Aims & Methods: Data was collected between December 2021 and December 2022 using Endoscopy UNISOFT system for all endoscopy procedures prompted by anaemia at Milton Keynes University Hospital, United Kingdom. Basic demographics, faecal immunochemical test (FIT) and 2WW referrals from both upper gastrointestinal (UGI) or colorectal pathway were recorded. Radiological images and multi-disciplinary team outcomes were reviewed.
Results: Total number of patients referred to our endoscopy unit was 389, 70% were referred via colorectal team while 30% were referred via UGI pathway. Age of patients was distributed between 19 to 98 years old with majority aged between 60 to 88 years old. 227 patients had both gastroscopy (OGD) + colonoscopy (COL), 76 had OGD+CT scan, 9 patients had OGD+COL+CT and 5 patients had COL+CT. The other patients had CT only, OGD only, or COL only, depending on fitness.
Data revealed that 33 (8.5%) patients referred with anaemia had cancer. 21 patients had colorectal cancer while 8 patients had upper GI cancer. Non-GI cancers were found in four patients, 2 of them lung cancer, 1 renal cancer and 1 tonsillar cancer. There were 187 patients (48%) that had UGI non-cancer pathology e.g. gastritis, duodenitis, peptic ulcer disease, oesophageal varices and coeliac disease. The remaining causes of anaemia are found in Table 1.

Total cause of Anaemia	Number of Patients
Cancer (Colon, UGI, Other)	33
Other UGI pathologies	187
Unknown	92
Other colorectal pathologies	55
Angiodysplasia (UGI + colon)	18
Anaemia of Chronic Disease	2
Gynaecological	2
Total	389

Table 1: Causes of Anaemia.

Positive FIT and colorectal cancer:
Out of the 389 patients, 100 patients (25%) had stool FIT. 37 patients had a positive FIT, and only 5 patients (14%) were diagnosed with colorectal cancer. In the remaining 16 patients with colorectal cancer, FIT was not performed.
Conclusion: The percentage of cancer in our population with anaemia was 8.5%. The main gastrointestinal cancer was colon cancer (5.4%), followed by upper gastrointestinal cancer (2.05%) and non-GI cancer was (1.02%) only. According to previous data, 8%-10% of cases with anaemia were found to have cancer which is not very different from our audit (1,2). The most common cause of anaemia was UGI non-cancer pathology, however, there was no clear aetiology identified in 23% of our population. Four non-GI cancer were discovered by radiological images/CT scans. Those patients with non-GI cancer were above the age of 60. Although the

number is small, radiological imaging remains an important tool to investigate anaemia in elderly people when both OGD and colonoscopy are unremarkable. FIT test revealed a high false positive rate with only 14% with positive FIT test had colorectal cancer.

References:

1. Snook, J. et al.(2021) British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults,Gut. 2021 Nov;70(11):2030-2051.
2. James MW, et al.(2005) Risk factors for gastrointestinal malignancy in patients with iron-deficiency anaemia.Eur J Gastroenterol Hepatol 2005;17:1197-203

Disclosure: Nothing to disclose.

PP0155

BIOPSY PRACTICE DURING DIAGNOSTIC UPPER GASTROINTESTINAL ENDOSCOPY IN THE UK: ANALYSIS OF 638 000 ENDOSCOPIES IN THE NATIONAL ENDOSCOPY DATABASE

A. Srinivasa¹, N. Trudgill¹

¹Sandwell and West Birmingham NHS Trust, Gastroenterology, West Bromwich, United Kingdom

Contact E-Mail Address: amarsrinivasa@nhs.net

Introduction: Appropriate tissue sampling is vital for lesion diagnosis during endoscopy. We have previously found an association between higher biopsy rates and reduced compliance with national biopsy recommendations (e.g. from ulcers) with higher rates of post endoscopy upper gastrointestinal cancers (PEUGIC).

Aims & Methods: The aim of this study was to examine biopsy practice in the UK, along with comparing results to the recommendations set out by the European Society of Gastrointestinal Endoscopy.

Upper gastrointestinal (UGI) endoscopies between 01/01/2019 and 29/02/2020 were analysed from the National Endoscopy Database (NED). Surveillance endoscopies were excluded. Logistic regression analysis examined associations with biopsy rate, biopsies from gastritis or duodenitis and biopsies from ulcers.

Results: 638,280 UGI endoscopies were analysed. 289,156 (45.3%) involved biopsies: esophagus 17.1%, stomach 18.0%, duodenal bulb (D1) 3.9%, second part of the duodenum (D2) 19.4%.

Biopsy rate was associated with: clinical endoscopists OR 1.31 (95% CI 1.29-1.33) and surgeons OR 0.84 (95% CI 0.90-0.95), compared to gastroenterologists; patient age 70-79 OR 1.12 (95% CI 1.05-1.19); male patients OR 1.07 (CI 95% 1.06-1.08); urgent endoscopy OR 1.38 (CI 95% 1.35-1.39); emergency endoscopy OR 0.37 (95% CI 0.36-0.39); and therapy during endoscopy OR 0.25 (95% CI 0.24-0.27).

During endoscopy for dysphagia with a normal appearance, only 5232 (36.3%) had biopsies to exclude eosinophilic esophagitis, with usually too few biopsies taken (mean 4.5 (SD±2.0)). When the endoscopic diagnosis was reportedly normal (excluding dysphagic indications), 35% involved potentially unnecessary biopsies (263557 biopsies). Biopsies were commonly taken from uncomplicated inflammatory conditions: 31% of endoscopic gastritis (58765 biopsies) and 31% of endoscopic duodenitis (15580 biopsies). Biopsies for gastritis/duodenitis were associated with surgeons OR 1.36 (95% CI 1.26-1.46) and clinical endoscopists OR 1.38 (95% CI 1.31-1.45), compared to gastroenterologists.

Mean number of biopsies from esophageal ulcers was 3.7 (SD±2.1) and from gastric ulcers 3.8 (SD±2.4).Biopsies of gastric or esophageal ulcers were associated with clinical endoscopists OR 1.51 (95% CI 1.37-1.65) and surgeons OR 0.53 (95% CI 0.50-0.56), compared with gastroenterologists; outpatient procedures OR 1.40 (95% CI 1.27-1.53); and emergency procedures OR 0.66 (95% CI 0.55-0.79).

Conclusion: Analysis of NED reveals a large number of apparently unnecessary biopsies for gastritis or duodenitis or during normal endoscopy. In contrast, in only 36% of normal endoscopies for dysphagia were biopsies taken to rule out eosinophilic esophagitis. Quality improvement efforts are needed to reduce unnecessary biopsies, increase appropriate biopsies, reduce costs and environmental impact.

References:

Pouw RE, Barret M, Biermann K, Bisschops R, Czako L, Gecse KB, de Hertogh G, Hucl T, Iacucci M, Jansen M, Rutter M, Savarino E, Spaander MCW, Schmidt PT, Vieth M, Dinis-Ribeiro M, van Hooft JE. Endoscopic tissue sampling - Part 1: Upper gastrointestinal and hepatopancreatobiliary tracts. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2021 Nov;53(11):1174-1188. doi: 10.1055/a-1611-5091. Epub 2021 Sep 17. PMID: 34535035.

Disclosure: Nothing to disclose.

PP0156

SEDATION PRACTICE IN THE UK: AN ANALYSIS OF 617,000 DIAGNOSTIC UPPER GI ENDOSCOPIES IN THE NATIONAL ENDOSCOPY DATABASE

A. Srinivasa¹, N. Trudgill¹

¹Sandwell and West Birmingham NHS Trust, Gastroenterology, West Bromwich, United Kingdom

Contact E-Mail Address: amarsrinivasa@nhs.net

Introduction: Sedation is commonly used during upper gastrointestinal (UGI) endoscopy to improve tolerability. We have previously reported an association between increased sedation use and lower rates of post endoscopy upper GI cancer. We have analysed sedation practices for diagnostic upper GI endoscopy in the National Endoscopy Database (NED).

Aims & Methods: The aim of this study was to examine endoscopy practice in the UK and quantify variation in sedation use during diagnostic endoscopy. Diagnostic endoscopies performed between 01/01/2019 and 29/02/2020 were analysed from NED data. Logistic regression analysis examined associations with sedation use and procedures abandoned due to tolerability.

Results: 314,725 (51%) UGI endoscopies involved sedation: midazolam alone 36%; combined midazolam + fentanyl 14%; midazolam + pethidine 0.9%. In patients over the age of 70, during 11 887 of 206 386 endoscopies (5.8%), more than the recommended 2.5mg of midazolam was given (mean 3.4mg (SD±0.76)), including 3320 in which fentanyl was co-prescribed (mean 67.0mcg (SD±29.1)).

Sedation use was associated with: compared to gastroenterologists, clinical endoscopists OR 0.57 (95% CI 0.56-0.58), surgeons OR 0.65 (95% CI 0.64-0.66), SAS doctors 0.65 (95% CI 0.64-0.66); younger patients; males OR 0.60 (95% CI 0.59-0.61); afternoon lists OR 0.98 (95% CI 0.97-0.99) and weekends (OR 0.88 (95% CI 0.87-0.90); compared with routine endoscopy, urgent 1.22 (95% CI 1.21-1.23) and surveillance OR 0.91 (95% CI 0.88-0.94). Sedation + opioid was most frequently used by gastroenterologists, but less by others: clinical endoscopists OR 0.26 (95% CI 0.25-0.27); surgeons OR 0.26, (95% CI 0.25-0.27); and SAS doctors 0.33 (95% CI 0.32-0.34).

3499 endoscopies were abandoned due to poor tolerance: age mean 59.1 (SD±17.1), female 59%, no sedation 57%, midazolam only 32% and midazolam + opioid 10%. This was associated with: surgeons OR 1.29 (95% CI 1.07-1.53) and clinical endoscopists OR 1.39 (95% CI 1.19-1.62), compared to gastroenterologists; addition of opioids OR 0.66 (95% CI 0.59-0.73); and no sedation OR 1.32 (CI 95% 1.23-1.40).

Conclusion: There is lower use of sedation overall, and combined midazolam and opioid particularly, among endoscopists other than consultant gastroenterologists, despite improved tolerability and reduced aban-

doned procedures. Sedation is used less in afternoons and at weekends, which may relate to recovery requirements and staffing.

Disclosure: Nothing to disclose.

PP0157

REMIMAZOLAM VS. MIDAZOLAM SEDATION IN UPPER GASTROINTESTINAL ENDOSCOPY IN ADULTS > 65 YEARS: RANDOMIZED CONTROLLED TRIAL

G.H. Lee¹, J.S. Park¹, J.H. Park¹, C.-K. Noh¹, S.G. Lim¹, S.J. Shin¹, K.M. Lee¹

¹Ajou University School of Medicine, Gastroenterology, Suwon, South Korea

Contact E-Mail Address: Shsj9128@ajou.ac.kr

Introduction: Safe and effective sedation are important factors when performing gastrointestinal endoscopy. However, clinicians should be cautious when using sedatives in older patients because of their decreased physiological reserves. Remimazolam is an ultrashort active benzodiazepine that has attracted attention because of its efficacy. This study aimed to determine the safety and efficacy of remimazolam compared with midazolam as a sedative for diagnostic upper gastrointestinal endoscopy in older patients aged ≥65 years.

Aims & Methods: We randomly assigned patients aged ≥65 years who were scheduled for diagnostic upper gastrointestinal endoscopy. The average induction time, average recovery time, and side effect profile of patients who received remimazolam as a sedative were compared with those of patients who received midazolam.

Results: Patients who received remimazolam had shorter average induction (102.0 sec vs. 327.5 sec, $p < 0.001$) and recovery times (5.8 min vs. 13.4 min, $p < 0.001$) than those who received midazolam. No significant difference in side effect profiles was observed between the groups.

Conclusion: In performing upper gastrointestinal endoscopy in older patients, remimazolam can be a good alternative sedative to midazolam, whether used as monotherapy or in combination therapy.

References: Kilpatrick GJ, McIntyre MS, Cox RF, et al. CNS 7056: a novel ultra-short-acting Benzodiazepine. *Anesthesiology* 2007;107:60-6. Borkett KM, Riff DS, Schwartz HI, et al. A Phase IIa, randomized, double-blind study of remimazolam (CNS 7056) versus midazolam for sedation in upper gastrointestinal endoscopy. *Anesth Analg* 2015;120:771-80. Chernik DA, Gillings D, Laine H, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. *J Clin Psychopharmacol* 1990;10:244-51.

Disclosure: Nothing to disclose.

PP0158

LCI (LINKED COLOR IMAGING) AND HISTOPATHOLOGICAL FINDINGS FOR MAP-LIKE REDNESS AFTER *HELICOBACTER PYLORI* ERADICATION THERAPY

E. Umegaki¹, T. Ninomiya¹, S. Monden¹, M. Sasahira¹, S. Yoi¹, M. Osawa¹, O. Handa¹, H. Matsumoto¹, A. Shiotani¹

¹Kawasaki Medical School, Gastroenterology & Hepatology, Kurashiki, Okayama, Japan

Contact E-Mail Address: eumegaki@med.kawasaki-m.ac.jp

Introduction: Mucosal redness (so called Map-like redness) after *Helicobacter pylori* (*H. pylori*) eradication therapy reflects intestinal metaplasia clarified by changes of intra-gastric condition and repairs for gastric mucosa. It is difficult to distinguish Map-like redness and gastric cancer. Map-like redness is a high risk condition for post *H. pylori* eradicated gastric

cancer. Consideration about histopathological findings of mucosal redness after *H. pylori* eradication therapy are not enough.

Aims & Methods: Image-enhanced endoscopy plays an important role in the detection and further examination of gastritis and early gastric cancer (EGC). LCI is also useful for detecting and evaluating gastritis, gastric intestinal metaplasia as a pre-cancerous lesion, and EGC. To investigate correlation between the color difference and immuno-histochemical findings for mucosal redness (map-like redness; intestinal metaplasia) detected by white light and LCI in patients with successful *H. pylori* eradication history. We get the endoscopic images by conventional white light image (WLI) and LCI with LASEREO system (FujiFilm, Tokyo, Japan), and evaluate color values (CIE L*a*b* color space and color analysis by Adobe Photoshop C54). Furthermore, we evaluate intestinal metaplasia histopathologically with the immuno-staining by MUC2/MUC5AC/HID-AB; phenotype (Gastro-intestinal Mixed type or Intestinal type, Incomplete type or Complete type) and relationship between color differences and phenotype of intestinal metaplasia.

Results: (1) Objects are 36 patients (24 males, range 56-87yo, median 71yo) and 43 lesions after successful *H. pylori* eradication therapy; cancer group 15 patients (20 lesions), non-cancer group 21 patients (23 lesions)

(2) Type of intestinal metaplasia in the cancer group and the non-cancer group: GI Mixed type 14/7(cancer group/non-cancer group), $p < 0.01$, Incomplete type 14/6(cancer group/non-cancer group), $p < 0.01$.

(3) In the cancer group, color differences Δa (Green to Red) with LCI between the lesion and the surrounding mucosa is significantly high compared with the non-cancer group (16.0 ± 6.6 vs 11.8 ± 7.0 ; $p < 0.05$).

(4) Compared severe intestinal metaplasia with none/mild/moderate intestinal metaplasia, color value b (Blue to Yellow) with LCI is significantly low (20.4 ± 9.5 vs 25.9 ± 8.0 ; $p < 0.05$)

(5) Compared GI mixed type with intestinal type of intestinal metaplasia, color values b (Blue to Yellow) with LCI is significantly low (19.2 ± 8.6 vs 26.4 ± 8.5 ; $p = 0.008$).

Conclusion: In this study, we observed differences in LCI color values of map-like redness appearing after *H. pylori* eradication depending on the type of intestinal metaplasia. In particular, the gastric cancer group has a high rate of Gastro-intestinal Mixed Type with a high risk of carcinogenesis. This suggests the usefulness of image enhancement by LCI as a marker for the high-risk group of gastric cancer.

References: Umegaki, E. et al. Linked Color Imaging for Stomach. *Diagnostics* 2023, 13, x. <https://doi.org/10.3390/xxxxx>

Disclosure: Nothing to disclose.

PP0159

BLOOD VESSEL RE-CONSTRUCTION IN THE SUBMUCOSAL LAYER OF THE POSTOPERATIVE STOMACH INDICATED FROM ESD SPECIMENS

S. Fushimi¹, Y. Horikawa^{1,2}, N. Mimori¹, Y. Kato¹, Y. Tahata¹, K. Sakaki¹

¹Hiraka General Hospital Dept. of Gastroenterology, Gastroenterology, Yokote, Japan, ²Crea Clinic, Sendai, Japan

Contact E-Mail Address: saki3040@gmail.com

Introduction: Advances in surgical treatments have improved mortality of postoperative patients with gastric cancer and esophageal cancer. Then, the number of residual and gastric-tube cancers is increasing. Re-surgical treatment for postoperative gastric cancers (Po-GCs) has a high incidence and mortality rate, so the contribution of endoscopic therapy might be large.

However, endoscopic submucosal dissection (ESD) for Po-GCs is considered technically difficult. Especially during mucosal incision, we sometimes encounter unexpected bleedings.

Aims & Methods: We investigated the re-construction of blood vessels in the submucosal layer on ESD specimens of Po-GCs. 8 cases of Po-GCs (4 cases of residual gastric cancer, 4 cases of gastric-tube cancer) underwent ESD in our hospital from 2016 to 2023 were included. Eligible specimens of cases include the lesion center. Vascular distribution in the shallow submucosal layer (a depth of 500µm from the muscularis mucosae) was well observed and the number of dilated arteries and veins with a diameter >100µm are counted and compensated by a specimen diameter. These number of vessels were compared with 16 cases of controls (1:2) extracted from general gastric ESD underwent in the same location and period.

Results: There were 0.4±0.5/cm arteries and 1.1±1.1/cm veins/mm in control. There were 2.3±1.4/cm arteries and 5.5±2.0/cm veins in the cases of residual gastric cancers. And there were 4.1±1.1/cm arteries and 2.7±0.4/cm veins in the cases of gastric-tube cancers. Both cases of residual and gastric-tube cancers involved many dilated arteries and veins ($P<0.05$) in superficial submucosal layer compared with control. On the other hands, the cases of residual gastric cancers have lots of veins compared with arteries ($P<0.05$), and the cases of gastric-tube cancers have lots of arteries compared with veins ($P<0.05$).

Conclusion: Residual stomach is small and arterial blood flow is maintained, but veins are resected on a process of surgery. These would be the reason for venous congestion is noticeably high in the residual stomach. On the other hand, the gastric-tube mucosa tends to be more abundant of blood flow due to the reconstruction method. As a result, branches of arteries remaining in submucosal layer would be developed. From the above, on the process of ESD, the probability of encountering venous oozing increases on residual gastric cancer, and arterial bleeding increases on gastric-tube cancer. It's suggested that paying more attention to these vascular distributions of the submucosal layer is needed while post-operative gastric ESD is performed.

Disclosure: Nothing to disclose.

PP0160

FEASIBILITY AND SAFETY OF COLLABORATIVE SURGERY FOR GASTROINTESTINAL TUMOURS BY ENDOSCOPISTS AND SURGEONS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS OF 131 PATIENTS

Y. Ishikawa¹, O. Goto^{1,2}, K. Higuchi¹, S. Nakagome¹, M. Niikawa¹, K. Yoshikata¹, T. Habu¹, E. Koizumi¹, K. Kirita¹, H. Noda¹, T. Onda¹, J. Omori¹, N. Akimoto¹, K. Iwakiri¹

¹Nippon Medical School, Department of Gastroenterology, Tokyo, Japan, ²Nippon Medical School, Endoscopy Center, Tokyo, Japan

Contact E-Mail Address: i-yumiko0@nms.ac.jp

Introduction: Endoscopic treatment using peroral/anal flexible endoscopy and dedicated through-the-scope electrocautery devices has been developed as a less-invasive intraluminal surgery. However, pure endoscopic treatment has limitations for lesions at the deeper layer or excessively close to the mouth/anus. Conversely, surgical approach sometimes leads to wider resection and subsequent decreases in the patient's quality of life. Collaborative surgery by both endoscopists and surgeons is considered effective for providing less-invasive local resection of gastrointestinal tumours to offset limitations either in pure endoscopic treatments or surgical intervention.

Aims & Methods: To investigate the feasibility and safety of this approach, we here retrospectively evaluated the clinical outcomes of collaborative surgery with endoscopists and surgeons. We consecutively collected data of patients who underwent collaborative surgery for lesions located from the laryngopharynx to the anus between October 2017 and December 2023. Collaborative surgery was indicated after the agreement on both flexible endoscopists and surgeons, considering possible benefits of the

cooperation in terms of invasiveness, technical difficulty, and safety. Laryngopharyngeal lesions and cervical oesophageal cancer were removed using the ESD technique under laryngeal expansion using a curved laryngoscope by the otolaryngologist's manipulation. With gastrointestinal surgeons, subepithelial tumours in the gastrointestinal tract and deeply invasive gastric cancers were removed in a full-layered fashion, followed by surgical suturing. Large duodenal cancers were principally treated by ESD followed by sero-muscular suturing for the reinforcement of the mucosal defects.

In large anal canal cancer with pagetoid spread, a dermatologist externally dissected the perianally expanded area following ESD from the rectal side. Collaboration completeness, technical success, procedure time, postoperative hospitalization period, and occurrence of adverse events were analyzed.

Results: Collaboration surgery was performed for 134 lesions (33 laryngopharyngeal, 2 oesophageal, 89 gastric, 8 duodenal, and 2 recto-anal lesions, respectively) in 131 patients. Collaboration completeness was achieved in 129 lesions (96%). The en-bloc resection and pathological R0 resection of lesions were obtained in 127 (95%) and 124 (93%) lesions, respectively. The mean procedure time was 188 min. Patients were discharged on the mean postoperative day of 11. Five patients (4%) developed relevant postoperative adverse events.

Conclusion: The results indicated that collaborative surgery by endoscopists and surgeons was feasible and safe, and should contribute to providing less-invasive treatment than conventional approaches. The frequency of adverse events was considered acceptable. Collaborative surgery is worth considering as a flexible and reliable surgical option when cooperation should outperform a single treatment by either of endoscopists or surgeons. To establish this concept, further accumulation of cases and pieces of evidence by well-designed studies is desired.

Disclosure: Nothing to disclose.

PP0161

FULL-THICKNESS RESECTION DEVICE (FTRD) FOR THE TREATMENT OF GASTROINTESTINAL TRACT (GIT) LESIONS : TREATMENT OUTCOMES AND PREDICTORS OF SUCCESS IN AN ASIAN COHORT

M. Chu^{1,2}, K.W. Lim², R. Ravi², C.P. Francisco³, R. Asokkumar⁴

¹Singapore General Hospital, Singapore, Singapore, ²Singapore General Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ³St. Luke's Medical Center - Global City, Institute of Digestive and Liver Diseases, Taguig City, Philippines, ⁴Singapore General Hospital, Gastroenterology, Singapore, Singapore

Contact E-Mail Address: michaelchu0712@gmail.com

Introduction: FTRD represents a novel treatment option for managing GIT lesions that are complex and not easily removed by conventional endoscopic resection techniques. However, there is limited data outside expert centers describing its efficacy and safety.

Aims & Methods: This study aims to evaluate the utility and safety of the FTRD to remove upper and lower GIT lesions and identify predictors for successful resection.

We included 34 patients (mean age 62.8±12.9 years; male-64.7%) who underwent FTRD at the Singapore General Hospital since 2021. We followed the recommended FTRD technique. The primary objective was to evaluate the technical success, defined as the correct application of the FTRD clip and immediate complete en-bloc resection of the lesion. The secondary objective was to assess the safety using the Clavien-Dindo classification and identify predictive factors for successful FTRD resection. Chi-squared test, Fisher's exact test, and logistic regression were used to analyze categorical data.

Results: FTRD was performed for both upper (35.3%) and lower GIT (64.7%) lesions (Table-1). The common lesions were neuroendocrine tumors (NET; 52.9%), mesenchymal neoplasms (23.5 %), and residual polyps/advanced adenomas (23.5 %). Most upper GIT lesions were in the stomach (58.3%), followed by duodenum (41.7%). Likewise, the lower GIT lesions were in the rectum (73%), left (3.5%) and right colon (13.5%). The average lesion size was 12.6 ± 6 mm. FTRD deployment was technically successful in 27 patients (79.4 %)(Table-2). We found the technical success was significantly higher for lower than upper GIT lesions (91% vs. 50%, $p=0.004$). Similarly, lesions in the rectum (100%) had substantially higher technical success than lesions in other locations ($p=0.01$). Technical success was significantly higher for NET than mesenchymal lesions or residual polyps (100% vs. 37.5% vs. 75%, $p=0.001$). Overall, the R0 resection rate with negative histological margin was noted in 25 (73.5%) patients and was significantly higher for NET (100%) than other lesions ($p=0.001$). The mean procedure time was 57.5 ± 25 min. Immediate complications occurred in 8 cases (23.5%) and delayed bleeding occurred in 1 patient (2.9%). Most of them were minor and treated conservatively, except one requiring endoscopic repositioning of duodenal FTRD clip causing gastric outlet obstruction. Follow-up endoscopy was performed in 11 patients at an average of 12-months. A retained clip with hyperplastic granulation change was seen in one patient. Multivariate analysis showed lesion size, location (rectum), and type of GIT lesion (NET) predicted significantly higher technical success ($p=0.02$).

Conclusion: Our results show that FTRD offers an acceptable technical success and R0 resection rate with a low risk of complications. Lower GIT location and non-mesenchymal lesion demonstrated better outcomes with FTRD.

Disclosure: None.

PP0162

VACUUM-STENT TREATMENT FOR TRANSMURAL DEFECTS IN THE UPPER GASTRO-INTESTINAL TRACT: CASE SERIES AND NEW INSIGHTS IN A TERTIARY REFERRAL CENTER

L. Pattynama^{1,2}, W.J. Eshuis², J.J. Bergman¹, M.I. van Berge Henegouwen², R.E. Pouw¹

¹Amsterdam UMC, Dept. of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Dept. of Surgery, Amsterdam, Netherlands

Contact E-Mail Address: l.m.pattynama@amsterdamumc.nl

Introduction: Transmural defects in the upper gastro-intestinal (GI) tract are associated with severe morbidity and mortality. Endoscopic vacuum therapy (EVT) has recently been established as promising endoscopic treatment option for such defects and is most often applied using endoscopically placed vacuum-sponges. The vacuum-stent is a novel device to apply EVT, combining the advantages of negative pressure wound therapy and an intraluminal stent, allowing for oral intake.

Aims & Methods: The aim of this prospective cohort study is to describe the experiences of, and lessons learned by a tertiary referral center with EVT experience since 2018, regarding the vacuum-stent for transmural defects in the upper GI tract. All patients treated with a vacuum-stent between November 2022 and October 2023 were included. Outcome measures included successful defect closure, reasons of treatment failure, adverse events and strictures.

Results: 31 patients were included. Baseline characteristics and outcomes are displayed in Table 1. Success rates of combined vacuum-stent and -sponge treatment and vacuum-stent treatment alone were respectively 83% and 78%. In this cohort, some notable reasons of failure were observed: a defect too close to the upper esophageal sphincter (UES), in-

adequate vacuum on the esophago-jejunal anastomosis, a carcinoma at a persisting perforated ulcer, and two adverse events (6%). The adverse events included two patients who developed a secondary defect at the site of the proximal vacuum-stent flange, of whom one had a cervical anastomosis with a narrow proximal esophagus and one Boerhaave syndrome. Three out of four patients with a severe stricture had undergone a McKeown esophagectomy (cervical anastomosis).

Etiology of defect, n (%)	31
Anastomotic leakage	18 (58%)
Boerhaave syndrome	5 (16%)
Iatrogenic	5 (16%)
Other	3 (10%)
Initial procedure in case of anastomotic leakage, n (%)	18
Ivor Lewis esophagectomy	9 (50%)
McKeown esophagectomy	6 (33%)
Gastrectomy	3 (17%)
Success rate, n (%)	31
Combined vacuum-stent and -sponge treatment	26 (83%)
Only vacuum-stent treatment	24 (78%)
Adverse events, n (%)	2 (6%)
Severe stricture requiring > 3 dilations, incision therapy or self dilation, n (%)	4 (13%)

Table 1. Baseline characteristics and outcomes.

Conclusion: The vacuum-stent is a valuable treatment option for AL after Ivor Lewis esophagectomy, Boerhaave syndrome and iatrogenic defects with success rates of 80-89%. Treating cervical anastomotic leaks is not recommended by us, due to the narrow lumen of the proximal esophagus, the proximity of the UES and high risk of severe strictures. Furthermore, caution is recommended in case of a narrow esophagus and the value of the vacuum-stent is yet to be determined in case of an esophago-jejunal anastomosis. In our experience, vacuum-stent and -sponge treatment complement each other and might be indicated in different situations. Sharing experiences on the topic is important to assess the best techniques and indications, to be able to reach the full potential of the vacuum-stent and further increase the success rate.

Disclosure: R.E. Pouw: consultant for Micro-Tech Europe and Medtronic, speaker fee for Pentax and Boston Scientific

M.I. van Berge Henegouwen: consultant for Mylan, Johnson & Johnson, Alesi Surgical, BBraun and Medtronic, and received unrestricted research grants from Stryker. All fees paid to institution.

PP0163

OUTCOME OF OESOPHAGEAL STENTING FOR MALIGNANT DYSPHAGIA: A 10-YEAR RETROSPECTIVE SURVIVAL ANALYSIS

D. Kapila¹, R. Rameshshanker¹

¹Hillingdon Hospital, London, United Kingdom

Contact E-Mail Address: r.rameshshanker@nhs.net

Introduction: Advanced oesophageal cancers (OC) exhibit poor median survival rates, and often self-expandable metal stents (SEMS) are used to address malignant dysphagia. Previous studies purport to a high prevalence of adverse events post stent insertion, without an impact on mortality. We aimed to review mortality outcomes of oesophageal stenting in both squamous cell carcinoma (SCC) and adenocarcinomas (AC).

Aims & Methods: One hundred and eighty-six patients who were diagnosed with OC between September 2010 - February 2021 were included. We retrospectively analysed the data for patient demographics, histology, oncological management, oesophageal stenting, and mortality, notably overall survival (OS). Survival probability was calculated using Kaplan-Meier survival curves and compared using Log-rank testing with statistical significance determined by p value <0.05.

Results: From the 186 OC diagnoses made. Male: Female 136 (73%) and 50 (27%). Mean age at diagnosis was 73 years (range 32-98). Histological findings showed 132 patients had AC (71%), and 54 patients had SCC (29%). Mean OS from date of diagnosis for AC and SCC were 21.6 and 10.6 months respectively.

SEMS were inserted for 98 patients (53%); 37 (38%) for SCC and 61 (62%) for AC. Mean OS for patients with stenting vs not stenting was 11.1 and 26.4 months respectively. Median OS for stenting was 8 months (95% CI, 6.0 - 10.0) vs 10 months for not stenting (95% CI, 7.0 -16.0) with a $p<0.0005$) (See Figure 1). 30-day mortality post stent insertion was 23%.

For patients who underwent oesophageal stent insertion, mean OS for AC and SCC 11.9 months (95% CI, 8.989 to 14.913) and 10.1 months (95% CI, 6.709 to 13.561) respectively. Median OS for stent population for SCC and AC were 6 months (95% CI, 5.0 -8.0) and 9 months (95% CI, 6.0 -12.0) respectively ($p = 0.3765$).

Conclusion: Patients with OC who underwent stent insertion had overall poor survival outcome. This could reflect advanced stage of OS. Stenting is often useful for malignant dysphagia in patients who harbor inoperable disease. Analysis of stent adverse events would be useful.

Disclosure: Nothing to disclose.

PP0164

GASTRIC INTESTINAL METAPLASIA DETECTION ACCURACY AND GENERALIZATION USING CURRENT STATE-OF-THE-ART AI ALGORITHMS

B. Magalhães¹, A. Neto¹, E. Almeida², A. Cunha¹, D. Libânio³, J. Chaves⁴, M. Dinis-Ribeiro⁵, M. Coimbra²
¹INESC TEC, Universidade de Trás os Montes e Alto Douro, Vila Real, Portugal, ²INESC TEC, Faculdade de Ciências da Universidade do Porto, Porto, Portugal, ³Instituto Português de Oncologia do Porto, Gastroenterology Department, Porto, Portugal, ⁴Ipo Porto, Porto, Portugal, ⁵IPO Porto, Dept. of Gastroenterology, Porto, Portugal

Contact E-Mail Address: mdinisribeiro@gmail.com

Introduction: Early detection of gastric cancer may result from adequate diagnosis and surveillance of individuals with gastric intestinal metaplasia (GIM). Computer-assisted diagnosis systems based on artificial intelligence, or more specifically Deep Neural Networks (DNN) applied to esophagogastroduodenoscopy may be crucial in optimizing and standardizing patients' final diagnosis. Literature has shown promising DNN results for single datasets, some of which reaching the 90% accuracy suggested by the European Society of Gastrointestinal Endoscopy for these algorithms [1].

Moreover, traditionally Wight-Light Endoscopy is referred as suboptimal to determine the presence of GIM. We aimed to determine the accuracy of current state-of-the-art AI algorithms for WLE from 2 different scopes' providers for GIM detection.

Aims & Methods: Two datasets were used in these experiments:

- Dataset A (Fujifilm) was used for training and testing, consisting of a private benchmark dataset [1] of which we have used 4876 endoscopic White Light (WL) images (2438 normal, 2438 GIM).
- Dataset B (Olympus) was used for external validation and was collected from a lower quality clinical routine dataset, including 373 WL images (170 normal, 203 GIM). All images were annotated by clinical experts and the primary outcome was GIM classification accuracy.

We conducted experiments comparing the performance of DNNs (ResNet50) in GIM detection by training the models with and without the integration of synthetic/artificially generated endoscopy images. This involved employing four different methods: using the default dataset, augmenting the dataset with classic data augmentation transformations, incorporating images generated by Deep Convolutional Generative Ad-

versarial Networks (DCGAN), and integrating images generated by Wasserstein GAN (WGAN). A part of dataset A (15%) was saved for testing in the different experiments and the remaining data (85%) was used to train the model, using a 5-fold cross-validation. In the end, dataset B was used as an external test set to evaluate the generalization capabilities of the different DNNs.

Results: The ResNet50 (dataset A – test set) achieved an accuracy of 92% for the default dataset, 93% for the data augmentation transformations, 93% for the DCGAN and 94% for the WGAN. The respective sensitivity values were 92%, 91%, 92% and 92%. Then, these models were evaluated in the dataset B, to infer its generalization capabilities. The ResNet50 achieved an accuracy of 63% for the default dataset, 68% for the data augmentation transformations, 65% for the DCGAN and 65% for the WGAN. The respective sensitivity values were 66%, 80%, 73% and 73%.

	Single Dataset (A->A) [Fujifilm WLE]				Generalization (A->B) [Olympus WLE]			
	Default	Augm.	DCGAN	WGAN	Default	Augm.	DCGAN	WGAN
Accuracy	0.92	0.93	0.93	0.94	0.63	0.68	0.65	0.65
Sensitivity	0.92	0.91	0.92	0.92	0.66	0.80	0.73	0.70

Conclusion: Even for WLE, current DNN architectures seem to obtain very good results for GIM detection. However, generalization is still insufficient, since validation in different datasets (different clinical settings, different endoscopic technologies) obtains average detection accuracy and sensitivity, illustrating the excessive specialization caused by maximizing accuracy results in single datasets.

References: 1] Messmann H, Bisschops R, Antonelli G, Libânio D, Sinonquel P, Abdelrahim M, Ahmad OF, Areia M, Bergman JJGHM, Bhandari P, Boskoski I, Dekker E, Domagk D, Ebigbo A, Eelbode T, Eliakim R, Häfner M, Haidry RJ, Jover R, Kaminski MF, Kuvaev R, Mori Y, Palazzo M, Repici A, Rondonotti E, Rutter MD, Saito Y, Sharma P, Spada C, Spadaccini M, Veitch A, Gralnek IM, Hassan C, Dinis-Ribeiro M. Expected value of artificial intelligence in gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2022 Dec;54(12):1211-1231. doi: 10.1055/a-1950-5694. Epub 2022 Oct 21. PMID: 36270318.
[2] Yang J, Ou Y, Chen Z, Liao J, Sun W, Luo Y, et al. A Benchmark Dataset of Endoscopic Images and Novel Deep Learning Method to Detect Intestinal Metaplasia and Gastritis Atrophy. IEEE J Biomed Health Inform 2022;1 10., <https://doi.org/10.1109/JBHI.2022.3217944>.

Disclosure: Nothing to disclose.

PP0165

FEASIBILITY, SAFETY, AND OUTCOMES OF UGI ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FROM UK ESD REGISTRY: A MULTICENTRE PROSPECTIVE STUDY ON WESTERN POPULATION

H. Htet¹, S. Subramaniam¹, K. Siggers¹, A. Haji², B. Hayee², N. Suzuki³, B.P. Saunders³, M. Banks⁴, J.E. East⁵, G. Longcroft-Wheaton¹, F. Thursby-Pelham¹, A.A. Alkandari¹, M. Baker-Moffatt¹, J. White⁶, A. Parra-Blanco⁶, P. Bhandari¹
¹Portsmouth Hospitals University NHS trust, Gastroenterology, Cosham, United Kingdom, ²King's College Hospital NHS Foundation Trust, London, United Kingdom, ³The National Bowel Hospital, London Northwest Healthcare NHS Foundation Trust, London, United Kingdom, ⁴University College London Hospitals NHS Foundation Trust, Endoscopy Unit, Gastrointestinal services, London, United Kingdom, ⁵Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, ⁶Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom

Contact E-Mail Address: heinmyat21@gmail.com

Introduction: The outcome of ESD in early gastrointestinal neoplasia in Japan is well established. However, in the west, ESD practice is variable given different disease prevalence in UGI tract and also the volume and experience of each centre.

Aims & Methods: We aim to evaluate ESD practice and outcomes in the UK and hence, multi centre registry was set up. This is a prospective observational study for patients undergoing ESD for early GI neoplasia. All technical and outcomes data was prospectively collected onto REDCap.

Results: There were 451 UGI ESD cases recruited between August 2016 to August 2023 from 6 large tertiary referral centres in the UK. Mean age of the patients was 70.8 years (range: 24-94 years) with male preponderance (318 males vs. 133 females). Majority were in oesophagus: 282 (62.53%), stomach: 159 (35.25%) and duodenum: 10 (2.22%).

Of 282 oesophageal ESDs, 277 (98.23%) were technically successful with en-bloc resection rate of 96%. There were 3 intra-procedural complications (2 oesophageal perforations and 1 oral laceration from overtube). All of them were managed endoscopically. There were 29 (10.28%) post ESD strictures requiring endoscopic dilatations. 3 (1.06%) delayed bleeding were noted and 3 were readmitted for decompensation of underlying co-morbidities.

There were 204/282 (72.34%) Barrett's cases with average length of C3 M5 and mean size 34.5mm. 34 cases (16.67%) had previous ESD or ablation at the same site. Post ESD resection showed deep submucosal (SM) invasion in 21 patients (deep R0 achieved in 42.9% and lateral R0 in 76.2%), 23 pT1bSM1 (deep R0 in 87.0% and lateral R0 in 87%), 107 pT1a (deep R0 in 89.7% and lateral R0 in 85.1%), 31 high grade dysplasia (HGD) (R0 in 97%) and 9 low grade dysplasia (LGD) (R0 in 78%) as shown in Table 1.

There were 44 squamous cell carcinoma (SCC), 26 gastro-oesophageal junctional neoplasia and 8 others (submucosal lesion and granular cell tumours). Of 44 SCC, there were 8 pT1b (5 achieved deep R0, 7 achieved lateral R0), 10 pT1a (all achieved both deep and lateral R0), 22 HGD (81.8% achieved R0), 3 LGD (all achieved R0) as shown in Table 1.

There were 160 gastric ESDs with completion rate of 96.25% and en-bloc rate of 95.5%. There were 8 (5%) intra-procedural perforation which required endoscopic clippings. There were 7 (4.36%) delayed bleeds which were managed endoscopically. Of 160 cases, 138 were epithelial neoplasia, 11 were submucosal lesions while 4 were large hyperplastic polyps. As shown in Table 1, of 138 epithelial neoplasia, 10 had deep SM invasion (7 achieved deep R0, 8 lateral R0), 14 pT1bSM1 (7 achieved deep R0, 10 lateral R0), 50 pT1a (90% achieved deep R0, 80% lateral R0), 35 HGD (94.3% R0) and 27 LGD (77.8% R0).

	Deep SM invasion (n)	Deep R0 (%)	Lateral R0 (%)	pT1b SM1 (n)	Deep R0 (%)	Lateral R0 (%)	IMC (n)	Deep R0 (%)	Lateral R0 (%)	HGD (n)	R0 (%)	LGD (n)	R0 (%)
Barrett's neoplasia	21	42.9	76.2	23	87.0	87.0	107	89.7	85.1	31	97.0	9	78.0
Oesophageal SCC	3	66.7	100.0	5	60.0	80.0	10	100.0	100.0	22	81.8	3	100.0
Gastric neoplasia	10	70.0	80.0	14	50.0	71.4	50	90.0	80.0	35	94.3	27	77.9

Table 1. Post ESD histology outcome in UGI tract.

Conclusion: Unlike in the East, most ESDs in our study were performed in Barrett's oesophagus rather than the stomach. Our data demonstrates the feasibility and safety of UGI ESD in Western setting with high en-bloc rate and low complication rates. We found that within indication of ESD, complete resection (R0) rate is high but lesions with deep submucosal invasion have poor R0 rate.

Disclosure: Professor Bhandari has received research grants or is the advisory board for Fujifilm, Boston, Olympus, Pentax, 3-D matrix, NEC (Japan), Medtronic.

PP0166

CLINICAL EFFICACY AND SAFETY OF ENDOSCOPIC DILATATION WITH ESOFILIP IN BENIGN ESOPHAGEAL STRICTURES

G. Pellegatta^{1,2}, R. Maselli^{1,2}, A. Fugazza¹, M. Colombo¹, M. Spadaccini^{1,2}, M. Andreozzi¹, G. Franchellucci^{1,2}, A. De Marco^{2,1}, C. Hassan^{2,1}, A. Repici^{1,2}

¹IRCCS Humanitas Research Hospital, Department of Gastroenterology, Rozzano, Italy, ²Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy

Contact E-Mail Address: gaia.pellegatta@humanitas.it

Introduction: EsoFLIP is a novel dilation balloon that utilizes high-resolution impedance planimetry to provide real-time, objective visualization and monitoring of dilation.

Aims & Methods: The aim of our prospective study is to evaluate clinical and technical success and safety of endoscopic dilation with EsoFLIP in patients affected by benign esophageal strictures (NCT05725473). Patients with symptomatic esophageal strictures, with exception of patients affected by motor disorders, were selected and endoscopic dilatations were performed with EsoFLIP (8-20 mm dilation range). Clinical condition was evaluated before and after procedure (one week and one month) using a specific questionnaire about severity and frequency of dysphagia (Brief Esophageal Dysphagia Questionnaire-BEDQ 10 items from 0 to 6). We also quantified rate of technical success, adverse events, total procedure time and fluoroscopy exposure time. We utilized EndoFLIP (impedance planimetry system) to evaluate stricture diameter (mm), cross-sectional area (CSA mm²), distensibility index (DI mm²/mmHg) before and after dilatation with EsoFLIP.

Results: We enrolled 15 patients affected by esophageal strictures due to lymphocytic (2) and eosinophilic esophagitis (2), caustic ingestion (2), Schatzki rings secondary to GERD (3), esophageal-gastric anastomosis (6). Strictures involved proximal-medial esophagus (18-30 cm from incisors) in 7 patients out of 15 and in 8 out of 15 patients medial-distal esophagus (30-42 cm). All dilation procedures were technically successful, and no adverse events occurred. The median procedure time was 52.67 min (±12.87) and fluoroscopy exposure time was 5.14 min (±1.23; 9.76% of procedure). After 1 week and 1 month from the dilatation there was a significant decrease of dysphagia severity and frequency shown by BEDQ total score (pre-BEDQ 6.87±5.82 vs 1 week-post-BEDQ 3.20±3.69, p-value 0.0486; pre-BEDQ 6.87±5.82 vs 1 month-post-BEDQ 2.33±2.81, p-value 0.0206). After procedure, there was a significant increase of stricture diameter (pre-di-

ameter 8.55±2.80 vs post-diameter 12.44±2.20 mm, p value=0.0002), distensibility index (pre-DI 1.72±1.63 vs post-DI 3.45±1.99 mm²/mmHg, p value= 0.0151) and cross-sectional area (pre-CSA 70.93 ± 45.69 vs post-CSA 114.93± 33.79 mm², p value=0.0075).

	Pre Eso-FLIP dilatation	Post Eso-FLIP dilatation	1 week post Eso-FLIP dilatation	1 month post Eso-FLIP dilatation
BEDQ total score	6.87±5.82		3.20±3.69 (p= 0.0486)	2.33±2.81 (p=0.0206)
Stricture diameter (mm)	8.55±2.80	12.44±2.20 (p=0.0002)		
Distensibility index (mm ² /mmHg)	1.72±1.63	3.45±1.99 (p= 0.0151)		
Stricture cross-sectional area (mm ²)	70.93 ± 45.69	114.93± 33.79 (p=0.0075)		

Conclusion: Our data showed that endoscopic dilatation of benign esophageal strictures with EsoFLIP is clinically effective and safe. EsoFLIP is a promising dilation technology that may yield a larger diameter change and may potentially reduce fluoroscopy time exposure when compared to traditional endoscopic dilation.

References: Ng K, Mogul D, Hollier J et al. Utility of functional lumen imaging probe in esophageal measurements and dilations: a single pediatric center experience. *Surg Endosc.* 2020 Mar;34(3):1294-1299
Baumann AJ, Carlson DA. EsoFLIP for esophageal dilation: proposed advantages. *Curr Opin Gastroenterol.* 2020 Jul;36(4):329-335.

Disclosure: Nothing to disclose.

PP0167

COMPARATIVE ANALYSIS OF TWO GRAPHICAL USER INTERFACES FOR COMPUTER AIDED DETECTION OF BARRETT’S NEOPLASIA

M.R. Jong¹, J. Jukema¹, C. Kusters², R. van Eijck van Heslinga¹, T. Boers², T. Jaspers², K. Fockens¹, J. van der Putten², R.E. Pouw¹, L. Duits¹, F. van der Sommen², P. de With², J. de Groof¹, J.J. Bergman¹, BONSAI Consortium
¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Technische Universiteit Eindhoven, Electrical Engineering, Eindhoven, Netherlands

Contact E-Mail Address: r.a.h.vaneijckvanheslinga@amsterdamumc.nl
Introduction: The development of artificial intelligence (AI) for endoscopy has significantly increased, yet the aspect of endoscopist-AI interaction remains insufficiently explored. This interaction is crucial as it could substantially influence the AI system’s performance in routine clinical practice.
Aims & Methods: This study aimed to evaluate two different graphical user interfaces (GUIs) for a computer aided detection (CAdE) system for recognition of early Barrett’s neoplasia. We performed a comparative analysis of two GUI designs—the frequently used bounding box GUI and a novel heatmap GUI—using an extensively evaluated CAdE system¹. Thirty-seven endoscopists from six countries participated. Each endoscopist assessed 70 Barrett’s esophagus. Every video was analyzed by the CAdE system and contained, at some point, a detection which was visualized by the GUI. The study was conducted in two phases, with each video initially shown using one of the GUIs, followed by a two-week washout period after which the same videos were displayed with the alternative GUI. Endoscopists were tasked with identifying potential neoplastic lesions, selecting biopsy sites, and stating their GUI preference.
Results: No significant differences were found for classification performance between the two GUIs (sensitivity 83% vs. 83%, p = 0.29; specificity 86% vs. 86%, p = 0.09). Both interfaces achieved similar scores in local-

ization accuracy, with a median of 97%. Among the participants, 23 expressed a preference for the heatmap GUI, while 14 favored the bounding box.

Conclusion: Despite a general preference for the heatmap GUI among endoscopists, there were no statistically significant differences in performance outcomes between the two interfaces.

References: 1. Fockens N, Jong MR, Jukema JB, Pouw RE, Duits LC, Van Munster SN, et al. A deep learning system for detection of early Barrett’s neoplasia: a model development and validation study. *The Lancet Digit Health.* 2023;5:905-21.

Disclosure: Nothing to disclose.

PP0168

DIAGNOSTIC ABILITY AND ADVERSE EVENTS OF MUCOSAL INCISION-ASSISTED BIOPSY FOR GASTRIC SUBEPITHELIAL TUMORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

E. Koizumi¹, O. Goto¹, A. Matsuda², Y. Ishikawa¹, S. Nakagome¹, M. Niikawa¹, T. Habu¹, K. Yoshikata¹, K. Kirita¹, H. Noda¹, K. Higuchi¹, T. Onda¹, J. Omori¹, N. Akimoto¹, H. Yoshida², K. Iwakiri¹
¹Nippon Medical School, Department of Internal Medicine, Division of Gastroenterology, Tokyo, Bunkyo-ku, Koishikawa, Japan,
²Nippon Medical School, Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Tokyo, Bunkyo-ku, Sendagi, Japan

Contact E-Mail Address: e-koizumi@nms.ac.jp
Introduction: Currently, the Japanese guidelines for GISTs suggest endoscopic ultrasound-guided fine-needle aspiration for sampling the tissue of subepithelial tumors (SETs) and as a first-line technique. Mucosal incision-assisted biopsy (MIAB) is another tissue sampling technique; in this technique, the mucous membrane covering the SET is cut to expose and sample the tissue directly under direct visualization. However, the Japanese guidelines do not clearly state how to handle this technique, and the MIAB procedure has not been standardized, especially in technical aspects, the need for local injection to the submucosa before mucosal incision to prevent perforation, and the need for acid secretion inhibitors to prevent postoperative bleeding.
Aims & Methods: This systematic review and meta-analysis aimed to evaluate diagnostic ability and examine the efficacy of countermeasures to adverse events of MIAB for gastric SETs. We performed a literature search and identified 533 relevant articles. Eleven articles, including 339 lesions, were ultimately used in the meta-analysis. The primary endpoint was the pathological diagnostic rate of MIAB for gastric SETs, and the secondary endpoint was the incidence of adverse events. The efficacy of acid secretion inhibitors in preventing postoperative bleeding and that of local injection before incision to prevent perforation were also examined.
Results: Nine studies were performed in Japan and two in South Korea, of which only two were prospective studies. The mean age of the patients was 60.7 years, and 48.4% were male. In all studies, endoscopic ultrasound was performed to assess tumors before incision-assisted biopsy. The mucosal incision procedure was the same in all studies: The mucosal incision on the tumor was made, and tissue was sampled directly from the tumor using biopsy forceps; however, in all cases in eight articles and six cases in one article, a local injection of saline or glycerol into the submucosa before the mucosal incision was performed. Nine articles reported the closure of the incision using clips. The mean tumor diameter was 20.6 mm, and the pathological results included 150 GISTs, 70 leiomyomas, 11 schwannomas, 37 ectopic pancreas, three lipomas, three cases of inflammatory fibrotic polyp, two malignant lymphoma lesions, two glo-

mus tumors, one neuroendocrine tumor, one adenocarcinoma, one old hematoma, and one renal cell carcinoma. In all cases in six articles and some in two, an intravenous or oral gastric acid suppressant such as esomeprazole or vonoprazan was administered after treatment. The pooled pathological diagnostic rate of MIAB for gastric SETs was 86.0% (95% confidence interval [CI]: 78.6–93.4; $P = 96\%$). The adverse event rate of the pooled population was 0.3% (95% CI: –1.15 – 1.76; $P = 0\%$). The acid secretion inhibitors significantly reduced postoperative bleeding (odds ratio: 0.06, 95% CI: 0.01– 0.66, $P = 0.02$). Perforation occurred in 0% and 2.6% of the local injection and non-local injection cohorts, respectively, and the pathological diagnostic rates were 50% and 66.7%, respectively.

Conclusion: MIAB is a reliable technique with a favorable diagnostic rate and few adverse events. Acid secretion inhibitors effectively prevent postoperative bleeding, but the effectiveness of local injection remains unclear. This technique is considered a robust tissue sampling method for gastric SETs.

Disclosure: Nothing to disclose.

PP0169

DIAGNOSIS AND SURVEILLANCE OF PREMALIGNANT GASTRIC LESIONS IN AN INTERMEDIATE-RISK POPULATION: WHERE ARE WE?

R. Reivytyte¹, I. Stundiene^{2,1}, E. Dieninyte - Misiune^{1,2}

¹Vilnius University, Faculty of Medicine, Vilnius, Lithuania,

²Vilnius University Santaros Klinikos, Center of Hepatology, Gastroenterology and Dietetics, Vilnius, Lithuania

Contact E-Mail Address: rositareivytyte@gmail.com

Introduction: Gastric cancer is associated with a poor prognosis due to the late stage of the disease at the time of diagnosis. Consequently, the detection and surveillance of the established premalignant gastric lesions becomes imperative. Despite Eastern Europe being a region of high – intermediate gastric cancer incidence, the guidelines (MAPS-II) (1) are mainly based on the data from Western countries due to a lack of research in this area in Eastern countries.

Aims & Methods: This study aimed to assess a) the incidence of gastric cancer in patients with proven histologically proven premalignant gastric lesions b) the efficacy of endoscopic diagnosis of premalignant gastric lesions and c) trends of subsequent management of patients at an intermediate risk for the development of gastric cancer in an academic center in Lithuania.

We conducted a retrospective cohort study of patients who underwent esophagogastroduodenoscopy with histological sampling between 2012 and 2020 in a single academic centre. The pathology database was filtered for keywords “atrophy” and/or “intestinal metaplasia” in pathological conclusions or descriptions to identify patients with possible premalignant gastric lesions. Demographic (age and gender), pathology report (histological findings, presence of *H.pylori*), endoscopic evaluation (diagnosis, location of biopsies, endoscopic recognition of premalignant or cancerous lesions), patient history (family history of gastric cancer) and subsequent management (recommended *H.pylori* eradication and follow-up) data were collected.

Results: This retrospective cohort study conducted in a single academic centre identified 1842 patients who underwent diagnostic esophagogastroduodenoscopy with histological sampling between 2012 and 2020. Out of 1842 patients screened in the pathology database, 1762 had histologically proven premalignant gastric lesions (extensive gastric mucosal atrophy, intestinal metaplasia or both).

The study cohort consisted of 51% males with an average age of 64.42 (SD ± 1.573). A positive family history of gastric cancer was reported in 0.7% of the patients.

Histological evaluation identified gastric atrophy in 9.9% ($n = 183$) of samples, distal atrophy in 6.1% ($n = 113$) of cases, and panatrophy in 3.8% ($n = 70$) of samples. Distal intestinal metaplasia was observed in 47.9% ($n = 883$) of cases, while extensive intestinal metaplasia was found in 47% ($n = 866$) of samples. Dysplasia was detected in 1.03% ($n = 19$) of the samples. Endoscopically precancerous lesions were identified in only 14.4% ($n = 254$) of cases, with follow-up recommendations provided for 3.4% ($n = 60$) of the patients.

Helicobacter pylori presence on biopsy samples was detected in 37.6% ($n = 662$) of cases, with eradication recommended only for 36.7% ($n = 243$) of these cases.

Subsequently, during follow-up 0.8% ($n = 14$) of patients with premalignant gastric lesions were diagnosed with gastric cancer.

Conclusion: This study reveals poor efficacy of endoscopic evaluation for precancerous gastric lesions and suboptimal adherence to current guidelines for their management. These findings underpin the importance of high-quality endoscopy, dissemination and adherence to the guidelines in the hopes of reducing the morbidity and mortality of gastric cancer.

References: (1) Pimentel-Nunes P, Libânio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy*. 2019;51(4):365–88.

Disclosure: Nothing to disclose.

PP0170

THE ROBOT-ASSISTED SYSTEM YUNSRBOT FOR REMOTE ENDOSCOPY: AN EXPLORATORY STUDY

Y. Yang¹, B. Yan¹, H. Liu², Y. Yang², L. Peng¹

¹The First Medical Center, Chinese PLA General Hospital, Beijing, China, ²Shenyang Institute of Automation, Shenyang, China

Contact E-Mail Address: sunny301ddc@126.com

Introduction: The introduction of robotic and communication technology into soft endoscopy allows remote endoscopy become a reality. The ability to perform upper gastrointestinal endoscopy from remote location will eliminate geographical constraints and make endoscopic expertise available throughout the world, improving patient treatment and healthcare management, especially when faced with a pandemic. Therefore, it is of great practical significance to develop a robot system that can be used for remote endoscopy.

Aims & Methods: This study aimed to evaluate the safety and effectiveness of the robot-assisted system YunSRobot for remote human upper gastrointestinal endoscopy and investigate the optimal network for remote endoscopy.

The robot-assisted system YunSRobot was developed by the Yunsheng Y group from the PLA General Hospital and Hao L group from the State Key Laboratory of Robotics, Shenyang Institute of Automation. The master manipulator is located in the Hainan Hospital of PLA general hospital (Sanya, Hainan Province, China), while the slave robot and the patient are located in the First Medical Center, PLA general hospital (Beijing, China)—a total distance of about 2,900 km. The two sites were connected through 5G network and remote upper gastrointestinal endoscopy were performed. The average network delay, operation time, standardized images collection and the adverse events were recorded.

Results: Three remote upper gastrointestinal endoscopy operations were safely performed through a 5G network, with an average time delay of 100–150 ms. The total operation time was 1370 $\pm$ 126.75 s, while average en-

try time for pharynx, esophagus, stomach and pylorus was 207.67±175.05 s, 78.00±29.68 s, 104.00±10.03 s, 30.67±30.40 s, respectively. The average operation time of duodenum was 141.67±40.88 s. Forty standardized images were collected from each patient. All patients successfully completed the biopsy (gastric body, gastric angle and gastric antrum) and no adverse events occurred during the procedures.

Conclusion: The robot-assisted system YunSRobot can realize remote human upper gastrointestinal endoscopy, which has high effectiveness and safety. The 5G network facilitate smooth operation and acceptable latency. Our exploratory study can provide insights for promoting the future development of remote endoscopic surgery.

Disclosure: Nothing to disclose.

PP0171

THE USEFULNESS OF ENDOSCOPIC HAND-SUTURING (EHS) FOR CLOSURE OF THE MUCOSAL DEFECT AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

M. Kobayashi¹, H. Chiba¹, M. Koga¹, A. Hayashi¹, Y. Ebisawa¹, J. Arimoto¹, H. Kuwabara¹, M. Nakaoka¹
¹Omori Red Cross Hospital, Gastroenterology, Ota-Ku, Japan

Contact E-Mail Address: m-kobayashi5@hotmail.co.jp

Introduction: ESD has become the standard treatment for early gastric cancer. Recently, the number of patients taking antithrombotic agents (ATAs) has increased, and the prevention of post-ESD bleeding is a main concern. EHS after gastric ESD has been developed to solve these problems, but the effectiveness and procedural success rate of EHS is not known. Here we investigate the successful introduction of EHS and evaluate the safety and effectiveness of the EHS.

Aims & Methods: 11 patients who underwent EHS after gastric ESD from December 2022 to April 2024 were included in this study. Patient and lesion background, endoscopic findings, and treatment outcomes were reviewed retrospectively. A V-loc 180 available barbed suture (VLOCL0604; Covidien, Mansfield, Mass, USA) and through-the scope flexible needle holder (SutuArt, Olympus, Tokyo, Japan) were used for EHS. The same endoscopist and the assistant performed Ex vivo training model prior to clinical introduction.

Results: Mean age was 74.8±7.3 years, 9 males and 2 females, and 4 with and 7 without ATAs. The lesion locations were as follows: upper/middle/lower = 4/0/7. Mean tumor size was 15.4±5.3 mm, mean defect size was 30.3±5.4 mm, and mean resection time was 46.6±26.4 minutes. The mean time needed for suturing was 30.6±9.6 minutes, and a mean of 4.7±0.4 stitches were placed. Suturing speed (resection area/suturing time) was 20.9±7.5 mm²/min. Complete suture was achieved in all patients, and they began clear fluid on POD1. There were no adverse events during EHS such as bleeding or perforation.

Conclusion: In EHS, complete suture was achieved in all cases, with no post-ESD bleeding or delayed perforation. Further data is needed to confirm its effectiveness.

References: 1) O. Goto et al. Endoscopic hand-suturing is feasible, safe, and may reduce bleeding risk after gastric endoscopic submucosal dissection: a multicenter pilot study (with video). *Gastrointest Endosc* 2020 ; 91(5): 1195-1202.

Disclosure: Nothing to disclose.

PP0172

THE FEASIBILITY AND SAFETY OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN PATIENTS TAKING GLUCOCORTICOIDS OR IMMUNOMODULATORS

H. Fukuya^{1,2}, Y. Iboshi^{1,2}, E. Ihara³, R. Okitsu^{1,2}, A. Ohkubo^{1,2}, T. Sasaki^{1,2}, S. Hamada^{1,2}, D. Yoshimura^{1,2}, N. Harada^{1,2}
¹National Hospital Organization Kyusyu Medical Center, Department of Gastroenterology, Fukuoka, Japan, ²Institute of Research Center, National Hospital Organization Kyusyu Medical Center, Fukuoka, Japan, ³Graduate School of Medical Sciences, Kyushu University, Department of Medicine and Bioregulatory Science, Fukuoka, Japan

Contact E-Mail Address: hiroki.fukuya2234@gmail.com

Introduction: Glucocorticoids (GC) and immunomodulators (IM) are frequently used to maintain clinical remission in various diseases, yet GC is implicated in delaying gastric ulcer healing [1], and IM is associated with post-endoscopic submucosal dissection (ESD) fever and post-coagulation syndrome on colon ESD [2]. The safety of gastric ESD in patients receiving oral GC or IM remains unknown.

Aims & Methods: This study evaluates the impact of oral GC or IM on gastric ESD outcomes, focusing on procedural safety and postoperative recovery. In a single-center, retrospective study, we analyzed clinical outcomes for 411 patients who underwent gastric ESD between April 2017 and April 2022 at our institute in Fukuoka, Japan. We compared data between patients using a GC or IM (32 patients) group and a standard group (379 patients), considering clinicodemographic characteristics and procedural details. Patients were further divided into three subgroups (SG) based on lesion size and procedure duration to consider treatment intensities: SG1 for lesions >20 mm and procedure times >60 minutes; SG2 for either lesions >20 mm or procedure times >60 minutes; and SG3 for lesions <20 mm and procedure times <60 minutes.

	GC Group (n=32)			Standard Group (n=379)			p-value*
Subgroup (n)	SG1 (9)	SG2 (10)	SG3 (13)	SG1 (125)	SG2 (164)	SG3 (90)	-
hospital stay(days)	10.8±7.1			8.6±3.7			0.0026
	14.1±2.3	9.3±2.2	9.8±1.9	9.4±4.8	8.3±3.3	8.1±2.0	-
□log WBC	0.12±0.12			0.20±0.15			0.005
	0.14±0.1	0.12±0.095	0.10±0.16	0.22±0.12	0.18±0.1	0.21±0.24	-
abdominal pain (%)	37.5%			16.9%			0.0066
	55.6%	40.0%	23.1%	20.0%	14.0%	15.6%	-
post-ESD fever (%)	12.5%			3.4%			0.035
	22.2%	0.0%	15.4%	6.4%	1.8%	2.2%	-

Table.
GC, glucocorticosteroid; SG, subgroup; log, logarithmic; WBC, white blood cell
*Analyzed by the Fisher exact test and the Student t-test. Values are shown as averages±standard deviation unless otherwise stated.

Results: The GC group (n=32, 93.8% on GC, median GC dose 5mg/day, 37.5% on IM) showed a higher prevalence of females (53.1%), were older (average age 77.5 vs. 73 years), and had poorer performance status than the standard group (n=379). Despite similar tumor characteristics, the GC group experienced more frequent abdominal pain (37.5% vs. 16.9%) and post-ESD fever (12.5% vs. 3.4%), resulting in longer hospital stays (average 10.8 days vs. 8.6 days) (Table). Meanwhile, the GC group's blood tests showed less elevation in white blood cell (WBC) and C-reactive protein

(CRP) levels compared to the standard group. Intraoperative perforation occurred in 6.2% of the GC group but was managed conservatively without any cases of delayed perforation. Subgroup analysis revealed that SG1 experienced the most significant increases in abdominal pain, post-ESD fever, and WBC/CRP levels (Table).

Conclusion: Gastric ESD in patients on GC or IM were feasible but poses higher procedural risks and more frequent postoperative complications, particularly at higher treatment intensities. These findings highlight the need for customized procedural strategies and increased postoperative care to enhance outcomes for this vulnerable patient population.

References: [1]Reitman D, Sacks HS, Smith H Jr, et al. Association of adrenocorticosteroid therapy and peptic-ulcer disease. *N Engl J Med.* 1983 Jul 7;309(1):21-4.

[2]Yamamoto S, Kinugasa H, Yamasaki Y, et al. H. Fever and electrocoagulation syndrome after colorectal endoscopic submucosal dissection for patients with immunosuppressants and steroids. *DEN Open.* 2021 Dec 9;2(1):e83.

Disclosure: Conflict of interest Hiroki Fukuya, Yoichiro Iboshi, Ryota Okitsu, Akito Ohkubo, Taisuke Sasaki, Shohei Hamada, Daisuke Yoshimura, and Naohiko Harada, declare that they have no conflict of interest. Eikichi Ihara participates in the funded research of Takeda Pharmaceutical Co., Ltd and belongs to an endowed course supported by companies including Ono Pharmaceutical Co., Ltd, Miyarisan Pharmaceutical Co., Ltd, Sanwa Kagaku Kenkyusho Co., Ltd, Otsuka Pharmaceutical Factory, Inc, Fujifilm Medical Co, Ltd, Terumo Corporation, Fancl Corporation, and Ohga Pharmacy.

PP0173

LOW ACCURACY OF ENDOSCOPIC DIAGNOSIS FOR DIMINUTIVE EARLY OROPHARYNGEAL CANCER

Y. Uenishi¹, Y. Shimodate¹, D. Miyaoka¹, Y. Iwado², T. Gotoda¹, H. Mori¹, M. Mizuno¹, Kurashiki Central Hospital, Department of Gastroenterology, Kurashiki, Japan

¹Kurashiki Central Hospital, Gastroenterology And Hepatology, Kurashiki, Japan, ²Okayama University Hospital, Gastroenterology, Okayama, Japan

Contact E-Mail Address: uenishi.yos@gmail.com

Introduction: Thanks to instrumental advances and accumulation of understandings of endoscopic features of early oropharyngeal neoplasia, we often encounter diminutive pharyngeal lesions. However, whether follow-up is permissible or therapeutic intervention is preferable for these lesions is uncertain. Accurate endoscopic diagnosis is pivotal for the decision-making process. This study aimed to assess the accuracy of endoscopic diagnosis for pharyngeal microlesions.

Aims & Methods: We evaluated pre-treatment endoscopic images of 121 lesions 3 mm or less in that pharyngeal neoplasia was endoscopically diagnosed with magnifying narrow-band imaging observation and resected by cold forceps biopsy. Two endoscopists, one with over 15 years of experience and another with 5 to 10 years (study A), made endoscopic diagnosis of each image and categorized the images into non-dysplasia, low-grade dysplasia, or squamous cell carcinoma (SCC)/high-grade dysplasia, and the accuracy of the endoscopic diagnosis was evaluated with the pathological findings of resected tissues. To assess interrater agreement, another physician joined to each experience group (study B), and the kappa coefficient was calculated.

Results: In study A, the overall accuracy rate of the endoscopic diagnosis was 60.7%. However, for SCC/high-grade dysplasia, the sensitivity was 12.5% (95% confidence interval [CI]: 3.5-29.0), specificity was 94.3% (95% CI: 90.2-97.0), positive predictive value was 25.0% (95% CI: 7.3-52.4), and

negative predictive value was 87.6% (95% CI: 82.6-91.6). Nearly 90% of malignant or high-grade dysplastic lesion were not correctly diagnosed by endoscopic observation even with magnifying narrow-band imaging. Although the concordance rate between study A and B was low (κ coefficient 0.07, 95% CI: -0.15-0.30), study B also exhibited low sensitivity (31.2%, 95% CI: 16.1-50.0), specificity (83.3%, 95% CI: 77.6-88.1), positive predictive value (22.2%, 95% CI: 11.2-37.1), and negative predictive value (88.8%, 95% CI: 83.6-92.9) for SCC/high-grade dysplasia.

	sensitivity	specificity	positive predictive value	negative predictive value
Study A				
Expert, (%)	25.0	93.3	36.4	89.1
Senior, (%)	0.0	95.2	0.0	86.2
Average, (%)	12.5	94.3	25.0	87.6
Study B				
Expert, (%)	37.5	76.2	19.4	88.9
Senior, (%)	25.0	90.5	28.6	88.8
Average, (%)	31.2	83.3	22.2	88.8

Conclusion: The accuracy of endoscopic diagnosis of diminutive malignant pharyngeal lesions was very low regardless of proficiency of endoscopist. Thus, given that such diminutive lesions can be resected with minimally invasive cold forceps biopsy, proactive excision for diagnostic treatment is recommended.

Disclosure: Nothing to disclose.

PP0174

WITHDRAWN

PP0175

THE NONINVASIVE ROLE OF SPLENO-PORTAL INDEX & PLATELET COUNT/SPLEEN RATIO IN THE DIAGNOSIS OF ESOPHAGEAL VARICES IN PATIENTS WITH COMPENSATED CIRRHOSIS

M. Abdel-Samiee¹, A.G. Badran²

¹National Liver Institute-Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt, ²Mansora, GIT and hepatology, Mansoura, Egypt

Contact E-Mail Address: drmohammed100@yahoo.com

Introduction: Varices are present in 30-40 % of patients with compensated cirrhosis (Child-Pugh class A). Although screening endoscopy for esophageal varices(O.V.) is recommended to all patients with cirrhosis, this recommendation is not a result of evidence-based data. We studied the association of (platelet count/spleen diameter ratio, insulin resistance and splenoportal index) and the presence of O.V. in patients with compensated cirrhosis.

Aims & Methods: 124 patients with compensated liver cirrhosis due to chronic hepatitis C virus were studied. After clinical, laboratory ultrasound examinations, all patients underwent screening endoscopy and O.V were reported as present or absent. According to presence or absence of varices; two groups were described: group I without varicesand group II with varices.

Results: Among 124 patients with mean age of (51.81±12.94), 2 groups were described: group I (30 patients) and group II (94 patients) with a male majority (20 patients in group I and 66 patients in group II). In group I and group II: the mean platelet count/spleen diameter ratio was (1022.6±73.36, 608.76±58.44) respectively, the mean insulin resistance value was (2.426±0.618, 3.081±0.474) respectively. The mean splenoportalindex (SPI) value was (2.878±0.870, 6.349±0.514) respectively.For platelet

count/spleen diameter ratio and SPI, the sensitivity was (95.7%), specificity (83.3%) and accuracy (92.7%). For platelet count/spleen diameter ratio and insulin resistance (IR), the sensitivity was (70.2%), specificity (86.7%) and accuracy (74.1%). For IR and SPI, the sensitivity was (70.2%), specificity (76.7%) and accuracy (71.7%). For the three predictors combined, the sensitivity was (78.7%), specificity (82.2%) and accuracy (79.5%).

	Platelet count / spleen diameter ratio & Splenoportal index	Platelet count / spleen diameter ratio & IR	IR & Splenoportal index	Platelet count / spleen diameter ratio & IR & Splenoportal index
Sensitivity (%)	95.7	70.2	70.2	78.7
Specificity (%)	83.3	86.7	76.7	82.2
Positive Predictive Value (%)	94.7	94.3	90.4	93.2
Negative Predictive Value (%)	86.2	48.1	45.1	55.2
Accuracy (%)	92.7	74.1	71.7	79.5

Table 1. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy when we combine (Platelet count / spleen diameter ratio & Splenoportal index), (Platelet count / spleen diameter ratio & IR) and (IR & Splenoportal index).

Conclusion: Low platelet count/spleen ratio and high SPI are very useful non invasive predictors for the presence of O.V. that could be used either separately or combined to decrease the number of upper GIT endoscopies needed in cirrhotic patients management, However, IR as a non invasive predictor is still in need for further evaluation.

References: Berzigotti A, Gilabert R, Abrales JG, Nicolau C, Bru C, Bosch J, et al. Noninvasive prediction of clinically significant portal hypertension and esophageal varices in patients with compensated liver cirrhosis. *Am J Gastroenterol* 2008; 103:1159-67.

Bolondi L, Zironi G, Gaiani S, Li Bassi S, Benzi G, Barbara L. Caliber of splenic and hepatic arteries and spleen size in cirrhosis of different etiology. *Liver* 1991; 11:198-205.

Bressler B, Pinto R, El-Ashry D, Heathcote EJ. Which patients with primary biliary cirrhosis or primary sclerosing cholangitis should undergo endoscopic screening for oesophageal varices detection? *Gut* 2005; 54:407-10.

Camma' C, Petta S, Vito Di Marco, Fabrizio Bronte, Stefania Ciminnisi, Giusalba Licata, Sergio Peralta, Fabio Simone, Giulio Marchesini, and Antonio Crax. Insulin Resistance Is a Risk Factor for Esophageal Varices in Hepatitis C Virus Cirrhosis. *Hepatology* 2009; 49:195-203.

Disclosure: Nothing to disclose.

PP0176
WITHDRAWN

PP0177
COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCULARIS PROPRIA

C.B. Ryu¹, M.S. Lee¹, J.Y. Bae²
¹Soon Chun Hyang University School of Medicine, Department of Internal Medicine, Bucheon, South Korea, ²Seoul Medical Center, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: ryuchb@gmail.com

Introduction: Endoscopic resection for gastric subepithelial tumors (SETs) originated from the muscularis propria (GSET-PM) has offered less invasive alternatives to surgical resection.

Aims & Methods: The aims of this study were to compare endoscopic sub-tumoral dissection (ESD) with surgical resection for the removal of GSET-PM. This study involved 17 patients with GSET-PM removed by ESD and 76 patients who underwent curative surgical resection. ESD was attempted in GSET-PM with well marginated tumors which was below 5cm and showed an endoluminal growth pattern according to endoscopic ultrasound (EUS) finding.

Results: ESD group were more likely to have upper portion (10/17, 58.8%) and surgery group were more likely to have mid portion (41/76, 53.8%) (p=0.039). ESD group were smaller median tumor size (25.6 mm vs 35.9 mm, p=0.037) and higher endoluminal ratio (58.5±9.1 % vs 45.8±15.4 %, p=0.002). ESD group were mostly to have Yamada type III (10/17, 58.8%) and surgery group were mostly Yamada type I (52/76, 68.4%) (p< 0.001). Complete resection by ESD was lower than by surgical resection (82.4% vs 100%, p< 0.001). In ESD group, 3 performed surgical resection after ESD (1 incompletely resection and 2 uncontrolled bleeding) and 1 showed perforation was completely resected with endoscopic closure. In surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group (p=0.006), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between two group.

Conclusion: ESD can be one of good options for the resection of endoluminal GSET-PM and could be replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.

Disclosure: Nothing to disclose.

PP0178
PROSPECTIVE EVALUATION OF AN EXPLAINABLE DEEP LEARNING MODEL FOR GASTROESOPHAGEAL VALVE ASSESSMENT VIA THE HILL CLASSIFICATION

I. Kafetzis¹, P. Sodmann¹, B.-E. Hergehelegiu¹, K.H. Fuchs¹, F. Seyfried², M. Brand³, A. Meining¹, A. Hann¹
¹University Hospital Würzburg, Interventional and Experimental Endoscopy (InExEn), Internal Medicine II, Würzburg, Germany, ²University Hospital Würzburg, Department of Experimental Surgery, Würzburg, Germany, ³University Hospital Würzburg, Internal Medicine II, Würzburg, Germany

Contact E-Mail Address: Hann_A@ukw.de

Introduction: Standardized classification of the gastroesophageal valve, achievable using the Hill classification, is a common step during gastroscopy. Given the visual nature of endoscopic examinations, artificial intelligence (AI) can support this task. We conducted a single-center prospective study to compare the performance of a self-developed AI model in determining the Hill classification with that of examiners.

Aims & Methods: From October 2023 to January 2024 consecutive patients with unaltered anatomy of the gastroesophageal junction were enrolled in the study. The AI model ran in the background during routine gastroscopy, providing real-time predictions, while physicians assessed the Hill grade without knowledge of the model's output. The Gold standard was established through a majority vote of a three-member expert committee in the cases where a clear image of the hiatus was available. The primary outcome was accuracy in Hill grade assessment, with secondary outcomes including precision and sensitivity for each grade.

Results: Out of 150 patients that participated, 131 were eligible for analysis. Our AI model exhibited an accuracy of 84.7%, surpassing the physicians' accuracy with 61.8% ($p<0.01$). Regarding rating the different Hill grades the AI's lowest accuracy, precision and sensitivity were 88%, 53% and 60% respectively, while physicians achieved lowest scores of 66%, 20%, and 30%. Post hoc analysis of the videos using the systems capability for real-time explainability via heatmaps highlighting image regions influencing the classification, revealed that the model used the correct anatomical region for classification.

Conclusion: Our AI system demonstrates superior accuracy compared to physicians in Hill grade assessment. Future research should explore the impact of physician-AI interactions during examinations through a randomized controlled trial. (ClinicalTrials.gov, Trial register number: NCT06040723)

Disclosure: Nothing to disclose.

PP0179

PREVALENCE, RISK FACTORS AND MANAGEMENT OF ENDOSCOPIC RESECTION RELATED DUODENAL STRICTURES

J. Gauci¹, R. Medas², F.V. Mandarino¹, C. Kerrison¹, A. Whitfield¹, H. Wang¹, M. Sidhu¹, L. Bracken¹, V. Peranathan¹, S. Gupta¹, O. Cronin¹, T. O'Sullivan¹, E. Lee¹, M.J. Bourke¹, N. Burgess¹
¹Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia, ²Centro Hospitalar São João, Gastroenterology, Pedroso - Vila Nova de Gaia, Portugal

Contact E-Mail Address: julia.gauci@yahoo.co.uk

Introduction: Endoscopic resection (ER) of large (>/-15mm) duodenal laterally spreading lesions (D-LSLs) is now standard of care. Data on prevalence, risk factors and outcomes of post-duodenal ER strictures are absent; we sought to evaluate this in a Western cohort.

Aims & Methods: We report a retrospective analysis of a prospectively collected cohort of D-LSLs following ER in an expert tissue resection centre. Strictures were considered "severe" if patients experienced obstructive symptoms, "moderate" if an adult gastroscope could not pass the stenosis, or "mild" if there was resistance on successful passage. If dilatation was performed, 2-4 weekly dilatation sessions were conducted until scope passage without resistance was achieved as well as symptom resolution where applicable. Primary outcomes included stricture prevalence, risk factors and management.

Results: Over 193 months until February 2023, 246 lesions in 239 patients were included (51.2% male, median age 70 years [IQR 14], median size 35mm [IQR 25]). 30 (12.2%) resections resulted in stenosis; 14 mild (46.7%), 4 moderate (13.3%) and 12 severe (40%). 18 (7.3%) required balloon dilatation (median number of sessions, 2 [IQR 6]). Stricture resolution following index-ER was achieved with balloon dilatation alone in 15/18 patients (83.3%). Two patients had an excellent response to lumen apposing metal stent insertion following ER of fully circumferential D-LSL. A patient with an incompletely resected fully circumferential D-LSL, in which adenocarcinoma was confirmed post-ER, required palliative stent placement after 3 sessions of balloon dilatation, due to gastric outlet ob-

struction caused by residual tumour. Post ER-defect circumference $\geq 80\%$ proved the strongest independent predictor for stricture formation (OR 62.9 (CI 17.9-276.7, $p<0.001$; Table 1). The incidence of stricture formation with an ER-defect $\geq 80\%$, 60-79% and $<60\%$ was 72.2% ($n=26/36$), 12.5% ($n=4/32$) and 0% ($n=0/178$) respectively. All severe strictures (12/12, 100%) occurred in ER-defects $\geq 80\%$.

Parameter		No stenosis n (%)	Stenosis n (%)	OR univariable (95% confidence interval, p value)	OR multivariable (95% confidence interval, p value)
Location involving a flexure	No (D1, D2 or D3)	210 (89.4)	25 (10.6)	-	-
	Yes (D1/D2 junction)	6 (54.4)	5 (45.5)	7.00 (1.9-24.9, $p=0.0002$)	4.05 (0.33-45.30, $p=0.28$)
Lesion length (mm)	<50	196 (95.1)	10 (4.9)	-	-
	≥ 50	13 (39.4)	20 (60.6)	30.2 (12.1-80.9, $p<0.001$)	5.25 (1.28-21.8, $p=0.02$)
Defect Circumference (%)	<80	206 (98.1)	4 (1.9)	-	-
	≥ 80	10 (27.8)	26 (72.2)	133.9 (43.2-526.7, $p<0.001$)	62.9 (17.9-276.7, $p<0.001$)
Histology	LGD/other*	188 (90.8)	19 (9.2)	-	-
	HGD/SMIC	28 (71.8)	11 (28.2)	3.89 (1.64-8.95, $p=0.002$)	2.23 (0.42-11.6, $p=0.33$)

Table 1: Logistic regression to determine lesion characteristics, endoscopic resection (ER) technique and post-ER outcomes which are risk factors for stricture development

*Other histology refers to non-adenomatous histology including Brunner's hyperplasia ($n=2$), gastric heterotopia ($n=2$) and duodenal lymphoma ($n=1$)

Conclusion: ER-defect circumference strongly predicts stricture formation following ER of D-LSL. These findings can be used to guide patient counselling and post-procedural care. Based on our findings, we recommend a management algorithm determined by the extent of the ER-defect. When the ER-defect extends $\geq 80\%$ of the luminal circumference, endoscopic assessment for stricture formation should be scheduled routinely at 3 weeks. When the ER-defect involves 60-79%, clinical consultation at 2-3 weeks should be conducted to screen for obstructive symptoms, and gastroscopy organised if the patient is symptomatic. ER-defects $<60\%$ can safely return to routine surveillance.

Disclosure: Nothing to disclose.

PP0180

COMPARISON OF SEDATION STRATEGIES IN DIAGNOSTIC UPPER GASTROINTESTINAL ENDOSCOPIES: A PROSPECTIVE STUDY

A. Samad¹

¹Hamdard University Hospital, Gastroenterology, Karachi, Pakistan

Contact E-Mail Address: samaddhedhi@gmail.com

Introduction: Sedation during upper gastrointestinal endoscopies (UGIEs) is a common practice aimed at improving patient comfort and procedural tolerance. However, the necessity of sedation remains a subject of debate, particularly regarding its impact on patient safety and experience. This prospective study aimed to compare the outcomes of sedated and non-sedated UGIEs, focusing on patient safety, procedural experience, and post-procedural comfort.

Aims & Methods: From January 1st, 2023, to December 31st, 2023, 150 patients undergoing diagnostic UGIEs were prospectively enrolled. Indications for endoscopy included dyspepsia, dysphagia, unexplained iron deficiency anemia, weight loss, and diarrhea. Patients were randomly assigned to one of three groups: Group 1 received local pharyngeal spray (lidocaine), Group 2 received pharyngeal spray with midazolam, and Group

3 received pharyngeal spray with nalbuphine. Parameters assessed included patient safety, procedural experience, technical safety, pharyngeal sensitivity, and post-procedural comfort.

Results: Out of 150 patients, 90 were male and 60 were female. In Group 1 (pharyngeal spray only), 12 out of 50 patients reported mild throat irritation. In Group 2 (pharyngeal spray with midazolam), 9 out of 50 patients experienced increased sleepiness during the procedure, with reduced discomfort. In Group 3 (pharyngeal spray with nalbuphine), 6 out of 50 patients reported post-procedural anxiety. The mean ages in Groups 1, 2, and 3 were 38.5 ± 2.25 , 41.25 ± 3.45 , and 45.5 ± 2.14 years, respectively.

Conclusion: This study sheds light on the feasibility and outcomes of non-sedated UGIEs using pharyngeal spray alone. While sedation can enhance procedural tolerance, it may also introduce risks and post-procedural effects. The findings suggest that UGIEs with pharyngeal spray alone may be well-tolerated, particularly for select patient populations. Further research on a larger scale is warranted to validate these findings and refine guidelines for sedation strategies in UGIEs.

Disclosure: Nothing to disclose.

PP0181

EFFICACY AND SAFETY OF SNARE TRACTION ASSISTED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR CIRCUMFERENTIAL SUPERFICIAL ESOPHAGEAL CANCER

S. Ullah¹, N. Dai¹, X. Cao¹

¹The First Affiliated Hospital of Zhengzhou University, Gastroenterology, Zhengzhou, China

Contact E-Mail Address: saifullah@gs.zzu.edu.cn

Introduction: Endoscopic submucosal dissection (ESD) has become a common treatment method for superficial esophageal cancer, allowing complete resection and accurate postoperative pathological evaluation, especially for relatively larger lesions^{1,2}. However, resection of larger lesions, especially circumferential lesions, can be time-consuming and challenging. The resected tissue can obstruct the esophageal lumen, leading to limited working space and poor visibility, thereby increasing the risk of adverse events such as perforation and muscular injury³. In recent years, several auxiliary traction techniques have been emerged, including positional adjustment traction, hemostatic clip elastic band traction, snare traction, line traction, and magnet anchor traction, which significantly improve the visibility of the submucosal layer during dissection and enhance the efficiency of the procedure^{4,5}. Among these techniques, snare traction allows bidirectional traction through “push and pull” maneuvers, offering flexibility and practicality in clinical practice. However, due to the difficulty and limited cases of circumferential esophageal ESD, there is currently no published literature demonstrating the advantages of snare traction-assisted ESD over traditional ESD techniques.

Aims & Methods: This study aims to investigate the efficacy and safety of snare traction assisted ESD for the management of circumferential superficial esophageal cancer. A total of 68 patients who underwent ESD for circumferential superficial esophageal cancer were included in this study. All the patients were divided into two groups based on whether the snare traction was used or not; the snare traction group (S-ESD, group n=35) and the control group (C-ESD, group n=33).

Results: There was no significant difference in the size of the resected area between the groups [21.98 (18.30, 27.00) cm² vs 24.00 (15.28, 30.72) cm², $P=0.976$]. The snare traction group had a shorter dissection time [92.00 (74.00, 121.00) min vs 110.00 (92.50, 137.00) min, $P=0.017$] and a faster resection speed [0.28 ± 0.13 cm²/min vs 0.22 ± 0.11 cm²/min, $P=0.040$] compared to the control group. There were no statistically significant differences between the two groups in terms of hospital stay, cost, en bloc

resection rate, R0 resection rate, curative resection rate, bleeding rate, perforation rate, stricture rate, and recurrence rate ($P>0.05$).

Conclusion: Snare traction-assisted ESD is a safe and efficient approach for the treatment of circumferential superficial esophageal cancer. Its advantages include shorter procedure so the anesthesia requirement, clear operative field view, improved mucosal dissection efficiency, simple, and easily accessible equipment.

References: 1 Ishihara R, Arima M, Iizuka T *et al.* Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. *Dig Endosc.* 2020; 32: 452-93.

2 Draganov PV, Wang AY, Othman MO, Fukami N. Aga institute clinical practice update: Endoscopic submucosal dissection in the united states. *Clin Gastroenterol Hepatol.* 2019; 17: 16-25.e1.

3 Zhang W, Zhai Y, Chai N *et al.* Endoscopic submucosal tunnel dissection and endoscopic submucosal dissection for large superficial esophageal squamous cell neoplasm: Efficacy and safety study to guide future practice. *Surg Endosc.* 2018; 32: 2814-21.

4 Fukami N. What we want for esd is a second hand! Traction method. *Gastrointest Endosc.* 2013; 78: 274-6.

5 Jin P, Yu Y, Fu KI, Yu DL, Li AQ, Sheng JQ. A new traction method with use of the snare as a “second hand” during endoscopic submucosal dissection. *Endoscopy* 2015; 47 Suppl 1 UCTN: E286-7.

Disclosure: Nothing to disclose.

PP0182

IS THE GASTRIC EMPTYING RATE PREDICTIVE FOR INTRAGASTRIC BALLOON TOLERABILITY?

Q. Shahed¹, M.C. Galavazi², H. Hesser³, J. Jendle⁴, M.A.v. Nieuwenhoven⁵

¹Örebro University, Department of Internal Medicine, Örebro,, Sweden, ²Örebro University, Department of Internal Medicine, Örebro, Sweden, ³Örebro University, School of Law, Psychology and Social Work, Örebro, Sweden, ⁴Örebro University, School of Medical Sciences, Faculty of Medicine and Health, Örebro, Sweden, ⁵Örebro University, Department of Internal Medicine, Division of Gastroenterology, Örebro, Sweden

Contact E-Mail Address: qays.shahed@regionorebrolan.se

Introduction: Obesity has reached pandemic proportions. According to the World Health Organization, 16% of the global adult population, or about 890 million people, have obesity(1). Intra-gastric balloon (IGB) is an alternative method to induce weight loss in subjects with obesity. However, not all subjects tolerate an IGB, and up to 15% of the cases, the IGB may be removed early due to intolerance(2). The factors that predict IGB tolerability remain poorly studied. In this study, we investigated whether there is an association between the baseline gastric emptying rate and IGB tolerability.

Aims & Methods: Twenty-eight subjects with a Body Mass Index (BMI) over 27.5 kg/m² were included. Orbera 365® IGBs were endoscopically inserted and filled with 550 ml saline solution and scheduled for removal after 12-months. Before insertion, the subjects underwent a standardized, FDA-approved 13C-Spirulina breath test to measure their gastric emptying half-time (T1/2). Gastrointestinal symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS) at baseline and at 4, 8, 16, and 24 weeks post-insertion, even after eventual early IGB removal.

Results: Six subjects had their IGBs removed earlier than planned due to tolerance issues, which we define as early removal. Early removal in our study refers to any removal that occurred before the planned 12-months. The specific timepoints of removal varied: one at four weeks, two at six months, one at eight months, and two at eleven months.

In the group that had their IGB removed earlier, the median baseline GSRS score was 28 (range 23-41), with a median T1/2 of 81.4 min (range 38.4-140.1). The median GSRS score at 4 weeks was 55.5 (range: 42-72), at 8 weeks 45 (range: 19-82), at 16 weeks 45.5 (range: 19-31), and at 24 weeks 37 (range 22-61).

In the group that tolerated the IGB, the median baseline GSRS score was 28 (range 19-77), with a median T1/2 of 61 min (range 34.5-108.4). The median GSRS score at 4 weeks was 53 (range: 24-133); at 8 weeks 37.5 (range: 19-79); at 16 weeks 37 (range: 21-85), and at 24 weeks 37 (range 19-104), respectively.

No statistically significant differences were observed in half-times (T1/2) and GSRS scores between the two groups at the examined time points. The p-value for T1/2 was 0.09. For GSRS, p-values were as follows: 0.89 at baseline, 0.63 at 4 weeks, 0.87 at 8 weeks, 0.45 at 16 weeks, and 0.73 at 24 weeks. Additionally, correlation analysis between GSRS scores and T1/2 values showed no significant relationships at baseline ($p = 0.50$), 4 weeks ($p = 0.89$), 8 weeks ($p = 0.93$), 16 weeks ($p = 0.983$), and 24 weeks ($p = 0.86$). These results suggest a consistent lack of significant association across all time points.

Conclusion: Early IGB removal cannot be predicted by the baseline gastric emptying rate or baseline GSRS in our study. The GSRS scores for subjects that tolerated the IGB, regardless of the time point, do not correlate with their baseline gastric emptying rate.

References:

1. World Health Organization. (2022). Obesity and overweight. Retrieved from <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>
2. Jamal MH, Al-Kanawati N, ElAbd R, et al. A Study Examining the Orbera365 Intragastric Balloon Safety and Effects on Weight Loss. *Obesity Surgery* 2021; 31(12); 5342-5347. <https://doi.org/10.1007/s11695-021-05729-8>

Disclosure: Nothing to disclose.

PP0183

LONG-TERM (MINIMUM 1 YEAR) OUTCOMES AFTER GASTRIC PERORAL ENDOSCOPIC MYOTOMY FOR REFRACTORY GASTROPARESIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

F.V. Mandarino¹, A. Barchi¹, F. Azzolini¹, N. Salmeri², E. Fasulo¹, E. Vespa¹, E. Sinagra³, G. Dell'Anna¹, J. Jacques⁴, S. Danese¹

¹San Raffaele Hospital, Gastroenterology and Gastrointestinal Endoscopy, Milan, Italy, ²San Raffaele Hospital, Gynecology/Obstetrics Unit, Milan, Italy, ³HSR Giglio, Endoscopy and Gastroenterology Unit, Cefalù, Italy, ⁴CHU Limoges - Hepato-Gastro-Enterology, CHU Limoges; Limoges/FR, Hepato-Gastro-Enterology, Limoges, France

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: Although Gastric Peroral Endoscopic Myotomy (G-POEM) has shown substantial efficacy in patients with medically refractory gastroparesis (GP), comprehensive long-term data on its effectiveness are lacking.

Aims & Methods: We conducted a systematic review and meta-analysis including observational studies assessing long-term outcomes after G-POEM in patients with refractory GP. Our primary outcome was the pooled rate of clinical success 1-year after G-POEM. Secondary outcomes included clinical success rates beyond 1 year, and the rate of adverse events (AEs).

Results: Fifteen studies, comprising 986 patients with refractory GP undergoing G-POEM, were eligible. The pooled 1 year-success rate was 0.722 (95% CI: 0.56, 0.86, $I^2=94.92\%$). In the subgroup analysis, which included only studies enrolling patients with 4-hour Postprandial Gastric

Residual (PGR) $\geq 10\%$, the clinical success rate was 0.610 (95% CI: 0.526, 0.709, $I^2=46.66\%$). The pooled success rates at 2 and 3 years calculated on followed-up patients were 0.861 (95% CI: 0.72, 0.96, $I^2=85.11\%$) and 0.838 (95% CI: 0.56, 0.99, $I^2=91.90\%$), respectively. In the subgroup analysis including studies that did not exclude non-responding patients from follow-up, the 2-year pooled success rate was 0.838 (95% CI: 0.60, 0.98, $I^2=89.49\%$). The pooled rate of AEs was 0.092 (95% CI: 0.06, 0.13, $I^2=81.35\%$), specifically 0.078 mild and 0.014 moderate AEs, according to the American Society for Gastrointestinal Endoscopy classification.

Conclusion: G-POEM is a safe procedure with 1-year success in more than 2/3 of treated cases and substantial benefit also at 2 and 3-years follow-ups. Future studies with strict patient selection and uniform outcome definitions are warranted.

Disclosure: Nothing to disclose.

PP0184

A SUB-EPITHELIAL LESION ALGORITHM FOR ENDOSCOPIC (SAFE) RESECTION IN THE UPPER GASTROINTESTINAL TRACT

S. Gupta^{1,2}, J. Gauci¹, T. O'Sullivan^{1,2}, O. Cronin^{2,1}, A. Whitfield^{1,2}, A. Craciun¹, H. Awadie¹, J. Yang¹, F.V. Mandarino¹, V. Kwan¹, E. Lee¹, N.G. Burgess^{1,2}, M.J. Bourke^{1,2}

¹Westmead Hospital, Gastroenterology & Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia

Contact E-Mail Address: julia.gauci@yahoo.co.uk

Introduction: Complete excision of upper gastrointestinal sub-epithelial lesions (SELs) eliminates diagnostic uncertainty, obviates the need for surveillance and may be necessary for definitive diagnosis and management. Current guidelines lack precision and cohesion, and surgery is associated with significant morbidity. Herein, we describe and report on the outcomes of our SEL algorithm for endoscopic (SAFE) resection.

Aims & Methods: SELs were enrolled prospectively over 115 months until March 2023. All underwent axial (CT) imaging and endoscopic-ultrasonography (EUS) to exclude a large exophytic component or invasion into local structures, and assess for muscularis propria involvement.

Results: 106 SELs were resected (mean age 60.6 $\pm$ 13.4, 51.9% male; 41 oesophageal, 65 gastric). Oesophageal SELs underwent ESD (n=22) or STER if MP involvement was suspected (n=19). Gastric SELs underwent STER (n=6 at cardia), ESD (n=47) or exposing-EFTR (n=12). Technical success was 97.6% and 92.3% respectively. Five (7.7%) were completed laparoscopically due to deep and broad full-thickness involvement. Five (7.7%) required laparoscopic gastrotomy and surgical retrieval after successful resection and closure due to a large lesion size (mean 47 mm). There was no delayed bleeding, perforation or recurrence at a median of 13 months.

Conclusion: Upper GI SELs are effectively and safely treated by endoscopic resection. The SAFE approach provides a framework that facilitates structured decision-making. Oesophageal SELs suspected to involve the MP should undergo STER. Gastric SELs can be best managed by ESD with a view to proceed to exposing-EFTR. A laparoscopic UGI surgeon should be available in case surgical retrieval of the specimen or laparoscopic completion is required.

Disclosure: Michael J. Bourke: Research Support: Olympus, Cook Medical, Boston Scientific.

PP0185

SUBTYPES OF GASTRIC ADENOMAS: PREVALENCE, RISK FACTORS AND OUTCOMES OF ENDOSCOPIC MANAGEMENT

N. El-Domiaty^{1,2}, F. Beuvon^{3,4}, M. Carpentier-Pourquier¹, W. Ibrahim⁵, S. Oumrani¹, P. Doumbe-Mandengue^{1,4}, J. Leroux^{1,4}, F. Corre^{1,4}, A. Belle¹, C. Stanislas^{1,4}, R. Coriat^{1,4}, A. Pellat^{1,4}, M. Barret^{4,1}

¹Cochin Hospital, Assistance Publique - Hôpitaux de Paris, Department of Gastroenterology and Digestive Oncology, Paris, France, ²Faculty of Medicine, Helwan University, Endemic Medicine Department, Cairo, Egypt, ³Cochin Hospital, Assistance Publique - Hôpitaux de Paris, Department of Pathology, Paris, France, ⁴Université de Paris, Paris, France, ⁵Cairo University, Faculty of Economics and Political Science, Statistics Department, Cairo, Egypt

Contact E-Mail Address: nadadomty@hotmail.com

Introduction: Gastric adenoma is recognized as a premalignant lesion.¹ Much of the literature lumps all adenomas together with different classifications. These are few western reports regarding the prevalence, associated risk factors and outcomes of endoscopic management of different subtypes of gastric adenoma.

Aims & Methods: Aims: The aim of this study is to determine the prevalence, potential predictors, and outcomes of endoscopic management of the different subtypes of gastric adenoma.

Methods: Of 162 consecutive patients who underwent endoscopic resection for gastric lesions between 2017 and 2022 at our center, 79 patients were enrolled. All the hyperplastic polyps (n=37) and subepithelial lesions (n=46) were excluded. The patient clinical characteristics, endoscopic and histopathological features of gastric lesions were retrospectively collected. Patients were divided according to the histological types of gastric adenoma into 4 groups: intestinal group (n= 49), foveolar group (n= 23), pyloric group (n= 6) and oxyntic group (n=1). We statistically compared the clinical and endoscopic features of the three groups. In addition to the analysis of the outcomes of endoscopic resection of gastric adenomas.

Results: Of the 79 patients with a mean follow-up of 26 ± 22 months, 51 patients were males (65 %) and 28 patients were females (35%). Forty-nine patients (49/79, 62%) had intestinal adenoma, 23 patients (29%) showed foveolar adenoma, 6 patients (8%) developed pyloric adenoma and only 1 patient (1%) had oxyntic adenoma. The mean age was significantly older in the intestinal group (71 ± 13 years vs. 64 ± 16 years vs. 58 ± 18 years, p = 0.03). Intestinal adenomas were significantly associated with family history of gastric adenocarcinoma (14% vs. 4% vs. 0%, p = 0.01) and history of statin intake (39% vs. 26% vs. 0%, p = 0.04). Foveolar adenomas were significantly associated with multiple lesions (≥3 lesions) (p < 0.001) and 0-IIa+IIc Paris classification (6/23, 26%). The size of largest polyp was significantly higher among pyloric group (28 ± 15, p = 0.00). Among intestinal group, 33/49 patients (67%) had atrophic gastritis. 82% of the adenomas were resected by ESD with histologically complete resection (R0) in 72/79 patients (91%). Although the difference was not statistically significant (p = 0.4), adenocarcinoma was most frequently encountered among the intestinal adenoma group (17/49, 35%). The post endoscopic resection outcome was comparable among 3 groups with overall recurrence rate (group 1: 8% vs. group 2: 17% vs group 3: 17%, P = 0.07) with a comparable mean time to recurrence among three groups (21 ± 17 months vs. 20 ± 17 months vs. 14 months, p = 0.8). Family history of gastric adenocarcinoma (HR=1.33, p < 0.001) and active helicobacter pylori infection (HR=1.14, p < 0.001) were identified as independent predictors of recurrence after endoscopic resection of different gastric adenoma. Among baseline endoscopic characteristics, polyp size ≥ 30mm (HR= 2.04, p < 0.001), more than 3 polyps (HR=1.51, p < 0.001), lesser curvature as lesion

location (HR=1.72, p < 0.001) and morphology as Paris classification IIc are potential predictors of post resection recurrence. In addition to specimen size ≥ 15mm (HR=2.19, p < 0.001) and T1b as lesion histology (HR=2.07, p < 0.001), in the histopathological examination.

Conclusion: The present study clarifies the endoscopic and histopathological characteristics of different gastric adenomas, in addition to the potential predictive factors for each subtype. Potential predictors of recurrence after endoscopic resection emphasize the importance of endoscopic follow up.

References: 1. Fujiwara, Y. *et al.* Diagnosis of borderline adenomas of the stomach by endoscopic mucosal resection. *Endoscopy* 28, 425–430 (1996).

Disclosure: Nothing to disclose.

PP0186

ENDOSCOPIC VACUUM THERAPY FOR THE MANAGEMENT OF GASTRO-ESOPHAGEAL PERFORATIONS

R. Valente¹, T. Irino¹, U. Arnelo¹

¹Umeå University, Department of Diagnostics and Intervention, Umeå, Sweden

Contact E-Mail Address: roberto.valente@umu.se

Introduction: Esophageal or gastric perforation is associated with systemic inflammatory response syndrome (SIRS), which can lead to multi-organ dysfunction and mortality in up to 50% of cases. Endoscopic vacuum therapy involves the use of a catheter with a sponge attached to its distal end, connected to a machine that applies negative pressure, allowing for continuous drainage of the perforation site and potentially promoting healing of the transmural defect. Previous series have reported promising results, indicating the potential effectiveness of this therapy in managing esophageal perforations. To evaluate the efficacy of endoscopic vacuum treatment in patients with primary or secondary gastroesophageal perforations.

Aims & Methods: Single-center retrospective cohort study on patients treated for gastroesophageal perforation between March 2019 and September 2022. The inclusion criteria for the study were patients with gastroesophageal perforation resulting from spontaneous rupture or iatrogenic damage (post-surgical or post-endoscopic treatment). The primary outcomes of the study were the success rate of endoscopic therapy, the length of hospital stay, and the specific survival at 30 and 90 days. The success rate of endoscopic therapy was assessed by considering the treatment successful if it led to the resolution of the fistula following vacuum endoscopic therapy. Secondary endpoints included the need for intensive care unit (ICU) stay between the start of vacuum endoscopic therapy and the patient's discharge.

Results: 27 patients, with a mean age of 69.8 years (95% CI 65.4-74.3), including 9 (33.3%) women, underwent endoscopic treatment with vacuum therapy for esophageal perforation. The causes of perforation were as follows: 6 (22.2%) cases were primary (Boerhaave syndrome), 15 (55.5%) cases were post-surgical (post-surgical anastomosis), and 6 (22.2%) cases were post-endoscopic treatment (endoscopic dilatation). Among the patients, 13 (48.1%) had previously undergone surgery for cancer, with 69.2% of them receiving intrathoracic stomach interposition reconstruction and the remaining patients undergoing reconstruction according to Roux-en-Y procedure. The treatment was successful in 21 (77.7%) patients, with a 14 days (9.0-24.4, 95% CI) median duration of treatment, and 4 (3-7, 95% CI) median number of endoscopic devices used per patient. One patient (3.7%) died within 30 days, and another one (3.7%) within 90 days. A total of 10 (38.4%) patients required an ICU stay, and there were no readmissions within 30 days. No procedure-related complication was reported.

Conclusion: In the current pilot study, the findings support the feasibility and safety of endoscopic vacuum therapy as a treatment modality for both primary and secondary gastro-esophageal perforations.

References:

- Kuehn F, Schiffmann L, Rau BM, Klar E. Surgical endoscopic vacuum therapy for anastomotic leakage and perforation of the upper gastrointestinal tract. *J Gastrointest Surg* 2012
- Pattynama LMD, Eshuis WJ, van Berge Henegouwen MI, Bergman J, Pouw RE. Vacuum-stent: A combination of endoscopic vacuum therapy and an intraluminal stent for treatment of esophageal transmural defects. *Front Surg* 2023
- Luttikhoud J, Pattynama LMD, Seewald S, et al. Endoscopic vacuum therapy for esophageal perforation: a multicenter retrospective cohort study. *Endoscopy* 2023
- Disclosure:** Dr Valente and Dr Arnelo are consultant to Boston Scientific. Dr Arnelo is Consultant to Ambu.

PP0187

ENDOSCOPIC ARGON PLASMA COAGULATION ABLATION SIGNIFICANTLY IMPROVES LARYNGOPHARYNGEAL SYMPTOMS IN SYMPTOMATIC CERVICAL INLET PATCHES PATIENTS: A PILOT STUDY IN THE ASIA-PACIFIC REGION

YY. Chuah¹, D.-E. Toh², YY. Lee³, P.-H. Tseng⁴, C.-K. Chou⁵

¹Ping Tung Christian Hospital, Department of Gastroenterology and Hepatology, Ping Tung, Taiwan, ²Flinders Medical Centre, Department of Gastroenterology, Adelaide, Australia, ³Universiti Sains Malaysia, Department of Gastroenterology and Hepatology, Kelantan, Malaysia, ⁴National Taiwan University Hospital, Department of Gastroenterology and Hepatology, Taipei, Taiwan, ⁵Ditmans Medical Foundation Chia-Yi Christian Hospital, Division of Gastroenterology and Hepatology, Department of Internal Medicine,, Chia-Yi, Taiwan

Contact E-Mail Address: yoenyoungchuah@gmail.com

Introduction: The cervical inlet patch (CIP) is an islet of heterotopic gastric mucosa that is observed in the upper esophagus during conventional diagnostic esophagogastroduodenoscopy. Commonly encountered laryngopharyngeal symptoms, including globus sensation, hoarseness, odynophagia, and dysphagia, have been linked to CIP. In most cases, medical intervention for symptomatic CIP commences with the administration of potent acid suppressive agents, such as proton-pump inhibitors (PPI); however, the efficacy of these agents is limited. A few Western studies have demonstrated that endoscopic therapy with argon plasma coagulation (APC) is increasingly effective in relieving laryngopharyngeal symptoms in patients with CIP.^{1,2} Additionally, long-term effects lasting up to 27 months of follow-up have been documented.³ Regarding the use of APC in patients with CIP, however, no pertinent research has been conducted in Asia-Pacific countries. Therefore, we retrospectively reviewed a cohort with six symptomatic CIP patients recruited for the APC ablation therapy. This case shed light on the possible use of APC for symptomatic CIP patients in Asia-Pacific countries.

Aims & Methods: We recruited a total of six symptomatic patients, proven to be CIP endoscopically and pathologically, from May 22, 2022, to April 20, 2024. We excluded patients who were less than 20 years old and who refused the option of argon plasma coagulation ablation. To ablate the CIP, all recruited patients underwent endoscopic ablation at 60 W and 2 L/min in one session. Questionnaires consisting of visual analog scores (from 0 to 10. The higher the score, the more severe the symptoms) for symptoms of dry throat, burning throat, globus sensation, hoarseness and clearing throat were distributed to patients at the time points of be-

fore the use of proton pump inhibitors, after the use of proton pump inhibitors and one month after the endoscopic ablation with APC to assess the efficacy endoscopic procedure. We defined symptomatic CIP with at least one any of the aforementioned symptoms with more than 5 out of 10 of pain score.

Results: The current study recruited a total of six patients. Two-thirds of patients were female (4/6) in gender and had an average age of 41 years. The CIP was located in the upper esophagus at 16.7cm from the incisors (15–18 cm), and two-thirds of the patients had more than one CIP. The average size of CIP was about 0.6 cm (ranging from 0.3cm to 0.8cm). The APC ablation significantly improved the five parameters (dry throat, burning sensation, foreign body sensation, and hoarseness) from more than 4/10 to less than 2/10. Foreign body sensation showed the most prominent improvement, decreasing from 7/10 to 1/10. (Figure1) There were no complications, such as perforation, infection, ulcers, or stricture, after the procedure. One month after the APC procedure, the follow-up EGD of all patients showed no residual CIP.

Conclusion: APC ablation shows a promising results for symptomatic CIP patients with laryngopharyngeal symptoms in Asia-Pacific population. However, further prospective randomized studies with a larger sample size are needed to validate the effectiveness and safety of APC ablation in symptomatic CIP patients in the region.

References: 1. Bajbouj M, Becker V, Eckel F, et al. Argon plasma coagulation of cervical heterotopic gastric mucosa as an alternative treatment for globus sensations.

Gastroenterology. 2009 Aug;137(2):440-4.

2. Brechmann T, Muhlenkamp M, Schmiegel W, et al. Argon Plasma Coagulation of Gastric Inlet Patches of the Cervical Esophagus Relieves Vocal and Respiratory Symptoms in Selected Patients. *Dig Dis Sci* 2023; 68: 1936-1943.

3. Klare P, Meining A, von Delius S, et al. Argon plasma coagulation of gastric inlet patches for the treatment of globus sensation: it is an effective therapy in the long term. *Digestion*. 2013;88(3):165-71.

Disclosure: There is no conflict of interest among authors.

PP0188

WITHDRAWN

PP0189

DEPTH ESTIMATION ALGORITHM-BASED LESION SIZE MEASUREMENT IN GASTROSCOPY: A COMPARATIVE STUDY WITH ENDOSCOPISTS

B. Kim¹, H. Chung², J.K. Ryu²

¹Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, South Korea, ²Seoul National University Hospital, Seoul, South Korea

Contact E-Mail Address: bkkim1119@gmail.com

Introduction: Precise measurement of lesion sizes during endoscopic procedures is crucial but often compromised by the reliance on visual estimations.

Aims & Methods: This study evaluates the precision of a novel depth estimation algorithm-based lesion size measurement function embedded in an electrically controlled endoscopy system, comparing its accuracy to visual and forceps-assisted estimations. A synthetic 3D-printed stomach model featuring 15 artificial lesions (6 ulcers and 9 polyps, size range: 6-39 mm) was used. Nineteen endoscopists (6 experts, 13 novices) measured the lesions using three methods: 1) visual estimation (VE) with a conventional endoscope, 2) forceps-assisted estimation (FE) with a conventional endoscope, and 3) depth estimation algorithm (DEA) with an electrically

controlled endoscope. Measurements were then compared to the actual lesion sizes according to endoscopic proficiency and lesion size (<1 cm, 1-2 cm, >2 cm).

Results: VE had the highest mean percentage error (MPE) at 39.97% (95% CI 36.66%-43.28%), followed by FE (MPE 31.39%, 95% CI 28.81%-33.98%). DEA was most accurate with an MPE of 13.59% (95% CI 11.46%-15.73%), significantly outperforming both VE and FE (all $P < 0.01$). For VE and FE, experts showed greater precision over novices (all $P < 0.01$). With DAE, the accuracy was consistent across experience levels ($P = 0.60$). Novices using DEA showed greater precision compared to both VE and FE (Table 1). Novices using VE had the least accuracy with an MPE of 43.93% (95% CI 39.67% - 48.19%). For experts, DEA was accurate than VE but was comparable to FE except in lesions over 2cm.

	VE (MPE ± 95% CI)	FE (MPE ± 95% CI)	DEA (MPE ± 95% CI)	VE vs FE (P value)	VE vs DEA (P value)	FE vs DEA (P value)
Total	39.97% (36.66% - 43.28%)	31.39% (28.81% - 33.98%)	13.59% (11.46% - 15.73%)	<0.01	<0.01	<0.01
All size	43.93% (39.67% - 48.19%)	37.67% (34.51% - 40.82%)	13.56% (10.77% - 16.35%)	0.01	<0.01	<0.01
Novice (N=13)						
<1 cm	43.49% (34.90% - 52.09%)	35.09% (28.96% - 41.22%)	19.58% (14.27% - 24.90%)	0.08	<0.01	<0.01
1-2 cm	44.24% (38.50% - 49.99%)	37.82% (33.77% - 41.86%)	12.79% (8.88% - 16.70%)	0.04	<0.01	<0.01
>2 cm	43.37% (33.94% - 52.79%)	42.16% (32.42% - 51.89%)	4.95% (3.49% - 6.42%)	0.7	<0.01	<0.01
All size	31.40% (26.77% - 36.02%)	17.80% (14.80% - 20.79%)	13.67% (10.57% - 16.78%)	<0.01	<0.01	0.09
Expert (N=6)						
<1 cm	33.15% (23.59% - 42.71%)	18.66% (13.89% - 23.43%)	20.80% (14.75% - 26.84%)	0.01	0.04	0.61
1-2 cm	31.21% (25.05% - 37.37%)	17.13% (12.77% - 21.49%)	11.64% (7.41% - 15.87%)	<0.01	<0.01	0.11
>2 cm	28.74% (15.89% - 41.60%)	19.07% (11.13% - 27.01%)	8.58% (5.22% - 11.95%)	0.02	0.01	0.03

Conclusion: The novel lesion size measurement function using a depth estimation algorithm outperforms traditional visual and forceps-assisted method, especially in novice. Its adoption in endoscopic practice and training could improve lesion sizing accuracy, enhancing clinical outcomes and decision-making.

Disclosure: Nothing to disclose.

PP0190

ENDOSCOPY IN THE SETTING OF INCIDENTAL HYPERMETABOLIC LESION ON PET SCAN

B. Soukaina¹, A. Moualif¹, F. Haddad¹, F.Z. Elrhaoussi¹, M. Tahiri Joutei Hassani¹, W. Hliwa¹, B. Ahmed¹, W. Badre¹
¹Hospital University Center IBN ROCHD, Gastroenterology, Casablanca, Morocco

Contact E-Mail Address: bannanisoukaina@gmail.com

Introduction: Positron emission tomography (PET) scan involves injecting a radioactive isotope (18-fluoro-2-deoxyglucose) to locate areas where the radiotracer accumulates. The established indications of PET scanning mainly concern oncology, where it is used for staging, treatment monitoring, and long-term surveillance. It is also useful in cases of secondary lesions for identifying the primary lesion. Outside of oncology, PET scan has

other clinical applications such as diagnosing and monitoring inflammatory diseases, and searching for infectious foci. The incidental discovery of metabolic hyperfixation in the digestive system on PET scan is becoming increasingly common, raising questions about the clinical significance of this hypermetabolism and the need for endoscopic exploration. The aim of our study is to report the endoscopic findings from examinations performed in our department where the indication was the incidental discovery of digestive hypermetabolism on PET scan.

Aims & Methods: This is a descriptive and analytical retrospective monocentric study including all patients referred for endoscopy due to the incidental discovery of digestive metabolic hyperfixation on PET scan, not corresponding to a previously known lesion, between January 2017 and September 2023. Only hypermetabolic fixations located in the stomach, colon, and rectum were included.

Results: 28 hypermetabolic fixations were included in the study, of which 46.4% were located in the colon, 42.9% in the rectum, and 10.7% in the stomach. The mean age was 54.9 years with a standard deviation [32,78]. The male-to-female sex ratio was 0.6. PET scan indications were mainly dominated by surveillance of treated cancers or during treatment (57.1%). In 21.4% of cases, PET scan was requested for staging a newly diagnosed tumor, and in 17.9% of patients, it was used to search for a primary tumor with hepatic, pulmonary, or bone metastases. Other indications were rarer, representing 3.6% of cases. Hypermetabolism on PET scan corresponded to a neoplastic lesion in 17.9% of cases, an adenoma in 14.3% of cases, and a benign lesion (non-specific ulceration, inflammatory lesion, or stenosis) in 32.2% of cases. In 35.7% of patients, endoscopic examination did not reveal detectable abnormalities. Hypermetabolism was most often focal (67.9%). According to this study, the presence of focal metabolic hyperfixation was significantly associated with the presence of a neoplastic lesion on digestive endoscopy ($P < 0.01$).

Conclusion: All metabolic hyperfixations on PET scan referred to our endoscopy center underwent endoscopic exploration to rule out a neoplastic lesion. However, additional studies, ideally prospective and multicentric with a larger sample size, are essential to establish the criteria for endoscopic exploration in the case of incidental discovery of digestive hypermetabolism on PET Scan

References: 1.Kousgaard SJ, Thorlacius-Ussing O. Incidental colorectal FDG uptake on PET/CT scan and lesions observed during subsequent colonoscopy: a systematic review. *Tech Coloproctol.* juill 2017;21(7):521-9.
2.van Hoeij FB, Keijzers RGM, Loffeld BC a. J, Dun G, Stadhouders PHGM, Weusten BL a. M. Incidental colonic focal FDG uptake on PET/CT: can the maximum standardized uptake value (SUVmax) guide us in the timing of colonoscopy? *Eur J Nucl Med Mol Imaging.* janv 2015;42(1):66-71.
3.Peng J, He Y, Xu J, Sheng J, Cai S, Zhang Z. Detection of incidental colorectal tumours with 18F-labelled 2-fluoro-2-deoxyglucose positron emission tomography/computed tomography scans: results of a prospective study. *Colorectal Dis.* nov 2011;13(11):e374-378.

Disclosure: Nothing to disclose.

PP0191

ENDOSCOPIC MANAGEMENT OF UPPER DYSPHAGIA OF UNKNOWN ETIOLOGY – A SINGLE CENTER PILOT EXPERIENCE

D. Simkova¹, J. Mareš², M. Vašátko¹, K. Hugova¹, J. Martinek¹

¹Institute for Clinical and Experimental Medicine (IKEM),

Department of Hepatogastroenterology, Prague, Czech Republic,

²Institute for Clinical and Experimental Medicine (IKEM),

Department of Statistical Analyses, Prague, Czech Republic

Contact E-Mail Address: drazilovad@gmail.com

Introduction: Upper dysphagia is a swallowing disorder associated with underlying pathology in the mouth, throat, or esophagus. Cricopharyngeal achalasia (CA) may cause upper dysphagia and its diagnosis is not well established. In case of CA, endoscopic myotomy of upper esophageal sphincter (C-POEM) may be offered to relieve symptoms.

Aims & Methods: We present our experience in diagnosing and managing upper dysphagia with suspicion on CA in patients referred to our center between May 2022 and April 2024. The patients with Zenker diverticulum or organic stricture were not enrolled. All patients underwent X-ray examination, high-resolution manometry and endoscopy. In patients with suspected CA, botulinum toxin injection (100 IU) was administered into the upper esophageal sphincter.

After botulinum toxin injection, the follow up visits were scheduled 1, 5 and 12 months after the procedure. In case of a positive effect of the injection, C-POEM (endoscopic myotomy of cricopharyngeal muscle) was considered after the effect of botulinum toxin had waned. FOSS Function Outcome Swallowing Score and Dakkak and Bennett score of dysphagia were used to assess the severity of the symptoms. The score systems are listed in the table.

Dakkak and Bennett score of dysphagia		FOSS Function Outcome Swallowing Score	
Grade	Characteristic	Grade	Characteristic
Grade 0	No dysphagia	Grade 0	Asymptomatic
Grade 1	Solids	Grade 1	Episodic or daily symptoms of dysphagia with normal meal time
Grade 2	Semi-solids	Grade 2	Dysphagia requiring significant dietary modifications or prolonged meal time
Grade 3	Liquids	Grade 3	Dysphagia with weight loss ≤10% of body weight with daily symptoms
Grade 4	Aphagia	Grade 4	Dysphagia with weight loss >10% of body weight or severe aspiration or requiring intermittent non-oral feeding for nutrition
		Grade 5	Non-oral feeding for all nutrition

Results: Ten patients (4 males, 6 female) were referred to our center with long term upper esophageal dysphagia and considered eligible for botulinum toxin injection. The mean age was 69.7 years (ranges 30, 85), mean duration of symptoms was 8.6 years (SD ± 11). Three patients were unable to swallow safely and PEG tube had to be placed for nutritional support. Aetiologies of dysphagia were cervical injury (n=2), radiotherapy (n=2) and previous neurosurgery (n=1) or idiopathic dysphagia.

All patients underwent botulinum toxin injection. One patient developed vocal cord paresis one week after the injection and her condition improved after corticoid administration. No other adverse events of botulinum toxin were observed.

Improvement of dysphagia occurred in 7 patients after botulinum toxin injection while no change in symptoms was present in 3 patients. One month after the procedure mean

FOSS Function Outcome Swallowing Score improved from 3.3 to 1.56 (p = 0.015) and Dakkak and Bennett score of dysphagia from 2.7 to 1.33 (p=0.012). Two patients received successful C-POEM, the remaining patients will be offered C-POEM once a recurrence of symptoms will occur.

Three patients without effect of botulinum toxin injection were considered endoscopically incurable and referred back to neurology or otorhinolaryngology departments.

Conclusion: Botulinum toxin injection may be effective in treating upper dysphagia caused by a spasm of cricopharyngeal muscle and may serve as a useful selection tool for endoscopic myotomy.

Disclosure: Nothing to disclose.

PP0192

IDENTIFICATION OF LIPIDOMICS AND PROTEOMIC SIGNATURES WHICH CORRELATE WITH RAMAN SPECTRA TO DIFFERENTIATE DYSPLASIA FROM NORMAL GASTRIC TISSUE

S. Quek¹, G. Kim², D.K.A. Chia², H. Chung³, G. Soon⁴, J.H.Y. Lum⁴, B.Y.J. So^{2,5}, A. Shabbir^{2,5}, L.K.Y. Ho^{1,5}, J. Lee^{1,5,6}

¹National University Hospital, Division of Gastroenterology and Hepatology, Singapore, Singapore, ²National University Hospital, Department of Surgery, Singapore, Singapore, ³Seoul National University, Seoul, South Korea, ⁴National University Hospital, Department of Pathology, Singapore, Singapore, ⁵National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore, ⁶National University of Singapore, iHealthtech, Singapore, Singapore

Contact E-Mail Address: jonathanlee@nus.edu.sg

Introduction: Early gastric cancer (GC) detection allows for early intervention and better patient outcomes. Yet, current diagnostic methods for early GC still need to be improved. Raman microscopy offers a noninvasive, label-free approach for a wide range of ex vivo (e.g. intraoperative tumour margin detection) and in vivo (e.g. early GC diagnosis) clinical applications. However, the specificity of Raman microscopy is limited by the high signal-to-noise ratio due to light scattering and the inherent molecular complexity of human tissues.

Aims & Methods: Aim: This study aims to identify lipidomic and proteomic tissue signatures that correlate with Raman microscopy, thereby shortlisting a more specific Raman spectrum to better differentiate GC from normal gastric tissue.

Methods: Real-time Raman spectrometry-based AI was applied to 19 consecutive patients (aged 51 - 85 years old, 14 male) with high risk for gastric dysplasia or cancer. Patients underwent high-definition white light upper endoscopy. Upon localisation of the lesion/s, the endoscopist used the SPECTRA IMDx™ probe to capture the Raman spectra (1251 features) from the dysplastic lesion and its adjacent normal mucosa. Biopsies paired to the sites of Raman readings were obtained for histopathologic examination, and lipidomic and proteomic profiling. 254 lipids (from 15 subclasses) and 4168 proteins were obtained through mass-spectrometry-based techniques. Differential abundance analysis of the lipid, protein and Raman spectra was undertaken using DESeq2 [1], which uses shrinkage estimation for dispersions and fold change to improve the stability and interpretability of estimates.

Results: Using 25 tissue samples (12 control, 13 with gastric dysplasia or cancer), we identified specific lipid species and protein markers as potential biomarkers (FDR <0.05) for GC; 45 lipid species (13 cholesterol esters, nine phosphatidylethanolamines, five diacylglycerols, five lysophosphatidylethanolamines, four hex ceramides, four phosphatidylcholines, two lysophosphatidylcholines and one sphingomyelin, one ganglioside) as well as ten proteins (PLOD2, GGPS1, C8G, COX7C, DCK, ACTBL2, EMC10, H2AC21, HDHD2). Integrating the putative lipid and protein features and the Raman spectra, only a shortlist of 56 Raman features were significantly correlated with only ten lipids (3 HexCeramides, three cholesterol esters, two diacylglycerols, one phosphatidylethanolamine and one lysophosphatidylethanolamine) and two protein features (C8G, ACTBL2).

Conclusion: Our findings demonstrate the potential of integrating Raman microscopy with lipidomics and proteomics. The potential lipid and protein signatures provide insight into the biochemical alterations associated with dysplastic transformation identified by Raman microscopy. This approach brings promise for improving the accuracy of Raman-based non-invasive GC early detection strategies.

References: 1. Love, M.I., Huber, W. & Anders, S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biol* 15, 550 (2014). <https://doi.org/10.1186/s13059-014-0550-8>

Disclosure: Prof Lawrence Ho Khek Yu is the Co-founder and Chief Medical Officer of Endofotonics (SPECTRA IMDx™).

PP0193

BLUE LIGHT IMAGING IS BETTER THAN LINKED COLOR IMAGING IN THE DETECTION OF GASTRIC INTESTINAL METAPLASIA

A. Schmal¹, C.N. Ferreira^{1,2}, F. Capinha¹, F. Faustino¹, F. Rodrigues³, A.T. Carvalho³, H. Siffert Pereira de Souza⁴, L. Carrilho-Ribeiro¹, L. Correia¹
¹Centro Hospitalar Universitário Lisboa Norte/ Hospital de Santa Maria, Serviço de Gastrenterologia e Hepatologia Hospital de Santa Maria, Lisbon, Portugal, ²Universidade de Lisboa/ Faculdade de Medicina de Lisboa., Clínica Universitária de Gastrenterologia, Lisbon, Portugal, ³Universidade Estadual do Rio de Janeiro/ Hospital Universitário Pedro Ernesto, Departamento de Gastroenterologia e Endoscopia Digestiva do Hospital Universitário Pedro Ernesto, Rio de Janeiro, Brazil, ⁴Universidade Federal do Rio de Janeiro/ Hospital Universitário Clementino Fraga Filho, Departamento de Gastroenterologia do Hospital Clementino Fraga Filho, Rio de Janeiro, Brazil

Contact E-Mail Address: aliceschmal@gmail.com

Introduction: Data evaluating the utility of Blue light Imaging (BLI) and Linked Color Imaging (LCI) in the diagnosis of gastric intestinal metaplasia (IM) and atrophic gastritis (AG) is limited.

Aims & Methods: We aimed to evaluate and compare the diagnostic accuracy of BLI and LCI without magnification for the detection of IM and AG. Single centre prospective study involving consecutive patients aged ≥18 years undergoing diagnostic upper gastrointestinal endoscopy (UGIE), endoscopic follow-up of intestinal metaplasia or gastric cancer screening. Exclusion criteria: previous gastrectomy, contraindication to UGIE due to comorbidities, no gastric mucosal biopsies, refusal of consent. Endoscopy was initially performed with white light image (WLI), followed by BLI and LCI. Standardized photodocumentation of stomach was performed with WLI, BLI and LCI. Imaging features suggestive of IM: lavender color sign and whitish flat elevation with LCI, and light blue crest and white opaque substance with BLI. EGGIM and Kimura-Takamoto Classification (KTC) were applied when IM and AG were suspected. Systematic random biopsies of the antrum, incisura angularis and corpus along with targeted biopsies of suspicious gastric mucosal lesions were obtained. Histology was considered gold standard. Performance of endoscopic imaging in the detection of IM, AG and EGC was evaluated.

Initially, 134 patients were evaluated and 64 were excluded: previous gastrectomy-22, pending histology-20, non-BLI imaging-15, intolerance to UGIE-3, refusal of consent-1, esophageal stenosis-1 and contra-indication to biopsies-2. Final sample included 70 patients.

Qualitative data expressed as percentage were compared with Chi-square test. A p value of <0.05 was considered significant.

Results: Median age was 56 (19-86), with 49 (63%) female. There was family history of gastric cancer in 12(15%) and history of smoking in 35 (44%). Histological AG was found in 15 (19%) and IM in 20 (26%) patients. WLI was

suggestive of IM in 14(20%), confirmed histologically in 9 (64%). IM was suspected by LCI and BLI in 24 (34%) and 23 (32%) cases, confirmed by histology in 16 (67%) and 17 (74%), respectively. WLI classified 56 (71%) as EGGIM 0 and after LCI and BLI, 10 (18%) and 8 (15%) of these cases had EGGIM 1 or 2. In 10 patients, EGGIM 1-2 with WLI, only 1 was upgraded to EGGIM 3-4 with LCI and BLI. In 3 (4%) EGGIM 3-4 with WLI, after LCI and BLI, 1 had extensive IM (EGGIM 6). Among 19(24%) patients EGGIM 1-2 with LCI, 3(16%) had EGGIM 0 with BLI. Atrophy was suspected by WLI and LCI in 9(12%) and 15(21%) patients, confirmed by histology in 6(67%) and 8(53%) cases, respectively. According to KTC, 5 (6%) were classified as C1, 2 (3%) as C2 and 4 (5%) as O3 with WLI. With LCI images, 8 (10%) were classified as C1, 3(4%) as C2 and 4(5%) as O3. The sensitivity (Sens), specificity (Spec), accuracy, positive predictive value (PPV), negative predictive value (NPV) of WLI, BLI and LCI in detecting AG and IM are shown in table 1.

	Sens (%)	Spec (%)	Accuracy (%)	PPV (%)	NPV (%)
Intestinal metaplasia					
WLI	47	90	79	61	83
LCI	80	84	83	62	92
BLI	85	88	97	70	94
Atrophic gastritis					
WLI	40	94	80	71	83
LCI	53	87	78	58	85

Table 1. Sens, Spec, accuracy, PPV and NPV in detecting AG and IM with WLI, LCI and BLI.

Conclusion: Both BLI and LCI are promising advanced endoscopic imaging techniques with BLI having higher accuracy than LCI in detection of IM.

- References:** 1. Chen H, Liu Y, Lu Y, Lin X, Wu Q, Sun J, et al. Ability of blue laser imaging with magnifying endoscopy for the diagnosis of gastric intestinal metaplasia. *Lasers Med Sci.* 2018 Nov 1;33(8):1757–62.
2. Ono S, Abiko S, Kato M. Linked color imaging enhances gastric cancer in gastric intestinal metaplasia. Vol. 29, *Digestive Endoscopy*. Blackwell Publishing; 2017. p. 230–1.
3. Ono S, Kato M, Tsuda M, Miyamoto S, Abiko S, Shimizu Y, et al. Lavender Color in Linked Color Imaging Enables Noninvasive Detection of Gastric Intestinal Metaplasia. *Digestion.* 2018 Nov 1;98(4):222–30.
4. Zhang G, Zheng J, Zheng L, Yu S, Jiang C, Lin W, et al. Gastric intestinal metaplasia assessment between linked color imaging based on endoscopy and pathology. *Scand J Gastroenterol.* 2021;56(1):103–10.
5. Shu X, Wu G, Zhang Y, Wang Y, Zheng Y, Guo Q, et al. Diagnostic value of linked color imaging based on endoscopy for gastric intestinal metaplasia: a systematic review and meta-analysis. *Ann Transl Med.* 2021 Mar;9(6):506–506.
6. Esposito G, Pimentel-Nunes P, Angeletti S, Castro R, Libânio D, Galli G, et al. Endoscopic grading of gastric intestinal metaplasia (EGGIM): A multi-center validation study. *Endoscopy.* 2019;51(6):515–21.

Disclosure: Nothing to disclose.

PP0194

SAFETY AND FEASIBILITY OF GASTROINTESTINAL ENDOSCOPY IN NEONATES AND INFANTS UNDER 3 MONTH OF AGE

H. Yang¹, S. Liu¹, Y. Fang¹

¹*Xi'an Children's Hospital, Department of Gastroenterology, Xi'an, China*

Contact E-Mail Address: liushan92263@163.com

Introduction: With the development of minimally invasive endoscopic diagnosis and treatment technology in children, the application age of pediatric digestive endoscopy is gradually expanded to infants and even neonates. Compared with older children, the gastrointestinal lumen of this population is more distorted and narrow, the wall is thinner, and the operation is more difficult and risky. This study aims to investigate the safety and feasibility of gastrointestinal endoscopy in neonates and infants under 3 months of age.

Aims & Methods: A retrospective analysis was performed on the clinical data of 145 neonates and infants under 3 months of age who underwent gastrointestinal endoscopy in Xi'an Children's Hospital from June 2018 to May 2023. The general condition, clinical manifestations, main diagnosis, endoscopic treatment and adverse events of all children were statistically analyzed.

Results: A total of 145 patients were enrolled in this study, including 30 neonates (20.7%). There were 96 males (66.2%) and 49 females (33.8%). The age ranged from 1 day (9 hours after birth) to February 29 days, with a mean age of January 17 days. The main symptoms of children undergoing gastrointestinal endoscopy were vomiting (79 cases, 54.5%), followed by hematochezia (25 cases), diarrhea (19 cases), bucking (10 cases), abdominal distension (6 cases), hematemesis (5 cases) and foreign body in digestive tract (1 case). All children underwent general anesthesia under tracheal intubation. Gastrosocopy was performed with XP290 electronic nasal gastroscope (external diameter of 5.8mm), gastroscopy was performed with H290 electronic gastroscope (external diameter of 8.9mm), and colonoscopy was performed with Q260 electronic colonoscopy (external diameter of 9.2mm). 114 cases (78.6%) underwent gastroscopy and 31 cases (21.4%) underwent colonoscopy. The most common diagnosis was congenital hypertrophic pyloric stenosis (55 cases, 37.9%), followed by allergic colitis (15 cases), esophageal stenosis (13 cases), erosive gastritis (11 cases), multiple colonic ulcers (7 cases), duodenal stenosis (5 cases), colonic stenosis (4 cases) and reflux esophagitis (3 cases). In addition, 25 cases (17.2%) showed no abnormalities after the examination, and gastrointestinal diseases were excluded. In addition to routine examination, a total of 63 children received endoscopic treatment. The most common endoscopic treatment was peroral endoscopic pyloromyotomy (G-POEM), 37 cases, accounting for 58.7% of all children who received endoscopic treatment. The others included 15 cases of endoscopic nutrition tube placement, 8 cases of endoscopic balloon dilatation, 1 case of endoscopic foreign body removal, 1 case of endoscopic magnetic ring placement and 1 case of endoscopic hemostasis. All children underwent gastrointestinal endoscopy successfully, with a success rate of 100%. No adverse events related to anesthesia and surgery occurred in all children.

Conclusion: The application of gastrointestinal endoscopy in neonates and infants under 3 months of age may be feasible and safe. Endoscopic diagnosis and treatment is minimally invasive, safe and fast recovery, which has a wide application prospect in young children.

Disclosure: Nothing to disclose.

PP0195

GASTRIC ENDOSCOPICAL SUBMUCOSAL DISSECTION: ARE WE EXCEEDING EXPECTED PROCEDURE TIMES?

M.I. Viegas¹, M. Areia¹, L. Elvas¹, S. Alves¹, D. Brito¹, S. Saraiva¹, A.T. Cadime¹

¹*Portuguese Oncology Institute of Coimbra, Department of Gastroenterology, Coimbra, Portugal*

Contact E-Mail Address: mariainesviegas96@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) stands as the gold standard treatment of gastric superficial lesions. Due to its technical complexity, ESD procedures often require extended durations, and longer procedural times are related to a higher level of adverse events. We intend to analyze our procedural time according to the predictive formula developed by Goto et al.

Aims & Methods: Prospective cohort study, single center, of patients who underwent gastric ESD between 2017 and 2023. The characteristics of the lesion were evaluated, and logistic regression of risk factors associated with longer procedural time (≥ 60 minutes) was performed. The predictive formula of procedural time was calculated for each patient and comparison between predictive and actual procedural time was performed using Pearson correlation coefficient.

Results: Included 101 gastric ESDs, 63.4% female, with a mean age of 69.7 ± 8 years. Among the analyzed lesions: 43.6% measured between 0-20mm, 56.4% ≥ 20 mm; 13.9% were sessile, 60.4% flat, 14.9% depressed and 10.9% subepithelial; 22.8% were located in the upper-third of the stomach, 17.8% in the middle-third and 59.4% in the lower-third. Ulcerative findings were identified in 10% of the lesions. The most frequent histological results were: 38.6% low grade dysplasia, 26.7% high grade dysplasia and 19.8% intramucosal adenocarcinoma. The mean procedure duration was 87 ± 43 minutes. Intra-procedure adverse events registered in 2% (perforation).

Evaluating the risk factors for longer procedures (≥ 60 minutes), the following revealed statistical significance: lesion size ≥ 20 mm (89.5% vs. 65.9%; $p=0.004$), histology indicative of intramucosal adenocarcinoma (95.7% vs. 74.4%; $p=0.027$) and location in the upper or middle-third of the stomach (95.1% vs. 68.3%; $p=0.001$), but not the Paris classification (78.6% vs. 75.4% vs. 93.3%; $p=0.4$), ulcerative findings (63.6% vs. 67.1%; $p=0.8$) and the use of anticoagulant therapy (64.3% vs. 81.6%; $p=0.138$). Logistic regression analysis revealed that lesion size ≥ 20 mm (OR 5.7; IC95%: 1.7-18.7) and location in the upper or middle-third of the stomach (OR 13.6; IC95%: 2.3-80.7) were significantly associated with longer procedural time.

When comparing predicted and actual procedural time, the overall Pearson correlation coefficient (r) was 0.58 ($p<0.01$), with the following values per consecutive 25 cases: 0.70, 0.67, 0.54 and 0.46.

Conclusion: Previous identification of risk factors for prolonged ESD procedures, such as lesion size ≥ 20 mm and proximal lesion location, can be useful in optimizing workflow scheduling. Our correlation between predicted and actual time demonstrated a decreasing value, probably due to a higher complexity of the lesions, giving room for improvement.

Disclosure: Nothing to disclose.

PP0196

DELAYED BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): ANALYSIS OF RISK FACTORS AND VALIDATION OF THE BEST-J SCORE

M.I. Viegas¹, L. Elvas¹, M. Areia¹, S. Alves¹, D. Brito¹, S. Saraiva¹, A.T. Cadime¹

¹Portuguese Oncology Institute of Coimbra, Department of Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: mariainesviegas96@gmail.com

Introduction: Delayed bleeding after gastric endoscopic submucosal dissection (ESD) is one of the most frequent complications (up to 7%). The BEST-J score is a risk predictive model for delayed bleeding following gastric ESD.

We aim to assess potential risk factors associated with bleeding and validate the BEST-J score in a population of patients undergoing ESD.

Aims & Methods: Prospective cohort study, single centre, of patients who underwent gastric ESD between 2017 and 2023. The characteristics of the lesion were evaluated, and logistic regression of risk factors associated with bleeding after ESD was performed. The BEST-J score was calculated for each patient and the discriminative ability was evaluated through the area under the receiver operating characteristic curve (AUC-ROC).

Results: Included 101 gastric ESDs (63.4% female), with a mean age of 69.7 ± 8 years. 17.8% of patients were on antiplatelet therapy and 13.9% were on anticoagulant therapy. Among the analyzed lesions: 43.6% measured between 0-20mm, 56.4% were ≥ 20mm; 13.9% were sessile, 60.4% flat, 14.9% depressed and 10.9% subepithelial; 22.8% were located in the cardia, fundus, or body, 17.8% in the incisura *angularis* and 59.4% in the antrum. The most frequent histological results were: 38.6% low-grade dysplasia, 26.7% high-grade dysplasia and 19.8% intramucosal adenocarcinoma. The mean procedure duration was 87±43 minutes. Delayed bleeding after ESD occurred in 5.9% (n=6) of cases. In the univariate analysis of risk factors, the lesion size ≥ 20mm showed statistical significance (10.5% vs. 0%; p=0.034), but not the location in the antrum (6.7% vs. 4.9%; p=0.5), lesion nature (7.1% vs. 8.2% vs. 0% vs. 0%; p=0.5) or procedure duration ≥60 minutes (5% vs. 9.5%; p=0.3). The BEST-J score predicted the risk of delayed bleeding after gastric ESD with an AUC of 0.70 (95% CI: 0.53-0.87; p=0.1).

Conclusion: The use of bleeding predictive scores may be useful in identifying high-risk patients; in our series, the BEST-J score was not very effective, with only lesion size ≥ 20mm being a relevant factor for bleeding after ESD.

Disclosure: Nothing to disclose.

PP0197

RISK FACTORS ASSOCIATED WITH METACHRONOUS LESIONS FOLLOWING GASTRIC SUBMUCOSAL DISSECTION (ESD): A SINGLE CENTRE EXPERIENCE

M.I. Viegas¹, L. Elvas¹, M. Areia¹, S. Alves¹, D. Brito¹, S. Saraiva¹, A.T. Cadime¹

¹Portuguese Oncology Institute of Coimbra, Department of Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: mariainesviegas96@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is the first-line treatment for superficial gastric lesions with a negligible or very low risk of lymph node metastasis. However, a permanent risk of developing metachronous lesions persists. We intend to analyze the risk factors associated with the development of metachronous lesions in a population of patients undergoing ESD.

Aims & Methods: Prospective cohort study conducted at a single centre, involving patients who underwent gastric ESD for lesions between 2017 and 2023, with a follow-up period of ≥ 6 months. Lesion characteristics were analyzed, including the rate of metachronous lesions, and logistic regression was performed to identify risk factors associated with the development of metachronous lesions.

Results: Included 78 ESDs performed on gastric epithelial lesions (59% female), with a mean age of 70.3±7.9 years. Regarding family history of gastric adenocarcinoma, 17.9% of patients had a first-degree relative. Among the analyzed lesions: 42.3% measured between 0-20mm, 57.7% ≥ 20mm; 12.8% were sessile, 71.8% flat and 15.4% depressed; 19.2% were located in the cardia, fundus or body, 21.8% in the incisura *angularis* and 59% in the antrum.

Regarding histological findings: 42.3% low-grade dysplasia, 30.8% high-grade dysplasia, 23.1% intramucosal adenocarcinoma and 3.8% adenocarcinoma with submucosal invasion. Nine metachronous lesions (11.5%) were detected, with a median time of occurrence of 24 [13-32] months. In the analysis of risk factors, statistical significance was found for location outside the antrum (21.6% vs. 1.9%; p=0.002) and the presence of adenocarcinoma (23.8% vs. 7%; p=0.039), but not for size ≥20mm (13.7% vs. 5.1%; p=0.178) or ulceration of the lesion (9.1% vs. 10.1%; p=0.915). Logistic regression analysis revealed that only location outside the antrum had a significant risk for the development of metachronous lesions (OR 13.4; 95% CI: 1.4-127.1).

Conclusion: Given the permanent risk of developing metachronous lesions, the identification of associated risk factors is important as it may eventually allow for the adaptation of surveillance programs.

Disclosure: Nothing to disclose.

PP0198

WITHDRAWN

PP0199

RISK FACTOR ANALYSIS FOR BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: A NATIONWIDE POPULATION-BASED STUDY OVER 11 YEARS

J.Y. Park¹, M.-S. Kim², J.G. Kim¹

¹Chung-Ang University College of Medicine, Seoul, South Korea,

²Division of Clinical Epidemiology, Medical Research Collaborating Center, Biomedical Research Institution, Seoul National University Hospital, Seoul, South Korea

Contact E-Mail Address: jay0park@cau.ac.kr

Introduction: Although an effective and relatively safe procedure, bleeding complications often occur after gastric endoscopic submucosal dissection (ESD). We aimed to comprehensively evaluate the risk factors of post-procedural bleeding following gastric ESD.

Aims & Methods: This study was designed as a nationwide, population-based, retrospective study utilizing the Korean National Health Insurance Service database, comprising patients who underwent gastric ESD for gastric cancer or adenoma from November 2011 to December 2022. Operational definitions were created to identify the target population and post-procedural bleeding using the diagnosis and procedure code, which underwent validation.

We established operational definitions to identify the target population and post-procedural bleeding by utilizing diagnosis and procedure codes, which underwent validation. The risk factors analyzed included age, sex, hospital volume, socioeconomic status (SES), histology, lesion numbers, comorbidities, and medication usage.

Results: During the study period, there were 191,932 procedures conducted on 175,779 patients, resulting in 9921 cases of bleeding events. Several factors were associated with increased post-ESD bleeding risk. Following multiple logistic regression, relevant factors with adjusted odds ratios (aORs) were identified. These factors included young age (aOR: 0.990, 95% CI 0.987-0.992), male sex (aOR: 1.377, 95% CI 1.311-1.448), low-volume center compared to high-volume center (aOR: 1.289, 95% CI 1.022-1.621), medical aid compared to the top 25% SES (aOR: 1.307, 95% CI 1.188-1.440), higher Charlson comorbidity index (aOR: 1.040, 95% CI 1.026-1.054), gastric cancer (aOR: 1.369, 95% CI 1.307-1.434), and multiple lesions (aOR: 1.144, 95% CI 1.032-1.267). Furthermore, bleeding risk was significantly higher in groups with several comorbidities and antithrombotic agent users, particularly showing Notably high aORs in groups with renal failure (aOR: 2.086, 95% CI 1.909-2.278), warfarin (aOR: 2.641, 95% CI 2.219-3.143), direct oral anticoagulants (aOR: 2.519, 95% CI 2.220-2.859), and antiplatelet combinations (aOR: 2.073, 95% CI 1.783-2.410).

Conclusion: This study revealed various factors associated with increased bleeding risk after gastric ESD using a large cohort, which could be an important issue in terms of risk stratification and personalized treatment.

Disclosure: Nothing to disclose.

PP0200

WITHDRAWN

PP0201

COMPREHENSIVE ANALYSIS OF ENDOSCOPIC ULTRASOUND (EUS) IN MEDIASTINAL LESIONS: PATIENT CHARACTERISTICS, DIAGNOSTIC OUTCOMES, SAFETY, AND EFFICACY: A MULTICENTER STUDY

H. Okasha¹, E. Gadour^{2,3}, G.U. Tayyab⁴, A. Seicean⁵, H. El Bacha⁶, E. Aljahdli⁷, T. Alamri⁸, N. Tehami⁹, A. Alzamzamy¹⁰, H. Hussein¹¹, M. Tag-Adeen¹², M. Elbasiony¹³, A. Al-Lehibi¹⁴, S. Saleh¹⁵, Z. Houmani¹⁶, M. Abdelghani¹⁷, Z. Ismaili¹⁸, D. Othmane¹⁹, E. Ghoneem²⁰, O. AbdAllah²¹, S. Rebiai Hadjmat²², N. Pausawasdi²³, F. Rouibaa²⁴, M. Farouk¹⁷, M. Borahma²⁵, H. Atalla²⁶, M. Alshair²⁷, K. Ragab²⁸, A. Altonbary²⁹

¹Faculty of Medicine, Cairo University, Cairo, Egypt, ²King Abdulaziz National Guard Hospital-Ahsa, Gastroenterology, Ahsa, Saudi Arabia, ³Zamzam University College, Faculty of Medicine, Department of Medicine, Khartoum, Sudan, ⁴Doctors Hospital and Medical Centre, Gastroenterology, Lahore, Pakistan, ⁵University of Medicine and Pharmacy Iuliu Hatieganu Cluj-Napoca, Romania, ⁶Regional Institute of Gastroenterology and Hepatology Cluj-Napoca, Romania, ⁷Cluj Napoca, Romania, ⁸Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ⁹King Abdulaziz University Hospital, Gastroenterology, Jeddah, Saudi Arabia, ¹⁰Imam Abdulrahman Bin Faisal University, Gastroenterology, Dammam, Saudi Arabia, ¹¹University Hospital Southampton NHS Foundation Trust, Gastroenterology, Southampton, United Kingdom, ¹²Maadi Armed Forces Medical Complex, Gastroenterology, Cairo, Egypt, ¹³Sulaimani Teaching Hospital, Gastroenterology, Sulaymaniyah, Iraq, ¹⁴Qena Faculty of Medicine, Gastroenterology, Qena, Egypt, ¹⁵Mansoura University, Internal Medicine, Mansoura, Egypt, ¹⁶King Fahad Medical City, Gastroenterology, Riyadh, Saudi Arabia, ¹⁷Ain Shams University, Internal Medicine, Cairo, Egypt, ¹⁸Najdeh Hospital, Gastroenterology and hepatology, Nabatieh, Lebanon, ¹⁹Assiut university, Tropical Medicine and Gastroenterology, Assuit, Egypt, ²⁰Medical School, Hepato Gastroentetology, Oujda, Morocco, ²¹Fatema el Azhar Oncology and Radiotherapy Centre, hepatologie, Algiers, Algeria, ²²Faculty of Medicine Mansoura University/ Egyptian Liver Hospital, Mansoura, Egypt, ²³Hepatogastroenterology, Mansoura- dakahleya, Egypt, ²⁴Mansoura University, Internal Medicine(Hepatology & Gastroenterology), Mansoura, Egypt, ²⁵Chifa Clinic Hydra, Gastroenterology, Algiers, Algeria, ²⁶Siriraj Hospital, Bangkok, Thailand, ²⁷Military hospital Mohamed V-Souissi University, Hay Ryad - 10100, Rabat, Morocco, ²⁸Mhammed V University, Ibn Sina Hospital, Gastroenterology, Rabat, Morocco, ²⁹Mansoura faculty of medicine, Internal medicine, gastroenterology and hepatology unit, Mansoura, Egypt, ³⁰Al-Azhar University, Gastroenterology, Cairo, Egypt, ³¹Theodor Bilharz Research Institute, Cairo, Egypt, ³²Mansoura Specialized Medical Hospital, Gastroenterology and Hepatology, Mansoura, Egypt

Contact E-Mail Address: eyadgadour@doctors.org.uk

Introduction: Mediastinal lesions develop from structures located in the mediastinal compartments and the paravertebral areas. The diagnosis of these lesions is primarily based on imaging studies such as computed tomography and magnetic resonance imaging, which confirm the presence of the lesions and suspected metastatic disease

Aims & Methods: This study aims to assess the factors that determine the diagnostic accuracy and yield of endoscopic ultrasound (EUS) in diagnosing mediastinal lesions. This multicenter study involved a list of centres providing EUS services across ten countries all over the globe. The appropriate information was collected regarding EUS-FNA and EUS-FNB

procedures, including nature of the lesion, needle types, needle passes, and complications of the techniques. The frequency/percentage conveyed data on the qualitative variables. The p-values were obtained using the Chi-square two-tailed exact test. The significance of the analysis was defined as $p < 0.05$. All the syntheses were performed using the Statistical Package for the Social Sciences (SPSS version 27; SPSS Inc., Chicago, IL). **Results:** A total of 439 participants were involved in this study, 255 (58.1%) males and 184 (41.9%) females, with a mean age of 55.7314.93 years. The average accuracy from the valid matched cases between EUS, cytopathy, and final diagnosis (300 out of 331) was 90.63%. EUS-FNA and EUS-FNB diagnostic yield was influenced by needle types, needle size, number of needle passes, and lesion size. Needles with smaller diameters (22G) offered greater diagnostic yield than needles with larger diameters (19G). However, the diagnostic matching accuracy of EUS in relation to needle sizes was statistically insignificant ($p = 0.774$). A minimal number of needle passes (between 2 and 4) showed a higher diagnostic yield than a higher number of needle passes (>5) with more diagnostic matching accuracy ($p = 0.009$). EUS-FNB accounted for a 0.5% complication incidence rate each for fever, pain, thoracic pain, and hemorrhage. Patients undergoing EUS-FNA, EUS-FNB, or both procedural examinations had no significant complications ($p = 0.085$) Table 1.

EUS diagnosis		Complications					P value
		Fever and Pain	Hemorrhage	None	Pain	Thoracic pain	
EUS-FNA or FNB	EUS-FNA	Count	0	0	75	0	0.085
		% within FNA	0.0%	0.0%	67.0%	0.0%	
	EUS-FNB	Count	1	1	178	1	
		% within FNB	0.5%	0.5%	82.8%	0.5%	
	FNA and FNB combined	Count	0	0	4	0	
		% FNB and FNA combined	0.0%	0.0%	1.6%	0.0%	

Table 1: Incidence rate of complications associated with EUS examination techniques.

Conclusion: The diagnostic yield of EUS procedures is affected by needle types, number of needle passes, lesion size, and needle size. Besides, EUS-FNA and EUS-FNB are infrequently associated with serious complications, these techniques are safe and offer higher diagnostic yield when utilised responsibly by endosonographers.

References: 1- Gadour E, Awad A, Hassan Z, Shrwani KJ, Miutescu B, Okasha HH. Diagnostic and therapeutic role of endoscopic ultrasound in liver diseases: A systematic review and meta-analysis. World J Gastroenterol. 2024 Feb 21;30(7):742-758. doi: 10.3748/wjg.v30.i7.742. PMID: 38515947; PMCID: PMC10950627.

2- Okasha HH, El-Meligui A, Pawlak KM, Żorniak M, Atalla H, Abou-Elmagd A, Abou-Elenen S, El-Husseiny R, Alzamzamy A. Practical approach to linear EUS examination of the mediastinum. Endosc Ultrasound. 2021 Nov-Dec;10(6):406-413. doi: 10.4103/EUS-D-21-00019. PMID: 34854401; PMCID: PMC8785678.

Disclosure: Nothing to disclose.

PP0202
USING NEEDLE BIOPSY UNDER ECHO-ENDOSCOPY (EEH-FNB) TO
DIAGNOSE STOMACH LINITIS: A MOROCCAN UNIVERSITY CENTER'S
EXPERIENCE

O. Nacir¹, F. Lairani¹, A. Ait errami², S. Oubaha^{1,3}, Z. Samlani¹, K. Krati¹
¹Department of GastroEnterology and Hepatology, Mohammed VI University Hospital Centrre, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco, ²UHC Mohammed VI, Hepatogastroenterology, Marrakech, Morocco, ³Department of Physiology, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco

Contact E-Mail Address: o.nacir@uca.ac.ma

Introduction: Gastric linitis is a kind of adenocarcinoma that invades the stomach and is composed of separate cells. The predicted survival rate for this condition over a five-year period ranges from 3 to 10%. The excessive cell growth that characterizes gastric linitis also results in the formation of fibrous tissue, which makes the stomach wall thicker and less flexible. Consequently, mucous biopsies frequently do not provide useful information.

Aims & Methods: The aim of this study is to evaluate the diagnostic performance of echo-endoscopic biopsy puncture (EUS-FNB) in the diagnosis of gastric linitis. This study is an observational retrospective monocentric analysis conducted over a period of 4 years from January 2018 to December 2022. It includes all patients who underwent a parietal gastric and/or ganglionic puncture under echo endoscopic guidance using a 20G or 22G Procore® or Acquire® type 22G FNB needle. The purpose of the procedure was to investigate suspected cases of gastric linitis. The study is conducted at the University Hospital Centre in Marrakech, which serves as a tertiary care department and is a point of reference for all regional and provincial hospitals. The appearance of parietal gastric thickness, abdominal DMT, an infiltrated aspect of the stomach, folds, or gastric stenosis in high digestive endoscopy led to the suspicion of gastric linitis. The data was obtained from various sources, including hospital registers, patient medical records, the computerized system "Hosix" for morphological and anatomopathological data, and the collaboration of the medical and paramedical staff from the departments of gastroenterology, visceral surgery, and anatomopathology. The statistical analysis was conducted using SPSS version 22.0. Socio-demographic, clinical and para-clinical data were collected taking into account the global ethical rules relating to confidentiality and protection of patient-specific data.

Results: Out of 42 patients who performed biopsy puncture under high echo-endoscopy on suspicion of diagnosis, ten patients had gastric linitis. The diagnosis of gastric linitis was obtained by puncture in 90% of cases (9/10). Eight patients (80%) had previously undergone at least one oeso-gastro-duodenal fibroscopy with returning negative mucous biopsies. Six patients were diagnosed as early as 1st EEH while 3 others required a second series of biopsies. While the mucous biopsies were also unsuccessful, echo-guided biopsy allowed the diagnosis of other more serious diseases in 43% of cases ($n = 18/42$) including gastric metastases of a breast cancer ($n=2$), other gastric adenocarcinomas of the intestinal type ($N=8$), and cases of T-type gastric lymphoma in one case and MALT type in 2 cases.

Conclusion: In case of suspicion of gastric linitis, guided biopsy puncture under echo-endoscopy is a cost-effective approach in 90% of cases, without noticeable side effects. It should be considered the procedure of choice for early diagnosis of gastric linitis when mucous biopsies return negative.

Disclosure: Nothing to disclose.

PP0203

PLATINUM FIDUCIAL SEEDS MADE IN HOUSE FOR EUS GUIDED IMPLANTATION

S. Abbott-Tate¹, A. Chatterjee¹

¹Ottawa Hospital Research Institute, Gastroenterology, Ottawa, Canada

Contact E-Mail Address: samabbott@ohri.ca

Introduction: Stereotactic Body Radiation Therapy (SBRT) has proven to be a safe and effective therapy for patients with deep abdominal malignancies who are ineligible/suboptimal candidates for surgery^{1,2}.

SBRT's effectiveness is dependent on precise targeting, achieved through both bone imaging and implantation of small markers (fiducials) that are visible during imaging which delineate margins of the target lesion³.

Fusion of computed tomography (CT) and magnetic resonance imaging (MRI) can provide enhanced soft tissue contrast and improved delineation of the tumor⁴, and is the preferred choice at our institution.

Fiducials have traditionally been made of gold due to its bioinertness and visibility on CT imaging, however gold is not accurately detected on MRI⁵. Platinum fiducials have recently emerged as an attractive alternative⁵, considering their improved detectability on MRI imaging.

Endoscopic ultrasound (EUS)-guided implantation techniques have largely supplanted percutaneous methods for deep abdominal targeting, due to improved access and visualization⁶.

Aims & Methods: The objective of this case series was to describe our novel platinum seed (PS) fiducials developed in house for EUS-guided fiducial SBRT application. We reviewed the adequacy of fiducial placement, quality of pre-treatment imaging, and migration rates of our fiducials. This single-center case series included patients diagnosed with cancers of the abdomen, including pancreas, adrenal, and liver, who were scheduled to undergo SBRT requiring EUS-guided fiducial implantation between January 2011-February 2024.

The cohort was derived from a prospectively collected EUS database at The Ottawa Hospital in Ottawa, Canada. Patient demographics (sex and age), procedure details (tumor site, number of fiducials implanted, complications), and radiologist's interpretation of MRI/CT imaging were assessed using hospital records. Approximately 70% of patients received antibiotics ((either IV x 1 does or oral antibiotics for 5 days post-procedure (eg. Ciprofloxacin, 500mg)). Our PS fiducials are made from 0.75mm wire cut into 3mm seeds which are then autoclaved in-house. Fiducials were implanted using a 19g FNA needle and advanced using an ERCP guidewire using EUS and fluoroscopic guidance.

Results: 55 patients underwent EUS implantation for a total of 176 fiducials. Preplanning CT/MRI imaging identified 166/176 (94.3%) fiducial signal voids. When evaluating fiducial placement adequacy, 52 of 55 (94.5%) patients had adequate placement for SBRT. Two patients required a repeat procedure with additional fiducial implantation. One case was due to suspected migration, and the second case was due to fiducials being placed too closely preventing adequate delineation. In a third case, no signal voids were visualized for an unknown reason, however, no repeat procedure was required as spine tracking was used. None of the patients developed post-procedure infection or other adverse events (AEs) in this case series (follow up at 1 month). Cost analysis revealed the fiducials made in-house were ~20-fold less expensive compared to commercially available solid gold, gold coil, or solid platinum fiducials.

Conclusion: Our platinum seed fiducials made in-house appear to have similar adequacy and no increased risk of AEs for EUS-implantation when compared to commercially available fiducials^{7,8}. For centres using fused CT-MRI imaging for SBRT planning, PS fiducials are recommended. Moreover, significant cost-saving can be achieved through in-house production.

References: 1. Rwigema JM, et al. Stereotactic body radiation therapy for abdominal and pelvic oligometastases: Dosimetric targets for safe and effective local control. *Pract Radiat Oncol.* 2015;5(3):e183-e191.

2. Almaghrabi MY, et al. Stereotactic body radiation therapy for abdominal oligometastases: a biological and clinical review. *Radiat Oncol.* Aug 01 2012;7:126. doi:10.1186/1748-717X-7-126

3. Moskalenko M, et al. Fiducial Markers Allow Accurate and Reproducible Delivery of Liver Stereotactic Body Radiation Therapy. *Curr Oncol.* May 16 2023;30(5):5054-5061.

4. Bryant JM, et al. Stereotactic Magnetic Resonance-Guided Adaptive and Non-Adaptive Radiotherapy on Combination MR-Linear Accelerators: Current Practice and Future Directions. *Cancers (Basel).* Mar 30 2023;15(7).

5. Nair VJ, et al. Feasibility, detectability and clinical experience with platinum fiducial seeds for MRI/CT fusion and real-time tumor tracking during CyberKnife. *J Radiosurg SBRT.* 2015;3(4):315-323.

6. Pishvaian AC, et al. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. *Gastrointest Endosc.* Sep 2006;64(3):412-7.

7. Choi JH, et al. Fiducial placement for stereotactic body radiation therapy under only endoscopic ultrasonography guidance in pancreatic and hepatic malignancy: practical feasibility and safety. *Gut Liver.* 2014;8(1):88-93.

8. Kataki K, et al. Prospective Evaluation Fiducial Migration after Placement for Liver SBRT and Influence on Treatment Delivery. *International Journ of Rad Onc.* 2019;105(1):E222.

Disclosure: Nothing to disclose.

PP0204

DIAGNOSIS OF GASTROINTESTINAL SUBEPITHELIAL LESIONS USING A NOVEL ENDOSCOPIC ULTRASONOGRAPHY IMAGING TECHNIQUE

C. Robles-Medrand¹, R. del Valle¹, M. Egas Izquierdo¹, M. Puga-Tejada¹, J. Baquerizo-Burgos¹, D. Cunto¹, M. Arevalo-Mora², J. Alcivar-Vasquez¹, H. Pitanga-Lukashok¹

¹Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Larkin Community Hospital, South Miami, United States of America

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Gastrointestinal stromal tumors (GIST) are the most common malignant subepithelial lesions (SELs) found in the gastrointestinal tract. Due to GIST's notable features including vascularity and deep location, endoscopic ultrasound (EUS) is the first-line diagnostic approach. Three models, color-doppler EUS, power-doppler EUS, and e-FLOW EUS, are useful for real-time vascularity detection; however, they are not effective for fine and slow flow vessel detection. Therefore, contrast enhanced EUS (CE-EUS) is proposed as a first-line approach. Nevertheless, the use of contrast may be detrimental, thus limited to some patients. To avoid contrast-related adverse events, a novel diagnostic method known as detective flow imaging endoscopic ultrasonography (DFI-EUS) has emerged.

Aims & Methods: To evaluate the utility of DFI-EUS in the diagnosis and differentiation of gastrointestinal SELs (GIST and leiomyomas) in comparison to CE-EUS.

A single-center, prospective, diagnostic study was conducted between December/2022 and October/2023 at IECED, Ecuador. The study protocol was approved by the Institutional Review Board and was conducted in accordance with the Declaration of Helsinki. Patients ≥18 years old with a suspected diagnosis of gastrointestinal SELs were enrolled for EUS vascularity assessment. Patients with contraindication for contrast agent administration, any clinical condition rendering EUS-DFI or CE-EUS unfeasible, pregnant and nursing were excluded. First, SELs' assessment was

performed by two expert endosonographers (blinded to patient's clinical information) using DFI-EUS, followed by a CE-EUS examination (using Sulphur hexafluoride contrast agent) for diagnostic confirmation. The identification rate along with diagnostic accuracy of DFI-EUS and CE-EUS based on histopathological confirmation was the primary endpoint. The type of vascularization (microvascular/microvascular) along with endosonographic appearance (hyper/hypovascular) were also recorded.

Results: A total of 24 patients were included, comprising 54.2% females. The examined lesions consisted of 70.8% GIST and 29.1% leiomyoma. Predominantly, lesions were found in the stomach (91.7%) and within the muscularis propria layer (91.7%). All GIST were hypoechoic and mainly heterogeneous, larger than leiomyoma in size (>2 cm; $p < 0.001$). Tortuous vessels were significantly identified in GIST ($p = 0.045$). Both CE-EUS (94.1%; $p = 0.003$) and DFI-EUS (94.1%; $p < 0.001$) successfully detected GIST (Table 1).

The overall sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of DFI-EUS was comparable with CE-EUS with rates of 94.12% vs 94.12, 100% vs 99.64%, 100% vs 99.85% and 87.5% vs 99.64%, respectively (Table 2).

A strong inter-rater agreement between CE-EUS vs DFI-EUS was detected with a kappa of 0.903 ($p < .001$).

Conclusion: DFI-EUS proves to be a reliable diagnostic tool, exhibiting high diagnostic accuracy, comparable to that of CE-EUS in the differentiation of GIST and SELs in the gastrointestinal tract. Larger multicenter studies are necessary to position this alternative for SELs' differentiation in clinical practice.

References:

1. Yamashita Y, Ashida R, Tamura T, Shimokawa T, Yamazaki H, Kawaji Y, Tamura T, Hatamaru K, Itonaga M, Kitano M. Novel Technique of Endoscopic Ultrasonography for the Differential Diagnosis of Gallbladder Lesions and Intraductal Papillary Mucinous Neoplasms: A Single-Center Prospective Study. *Diagnostics (Basel)*. 2023 Jun 21;13(13):2132. doi: 10.3390/diagnostics13132132. PMID: 37443527; PMCID: PMC10341113.
2. Yamashita Y, Yoshikawa T, Yamazaki H, Kawaji Y, et al. A Novel Endoscopic Ultrasonography Imaging Technique for Depicting Microcirculation in Pancreatobiliary Lesions without the Need for Contrast-Enhancement: A Prospective Exploratory Study. *Diagnostics (Basel)*. 2021 Oct 30;11(11):2018. doi: 10.3390/diagnostics11112018. PMID: 34829364; PMCID: PMC8621279.
3. Casali PG, Blay JY, Abecassis N, Bajpai J, et al; ESMO Guidelines Committee, EURACAN and GENTURIS. Electronic address: clinicalguidelines@esmo.org. Gastrointestinal stromal tumours: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2022 Jan;33(1):20-33. doi: 10.1016/j.annonc.2021.09.005. Epub 2021 Sep 21. No abstract available. PubMed ID: 34560242

Disclosure: Carlos Robles-Medrandia is a key opinion leader and consultant for Pentax Medical, Steris, Medtronic, Motus, Micro-tech, G-Tech Medical Supply, CREO Medical, EndoSound, and mdconsgroup.

The other authors declare no conflict of interest.

PP0205

THE ROLE OF EUS IN THE ASSESSMENT OF SUBEPITHELIAL LESIONS OF THE UPPER GASTROINTESTINAL TRACT: A SINGLE CENTER EXPERIENCE

G. Georgiadou¹, E. Athanasiadou¹, G. Lazaraki¹, K. Soufleris¹, S. Mamalis¹, B. Molayusufoglou¹, M. Stafylidou¹, D. Tzilves¹
¹Theageneio Anticancer Hospital of Thessaloniki, Gastroenterology Department, Thessaloniki, Greece

Contact E-Mail Address: eftychiaath1@gmail.com

Introduction: The increasing number of performed gastroscopies worldwide has led to higher detection rates of the subepithelial lesions (SELs) of the upper gastrointestinal tract. This study aims to describe the role of endoscopic ultrasonography (EUS) in the diagnosis and management of SELs at a tertiary public reference hospital in Northern Greece.

Aims & Methods: Records of patients who were referred to the Endoscopy Unit of Theageneio Hospital between 2018 and 2023 for upper EUS evaluation were retrospectively reviewed. We conducted data concerning patient characteristics, SELs features, details of the procedure and the final management of each case. All the examinations were performed by a single operator (DT).

Results: A total of 310 patients, male:130 and female:180, with a median age of 59 (range:17-86) were referred to EUS examination. EUS showed extraluminal compression in 16 cases (5.2%), gastric folds in 8 cases (2.6%), vascular structure in 8 cases (2.6%), and in 26 patients (8.4%) no lesion could be identified. A total of 252 (81.3%) patients had confirmed SELs. The lesion's location was: gastric body/corpus in 40.0% (101/252), antrum 34.5% (87/252), duodenum 15.1% (38/252), esophagus 10.3% (26/252). Regarding the size of the lesion in 31.7% of the cases (80/252) was <10 mm, 41.3% (104/252) 10-19mm and in 27% (68/252) was >20 mm. The most common EUS features were the following: regular borders 98.8% (249/252), hypoechoic lesions 67.5% (170/252), homogenous 77.8% (196/252), without vascularity 90.5% (228/252), and 69.5% (155/252) were originating from the third layer. Sixty-nine SELs (69/252, 27.4%) were malignant or had malignant potential as defined by the EUS findings. More specifically, forty-three patients (43/69, 62.3%) were referred for surgical resection. Twenty-three patients (23/69, 33.3%) were referred for further radiological evaluation and one patient (1/69, 1.4%) was referred for endoscopic resection. Endoscopic reassessment was recommended in 155 patients (155/252, 61.5%). Only one patient had persistent regurgitation, as an examination-related complication, probably due to the periprocedural

anesthesia that led to discontinuation of the examination.

Conclusion: EUS is a practical and safe tool for characterizing and assessing the features and malignant potential of SELs. In our center we could identify the malignant or potential malignant lesions and refer them to surgery.

References: 1. Deprez, P. H., Moons, L. M., O'Toole, D., Gincul, R., Seicean, A., Pimentel-Nunes, P., Fernández, Esparrach, G., Polkowski, M., Vie th, M., Borbath, I., Moreels, T. G., Van Dijkum, E. N., Blay, J., & VanHooft, J. E. (2022). Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*, 54(04),412–429. <https://doi.org/10.1055/a-1751-5742>

Disclosure: Nothing to disclose.

PP0206

EUS-GUIDED GASTROENTEROSTOMY TO TREAT REFRACTORY GASTROPARESIS: PRELIMINARY RESULTS OF THE FIRST GERMAN EXPERIENCE

M. Heilmaier¹, J. Wiessner¹, J. Ulrich¹, D. Schulz², M. Elnegouly¹, R.M. Schmid¹, M. Abdelhafez¹

¹Klinikum rechts der Isar der Technischen Universität München, Gastroenterologie, München, Germany, ²Universitätsklinikum Augsburg, Gastroenterologie, Augsburg, Germany

Contact E-Mail Address: markus.heilmaier@gmail.com

Introduction: Gastroparesis is a motility disorder of the stomach characterized by a delayed emptying of food into the small bowel in the absence of mechanical obstruction. Medical treatment is difficult and symptoms such as epigastric pain, nausea and vomiting can lead to a significantly reduced quality of life. As endosonographic-guided gastroenterostomy facilitates gastric emptying and has been used successfully in patients with gastric outlet obstruction over years, it might be a viable option to treat refractory gastroparesis. The aim of the study was to report the first experience with that approach and to evaluate its feasibility and efficacy.

Aims & Methods: The data of 7 patients with refractory gastroparesis undergoing EUS-GE between march 2021 and August 2023 were retrospectively collected and analyzed. Primary endpoint was to assess the clinical and technical success of the intervention. Secondary endpoints were to assess the stent patency, adverse events and the rate of reinterventions.

Results: Technical and clinical success rate was 100% with a mean reduction in gastroparesis cardinal symptom index of 71%. During the ongoing surveillance, 2 stents had to be replaced after 12 months due to ingrowth, the other 5 stents remained patent after up to 36 months. We observed 2 stent obstructions in one patient due to food which had to be removed gastroscopically.

Conclusion: EUS-GE can effectively reduce the symptom burden in patients with gastroparesis refractory to medical treatment.

Disclosure: Nothing to disclose.

PP0207

PEDIATRIC DEVICE-ASSISTED ENTEROSCOPY – INSIGHTS FROM A TERTIARY CENTER

F. Mendes¹, M. Martins¹, J. Afonso¹, T. Ribeiro¹, M. Marques¹, A.P. Andrade¹, E. Trindade², H. Cardoso¹, G. Macedo¹

¹Centro Hospitalar Universitário São João, Department of Gastroenterology, Porto, Portugal, ²Centro Hospitalar Universitário São João, Paediatrics Department, Porto, Portugal

Contact E-Mail Address: francisco.cnm@gmail.com

Introduction: Device-assisted enteroscopy (DAE) is the only exam capable of a panendoscopic diagnostic and therapeutic intervention in gastrointestinal tract. Despite the limited data, DAE appears to be a safe procedure in pediatric population. In fact, a few studies demonstrate the feasibility and safety of DAE in several clinical contexts, namely small bowel bleeding, polyposis syndromes or inflammatory bowel disease.

Aims & Methods: With this study, the authors aim to describe DAE experience, specifically balloon assisted enteroscopy, in a pediatric population of a tertiary center.

A unicentric retrospective study was performed in patients up to 18 years old undergoing DAE (either by antegrade or retrograde pathway), between January 2011 and February 2024.

Results: A total of 23 DAE exams from 16 patients were included in the study, 56% from the male gender. The study population had a medium age of 13 years (ranging from 4 to 18 years old). DAE was performed due

to polyposis syndromes in 8 cases (6 cases of Peutz-Jeghers syndrome and 2 cases of juvenile polyposis) and in suspicious cases of middle gastrointestinal bleeding in 8 patients (5 with melena and 3 with ferropenic anemia). There was a total of 17 antegrade DAE, 5 retrograde DAE and 1 intraoperative enteroscopy. 35% of the procedures were performed in an inpatient setting.

DAE had a diagnostic yield of 95%, identifying polyps in the small bowel or other locations, ulcers, small bowel stenosis and foreign body. A therapeutic procedure was performed in 56% of the cases, namely polypectomy, argon plasma coagulation and foreign body removal. A self-limited bleeding was observed in the first 24 hours after an antegrade DAE, solved without the need of an additional endoscopic or surgical procedure. DAE led to a modification in the clinical outcome in over 90% of the patients.

Conclusion: The present study confirms the safety profile of DAE in the pediatric population. In a cohort from a tertiary referral center, DAE led to therapeutic procedure in the majority of patients, without significant procedure related complications.

References:

1. Pennazio, Marco et al. "Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022." *Endoscopy* vol. 55,1 (2023): 58-95.
2. Di Nardo, Giovanni et al. "Enteroscopy in children." *United European gastroenterology journal* vol. 6,7 (2018): 961-969.

Disclosure: Nothing to disclose.

PP0208

EVEROLIMUS-COATED LASER-CUT SELF-EXPANDABLE METALLIC STENT SUPPRESSES STENT-INDUCED TISSUE HYPERPLASIA IN THE RAT GASTRIC OUTLET

C.E. Yun^{1,2}, Y. Park^{1,2}, S.H. Kim^{1,3}, D.H. Kim³, J.-H. Park^{1,2}

¹Asan Medical Center, Biomedical Engineering Research Center, Asan Institute for Life Sciences, Seoul, South Korea, ²University of Ulsan College of Medicine, Department of Convergence Medicine, Asan Medical Center, Seoul, South Korea, ³University of Ulsan College of Medicine, Department of Gastroenterology, Asan Medical Center, Seoul, South Korea

Contact E-Mail Address: ybeen9733@amc.seoul.kr

Introduction: Self-expandable metallic stents (SEMS) are commonly used to relieve malignant gastric outlet obstruction (GOO). However, SEMS with high radial force can cause tissue proliferation caused by mechanical injury. To overcome these problems, drug-eluting stents using antiproliferative drugs have been developed. Specially, everolimus have demonstrated efficacy in reducing restenosis rates in arteries, but their potential application in the gastrointestinal tract remains unexplored. Additionally, recent studies have reported that stents with thinner struts have a reduced risk of clinical restenosis compared to stents with thicker struts. However, the application of everolimus-coated laser-cut stents, which offer robust antiproliferative properties, has not yet been investigated or established in the gastrointestinal tract.

Aims & Methods: This study aims to investigate the efficacy and safety of everolimus-coated laser-cut SEMS in suppressing stent-induced tissue hyperplasia in a rat gastric outlet model.

Everolimus-coated laser-cut SEMS were prepared using ultrasonic spray technology, and the characteristics of the SEMS before and after coating process were evaluated. Twelve male rats were randomly divided into two groups: control (laser-cut SEMS, n = 6) and everolimus (everolimus-coated laser-cut SEMS, n = 6). The effectiveness of everolimus-coated laser-cut SEMS were assessed by comparing results of fluoroscopy, endoscopy, and histopathological analyses.

Results: Everolimus were uniformly coated onto the surface of the laser-cut SEMS and approximately 80% of everolimus was slowly released for a week. Stent placement was successful in all rats. Stent-induced tissue hyperplasia variables were significantly lower in the everolimus group compared to the control group (all $p < 0.05$). The luminal diameter was significantly larger in the everolimus group than in the control group ($p < 0.05$). The degrees of α -SMA-, Ki-67-, and BrdU-positive deposition were significantly lower in the everolimus group ($p < 0.001$), while the degree of TUNEL-positive deposition was significantly higher than in the control group ($p < 0.001$).

Conclusion: Everolimus-coated laser-cut SEMS effectively suppressed stent-induced tissue hyperplasia in a rat gastric outlet model. Local treatment with everolimu via laser-cut SEMS was safe and effective to maintain the stent patency and has therapeutic potential in the prevention of restenosis after stent placement in the gastrointestinal tract.

Disclosure: Nothing to disclose.

PP0209
OCCURRENCE AND RISK FACTORS OF MISSED CARCINOMA IN THE UPPER GASTROINTESTINAL TRACT (PEUGIC) 2013-2023 – RETROSPECTIVE OBSERVATIONAL STUDY

J. Langner¹, I. Mikoviny Kajzrlkova¹, P. Vitek^{1,2}, B. Horavova³, M. Chrostek⁴
¹Beskydy Gastrocentre, Department of internal medicine, Frydek-Mistek Hospital, Frydek-Mistek, Czech Republic, ²University of Ostrava, Faculty of Medicine, Ostrava, Czech Republic, ³Frydek-Mistek Hospital, Department of Pathology, Frydek-Mistek, Czech Republic, ⁴Frydek-Mistek Hospital, Department of Surgery, Frydek-Mistek, Czech Republic

Contact E-Mail Address: langnerjakub@gmail.com

Introduction: PEUGIC (Post-Endoscopy Upper Gastrointestinal Cancer) is defined as carcinoma in the upper gastrointestinal (GI) tract which was preceded by negative upper endoscopy in the last 3 years. According to current knowledge, the rate of PEUGIC is an important parameter of quality and should not exceed 10 %. The aim of this study was to evaluate the occurrence and risk factors of PEUGIC at non-university hospital in Frydek-Mistek (Czech Republic) between 2013 and 2023.

Aims & Methods: This is a retrospective analysis of the patients diagnosed with upper GI cancer from January 2013 to December 2023. The data analyzed included family history of upper GI cancer, indications of the examination, therapy, tumor location and histological type. Risk factors for PEUGIC were calculated using the Chi-squared test and Fisher's exact test, with $p < 0,05$ considered significant.

Results: During the study period, a total of 22727 gastroscopies were performed in total, and 122 patients were diagnosed with upper GI cancer (88 men and 34 women), including 35 esophageal tumors, 80 gastric tumors, and 7 duodenal tumors. Family history of upper GI tumor was reported in 10 patients. PEUGIC was identified in 12 patients (9,84%, 9 men and 3 women, mean age 69,25 years), including 6 in the esophagus, 5 in the stomach, and 1 in the duodenum. Two patients had early detection as part of adequate surveillance (Barrett's esophagus, post-polypectomy). Thus, we can evaluate 10 patients as true PEUGIC (8,20%). The rate of PEUGIC was 17,14 % (6/35) in the esophagus, 6,25 % (5/80) in the stomach, and 14,3 % (1/7) in the duodenum. Tumor location (for esophagus $p=0,086$, for stomach $p=0,065$, for duodenum $p=0,525$), histology (for adenocarcinoma $p=0,332$, for spinocelular cancer $p=0,402$, for neuroendocrine tumor $p=0,25$), male gender ($p=0,815$), or family history of upper GI tumor ($p=0,335$) were not statistically significant risk factors for detecting PEUGIC.

Conclusion: The overall rate of PEUGIC at our institution over the 11-year study period was 9,86 %, without early detected lesions as part of adequate surveillance, it was 8,20 %. Early detection of PEUGIC, which indicate poorer endoscopy quality, need to be distinguished from early detection of carcinoma within adequate surveillance.

Disclosure: Nothing to disclose.

PP0210
IMPACT OF USING SELF-ASSEMBLING PEPTIDE (PURASTAT) ON ANASTOMOTIC ULCERS – A MULTI-CENTER US EXPERIENCE

V. Oza¹, N. Mittal², C. Winchester¹, Y. Fazal³, A. Manver³, A. Goodman³, M. Girotra⁴, H. Khara⁵, S. Kothari⁶, T. Kothari^{7,7}
¹Bon Secours Mercy Health, Gastroenterology, Greenville, United States of America, ²University of Texas at Houston, Houston, United States of America, ³New York University Langone Medical Center, New York City, United States of America, ⁴Swedish Medical Center, Seattle, United States of America, ⁵Geisinger Medical Center, Danville, United States of America, ⁶University of Rochester, Gastroenterology, Rochester, United States of America, ⁷University of Rochester, Rochester, United States of America

Contact E-Mail Address: Veerubhai@gmail.com

Introduction: Treatment of gastrojejunal anastomotic ulcers, also known as marginal ulcers, is challenging, especially when established techniques such as proton pump inhibitor have failed.

Pura Stat, is a biocompatible transparent synthetic peptide hemostatic gel that is indicated for hemostatis of bleeding in small blood vessels or capillaries of the GI tract and vascular anastomoses. Our aim was to evaluate the feasibility of PuraStat in the setting of non-healing marginal ulcers when used in addition to proton pump inhibitor (PPI) therapy after failed standard therapies

Aims & Methods: We conducted a multi-center prospective case study of adult patients that underwent PuraStat application (3 ml) for marginal ulcers after failing multiple initial therapies with proton pump inhibitors for at least 8 weeks

Results: A total of 10 patients were included in the study. Patients who had an initial presentation of pain, nausea, anemia, with confirmed anastomotic ulceration seen on endoscopy were included. A total of 3mL of Pura-stat was applied on each of these patients' ulcers, and a repeat endoscopy was performed to evaluate ulcers at ~3months. 9 out of 10 patients showed healing of marginal ulcer on repeat endoscopy in 3 months, while one patient did not present for repeat endoscopy. 9 out of 10 patients showed clinical improvement in their symptoms (90%), and one patient did not show improvement in their symptoms.

Surveillance EGD 3 months post PuraStat	No. (%)
Healing of Marginal Ulcer	
Yes	9 (90)
No	0 (00)
No follow-up EGD	1 (10)
Improvement in Clinical Symptoms (Abdominal pain, nausea, GI Bleed)	
Yes	9 (90)
No	1 (10)

Table 1. Post-PuraStat application results.

Conclusion: PuraStat is an important useful addition to the therapeutic toolbox for the treatment of anastomotic ulcers. Our small prospective case series shows effectiveness in symptom relief as well as clinical healing of anastomotic ulcers. Larger randomized clinical trials are needed.

References: 1. Branchi F, Klingenberg-Noftz R, Friedrich K, Bürgel N, Daum S, Buchkremer J, Sonnenberg E, Schumann M, Treese C, Tröger

H, Lissner D. PuraStat in gastrointestinal bleeding: results of a prospective multicentre observational pilot study. *Surgical Endoscopy*. 2022 May;36(5):2954-61

2. Tian Y, Rogers AM. Marginal ulcer: diagnosis and treatment. *Clinical Algorithms in General Surgery: A Practical Guide*. 2019:827-9.

Disclosure: Nothing to disclose.

PP0211

WITHDRAWN

PP0212

WITHDRAWN

PP0213

COLONOSCOPY INDICATIONS ACCORDING TO EPAGE II CRITERIA

B. Soukaina¹, F. Amkhaoui¹, F. Haddad¹, F.Z. Elrhaoussi¹, M. Tahiri Joutei Hassani¹, W. Hliwa¹, B. Ahmed¹, W. Badre¹

¹Hospital University Center IBN ROCHD, Gastroenterology, Casablanca, Morocco

Contact E-Mail Address: bannanisoukaina@gmail.com

Introduction: The prescription of colonoscopies is constantly increasing for the screening and diagnosis of colorectal cancer, precancerous lesions, polyps, and adenomas. Sometimes, indications become excessive due to the availability of this examination on one hand and the fear of missing a neoplastic lesion on the other. The EPAGE II criteria (European Panel on the Appropriateness of Gastrointestinal Endoscopy) was developed to assess the relevance of colonoscopy indications and to rationalize its prescription.

The aim of our study was to evaluate the relevance of colonoscopy indications performed in our department according to EPAGE II criteria and to investigate a possible correlation between the appropriateness of the examination and the endoscopic result.

Aims & Methods: A retrospective study was conducted at a hepatogastroenterology department including all colonoscopies performed during the period from January 2022 to June 2023. The relevance of colonoscopy indications according to EPAGE II criteria was classified as appropriate, uncertain, or inappropriate.

Results: The relevance of the indication was evaluated in 406 colonoscopies. The sex ratio (Male / Female) was 1.15. The median age was 51 with an IQ [15.93]. Rectal bleeding represented the most frequently found indications (30%), followed by Crohn's disease (12.8%), then chronic diarrhea (11.1%). 49% of colonoscopies had satisfactory preparation (Boston ≥ 7). Colonoscopy was complete in 86% of patients, with catheterization of the terminal ileum in 36.2% of cases.

A significant endoscopic lesion was found in 63% of colonoscopies, represented mainly by inflammatory lesions of inflammatory bowel disease (20.7%) followed by neoplastic lesions (15.3%) of colorectal cancer, then polyps (10%), benign strictures (6.4%), and diverticulosis (5.7%).

Overall, colonoscopy indication was appropriate in 83.5% of cases, uncertain in 10.8%, and inappropriate in 5.7%. A significant endoscopic lesion was found in 63% of patients with an appropriate indication.

Conclusion: The indication for colonoscopies performed in our department was considered appropriate in more than 80% of cases, with rectal bleeding being the main indication.

Significant endoscopic lesions were mostly found in cases of appropriate indication, leading us to encourage the use of this software to regulate colonoscopy indications

References:

1. Ardit C et al ; EPAGE II Study Group. Appropriateness of colonoscopy in Europe (EPAGE II). Screening for colorectal cancer. *Endoscopy*. 2009 Mar;41(3):200-8. doi: 10.1055/s-0028-1119626. Epub 2009 Mar 11. PMID: 19280531.

2. Juillerat P et al. Appropriateness of colonoscopy in Europe (EPAGE II). Presentation of methodology, general results, and analysis of complications. *Endoscopy*. 2009 Mar;41(3):240-6. doi: 10.1055/s-0028-1119643. Epub 2009 Mar 11. PMID: 19280536.

3. Gimeno García AZ et al. Clinical validation of the European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE) II criteria in an open-access unit: a prospective study. *Endoscopy*. 2012 Jan;44(1):32-7. doi:10.1055/s-0031-1291386. Epub 2011 Nov 22. PMID: 22109649; PMCID: PMC4086891.

Disclosure: Nothing to disclose.

PP0214

GASTRIC ULCER FOLLOW UP - IS ONE LOOK ENOUGH?

M. Clarke¹, T. Sheehan¹, R. Connaughton¹, H. Kerr¹, A. Omar¹, C. Smyth¹, R.J Farrell¹, C. Egan¹, B. Hall¹, M.M. Elsiddig¹, O. Kelly¹

¹Connolly Hospital, Blanchardstown, Gastroenterology Department, Dublin, Ireland

Contact E-Mail Address: maeve.j.clarke@gmail.com

Introduction: Current guidelines recommend 12 week follow up for gastric ulcer surveillance. This represents a significant proportion of follow up oesophago-gastro-duodenoscopies (OGDs). Debate is ongoing regarding the need for universal endoscopic follow-up to ensure gastric ulcer healing.

Aims & Methods: **Aims:** We aimed to assess the value of follow-up OGD for gastric ulcer healing in Connolly Hospital Endoscopy Unit with regards to cancer diagnosis and the yield of index biopsies.

Methods: Patient endoscopy data for gastric ulcers diagnosed 2021-2023 via Endoraad were examined. All gastric biopsies including index biopsy of ulcers were reviewed. Time to repeat procedure was recorded.

Results: 147 documented diagnoses of gastric ulcers were identified for the study period (51% female, mean age 60.2). 56% (n=83) of ulcers were biopsied at index OGD. 6 (4% of total) malignancies were diagnosed at index biopsy with no malignancies diagnosed on repeat, chi sq., p = 0.02. 76% (n=111) had a repeat procedure, with 43% (n=63) meeting the target of 12 weeks. 16% (n=24) index biopsies taken were HLO positive. Following review of the images by three gastroenterology consultants; 26% (n=38) were deemed erosions rather than ulcers. Of those deemed ulcers their Forrest classification are as follows; 34% (n=50) Forrest 3, 8% (n=13) Forrest 2c, 2% (n=3) Forrest 2b, 2% (n=3) Forrest 2a and 6% (n=10) Forrest 1b. The remaining 20% of images (n=30) deemed not a gastric ulcer included: malignancy, healed ulcers and severe gastritis. Regarding findings at second scope, 20 patients (18.3%) had persistent ulceration, with no new malignancies identified. Of note, of those not followed, 95% were biopsied at index procedure and had benign features. The average time to repeat procedure was 9.7 weeks.

Conclusion: The Covid pandemic and HSE ransomware attack may have significantly contributed to delay in repeat procedures. However, the majority of patients had either index ulcer biopsies or repeat endoscopy performed. The cancer yield of FU-OGD after benign biopsies remains low. Strategies to reduce the burden of FU-OGD such as risk stratification approach using high quality index examination, ulcer features and index biopsies may aid selective patient follow-up, improve yield of repeat procedures and reduce burden on the patient and health service.

Disclosure: Nothing to disclose.

PP0215

WITHDRAWN

PP0216

EFFECT OF SELF-ASSEMBLING PEPTIDE HYDROGEL ON GASTRIC ULCER HEALING AFTER ENDOSCOPIC MUCOSAL RESECTION IN PIGS

S. Hayasaka¹, S. Ono², Z. Yang^{1,3}, K. Yamamoto², E. Ishibe¹, H. Egami¹, S. Nakajima¹, M. Higashino¹, M. Inoue², S. Miyamoto¹, M. Ono¹, N. Sakamoto¹

¹Hokkaido University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ²Hokkaido University Hospital, Department of Gastroenterology, Sapporo, Japan, ³The First Affiliated Hospital of Sun Yat-Sen University, Department of Gastroenterology, Guangzhou, China

Contact E-Mail Address: mtda.hum@gmail.com

Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are both standard endoscopic treatments for early-stage gastrointestinal tumors. Submucosal fluid injection is an important part of endoscopic procedure, increasing the space between the lesion and the muscle layer and enabling easy and safe resection. Recently, PuraLift™ (3-D Matrix Ltd, Tokyo, Japan), a novel submucosal injection solution made from self-assembling peptide hydrogel (SAP) was developed in Japan. SAP is fully synthetic and consists only of amino acids present in the human body, giving it the advantages of biodegradability and biocompatibility over conventional solutions.

In addition, the 3D structure of the hydrogel supports cell proliferation in vitro, and self-assembling peptide hydrogel (SAPH) may promote wound healing. However, there are no reports on the effect of SAPH on ulcer healing after endoscopic resection.

Aims & Methods: The aim of this study was to assess the effect of SAPH on wound healing after endoscopic resection. EMR procedures were performed in the stomach of 4 living pigs with 3 patterns of submucosal injection solution; normal saline injection group (NS); sodium alginate injection group (SA); PuraLift™ injection group (SAPH). Each pig received 3 separate submucosal injections with 3 mL of the different solutions and then EMR was performed using a 15mm diameter snare. Immediately after EMR (W0) and on week 1(W1) and week 2(W2), we measured the ulcer diameter endoscopically using a measuring device. On week 3(W3) after EMR, all pigs were sacrificed and necropsied by en-bloc gastrectomy, followed by macroscopic measurement of ulcer diameter. All wound sites of the resected specimens were examined histopathologically by haematoxylin and eosin (HE) and Masson's trichrome (MT) and immunohistochemistry staining (α SMA, CD3, CD 31, CD107a). The ulcer reduction rate was calculated as follows: [(ulcer diameter at W0) - (ulcer diameter at week X)] / (ulcer diameter at W0) x 100(%). Ulcer epithelialisation and submucosal foreign bodies were assessed by HE staining, tissue damage in the muscle layer and the thickness of the fibrotic layer by MT staining. Five random fields at each wound site were photographed, and the average rate of positive areas by immunostaining in each injection solution group was calculated.

Results: Ulcer reduction rate at W1 was higher in SAPH group and SA group than NS group (24.1±13.5%; 24.6±17.9%; -6.9±7.6%; p<0.05), but there were no significant differences at W2 and W3 among three groups. Complete epithelialisation of the ulcer occurred in all except one case of NS group. In SA group, all four cases showed residual injection solution in the submucosal layer with foreign body giant cell reaction and fibrous tissue growth. In contrast, in SAPH group, only one case showed a focal foreign body giant cell reaction without residual injection solution. The thickness of the fibrotic layer is greater in SA group than SAPH and NS

groups (SA: 4.2±0.8mm, SAPH: 1.6±0.4mm, NS: 2.0±1.2mm, p<0.05). Tissue damage was not observed in either group. There were no differences in the rates or positive area of α SMA, CD3 and CD31 staining between groups. In contrast, the rates of positive area of CD107a staining were significantly higher in SA group than SAPH and NS group (SA: 13.9±1.0%, SAPH: 5.7±2.2%, NS: 1.2±2.1%, p<0.001), indicating a high degree of macrophage accumulation.

Conclusion: SAPH induced good healing after EMR and was more biodegradable and biocompatible than sodium alginate.

Disclosure: Nothing to disclose.

PP0217

SAFETY, EFFICACY AND CARBON FOOTPRINT OF A CAPSULE SPONGE PATHWAY IN PATIENTS WITH REFLUX - A 3YR FOLLOW-UP

D. Angel¹, K. Shaw¹, F. Cole¹, K. Mohanathass¹, D. Corrigan¹, D. Morris¹

¹East and North Hertfordshire NHS Trust, Gastroenterology and Hepatology, Stevenage, United Kingdom

Contact E-Mail Address: dylan.angel@nhs.net

Introduction: With the need to reduce the burden of endoscopy, capsule sponge enables cost effective and efficient triage for patients with reflux as shown in the National Health Service England (NHSE) pilot study whilst achieving a smaller carbon footprint in comparison to gastroscopy. Negative sponge follow up has yet to be reported. Using the largest single UK site database, we describe 1, 2 and 3 year follow up and quantify the effect of gastroscopy avoidance on the endoscopic carbon footprint.

Aims & Methods: Patients routinely referred between November 2020 and November 2023 to gastroscopy or gastroenterology clinic with reflux were selected as part of the DELTA or NHSE pilot studies and triaged to a new nurse led early diagnosis teleclinic where they were first offered a capsule sponge. Patients with positive tests, (Trefoil factor 3 TFF3 and/or atypia/p53 positivity indicating possible Barrett's/gastric intestinal metaplasia or dysplasia respectively) all underwent mandatory gastroscopy and were excluded from this analysis. In the event of a negative test, nurse led teleclinic follow up occurred by 3 months and gastroscopy was only requested for ongoing/concerning symptoms. The endoscopy database for patients with a negative capsule sponge was reviewed at 1, 2 and 3 year intervals to review if gastroscopy had occurred and what findings were identified.

Results: At the 1, 2 and 3 year follow up intervals, 429 and 204 and 41 patients were identified respectively. 86% of the 1 year follow ups (n=371) had not represented for a gastroscopy. The most frequent findings in the 14% (n=57) who did undergo gastroscopy were gastritis (n=14), hiatus hernia (n=9) and normal (n=16).

The most significant finding in this cohort was one case of gastric cancer, identified two weeks post capsule due to new concerning symptoms. In total 371 gastroscopies were avoided in year 1, equating to 42294L of water and 1846 kgeCO₂. Of the 204 2 year follow up group, 92% (n=187) had not had a gastroscopy.

There was no significant pathology (including Barrett's) identified in any of the remaining 8% (n=17) and the most common endoscopic conclusion in this cohort was normal. Only 2/17 patients underwent their gastroscopy in the second year of follow up.

Finally, of the 41 patients with a negative capsule sponge available to review at 3 year follow up, 21% (n=9) had undergone a gastroscopy however only 3 of these had been performed in year 3 and they were all normal. Importantly, no patient who represented for OGD at any of the intervals after a negative capsule sponge were found to have Barretts.

Conclusion: Over 1, 2 and 3 year follow up periods, our study provides reassuring data from the largest UK capsule sponge site. Our data shows

that capsule sponge safely excluded significant upper GI pathology in a less invasive manner, enabling symptomatic management without necessitating gastroscopy in the majority of patients. Nurse led teleclinic safety netting proved effective in identifying patients needing additional investigations whilst reducing the number of gastroscopies performed. This has helped improve endoscopy access overall, whilst also tackling the growing concern surrounding the endoscopic carbon footprint. Our study supports a new paradigm for the investigation of reflux symptoms which can be incorporated in both community and secondary care pathways.

References: Greenhouse gas reporting: conversion factors 2022. GOV.UK. Published September 20, 2022. Accessed January 26, 2023. <https://www.gov.uk/government/publications/greenhouse-gas-reporting->

Disclosure: Nothing to disclose.

PP0218

AUGMENTED PRO-MOTILITY PROTOCOL FOR PATIENTS WHO PREVIOUSLY FAILED PATENCY CAPSULE IS SAFE AND EFFECTIVE

T. Borkovksy^{1,2}, T. Thurm^{2,1}, N. Maharshak^{2,1}, L. Deutsch (Mlynarsky)^{2,1}

¹Tel Aviv Sourasky Medical Center, Department of Gastroenterology and Hepatology, Tel Aviv, Israel, ²Tel Aviv University, Faculty of Medicine and Health Sciences, Tel Aviv, Israel

Contact E-Mail Address: tombor@tlvmc.gov.il

Introduction: A patency capsule (PC) test is advised before video capsule endoscopy (VCE) to prevent capsule retention in high-risk patients. Although up to 30% of patients cannot expel the PC within 30 hours and are ineligible for VCE, those without strictures, but with slow transit time, can safely undergo VCE. Currently there are no recommendations regarding PC protocol.

Aims & Methods: In this prospective cohort study, we aimed to evaluate the success rate of a 2nd PC attempt with augmented pro-motility preparation protocol, in patients who previously failed to pass PC and to ascertain the risk factors for failure in PC test.

During 2019-2023, Patients who failed their initial PC test in our referral center were offered to undergo a 2nd augmented pro-motility bowel preparation protocol (Table 1). Exclusion criteria: age<18 years, total colectomy or ileostomy and inability to sign informed consent. Patients were followed during the 2nd PC test and the subsequent VCE for success rates and safety outcomes, i.e. VCE retention. Demographic and clinical characteristics were collected for assessing potential risk factors for 1st PC failure and successful 2nd PC by multivariate regression analysis.

		Pro-motility protocol 1 st PC	Augmented pro-motility protocol 2 nd PC
-2 day	All day	Low residue diet	
	12:00-20:00	Clear liquid diet	
-1 day	14:00	-	Bisacodyl 10mg
	19:00-21:00	-	PEG 3350 1.5L
	20:00-till PC ingestion	Fasting	
	Morning	PC ingestion + Bisacodyl 10mg	
PC day	2hours post-ingestion	Drink clear liquids	
	4 hours post ingestion	A light meal	
+1 day	30 hours post ingestion	X-ray or confirmed expulsion	

Table 1: Patency Capsule Preparation Protocols

PC, patency capsule; PEG3350, Poly-ethylene Glycol

Results: A total of 396 patients performed a PC test and were included in the study (age 45.4±18.6 years, male gender 47.7%). The indications for VCE were suspected/established Crohn's disease (86.1%); anemia/bleeding (8.3%) and radiologic findings (5.6%).

Successful PC expulsion was documented in 323 (81.6%) patients, while 73 (18.4%) failed. A 2nd attempt with augmented pro-motility protocol was accepted by 35/73 patients (48%) and rejected by 38/73 patients (52%). no clinico-demographic differences between the groups.

Successful 2nd PC attempt was documented in 20/35 patients (57%), with all of them completing VCE without adverse events. Failed 2nd PC was documented in 15/35 patients (43%) without adverse events, while 3/15 performed tandem abdominal CT confirming PC in colon (i.e false failure) followed by uneventful VCE.

Performance of a 2nd PC attempt reduced the failed PC rate by 57% (Absolute risk reduction) and the number needed to treat (NNT) is 1.8 for a successful 2nd attempt. Multivariate regression for success with 2nd PC vs. 1st PC was limited by small numbers.

However, diabetes mellitus showed a trend as a risk factor (9.6% in 1st PC test success vs. 20% in 2nd PC test success, OR 3.7, p=0.057, adjusted for age, gender, BMI and stools/day).

Conclusion: In this prospective cohort study, a novel augmented pro-motility PC test preparation protocol improved the success rate in patients who previously failed an initial PC test, without any adverse events. Subsequent abdominal CT should be considered in selected cases to further reduce false positive results. Patients with diabetes mellitus might benefit from performing the augmented protocol upfront, but further large-scale studies are required to establish that.

Disclosure: Nothing to disclose.

PP0219

INCRETIN EFFECT DURING A LOW-CALORIE MIXED BREAKFAST SMARTPILL® INVESTIGATION: TIMING OF POST-PRANDIAL METABOLIC HORMONE AND GLUCOSE CHANGES IN HEALTHY VOLUNTEERS

M.A. Halim¹, D. Javidi¹, P. Kalamees¹, M.u. Din¹, H.O. Diaz Tartera¹, P.M. Hellström¹, D.-L. Webb¹

¹Uppsala University, Gastroenterology & Hepatology, Medical Sciences, Uppsala, Sweden

Contact E-Mail Address: dominic-luc.webb@medsci.uu.se

Introduction: The "incretin effect", the concept that gut hormones amplify insulin secretion, has been around for decades. In the 1960's, it was discovered that oral glucose leads to greater circulating insulin response than IV glucose (1). This was later attributed to gut hormones, such as GLP-1 and GIP. Activation of their receptors on pancreatic β-cells raises cAMP, accounting for amplified insulin secretion. This study aimed to determine if incretin and related metabolic analytes consistent with the incretin effect are detectable during SmartPill® wireless motility capsule (WMC) investigations. These increasingly common investigations represent a convenient resource to study metabolism and relate this to gut physiology.

Aims & Methods: Healthy volunteers (n=41) arrived following overnight fasting. They consumed a standardized 270 kcal mixed meal breakfast. Details of methods including validation of motility data have been published (2). Blood was tapped -10, 0, 10, 20, 30, 40, 50, 60, 90, 120, 180 and 240 min into the meal. Protease inhibitors, including DPP4 inhibitor KR-62436, were added and plasma was prepared. Glucose was measured by the clinical chemistry unit. Active GLP-1, total GIP, acyl-ghrelin and insulin were measured by multiplex ELISA (MesoScale Discovery, USA). Glucagon was measured by ELISA (Mercodia, Sweden). Statistics for comparing pairs of peak or trough timing was done by rank-sum test. Data is presented as median ±SD.

Results: Following meal ingestion, the GLP-1 peak (30 ± 11 min) preceded those of glucose (40 ± 16 min), insulin (40 ± 12 min) and GIP (50 ± 26 min) (p<0.01, all comparisons). Glucose peaked about same time as insulin and before GIP (p<0.01).

However, the rising phase of insulin and GIP overlapped somewhat, with no statistical difference in time to peak. GLP-1 peaked before insulin in 68% (28/41) of subjects, at the same time in 29% (12/41) of subjects, and after insulin in only 2% (1/41) cases in which insulin appeared to peak at 10 min and GLP-1 at 30 min. GIP peaked before insulin in 20% of subjects (8/41), at the same time as insulin in 49% of subjects (20/41), and after insulin in 32% of cases (13/41). Ghrelin and glucagon deflected downward at 30 min. Ghrelin reached trough at 60 ± 31 min, which was later than peaks of GLP-1 (p<0.01), glucose (p<0.01), insulin (p<0.01) and GIP (p<0.05). Glucagon reached trough at 55 ± 44 min, which was also later than peaks of GLP-1 (p<0.01), glucose (p<0.01), insulin (p<0.01) and GIP (p<0.05). GLP-1 peaked before glucagon reached trough in 95% of cases (38/40)(p<0.01) and at the same time or after glucagon in only 5% (2/40) of cases. GIP peaked before glucagon reached trough in 75% (30/40) of cases (p<0.01). Expulsion of the WMC from the stomach (gastric emptying time 185 ± 72 min) occurred after all peaks and troughs were reached in 95% (39/41) of subjects (p<0.001).

Conclusion: GLP-1 rise to peak is detectable as an early event during SmartPill® WMC investigation, usually preceding peaks or troughs of any of the other analytes. This is consistent with GLP-1 raising intracellular cAMP in pancreatic β-cells to prime them for insulin secretion. GIP rise to peak trails GLP-1, implying a later, prolonged action that parallels insulin. Ghrelin and glucagon start to decline when GLP-1 peaks, tending to reach trough after other hormones peak. Studies of these events require blood taps at a number of time points during a meal.

References:

1. Unger RH & Eisentraut AM. Arch Intern Med. 123(3):261–6. 1969
2. Diaz Tartera HO, et al. Neurogastroenterol Motil. 29(10):e13107:1-9. 2017

Disclosure: Nothing to disclose.

PP0220

COMPARATIVE EVALUATION OF ATMO GAS CAPSULE SYSTEM AND SMARTPILL GI MONITORING SYSTEM FOR TRANSIT TIME ASSESSMENT IN MOTILITY DISORDERS

B. Kuo¹, A. Lee², T. Abell³, A. Attaluri⁴, M. Cline⁵, W. Hasler⁶, V. Ho⁷, A. Lembo⁵, A. Masoud⁸, R. McCallum⁹, B. Moshiree¹⁰, E. Quigley¹¹, S. Rao¹², M. Sanchez⁸, I. Sarosiek⁹, A. Stocker³, B. Surjanhata¹, J. Zhou⁷, W. Chey²

¹Massachusetts General Hospital, Boston, United States of America, ²University of Michigan, Ann Arbor, United States of America, ³University of Louisville, Louisville, United States of America, ⁴Alliance for Multispecialty Research, Kansas, United States of America, ⁵Cleveland Clinic, Cleveland, United States of America, ⁶Mayo Clinic, Scottsdale, United States of America, ⁷Western Sydney University, Campbelltown, Australia, ⁸Hartford Health, Fairfield, United States of America, ⁹Texas Tech University, El Paso, United States of America, ¹⁰Atrium Health Wake Forest Medical University, Charlotte, United States of America, ¹¹Houston Methodist Research Institute, Houston, United States of America, ¹²Augusta University, Augusta, United States of America

Contact E-Mail Address: bkuo@mgh.harvard.edu

Introduction: Motility disorders, such as gastroparesis and slow transit constipation (STC), are common gastrointestinal (GI) conditions affecting up to 5% of individuals worldwide. The symptoms of motility disorders can be debilitating, affecting quality of life and driving utilisation of healthcare systems. Diagnosis relies on evaluation of regional transit times, with delayed gastric and colonic transit indicated for gastroparesis and STC, respectively. The SmartPill GI Monitoring System (SmartPill), an

FDA-cleared wireless motility capsule (WMC), has been used in the assessment of gastroparesis and STC since 2008 but has recently been discontinued, leaving a need for a like replacement.

This study aimed to assess a new WMC, the Atmo Gas Capsule System (Atmo Capsule), against SmartPill for the assessment of regional transit times in these conditions.

Aims & Methods: Individuals with upper, lower, or overlapping GI symptoms were recruited in a prospective multi-centre study. Participants concomitantly ingested the Atmo Capsule and SmartPill in a randomized order. Regional transit times including Gastric Emptying Time (GET) and Colonic Transit Time (CTT) were measured and compared between the devices, where paired data were available. GET >5 hours and CTT >59 hours were defined as delayed.

Results: 213 participants (median age 41 [range 20-77], 188 female) were recruited across 12 sites: 177 yielded paired GET results, and 147 for CTT. Pearson correlation coefficients for GET and CTT comparisons between Atmo Capsule and SmartPill were 0.86 (0.81-0.89) and 0.74 (0.66 – 0.81) respectively. GET demonstrated a positive predicted value (PPV) of 78.00% (SE: 5.86%), negative predictive value (NPV) of 85.83% (SE: 3.09%), and overall agreement (OA) of 83.62% (SE: 2.78%). For CTT, PPV was 67.35% (SE: 6.70%), NPV was 92.89% (SE: 2.60%), and OA was 84.35% (SE: 3.00%). No serious adverse device events were reported. 32.2% of the total GET evaluable cohort had delayed GET, 27.2% of the CTT evaluable cohort had delayed CTT. For the cohort that had measurements for all transit regions (n=142), 20% had delayed CTT only, 11% had delayed GET only and 18% had a delay in multiple GI regions as measured by the Atmo capsule.

Regional Transit Times		Atmo Result	SmartPill Result	Pearson Correlation
		Mean (SD) hours	Mean (SD) hours	P-value
	GET (n=177)	3.84 (1.57)	4.05 (1.45)	<0.0001
	SBTT (n=183)	5.13 (2.56)	5.18 (2.23)	<0.0001
	CTT (n=147)	47.01 (29.67)	41.79 (27.73)	<0.0001
Multi-regional transit delays as determined by Atmo Capsule	Overall (n=142)	No regional delay	62 (43.7%)	
		Single region delay	55 (38.7%)	
		Multi-region delay	25 (17.6%)	
	Single region delay only (n=55)	GET	16 (11.3%)	
		SBTT	10 (7.0%)	
		CTT	29 (20.4%)	
	Multi-region delay (n=25)	GET & SBTT	6 (4.2%)	
Safety		GET & CTT	9 (6.3%)	
		SBTT & CTT	6 (4.2%)	
		All regions	4 (2.8%)	
	Adverse events related to study devices	17 (8.1%): Abdominal Pain: 1 (0.47%), Capsule Retention: 15 (7.1%), Headache: 1 (0.47%)		
	Serious adverse device effects	0 (0%)		

Conclusion: The Atmo Capsule exhibited substantial agreement with SmartPill in measuring both GET and CTT, highlighting its utility as a potential replacement for the discontinued SmartPill for assessment of motility disorders. Nearly 1 in 5 patients studied had delayed upper and lower transit times highlighting the benefit of evaluating multiple regions of the GI tract with a single test.

Disclosure: Nothing to disclose.

PP0221

USE OF A NOVEL PHOTOMETRIC CAPSULE IN SUSPECTED NONVARICEAL UPPER GASTROINTESTINAL BLEEDING - A PROSPECTIVE MULTICENTER STUDY

M. Brand¹, G. Vogt¹, A. Weich¹, A. Hann¹, T. Kudlich¹, M. Weber², E. Wedi², A. Kuellmer³, A. Schmidt⁴, T. Brunk⁵, A. Meining¹

¹University Hospital Wuerzburg, Medical Department II - Gastroenterology, Wuerzburg, Germany, ²Sana Klinikum Offenbach, Gastroenterology, Gastrointestinal Oncology and Interventional Endoscopy, Offenbach, Germany, ³University of Freiburg, Faculty of Medicine, Department of Medicine II, Medical Center, Freiburg, Germany, ⁴Robert Bosch Hospital, Department of Gastroenterology, Stuttgart, Germany, ⁵Hospital Friedrichshain, Department of Internal Medicine and Gastroenterology, Berlin, Germany

Contact E-Mail Address: Hann_A@ukw.de

Introduction: In accordance to current European guidelines, an emergency endoscopy in hemodynamically stable patients with suspected nonvariceal, upper gastrointestinal bleeding (nvoGI bleeding) should be performed within the first 24 hours. This practice consumes scarce human resources, especially at weekends. A recently available photometric capsule enables a prompt, non-invasive assessment of blood or haematin in the gastrointestinal tract.¹

Aims & Methods: We investigated whether this capsule is a proficient tool to identify patients for whom an emergency endoscopy (within 24h) can be avoided.

A total of 73 patients with suspected hemodynamically stable nvoGI bleeding were included at four different sites using the photometric capsule. Capsule data were assessed after 120 minutes. All patients with a positive capsule result (bleeding index, HI $\geq$ 1) underwent an upper gastrointestinal endoscopy within 12 hours (Group A). Patients with a negative result (HI<1.0) received a proton pump inhibitor at a standard dose twice daily and underwent endoscopy within 48 to 96 hours (Group B). If clinical or laboratory signs of acute bleeding became apparent in the meantime, an early endoscopy (within 12h) was performed.

Results: Mean modified Glasgow-Blatchford score (mGBS) was 8.9 for all 73 patients. Among the 41 patients of Group B, two patients (4.8%) received early endoscopy due to persistent hypotension (<90mmHg syst.) (1x cardiac tumor, 1x Forrest III ulcer, both without active bleeding). Two patients received no endoscopy (1 patient refused, 1 patient suffered from a stroke).

Active bleeding was excluded in the remaining 37 patients (sensitivity regarding active bleeding = 100%, negative predictive value = 100%). In Group A, (n=32), emergency endoscopy was performed on average within 2.7 h and detected active bleeding sources in nine patients (28.1%). There were no technical, capsule-associated or bleeding-associated complications as assessed within 30 days of follow-up.

Group	B (capsule negative)	A (capsule positive)	p-value
number	41	32	
mGBS	8.45 $\pm$ 2.9	9.3 $\pm$ 3.1	n.s.
anticoagulation	25 (61.0%)	19 (59.4%)	n.s.
mean time to endoscopy (EGD)	65.0h (21-97)	2.7h (0.25 - 18)	<0.05
active bleeding in EGD	0 (0%)	9 (28.1%)	<0.05

Conclusion: Due to the very high negative predictive value in detecting active upper GI-bleeding, the applied novel photometric capsule can reliably identify patients in whom emergent endoscopy is not necessary.

References: ¹Schmidt et al. Endosc Int Open 2019 Jun;7(6):E774-E781. doi: 10.1055/a-0880-531

Disclosure: M. Brand: Ovesco: study funding.

A. Meining: Ovesco: consultant.

A. Kuellmer: Ovesco: lecture fees, study funding.

A. Schmidt: Ovesco: lecture fees, study funding.

PP0222

PASSING YOUR PATENCY TEST: DO PRUCALOPRIDE AND FASTING MAKE A DIFFERENCE?

D. Alsharqi¹, P. Maligaya¹, S. Ismail¹, E. Gibbons², L. Keating², B. Hall², E. Coughlin³, M. Ferry³, V. Parihar³

¹Beaumont Hospital, Dublin, Ireland, ²Connolly Hospital Blanchardstown, Dublin, Ireland, ³Letterkenny University Hospital, Gastroenterology, Letterkenny, Ireland

Contact E-Mail Address: Dana_alsharqi@hotmail.com

Introduction: Capsule endoscopy (VCE) is generally safe, however a subset of patients require confirmation of bowel patency before undergoing the procedure, using a self-dissolvable patency capsule of similar calibre to the video capsule, with interval imaging to confirm excretion. Patency capsule absence on imaging confirms bowel patency. Prucalopride, a 5-HT₄ agonist that enhances bowel motility, has been used in VCE to improve completion rates¹, but its use in the context of patency testing remains unknown. Similarly, the role of fasting in improving pass rate is unclear.

Aims & Methods: This study aims to determine whether Prucalopride and fasting enhance the pass rate of patency tests. Data from procedures performed in 3 centers in the Republic of Ireland was reviewed retrospectively. We compared the pass rate in the context of Prucalopride (Group A), fasting (B), and non-fasting (C) states. All patients had an abdominal x-ray between 24-30 hours post-patency capsule ingestion to confirm passage. ANOVA test was used to compare means between all groups, and student t-test between individual groups.

Results: A total of 127 patients were included. Group A (Prucalopride): 59 patients, Group B (fasting, no Prucalopride): 22 patients, Group C (non-fasting, no Prucalopride): 46 patients.

Demographics:

Group A: 47.5% males and 52.5% females, Group B: 45.5% males and 54.5% females, Group C: 32.6% males and 67.4% females

Mean age – Group A: 50.3 years (range 18-82), Group B: 48.4 years (24-82), Group C: 47.9 (17-79).

Indication based on European Society of Gastrointestinal Endoscopy guidelines

Appropriate: 80 (63%)

Inappropriate: 35 (27.6%)

Undocumented: 12 (9.4%)

Pass Rate:

Group A: 36/59 (61%), Group B: 17/22 (77%), Group C: 19/46 (67%).

ANOVA test f-ratio 4.55, p=0.012.

T-test: Group A vs B (61% vs 77%, p=0.087). A vs C (61%vs 67%, p=0.023), B vs C (77% vs 67%, p=0.002).

Group	Description / Intervention	Male	Female	Mean Age (Range)	Pass Rate
A	Prucalopride	47.5%	52.5%	50.3 years (18-82)	36/59 (61%)
B	No Prucalopride, fasting	45.5%	54.5%	48.4 years (24-82)	17/22 (77%)
C	No Prucalopride, non-fasting	32.6%	67.4%	47.9 years (17-79)	19/46 (67%)

Conclusion: This study shows that fasting improves patency tests pass rates, but Prucalopride does not. Fasting and subsequent patency capsule ingestion promoting the gastro-ileal reflex is a possible explanation. It is

unclear in this study why Prucalopride, a prokinetic and laxative, failed to show an improvement in pass rates despite being shown to improve VCE completion rates in other studies. Longer duration of Prucalopride at split intervals is a potential area for further studies.

References:

1. Deding U, Kaalby L, Baatrup G, Kobaek-Larsen M, Thygesen MK, Epstein O, et al. The effect of prucalopride on the completion rate and polyp detection rate of colon capsule endoscopies. *Clinical Epidemiology* 2022;Volume 14:437–44. doi:10.2147/clep.s353527.

Disclosure: None.

PP0223

EVALUATION OF “PATENCY AT HOME” PILOT PROGRAM; SUCCESS, SATISFACTION AND SAVING

G. Madders¹, R. Grainger¹, C. Costigan¹, D. McNamara¹

¹Tallaght University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: gillianmadders@gmail.com

Introduction: Capsule retention is the major risk associated with Video Capsule Endoscopy (VCE) with a frequency reported between 2-8% depending on indication. To mitigate this risk, a Patency Capsule (PC) is used to confirm functional patency of the GI tract. Ingestion of a dissolvable capsule followed by plain film radiography 28 hours post ingestion confirms patency. We established a pilot “Patency at Home” programme with the goal of providing a more efficient service for both patients and the hospital.

Aims & Methods: The aim of this study was to evaluate the pass rate of the service as well as patient satisfaction and cost saving. Patients referred for VCE between October 2023 and March 2024 were randomly selected to undergo a home patency test. Pre-assessment for VCE by phone call was carried out prior to postage of the home patency test kit. Written instructions were provided in the kit and an X-ray for a designated day was booked. Questionnaires to evaluate patient experience were included in the testing kit and returned on the day of X-ray. Follow-up phone calls were also offered to those who did not submit questionnaires.

Results: A total of 53 home patency tests were carried out. 68% of referrals were female (n=36). Suspected Crohn's Disease was the most frequent indication for VCE (36%, n=19). NSAID exposure was the most common reason for PC (30%, n=16). The pass rate in this study was 45%, similar to our institution's reported pass rate for hospital patency testing. 96% of patients felt home testing was logistically easier and 94% would choose home patency testing if offered a choice. A cost of €129 per patient visit was offset by this program, totalling a saving of €6,837.

Conclusion: “Patency at Home” is an effective and agreeable method for confirming functional patency of the GI tract prior to VCE. Pass rates in home patency testing proved to be similar to those achieved for hospital patency testing. The programme was cost effective with a saving of €129 per patient visit.

References: Patency testing improves capsule retention rates but at what cost? A retrospective look at patency testing. F.O'Hara, C.Walker, D.McNamara, *Front. Med.*, 09 August 2023

Sec. Gastroenterology Volume 10 - 2023

Disclosure: Nothing to disclose.

PP0224

SAFETY AND FEASIBILITY OF MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY IN CHILDREN

H. Yang¹, S. Liu², F. Wang², Y. Fang²

¹Xi'an Children's Hospital, Department of Gastroenterology, Xi'an, China, ²Xi'an Children's Hospital, Department of Gastroenterology, Xi'an, China

Contact E-Mail Address: liushan92263@163.com

Introduction: In recent years, Magnetically controlled capsule endoscopy (MCE) has become increasingly popular in the diagnosis of gastrointestinal diseases in children. This study aims to investigate the safety and feasibility of MCE in the diagnosis of gastric and small intestinal diseases in children by retrospective investigation of the application of MCE in Xi'an Children's Hospital in a single center.

Aims & Methods: The data of 109 patients who underwent MCE in Xi'an Children's Hospital from September 2022 to May 2023 were retrospectively analyzed. The general condition, clinical manifestations, completion of gastric and small intestinal examinations, detection of lesions and adverse events of all patients were statistically analyzed.

Results: A total of 109 patients were enrolled in this study, including 56 males (56/109, 51.4%) and 53 females (53/109, 48.6%). The age ranged from 6 to 18 years (mean, 9.9 years). There were 94 outpatients (94/109, 86.2%) and 15 inpatients (15/109, 13.8%). The main indications for MCE examination were abdominal pain (102/109, 93.6%), nausea, vomiting and acid reflux (46/109, 42.2%), abdominal distension (31/109, 28.4%) and anorexia (3/109, 2.7%). Among them, 59 patients (59/109, 54.1%) underwent gastric examination, and 50 patients (50/109, 45.9%) underwent gastric and small intestine combined examination. The completion rate of both examinations was 100% (the capsule reaching the ileocecal junction during the battery life was defined as completion). A total of 91 cases (91/109) of gastric lesions were detected, and the detection rate of lesions was as high as 83.5%. The main manifestations were gastritis, erosion, bile reflux and reflux esophagitis. Nine cases (9/50) of small intestinal lesions were detected, and the detection rate of lesions was 18.0%. The main manifestations were mucosal erosion, ulcer, lymphangiectasis and villous atrophy. The capsule excretion time of all patients was within 1-10 days, and no adverse events such as abdominal pain, hematochezia and capsule retention occurred during the period.

Conclusion: MCE is feasible and safe in the diagnosis of gastric and small intestinal lesions in children. The main indication of MCE in children is abdominal pain. However, most of the abdominal pain in children is caused by functional factors. MCE has great advantages in the exclusion diagnosis of organic diseases in these children because of its safety, non-invasive examination, no need for anesthesia and outpatient examination.

Disclosure: Nothing to disclose.

ENDOSCOPIC LUMINAL IMPEDANCE PLANIMETRY OF THE LOWER OESOPHAGEAL SPHINCTER AND PYLORUS IN EXPERIMENTAL PIGS: A PILOT STUDY. METHODS AND INITIAL EXPERIENCE

J. Bures¹, V. Radochova², D. Kohoutova³, M. Zavoral¹, K. Hugova⁴, S. Suchanek¹, O. Soukup⁵, J. Martinek⁴
¹Charles University First Faculty of Medicine and Military University Hospital Prague, Institute of Gastrointestinal Oncology, Prague, Czech Republic, ²University of Defence, Military Faculty of Medicine, Animal Laboratory, Hradec Kralove, Czech Republic, ³The Royal Marsden NHS Foundation Trust, London, United Kingdom, ⁴Institute of Clinical and Experimental Medicine, Department of Hepatogastroenterology, Prague, Czech Republic, ⁵University Hospital Hradec Kralove, Biomedical Research Centre, Hradec Kralove, Czech Republic

Contact E-Mail Address: bures.jan@uvn.cz

Introduction: The functional lumen imaging probe (FLIP) relies on the principle of impedance planimetry that enables direct measurement of intraluminal cross-sectional areas, allowing the assessment of intraluminal diameters, lumen geometric profiles, and wall biomechanical properties. Electrical impedance refers to the opposition to alternating current presented by the combined effect of resistance and reactance in a closed circuit.

Planimetrics is the study of plane measurements, including distances and areas. Since the early 2000s, impedance planimetry has been introduced into clinical practice, allowing principally assessment of any sphincter function / dysfunction.

In humans, the functional lumen imaging probe is applied mostly to diseases of the oesophagus (achalasia, dysphagia, gastro-oesophageal junction outflow obstruction, eosinophilic oesophagitis, gastro-oesophageal reflux disease), pyloric distensibility (gastroparesis), and ano-rectal disorders (faecal incontinence).

The physiology of the gastrointestinal tract of pigs is similar to that of humans, and therefore porcine experimental models are suitable for various endoscopic and preclinical studies.

Aims & Methods: Aims: The aim of our pilot project was to introduce this method to assess function of the lower oesophageal sphincter and pyloric muscle in experimental pigs.

Methods: All measurements were accomplished in one session under general anaesthesia in six adult female pigs (mean weight 34.2 ± 3.6 kg). EndoFLIP 1.0 System with EndoFLIP catheters (length of measuring zone 80 mm; 16 paired impedance planimetry sensors; filling volumes: 20, 30 and 40 mL). Five major parameters were evaluated for each filling volume: balloon pressure (mm Hg), estimated diameter (mm), cross-sectional area (mm²), distensibility defined as cross-sectional area divided by balloon distending pressure (mm²/mm Hg), and zone compliance defined as the change in volume over a 2-cm long segment spanning five electrodes, centred around the gastro-oesophageal junction or pylorus (mm³/mm Hg).

Results: In total, 180 particular readings were successfully accomplished, see Table 1.

Most of the measured values were nearing lower average figures for the lower oesophageal sphincter and upper average figures for the pylorus in healthy humans. The porcine pyloric sphincter is composed of the *torus pyloricus*. It serves as a sturdy “gatekeeper” between the stomach and D1 duodenum, thus explaining higher pyloric readings.

There was a clear trend for increasing values of CSA, diameter, and balloon pressure with increased filling balloon volumes. However, the sphincter distensibility did not change with increasing filling volumes either for the lower oesophageal sphincter or pylorus.

Conclusion: Endoscopic functional luminal planimetry in experimental pigs is feasible, both for the lower oesophageal sphincter and the pylorus. This is an important starting point for future experimental endoscopic trials and pharmacology studies.

Disclosure: Nothing to disclose.

Parameter	Filling volume 20 mL	Filling volume 30 mL	Filling volume 40 mL
	mean ± standard deviation median	mean ± standard deviation median	mean ± standard deviation median
	interquartile range	interquartile range	interquartile range
Oesophagus	18.7 ± 20.3	28.8 ± 10.2	44.9 ± 28.9
Balloon pressure	10.4	20.4	36.3
(mm Hg)	6.6 - 22.1	18.4 - 33.9	24.2 - 56.2
Oesophagus	5.9 ± 0.9	7.1 ± 1.8	9.0 ± 3.2
Diameter	5.9	7.2	8.9
(mm)	5.0 - 6.5	5.2 - 8.6	5.7 - 10.9
Oesophagus	25.8 ± 8.7	38.4 ± 22.7	66.4 ± 44.7
Cross-sectional area	21.5	29.5	56.5
(mm ²)	20.0 - 33.0	20.0 - 50.0	25.0 - 91.0
Oesophagus	1.7 ± 1.5	1.5 ± 1.5	2.1 ± 2.8
Distensibility	1.6	1.0	1.2
(mm ² /mm Hg)	0.3 - 1.9	0.3 - 2.0	0.3 - 2.1
Pylorus	15.9 ± 13.8	20.9 ± 17.3	28.6 ± 17.0
Balloon pressure	11.0	14.8	25.6
(mm Hg)	10.5 - 17.6	13.1 - 23.6	17.1 - 31.3
Pylorus	5.9 ± 1.4	6.9 ± 1.3	9.2 ± 3.2
Diameter	5.3	6.7	8.2
(mm)	5.0 - 6.0	5.9 - 8.1	6.5 - 12.0
Pylorus	28.5 ± 14.1	38.5 ± 14.4	73.8 ± 52.2
Cross-sectional area	22.0	35.0	52.5
(mm ²)	20.0 - 28.0	27.3 - 51.0	29.0 - 118.0
Pylorus	2.4 ± 1.9	2.0 ± 1.1	2.1 ± 1.3
Distensibility	1.6	1.8	1.6
(mm ² /mm Hg)	0.3 - 1.9	1.0 - 2.9	0.8 - 3.2

Table 1. Endoscopic functional luminal imaging probe panometry of the lower oesophageal sphincter and pylorus in six experimental pigs

SAFETY OF OESOPHAGEAL SELF-EXPANDABLE METALLIC STENT PLACEMENT IN PATIENTS WITH MALIGNANT DYSPHAGIA UNDERGOING ONCOLOGIC THERAPY

B. Abreu¹, L.M. Roque Ramos¹, C. Gouveia¹, B. Morão¹, R. Loureiro¹
¹Unidade de Saúde Local de Loures-Odivelas, Hospital de Loures, EPE, Gastroenterology, Loures, Portugal

Contact E-Mail Address: barbara.abreu.45@gmail.com

Introduction: Oesophageal self-expandable metallic stent (SEMS) placement is useful in malignant dysphagia palliation. However, its safety in patients undergoing chemoradiotherapy (CRT) remains unclear.

Aims & Methods: Our aim was to evaluate the safety of SEMS placement in these patients.

Retrospective study of consecutive patients between July 2012 and August 2023, with malignant dysphagia and inoperable tumors, who underwent SEMS placement alone or with oncologic treatment (CRT or chemotherapy (CT)) in a tertiary center. Demographic, tumor and stent characteristics, complications and follow-up data were collected.

Results: 44 patients were included; 86.4% male; median age 68.3 IQR 39-97 years; 70.5% (n=31) with esophageal squamous cell carcinoma and 29.5% (n=13) with esophagogastric junction adenocarcinoma. Patients were in stage IV (72.7%, n=32) and stage III (27.3%, n=12).

A partially covered SEMS was placed in most cases (90.9%, n= 40), and a fully covered SEMS in the remainder 4 patients. Median follow-up was 76 days (IQR 2-417 days). One third of patients (n=15) underwent CRT: nine priors, four after and two before and after SEMS placement. Seven patients only had CT: five after and two before and after stent placement. The remaining 50% did not undergo CRT nor CT. The overall median sur-

vival was 81.5 days (IQR 42.8-115). Survival was similar between patients with and without oncologic treatment 81.5 versus 77.5 days. Major complications occurred in 15.9%: six perforations and one hemorrhage. Severe complications were similar between patients with or without oncologic treatment peri stent placement. Similarly, there was no difference in complications between partially and fully covered SEMs (15% vs 25%, $p=0.602$).

Conclusion: In our cohort, CRT or CT did not increase the rate of major complications of SEMs placement for malignant dysphagia palliation.

References: Adamson D, et al. Palliative radiotherapy after oesophageal cancer stenting (ROCS): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2021 Apr; 6(4):292-303. Kinsman KJ, et al. Prior radiation and chemotherapy increase the risk of life-threatening complications after insertion of metallic stents for esophagogastric malignancy. *Gastrointest Endosc*. 1996 Mar; 43(3):196-203. Machado AA, et al. Impact of radiotherapy on adverse events of self-expanding metallic stents in patients with esophageal cancer. *Dis Esophagus*. 2023 Sep 30; 36(10): doad019.

Disclosure: Nothing to disclose.

PP0227

SELF-DILATATION FOR THE MANAGEMENT OF REFRACTORY BENIGN OESOPHAGEAL STRICTURES: OUTCOMES FROM THE LARGEST EUROPEAN TERTIARY CENTRE EXPERIENCE TO DATE

G. Ioannidis¹, P. Pilavaki¹, R. Basra¹, J. Gertner¹, N. Aslam¹, M. Duku¹, S. Thorpe¹, R.J. Haidry¹, O.F. Ahmad^{1,2,3}, R. Sweis¹, D.G. Graham¹, M. Banks¹, L.B. Lovat^{1,2,3}, V. Sehgal¹

¹University College London Hospitals NHS Foundation Trust, Gastrointestinal Services, London, United Kingdom, ²University College London, Wellcome/EPSCRC Centre for Interventional & Surgical Sciences, London, United Kingdom, ³University College London, Division of Surgery & Interventional Science, London, United Kingdom

Contact E-Mail Address: giannis.ioannidis@nhs.net

Introduction: Benign oesophageal strictures are commonly encountered in endoscopy and often effectively managed with endoscopic dilatation. However, up to 40% of patients may develop refractory benign oesophageal strictures (RBES), necessitating frequent endoscopic intervention that is challenging, poses a greater risk of complication and negatively impacts patients' quality of life.

Oesophageal self-dilatation (SD) offers an alternative treatment that potentially reduces the need for repeat hospital visits while allowing greater autonomy in managing their condition.

Aims & Methods: We describe the efficacy and safety of oesophageal SD at a tertiary referral centre. We retrospectively reviewed electronic records of patients with RBES who started SD between 2013 and 2024. Data were collected on stricture characteristics, endoscopies, dysphagia scores, and adverse events. The primary outcomes were the endoscopic dilatation-free interval (longest period of time patients did not require endoscopic dilatation) and the number of endoscopic procedures performed within 12 months of starting SD. Secondary outcomes included improvement in dysphagia score, technical success rate, and complications.

Results: We identified 43 patients who initiated SD during the study period. The technical success rate was 95.3%, with 41 out of 43 patients learning to perform SD successfully.

Among the remaining patients, the median age was 57 years (range 27-84 years), and 28/41 patients (68.3%) were female. Patients initiated SD for refractory peptic (32%), post-radiation (19.5%), post-surgical (12.2%), post-endoscopic resection (11.6%), caustic (7.3%), and other aetiology-re-

lated strictures. Stricture location varied, with 10/41 patients (24.4%) having proximal, 12/41 (29.3%) having middle, and 14/41 (34.1%) having lower oesophageal strictures, while the remainder had strictures involving multiple segments. Before initiating SD, patients had a median of 9 endoscopic interventions (IQR 7-17). The median follow-up post-SD was 23.2 months (IQR 6.8-49.4). The median dilatation-free interval significantly increased from 68.5 days (IQR 41-106 days) to 161 days (IQR 121-279 days) within 12 months before and after SD, respectively ($P < 0.001$). The median all-time intervention-free interval after SD was 405 days (IQR 130-705 days). Additionally, there was a significant reduction in the number of endoscopic interventions from a median of 7 (IQR 4.7-10) to 1 (IQR 0.75-3) within 12 months before and after SD, respectively ($P < 0.001$). Dysphagia scores improved, with a median Dakkak and Bennett Dysphagia Score of 2 (IQR 2-2) at baseline and 0 (IQR 0-1) after SD ($p<0.001$). Two adverse events were reported: one patient experienced clinically significant haematemesis while another patient suffered presumed iatrogenic oesophageal perforation secondary to SD. Both patients were managed endoscopically but discontinued SD.

Conclusion: To our knowledge, we have described the largest European case series of oesophageal SD that has been published to date. Oesophageal SD appears to be an effective, well-tolerated, and safe approach in managing often complex patients with RBES providing a viable alternative to conventional endoscopic interventions. However, the occurrence of adverse events highlights the importance of careful patient selection and ongoing monitoring. Further research is warranted to validate these findings and identify predictive factors for treatment success.

Disclosure: Nothing to disclose.

PP0228

ESOPHAGEAL ATRESIA WITH TRACHEOESOPHAGEAL FISTULA IS ASSOCIATED WITH CONSANGUINITY

O.E. Hougui¹, M. Zerem¹, M. Omary¹, Z. Assi², G. Ling¹, B. Yerushalmi¹, R. Nassar¹

¹Soroka University Medical Center, Pediatric Gastroenterology Unit, Beer Sheva, Israel, ²Soroka University Medical Center, Pediatric Surgery Department, Beer Sheva, Israel

Contact E-Mail Address: OEH8811@yahoo.com

Introduction: Esophageal atresia with tracheoesophageal fistula (EA-TEF) is a rare congenital malformation. The incidence of TEF is 1.3-4.6 cases per 10,000 live births. The specific etiology of EA-TEF is unknown. Environmental risk factors such as maternal use of medications and alcohol consumption during pregnancy are suggested. Genetic factors have also been described, especially among the syndromic types such as VACTERL, CHARGE, and Down syndrome, but less among non-syndromic types.

Aims & Methods: Aim: To examine the association between non-syndromic EA-TEF and consanguinity.

Methods: A retrospective study comparing the incidence of EA-TEF between low-consanguineous Jewish population and high-consanguineous Bedouin population. All patients were treated at Soroka University Medical Center, the only tertiary medical center in southern Israel.

Results: During the years 2000-2022, 579,130 children were born in southern Israel, 386,915 (67%) were Jewish and 192,215 were Bedouin Muslims. A total of 96 patients were diagnosed with EA-TEF, 83 of them were non-syndromic EA-TEF. The incidence of non-syndromic EA-TEF was 1.43 cases per 10,000 live-births and was statistically higher among the Bedouin population (2.65 vs. 0.83 cases per 10,000 live-births, $P<0.001$). The consanguinity rate among the Bedouin group was higher comparing with the Jewish (71% vs 0% $P<0.001$). There were no differences in other risk factors.

Conclusion: The incidence of EA-TEF is exceptionally higher among the Bedouin population that live in the same geographic region and the same medical access as the Jewish population, proposing consanguinity as an important/essential risk factor of EA-TEF.

References: 1. Prevalence of consanguineous marriages and associated factors among Israeli Bedouins. Wasef Na'amni, Orly Romano-Zelekha et al.

2. Risk factors for congenital heart defects in two populations residing in the same geographic area: a long-term population-based study, Southern Israel. Author(s) Robinson, R, Stavsky, et. al.

4. Jaber L, Bailey-Wilson JE, et. al. (1994) Consanguineous matings in an Israeli-Arab community. Arch Pediatr Adolesc Med 148:412-415

5. Weitzman D, Shoham-Vardi I et. al. (2000) Factors affecting the use of prenatal testing for fetal anomalies in a traditional society. Community Genetics 3:61-70

6. Cassina M, Ruol M, et al. Prevalence, characteristics, and survival of children with esophageal atresia: A 32-year population-based study including 1,417,724 consecutive newborns. Birth Defects Res A Clin Mol Teratol 2016; 106:542.

7. Oesophageal atresia, tracheoesophageal fistula, and the VACTERL association: review of genetics and epidemiology. C Shaw-Smith. J Med Genet 2006;43:545-554. doi: 10.1136/jmg.2005.038158

8. Oesophageal atresia. van Lennep M, Singendonk MMJ, et. al. Nat Rev Dis Primers. 2019 Apr 18;5(1):26. doi: 10.1038/s41572-019-0077-0. PMID: 31000707.

9. Esophageal morbidity in patients following repair of esophageal atresia: A systematic review. Comella A, Tan Tanny SP, Hutson JM, et al. J Pediatr Surg. 2021;56(9):1555-1563. doi:10.1016/j.jpedsurg.2020.09.010

Disclosure: Conflict of Interest: None.

PP0229

PROPHYLACTIC ENDOLUMINAL VACUUM THERAPY – TOWARDS AN ERA OF REDUCING LEAK RELATED MORBIDITY AFTER ELECTIVE OESOPHAGO-GASTRIC RESECTION

I.-u.-d. Saqib¹, Z. Al-Ani², S. Gourgiotis¹, R. Hardwick¹, P. Safranek¹, V. Sujendran¹, A. Hindmarsh¹, A. Noorani^{3,1}

¹Cambridge Oesophago-Gastric Unit, Addenbrooke's Hospital, Cambridge, United Kingdom, ²Auckland City Hospital, Auckland, New Zealand, ³Wellcome Sanger Institute, Hinxton, United Kingdom

Contact E-Mail Address: imaduddinsaib@gmail.com

Introduction: Uncontrolled sepsis following leak from major oesophago-gastric surgery is a devastating condition with increased morbidity and mortality and intensive care stay. We hypothesised that endoluminal vacuum therapy (EVT) could be used in the prophylactic setting to provide source-control, prevent mediastinitis and minimise sepsis related morbidity from leaks.

Aims & Methods: An ad-hoc EVT device was created using VAC granufoam (KCI) and a nasogastric-tube (16/18Fr), and placed intraluminally across the high risk anastomosis/area of repair. Continuous negative pressure (75–125mmHg) was applied. Assessment of the repair site/anastomosis was performed by radiology, endoscopy, clinical assessment or a combination following cessation of EVT and removal of the prophylactic EVT device.

Results: Twenty-seven patients had prophylactic EVT; M:F ratio was 3:1 and the median age was 68 years (range: 41-82 years). Twenty-six patients had cancer resections while 1 had benign surgery. The rationale for prophylactic EVT included preoperative factors (10), intra-operative factors (16) or both (1). The median duration of prophylactic EVT was 7

days (range: 4-14 days). The median length of stay was 19.7 days (range: 6-96 days), the two longest admissions were unrelated to the anastomosis (prolonged chyle leak, and long-term-sequelae of life-threatening bleed). One patient developed full-thickness microleak at endoscopic evaluation, remained clinically well with no systemic signs of sepsis, and was successfully managed with luminal EVT for a further 6 days in a ward-based environment. Though prophylactic EVT did not prevent the leak, it significantly minimised the systemic hit that traditionally results from leak and associated mediastinal sepsis.

Conclusion: Prophylactic EVT is a useful adjunct for management of patients with a high-risk for leak and can serve as a risk reducing strategy in select cases. There are no short-term complications, yet the additional morbidity, mortality, and length of stay associated with a fully-fledged leak is avoided. Our results lay the foundation for the use of prophylactic EVT in randomised controlled trials to further standardise selection criteria, assess longer term potential patient benefit and impact on survivorship.

References: 1. Pournaras DJ, Hardwick RH, Safranek PM, Sujendran V, Bennett J, Macaulay GD, Hindmarsh A. Endoluminal vacuum therapy (E-Vac): a treatment option in oesophagogastric surgery. World journal of surgery. 2018 Aug;42:2507-11.

2. Afzal Z, Gourgiotis S, Hardwick R, Safranek P, Sujendran V, Bennett J, O'Neill R, Noorani A, Hindmarsh A. O-EGS08 Endoluminal Vacuum Therapy (EVT) for leaks in the upper gastrointestinal (UGI) tract; 10-years' experience in a specialist Oesophagogastric centre. British Journal of Surgery. 2021 Dec 1;108(Supplement_9):znab429-022.

3. Müller PC, Morell B, Vetter D, Raptis DA, Kapp JR, Gubler C, Gutschow CA. Preemptive endoluminal vacuum therapy to reduce morbidity after minimally invasive Ivor Lewis esophagectomy: including a novel grading system for postoperative endoscopic assessment of GI-anastomoses. Annals of Surgery. 2021 Nov 1;274(5):751-7.

Disclosure: Nothing to disclose.

PP0230

ESOPHAGEAL PERFORATION – ANALYSIS OF ETIOLOGY, MANAGEMENT AND OUTCOME – A 10YRS EXPERIENCE AT A TERTIARY UNIVERSITY MEDICAL CENTER

D. Voll¹, M.A. Kölling¹, N. Friedrich¹, P. Rösel¹, T. Perl¹, V. Ellenrieder², M. von Heesen¹, M. Ghadimi¹, J. Reinecke², L.-C. Conrad¹

¹University Medical Center Göttingen, Department of General, Visceral and Paediatric Surgery, Göttingen, Germany, ²University Medical Center Göttingen, Department of Gastroenterology, Gastrointestinal Oncology and Endocrinology, Göttingen, Germany

Contact E-Mail Address: diana.voll1@med.uni-goettingen.de

Introduction: Esophageal perforation is a rare condition with a high mortality rate. Often it has an iatrogenic origin, being caused by transesophageal echocardiography, different endoscopic and surgical procedures. Furthermore, there are other causes such as foreign body ingestion, tumor associated perforation and Boerhaave's syndrome. Esophageal perforation can be difficult to diagnose since the clinical presentation is often unspecific. This can lead to a delay in appropriate treatment. Optimal management of this condition challenges clinicians in daily practice. Therefore, we present a monocentric retrospective study, evaluating our experience in treating esophageal perforations over more than a decade as a tertiary referral University Medical Center in Germany.

Aims & Methods: This study comprises the retrospective analysis of data from all patients treated for esophageal perforation in our clinic in the departments of general and visceral surgery and gastroenterology between

2012 and 2024. Only patients with confirmed esophageal perforation were included. Data was collected by means of a retrospective analysis of digital and analogous data archives as well as information from the physicians providing further treatment.

Results: A total of 78 cases (47 male, 31 female) of esophageal perforation were included. The leading cause was iatrogenic (n=45), consisting of endoscopic procedures (n=22), operative complications (n=11), TEE (n=6), diagnostic EGD (n=5) and one case of endotracheal intubation. The second most common cause of perforation was Boerhaave's syndrome (n=23), followed by perforations associated with foreign body ingestion (n=5) or tumors of the esophagus (n=4). Traumatic perforations were rare (n=1). Most perforations occurred in the lower third of the esophagus (58 cases), 11 perforations were located in the mid esophagus and 9 in the upper third. Primary treatment consisted of direct surgical management in 26 cases (suture of the esophagus, gastrectomy, esophagectomy, definitive cervical esophagostomy, thoracic drainage, lavage), endoscopic therapy in 38 cases (Endo-VAC, stenting and application of OTSC or TTSC clips) and a conservative approach in 14 cases. Eventually a total of 48 patients underwent surgical treatment. Survival was poorest in spontaneous and tumor associated perforations (mean survival 22 and 23 months). Iatrogenic perforations showed an intermediate outcome.

The best outcome was observed in perforations associated with foreign body ingestion (mean survival 50 months). In correlation with perforation location, the survival was best for perforations in the upper esophagus, followed by those in the lower esophagus, while lesions in the mid esophagus showed the worst outcome. Perforation associated death was recorded in 17 cases.

Conclusion: Esophageal perforations are a life-threatening event that require immediate and adequate treatment. Our analysis identified risk groups resulting in poorer survival: perforations in the mid esophagus, primary surgical treatment, advanced age. Within the last years, endoscopic techniques have reduced the need for surgical interventions. Nevertheless, surgical treatment remains the therapy of choice for patients not eligible for endoscopic treatment or after failure of endoscopic therapy. Our analysis emphasizes the importance of multidisciplinary, close monitoring and continuous reassessment of treatment strategy. Further investigation will help to improve the outcome via prospective studies or the establishment of a local or interregional database seem promising to underline suggestions derived from our analysis.

Disclosure: Nothing to disclose.

PP0231

WITHDRAWN

PP0232

ENDOSCOPIC TRANS-ORAL OUTLET REDUCTION IS SAFE AND EFFECTIVE FOR WEIGHT REGAIN AFTER ONE-ANASTOMOSIS GASTRIC BYPASS

S. Fishman¹, M. Shnell¹, F. Kinaany¹, R. Reicher¹, W. Mathur², M. Galvao Neto³, M. Bhandari³

¹Tel Aviv Sourasky Medical Center affiliated to Tel Aviv University, Dept. of Gastroenterology, Tel Aviv, Israel, ²Sri Aurobindo Medical College and PG Institute, Department of Surgery, Indore, India, ³Mohak Bariatric and Robotic Center, Bariatric Endoscopy department, Indore, India

Contact E-Mail Address: rellyr@tlvmc.gov.il

Introduction: Obesity is a global health concern with increasing prevalence, and bariatric surgery remains a prominent treatment option. One-anastomosis gastric bypass (OAGB) has gained popularity for its advantages, including significant weight loss and fewer early complications. However, concerns arise regarding nutritional deficiencies, weight regain, and other complications. This study aims to assess the effectiveness and safety of endoscopic transoral outlet reduction (TORe) as a treatment for weight regain after OAGB.

Aims & Methods: Consecutive Patients with weight regain following OAGB were evaluated. Weight regain was defined as a 10% increase in total body weight from the post-surgery weight nadir. Diagnostic gastroscopy determined anastomosis diameter, pouch dimensions and ruled out contraindications for TORe. The procedure involved circumferential argon plasma coagulation and full thickness endoscopic suturing to narrow the anastomosis. Patient data was collected, and outcomes assessed in accordance with ethical standards

Results: sixty four patients were treated during a 4 years duration and followed up for 1 a minimum of 1 year. Fourty seven percents were females, mean pre-treatment BMI 35.5. Average weight loss was 7% of total body weight after 6 months and 8% after 12 months (p=0.03). A reduction of at least 5% and 10% was seen in 65% and 31%, respectively. Additional treatment was needed in 17% of patients. Major complication that required surgical intervention occurred in only one patient

Conclusion: Endoscopic transoral outlet reduction appears safe and effective for the treatment of weight regain s/p OAGB. Sustained weight loss was seen during a 1 year follow up. Further investigation is needed to assess the long term durability of the effect.

Disclosure: Nothing to disclose.

PP0233

ENDOSCOPIC TREATMENT OF REFRACTORY MARGINAL ULCERS - A CASE SERIES

T. Bar-on¹, S. Fishman², M. Shnell³, R. Reicher³

¹Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ²TASMC Dept. of Gastroenterology, Dept. of Gastroenterology, Tel Aviv, Israel, ³Tel-Aviv Medical Center Dept. of Gastroenterology, Tel Aviv, Israel

Contact E-Mail Address: talibaron07@gmail.com

Introduction: Ulceration at the gastrojejunostomy is a late complication following gastric bypass surgery, usually responsive to high dose PPI. However, in refractory cases, patients may require surgical treatment. Recently, a new technique of endoscopic jejunal flap over-suturing has been reported with exceptional success rates. We aimed to evaluate the implementation of this approach in our practice.

Aims & Methods: Consecutive patients with symptomatic marginal ulcers, who failed to response to a two-month course of high dose PPI were included. Patients were treated with endoscopic suturing of a jejunal flap

over the ulcer. In case of a narrow anastomosis, a self-expandable metallic stent (SEMS) was used alone or in combination with suturing. The stent was removed after 2 months. Endoscopy was repeated 8 weeks after the procedure. Technical success was defined as a fully covered marginal ulcer. Clinical success was defined as an ulcer heal on repeat endoscopy, while persistent ulcer, perforation or need for surgical repair was considered as failure.

Results: Ten patients were included, seven after Roux-en-Y gastric bypass and after 3 single anastomosis gastric bypass. All patients were negative for *Helicobacter Pylori*, deny alcohol abuse or NSAIDS use, 2 patients were active smokers at the time of diagnosis. All patients were on chronic PPI at the time of diagnosis, and the average therapy duration was 27 months. Jejunal over-suturing was performed in 9 patients of them 3 in combination with a SEMS, and 1 patient was treated only with a SEMS. Overall technical success rate was 100%, and a clinical success rate was 50% with 4 patients going through surgery thereafter. No adverse events occurred during the procedure or follow up period.

Conclusion: To date, marginal ulcers remain a dreaded late adverse event necessitating prolonged PPI use, repeat endoscopies and even revisional surgery. Endoscopic treatment to promote healing of refractory marginal ulcers appears safe. Technical success was achieved in all patients while clinical success only in half. However, since the only alternative treatment is surgery the endoscopic approach should still be considered. The lower than expected clinical success might be related to a more PPI resistant population compared with previous published series. Further research is needed to determine the appropriate therapeutic algorithm.

Disclosure: Nothing to disclose.

PP0234

INFLUENCE OF RECURRENT LARYNGEAL NERVE PALSY AFTER ESOPHAGECTOMY AND FUTURE PLAN OF TREATMENT USING AMNION MEMBRANE SHEET

Y. Taniyama¹, Y. Watanabe¹, K. Tokokdai¹, H. Okamoto¹, C. Sato¹, Y. Ozawa¹, H. Ishida¹, R. Ando¹, M. Unno¹, T. Kamei¹

¹Tohoku University Hospital, Department of Surgery, Sendai, Japan

Contact E-Mail Address: yusuketaniyama@gmail.com

Introduction: The therapeutic effect of recurrent laryngeal nerve (RLN) dissection in the treatment of esophageal cancer, particularly squamous cell carcinoma, is well-established. However, due to the risk of RLN palsy as a consequence, this procedure is often avoided. Nonetheless, the prevalence of this adverse event and its impact on prognosis remain unclear.

Aims & Methods: In this study, we aimed to evaluate the influence of recurrent laryngeal nerve palsy and long-term effects on prognosis. Moreover, we introduce some basic science of treating injured nerve using amnion membrane sheet.

We analyzed 726 cases of esophageal cancer who underwent bilateral recurrent laryngeal nerve lymphadenectomy during esophagectomy between 2000 and 2021. Cases with combined nerve resection and R2 resection were excluded. Recurrent laryngeal nerve palsy was confirmed by bronchoscopy on the first postoperative day, if even a slight difference in the movement of the vocal cords between the left and right sides was detected.

Results: RLN palsy was observed in 40.7% of cases (left: 234 cases, right: 31 cases, bilateral: 30 cases), with 12 cases experiencing paralysis lasting over a year. Analysis revealed significantly higher rates of complications such as aspiration ($p < 0.0001$), postoperative pneumonia ($p = 0.0004$), and prolonged hospital stay ($p < 0.0001$) in RLN palsy cases. Furthermore, there were associations between postoperative pneumonia and patient

factors including age ($p = 0.0364$), sex ($p = 0.0066$), RLN palsy ($p = 0.0005$), and reconstruction route ($p = 0.0098$), each identified as independent risk factors in multivariate analysis. However, only age and sex showed associations with pneumonia-related mortality. Long-term prognosis analysis using propensity score matching revealed slightly poorer outcomes in the RLN palsy group, although no statistically significant difference was observed.

Additionally, we are conducting research on a treatment method using amniotic membrane sheets in a sciatic nerve injured rat model. Electromyography studies showed a trend toward improved motor function in the amniotic membrane sheet treatment group compared to the control group at 8 weeks post-injury ($p = 0.0887$). Further investigation with increased sample size is planned to refine this approach for future clinical application.

Conclusion: Although RLN palsy after esophageal cancer surgery did not affect patient prognosis in the long term, we discovered it as a cause of aspiration and postoperative pneumonia in the short term. With the growing understanding of respiratory complications as important prognostic factors in various cancers, including esophageal cancer, strategies to prevent RLN palsy are crucial. Amniotic membrane sheets represent a potential intervention for the early recovery of RLN palsy.

Disclosure: Nothing to disclose.

PP0235

WITHDRAWN

PP0236

ASSESSING THE EFFICACY OF SELF-EXPANDING METAL STENTS FOR POSTOPERATIVE UPPER DIGESTIVE LEAKS AND FISTULAE: A DECADE OF EXPERIENCE AT A TERTIARY CENTER

D. Feijó¹, A.E.P. Silva¹, M. Costa¹, M. Gravito-Soares¹, E. Gravito-Soares¹, P. Amaro¹, C. Agostinho¹, M. Ferreira¹, P. Narra Figueiredo¹

¹ULS Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: diogofeijo96@gmail.com

Introduction: Postoperative anastomotic leaks and fistulae in the upper digestive tract are severe complications that can lead to significant morbidity and mortality. Traditionally, surgical intervention has been the primary approach to address these complications. However, self-expanding metal stents (SEMS) have emerged as a less invasive alternative, offering a potential pathway to achieve closure of these leaks and fistulae. Despite their growing use, the efficacy and safety profile of SEMS in this context is not fully understood.

Aims & Methods: This study aims to evaluate the success rates, safety, and predictive factors of therapeutic success for SEMS in managing postoperative upper digestive tract leaks and fistulae, drawing on a 10-year experience at a tertiary center.

We conducted a retrospective review of patients with postoperative anastomotic leak or fistula who underwent endoscopic SEMS placement at our tertiary center between 2014 and 2022, and prospectively from 2022 onwards. Therapeutic success was defined as complete closure of the leak/fistula, while failure indicated non-closure.

Results: We included a total of 43 patients (69.8% male) with a median age of 61 years (IQR 17). There were no statistically significant differences regarding distribution by gender, age, Charlson comorbidity index, benign vs malignant disease, time from surgery to endoscopic treatment and leak size between the different types of stents ($p > 0.05$). The technical efficacy was 100%, with a therapeutic success rate of 55.8%. Bariatric stents ex-

hibited the highest success rate (85.7%), followed by fully covered SEMS (60.0%) and partially covered SEMS (46.2%) ($p = 0.166$). Success was significantly higher in patients with a smaller leak size (10 mm vs. 12 mm, $p < 0.05$).

Therapeutic failure was associated with greatest need for endoscopic adjuvants (57.9% vs. 37.5%, $p = 0.183$). The overall mortality rate was 34.9%.

Conclusion: This study indicates that self-expanding metal stents (SEMS) offer a viable and safe treatment option for postoperative upper digestive tract leaks and fistulae. With a technical efficacy of 100% and a therapeutic success rate of 55.8%, SEMS demonstrated promising results. The success rate was influenced by stent type, with bariatric stents showing the highest rate, followed by fully covered SEMS and partially covered SEMS. Smaller leak size emerged as a significant predictor of therapeutic success, emphasizing the importance of early detection and timely intervention. Although the overall mortality rate was 34.9%, this study's outcomes suggest that SEMS can play a crucial role in managing these complications, with early diagnosis and prompt stent placement being pivotal for success. Further research is needed to better understand the factors contributing to therapeutic success and to optimize endoscopic strategies for patients with upper digestive tract leaks and fistulae.

Disclosure: Nothing to disclose.

PP0237

CGAS-STING PATHWAY ACTIVATION ENHANCES ANTI-TUMOR EFFECT OF TALAPORFIN PHOTODYNAMIC THERAPY THROUGH REACTIVE OXYGEN SPECIES PRODUCTION AND DNA DAMAGE

M. Sasaki¹, M. Tanaka¹, Y. Kojima¹, Y. Sasaki¹, T. Suzuki¹, H. Nishie¹, H. Kataoka¹

¹Nagoya City University Graduate School of Medical Science, Department of Gastroenterology and Metabolism, Nagoya, Japan

Contact E-Mail Address: sasakimakiko@gmail.com

Introduction: Photodynamic therapy (PDT) is a relatively non-invasive anti-cancer therapy that employs a photosensitizer and a specific wavelength of light irradiation. PDT induces tumor shrinkage in various malignancies due to three main mechanisms, direct effects of reactive oxygen species (ROS), vascular shutdown leading to tumor infarction, and acute inflammation with immune response. Among them, ROS is important factor of DNA damage. It was reported that cGAS (cyclic GMP-AMP synthase)-STING (stimulator of interferon genes) pathway regulates a transcriptional program that controls the generation of ROS and that STING loss alters ROS homeostasis. STING loss reduces ROS induction and that causes therapeutic resistance.

Thus, we predicted that pharmacological activation of cGAS-STING pathway would be an actionable target for reducing therapeutic resistance and enhance DNA damage caused by PDT. Our study investigated the efficacy of STING agonist (2'-3'-cyclic GMP-AMP sodium or AUS-100) combined with talaporfin sodium PDT.

Aims & Methods: 1. We established STING knockout cells in a colon cancer cell line (HCT116) using CRISPER-Cas9.

2. We compared the induction of cell death after *in vitro* talaporfin PDT in parental and knockout cells. We analyzed IC50 by MMT assay.

3. We measured ROS generation, using DCFDA assay after *in vitro* talaporfin PDT in parental and knockout cells.

4. We analyzed the induction of cell death treated with ROS scavenger (N-acetyl cysteine; NAC) after *in vitro* talaporfin PDT in parental and knockout cells.

5. We measured DNA damage by immunofluorescence microscopy with an anti- γ -H₂AX antibody after *in vitro* talaporfin PDT in parental and knockout cells.

6. We investigated PDT-induced STING pathway activation of STING-regulated genes by western blot analyses after *in vitro* PDT in parental and knockout cells.

7. We compared the *in vivo* efficacy of talaporfin PDT between the parental and knockout cells.

8. We assessed the *in vivo* efficacy of talaporfin PDT, STING agonist (2'-3'-cyclic GMP-AMP sodium or AUS-100), and their combination in a xenograft tumor model bearing HCT116.

Results: 1. We established STING knockout cell. STING knockout was confirmed by western blot analyses.

2. STING KO suppressed cell death induction of TS-PDT (IC₅₀ 12.5 ($\pm$ 1.35) vs 14.5 ($\pm$ 1.18) μ mol/L).

3. STING KO suppressed TS-PDT induced ROS generation (M.F.I. 4491 vs 1706).

4. STING KO suppressed cell death induction of TS-PDT with NAC.

5. Treating parental cell lines with talaporfin PDT led to significantly more γ -H₂AX foci formation than in STING knockout cells.

6. At the protein level, TS-PDT enhanced TBK-1 phosphorylation in parental cell. STING dependent signaling was enhanced by TS-PDT, and the effects were eliminated by STING loss.

7. The *in vivo* efficacy against towards parental cells was significantly greater than that towards STING knockout cells.

8. The combination exhibited significantly greater tumor growth inhibition than by single agents alone in a xenograft tumor model.

Conclusion: We have established STING knockout cell using CRISPR-Cas9 and identified novel regulators of DNA damage in Photodynamic therapy. Our results point to a role for STING in DNA damage sensing and cyclic dinucleotide detection that goes beyond its conventional function. According to these results, talaporfin PDT is more effective when a STING agonist is used to control the degree of DNA damage. Combining talaporfin PDT with a STING agonist would offer a potentially strong combination for next-generation anticancer treatments.

Disclosure: Nothing to disclose.

PP0238

OLGA AND OLGIM STAGING ARE POOR PREDICTORS OF GASTRIC CANCER RISK

P. Nalivaiko¹, I. Bogdanova^{1,2}, I. Liepniece-Karele², I. Polaka^{1,3}, E. Syundyukov⁴, I. Tolmanis⁵, Y. Tarasenko⁶, L. Morozova⁷, S. Abdelmassi⁸, M. Leja^{1,5}

¹Institute of Clinical and Preventive Medicine and Faculty of Medicine, University of Latvia, Riga, Latvia, ²Academic Histology Laboratory, Riga, Latvia, ³Riga Technical University, Riga, Latvia, ⁴Longenes, Ltd., Riga, Latvia, ⁵Digestive Diseases Centre GASTRO, Riga, Latvia, ⁶Giann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, United States of America, ⁷Hospital Jurmala, Jurmala, Latvia, ⁸Riga 1st Hospital, Riga, Latvia

Contact E-Mail Address: paula.nalivaiko@gmail.com

Introduction: Gastric cancer continues to be one of the main challenges worldwide, with a predictable increase in the number of new cases in the coming decades. Staging systems for gastric precancerous lesions: Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia (OLGIM) are considered to be the best predictors for gastric cancer development. Only OLGA/OLGIM stages III-IV are considered high-risk lesions with a significant potential of progressing towards gastric cancer.

Aims & Methods: The purpose of this study was to evaluate the predictive role of OLGA and OLGIM staging in gastric cancer development.

We conducted a retrospective cohort study by matching gastric adenocarcinoma cases registered in the Latvian Cancer Registry between 2005 and 2022 to the pathology reports in the database of Academic Histology Laboratory from upper endoscopies performed in the Digestive Diseases Centre GASTRO, Jurmala hospital and Riga 1st hospital. Only cases with antral and corpus biopsies (as the minimum) available from the index endoscopy allowing OLGA / OLGIM staging were included in the study. If data from several endoscopies were available for the same patient, the case with the highest OLGA/OLGIM stage was used as the index endoscopy; if OLGA/OLGIM staging was identical across several endoscopies, the first endoscopy was used as the index case. The presence of dysplasia in any of the previous pathology reports was also considered. Patients with suspected cancer at the enrolment or having been recorded in the cancer registry less than 6 months after the index endoscopy were excluded from the study.

Results: Altogether 54 patients were available for the analysis; 38.9% were male. The mean age at the time gastric cancer detection 69.2 years, range 40-90. The median time between the index endoscopy and gastric cancer diagnosis was 1403.5 days (IQR: 826.5-2793.3). Forty-one patients (75.9%) had one endoscopy, eleven (20.4%) had two, one (1.9%) had four and one (1.85%) – 8 endoscopies. Biopsies from incisura angularis of the stomach were available for 43 patients (79.6%).

Altogether 16 patients (29.6%) had dysplasia reported at one of the preceding endoscopies, of those 14 were low grade, 2 – high grade. Patient distribution per OLGA and OLGIM stages at the index endoscopy is shown in Table 1. Among patients ultimately diagnosed with gastric cancer, only 11 (20.4%) had OLGA III-IV stages and 10 (18.6%) had OLGIM III-IV stages at the time of the index endoscopy. Excluding cases with dysplasia reported during any of the preceding endoscopies did not make a substantial change in the OLGA and OLGIM stage distribution at the index endoscopy.

	Stage 0	Stage I	Stage II	Stage III	Stage IV
OLGA (all cases)	7 (13.0%)	17 (31.5%)	19 (35.2%)	6 (11.1%)	5 (9.3%)
OLGIM (all cases)	12 (22.2%)	15 (27.8%)	17 (31.5%)	5 (9.3%)	5 (9.3%)
OLGA (excluding cases with previously reported dysplasia)	7 (18.4%)	15 (39.5%)	10 (26.3%)	4 (10.5%)	2 (5.3%)
OLGIM (excluding cases with previously reported dysplasia)	12 (31.6%)	12 (31.6%)	9 (23.7%)	3 (7.9%)	2 (5.3%)

Table 1. OLGA and OLGIM stages at the time of the index upper endoscopy in patients having developed gastric cancer thereafter.

Conclusion: The majority of patients having undergone upper endoscopy before the diagnosis of gastric cancer were in low-risk OLGA and OLGIM stages. Continued research is warranted to identify the best approach for risk stratification of gastric precancerous lesions. Yet, the current study demonstrates that the assessment should not be solely based on OLGA or OLGIM staging.

Disclosure: Nothing to disclose.

PP0239

WITHDRAWN

PP0240

ENDOSCOPIC SUTURING FOR DEFECT CLOSURE IN THE UPPER GASTROINTESTINAL TRACT: A RETROSPECTIVE COHORT STUDY

A. Papaefthymiou¹, N. Aslam², B. Norton¹, A. Telese¹, C. Murray¹, A. Murino¹, G. Johnson¹, C.R. Simons-Linares³, R.J. Haidry³

¹Cleveland Clinic London, Gastroenterology, London, United Kingdom, ²University College London Hospital, Department of Gastrointestinal Services, London, United Kingdom, ³Cleveland Clinic, Advanced Endoscopy - Gastroenterology, Cleveland, United States of America

Contact E-Mail Address: Andrea.Telese@nhs.net

Introduction: The increasing availability of gastrointestinal (GI) interventions has raised the need to treat luminal defects. Endoscopic suturing (ES) is a minimally invasive technique, used for a wide range of indications.

Aims & Methods: This retrospective cohort study aimed evaluate the performance of ES in treating upper GI defects. Data from a tertiary centre were collected for patients undergoing ES to treat upper GI defects. The primary outcome was technical success, defined as the successful sutures' deployment. Secondary outcomes included immediate clinical success (confirmation of closure at the time of the procedure), recurrence, long-term outcomes and complications. Descriptive statistics and χ^2 test were used to calculate the rates of the outcomes and assess any link between independent variables and results.

Results: Forty-two procedures were performed on 25 patients between 2018 and 2023. The mean age was 55 (± 16.2) years and 56% were female. The technical success rate was 88.1% (37/42) and immediate clinical success 91.9% (34/37), with only two (4.8%) adverse events. The overall recurrence rate was 61.8% (21/34), with a long-term clinical success rate of 69.6% (16/23). Technical success was higher in oesophagus (92.3%), and stomach (100%) ($p=0.002$), and immediate clinical success was more likely in patients with leak (88.9%) or fistula (95.2%) compared to perforation (50%; $p=0.005$).

Conclusion: ES demonstrated high rates of technical and immediate clinical success for defect closure in the upper GI tract, with low rates of complications. The benefit is most prominently seen among patients with leaks and fistulas in the stomach and oesophagus.

Disclosure: Nothing to disclose.

PP0241

LONG TRANSPARENT CAP SUTURING TECHNIQUE FOR THE CLOSURE OF ENDOSCOPIC FULL-THICKNESS RESECTION DEFECTS: A NOVEL ALTERNATIVE

N. Dai¹, S. Ullah¹, X. Cao¹

¹The First Affiliated Hospital of Zhengzhou University, Gastroenterology, Zhengzhou, China

Contact E-Mail Address: xinguangcao@126.com

Introduction: Gastric submucosal tumors (SMTs) are elevated lesions originating from below the gastric mucosal layer. Pathological types of SMTs include stromal tumors, leiomyomas, lipomas, etc., with stromal tumors being the most common¹. Endoscopic full-thickness resection (EFTR) has gradually become the main treatment modality for SMTs². However, in order to completely remove lesions involving the submucosal and deeper layers, EFTR often involves intentional perforation during the procedure. Therefore, successful closure of the full-thickness defect after the procedure is crucial to prevent serious complications such as pneumothorax and pneumoperitoneum³. Currently, available techniques for the full-thickness GI wall defects closure includes metal clip closure, ny-

lon suture purse-string closure, Over-The-Scope-Clip system (OTSC), and the OverStitch suture system^{4,5}. However, due to variations in endoscopic center equipment, individual physician skills, and patient economic conditions, most of the suture devices are not widely available including in China. Using metal clips alone may sometimes be insufficient for closing the large GI defects, while the purse-string suture technique can be relatively cumbersome.

Aims & Methods: The aim of this study was to evaluate the safety and efficacy of the long transparent cap suturing technique for the closure of large endoscopic full-thickness resection (EFTR) defects. A total of 62 patients who underwent EFTR for their large gastric submucosal tumors at the First Affiliated Hospital of Zhengzhou University between January 2017 and March 2023 were included in this study. The novel long transparent cap suturing technique was used for EFTR defect closure in all the patients.

Results: The procedure technical success rate was 100%. The median tumor size was 1.5 cm (range: 0.6-6.5 cm), and the median number of metal clips used was 7 (range: 4-14). The median EFTR procedure time was 53.5 minutes (range: 22-136 minutes), and the median suturing time was 14 minutes (range: 3-45 minutes). The median length of postoperative hospital stay was 4.5 days (range: 3-7 days). Postoperative complications including bleeding occurred in 1 case, fever in 3 cases, and abdominal pain in 2 cases. During the median 29 months (range: 7-79 months) of follow up, no residual lesions, tumor recurrence, or metastasis were detected, and no formation of digestive tract fistulas or sinuses was observed.

Conclusion: The long transparent cap suturing technique is a simple, safe, and effective method for wound closure after EFTR. It is beneficial for clinical application and widespread use.

References:

- Sharzei K, Sethi A, Savides T. Aga clinical practice update on management of subepithelial lesions encountered during routine endoscopy: Expert review. *Clin Gastroenterol Hepatol* 2022; 20: 2435-43.e4.
- Liu S, Zhou X, Yao Y, Shi K, Yu M, Ji F. Resection of the gastric submucosal tumor (g-smt) originating from the muscularis propria layer: Comparison of efficacy, patients' tolerability, and clinical outcomes between endoscopic full-thickness resection and surgical resection. *Surg Endosc* 2020; 34: 4053-64.
- Zhou PH, Yao LQ, Qin XY *et al*. Endoscopic full-thickness resection without laparoscopic assistance for gastric submucosal tumors originated from the muscularis propria. *Surg Endosc* 2011; 25: 2926-31.
- Verlaan T, Voermans RP, van Berge Henegouwen MJ, Bemelman WA, Fockens P. Endoscopic closure of acute perforations of the gi tract: A systematic review of the literature. *Gastrointest Endosc* 2014; 82: 618-28.e5.
- Shi D, Li R, Chen W *et al*. Application of novel endoloops to close the defects resulted from endoscopic full-thickness resection with single-channel gastroscope: A multicenter study. *Surg Endosc* 2017; 31: 837-42.

Disclosure: Nothing to disclose.

PP0242

HIGH RESOLUTION ESOPHAGEAL MANOMETRY IN EVALUATION OF EFFICACY OF PERORAL ENDOSCOPIC MYOTOMY

E. Valitova^{1,2}, O. Berezina¹, D.S. Bordin^{3,4,5}, I. Kanischev⁶, K. Shishin⁷

¹A.S. Loginov Moscow Clinical Scientific Center, Laboratory of functional diagnostics of diseases of esophagus and stomach, Moscow, Russian Federation, ²Organizational and Methodological Department on Gastroenterology of Moscow Department of Health, 111111, Russian Federation, ³A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ⁴Russian University of Medicine, Moscow, Russian Federation, ⁵Tver State Medical University, Tver, Russian Federation, ⁶A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ⁷A.S. Loginov Moscow Clinical Scientific Center, Operative Endoscopy, Moscow, Russian Federation

Contact E-Mail Address: dbordin@mail.ru

Introduction: Achalasia is a primary motility disorder, which presented by dysphagia. The most effective treatment of the disease is surgical (peroral myotomy or laparoscopic myotomy). However, there are few studies which assess the changes in esophageal motility after surgery.

Aims & Methods: The aim of our study was evaluating the changes in esophageal manometry in patients with achalasia after peroral endoscopic myotomy (POEM).

Subjects and methods: 43 patients with achalasia were consequently observed before and 1 year after POEM. Females predominated (28 subjects). All patients examined endoscopically, then high resolution manometry (HRM) was performed by Solar™ GI (MMS/Laborie, Netherland). Achalasia was defined as described in Chicago Classification 4.0. Eight patients had I type of achalasia, 24 – II type and 11 – III type.

Results: The median Eckardt score was 7 on the start and 2 – after POEM in 35 patients (group A). However, 8 patients were dissatisfied with the surgery (4 pts with II type achalasia and 4 – III type). They continued to suffer from dysphagia and/or noncardiac chest pain (group B).

According to HRM the mean resting pressure of LES in group A reduced 2 folds from 39,1±2,7 mmHg to 18,9±1,4 mmHg. Also we revealed the dramatic decrease in integrated residual pressure (IRP) from 22,8±0,7 mmHg to 9,8±0,6 mmHg and DCI: from 1865,5±286,9 to 128,2±53,8. In a group B the mean resting pressure of LES reduced from 48,8±2,4 mmHg to 33,6±2,4 mmHg. The integrated residual pressure (IRP) decreased from 22,8±0,7 mmHg to 15,01±0,6 mmHg and DCI: from 2999,6±417,6 to 1038,1±107,7.

Even though, we didn't observed the peristaltic waves in two groups before and after POEM as a normal manometric criteria: the consistent contraction of upper part of esophagus and then lower part of esophagus. Besides, HRM evaluated persisting spastic contraction in the middle and lower part of esophagus in patients with type III achalasia from group B. Two patients from group B with type II had good results in esophageal manometry.

Conclusion: The reduction of resting pressure, integrated resting pressure and distal contractile interval in several times can be accepted as criteria of POEM effectiveness. Besides, in patients with III type of achalasia we must assess the absence of spastic contraction as additional criteria of POEM satisfaction.

Disclosure: Nothing to disclose.

PP0243

LUMEN-APPPOSING METAL STENTS: A MINIMALLY INVASIVE TREATMENT OPTION FOR GASTROINTESTINAL OUTFLOW OBSTRUCTION

E. Gökce¹, P. Hindryckx¹

¹Ghent University Hospital, Dept. of Gastroenterology, Ghent, Belgium

Contact E-Mail Address: Emine.gokce@ugent.be

Introduction: The introduction of lumen-apposing metal stents (LAMSs) has revolutionized the field of therapeutic endoscopic ultrasound (EUS). LAMSs were initially developed for drainage of pancreatic fluid collections, but in the last decade its use for off-label indications has increased significantly. One of the most common off-label indications is treatment of gastrointestinal outflow obstruction.

Aims & Methods: This study aims to evaluate the effectiveness and safety of LAMS in creating EUS-guided gastro-enterostomy (EUS-GE) and entero-enterostomy (EUS-EE) anastomoses for the treatment of gastrointestinal (GI) outflow obstruction.

We collected data on all LAMS procedures conducted in patients with gastrointestinal (GI) outflow obstructions, including malignant gastric outlet obstruction (mGOO), benign gastric outlet obstruction (bGOO), candy cane syndrome, and afferent loop syndrome, between October 2019 and November 2023 at the University Hospital of Ghent. We used our prospective LAMS database and retrieved missing data from retrospective analysis of the medical patient records. The main outcome data of interest were technical success, clinical success, and adverse events. Technical success was defined as a successful placement of LAMS in the desired position. Clinical success was defined as either successful re-initiation of oral food intake in patients with mGOO and bGOO, or achievement of the intended therapeutic goal for the remaining conditions. Adverse events were classified according to the AGREE criteria.

Results: A total of 72 LAMS procedures were performed for GI outflow obstructions. The indications included 50 (69.4%) cases of mGOO, 19 (26.4%) cases of bGOO, 2 (2.8%) cases of afferent loop syndrome, and 1 (1.4%) case of candy cane syndrome. The overall technical and clinical success rates were very high (97.2% and 94.4%, respectively). Adverse events were observed in 9/72 (12.5%) cases, including 4 (5.6%) minor events (AGREE < 3) and 5 (6.9%) major events (AGREE ≥ 3). Major events included persisting fistula (N=1), and bleeding (N=4). All could be successfully managed, and there were no procedure-related deaths. Loss of LAMS patency occurred in 3/72 (4.2 %) cases and could be endoscopically managed in all cases.

Conclusion: In conclusion, our study shows that EUS-GE and EUS-EE offer an effective and safe approach when performed by experts. With high technical (97.2%) and clinical (94.4%) success rates, LAMS proves beneficial for treating GI outflow obstruction. Adverse events (12.5%) were manageable, with no procedure-related mortality. The extended patency duration and low re-intervention rate highlight LAMS as a minimally invasive and durable therapeutic option. Further prospective studies are needed.

Disclosure: Nothing to disclose.

PP0244

ENDOSCOPIC TREATMENT FOR SHORT-SEPTUM ZENKER'S DIVERTICULUM: A COMPARISON OF TRADITIONAL FLEXIBLE ENDOSCOPY SEPTOTOMY AND PERORAL ENDOSCOPIC SEPTOTOMY

R. de Sire¹, G. Franchellucci¹, A. Capogreco¹, D. Massimi¹, E. Mastrococco¹, L. Alfarone¹, M. Spadaccini¹, G. Marcozzi¹, A. Facciorusso², C. Hassan¹, A. Repici¹, R. Maselli¹

¹Humanitas Research Hospital, IRCCS, Gastroenterology, Endoscopy Unit, Rozzano, Italy, ²University of Foggia, Gastroenterology, Foggia, Italy

Contact E-Mail Address: roberto.desire@libero.it

Introduction: Short-septum Zenker's diverticulum (ZD) is considered difficult-to-treat because the limited anatomical space which restricts the operating area. Recently, peroral endoscopic septotomy (POES) emerged as a novel third-space technique for addressing this condition.

Aims & Methods: This study aims to compare the effectiveness and safety of POES with traditional flexible endoscopic septotomy (FES) for the treatment of symptomatic patients with short-septum ZD (<25 mm). In this single-center, prospective study we included all consecutive patients referred to Humanitas Research Hospital with symptomatic short-septum ZD who were scheduled to undergo either FES or POES. The primary outcome was the rate of technical success and adverse events (AEs). The secondary outcome was the rate of clinical success at 12 months and recurrence requiring a retreatment. A sensitivity analysis was conducted using propensity score matching. Hazard Ratio (HR) and its associated 95%CI were used for a time-dependent analysis of recurrence.

Results: A total of 94 patients (63.8% male; mean age 72.7 ± 10.7 years) underwent endoscopic treatment for a short-septum ZD (mean size 17.0 ± 4.3 mm) were included. Among them, 41.5% (n=39) were treated with FES and 58.5% (n=55) with POES (p=n.s.). Overall, the mean procedural duration was 25.3 ± 15.7 min, while the mean hospital stay was 0.3 days. Septotomies were performed under deep sedation in 91.5% of patients (n=86), while in 8.5% of them (n=8) the procedure was performed under general anesthesia. Technical success was achieved in 98.9% of patients (n=93), while AEs occurring in 5.3% of cases (n=5), with no statistical difference between groups (p=n.s.). Clinical success was observed in 91.5% of patients (n=86), while recurrence necessitating retreatment in 14.9% of cases (n=14) with no statistical difference between groups (p=n.s.).

Conclusion: Our findings suggest that POES is an effective and safe technique for the treatment of short-septum ZD, showing comparable outcomes to traditional FES.

References: Repici A, Spadaccini M, Belletrutti PJ, et al. Peroral endoscopic septotomy for short-septum Zenker's diverticulum. *Endoscopy*. 2020 Jul;52(7):563-568.

Disclosure: Nothing to disclose.

PP0245

BESPOKE, IN-HOUSE MADE ENDOSCOPIC VACUUM THERAPY DEVICES FOR THE TREATMENT OF UPPER GASTRO-INTESTINAL ANASTOMOTIC LEAKS: A SINGLE, TERTIARY CENTER EXPERIENCE

T. Alexopoulos¹, V. Lekakis¹, M. Tampaki¹, S. Papadakos¹, G. Mpouga¹, P. Fytili¹, A. Koutsoumpas¹

¹Laiko Hospital, Academic Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: thodorisalexo1990@gmail.com

Introduction: Anastomotic leaks (AL) are a challenging complication after upper gastro-intestinal (UGI) surgery, with significant mortality and morbidity. Endoscopic vacuum therapy (EVT) has recently emerged as the

mainstream tool for the management of UGI AL, both with commercially available devices and with in-house devices. Our group has recently (since July 2022) started to use bespoke, in-house made devices for EVT.

Aims & Methods: The aim of this study is to describe our experience with EVT for UGI AL in oncological patients undergoing surgery. We retrospectively collected and analysed data from all our patients who underwent EVT for AL after UGI oncological surgery, between July 2022 and December 2023 (18 months period). EVT was offered with bespoke, in house, hand-made negative pressure endoscopic devices connected to commercial, medical vacuum pumps. EVT was performed twice per week and initial response was assessed during the 5th EVT (after the completion of two weeks of endoscopic therapy) at latest; if AL had not improved endoscopically and radiologically by that point, no further EVT was offered and alternative therapies were considered.

Results: In total, 8 patients (5 male; mean age 61) underwent EVT over the above-mentioned period. Six of them underwent Ivor-Lewis esophagectomy with esophago-gastric anastomosis and 2 underwent total gastrectomy with esophago-jejunal anastomosis. Five of them had received neo-adjuvant chemotherapy prior to surgery. EVT was placed intracavitary initially if technically possible (5 patients) and then intraluminally as the leak site decreased in size, or directly intraluminally (3 patients) if the anastomotic leak was <5mm and could not accommodate our smallest in-house device.

EVT was successful in 7 out of 8 patients (success rate 87,5%). Only one patient had no response on day 15, and after discussion at our MDT he was offered a redo surgery (this was a patient with esophago-jejunostomy) with good final result. The mean time between AL diagnosis and first EVT was 9 days. A median of 6 endoscopic EVT procedures was needed (range 2- 15) for total AL closure. There were no technical issues related to the device itself, all patients tolerated EVT well and no adverse event directly related to EVT was recorded (the one patient who underwent reconstructive surgery experienced worsening of extraluminal cavity/collection but this was deemed secondary to the leak itself rather than EVT).

Conclusion: EVT is an effective therapy for UGI post-surgical anastomotic leaks, with a success rate of 87,5% in our experience. It is demanding in terms of resources (high number of repeat endoscopies needed), but it is well tolerated and safe.

Disclosure: Nothing to disclose.

PP0246

COMPARING TRANSNASAL PEG TUBE PLACEMENT WITH AND WITHOUT SEDATION IN PATIENTS WHERE TRANSORAL PEG TUBE PLACEMENT NOT POSSIBLE

N. Ahmed¹

¹*Sindh institute of advanced endoscopy and gastroenterology karachi, Gadtroenterology, Karachi, Pakistan*

Contact E-Mail Address: nasierahmedkhan@gmail.com

Introduction: In patients with indications for transnasal PEG tube placement, such as oral cavity, head and neck tumors where the conventional upper gastrointestinal endoscopic procedure to place a PEG tube through the oral cavity can be difficult due to complete or partial occlusion of mouth and/or pharynx. In such cases transnasal placement of a PEG tube is proven to be useful.

Aims & Methods: The aim of this study was to compare the efficacy, safety, procedure time, patient tolerance ,recovery time, immediate and late complication of transnasal PEG tube (T-PEG) placement with and without conscious sedation. A total of 150 patients had a successful PEG tube placement. Out of which 49 patients required transnasal PEG tube placement through ultra-thin video gastroscope with an external diame-

ter of 5.9 mm. patients were selected randomly for sedation and without sedation. After all aseptic measures,transillumination18-Fr PEG tube was placed transnasally by the Gauderer-Ponsky pull technique. 25 of the patients underwent T-PEG without any sedation and the remaining 24 patients were placed under conscious sedation with 2 mg midazolam. All patients were followed immediately and after 1 month of the procedure.

Results: T-PEG tube was placed successfully in all 49 patients.very surprisingly all patients for transnasal were male.all had history of tobacco chewing in the form of ghutka/mawa. mean age was 38 years. 24 patients had a transnasal-PEG tube placed under conscious sedation of 2 mg midazolam.2 patients in the sedated group had drop in oxygen saturation which was managed during procedure.one patient in sedated and one in unsedated group had minor nasal trauma during peg tube placement. procedure time, procedure tolerance in both groups were almost similar.while post procedure recovery,observation,monitoring and discharge time by the staff was shorter for unsadated group 10mins +-5 min as compared to the sadated group 60mins +-10mins.two patients in sedated group While only one patient in the unsedated group had stoma site infection which were treated according to c/s report. The overall tolerance and success rate was similar in both groups.

Conclusion: In patients with oral cavity obstructing mass or trismus where oral route of PEG tube placement cannot be done, a transnasal route can be considered for placement of PEG tube safely with no requirement of sedation.it decreases the patient hospital stay,staff nurse monitoring,risk of resuscitation tracheostomy.This method is especially useful if the procedure is done in remote settings where anesthesiologists are not available.

References: Unsedated transnasal percutaneous endoscopic gastrostomy placement in selected patientsM A Vitale et al. Endoscopy. 2005 Jan.

Unsedated transnasal percutaneous endoscopic gastrostomy carried out by a single physicianLian-Feng Lin et al. Dig Endosc. 2013 Mar.

Transnasal PEG tube placement in patients with head and neck cancer-Moises I Nevah et al. Gastrointest Endosc. 2014 Apr.

Nasal unsedated seated percutaneous endoscopic gastrostomy (nuPEG): a safe and effective technique for percutaneous endoscopic gastrostomy placement in high-risk candidatesAdam McCulloch et al. Frontline Gastroenterol. 2018 Apr.

Nasal unsedated seated percutaneous endoscopic gastrostomy (nuPEG): a safe and effective technique for percutaneous endoscopic gastrostomy placement in high-risk candidatesNeil C Fisher et al. Frontline Gastroenterol. 2019

Disclosure: Nothing to disclose.

PP0247

ENDOSCOPIC SLEEVE GASTROPLASTY AS A THERAPEUTIC OPTION FOR CLASS III OBESITY

L. Gualtieri¹, G. Carlino², V. Pontecorvi³, M.V. Matteo¹, M. De Siena⁴, C. Spada⁵, I. Boskoski⁶, V. Bove⁷

¹Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Digestive Endoscopy Unit, Rome, Italy, ²Policlinico Universitario Agostino Gemelli, Università Cattolica Del Sacro Cuore, 00168, Italy, ³IRCCS Fondazione Policlinico Gemelli, Endoscopia Digestiva Chirurgica, Rome, Italy, ⁴POLICLINICO A. GEMELLI, Roma, Italy, ⁵Catholic University Rome - Digestive Endoscopy unit, Catholic University Rome; Rome/IT, Digestive Endoscopy unit, Rome, Italy, ⁶Catholic University of Rome Digestive Endoscopy Unit, Digestive Endoscopy Unit, Rome, Italy, ⁷Fondazione Policlinico Universitario A. Gemelli, Roma, Italia - IRCCS, Digestive Endoscopy Unit, Roma, Italy

Contact E-Mail Address: loredana.gualtieri.15@gmail.com

Introduction: The spread of Endoscopic Sleeve Gastroplasty (ESG) as an effective bariatric endoscopic technique has been notable, particularly for treating patients with class I and II obesity with related comorbidities. Our study aimed to assess the efficacy of ESG in class III obese patients [Body Mass index (BMI) >40 kg/m²] focusing on weight loss and comorbidities improvement.

Aims & Methods: This retrospective analysis on a prospective dataset, focused on subjects with a baseline BMI >40 kg/m² who underwent ESG from June 2017 to November 2023. Weight loss outcomes [BMI, Excess Weight Loss (%EWL), Total Body Weight Loss (%TBWL), BMI loss (BMIL) and Absolute Weight Loss (AWL)] were assessed at 3, 6, 12 and 24 months. Additionally, the impact of ESG on Type 2 Diabetes (T2D), Hyperinsulinemia (H-INS), Arterial Hypertension (AH), and Obstructive Sleep Apnea Syndrome (OSAS) was analyzed.

Results: A total of 129 patients were included (74 female, mean age 47 ± 12.7, mean BMI: 44.4 ± 4.1 kg/m²). We observed a significant regression to grade II obesity starting within the first three months postoperatively, with a BMI reduction of 7.1 ± 4.8 at 24-months follow-up (Table 1).

At 12-month follow-up, our data showed improvement or complete remission of T2D, H-INS, AH and OSAS, in 50% (7/14), 36.3% (12/33), 41% (20/49) and 31% (9/29) of patients, respectively.

Follow-up	n	Weight (kg)	p	AWL (kg)	EWL (%)	TBWL (%)	BMI (kg/m ²)	p	BMIL (kg/m ²)
3m	99	106.1 (15.7)	<0.01	19.3 (8.0)	25.3 (11.1)	15.3 (5.0)	37.7 (3.8)	<0.01	6.8 (2.6)
6m	90	103.8 (17.1)	<0.01	21.6 (9.5)	39.9 (16.0)	17.2 (6.9)	36.6 (4.7)	<0.01	7.7 (3.3)
12m	83	105.4 (21.5)	<0.01	19.9 (13.1)	37.2 (23.2)	16.0 (10.0)	37.5 (5.9)	<0.01	7.2 (4.6)
24m	44	106.1 (17.4)	<0.01	19.8 (13.4)	34.7 (22.2)	15.4 (10.0)	37.7 (4.3)	<0.01	7.1 (4.8)

Weight loss outcomes of primary ESG in subjects with BMI >40 kg/m².

Data are reported as mean value (standard deviation).

A two sample T-Test was used to compare baseline weight and weight loss outcomes.

Conclusion: Based on our observations, while Endoscopic Sleeve Gastroplasty (ESG) demonstrated effectiveness in inducing weight loss and ameliorating comorbidities in class III obese patients, it did not fully resolve obesity, potentially due to the high baseline BMI. Consequently, surgical intervention should continue to be the primary treatment modality for class III obesity. However, when surgery is contraindicated or refused by the patient, ESG represents a less invasive option and could be considered as an effective first-stage or multi-step treatment.

Disclosure: Nothing to disclose.

PP0248

TWO HUNDRED CASES OF PERCUTANEOUS TRANSESOPHAGEAL GASTROTUBING (PTEG) FOR THE PATIENTS WITHOUT INDICATION OF PEG

M. Murakami¹, K. Nishino¹, S. Murakami¹, H. Yano¹, K. Hino¹, K. Mori¹, K. Ishido², S. Tanabe³, M. Kida⁴, C. Kusano²

¹Murakami Memorial Hospital, Dept. of Internal Medicine, Saijo, Japan, ²Kitasato University School of Medicine, Gastroenterology, Sagami-hara, Japan, ³Kitasato University School of Medicine, Department of Advanced Medicine Research and Development Center for New Medical Frontiers, Sagami-hara, Japan, ⁴Kitasato University, Endoscopy & Gastroenterology, Sagami-hara, Japan

Contact E-Mail Address: masato@murakami-kinen.or.jp

Introduction: Percutaneous transesophageal gastrotubing (PTEG) was established as an alternative route to access the gastrointestinal tract for the patients that Percutaneous Endoscopic Gastrostomy was contraindicated. More than two hundred cases without indication of PEG were rescued by this ideal method.

Aims & Methods: The aim of this study is to evaluate the clinical usefulness of PTEG. A rupture-free balloon (RFB) catheter is inserted into the upper esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient's neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. Double Balloons equipped Over tube type RFB were used instead of primary RFB in fifty-seven cases that the puncture needle is punctured into the over tube trough the balloon. We perform PTEG in a total of 204 patients (124 men and 80 women, mean age 71.5 years) PTEG was performed for nutrition in 116 patients and for decompression in 88. Eighty-five patients had peritoneal carcinoma, 62 patients had prior gastrectomy, 30 patients had gastric herniation into the thoracic cavity.

Results: Satisfactory results were achieved in all 204 patients. Median follow-up was 65.0 days in patients who received decompression because of the obstruction due to mainly malignancies and 359.0 days in those who received nutrition. Nine patients who were started in the fluoroscopically assisted according to the original method needed endoscopic assistance to complete the procedure in first 30 cases.

Another 174 patients were performed in endoscopic assistance instead of fluoroscopy.

About the complications, there was 2 patient with severe bleeding requiring blood transfusion, Two patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in thirteen patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. Complication rate was 9.8%. No patient required surgical treatment or died after PTEG.

Conclusion: PTEG is feasible, safe, and useful for long-term nutrition and/or decompression for the patient who is contraindicated to PEG. PTEG may become the only procedure of the liberation from nasogastric tube for the patient who is contraindicated to PEG. PTEG is the ideal solution for the patients with PEG contraindicated.

Disclosure: Nothing to disclose.

PP0249

ACUTE ESOPHAGEAL NECROSIS IS ASSOCIATED WITH CELIAC TRUNK STENOSIS: A SINGLE CENTER EXPERIENCE OF 15 CASES

M. Maibier¹, D. Geisel², A. Arnold³, M. Schulz¹, J. Wizenty¹, M. Sigal¹, A. Wree¹, F. Tacke¹, A. Fischer¹

¹Charité Universitätsmedizin Berlin, Department of Hepatology & Gastroenterology, Berlin, Germany, ²Charité Universitätsmedizin Berlin, Department of Radiology, Berlin, Germany, ³Charité Universitätsmedizin Berlin, Department of Pathology, Berlin, Germany

Contact E-Mail Address: martin.maibier@charite.de

Introduction: Acute esophageal necrosis (AEN) is an uncommon but often fatal esophageal condition with a mortality rate of approximately 30%. AEN predominantly affects elderly, male patients with significant comorbidities and typically presents with signs of upper gastrointestinal hemorrhage. The pathophysiology of AEN is attributed to a combination of local hypoperfusion, loss of mucosal barrier function and acid reflux. However, AEN still remains poorly understood due to its low incidence. In example, it has not been investigated whether celiac trunk stenosis might contribute to AEN development.

Aims & Methods: In this case series, we aimed to review clinical, laboratory and endoscopic features of AEN patients with an additional focus on celiac trunk diameter. 15 patients diagnosed with AEN between 2014 and 2024 at a single center in Berlin, Germany, were included in this study. Clinical data were reviewed and retrospectively analyzed on a case-by-case basis. AEN diagnosis was made endoscopically applying well-described criteria including diffuse, circumferential livid or black discoloration of esophagus mucosa with sparing of the gastroesophageal junction. Celiac trunk was assessed using contrast-enhanced computed tomography imaging to measure the extent of narrowing in the celiac trunk artery. The stenosis was classified into atherosclerotic or median arcuate ligament compression and graded into < 30% (grade 0), 30 - 50% (grade 1), 50 - 80% (grade 2) and > 80% narrowing (grade 3). Laboratory tests were carried out for each patient. However, in some cases not all parameters were available in retrospect.

Results: 73% (11/15) of AEN patients were male with a median age of 63.4 years (23 - 85 years). In 47% (7/15) of cases, cardiovascular disease was present. 67% (10/15) of patients presented with gastrointestinal hemorrhage, other clinical presentations included dysphagia, abdominal pain, dyspnea, and shock. 100% (15/15) of patients showed elevated CRP (mean: 70.9 mg/dl, 13.8 - 224.5 mg/l), 92% (11/12) hypalbuminemia (mean: 22.4 g/dl, 6.0 - 36.3 g/dl), 90% (9/10) lactatemia (mean: 97.5 mg/dl, 17 - 259 mg/dl), 82% (9/11) hyperglycemia (mean blood glucose: 146 mg/dl, 73 - 200 mg/dl), 67% (10/15) leukocytosis (mean: 17.96/nl, 4.64 - 42.02/nl) and 67% (10/15) anemia (mean hemoglobin: 11.0 g/dl, 5.0 - 16.1 g/dl). Endoscopy revealed panesophageal necrosis in 71% (10/14) of cases and mid-distal disease in 21% (3/14). Duodenal involvement, mostly reflected by duodenal ulcers, was found in 79% (11/14) of cases. 87% (13/15) of AEN patients showed celiac trunk stenosis. Grade 2 or 3 stenosis was present in 47% (7/15) of cases. 85% (11/13) of celiac trunk stenoses were atherosclerotic, 15% (2/13) were caused by median arcuate ligament compression. Case fatality rate was 40% (6/15) in this series.

Conclusion: Our study confirms that AEN is a potentially life-threatening medical condition often observed in critically ill patients. For the first time, we show that celiac trunk stenosis is associated with this condition. Future research is needed to confirm this data and carve out a possible role for endovascular revascularization in the treatment of AEN patients.

Disclosure: Nothing to disclose.

Poster
H.pylori

H.pylori

09:00-18:00 / Poster Exhibition

P0250

EFFECT OF HELICOBACTER PYLORI ERADICATION ON BODY WEIGHT AND LIPID PROFILE; A PROSPECTIVE COHORT STUDY AT A UNIVERSITY HOSPITAL IN SOUTH KOREA

J.W. Kim¹, N.H. Kim²

¹Inje University Ilsan Paik Hospital, Internal Medicine, Goyang, South Korea, ²Inje University Ilsan Paik Hospital, Gastroenterology, Goyang, South Korea

Contact E-Mail Address: jongman12@gmail.com

Introduction: The effect of *Helicobacter pylori* eradication (HPE) on body weight and lipid profile is not well known.

Aims & Methods: We prospectively enrolled 102 patients who were treated for *H. pylori* eradication from Apr 2021 to Jan 2024 at a university hospital in Goyang, South Korea (Inje University Ilsan Paik Hospital). Patients who had active peptic ulcer were excluded. Patients' body weight and lipid profile were measured before enrollment and 3 months after taking medications for HPE. The difference between before-and-after measurements were compared using the paired t-test. To test the difference in lipid profile, patients who had newly started lipid lowering drugs before the three-month follow-up visit were excluded from the analysis.

Results: Among 102 patients who were enrolled to treat *H. pylori*, 87 patients (46 males, 41 females) were followed up three months after taking HPE prescriptions. The median age was 59 years (range, 19-82). The baseline body mass index was 25.0 kg/m² (range, 16.2-37.5).

There were 39 patients (44.8%) who were using lipid lowering drugs at the baseline. Five patients who had started lipid lowering drugs before the follow-up visit were excluded when analyzing the lipid profile change. Hp eradication rate was 91.9% (80/87). The HPE regimen included triple therapy (n=46 [52.9%]), quadruple therapy (n=31 [35.6%]), and concomitant therapy (n=10 [11.5%]).

	Baseline, mean (95% CI)	3 month follow-up after H. pylori eradication, mean (95% CI)	P-value (before-and-after t-test)	Difference among HPE successful (n = 80), median (interquartile range)	Difference among HPE failed (n = 7), median (interquartile range)	P-value (according to H. pylori eradication)
Body weight (kg)	67.4 (64.7-70)	66.9 (64.3-69.5)	0.079	-0.15 (-1.55, 1)	-1 (-2.8, 0)	0.386
Serum glucose (mg/dL)	111.7 (106.9-120.5)	109.4 (104.1-114.5)	0.068	-1 (-11, 7)	-14.5 (-18, 23)	0.465
Total cholesterol (mg/dL)	166.5 (157.5-175.6)	162.1 (152.7-171.5)	0.172	-5 (-17, 7)	14 (-13, 43)	0.770
LDL cholesterol (mg/dL)	93.4 (84.9-101.8)	84.2 (76.4-92.1)	0.009	-7 (-21, 6)	-1.5 (-70, 19)	0.264
HDL cholesterol (mg/dL)	52.7 (49.6-55.8)	54.5 (51.2-57.9)	0.074	1 (-3, 7)	3 (-1, 22)	0.113
Triglyceride (mg/dL)	120.0 (105.3-134.7)	122.4 (103.9-140.9)	0.702	-3 (-30, 31)	-12 (-44, -1)	0.507

The body weight decreased from mean 67.4 kg (95% confidence interval [CI], 64.7-70.0) to mean 66.9 kg (95% CI, 64.3-69.5; p = 0.079). Serum glucose decreased from mean 111.7 mg/dL (95% CI, 106.9-120.5) to mean 109.4 (95% CI, 104.1-114.5; p = 0.068).

Total cholesterol decreased from mean 166.5 mg/dL (95% CI, 157.5-175.6)

to mean 162.1 (95% CI, 152.7-171.5; p = 0.172). Low-density lipoprotein (LDL) cholesterol decreased from mean 93.4 mg/dL (95% CI, 84.9-101.8) to mean 84.2 (95% CI, 76.4-92.1; p = 0.009). High-density lipoprotein (HDL) cholesterol increased from mean 52.7 mg/dL (95% CI, 49.6-55.8) to mean 54.5 (95% CI, 51.2-57.9; p = 0.074). Triglyceride changed slightly from 120.0 mg/dL (95% CI, 105.3-134.7) to 122.4 mg/dL (95% CI, 103.9-140.9; p = 0.702). The number of non-Hp eradicated subjects was too small (n = 7) to compare the differences in body weight and lipid profile according to actual *H. pylori* eradication.

Conclusion: In a short-term prospective study among Korean patients who were treated for *H. pylori*, there was a decrease in body weight and a favorable effect on serum lipid levels. The number of non-Hp eradicated subjects was too small to draw conclusions about the effect of successfully eradicated Hp on body weight and lipid profile. The long-term effect of HPE on body weight and lipid profile remains to be analyzed, and a randomized study is required to achieve non-biased results.

References: 1. Effect of *Helicobacter pylori* Eradication on Body Weight: A Multicenter Propensity Score-matched Analysis in Korea. *J Neurogastroenterol Motil.* 2023 Jul 30; 29(3): 352-359.

2. Eradication of *Helicobacter pylori* alleviates lipid metabolism deterioration: a large-cohort propensity score-matched analysis. *Lipids Health Dis* 21, 34 (2022).

Disclosure: Nothing to disclose.

PP0251

WITHDRAWN

PP0252

GUINEA PIG - A CONVENIENT MODEL TO STUDY THE PATHOGENESIS OF HELICOBACTER PYLORI INFECTIONS

W. Gonciarz¹, P. Płoszaj¹, M. Chmiela¹

¹University of Lodz, Institute of Microbiology, Biotechnology and Immunology, Faculty of Biology and Environmental Protection, Department of Immunology and Infectious Biology, Łódź, Poland

Contact E-Mail Address: weronika.gonciarz@biol.uni.lodz.pl

Introduction: *Helicobacter pylori* (Hp) is an etiological agent of chronic gastritis, gastric and duodenal ulcers and gastric cancers. The use of an appropriate animal model for experimental studies on the pathogenesis of *H. pylori* infections is necessary due to the chronic character of such infections and difficulties in identifying their early stage in humans.

Aims & Methods: The aim of this study was to develop a guinea pig model of *H. pylori* infection and identify its microbiological, histological, molecular and serological determinants. Guinea pigs (*Cavia porcellus*) were inoculated *per os* with *H. pylori* strain: CCUG 17874 positive for vacuolating cytotoxin A (VacA) and cytotoxin associated gene A (CagA) protein, suspended in *Brucella* broth with fetal calf serum (FCS) and Skirrow supplement (on permission of Local Ethics Committee for Anima Experiments, Medical University of Lodz Poland, Decision 58/ŁB45/2016).

To determine *H. pylori* colonization, 7 and 28 days after inoculation, a gastric tissue was used for culturing Hp histopathological examination of gastric tissue sections, stained by Mayer's haematoxylin and eosin, Giemsa staining or Warthin-Starry silver staining to assess inflammatory

response, or to visualize *Helicobacter*-like organisms (HLO). Furthermore an immunostaining with anti-Ki-67 antibodies was developed to assess epithelial cell proliferation. *H. pylori* infection was also confirmed by polymerase chain reaction (PCR) for detection in gastric tissue of *ureC* and *cagA* genes and by serological assessment of *Hp* antigens in feces and serum anti-*Hp* antibodies.

Results: This study showed the successful colonization of guinea pigs with *Hp* on the basis of microbiological, histological, molecular and immunological determinants. In the light of obtained results *Cavia porcellus* can be a good model for studying *Hp* pathogenesis and the related immune response against this pathogen.

Conclusion: The ability to induce and confirm the *Hp* infection in guinea pig makes this animal model suitable for studying the pathogenesis of infection and the course of related immune response, which *in vivo* is modulated by the components of these bacteria.

Financing: The research was financially supported by the National Science Center by the grant SONATA 18 "Assessment of the ability of *Mycobacterium bovis* BCG-onco bacilli to control the development of *Helicobacter pylori* infection", UMO-2022/47/D/NZ7/01097.

Disclosure: Nothing to disclose.

PP0253

BARRIERS TO EFFECTIVE GERD SYMPTOM CONTROL POST-H. PYLORI TREATMENT IN SOCIO-ECONOMICALLY DIVERSE POPULATIONS

R. Rammohan¹, M. Joy¹, S.G. Magam¹, D. Natt¹, W. Lau¹, A. Tadikonda¹, S.R. Magam¹, L. Pannikodu¹, J. Desai¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rammoha@numc.edu

Introduction: The interplay of race and gender significantly influences the manifestation of Gastroesophageal Reflux Disease (GERD) symptoms following *Helicobacter pylori* (*H. pylori*) treatment.

This multifaceted relationship, deeply rooted in biological, cultural, and socioeconomic factors, presents a complex medical challenge. Understanding these disparities is crucial for tailoring effective treatment strategies, ensuring equitable healthcare outcomes, and advancing personalized medicine in managing GERD symptoms in diverse populations post-*H. pylori* eradication.

Aims & Methods: Our research, spanning 2009 to 2023, retrospectively analyzed patients treated for *H. Pylori*, ensuring a minimum one-year follow-up. We collected data encompassing comorbidities, insurance status, and socioeconomic factors, particularly targeting the emergence of GERD symptoms, Esophagitis, and duodenal ulcers, identified using CPT and ICD codes. Initially, we employed a Chi-square test of independence to evaluate the association between race and GERD symptoms.

We conducted a post-hoc analysis with adjusted standardized residuals to delve deeper, pinpointing specific races with notably higher or lower GERD symptom frequencies than expected. We performed pairwise race comparisons via Chi-square tests, applying a Bonferroni correction for multiple comparisons.

Results: Between 2009 and 2023, 4,205 patients received *H. Pylori* treatment, with 3,329 qualifying for our study after excluding those lost to follow-up. The average age was 54.5 years, with 64% female (2,134) and 48% Caucasian (1,664).

The Chi-square test revealed a significant association between Race and GERD symptoms (Chi sq stat:8.69 p-value <0.01). In-depth post-hoc pairwise comparisons showed that the Hispanic race had significantly higher rates of GERD symptoms when compared to other races. Other races (p

<0.01), White (p <0.01), Black (p <0.01), and Asian races (<0.01). Adjusted residual analysis further confirmed that the Hispanic race (5.54, p<0.023) showed a higher-than-expected number of GERD symptom cases.

Among the Hispanic races, Patients with low socioeconomic status showed increased GERD symptoms (Chi. Sq: 7.65, P<0.01). Gender does not significantly impact GERD symptoms (Chi. sq: 0.831, P = 0.512).

Conclusion: Our study, analyzing data from 2009 to 2023 on patients treated for *H. Pylori*, underscores the significant influence of race and gender on GERD symptoms post-treatment.

Notably, the Hispanic population exhibited a higher incidence of GERD symptoms compared to other races, with socioeconomic status further intensifying this trend.

These findings highlight the need for more personalized, culturally sensitive approaches in healthcare, emphasizing the importance of considering race, gender, and socioeconomic factors in the treatment and management of GERD following *H. Pylori* eradication.

References:

Lai Y, Shi H, Wang Z, Feng Y, Bao Y, Li Y, Li J, Wu A. Incidence trends and disparities in *Helicobacter pylori* related malignancy among US adults, 2000-2019. *Front Public Health*. 2022 Nov 28;10:1056157. doi: 10.3389/fpubh.2022.1056157. PMID: 36518580; PMCID: PMC9743990.

Disclosure: Nothing to disclose.

PP0254

CHANGES OVER TIME IN THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN THE NORTH-WESTERN REGION OF THE RUSSIAN FEDERATION FROM 2015 TO 2023

N.V. Bakulina¹, S.V. Tikhonov¹, I.V. Savilova¹, A.V. Zharkov^{1,2}, V.A. Ponomarenko¹, I.G. Bakulin¹

¹North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russian Federation, ²Healthcare Committee of the Leningrad Region, Saint Petersburg, Russian Federation

Contact E-Mail Address: nv_bakulina@mail.ru

Introduction: Russia is among the countries with a high prevalence of *Helicobacter pylori* (*H. pylori*) infection. The North-Western Federal District, comprising one-tenth of Russia's population, is predominantly urban. As of 2023, its population is over 13 million people. Current information on *H. pylori* infection prevalence is necessary for the development of clinical guidelines for the prevention of *H. pylori*-associated disorders.

Aims & Methods: To evaluate the dynamics of *H. pylori* infection prevalence among patients with dyspepsia between 2015 and 2023 based on ¹³C-urea breath test (¹³C-UBT).

The study was conducted in the North-Western Federal District. Patients with dyspepsia (n=50,884) who underwent ¹³C-UBT between 2015 and 2023 were included in this descriptive study. If Delta Over Baseline (DOB, δ¹³CO₂) was less than 2.5‰, the result of the test was considered negative, while δ¹³CO₂ value ≥2.5‰ indicated the presence of *H. pylori* infection.

The criteria for the infection grade (IG) were defined as follows: IG I (2.5–3.4‰), IG II (3.5–6.4‰), IG III (6.5–9.4‰), and IG IV (>9.5‰). The database for subsequent statistical analysis included such parameters as the patients' age, gender, history of prior eradication therapy, and the result of the ¹³C-UBT test.

Results: Among all included individuals (mean age 43.3 years (31.0; 55.0); 57.5% of whom were female), there were 83.6% (n=42,543) of primary "naïve" patients (who had had no history of prior eradication therapy) (95% confidence interval (CI) 83.3–83.9). The proportion of treated patients was 16.4% (n=8,341; 95% CI 16.1–16.7).

The prevalence of *H. pylori* infection among the primary patients was 51.4% in 2015 (874/1701 subjects; 95% CI 49.0–53.8) and gradually decreased to 32.2% (1904/5916 subjects; 95% CI 31.0–33.4) in 2022. In 2023 *H. pylori*-positive was 32.7% (1450/4433 subjects; 95% CI 31.3–34.1). Eradication failure was 39.1% in 2015 (148/379 subjects; 95% CI 34.5–44.3). Eradication rate in 2016 was 80.2% (684/853 subjects; 95% CI 77.4–82.7) and increased to 86.8% (702/809 subjects; 95% CI 84.3–88.9) in 2023. Naive and unsuccessful treated patients demonstrated a very high IG - 73.0 and 66.5%, respectively. *H. pylori* was detected more often in young adults (18–44 years old (y.o.)). The infection was less commonly detected among children (1.6% of primary and 1.3% of treatment-failure patients).

Total, n	Naive, 15358	Treatment failure, 1284
Women, n (%)	8804 (57,3)	728 (56,7)
Men, n (%)	6554 (42,7)	556 (43,3)
2–17 y.o., n (%)	247 (1,6)	17 (1,3)
18–44 y.o., n (%)	7918 (51,5)	613 (47,7)
45–59 y.o., n (%)	4401 (28,7)	403 (31,4)
Over 60 y.o., n (%)	2792 (18,2)	251 (19,6)
IG I, n (%)	736 (4,8)	119 (9,3)
IG II, n (%)	1605 (10,5)	179 (13,9)
IG III, n (%)	1802 (11,7)	132 (10,3)
IG IV, n (%)	11215 (73,0)	854 (66,5)

Table 1. Characteristics of the *H. pylori*-positive primary and treatment failure patients.

Conclusion: Overall, our study highlighted a significant decrease of *H. pylori*-infection from 2015 to 2023. However, the eradication rates in the North-Western district of Russia remain low and do not reach the threshold value of 95%.

References:

1. Li Y, Choi H, Leung K. et al. Global prevalence of *Helicobacter pylori* infection between 1980 and 2022: a systematic review and meta-analysis // *Lancet Gastroenterol. Hepatol.* 2023. Vol. 8, No. 6. P. 553–564. DOI: 10.1016/S2468-1253(23)00070-5

2. Malfertheiner P, Megraud F, Rokkas T. et al; European *Helicobacter* and Microbiota Study group. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report // *Gut.* 2022;gutjnl-2022-327745. DOI: 10.1136/gutjnl-2022-327745

Disclosure: Nothing to disclose.

PP0255

PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AND ANTIMICROBIAL RESISTANCE IN PORTUGAL: A MULTICENTRIC POPULATION STUDY

M. Rocha¹, P. Pimentel-Nunes², D. Libânio², R.P. Bastos², M. Bento-Miranda², M.T.d.A.P. Pais², C. Bernardes¹, S. Mendez Santos¹, V. Gamelas¹, M. Cruz Costa³, L. Prado Castro⁴, G. Esquerda⁴, H. Baldaia⁴, L. Raimundo³, L. Costa³, L. Rafael⁵, R. Panseri-Rodrigues⁵, F. Barreto⁴, A. Maia-Gonçalves⁵, C. Sousa³

¹Unilabs Portugal, Gastroenterology Department, Lisbon, Portugal, ²Unilabs Portugal, Gastroenterology Department, Porto, Portugal, ³Unilabs Portugal, Molecular Biology Department, Porto, Portugal, ⁴Unilabs Portugal, Pathology Department, Porto, Portugal, ⁵Unilabs Portugal, Porto, Portugal

Contact E-Mail Address: pedronunesml@gmail.com

Introduction: Portugal is an intermediate-high risk country for gastric cancer and *Helicobacter pylori* (Hp) infection is an important risk factor for such condition. All of infected patients should be treated; however, the increasing frequency of antibiotic resistance reduces its eradication rate.

Aims & Methods: Aims: To analyze the prevalence of Hp infection in Portugal and its antimicrobial resistance profile. To evaluate the prevalence of premalignant gastric conditions.

Methods: A multicentric cross-sectional study involving 9 endoscopy units from Portugal, distributed across the country (north, central and south regions). We included patients aged ≥40 who underwent upper endoscopy in these units between February and March 2024. Hp detection was performed using immunohistochemistry (IHC). In positive IHC samples, clarithromycin, fluoroquinolones and metronidazole resistances were assessed in biopsy samples using real-time polymerase chain reaction.

Results: Four hundred twenty-one patients were included (58% women, mean age 60), 172 of which were Hp-positive (41%). Excluding patients with prior eradication therapy, the prevalence of Hp infection was 47.4%. Infection was more prevalent in the north region of the country (north 46.8%; central 36%; south 36.5%). The antimicrobial resistance rates were: clarithromycin 26%; fluoroquinolones 16%; metronidazole 2%; clarithromycin/fluoroquinolones 4%. Intestinal metaplasia (IM) was identified in 138 patients (32.8%), 24 of which (6%) had extensive IM (both antrum and corpus) and 31 (7%) had an endoscopic grading of gastric IM (EGGIM) ≥5.

Conclusion: Hp infection in Portugal is frequent, showing a north-south gradient, albeit smaller than expected. More than half of the strains showed no antibiotic resistance and only 4% exhibited dual resistance to clarithromycin/fluoroquinolones. We demonstrate the feasibility of studying resistance profile in endoscopic biopsies, suggesting that such tests may lead to reduce antibiotic consumption and associated side effects, as well as lower therapeutic costs. The presence of IM in approximately one-third of patients, in a predominantly young population, reinforces the relevance of endoscopic screening in Portugal.

References:

1. Malfertheiner P, Megraud F, Rokkas T, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut.* 2022;71:1724-62.

2. Hooi JKY, Lai WY, Ng WK, et al. Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. *Gastroenterology.* 2017;153:420-9.

3. Howden CW, Graham DY. Recent Developments Pertaining to *H. pylori* Infection. *Am J Gastroenterol.* 2021;116:1-3.

4. Savoldi A, Carrara E, Graham DY, et al. Prevalence of Antibiotic Resistance in *Helicobacter pylori*: A Systematic Review and Meta-analysis in World Health Organization Regions. *Gastroenterology.* 2018;155:1372-82.

5. Lopo I, Libânio D, Pita I, et al. *Helicobacter pylori* antibiotic resistance in Portugal: Systematic review and meta-analysis. *Helicobacter.* 2018;23:e12493.

6. Kovacheva-Slavova M, Valkov H, Angelov T, et al. Screening for *Helicobacter pylori* infection and Clarithromycin resistance using Real-Time Polymerase Chain Reaction. *Eur Rev Med Pharmacol Sci.* 2021;25:5042-46.

7. Egli K, Wagner K, Keller PM, et al. Comparison of the Diagnostic Performance of qPCR, Sanger Sequencing, and Whole-Genome Sequencing in Determining Clarithromycin and Levofloxacin Resistance in *Helicobacter pylori*. *Front Cell Infect Microbiol.* 2020;10:596371.

8. Nyssen OP, Espada M, Gisbert JP. Empirical vs. Susceptibility-Guided Treatment of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis. *Front Microbiol.* 2022;13:913436.

Disclosure: Nothing to disclose.

PP0256

PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AND VIRULENCE GENES IN PATIENTS WITH UPPER GASTROINTESTINAL DISEASES FROM SOUTHWEST OF IRANP. Alavinejad¹, N. Karimi², M. Savari², E. Abbasi Montazeri²¹Ahvaz Jundishapur university of medical sciences, GI department, Copenhagen, Denmark, ²Ahvaz Jundishapur university of medical sciences, GI department, Ahvaz, Iran**Contact E-Mail Address:** Pezhmanalavinejad@gmail.com

Introduction: Various virulence factors of *H. pylori* have been identified that play an important role in pathogenesis. The aim of this study was to investigate the prevalence of *H. pylori* infection by rapid urea test and histopathology examination and determining the prevalence of the cytotoxin associated gene A (*cagA*), vaculating cytotoxin A (*vacA*) and restriction endonuclease-replacing gene (*hrgA*) in *H. pylori* strains isolated from patients with upper gastrointestinal diseases from Khuzestan.

Aims & Methods: Gastric biopsy specimens were obtained from 426 patients with gastrointestinal disorders undergoing endoscopy in Imam Khomeini Hospital, Ahvaz, the capital of Khuzestan province. *H. pylori* infection was investigated in patients by rapid urea test and histopathology examination and positive specimens were reconfirmed by PCR of the *ureB* gene. The presence of *cagA*, *vacA* s/m and *hrgA* genotypes were determined by PCR from culture or gastric biopsies.

Results: *H. pylori* was detected in 33.8% (144/426) of patients by rapid urea test and in 44.13% (188/426) by histopathology. 60.2% of infected patients were female and 39.8% were male and the mean age of patients was 47.1 years (range 14 to 89 years old). Epigastric pain was the most commonly reported symptom (62.7%), followed by anorexia (24.9%), nausea (21.4%), epigastric burning (20.4%), gastrointestinal bleeding (14.9%), fullness (12.4%), vomiting (12.4%), weight loss (12.9%) and bloating (11.9%). The main endoscopic findings were non-ulcer dyspepsia 56.7%, erosive gastritis 20.9%, gastric ulcer 13.4%, duodenal ulcer 7.5% and gastric cancer 1%. The *cagA*, *vacAs1*, *vacAs2*, *vacAm1*, *vacAm2* and *hrgA* genotypes were detected in 93.3%, 71.6%, 23.1%, 25.4%, 70.1% and 67.2% of isolates, respectively. The allelic variant *vacAs1m2* was more prevalent (45.5%) than *vacAs1m1* (23.9%) and *vacAs2m2* (23.1%).

There was a statistically significant association between the presence of *vacAs1m2* genotype and gastric ulcer ($P = 0.004$), while the *vacAs2m2* significantly was observed in strains isolated from patients with non-ulcer dyspepsia ($P = 0.017$). Also the presence of *hrgA* gene was associated with duodenal ulcer ($P = 0.043$).

Conclusion: the histopathology examination is more specific than the rapid urea test especially in gastric ulcer bleeding cases and the use of both tests can help to more accurate diagnosis of *H. pylori* infection. Based on the results *vacAs1*, *vacAs2* and *hrgA* genotypes may be the predictors of gastric ulcer, non-ulcer dyspepsia and duodenal ulcer, respectively.

Disclosure: Nothing to disclose.

PP0257

PREVALENCE OF PRIMARY CLARITHROMYCIN RESISTANCE IN PATIENTS INFECTED WITH *HELICOBACTER PYLORI* IN EUROPE IN THE LAST FOUR DECADESB. Nafria^{*1}, O.P. Nyssen^{*2}, L. Bujanda^{**3}, J.P. Gisbert^{**2},^{*}co-first authors ^{**}co-last authors

¹Instituto de Investigación Sanitaria Biodonostia, Área de Enfermedades Hepáticas y Gastrointestinales, San Sebastián, Spain, ²Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Digestive Services, Madrid, Spain, ³Instituto de Investigación Sanitaria Biodonostia, Hospital Universitario Donostia-San Sebastián, Servicio de Aparato Digestivo, San Sebastián, Spain

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: Global rise in primary *Helicobacter pylori* (*H. pylori*) antibiotic resistance has led to a decrease in the treatment efficacy. Understanding the rates of clarithromycin resistance in *H. pylori* management is essential for determining the optimal eradication therapy and achieve successful clinical outcomes.

Aims & Methods: This review aimed to evaluate the prevalence and geographical distribution of *H. pylori* primary clarithromycin resistance in Europe. Bibliographical searches were performed in PubMed up to March 2024. Selection: Included studies assessing rates of *H. pylori* primary resistance to clarithromycin with no time restriction. Publications in any language were considered. Studies that focused on children only or non-European countries were excluded.

Country (number of studies)	Clarithromycin resistance prevalence % (n/N) 1990-1999	Clarithromycin resistance prevalence % (n/N) 2000-2009	Clarithromycin resistance prevalence % (n/N) 2010-2019	Clarithromycin resistance prevalence % (n/N) 2020-2024
Armenia (1)	NA	NA	2.2 (2/91)	NA
Austria (5)	3.3 (11/331)	NA	19.6 (133/680)	NA
Belgium (9)	9.9 (125/1260)	6.1 (825/13587)	3.6 (131/3661)	18.9 (51/269)
Bosnia and Herzegovina (1)	NA	NA	NA	28.26 (13/46)
Bulgaria (10)	9.3 (26/278)	18.1 (338/1869)	23.1 (131/569)	30 (15/50)
Croatia (7)	NA	13.2 (146/1105)	21.2 (73/345)	NA
Denmark (1)	NA	7.1 (63/894)	NA	NA
Estonia (2)	2.8 (3/106)	NA	NA	NA
Finland (2)	NA	13.1 (173/1329)	NA	NA
France (8)	25.8 (81/314)	21.8 (172/786)	17.7 (370/2093)	NA
Germany (13)	2.4 (52/2143)	3.2 (81/2567)	11.7 (315/2682)	NA
Greece (2)	NA	30 (15/50)	30.7 (59/192)	NA
Iceland (1)	NA	NA	6 (6/100)	NA
Ireland (5)	4.5 (25/557)	14.2 (21/148)	50.5 (53/105)	NA
Israel (2)	NA	7.9 (11/138)	44.1 (198/449)	NA
Italy (33)	9.5 (65/686)	16.5 (271/1645)	23.2 (1499/6456)	27.1 (79/292)
Lithuania (1)	1.1 (1/89)	4.4 (4/90)	NA	NA
Netherlands (5)	0.7 (7/893)	7.8 (61/778)	18.2 (61/336)	NA
Norway (2)	NA	5.8 (6/102)	9.5 (4/42)	NA
Poland (9)	9.1 (6/66)	24.88(158/635)	39.1 (81/207)	NA
Portugal (3)	13.9 (47/336)	NA	40 (58/145)	NA
Romania (1)	NA	NA	NA	20 (18/90)
Russia (4)	NA	5.3 (7/133)	9.5 (116/1220)	NA
Scotland (1)	1.8 (3/162)	NA	NA	NA
Serbia (1)	NA	NA	NA	24.03 (68/283)
Slovenia (2)	NA	NA	10.7 (44/412)	NA
Spain (26)	8.9 (143/1599)	15.8 (730/4623)	17.1 (2835/30697)	15.1 (193/1283)
Sweden (3)	2.7 (3/109)	1.3 (7/538)	NA	NA
Switzerland (4)	11.6 (13/112)	17.6 (29/165)	67.1 (145/216)	NA
Turkey (15)	NA	28.9 (128/442)	28.4 (173/609)	15.5 (64/413)
United Kingdom (9)	5.5 (23/415)	10.7 (198/1845)	35.8 (97/271)	NA

Table 1. Clarithromycin primary resistance prevalence in Europe in the last four decades (1990-2024). Number of patients tested for Clarithromycin: n (positive resistance results)/N (total with *H. pylori*). NA: not available.

Results: Overall, 188 studies were included, evaluating 81,458 patients over more than 30 years (1990-2024). In this time span, the mean prevalence of primary *H. pylori* clarithromycin resistance in Europe was 17%.

This rate increased from 7.3% in the period 1990-1999, to 13% in 2000-2009, reaching 26% in 2010-2019; and then reported a decreased rate to 22% in 2020-2024. In almost all European countries, the clarithromycin resistance rate increased over time, reporting the highest rates in Switzerland (67%), Ireland (50%), Israel (44%), Portugal (40%) and Poland (39%) (2010-2019). The prevalence remained stable in recent years in France (decreasing from 21% to 17%), in Spain (around 15%), and in Turkey (decreasing from 28% to 15%). Southern European countries reported higher rates (>15-20%) than in northern countries (<10-15%).

Conclusion: In Europe, overall *H. pylori* primary clarithromycin resistance was above 15% in the last 30 years. Variability exists between countries, with Southern European and Mediterranean countries showing higher levels of resistance.

References: Bujanda, Luis et al. "Antibiotic Resistance Prevalence and Trends in Patients Infected with *Helicobacter pylori* in the Period 2013-2020: Results of the European Registry on *H. pylori* Management (Hp-Eu-Reg)." *Antibiotics (Basel, Switzerland)*. 2021,10(9):1058.

Macías-García, Fernando et al. "High primary antibiotic resistance of *Helicobacter Pylori* strains isolated from dyspeptic patients: A prevalence cross-sectional study in Spain." *Helicobacter*. 2017,22(6):10.1111/hel.12440.

Tamayo, Esther et al. "Clarithromycin resistance in *Helicobacter pylori* and its molecular determinants in Northern Spain, 2013-2015." *Journal of global antimicrobial resistance*. 2017,9:43-46.

Saracino, Ilaria Maria et al. "Trends in Primary Antibiotic Resistance in *H. pylori* Strains Isolated in Italy between 2009 and 2019." *Antibiotics (Basel, Switzerland)*. 2020,9(1):26.

Megraud, Francis et al. "*Helicobacter pylori* resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community." *Gut*. 2021,70(10):1815-1822.

Disclosure: Nothing to disclose.

PP0258

WITHDRAWN

PP0259

ASSOCIATION OF AUTOIMMUNE ATROPHIC GASTRITIS WITH *HELICOBACTER PYLORI* INFECTION

G. Gharbi¹, A. Khsiba¹, A. Ben Mohamed¹, M. Yakoubi¹, M. Moufida¹, M. Medhioub¹, M.L. Hamzaoui¹

¹Faculty of medicine Tunis, Tunisia Mohamed taher Maamouri hospital Nabeul Tunisia, Gastroenterology and Hepatology departement, Nabeul, Tunisia

Contact E-Mail Address: gharbighada1801@gmail.com

Introduction: In patients with *Helicobacter pylori* (HP) infection, superficial gastritis proceeds to atrophic gastritis in about half of the patients. Although, it usually involves the antrum, it can also proceed to the corpus with sometimes neuroendocrine cell hyperlasia and chromogranin A antibody positivity, like in classic autoimmune gastritis.

Aims & Methods: The aim of our study was to determine the frequency of HP infection in autoimmune atrophic gastritis and its characteristics. A retrospective study was conducted over patients with autoimmune atrophic gastritis diagnosed in the gastroenterology department in Mohamed taher maamouri hospital between January 2019 and December 2021. Clinical, biological, endoscopic and pathology features were abstracted from medical records.

Results: A total of 31 patients were included in this study. The sex ratio M/F was 0.8 and the mean age was 56 years [28- 82 years]. The average

haemoglobin level was 9,9 g/dl and the average mean corpuscular volume was 95,6 fL. Serum markers were available in 13 patients. Intrinsic factor antibodies were positive in five patient and anti-parietal cell antibodies in 11 patients. Pathology findings of fundal biopsies showed mild atrophy in 16,1% patients, moderate in 48,4% and severe in 35,5% with presence of intestinal metaplasia in 90,3%. The antrum was atrophic in one patient and antral intestinal metaplasia was detected in 11 patients (35,5%). HP infection was diagnosed in 23 patients (74,2%). The presence of HP infection was correlated with the severity of anaemia ($p=0.048$). No correlation was found between HP infection and the degree of atrophy or the presence of intestinal metaplasia ($p=0.35$ et 0.38 respectively).

Conclusion: Our study showed the presence of HP in 74.2% of patients with autoimmune atrophic gastritis, which may support the implication of HP infection in the development of autoimmune gastritis. The presence of HP infection was correlated with the severity of anaemia, hence the importance of HP eradication treatment.

Disclosure: Nothing to disclose.

PP0260

WITHDRAWN

PP0261

PREVALENCE AND PREDICTIVE FACTORS OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: EXPERIENCE FROM A TERTIARY CARE GASTROENTEROLOGY CENTER

F. Adamou¹, H. Koulali¹, O. Elmqaddem¹, Z. Abdelkrim¹, Z. Ismaili¹, G. Kharrasse¹

¹Faculty of Medicine and Pharmacy, Mohammed I University, Department of Hepato-gastroenterology, Mohammed VI University Hospital Center. Digestive Disease Research Laboratory, Medical School, Mohammed First University, Oujda, Morocco

Contact E-Mail Address: adachou299@gmail.com

Introduction: Inflammatory Bowel Diseases (IBD) are chronic conditions whose etiology remains elusive. Several hypotheses, including a potential association with *Helicobacter pylori* (HP), have been proposed, as evidenced by declining prevalence due to eradication protocols. However, literature data exhibit considerable variability. Our study aims to determine the prevalence of HP infection in a population of IBD patients based on gastric biopsy results, alongside predictive factors for HP infection in this population, integrating epidemiological, endoscopic, and histological analyses.

Aims & Methods: This retrospective descriptive study spanned four and a half years from January 2019 to July 2023, encompassing all IBD patients who underwent gastroscopy with biopsy. Patients with fewer than four gastric biopsies were excluded. Data were collected from medical records, and statistical analysis was performed using SPSS software version 21.0.

Results: 150 patients were included, with a median age of 39.9 years [range: 18-71 years; ± 13.49], including 80 females (53.3%) and a sex - ratio of 0.8. All patients reported tea consumption (100%), while 25 patients (16.66%) were smokers, and 18 (12%) reported alcohol use. NSAID use was noted in 17 patients (11.3%), and proton pump inhibitor (PPI) use in 5 patients (3.3%). Additionally, 15 patients reported herbal therapy. All patients underwent gastroscopy with at least 3 antral and 2 fundic biopsies. 93.3% of patients underwent systematic gastroscopy. Among participants, 66 tested positive for HP (HP+), including 61 asymptomatic individuals. Symptomatically, 4 patients experienced epigastric pain, and one case of gastroesophageal reflux disease (GERD) was observed. HP prevalence in our sample was 44%, with a higher prevalence among females (56% vs. 44% males). HP infection was more common among individuals

aged 21-45 and over 60, peaking between 30 and 40. Endoscopic findings in HP+ patients included esophagitis in 6 patients (9%), erythematous and erosive gastritis in 4 patients (6%), hiatal hernia in 3 patients (4.5%), and micronodular antritis in 1 patient (1.5%). Duodenal and bulbar aphthoid ulcers were observed in 5 patients (7.5%). Notably, gastroscopy was normal in 112 patients. Epidemiological data analysis revealed that chronic NSAID use ($P=0.01$), herbal therapy ($P=0.05$), tea consumption ($P=0.03$), history of digestive cancer ($P=0.01$), young age (<37 years; $P=0.05$), and patients with ulcerative colitis ($P=0.001$) were significant risk factors for HP infection.

Conclusion: In our study, the prevalence of *Helicobacter pylori* infection was 44%. Ulcerative colitis was a significant risk factor for HP infection in our sample, with a highly significant P value of 0.0001. Therefore, should all IBD patients be systematically screened for HP infection?

Disclosure: No there is no Conflict of Interest into the text field below.

PP0262

WITHDRAWN

PP0263

DIAGNOSIS OF HELICOBACTER PYLORI IN PATIENTS WITH OBESITY: COMPARISON BETWEEN ^{13}C -UBT AND PCR

L. Miranda Fernandes¹, C. Garcia Montes², E. Cazzo³, G. Fernanda Soares Ruppert Reis², C. Rodrigues dos Santos⁴, M. Viviane Sá dos Santos Rondon⁴, N. Hifumi Hara⁴, C. Regina Pavan⁴, E. Adami Chaim³, C. Kibune Nagasako²

¹UNICAMP - Universidade Estadual de Campinas, Pós Graduação em Clínica Médica - Disciplina de Gastroenterologia, Campinas, Brazil, ²UNICAMP - Universidade Estadual de Campinas, Departamento de Clínica Médica - Disciplina de Gastroenterologia, Campinas, Brazil, ³UNICAMP - Universidade Estadual de Campinas, Departamento de Cirurgia, Campinas, Brazil, ⁴UNICAMP - Universidade Estadual de Campinas, Laboratório de Hepatologia e Gastroenterologia, Campinas, Brazil

Contact E-Mail Address: liviamfernandes@hotmail.com

Introduction: The prevalence of gastric infection by *Helicobacter pylori* (Hp) in individuals with obesity ranges from 8.7% (1) to 85.5% (2). In candidates for bariatric surgery, Hp infection is associated with an increased risk of perioperative complications, including marginal ulcers, ulcer perforations, anastomotic dehiscence, fistulas, and bleeding. It also exacerbates symptoms related to pre-existing gastrointestinal diseases (3,4). Preoperative eradication of Hp reduces complication rates. However, there is a lack of standardization in the diagnostic methods and eradication control of this bacterium in the population with obesity (5).

Aims & Methods: To compare the performance of the carbon-13 urea breath test (^{13}C -UBT) with molecular test based on PCR in diagnosing Hp infection in candidates for bariatric surgery. To assess the prevalence of Hp infection in these individuals and analyze the correlation with gastrointestinal symptoms and endoscopic findings.

Results: Ninety-two patients were evaluated, 83.7% female, with an average age of 41 ± 10.8 years and a mean body mass index of 41.8 ± 5.2 kg/m². The majority of participants (71.7%) had at least one comorbidity (arterial hypertension in 42.4%). The prevalence of Hp infection was 55.4% by PCR. Among the participants, 33.4% were symptomatic, predominating gastric symptoms. Abnormal endoscopic findings were observed in 56.5%, with no significant differences between the Hp negative and positive groups (51.2% vs. 60.7%, $p=0.47$). The most common endoscopic finding was erosive gastritis (45.6%). Table 1.

The sensitivity of the ^{13}C -UBT was 86.2% (CI95%: 73.1 to 93.8), with a specificity of 100% (CI95%: 89.3 to 100) and diagnostic accuracy of 92.3% (CI95%: 84.4 to 96.6). There was good concordance between the ^{13}C -UBT and PCR (kappa value 0.84, CI95%: 0.74 to 0.95), supporting the use of ^{13}C -UBT as a noninvasive test for the diagnosis of Hp in patients with obesity. Considering that Hp eradication therapy in obese individuals can contribute to reducing postoperative complications, this method becomes an alternative to endoscopy after eradication therapy, minimizing risks and costs in the preoperative period.

Parameter	Total (n=92)	Hp negative (n=41)	Hp positive (n=51)	p value
Abnormalities in endoscopy	52 (56.5)	21 (51.2)	31 (60.7)	0.47
Erosive gastritis	42 (45.6)	18 (43.9)	24 (47)	0.92
Esophagitis	17 (18.4)	6 (14.6)	11 (21.5)	0.56
Nodular gastritis	5 (5.4)	0 (0)	5 (9.8)	0.06*

Table 1. Comparison between endoscopic findings and Hp diagnosis, n (%).

*calculation using Fisher's exact test, as the value of n for Hp-negative group was zero.

Conclusion: The prevalence of Hp infection is 55.4% in obese individuals, with no correlation with symptoms and endoscopic findings. The ^{13}C -UBT showed high sensitivity, specificity, and good correlation with PCR in detecting Hp in candidates for bariatric surgery. This non-invasive test can be used in the eradication control of Hp in the preoperative of bariatric surgery.

References:

- Küper MA, Kratt T, Kramer KM, Zdichavsky M, Schneider JH, Glatzle J, et al. Effort, safety, and findings of routine preoperative endoscopic evaluation of morbidly obese patients undergoing bariatric surgery. *Surg Endosc.* 2010;24(8):1996–2001.
- Al-Akwaa A. Prevalence of *Helicobacter pylori* Infection in a Group of Morbidly Obese Saudi Patients undergoing Bariatric Surgery: A Preliminary Report. *Saudi J Gastroenterol.* 2010;16(4):264.
- Makristathis A, Hirschl AM, Mégraud F BE. Review: Diagnosis of *Helicobacter pylori* infection. *Helicobacter.* 2019;1(24):1–7.
- Pintar T, Kaliterna N, Carli T. The need for a patient-tailored *Helicobacter pylori* eradication protocol prior to bariatric surgery. *J Int Med Res.* 2018;46(7):2696.
- Carabotti M, D'Ercole C, Iossa A, Corazziari E, Silecchia G, Severi C. *Helicobacter pylori* infection in obesity and its clinical outcome after bariatric surgery. *World J Gastroenterol.* 2014;20(3):647–53.

Disclosure: Nothing to disclose.

PP0264

A RETROSPECTIVE, OBSERVATIONAL, REAL-WORLD STUDY EVALUATING THE DIAGNOSTIC PATTERN IN CHINESE PATIENTS WITH HELICOBACTER PYLORI

W. Pan¹, Y. Zhao², P. Li³, F. Zhaou³, L. Xie³, H. Xu⁴

¹Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou, China, ²Shanghai Tenth People's Hospital, Shanghai, China, ³Takeda (China) International Trade Co, Shanghai, China, ⁴Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China

Contact E-Mail Address: fang.zhou1@takeda.com

Introduction: *Helicobacter pylori* (*H. pylori*) infection is a common etiological cause of gastritis, peptic ulcer, atrophic gastritis, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma. Accurate diagnosis and sufficient efficacy evaluation duration are both critical for effective treatment to avoid precancerous conditions.

Aims & Methods: This retrospective, observational, multicenter, real-world study (NCT05073367) was performed across 3 hospitals using a preexisting electronic medical record (EMR) database between January 1, 2019, and March 31, 2021, to evaluate the diagnosis and treatment pattern of *H. pylori* infection in China. The study included adult patients (aged ≥ 18 years) with a record of diagnostic tests or positive results of *H. pylori* infection.

Here we analyzed the current pattern of diagnosis testing, eradication efficacy testing after eradication therapy, and the duration (≤ 4 or > 4 weeks) from the termination of eradication therapy to efficacy evaluation testing.

Results: A total of 22,971 patients with *H. pylori* infection data was extracted from EMR databases. Among them, 15,712 patients had 15713 initial diagnostic testing records before the eradication therapy (One participant had both RUT testing and UBT at the index date), and 1,626 patients received efficacy evaluation after the eradication therapy. Of 15,713 initial diagnostic testing records, non-invasive testing was the main diagnostic test used by 99.99% ($n=15,712$) of records, and invasive testing was used by only 0.01% ($n=1$).

Among non-invasive testing, ^{13}C - Urea breath testing (UBT) was used by 76.8% and ^{14}C -UBT was used by 23.19%. An increasing trend was observed in the use of ^{13}C -UBT diagnostic test with 47.54%, 73.20%, and 99.98% in 2019, 2020, and 2021, respectively. ^{14}C -UBT was 52.46% in 2019, 26.80% in 2020, 0% in 2021. Among 1,426 patients with eradication efficacy evaluation (duration ≥ 4 weeks), non-invasive testing- UBT was the only evaluation method used, with ^{13}C -UBT in 72.3% and ^{14}C -UBT in 27.7%. In 2019, ^{13}C -UBT was used by 53.69%, in 2020 it was 69.88%, and in 2021, ^{13}C -UBT was the only evaluation method to assess the efficacy (Table 1).

The mean (Standard Deviation) duration from the termination of eradication therapy until the eradication efficacy evaluation testing was 7.0 weeks (4.37).

Of 1626 patients with efficacy evaluation, 87.7% had > 4 weeks duration and 12.3% had ≤ 4 weeks. In 2019, 83.4% had a duration of > 4 weeks, 91.21% in 2020, and in 2021, 90.68% had a duration of > 4 weeks to receive an efficacy evaluation.

Testing condition	Total count (N)	Invasive testing, RUT, n (%)	Overall Noninvasive testing, UBT, n (%)	Noninvasive testing, ^{13}C -UBT, n (%)	Noninvasive testing, ^{14}C -UBT, n (%)
Diagnostic testing used before eradication therapy	15,713*	1 (0.01)	15,712 (99.99)	12,068 (76.80)	3644 (23.19)
Year 2019	4516	0 (0)	4516 (100)	2147 (47.54)	2369 (52.46)
Year 2020	4757	0 (0)	4757 (100)	3482 (73.20)	1275 (26.80)
Year 2021	6440	1 (0.02)	6439 (99.98)	6439 (99.98)	0 (0)
efficacy evaluation testing used after eradication therapy ≥ 4 weeks	1426	0 (0)	1426 (100)	1031 (72.30)	395 (27.70)
Year 2019	583	-	583 (100)	313 (53.69)	270 (46.31)
Year 2020	415	-	415 (100)	290 (69.88)	125 (30.12)
Year 2021	428	-	428 (100)	428 (100)	0 (00.00)

Table 1. Diagnostic Testing Used Before and After Eradication Therapy

Abbreviations: RUT, Rapid Urease Test; UBT, Urea Breath Testing

*A patient may have ≥ 1 diagnostic test. One participant had both RUT testing and UBT at the index date.

Conclusion: In China, non-invasive testing was dominant for the initial diagnosis of *H. pylori* infection, and ^{13}C UBT was commonly used compared with ^{14}C -UBT. The eradication efficacy evaluation testing was the same. Even over a tenth had insufficient evaluation duration, a higher proportion of evaluation duration > 4 weeks was discovered with an increasing tendency.

Disclosure: The study was funded by Takeda China. Wensheng Pan, Yan Zhao, and Hongwei Xu have no conflicts of interest. Pengfei Li, Fang Zhou, and Li Xie are the employees of Takeda, and they hold Takeda stock op-

tions. Medical writing for the development of this abstract was provided by Kusuma Kumari G, Ph.D., of Indegene Private Limited, and funded by Takeda China. Authors retained full control of the abstract content.

PP0265

EVALUATE THE DIAGNOSTIC ACCURACY OF PYLORI DUOTECT (QUALITATIVE DETECTION OF 2 ANTIBODIES SPECIFIC TO FLID AND CAGA) IN PATIENTS WITH SYMPTOMS OF UPPER GASTROINTESTINAL DISORDERS

V.H. Dao^{1,2}, P.B. Nguyen², T.T. Dang², T.H.T. Nguyen², T.T. Nguyen², T.U. Vu², V.L. Dao^{1,2}

¹Hanoi Medical University, Internal Medicine Faculty, Hanoi, Vietnam, ²Institute of Gastroenterology and Hepatology, Hanoi, Vietnam

Contact E-Mail Address: hangdao.fsh@gmail.com

Introduction: *H. pylori* infection is common in developing countries leading to of high prevalences of peptic ulcers and gastric cancer. However, the diagnostic tests such as rapid urease test or urease breath test requires facilities and patients need to go to medical sites, which raise a more and more need for non-invasive and convenient tests appropriate to community.

Aims & Methods: A cross-sectional study was conducted at the Institute of Gastroenterology and Hepatology, Hanoi, Vietnam to compare the *H. pylori* determination results of the qualitative detection of 2 antibodies specific to Flid and CagA with the rapid urease test and urease breath test in Vietnamese patients with upper gastrointestinal symptoms. Patients over 18 years old with upper GI symptoms and no prior history of treated peptic ulcers or *H. pylori* eradication were invited to participate in the study. Patients were indicated with upper GI endoscopy and three methods to diagnose *H. pylori* infection: Rapid Urease Test (RUT), Urease Breath Test (UBT), and qualitative detection of 2 antibodies specific to Flid and CagA (Pylori Duotect). Pylori Duotect is considered positive if either antibody for Flid and CagA are positive. The parameters for evaluating the diagnostic accuracy of Pylori Duotect include sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV). Patients are considered *H. pylori* positive if both RUT and UBT are positive.

Results: From December 1, 2023, to April 20, 2024, 189 patients were recruited for the research. The mean age were 45.8 years old (min-max: 18-76 years old), 40.7% were female. The most common symptom of patients was epigastric pain (46.6%). There were 172 patients (91%) with gastritis, 27 patients (14.3%) with gastric ulcers and 16 (8.5%) with duodenal ulcers. Using the Pylori Duotect test, 50.8% of the patients were positive, in which 39.6% were positive with Flid and 86.5% were positive with CagA. Based on RUT and UBT results, 31.2% of patients were diagnosed with *H. pylori* infection. Pylori DuoTect's sensitivity, specificity, PPV, and NPV were 81.4%, 63.8%, 50.5%, and 88.3%, respectively.

Conclusion: The Pylori DuoTect test had low sensitivity and specificity in diagnosis *H. pylori* infection in patients with upper gastrointestinal symptoms.

Disclosure: Nothing to disclose.

PP0266

UREA BREATH TESTS IN IRELAND: AN 8 YEAR RETROSPECTIVE ANALYSIS

C. Costigan^{1,2}, O. Costigan², M. Comerford², D. Scaiscia², G. Madders², T. Butler¹, F. O'Hara², D. McNamara^{2,1}

¹Trinity College Dublin, Clinical Medicine, Dublin, Ireland, ²Tallaght University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: conorcostigan92@gmail.com

Introduction: *Helicobacter pylori* (*H. pylori*) is a bacterium which inhabits the gastric epithelium and has been associated as a causative agent for dyspepsia, chronic gastritis, peptic and duodenal ulceration and gastric cancer. Testing for this pathogen is by Urea Breath Test (UBT) or OGD, and treatment varies according to local sensitivities and guidelines. *H. pylori* rates in developed countries have been falling in recent years as have those of associated conditions including gastric cancer, however increases in antimicrobial resistance recently has slowed this trend.

The current burden of disease either in asymptomatic population or symptomatic in Ireland is unknown, as are the rates of reinfection and recrudescence. Having up-to-date data on local epidemiology could have an effect on our strategy to detect and manage this class 1 carcinogen.

Aims & Methods: All UBTs performed in a tertiary hospital since 2016 were retrospectively assessed.

Demographic data & test results were taken from the UBT computer database and electronic patient record. All patients returning positive tests were offered appropriate antimicrobial therapy based on up to date local guidelines, and follow-up post-eradication testing by repeat UBT.

Results: From 2016-2023, 6716 UBTs were performed. 32 were excluded due to incomplete data. N=6684. 2752 (41.16%) were male, mean age was 43. Overall, 1589 (23.77%) tests were positive. There was no significant difference in positivity by gender ($p=0.321$). However there was a slight positive correlation with increasing age (AUC=0.5178 $p=0.035$). The positivity rate in our cohort reduced by roughly 2% per annum from 2016-22 (30%-18.5%).

Data on UBT type (Diagnostic vs Post-Eradication) was available from 2020-2023 when 3496 tests were performed and 2570 (73.5%) were diagnostic tests: 1060 (41.2%) male, mean age 41 years, 48 (19%) were positive. Positivity between genders was similar ($p=0.3771$). Conversely, in the post-eradication group $n=926$ (412, 44.5% Male), 259 (28%) were positive, females were more likely to remain positive post-therapy (32% vs 23%, $X^2=8.031$, $p=0.0046$).

Over the 8 years, 747 patients returned positive tests (306 (41%) male). All were offered follow up testing. Males were significantly less likely to attend follow-up testing (140/306, 46% vs 254/441, 58%, $p=0.0017$)

In all 83 (2.4%) patients were re-tested for *H. pylori* after returning negative UBT tests due to persistent symptoms. Mean time to re-testing was 270 days, 34 (40%) were positive, representing 0.97% of the cohort. Both genders were equally likely to have had a false negative UBT, male 10/30 versus 24/77 women, $p=0.8214$)

Conclusion: The overall positivity rate for diagnostic tests over the past 8 years was (19%) and is falling year on year.

The high positivity rate for post-eradication tests (28%) reflects rising antibiotic resistance.

The overall attendance rates for post-eradication tests after positive results were disappointing

Finally, the false negative rate in patients with persistent symptoms was high, 40% retested remained positive, raising the possibility of residual infection in our asymptomatic cohort.

References:

1. Chen, Y.C., et al., Global Prevalence of *Helicobacter pylori* Infection and Incidence of Gastric Cancer Between 1980 and 2022. *Gastroenterology*, 2024. 166 (4): p. 605-619.

2. Warren, J.R. and B. Marshall, Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet*, 1983. 1 (8336): p. 1273-5.

3. Marshall, B.J. and J.R. Warren, Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet*, 1984. 1 (8390): p. 1311-5.

4. Zullo, A., et al., Gastric MALT lymphoma: old and new insights. *Ann Gastroenterol*, 2014. 27 (1): p. 27-33.

5. Mulder, D.T., et al., Prevalence of Gastric Precursor Lesions in Countries With Differential Gastric Cancer Burden: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol*, 2024.

6. Malfertheiner, P., et al., Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*, 2022.

Disclosure: Nothing to disclose.

PP0267

FERRITIN LEVEL AS A DIAGNOSTIC PREDICTOR OF H. PYLORI INFECTION

I. Baculin¹, A. Sushilova¹, A. Zharkov¹

¹Federal state budgetary educational institution of higher education "Mechnikov North-Western State Medical University" of the Ministry of Healthcare of the Russia, Department of the Propedeutics of Internal Diseases, Gastroenterology and Dietology at SM Ryss, St. Petersburg, Russian Federation

Contact E-Mail Address: anastasiya.s1311@yandex.ru

Introduction: The Maastricht VI consensus recognizes the ¹³C-urease breath test (¹³C-UBT) as the "gold standard" in the diagnosis of *H. pylori* infection, including in patients with dyspepsia, in which this infection is detected quite often [1, 2]. Atrophic gastritis of the body of the stomach can cause both false-positive (due to the increased activity of urease producers other than *H. pylori*) and false-negative ¹³C-UBT result (due to a decrease in the microbial load of *H. pylori* associated with severe atrophy and metaplasia of the gastric mucosa and deterioration of habitual living conditions bacteria) [3]. Serological tests for the detection of *H. pylori* IgG are the primary screening method for *H. pylori* infection, recommended by the Maastricht VI consensus [1]. However, negative ¹³C-UBT and *H. pylori* antigen in stool with positive antibodies in patients with CAG, it often causes difficulties in assessing the *H. pylori* status, which emphasizes the relevance of searching for new diagnostic predictors.

Aims & Methods: Aim: evaluate the role of ferritin in determining the presence of *H. pylori* infection. 143 patients aged from 20 to 79 years were examined. The mean age was 59 (49–66) years. All participants underwent serum determination of pepsinogen-I (P-I), pepsinogen-II (P-II), gastrin-17 and antibodies to *H. pylori*; esophagogastroduodenoscopy with biopsy according to the OLGA system. Confirmation of *H. pylori* infection was performed by assessing the presence of antigen in stool using immunochromatography. To confirm autoimmune gastritis (AIG), the level of antibodies to parietal cells and intrinsic factor was determined in the blood. The indicators of clinical and biochemical blood analysis of patients (iron levels, ferritin) were assessed. When not normally distributed, quantitative data were described using the median (Me) and lower and upper quartiles (Q1–Q3). Comparison of two groups according to a quantitative indicator, the distribution of which differed from normal, was carried out using the Mann–Whitney U test. Comparisons of percentages in the analysis of multifield contingency tables were performed using the Pearson chi-square test.

Results: In 69.2% of cases, when verifying the etiology of CAG, AIH was identified, in 21.7% *H. pylori*-associated gastritis was identified, in 9.1% - CAG of mixed etiology. There was a weak positive correlation between P-I and iron levels ($p=0.220$, $p=0.01$), as well as between P-I and ferritin levels ($p=0.229$, $p=0.007$), the ratio P-I/ P-II and ferritin $p=0.286$, $p<0.001$), P-I/P-

II and iron level ($p=0.229$, $p=0.007$). There was no relationship between P-II and iron content in the blood ($p=0.025$, $p=0.775$), as well as no association of P-II with ferritin levels ($p=0.085$, $p=0.323$). When analyzing the concentrations of iron and ferritin, no statistically significant differences were revealed in these indicators depending on the stage of atrophy in CAG. When comparing groups of patients with IDA and iron deficiency, no statistically significant differences in the etiology of CAG could be found ($p=0.167$). When comparing ferritin values depending on the presence/absence of *H. pylori* antigen in stool, statistically significant differences were noted in this parameter (negative – Me = 43.0, 19.8–59.0, positive – Me = 67.0, 51, 7–80.5, $p<0.001$).

Conclusion: The presence of iron deficiency does not depend on the etiology of chronic atrophic gastritis. A positive correlation was revealed between P-I, P-I/P-II and iron deficiency. Ferritin levels may be a promising diagnostic predictor of *H. pylori* infection in patients with CAG.

References:

1. Malfertheiner, Peter, et al. "Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report." Gut 71.9 (2022): 1724-1762.
2. Zakharova, N. V., et al. "Prevalence of helicobacter pylori infection in gastroenterological patients in Saint Petersburg." Pharmateca 5S (2016): 33-39.
3. Best, Lawrence MJ, et al. "Non-invasive diagnostic tests for Helicobacter pylori infection." Cochrane Database of Systematic Reviews 3 (2018).

Disclosure: The authors declare that there is no conflict of interest.

PP0268

FACTORS ASSOCIATED WITH HELICOBACTER PYLORI ERADICATION IN THE ADULT POPULATION IN COLOMBIA: A MULTIVARIABLE ANALYSIS

S.F. Niño Ramirez¹, M.A. Saffon², L. Roldan³, J.N. Zuluaga Aguilar⁴, N. Zuluaga¹, J. Londoño castillo³, H.M. Perez Useche³, E. Nunez³, J. Bejarano Rengifo², J. Zuleta³, O. Ardila⁵, E. Licona⁶
¹Gastroclinic institute, UCES, Gastroenterology, Medellin, Colombia, ²Gastroclinic institute, Bogota, Colombia, ³Gastroclinic institute, Medellin, Colombia, ⁴Gastroclinic institute, Gastroenterologia, Bogota, Colombia, ⁵Clinica CES, Gastroenterologia, Medellin, Colombia, ⁶Universidad CES, Medellin, Colombia

Contact E-Mail Address: ardilagastro@gmail.com

Introduction: Helicobacter pylori infection involves a high proportion of the Colombian population (1). It has been established that Helicobacter pylori infection increases the risk of developing gastric cancer (2). Multiple treatment regimens have been proposed to eradicate Helicobacter pylori, but it is not known which one could be associated with the best eradication rate in our population (3).

Aims & Methods: The aim of this research was to determine the factors most associated with the successful eradication of Helicobacter pylori in an adult population in Colombia.

An analytical cross-sectional study was conducted to assess risk factors associated with the eradication of Helicobacter pylori in an adult population in Colombia. The cross-sectional design facilitated data collection at a specific time point, while the analytical approach aimed to uncover connections between risk factors and the success of eradication.

A sample size calculation was performed for logistic regression using the Freeman formula. Based on estimated proportions of patients experiencing treatment failure, an approximate sample size of 400 patients was determined for the evaluation of 10 variables. Participant patients were adults diagnosed with Helicobacter pylori infection who were prescribed

eradication treatment and underwent verification of eradication between January 1, 2022, and December 31, 2022. Patients with incomplete information, the pediatric population, or those without eradication verification were excluded from the analysis.

A descriptive analysis was conducted to characterize the sample and risk factors. Subsequently, a bivariate analysis examined the relationship between each independent variable and Helicobacter pylori eradication. Variables with a p-value < 0.05 in the bivariate analysis were included in a multivariate logistic regression model to identify independent risk factors associated with successful eradication. The multivariate analysis was adjusted for treatment adherence and compliance.

Results:

Variable	Odds ratio	95% Confidence Interval	p value
Proper treatment adherence*	13.72	3.1840 59.0874	< .001
Regimen with esomeprazole	4.97	1.1034 22.3592	0.037
Regimen with bismuth	2.04	1.1580 3.5977	0.014
Duration of the regimen: 14 days	7.21	1.2304 42.2908	0.029
Lactobacillus reuteri	1.79	0.8633 3.7249	0.117
Eradication regimen with amoxicillin	2.58	0.1512 43.9183	0.513
Eradication regimen with clarithromycin	6.88	0.4417 107.1126	0.169
Eradication regimen with metronidazole	6.94	0.4185 115.1961	0.176
Eradication regimen with levofloxacin	11.76	0.7801 177.1968	0.075

Table 1. Multivariable analysis, factors associated with Helicobacter pylori eradication. * Adherence assessed by the Morisky-Green Test.

A total of 386 patients were included in the study, of whom 74% achieved successful eradication of Helicobacter pylori. The multivariate analysis identified factors associated with successful eradication of Helicobacter pylori: proper adherence to the treatment, the inclusion of esomeprazole and bismuth subsalicylate in the treatment, and a eradication regimen duration of 14 days (Table 1).

Conclusion: Our results support the promotion of treatment regimens lasting 14 days. Strategies to ensure proper adherence to treatment should be encouraged, always incorporating esomeprazole and bismuth subsalicylate in the regimen.

References: 1. Virulence Genes of Helicobacter pylori Increase the Risk of Premalignant Gastric Lesions in a Colombian Population - PMC [Internet]. [citado 12 de agosto de 2023]. Disponible en: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9534724/>

2. Valladales-Restrepo LF, Correa-Sánchez Y, Aristizábal-Carmona BS, Machado-Alba JE. Treatment regimens used in the management of Helicobacter pylori in Colombia. Braz J Infect Dis. 16 de febrero de 2022;26(1):102331.

3. Piazueto MB, Bravo LE, Mera RM, Camargo MC, Bravo JC, Delgado AG, et al. The Colombian chemoprevention trial. Twenty-year follow-up of a cohort of patients with gastric precancerous lesions. Gastroenterology. marzo de 2021;160(4):1106-1117.e3.

Disclosure: The authors declare no conflict of interest.

PP0269

HELICOBACTER PYLORI SECONDARY ANTIBIOTIC RESISTANCES:
A GENOTYPIC STUDY ON STOOL SAMPLES

M. Mezzapesa¹, M. Piazzolla¹, I. Ditonno¹, M. Pricci²,
B. Girardi², F. Celiberto¹, G. Galeano³, G. Riezzo³, F. Russo³,
A. Iannone¹, E.G. Ierardi¹, A. Di Leo¹, G. Losurdo¹

¹University of Bari, Section of Gastroenterology, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy, ²THD spa, Correggio, Italy, ³IRCCS De Bellis, Functional Gastrointestinal Disorders Research Group, Castellana Grotte, Italy

Contact E-Mail Address: martino.mezzapesa@gmail.com

Introduction: Helicobacter pylori (H. pylori) antibiotic resistances are the leading cause for unsuccessful eradication therapy. After one or more failures, the chance of encountering secondary antibiotic resistances increases. The aim of this study was to characterize genotypic secondary resistances in a cohort of Southern Italy H. pylori patients with at least one previous failure.

Aims & Methods: Patients with at least one previous eradication failure collected stool samples by a dedicated kit (THD fecal testTM) and bacterial DNA was extracted and amplified by RT-PCR. Resistance to clarithromycin, amoxicillin, metronidazole, levofloxacin and tetracycline was assessed by high-resolution melting curve.

Results: We enrolled 50 patients. The 72% failed one previous antibiotic course, the 16% two, the 10% three and the 2% four. The rate of secondary antibiotic resistance was 16% for clarithromycin, 18% for metronidazole, 14% for amoxicillin, 14% for levofloxacin and 2% for tetracycline. Multi-resistance was detected in 9 patients (18%) and double resistance to clarithromycin + metronidazole was the most common one (n = 5). Among patients with a previous failure to an amoxicillin-containing regimen, amoxicillin resistance was found in 4 out of 20 (20%). Among patients with a previous failure to a clarithromycin-containing regimen, resistance to such antibiotic was detected in 6 out of 19 (31.6%). Among patients with a previous failure to a metronidazole-containing regimen (n = 21), metronidazole resistance was found in 3 cases (14.3%). A failed levofloxacin-based therapy was given in 3 patients, but in none of them resistance was found (0%). Finally, among patients with a previous failure to a tetracycline-containing therapy, resistance to such antibiotic was detected in 1 out of 12 (8.3%)

Conclusion: In conclusion, our data seem to show that, despite secondary resistances are not so high, a resistance to clarithromycin could be very likely related to previous exposure to this antibiotic.

Disclosure: Nothing to disclose.

PP0270

THE FREQUENCY OF HELICOBACTER PYLORI INFECTION AND THE
EFFECT OF ERADICATION THERAPY ON SYMPTOM IMPROVEMENT
IN FUNCTIONAL DYSPESIA SUBGROUPS ACCORDING TO ROME IV
CRITERIA: A STUDY FROM TURKEY WITH A HIGH PREVALENCE OF
HELICOBACTER PYLORI

S. Demirbaş Yücel¹, M. Sadeçolak², A. Bilgili², M. Tozlu²,
A.T. Eminler², M.I. Uslan²

¹Sakarya Training and Research Hospital, Gastroenterology, Sakarya, Turkey, ²Sakarya University Medical Faculty Hospital, Gastroenterology, Sakarya, Turkey

Contact E-Mail Address: selmademirbas@yahoo.com

Introduction: Different pathophysiological mechanisms are thought to play a role in functional dyspepsia (FD) subgroups defined by Rome IV criteria. Studies are needed to determine whether Rome IV subgroups are linked to distinct pathophysiologies and treatment responses.

This study aims to investigate the impact of Helicobacter pylori (H. pylori) infection in the pathogenesis of each FD subgroups, subdivided according to the Rome IV consensus, within a high H. pylori prevalence country, Turkey.

The investigation centered on assessing the frequency of H. pylori and examining the impact of eradication therapy on alleviating symptoms, in each Rome IV subgroup.

Aims & Methods: Eradication treatment was applied to cases who were initially diagnosed with FD using the Rome IV criteria and subsequently found to have H. pylori gastritis through endoscopic biopsy. 8-12 weeks after treatment, H. pylori state was evaluated with fecal antigen test. Symptom responses were evaluated in each subgroup at 2, 6, and 12 months post-therapy using a Likert scale and statistically with SPSS version 23.0.

Results: The H. Pylori frequency was statistically more common in individuals with symptoms consistent with epigastric pain syndrome (EPS) (73.1% in EPS, 41% in postprandial distress syndrome (PDS), and 43.9% in overlapping subgroups (p<.001)).

With eradication treatment of H. pylori-positive cases, all subgroups demonstrated a significant response and the response rates didn't exhibit significant difference between subgroups (73.7% in total cases; 70.5% in EPS; 71.4% in PDS; 82.6% in overlapping, in the 12th month (p>0.05)). Eradicated patients showed significant symptomatic improvement with 70.2% in the 12th month. None of the non-eradicated patients experienced symptomatic improvement.

Subgroups	In EPS cases Responsive(n) / Total(n) (%)	In PDS cases Responsive(n) / Total(n) (%)	In overlapping cases Responsive(n) / Total(n) (%)	In all cases Responsive(n) / Total(n) (%)
Respond rate at 2nd month (%)	23/51 (45.1%)	15/39 (38.5%)	11/26 (42.3%)	49/116 (42.2%)
Respond rate at 6th month (%)	31/46 (67.4%)	18/35 (51.4%)	18/25 (72%)	67/106 (63.2%)
Respond rate at 12th month (%)	31/44 (70.5%)	20/28 (71.4%)	19/23 (82.6%)	70/95 (73.7%)

FD, functional dyspepsia; PDS, postprandial distress syndrome; EPS, epigastric pain syndrome

Table 2. The ratios of symptomatic response after H. pylori eradication therapy among FD Rome IV subgroups that received therapy, at 2nd, 6th, 12th month visits.

Conclusion: Using Rome IV consensus confirmed the data that H. pylori plays a notable role as a pathogenic factor in FD, particularly in EPS, and it is recommended to screen all FD subgroups, particularly EPS, for H. pylori and eradicate, if detected. Additionally, this study suggests that regions with a high H. pylori prevalence tend to have a higher H. pylori-associated dyspepsia prevalence.

References:

1. Wauters L, Dickman R, Drug V, et al. United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on functional dyspepsia. *United European Gastroenterol J*. 2021 Apr;9(3):307–331.
2. Houte KVD, Carbone F, Goelen N, et al. Effects of Rome IV Definitions of Functional Dyspepsia Subgroups in Secondary Care. *Clinical Gastroenterology and Hepatology* 2021;19:1620–1626.
3. Carbone F, Vanuytsel T, and Tack J. Analysis of Postprandial Symptom Patterns in Subgroups of Patients With Rome III or Rome IV Functional Dyspepsia. *Clinical Gastroenterology and Hepatology* 2020;18:838–846.
4. Vanheel H, Vanuytsel T, Van Oudenhove L, Farre R, Verbeke K, Tack J. Postprandial symptoms originating from the stomach in functional dyspepsia. *Neurogastroenterol Motil* 2013;25:911–e703
5. Ford AC, Tsipotis E, Yuan Y, Leontiadis GI, Moayyedi P. Efficacy of Helicobacter pylori eradication therapy for functional dyspepsia: updated systematic review and meta-analysis. *Gut*. 2022 Jan 12;gut-jnl-2021-326583. doi: 10.1136/gutjnl-2021-326583.
6. Kang SJ, Park B, Shin CM. Helicobacter pylori Eradication Therapy for Functional Dyspepsia: A Meta-Analysis by Region and H. pylori Prevalence. *J Clin Med*. 2019 Aug 28;8(9):1324. doi: 10.3390/jcm8091324.
7. Malfertheiner P, Megraud F, Rokkas T, et al. European Helicobacter and Microbiota Study group. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. *Gut*. 2022 Aug 8;gut-jnl-2022-327745. doi: 10.1136/gutjnl-2022-327745.

Disclosure: The authors declare that they have no conflict of interest.

PP0271

EMPIRICAL SECOND-LINE TREATMENTS IN EUROPE: DATA FROM 9,000 CASES FROM THE EUROPEAN REGISTRY ON HELICOBACTER PYLORI MANAGEMENT (HP-EUREG)

Q. P. Nyssen¹, L. Jonaitis², Á. Pérez-Aísa³, L. Rodrigo⁴, S.J. Martínez-Domínguez⁵, B. Tepeš⁶, L. Vologzanina⁷, A. Garre¹, L. Bujanda⁸, M. Pabón-Carrasco⁹, M. Castro-Fernández⁹, F. Lerang¹⁰, I. Voynovan¹¹, A.J. Lucendo¹², J.M. Huguet¹³, J. Tejedor-Tejada¹⁴, R. Bumane¹⁵, J. Barrio¹⁶, P. Bogomolov¹⁷, M. Pavoni¹⁸, V. Milivojevic¹⁹, B. Velayos²⁰, M. Denkovski²¹, B.J. Gómez Rodríguez²², T. J. Butler²³, F. Bermejo²⁴, G. Losurdo²⁵, M. Areia²⁶, A. S. Sarsenbaeva²⁷, A. Keco-Huerga⁹, Ó. Núñez²⁸, A. Gasbarrini²⁹, R. Abdulkhakov³⁰, D. Boltin³¹, G. Kamto³², I. L. P. Beales³³, J. Kupcinskas², L. Hernández³⁴, D.S. Bordin³⁵, M. Leja¹⁵, S.M. Smith³⁶, R. Marcos-Pinto³⁷, W. Marlicz³⁸, P.S. Phull³⁹, A. Cano-Català⁴⁰, P. Parra¹, L. Moreira⁴¹, F. Megraud⁴², C. O'Morain³⁶, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania, ³Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ⁴Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ⁵Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁶Department of Gastroenterology, DC Rogaska, Rogaska Slatina, Slovenia, ⁷Gastrocentr, Perm, Russian Federation, ⁸Department of Gastroenterology, Biodonostia Health Research

Institute, Department of Medicine, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ⁹Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ¹⁰Østfold Hospital Trust, Grålum, Norway, ¹¹A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ¹²Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ¹³Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ¹⁴Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ¹⁵Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia, ¹⁶Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ¹⁷Universal Clinic Private Medical Center, Moscow, Russian Federation, ¹⁸Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ¹⁹Clinical Center of Serbia and School of Medicine, University of Belgrade, Belgrade, Serbia, ²⁰Department of Gastroenterology, Hospital Clínico de Valladolid, Valladolid, Spain, ²¹Interni oddelek, Diagnostic Centre, Bled, Slovenia, ²²Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ²³Clinical Medicine, Trinity College Dublin, Department of Gastroenterology, Tallaght University Hospital, Dublin, Ireland, ²⁴Department of Gastroenterology, Hospital Universitario de Fuenlabrada, Fuenlabrada, Spain, ²⁵Department of Gastroenterology, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari, Bari, Italy, ²⁶Department of Gastroenterology, Portuguese Oncology Institute of Coimbra, Faculty of Medicine of the University of Porto (FMUP), Center for Health Technology and Services Research (CINTESIS), Coimbra, Portugal, ²⁷Department of Gastroenterology, Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁸Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ²⁹Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ³⁰Department of Hospital Medicine, Kazan State Medical University, Kazan, Russian Federation, ³¹Department of Gastroenterology, Rabin Medical Center, Tel Aviv University, Tel Aviv, Israel, ³²Hepatic Medical, Private Medical Center, Krakow, Poland, ³³Norwich Medical School, University of East Anglia, Norwich, United Kingdom, ³⁴Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁵Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow clinical scientific center, Department of outpatient therapy and family medicine, Tver State Medical University, Department of propaedeutic of internal diseases and gastroenterology, Russian University of Medicine, Moscow, Russian Federation, ³⁶School of Medicine, Trinity College Dublin, Dublin, Ireland, ³⁷Gastroenterology Department, Centro Hospitalar do Porto, Universidade do Porto, Instituto De Ciências Biomédicas de Abel Salazar, Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal, ³⁸Department of Gastroenterology, Pomeranian Medical University in Szczecin, The Centre for Digestive Diseases, Endoklinika, Szczecin, Poland, ³⁹Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom, ⁴⁰Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ⁴¹Department

of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ⁴²INSERM U1312, Université de Bordeaux, Bordeaux, France

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: After a first eradication attempt, approximately 10-20% of patients will fail to achieve *H. pylori* eradication.

Aims & Methods: To evaluate the effectiveness of second-line empirical treatment.

A systematic, prospective, registry of the clinical practice of European gastroenterologists (38 countries) on *H. pylori* management was established. All infected adult patients were systematically registered at AEG-RED-Cap e-CRF until December 2023. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed.

Results: Overall, 8,984 patients received a second-line empirical therapy. Mean age was of 50 years, 66% were women, and 5% had penicillin allergy. Most frequent treatment indications were dyspepsia (70%) and gastroduodenal ulcer (15%). Overall effectiveness was 83% (both by mITT and PP). Over 96.5% of patients were compliant.

Adverse events were reported in 23% of the cases, most of them mild. Most frequent second-line prescriptions and their effectiveness by region is shown in table 1.

None of the European regions achieved an optimal effectiveness. However, in those patients receiving optimised therapy (i.e., 14-days and high dose PPIs), triple regimens containing levofloxacin and bismuth quadruple therapies either with metronidazole-tetracycline or clarithromycin-amoxicillin, as well as quadruple therapy with clarithromycin-amoxicillin-metronidazole, showed optimal effectiveness. Also, 10-day bismuth quadruple therapy as single-capsule achieved over 90% cure rates when prescribed with standard PPI doses. After failure of first-line clarithromycin-containing therapy, optimal eradication was only obtained with moxifloxacin-containing triple therapy (92%). Quadruple therapy with clarithromycin-amoxicillin-metronidazole and bismuth quadruple therapies either with clarithromycin-amoxicillin, amoxicillin-levofloxacin or the single-capsule provided encouraging results (>85%).

Treatment	N	Use (%)	mITT, N (%)	(95% CI)	PP, N (%)	(95% CI)
Triple-A+L	2,212	25.5	1,959 (81)**	(79-83)	1,936 (81)	(79-83)
Single-capsule*	1,783	20.6	1,659 (88)**	(86-89)	1,621 (89)	(87-90)
Quadruple-A+L+B	1,170	13.5	929 (85)	(83-87)	910 (85)	(83-88)
Quadruple-C+A+M	560	6.5	534 (85)**	(82-88)	523 (85)	(82-89)
Triple-C+A	525	6.1	424 (79)**	(75-83)	416 (79)	(75-83)
Quadruple-M+Tc+B	451	5.2	405 (83)**	(79-87)	386 (85)	(81-88)
Quadruple-C+A+B	370	4.3	251 (89)**	(85-93)	240 (90)	(86-94)
Triple-A+M	225	2.6	198 (62)	(55-69)	195 (63)	(56-70)
Triple-A+R	212	2.4	189 (83)	(77-88)	187 (83)	(77-89)
Triple-A+Mx	153	1.8	147 (92)	(87-97)	147 (92)	(87-97)
Other	1,013	11.5	NA	NA	NA	NA
Overall	8,674	100	7,563 (83)	(82-84)	7,410 (83)	(83-84)
Overall (optimised conditions)	2,005	23.1	1,747 (89)	(87-90)	1,709 (89)	(88-91)
East	1,425	15.9	1,159 (84)	(82-86)	1,121 (84)	(82-87)
East-Centre	1,625	18.1	1,160 (84)	(82-86)	1,147 (84)	(82-87)
South-West	4,190	46.7	3,973 (83)	(82-85)	3,895 (84)	(83-85)
West-Centre	1,103	12.3	979 (84)	(82-87)	962 (85)	(82-87)
North	631	7.0	547 (72)	(68-76)	530 (73)	(69-77)
Total	8,974	100	7,803 (83)	(82-84)	7,641 (83)	(83-84)

95% CI –confidence interval; mITT: modified intention-to-treat; PP: per-protocol; N: total number of patients analysed; C – clarithromycin; M – metronidazole; A – amoxicillin; L – levofloxacin; B – bismuth salts; Tc – tetracycline; R – rifabutin; Mx – moxifloxacin; Other – Other second-line empirical treatments with less than 150 patients treated in each category; East – Ukraine, Serbia, Bulgaria, Turkey, Russia, Romania, Albania, North Macedonia; East-Centre – Croatia, Poland, Hungary, Latvia, Lithuania, Greece, Slovenia, Czech Rep, Azerbaijan, Slovakia, Malta; South-West – Portugal, Spain; West-Centre – France, Austria, Belgium, Germany, Italy; North – United Kingdom, Finland, The Netherlands, Ireland, Israel, Norway, Switzerland, Sweden, Denmark; *three-in-one single-capsule containing metronidazole tetracycline and bismuth; **achieved over 90% effectiveness when optimised (high-dose PPIs and 14-days length in all schemes but the single-capsule optimised with standard-dose PPIs).

Table 1. Second-line empirical treatment prescriptions and effectiveness by treatment scheme and geographical region.

Conclusion: In Europe, empirical second-line treatment achieves optimal effectiveness with bismuth quadruple therapy as single-capsule when prescribed standard doses of PPIs, and when regimens including triple therapy with levofloxacin, quadruple therapy with clarithromycin-amoxicillin-metronidazole and bismuth quadruple therapies with metronidazole-tetracycline or clarithromycin-amoxicillin are prescribed for 14 days and with high-dose PPIs.

Many other second-line treatments evaluated achieved low eradication rates.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

PP0272

EFFECTIVENESS OF FIRST-LINE TREATMENT FOR *H. PYLORI* INFECTION IN ISRAEL: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

D. Boltin^{1,2}, A. Mari³, L. Brickner⁴, S. Odeh⁴, J. Wardi⁵, H. Schweistein¹, A. Shitrit⁶, A. Stein⁷, Y. Niv⁸, A. Cano-Català⁹, L. Moreira Ruiz¹⁰, P. Parra¹¹, O. P. Nyssen¹¹, F. Megraud¹², C. O'Morain¹³, J. Gisbert¹¹, on behalf of the Hp-EuReg investigators.

¹Rabin Medical Center, Gastroenterology, Petah Tikva, Israel, ²Tel Aviv University, Faculty of Medicine, Tel Aviv, Israel, ³Nazareth Hospital EMMS, Gastroenterology Department, Nazareth, Israel, ⁴Bnai Zion Medical Center, Haifa, Israel, ⁵Gastroenterology And Hepatology, Haifa, Israel, ⁶Wolfson Medical Center Dept. of Gastroenterology, Gastroenterology, Hod Hasharon, Israel, ⁷Shaare Zedek Medical Center, IBD and Pregnancy Unit, Jerusalem, Israel, ⁸Meir Medical Center, Gastroenterology, Kfar Saba, Israel, ⁹Adelson Faculty of Medicine, Ariel University, Risk Management Education Center, Ariel, Israel, ¹⁰Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Manresa, Spain, ¹¹Hospital Clínic de Barcelona, Gastroenterology, Gava, Spain, ¹²Hospital Universitario de La Princesa, IIS-IP, and CIBERehd, Gastroenterology Unit, Madrid, Spain, ¹³Hopital Pellegrin, Laboratoire de Bactériologie, Bordeaux, France, ¹³Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: dboltin@gmail.com

Introduction: The effectiveness of first-line treatment for *H. pylori* infection varies between countries. Local data are necessary to guide clinical practice. We aimed to assess the effectiveness of first-line eradication treatments for *H. pylori* in Israel.

Aims & Methods: International, multicenter, prospective, non-interventional registry aiming to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists (Hp-EuReg).

All infected adult patients treated with a first-line therapy at 10 centers in Israel between 2013 and 2023 were registered at e-CRF AEGRedCap and were included in the current study.

Effectiveness was assessed by modified intention-to-treat (mITT) and per-protocol (PP) analyses.

Results: A total of 663 cases were registered, where 320 (48%) had received a 1st line empirical therapy with an average age of 51±18 years and 183 (57%) were females. The most common indication for *H. pylori* investigation was dyspepsia (67%). Infection was diagnosed with histology (56%), ¹³C-Urea breath test (22%), rapid urease test (17%) and monoclonal stool Ag test (5.3%). Quadruple concomitant therapy with PPI-clarithromycin-amoxicillin-tinidazole was the most frequent 1st line treatment (43%), mostly prescribed for 14 days (87% of the patients) and with high-dose PPIs (91% of the cases), followed by triple therapy with PPI-clarithromycin-amoxicillin (16%) and quadruple concomitant therapy with PPI-clarithromycin-amoxicillin-metronidazole (12%). The majority of prescriptions were of 14-day (70%) length, followed by 10-day (22%) and 7-day (7.3%) duration. High potency proton pump inhibition (PPI) was prescribed to most patients (75%).

Overall treatment success was 84% (160/191) and 86% (155/181) by mITT and PP, respectively, with the highest effectiveness provided by 10-day and high-dose PPIs of sequential therapy with clarithromycin-amoxicillin-tinidazole (89.5% by mITT), and by 14-day and high-dose PPIs of concomitant therapy with clarithromycin-amoxicillin-tinidazole (85% by mITT). Longer treatment durations and higher PPI doses provided better cure rates. Treatment effectiveness did not change significantly during the study period, and remained suboptimal (<90%) over the years. Compliance (>90% drug intake) was 97%. The incidence of at least one adverse event was reported in 10%, necessitating treatment cessation in 1.5%.

	Use, n (%)	mITT Success n/N (%)	PP Success n/N (%)
Treatment scheme			
Triple-C+A	49 (16.1)	36/44 (81.8)	36/44 (81.8)
Sequential-C+A+T	20 (6.6)	17/19 (89.5)	17/19 (89.5)
Quadruple-C+A+T	132 (43.3)	73/86 (84.9)	71/80 (88.8)
Quadruple-C+A+M	38 (12.5)	13/13 (100)	13/13 (100)
Treatment Duration			
7 days	22 (7.3)	16/20 (80)	16/20 (80)
10 days	68 (22.4)	43/50 (86)	42/49 (85.7)
14 days	213 (70.3)	92/111 (82.9)	88/102 (86.3)
Potency of acid inhibition*			
Low	63 (20.6)	48/58 (82.8)	47/57 (82.5)
Standard	12 (3.9)	6/6 (100)	6/6 (100)
High	231 (75.5)	105/125 (84)	101/116 (87.1)
Overall	320 (100)	160/191 (83.8)	155/181 (85.6)

Abbreviations: n: total number of patients analysed; mITT, modified intention to treat; PP, per-protocol; C, clarithromycin; A, amoxicillin; T, tinidazole; M, metronidazole; *Low dose PPI – 4.5 to 27 mg omeprazole equivalents. b.i.d.; standard dose PPI – 32 to 40 mg omeprazole equivalents. b.i.d.; high dose PPI – 54 to 128 mg omeprazole equivalents. b.i.d.

Table: Empirical first-line therapy effectiveness by modified intention-to-treat and per-protocol analyses, by treatment duration and acid inhibition in Israel.

Conclusion: In Israel, empirical first-line treatment for *H. pylori* eradication is still suboptimal (<90%). Treatments should consist of four drugs and should be optimised with a 14-day duration and standard/high doses of PPIs.

Disclosure: None.

PP0273

H. PYLORI FIRST-LINE EMPIRICAL THERAPY EFFECTIVENESS AND ITS RELATIONSHIP TO ANTIBIOTIC CONSUMPTION IN THE COMMUNITY: DATA FROM THE EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG)

O. P. Nyssen¹, G.J. Ortega², L. Jonaitis³, Á. Pérez-Aísa⁴, B. Tepeš⁵, U. Mahmudov⁶, I. Voynovan⁷, S.J. Martínez-Domínguez⁸, L. Bujanda⁹, A.J. Lucendo¹⁰, L. Rodrigo¹¹, L. Vologzanina¹², E. Mammadov¹³, F. Lerang¹⁴, R. Bumane¹⁵, M. Denkovski¹⁶, G. Fadieienco¹⁷, I. Tatiana¹⁸, J. Tejedor-Tejada¹⁹, A. Garre¹, G. Babayeva¹³, A. S. Sarsenbaeva²⁰, J.M. Huguet²¹, O. Zaytsev²², Q. Farid Vidadi Oğlu²³, M. Pabón-Carrasco²⁴, M. Perona²⁵, S. Alekseenko²⁶, M. Castro-Fernández²⁴, Ó. Núñez²⁷, I. Bakulin²⁸, M. Areia²⁹, P. Bogomolov³⁰, J. Barrio³¹, N. Brglez Jurecic¹⁶, A. Moreno Loro³², B.J. Gómez Rodríguez³³, J. Kupcinskas³, A. Gasbarrini³⁴, L. Hernández³⁵, D.S. Bordin³⁶, M. Leja¹⁵, O. Gridnyev¹⁷, R. Marcos-Pinto³⁷, A. Cano-Català³⁸, P. Parra¹, L. Moreira³⁹, F. Megraud⁴⁰, C. O'Morain⁴¹, J. P. Gisbert¹, on behalf of the Hp-EuReg investigators.

¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Unidad de Análisis de Datos, Hospital Universitario de la Princesa, CONICET, Universidad Nacional de Quilmes – Argentina, Madrid, Spain, ³Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania, ⁴Department of Gastroenterology, Hospital Universitario Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, ⁵Department of Gastroenterology, DC Rogaska, Rogaska Slatina, Slovenia, ⁶Modern Hospital, Baku, Azerbaijan, ⁷A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ⁸Department of Gastroenterology, Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Zaragoza, Spain, ⁹Department of Gastroenterology, Biodonostia Health Research Institute, Department of Medicine, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ¹⁰Department of Gastroenterology, Hospital General de Tomelloso, IIS-Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Tomelloso, Spain, ¹¹Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ¹²Gastrocentr, Perm, Russian Federation, ¹³Department of Internal Medicine and Gastroenterology, Azerbaijan State Advanced Training Institute for Doctors named by A. Aliyev, Baku, Azerbaijan, ¹⁴Østfold Hospital Trust, Grålum, Norway, ¹⁵Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia, ¹⁶Interni oddelek, Diagnostic Centre, Bled, Slovenia, ¹⁷Departments the Division for the Study of the Digestive diseases and its Comorbidity with Noncommunicable Diseases, Government Institution L.T. Malaya Therapy National Institute of NAMS of Ukraine, Kharkiv, Ukraine, ¹⁸Department of Gastroenterology, SM-clinic, Saint-Petersburg, Russian Federation, ¹⁹Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ²⁰Department of Gastroenterology, Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²¹Department of Gastroenterology, Hospital General Universitario de Valencia, Valencia, Spain, ²²First Clinical Medical Centre, Kovrov, Russian

Federation, ²³National Oncology Centre, Baku, Azerbaijan, ²⁴Department of Gastroenterology, Hospital Universitario Virgen de Valme, Sevilla, Spain, ²⁵Department of Gastroenterology, Hospital Quirón Marbella, Marbella, Spain, ²⁶Far Eastern State Medical University, Khabarovsk, Russian Federation, ²⁷Department of Gastroenterology, Hospital Universitario Sanitas La Moraleja, Madrid, Spain, ²⁸I. I. Mechnikov North-Western State Medical University, Saint-Petersburg, Russian Federation, ²⁹Department of Gastroenterology, Portuguese Oncology Institute of Coimbra, Faculty of Medicine of the University of Porto (FMUP), Center for Health Technology and Services Research (CINTESIS), Coimbra, Portugal, ³⁰Universal Clinic Private Medical Center, Moscow, Russian Federation, ³¹Department of Gastroenterology, Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Valladolid, Spain, ³²Department of Gastroenterology, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ³³Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ³⁴Department of Internal Medicine and Gastroenterology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ³⁵Department of Gastroenterology, Hospital Santos Reyes, Aranda de Duero, Spain, ³⁶Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow clinical scientific center, Department of outpatient therapy and family medicine, Tver State Medical University, Department of propaedeutic of internal diseases and gastroenterology, Russian University of Medicine, Moscow, Russian Federation, ³⁷Gastroenterology Department, Centro Hospitalar do Porto, Universidade do Porto, Instituto De Ciências Biomédicas de Abel Salazar, Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal, ³⁸Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universitària de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ³⁹Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ⁴⁰INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴¹School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: The link between the misuse in global antibiotic consumption and increased antimicrobial resistance is well documented. Clarithromycin-based anti-*H. pylori* eradication therapy as a triple regimen (encompassing a PPI plus two antibiotics) has been used empirically worldwide without antimicrobial susceptibility testing. In the last decade, a marked decrease in the effectiveness of clarithromycin-based regimens has been observed globally.

Aims & Methods: This study aimed at exploring the potential relationship between the consumption of macrolides in the overall population as a factor influencing the effectiveness of *H. pylori* clarithromycin-containing regimens.

Data from the European Registry on *Helicobacter pylori* management (Hp-EuReg) were used for this analysis. A multivariate logistic regression was built using the modified intention-to-treat (mITT) effectiveness analysis as the outcome and the following main effects: first-line treatment scheme (using the 10 most frequent antibiotic combinations), duration of treatment (as 7, 10 or 14-day lengths), proton-pump inhibitor (PPI) dose (categorised as low, standard, or high; that is, 20 mg, 40 mg or 80 mg omeprazole equivalent twice a day), compliance (that is, >90% of drug intake), and clarithromycin consumption expressed as daily doses per 1,000 in-

habitants per day. Data of macrolide community consumption was taken from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net). Hierarchical nested models were constructed by adding macrolide consumption, matching by year and country with the corresponding patients' therapy, and the interaction between consumption and treatment scheme (taken from the Hp-EuReg).

Results: In total, 28,590 first-line treated patients from 24 European countries participating in the Hp-EuReg, on which data of macrolides consumption in the period 2013-2022 was available, were evaluated. Three nested models were analysed: the first one with the main effects without including macrolides consumption (A), the second with the full set of main effects (including macrolides consumption) (B) (likelihood ratio test A-B p-value=2.11.10⁻²), and the third one included both macrolides consumption and interactions between this main effect and treatments (C) (likelihood ratio test B-C p-value=4.08 10⁻¹⁰). Model B (without interactions) showed a global decrease in treatment mITT effectiveness (OR: 0.95 [0.91-0.99]). Model C (with interactions) showed a significant decrease in the mITT effectiveness in three different treatments (Table): triple-clarithromycin-metronidazole (OR: 0.37 [0.25-0.53]), triple-clarithromycin-amoxicillin (OR: 0.60 [0.43-0.82]), and sequential-clarithromycin-amoxicillin-metronidazole/tinidazole (OR: 0.60 [0.43-0.84]); whereas, bismuth quadruple therapy (single capsule) remained unaffected.

	OR	95% CI	p-value
Intercept	0.42	0.15-1.22	0.17
Compliance (>90% of drug intake)	7.41	6.30-8.71	1.01e-92
10 days prescriptions	0.92	0.92-1.04	0.25
14 days prescriptions	1.06	0.94-1.21	0.43
Standard-dose PPI *	1.58	1.44-1.74	1.08e-15
High-dose PPI*	1.79	1.65-1.95	7.23e-31
Triple- PPI+C+A	2.32	0.80-6.34	0.18
Triple- PPI+C+M	3.95	1.25-11.93	0.04
Triple- PPI+A+M	1.90	0.64-5.43	0.32
Triple- PPI+A+L	1.29	0.36-4.40	0.74
Conco- PPI+C+A+T/M	1.97	0.68-5.42	0.28
Seq- PPI+C+A+T/M	4.71	1.55-13.66	0.02
Quadruple- PPI+C+A+B	0.99	0.21-4.88	0.99
Quadruple- PPI+single capsule**	2.32	0.76-6.69	0.20
Other	1.45	0.47-4.22	0.58
C cons	1.42	1.04-1.96	0.07
Triple- PPI+C+A: C cons	0.60	0.43-0.82	0.01
Triple- PPI+C+M: C cons	0.37	0.25-0.53	1.58e-05
Triple- PPI+A+M: C cons	0.71	0.49-1.01	0.11
Triple- PPI+A+L: C cons	0.76	0.51-1.12	0.24
Conco- PPI+C+A+T/M: C cons	0.76	0.54-1.04	0.15
Seq- PPI+C+A+T/M: C cons	0.60	0.43-0.84	0.01
Quadruple- PPI+C+A+B: C cons	0.89	0.52-1.48	0.72
Quadruple-PPI+Single capsule**: C cons	0.86	0.60-1.20	0.46
Other: C cons	0.72	0.51-1.00	0.10

OR: odds ratio; CI: confidence interval; *low dose PPI – 4.5 to 27 mg omeprazole equivalents. b.i.d.; standard dose PPI – 32 to 40 mg omeprazole equivalents. b.i.d.; high dose PPI – 54 to 128 mg omeprazole equivalents. b.i.d.; A: amoxicillin; B: bismuth; C: clarithromycin; L: levofloxacin; M: metronidazole; tetracycline.; **Three-in-one single-capsule containing metronidazole, tetracycline and bismuth; C cons: clarithromycin consumption.

Table. Multivariate logistic regression (model C) evaluating the interaction between clarithromycin consumption and first-line empirical treatment effectiveness (by modified intention-to-treat) in Europe between 2013 and 2022.

Conclusion: The models showed an inverse association between the clarithromycin consumption and empirical first-line therapy overall effectiveness in Europe; particularly, in those clarithromycin-containing regimens. Further research will consider a broader time lag to assess this association.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.

Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

PP0274

WITHDRAWN

PP0275

EFFECTIVENESS OF FIRST-LINE EMPIRICAL TREATMENT IN AZERBAIJAN: RESULTS FROM THE EUROPEAN REGISTRY ON HELICOBACTER PYLORI MANAGEMENT (HP-EUREG)

G. Babayeva¹, U. Mahmudov², E. Mammadov^{1,3}, F. Guliyev⁴, E. Verdiyev⁵, U. Machanov⁶, R. Ibishev⁷, H. Huseynov⁸, Z. Zalov⁹, S. Ismayilova¹⁰, R. Hasanov^{1,11}, H. Ibrahimli¹², A. Cano-Català¹³, P. Parra¹⁴, L. Moreira¹⁵, O.P. Nyssen¹⁴, F. Mégraud¹⁶, C. O'Morain¹⁷, J.P. Gisbert¹⁴

¹Azerbaijan State Advanced Training Institute for doctors named after A.ALIYEV, Department of Terapiya, Baku, Azerbaijan, ²Modern Hospital, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ³MediLand Hospital, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ⁴National Centre of Oncology, Department of Invasive Diagnosis And Treatment, Baku, Azerbaijan, ⁵Central Hospital, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ⁶Ganja International Hospital, Department of Gastroenterology and Endoscopy, Ganja, Azerbaijan, ⁷Zafaran Hospital, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ⁸Azerbaijan Medical University, Oncology clinic, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ⁹Istanbul NS Klinika, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ¹⁰StarLab Medical Center, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ¹¹German Hospital, Department of Gastroenterology and Endoscopy, Baku, Azerbaijan, ¹²Azerbaijan State Advanced Training Institute for doctors named after A.ALIYEV, Department of Health Organization, Baku, Azerbaijan, ¹³GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain, ¹⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ¹⁵Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain, ¹⁶INSERM U1312, Université de Bordeaux, Bordeaux, France, ¹⁷Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: doctorabu@mail.ru

Introduction: Gastric lesions associated with *Helicobacter pylori*, eradication issues and problems of its sometimes-insufficient effectiveness continue to remain one of the most pressing topics in modern healthcare. **Aims & Methods:** The analysis aimed to assess the usage, efficacy, and safety of initial empirical treatment for *H. pylori* infection in Azerbaijan. Data were collected at e-CRF AEG-REDCap from the European Registry on *Helicobacter pylori* Management (Hp-EuReg) and quality reviewed from January 2020 to May 2023. All treatment-naïve cases were assessed for effectiveness by modified intention-to-treat (mITT), per-protocol (PP) analyses, and a separate multivariate analysis was performed. **Results:** The study included 3,898 patients (67% reported dyspepsia). In 1.9% of patients, at least one type of allergy was reported (1.6% to penicillin). A total of 226 patients (5.8%) received concurrent medication: PPI (5.1% on demand, 0.1% daily), acetylsalicylic acid (1.2% on demand, 0.2% daily), NSAIDs (1.3% on demand), statins (1.2% on demand, 0.1% daily).

The most frequent indication for treatment was dyspepsia with normal endoscopy in 2,610 patients (67%). In total, 3,853 (99%) patients were diagnosed pre-treatment using the rapid urease test, which was the most frequently used. The following tests were likewise used in a lower number of cases: monoclonal stool antigen test (MSAT)(0.7%) and polyclonal stool antigen test (0.1%). In 2,661 (68%) cases a MSAT was used, being the most frequent post-treatment confirmation method. Additionally, in 55 (1.4%) cases an invasive method, that is endoscopy, was performed, to confirm the eradication. First-line empirical treatment prescriptions and mITT effectiveness by treatment schemes is presented in Table 1. Triple regimens were the most frequently prescribed in over 3,000 (82%) patients, where the PPI-C+A treatment scheme represented 54% of the total of first-line prescriptions. Treatment length varied from 14 days in 56% of cases, 10 days in 27%, and 7 days in 17%. Following 14-day treatments prescriptions achieved optimal (>90%) mITT effectiveness: PPI-C+A (94%), PPI-C+M (97%), PPI-C+M+ B (96%) and PPI-C+A+B (98%). Following schemes also provided optimal results when combined with standard-dose (i.e., 40 mg omeprazole equivalent twice a day) PPIs: PPI-A+Tc (100%) and PPI-C+A+B (96%). Additionally, prescriptions concomitantly administered with high-dose (i.e., 80 mg omeprazole equivalent twice a day) PPIs provided also over 90% eradication rates: PPI-C+A (94%), PPI-C+M (97%), PPI-C+M+B(100%) and PPI-C+A+B (99%). Compliance with treatment was over 90% in the vast majority of cases. The incidence of at least one adverse event was reported in 12% of cases.

Treatment	Number of prescriptions	Use (%)	mITT, N (%)	PP, N (%)	mITT, N (%) Low-dose PPI	mITT, N (%) Standard-dose PPI	mITT, N (%) High-dose PPI
Triple-C+A	2,117	54.3	1,832 (91.2%)	1,819 (95.2%)	873 (91.2%)	527 (89.3%)	420 (93.8%)
Triple-C+M	760	19.5	584 (93.3%)	581 (96.5%)	326 (93.4%)	89 (86.4%)	167 (97.1%)
Quadruple-C+A+B	610	15.6	579 (98%)	574 (99.8%)	219 (98.2%)	187 (96.4%)	178 (99.4%)
Triple-A+L	159	4.1	124 (82.1%)	124 (99.2%)	52 (82.5%)	68 (81.9%)	4 (80.0%)
Triple-A+Tc	75	1.9	71 (94.7%)	71 (100.0%)	28 (93.3%)	43 (95.6%)	NA
Quadruple-C+M+B	44	1.1	40 (95.2%)	40 (100.0%)	26 (100.0%)	6 (75.0%)	8 (100.0%)
Other	44	1.1	114 (90.5%)	113 (97.4%)	55 (93.2%)	55 (90.2%)	4 (66.7%)
Total	3,809	97.6	3,344 (92.4%)	3,322 (96.6%)	68 (92.5%)	975 (89.9%)	776 (95.4%)
A-amoxi-cillin, C- clarithro-mycin, M- metroni-dazole, L- levoflo-xacin, Tc- tetracy-cline, B - bismuth			mITT-modified Intention-to-treat;	PP: per protocol analysis;	low-dose PPI, between 4.5 and 27 mg omepra-zole equi-valents given twice a day;	standard-dose PPI, between 32 and 40 mg omepra-zole equi-valents given twice a day;	high-dose PPI, between 54 and 128 mg omepra-zole equi-valents given twice a day; NA: not avail-able data.

Table 1. Most frequent first-line empirical treatment prescriptions and modified intention-to-treat effectiveness in Azerbaijan.

Conclusion: The prescribed *H. pylori* eradication regimens during the period 2020–2023 in Azerbaijan adhered only partially to the Maastricht VI recommendations; however, most of first-line empirical therapies achieved high (≥90%) cure rates, providing a good safety profile.

Disclosure: Nothing to disclose.

THE PATTERN OF *HELICOBACTER PYLORI* PCR-ASSESSED ANTIBIOTIC RESISTANCE: EXPERIENCE FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

V. Milivojevic¹, D. Kekic², T. Milosavljevic³, I. Babic⁴, G. Losurdo⁵, J. Tejedor-Tejeda⁶, T. Matysiak-Budnik⁷, L. Vologzanina⁸, T. Ilchishina⁹, I. Linas¹⁰, I. Voinovan¹¹, L. Rodrigo¹², N. Bakulina¹³, I. Bakulin¹⁴, M. Romano¹⁵, M. Pavoni¹⁶, B.J. Gómez Rodríguez¹⁷, G.M. Buzás¹⁸, M. Ražov-Radas¹⁹, A.G. Gravina²⁰, N.V. Baryshnikova²¹, G. Fiorini²², M. Nikolic²³, L. Belousova²⁴, K. Jankovic²⁵, K. Priadko²⁶, I. Hasukic²⁷, A. Di Leo²⁸, A. Osmanovic²⁹, C. Paéz Cumpa³⁰, D. Vaira³¹, A. Sushilova³², S. Hodzic²⁹, A. Perelló Juan³³, A. Gasbarrini³⁴, L. Hernández Villalba³⁵, D.S. Bordin³⁶, M. Doulberis³⁷, A. Mestrovic³⁸, V. Papp³⁹, A. Cano-Catala⁴⁰, P. Parra⁴¹, L. Moreira Ruiz⁴², O. P. Nyssen⁴³, F. Megraud⁴³, C. O'Morain⁴⁴, J. P. Gisbert⁴¹, on behalf of the Hp-EuReg investigators

¹University Clinical Centre of Serbia, Belgrade University, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia, ²Medical Faculty University of Belgrade, Institute of Microbiology and Immunology, Belgrade, Serbia, ³General hospital Euromedic, Belgrade, Serbia, ⁴Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia, ⁵University of Bari, Section of Gastroenterology, Dept. Emergency and organ transplantation, Bari, Italy, ⁶Department of Gastroenterology, Hospital Universitario de Cabueñes, Gijón, Spain, ⁷CHU de Nantes IMAD, Institut des maladies de l'appareil digestif, Nantes, France, ⁸Gastrocentr, Perm, Russian Federation, ⁹Department of Gastroenterology, SM-clinic, Saint-Petersburg, Russian Federation, ¹⁰Department of Gastroenterology, GGP Bern, Department of Gastroenterology, Hirslanden Klinik Beau-Site, Gastroenterology, Bern, Switzerland, ¹¹A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ¹²Department of Gastroenterology, Universidad de Oviedo, Oviedo, Spain, ¹³North-Western State Medical University n. a. I. I. Mechnikov, St. Petersburg, Russian Federation, ¹⁴Mechnikov North-Western State Medical University, Saint-Petersburg, Russian Federation, ¹⁵Department of Gastroenterology and Endoscopy, Department of Precision Medicine, Università Vanvitelli, Napoli, Italy, ¹⁶Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, Bologna, Italy, ¹⁷Department of Gastroenterology, Hospital Universitario Virgen Macarena, Sevilla, Spain, ¹⁸Ferencvaros Health Centre, Dr., Budapest, Hungary, ¹⁹Department of Gastroenterology and Hepatology, General Hospital Zadar, Health Studies, University of Zadar, Zadar, Croatia, ²⁰Division of Hepatogastroenterology, University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy, ²¹Pavlov First Saint Petersburg State Medical University, Saint-Petersburg, Russian Federation, ²²Cardiovascular Medicine Unit, Heart, Chest and Vascular Dept., IRCCS Azienda Ospedaliero-Universitaria di Bologna, Hypertension and Cardiovascular Risk Research Center, Medical and Surgical Sciences Dept., University of Bologna, Bologna, Italy, ²³University Centre Sestre Milosrdnice, Gastroenterology And Hepatology, Zagreb, Croatia, ²⁴University Hospital Peter The Great, St. Petersburg, Russian Federation, ²⁵Clinic for Gastroenterohepatology, University Clinical Centre of Serbia, Sabac, Stitar, Serbia, ²⁶Hepato-Gastroenterology & Digestive Oncology Unit, University Hospital of Nantes, Nantes, France, ²⁷UKC Tuzla, Tuzla, Bosnia and Herzegovina, ²⁸Section of gastroenterology, DETO, University of Bari, Dr., Bari, Italy,

²⁹Department of Gastroenterology and Hepatology, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina, ³⁰Hospital Cruz Roja Palma de Mallorca, Palma de Mallorca, Spain, ³¹Cardiovascular Medicine Unit, Heart, Chest and Vascular Dept., IRCCS Azienda Ospedaliero-Universitaria di Bologna, Hypertension and Cardiovascular Risk Research Center, Medical and Surgical Sciences Dept., University of Bologna, Bologna, Italy, ³²University Hospital Peter The Great, Saint-Petersburg, Russian Federation, ³³Department of Gastroenterology, Hospital Universitario Son Espases, Palma de Mallorca, Spain, ³⁴Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ³⁵Santos Reyes, Gastroenterology, Aranda de Duero, Spain, ³⁶A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ³⁷Department of Gastroenterology, Kantonsspital Aarau, Aarau, Switzerland, ³⁸KBC SPLIT, Split, Croatia, ³⁹Semmelweis University, II. departement of internal medicine, Budapest, Hungary, ⁴⁰Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Università de Manresa, Institut de Recerca i Innovació en Ciències de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ⁴¹Department of Gastroenterology, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Madrid, Spain, ⁴²Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ⁴³Hopital Pellegrin, Laboratoire de Bacteriologie, Bordeaux, France, ⁴⁴Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: dotorevlada@gmail.com

Introduction: In light of the growing global problem of antibiotic resistance, eradication of clarithromycin (CLA)-resistant *Helicobacter pylori* (*H. pylori*) strains has been recognized as a top priority health problem. Poor antibiotic stewardship, and the complexity of antibiotic resistance patterns, has made *H. pylori* gastritis the most prevalent infectious disease. Pretreatment assessment of *H. pylori* antibiotic sensitivity has been suggested as a reasonable solution in overcoming antibiotic resistance and treatment failure.

Aims & Methods: The aim of the study was to assess the prevalence and pattern of *H. pylori* resistance towards most common prescribed antibiotics, through the use of molecular, PCR-based technique. A multicentric, prospective registry of the clinical practice of European gastroenterologists on the management of *H. pylori* (Hp-EuReg) collects since 2013 the real clinical practice of European gastroenterologists. Adults *H. pylori*-infected and PCR-tested patients registered at AEG REDCap e-CRF were analysed. Two types of molecular testing were performed: a non-invasive (stool sample PCR) and an invasive (gastric sample PCR) test.

Results: In total, 265 *H. pylori* patients were tested, of which 130 were treatment-naïve cases and 135 had already received at least one eradication attempt. In treatment-naïve cases, CLA resistance (CLA-R) was 31%, fluoroquinolone resistance (FLQ-R) was 33% and metronidazole resistance (MET-R) was 14% (Table).

There was no statistically significant difference in the bacterial resistance rate of tested antibiotics based on the gender and age distribution. In the rescue line, CLA-R was 62%, FLQ-R was 53% while MET-R was 7% (Table). Multiple eradication attempts significantly increased CLA-R (53% vs. 79% vs. 100%, for the 2nd, 3rd and 4th line respectively, p=0.001).

Antibiotics	First line (n, %)	Rescue line (n, %)
Clarithromycin	40, 31%	84, 62%
Fluoroquinolones	43, 33%	72, 53%
Metronidazole	18, 14%	10, 7%

Table. PCR-detected resistance to most common prescribed antibiotics in Europe.

Conclusion: Alarmingly high *H. pylori* resistance to CLA and FLQ as well as its steep increase following multiple eradication attempts, implies an urgent need of continuous and systematic antibiotic stewardship, in order to further optimise *H. pylori* eradication strategies.

Disclosure: Olga P. Nyssen received research funding from Mayoly and Allergan. Javier P. Gisbert served as speaker, consultant, and advisory member for or received research funding from Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

PP0277

HELICOBACTER PYLORI ERADICATION FIRST- AND SECOND-LINE REGIMENS PRESCRIPTIONS AND EFFECTIVENESS IN LITHUANIA DURING THE YEARS 2013-2023: ANALYSIS OF THE EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG)

P. Jonaitis¹, J. Kupcinskas¹, O. P. Nyssen², P. Parra², L. Moreira³, A. Cano-Catala⁴, F. Megraud⁵, C. O'Morain⁶, J. P. Gisbert^{*2}, L.V. Jonaitis^{*1}, *co-last authors
¹Lithuanian University of Health Sciences, Department of Gastroenterology and Institute for Digestive Research, Kaunas, Lithuania, ²Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Gastroenterology, Madrid, Spain, ³Hospital Clínic Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBEREHD), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Department of Gastroenterology, Barcelona, Spain, ⁴Althaia Xarxa Assistencial Universitària de Manresa, GOES Research Group, Manresa, Spain, ⁵Université de Bordeaux, INSERM U131, Bordeaux, France, ⁶Trinity College Dublin, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: pjonaitis95@gmail.com

Introduction: Lithuania remains in the area with a high prevalence of *H. pylori* infection, which is estimated to be ~30-40%. Therefore, it is important to analyze the local *H. pylori* management in order to achieve better treatment results.

Aims & Methods: To evaluate the trends and effectiveness of *H. pylori* first- and second-line treatment prescriptions in Lithuania during 2013-2023. Prospective, multicenter, international, non-interventionist registry on the management of *H. pylori* (Hp-EuReg) by European gastroenterologists. Lithuanian data from 2013 to 2023 were analysed. The effectiveness of the five most frequent first- and second-line *H. pylori* eradication prescriptions was evaluated using the modified intention-to-treat (mITT) analysis.

Results: In total 4,168 patients from Lithuania were included in the Hp-Eu-Reg. The confirmation of *H. pylori* eradication was assessed in 37% of the first-line and 44% of the second-line cases. The overall first-line treatment effectiveness was 88%; the effectiveness of the most frequent first-line treatment prescription (standard triple therapy with amoxicillin and clarithromycin) increased from 78% in 2013 to 95% in 2023, obtaining the optimal (>90%) cure rates during the last 4 years. The overall second-line treatment effectiveness was 91%; the overall effectiveness of the most fre-

quent second-line treatment prescription (triple therapy with amoxicillin and levofloxacin) was 92%. Since 2020 this triple therapy was taken over by bismuth quadruple therapy with amoxicillin and levofloxacin in prescription frequency – this quadruple regimen managed to maintain optimal eradication effectiveness rates during the last 6 years. The trends and effectiveness of other most frequent first- and second line prescriptions are presented in Table 1.

First-line treatment	Years period							
	2013-2016			2017-2020			2021-2023	
	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)	mITT (95% CI)	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)	mITT (95% CI)	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)
Triple C+A	662 (97.1%)	301 (45.5%)	84.4% (80-88%)	1477 (89.5%)	553 (37.4%)	85.7% (83-89%)	686 (68.5%)	267 (38.9%)
Quadruple C+A+B	0 (0%)	N/A	N/A	72 (4.4%)	20 (27.8%)	100% (83-100%)	155 (15.5%)	35 (8%)
Triple A+L	2 (0.3%)	1 (50%)	100% (3-100%)	35 (2.1%)	23 (65.7%)	100% (85-100%)	11 (1.1%)	7 (63.6%)
Triple C+M	18 (2.6%)	7 (46.6%)	100% (59-100%)	39 (2.4%)	14 (95.9%)	92.9% (66-100%)	13 (1.3%)	8 (61.5%)
Quadruple A+M+B	0 (0%)	N/A	N/A	27 (1.6%)	6 (22.2%)	83.3% (36-100%)	137 (13.7%)	7 (5.1%)

Second-line treatment	Years period							
	2013-2016			2017-2020			2021-2023	
	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)	mITT (95% CI)	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)	mITT (95% CI)	Prescription frequency, n (% of top 5)	Test post-treatment, n (follow-up %)
Quadruple A+L+B	0 (0%)	N/A	N/A	110 (39.4%)	48 (43.6%)	97.9% (89-100%)	167 (65.2%)	40 (24%)
Triple A+L	57 (79.2%)	24 (42.1%)	87.5% (68-97%)	124 (44.4%)	84 (67.7%)	91.7% (84-97%)	44 (17.8%)	26 (59.1%)
Quadruple A+M+B	0 (0%)	N/A	N/A	21 (7.5%)	7 (33.3%)	71.4% (29-96%)	32 (12.5%)	9 (28.1%)
Triple C+A	15 (20.8%)	8 (53.3%)	100% (63-100%)	13 (4.7%)	9 (69.2%)	100% (66-100%)	9 (3.5%)	5 (55.6%)
Quadruple C+A+B	0 (0%)	N/A	N/A	11 (3.9%)	4 (36.4%)	100% (40-100%)	11 (4.3%)	6 (54.5%)

Table 1. Most frequent first- and second-line prescriptions and their modified intention-to treat (mITT) effectiveness in Lithuania during 2013-2023.

Conclusion: During 2013-2023 there was a trend of increasing *H. pylori* eradication effectiveness of the main first-line prescription, managing to maintain optimal cure rates in the last 4 years. There has been an increase in first- and second-line quadruple therapies prescriptions since the year 2018.

Disclosure: Nothing to disclose.

PP0278

COMPARISON OF ERADICATION EFFICACY OF 1-WEEK METRONIDAZOLE TRIPLE REGIMEN WITH BISMUTH ADD-ON AND 2-WEEK BISMUTH QUADRUPLE REGIMEN FOR H PYLORI WITH CLARITHROMYCIN RESISTANCE-RELATED GENE MUTATION (A2143G)

K.A. Jang¹, D.Y. Cheung¹, T.H. Kim²

¹College of Medicine, The Catholic University of Korea, Internal Medicine, Seoul, South Korea, ²The Catholic University Of Korea, Department Of Internal Medicine, Bucheon, South Korea

Contact E-Mail Address: adagio@catholic.ac.kr

Introduction: In regions where there is a prevalence of clarithromycin resistant strains, 2-week bismuth quadruple therapy (PBMT) is recommended as the first-line treatment. In cases where CLA resistance-related genetic mutations are identified, 1-week metronidazole triple therapy is recommended. The aim of this study is to investigate whether 1-week bismuth-added metronidazole triple therapy (PBMA) therapy can achieve equivalent efficacy to 2-week PBMT therapy.

Aims & Methods: This study was a multicentred retrospective analysis using electronic medical records, employing propensity score matching to analyze the results. The study population consisted of individuals who were confirmed to have H. pylori infection with clarithromycin resistance-associated genetic mutation (A2143G) using PCR and who were administered either 2-weeks PBMT or 1 week PBMA.

Results: From October 2019 to May 2023, a total of 121 patients were confirmed for H. pylori infection and clarithromycin resistance-related genetic mutations using PCR. Among them, 6 patients with the A2142G mutation were excluded, leaving 115 patients with the A2143G mutation for analysis. Out of these 115 patients, retrospective analysis was conducted on 82 patients who underwent UBT testing at least 4 weeks after completing the antibiotic regimen and had complete medical records.

Among the 82 patients analyzed, 51 had received the conventional 2-week PBMT while 31 had received a 1-week PBMA. Propensity score matching was performed for gender, age, and body mass index, factors suspected to influence the efficacy of eradication, resulting in 25 matched cases in each group.

The baseline characteristics, including age and gender distributions, did not differ significantly between the two groups of analyzed subjects.

The efficacy of eradication therapy was confirmed through UBT conducted 4-8 weeks after treatment. In the analysis before propensity score matching (PSM), the eradication rates for the 2-week PBMT group and the 1-week PBMA group were 70.6% and 77.4% in the intention-to-treat (ITT) analysis, respectively, and 94.7% and 85.7% in the per-protocol (PP) analysis, respectively. There was no significant difference between the two groups in both analyses.

After PSM, the analysis still showed no significant difference between the 2-week PBMT group and the 1-week PBMA group. In the ITT analysis, the eradication rates were 68.0% for the OBMT2w group and 80.0% for the OAM+B1w group, while in the PP analysis, the rates were 94.4% for the OBMT2w group and 87.0% for the OAM+B1w group.

Regarding adverse events, there was no difference in the frequency of adverse events between the two groups. However, the need to discontinue medication occurred in 5.3-5.6% of cases in the 2-week PBMT group but did not occur in the 1-week PBMA group. Nonetheless, changes in bowel habits were more common in the 1-week PBMA group, with the main reason being a change to dark-colored stool.

Conclusion: For patients infected with H. pylori carrying the A2143G point mutation, there was no difference in the eradication rate between the 2-week PBMT regimen and the 1-week PBMA regimen. The 1-week PBMA regimen showed superior drug compliance and a tendency for fewer adverse effects compared to the 2-week PBMT regimen.

References: 1. Malfertheiner P, Megraud F, Rokkas T, et al. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut 2022;71:1724-1762.

2. Jung HK, Kang SJ, Lee YC, et al. Evidence-Based Guidelines for the Treatment of Helicobacter pylori Infection in Korea 2020. Gut Liver 2021;15:168-195.

3. Seo SI, Lim H, Bang CS, et al. Bismuth-Based Quadruple Therapy versus Metronidazole-Intensified Triple Therapy as a First-Line Treatment for Clarithromycin-Resistant Helicobacter pylori Infection: A Multicenter Randomized Controlled Trial. Gut Liver 2022;16:697-705.

4. Moon SG, Lim CH, Kang HJ, et al. Seven Days of Bismuth-Based Quadruple Therapy Is as Effective for the First-Line Treatment of Clarithromycin-Resistant Confirmed Helicobacter pylori Infection as 14 Days of Bismuth-Based Quadruple Therapy. J Clin Med 2022;11.

5. Bang CS, Lim H, Jeong HM, et al. Amoxicillin or tetracycline in bismuth-containing quadruple therapy as first-line treatment for Helicobacter pylori infection. Gut Microbes 2020;11:1314-1323

Disclosure: Nothing to disclose.

PP0279

INITIAL RESULTS OF THE FOLLOW-UP OF A GISTAR PARTICIPANT COHORT FOR ASSESSING THE POTENTIAL NEGATIVE LONG-TERM EFFECTS OF HELICOBACTER PYLORI TEST AND TREAT

D. Razuka-Ebela¹, N. Sapurovs¹, I. Polaka¹, S. Parshutin¹, I. Ebela², Y. Tarasenko¹, D. Santare², M. Leja¹

¹University of Latvia, Institute of Clinical and Preventive Medicine, Riga, Latvia, ²University of Latvia, Faculty of Medicine, Riga, Latvia

Contact E-Mail Address: d.razuka.ebela@gmail.com

Introduction: These are the initial results based on currently ongoing follow-up of the participants in the GISTAR study in Latvia (Multicentric randomized study of H. pylori eradication and pepsinogen testing for prevention of gastric cancer mortality) within the EUROHELICAN project.

Aims & Methods: The aim was to investigate the potential adverse health effects of the Helicobacter pylori (H. pylori) test-and-treat strategy in the long term. Baseline data on sociodemographic and lifestyle factors, medical history, body mass index (BMI), waist to hip ratio (WHR), and blood pressure were collected 5 to 11 years ago. Blood samples were also drawn. Participants in the intervention group were tested for H. pylori (initially with serology, then urea breath test (UBT)). Those who tested positive were offered eradication therapy. Participants in the control group were not tested for H. pylori and received regular healthcare. During follow-up, data on the same characteristics were collected. UBT was performed for those who were H. pylori positive at baseline. The symptom-based GERDQ score was assessed at the follow-up. The change in parameters from baseline to follow-up was examined between groups using chi-square and Mann-Whitney tests in SPSS 29.0.

Results: A total of 1305 GISTAR participants were recruited at follow up within EUROHELICAN. Their median age was 60 years (IQR 11). Among them, 57 % were female, of whom 691 (53%) were in the intervention group. Baseline data on H. pylori status and eradication were available for 687 participants, of whom 423 (61.6%) were positive at baseline.

When comparing differences in the change of characteristics between baseline and follow-up in the treated (n = 356, 51.8%) and non-treated groups (331, 48.2%), there were no significant differences in BMI, WHR, systolic and diastolic blood pressures (Table 1).

When examining changes in characteristics of participants in the eradicated (n = 281, 84%) and non-eradicated (53, 15.9%) groups, there were no significant differences in BMI and blood pressure. There was a significant difference in the WHR change.

Charac- teristics	Treated (n = 356, 51.8%)	Not treated (n = 331, 48.2%)	p value	Eradicated (n = 281, 84%)	Non-eradicated (n = 53, 15.9%)	p value
	Median, inter- quartile range (IQR)	Median, interquartile range (IQR)		Median, interquartile range (IQR)	Median, interquarti- le range (IQR)	
BMI	1.01 (2.55)	0.91 (2.90)	0.38	1.06 (2.65)	1.05 (2.61)	0.75
WHR	0.00 (0.05)	0.01 (0.05)	0.06	0.0003 (0.05)	0.02, 0.07	0.03

Table 1. Comparison of the change in values from baseline to follow-up between groups.

Using GERDQ at least 8 points, 40 (11.3%) met the cut-off for GERD in the treated group versus 48 (14.9%) in the non-treated group ($p = 0.16$). The prevalence of GERD was 30 (10.9%) in the eradicated versus 5 (9.6%) in the non-eradicated group ($p = 0.78$).

Conclusion: The project will provide data missing on the potential negative effects of eradication. So far, no negative effects were confirmed. The study is ongoing, and a larger number of participants will be included. More data will be available to better assess whether there is a significant change in parameters covered in this abstract as well as additional variables pertaining to GERD, and potential metabolic and cardiovascular effects.

The EUROHELICAN project “Accelerating gastric cancer reduction in Europe through *Helicobacter pylori* eradication” received funding from EU-4Health program, grant no. 101079944.

Disclosure: Nothing to disclose.

PP0280

EFFECTIVENESS OF THE FIRST-LINE ERADICATION THERAPY IN 14 CITIES IN RUSSIA: RESULTS FOR THE PERIOD 2013-2022 OF THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

D.S. Bordin^{1,2,3}, S.R. Abdulkhakov^{4,5}, D.N. Andreev², I. Voynovan¹, I.G. Bakulin⁶, N.V. Bakulina⁶, N.V. Baryshnikova⁷, T.A. Ilchishina⁸, B.D. Starostin⁹, L.G. Vologzhanina¹⁰, O.V. Zaytsev¹¹, A.S. Sarsenbaeva¹², S.A. Alekseenko¹³, G.N. Tarasova¹⁴, N.N. Dekhnich¹⁵, L.V. Tarasova¹⁶, M.A. Livzan¹⁷, V.V. Tsukanov¹⁸, M.F. Osipenko¹⁹, N.V. Bakanova²⁰, R.A. Abdulkhakov⁵, P.O. Bogomolov^{2,21,22}, O.A. Kolokolnikova²³, S.G. Burkov²⁴, I.V. Maev², A. Cano-Català²⁵, P. Parra²⁶, L. Moreira²⁷, F. Megraud²⁸, C. O'Morain²⁹, O.P. Nyssen²⁶, J.P. Gisbert²⁶, on behalf of the Hp-EuReg scientific committee and the researchers
¹Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ²Russian University of Medicine, Moscow, Russian Federation, ³Tver State Medical University, Tver, Russian Federation, ⁴Kazan Federal University, Kazan, Russian Federation, ⁵Kazan State Medical University, Kazan, Russian Federation, ⁶Mechnikov North-Western State Medical University, Saint Petersburg, Russian Federation, ⁷Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation, ⁸Multidisciplinary Medical Holding “SM-clinic” (Medi Com LLC), Saint Petersburg, Russian Federation, ⁹City Polyclinic №38, Saint Petersburg, Russian Federation, ¹⁰Vagner Perm State Medical University, Perm, Russian Federation, ¹¹First Clinical Medical Centre, Kovrov, Russian Federation, ¹²South Ural State Medical University, Chelyabinsk, Russian Federation, ¹³Far Eastern State Medical University, Khabarovsk, Russian Federation, ¹⁴Rostov State Medical University, Rostov-on-Don, Russian Federation, ¹⁵Smolensk State Medical University, Smolensk, Russian Federation, ¹⁶Ulyanov Chuvash State University, Cheboksary, Russian Federation, ¹⁷Omsk State Medical University, Omsk, Russian Federation,

¹⁸Federal Research Center “Krasnoyarsk Science Center of the Siberian Branch of the Russian Academy of Sciences, Research Institute for Medical Problems in the North, Krasnoyarsk, Russian Federation, ¹⁹Novosibirsk State Medical University, Novosibirsk, Russian Federation, ²⁰Medical Center “Medicea”, Izhevsk, Russian Federation, ²¹Private Medical Center “Universal”, Moscow, Russian Federation, ²²Vladimirsky Moscow Regional Clinical Research Institute, Moscow, Russian Federation, ²³Clinical Hospital №1 MEDSI, Moscow, Russian Federation, ²⁴Polyclinic №3, Moscow, Russian Federation, ²⁵Gastrointestinal Oncology, Endoscopy and Surgery (GOES) research group, Althaia Xarxa Assistencial Universit ria de Manresa, Institut de Recerca i Innovaci n en Ci ncies de la Vida i de la Salut de la Catalunya Central (IRIS-CC), Manresa, Spain, ²⁶Hospital Universitario de La Princesa, Instituto de Investigaci n Sanitaria Princesa (IIS-Princesa), Universidad Aut noma de Madrid (UAM), Centro de Investigaci n Biom dica en Red de Enfermedades Hep ticas y Digestivas (CIBERehd), Madrid, Spain, ²⁷Department of Gastroenterology, Hospital Cl nic de Barcelona, Centro de Investigaci n Biom dica en Red en Enfermedades Hep ticas y Digestivas (CIBERehd), Institut d’Investigacions Biom diques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain, ²⁸INSERM U1312, Universit  de Bordeaux, Bordeaux, France, ²⁹School of Medicine, Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: dbordin@mail.ru

Introduction: According to recent studies, the prevalence rate of *H. pylori* infection in Russia is over 30%, but a decreasing trend has recently been observed. Comprehensive multicenter evaluation of effectiveness of different eradication treatments in Russia has not yet been performed. One of the most efficient tools of such analysis is the on-going European Registry on *H. pylori* Management (Hp-EuReg), an international, prospective, multicenter, observational study, which begun in 2013.

Aims & Methods: The objective of our study was to evaluate the effectiveness of first-line empirical eradication therapy in Russia between 2013-2022 according to the data of Hp-EuReg. The treatment effectiveness was analysed by per-protocol (PP), and modified intention-to-treat (mITT), also stratifying by PPI dose (low dose - 4.5 to 27 mg omeprazole equivalent, twice daily; standard dose - 32 to 40 mg omeprazole equivalent, twice daily; high dose - 54 to 128 mg omeprazole equivalent, twice daily) and duration of treatment (7, 10 or 14 days).

Results: Overall, 8,354 patients from 14 cities in Russia who had received a first-line empirical eradication therapy between 2013 and 2022, were included. Invasive (i.e. endoscopic) methods (rapid urease test, histology/cytology) for the *H. pylori* primary evaluation were mostly used in almost all cities. The highest rate of ¹³C-urea breath test was observed in Rostov-on-Don (89% of cases), Saint-Petersburg (37%), Omsk (25%), Perm (25%), and Moscow (23%). The most frequently used first-line treatments were: triple (PPI, amoxicillin, clarithromycin) and triple plus bismuth (PPI, amoxicillin, clarithromycin, bismuth) therapies, accounting for more than 60% of prescriptions in almost all cities. Most cities prescribed 14-day length therapies; whereas standard PPI doses were most frequently used in Chelyabinsk (94%), Smolensk (84%), Saint-Petersburg (68%), Moscow (67%), Khabarovsk (66%) and Rostov-on-Don (54%), low PPI doses prevailed in Krasnoyarsk (80%), Izhevsk (70%), Novosibirsk (65%), Omsk (60%), and Kazan (52%). Quadruple therapy with PPI, amoxicillin, clarithromycin and bismuth achieved optimal (>90%) mITT effectiveness in Saint-Petersburg, Perm, Chelyabinsk, and Khabarovsk, where it was more frequently used than in the remaining cities. Effectiveness of triple therapy (PPI, amoxicillin, clarithromycin) varied from 62% (Novosibirsk) to 99% (Omsk), achieving over 85% across all cities. However, high eradication rates with triple therapy prescriptions were observed in the cities with a small number of

patients or in those cases where histology were the unique tests used for eradication control, possibly giving false negative results. Classic bismuth quadruple therapy (PPI, tetracycline, metronidazole, bismuth) provided optimal (>90%) mITT effectiveness in Moscow and Saint-Petersburg, where it was predominately used as compared to other cities (table 1).

Eradication therapy	Moscow	St. Petersburg	Kazan	Perm	Kovrov	Chelyabinsk	Khabarovsk	Rostov-On-Don	Smolensk	Cheboksary	Omsk	Krasnoyarsk	Novosibirsk	Izhevsk	Overall
Triple therapy (PPI+ A+C)	83.4%	87%	77.2%	89.2%	76.1%	96.3%	72.6%	88.3%	78%	94%	99.1%	81.7%	62%	100%	83.1%
Quadruple therapy (PPI+M+Tc+ bismuth)	92.1%	91.4%	100%	100%	80%	100%	100%	-	100%	100%	100%	-	-	-	92.9%
Quadruple therapy (PPI+ A+C+ bismuth)	88.3%	93.1%	86.4%	95.2%	87.3%	100%	92.4%	100%	86.7%	96.2%	100%	-	71.4%	91.2%	92.7%

Table 1 Effectiveness by modified intention-to-treat of most common first-line empirical therapies in 14 cities of Russia in 2013-2022

PPI: proton pump inhibitor; A: amoxicillin; C: clarithromycin; M: metronidazole; B: bismuth salts; Tc: tetracycline

Conclusion: To date, in Russia, bismuth quadruple therapies either with classical metronidazole-tetracycline-bismuth or amoxicillin-clarithromycin-bismuth achieve optimal (> 90%) results, providing significantly better rates when prescribed for 14 days

Disclosure: Nothing to disclose.

PP0281

TREATMENT PATTERNS IN CHINESE PATIENTS WITH HELICOBACTER PYLORI: A MULTICENTER, RETROSPECTIVE, REAL-WORLD STUDY

W. Pan¹, Y. Zhao², P. Li³, F. Zhou³, L. Xie³, H. Xu⁴

¹Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou, China, ²Shanghai Tenth People's Hospital, Shanghai, China, ³Takeda (China) International Trade Co, Shanghai, China, ⁴Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China

Contact E-Mail Address: fang.zhou1@takeda.com

Introduction: *Helicobacter pylori* (HP) is regarded as a class I carcinogenic factor and eradication therapy can reduce the risk of gastric cancer. Patients with HP infections are administered with bismuth quadruple therapy (BQT), triple and dual therapies based on their eradication effectiveness. BQT (bismuth + acid suppressants + 2 antibiotics) and dual therapy are both recommended in China now. Comprehensive understanding on the distribution of current eradication therapies is required to identify gaps observed in real-world practice.

Aims & Methods: This multicenter, retrospective, real-world study (NCT05073367) extracted preexisting electronic data including adult patients (aged ≥18 years) with HP infection between January 1, 2019 and March 31, 2021 from 3 hospitals to assess the diagnosis and treatment pattern of HP infection and effectiveness of eradication therapy in China. In this abstract, we reported the distribution of eradication therapies, difference in initiation year for treatment, and treatment duration.

Results: Of the 22,971 eligible patients with HP infection, 13,233 (57.61%) were prescribed eradication regimens. Mean ± SD age of patients with eradication treatment was 43.7 ± 14.0 years; 65.94% of patients had medical insurance; and 54.50% of patients were women.

In patients who received eradication therapy, the BQT therapy was predominantly prescribed (85.39%; n=11301), followed by triple therapy (7.55%; n=999) and dual therapy (7.06%; n=934). Among those receiving BQT, use of amoxicillin + clarithromycin based regimens (38.72%; n=4376) were the most prevalent, followed by amoxicillin + furazolidone (18.35%; n=2074) and amoxicillin + levofloxacin (17.76%; n=2007) based combina-

tion regimens. Proportion of patients receiving BQT decreased over years: 97.24% patients in 2019, 79.98% in 2020, and 78.71% in 2021. The proportion of patients receiving dual and triple therapy increased over the years in 2019, 2020, and 2021 were shown in Table 1. A total of 10,903 patients were analyzed according to various treatment durations with the usage of various eradication therapies. Treatment duration is defined as the number of days that prescribed drugs can cover. Out of the three types of treatments, BQT had the highest proportion of 14-day treatment duration at 90.16%, followed by triple therapy at 76.78%, while dual therapy had the least proportion at 14.42%. For treatment duration >14 days, BQT, dual and triple therapy had a proportion of 4.38%, 82.35%, and 17.27% respectively.

Treatment	Type of Eradication therapy (N=13, 234) n (%) ^a	Year of treatment initially prescribed, 2019 (N=4492) n (%) ^a	Year of treatment initially prescribed, 2020 (N=4125) n (%) ^a	Year of treatment initially prescribed, 2021 (N=4616) n (%) ^a
Total	13,234 (-)	4492 (-)	4125 (-)	4617 (-)
Bismuth quadruple therapy	11,301 (85.39)	4368 (97.24)	3299 (79.98)	3634 (78.71)
Amoxicillin and Clarithromycin	4376 (38.72)	1800 (41.21)	1324 (40.13)	1252 (34.45)
Amoxicillin and Furazolidone	2074 (18.35)	689 (15.77)	480 (14.55)	905 (24.90)
Amoxicillin and Levofloxacin	2007 (17.76)	1021 (23.37)	516 (15.64)	470 (12.93)
Amoxicillin and Metronidazole	76 (0.67)	27 (0.62)	10 (0.30)	39 (1.07)
Amoxicillin and Tetracycline	9 (0.08)	5 (0.11)	1 (0.03)	3 (0.08)
Furazolidone and Tetracycline	12 (0.11)	1 (0.02)	0 (0.00)	11 (0.30)
Other Bismuth quadruple	2747 (24.31)	825 (18.89)	968 (29.34)	954 (26.25)
Triple therapy^c	999 (7.55)	105 (2.34)	551 (13.36)	343 (7.43)
Dual therapy^c	934 (7.06)	19 (0.42)	275 (6.67)	640 (13.86)

Table 1. Distribution of eradication therapy based upon the type and year of treatment initiation

Abbreviations: N, total number; n, number in respective category.

^a% = The total usage count of BQT or Triple or Dual eradication therapy/the total usage count of all standard eradication therapies received by eligible participants.

Of BQT, the total usage count of different BQT/the total usage count of all BQT.

^bThere is a recurrent patient who changed the treatment pattern from triple therapy (ilaprazole, clarithromycin, levofloxacin) to dual therapy (ilaprazole, ornidazole) after the recurrence.

^cConsidering the table size, outcomes of different treatment regimens under dual and triple therapy were not included in the table.

Conclusion: BQT-based regimen for 14 days was the predominant eradication regimens in all therapies, amoxicillin + clarithromycin based BQT was the most prevalent. Use of dual therapy gradually increased with years for HP eradication in the Chinese real-world clinical practice.

Disclosure: The study was funded by Takeda China. Wensheng Pan, Yan Zhao, and Hongwei Xu have no conflicts of interest. Pengfei Li, Fang Zhou, Li Xie are the employees of Takeda, and they hold Takeda stock options. Medical writing for the development of this abstract was provided by Kusuma Kumari G, PhD, of Indegene Private Limited, and funded by Takeda China. Authors retained full control of the abstract content.

PP0282

TREATMENT EFFECTIVENESS OF DIFFERENT ERADICATION TREATMENTS IN CHINESE PATIENTS WITH HELICOBACTER PYLORI: A RETROSPECTIVE REAL-WORLD STUDY

W. Pan¹, Y. Zhao², P. Li³, F. Zhou³, L. Xie³, H. Xu⁴

¹Zhejiang Provincial People's Hospital (Affiliated People's Hospital), Hangzhou, China, ²Shanghai Tenth People's Hospital, Shanghai, China, ³Takeda (China) International Trade Co, Shanghai, China, ⁴Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China

Contact E-Mail Address: fang.zhou1@takeda.com

Introduction: *Helicobacter pylori* (*H. pylori*) infection has a high prevalence (44.8%) in China and is an important risk factor of gastrointestinal diseases including gastric cancer. Bismuth quadruple therapy (BQT; bismuth + acid suppressant + 2 antibiotics [ABs]) is the currently recommended first-line regimen for *H. pylori* in China. Increasing AB resistance poses a vital challenge and remarkably reduces the eradication rate (ER) from 95% to 80% globally and 89% to 78% in China. Real-world ER analysis assessed only quadruple therapy in a few single centers and did not focus on different antibiotic combinations and other different regimens.

Aims & Methods: This study was designed to evaluate the diagnosis and treatment pattern of *H. pylori* infection and the effectiveness of eradication therapy in real-world settings in China. In this retrospective, multi-center study (NCT05073367), de-identified patient data were extracted from the electronic medical records database of 3 hospitals between January 1, 2019, and March 31, 2021. Patients aged ≥18 years with a record of *H. pylori* infection diagnosis were included. Here we presented the eradication rate of different treatment regimens and the eradication rate of different years with different treatment regimens.

Total (N=1426) → /Treatment regimens ↓	ER-success n (%) ^a	Year 2019 Success n (%) ^b	Year 2020 Success n (%) ^b	Year 2021 Success n (%) ^b
Total	1028 (72.09)	454 (77.87)	253 (60.96)	321 (75.00)
Bismuth Quadruple Therapy	879 (76.70)	443 (77.86)	186 (67.64)	250 (82.78)
Amoxicillin and Clarithromycin	391 (76.07)	169 (78.24)	106 (67.95)	116 (81.69)
Amoxicillin and Furazolidone	181 (87.44)	55 (87.30)	44 (83.02)	82 (90.11)
Amoxicillin and Levofloxacin	159 (77.94)	126 (79.25)	10 (55.56)	23 (85.19)
Amoxicillin and Metronidazole	2 (50.00)	2 (50.00)	0 (0.00)	0 (0.00)
Other Bismuth Quadruple Therapy	146 (67.28)	91 (71.65)	26 (54.17)	29 (69.05)
Triple therapy^c	59 (48.36)	11 (78.57)	37 (46.25)	11 (39.29)
Dual therapy^c	90 (56.96)	0 (0.00)	30 (50.00)	60 (61.22)

Table 1. Eradication rate of *H. pylori* positive patients based on the type of eradication therapy.

Abbreviations: N, total number; n, number in respective category.

^a% = The total usage count of BQT/Triple therapy/Dual therapy eradication therapy/ the total usage count of all standard eradication therapies taken by eligible participants. Of BQT, the total usage count of different BQT/the total usage count of all BQT.

^b% = The number of participants with a negative efficacy evaluation result/the number of participants receiving certain eradication therapy.

^cConsidering the table size, outcomes of different treatment regimens under dual and triple therapy were not included in the table.

Results: A total of 1426 patients received ET with efficacy evaluation duration >4 weeks after the eradication therapy and the total eradication rate was 72.09% (n=1028). Most patients (80.36%; n=1146) received standard BQT with an ER of 76.70% (n=879). 158 patients (11.08%) received dual therapy (ER=56.96%; n=90) and 122 patients (8.56%) received triple therapy (ER=48.36%; n=59). Compared with triple and dual therapies, BQT was the predominant regimen in all the years with an ER of 77.86%, 67.64%, and 82.78% in 2019, 2020, and 2021, respectively. The ER of dual therapy was 50% in 2020 and 61.22% in 2021. The triple therapy ER showed a

decreasing trend with 78.57% (n=11), 46.25% (n=37), 39.29% (n=11) from 2019 to 2021. Among the BQT regimens, amoxicillin plus furazolidone based regimens showed a higher ER (87.44%; n=181), while the ER of amoxicillin plus levofloxacin, amoxicillin plus clarithromycin based BQT was 77.94% (n=159) and 76.07% (n=391), respectively. Amoxicillin plus furazolidone based BQT showed a higher ER of 87.30%, 83.02%, and 90.11% in 2019, 2020, and 2021 respectively (Table 1).

Conclusion: BQT-based regimens were predominantly prescribed for *H. pylori* management and the current *H. pylori* treatment regimens have a suboptimal eradication rate in the real-world settings.

Disclosure: The study was funded by Takeda China. Wensheng Pan, Yan Zhao, and Hongwei Xu have no conflicts of interest. Pengfei Li, Fang Zhou, and Li Xie are employees of Takeda, and they hold Takeda stock options. Medical writing for the development of this abstract was provided by Swathirajan CR, PhD, and Kusuma Kumari G, PhD, of Indegene Private Limited, and funded by Takeda China. Authors retained full control of the abstract content.

PP0283

ESOMEPRAZOLE/VONOPRAZAN COMBINED WITH HIGH-DOSE AMOXICILLIN DUAL THERAPY FOR PRIMARY ERADICATION OF HELICOBACTER PYLORI INFECTION: A MULTI-CENTER, PROSPECTIVE, OPEN-LABEL, RANDOMIZED CONTROLLED CLINICAL TRIAL

X. Yang¹, S. Zhang², Y. Liu³, S. Yao¹, S. Zhang¹, X. Liu¹, F. Wang¹

¹The Third Xiangya Hospital, Central South University, Department of Gastroenterology, Changsha, China, ²The Second People's Hospital of Huaihua, Department of Gastroenterology, Huaihua, China, ³Yueyang Hospital of Traditional Chinese Medicine, Department of Gastroenterology, Yueyang, China

Contact E-Mail Address: wfen-judy@csu.edu.cn

Introduction: Due to certain shortcomings of traditional triple and quadruple therapy for *Helicobacter pylori* (*H. pylori*), high-dose dual therapy (HDDT) is proposed as another option.

Aims & Methods: Our study aims to evaluate the efficacy and safety of HDDT, and provide more reference for clinical eradication of *H. pylori*. The subjects were untreated *H. pylori* patients from three medical centers in Central China. Totally, 439 subjects were randomly assigned to EA (esomeprazole-amoxicillin) or B-quadruple (esomeprazole-amoxicillin-clarithromycin-bismuth) group. A total of 367 subjects were randomly assigned to VA (vonoprazan-amoxicillin) or VAC (vonoprazan-amoxicillin-clarithromycin) group. The effect, adverse events, compliance, symptom relief and cost were recorded.

Results: EA-dual was non-inferior to B-quadruple regimen in mITT and PP analysis ($P < 0.025$). But the eradication rate of EA was lower than that of B-quadruple group (70.59% vs. 83.49%, 92.86% vs. 98.38%, 93.94% vs. 98.38%, ITT, mITT, PP respectively, $P < 0.05$). In ITT, mITT and PP analysis, VA-dual was non-inferior to VAC treatment (84.15% vs. 83.15%, 96.25% vs. 92.73%, 96.75% vs. 93.75%, $P < 0.025$).

There was no significant difference in adverse events, compliance, and symptom relief between groups. Cost of VA was the lowest. Antibiotics use within 2 years, poor compliance and suburban area residence reduced the eradication efficacy ($P < 0.05$).

Conclusion: The HDDT based on esomeprazole or vonoprazan was non-inferior to the classical B-quadruple or VAC triple regimen. So, the HDDTs should be recommended as first-line therapies of *H. pylori* eradication. Antibiotics use in 2 years, adherence and residence were crucial for eradication.

Disclosure: The authors declare that they have no conflict of interest.

PP0284

EVALUATION OF THE EFFECTIVENESS AND SAFETY OF *HELICOBACTER PYLORI* EMPIRICAL ERADICATION REGIMENS IN SWITZERLAND: AN INTERIM ANALYSIS WITH DATA FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

M. Doulberis¹, D. Riva², I. Linas³, O. P. Nyssen⁴, A. Cano Català⁵, L. Moreira Ruiz⁶, P. Parra⁴, T. Kuntzen⁷, J. Gisbert⁸

¹Kantonsspital Aarau, Gastroenterology & Hepatology, Dietikon, Switzerland, ²Gastro, Gastrocentro Plus Lugano, Lugano, Switzerland, ³Gastroenterologische Gruppenpraxis / Hirslanden Clinic Beau-Site, Gastroenterology, Münsingen, Switzerland, ⁴Hospital Universitario de La Princesa, IIS-IP, and CIBERehd, Gastroenterology Unit, Madrid, Spain, ⁵GOES Research Group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain., GOES Research Group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain., Manresa, Spain, ⁶Hospital Clinic de Barcelona, Gastroenterology, Gava, Spain, ⁷Kantonsspital Aarau, Gastroenterology And Hepatology, Department Of Internal Medicine, Aarau, Switzerland, ⁸Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Digestive Services, Madrid, Spain

Contact E-Mail Address: doulberis@gmail.com

Introduction: Prevalence of *Helicobacter pylori* (*H. pylori*) infection remains high. Despite the reported relatively low prevalence in Switzerland, the real burden is considered to be much higher, primarily due to the phenomenon of migration. Till now, there is scarce evidence regarding effectiveness of *H. pylori* eradication schemes in Switzerland.

Aims & Methods: Sub-study of the “European Registry on *H. pylori* Management” (Hp-EuReg), an international, multicenter, prospective non-interventional registry of the routine clinical practice. All infected adult patients were systematically registered at AEG-REDCap e-CRF from 2013 to December 2023. Swiss data were analysed for effectiveness on a modified intention-to-treat (mITT) basis.

Results: A total of 486 adult patients, diagnosed with *H. pylori* infection, were collected. Out of them, 428 (88.1%) were treatment-naïve patients. Two prescription regimes included more than 90% of the cases (triple with Clarithromycin and Amoxicillin in 49% and single-capsule bismuth quadruple in 42%). For the effectiveness analysis, 280 naïve patients were eligible, due to their availability of a confirmatory *H. pylori* eradication test. The overall effectiveness of 1st line empirical therapy was 92% by mITT. The lowest effectiveness was recorded with triple therapy with amoxicillin and clarithromycin (28/34 cases, 82.4 % for seven days duration, and 86.9% overall (126/145). On the other hand, the highest effectiveness was reached with the single-capsule bismuth quadruple therapy (97.1%, 100/103). In respect to potency of gastric acid inhibition by proton pump inhibitors (PPI), the group with low-dose (i.e. 20 mg omeprazole equivalent twice daily) PPI yielded an overall eradication success of 90.8%, whereas for the standard-dose (i.e. omeprazole equivalent 40mg bid) and high-dose (i.e. omeprazole equivalent 80mg bid) PPI inhibition the rates increased up to 100% and 96.3%, respectively. Regarding safety, the eradication treatments were generally well tolerated, and serious adverse events were reported in 16 cases (5.7%). Mild adverse effects were rather uncommon and included dysgeusia (n=1), diarrhoea (n=6), nausea (n=6) and dyspepsia (n=3).

Conclusion: This first interim analysis of Swiss population as sub-study of the Hp-EuReg suggests that bismuth quadruple therapy prescribed as single-capsule represents a reliable option as first-line empirical therapy.

Disclosure: Nothing to disclose.

PP0285

EFFECTIVENESS OF EMPIRICAL FIRST-LINE *H. PYLORI* ERADICATION THERAPY IN ITALY FROM 2013 TO 2023: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

L. Gatta¹, O. P. Nyssen², M. Pavoni³, G. Fiorini³, M. Romano⁴, A.G. Gravina⁴, L. Granata⁴, R. Pellicano⁵, A. Gasbarrini⁶, D.L. Alfredo⁷, G. Losurdo⁷, F. Franceschi⁸, G. Nardone⁹, A. Rocco¹⁰, M.P. Dore¹¹, F. Farinati¹², M. Ghisa¹², M. Bellini¹³, R. Manta¹⁴, J. Holton¹⁵, B. Vaira³, C. Borghi³, A. Cano-Català¹⁶, P. Parra², L. Moreira Ruiz¹⁷, F. Megraud¹⁸, C. O’Morain¹⁹, J. Gisbert²

¹Azienda USL Toscana Nord Ovest (ATNO), Department of Oncology Screenings, Carrara, Italy, ²Hospital Universitario de La Princesa, IIS-IP, and CIBERehd, Gastroenterology Unit, Madrid, Spain, ³University of Bologna, Department of Medical and Surgical Sciences, IRCCS S. Orsola, Bologna, Italy, ⁴University of Campania “Luigi Vanvitelli”, Department of Precision Medicine, Division of Hepatogastroenterology, Naples, Italy, ⁵University of Turin, Molinette-SGAS Hospital, Turin, Italy, ⁶Università Cattolica Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁷University “Aldo Moro” of Bari, Section of Gastroenterology, Department of Emergency and Organ Transplantation, Bari, Italy, ⁸Università Cattolica Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Emergency, Anesthesiological, and Reanimation Sciences, Rome, Italy, ⁹University Federico II of Naples, Gastroenterology Unit, Department of Clinical Medicine and Surgery, Naples, Italy, ¹⁰University Federico II Naples, Gastroenterology Unit, Department of Clinical Medicine and Surgery, Naples, Italy, ¹¹University of Sassari, Department of Medical, Surgical and Experimental Science, Sassari, Italy, ¹²Padua University Hospital, Dept Surgery, Oncology and Gastroenterology, Padova, Italy, ¹³University of Pisa, Dept. of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ¹⁴Azienda USL Toscana Nord Ovest (ATNO), Digestive Endoscopy Unit, “Spedali Riuniti” Hospital, Livorno, Italy, ¹⁵Middlesex University, The Burroughs, Hendon, Department of Natural Sciences, Faculty of Science and Technology, London, United Kingdom, ¹⁶Università de Manresa, GOES Research Group, Althaia Xarxa Assistencial, Manresa, Spain, ¹⁷University of Barcelona, Department of Gastroenterology, Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Gava, Spain, ¹⁸Université de Bordeaux, Hopital Pellegrin, Laboratoire de Bactériologie, Bordeaux, France, ¹⁹Trinity College Dublin, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: opn.aegredcap@aegastro.es

Introduction: It is not yet clear what is the best first-line empirical therapy in patients with *Helicobacter pylori* (*H. pylori*) infection. For this reason, it is important to constantly monitor the effectiveness of the different therapies used in clinical practice.

Aims & Methods: The aim of this study was therefore to assess the effectiveness of empirical first-line treatment prescribed in Italy evaluating the European Registry on *H. pylori* Management (Hp-EuReg). The Hp-EuReg is an international multicentre prospective non-interventional registry recording information on *H. pylori* infection management since 2013. All infected adult patients enrolled were systematically registered at AEG-REDCap e-CRF. Data of all *H. pylori*-positive treatment-naïve patients enrolled from 2013 to December 2023 by Italian centres participating in the Hp-EuReg, were extracted, subject to quality control, and analysed. The effec-

tiveness of the first-line treatment empirically prescribed was evaluated according to the modified intention-to-treat (including all patients that completed follow-up, *i.e.*, a confirmatory test of success or failure available after eradication treatment), and per-protocol analysis (including all patients that completed follow-up and took at least 90% of the treatment drugs).

Results: In total, 4,144 patients were included for analysis; the mean age was 52 years (SD ± 5), and 60% of patients were women. Overall, 1.0% of the cases were allergic to penicillin. Among those non-allergic to penicillin, 10-day sequential therapy (mainly as PPI-clarithromycin-amoxicillin-tinidazole) was most commonly prescribed (54%), followed by 10-day single capsule bismuth quadruple therapy with metronidazole and tetracycline (19 %), and 10 or 14-day non-bismuth concomitant treatment (mainly as clarithromycin-amoxicillin-tinidazole) (9.3%), providing these regimens optimal cure rates (91.5%, 95.5%, 92% and 97%; respectively). Additional first-line prescriptions encompassed 7, 10 or 14-day triple therapy with PPI-clarithromycin-amoxicillin (5.5%), and 10-day triple therapy with PPI-levofloxacin-amoxicillin (2.9%) (see Table 1).

First-line treatment	Length (days)	mITT % (95% CI)	PP % (95% CI)
Sequential (PPI + C-A-T/M)	10	91.5 (90.2 to 92.7)	90.9 (89.5 to 92.1)
PPI + Single capsule (M+Tc+B)	10	95.5 (93.7 to 96.8)	96.6 (94.9 to 97.7)
Concomitant (PPI + C-A-M/T)	10	92.2 (86.6 to 95.6)	93.5 (88.1 to 96.5)
	14	96.6 (93.6 to 98.4)	98.1 (95.6 to 99.2)
Triple PPI-C-A	7	83.6 (72.9 to 90.6)	86.2 (75.7 to 92.5)
	10	80 (71.1 to 86.7)	80.4 (71.4 to 87.1)
	14	100 (0.77 to 100)	100 (0.77 to 100)
Triple PPI-A-L	10	81.4 (72.7 to 87.7)	82.8 (74.2 to 89)

mITT: modified intention-to-treat; PP, per protocol; A, amoxicillin; B, bismuth salt; C, clarithromycin; L, levofloxacin; M, metronidazole; PPI, proton pump inhibitor; T, tinidazole; Tc, tetracycline.

Table 1; Effectiveness by modified intention-to-treat (mITT), and per-protocol (PP) analyses of first-line empirical treatment in patients not allergic to penicillin enrolled in the Italian centres participating in the European Registry on H. pylori management (Hp-EuReg).

Conclusion: Among the first-line empiric treatments prescribed by the Italian centres participating in the Hp-EuReg, only single-capsule bismuth quadruple therapy with metronidazole-tetracycline-bismuth, sequential therapy with clarithromycin-amoxicillin-tinidazole, and non-bismuth concomitant therapy with clarithromycin-amoxicillin-tinidazole, achieved over 90% effectiveness.

Disclosure: Olga P. Nyssen received research funding from Mayoly and Allergan; Antonio Gasbarrini served as consultant for Abbvie, Actial, Alpha-Sigma, Eisai, Gilead, Malesci; Maria Pina Dore received funding from Sanofi, Takeda; Alfredo Di Leo served as a consultant for THD SpA; Gerardo Nardone received research grant from Sofar S.p.a and Alfasigma; Francis Mégraud received research grant from Allergan, bioMerieux, Mobidiag (to the institution), and as speaker from Biocodex and Mayoly; Claudio Borghi served as speaker, consultant, and advisory member for Servier, Novo-Nordisk, Astra-Zeneca, Sanofi; Javier P. Gisbert served as speaker, consultant, and advisory member for or received research funding from Mayoly, Allergan, Diasorin, GebroPharma, and Riche.

PP0286
NON-BISMUTH QUADRUPLE CONCOMITANT TREATMENT FOR H. PYLORI ERADICATION: SYSTEMATIC REVIEW AND META-ANALYSIS

P. Parra¹, O. P. Nyssen^{*1}, J.P. Gisbert^{*1}, ^{*}co-last authors
¹Department of Gastroenterology, Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain

Contact E-Mail Address: pablo.parra.hlp@gmail.com
Introduction: *Helicobacter pylori* eradication with standard triple therapy fails in ≥20% of the cases, mainly due to bacterial antibiotic resistances. Non-bismuth quadruple concomitant therapy is among the most widely used first-line treatments against *H. pylori* infection, even in high clarithromycin resistance areas.

Aims & Methods: To evaluate the efficacy and safety of non-bismuth quadruple concomitant therapy (proton pump inhibitor, clarithromycin, amoxicillin and nitroimidazole) in the treatment of *H. pylori* infection, and to compare it with other triple and quadruple regimens. Bibliographical searches were performed in PubMed up to April 2024. We performed a meta-analysis of the studies evaluating the concomitant therapy as a first-line regimen, and of the randomised controlled trials comparing concomitant vs. standard triple, sequential, hybrid, and bismuth quadruple therapies.

Results: 115 studies (78 randomised trials) were included (23,454 patients); 39 studies compared concomitant vs triple (13,494 patients), 38 studies vs sequential (11,907 patients), 12 studies vs hybrid (3,719 patients) and 11 studies vs bismuth quadruple (3,258 patients). Concomitant regimen achieved an overall eradication rate of 86% (95%CI=85-86%) by intention-to-treat, and 90% (90-91%) by per-protocol. Concomitant therapy achieved high eradication rates even in single clarithromycin resistant (89%) and metronidazole resistant (95%) patients, but poor cure rates in dual (clarithromycin and metronidazole) resistance (68%). The overall efficacy by intention-to-treat with concomitant therapy was significantly higher as compared to both triple therapy (risk difference [RD]=0.11; 95%CI=0.09-0.14; 39 studies) and sequential therapy (RD=0.04; 0.02-0.06; 38 studies); however, in the latter comparison, when only 14-day prescriptions were considered, no significant differences were observed (RD=0.01; -0.05-0.06; 4 studies). Likewise, the overall efficacy of concomitant therapy was similar to hybrid (RD=0.01; -0.01-0.03; 12 studies), and to bismuth quadruple therapy (encompassing the classical form and the single-capsule (RD=0.01; -0.03, 0.06; 11 studies). The overall incidence of adverse events with concomitant therapy was 37% (36-38%) (85 studies). When comparing only the studies with the same treatment durations, the incidence of adverse events with concomitant therapy was similar to that of triple (RD=0.04; -0.01-0.09; 15 studies), sequential (RD=0.03; -0.00-0.06; 16 studies), and bismuth quadruple therapies (RD=0.02; -0.06-0.09; 7 studies), but higher than that of hybrid therapies (RD=0.10; 0.04-0.15; 7 studies).

Conclusion: Non-bismuth quadruple concomitant therapy is highly effective for *H. pylori* eradication (achieving a cure rate of approximately 90%), even in the presence of clarithromycin or metronidazole resistance, being superior to standard triple and sequential therapies, and similar to hybrid and bismuth quadruple regimens. The incidence of adverse events with concomitant treatment is relatively high (37%), similar to that of triple and bismuth quadruple regimens.

Disclosure: Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from: Mayoly, Allergan/Abbvie, Diasorin, Richen, Juvisé and Biocodex.
Olga P. Nyssen received research funding from: Mayoly, Allergan/Abbvie, Richen, Juvisé and Biocodex.

PP0287

LEVOFLOXACIN VERSUS MOXIFLOXACIN IN NITAZOXANIDE-BASED QUADRUPLE THERAPY AS A FIRST- AND SECOND-LINE TREATMENT FOR *HELICOBACTER PYLORI* INFECTION. A RANDOMIZED, COMPARATIVE, MULTICENTER STUDY

G. El-Azab¹, S. Abd-Elsalam², M. Elsabaawy¹, M. Magdy¹, B. Hussein², A.M. Shamseya³, A. Ellakany³, F. Khalil⁴, N. Zaghloul⁵, M. Ezz-Eldin⁵, S. Hassany⁵, E. Moustafa⁵, A. Abuouelhasan⁶, U.M Abdelaal⁷, A. Mahmoud⁸, M. Assem^{1,9}

¹National Liver Institute - Menoufia University, Hepatology and Gastroenterology, Menoufia, Egypt, ²Tanta University, Tropical Medicine, Tanta, Egypt, ³Faculty of Medicine, University of Alexandria, Gastroenterology, Alexandria, Egypt, ⁴National Liver Institute - Menoufia University, Clinical Microbiology and Immunology, Menoufia, Egypt, ⁵Faculty of Medicine, Assiut University, Tropical Medicine and Gastroenterology, Assiut, Egypt, ⁶Faculty of Medicine, Al-Azhar University, Gastroenterology, Hepatology and Infectious Diseases, Cairo, Egypt, ⁷Faculty of Medicine, Sohag University, Gastroenterology Unit, Internal Medicine, Sohag, Egypt, ⁸Faculty of Medicine, Assiut University, Clinical Pathology, Assiut, Egypt, ⁹Faculty of Medicine, University of Bisha, Internal Medicine, Bisha, Saudi Arabia

Contact E-Mail Address: Dr.ayman1977@gmail.com

Introduction: Increasing resistance to antibiotics represents a significant challenge for the successful eradication of *Helicobacter pylori* (*H. pylori*). Therefore, there is a growing need to find novel modalities to improve treatment outcomes.

Aims & Methods: This study aimed to assess the efficacy and safety of levofloxacin- or moxifloxacin-containing nitazoxanide-based regimens for eradicating *H. pylori* as first- and second-line therapies. Patients with dyspeptic symptoms and a positive *H. pylori* antigen test in the stool were eligible for inclusion in this study. Naïve patients were randomized into three groups according to treatment regimens: levofloxacin, nitazoxanide, doxycycline, and lansoprazole (LNDL); moxifloxacin, nitazoxanide, doxycycline, and lansoprazole (MNDL); or amoxicillin, clarithromycin, and lansoprazole (ACL) for 14 days. Treatment-experienced patients received the LNDL or MNDL regimen. *H. pylori* eradication was confirmed by stool antigen testing at least 4 weeks after the cessation of therapy.

Results: In naïve patients, eradication rates were significantly greater by intention to treat (ITT) analysis in patients treated with the LNDL regimen (83.3%) than in those treated with standard triple therapy (ACL) (59.2%). According to the per-protocol analysis (PP), both the LNDL and MNDL regimens had significantly greater eradication rates (87.7% and 81.6%, respectively) than did the ACL regimen (60.9%). Regarding treatment-experienced patients, eradication rates were comparable for the LNDL and MNDL regimens in both ITT (65.9% and 77.5%, respectively) and PP analyses (72.5% and 82.7%, respectively). All treatment regimens were well tolerated.

H. pylori stool antigen test result	Eradication regimen			p-value
	LNDL	MNDL	ACL	
Intention to treat	n: 90	n: 102	n: 71	
Negative (%)	75 (83.33%)	71 (69.61%)	42 (59.15%)	0.003
95% CI	75.73-91.27	60.92-78.90	47.96-71.16	
Per-protocol	n: 86	n: 87	n: 69	
Negative (%)	75 (87.21%)	71 (81.61%)	42 (60.87%)	< 0.001
95% CI	80.21-94.47	73.57-90.01	49.57-72.95	

Table 1 Eradication Rates of *Helicobacter pylori* infection in treatment-naïve patients

Conclusion: levofloxacin- and moxifloxacin-containing nitazoxanide-based regimens exhibit substantial efficacy for the eradication of both naïve and resistant *H. pylori* infections over a 14-day course with a considerable safety profile.

Disclosure: The authors declare to have no competing interests related to this work.

PP0288

EFFICACY OF TEGOPRAZAN-BASED BISMUTH QUADRUPLE THERAPY COMPARED WITH BISMUTH QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* INFECTION: A REAL WORLD EVIDENCE EXPERIENCE

J.M. Remes-Troche¹, E. Coss-Adame², L.R. Valdovinos-García³, A. Cano-Contreras¹, G. Martinez¹

¹Ins Inv Medico-Biol, Veracruz, Neurogastroenterology, Veracruz, Mexico, ²Instituto Nacional de la Nutrición Salvador Zubiran, Motility and Gastroenterology, Mexico City, Mexico, ³Hospital Medica Sur, Gastroenterology, Mexico City, Mexico

Contact E-Mail Address: jose.remes.troche@gmail.com

Introduction: Bismuth-based quadruple therapy (BQT) is recommended as the first-line therapy for *Helicobacter pylori* eradication as it is not associated with resistance. Tegoprazan, a new, fast, and strong potassium-competitive acid blocker, has been approved for the treatment of gastric acid-related diseases in México. However, real-world clinical data regarding this drug are scarce. We aimed to compare the *Helicobacter pylori* eradication rates of tegoprazan- and omeprazole-based quadruple therapy.

Aims & Methods: Aim: To investigate the efficacy and safety profiles of tegoprazan-based BQT (TBMT) versus omeprazole-based BQT (OBMT) for *H. pylori* eradication.

Methods: We included patients older than 18 with an *H. pylori* infection without a history of *H. pylori* eradication who visited two centers between January 2024 and April 2024. *H. pylori* infection was diagnosed using histology. Patients received tegoprazan 50 mg BID, bismuth subcitrate 300 mg QID, metronidazole 500 mg QID, and doxycycline 100 mg QID for 14 days. An historic control groups was used as comparator. Historic controls were age-sex matched subjects that received omeprazole 40 mg BID, bismuth subcitrate 300 mg QID, metronidazole 500 mg QID, and doxycycline 100 mg QID, in the previous year.

Results: Until now, 80 patients have been included (40 TBMT and 40 OBMT). Most common indication for eradication was dyspeptic symptoms (78%), followed by peptic ulcer disease (10%), follicular gastritis (9%) and familiar history of cancer (2.5%). Eradication rates of TBMT and OBMT were 90% and 77.4% (=OR 2.61, CI 95% 0.73-9.37, p=0.12), respectively. There was no significant difference in the rate of adverse events between the TBMT and OBMT groups (42.5% vs. 55.5%, p = 0.37). Nausea was the most common adverse effect (37.5% vs 40%, p=0.92), followed by abdominal pain (12.5% vs 17.5%, p=0.16%) Adherence to the treatments was similar between groups (> 90%, 10% vs 12%, p=0.98)

Conclusion: TBMT showed a noninferior eradication rate and similar adverse events to OBMT as a first-line eradication regimen. Our results suggest that tegoprazan might be substituted for proton pump inhibitors in *H. pylori* eradication regimens in Mexico. A further randomized controlled trial is required to confirm our findings.

Disclosure: JMRT has served as advisory board for Takeda, Asofarma, Carnot and Biocodex. Also is a speaker for Takeda, Asofarma, Alfasigma, Carnot, Chinoin, Medtronic, Ferrer, and Sanofi. ECA and LRVD are speakers for Carnot and Asofarmna. ACC and GM do not have any conflict of interest.

PP0289

FIRST-LINE PRESCRIPTION PATTERNS AND ERADICATION RATES IN IRELAND OVER A 10-YEAR PERIOD: DATA FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

S. Smith¹, O. P. Nyssen², R. FitzGerald¹, T. Butler¹, D. McNamara³, A. Qasim⁴, A. Cano-Catalá⁵, P. Parra², L. Moreira⁶, F. Megraud⁷, C. O'Morain¹, J.P. Gisbert²

¹Trinity College Dublin, School of Medicine, Dublin, Ireland,

²Hospital Universitario de La Princesa, IIS-IP, and CIBERehd, Gastroenterology Unit, Madrid, Spain, ³Gastroenterology, Tallaght University Hospital, School of Medicine, Trinity College Dublin, Dublin, Ireland, ⁴UPMC Beacons Hospital, Gastroenterology, Dublin 16, Ireland, ⁵Althaia Xarxa Assistencial Universitària de Manresa, GOES research group, Manresa, Spain, ⁶Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain, ⁷Hopital Pellegrin, Laboratoire de Bacteriologie, Bordeaux, France

Contact E-Mail Address: SMITHSI@tcd.ie

Introduction: The emergence of antimicrobial resistant *Helicobacter pylori* (*H. pylori*) has impacted treatment success rates. Local audits of prescription patterns and eradication rates are necessary to assess treatment efficacy and compliance with clinical guidelines. The first Irish consensus guidelines on the management of *H. pylori* were published in 2017. Clarithromycin-amoxicillin triple therapy (CTT) or bismuth quadruple therapy (BQT) were the recommended first-line options. Other key recommendations included extending treatment durations to 14 days and the use of high-dose proton pump inhibitors (PPIs).

Aims & Methods: This study aimed to (i) investigate first-line *H. pylori* prescription patterns and cure rates over a 10-year period in Ireland, and (ii) evaluate the impact of the first Irish consensus guidelines on these trends. Data were collected at e-CRF AEG-REDCap from the European Registry on *Helicobacter pylori* Management (Hp-EuReg) and quality reviewed from 2013 to 2022. All treatment-naïve cases were assessed for effectiveness by modified intention-to-treat (mITT) analysis. Multivariate analysis was performed using a logistic regression model to evaluate the relationship between mITT rates and age, sex, indication, compliance, PPI dose and treatment duration.

Results: In all, data from 1,000 patients (mean age 50±15 years; 54% (n=536) female) were included in the analysis, from those 78% (n=784) were from Tallaght University Hospital, Dublin and 22% (n=216) were from Beacons Hospital, Dublin. The most common indication was dyspepsia (92%; n=920), followed by duodenal ulcer and gastric ulcer (2%; n=20 and 1%; n=10, respectively). CTT was the most common first-line treatment (88%; n=880). BQT represented 1.7% (n=17) of prescriptions. Of the reported treatment durations (n=998), 87% (n=868) were for 14 days, 4.5% (n=45) were for 10 days and 8.5% (n=85) were for 7 days. Of the reported PPI dose prescribed (n=999), 86% (n=860) were high (i.e., 80 mg omeprazole equivalent twice daily), 0.9% (n=9) were standard (i.e., 40 mg omeprazole equivalent twice daily), and 13% (n=130) were low (i.e., 20 mg omeprazole equivalent twice daily).

The eradication rate was 80.1% (95% confidence interval (CI) 77.5-82.5%) overall and 81.4% (95% CI 78.9-83.7%) for CTT. Multivariate analysis revealed that good compliance and the use of high dose PPI were significantly associated with higher overall mITT rates (odds ratio (OR) 4.5, 95% CI 1.4-14.2, p<0.05 and OR 1.9, 95% CI 1.2-2.8, p<0.005, respectively) and CTT mITT rates (OR 4.2, 95% CI 1.2-14.2, p<0.05 and OR 1.9, 95% CI 1.1-3.2, p<0.05, respectively).

Following publication of the Irish consensus guidelines in 2017, prescriptions for 14 days therapy increased from 39% (n=82/208) pre-2017 to 99% (n=786/790; p<0.0001) and the use of high dose PPI increased from 37% (n=77/207) pre-2017 to 99% (n=783/792; p<0.0001). In line with this, overall eradication rates significantly increased from 74.5% (95% CI 68.2-80.0%) pre-2017 to 81.6% (95% CI 78.7-84.1%; p<0.05). CTT eradication rates significantly increased from 75.7% (95% CI 68.2-81.8%) pre-2017 to 82.6% (95% CI 79.6-85.1%; p<0.05).

Conclusion: CTT was the most frequently prescribed first-line therapy between 2013-2022. BQT was rarely prescribed, reflecting difficulty accessing bismuth in Ireland. While treatment success increased following publication of the Irish consensus guidelines, cure rates remain below 90%. Alternative first-line treatment strategies are required in the Irish healthcare setting.

Disclosure: Nothing to disclose.

PP0290

PHARMACOGENOMICS OF ANTIBIOTIC RESISTANCE IN *HELICOBACTER PYLORI* FROM COLOMBIA

K. Guzman¹, A.J. Pazos^{2,3}, A. Hidalgo^{4,3}

¹Kevin Guzman, Centro de Estudios en Salud Universidad de Nariño (CESUN), San Juan de Pasto, Colombia, ²Universidad de Nariño, Biology Department, San Juan de Pasto, Colombia, ³Universidad de Nariño, Centro de Estudios en Salud Universidad de Nariño (CESUN), San Juan de Pasto, Colombia, ⁴Universidad de Nariño, Departamento de Matemáticas, San Juan de Pasto, Colombia

Contact E-Mail Address: keving346@gmail.com

Introduction: *Helicobacter pylori* is a microaerophilic gram-negative bacillus that colonizes the gastric mucosa and is associated with gastroduodenal diseases such as chronic gastritis and gastric adenocarcinoma. Although triple therapy is the recommended treatment for its eradication, its effectiveness has decreased due to the lack of knowledge about bacterial susceptibility patterns and the emergence of resistant strains, a phenomenon related to the bacterium's adaptation to hostile environments and antibiotic use. This infection is associated with gastroduodenal diseases such as chronic gastritis, peptic ulcer, and gastric adenocarcinoma, and although various therapeutic regimens are available, the indiscriminate use of antibiotics has led to resistance, highlighting the need to study alternatives and reevaluate the criteria that determine the selection of a specific therapeutic regimen.

Aims & Methods: We analyzed 169 *Helicobacter pylori* Whole Genome Sequences (WGS) from Colombian participants. Bioinformatics analyses were performed using the ATCC 26695 genome as a reference strain. We searched for mutations in specific genes to assess resistance rates to different antibiotics: 23S rRNA for clarithromycin, 16S rRNA for tetracycline, *pbp1A* for amoxicillin, *gyrA* for levofloxacin, *rdxA* for metronidazole, *rpoD* for rifampicin, and *porD* for furazolidone. The phylogenomic analysis was conducted using the core genome consisting of 1,594 genes of *Helicobacter pylori*-ATCC 26695

Results: Our findings revealed that the resistance rate of *Helicobacter pylori* to clarithromycin was 3.62%, mainly associated with the A2143G and A2142G mutations in the 23S rRNA gene. For tetracycline, the resistance rate was 7.23%, with mutations A926G, A926T, and A928C observed in the 16S rRNA gene. Resistance to amoxicillin was found in 25.9% of cases, with mutations observed in the *pbp1A* gene, including T556S, T593, R649K, R656P, and R656H. In the *gyrA* gene, mutations N87K, N87I, D91G, D91N, and D91Y were identified, resulting in a resistance rate of 12.04% to levofloxacin. The most common mutations in the *rdxA* gene associated with

metronidazole resistance were a stop codon and mutations at D59N and D59S, resulting in a resistance rate of 99.3%. No mutations were found for rifampicin in the *rpoD* gene, and a resistance rate of 0.84% was found for furazolidone due to mutations C357T in the *porD* gene.

Conclusion: The high rate of *Helicobacter pylori* resistance to metronidazole indicates that this drug should be excluded from eradication therapy. However, resistance rates for tetracycline and clarithromycin did not exceed the 10% threshold established in Colombia. The increased resistance rate of *Helicobacter pylori* to levofloxacin and amoxicillin may partially explain the therapeutic failures observed in Colombia. As rescue therapy, rifampicin and furazolidone antibiotics can be used along with bismuth in *Helicobacter pylori* treatment, following the guidelines recommended by the Maastricht VI/Florence consensus report. Phylogenomic analysis showed that the *Helicobacter pylori* isolate belongs to its own lineage (hspColombia). These findings provide valuable information to improve the characterization of treatment protocols for the specific *Helicobacter pylori* lineage (hspColombia) at the local level.

References: Malfertheiner, P., Megraud, F., Rokkas, T., Gisbert, J. P., Liou, J. M., Schulz, C., & El-Omar, E. M. (2022). Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*, 71(9), 1724-1762.

Disclosure: Nothing to disclose.

PP0291

EFFICACY AND SAFETY OF HELICOBACTER PYLORI ERADICATION THERAPY IN PORTUGAL: A BLIND RANDOMIZED CONTROLLED CLINICAL TRIAL

E. Gravito-Soares¹, N.P. Almeida¹, M. Gravito-Soares¹, B. Rocha², M.M. Donato³, P. Narra Figueiredo¹

¹Centro Hospitalar e Universitário de Coimbra, Unidade Local de Saúde de Coimbra; Faculty of Medicine, University of Coimbra, Gastroenterology, Coimbra, Portugal, ²Faculty of Pharmacy, University of Coimbra; Center for Neuroscience and Cellular biology, University of Coimbra, Gastroenterology, Coimbra, Portugal, ³Faculty of Medicine, University of Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: es18497@gmail.com

Introduction: *Helicobacter pylori* (Hp) infection remains a major public health problem, associated with significant morbidity and mortality, whose eradication therapy has proven to be effective in preventing these complications.^{1,2} Given the high resistance to antibiotics and the scarcity of available antibiotic therapy worldwide, there is not enough data on the best eradication strategy.^{3,4}

Aims & Methods: Aim: The aim of this study was to perform a comparative evaluation of the efficacy and safety of the different quadruple therapy regimens currently recommended for the Hp eradication, including Esomeprazole 40 mg bid.

Methods: A blind randomized controlled clinical trial of consecutive patients with gastric infection by Hp, diagnosed by 13C-urea breath test (UBT) or histological analysis were randomized in 5 therapy arms (A: Quadruple with metronidazole 500 mg tid, 14 days; B: Quadruple with metronidazole 500 mg bid, 14 days; C: Quadruple with bismuth, 10 days; D: Sequential, 7 days; E: Hybrid, 7 days). Hp eradication with evaluation of the efficacy and safety rates at 1-2 months after the eradication therapy was made.

Results: From a total of 200 patients currently included, 193 concluded the protocol study (164-histological analysis; 29-UBT), 102 males (52.8%), mean age of 57.2±16.3 (A: 38; B: 39; C: 38; D: 41; E: 37). Overall efficacy rate of quadruple therapy regimens was 95.9% (n=185), being 100.0% for arm

A, 92.3% for arm B, 97.3% for arm C, 97.6% for arm D and 91.9% for arm E (p=0.431). Overall adverse events rate of quadruple therapy regimens was 53.9% (n=104), being diarrhea (27.5%) and nausea (26.9%) the most common. Major symptoms (need for therapy or impairment of daily living activities) occurred in 8.3%. Adverse events/Major adverse events rates for the different regimens were 50.0%/5.3% for arm A, 69.2%/15.4% for arm B, 48.6%/7.9% for arm C, 48.8%/4.9% for arm D and 54.0%/8.1% for arm E (p=0.287/p=0.451).

Conclusion: In Portugal, all the quadruple therapy regimens currently recommended for the eradication of Hp, with or without bismuth, have been effective in eradicating Hp gastric infection. However, concomitant therapy with metronidazole bid seems to have a higher rate of adverse effects, including major adverse effects.

References: 1. Zamani, M., Ebrahimitabar, F., Zamani, V., et al. Systematic review with meta-analysis: the worldwide prevalence of *Helicobacter pylori* infection. *Aliment Pharmacol Ther* 2018; 47(7): 868-876.

2. Malfertheiner, P., Megraud, F., O'Morain, C.A., et al. Management of *Helicobacter pylori* infection – the Maastricht VI/Florence Consensus Report. *Gut* 2017; 66(1): 6-30.

3. Savoldi, A., Carrara, E., Graham, D.Y., et al. Prevalence of antibiotic resistance in *Helicobacter pylori*: a systematic review and meta-analysis in World Health Organization Regions. *Gastroenterology* 2018; 155(5): 1372-1382.

4. Lopo, I., Libânio, D., Pita, I., et al. *Helicobacter pylori* antibiotic resistance in Portugal: Systematic review and meta[1]analysis. *Helicobacter* 2018; 23(4): e12493.

Disclosure: Nothing to declare.

PP0292

THE EFFECTIVENESS OF THE ALPHA-GLUTAMYL-TRYPTOPHAN AS A LOCAL CYTOPROTECTOR FOR GASTRIC MUCOSA CELLS IN PATIENTS WITH CHRONIC ATROPHIC GASTRITIS: RESULTS OF MULTICENTER DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED STUDY

N.V. Baryshnikova^{1,2,3}, Y. Uspenskiy^{1,3}, Y. Fominykh³, A. Krasnov⁴, S. Petlenko⁵, V. Apriyatina⁶

¹First Pavlov St. Petersburg medical University, St-Petersburg, Russian Federation, ²Institute of Experimental Medicine, St. Petersburg, Russian Federation, ³St. Petersburg State Peadiatric University, St. Petersburg, Russian Federation, ⁴Herzen State Pedagogical University of Russia, St. Petersburg, Russian Federation, ⁵Golikov Research Clinical Center of Toxicology under the Federal Medical-Biological Agency, St. Petersburg, Russian Federation, ⁶Institute of Translational Biomedicine, Saint-Petersburg State University, St. Petersburg, Russian Federation

Contact E-Mail Address: baryshnikova_nv@mail.ru

Introduction: Prevention of gastric cancer, both primary and secondary, is an extremely important component of the management of patients infected with *Helicobacter pylori*. An important component of secondary prevention of gastric cancer is the use of gastroprotectors and repair stimulants, in particular the alpha-glutamyl-tryptophan, especially in people with a potentially precancerous condition – chronic atrophic gastritis

Aims & Methods: The aim is to estimate the effectiveness of the alpha-glutamyl-tryptophan as a local cytoprotector for gastric mucosa cells in patients with chronic atrophic gastritis (CAG).

116 patients with H. pylori-associated CAG took two treatment lines: 1. standard eradication therapy 10 days, 2. alpha-glutamyl-tryptophan(58 patients)/placebo(58 patients) 28 days. For all patients before and after treatment we performed gastroscopy with two biopsies from atrophic area, histological study of these biopsies, daily pH-metry and Gastropan-el.

Results: Alpha-glutamyl-tryptophan in comparison with placebo have statistically significant: *regenerative effect* (26.1% increase in the number of glands per 1 mm² of the gastric mucosa (GM) by histological study) and *anti-inflammatory effect* (decrease of GM edema and hyperemia by endoscopy data, reduction of the number of inflammatory infiltration cells per 1 mm² of GM: eosinophilic granulocytes – 3 times, neutrophilic leukocytes – 4 times, macrophages – 1.5 times, lymphocytes – 28.2%, plasmocytes – 29.6% by histological study). Also alpha-glutamyl-triaphan improved the functional possibilities of stomach: a decrease in the level of gastrin-17 ($p = 0.005$) and an increase in the value of the PG I/PG II ratio ($p=0.003$), there was a shift in the acidic side of the pH values ($p=0.001$) when comparing indicators before and after treatment. There were no statistically significant changes in these parameters in the placebo group. According to the results of gastroscopy, a statistically significant decrease in the severity of edema of the gastric mucosa ($p=0.008$), the total set of signs of an acute inflammatory process ($p=0.006$), and a decrease in the proportion of outcomes with negative dynamics of the inflammatory process ($p=0.038$) were revealed in alpha-glutamyl-tryptophan group.

Conclusion: Alpha-glutamyl-tryptophan can be recommended for local cytoprotection in CAG, especially for *H. pylori* associated gastritis for prevention the progression of atrophy and inflammation, and also lowering the risk of gastric cancer.

Disclosure: nothing to disclose.

PP0293

THE EPIDEMIOLOGICAL PROFILE OF GASTRIC CANCER PATIENTS IN GROOTE SCHUUR HOSPITAL CAPE TOWN, SOUTH AFRICA

I.E. Francis¹, G. Chinnery², M. Scriba², F. Patel³, M. Setshedi¹

¹Groote Schuur Hospital, University of Cape Town, Gastroenterology Unit, department of Medicine, Cape Town, South Africa, ²Groote Schuur Hospital, University of Cape Town, Upper Gastroenterology Surgery, Cape Town, South Africa, ³University Of Cape Town, Microbiology department, Cape Town, South Africa

Contact E-Mail Address: francisino@gmail.com

Introduction: Gastric cancer (GCA) is the 5th most common cancer and 3rd leading cause of cancer-related death. *Helicobacter pylori* (*H. pylori*) is the chief risk factor. The prevalence of *H. pylori* in Africa is between 60-90%, despite this GCA appears to be low, the so-called African enigma.

Aims & Methods: To document the epidemiological profile and risk factors of GCA in a South African cohort.

A retrospective folder review of patients with GCA from 2018-2022

Results: 443 patients were included; median age= 63 (range 29-86), 65% male (61% ≥ 60 years old). HPT (38.2%) and diabetes (17.6%) were the main comorbidities. 46% and 8.4% had history of smoking and alcohol use respectively. NSAID and PPI use were reported in 8.8% and 7% respectively. The commonest symptom was loss of weight (38.6%) and epigastric pain (29%). 68% had a Hb<12g/dl with a median Hb=10 (range 3.8-17). Endoscopically, gastritis or duodenitis or ulcers were recorded in 63% of cases. The commonest site of GCA was non-cardia (82.2%); antral and corpus cancers in 40.9% and 53.2% respectively. Histologically, *H. pylori* was reported in 11.5%, while chronic atrophic gastritis (CAG) in 15.6%. *H. pylori* was not associated with either antral or corpus cancer, or CAG, however PPIs were associated with a reduced odd of antral cancer, OR=0.42, CI=0.18-0.97, $p=0.04$. None of the other demographic or clinical factors were associated with the location of GCA.

Conclusion: GCA is higher in males and those ≥60 years. Loss of weight and anaemia are key red flags. Non-cardia gastric cancers are the commonest in this cohort. The low prevalence of *H. pylori* suggests previous eradication, although CAG was high, thus maintaining the increased risk of non-cardia

GCA. Interestingly, PPI use was significantly protective against developing antral cancer. This highlights the need to treat *H. pylori* before CAG occur.

Disclosure: None.

PP0294

ASSESSMENT OF OLGA AND OLGIM STAGING SYSTEMS IN HELICOBACTER PYLORI INFECTION

G. Gharbi¹, A. Khsiba¹, M. Yakoubi¹, A. Ben Mohamed¹, M. Moufida¹, M. Medhioub¹, M.L. Hamzaoui¹

¹Faculty of medicine Tunis, Tunisia Mohamed taher Maamouri hospital Nabeul Tunisia, Gastroenterology and Hepatology departement, Nabeul, Tunisia

Contact E-Mail Address: gharbighada1801@gmail.com

Introduction: *Helicobacter pylori* (HP) infection induces chronic gastritis and represents a major factor in gastric cancer. The histological sequence leading to gastric cancer is well known: gastritis induces atrophy and intestinal metaplasia, two precancerous lesions detectable by early endoscopy and meticulous anatomopathological examination.

Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) are two systems designed to detect patients at high risk of developing gastric cancer by assessing, respectively, the degree of atrophy and intestinal metaplasia in the gastric mucosa.

Aims & Methods: The aim of our study was to evaluate the OLGA and OLGIM staging systems in HP infection.

A retrospective study was conducted over patients who had upper gastrointestinal endoscopy between January 2018 and December 2019 with the presence of HP infection on pathological examination of gastric biopsies. Patients with stage III or IV gastritis according to the OLGA or OLGIM systems were considered at high risk of progression to gastric cancer.

Results: Two hundred patients were included in this study. The mean age was 52.5 years [10-92], with a F/M sex ratio of 1.67. The main indications for upper GI endoscopy were epigastralgia (66.5%) and anemia (18.5%). Various morphological aspects were observed. The gastric body was normal in 59.5% of cases, with gastroraphy present in 40.5%, mainly congestive (17.5%), but also mosaic (11%), nodular (6.5%), atrophic (4.5%), erosive (3%) and ulcerated (2.5%). The antrum was normal in only 23.5% of cases. Antral gastroraphy was congestive (46.5%), nodular (14.5%) or ulcerated (14%).

On anatomopathological examination of gastric biopsies, atrophy was present in 15.5% of patients and intestinal metaplasia in 45%. Only 3 patients (1.5%) were considered at high risk of developing gastric cancer according to the OLGA system, while this risk was estimated at 13.5% according to the OLGIM classification.

There was no statistically significant association between the OLGA and OLGIM staging systems in the selection of patients at high risk of developing gastric cancer ($p=0.09$). Nevertheless, an association was noted between OLGA classification and the presence of intestinal metaplasia ($p=0.009$), the presence of a high risk of developing gastric cancer according to the OLGA system and the finding of moderate to severe intestinal metaplasia on gastric biopsies ($p=0.018$), and between the existence of a high risk of progression to gastric cancer according to the OLGIM system and the presence of moderate to severe atrophy ($p=0.005$).

Conclusion: The OLGA and OLGIM staging systems assess the risk of developing gastric cancer in HP infection. Our study didn't found a correlation between the two systems. A concomitant assessment of this risk by the two systems will enable a better selection of high-risk patients for appropriate surveillance and early management.

Disclosure: Nothing to disclose.

Poster
Small intestinal

Small intestinal

09:00-18:00 / Poster Exhibition

PP0295

THE EFFECTS OF HIGH FAT, HIGH FRUCTOSE DIET ON HEPATIC
STEATOSIS AND SMALL BOWEL TIGHT JUNCTION PROTEINS
DEPENDING ON AGE AND SEX IN RATS

S. Ha^{1,2}, N. Kim^{1,2,3,4}, S.I. Choi², R.H. Nam², J.Y. Jang^{2,4}, E.H. Kim²,
C.-H. Song², H.Y. Na⁵

¹Seoul National University, Department of Health Science and
Technology, Graduate School of Convergence Science and
Technology, Seoul, South Korea, ²Seoul National University
Bundang Hospital, Department of Internal Medicine and Research
Center for Sex- and Gender-specific Medicine, Seongnam,
South Korea, ³Seoul National University College of Medicine,
Department of Internal Medicine and Liver Research Institute,
Seoul, South Korea, ⁴Seoul National University College of Medicine,
Department of Medical Device Development, Seoul, South Korea,
⁵Seoul National University Bundang Hospital, Department of
Pathology, Seongnam, South Korea

Contact E-Mail Address: tjdc6101@naver.com

Introduction: The aging with weight gain induces pathological changes in the liver, exacerbating non-alcoholic fatty liver disease (NAFLD). In the reproductive age, NAFLD is more prevalent and severe in males, however, NAFLD occurs at a higher rate among postmenopausal females. The liver and small bowel are closely interrelated through enterohepatic circulation, such that damage to the small bowel can significantly impact hepatic function. In small intestine, the expression of tight junction protein (TJP) in nearly associated with the development of NAFLD.

The aim of this study was to investigate the effects of age and sex on hepatic steatosis and the small bowel under conditions of a high fructose, high-fat diet (HFHFD) in rats.

Aims & Methods: 6-week-old male and female F344 rats divided into control and HFHFD groups, along with 2-year-old F344 rats. Over an 8-week period, the high fat diet (Raonbio, 60 kcal% fat) provided twice weekly and high fructose water (20%) gave once weekly for HFHFD groups. After 8 weeks, all animals were sacrificed, and both liver and small intestinal tissue were collected.

All tissue samples were subjected to hematoxylin and eosin staining for histological analysis. RNA extraction from the jejunum mucosa was followed by qRT-PCR analysis to assess claudin-2 (cldn-2, one of TJP) gene expression.

Results: The body weight change (%) and the hepatic steatosis scores were significantly higher in the HFHFD groups compared to both male and female control groups (Table).

Histological scores of old rat HFHFD groups were significantly higher than those of 6 week HFHFD groups, regardless of sex (Table).

In terms of histological inflammation scores of old control group small bowel were higher than those of 6 week control group regardless of sex (Table).

The jejunum villus/crypt ratio of 6-week-old rats significantly decreased only among males (Table).

In contrast, in the 2-year-old groups, the villus/crypt ratio resulted in a reduction only among females and the mRNA expression of cldn-2 observed in females with significant elevation (Table).

	Weight	Steatosis score	Inflammation score			Jejunum villus/crypt length ratio	Cldn-2 mRNA expression
			Duodenum	Jejunum	Ileum		
Male	6-week Con vs. 6-week HFHFD	increase (p = 0.006)	increase (p = 0.003)	increase (p = 0.072)	increase (p = 0.026)	increase (p = 0.049)	decrease (p = 0.072)
	2-year Con vs. 2-year HFHFD	increase (p = 0.006)	increase (p = 0.002)	-	increase (p = 0.015)	-	-
	6-week Con vs. 2-year Con	-	-	increase (p = 0.005)	-	increase (p = 0.022)	-
	6-week HFHFD vs. 2-year HFHFD	-	increase (p = 0.007)	-	-	-	-
	6-week Con vs. 6-week HFHFD	increase (p = 0.004)	increase (p = 0.002)	-	increase (p = 0.007)	increase (p = 0.104)	increase (p = 0.056)
	2-year Con vs. 2-year HFHFD	increase (p = 0.004)	increase (p = 0.002)	-	-	decrease (p = 0.076)	increase (p = 0.005)
Female	6-week Con vs. 2-year Con	-	-	increase (p = 0.007)	increase (p = 0.002)	increase (p = 0.002)	-
	6-week HFHFD vs. 2-year HFHFD	-	increase (p = 0.011)	-	-	-	-

Con, control; HFHFD, high fructose high fat diet; Cldn-2, Claudin-2; vs., versus.

Conclusion: Our data showed that high fructose, high-fat diet induced hepatic steatosis and inflammation of small bowel, especially in old rats. This indicates that NAFLD is related with damage of small bowel brush border membrane. The upregulated gene expression of cldn-2 (p = 0.005) and the decreased tendency of jejunum villus/crypt ratio (p = 0.076) in the aged females rats suggests a potential role of TJP in advancing NAFLD in postmenopausal females.

References: Lee, Sun Min, et al. "Microbial changes and host response in F344 rat colon depending on sex and age following a high-fat diet." *Frontiers in microbiology* 9 (2018): 386521.

He, Yongyuan, et al. "Emerging role of aging in the progression of NAFLD to HCC." *Ageing Research Reviews* 84 (2023): 101833.

Hollander, Daniel, and Jonathan D. Kaunitz. "The "leaky gut": tight junctions but loose associations?." *Digestive diseases and sciences* 65.5 (2020): 1277-1287.

Ahmad, Rizwan, et al. "Obesity-induces organ and tissue specific tight junction restructuring and barrier deregulation by claudin switching." *Scientific reports* 7.1 (2017): 1-16.

Zhou, Xiaoqiong, et al. "Gut microbiota induces hepatic steatosis by modulating the T cells balance in high fructose diet mice." *Scientific Reports* 13.1 (2023): 6701.

Amasheh, Salah, et al. "Claudin-2 expression induces cation-selective channels in tight junctions of epithelial cells." *Journal of cell science* 115.24 (2002): 4969-4976.

Lonardo, Amedeo, et al. "Sex differences in nonalcoholic fatty liver disease: state of the art and identification of research gaps." *Hepatology* 70.4 (2019): 1457-1469.

Disclosure: Nothing to disclose.

PP0296

THE IMPACT OF SMALL INTESTINAL BACTERIAL OVERGROWTH ON THE EFFICACY OF FECAL MICROBIOTA TRANSPLANTATION IN PATIENTS WITH CHRONIC CONSTIPATION

H. Tian¹, L. Wang¹, H. Qin¹, Q. Chen¹¹Tongji University School of Medicine, General Surgery of Shanghai Tenth People's Hospital, Shanghai, China

Contact E-Mail Address: kevin_thl@163.com

Introduction: To investigate the impact of small intestinal bacterial overgrowth (SIBO) on the efficacy of Fecal Microbiota Transplantation (FMT) in patients with chronic constipation

Aims & Methods: Inclusion of 218 chronic constipation patients treated with FMT, divided into constipation with SIBO group (SIBO) based on breath test results for SIBO, and constipation without SIBO group (Non-SIBO). The efficacy of the two groups was evaluated using constipation-related scoring scales. At the same time, feces and small intestinal fluid samples were collected from both groups before and after FMT to compare the changes in the intestinal microbiota through 16S rRNA sequencing

Results: In this study, it was found that the clinical efficacy of FMT in the SIBO group was superior to that in the Non-SIBO group. After FMT treatment, both groups showed a significant increase in bowel frequency and improvement in stool characteristics. Abdominal symptoms, rectal symptoms, and defecation symptoms were significantly alleviated ($P < 0.05$), and patients' quality of life was significantly enhanced ($P < 0.05$). After FMT, except for the CAS scale scores, other scale scores showed significant differences between the two groups, the SIBO group scoring significantly better than the Non-SIBO group ($P < 0.05$).

After FMT, there were minor changes in the colonic microbiota but more substantial changes in the small intestinal microbiota. At baseline, the SIBO group had a higher abundance of *Veillonella*, and lower abundances of *Escherichia-Shigella* and *Acinetobacter* compared to the Non-SIBO group.

Characteristics	Overall (N=218)
Age (mean $\pm$ standard deviation)	55.62 $\pm$ 16.48
Gender (Male/Female)	95/123
SIBO (Positive/Negative)	88/130
Disease Duration (year)	13.46 $\pm$ 7.98
Complete Spontaneous Bowel Movements (CSBM) time/week	1.32 $\pm$ 0.66
Spontaneous Bowel Movements (CSBM) time/week	1.76 $\pm$ 0.59
Wexner Scale	16.27 $\pm$ 1.68
Bristol Stool Form Scale (BSFS)	1.30 $\pm$ 0.46
PAC-SYM	2.95 $\pm$ 1.32

Table 1 General Information of the Patients

Conclusion: Chronic constipation patients with SIBO have a better response to FMT than those without SIBO.

References: [1]Pimentel M, Saad R J, Long M D, *et al.* ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth[J]. The American journal of gastroenterology, 2020, 115(2): 165-178.

[2]Ghoshal U C,Ghoshal U. Small Intestinal Bacterial Overgrowth and Other Intestinal Disorders[J]. Gastroenterology clinics of North America, 2017, 46(1): 103-120.

[3]Polkowska-Pruszyńska B, Gerkowicz A, Szczepanik-Kuś P, *et al.* Small intestinal bacterial overgrowth in systemic sclerosis: a review of the literature[J]. Archives of dermatological research, 2019, 311(1): 1-8.

[4]Rezaie A, Buresi M, Lembo A, *et al.* Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus[J]. The American journal of gastroenterology, 2017, 112(5): 775-784.

[5]Levitt M D,Bond J H, Jr. Volume, composition, and source of intestinal gas[J]. Gastroenterology, 1970, 59(6): 921-929.

[6]Gasbarrini A, Corazza G R, Gasbarrini G, *et al.* Methodology and indications of H₂-breath testing in gastrointestinal diseases: the Rome Consensus Conference[J]. Alimentary pharmacology & therapeutics, 2009, 29 Suppl 1(1-49).

[7]Bharucha A E, Pemberton J H,Locke G R, 3rd. American Gastroenterological Association technical review on constipation[J]. Gastroenterology, 2013, 144(1): 218-238.

Disclosure: Nothing to disclose.

PP0297

INCREASING PREVALENCE OF INCIDENTAL ILEITIS FOLLOWING THE COVID-19 PANDEMIC

S. Helou¹, L. Amer¹, E. Mikhael¹, R. Slim Karam¹,J. Amara¹,K. Honein¹, E. Mahfouz¹, C. Yaghi¹¹Hotel Dieu de France Hospital - Saint Joseph University, Gastroenterology and Hepatology, Beirut, Lebanon

Contact E-Mail Address: santaelhelou@gmail.com

Introduction: The incidental finding of terminal ileal inflammation during routine colonoscopy is not uncommon and is of unclear significance. It has been reported among asymptomatic persons undergoing non-diagnostic colonoscopy. There is limited data on long term follow-up and outcomes of such findings.(1)

Aims & Methods: This is a monocentric retrospective observational study spanning from 2018 to 2023, comparing two periods: the first period (P1) before the impact of the Covid-19 pandemic in 2020, and the second period (P2) starting 2020 reflecting the impact the pandemic left on colonoscopies. For each patient, variables were collected from medical records.

Results: Our initial database included 11200 colonoscopies, from which we randomly selected 2394 patients proportionally to the annual activity (mean of 1686/year before 2020 and 1189/year after 2020). Among indications of colonoscopy were screening and follow-up, change in bowel habits, anemia and bleeding. We excluded 287 patients (known history of inflammatory bowel disease and no ileum intubation). Then the sample was divided into P1 (681 patients) and P2 (1483 patients). Characteristics and findings are shown in Table 1. We noted better bowel preparation (77.1 vs 91.7%) and a higher ileum intubation in P2 (79.7 in P1 vs 93.8% in P2).

N=2164		P1 (N1=681)	P2 (N2= 1483)	P
Overall endoscopic findings n(%)	Age (years)	57.5	56.9	NS
	Endoscopic aspect of ileitis	0 (0)	71 (5.8)	<0.001
	Abnormal ileal findings on histology	23 (3.4)	169 (11.4)	<0.001
	Diagnosis of Crohn's disease	0 (0)	19 (0.9)	<0.001
Overall histological findings n(%)	Active ileitis	19 (2.8)	147 (9.9)	<0.001
	Focal ileitis	10 (1.5)	89 (6)	<0.001
	Ulcerative ileitis	11 (1.6)	48 (3.2)	0.031
	Erosive ileitis	3 (0.4)	31 (2.1)	0.004
	Architectural distortion	1 (0.1)	16 (1.1)	0.023

Overall ileoscopy findings showed an increased aspect of ileitis on endoscopy (0% in P1 and 5.8% in P2, with $p < 0.001$), correlating with a significant increase in the incidence of histological findings on ileal biopsies (3.4% in P1 vs 11.4% in P2; $p < 0.001$). These histological findings included active, focal and ulcerative ileitis, with more architectural distortion. However, these results corresponded to a less severe ileitis (0.3 vs 2.3%; $p = 0.001$). Nineteen of these patients with positive results of ileitis were diagnosed with Crohn's disease.

Conclusion: This study showed an increase in endoscopic and histologic ileitis on colonoscopy following the Covid-19 era. This could be the result of the direct virologic effect that the virus has on intestinal inflammation, its indirect effect on immunity triggering the onset of enteritis, or the consequence of the mass vaccination campaign held to protect from the virus. Furthermore, histology showed granulomatous inflammation similar to Crohn's disease, which may lead to misdiagnosis and probably over-treatment.

References: 1. Agrawal M, Miranda MB, Walsh S, Narula N, Colombel JF, Ungaro RC. Prevalence and Progression of Incidental Terminal Ileitis on Non-diagnostic Colonoscopy: A Systematic Review and Meta-analysis. *J Crohns Colitis*. 2021 Feb 14;15(9):1455–63.

Disclosure: Nothing to disclose.

PP0298

EXAMINING LONG-TERM ANTITHROMBOTIC TREATMENT PATTERNS IN PATIENTS WITH SHORT BOWEL SYNDROME POST ACUTE MESENTERIC ISCHEMIA: INSIGHTS FROM AN INTERNATIONAL SURVEY

B. Deleenheer^{1,2,3}, C. Cuerda⁴, P.B. Jeppesen⁵, F. Joly⁶, S. Lal⁷, G. Lamprecht⁸, M. Manpreet⁹, L. Pironi¹⁰, K. Szczepanek¹¹, T. Vanassche¹², L. Van der Linden^{13,3}, A. Van Gossum¹⁴, G.J. Wanten¹⁵, T. Vanuytsel^{1,2}

¹KU Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism (ChroMeta), Leuven, Belgium, ²University Hospitals Leuven, Leuven Intestinal Failure and Transplantation Center (LIFT), Leuven, Belgium, ³University Hospitals Leuven, Hospital Pharmacy Department, Leuven, Belgium, ⁴Hospital General Universitario Gregorio Marañón, Nutrition Unit, Madrid, Spain, ⁵Rigshospitalet, Department Of Gastroenterology Ca-2121, Copenhagen, Denmark, ⁶Beaujon Hospital Service de Gastroenterologie, Gastroenterology, Clichy, France, ⁷Salford Royal Foundation Trust, Intestinal Failure Unit, Salford, United Kingdom, ⁸Rostock University Medical Center, Department of Medicine II, Division of Gastroenterology and Endocrinology, Rostock, Germany, ⁹Mayo Clinic, Division of Endocrinology, Diabetes, Metabolism and Nutrition, Rochester, United States of America, ¹⁰University of Bologna S. Orsola-Malpighi Hospital, Dept. of Clinical Medicine, Bologna, Italy, ¹¹Stanley Dudrick's Memorial Hospital, General and Cancer Surgery Departement with Intestinal Failure Center, Skawina, Poland, ¹²University Hospitals Leuven, Department of Cardiovascular Diseases, Leuven, Belgium, ¹³KU Leuven, Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium, ¹⁴Hôpital Erasme, University of Brussels, Department of Gastroenterology and Hepatology, Bruxelles, Belgium, ¹⁵Radboud University Nijmegen, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands

Contact E-Mail Address: barbara.deleenheer@uzleuven.be

Introduction: Long-term antithrombotic therapy is recommended in short bowel syndrome (SBS) caused by acute mesenteric ischemia (AMI). However, evidence-based recommendations on drug choice, duration and monitoring of treatment are lacking. Also, guidelines are based on data on other artery diseases and overlook the altered drug absorption in patients with SBS. To understand current practices, we aimed to assess the long-term antithrombotic management of AMI.

Aims & Methods: An online survey was sent to centers contributing to the chronic intestinal failure database of the HAN-CIF (Home Artificial Nutrition – Chronic Intestinal Failure) special interest group of ESPEN (European Society on Clinical nutrition and Metabolism), treating patients with

SBS post-AMI. The survey featured 10 cases varying in postsurgical intestinal anatomy, revascularization and etiology and focused on drug class, administration route, duration and monitoring of antithrombotic therapy. **Results:** The survey was completed by 43 centers. In case of idiopathic AMI leading to SBS, anticoagulation (65.1% of all physicians) or antiplatelet (32.6%) therapy were mostly prescribed (Figure 1; jejuno-colic anastomosis, idiopathic).

Antiplatelet therapy was prescribed more often to patients with type 3 anatomy (37.2%, largest absorptive capacity) than to other anatomy groups (30.2 and 32.6% in type 1 and 2 respectively). Antiplatelet drugs (39.5%) or combination therapy (18.6%) were more commonly prescribed in case of revascularization compared to no revascularization (32.6% or 2.3% respectively).

Anticoagulants were very common in patients with atrial fibrillation (90.7%), venous thrombosis (95.3%) and antiphospholipid syndrome (83.7%). More antiplatelet drugs (27.9%) or combination therapy (18.6%) were preferred with concomitant peripheral artery disease. In hypovolemic shock, no therapy (41.9%) or anticoagulants (51.2%) were common. Parenteral drugs were more prescribed to patients with type 1 anatomy (51.2% of all physicians; lowest absorptive capacity) than to patients with type 2 (44.2%) or 3 (20.9%) anatomy.

Antiplatelet drugs were mainly prescribed lifelong (94.7% of this drug class), while anticoagulants were prescribed for 6 (19.4%) to 12 (16.1%) months or lifelong (51.6%), irrespective of anatomy, revascularization or etiology.

Vitamin K antagonists were consistently monitored, whereas aspirin was not. Monitoring of subcutaneous low molecular weight heparins (no monitoring, 36.8% - always monitoring, 42.1% - in specific circumstances, 21.0%) and non-vitamin K oral anticoagulants varied (no monitoring, 50.0%).

Conclusion: In a case-based survey, anticoagulant versus antiplatelet drug choice depended on the anatomy, revascularization and etiology. However, there was a high variability in case of idiopathic AMI. Administration route depended on anatomy. More detailed practice guidelines are needed.

Disclosure: TV has participated in advisory boards, as a consultant and/or as a speaker on behalf of Boehringer Ingelheim, Bayer, Daiichi Sankyo, BMS/Pfizer, Sanofi Aventis, and Leo Pharma.

PP0299

PREDICTIVE FACTORS IMPACTING THE RESULT OF A GLUCOSE BREATH TEST: A RETROSPECTIVE ANALYSIS OF 2373 TESTS

H. Soliman^{1,2}, P.-E. Cailleaux³, C. Desprez², A.-M. Leroi², C. Melchior⁴, G. Gourcerol²

¹Hôpital Louis Mourier - AP-HP, Gastro-enterology Department, Colombes, France, ²CHU Rouen Hopital C. Nicolle, Dept. of Digestive Physiology, Rouen Cedex, France, ³CHU Rouen, INSERM UMR 1073, Geriatrics Department, Rouen, France, ⁴Rouen University Hospital, INSERM U1073, CIC-CRB-1404, Gastroenterology, Rouen, France

Contact E-Mail Address: heithemsoliman90@hotmail.com

Introduction: Glucose breath test (GBT) is the most commonly used method for the diagnosis of small intestinal bacterial overgrowth (SIBO). SIBO is a common condition with very unspecific symptoms (bloating, abdominal pain, diarrhea or constipation).

Recently, American and European recommendations have been published to standardize the indications and the conditions to perform these tests.^{1,2} However, some discrepancies remain between the European and American recommendations, and many statements were supported by

low quality of evidence.^{1,2} Moreover, several confounding factors related to the patient's condition may impact the result of the test, leading to a difficult interpretation.

Aims & Methods: This study aimed to assess the factors that could impact the results of a GBT. Therefore, we retrospectively reviewed the results of the GBT performed in our physiology department from 2013 to 2023. The test was performed after ingestion of 75g of glucose, with breath samples collected every 15min during 2 hours. The result was considered positive for hydrogen (H₂) if a rise ≥ 20 ppm was observed or positive for methane (CH₄) if a rise ≥ 10 ppm was observed. Demographic data were collected, such as symptoms and questionnaires during the exam including Rome questionnaire, and the Gastro-Intestinal Quality of Life Index (GIQLI). Severity of symptoms was based on the GIQLI questionnaire, where a higher score represents a better condition. Medical and surgery history, such as drug treatments were then retrospectively collected from medical records, using a computerized research.

Results: A total of 2373 tests from different patients were included. The mean age was 46.0 ± 15.8 years old, with 1727 females (73.7%). The number of positive GBT was 576 tests (24.3%), with 294 tests positive for H₂ only, 214 tests positive for CH₄ only, and 69 tests positive for both. In univariate analysis, a higher age, female sex, and a lower body mass index (BMI) were associated with a positive GBT (Table). A history of diabetes, and a previous gastric surgery (sleeve, or bypass) were associated with a positive test, while proton pump inhibitors (PPI) or opioids intake did not change the outcome (Table). Regarding the symptoms, more severe abdominal bloating and constipation were associated with a positive test (1.28 ± 1.0 vs 1.41 ± 1.1 ; $p=0.02$, and 2.67 ± 1.3 vs 2.82 ± 1.2 ; $p=0.03$), while abdominal pain and diarrhea were not statistically different (1.57 ± 1.1 vs 1.67 ± 1.1 ; $p=0.07$; and 2.23 ± 1.3 vs 2.33 ± 1.4 ; $p=0.14$). In multivariate analysis, age (Odds Ratio (OR) = 1.02 [1.01 – 1.03]; $p<0.001$), BMI (OR=0.93 [0.90 – 0.96]; $p<0.001$), a previous gastric surgery (OR=9.32 [3.74 – 24.86]; $p<0.001$) and more severe constipation (OR=0.88 [0.79 – 0.98]; $p=0.02$) were associated with a positive GBT.

	Negative GBT (n=1797)	Positive GBT (n=576)	p value
Age (years)	44.7 ± 15.5	50.0 ± 16.2	<0.001
Sex (female)	1280 (71.2%)	447 (77.6%)	0.005
BMI (kg/m ²)	25.0 ± 5.5	23.9 ± 5.2	<0.001
Diabetes	62 (3.5%)	30 (5.2%)	0.02
Gastric sleeve	8 (0.4%)	14 (2.4%)	<0.001
PPI intake	361 (20.1%)	123 (21.4%)	0.50
Opioids intake	183 (10.2%)	57 (9.9%)	0.91
Irritable bowel syndrome	561 (31.2%)	148 (25.7%)	0.09
Functional dyspepsia	704 (39.2%)	190 (33.0%)	0.08

Conclusion: The result of GBT is more likely to be positive in patients with constipation. A previous gastric surgery is a cofounding factor, leading to a non-interpretable result of the test. A diagnosis of irritable bowel syndrome or functional dyspepsia did not change the result of the test, such as PPI or opioid intake.

References: 1. Hammer HF, Fox MR, Keller J, et al. European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition consensus. United European Gastroenterol J 2022;10:15-40.

2. Pimentel M, Saad RJ, Long MD, et al. ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. Am J Gastroenterol 2020;115:165-178.

Disclosure: Nothing to disclose.

PP0300

THE IMPACT OF GUT MICROBIOTA MODULATION ON THE EVOLUTION OF CELIAC DISEASE

A. Franculescu-Berteau¹, L. Micu¹, E.L. Iliescu¹, I. Copaci¹

¹Fundeni Clinical Institute, Center of Internal Medicine, Bucharest, Romania

Contact E-Mail Address: a.franculescu1989@gmail.com

Introduction: The only effective treatment for celiac disease (CD) is life-long compliance with a gluten-free diet. *Lactobacilli* and *Bifidobacterium* spp. may play a role in the breakdown of gluten. It has been demonstrated that *Lactobacilli* can detoxify gliadin peptides after partial digestion by human proteases. These findings could suggest the use of probiotics as complementary therapy for CD.

Aims & Methods: We designed a study to determine the potential effect of a combination of *Lactobacillus* (acidophilus HA-122, casei HA-108) and *Bifidobacterium bifidum* HA-132 on perception of symptoms and on the inflammatory-immunological markers in patients with active CD.

25 adult patients were randomized to receive bid of a probiotic combination of *Lactobacillus* and *Bifidobacter* for six weeks (13 pts) vs a placebo group (12 pts) while being on gluten-free diet. Laboratory studies included routine blood tests, CD specific antibodies, determination of IL-1b, IL-6 and TNF-alpha. CD serology and duodenal histology were performed at baseline, at the end of treatment and at 30 days after therapy. Histological damage in intestinal biopsy samples was graded according to the Marsh modified classification. At baseline and follow-up visit, patients completed the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire. Histological damage in intestinal biopsy samples was graded according to the Marsh modified classification.

Results: 25 patients, 13 in the probiotic associated arm, 12 in the placebo arm, with median age of 40, BMI 21.2, 18 with symptomatic CD (equal distributed) and 7 with subclinical CD (4 in the probiotic arm, 9 in the placebo arm). Baseline serology: IGA tTG 1986.6 (group A) vs 1507.1 (placebo group). Baseline histology (Marsh classification)- Marsh 3a 1 patient in probiotic group, 2 in the placebo arm. 5 pts Marsh 3b3 in group A and 2 in the placebo arm and 17 pts Marsh 3c (9 pts probiotic, 8 pts placebo). IELs density (mean range) was 44.5 in the first group vs 42.5

After treatment: clinical alleviation of indigestion and diarrhea ($p=0.002$), constipation ($p=0.0396$), gastro-esophageal reflux ($p=0.0493$) and abdominal pain ($p=0.0378$)-superior in the probiotic associated treatment.

Serologic parameters: IgA tTG 0.96 in the probiotic arm vs 1.16 in the placebo ($p=0.048$), IgA EMA 1.05 vs 0.97 ($p=0.028$), IgG DGP 0.91 vs 1.12 ($p=0.21$).

Improvement of the inflammatory status: decrease of IL-1b, IL 6 and TNF-a was superior in the probiotic associated group ($p=0.071$, $p=0.083$, $p=0.078$).

Regarding the histologic response: IELs 0.83 vs 1.07 in the placebo arm ($p=0.049$).

Conclusion: Tests and the lymphocyte infiltrates in the mucosal biopsy specimen in our study suggests that prebiotic/probiotic treatment may improve symptoms and serology in celiac disease.

Disclosure: I don't have any conflict of interest to declare.

PP0301

SLEEP DISTURBANCES IN CELIAC PATIENTS UNDER GLUTEN FREE DIET: A PROSPECTIVE STUDY

F. Squeo¹, A. Marotti¹, A. Giangaspero¹, A. Di Leo¹, G. Losurdo¹

¹University of Bari, Section of Gastroenterology, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy

Contact E-Mail Address: dott.francescosqueo@gmail.com

Introduction: Celiac disease (CD) is an immune-mediated enteropathy associated with extraintestinal manifestations. It has been hypothesized that sleep disorders may be more frequent in CD patients.

Aims & Methods: The purpose of this study was to investigate the quality of sleep in CD patients and to assess the relationship between poor sleep quality and biochemical parameters.

We included patients with a proven diagnosis of CD at least twelve months prior to enrollment. Patients not fully adhering to a gluten free diet were excluded. All the participants completed the Sleep Scale from the Medical Outcomes Study (MOS sleep scale) and Sleep Problems Index II (SLP9) was calculated. A high SLP9 scale indicated worse quality of sleep and values >20 indicated significant sleep disturbance. Stress was evaluated by PSS-4 scale. Simultaneously, blood samples from each subject were collected and demographic and clinical data were recorded. Linear logistic regression was used for uni- and multivariate analysis, and b coefficient and 95% confidence intervals (CI) were calculated.

Results: We enrolled 53 patients, mean age 42.75±11.19, 84.9 % female. The average hours of sleep per night was 6.47±1.11. Mean SLP9 was 37.44±20.65. Forty patients (75.5%) showed sleep disturbance. At univariate analysis, high SLP9 values (worse sleep) were inversely related to the number of hours of sleep (b=-0.38, 95% CI -11.8 to -2.2, p=0.005) and to vitamin D blood levels (b=-0.57, 95% CI -2.7 to -0.46, p=0.009). In multivariate analysis only serum levels of vitamin D were inversely related to SLP9 (b=-0.47, 95% CI -12.8 to -0.43, p=0.05).

Conclusion: Our study demonstrates that low serum levels of vitamin D are independently associated with poor sleep quality in celiac patients. These findings need to be confirmed in future experimental and clinical studies.

Disclosure: Nothing to disclose.

PP0302

DIGESTION SUPPLEMENTED WITH COMMERCIAL GLUTENASES: EVALUATION OF THE FATE OF GLUTEN IN PIZZA BY PROTEOMICS AND IMMUNOCHEMISTRY

G. Mazzarella¹, G. D'Auria², D.A. Leffler³, V. Rotondi Aufiero¹, A. Camarca¹, C. Nitride², P. Ferranti²

¹Institute of Food Sciences-CNR, ImmunoMorphology, Avellino, Italy, ²University of Naples Federico II, Department of Agricultural Sciences, Naples, Italy, ³Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School, Boston, MA, USA., Celiac Center, Boston, United States of America

Contact E-Mail Address: Daniel.leffler@takeda.com

Introduction: Celiac disease (CD) is an autoimmune disorder caused by gluten in genetically predisposed subjects. Recently, the market has introduced enzymatic supplements, known as glutenases, that individuals can ingest before a meal. These supplements can include single enzymes or mixtures facilitating the digestion; however, their potency is unclear.

Aims & Methods:

We developed an analytical process for assessing the effect of supplements on gluten digestion. A standardized pizza recipe was created and used as substrate in a novel *in vitro* model of gastroduodenal digestion

(INFOGEST)[DL1] [GDA2] . 3 different commercial supplements (S1, S2 and S3) were tested. The digestion products were qualitatively monitored in the gastric and duodenal phases using electrophoresis. Primary amines were used to quantify the production of proteinaceous degradation products. Finally, we assessed the digestion resistance of immune-toxic gluten epitopes by using a commercial G12-based ELISA.

Results: Samples treated with supplements showed a reduced number of electrophoretic gluten-related bands [DL3] [GDA4] [GDA5] after gastric digestion as compared with the control. This suggests a faster gluten digestion in the stomach. The highest content of primary amines was determined in the presence of S1 and S2, supplements formulated to contain proteases, peptidases, and starch-degrading enzymes which are active at various pH levels, assisting gluten degradation by gastroduodenal enzymes. The ELISA assay showed a more rapid degradation of G12-immune-toxic epitopes in the presence of S3-a supplement containing prolyl-oligopeptidases, that cleave proline-rich motifs.

Conclusion: The developed approach was effective in assessing the ability of commercial glutenase supplements to reduce the potential immune toxicity of gluten-containing ingredients.

Disclosure: This study was supported by an unrestricted grant from Takeda Pharmaceuticals.

PP0303

THE FREQUENCY OF CELIAC DISEASE AND ITS ASSOCIATION WITH INFERTILITY IN WOMEN REFERRING TO INFERTILITY CLINICS; A CASE-CONTROL STUDY IN SOUTHERN IRAN

E. Rahimpour¹, A.R. Safarpour², S. Shojaei-Zarghani¹, S. Amooee¹, B. Geramizadeh¹, M. Mehrabi¹, M. Zahmatkeshan¹

¹Shiraz University of Medical Sciences, Shiraz, Iran, ²Gastroenterohepatology Research Center, Gastroenterohepatology Research center, Shiraz, Iran

Contact E-Mail Address: mehrabi.manoosh@gmail.com

Introduction: Celiac disease (CD) is a multifactorial systemic disease causing enteropathy that can cause a wide spectrum of disorders related to infertility.

Aims & Methods: This case-control study aimed to evaluate the frequency of CD and its association with infertility in women.

This study was conducted on women referred to the Ghadir Mother and Child Hospital in Shiraz. Infertile women were considered as the case group, and fertile women were considered as the control group. Blood samples were taken from participants, and tissue anti-transglutaminase (Anti-TTG Ab) levels were measured. Patients with high levels of Anti-TTG Ab were referred for duodenal biopsy.

Results: One hundred subjects were enrolled in the case group and 200 in the control group. Eight patients in the case group had positive serology, and duodenal biopsy results of four were positive for CD. Among the control group, one had a positive serology, and the duodenal biopsy result was negative (*P* for between-group differences: 0.001 for serology and 0.012 for biopsy results). There was a positive association between high levels of Anti-TTG Ab and infertility (odds ratio=17.30, 95% CI: 2.13-140.39), even after adjusting for age and body mass index (odds ratio =9.92, 95% CI: 1.17-84.21).

Conclusion: The frequency of CD among infertile women was higher than that of fertile women. The increased levels of Anti-TTG Ab were independently associated with infertility.

Disclosure: None.

PP0304

PATIENT PREFERENCES FOR THE DIAGNOSIS OF COELIAC DISEASE:
A DISCRETE CHOICE EXPERIMENT

M.G. Shiha^{1,2}, N. Wickramasekera³, S. Raju^{1,2}, H.A. Penny^{1,2},
D.S. Sanders^{1,2}

¹Sheffield Teaching Hospitals, Academic Unit of Gastroenterology, Sheffield, United Kingdom, ²University of Sheffield, Division of Clinical Medicine, School of Medicine and Population Health, Sheffield, United Kingdom, ³University of Sheffield, Sheffield Centre for Health and Related Research, Sheffield, United Kingdom

Contact E-Mail Address: shiha202@gmail.com

Introduction: There is potential for a paradigm shift from a biopsy- to a serology-based diagnosis of coeliac disease in selected adults. However, it remains unknown if this approach would be acceptable to patients. We aimed to explore patients' views and preferences regarding the no-biopsy approach for coeliac disease diagnosis.

Aims & Methods: We developed a discrete choice experiment survey containing 12 different scenarios with 2 possible alternatives (endoscopy & biopsy or serology), to estimate patient preferences. The scenarios were based on 5 attributes: risk of false positive results, risk of missed diagnosis, waiting time to start treatment, risk of complications, discomfort, or pain. Patient preferences and the relative importance of the attributes were estimated using a mixed logit model.

Results: In total, 385 people (70.6% female, 98.2% white) completed the survey. Respondents preferred a serology-based diagnosis over endoscopy and duodenal biopsies (59% vs 41%, β coefficient = 1.88, $p < 0.001$). Diagnostic test accuracy ($p < 0.001$), shorter waiting time to start treatment ($p < 0.001$), and discomfort levels during the procedure ($p < 0.001$) were the most important attributes to respondents. The risk of complications, including perforation and bleeding, did not significantly influence respondents' choices. Respondents with previous endoscopy experience were more willing to undergo endoscopy compared with those who never had one.

Conclusion: The no-biopsy approach to diagnosing coeliac disease is acceptable and preferred by patients over endoscopy and biopsy. Our findings highlight the importance of patient-centred care and shared decision-making in guiding diagnostic strategies for optimal patient outcomes.

Disclosure: Nothing to disclose.

PP0305

EXPLORING THE VIEWS OF PRIMARY AND SECONDARY CARE
PHYSICIANS ON THE NO-BIOPSY DIAGNOSIS OF COELIAC DISEASE
IN ADULTS: A QUALITATIVE INTERVIEW STUDY

M.G. Shiha^{1,2}, F.J. Bowker-Howell^{1,2}, A.M. Harper¹,
M. Elwenspoek², H.A. Penny^{3,4}, J. Banks⁵, D.S. Sanders^{3,4}

¹Sheffield Teaching Hospitals, Academic Unit of Gastroenterology, Sheffield, United Kingdom, ²University of Sheffield, Division of Clinical Medicine, School of Medicine and Population Health, Sheffield, United Kingdom, ³University of Bristol, Centre for Academic Primary Care, Population Health Sciences, Bristol Medical School, Bristol, United Kingdom, ⁴University of Bristol, NIHR ARC West; Population Health Sciences, Bristol Medical School, Bristol, United Kingdom, ⁵University of Bristol, NIHR Applied Research Collaboration (ARC) West; Population Health Sciences, Bristol Medical School, Bristol, United Kingdom

Contact E-Mail Address: mohamed.shiha1@nhs.net

Introduction: Despite mounting evidence supporting a no-biopsy approach for the diagnosis of coeliac disease in adults, established clinical pathways in primary and secondary care could hinder implementation in clinical practice. The aim of this study was to identify the barriers and facilitators to a no-biopsy diagnostic pathway of coeliac disease in primary and secondary care.

Aims & Methods: We conducted a qualitative study using semi-structured interviews with gastroenterologists and general practitioners (GPs). We used a pre-defined interview topic guide consisting of open-ended questions and prompts to facilitate discussion about the views of primary and secondary care physicians on the no-biopsy diagnosis of coeliac disease in adults. The interviews were conducted in person or virtually, then transcribed verbatim and analysed using reflexive thematic analysis.

Results: We interviewed 24 physicians (12 gastroenterologists and 12 GPs) across England between February and March 2024. Participants (62.5% male, 58.3% from North of England, and 50% non-white) had different levels of experience ranging between 2 and 30 years. Gastroenterologists were more aware of the no-biopsy approach and the evidence supporting it compared with GPs (100% vs. 50%, $p = 0.01$). Both groups were supportive of the no-biopsy approach but acknowledged the lack of clear guidelines as a major barrier to implementation in clinical practice. Increased patient satisfaction, shorter waiting times to start treatment, and reduced endoscopy services pressures and costs were perceived as the main advantages of the no-biopsy approach. However, participants had concerns regarding false positive results, missing concurrent pathology, dealing with persistent symptoms after treatment without biopsy confirmation, and the increased workload in primary care.

Conclusion: Primary and secondary physicians are willing to adopt a serology-based diagnosis of coeliac disease in adults. The safe and effective implementation of this no-biopsy approach depends on developing clear evidence-based clinical guidelines and referral pathways, along with comprehensive education for all healthcare providers involved.

Disclosure: Nothing to disclose.

PP0306

BODY COMPOSITION AND MEDITERRANEAN DIET ADHERENCE OF COELIAC PATIENTS. A PROSPECTIVE, MULTICENTER STUDY (ARCTIC STUDY)

Z. Vereczkei¹, P. Fülöp², S. Lada³, S. Dakó⁴, E. Dakó⁴, D.D. Füstös⁴, M.Z. Peresztegi⁵, J. Bajor⁶

¹Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ²First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary, ³Department of Medicine, University of Szeged, Albert Szent-Györgyi Medical School, Szeged, Hungary, ⁴Department of Surgery, Transplantation and Gastroenterology, Faculty of Medicine, Semmelweis University, Budapest, Hungary, ⁵Medical School, University of Pécs, Pécs, Hungary, ⁶University of Pécs, Medical School, First Department of Medicine, Division of Gastroenterology, Pécs, Hungary

Contact E-Mail Address: vereczkei47@gmail.com

Introduction: Coeliac disease (CD) is an immune-mediated systemic disorder caused by gluten proteins, affecting approximately 1% of the population. The cardiovascular (CV) and metabolic effects of the disease and the gluten-free diet (GFD) used for its treatment are controversial. Current guidelines suggest that the Mediterranean diet is the most suitable for reducing the risk of CV and metabolic disease, both in terms of primary and secondary prevention. The optimal GFD is based on the Mediterranean diet.

Aims & Methods: Our aim was to assess the body composition and adherence to the Mediterranean diet of CD patients who have been on a GFD for at least 1 year. Body composition was measured with an InBody 770 device and adherence to the Mediterranean diet was assessed with a 14-item questionnaire. Descriptive statistics and Spearman's rank correlation test were applied to analyze our data, provided as mean $\pm$ standard deviation.

Results: Data from 105 patients (84 females, 21 males, mean age 36 $\pm$ 13 years) were analyzed. Regarding body composition, body weight was 68 $\pm$ 17 kg, BMI was 23.9 $\pm$ 5.5 kg/m², waist-hip ratio was 0.89 $\pm$ 0.07, body fat percentage was 27 $\pm$ 10%, skeletal muscle mass was 27 $\pm$ 7 kg and visceral fat area was 89 $\pm$ 50 cm² on average. CD patients' Mediterranean diet adherence was low (5.44 $\pm$ 1.54 points), due to an inadequate consumption of whole grains (34.3%), fish (22.9%), avocado (13.4%) and red wine (29.5%).

Conclusion: Despite the lack of correlation between body composition parameters and adherence rates, patients with CD have an elevated waist-hip ratio and visceral fat area, as well as insufficient intakes of fibre, fish and red wine. Our data suggest that, in addition to maintaining a GFD, an increased fibre consumption and adherence to a Mediterranean diet are necessary for the prevention of CV and metabolic complications, which should be emphasized during patient follow-up.

Disclosure: Nothing to disclose.

PP0307

ASSOCIATION BETWEEN CELIAC DISEASE SYMPTOM SEVERITY AND QUALITY OF LIFE AMONG PATIENTS IN A US LONGITUDINAL OBSERVATIONAL STUDY

M. Arvizu¹, J.R. Marden², E. Swallow², D. Adams³, N. Cheinquer⁴, M. Geller⁵, L. M. Meckley⁶, S. Ghura¹, E. Liu⁷, R. Saad¹, D.A. Leffler^{1,8}

¹Takeda Development Center Americas, Inc., Cambridge, United States of America, ²Analysis Group, Inc., Boston, United States of America, ³Vanderbilt University Medical Center, Nashville, United States of America, ⁴Takeda Pharmaceuticals USA, Inc., Boston, United States of America, ⁵Celiac Disease Foundation, Woodland Hills, United States of America, ⁶At the time of this study: Takeda Development Center Americas, Inc., Cambridge, United States of America, ⁷Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, United States of America, ⁸Celiac Center, Beth Israel Deaconess Medical Center, Harvard Medical School Celiac Research Program, Boston, United States of America

Contact E-Mail Address: Daniel.leffler@takeda.com

Introduction: Quality of life (QoL) measures and symptom frequency/severity are common patient-centred outcomes in clinical practice and drug trials. However, the relationship between QoL measures and symptom burden among patients with celiac disease (CeD) is poorly understood. This study evaluated QoL scores in relation to self-reported symptom severity.

Aims & Methods: The Virtual Celiac Symptoms Study (NCT05309330) is a patient survey that followed US adults ($\geq$ 18 years) and adolescents (12–17 years) with CeD currently adhering to a gluten-free diet, for a study period of 12 weeks. Participants self-reported daily symptom severity through the Celiac Disease Symptom Diary 2.1[®] (CDS 2.1) and completed the Celiac Disease Quality of Life 20-item questionnaire (CD-QoL) covering a 30-day recall period through a web application. The CDS 2.1 included five core CeD symptoms (abdominal pain, bloating, diarrhoea, nausea, and tiredness) scored 1 to 5 as none, mild, moderate, severe, and very severe, respectively. The CD-QoL total scores range from 20 to 100, with higher scores corresponding to better QoL. The CDS 2.1 score was calculated as the daily average symptom severity during the 4 weeks prior to completing the CD-QoL and was categorized as increasing score quartiles; quartile 1 (Q1, reference) represented the lowest possible score and Q4 the highest possible score. In addition, individual CDS 2.1 symptoms were categorized by severity (none/mild [reference], moderate, and severe/very severe). The mean adjusted percentage difference and 95% confidence interval (95% CI) in CD-QoL scores was estimated by generalized linear regression which included terms for age, sex, race, years since CeD diagnosis, and body mass index.

Results: At Week 7, 404 participants in total had complete information on CD-QoL and CDS 2.1 scores. The mean (standard deviation [SD]) CD-QoL score was 56.83 (19.21) and the mean (SD) score for CDS 2.1 was 0.72 (0.56). The CD-QoL scores had a positive linear association with CDS 2.1 overall scores as well as with individual symptom severity scores. Participants had a 52.7% (95% CI: 39.2%, 67.4%) higher CD-QoL score when comparing those in CDS 2.1 Q4 (median [min-max] score 1.19 [0.85–3.00]) with those in Q1 (reference; median [min-max] score 0.07 [0.00–0.19]), which was unchanged when tiredness was excluded from the CDS 2.1 score (53.2% [95% CI: 39.9%, 67.8%]). The positive association between CD-QoL and CDS 2.1 was mainly driven by abdominal pain, tiredness, and bloating. Comparing participants with severe/very severe symptoms with those with none/mild symptoms, the CD-QoL score was 38.8% (95% CI: 28.2%, 50.2%) higher for abdominal pain, 37.8% (95% CI: 25.5%, 51.3%) higher for tiredness, and 32.2% (95% CI: 21.7%, 43.6%) higher for bloating.

Conclusion: In patients with CeD assessed via a digital platform, those with a higher symptom severity burden, assessed with CDS 2.1, had significantly greater (worse) CD-QoL scores, which suggests that the CDS 2.1 might be a good indicator of clinically active disease among patients with CeD.

Disclosure: MA, NC, SG, RS, and DAL are employees and shareholders of Takeda. LMM was an employee of Takeda at the time of the study. JRM and ES are employees of Analysis Group, Inc., which received research support from Takeda Development Center Americas, Inc. DA has served as a consultant for Takeda Pharmaceuticals and Ironwood Pharmaceuticals. MG is an employee of the Celiac Disease Foundation, which received financial support from Takeda Development Center Americas, Inc. EL serves as a consultant for Takeda Pharmaceuticals and is an author for UpToDate (celiac section) for which he receives royalties.

PP0308

COMORBIDITIES, MEDICATION USE AND PROCEDURES AMONG PATIENTS WITH CELIAC DISEASE BEFORE AND AFTER DIAGNOSIS: A US HEALTH CLAIMS DATABASE STUDY

F. Zingone¹, M. Arvizu², S. Manne², V. Gandhi², S. Ghura², R. Saad², D.A. Leffler², I. Petrakis², N. Cheinquer², B. Lebowitz³

¹University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ²Takeda Development Center Americas, Inc., Cambridge, United States of America, ³Columbia University Irving Medical Center, Division of Gastroenterology, Department of Medicine, New York, United States of America

Contact E-Mail Address: fabiana.zingone@unipd.it

Introduction: The healthcare burden among patients with celiac disease (CeD) following a gluten-free diet is still uncertain. The aim of this study was to compare the frequency of comorbidities, medication use and medical procedures among patients with CeD, pre- and post-diagnosis.

Aims & Methods: This case-control study was conducted in US individuals with and without CeD (1:5 ratio), matched for age, sex, region and diagnosis year using MarketScan claims data (2002-2023). CeD diagnosis was defined as ≥ 1 inpatient or ≥ 2 outpatient International Classification of Diseases (ICD)-9/-10 diagnostic codes and all individuals had continuous medical/pharmacy enrolment for 2 years pre-/post-index. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by logistic regression comparing CeD cases and controls.

Results: The 21-year data coverage period included 39,814 patients with CeD and 198,961 individuals without CeD (matched controls) with similar baseline demographics (mean age 41.6 years [standard deviation 20.1]; 70.5% female). Comorbidities, medication use, and medical procedures were higher among individuals with CeD versus controls at 2 years pre- and post-diagnosis.

Two years pre-diagnosis, the frequency of depression/anxiety and use of antidepressants and anxiolytics was greater for individuals with CeD versus without CeD (OR: 2.0 [95% CI 1.9–2.0]), 1.5 [1.5–1.5] and 1.5 [1.4–1.5], respectively), and remained higher 2 years post-diagnosis (OR: 2.2 [2.1–2.3], 1.6 [1.5–1.6] and 1.6 [1.6–1.7], respectively).

The odds of medical procedures were higher comparing individuals with CeD versus without CeD, with the strongest associations for video capsule endoscopy and oesophagogastroduodenoscopy (OR: 9.6–19.9 pre- and post-diagnosis).

Conclusion: Comorbidities, medication use, and medical procedures were greater in individuals with CeD than matched controls, both pre- and post-diagnosis, indicating a continued burden for patients with CeD as well as the healthcare system.

Disclosure: MA, SM, VG, SG, RS, DAL, IP and NC are employees and shareholders of Takeda. BL has nothing to disclose. FZ served as a speaker for Werfen and a consultant for Takeda.

PP0309

THE PHENOTYPE AND TREATMENT OPTIONS FOR MESENTERIC LYMPH NODE CAVITATING SYNDROME IN COELIAC DISEASE: A CASE SERIES AND SYSTEMATIC REVIEW

F. Marchetti¹, S.A. Raju^{2,3}, N. Nandi⁴, M. Shiha^{2,3}, S.S. Cross³, B. Rea⁵, G. Caio⁶, D.S. Sanders^{2,3}

¹University of Ferrara, Ferrara, Italy, ²Academic Unit of Gastroenterology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom, ³Division of Clinical Medicine, Faculty of Medicine and Population Health, University of Sheffield Medical School, Sheffield, United Kingdom, ⁴University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ⁵Sheffield Teaching Hospitals NHS Foundation Trust, Department of Clinical Radiology, Sheffield, United Kingdom, ⁶University of Ferrara, Department of Translational Medicine, Ferrara, Italy

Contact E-Mail Address: federic.marchetti@edu.unife.it

Introduction: There is a paucity of data on mesenteric lymph node cavitating syndrome (MLNCS); a rare complication of coeliac disease, characterized by central necrosis within enlarged mesenteric lymph nodes.

Aims & Methods: A case series of all patients with MLNCS at Sheffield Teaching Hospitals, UK between 2000 and 2022.

A further systematic review using PubMed and Google Scholar for patients with MLNCS and coeliac disease until 2022.

Results: In our case series, 5/6 patients were female (mean age: 58 years (SD: 14.1 years)). Half of patients presented with weight loss, and all were diagnosed by CT scan. Five patients followed a gluten free diet (GFD) and 3 were still alive 1-6 years later, 2 died after 5 and 9 years. One did not follow a GFD and died at 1 year.

From the literature 44 patients were identified with MLNCS (52% female, mean age 52 years (SD: 14.0 years)) and 16% had refractory coeliac disease (RCD). Common features were persistent villous atrophy (90%), weight loss (82%) and hyposplenism (80%). Forty followed a strict GFD, and 28 had partial or complete improvement of their symptoms whilst 19 died. Twenty-one were treated with steroids and 12 of them died.

The overall mortality was 44% and associated with cachexia (5), lymphoma (4), and infectious complications (4).

Conclusion: MLNCS was indicative of a poor prognosis and commonly presented with weight loss, hyposplenism, persistent villous atrophy and RCD. An early diagnosis and strict GFD may lead to a better prognosis. The role of immunosuppression is unclear and needs further investigation.

Disclosure: Nothing to disclose.

PP0310

CELIAC DISEASE: A FORTY-YEAR ANALYSIS IN AN ITALIAN REFERRAL CENTER

L. Lungaro¹, G. Caio^{1,2}, A. Costanzini¹, F. Manza¹, F. Caputo¹, F. Remelli³, S. Volpato³, R. De Giorgio¹, U. Volta⁴

¹University of Ferrara, Department of Translational Medicine, St. Anna Hospital, Cona -Ferrara, Italy, ²Massachusetts General Hospital-Harvard Medical School, Mucosal Immunology and Biology Research Center, Boston, United States of America, ³University of Ferrara, Department of Medical Sciences, Ferrara, Italy, ⁴University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: lisa.lungaro@gmail.com

Introduction: Celiac disease (CD) is a gluten-related autoimmune enteropathy affecting human leukocyte antigen (HLA) DQ2 or DQ8 positive subjects.¹ CD onset can occur at any age and with several clinical phenotypes. Modern serological markers have significantly improved the diagnosis of the disease, which affects about 1% of the population worldwide.¹⁻³ Hence, CD serology helps to detect CD in patients with non-classical symptoms or even in those who are asymptomatic.

Aims & Methods: This study aims to analyze the clinical presentation, serology, histology, associated diseases, complications, and death rate of a large cohort of CD patients diagnosed and followed up over forty years. This is a retrospective study on 1547 CD patients (1170 females and 377 males; mean age at diagnosis: 33.1±24.4 years; F:M ratio = 3.1:1), consecutively diagnosed from January 1980 to December 2020 at our referral center (Department of Medical and Surgical Sciences, St. Orsola-Malpighi Hospital, Bologna, Italy). CD diagnosis was established following positive serological tests and confirmed by duodenal histology. The evaluated serological markers included: total immunoglobulin A (IgA), anti-transglutaminase (TG)-2 and anti-endomysium (EmA), both of IgA type; in cases with IgA deficiency, the immunoglobulin G (IgG) antibody anti-TG2 or against deamidated gluten peptides were considered.⁴ Comorbidities and complications were recorded at diagnosis and during follow-up.

Results: The rate of CD diagnoses quadrupled after the year 2000. The most prevalent phenotype was the non-classical CD (63.3%), and the most frequent histotype was Marsh 3C (44.7%). Gastrointestinal manifestations, affecting about half of patients (51%), included diarrhea (24.3%), bloating (28%), and aphthous stomatitis (19.7%). Among the CD-associated disorder, osteopenia was the most common (59.9%) and predominantly affecting females (64.3%). Extraintestinal manifestations were anemia (35.8%, with low levels of ferritin and folic acid malabsorption detectable in 87% of patients), cryptogenic hypertransaminasemia (27.9%), and recurrent miscarriages (11.5%). The prevailing CD-related autoimmune disorders were thyroiditis (26.9%), type 1 diabetes mellitus (2.9%), and dermatitis herpetiformis (1.4%). Six patients had inflammatory bowel disease (2 Crohn's disease and 4 ulcerative colitis). Complications occurred in 1.8% of cases, and the mortality rate was 1.9%.

Conclusion: This forty-year, single-center, large cohort analysis showed that the clinical presentation of CD changed over the years, with an increase of non-classical and subclinical phenotypes. Our study highlighted three main aspects: i) the non-classical and subclinical phenotypes prevailed over the classical forms, according to the recently established criteria; ii) modern serological tests allowed an earlier, faster, and more precise CD diagnosis, even at the subclinical stage, thus contributing to explain the increased diagnostic yield; iii) some CD-associated disorders correlated with gender (e.g., osteopenia which prevailed in women). In conclusion, our data confirmed and broadened current knowledge on CD, and help physicians to recognize new CD presentations, thus avoiding diagnostic delay and inappropriate management.

References:

1. Caio, G., Volta, U., Sapone, A., Leffler, D. A., De Giorgio, R., Catassi, C., & Fasano, A. (2019). Celiac disease: a comprehensive current review. *BMC medicine*, 17(1), 142. <https://doi.org/10.1186/s12916-019-1380-z>
2. Volta, U., Caio, G., Stanghellini, V., & De Giorgio, R. (2014). The changing clinical profile of celiac disease: a 15-year experience (1998-2012) in an Italian referral center. *BMC gastroenterology*, 14, 194. <https://doi.org/10.1186/s12876-014-0194-x>
3. Dieterich, W., Laag, E., Schöpper, H., Volta, U., Ferguson, A., Gillett, H., Riecken, E. O., & Schuppan, D. (1998). Autoantibodies to tissue transglutaminase as predictors of celiac disease. *Gastroenterology*, 115(6), 1317-1321. [https://doi.org/10.1016/s0016-5085\(98\)70007-1](https://doi.org/10.1016/s0016-5085(98)70007-1)
4. Villalta, D., Tonutti, E., Prause, C., Koletzko, S., Uhlig, H. H., Vermeersch, P., Bossuyt, X., Stern, M., Laass, M. W., Ellis, J. H., Ciclitira, P. J., Richter, T., Daehrich, C., Schlumberger, W., & Mothes, T. (2010). IgG antibodies against deamidated gliadin peptides for diagnosis of celiac disease in patients with IgA deficiency. *Clinical chemistry*, 56(3), 464-468. <https://doi.org/10.1373/clinchem.2009.128132>

Disclosure: Nothing to disclose.

PP0311

IMPACT OF SEROLOGY-BASED CELIAC DISEASE DIAGNOSIS ON PEDIATRIC PATIENTS' OUTCOME

I. Enache^{1,2}, A. Palaga³, D.V. Balaban^{1,2}, D. Czika³, M. Jinga^{1,2}, A. Popp^{1,3}

¹University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, ²Dr. Carol Davila Central Military Emergency University Hospital, Bucharest, Romania, ³National Institute for Mother and Child Health, Bucharest, Romania

Contact E-Mail Address: iuliaenache.89@gmail.com

Introduction: Celiac disease (CD) is an immune-mediated systemic disease, triggered by the ingestion of gluten, which only develops in genetically predisposed individuals. The main characteristics of the disease are the gluten-dependent small intestinal mucosal lesion, villous atrophy and crypt hyperplasia, and the production of the specific serum autoantibodies. The gold standard for diagnosis has been based on the biopsy findings. In 2012, new ESPGHAN diagnostic guidelines removed the necessity of duodenal biopsy in symptomatic children showing a high serum transglutaminase 2 titers (TG2-IgA) together with the presence of endomysial antibodies (EmA) and HLA DQ2 and/or DQ8.

Aims & Methods: Our aim was to assess the clinical outcome of the diagnostic change in children by comparing new serology-based diagnosed patients to the biopsy-based ones.

We conducted a retrospective analysis of data collected from the medical charts of the patients diagnosed during a four-year period, from 2010 to 2014, being a time overlapping the guideline change. From a total of 63 patients, 30 were biopsy-diagnosed and 33 diagnoses were based on serology only. Clinical data and laboratory parameters were compared between the groups at diagnosis and at follow-ups at 1 year, 2 years and at their latest follow-up visit during the gluten-free diet (GFD) treatment, median time 8.7 years for the serology-based group and 10 years for the biopsy-based group.

Results: Our results show clear improvement upon GFD in gastrointestinal symptoms in both groups. However, there was a general trend for better treatment outcomes in the biopsy-based group compared to the serology-based group at 1 and 2 years of follow-up. Body mass index Z score was in the biopsy group at baseline -1.5, at 1 year on GFD -0.2 and at 2 years -0.2. The corresponding results in the serology group was -1.51, -0.8 (p=0.056), and -1.35 (p=0.023). Anemia was observed in the serology group

at one year as frequently (25%) as at baseline (26.7%) but in the biopsy group improvement from baseline was seen, 27.4% to 7.1 % of patients. At two years, anemia was present in 16.6% of patients. Ferritin values were significantly lower in the serology group at one year (27.5 µg/L vs 59, $p=0.040$) but not anymore at 2 years. After two years on GFD both TG2-IgA and EmA were often still above the cut-off for positivity in both diagnostic groups (serology group 58.3 % and 50% respectively and in the biopsy group somewhat less, 50% and 28.6% respectively). At long term, no anemia was present anymore. However, 4 children from serology group and 8 from the biopsy group showed antibodies above cut-off even after 8.7 and 10 years of treatment, respectively. Upon long-term follow-up the patients from the biopsy-proven group seemed to be more compliant with the follow-up visits and more adherent to the gluten-free diet.

Conclusion: Both clinical and laboratory results show slow recovery upon gluten-free diet. High percentage of autoantibody positivity still at 2 years on GFD indicates substantial amounts of gluten in the diet. Biopsy-proven patients seemed to have a faster recovery than the serology-diagnosed. Serological diagnosis also appears to negatively influence the adherence and compliance to treatment and follow-up. Novel (drug/vaccine) treatments adjunctive to GFD are an unmet need also in children. Duodenal mucosal recovery results on long-term GFD are warranted.

Disclosure: Nothing to disclose.

PP0312

PREVALENCE OF ANTI-SACCHAROMYCES CEREVISIAE AND ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES IN PATIENTS WITH NEWLY DIAGNOSED CELIAC DISEASE

D.V. Balaban^{1,2}, L. Sauciuc³, I. Enache^{4,2}, L. Coman⁴, M. Balaban⁵, D. Czika⁶, A. Pop^{7,6}, M. Jinga^{1,2}

¹University of Medicine and Pharmacy Carol Davila, Internal Medicine and Gastroenterology, Bucharest, Romania, ²Central Military Emergency University Hospital, Gastroenterology, Bucharest, Romania, ³Diamedix Impex, Bucharest, Romania, ⁴Carol Davila University of Medicine and Pharmacy, Internal Medicine and Gastroenterology, Bucharest, Romania, ⁵University of Medicine and Pharmacy Carol Davila, Doctoral School, Bucharest, Romania, ⁶IOMC Alfred Rusescu Dept. of Pediatrics, Paediatrics, Bucarest, Romania, ⁷University of Medicine and Pharmacy Carol Davila, Pediatrics, Bucharest, Romania

Contact E-Mail Address: vbalaban@yahoo.com

Introduction: Anti-Saccharomyces cerevisiae antibodies (ASCA) and anti-neutrophil cytoplasmic antibodies (ANCA) are well recognized as serological markers in inflammatory bowel diseases (IBD). With the growing evidence of a bidirectional association between IBD and celiac disease (CD), there has been an increased interest in identifying shared biomarkers for both conditions.

Aims & Methods: We aimed to assess seroprevalence of ANCA, IgA and IgG ASCA, in newly diagnosed CD patients. CD diagnosis was set according to 2013 ACG guideline and 2019 ESSCD guideline. Serum collected at the time of diagnosis for all CD patients was analyzed for IgA and IgG ASCA, and ANCA concentration, using INOVA Quanta Lite® assays. Positivity cut-off was defined as $\geq 25U$ for ASCA and $> 30U$ for ANCA.

Results: Altogether 82 newly diagnosed CD patients, 82.9% female, were recruited, all of them having atrophic mucosal injury on duodenal biopsy sampling and one being seronegative CD. While none of the CD patients had positive ANCA, seroreactivity against Saccharomyces cerevisiae was seen in 32.93% of cases for IgG ASCA. A lower prevalence for IgA ASCA was recorded, of 4.88%, due to associated IgA deficiency. Moreover, 7.32% of newly diagnosed CD patients had equivocal result for IgG ASCA.

Conclusion: A high prevalence of ASCA, particularly IgG type, was seen in newly diagnosed, biopsy-proven CD patients. Future research should investigate the clinical significance of the seroreactivity to IBD-specific antibodies in CD patients.

References:

1. Pinto-Sanchez MI, Seiler CL, Santesso N, Alaedini A, Semrad C, Lee AR, Bercik P, Lebwohl B, Leffler DA, Kelly CP, Moayyedi P, Green PH, Verdu EF. Association Between Inflammatory Bowel Diseases and Celiac Disease: A Systematic Review and Meta-Analysis. *Gastroenterology*. 2020 Sep;159(3):884-903.e31. doi: 10.1053/j.gastro.2020.05.016. Epub 2020 May 13. PMID: 32416141.
2. Damoiseaux JG, Bouten B, Linders AM, Austen J, Roozendaal C, Russel MG, Forget PP, Tervaert JW. Diagnostic value of anti-Saccharomyces cerevisiae and antineutrophil cytoplasmic antibodies for inflammatory bowel disease: high prevalence in patients with celiac disease. *J Clin Immunol*. 2002 Sep;22(5):281-8. doi: 10.1023/a:1019926121972. PMID: 12405161.

Disclosure: None.

PP0313

SEROLOGICAL DIAGNOSIS OF COELIAC DISEASE - A WEB-BASED SURVEY AMONG NORWEGIAN GASTROENTEROLOGISTS

N. Gjerstad¹, K.E. Lundin²

¹Institute of Clinical Medicine, Oslo, Norway, ²Norwegian Coeliac Disease Research Centre, University of Oslo and Oslo University Hospital, Gastroenterology, Oslo, Norway

Contact E-Mail Address: knut.lundin@medisin.uio.no

Introduction: Serological diagnosis of coeliac disease (CeD) is accepted for pediatric patients in Europe [1]. Both the 2019 European guidelines and the 2023 American guidelines from the American College of Gastroenterology required a diagnostic biopsy in adults [2, 3]. In recent years we have seen several studies addressing the no-biopsy approach in adults [4-6]. Wide-spread implementation of no-biopsy approach demands precise instructions on how the diagnosis can be made and by whom.

Aims & Methods: We aimed at investigation the acceptance among clinicians for a no-biopsy approach, and how they follow current guidelines. A digital survey was sent in November 2023 to members of the Norwegian Society for Gastroenterology. It was sent out once, no reminder, and was open for one month. Replies were collected anonymously. The Society has 452 members including 256 gastroenterologists. Almost all specialists are members of this Society.

Results: We received 72 replies. Of the respondents, 48 were male and 22 female, 1 not-binary and 1 did not answer. Five of them were not clinically active. Fifty-eight of 72 adhered to guidelines and routinely took biopsies both from the bulb and the distal duodenum. Forty-five took 4 biopsies from the distal duodenum, only five of them 2 biopsies. Negative serology was considered insufficient to exclude CeD by 52 respondents. All used IgA-TG2 for diagnosis, 41 also IgG-DGP, whereas 6 used endomysium test (EMA) and 4 also anti-gliadin antibodies. We initially asked if positive serology alone could diagnose CeD and received mixed response; 26 supported the notion, 37 did not and 9 did not know. We thereafter provided information on no-biopsy diagnosis for children. With this information, forty respondents supported serological diagnosis without biopsy, 10 were negative and 21 uncertain. The majority (32) requested 2 strongly positive (more than 10 x ULN) IgA-TG2, whereas 14 considered a single strongly positive test as sufficient. Specialists deemed capable of setting the diagnosis was gastroenterology (48 votes), general practitioner (22 votes), internists (21 votes) any doctor (10 votes). However, half of the respondents considered it not necessary to personally meet the patient to make a diagnosis.

Conclusion: The no-biopsy approach receives support; but the precise set-up is not clear. If a no-biopsy approach is agreed upon, we should decide on single or repeated tests, on the use of EMA or rely on only IgA-TG2, and if IgG-DGP has a role. The coeliac community should agree on precise guidelines to minimize misdiagnosis and provide the patients with a clear and definite diagnosis.

References: 1. Husby, S., et al., European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. *J Pediatr Gastroenterol Nutr*, 2020. 70(1): p. 141-156.
2. Al-Toma, A., et al., European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *United European Gastroenterol J*, 2019. 7(5): p. 583-613.
3. Rubio-Tapia, A., et al., American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. *Am J Gastroenterol*, 2023. 118(1): p. 59-76.
4. Penny, H.A., et al., Accuracy of a no-biopsy approach for the diagnosis of coeliac disease across different adult cohorts. *Gut*, 2021. 70(5): p. 876-883.
5. Ciacci, C., et al., Serum anti-tissue transglutaminase IgA and prediction of duodenal villous atrophy in adults with suspected coeliac disease without IgA deficiency (Bi.A.CeD): a multicentre, prospective cohort study. *Lancet Gastroenterol Hepatol*, 2023. 8(11): p. 1005-1014.
6. Fuchs, V., et al., Serology-based criteria for adult coeliac disease have excellent accuracy across the range of pre-test probabilities. *Aliment Pharmacol Ther*, 2019. 49(3): p. 277-284.

Disclosure: Nothing to disclose.

PP0314

VARIABLE PRESENTATIONS OF CELIAC DISEASE & SOCIAL IMPLICATIONS OF CELIAC DISEASE, DATA FROM DEVELOPING COUNTRY

M.F. Muslim¹, T. Bhatti², M. Irfan³, H. Sanekommu⁴, A. Sufyan^{2,2}
¹Allama Iqbal Medical College, Lahore, Pakistan, Internal Medicine, Lahore, Pakistan, ²SZABMU, Islamabad, Gastroenterology, Islamabad, Pakistan, ³Holy Family Hospital, Rawalpindi, Internal Medicine, Rawalpindi, Pakistan, ⁴Hackensack Meridian Jersey Shore University Medical Center, Internal Medicine, Neptune, United States of America

Contact E-Mail Address: alisufyan92@gmail.com

Introduction: Celiac disease (CD) is an autoimmune enteropathy triggered by ingestion of gluten in genetically susceptible individuals. It has extremely varied clinical presentations. Diagnosis of celiac disease is made by history and clinical presentation compatible with CD, serological screening compatible with CD, histological findings compatible with CD, obvious clinical and serological response to a gluten-free diet, and exclusion of other clinical conditions mimicking CD. Not much is known about presentation of this disease in Pakistani adults.

Aims & Methods: The study is cross-sectional in nature, gathering data from celiac support communities on social media platforms throughout Pakistan. Patients who were diagnosed cases of Celiac disease on the basis of serology and/or histopathology were interviewed via a structured questionnaire via non probability consecutive sampling technique. Patient's age, gender, age of diagnosis, diagnostic modality, intestinal and extra-intestinal symptoms, gluten free diet status and response and challenges in gluten free diet were recorded while ensuring patient anonymity. Data was entered and statistical analysis was performed via IBM SPSS version 25.

Results: A total of 340 patients were enrolled in present study. Most predominant intestinal symptom was Diarrhea reported by 46.8% of participants followed by Abdominal pain/Bloating in 44.7% (Figure I). Most common Extra-intestinal features were Anemia reported by 51.5% of pa-

tients (Figure II). Of note constipation was reported by 21.5% and Stunted growth by 35.3% of patients. Most common utilized diagnostic modality was Serology in 62.9% of patients (Figure III). 86.8% of patients reported symptom resolution with Gluten free diet. This association was statistically significant. Patients who reported Abdominal pain/Bloating were significantly more likely to report improvement in symptoms following Gluten free diet (Figure IV). Challenges in Gluten free diet were availability issues reported by 37.5% followed by financial issues in 25%, social challenges in 19.2% and other issues including compliance and cross contamination by 40% (Figure V)

Pie & Bar Charts for Abstract

Conclusion: Celiac Disease has an extremely Variable Presentation in Pakistani patients. It can present with Classical Diarrhea and Non classical presentation with abdominal pain and bloating as well. Adherence to Gluten free diet was associated with reduction in Symptoms and improvement.

Financial constraints and limited availability of gluten-free products are contributing factors to non-adherence to gluten-free diet. Further Studies are needed to know more about the Variability of Symptoms in underdeveloped Countries.

Disclosure: Nothing to disclose.

PP0315

WORK ABSENTEEISM, QUALITY OF LIFE AND PSYCHOLOGICAL MORBIDITY IN COELIAC PATIENTS ON A GLUTEN-FREE DIET: AN ITALIAN CROSS-SECTIONAL STUDY

M. Dota¹, L. Rubbini¹, A. Schieppatti^{1,2}, S. Maimaris^{1,2}, F. Biagi^{2,1}, F. Zingone^{3,4}

¹University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy, ²Istituti Clinici Scientifici Maugeri IRCCS, Gastroenterology Unit of Pavia Institute, Pavia, Italy, ³Azienda Ospedale Università Padova, Gastroenterology Unit, Padua, Italy, ⁴University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy

Contact E-Mail Address: michele.dota01@universitadipavia.it

Introduction: The data on the impact of coeliac disease on work loss are still scarce [1-3]. We aimed to evaluate the amount of hours lost at work in adult coeliac patients on a gluten-free diet (GFD), focusing on the reasons behind the work loss (WL), and the relationship with quality of life (QOL) and psychological morbidity.

Aims & Methods: Adult patients with biopsy-proven CD under regular follow-up at two Italian centres were surveyed between October 2022 and January 2024. The survey consisted of specific questionnaires, including the Work Productivity and Activity Impairment questionnaire (WPAI:CD), gastrointestinal symptoms severity score (Visual Analog Scale, VAS), the Coeliac Disease-specific Quality Of Life scale (CD:QOL), the State-Trait Anxiety Inventory scale (STAI-Y1 & STAI-Y2), and the Beck Depression Inventory scale (BDI-II). Amount of hours lost at work in the previous 7 and 30 days were specifically investigated and statistically analysed.

Results: 160 patients on a GFD (121 F, mean age at CD diagnosis 32±14 years, 6% in a GFD for less than 1 year, 63% for more than 5 years, 31% for 1 to 5 years) were enrolled. Eight/160 (6.0%) patients reported having lost working hours in the previous 7 days and 15/132 (11.3%) in the previous 30 days. Reasons for work loss at 30 days included symptoms persistence despite the GFD (40%), attendance of outpatient clinic (40%) and issues with GFD adherence (20%).

The patients had a mean of 3.1 hours of missed work at 7 days and 5.0 hours at 30 days. Focusing on the patients that experienced WL in the previous 30 days, we have found that they were more likely to have on-

going symptoms despite the GFD (67% vs 93%, $p=0.04$), scored higher on the survey items regarding depression (median BDI-II score 7.00 vs 12.00, $p=0.04$), and self-reported a lower QOL (median CD:QOL score 85.00 vs 75.00, $p=0.03$).

Conclusion: Our clinical data-based study has shown that CD patients can experience a substantial work loss at 30 days, particularly in case of persistence of symptoms despite a GFD, which can have negative impacts on psychological health, as well as overall QOL. This aspect should be considered when trying to develop personalized strategies for the individual follow-ups of coeliac patients.

References: 1. Bozorg SR et al. Clin Gastroenterol Hepatol. 2022; 20: 1068-1076.e6

2. Norström F et al. BMC Gastroenterol 2012; 12: 125

3. Ukkola A et al. BMC Gastroenterol 2012; 12: 136

Disclosure: Nothing to disclose.

PP0316

A DECADE OF COELIAC DISEASE: A COMPARATIVE STUDY OF THE MALTESE ISLANDS (2013-2023)

L. Miruzzi¹, J. Schembri¹, M.D. Grixti¹, P. Ellul¹, M. Sciberras¹

¹Mater Dei Hospital, Msida, Malta

Contact E-Mail Address: lara.g.miruzzi@gmail.com

Introduction: Coeliac disease (CeD) is a chronic autoimmune condition affecting the small intestine triggered by gluten.

Aims & Methods: To assess the national management of newly diagnosed CeD patients between 2013 and 2023 in Malta and whether this was carried out in accordance with “European Society for the Study of Coeliac Disease (ESsCD) guideline for CeD and other gluten-related disorders”¹.

The national statistics data of all the newly diagnosed patients with CeD between 2013 and 2023 in the Maltese Islands, were retrospectively analysed. Several factors were considered including patient demographics, serology, histology, imaging and dietitian referral.

Results: 171 patients with newly diagnosed CeD (2013 n=46, 2023 n=125) were recruited. Adults, defined as ≥ 18 years, accounted for 72.5% (n=124) of the total cohort.

In 2013, 80.4%(n=37) were female while in 2023, 66.4% (n=83) were female ($p=0.07$). The mean age at diagnosis was 38.5 years (SD19.6) in 2013 and 36.6 years (SD23.4) in 2023. The largest proportion, 17.0%(n=29), were diagnosed in the 31 to 40 age group.

Anti-Tissue Transglutaminase Antibody (anti-TTG IgA-Ab) was taken in 99.4%(n=170), with 92.4%(n=158) having a positive anti-TTG. 4.1%(n=7) had negative anti-TTG IgA-Ab while 2.9%(n=5) had borderline anti-TTG IgA-Ab. Of these 12 patients, 11 patients had biopsies taken with histology confirming the diagnosis of CeD. The other patient was 8 years old with IgA deficiency and had a positive anti-TTG IgG-Ab, with a value of >250 U/mL.

73.1%(n=125) of the total cohort had biopsies taken, with 56.0%(n=70) taken from D2, 3.2%(n=4) taken from D1 and 37.6%(n=47) taken from both D1 and D2. In 3.2%(n=4), the biopsy site was not specified. In 2023, 48.2%(n=41) of patients had D1+D2 biopsies taken, versus only 15%(n=6) in 2013 ($p<0.001$). Of the remaining 26.9%(n=46) who did not have biopsies taken, 73.9%(n=34) were children.

48%(n=60) of the patients in 2023 were referred to the dietitian versus 15.2%(n=7) in 2013 ($p<0.001$). From the total cohort, only 39.2%(n=67) were referred to the dietitian. DEXA scan was carried out in 49.1%(n=84), 40% referred patients in 2023 versus 74% in 2013. 11 patients, 6.4%, required small bowel imaging.

73.7%(n=126) had repeat TTG taken after diagnosis. Only 9 patients, (7.2%), had repeat biopsies taken.

Conclusion: This is the first review of CeD in the Maltese Islands showing a percentage increase over ten years of 171% in diagnosis. The incidence rate was 9.2 new cases per 100,000 in 2013 and 24.3 new cases per 100,000 in 2023. CeD diagnosis was x2.4 times commoner in females. This significant change is also accompanied by the increase in D1 biopsies taken in addition to D2 ($p<0.001$).

An improvement was noted in the number of dietitian referrals carried out from 2013 to 2023. DEXA scan testing was carried out in nearly half the total cohort emphasizing the need to consider this investigation especially in those patients who are at high risk of osteoporosis.

A limitation of this study was the fact that biopsies taken in the private sector were not available for review. Therefore from the total cohort only 7%(n=12) did not have an available biopsy result or review.

A multidisciplinary team approach to the management of CeD is crucial and will help to provide the best outcomes for the patient.

References: ¹ Al-Toma, A., Volta, U., Auricchio, R., Castillejo, G., Sanders, D. S., Cellier, C., Mulder, C. J., & Lundin, K. E. A. (2019). European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. United European gastroenterology journal, 7(5), 583–613. <https://doi.org/10.1177/2050640619844125>.

Disclosure: No disclosures or Conflict of Interest.

PP0317

SCREENING FOR COELIAC DISEASE IN INFLAMMATORY BOWEL DISEASE

J. Schembri¹, L. Miruzzi¹, M.D. Grixti¹, N. Sciberras¹, J. Barbara¹, D. Gauci¹, P. Ellul¹, M. Sciberras¹

¹Mater Dei Hospital, Msida, Malta

Contact E-Mail Address: lara.g.miruzzi@gmail.com

Introduction: Coeliac disease (CeD) is an autoimmune condition affecting the small intestine. Research has shown a likely bidirectional association between CeD and Inflammatory Bowel Disease (IBD)¹.

Aims & Methods: Our aim is to retrospectively assess whether patients with IBD are screened for CeD in Malta.

284 patients with a histological diagnosis of IBD were randomly selected from the hospital IBD pool. They were grouped into those receiving biological therapy and those solely on immunomodulators. Data collected included age, sex and whether coeliac serology (TTG – IgA or EMA) and/or duodenal biopsies were taken and whether the results were compatible with a diagnosis of CeD.

Results: From 284 patients (58.1% male, mean age 44.5 years SD=16.4). 58.5% had Crohn's disease, 41.5% had Ulcerative Colitis. 65.1%(n=185) were on biological treatment (Infliximab=21.5%, Adalimumab=22.2%, Vedolizumab=17.6%, Ustekinumab=3.9%).

Out of all patients, 79.9%(n=227) underwent CeD immunology tests either at the time of diagnosis or during follow-up, with no difference in gender ($p=0.79$) or IBD subtype ($p=0.32$) whether serology was taken or not. Among them, five patients (2.2%) tested positive for coeliac antibodies. However, only three of these individuals proceeded to have duodenal biopsies performed.

One of these patient's biopsies yielded results consistent with Coeliac disease. All these five patients had repeat TTGs, while four of them had DEXA scan performed. 3 patients with positive CeD serology had small bowel imaging. 33.5% of IBD patients had duodenal biopsies taken during upper GI endoscopy.

Conclusion: It's reassuring to observe that a significant majority (79.9%) of patients with IBD underwent testing for CeD. However, despite consistent follow-up in gastroenterology clinics, one-fifth of IBD patients in our cohort were never tested. Our findings reveal a local incidence of CeD in IBD of 0.4%, which is slightly lower than the reported 0.75% [1].

This underscores the significance of considering CeD as a potential pathology that may contribute to ongoing symptoms and abnormal blood test results in IBD patients.

References: [1] Pinto-Sanchez MI, Seiler CL, Santesso N, Alaedini A, Semrad C, Lee AR, Bercik P, Lebowitz B, Leffler DA, Kelly CP, Moayyedi P, Green PH, Verdu EF. Association Between Inflammatory Bowel Diseases and Celiac Disease: A Systematic Review and Meta-Analysis. *Gastroenterology*. 2020 Sep;159(3):884-903.e31. doi: 10.1053/j.gastro.2020.05.016. Epub 2020 May 13. PMID: 32416141.

Disclosure: No disclosures or Conflict of Interest.

PP0318

EVALUATION OF GLUTEN-FREE DIET ADHERENCE AND QUALITY OF LIFE IN COELIAC PATIENTS

H. Yacoub¹, H. Debbabi¹, D. Cherif¹, H. Hassine¹, H. Kchir¹, N. Maamouri¹

¹La Rabta Hospital, Tunis, Tunisia

Contact E-Mail Address: yacoubhaythem@hotmail.com

Introduction: As there is currently no drug treatment available to cure celiac disease (CD), treatment is based on a strict, lifelong gluten-free diet (GFD). The GFD is very restrictive and patient adherence is not always a guaranty.

Aims & Methods: The aim of our study was to evaluate adherence to the GFD and the impact of the disease on quality of life.

We conducted a cross-sectional study, including celiac patients followed up at the consultation during the period from January to March 2023. Adherence to the GFD was assessed using the validated Biagi questionnaire, and patients' quality of life was assessed using the CD-QoL questionnaire, which we translated into Tunisian dialect.

Results: We included 33 patients followed for celiac disease with confirmed diagnosis assessed by anatomopathological examination according to Marsh classification. The mean age of included patients was 42.2 years. The sex ratio (M/F) was 0.32. The mean course of the disease was 13.3 years. The dietary survey revealed insufficient macronutrient intake and unbalanced macronutrient distribution (67% of patients). Assessment of adherence to the GFD revealed that 44.4% of patients followed the diet strictly, 33.3% followed the GFD non-strictly, and 22.2% did not follow the GFD at all. The most frequent reason for non-adherence to the GFD was economic issues (87.9%). With regard to quality of life, 57.7% of patients had a good quality of life, as evidenced by a high CD-QoL score > 73. Only 12.1% of patients had poor quality of life (low score < 46). Patients with good adherence to RSG had better quality of life (p=0.027).

Conclusion: Our study demonstrates the link between adherence to the RSG and quality of life in celiac patients, hence the importance of encouraging patients to follow the diet properly.

Disclosure: No conflict of interest.

PP0319

AWARENESS AND KNOWLEDGE OF CELIAC DISEASE AMONG THE HEALTH CARE PROFESSIONALS: A CROSS-SECTIONAL SURVEY FROM THE LARGEST PUBLIC SECTOR HOSPITAL OF KARACHI, PAKISTAN

M. Mujahid¹

¹Jinnah Postgraduate Medical Center, Gastroenterology and Hepatology, Karachi, Pakistan

Contact E-Mail Address: murk.mujahid@hotmail.com

Introduction: Celiac disease (CD) is a common chronic illness with various clinical presentations. Despite a rise in prevalence, 95% of patients go undetected, often misdiagnosed or ignored. Inadequate understanding among healthcare professionals contributes to this delay.

Aims & Methods: To evaluate the knowledge of HCPs regarding celiac disease.

Results: Out of 374 participants, 196 (52.4%) were male and 178 (47.5%) were female, indicating sample diversity. Furthermore, the split of professional roles demonstrates the vocational diversity of the sample, with nurses comprising the largest group at 147 (39.3%), followed by interneers 106 (28.3%), house officers 93 (24.8%), and medical officers 28 (7.49%). The study reveals that a majority of the population perceives the disease as autoimmune, with a higher percentage believing it can be hereditary.

The perception of the illness as lifelong is prevalent, with a high confidence in a cure. A significant proportion acknowledge the potential reversal of symptoms through a strict gluten-free diet, but also associate gluten with sensitivity and allergies.

According to the poll, most people are aware of the symptoms of celiac disease, including chronic diarrhea, bone pain, stomach pain, bloating, exhaustion, weight loss, and skin/nail manifestations.

Conclusion: The study highlights the unsatisfactory knowledge level among HCPs regarding CD, suggesting the need for increased awareness and e-learning activities to improve CD knowledge.

Disclosure: Nothing to disclose.

PP0320

POTENTIAL CELIAC DISEASE IN CHILDREN: HEALTH STATUS ON A LONG-TERM GLUTEN-CONTAINING DIET

R. Mandile¹, L. D'Antonio¹, M. Carpinelli¹, F. Lerro¹, L. Greco¹, R. Troncone¹, R. Auricchio¹

¹University Federico II, Translational Medical Science, Naples, Italy

Contact E-Mail Address: r.auricchio@unina.it

Introduction: Potential celiac disease (PCD) is a clinical condition characterized by the presence of a positive CD-specific serology and a normal intestinal architecture. Asymptomatic PCD patients are generally addressed to continue on a gluten containing diet (GCD), but long-term risks of this approach have never been explored.

Aims & Methods: In the present study we aim at investigating nutritional and autoimmune complications possibly developing overtime in a cohort of asymptomatic PCD children left on a GCD. We compared parameters of growth, nutritional status, and autoimmunity between time of diagnosis and in occasion of last medical check, after a long-term gluten containing diet.

Results: Altogether we collected data from 171 PCD children with a mean follow-up time of 3 years (range 0.35-15.3 years). During follow-up, despite patients did not reduce the amount of daily gluten intake, anti-tissue transglutaminase (anti-TG2) antibodies spontaneously and significantly decreased. Most of parameters analysed did not change over follow-up (height centile, ferritin, albumin, cholesterol, calcium, alkaline phosphatase, parathormone, vitamin D, p>0.05) or even improved (weight and BMI

centile, haemoglobin, blood iron, HDL, glycaemia and HbA1C, $p < 0.05$), always remaining in the limit of normality. Equally autoantibodies for other concomitant autoimmune disorders did not increase overtime. Similar results were obtained excluding from the analysis patients that stopped producing anti-TG2 and those with a follow up < 3 years.

Conclusion: Our pilot study provides reassuring results on the maintenance of a gluten containing diet in asymptomatic PCD children, even when a long term follow-up is considered.

Disclosure: no conflict of interest to declare.

PP0321

EVIDENCES OF SENESENCE AND OXIDATIVE STRESS IN THE DUODENAL MUCOSA OF ACTIVE CELIAC DISEASE. AN EXPLORATORY STUDY

E.G. Smecuol¹, M. Kujaruk², M.L. Espinet¹, M.E. Oregui¹, R.A. Puebla³, P. Temprano¹, J.P. Stefanolo¹, M.L. Moreno¹, S. Niveloni¹, M. Toigo⁴, N. Ortonne⁴, J. Bai⁵, J. Boczkowski⁴
¹Hospital de Gastroenterología 'Dr. C. Bonorino Udaondo', Medicine, Buenos Aires, Argentina, ²Hospital de Gastroenterología 'Dr. C. Bonorino Udaondo', Pathology Department, Buenos Aires, Argentina, ³Hospital de Gastroenterología 'Dr. C. Bonorino Udaondo', Laboratory Department, Buenos Aires, Argentina, ⁴Mondor Institut of Biomedical Research, UMR 955 Inserm-UPEC, Créteil, France, ⁵Del Salvador University, Research Institutes, Buenos Aires, Argentina

Contact E-Mail Address: esmecuol@intramed.net

Introduction: The exact molecular pathways contributing to epithelial abnormalities in celiac disease (CeD) remain incompletely understood. Cellular senescence, characterized by cell-cycle arrest and involving oxidative stress (OS), has been associated with the onset of chronic diseases, and attributed to the decline in regenerative capacity and the release of inflammatory agents. However, the potential involvement of senescence and OS in the context of intestinal mucosal damage in CeD remains to be investigated.

Aims & Methods: Aim: To investigate the presence of senescence and OS markers in the duodenal mucosa of both CeD patients and non-CeD controls.

Methods: This was an exploratory study wherein we analyzed duodenal biopsies obtained from 4 adult patients diagnosed with CeD and 5 non-CeD controls. Senescence was analyzed through the expression of the protein p21 and its relevance in terms of cell proliferation was evaluated by the expression of the protein Ki67 (detection with specific primary antibodies and peroxidase immunostaining). Positive cells were semi-quantified in the surface epithelium and crypts according to the percentage of positive cells among the total cells of the analyzed section (no staining reaction = 0; 1-30% stained nuclei = 1; 31-60% = 2; > 60% = 3). Carbonylated proteins were detected using amino-oxyfunctionalized fluorophores. The intensity of fluorescence was quantified in villi and crypts and expressed as relative fluorescence units (RFU) by surface. The statistical analysis was performed by non-parametric tests.

Results: Intestinal biopsies from CeD patients (3 females; median age 26.5 yr; 25%-75% IQR: 21-29) and non-CeD controls (3 females; median age 38 yr; 25%-75% IQR: 33-38) were studied. The percentage of p21-positive cells in the surface epithelium was not different between CeD patients and controls (median [25-75% IQR]): 100% (95-100%) vs 98% (98-100%), respectively ($p = 0.6$).

By contrast, the expression of p21 in the epithelium of crypts was significantly higher in CeD patients vs. controls (45% [40-67.5%] and 0 [0-1]), respectively ($p = 0.02$). Ki-67 expression in the surface epithelium was higher in CeD patients vs. controls (2% [2-3]) and 0% [0-0%]), respective-

ly ($p = 0.04$), while the determinations were similar in the crypts of both groups. Finally, carbonylated proteins were detected with greater intensity in CeD patients compared to controls both in the surface epithelium (5050 RFU [3862-5622]) vs. 2335 RFU [2324-2477]), respectively ($p = 0.03$), and in crypts (2260 RFU [2197-2598]) vs. (1403 RFU [1313-1476]), respectively ($p = 0.03$).

Conclusion: This exploratory study presents the first evidence of senescence and OS in the duodenal mucosa of CeD patients at diagnosis and compared to controls suggesting that these phenomena could be involved in a dysfunctional epithelial regenerative process in CeD. These novel findings offer new perspectives for understanding CeD mucosal damage. However, further confirmation in a larger series of cases is required to validate these findings.

Disclosure: Nothing to disclose.

PP0322

CARBOHYDRASE ACTIVITY IN PROXIMAL AND DISTAL SEGMENTS OF SMALL INTESTINE IN HEALTH, IRRITATED BOWEL SYNDROME AND ENTEROPATHY WITH MEMBRANE DIGESTION DISTURBANCE

E. Kondrashova¹, A. Parfenov², N. Belostotsky³
¹Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation, ²A. S. Loginov Moscow Clinical Scientific Center MHD, Department of Intestinal Pathology, Moscow, Russian Federation, ³A. S. Loginov Moscow Clinical Scientific Center MHD, Laboratory of preclinical research methods, Moscow, Russian Federation

Contact E-Mail Address: doktor_alena@mail.ru

Introduction: Diagnostics of enteropathy with membrane digestion disturbance (EMDD) is based on the evaluation of carbohydrase activity in duodenal mucosa (DM). There is no information about diagnostic value of ileum mucosa (IM) carbohydrases.

Study objective. Assess the diagnostic value of carbohydrases activity in mucous membrane of duodenum and distal ileum in patients with EMDD and irritable bowel syndrome (IBS).

Aims & Methods: The study includes 12 patients with EMDD, 16 patients with IBS and 12 relatively healthy persons (control group). Study design included analysis of food tolerance and evaluation of activity of sucrase (S), glucoamylase (GA), maltase (M) and lactase (L) in mucous membrane of duodenum and ileum based on the method of Dahlquist with N.I. Belostotsky modification. Microsoft Office Excel and STATISTICA 10.0 were used for statistical evaluation of material. Mann-Whitney criterion was used to evaluate the differences between quantitative parameters. The differences were considered to be significant at $p < 0.05$. Control group was used for comparison.

Results: Ratio of carbohydrase activity in duodenum and ileum in control group and patients with IBS and EMDD.

		Glucoamylase	Maltase	Sucrase	Lactase
Control	Duodenum	776 ± 163	2664 ± 317	175 ± 25	83 ± 17
	Ileum	714 ± 121	2532 ± 438	130 ± 27	16 ± 4
	P	0.763	0.81	0.2	0.001
IBS	Duodenum	590 ± 91	2118 ± 124	194 ± 33	84 ± 6
	Ileum	1275 ± 158	4142 ± 489	191 ± 27	14.4 ± 6
	P	0.008	0.0004	0.934	0.002
EMDD	Duodenum	164 ± 23	859 ± 76	69 ± 7	27 ± 6
	Ileum	858 ± 182	3259 ± 59.6	143 ± 30	10 ± 3
	P	0.0014	0.0009	0.03	0.004

In control group the carbohydrases activity in duodenum mucosa was not significantly statistically different from the one in ileum mucosa.

In patients with IBS glucoamylase and maltase activity parameters in IM were significantly different from activity in DM, which can be interpreted as functional inequality of enzyme activity of various departments of small intestine.

In patients with EMDD GA level in ileum mucosa is 5.2 times higher, maltase level is 3.8 times higher and sucrose level is 2 times higher than duodenum enzyme levels, which demonstrates the possibility of formation of compensatory reaction of adaptive shift type towards distal segments of small intestine, initially described by A.M. Ugolev et al. in 1985

Conclusion: Enzyme activity distribution along small intestine is an adaptor function of its segments. Our study confirmed the need and promising outlook of further investigations in terms of evaluation of proximo-distal gradients of enzyme activity to study compensatory reactions which can be fulfilled by distal segment of small intestine in case of duodenum damage.

The evaluation of carbohydrase activity in ileum mucosa provides additional opportunities for diagnostics of EMDD and its differentiation from IBS, which can be used to improve therapeutic approaches.

Disclosure: Nothing to disclose.

PP0323

WHAT IS THE SIGNIFICANCE OF SYMPTOMS DURING THE GLUCOSE SIBO BREATH TEST IN PATIENTS WITH DISORDERS OF GUT-BRAIN INTERACTION (DGBI)?

C.H. Wilder-Smith¹, A. Materna¹, S.S. Olesen^{2,3}

¹Brain-Gut Research Group, Gastroenterology Group Practice, Bern, Switzerland, ²Aalborg University Hospital, Department of Gastroenterology, Aalborg, Denmark, ³Aalborg University Hospital, Department of Clinical Medicine, Aalborg, Denmark

Contact E-Mail Address: info@ggp.ch

Introduction: Small intestinal bacterial overgrowth (SIBO) is a commonly diagnosed finding in diverse conditions ranging from DGBI to GI motility, connective tissue and neurodegenerative disorders (1). A wide spectrum of signs and symptoms have been attributed to SIBO (1,2). Diagnosis is achieved either by direct culture of duodenal aspirate or indirectly, by demonstrating exhaled fermentation gases with ingested sugars, such as glucose or lactulose (3,4). In the breath tests used for carbohydrate intolerances, the symptoms provoked are at least as important for the diagnostic interpretation as the measured gas concentrations. However, the symptoms generated during SIBO breath tests are neither evaluated nor mentioned in most testing guidelines. SIBO exists in asymptomatic populations and the association with symptoms remains uncertain (1,2).

Aims & Methods: We examined the acute relationship between breath gases and the symptoms generated during glucose breath tests in DGBI. A standardised breath test with glucose (50g in 150ml water) was performed after a 24-hour low-FODMAP diet and >8-hour fast. Exhaled hydrogen and methane concentrations were measured and symptom assessments (composite symptom index score, SI used for intolerance breath tests)(5) were performed every 15 minutes for 2 hours in 790 male (30%) and female patients of average age 40.0 years referred to our gastroenterology practice with DGBI (Rome 4 criteria). Breath gas concentration thresholds of >20ppm and >10ppm above baseline were considered positive tests for hydrogen and methane, respectively.

Results: Overall, 59 (7.5%) and 111 (14.1%) DGBI patients were SIBO positive using the hydrogen and methane thresholds, respectively. The composite SI was positive in 208 (26.3%) of patients. The most common individual symptoms were fullness, nausea, tiredness, headache (each in

>30% of patients), followed by bloating, flatulence, abdominal cramps or pain, GORD and problems concentrating (each in 20-30% of patients). A positive SI with a negative hydrogen test was seen in 151 (19.1%) of DGBI patients, in 108 (13.0%) with a negative methane test and in 55 (7.0%) with both negative hydrogen and methane tests. A negative SI occurred in 2.4% of patients if either of the gas tests was positive.

Conclusion: During the glucose SIBO breath test, positive gas results and evoked symptoms are closely associated. However, glucose frequently provokes symptoms in DGBI patients with negative hydrogen and/or methane breath test results. This may be due to a discrepancy between breath and intestinal gases, production of gases beyond hydrogen and methane, or the induction of symptoms by glucose or its metabolites via alternative mechanisms.

References:

1. Quigley EMM, et al. Expert Review. Gastroenterology 2020;159:1526-1532.
2. Bushyhead D, et al. Gastroenterology 2022;163:593-607.
3. Losurdo G, et al. J Neurogastroenterol Motil 2020;26:16-28.
4. Tansel A, et al. Clin Transl Gastroenterol 2023;14:e00567.
5. Wilder-Smith CH, et al. Aliment Pharmacol Ther 2013;37:1074-83.

Disclosure: Nothing to disclose.

PP0324

REDUCING THE NUMBER OF BREATH SAMPLES IS A COST-EFFECTIVE STRATEGY TO OPTIMIZE THE LACTOSE BREATH TEST

G. Scalese¹, A. Cesarini¹, L. Pallotta¹, E. Ribichini¹, L. Spina¹, A. Citarella², S. Cammarota², C. Severi¹

¹Sapienza University, Department of Translational and Precision Medicine, Rome, Italy, ²LinkHealth Health Economics, Outcomes & Epidemiology S.R.L., Naples, Italy

Contact E-Mail Address: scalese.giulia@gmail.com

Introduction: The lactose breath test (LBT), through the measurement of hydrogen (H₂) and methane (CH₄), is the test of choice in assessing lactose malabsorption (LM). Although direct costs of LBTs are low, indirect costs are high due to the long test duration requiring prolonged involvement of qualified staff and available infrastructures. Sampling frequency represents the principal time-consuming part of the test. The current European guidelines recommend a test duration of 3-5 hours (hrs) and sample intervals of 30-60 minutes (min). In our center, the standard LBT consists of 9 samples collected every 30 min up to 4 hrs after the ingestion of 25 g of lactose.

Aims & Methods: The study aimed to optimize the methodology of LBT either by reducing the test duration by up to 3 hrs (Shortened-test: ST) or reducing the number of breath samples with hourly intervals by up to 4 hrs (Five-sample test: FST). Retrospectively, patients (pts) undergoing LBT at the Gastroenterology Unit from January 2022 to October 2023, were included. Gas peak ≥20 ppm for H₂ and/or ≥10 ppm for CH₄ above baseline was diagnostic for LM. Results of ST and FST were calculated from the standard LBT and compared with them. The delta-ppm (Δ-ppm) and the area under the curve (AUC) were calculated to stratify gas excretion into 3 grades of malabsorption (mild, moderate, severe) according to the percentile distribution. Data were expressed as mean (±DS), and analyzed with Chi-square, Mann-Whitney and Pearson correlation. p<0.05 was considered statistically significant. Specificity was always 100% due to the lack of an independent gold-standard test.

Results: Of the 543 pts enrolled (F 71.5%, mean age 43.7 ± 17.6 yrs), 60.4% (328/543) were positive for LM and were significantly older (44.7±17 years) than negative ones (40.5±17.6 years) (p=0.006). LBTs were mainly positive for H₂ (80.8% for H₂, 8.2% for CH₄, and 11% for both gases; p<0.0001).

FST showed higher accuracy than ST. In the ST, the positivity rate was 54.1% (294/543), sensitivity was 89.6% with a false negative rate of 10.4% (34/328) and accuracy was 93.7%. In FST, the positivity rate was 57% (309/543), sensitivity was 94.2% with a false negative rate of 5.8% (19/328) and accuracy was 96.5%.

A statistically positive correlation was found between the Δ -ppm value and the AUC, both for H_2 ($r=0.94$) and CH_4 ($r=0.78$). In the FST, according to the percentile stratification of Δ -ppm, 84% (16/19) of negative pts showed mild LM (≤ 25 th percentile) and the remaining 16% (3/19) had Δ -ppm values slightly higher.

Conclusion: Comparing FST and ST, only FST proved to be a cost-effective strategy to optimize LBT without reducing test sensitivity. Extending the interval of breath sampling collection with hourly measurements reduces the indirect costs, by decreasing the involvement of qualified staff and maximizing the procedure by doubling the number of pts who could be tested in a day.

Disclosure: Nothing to disclose.

PP0325

EFFICACY AND QUALITY OF LIFE IMPACT OF INTRAVENOUS FERRIC CARBOXYMALTOSE TREATMENT IN PATIENTS WITH IRON DEFICIENCY ANAEMIA DUE TO IRON MALABSORPTION

S. Scalamonti¹, E.P. Schiavone¹, L. Dottori¹, C. Palumbo¹, E. Dilaghi¹, G. Pivetta¹, I. Ligato¹, M. Pompili¹, M. Magnante¹, B. Annibale¹, E. Lahner¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea University Hospital, Gastroenterology Unit, Roma, Italy

Contact E-Mail Address: schiavone.1794884@studenti.uniroma1.it

Introduction: Iron malabsorption (FeM) may lead to iron deficiency anaemia (IDA). Its most common causes are celiac disease (CD) due to atrophy of the small intestine mucosa, corpus atrophic gastritis (CAG), and gastric surgery (GS): reduced hydrochloric acid secretion derived from corpus oxyntic mucosa atrophy or surgical resection causes a decreased conversion of Fe(III)ion to Fe(II)ion, the latter being the more easily absorbable form. IDA affects more than two billion people over the world and it can cause troublesome symptoms as asthenia and fatigability. Iron oral supplementation is considered the standard therapy but frequently it leads to side effects reducing long-term compliance. Ferric carboxymaltose (FCM) is an intravenous (iv) preparation shown to be safe and effective in improving the iron status (FeS), but its efficacy in patients with FeM and IDA has not been investigated so far.

Aims & Methods: To evaluate the safety, efficacy and quality of life impact of iv FCM in treating pts with IDA due to FeM. A prospective observational single centre study was conducted on 37 pts with IDA caused by CAG ($n=19/51.4\%$), CD ($n=9/24.3\%$), and GS ($n=9/24.3\%$). Pts with other causes of IDA as GI bleeding were excluded. At baseline (T0), pts were clinically and biochemically evaluated (symptoms, SF12, CBC and FeS: ferritin, iron, transferrin, transferrin saturation (TS)). FCM dosage was calculated according to Ganzoni formula considering Hb values and body weight. If the dosage needed was up to 1000mg, iv infusion was scheduled in a single session, otherwise a 2 nd infusion after 1 wk was planned. After treatment, CBC and FeS were assessed at 4 (T4) and 12 (T12) wks. SF12 was reevaluated after 12 wks (cut-off physical component summary (PCS)<44, mental component summary (MCS)<46). IDA was defined as Hb<13 and <12 g/dl for men and women, ferritin<45 ng/dl or TS<15%. Moderate and severe anemia were defined as Hb 8-10 and Hb<8 g/dl. Student's t-test was used to compare CBC and FeS parameters at baseline (T0), 4 weeks (T4) and 12 weeks (T12).

Results: All 37 patients completed 12-wks-follow-up. At T0 Hb was mean $\pm$ SEM 10.9 $\pm$ 0.2g/dl, 18.9% had moderate and 2.7% severe anaemia. In pts treated in a single-session-infusion (64.9%), dosage of FCM was mean $\pm$ SEM 975 $\pm$ 12mg; in pts treated in two sessions (35.1%), FCM dosage was mean $\pm$ SEM 1400 $\pm$ 77mg. One patient reported mild side effects (pruritus, cutaneous erythema) not requiring FCM interruption and reversing after H_2 antagonist treatment within 15 minutes. At T4 and T12, 70.4% and 78.4% of pts recovered from IDA. At T4 mean Hb significantly increased compared to T0 (12.7 $\pm$ 0.2 vs 10.8 $\pm$ 0.2 g/dl, $p<0.0001$). At T12 a further increase was observed (13.1 $\pm$ 0.2 g/dl, $p<0.05$). Also, TS increased from 6% at T0 to 20% at T12, $p<0.0001$. At T4 ferritin levels (ng/dl) significantly increased compared to T0, but slightly decreased at T12 (T0 28.5 $\pm$ 11.2 vs T4 188.2 $\pm$ 25.7, $p<0.0001$; T12 124.9 $\pm$ 25.7, $p=0.10$). RDW (%) significantly increased at T4 and significantly decreased at T12 (T0 15.4 $\pm$ 0.5 vs T4 18.6 $\pm$ 0.7, $p=0.0003$; T12 14.8 $\pm$ 0.4, $p<0.0001$). The proportion of patients with SF12 MCS>46 and PCS>44 scores significantly increased at T12 compared to T0 indicating improved mental and physical health perception after FCM treatment.

Conclusion: In pts with IDA due to FeM, ivFCM is an effective and safe treatment, leading to recovery of IDA in nearly 80% of cases at 12 weeks after treatment and concomitantly to an improved mental and physical health perception. These data show that ivFCM treatment could be considered as a first line treatment for IDA patients with FeM.

References: Lahner E, et al. Dig Liver Dis. 2019 Dec;51(12):1621-1632. doi: 10.1016/j.dld.2019.09.016. Epub 2019 Oct 19. PMID: 31635944.

Elli L, et al. Nat Rev Gastroenterol Hepatol. 2024 Mar;21(3):198-215. doi: 10.1038/s41575-023-00872-2. Epub 2023 Dec 18. PMID: 38110546.

Carabotti M et al. Nutrients. 2021 Jan 13;13(1):208. doi: 10.3390/nu13010208. PMID: 33450823; PMCID: PMC7828248.

Kodraliu G et al. J Epidemiol Biostat. 2001;6(3):305-16. doi: 10.1080/135952201317080715. PMID: 11437095.

Disclosure: Nothing to disclose.

PP0326

CLINICAL AND HISTOLOGICAL SPECTRUM OF MALABSORPTION SYNDROME: INSIGHTS FROM ENDOSCOPIC EVALUATION AND HISTOLOGICAL ANALYSIS

A. Samad¹

¹Hamdard University Hospital, Gastroenterology, Karachi, Pakistan

Contact E-Mail Address: samaddhedhi@gmail.com

Introduction: Malabsorption syndrome encompasses a spectrum of gastrointestinal disorders characterized by impaired absorption of nutrients, leading to various clinical manifestations. Endoscopic and histological evaluations play crucial roles in diagnosing underlying etiologies, including celiac disease.

Aims & Methods: This retrospective study aimed to analyze the clinical presentation, endoscopic findings, and histological yield in patients with malabsorption syndrome, focusing on the subset exhibiting villous atrophy to investigate the prevalence of celiac disease. We conducted a retrospective analysis of 100 patients with malabsorption syndrome who underwent endoscopic evaluation between January 1, 2023, and December 31, 2023. Clinical data, endoscopic findings, and histological results were collected and analyzed.

Results: Among the 100 patients, 60 were males and 40 were females. Common presenting symptoms included fatigue (33 patients), recurrent mouth ulcers (15 patients), bloating (12 patients), diarrhea (24 patients), and abdominal discomfort (16 patients). Endoscopic findings revealed normal mucosa in 34 patients, decreased height of duodenal folds in 24,

and fissured mucosa in 42. Histological analysis showed increased intraepithelial lymphocytes in 36 patients, crypt hyperplasia with increased intraepithelial lymphocytes in 20, partial villous atrophy in 22, subtotal villous atrophy in 12, and total villous atrophy in 10 patients. Giardia was detected in histological specimens from 4 patients with partial villous atrophy. Interestingly, only 12 patients had positive celiac serology despite a substantial number exhibiting villous atrophy on histological examination.

Conclusion: This study highlights the diverse clinical presentation and histological spectrum of malabsorption syndrome. Despite significant villous atrophy, celiac disease was diagnosed in only a minority of patients, suggesting the need for further investigation into the etiology of villous atrophy in this subset of patients.

Disclosure: Nothing to disclose.

PP0327

ENDOSCOPIC SMALL BOWEL SURVEILLANCE IN PATIENTS WITH SHORT BOWEL SYNDROME IN TREATMENT WITH TEDUGLUTIDE

A. Sorge^{1,2}, L. Scaramella³, V. Smania¹, N. Nandi¹, A. Costantino³, M. Michelon¹, T. Pessarelli¹, M. Vecchi^{4,1}, G.E. Tontini^{4,1}, L. Elli⁴

¹University of Milan, Milan, Italy, ²Ghent University Hospital, Ghent, Belgium, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico University of Milan, Milan, Italy

Contact E-Mail Address: andreasorge6@gmail.com

Introduction: Concerns regarding colorectal cancer in short bowel syndrome (SBS) patients receiving teduglutide (TED) treatment have led to the recommendation of colonoscopy for screening and surveillance.^{1,2} While there are reports of new small bowel polyps in TED patients, data on small bowel cancer risk and surveillance are lacking.^{3,4} This study aims to evaluate the feasibility and effectiveness of using double-balloon enteroscopy (DBE) for surveillance in SBS patients undergoing TED treatment.

Aims & Methods: Data from patients with SBS in TED treatment who underwent DBE within a year of starting TED at a tertiary referral center for enteroscopy between December 2019 and October 2023 were collected. The primary endpoints were technical success, adverse events, and total enteroscopy rates. Secondary endpoints included the incidence of small bowel polyps and residual small bowel length measurement.

Results: Nine patients (7 female, median age 65.5, IQR 58-79) with SBS (22% type 1, 55.6% type 2, 22.2% type 3-SBS) underwent DBE (10 antero-grad, 2 retrograde) under procedural sedation. Crohn's disease (33.3%) and post-surgical complications (33.3%) were the most frequent causes of SBS. The median interval from TED prescription to DBE surveillance was 9.1 months (IQR 3.2-32.9). The median depth of maximal insertion was 85 cm (IQR 50-187). No adverse events occurred during all the procedures. The total enteroscopy rate was 75% (80% [8/10] of antero-grad DBEs, 50% [1/2] of retrograde DBEs). Panenteric DBE allowed the estimation of small bowel residual length in all cases (2/2) where this important clinical information was unknown and revealed a different residual small bowel length compared to surgery in 44% of patients. No small bowel malignancies were detected during the study period.

Conclusion: DBE surveillance for small bowel malignancy in SBS patients undergoing TED treatment is feasible and effective. Total enteroscopy can be frequently achieved with a single endoscopy in these patients, allowing easy oncologic surveillance.

References: 1. Revestive (teduglutide). Summary of product characteristics. Takeda; August 2022. Accessed 23 March 2024. <https://www.medicines.org.uk/emc/product/3382/smpc>

2. Pironi L, Allard JP, Joly F, et al. Use of teduglutide in adults with short bowel syndrome-associated intestinal failure. *Nutr Clin Pract* 2024;39:141-153.

3. Pevny S, Pape UF, Elezkurtaj S, et al. De Novo Development of Distal Jejunal and Duodenal Adenomas After 41 Months of Teduglutide Treatment in a Patient With Short-Bowel Syndrome: A Case Report. *JPEN J Parenter Enteral Nutr* 2021;45:652-656.

4. Ukleja A, Alkhairi B, Bejarano P, et al. De Novo Development of Hamartomatous Duodenal Polyps in a Patient With Short Bowel Syndrome During Teduglutide Therapy: A Case Report. *JPEN J Parenter Enteral Nutr* 2018;42:658-660.

Disclosure: Nothing to disclose.

PP0328

UTILITY OF ENDOSCOPIC ISCHEMIC POLYPECTOMY FOR THE TREATMENT OF POLYPS IN THE SMALL INTESTINE OF PEUTZ-JEGHERS SYNDROME

T. Taida^{1,2}, Y. Ohta¹, R. Horio¹, C. Goto¹, A. Kurosugi¹, M. Sonoda^{1,2}, T. Kaneko¹, T. Ishikawa^{1,2}, K. Saito¹, K. Okimoto¹, T. Matsumura¹, J. Kato^{1,2}, N. Kato¹

¹Graduate School of Medicine, Chiba University, Department of Gastroenterology, Chiba, Japan, ²Chiba University Hospital, Endoscopy Center, Chiba, Japan

Contact E-Mail Address: taida@chiba-u.jp

Introduction: Peutz-Jeghers polyps (PJPs), seen in Peutz-Jeghers syndrome (PJS), are found throughout the gastrointestinal tracts except for the esophagus. Of these, polyps in the small intestine are likely to become numerous developed and enlarged, resulting in intestinal intussusception which requires surgical treatment. Therefore, endoscopic treatment is recommended to prevent intestinal intussusception.

Recently, endoscopic ischemic polypectomy (EIP) as the strangulation of the polyps using endoclips without polypectomy has been a treatment option for PJPs of the small intestine as well as conventional endoscopic mucosal resection (EMR). However, there has been insufficient data on the clinical utility and safety of EIP compared to EMR, and that needs to be clarified.

Aims & Methods: The purpose of this study was to evaluate the utility and safety of EIP for PJP in the small intestine. We retrospectively recruited PJS patients who underwent balloon-assisted enteroscopy at Chiba University Hospital between February 2010 and December 2023. The clinical information such as patient clinical backgrounds, treatment option, number of polyps, maximum diameter of polyps, and incidence of bowel obstruction after treatment were analyzed in patients who underwent endoscopic treatment for PJPs of the small intestine. The safety profile per-treatment was evaluated using the inverse probability weighting (IPW) method regarding the incidence of bleeding and intussusception after treatment.

Results: During the research period, 55 enteroscopies were performed, of which 37 (20 EMR and 17 EIP) endoscopic treatments were performed for a total of 239 PJPs (diameter 10-40 mm) in 10 PJS patients. The pathological evaluation was performed for 15 lesions (diameter 15-40 mm) treated with EMR, and all were diagnosed as PJPs.

While there was no difference in the total time for endoscopic procedures including insertion and treatment between the EMR and EIP groups (182.5 min vs. 179.1 min, $P=0.497$), the number of treated polyps at one procedure was significantly higher in the EIP group (3.0 ± 2.1 polyps by EMR v.s. 10.5 ± 13.0 polyps by EIP, $P=0.015$). Post-treatment complications included bleeding in 5 treatments while no intussusception was observed. IPW analysis revealed that EIP was associated with a significantly lower risk of complications ($P=0.017$, $OR=0.186$, 95% CI 0.047-0.738) (Table).

	OR	95%CI	P value
EIP	0.186	0.047 - 0.738	0.017

Table. Weighted logistic regression analysis of the risk of bleeding after treatment for PJP.

Adjusted for gender, age at treatment, presence of intestinal adhesion, scope approach (via-oral or via anal), endoscopist (expert or non-expert), insert length, number of treated polyps, maximum diameter of polyps, and total time as confounding factors.

Conclusion: EIP for PJPs in the small intestine is a safer treatment option for numerous lesions than EMR.

Disclosure: Nothing to disclose.

PP0329

DEEP LEARNING AND CAPSULE ENDOSCOPY: AUTOMATIC PANENDOSCOPIC DETECTION OF PROTRUDING LESIONS

P. Cardoso¹, M. Mascarenhas¹, M. Martins¹, F. Mendes¹, M.J. Almeida¹, J. Mota¹, T. Ribeiro¹, J. Afonso¹, A.P. Andrade¹, H. Cardoso¹, M. Mascarenhas-Saraiva², J. Ferreira³, G. Macedo¹

¹Department of Gastroenterology, University Hospital Center of São João, Department of Gastroenterology, Porto, Portugal,

²ManoPH, Porto, Portugal, ³DigestAid, Porto, Portugal

Contact E-Mail Address: pedromarilio@gmail.com

Introduction: While capsule endoscopy (CE) offers a minimally invasive way to examine the entire digestive tract, current analysis methods are time-consuming and susceptible to errors. Protruding lesions are frequently encountered with varying significance throughout the GI tract. This study aims to develop and test a Convolutional Neural Network for panendoscopic automatic detection of protruding lesions on CE exams.

Aims & Methods: A multicentric retrospective study was performed on 1222 CE exams. A total of 191455 images from six different CE device types were evaluated, with 52717 confirmed protruding lesions (epithelial and subepithelial lesions) after a rigorous triple-validation process. First, we conducted a 5-fold cross validation with exam-split for assessing CNN's robustness. Then, we evaluated CNN's global performance in an exam-split train and test division of data, assessing the latter. Primary outcomes measures were sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV) and area under the conventional receiver operating characteristic curve (AUC-ROC) and the precision-recall curve (AUC-PR).

Results: Regarding test set, the sensitivity were 90.7% and specificity 94.0%. The PPV and NPV were 95.3% and 88.3%, respectively. The global accuracy was 92.1%. The CNN processed 112 frames per second.

Conclusion: This study aims to address the gap in AI-enhanced capsule panendoscopy by investigating the development of the first CNN for the detection of protruding lesions across the GI tract. AI's improvement of CE's diagnostic accuracy, along with the growing interest in minimally invasive procedures, may contribute to increasing access to this diagnostic tool.

Disclosure: Nothing to disclose.

PP0330

DIAGNOSTIC YIELD AND OUTCOMES OF SMALL BOWEL CAPSULE ENDOSCOPY IN PATIENTS WITH SMALL BOWEL BLEEDING RECEIVING ANTITHROMBOTICS

N. Viazis¹, D.K. Christodoulou², V. Papastergiou¹, K. Mousourakis¹, D. Kozompoli¹, P. Kanellopoulos¹, I. Stasinou³, K. Dimopoulou⁴, P. Apostolopoulos³, F. Fousekis², C. Liatsos⁵, N. Kyriakos⁵, T. Argyropoulos⁴, G. Trimponias⁴

¹"Evangelismos" General Hospital, Gastroenterology Department, Athens, Greece, ²Gastroenterology Unit University Hospital, 1st Division Of Internal Medicine And Hepato-Gastroenterology Unit, Ioannina, Greece, ³417 (NIMTS) Army Equity Fund Hospital, Athens, Greece, ⁴Red Cross Hospital, Gastroenterology Department, Athens, Greece, ⁵401 Army General Hospital of Athens, Dept. of Gastroenterology, Rafina-Pikermi, Greece

Contact E-Mail Address: konstantinosmousourakis@gmail.com

Introduction: Use of antithrombotics including antiplatelet agents and anticoagulants is associated with upper and lower GI bleeding, thus a higher rate of positive findings is reasonable to be expected when patients receiving these drugs undergo SBCE for the investigation of SBB. However, the results of published studies concerning the impact of antithrombotics on the SBCE diagnostic yield remain conflicting. Furthermore, the clinical outcome of patients under antithrombotics who undergo SBCE for the investigation of SBB is not currently known.

Aims & Methods: We aimed to determine the diagnostic yield and outcome of patients receiving antithrombotic drug therapy subjected to small bowel capsule endoscopy (SBCE) for the investigation of small bowel bleeding (SBB). Multicenter retrospective analysis of collected data from all patients undergoing SBCE for the investigation of SBB from March 2003 to June 2023. The diagnostic yield of SBCE was defined as the detection of positive findings that could explain the cause of the patient's bleeding. Rebleeding was defined as evidence of bleeding within 1 year after the index episode.

Results: During the study period, 8401 patients underwent SBCE for SBB investigation. Bleeding lesions were detected in 1103/2535 (43.5%) patients receiving antithrombotics, compared to 1113/5866 (18.9%) not receiving these drugs (p<0.00001). Following capsule endoscopy, a therapeutic intervention was possible in 390/2216 (17.5%) patients with a bleeding lesion. Rebleeding occurred in 927 (36.5%) of patients receiving antithrombotics (36.5%), compared to 795 (13.5%) not receiving these drugs (13.5%, p<0.00001).

Conclusion: Both the diagnostic yield of SBCE and the rebleeding rate were higher in patients with SBB receiving antithrombotics. Therapeutic intervention was possible in a real world setting only in a minority of patients with positive findings.

References:

1. Sherwood MW, Nessel CC, Hellkamp AS, et al. Gastrointestinal bleeding in patients with atrial fibrillation treated with rivaroxaban or warfarin: ROCKET AF trial. *J Am Coll Cardiol* 2015; 66: 2271–2281.
2. Abraham NS, Hlatky MA, Antman EM, et al. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of PPI and thienopyridines: focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. *Am J Gastroenterol* 2010; 105:2533–2549.
3. Maiden L, Thjodleifsson B, Seigal A, et al. Long-term effects of nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 selective agents on the small bowel: a cross-sectional capsule enteroscopy study. *Clin Gastroenterol Hepatol*. 2007;5:1040–1045.

4. Nagata N, Niikura R, Yamada A, et al. Acute middle gastrointestinal bleeding risk associated with NSAIDs, antithrombotic drugs, and PPIs: a multicenter case-control study. *PLoS ONE*. 2016;11:e0151332.
5. Lepileur L, Dray X, Antonietti M, et al. Factors associated with diagnosis of obscure gastrointestinal bleeding by video capsule enteroscopy. *Clin Gastroenterol Hepatol*. 2012;10:1376–1380.
6. Shiotani A, Honda K, Murao T, et al. Combination of low-dose aspirin and thienopyridine exacerbates small bowel injury. *Scand J Gastroenterol*. 2011;46:281–286.

Disclosure: Nothing to disclose.

PP0331

EFFICACY OF YOGURT CONTAINING *LACTOBACILLUS PARAGASSERI* IN ALLEVIATING ON SMALL INTESTINAL INJURY INDUCED BY COMBINED TREATMENT OF ASPIRIN AND A POTENT ACID SECRETION INHIBITOR

E. Teramura¹, T. Cho², S. Tsuda², S. Hirose², J. Nagata², M. Matsushima¹, Y. Koga¹, S. Fujiwara³, K. Kimura³, T. Suzuki²

¹Tokai University School of Medicine, Isehara, Japan, ²Tokai University Hachioji Hospital, Gastroenterology, Hachioji, Japan, ³Wellness Science Labs, Meiji Holdings Co., Ltd., Hachioji, Japan

Contact E-Mail Address: takayosh@is.icc.u-tokai.ac.jp

Introduction: Our previous study using capsule endoscopy has demonstrated that low-dose aspirin (LDA) frequently induces small intestinal injury, which is shown to be alleviated by some probiotics. However, the mechanism underlying the effects of probiotics remains elusive.

Aims & Methods: Aim: To clarify the mechanism underlying the alleviating effects of probiotics on LDA-induced mucosal injury using gut microbiota analysis.

Methods: Twenty patients in each of the three groups were recruited: control, received no treatment; PPI, treated with either a proton pump inhibitor (PPI) or potassium-competitive acid blocker (P-CAB); and Aspirin+P, treated with aspirin and PPI/P-CAB. Ileal fluid was collected using colonoscopy for ileal microbiota analysis. All patients were treated with *Lactobacillus paragasseri* OLL2716 (LG) for 6 weeks after colonoscopy, and stool samples were collected for faecal microbiota analysis before and after LG treatment. The participants were asked to complete the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire before (at 0 weeks) and after 6 weeks of LG intake.

Results: Faecal microbiota analysis revealed no significant difference in α -diversity among the three groups before and after LG intake. In contrast, β -diversity indices differed significantly between the control and PPI groups as well as between the control and Aspirin+P groups before LG intake. However, no such significant differences between them were found any more after LG intake. The composition of microbiota structures in the PPI and Aspirin+P groups did not differ before or after LG intake. Ileal microbiota analysis revealed no differences among the three groups. The GSRS scores in the control and Aspirin+P groups significantly decreased after LG intake compared to those before LG intake. However, the GSRS scores in the PPI group did not differ significantly before and after LG intake.

Conclusion: The effect of aspirin itself on the microbiota structure and composition was minimal when combined with PPI or P-CAB. The remodelling effect of probiotics on Aspirin+P-induced dysbiosis may be one of the mechanisms underlying the alleviating effects of probiotics on aspirin-induced mucosal injury.

Disclosure: T.S. has received research grants from Meiji Co., Ltd. S.F. and K.K. are employees of Meiji Holdings Co., Ltd.

This study was supported in part by JSPS KAKENHI Grant Number 19K05867.

PP0332

GASTROINTESTINAL ANGIODYSPLASIA RESOLUTION FOLLOWING TRANSCATHETER AORTIC VALVE IMPLANTATION: A PROSPECTIVE COHORT STUDY

L. Goltstein¹, M.J. Rooijackers², N.D. Thierens¹, S.C. Schoormans³, H. Beaumont⁴, C. Houdeville⁵, M.P. Hoeks⁶, E.J.M. van Geenen¹, S.R. Rijpma³, X. Dray⁵, N. van Royen², J.P. Drenth^{1,4}

¹Radboud University Medical Center, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands, ²Radboud University Medical Center, Department of Cardiology, Nijmegen, Netherlands, ³Radboud University Medical Center, Department of Laboratory Medicine, Laboratory of Hematology, Nijmegen, Netherlands, ⁴Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁵Sorbonne University, Centre for Digestive Endoscopy, Saint Antoine Hospital, APHP, Hepatology and Gastroenterology, Paris, France, ⁶Radboud University Medical Center, Department of Hematology, Nijmegen, Netherlands

Contact E-Mail Address: lia.goltstein@radboudumc.nl

Introduction: Heyde syndrome is the co-occurrence of aortic stenosis and gastrointestinal bleeding secondary to vascular lesions, including angiodysplasias. Several studies have demonstrated cessation of gastrointestinal bleeding after transcatheter aortic valve implantation (TAVI), but the etiology and effects on vascular lesions are largely unknown.

Aims & Methods: We aimed to establish the effects of TAVI on gastrointestinal vascular lesions and identify the factors associated with recovery. In this prospective, single-center cohort study, patients with iron-deficiency anemia on the TAVI waitlist from September 2020 to February 2022 were assessed by capsule endoscopy. Those with vascular lesions were reassessed six months after TAVI. Endoscopic images were anonymized and evaluated by two independent researchers.

Results: Twenty-four patients underwent capsule endoscopy, and vascular lesions were present in 18 (prevalence 75%). TAVI was performed in 15/18 patients with vascular lesions, of which 11 agreed to a second capsule endoscopy. The mean number of vascular lesions across the gastrointestinal tract decreased from 6.4 (SD 5.6) to 2.0 (SD 2.1) ($P = .036$). The number of vascular lesions decreased in 9/11 (82%) patients, including 6/11 (55%) who no longer had typical angiodysplasias. Cessation of angiodysplasias was less frequent in patients who had multiple valvular heart disease before TAVI (0/3 [0%] vs 6/8 [75%]) and patients with significant paravalvular leakage after TAVI (2/5 [40%] vs 4/6 [67%]).

Conclusion: Angiodysplasias are present in 75% of anemic patients with severe aortic stenosis. TAVI effectively reduces the size and number of angiodysplasias in these patients.

Disclosure: Lia Goltstein, Maxim Rooijackers, Naomi Thierens, Selene Schoormans, Charles Houdeville, Marlijn Hoeks, and Sanna Rijpma do not have potential conflicts of interest or disclosures to report. Hanneke Beaumont has received speaker fees from Medtronic. Erwin van Geenen has received research funding from Viatrix, Boston Scientific, and Olympus and serves as a consultant for MTW-Endoskopie and Microtech. Xavier Dray is cofounder and shareholder of Augmented Endoscopy, has served as a consultant for Norgine and Provepharma, and received speaker fees from Bouchard Recordati, Fujifilm, Medtronic, Norgine, and Sandoz. Niels van Royen has received research funding from Abbott, Philips, Medtronic, and Biotronik, has served as a consultant for RainMed, Castor, and Medtronic, and received speaker fees from Abbott. The Radboudumc, on behalf of Joost Drenth, has received research funding from Gilead to support Hepatitis C elimination in The Netherlands.

PP0333

IS FIT FIT FOR DETECTION OF SMALL BOWEL PATHOLOGY?
A PROSPECTIVE STUDYP. Oka¹, R. Sidhu², M. McAlindon²¹Royal Hallamshire Hospital, Sheffield Teaching Hospitals,
Academic Dept of Gastroenterology, Sheffield, United Kingdom,²Royal Hallamshire Hospital, Sheffield Teaching Hospitals,
Academic Dept of Gastroenterology, Sheffield, United Kingdom**Contact E-Mail Address:** oka.priya@gmail.com**Introduction:** The role of faecal immunochemical testing (FIT) as a biomarker to stratify patients with lower gastrointestinal (GI) symptoms is well established. However, its use in patients with iron deficiency anaemia (IDA) is unclear. The aim of this study was to investigate the role of FIT in predicting small bowel (SB) pathology in patients with IDA.**Aims & Methods:** This was a single tertiary centre prospective study. Inclusion criteria was adults (>18 years and < 80 years) with IDA who were referred to secondary care for upper and lower gastrointestinal tract (GI) endoscopy. These patients also had a FIT test done in primary care. All participants had a small bowel capsule endoscopy (SBCE) prior to their endoscopic investigations. Participants with subsequent upper or lower gastrointestinal tract malignancy were excluded from the study as this was considered as the most likely cause of IDA. IDA was defined as a Hb < 131g/L for men and < 110 g/L for women with ferritin < 30ug/L and/or iron levels < 11umol/L.**Results:** In total 79 patients were included in the final analysis with a median age of 67yrs (IQR 52-74); haemoglobin 103(IQR 95- 118) and ferritin 11(IQR 6-11). There were 13 patients on NSAID's at the time of their investigations. There were 35 (44%) patients with significant findings on SBCE which was classed as contributing to IDA. These findings included angioectasia in n= 21 (26%) of the patients which was the most common finding. The other findings included erosions= 5 (6.3%); inflammatory strictures= 3 (3.8%); active Crohn's n=1 (1%); visible blood with no clear source n=3 (3.8%); bleeding angioectasia n=1 (1%); and ulcer=1 (1%). A positive FIT (>10) had a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 34.29%, 54.55%, 37.5% and 51.08% respectively.**Conclusion:** Patients with IDA have a high diagnostic yield on SBCE and should routinely have SBCE as part of the work up for IDA. There is a pressing need for biomarkers to help triage SBCE referrals, however FIT is not a reliable biomarker for the presence of small bowel pathology in patients with IDA.**Disclosure:** Nothing to disclose.

Poster
Nutrition

Nutrition

09:00-18:00 / Poster Exhibition

PP0334

USEFULNESS OF LAPAROSCOPIC SLEEVE GASTRECTOMY FOR NAFLD (MASLD)

B. Matsuura¹, H. Nakaguchi¹, M. Miyazaki², A. Shiomi², A. Kanamoto², T. Miyake², S. Furukawa³, Y. Hiasa²
¹Ehime University Graduate School of Medicine, Lifestyle-related Medicine & Endocrinology, Toon, Japan, ²Ehime University Graduate School of Medicine, Gastroenterology & Metabology, Toon, Japan, ³Ehime University, Health Service Center, Matsuyama, Japan

Contact E-Mail Address: bmatsu@m.ehime-u.ac.jp

Introduction: Since 2006 at our hospital, lifestyle modification for obese patients has been provided through a team approach with a physician, dietician, nurse, physical therapist and psychologist. From 2016, a surgeon and anesthesiologist were added to the team for metabolic/bariatric surgery (laparoscopic sleeve gastrectomy: LSG).

Aims & Methods: The aim of this study is to clarify the characteristics of obese patients with NAFLD for whom LSG was effective. Of 40 obese patients who were received LSG between 2017 and 2021 with follow-up period of more than 1 year, 19 were male and 21 were female, 24 were with diabetes, 16 with other complications. The diagnosis of NAFLD was made by liver imaging for fat deposit and stiffness by Fibroscan, and liver biopsy in some cases.

Results: The mean preoperative BMI was 43, the mean Fib-4 index was 0.98, and the postoperative insulin resistance (CPI) of diabetic patients improved significantly, with 15 patients in complete remission and 6 in incomplete remission after surgery. One year after surgery, the mean weight loss was 18.3%, the Fib-4 index did not decrease significantly, but the mean AST (U/L) improved from 38 to 18, ALT (U/L) from 55 to 15, GGT (U/L) from 78 to 40, CAP (dB/m) from 348 to 279, and liver stiffness (kPa) from 12.1 to 7.6, significantly. In patients who underwent follow-up biopsy, there was a trend toward improvement in liver fibrosis.

Conclusion: Since LSG significantly improves hepatic markers in obese patients with NAFLD, metabolic/bariatric surgery should be positively considered.

Disclosure: Nothing to disclose.

PP0335

HYPERTRIGLYCERIDEMIA IS A DOSE-DEPENDENT RISK FACTOR OF DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

L. Havelda^{1,2}, E.Á. Szalai^{1,3}, M. Obediat¹, D. Dobszai^{1,4}, D.S. Veres^{1,5}, M. Bucur¹, A. Molnár^{1,2}, L.K. Vámosy^{1,2}, P. Hegyi^{1,2,4,6}, A. Szentesi^{1,4}
¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ³Semmelweis University, Department of Restorative Dentistry and Endodontics, Budapest, Hungary, ⁴University of Pécs, Institute for Translational Medicine, Medical School, Pécs, Hungary, ⁵Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁶University of Szeged, Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, Szeged, Hungary

Contact E-Mail Address: haveldaluca97@gmail.com

Introduction: The prevalence of type 2 diabetes has more than doubled in the past 20 years, and literature suggests that nearly 90% of diabetes cases are preventable if risk factors are eliminated early. One of these potential risk factors is hypertriglyceridemia. Given the high prevalence of hypertriglyceridemia (which can affect nearly one-third of the population), the link between the two conditions is of crucial importance. Therefore, we aimed to investigate the dose-dependent effect of hypertriglyceridemia on the development of diabetes mellitus.

Aims & Methods: We carried out a systematic search in three databases (MEDLINE, Embase, and CENTRAL) on the 9th of November, 2023 with no restriction. In the final analysis, we investigated adult population with different triglyceride levels (exposure) and our outcome of interest was the development of diabetes mellitus. We calculated pooled odds ratios (OR) with 95% confidence intervals (CIs) and assessed the risk of bias with the Quality In Prognosis Studies (QUIPS) tool. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42023471288.

Results: According to the meta-analysis result of eight cohorts with a total population number of 127431, those who had hypertriglyceridemia had more than a 2-fold higher risk (OR:2.17[CI 1.52-3.10]) of developing diabetes mellitus during the follow-up period than those whose triglyceride levels were below 1.7 mmol/L. Those who had borderline high triglyceride levels at baseline (1.7-2.3 mmol/L) had significantly higher odds of developing diabetes mellitus during follow-up (OR 1.45[CI 1.29-1.63]) according to the data of six cohorts with 36807 patients. Those whose baseline triglyceride levels were higher than 2.3 mmol/L also had significant and even higher odds of the development of diabetes mellitus (OR:2.16 [CI 1.74-2.67]) than patients with normal triglyceride levels, based on the results of 6 cohorts with data on 39068 patients.

Conclusion: Hypertriglyceridemia is a dose-dependent risk factor of diabetes mellitus.

Disclosure: Nothing to disclose.

PP0336

THE IMPACT OF OBESITY ON DEVELOPMENT OF NON-CARDIA GASTRIC CANCER ACCORDING TO SEX IN SOUTH KOREA: A RETROSPECTIVE COHORT STUDY

J. Jang¹, N. Kim^{2,3}, Y. Choi²

¹National Cancer Center Korea, Research Institute, Division of Clinical Research, Goyang-si, Gyeonggi-do, South Korea, ²Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, Gyeonggi-do, South Korea, ³Seoul National University College of Medicine, Department of Internal Medicine and Liver Research institute, Seoul, South Korea

Contact E-Mail Address: jjencn@ncc.re.kr

Introduction: Several studies have recently reported an increased risk of gastric cancer (GC) risk in both underweight and obese population in East Asia. However, the impact of underweight or obesity on the development of non-cardia GC is not fully established yet. In addition, GC is a male dominant cancer, and considering the phenotype differences in body composition between males and females, sex differences must be considered in evaluating the association between obesity and the risk of developing non-cardia GC.

Aims & Methods: Therefore, we aimed to evaluate associations between body mass index (BMI) and non-cardia GC risk with consideration of sex. This study was performed based on a retrospective cohort, which consists of Koreans randomly sampled from participants who underwent the National Health Screening programs and is termed National Health Insurance Service–Health Screening Cohort (NHIS-HEALS). The National Health Insurance system provides health checkups biennially for adults aged ≥ 20 years through the National Health Screening program. This program covers over 70% of total population in Korea, thus the NHIS-HEALS is a nationwide representative database in South Korea. This study includes a total of 341,999 subjects including 4,103 incident non-cardia GC cases identified during a median follow-up period of 10 years after exclusion of incident GC cases identified within 2 years from the follow-up start. We classified subjects into five groups according to BMI (<18.5 , 18.5–22.9, 23.0–24.9, 25.0–29.9, ≥ 30.0 kg/m²) and evaluated the association between BMI level and GC risk by calculating hazard ratio (HR) and corresponding 95% confidence interval (95% CI) based on the Cox proportional hazard regression.

Results: Increased non-cardia GC risks were observed in severely obese (BMI ≥ 30.0 kg/m²) males and obese (BMI 25.0–29.9 kg/m²) females, respectively (HR, 1.40; 95% CI, 1.11–1.75 for severely obese males; HR, 1.25; 95% CI, 1.06–1.46 for obese females).

Age ¹	Sex	Body mass index (kg/m ²)				
		<18.5	18.5–22.9	23.0–24.9	25.0–29.9	≥ 30.0
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
<50 years	Total	1.53 (0.74–3.16)	1.01 (0.77–1.32)	1.00	0.88 (0.66–1.17)	1.41 (0.77–2.58)
	Males	1.74 (0.75–4.02)	1.06 (0.77–1.46)	1.00	0.94 (0.69–1.30)	1.91 (1.03–3.55)
	Females	1.39 (0.17–11.02)	0.88 (0.38–2.02)	1.00	0.91 (0.34–2.44)	N/A
≥ 50 years	Total	1.06 (0.85–1.32)	1.01 (0.93–1.10)	1.00	1.13 (1.04–1.23)	1.17 (0.96–1.44)
	Males	1.09 (0.85–1.39)	0.96 (0.87–1.06)	1.00	1.08 (0.99–1.19)	1.33 (1.04–1.70)
	Females	0.97 (0.61–1.54)	1.17 (0.99–1.38)	1.00	1.30 (1.10–1.53)	0.98 (0.68–2.26)

Table. Association between body mass index and non-cardia gastric cancer risk according to sex in Korea.

Abbreviations: HR, Hazard ratio; CI, Confidence interval

1. Age at BMI measurement

In contrast, evidences supporting that underweight (BMI <18.5 kg/m²) is associated with increased non-cardia GC risk was not found overall (HR, 1.08; 95% CI, 0.88–1.33). In males, the increased risk of non-cardiac GC in the severely obese group remained regardless of age at BMI measurement.

However, the increased risk of non-cardia GC risk related to obesity was confirmed only in elderly females, and was not found in females under 50 years of age. In addition, increased non-cardia GC risk in the normal weight group (18.5–22.9 kg/m²) was found compared to that in overweight group among females over 50 years of age.

Conclusion: Results suggest that elevated risk of non-cardia GC development might be originated from obesity, especially in elderly populations in East Asia regardless of sex. However, this study proposes that being overweight, which is the pre-obesity stage, may rather have a lower risk of developing non-cardia GC than being normal weight in elderly females.

Disclosure: Nothing to disclose.

PP0337

GASTROINTESTINAL ADVERSE EVENTS WITH GLP-1 RAS IN NON-DIABETIC OVERWEIGHT AND OBESE INDIVIDUALS: SYSTEMATIC REVIEW AND DOSE-RESPONSE META-ANALYSIS

A. Ismaiel¹, G.G.M. Scarlata², I. Boitos³, D.-C. Leucuta⁴, P. Stefan-Lucian¹, L. Montebianco Abenavoli², D.L. Dumitrascu¹

¹“Iuliu Hatieganu” University of Medicine and Pharmacy, 2nd

Department of Internal Medicine, Cluj-Napoca, Romania,

²University Magna Graecia, Campus “Salvatore Venuta”,

Department of Health Sciences, Catanzaro, Italy, ³“Iuliu

Hatieganu” University of Medicine and Pharmacy, Faculty of

Medicine, Cluj-Napoca, Romania, ⁴“Iuliu Hatieganu” University of

Medicine and Pharmacy, Department of Medical Informatics and

Biostatistics, Cluj-Napoca, Romania

Contact E-Mail Address: abdulrahman.ismaiel@yahoo.com

Introduction: Overweight and obesity present global health challenges, often managed through lifestyle changes and medications like glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which can cause gastrointestinal (GI) adverse events. However, research on their effects in non-diabetic populations is lacking.

Aims & Methods: This review addresses this gap by examining the impact of GLP-1 RAs on GI adverse events in non-diabetic overweight or obese individuals. We systematically reviewed the literature by conducting a search using PubMed and EMBASE, adhering to predefined inclusion and exclusion criteria, to assess GI adverse events linked with GLP-1 RAs in non-diabetic overweight or obese populations. We conducted a dose response meta-analysis to evaluate each adverse event associated with different GLP-1 RAs. The quality of the included studies was appraised utilizing the Cochrane Collaboration’s assessment tool.

Results: Our systematic review and meta-analysis encompassed thirty-eight articles, incorporating data from a total cohort of 32,882 individuals. Predominant GI adverse effects observed included nausea, vomiting, diarrhea, constipation, and abdominal pain. Across all evaluated GLP-1 RAs, a notable elevation in nausea risk was noted, with orforglipron exhibiting the highest risk, succeeded by exenatide, tirzepatide, semaglutide, and liraglutide. Moreover, liraglutide, orforglipron, semaglutide, and tirzepatide were associated with heightened vomiting risk, while cagrilinitide and exenatide displayed no significant increase. Exenatide, cagrilinitide, and orforglipron demonstrated no significant association with diarrhea risk. Conversely, semaglutide and liraglutide correlated with an elevated risk of constipation, while cagrilinitide and exenatide did not exhibit a significant increase. Notably, certain GLP-1 RAs were linked to a heightened

risk of abdominal pain, with liraglutide, semaglutide, and tirzepatide displaying significant increases, whereas orforglipron showed no significant elevation in abdominal pain risk.

Conclusion: In conclusion, GLP-1 RAs are associated with an increased risk of GI adverse effects, including nausea, vomiting, diarrhea, constipation, and abdominal pain. Importantly, distinct GLP-1 RAs exhibited varying degrees of risk for these adverse effects, underscoring the importance of tailored risk assessment and management strategies in clinical practice.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

PP0338

EXPLORING THE IMPACT OF BREASTFEEDING DURATION ON NEURODEVELOPMENT IN FIVE-YEAR-OLD CHILDREN

M. Dzhogova¹, V. Atanasova¹, D. Zhelyazkova¹, M. Petrov¹, S. Popova¹, R. Yordanova², I. Ivanov², R. Pancheva¹

¹Medical University of Varna "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria, ²Medical University of Plovdiv, Plovdiv, Bulgaria

Contact E-Mail Address: mod2506mod@gmail.com

Introduction: Breastfeeding, recognized for its essential nutrition and health benefits, potentially influences central nervous system development. This study delves into the nuanced relationship between breastfeeding duration and neurodevelopment in five-year-old children.

Aims & Methods: A cohort of 72 children living in Varna, Bulgaria was followed up from birth to age five, all of them being term-born infants with normal birth weight and devoid of perinatal infections or abnormalities. Comprehensive data on demographics and dietary practices were collected. Neurodevelopmental assessments at five years included motor and speech development, articulation, nonverbal intelligence, and behavior, evaluated using the validated NDT5 tool. Children were stratified into 2 groups based on breastfeeding duration (up to age six months vs. over six months). Statistical analysis was performed using Jamovi 2.0.0.0.

Results: Children in both groups exhibited similar demographic characteristics and BMI distributions. Notably, significant differences emerged between the groups in girls' motor development ($U=54$, $p=0.018$) and overall development ($U=52$, $p=0.045$). Similarly, boys showed disparities in nonverbal intelligence ($U=66.5$, $p=0.008$), as evidenced by both intention-to-treat (ITT) and per-protocol (PP) analyses.

Conclusion: Breastfeeding duration appears to exert a discernible influence on neurodevelopment in five-year-old children. Notably, distinct effects were observed in girls' motor development and boys' nonverbal intelligence. Further longitudinal investigations are warranted to optimize neurodevelopmental outcomes based on breastfeeding duration.

Disclosure: Nothing to disclose.

PP0339

PROBIOTIC INTERVENTION IMPROVES QUALITY OF SLEEP – A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TELEMEDICAL STUDY

A. Horvath^{1,2}, N. Feldbacher^{1,2}, V. Stadlbauer^{1,2}

¹Center for Biomarker Research in Medicine, Translational Precision Medicine, Graz, Austria, ²Medical University of Graz, Division of Gastroenterology und Hepatology, Graz, Austria

Contact E-Mail Address: angela.horvath@medunigraz.at

Introduction: Poor quality of sleep has detrimental effects on job performance, accident rates and health risks, with a potential link to the gut microbiome composition. First pilot trials have indicated beneficial effects of probiotic modulation of the microbiome on quality of sleep.

Aims & Methods: We conducted a randomized, double-blind, placebo-controlled trial testing the effects of a probiotic intervention on quality of sleep, quality of life and intestinal microbiome.

In total, 130 volunteers with impaired quality of sleep ($PSQI>5$) were included in the study. They were randomized in a 1:1 ratio to a 28-day intervention with either a multispecies probiotic (Omnibiotic-Stress Repair) or a placebo. Participants completed validated questionnaires to estimate quality of sleep (PSQI), quality of life (SF12, GIQLI) and perceived stress (PSQ20) before, during and after the intervention. Furthermore, stool samples for 16S rRNA gene sequencing were collected before and after the intervention. Ninety-four participants finished the study and could be included in the analysis.

Results: The 50 participants (88.6% female, 41.2 ± 10.6 years old) analysed in the probiotic group and 44 participants (88.0% female, 40.1 ± 10.7 years old) in the placebo group were well comparable at baseline, including the initial PSQI-score (10.1 ± 2.7 vs. 10.5 ± 2.6). After two weeks of intervention, both groups showed a comparable improvement in their PSQI-scores. After four weeks of intervention, the improvement of the PSQI score was significantly more pronounced in the probiotic group compared to the placebo group (6.8 ± 2.9 vs. 7.7 ± 3.1 ; $p=0.036$), mainly due to improved sleep efficiency and latency. The intervention did not influence quality of life or perceived stress. Ingested bacteria were partially recovered in the microbiome, causing a slight shift in beta diversity in the probiotic group, while alpha diversity and the overall composition of the microbiome remained unaffected.

Conclusion: In conclusion, the intervention with a multispecies probiotic was able to improve quality of sleep of participants with poor quality of sleep beyond an observable placebo-effect. Participants reported falling asleep more quickly and spending less time awake in bed. This well-powered RCT confirms that the probiotic modulation of the intestinal microbiome can be effective in alleviating sleep disturbances.

Disclosure: VS received research funding and speaker honoraria from Institut Allergosan (Graz, Austria) and Winlove Probiotics (Amsterdam, The Netherlands).

PP0340

THE IMPACT OF NUTRITIONAL SUPPLEMENTATION ON CLINICAL ACTIVITY, QUALITY OF LIFE AND DISABILITY OF PATIENTS WITH IBD: A BRAZILIAN MULTICENTER LONGITUDINAL STUDY

M. Amorim Lopes¹, R. Nunes Yoshio Yoshihara¹, N. Salvador Castelhana¹, L. Ferreira Pereira¹, L.J. de Pinho Morais¹, E. Zucari Nogueira², J. Baima³, J.M. Parente⁴, R. Parra⁵, S. Jankiel Miszputen⁶, L. Yukie Sassaki¹
¹São Paulo State University, Medical School - Department of Internal Medicine, Botucatu, Brazil, ²São Paulo State University, Institute of Biosciences, Botucatu, Brazil, ³UNESP Botucatu / Uninove Bauru, Botucatu, Brazil, ⁴Universidade Federal do Piauí - Centro de Ciências da Saúde, Terezina, Brazil, ⁵HC Ribeirão Preto, Ribeirão Preto, Brazil, ⁶EPM UNIFESP, São Paulo, Brazil

Contact E-Mail Address: ma.lopes@unesp.br

Introduction: Inflammatory Bowel Diseases (IBD), including Crohn's Disease (CD) and Ulcerative Colitis (UC), pose significant global health challenges. Nutrient deficiencies and malnutrition are common in both forms of the disease. Dietary supplementation with TGF- β has been suggested to enhance patients' nutritional status, quality of life, and improvement of the symptoms. However, comprehensive evaluations of its clinical impact are needed.

Aims & Methods: This study aims to assess the efficacy of nutritional supplementation in improving clinical outcomes, nutritional status, quality of life, fatigue, disability, and body image among IBD patients.

Methods: Multicenter longitudinal study, enrolling 42 IBD patients in clinical activity and/or at nutritional risk. Patients received the nutritional supplement enriched with TGF- β and underwent assessments before supplementation (M0), at 30 days (M30), and at 60 days (M60) of supplement use. Clinical parameters, disease activity (Harvey-Bradshaw score for CD and partial Mayo score for UC), nutritional evaluation, body composition, presence of fatigue, anxiety and depression, disability, and body image were evaluated. Statistical analyses included descriptive statistics and ANOVA ($p < 0.05$).

Results: 42 patients were included: 30 (71%) with CD and 12 (29%) with UC; 48% women, age of 35.1 ± 15.65 years. Among CD patients, 30% were in remission, 16.67% had mild, 43.33% moderate, and 10% severe activity. According to Montreal classification, 36.67% presented ileocolonic disease, 36.67% fistulizing behavior, 26.67% stenosing behavior, 33.33% perianal disease. For UC patients, 41.67% had mild and 58.33% moderate activity; 41.67% presented pancolitis. All patients presented malnutrition or nutritional risk at enrollment. Significant improvements were observed in HBI score comparing M0 (7.97 ± 5.70) vs M30 (4.61 ± 3.16) vs M60 (3.27 ± 1.75), $p = 0.0055$. There was also an improvement of the number of bowel movements (5.45 ± 4.65 vs 2.90 ± 2.02 vs 2.65 ± 1.55). Nutritional assessment revealed a significant increase in brachial circumference (24.23 ± 3.68 vs 25.37 ± 3.51 vs 26.03 ± 4.10 , $p = 0.0182$). Fatigue decreased (40.58 ± 14.07 vs 33.12 ± 15.72 vs 30.38 ± 14.88 , $p = 0.0293$), as well as disability (51.14 ± 25.34 vs 36 ± 20.89 vs 30.33 ± 22.64 , $p = 0.0032$). It was observed an improvement of IBD score (135.08 ± 38.88 vs 145.20 ± 48.27 vs 152.71 ± 58.96 ; $p = 0.3737$) and body image (10.78 ± 7.37 vs 9.68 ± 8.42 vs 5.57 ± 6.04 ; $p = 0.1395$), with no significance.

Conclusion: Nutritional supplementation demonstrated notable improvements in clinical and nutritional parameters, as well as reduction in fatigue and disability, underscoring its potential as an adjunctive therapy for IBD management

Disclosure: Nothing to disclose.

PP0341

PREVALENCE OF FOOD ALLERGY AMONG JORDANIAN CHILDREN

E. Altamimi¹, N. Yousef², R. Nimer², M. Abdelraheem²

¹Jordan University of Science and Technology, Pediatrics, Irbid, Jordan, ²Jordan University of Science and Technology, Faculty of Medicine, Irbid, Jordan

Contact E-Mail Address: eyadtamimi@gmail.com

Introduction: Food allergy, characterized by an immune reaction to proteins in food, presents a significant global health challenge, especially among children. It is a growing concern worldwide, impacting over 10% of the general population. Epidemiological studies suggest a rising prevalence of food allergy, with estimates indicating that approximately 1 in 10 adults and 1 in 12 children are affected.

Aims & Methods: Our aim was to assess the prevalence of food allergies among schoolchildren aged 5 to 14 years in central and northern Jordan. We conducted a randomized cross-sectional online questionnaire among schoolchildren aged 5 to 14 in central and northern Jordan. A total of 1629 parents completed the questionnaire, providing information on their children's demographic details, feeding history, food allergy occurrences, as well as atopic history for both the child and their family.

Results: The prevalence of parent-reported food allergy was 11.5% (95% CI = 10-13%). Among these cases, 10.1% (95% CI = 8.6-11.7%) were identified as having convincing food allergies, while 5.7% (95% CI = 4.5-6.8%) were diagnosed by a physician. The most common allergens reported were eggs (17.8%), cow's milk (15.8%), peanuts (14.5%), and strawberries (13.8%). A majority (67.1%) reported having a single allergen, while 15.8% reported two allergens, and 17.2% reported more than two allergens.

Among the participants, Food allergy prevalence was higher among children with coexisting atopic diseases and those with a family history of allergies. Regional variations in prevalence were observed, with urban areas showing higher rates.

Conclusion: This study sheds light on the prevalence of food allergy among schoolchildren in Jordan, emphasizing the importance of considering convincing food allergy alongside parent-reported data. The findings underscore the significant burden of food allergy and its association with other atopic conditions, highlighting the need for comprehensive management strategies and further research to understand underlying factors.

References:

1. Sampson, H. A. (1999). Food allergy. Part 1: Immunopathogenesis and clinical disorders. *The Journal of Allergy and Clinical Immunology*, 103(5), 717-728. [https://doi.org/10.1016/s0091-6749\(99\)70411-2](https://doi.org/10.1016/s0091-6749(99)70411-2)
2. Sampson, H. A., Aceves, S., Bock, S. A., James, J., Jones, S., Lang, D., Nadeau, K., Nowak-Węgrzyn, A., Oppenheimer, J., Perry, T. T., Randolph, C., Sicherer, S. H., Simon, R. A., Vickery, B. P., Wood, R., Sampson, H. A., Randolph, C., Bernstein, D., Blessing-Moore, J., . . . Wood, R. (2014). Food allergy: A practice parameter update—2014. *The Journal of Allergy and Clinical Immunology*, 134(5), 1016-1025.e43. <https://doi.org/10.1016/j.jaci.2014.05.013>
3. Renz, H., Allen, K. J., Sicherer, S. H., Sampson, H. A., Lack, G., Beyer, K., & Oettgen, H. C. (2018). Food allergy. *Nature Reviews Disease Primers*, 4(1). <https://doi.org/10.1038/nrdp.2017.98>
4. Branum, A. M., & Lukacs, S. L. (2009). Food allergy among children in the United States. *Pediatrics*, 124(6), 1549-1555. <https://doi.org/10.1542/peds.2009-1210>

Disclosure: Nothing to disclose.

PP0342

SARCOPENIA RELATED FUNCTIONAL STRAINS AND EXPLORE THEIR MECHANISMS BASED ON GERM-FREE ANIMALS

Y. Bo¹, Q. Chen², H. Tian³¹School of Medicine, Tongji University, Department of Colorectal Disease, Tenth People's Hospital of Tongji University, Shanghai, China, ²Shanghai Tenth People's Hospital, Shanghai, China,³School of Medicine, Tongji University, Department, Shanghai, China**Contact E-Mail Address:** docyangbo@126.com**Introduction:** Sarcopenia is a progressive, systemic skeletal muscle disease associated with aging that severely affects the quality of life and overall health of older adults. Emerging research demonstrates a strong association between the onset of sarcopenia and gut microbiota.**Aims & Methods:** 16 out of 30 sarcopenia patients who showed significant skeletal muscle improvement after fecal microbiota transplantation (FMT) were selected and validated by metagenomic, cultured and animal experiments.**Results:** Our clinical observations show a marked improvement in sarcopenia symptoms among older patients post FMT, leading to a notable rise in muscle mass ($P < 0.05$). To delve deeper into this occurrence, we conducted metagenomic sequencing of patient fecal samples pre- and post-treatment. FMT distinctly modified the intestinal microbiota composition. Utilizing germ-free animal models and culturomics, we identified Roseburia inulinivorans as a potentially beneficial strain for the alleviation of sarcopenia. Further experimental validation displayed that Roseburia inulinivorans escalated MyoG and MyoD expression ($P < 0.05$), augmented muscle mass ($P < 0.01$) and grip strength ($P < 0.01$) in mice by boosting branched-chain amino acid metabolism within the host, diminishing sarcopenia symptoms in the process.**Conclusion:** These outcomes not only validate the intestinal microbiota-sarcopenia relationship but also introduce novel insights and strategies for sarcopenia management.**References:** [1] Tournadre A, Vial G, Capel F, Soubrier M, Boirie Y. Sarcopenia. Joint Bone Spine. 2019. 86(3): 309-314.

[2] DeJong EN, Surette MG, Bowdish D. The Gut Microbiota and Unhealthy Aging: Disentangling Cause from Consequence. Cell Host Microbe. 2020. 28(2): 180-189.

[3] Wang T. Searching for the link between inflammaging and sarcopenia. Ageing Res Rev. 2022. 77: 101611.

[4] Hanna BS, Wang G, Galván-Peña S, et al. The gut microbiota promotes distal tissue regeneration via ROR γ + regulatory T cell emissaries. Immunity. 2023. 56(4): 829-846.e8.

[5] Chen YM, Wei L, Chiu YS, et al. Lactobacillus plantarum TWK10 Supplementation Improves Exercise Performance and Increases Muscle Mass in Mice. Nutrients. 2016. 8(4): 205.

[6] Lee MC, Hsu YJ, Ho HH, et al. Lactobacillus salivarius Subspecies salicinius SA-03 is a New Probiotic Capable of Enhancing Exercise Performance and Decreasing Fatigue. Microorganisms. 2020. 8(4): 545.

[7] Liu X, Wu J, Tang J, et al. Prevotella copri alleviates sarcopenia via attenuating muscle mass loss and function decline. J Cachexia Sarcopenia Muscle. 2023. 14(5): 2275-2288.

[8] Chen LH, Chang SS, Chang HY, et al. Probiotic supplementation attenuates age-related sarcopenia via the gut-muscle axis in SAMP8 mice. J Cachexia Sarcopenia Muscle. 2022. 13(1): 515-531.

Disclosure: Nothing to disclose.

PP0343

EXPLORING THE RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND NON-ALCOHOLIC FATTY LIVER DISEASE IN INFLAMMATORY BOWEL DISEASE: A CROSS-SECTIONAL ANALYSIS

N. Castelhana¹, M. Amorim Lopes², E. Zucari Nogueira¹, R. Fedatto Beraldo¹, E. Oliveira³, G. Herrerias¹, D. Salate Biagioni Vulcano¹, J. Baima⁴, W. Barbosa¹, L. Yukie Sasaki¹¹Universidade Estadual Paulista "Júlio de Mesquita Filho" UNESP -FACULDADE DE MEDICINA DE BOTUCATU, Botucatu, Brazil, ²São Paulo State University, Botucatu, Brazil, ³Universidade Estadual Paulista Júlio De Mesquita Filho / Faculdade De Medicina/ Departamento De Clínica Médica, Botucatu, Brazil, ⁴UNESP BOTUCATU / UNINOVE BAURU, Botucatu, Brazil**Contact E-Mail Address:** nutri.nacastelhana@gmail.com**Introduction:** Inflammatory Bowel Disease (IBD), encompassing Crohn's Disease (CD) and Ulcerative Colitis (UC), shares chronic and inflammatory characteristics with Non-Alcoholic Fatty Liver Disease (NAFLD). While their precise pathogenesis remains unclear, emerging evidence implicates dysbiosis and metabolic changes. This study aims to investigate the association between IBD and NAFLD, focusing on metabolic syndrome and its nutritional implications**Aims & Methods:** Objective: To evaluate the nutritional status and body composition in IBD patients, comparing groups with and without NAFLD, and identifying the associated factors.

Methods: A cross-sectional study was conducted, assessing clinical data, metabolic syndrome presence, nutritional status, and biochemical markers. Patients were categorized into IBD+NAFLD and IBD-only groups based on hepatic ultrasound findings. Statistical analysis included descriptive statistics and logistic regression.

Results: 127 patients were included, comprising 58 CD and 69 UC, with a mean age of 45.56 years. Most patients were female and did not engage in physical activity. Patients were mostly in clinical remission and endoscopic activity. 58 patients (45.67%) had hepatic steatosis on ultrasound, forming the IBD+NAFLD group. The IBD+NAFLD group had higher BMI, fat mass, and all circumference values, Table 1, as well as a higher prevalence of hypertension ($p=0.0446$) and dyslipidemia ($p=0.0377$). It is noteworthy that, although most of these patients were classified as overweight by BMI, considering anthropometric data, most IBD+NAFLD patients were classified as eutrophic. 86.21% of patients in the IBD+NAFLD group met the criteria for MAFLD. No difference was observed regarding medication in use. Regarding biochemical tests, the IBD+NAFLD group had higher values of hematocrit ($p=0.0023$), liver enzymes (AST, $p=0.0141$ and ALT, $p<0.0001$), fasting glucose ($p=0.0107$), glycated hemoglobin ($p=0.0146$), basal insulin ($p=0.0003$), and triglycerides ($p=0.0001$), with lower HDL cholesterol ($p=0.0101$)**Conclusion:** The study highlights a significant association between nutritional status and NAFLD in IBD patients. Those categorized as eutrophic had a higher prevalence of hepatic steatosis, potentially linked to dietary factors.**References:** Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Alimentary pharmacology & therapeutics. 2011;34(3):274-285./ Silva A.F; Schieferdecker M.H; Amarante M. B. Ingestão alimentar em pacientes com doença inflamatória intestinal ABCD, arq. bras. cir. dig. 24 (3) • Set 2011/ Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015;313(22):2263-73**Disclosure:** Nothing to disclose.

PP0344

WITHDRAWN

PP0345

CAN DIETARY PATTERNS AND DIET QUALITY BE ASSOCIATED WITH DISEASE ACTIVITY?

L.J. Koppelman¹, C.L. Stevens², I. Barth², R.J. Jacobs³, A.E. Van Der Meulen - De Jong¹, M.J. Campmans-Kuijpers²
¹Leiden University Medical Centre, Gastroenterology and Hepatology, Leiden, Netherlands, ²University Medical Centre Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ³Alrijne Hospital, Gastroenterology and Hepatology, Leiderdorp, Netherlands

Contact E-Mail Address: l.j.m.koppelman@lumc.nl

Introduction: Inflammatory bowel disease (IBD) is characterised by a relapsing-remitting disease course, known to be influenced by dietary factors. Therefore, this study aims to examine the relationship between dietary patterns and diet quality with disease activity in IBD patients.

Aims & Methods: From a one-year study of IBD patients from two Dutch hospitals, a cross-sectional analysis of the baseline data was conducted. The GINQ-FFQ¹, an IBD-specific food frequency questionnaire was used to assess dietary intake. Consumed foods were categorised into 26 food groups and analysed for dietary patterns using principal component analysis (PCA)². The Dietary Inflammatory Index (DII), a dietary quality score reflecting inflammatory potential, was calculated according to Shivappa et al.³, using 28 of the 45 components. Patients were categorised by sex, disease type (Crohn's Disease (CD) or ulcerative colitis (UC)), and biochemical disease activity (remission: CRP ≤ 5 mg/L and/or FCP ≤ 150 µg/g). Mann-Withey U and T-tests were performed to assess differences in dietary patterns and diet quality between patient groups.

Results: A total of 177 patients (52% female, 55.4% CD, median age 50 years) correctly filled out the GINQ-FFQ. Three dietary patterns were identified: a western diet, a flexitarian diet, and a convenience diet. The western diet was high in bread, meat and poultry, pastries and biscuits, cold meats, potatoes and root vegetables, sugar and sweets, sweet sauces, and cheese. It was low in nuts and seeds, vegetables, soups, and fruit. The flexitarian diet consisted of many savoury sauces, eggs, vegetables, potatoes and root vegetables, fats and oils, soups, herbs and spices, savoury snacks and crisps, fish, legumes, and grain products and thickeners. Lastly, the convenience diet was high in grain products and thickeners, composite dishes, non-alcoholic drinks, and meat and poultry, but low in fats and oils, cold meats, alcoholic drinks, and cheese. No differences in consumption of these dietary patterns were observed between patients with active (n=40) and remitted disease (n=137) (p=0.779, p=0.087, p=0.212, respectively). Females adhered less to Western (p=0.001) and convenience food patterns (p=0.009) compared to males. UC patients favoured a flexitarian diet more than CD patients (p=0.030). No differences in DII scores were found (p=0.802). Patients in biochemical remission consumed more alcohol (p=0.04) compared to those with active biochemical disease.

Conclusion: This analysis found no direct association between dietary patterns or dietary inflammatory potential and disease activity. However, patients in remission consumed more alcohol, and a trend towards a flexitarian diet was observed in those with active disease. The full study will follow these patients for a year to assess potential changes in diet and disease activity.

References: ¹ Peters, V., Alizadeh, B. Z., de Vries, J. H., Dijkstra, G., & Campmans-Kuijpers, M. J. (2019). Nutritional assessment in inflammatory bowel disease (IBD)—development of the Groningen IBD Nutritional Questionnaires (GINQ). *Nutrients*, 11(11), 2739.

² Zhao, J., Li, Z., Gao, Q., Zhao, H., Chen, S., Huang, L., ... & Wang, T. (2021). A review of statistical methods for dietary pattern analysis. *Nutrition journal*, 20, 1-18.

³ Shivappa, N., Steck, S. E., Hurley, T. G., Hussey, J. R., & Hébert, J. R. (2014). Designing and developing a literature-derived, population-based dietary inflammatory index. *Public health nutrition*, 17(8), 1689-1696.

Disclosure: AEvdMdJ received research grants from Nestle, Norgine, Cablon, Galapagos, and ZonMw, including speaker's fees from, Tramedico, Janssen Pharmaceuticals, Takeda, Galapagos, Vedanta, Ferring, and AbbVie. MJECK received speaking fees from Janssen Pharmaceuticals and Takeda. These are not related to this work. All other authors have no conflicts of interest to declare.

PP0346

IMPACT OF ANAL FISSURE ON QUALITY OF LIFE AND THE EFFECTIVENESS OF HIGH-FIBER DIET IN TREATMENT

R. Saidani¹, D. Cherif², H. Yacoub², H. Dabbebi², H. Hassine², H. Kchir², N. Maamouri²

¹La Rabta Hospital, Bizerte, Tunisia, ²La Rabta Hospital, Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: raouia.saidani@etudiant-fmt.utm.tn

Introduction: Anal fissures are painful benign conditions that significantly impact patients' quality of life (QoL).

Aims & Methods: This study aimed to evaluate the QoL of patients with anal fissures and assess the effectiveness of a high-fiber diet in treatment. A prospective cross-sectional study was conducted over 4 months (September-December 2023) on patients with anal fissures. QoL was assessed using the Hemo/Fiss Burden score and the newly validated REALISE Score. The REALISE Score measures pain severity, post-defecatory pain, analgesic use, bleeding frequency, and impact on QoL.

Results: 62 patients were included, with a female predominance (sex ratio: 1/2). The average age was 54.3 years. Both scores revealed significant impairments in QoL across all domains, including physical discomfort, psychological distress, and sexual dysfunction. A strong correlation was found between the Hemo/Fiss and REALISE scores (r: 0.71; p <10-4), indicating the validity of the REALISE Score for QoL assessment.

Treatment and Effectiveness: All patients were advised to adopt a high-fiber diet, which resulted in healing in 73% of cases within 4 weeks. This improvement is likely due to the softening of stool and facilitation of regular bowel movements, which reduces pain and discomfort associated with anal fissures.

Additionally, the high-fiber diet significantly improved QoL scores compared to those who did not take fiber (p=0.039). Bleeding and pain at defecation were significantly reduced during six weeks of high fiber diet associated to medical treatment compared to those using medical treatment only (p=0.041).

Conclusion: This study demonstrates the significant impact of anal fissures on QoL and highlights the effectiveness of a high-fiber diet in promoting healing and improving QoL. The REALISE Score offers a valuable tool for assessing the severity of anal fissures and monitoring treatment progress.

Disclosure: Nothing to disclose.

PP0347

NON-CELIAC GLUTEN/WHEAT SENSITIVITY: GUT MICROBIOME AS A DIAGNOSTIC TOOL AND THERAPEUTIC TARGET

A. Costanzini¹, M. Punčochář², L. Lungaro¹, F. Manza¹, F. Armanini², F. Pinto², F. Asnicar², E. Boschetti³, A. Seidita⁴, P. Mansueto⁴, A. Carroccio⁴, A. Calabrò⁵, D. Cavalieri⁶, R. Ciccocioppo⁷, F. Zingone⁸, G. Barbara^{9,10}, V. Stanghellini^{9,10}, U. Volta⁹, N. Segata², G. Caio¹, R. De Giorgio¹

¹University of Ferrara, Department of Translational Medicine, Ferrara, Italy, ²University of Trento, Department of Cellular, Computational and Integrative Biology, Trento, Italy, ³University of Bologna, Department of Biomedical and NeuroMotor Sciences, Bologna, Italy, ⁴University of Palermo, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine, and Medical Specialties (PROMISE), Internal Medicine Unit, Palermo, Italy, ⁵University of Florence, Department of Biomedical Experimental and Clinical Sciences "Mario Serio", Florence, Italy, ⁶University of Florence, Department of Biology, Sesto Fiorentino, Italy, ⁷University of Verona, Department of Medicine, Verona, Italy, ⁸University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ⁹University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ¹⁰IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Contact E-Mail Address: anna.costanzini90@gmail.com

Introduction: Non-celiac gluten/wheat sensitivity (NCG/WS) is a clinical condition in which gluten/wheat ingestion evokes, while withdrawal ameliorates or reverts gastrointestinal (GI) and extra-GI symptoms. The pathogenetic mechanisms of NCG/WS are poorly understood and no diagnostic biomarker is so far available. NCG/WS diagnosis is established by excluding celiac disease (CD) and wheat allergy (WA), evaluating response to a gluten-free diet (GFD) and the effects of gluten reintroduction. Initial evidence suggests a central role played by the gut microbiota in NCG/WS. **Aims & Methods:** This study aimed to identify: i) microbiota species valid as biomarkers for rapid and non-invasive NCG/WS diagnosis; ii) the effects of GFD on microbiota in NCG/WS. Subjects with a clinical suspect of either NCG/WS or CD and healthy volunteers (Ctrl) were enrolled while on a free diet. A thorough work-up (including clinical, endoscopic, allergologic and serological evaluations) was applied to diagnose NCG/WS or CD while excluding WA. Instructions for GFD were provided to all participants. Stool samples for gut microbiome were obtained from NCG/WS and CD before (t0) and after 3, 7, 30 and 200 days of GFD (t1, t2, t3, t4). Stool samples from Ctrl were obtained at t0, t1, t2, and t3. The presence and severity of GI (GI Symptom Rating scale) and extra-GI symptoms of NCG/WS were recorded at each time point (t0-t4). NCG/WS diagnosis was confirmed in participants with a 30% improvement in symptom scores in t3 vs. t0. Metagenome from stools was shotgun-sequenced. Data were processed and microbiome profiled with MetaPhlAn v.4.1 (Jun.23). Alpha-diversity (Shannon index, SI), beta-diversity and relative abundances were computed. Principal coordinates analysis was performed (Bray-Curtis dissimilarity test) and groups were compared (PERMANOVA test). Differences in SI at t0 among cohorts were assessed (Mann-Whitney U-test). Species present at any time point in at least 10 subjects were assessed. Candidate biomarkers were validated in newly diagnosed NCG/WS and CD cohorts. Species varying relative abundance during the GFD were identified (linear mixed model and Friedman's ANOVA). P-values were combined with the harmonic mean and corrected for multiple testing (Benjamini-Hochberg method, q-value).

Results: Twenty-eight NCG/WS (F, 37±16 yrs), 11 CD (9 F, 32±15 yrs) and 37 Ctrl (25 F, 33±14 yrs) were enrolled. Alpha-diversity at t0 was comparable (p>0.19) in NCG/WS (SI=4.0), CD (SI=3.7) and Ctrl (SI=4.1), whereas beta-di-

versity was different among groups (p=0.026). A total of 507 species were identified. The candidate biomarker *Clostridiaceae bacterium* (SGB47672) showed lower abundance in NCG/WS vs. Ctrl (q<0.2), data confirmed in validation cohorts (172 NCG/WS, 243 CD). Alpha-diversity was preserved (p>0.05) in NCG/WS and CD up to t4 and in Ctrl (t3) in GFD, whereas concerning changes in relative abundance (q<0.2; p<0.05) we identified a reduction of *Bifidobacterium longum* (SGB17248).

Conclusion: We showed that NCG/WS exhibits a peculiar metagenomic signature with *C. bacterium* (SGB47672) being a potential biomarker for NCG/WS diagnosis. Our study suggests that the use of probiotic supplements can help to restore *B. longum* (SGB17248) deficiency during GFD. Beyond integrating GFD treatment, probiotics containing *Bifidobacteria* can positively contribute by exerting anti-inflammatory and protective effects on the intestinal epithelial barrier in NCG/WS.

References: Volta U, De Giorgio R, Caio G, Uhde M, Manfredini R, Alaedini A. Nonceliac Wheat Sensitivity: An Immune-Mediated Condition with Systemic Manifestations. *Gastroenterol Clin North Am.* 2019 Mar;48(1):165-182

Beghini F, McIver LJ, Blanco-Míguez A, Dubois L, Asnicar F, Maharjan S, Mailyan A, Manghi P, Scholz M, Thomas AM, Valles-Colomer M, Weingart G, Zhang Y, Zolfo M, Huttenhower C, Franzosa EA, Segata N. Integrating taxonomic, functional, and strain-level profiling of diverse microbial communities with bioBakery 3. *Elife.* 2021 May 4;10:e65088.

Yao S, Zhao Z, Wang W, Liu X. *Bifidobacterium Longum*: Protection against Inflammatory Bowel Disease. *J Immunol Res.* 2021 Jul 23;2021:8030297.

Disclosure: Nothing to disclose.

PP0348

DIET AND EARLY-ONSET COLORECTAL CANCER: VALIDATION OF A NOVEL AD HOC DESIGNED FOOD FREQUENCY QUESTIONNAIRE

M. Puzzono¹, S. Sieri², V. Pala², A. Mannucci¹, G. Artuso³, G.M. Cavestro¹

¹Gastroenterology and Gastrointestinal Endoscopy Unit, Vita-Salute San Raffaele University, IRCCS San Raffaele Scientific Institute, Milan, Italy, ²Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Italy, ³Vita-Salute San Raffaele University, Milan, Italy

Contact E-Mail Address: cavestro.giuliamartina@hsr.it

Introduction: The incidence of early-onset colorectal cancer (eoCRC), defined as colorectal cancer occurring in young adults under the age of 50, is increasing globally. Questionable eoCRCs' exogenous risk factors are represented by diet and lifestyle, even though a scant literature is available to date. The DEMETRA study is being conducted to assess diet and lifestyle as potential risk factors for eoCRC in various European and non-European countries with populations characterized by large variations in dietary/drinking habits and eoCRC incidence.

Aims & Methods: Therefore, our aims were to (i) develop a unique and shared semi-quantitative food frequency questionnaire (SQFFQ) able to accurately describe dietary and drinking habits of eoCRCs and healthy age-matched controls of different countries at global level that will be involved in the DEMETRA study; (ii) validate the SQFFQ.

We designed an ad-hoc, shared, online SQFFQ to investigate the usual consumption of 329 foods over the past year. These foods were classified in groups and subgroups using the same criteria as the EPIC Italy study [1]. In addition to frequency of consumption, the tool investigates the portions habitually consumed using validated photographs, household measures, and standard units, as well as types of seasoning and methods of cooking and storage. A special software was then developed to analyze responses and link them to food composition tables in order to provide a nutritional

breakdown of individual and collective diets. The SQFFQ was then validated for repeatability by administering it twice, 3 weeks apart, to a sample of 30 young adults under 50 years (mean age 35.1 y $\pm$ sd 7.71; 63,3% females, 33,3% males, 3% preferred not to answer). To evaluate repeatability, the measurement error for each food group was estimated as the percentage change between the estimates of food consumption for the same individual. Afterwards, the agreement between the two measurements for each food group was measured with Cohen's kappa coefficient.

Results: For 40 out of 65 food groups, the difference between the two SQFFQs was less than 20%. The greatest percentage differences were found, as expected, for food groups with sporadic consumption (snacks, barbecue sauces, ketchup, mayonnaise) or consumed in minimal quantities (spices). Agreement levels, represented by the calculation of Cohen's kappa coefficient, were as follows: 12 food groups showed fair/sufficient agreement (Cohen's kappa 20-40), 23 foods exhibited good/moderate agreement (Cohen's kappa >40-60), and 22 food groups demonstrated high substantial agreement (Cohen's kappa >60). Insufficient agreement, with Cohen's Kappa values < 0.21, was observed for only three food groups (snacks, sauces, mayonnaises).

Conclusion: The ad hoc designed SQFFQ provides a reasonably repeatable measure of dietary intake and can be used to assess the dietary and drinking habits of volunteers in this age group. Indeed, most staple foods in the Italian diet, including pasta, fruit, vegetables, legumes, eggs, meat, coffee, and tea, are well estimated by the SQFFQ. However, as yet described in literature, challenges persist in estimating the consumption of foods assumed sporadically (such as snacks) or in small quantities such as spices. Definitive conclusions will be drawn after the completion of the external validation, in which the SQFFQ will be validated against the gold standard, represented by the completion of a 4-day food diary followed by a dietary recall.

References: 1. Pala V, Sieri S, Palli D, Salvini S, Berrino F, Bellegotti M, et al. Diet in the Italian EPIC cohorts: presentation of data and methodological issues. *Tumori*. 2003;89: 594–607.

Disclosure: Nothing to disclose.

PP0349

PREVALENCE AND IMPACT OF SARCOPENIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: A PROSPECTIVE COHORT STUDY

S. Dermine¹, F. Adam Hassan², A. Nuzzo³, A. Mohamed Gouse², L. Billiauws², J. Bourdille², F. Joly⁴

¹Beaujon Hospital, Gastroenterology, Clichy la Garenne, France, ²Beaujon Hospital, Clichy la Garenne, France, ³Beaujon Hospital, Intestinal Stroke Center unit, Department of Gastroenterology, IBD, Intestinal Failure, Clichy la Garenne, France, ⁴Beaujon Hospital Service de Gastroenterologie, Gastroenterology, Clichy, France

Contact E-Mail Address: solene.dermine@gmail.com

Introduction: Sarcopenia is associated with increased morbidity and mortality in IBD. The main objective of this study was to prospectively evaluate sarcopenia by combining morphological and functional criteria in an outpatient IBD population.

Aims & Methods: In a prospective cohort study, we included all IBD patients admitted to the Day Hospital (DH) of our department between March 1st and 31st, 2023. Patients with short bowel syndrome were not included. Muscle mass was assessed using a Bodystat[®]1500MDD dual-frequency impedance meter, and muscle function was assessed by measuring handgrip strength, Carym[®] digital dynamometer. Pre-sarcopenia was defined by a handgrip measurement < 16 to 26, and myopenia was defined by an appendicular muscle mass index (AMMI) < 5.5 to 7 kg/m² or a fat-free mass index (FFMI) < 15 to 17 in women or men. Sarcopenia was defined by the

association of pre-sarcopenia and myopenia. Patients were followed-up at 6 months to measure a composite criterion of disease activity combining one of the factors: FC > 250 µg/g, endoscopic activity, therapeutic change, hospitalization, or IBD-related surgery.

Results: In total, 60 patients were included, median age 37 years (IQR 28-54), 55% women, with CD (52%) or UC (48%) diagnosed 9 years (4-17) ago, mostly in remission (67%, n=40). Patients with CD had ileocolic (48%), ileal (35%), or colonic (16%) involvement. Patients with UC had E1 (7%), E2 (41%), or E3 (52%) involvement. A history of digestive surgery linked to IBD was noted in 30% of cases. The biologics administered were infliximab (61%), vedolizumab (25%), or ustekinumab (14%). The BMI was 24 (21-27) and serum albumin was 41 g/l (39-44). The prevalence of sarcopenia, pre-sarcopenia and myopenia was 10%, 11% and 20%, respectively. Sarcopenic patients were significantly older (59 vs. 36 years, p=0.01), with older disease (20 vs. 8 years, p=0.003), and associated joint damage (40% vs. 2%, p=0.002) and tended to involve CD more frequently (80 vs. 49%, p=0.36). There was no significant difference between biologics, BMI or albuminemia in sarcopenic patients, but vitamin D levels tended to be lower (15 vs. 43, p=0.27). Myopenia was significantly associated with a history of surgery (67 vs. 21%, p=0.004), a lower BMI (21 vs. 24, p=0.001) and a more active disease at M6 according to the composite criterion (50 vs. 21%, p=0.04 after adjustment for age, sex, and disease activity at baseline). Myopenia indices were strongly correlated with handgrip values (r=0.7, p<0.001).

Conclusion: In a prospective study of Day Hospital IBD patients, sarcopenia was identified by impedanceometry in 11% and myopenia in 20% of cases, and associated with an increase in morbidity.

Disclosure: No conflict of interest.

PP0350

DIETARY BELIEFS AND HABITS IN INFLAMMATORY BOWEL DISEASES: A CROSS-SECTIONAL STUDY

R. Saidani¹, D. Cherif², H. Dabbebi³, H. Yacoub³, H. Kchir², N. Maamouri²

¹La Rabta Hospital, Gastroenterology B, Bizerte, Tunisia,

²La Rabta Hospital, Gastroenterology B, Tunis, Tunisia, ³La Rabta Hospital, Tunis, Tunisia

Contact E-Mail Address: raouia.saidani@etudiant-fmt.utm.tn

Introduction: Inflammatory bowel diseases (IBD) are characterized by recurrent flares and periods of remission. Dietary modifications are commonly made by patients with IBD to manage their symptoms. However, there is no single dietary recommendation for all patients with IBD and little is known about the impact of diet on these patients.

Aims & Methods: This study aimed to identify patients' beliefs, attitudes, and behaviors regarding diet in the management of symptoms and flares in patients with IBD, and to assess the impact on their social life.

Methods: This was a cross-sectional, single-center study involving 50 patients with IBD who were followed up in our department. All patients completed a semi-structured questionnaire.

Results: The majority of patients were male (56%) and had Crohn's disease (84%). Four main themes emerged from the analysis: beliefs about the role of diet in disease onset and flares, attempts to control symptoms through diet, changes in appetite during and outside of flares, and the impact of dietary beliefs on social life. Fifty-six percent (n=28) of patients believed that their diet had triggered their disease, while 84% (n=42) believed that diet could trigger flares. Seventy percent of patients identified specific foods as triggers. Participants described a process of trial and error, identifying foods that worsened their symptoms and others that helped them feel better. Twenty-four percent of patients reported that

avoiding fiber improved their symptoms during flares. Two patients used diet as their primary treatment for IBD, but 96% of patients considered diet to be complementary to prescribed medication. Eighty-eight percent of respondents reported having received dietary advice at some point. The majority of patients (68%, $n = 34$) reported that their disease had changed their enjoyment of food. Appetite was lower during flares than during remission.

Only 8% of patients followed a normal diet during flares. Dietary beliefs and behaviors had an impact on social life for 56% of patients. Avoiding eating out was reported by 56% of patients and not sharing meals with others was reported by 44% of patients.

Conclusion: Our findings confirm those of previous studies that patients with IBD perceive that certain foods can trigger their disease or symptoms, and dietary control is one of the ways they choose to manage their IBD symptoms. We also noted that patients used a personalized approach to diet, combining experience and knowledge.

Disclosure: No conflict of interest.

PP0351

INCIDENCE AND RISK PREDICTION SCORE OF REFEEDING SYNDROME IN HOSPITALIZED PATIENTS ADMITTED IN A PUBLIC TERTIARY HOSPITAL: A PROSPECTIVE, ANALYTICAL SINGLE CENTER STUDY

J.L. Gargaritano¹, M. Malazarte¹, K. Batocoy¹

¹Vicente Sotto Memorial Medical Center, Internal Medicine - Section of Gastroenterology, Cebu, Philippines

Contact E-Mail Address: janelouegargaritanomd@gmail.com

Introduction: Among critically ill older patients who are hospitalized, malnutrition is prevalent and is also considered a risk factor to develop refeeding syndrome (RFS). There is not enough data on the incidence of refeeding syndrome among them.

This study was conducted to identify the prevalence, severity and risk factors of refeeding syndrome among malnourished hospitalized patients.

Aims & Methods: In this prospective, analytical study conducted in Vicente Sotto Memorial Medical Center in Cebu, Philippines from October 2022 to December 2023, 217 patients were evaluated for malnutrition and risk for developing refeeding syndrome. Malnutrition assessment was conducted using Nutrition Risk Screening 2002 (NRS-2002) through bedside patient interview. The criteria for refeeding syndrome (RFS) were based on the consensus recommendations of the American Society for Parenteral and Enteral Nutrition (ASPEN) for RFS.

Data on electrolyte levels and daily caloric and intake of protein were taken within five days post resumption of nutrition. Significant risk factors in predicting refeeding syndrome were analyzed using Chi-square testing and Pearson rho correlations then subjected to a binary logistic regression to ascertain the effect size.

Results: Among 217 patients, 70 (32%) were at risk for RFS and assessed to have severe nutrition risk with an NRS 2002 score of at least 4 via bedside interview. Refeeding syndrome occurred in 14 patients (20%). Patients with RFS were older (54.71 ± 18.20) than those who were not diagnosed with RFS (50.91 ± 15.77). The total protein (g/day) and total caloric intake of patients who had RFS were significantly lower ($41.25\text{g/day} \pm 12.88$ and $884.64\text{ kcal/day} \pm 559.25$, respectively) than those who did not develop RFS ($51.20\text{ g/day} \pm 11.02$ and $1275.59\text{ kcal/day} \pm 295.77$, respectively).

Serum albumin (2.59 ± 0.27) and electrolyte levels, particularly, serum phosphorus (1.66 ± 0.29), magnesium (1.96 ± 0.36) and potassium (3.13 ± 0.43) were lower among the RFS patients than the non-RFS group. RFS diagnosis was associated with higher incidence of arrhythmia (50% vs 21%), use of vasopressors (64% vs 32%), ventilatory support (71% vs 23%) and mortality (64.29% vs 21.43%) compared to patients who did not have re-

feeding syndrome. Predictors of RFS include lower serum magnesium and potassium levels within 5 days of feeding initiation, lower total protein delivered and lower serum albumin level.

Conclusion: Among patients referred to the Section of Gastroenterology and Nutrition Medicine in Vicente Sotto Memorial Medical Center, Cebu City, Philippines, the incidence of refeeding syndrome (RFS) among malnourished patients is 20%. Refeeding syndrome is associated with high morbidity (arrhythmia incidence, use of ventilatory support and vasopressors) and mortality. Parameters such as malnutrition, low total protein intake, low serum electrolyte levels (serum magnesium, serum potassium, serum phosphorus) and low serum albumin were identified to predict the development of refeeding syndrome, with high accuracy, sensitivity, and specificity. However, despite the high morbidity and mortality associated in RFS, most clinicians lack awareness in identifying and managing this syndrome. Clinicians should be able to identify patients at risk to reduce its occurrence.

References: 1. Indraspati A. et al, "Prevention and Management of Refeeding Syndrome," The Indonesian Journal of Gastroenterology, 2016
2. Rio, A. et al, "Occurrence of Refeeding Syndrome in Adults Started on Artificial Nutrition Support: Prospective Cohort Study," British Medical Journal, 2013

3. Mustofa, N. et al, "Refeeding Syndrome: Frequency of Hypophosphatemia and other Electrolyte Abnormalities Experience from a Private Tertiary Care Hospital in the Philippines," Journal of Parenteral and Enteral Nutrition, January 2017

4. Brown, C. et al, "Predictors of Hypophosphatemia during Refeeding of Patients with Severe Anorexia Nervosa," International Journal of Eating Disorders, 2015

5. Mehanna H. et al, "Refeeding Syndrome: What it is, and how to prevent and treat it," British Medical Journal, 2008

6. Camp M, "Severe hypophosphatemia in hospitalized patients." Minerals and Electrolyte Metabolism, 1990

7. Marik PE et al, "Refeeding hypophosphatemia in critically ill patients in an intensive care unit: A Prospective Study," Archives of Surgery 1996

8. Olthof, L. E., Koekkoek, W. A. C. K., van Setten, C., Kars, J. C. N., van Blokland, D., & van Zanten, A. R. H. "Impact of caloric intake in critically ill patients with, and without, refeeding syndrome: A retrospective study." Clinical Nutrition, 2017 doi:10.1016/j.clnu.2017.08.001

Disclosure: Nothing to disclose.

PP0352

A RETROSPECTIVE EXAMINATION OF RISK FACTORS FOR CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN HOME PARENTERAL NUTRITION PATIENTS FROM A QUEENSLAND TERTIARY HOSPITAL

P. Hoey^{1,2}, D. Roche^{1,2}, P. Chapman³, V. Kaushik¹, S. Llewellyn⁴, N. Adris¹

¹Royal Brisbane and Women's Hospital, Department of Gastroenterology and Hepatology, Brisbane, Australia, ²University of Queensland, Faculty of Medicine, Brisbane, Australia, ³Royal Brisbane and Women's Hospital, Department of Infectious Disease, Brisbane, Australia, ⁴QIMR Berghofer Medical Research Institute, Brisbane, Australia

Contact E-Mail Address: phoey@contexto.com.au

Introduction: A central line-associated bloodstream infection (CLABSI) is a common and potentially life-threatening complication for patients with intestinal failure (IF) receiving home parenteral nutrition (HPN). In uncomplicated infections, The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines advocate for central venous access (CVC) salvage for venous access preservation (1).

Existing knowledge regarding the risk factors of HPN-related CLABSIs have been extrapolated from European and North American studies (2-4), and the effects of tropical climates and its potentially higher support requirements on the incidence of infection has not yet been studied.

Aims & Methods: We sought to analyse the risk factors of developing HPN-related CLABSI, and assess CLABSI management, in a large Australian state with a highly dispersed population. A retrospective observational cohort study was conducted on 34 adult patients receiving HPN via a central venous catheter (CVC) at a Queensland tertiary referral centre, between 2016 and 2023. CLABSI was defined according to the criteria of the Australian Commission on Safety and Quality in Health Care (5). Patient charts were reviewed, and a univariate cox regression analysis model was used to identify predictors of CLABSI in the first CVC during the study period. Kaplan-Meier analysis was employed to build survival curves of time to CLABSI, and log-rank tests analysed survival between patient and CVC characteristics.

Results: Nineteen patients had ≥ 1 CLABSI(s) episode, accounting for a total of 39 episodes. Patients with ≥ 1 CLABSI(s) used regular opioids more than those who did not develop CLABSI ($p=0.016$) but did not differ by age, gender, body mass index, geography, aetiology of intestinal failure or catheter weeks. Fourteen patients (41%, $n=14/34$) developed a CLABSI in their first CVC. No patient or line characteristics, including geographical remoteness and tropical climate, were found to be predictive of CLABSI in their first CVC. The overall infection rate was 1.02 per 1000 catheter days. Most CLABSIs were caused by Enterobacterales (22%, $n=12/55$), followed by coagulase-negative Staphylococcus (18%, $n=10/55$). Administration of empiric antimicrobials within the standardised 3-hour sepsis timeframe was inadequate (50%, $n=14/28$), with only 25% ($n=7/28$) providing adequate cover of causative pathogens. The median time to effective antibiotic therapy was 22.7 hours (IQR 4.8-29.8). There were 3 CVC salvages (8%, $n=3/39$), all of which were successful.

Conclusion: In this cohort of patients, regular opioid use was associated with an increased risk of developing CLABSI which is consistent with international studies (2-4). We also found a low CVC salvage rate in our cohort, representing potential missed opportunities for venous access preservation. Based on our findings, an empiric antimicrobial regime of vancomycin, cefepime and caspofungin for all HPN-related CLABSI cases would be expected to be effective for 84.6%. We recommend that Australian IF units with a similar antimicrobial distribution and resistance pattern adopt this regime.

References:

1. Pironi L, Boeykens K, Bozzetti F, Joly F, Klek S, Lal S, et al. ESPEN guideline on home parenteral nutrition. Clin Nutr. 2020;39(6):1645-66.
2. Gompelman M, Causevic E, Bleeker-Rovers CP, Wanten GJA. Catheter-related bloodstream infection management in patients receiving home parenteral nutrition: An observational cohort study. Clin. Nutr. ESPEN. 2022;50:155-61.
3. Adgey C, Raine T, Lawrence H, Sharkey LM, Woodward JM, Massey DCO. ADWE-10 Risk factors for line infections in a cambridge HPN cohort. Gut. 2018;67(1):A7.
4. Ashley B, Paul C, Trevor RS, Jeremy MDN, Simon L. Diagnosis and management of catheter-related bloodstream infections in patients on home parenteral nutrition. Frontline Gastroenterol. 2020;11(1):48.
5. Australian Commission on Safety and Quality in Health Care. Surveillance of Central Line-Associated Bloodstream Infection. [Internet]. Sydney: Australian Commission on Safety and Quality in Health Care; July 2019. Available from: <https://www.safetyandquality.gov.au/sites/default/files/2019-08/implementation-guide-for-surveillance-of-central-line-associated-blood-stream-infection-2019-final.pdf>.

Disclosure: Nothing to disclose.

PP0353

EVALUATION OF MALNUTRITION RISK WITH THE MUST SCORE AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE

O. M'solli¹, S. Emna¹, W. Dahmani¹, A. Hammami¹, N. Elleuch¹, M. Ksiao¹

¹Sahloul University Hospital, Gastroenterology, Sousse, Tunisia

Contact E-Mail Address: Oussamamsolli7@gmail.com

Introduction: Inflammatory bowel disease patients are at risk of malnutrition due to the nature of the disease, the drugs used, and some dietary restrictions. Several screening tools are available, including the MUST score: the Malnutrition Universal Screening Tool, a simple and an easy-to-use tool.

Aims & Methods: The aim of our study was to assess the frequency of malnutrition risk using MUST score in IBD patients.

We conducted a prospective study that included 142 patients with IBD. All patients with IBD completed a self-administered nutrition screening assessment using the MUST score. Patients with a MUST score of ≥ 2 were concluded as high-risk for malnutrition.

Results: A total of 142 IBD patients were studied over 2 month period. We enrolled a total of 116 (82,1%) patients from outpatient and 26 (18,3%) from inpatient. Risk of malnutrition was identified in 21,1 % of patients according to MUST score. Number of hospitalized patients with malnutrition risk was significantly higher than the outpatient ones (84,6% vs 6.9 %, $p<0.01$). The frequency of high malnutrition risk was 36,8 % in ulcerative colitis (UC) patients and 15,4% in Crohn's disease (CD) patients ($p=0.006$). A high MUST score was strongly associated with an elevated Harvey Bradshaw Index score ($p<0.01$) for patients with Crohn's disease, and with Partial Mayo Index scores ($p<0.01$) for patients with ulcerative colitis.

Conclusion: In our study, we found that the risk of malnutrition was high in both CD and UC patients, especially inpatients, and it correlates to the disease activity. Considering the effect of malnutrition on the prognosis of the disease, IBD patients should be evaluated in terms of malnutrition risk both during their routine follow-ups and during hospitalizations.

Disclosure: Nothing to disclose.

Poster
IBD

IBD

09:00-18:00 / Poster Exhibition

PP0354

THE IMPACT OF ETASIMOD ON THE TRANSCRIPTOME IN COLON BIOPSIES USING RNA-SEQ: DATA FROM ELEVATE UC 52 AND ELEVATE UC 12 PHASE 3 CLINICAL TRIALS

B. Siegmund^{1,2}, R.D Ryan³, C.M. Crosby⁴, M.T. Abreu⁵, S. Vermeire⁶, I. Dotan^{7,8}, K.M Rabinowitz^{7,9}, X. Guo¹⁰, HK. Komori¹¹, M. Goetsch¹², J.C. Woolcott¹⁰, S. Danese¹³
¹Charité – Universitätsmedizin Berlin, Med. Klinik für Gastroenterologie, Infektiologie, Rheumatologie, Berlin, Germany, ²Freie Universität Berlin, Humboldt-Universität zu Berlin, Campus Benjamin Franklin, Berlin, Germany, ³Pfizer Inc, South San Francisco, United States of America, ⁴Pfizer Inc, La Jolla, San Diego, United States of America, ⁵University of Miami Miller School of Medicine, Department of Medicine, Division of Gastroenterology, Crohn's and Colitis Center, Miami, United States of America, ⁶University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁷Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ⁸Tel Aviv University, Faculty of Medical and Health Sciences, Tel Aviv, Israel, ⁹Felsenstein Medical Research Centre, Medical and Health Sciences, Tel Aviv, Israel, ¹⁰Pfizer Inc, Collegeville, United States of America, ¹¹Formerly Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, United States of America, ¹²Pfizer AG, Zürich, Switzerland, ¹³IRCCS San Raffaele Hospital and Vita Salute San Raffaele University, Division of Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: britta.siegmund@charite.de

Introduction: Etrasimod is an oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC). S1P₁ receptor modulation is believed to reversibly sequester lymphocytes¹; its impact on UC intestinal tissue is unknown.

Aims & Methods: We characterised the impact of etrasimod in inflamed colonic biopsy tissue using ribonucleic acid sequencing (RNA-seq) to examine transcriptional-level impacts on disease, in terms of mucosal barrier inflammatory pathways and immune cell populations. In ELEVATE UC 52 (NCT03945188) and ELEVATE UC 12 (NCT03996369), patients (pts) aged 16–80 years with moderately to severely active UC were randomised 2:1 to etrasimod 2 mg QD or placebo (PBO).

Etrasimod treatment effects were characterised by RNA-seq at Week 12 vs baseline (both trials), and in responders achieving clinical remission vs nonresponders. CytoPro (CytoReason) was used for colon-specific cell type deconvolution analysis and single sample Geneset Enrichment Analysis was used for pathway analysis.

Results: At baseline in ELEVATE UC 52/ELEVATE UC 12, colon biopsy samples were available for 245/166 pts receiving etrasimod and 114/84 pts receiving PBO. There were significant reductions in T cell subsets (CD4+, CD8+, helper [Th]1 and Th17), plasma/mature B cell subsets and innate immune cell subsets (monocytes, macrophages, dendritic cells and natural killer cells) in the colon of pts receiving etrasimod (false discovery rate [FDR] < 0.05); significant changes were not seen among pts receiving PBO. There were also reductions in inflammatory fibroblasts and increases in

epithelial cells in the colon of pts receiving etrasimod but not PBO. The change in immune cell populations for responders vs nonresponders at Week 12 was similar to that for etrasimod Week 12 vs baseline. At Week 12, several inflammatory pathways were reduced in responders vs nonresponders to etrasimod; IL-17 signalling was among the most affected (both trials). Nonimmune pathways related to mucosal healing were significantly increased in Week 12 responders.

Conclusion: Decreases in activated immune cell subset and inflammatory signalling pathway changes in responders to etrasimod suggest reductions in local inflammation may contribute to remission and mucosal healing. RNA-seq with cell type deconvolution and pathway analysis contributes to the understanding of etrasimod's mechanism of action.

References: 1. Scott FL et al. *Br J Pharmacol* 2016; 173: 1778–1792.

Disclosure: BS has received lecture fees from AbbVie, CED Service GmbH, Chiesi, Dr. Falk, Forga Software, Galapagos, IBD Passport, Janssen, Materia Prima, Pfizer Inc and Lilly; consultancy fees from AbbVie, Arena Pharma, Boehringer Ingelheim, BMS, Celgene, CT-Scout, Endpoint Health, Galapagos, Gilead Sciences, Janssen, Landos, Lilly, Pfizer Inc, PredictImmune and PsiCro. RDR is an employee of and holds stock options with Pfizer Inc. CMC, XG and JCW are employees and shareholders of Pfizer Inc. MTA has received consultancy fees from AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celisus, Eli Lilly, Gilead, Janssen, Microba Life Sciences, Pfizer, Prometheus, Prometheus Bioscience, Takeda and UCB Biopharma. SV has received lecture/speaker fees from AbbVie, Dr. Falk Pharma, Ferring, Galapagos, Hospira, Janssen, MSD, Takeda and Tillotts; consultancy/advisory fees from AbbVie, Abolentis Pharma, Alimentiv, Arena, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Dr. Falk Pharma, Ferring, Galapagos, Genentech/Roche, Gilead, Hospira, Imidomics, Janssen, Johnson & Johnson, Lilly, Materia Prima, MiroBio, Morphic, MrMHealth, MSD, Mundipharma, Pfizer Inc, Prodigest, Progenity, Prometheus, Roberts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma AG and Zealand Pharma; grant/research support from AbbVie, MSD, Pfizer Inc, Galapagos, Janssen and Takeda. ID has received consultancy fees, research grants or honoraria from Abbott, AbbVie, Altman, Arena, Athos, Cambridge Healthcare, Celgene/BMS, Celltrion, Falk Pharma, DSM, Ferring, Food Industries Organisation, Galapagos, Genentech/Roche, Gilead, GSK, Hospital for Sick Children, Integra Holdings, Iterative Scopes, Janssen, Mediahuset, Medscape, Neopharm, Nestle, Peer voice, Pfizer, Rafa Laboratories, Sangamo, Sublimity, Takeda, Wilbio. KMR has received grant/research support from Bristol Myers Squibb. HKK has received consultancy fees from Kinevant Sciences and is an employee/shareholder for Uniquity Bio. MG is an employee and shareholder of Pfizer AG. SD has received lecture/speaker fees from AbbVie, Amgen, Ferring Pharmaceuticals Inc, Gilead, Janssen, Mylan, Pfizer and Takeda; consultancy/advisory fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Gilead Sciences, Hospira, Janssen, Johnson & Johnson, MSD, Mundipharma, Pfizer Inc, Roche, Sandoz, Takeda, TiGenix, UCB, and Vifor; holds directorship/ownership for Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele.

CHARACTERISATION OF THE EFFECT OF ETASIMOD ON PERIPHERAL BLOOD MONONUCLEAR CELLS: DATA FROM ELEVATE UC 52 AND ELEVATE UC 12 PHASE 3 CLINICAL TRIALS

B. Siegmund^{1,2}, C.M. Crosby⁴, R.D Ryan³, M.T. Abreu⁵, S. Vermeire⁶, I. Dotan^{7,1}, K.M Rabinowitz^{7,9}, X. Guo¹⁰, H.K. Komori¹¹, M. Goetsch¹², J.C. Woolcott¹⁰, S. Danese¹³

¹Charité – Universitätsmedizin Berlin, Med. Klinik für Gastroenterologie, Infektiologie, Rheumatologie, Berlin, Germany, ²Freie Universität Berlin, Humboldt-Universität zu Berlin, Campus Benjamin Franklin, Berlin, Germany, ³Pfizer Inc, La Jolla, San Diego, United States of America, ⁴Pfizer Inc, South San Francisco, United States of America, ⁵University of Miami Miller School of Medicine, Department of Medicine, Division of Gastroenterology, Crohn's and Colitis Center, Miami, United States of America, ⁶University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁷Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ⁸Tel Aviv University, Faculty of Medical and Health Sciences, Tel Aviv, Israel, ⁹Felsentstein Medical Research Centre, Medical and Health Sciences, Tel Aviv, Israel, ¹⁰Pfizer Inc, Collegeville, United States of America, ¹¹Formerly Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, United States of America, ¹²Pfizer AG, Zürich, Switzerland, ¹³IRCCS San Raffaele Hospital and Vita Salute San Raffaele University, Division of Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: britta.siegmund@charite.de

Introduction: Etrasimod is an oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC). S1P receptor modulation reversibly sequesters specific lymphocyte subsets in lymph nodes.¹

Aims & Methods: This study aimed to better understand immune cell type selectivity of etrasimod using in-depth immunophenotyping of peripheral blood mononuclear cells (PBMC). In ELEVATE UC 52 (NCT03945188) and ELEVATE UC 12 (NCT03996369), patients (pts) aged 16–80 years with moderately to severely active UC were randomised 2:1 to etrasimod 2 mg QD or placebo (PBO). PBMCs were collected and characterised using flow cytometry and epigenetic immune monitoring by Epiontis ID for baseline and Week 12 assessments (both trials).

Outputs were expressed as mean percent change from baseline (%CFB) of cell frequencies. Statistical tests were performed with t-tests at a nominal significance level of 0.05.

Results: In ELEVATE UC 52 and ELEVATE UC 12, 185 (64.0%) and 120 (50.4%) pts receiving etrasimod 2 mg QD, and 98 (68.1%) and 68 (58.6%) receiving PBO, respectively, were included in the biomarker analysis set. Baseline demographics and disease characteristics were similar to the full analysis set.

Using flow cytometry, in both trials, %CFB reductions were observed in total T and B cells with etrasimod (62.24–72.46% decrease) but not PBO. Among CD4+ T cell subsets, the greatest %CFB reductions with etrasimod were for naïve (Tn) cells. Reductions were also seen in central memory (Tcm), helper (Th)2, regulatory, Th1, Th17 and effector memory (Tem) cells (61.00–87.07% decrease) in both trials.

Similarly, CD8+ Tn and Tcm subsets were reduced (69.33–78.48% decrease) with etrasimod; minimal changes were seen in CD8+ Tem cells. For B cell subsets, memory cells and naïve cells were reduced with etrasimod in both trials (62.45–78.03% decrease). In both trials, minimal changes were observed for natural killer cells. With Epiontis ID, etrasimod induced significant reductions in peripheral CD3+, CD4+, GATA3+, IL17A+, FOXP3+, CCR7+ and LRP5A+ cells vs PBO (both trials; Table).

n, mean CFB, % (SD)	ELEVATE UC 52		ELEVATE UC 12	
	PBO (N = 98)	Etrasimod 2 mg QD (N = 185)	PBO (N = 68)	Etrasimod 2 mg QD (N = 120)
CD3+ (T cells)	28, -1.61 (62.62)	64, -45.05 (52.48)*	25, 7.07 (41.22)	47, -32.57 (50.77)***
CD4+ (CD4 T cells)	28, -1.63 (67.21)	62, -65.29 (31.33)***	25, 11.20 (45.41)	47, -49.51 (41.10)***
GATA3+ (Th2 cells)	27, 0.91 (74.49)	58, -62.56 (33.11)***	25, -3.60 (44.35)	45, -43.15 (39.43)***
IL17A+ (Th17 cells)	28, -4.61 (69.25)	60, -59.85 (35.28)***	25, 3.96 (42.72)	46, -34.43 (48.66)***
FOXP3+ (Treg cells)	27, -2.01 (52.99)	59, -52.40 (37.59)***	24, 3.36 (56.09)	44, -41.86 (38.78)**
CD8B+ (CD8 T cells)	28, -6.53 (52.03)	60, -28.65 (70.59)	25, 10.96 (50.60)	47, -11.67 (65.27)
CCR7+ (LN homing cells)	27, -7.18 (48.44)	61, -56.64 (24.04)***	25, 8.35 (46.89)	46, -47.71 (25.33)***
CXCR3+ (Th1, activated T cells)	28, 5.16 (63.25)	56, 1.92 (105.60)	25, 2.16 (41.96)	46, 28.54 (93.48)
LRP5A+ (B cells)	28, -9.45 (54.26)	62, -59.22 (33.40)***	25, 13.94 (64.45)	47, -44.60 (55.28)***
MVD+ (NK cells)	28, 13.72 (50.83)	62, 39.96 (91.54)	25, 17.79 (31.80)	46, 71.31 (89.23)***

*p < 0.05, **p < 0.01 and ***p < 0.001. Significant differences for etrasimod vs placebo are denoted with asterisks. The p-values were determined with a 2-sided t-test of the null hypothesis that the etrasimod-treated population parameter mean is equal to the PBO-treated population parameter mean. Values shown are for Epiontis ID parameters in PBMC by visit.

%CFB, percent change from baseline; CD, cluster of differentiation; CCR, C-C chemokine receptor; CXCR, C-X-C motif chemokine receptor; GATA, GATA binding protein; FOXP, forkhead box protein; IL, interleukin; LN, lymph node; LRP, low-density lipoprotein receptor-related protein; MVD, mevalonate diphosphate decarboxylase; N, number of patients in cohort; n, number of patients in group; NK, natural killer; PBMC, peripheral blood mononuclear cell; PBO, placebo; QD, once daily; SD, standard deviation; Th, helper T cell; Treg, regulatory T cell; UC, ulcerative colitis.

Table. Epiontis ID PBMC %CFB at Week 12 (biomarker analysis set).

Conclusion: Etrasimod induces selective, pharmacodynamic changes in certain PBMC subsets. Results of cell-type characterisation by flow cytometry and Epiontis ID were complementary.

References: 1. Scott FL et al. Br J Pharmacol 2016; 173: 1778–1792

Disclosure: BS has received lecture fees from AbbVie, CED Service GmbH, Chiesi, Falk, Forga Software, Galapagos, IBD Passport, Janssen, Materia Prima, Pfizer Inc and Lilly; consultancy fees from AbbVie, Arena Pharma, Boehringer Ingelheim, BMS, Celgene, CT-Scout, Endpoint Health, Galpagos, Gilead Sciences, Janssen, Landos, Lilly, Pfizer Inc, PredictImmune and PsiCro. CMC, XG and JCW are employees and shareholders of Pfizer Inc. RDR is an employee of and holds stock options with Pfizer Inc. MTA has received consultancy fees from AbbVie Inc, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celsius, Eli Lilly, Gilead, Janssen, Janssen Biotech Inc, Microba Life Sciences, Pfizer, Prometheus, Prometheus Bioscience, Takeda, and UCB Biopharma. SV has received lecture/speaker fees from AbbVie, Dr. Falk Pharma, Ferring, Galapagos, Hospira, Janssen, MSD, Takeda and Tillotts; consultancy/advisory fees from AbbVie, AbolerIS Pharma, Alimentiv, Arena, AstraZeneca, Avaxia, BMS, Boehringer Ingelheim, Celgene, CVasThera, Dr Falk Pharma, Ferring, Galapagos, Genentech/Roche, Gilead, Hospira, Imidomics, Janssen, Johnson and Johnson, Lilly, Materia Prima, MiroBio, Morphic, MrMHealth, MSD, Mundipharma, Pfizer Inc, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Second Genome, Shire, Surrozen, Takeda, Theravance Biopharma, Tillots Pharma AG and Zealand Pharma; grant/research support from AbbVie, MSD, Pfizer Inc, Galapagos, Janssen and Takeda. ID has received consultancy fees, research grants or honoraria from Abbott, AbbVie, Altman, Arena, Athos, Cambridge Healthcare, Celgene/BMS, Celltrion, Falk Pharma, DSM, Ferring, Food Industries Organisation, Galapagos, Genentech/Roche, Gilead, GSK, Hospital for Sick Children, Integra Holdings, Iterative Scopes, Janssen, Mediaset, Medscape, Neopharm, Nestle, Peer voice, Pfizer, Rafa Laboratories, Sangamo, Sublimity, Takeda and Wilbio. KMR has received grant/research support from Bristol Myers Squibb. HKK has received consultancy fees from Kinevant Sciences and is an employee/ shareholder for Uniquity Bio. MG is an employee and shareholder of Pfizer AG. SD has received lecture/speaker fees from AbbVie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer and Takeda; consultancy/advisory fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Gilead Sciences, Hospira, Janssen, Johnson & Johnson, MSD, Mundipharma, Pfizer Inc, Roche, Sandoz, Takeda, TiGenix, UCB, and Vifor; holds directorship/ownership for Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele.

EVALUATION OF FECAL SHORT-CHAIN FATTY ACIDS CONTENT IN PATIENTS WITH ULCERATIV COLITIS.

M. Stoykevych¹, T. Tarasova¹, I. Klenina¹¹SI "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Department of intestinal diseases, Dnipro, Ukraine**Contact E-Mail Address:** stoykevich.marina@gmail.com

Introduction: It is known that disorders of the intestinal microbiota in patients with ulcerativ colitis (UC) lead to increased intestinal permeability, impaired production and intestinal absorption of short-chain fatty acids (SCFA). The ratio of fecal SCFA is an important indicator of the integrity of the intestinal microbial community. The study of the concentrations of SCFA is a very attractive approach to broadening the understanding of the pathogenesis of UC.

Aims & Methods: To study the content of SCFA in the coprofiltrate of patients depending on the degree of severity of the course of UC.

We included in this study 86 patients with UC with a mean age of 43.2 ± 1.8 years. They were divided according to the Mayo index: 7 milds, 64 moderate and 15 severe. The control group consisted of 7 relatively healthy people. The diagnose UC were established according to generally accepted diagnostic standards in gastroenterology. Determination of SCFA was carried out by the method of chromatographic research. Was determined anaerobic index (AI) - the ratio of the sum of propionic and butyric acids concentrations to the concentration of acetic acid. AI values are used as an indicator of the infrastructure of the microbiocenosis - the ratio of anaerobic and aerobic microorganisms.

Results: The total content of SCFA did not show significant changes in patients with mild and moderate severity of UC (only a moderate tendency to decrease by 1.6 times ($p>0.05$) and 1.8 times ($p>0.05$), respectively), while in severe severity there was a statistically significant decrease by 3.9 times ($p=0.008$) compared to control. Also, in severe UC, this indicator had a pronounced tendency to decrease by 2.4 times ($p>0.05$) and 2.2 times ($p>0.05$), respectively, compared with mild and moderate severity, respectively. In mild and moderate severity of the disease, only a weak tendency to reduce the content of acetic acid in the coprofiltrate of patients by 1.4 times ($p>0.05$) and 1.3 times ($p>0.05$), respectively, and in severe severity - a significant decrease by 1.7 times ($p=0.02$), compared to the control. The content of propionic acid in the experimental samples of patients did not change significantly, there was only a moderate/weak tendency to its decrease by 1.6 times ($p>0.05$), 1.3 times ($p>0.05$) and 1.2 times ($p>0.05$), respectively, for the three severity levels of UC compared to the control. A significant decrease in the content of butyric acid in the coprofiltrate of patients with moderate and severe UC severity was found by 2.1 times ($p=0.049$) and 10.4 times ($p=0.001$), respectively, compared to the control. It is characteristic that in severe UC, the content of butyric acid was significantly reduced by 5.7 times ($p=0.034$) and 5 times ($p=0.022$), respectively, compared with mild and moderate severity of this disease.

IA significantly decreased by 1.5 times ($p=0.028$) and 1.9 times ($p=0.033$) in moderate and severe UC severity compared to the control group.

Thus, in severe UC severity, there was a marked decrease in the total content of FFAs mainly due to a significant decrease in butyric acid and a moderate decrease in acetic acid.

Conclusion: The obtained results showed that changes in SCFA concentrations in patients with UC differed significantly from the control group, what can lead to deterioration of the course and prognosis of UC. Estimation of the ratio of SCFA fractions with the calculation of the anaerobic index may be useful for the diagnosis of violation of the quantitative and qualitative composition of the intestinal microbiota in patients with UC.

References: 1. Parada Venegas D, De la Fuente MK, Landskron G, et al.

Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. *Front Immunol.* 2019;10:277. Published 2019 Mar 11. doi:10.3389/fimmu.2019.00277

2. Shin Y, Han S, Kwon J, et al. Roles of Short-Chain Fatty Acids in Inflammatory Bowel Disease. *Nutrients.* 2023;15(20):4466. Published 2023 Oct 21. doi:10.3390/nu15204466

3. Lee S.H., Kwon J.E., Cho M.L. Immunological pathogenesis of inflammatory bowel disease. *Intestinal Research*, 2018. Vol. 16, №1. P.26-42. doi: 10.5217/ir.2018.16.1.26.

Disclosure: Nothing to disclose.

PP0357

ACCURATE AND ROBUST COLLAGENOUS COLITIS DETECTION IN HISTOLOGICAL IMAGES USING FEATURES EXTRACTED FROM SEGMENTED AREAS BASED ON SUPERPIXELS TOGETHER WITH DEEP LEARNING

V. Kiudelis^{1,2}, R. Petrolis^{3,4}, R. Ramonaitė^{2,1}, D. Jančiauskas⁵, J. Kupčinskas^{1,2}, J. Skiecevičienė², P. Šabanas^{1,2}, A. Kriščiukaitis^{3,4}

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³Lithuanian University of Health Sciences, Department of Physics, Mathematics and Biophysics, Kaunas, Lithuania, ⁴Lithuanian University of Health Sciences, Neuroscience Institute, Kaunas, Lithuania, ⁵Lithuanian University of Health Sciences, Department of Pathology, Kaunas, Lithuania

Contact E-Mail Address: Juozas.Kupcinskas@lsmu.lt

Introduction: Collagenous colitis (CC) is a form of microscopic colitis (MC), the others being lymphocytic colitis (LC), incomplete CC and incomplete LC (1). It is an inflammatory disease of the large bowel that causes chronic watery diarrhoea, abdominal pain, faecal incontinence, nightly defecation, and weight loss, resulting in significantly impaired quality of life (2). Incidence of MC has increased significantly during the past decades in some countries and the main reason for this increase is thought to be an enhanced disease recognition (3). The diagnosis of MC is challenging as it can only be diagnosed upon histological examination of colonic biopsies taken from normal or near normal appearing mucosa (1).

Histological interpretation of biopsies involves subjective evaluation leading to inter-rater variability discrepancies in diagnosis and treatment plan. Deep learning-based assistance system can objectivise diagnostic key feature selection leading to minimisation of inter-rater variability and improvement of diagnostic accuracy.

Aims & Methods:

The aim of this pilot study was to develop an algorithm for robust segmentation of light microscopy images of histological specimen slides (tissue slides) emphasizing key diagnostic features of CC.

Histological specimens were fixed with formalin, embedded in paraffin, cut into 3 µm sections, and stained with haematoxylin and eosin (H&E) for histological examination. Images were taken using OLYMPUS IX71 light microscope (x20 magnification) equipped with Q IMAGING EXI aqua camera at (1392 x 1040 pix.) resolution and 24-bit pixel encoding. Registered image pixel values were normalized in RGB colour space by histogram alignment using empty tissue-less areas using an algorithm described previously (4).

Superpixel technique using Simple Linear Iterative Clustering algorithm (5) was used for initial segmentation of the images. All 1000 superpixels defined in each image were annotated by the expert, indicating ones containing thickened subepithelial collagen layer as the sought class among the others containing the rest of the tissue indicated as normal class. The

feed – forward neural network (implemented in MatLab environment) was trained to classify superpixels using their normalized histogram bin-counts of the pixel values as a feature.

Due to significant inequality in the data set, where the number of sought class superpixels was significantly smaller than the number of the remaining ones, the training set was formed by equalising it to the lowest class case's value (18761). Only randomly selected cases of the bigger class were included in the training set.

Results: The proposed algorithm was tested on images from 5 treatment-naïve patients with newly diagnosed CC. Patients' histological specimens were rated by an expert pathologist and 50 images were chosen (with changes characteristic of CC and without). The classification training process with extracted data set took 0.13 seconds on personal computer with an AMD Ryzen Threadripper 3970X 32-Core, 3.70 GHz processor and 128GB of RAM memory, epochs for training was set to 30 (after tests the model was not improving after 30 epochs) and data shuffling was set to every-epoch. The algorithm showed 0.807 accuracy, 0.801 sensitivity and 0.813 specificity.

Conclusion: The shown ability of deep learning algorithm to classify histology image segments can assist the diagnostic process of CC emphasizing thickened subepithelial collagen layer – the essential diagnostic feature.

References: 1. Miehke S, Guagnozzi D, Zabana Y, Tontini GE, Fiehn AMK, Wildt S, et al. European guidelines on microscopic colitis: United European Gastroenterology (UEG) and European Microscopic Colitis Group (EMCG) statements and recommendations. *United European Gastroenterol J*. 2020;

2. Verhaegh BPM, Münch A, Guagnozzi D, Wildt S, Cebula W, Diac AR, et al. Course of Disease in Patients with Microscopic Colitis: A European Prospective Incident Cohort Study. *J Crohns Colitis*. 2021;15(7):1174–83.

3. Weimers P, Ankersen DV, Lophaven S, Bonderup OK, Münch A, Løkkegaard ECL, et al. Incidence and Prevalence of Microscopic Colitis between 2001 and 2016: A Danish Nationwide Cohort Study. *J Crohns Colitis*. 2021;14(12):1717–23.

4. Petrolis R., Čižas P., Borutaitė V., Kriščiukaitis A. Method of fluorescence imaging for evaluation of membrane potential in cultured neurons using transmembrane voltage sensitive dye. *Biomedical engineering 2011: Proceedings of International Conference*. 14:16–19, 2011.

5. Achanta R, Shaji A, Smith K, Lucchi A, Fua P, Susstrunk S. SLIC Superpixels Compared to State-of-the-art Superpixel Methods. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, Volume 34, Issue 11, pp. 2274–2282, May 2012

Disclosure: Nothing to disclose.

PP0358

A MULTI-OMICS ANALYSIS REMINDS THE RELATIONSHIP AMONG GUT MICROBIOTA, BILE ACID METABOLISM, AND THE DISORDER OF INTESTINAL BARRIER FUNCTION IN CROHN'S DISEASE

J. Jiang¹, L. Chen², Y. Liu¹, W. Chen¹, H. Chen²

¹Southeast University, School of Medicine, Nanjing, China,

²Zhongda Hospital, Southeast University, Department of Gastroenterology, Nanjing, China

Contact E-Mail Address: yc_jjj@126.com

Introduction: Crohn's disease (CD) is a complex chronic intestinal inflammatory disease with unknown etiology¹. Gut microbiota is involved in the bile acid metabolism in the intestine and the regulation of intestinal mucosal immunization to maintain intestinal homeostasis². The histological changes in the intestinal mucosa of CD are closely related to impaired intestinal barrier function^{3–5}. Abnormal gut microbiota and metabolic dis-

orders can destroy the normal intestinal barrier function and intestinal homeostasis, thereby continuously aggravating the inflammatory reactions^{6,7}.

Aims & Methods: To further explore the related factors affecting the incidence and provide essential guidelines for clinical prevention and treatment of CD, the prospective case-control study conducted a multi-omics analysis of gut microbiota, fecal bile acid profiles, serum cytokines and intestinal barrier function in patients with active CD, patients in remission and normal controls.

Results: The study found that CD patients had unique gut microbiota and fecal bile acid profiles compared with normal controls, which were related to the disease activity. The beneficial bacteria represented by Romboutsia were positively correlated with the concentrations of fecal secondary bile acids, while negatively correlated with the concentrations of primary bile acids. When patients were active, their gut-beneficial bacteria decreased, affecting the bile acid metabolism. The variation of CD patients' bile acid profile was increased. The production of secondary bile acids was decreased. The levels of proinflammatory cytokines in peripheral blood were increased, such as FC, ESR, CRP and HBP, with P values all below 0.001. And the CD active group had significantly higher levels of IL-6, IL-8, IL-10 and IL-1 β than those in remission, with P values of <0.001, 0.005, 0.04 and 0.044, respectively. The intestinal physical barrier and mucosal barrier were damaged with disease activity of CD.

Conclusion: The study suggested that the occurrence and development of CD might be caused by the interaction between gut microbiota and the metabolic product bile acid, which leads to the consequence of immune response in the body and the damage to the intestinal barrier.

References: 1. Suau R, Pardina E, Domènech E, Lorén V, Manyé J. The Complex Relationship Between Microbiota, Immune Response and Creeping Fat in Crohn's Disease. *J Crohns Colitis*. 2022;16(3):472–89.

2. Leonardi I, Gao IH, Lin WY, et al. Mucosal fungi promote gut barrier function and social behavior via Type 17 immunity. *Cell*. 2022;185(5):831–46.e14.

3. Leibovitz H, Lee SH, Raygoza Garay JA, et al. Immune response and barrier dysfunction-related proteomic signatures in preclinical phase of Crohn's disease highlight earliest events of pathogenesis. *Gut*. 2023;72(8):1462–71.

4. Rath T, Atreya R, Bodenschatz J, et al. Intestinal Barrier Healing Is Superior to Endoscopic and Histologic Remission for Predicting Major Adverse Outcomes in Inflammatory Bowel Disease: The Prospective ERIca Trial. *Gastroenterology*. 2023;164(2):241–55.

5. Maddipati SC, Kolachala VL, Venkateswaran S, et al. Assessing Cellular and Transcriptional Diversity of Ileal Mucosa Among Treatment-Naïve and Treated Crohn's Disease. *Inflamm Bowel Dis*. 2023;29(2):274–85.

6. Caparrós E, Wiest R, Scharl M, et al. Dysbiotic microbiota interactions in Crohn's disease. *Gut Microbes*. 2021;13(1):1949096.

7. Leibovitz H, Lee SH, Xue M, et al. Altered Gut Microbiome Composition and Function Are Associated With Gut Barrier Dysfunction in Healthy Relatives of Patients With Crohn's Disease. *Gastroenterology*. 2022;163(5):1364–76.e10.

Disclosure: All authors declared no potential conflicts of interest with respect to the study.

PP0359

WITHDRAWN

PP0360

THE CONTACT SYSTEM - AN INFLAMMATORY CONTRIBUTOR IN ULCERATIVE COLITIS

M.L. Halling^{1,2,3,4}, S.T.D. Pham⁴, M. Wrenfeldt^{3,5}, Y. Palarasah^{2,4}, T. Knudsen^{1,3}

¹Esbjerg and Grindsted Hospital, Department of Internal Medicine, Section of Gastroenterology, Esbjerg, Denmark,

²Esbjerg and Grindsted Hospital, Department of Clinical Biochemistry, Unit for Thrombosis Research, Esbjerg, Denmark, ³University of Southern Denmark, Department of Regional Health Research, Odense, Denmark, ⁴University of Southern Denmark, Department of Cancer and Inflammation Research, Institute for Molecular Medicine, Odense, Denmark, ⁵Esbjerg and Grindsted Hospital, Department of Pathology, Esbjerg, Denmark

Contact E-Mail Address: morten.halling@rsyd.dk

Introduction: Previous research indicate the contact system (CAS) is associated with ulcerative colitis (UC). The activation of coagulation factor XII leads to the activation of plasma kallikrein. Plasma kallikrein generates bradykinin and cleaved H-kininogen (CHK) by cleaving H-kininogen. Bradykinin induces inflammation.

C1 inhibitor (C1-INH) is the most important regulator of CAS, while activated factor XII and plasma kallikrein are the accelerators. Interestingly, experimental colitis can be induced and alleviated in UC animal models by respectively activating and inhibiting CAS¹⁻³.

Increased activity of CAS in plasma and colonic tissue was detected in patients with active disease^{4,5}.

Human studies are still limited. We, therefore, aimed to characterise CAS in patients with active UC by employing our unique panel of CAS assays.

Aims & Methods: We included adults with active UC at the Section of Gastroenterology, Esbjerg and Grindsted Hospital, Denmark from May 2021 to June 2023. Inclusion criteria were: Patient reported outcome 2 (PRO2) score ≥ 1 , Mayo endoscopic subscore (MES) ≥ 1 and negative stool culture. The PRO2 considers stool frequency and passage of blood.

Pregnancy and conditions influencing CAS or inflammation was prohibited. Patient were not allowed to use oral contraceptives, non-steroid anti-inflammatory drugs, systemic corticosteroids or anticoagulants. Controls were gender-matched blood donors recruited at the Unit for Thrombosis Research, Esbjerg and Grindsted Hospital, Denmark from 2019 to 2021. In- and exclusion criteria were the Danish blood donation criteria. We used the Montreal classification, MES, Nancy histological index, PRO2, CRP, and fecal calprotectin to describe the UC activity.

Biochemical assays determined the kallikrein generation and plasma concentrations of coagulation factor XII, prekallikrein, H-kininogen, C1-INH and CHK (a surrogate marker of bradykinin generated by plasma kallikrein).

Results: We included 94 patients and 100 controls. Patients were primarily female (n=53) non-smokers (n=91) with a median age of 43 years and limited comorbidity (n=26). Half of the patients had proctitis. Patients displayed mild to moderate disease with medians: MES 2, Nancy histologic index 2, PRO2 4, CRP 2.5 mg/L and fecal calprotectin 515 mg/kg.

Although, patients and controls generated similar amounts of plasma kallikrein, patients still had higher CHK levels in plasma than controls (1.38 [0.21-3.98] $\mu\text{g/mL}$ vs 0.83 [0.02-2.88] $\mu\text{g/mL}$, $p < 0.0001$). The same applied for C1-INH levels (0.22 [0.14-0.33] g/L vs 0.21 [0.16-0.29] g/L, $p = 0.0340$).

The remaining CAS components were similar in patients and controls. Nor, did CAS correlate to UC extension or severity. Interestingly, CHK remained higher even in patients displaying mild disease (see Table 1).

Patient subgroups	CHK in patients	CHK in controls	p-value
Proctitis, n=50	1.40 [1.13-1.70]	0.83 [0.64-1.16]	<0.0001
Mayo endoscopic subscore 1, n=14	1.35 [1.07-1.61]	0.83 [0.64-1.16]	0.0012
Nancy histological index grade ≤ 1 , n=24	1.29 [0.90-1.56]	0.83 [0.64-1.16]	0.0013
Patient reported outcome 2 score ≤ 2 , n=19	1.33 [0.92-1.61]	0.83 [0.64-1.16]	<0.0001
CRP in plasma ≤ 5 mg/L, n=63	1.40 [1.13-1.61]	0.83 [0.64-1.16]	<0.0001
Fecal calprotectin ≤ 250 mg/kg, n=20	1.45 [1.13-1.76]	0.83 [0.64-1.16]	0.0004

Results are expressed as medians [interquartile range 25-75%]. Significance was tested with the Mann-Whitney U test.

Table 1 Cleaved HK in patients with mild disease vs controls.

Conclusion: This is currently the largest study to profile CAS in patients with UC. By employing unique and novel assays, we can conclude that CAS contributes to active UC as verified by increased plasma levels of CHK and C1-INH in patients. Further, CHK might be useful as a serological marker for distinguishing patients with UC from healthy subjects.

References: 1. Wang B, Yang A, Zhao Z, et al. The Plasma Kallikrein-Kininogen Pathway Is Critical in the Pathogenesis of Colitis in Mice. *Front Immunol* 2018;9:21.

2. Arai Y, Takanashi H, Kitagawa H, et al. Effect of icatibant, a bradykinin B2 receptor antagonist, on the development of experimental ulcerative colitis in mice. *Dig Dis Sci* 1999;44:845-51.

3. Lu F, Fernandes SM, Davis AE, 3rd. The role of the complement and contact systems in the dextran sulfate sodium-induced colitis model: the effect of C1 inhibitor in inflammatory bowel disease. *Am J Physiol Gastrointest Liver Physiol* 2010;298:G878-83.

4. Stadnicki A, Gonciarz M, Niewiarowski TJ, et al. Activation of plasma contact and coagulation systems and neutrophils in the active phase of ulcerative colitis. *Dig Dis Sci* 1997;42:2356-66.

5. Stadnicki A, Pastucha E, Nowaczky G, et al. Immunolocalization and expression of kinin B1R and B2R receptors in human inflammatory bowel disease. *Am J Physiol Gastrointest Liver Physiol* 2005;289:G361-6.

Disclosure: Nothing to disclose.

PP0361

MYENTERIC AND SUBMUCOSAL PLEXITIS AS PREDICTIVE FACTORS FOR POSTOPERATIVE ENDOSCOPIC AND CLINICAL RECCURENCE AFTER SURGERY IN CROHN'S DISEASE

S. Riahi¹, F. Khanchel², M. Sabbah¹, R. Hedhli², I. Helal², R. Jouini², E. Ben Brahim², A. Chadli²

¹Habib Thameur Hospital, Gastroenterology, Tunis, Tunisia,

²Habib Thameur Hospital, Pathology, Tunis, Tunisia

Contact E-Mail Address: Samehsam888@gmail.com

Introduction: Postoperative recurrence (POR) in Crohn's disease (CD) affects nearly half of patients one year after surgery. The identification of histological features, predictive of POR is relevant. Although it has been suggested that the presence of plexitis is associated with an increased risk of POR, it is not yet common practice to look for plexitis during pathological examination. Therefore, the predictive value of myenteric and submucosal plexitis in POR remains unclear.

Aims & Methods: The aim of our work was to evaluate the histopathological and clinical factors associated to POR after bowel resection in CD patients. We conducted a retrospective study using the Database of the Department of Pathology of Habib Thameur hospital (Tunis). Patients with ileocolonic or ileal resection for CD between 2000 and 2020 were included. The proximal resection margin was analyzed to detect the presence of myenteric and/or submucosal plexitis and assess its grade and the inflammatory cells involved. Plexitis was evaluated based on the appearance of the most severely inflamed ganglion or nerve bundle. Endoscopic recurrence was defined as a Rutgeerts score of ≥ 2 during a colonoscopy performed

between the 6th and 12th month after anastomotic surgery. Clinical recurrence was defined as the reappearance of disease-related symptoms, confirmed by endoscopy and imaging.

Results: Seventy patients were included in the study. The mean age was 35 ± 10.7 years and the sex ratio was 1.33. Endoscopic recurrence occurred in 56% of cases. Clinical POR concerned 50% of patients within 62 ± 49.2 months. The time to onset of clinical recurrence was significantly shorter in case of endoscopic recurrence ($p=0.05$). Age > 30 years at the time of surgery increased the rate of endoscopic POR ($p=0.02$) and its severity ($p=0.015$). Endoscopic recurrence was more frequent in cases of a previous bowel resection ($p=0.03$). An ileal resection > 30 cm was associated with clinical POR ($p=0.012$). Ileocolic disease location was associated with a significant increase in clinical POR ($p=0.04$). A macroscopically affected proximal margin was associated with endoscopic ($p=0.017$) and clinical ($p=0.024$) recurrence. Histologic activity at the proximal margin was present in 28% of cases and was associated with endoscopic POR ($p=0.042$). Myenteric plexitis was reported in 49% of cases. Submucosal plexitis was present in 21% of patients.

The presence of myenteric plexitis and its grade did not increase endoscopic ($p=0.28$) and clinical ($p=0.54$) POR. However, plasma cell plexitis was associated with clinical POR ($p=0.043$). The presence of submucosal plexitis and its grade were not significantly related with a higher risk to endoscopic and clinical recurrence ($p=0.94$, $p=0.31$ respectively).

Inflammatory cells involved in submucosal plexitis had no influence on endoscopic and clinical recurrence ($p=0.18$, $p=0.5$ respectively). In multivariate analysis, factors associated with endoscopic POR were age > 30 years at the time of surgery (Odds ratio (OR) = 1.069; 95% CI 1.002 to 1.14; $p=0.044$) and the presence of histologic activity (OR= 4.969; 95% CI 1.175 to 21.01; $p=0.029$). Ileal resection > 30 cm was independently associated with clinical POR (OR= 1.043; 95% CI 1.002 to 1.086; $p=0.04$).

Conclusion: In this present study, histologic activity at proximal margin, age > 30 at surgery and ileal resection > 30 cm were associated with POR. No association was revealed between myenteric/submucosal and POR. Looking for plexitis should be more regular with a common search methodology to better assess its predictive value in POR.

Disclosure: Nothing to disclose.

PP0362

ANALYSIS OF FECAL MICROBIOTA COMPOSITION IN NEWLY DIAGNOSED PATIENTS WITH INFLAMMATORY BOWEL DISEASE BASED ON DISEASE LOCATION

M. Orejudo del Río¹, M.J Gómez², R.M. de Francisco García³, M. Rivero⁴, A. Gutiérrez-Casbas⁵, I. Rodríguez-Lago⁶, L. Fernández-Salazar⁷, D.S. Ceballos Santos⁸, J.M. Benítez Cantero⁹, M. Aguas¹⁰, I. Bastón-Rey¹¹, F. Bermejo¹², M.J. Casanova¹, R. Lorente Poyatos¹³, Y. Ber¹⁴, V. Royo¹⁵, M. Esteve Comas¹⁶, C. Ramírez¹, I. Soletó¹, M. Baldán-Martín¹, F. Sánchez-Cabo², J. P. Gisbert^{*1}, M. Chaparro^{*1}, * co-last authors
¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain, ³Hospital Universitario Central de Asturias, Oviedo, Spain, ⁴Marqués de Valdecilla University Hospital, Santander, Spain, ⁵Hospital General Universitario Alicante, Gastroenterology, Alicante, Spain, ⁶Hospital Universitario de Galdakao, Gastroenterology, Bilbao, Spain, ⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ⁸Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain, ⁹Hospital Universitario Reina Sofía, Gastroenterology, Cordoba, Spain, ¹⁰La Fe University And Politecnico Hospital, Gastroenterology Unit, Valencia, Spain, ¹¹University Hospital of Santiago de Compostela, La Coruña, Spain, ¹²Hospital Universitario de Fuenlabrada, Madrid, Spain, ¹³Hops. General Ciudad Real, Ciudad real, Spain, ¹⁴Hospital San Jorge, Huesca, Spain, ¹⁵Hospital Universitari Son Espases, Palma de Mallorca, Spain, ¹⁶Gastroenterology, Hospital Universitari Mutua Terrassa, Barcelona, Spain

Contact E-Mail Address: macaoorejudo@gmail.com

Introduction: Patients diagnosed with inflammatory bowel disease (IBD) may have damage in different parts of the gut. The development of this disease involves an intricate interaction between a host with genetic susceptibility, environmental factors, an imbalanced immune response, and intestinal microbiota. Several studies have revealed discrepancies in the composition of gut microbiota between IBD patients and healthy individuals, especially concerning microbial diversity and relative abundance of specific bacteria.

Nonetheless, previous research typically involves patients who have undergone immunosuppressive treatment, potentially altering the microbiota and affecting the integrity of study findings.

Aims & Methods: The aim of this study was to elucidate the differences in the microbiota of newly diagnosed patients with Crohn's disease (CD) and ulcerative colitis (UC) compared to healthy controls (HC), based on the location of the affected area. Stool samples were obtained from IBD patients who had not yet initiated treatment for the disease, and from HC. Each sample underwent shotgun metagenomic sequencing, followed by bioinformatic analysis using the Cutadapt, Kraken2, and Bracken programs. Shannon index (α -diversity) and Bray-Curtis dissimilarity (β -diversity) were used as tests of within-species diversity and within-group diversity, respectively.

Results: We included 103 patients with CD, 144 with UC and 49 HC. Patients with CD, which have been classified depending on disease location (ileal, colonic and ileocolonic), showed lower α -diversity compared to HC in each subgroup, showing the lowest index in those with ileocolonic location. In UC patients, divided according to disease extension (proctitis, left-sided colitis and extensive colitis), those with extensive involvement,

exhibited the lowest α -diversity compared to HC and other groups. β -diversity in CD patients revealed the highest differences between the comparisons ileal vs ileocolonic and colonic vs ileocolonic, suggesting that patients with ileocolonic pattern showed a more different microbiota profile compared to the other groups studied; however, there were no differences in UC patients.

Examination of taxonomic abundance revealed a decrease in *Phocaeicola coprocola* and several species of *Adlercreutzia*, and an increase in *Shigella flexneri*, in CD patients, compared to HC. In UC patients, an increase in *Toxoplasma gondii* and *Gemella morbillorum* was observed in all three extension subgroups compared to HC. However, several species of *Adlercreutzia* and *Alistipes* were decreased in patients with extensive colitis compared to HC.

Conclusion: Our data suggest that newly diagnosed CD and UC patients showed relevant differences in the microbiota depending on the location of the disease, with a reduction in beneficial genus such as *Adlercreutzia* and *Alistipes*, and an increase in pathogenic species.

Disclosure: Nothing to disclose.

PP0363

PHYSICAL ACTIVITY SUPPRESSES THE DELETERIOUS EFFECTS OF HIGH-FAT DIET ON INTESTINAL HOMEOSTASIS THROUGH THE ACTIVATION OF AUTOPHAGY

H.T.M. Hoang¹, A. Couvert², A. Duval¹, P. Sauvanet¹, C. Rozotte¹, L. Combaret³, J. Delmas⁴, G. Dalmasso¹, N. Barnich⁵, V. Martin², N. Boisseau², H.T.T. Nguyen⁶

¹University Clermont Auvergne, Microbes, Intestine, Inflammation And Susceptibility Of The Host (M2iSH), Clermont Ferrand, France, ²University Clermont Auvergne, AME2P - Laboratoire des Adaptations Métaboliques à l'Exercice en Conditions

Physiologiques et Pathologiques, Clermont-Ferrand, France, ³University Clermont Auvergne, INRAE, UNH, Unité de Nutrition Humaine, CRNH Auvergne, Clermont-Ferrand, France, France, ⁴CHU Gabriel-Montpied, Department of Bacteriology, Clermont-Ferrand, France, ⁵Université Clermont Auvergne, M2iSH, Clermont-Ferrand, France, ⁶Université Clermont Auvergne, UMR 1071 Inserm, Clermont-Ferrand, France

Physiologiques et Pathologiques, Clermont-Ferrand, France, ³University Clermont Auvergne, INRAE, UNH, Unité de Nutrition Humaine, CRNH Auvergne, Clermont-Ferrand, France, France, ⁴CHU Gabriel-Montpied, Department of Bacteriology, Clermont-Ferrand, France, ⁵Université Clermont Auvergne, M2iSH, Clermont-Ferrand, France, ⁶Université Clermont Auvergne, UMR 1071 Inserm, Clermont-Ferrand, France

Physiologiques et Pathologiques, Clermont-Ferrand, France, ³University Clermont Auvergne, INRAE, UNH, Unité de Nutrition Humaine, CRNH Auvergne, Clermont-Ferrand, France, France, ⁴CHU Gabriel-Montpied, Department of Bacteriology, Clermont-Ferrand, France, ⁵Université Clermont Auvergne, M2iSH, Clermont-Ferrand, France, ⁶Université Clermont Auvergne, UMR 1071 Inserm, Clermont-Ferrand, France

Contact E-Mail Address: hoangthimyanh@hus.edu.vn

Introduction: Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract, with its etiology involving genetic, microbial and environmental factors. Dysregulated autophagy, high-fat (HF) diet and abnormal colonization of adherent-invasive *E. coli* (AIEC) have been identified as risk factors for CD. Physical activity (PA) represents a fundamental intervention that offers significant health benefits and has been associated with a reduced risk of developing various diseases, including CD. Although PA has been shown to induce autophagy in different tissues, exerting beneficial effects for the organism, its impact on autophagy in the intestine and its ability to suppress the deleterious effects of HF diet via the modulation of autophagy have not been investigated.

Aims & Methods: This study aims to:

- (i) explore the influence of PA on the autophagy process in intestinal tissue, and;
- (ii) assess the potential of PA to restore intestinal homeostasis and decrease inflammation caused by HF consumption.

Mice deficient for the autophagy-related gene *Atg16l1* specifically in intestinal epithelial cells (*Atg16l1*^{flax/flax}CreVillin, called by *Atg16l1*^{ΔIEC} mice) or wild-type mice (WT or *Atg16l1*^{flax/flax}) were fed either a control or HF diet for 12 weeks, and then engaged in spontaneous PA on running wheels (active group) or not (sedentary control group) for the same duration.

The travelled distance (km), and the speed (m/min) on the wheels were recorded continuously. At the end of the experiment, total fat mass and fat-free mass were measured with echoMRI. The weight of total mesenteric and epididymal adipose tissues were also determined post-mortem. Levels of autophagy markers were assessed by Western blot and qRT-PCR. Intestinal inflammation was assessed by quantification of fecal lipocalin-2 and intestinal pro-inflammatory cytokine levels.

Results: Under HF diet, both *Atg16l1*^{ΔIEC} and WT mice exhibited substantial weight gain compared to the groups fed the control diet. Spontaneous PA notably attenuated weight gain, particularly in the HF diet-fed groups. Spontaneous PA also diminished the increase in total fat mass and the weight of mesenteric adipose tissue induced by HF consumption, while concurrently augmenting total fat-free mass. HF diet-fed mice exhibited a lower total running distance over the 12 weeks compared to those fed the control diet. Importantly, HF diet consumption led to increased fecal lipocalin-2 level compared to control diet, with a more pronounced effect in *Atg16l1*^{ΔIEC} versus WT mice, and this level was reduced with spontaneous PA. In the absence of PA, HF diet-fed *Atg16l1*^{ΔIEC} mice exhibited increased *E. coli* abundance compared to other mouse groups, and this was not observed in the active groups.

Compared to control diet, HF diet led to dysregulation of expression levels of several autophagy markers and autophagy flux in intestinal tissues, and this was corrected by PA. In particular, there was a positive correlation between the total travelled distance and levels of several autophagy-related mRNAs.

Conclusion: Spontaneous PA can correct the dysregulation of autophagy and mitigate intestinal inflammation induced by the HF diet. This suggests that combining spontaneous PA with other therapeutic interventions may be a valuable strategy for CD patients with dysregulated autophagy.

Disclosure: Nothing to disclose.

PP0364

UNREVEALING NEW POTENTIAL KEY MECHANISMS IMPLICATED IN INFLAMMATORY BOWEL DISEASE BY MULTIOMIC APPROACH

M. Baldan Martín¹, M. Azkargorta², A.M. Aransay³, R. Gil-Redondo⁴, I. Moreno-Indias⁵, I. Iloro², I. Soletto¹, M. Orejudo del Río¹, C. Ramirez¹, A.J. Lucendo⁶, C. Rodríguez Gutiérrez⁷, A. Gutiérrez-Casbas⁸, E. Martín Arranz⁹, L. Bujanda Fernández de Piérola¹⁰, I. Rodríguez-Lago¹¹, R. De Francisco¹², E. Iglesias-Flores¹³, F. Bermejo¹⁴, M. Van Domselaar¹⁵, M.J. García¹⁶, L. Fernández Salazar¹⁷, J. Barrio Andrés¹⁸, X. Calvet¹⁹, L. Torrealba Medina²⁰, I. Bastón-Rey²¹, H. Pallares Manrique²², Y. Ber Nieto²³, E. Leo-Carnerero²⁴, M.J. Casanova¹, F. Casals Seoane¹, J. Mendoza¹, J.A. Moreno-Monteagudo¹, O. Millet⁴, F. Elortza², J. Mato⁴, F.J. Tinahones⁵, M. Chaparro^{*1}, J.P. Gisbert^{*1}, *co-last authors

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Proteomics Platform, CIC bioGUNE, BRTA (Basque Research & Technology Alliance), CIBERehd, Derio, Spain, ³Genome Analysis Platform, CIC bioGUNE, Basque Research and Technology Alliance (BRTA), CIBERehd, Derio, Spain, ⁴Precision Medicine and Metabolism Lab, CIC bioGUNE, Derio, Spain, ⁵Virgen de la Victoria University Hospital, Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y la Nutrición (CIBEROBN), Instituto de Salud Carlos III, Department of Endocrinology and Nutrition, Madrid, Spain, ⁶Hospital General de Tomelloso, Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), CIBERehd, Ciudad Real, Spain, ⁷Hospital Universitario de Navarra, Pamplona, Spain, ⁸Hospital General Universitario Alicante, CIBERehd and Instituto de Investigación Sanitaria y Biomédica de Alicante, Gastroenterology, Alicante, Spain, ⁹Hospital Universitario La Paz and Instituto de Investigación Sanitaria La Paz (IdiPaz) and UAM, Madrid, Spain, ¹⁰Hospital Universitario Donostia and Instituto Bionostia and Universidad de País Vasco (UPV/EHU), San Sebastián, Spain, ¹¹Hospital Universitario de Galdakao, Biocruces Bizkaia HRI, Vizcaya, Spain, ¹²Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ¹³Hospital Universitario Reina Sofía, Digestive, Cordoba, Spain, ¹⁴Hospital Universitario de Fuenlabrada, Madrid, Spain, ¹⁵Hospital Universitario de Torrejón and Universidad Francisco de Vitoria, Madrid, Spain, ¹⁶Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology and Hepatology Unit, Santander, Spain, ¹⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ¹⁸Hospital Universitario Río Hortega, Valladolid, Spain, ¹⁹Consorti Corporació Sanitaria Parc Taulí, CIBERehd, Sabadell, Spain, ²⁰Hospital Universitario Dr. Josep Trueta, Girona, Spain, ²¹Hospital Clínico Universitario de Santiago, Gastroenterology and Hepatology, Santiago de Compostela, Spain, ²²Hospital Juan Ramón Jiménez, Huelva, Spain, ²³Hospital San Jorge, Huesca, Spain, ²⁴Hospital Universitario Virgen del Rocío, Sevilla, Spain

Contact E-Mail Address: mbaldanm@gmail.com

Introduction: Inflammatory bowel diseases (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), are characterised by chronic, relapsing and remitting inflammation of the gastrointestinal tract. Despite significant efforts to understand the pathogenetic mechanisms of IBD, the elucidation of its etiopathology and progression remains incomplete. This study aimed to clarify IBD pathogenesis using a multiomic approach in serum, urine, intestinal tissue and stool samples.

Aims & Methods: We performed a multiomic analysis (transcriptomic, proteomic, metabolomic and metagenomic) in a discovery cohort of 53 patients with active CD, 50 patients with active UC, and 33 healthy controls (HC). Transcriptomic and proteomic analysis of intestinal tissue was performed by RNA-seq and liquid chromatography-mass spectrometry, respectively. Serum and urine samples were used for metabolome study using nuclear magnetic resonance, and metagenomic analysis of stool samples was performed by 16rRNA gene sequencing.

Results: Gene expression profiles showed a detailed transcriptome landscape of intestinal tissue in patients with CD and UC. A total of 4,105 proteins were identified in mucosal biopsies, of which 2,128 were differentially expressed (DE) between CD and HC, 2,715 proteins DE in UC compared with HC, and 1,653 proteins DE between CD and UC. Metabolomic analyses revealed metabolites and pathways related to ketone, amino sugar and methyl histidine metabolism, Warburg effect, and ammonia recycling deregulated in IBD patients. Moreover, metagenomic results indicated that CD and UC differ in their microbial populations according to beta diversity. In comparison to HC, the microbial population in CD was different, and its alpha diversity was significantly lower.

Conclusion: The results showed that some of the identified analytes could play essential roles in the pathogenesis of CD and UC. New potential key mechanisms that could help to understand the information of omics layers that underlies the pathogenesis of IBD have been outlined.

Disclosure: Nothing to disclose.

PP0365

LIVER FIBROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL STUDY FROM AN IBD CENTER

D. Feijó¹, C. Borges Chaves¹, S. Mendes¹, M. Ferreira¹, S. Lopes¹, M. Ferreira¹, F. Portela¹, P. Figueiredo¹

¹ULS Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: diogofeijo96@gmail.com

Introduction: Inflammatory Bowel Disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory condition affecting the gastrointestinal tract. Although primarily associated with intestinal symptoms, IBD has also been linked to various extraintestinal complications, including liver fibrosis (LF). Additionally, metabolic-associated steatotic liver disease (MASLD), a common liver condition driven by metabolic risk factors such as obesity and insulin resistance, could intersect with IBD, given its systemic nature.

While both LF and MASLD are prevalent among the general population, their incidence and associated risk factors in IBD patients remain underexplored. Understanding these liver-related complications is crucial for developing effective screening and management strategies for patients with IBD.

Aims & Methods: We aimed to assess the prevalence of LF and MASLD in IBD patients compared to matched controls. In this cross-sectional, case-control study, we enrolled consecutive IBD patients from an IBD referral center and matched controls from the general population based on age, sex, type 2 diabetes (T2D) status, and body mass index (BMI) in a 1:1 ratio. Liver fibrosis and MASLD were confirmed through shear-wave elastography (SWE) measurements of stiffness and attenuation coefficient. Potential risk factors were analyzed using multivariate logistic regression.

Results: We included 378 participants, comprising 200 IBD patients (106 with CD and 94 with UC) and 178 controls. There were no statistically significant differences regarding distribution by gender, age, T2D status and BMI. The prevalence of LF (SWE ≥ 6.78 kPa) and advanced LF (SWE ≥ 9.15 kPa) was 42.5% and 16.0%, respectively, in IBD patients (48.1% in CD vs. 36.2% in UC; $p=0.088$) and 28.1% and 9.0%, respectively, in the control

group ($p<0.05$). For UC, history of complicated disease (OR 7.5, CI95% 1.2-46.2 $p<0.05$) and multiple hospitalizations due to acute disease (OR 5.6, CI95% 1.3-24.8; $p<0.05$) were significant risk factors. As for CD, previous hospitalizations (OR 9.7, CI95% 1.4-65.8; $p<0.05$) and heavy smoking habits (OR 4.9, CI95% 2.0-12.4; $p<0.001$) were the main risk factors.

Extraintestinal manifestations, higher fecal calprotectin level at the time of liver stiffness measurement and latest endoscopic activity were not associated with presence of LF. MASLD was not significantly different between IBD and control group (42.0% vs. 51.7%, respectively; $p>0.05$). Higher BMI, higher waist circumference, higher abdominal wall thickness and metabolic syndrome were significant risk factors for MASLD ($p<0.001$).

Conclusion: Our case-control study demonstrates that patients with IBD have a higher prevalence of liver fibrosis compared to matched controls, with significant risk factors including a history of complicated disease, multiple hospitalizations, and heavy smoking habits.

Conversely, the prevalence of MASLD does not significantly differ between IBD patients and controls, suggesting that metabolic factors might play a more substantial role in MASLD risk. Given these findings, it is critical for clinicians to implement routine liver fibrosis surveillance in IBD patients, especially in those with identified risk factors. Proactive management strategies aimed at reducing risk factors, such as smoking cessation and minimizing hospitalizations through effective disease management, could mitigate liver fibrosis risk in this population. These insights emphasize the need for integrated care approaches that address both IBD-related complications and associated liver health.

Disclosure: Nothing to disclose.

PP0366

MIRNA EXPRESSION CHANGES IN COLONIC EPITHELIAL CELLS AND THEIR RELEASED EXTRACELLULAR VESICLES IN RESPONSE TO COMMENSAL BACTERIA IN ULCERATIVE COLITIS

R. Steponaitienė¹, R. Inčiūraitė¹, D. Tilindė¹, V. Šaltenienė¹, G. Kiudelis¹, L.V. Jonaitis¹, J. Kupčinskas¹, S. Juzėnas^{1,2}, J. Skiecevičienė¹

¹Lithuanian University of Health Sciences, Kaunas, Lithuania,

²Vilnius University, Vilnius, Lithuania

Contact E-Mail Address: ruta.steponaitiene@lsmu.lt

Introduction: Ulcerative colitis (UC) is an inflammatory bowel disease marked by chronic inflammation of the colon's inner lining. Its pathogenesis involves a multifactorial interplay between genetic and environmental factors, dysregulated immune responses, and alterations in the gut microbiome. MicroRNAs (miRNAs) have emerged as critical regulators of gene expression implicated in UC pathogenesis.

Understanding the differential expression of miRNAs in colonic epithelial cells and their extracellular vesicles (EVs) during bacterial exposure could offer potential insights into the interplay between gut microbiota and epithelial cell-mediated inflammatory responses.

Aims & Methods: The objective of this study was to investigate the expression of UC-associated miRNAs in colonic epithelial cells and their EVs, using UC patients and control subjects-derived colonic epithelial cells co-cultures with *Escherichia coli* and *Phocaeicola vulgatus* bacteria.

Colonic stem cells from healthy controls (HC) ($n=10$) and patients with active UC ($n=10$) were used to generate 3D colonic epithelial organoids, which subsequently served as a cell source for constructing polarized monolayers of colonic epithelial cells. These monolayers were co-cultured with commensal *E. coli* or *P. vulgatus* bacteria for 2 hours, washed, replenished with fresh culture medium, and further incubated for an additional 24 hours. EVs from cell-conditioned media were isolated using precipita-

tion method and characterized by ELISA (CD63, HSP70, Apo-A1), Dynamic Light Scattering and cryo-TEM. RNAs from colonic epithelial cells and precipitated EVs were isolated using silica-column based method. MiRNAs expression was evaluated by TaqMan qPCR. Statistical analysis and visualization of the results were performed using R studio.

Results: Although statistically insignificant, but the expression of miR-183-5p and miR-135b-5p in epithelial cells of HC group was tended to decrease after contact with *E. coli* compared to untreated cells (resp. FC=0.84 ($p=0.574$) and FC=0.87 ($p=0.798$)), while miR-146a-5p increased (FC=1.37 ($p=0.798$)). In the EVs samples of HC, the same trends were observed. Interestingly, in the UC patients' cells, after incubation with *E. coli*, the expression of all studied miRNAs - miR-183-5p, miR-135b-5p, miR-146a-5p - tended to increase (resp. FC=1.53 ($p=0.730$), FC=1.71 ($p=0.666$), and FC=2.39 ($p=0.258$)).

Similar expression changes were observed in the EVs of colonic epithelial cells from UC patients following stimulation with *E. coli* (resp. FC=1.32 ($p=0.730$) (miR-183-5p), FC=1.32 ($p=0.666$) (miR-135b-5p), and FC=2.07 ($p=0.258$) (miR-146a-5p)).

After culturing colonic epithelial cells with *P. vulgatus* the expression of all investigated miRNAs, compared to unstimulated cells, remained almost unchanged, both in HC and in UC patients' monolayers. Meanwhile, in both the HC and UC groups, a decrease in miR-183-5p and miR-135b-5p expression was observed in EVs following contact with *P. vulgatus*, compared to control conditions (in the HC group resp. FC=0.59 ($p=0.382$) and FC=0.51 ($p=0.234$); in the UC group resp. FC=0.70 ($p=0.605$) and FC=0.73 ($p=0.489$)). However, the expression of miR-146a showed a decreasing trend only in the HC group compared to unstimulated cells (FC=0.53 ($p=0.161$)).

Conclusion: Due to the considerable variation in the response between study subjects, the observed expression changes did not reach statistical significance. The experimental study revealed a tendency that the expression of miRNAs associated with UC can be modulated by commensal gut bacteria, particularly *E. coli*, both in colonic epithelial cells and their EVs.

Disclosure: Nothing to disclose.

PP0367

THE IMPACT OF TOFACITINIB AND BUDESONIDE ON STEMNESS, CELL DEATH, AND CHEMOKINE RELEASE IN IBD PATIENT-DERIVED COLONOIDS

A. Sridhar¹, I. Bakke², S. Gopalakrishnan³, N.M. Mohamud Osoble³, E.P. Hammarqvist³, H.P. Sahlin Pettersen^{1,4}, A.K. Sandvik¹, A.E. Østvik¹, M. Doré Hansen², T. Bruland¹

¹Norwegian University of Science and Technology (NTNU), Department of Clinical and Molecular Medicine (IKOM), Department of Gastroenterology and Hepatology, Clinic of Medicine, St. Olav's University Hospital, Trondheim, Norway,

²Norwegian University of Science and Technology (NTNU), Department of Clinical and Molecular Medicine (IKOM), Clinic of Laboratory Medicine, St. Olav's University Hospital, Trondheim, Norway, ³Norwegian University of Science and Technology (NTNU), Department of Clinical and Molecular Medicine, Trondheim, Norway, ⁴Norwegian University of Science and Technology (NTNU), Department of Clinical and Molecular Medicine (IKOM), Department of Pathology, St. Olav's University Hospital, Trondheim, Norway

Contact E-Mail Address: arun.sridhar@ntnu.no

Introduction: Mucosal healing, defined as the resolution of inflammation and restoration of the intestinal epithelial barrier¹, is believed to cause long-term remission in patients treated for Inflammatory bowel disease (IBD). However, most current therapeutic strategies only alleviate the symptoms and induce endoscopic remission rather than directly addressing histological and molecular healing, and little is known about how IBD drugs may contribute to epithelial repair in the colon².

During homeostasis, epithelial renewal is maintained by leucine-rich repeat-containing G-protein coupled receptor 5+ (Lgr5+) intestinal stem cells in the crypts, producing proliferative progenitors that gradually cease to divide as they move towards the surface and differentiate into mature cytokeratin 20 (CK20) expressing colonocytes. Inflammation is a major effector of intestinal mucosal damage in IBD and has been found to affect epithelial stemness, regeneration and cellular functions³.

Thus, we need more knowledge about how IBD drugs, developed to modulate immune cells, also affect intestinal epithelial cells. Here, we used human colon organoids (colonoids) to recapitulate important features of colonic epithelium in a donor-specific manner⁴.

Aims & Methods: Our hypothesis is that mechanisms of action (MOA) of IBD drugs in intestinal epithelium are relevant for homeostasis, and drug classes such as targeted small molecules and broad-spectrum first-line corticosteroids will have distinct MOA and varied effects among patients. Here, we use colonoids from healthy donors and ulcerative colitis patients to elucidate MOA for budesonide and the pan-JAK inhibitor tofacitinib, especially their impacts on stemness in differentiated cells.

The effects of tofacitinib and budesonide treatment during differentiation were examined in uninflamed and TNF+Poly(I:C) stimulated colonoids. Colonoid growth, stemness, cell death, and chemokine release were analyzed by brightfield and confocal imaging, immunohistochemistry, western blot, 40-chemokine plex, and single ELISAs. Scripts were developed for automated size and protein quantifications.

Results: When added during the differentiation process, tofacitinib led to an increase, while budesonide resulted in a decrease in colonoid size. Tofacitinib treatment was associated with increased Ki67 expression in general and specifically in mature CK20-positive cells. We observed large inter-individual differences, but tofacitinib treatment enhanced expression of the stem cell markers LGR5 and EPHB2 receptor in colonoids from most donors. Budesonide treatment did not seem to affect proliferation or

stemness consistently. Neither tofacitinib nor budesonide pre-treatment showed definite harmful or protective effects on TNF+Poly(I:C) induced cell death in colonoids, but both drugs attenuated TNF+Poly(I:C) induced chemokine release from colonoids.

Conclusion: Although both budesonide and tofacitinib show anti-inflammatory effects in colonoids, their effects on stemness may differ. Notably, our study represents the first to demonstrate that treatment of colonoids with the pan JAK-inhibitor tofacitinib during differentiation promotes a heightened tendency for proliferation in terminally differentiated colonoids.

Furthermore, our research reveals that tofacitinib enhances the expression of stem cell markers. Our study also demonstrates the utility of human colonoids in investigation of drug effects and inter-individual variations in the intestinal epithelium.

References:

1. Villablanca, E.J., Selin, K. & Hedin, C.R.H. Mechanisms of mucosal healing: treating inflammatory bowel disease without immunosuppression? *Nat Rev Gastroenterol Hepatol* (2022).
2. Turner, D., et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology* 160, 1570-1583 (2021).
3. Khaloian, S., et al. Mitochondrial impairment drives intestinal stem cell transition into dysfunctional Paneth cells predicting Crohn's disease recurrence. *Gut* 69, 1939-1951 (2020).
4. Gopalakrishnan, S., et al. Tofacitinib Downregulates TNF and Poly(I:C)-Dependent MHC-II Expression in the Colonic Epithelium. *Frontiers in Immunology* 13, 882277 (2022).

Disclosure: Nothing to disclose.

PP0368

VALERIC ACID: A POTENTIAL THERAPEUTIC TARGET FOR MODULATING INTESTINAL BARRIER FUNCTION IN INFLAMMATORY BOWEL DISEASE

M. Liu¹, R. Gacesa¹, D. Jansen¹, S. Sun¹, E.A.M. Festen¹, K.D. Camacho¹, K.N. Faber¹, R.K. Weersma¹, M. Hermoso^{1,2}

¹University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands,

²Universidad de Chile, Institute of Biomedical Sciences, Santiago, Chile

Contact E-Mail Address: m.liu@umcg.nl

Introduction: Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic inflammation of the gastrointestinal tract. Emerging evidence suggest critical role of gut microbial metabolites in IBD progression. Among these, valeric acid (VA), a short-chain fatty acid (SCFA) produced by bacterial fermentation, is known to be decreased in the feces of IBD patients and to exert an anti-inflammatory effect on macrophages. However, it remains under-explored whether VA could alleviate intestinal inflammation and improve the epithelial barrier in IBD.

Aims & Methods: This study aimed to investigate the effects of VA on intestinal epithelial barrier function and delineate its molecular mechanisms in IBD. VA pathway-related gene expression in human colon biopsies was measured by bulk and single-cell RNA sequencing. In addition, we investigated changes in microbial enzymes involved in VA biosynthesis via microbiome sequencing.

Furthermore, we used human colon organoid *in vitro* model to examine the effects of VA on the intestinal epithelial inflammatory response.

Results: Expression of VA receptors (*Ffar2*, *Ffar3*, *Hcar2*), transporters (*Slc5a8*, *Slc16a1*), and histone deacetylases (*HDACs*) are altered in the colonic mucosa of IBD patients, compared to healthy individuals. The abundance of microbial enzymes responsible for VA synthesis shows significant differences in the microbiota of IBD patients.

Finally, VA treatment decreases the secretion of the inflammatory IL-8 cytokine in a dose-dependent manner and downregulates genes such as *Ffar2* and *Cxcl8* in the colon organoids model.

Conclusion: VA is involved in IBD pathogenesis by affecting the epithelial barrier and modulating immune response.

References: 1. Vich Vila, Arnau et al. "Faecal metabolome and its determinants in inflammatory bowel disease." *Gut* vol. 72,8 (2023): 1472-1485. doi:10.1136/gutjnl-2022-328048

2. Liu, Moting et al. "Revisiting the Role of Valeric Acid in Manipulating Ulcerative Colitis." *Inflammatory bowel diseases* vol. 30,4 (2024): 617-628. doi:10.1093/ibd/izad187

Disclosure: Nothing to disclose.

PP0369

SMALL MOLECULE INHIBITORS FOR A4B7 AND IRAK4 SHOW PROMISING EFFECTS IN A PRECLINICAL MODEL OF SPONTANEOUS COLITIS

M.R. Spalinger¹, M. Schwarzfischer¹, D. Pöhlmann¹, M. Determann¹, K. Atrott¹, A. Leimbacher¹, P. Blomgren², L. Patel², V. Gorney², A. Clarke³, K.S. Currie², T. Yi², M. Scharl⁴

¹University Hospital Zürich, Departement for Gastroenterology and Hepatology, Zürich, Switzerland, ²Gilead Sciences Inc, Inflammation Biology Department, Seattle, United States of America, ³Gilead Sciences, Inc., Foster City, United States of America, ⁴University Hospital Zürich, Division of Gastroenterology and Hepatology, Zürich, Switzerland

Contact E-Mail Address: marianne.spalinger@usz.ch

Introduction: Current IBD therapy regimens are still frequently inefficient, can exert severe side effects, and loss of treatment response is common. Thus, the development of novel therapeutic approaches is an unmet clinical need – especially for patients featuring a primary non-response, refractory disease and/or severe side effects.

Here we assessed novel small molecule inhibitors targeting a4b7 integrin or IRAK4 regarding their efficacy to relieve colitis in a model of spontaneous intestinal inflammation either as a stand-alone treatment or in combination.

Aims & Methods: IL-10 knockout (IL-10KO) mice, which develop spontaneous immune-driven intestinal inflammation resembling human IBD, were used for all studies. Mice with established disease were fed for three weeks *ad libitum* with control chow or chow containing the inhibitors at two previously defined concentrations: a higher concentration intended to induce optimal treatment response or a lower, sub-optimal concentration that did not induce therapeutic effect as stand-alone therapy.

Results: When administered as stand-alone treatment at the higher dose, a4b7 and IRAK4 inhibitors both significantly reduced colitis severity (reduced endoscopic and histological colitis scores [$p < 0.001$ and $p < 0.01$], reduced disease activity index scores [$p < 0.001$]). This effect was accompanied by a normalization of immune cell populations in the colonic lamina propria.

Particularly, we found reduced numbers of granulocytes, Th1, Th17, and cytotoxic T cell in a4b7 and IRAK4 treated mice. Furthermore, mRNA and protein levels of inflammatory cytokines (IFN γ , IL17, TNF α and IL-1b) were normalized in intestinal tissue of a4b7 and IRAK4 inhibitor-treated mice ($p < 0.01$, each). When administered in lower concentrations, however, the a4b7 and IRAK4 inhibitors were not able to reduce disease activity

as a stand-alone treatment. Of note, a combination of the low doses of the a4b7 inhibitor and the IRAK4 inhibitor significantly reduced the disease severity as evidenced by reduced endoscopic and histologic colitis scores [$p < 0.001$, each], reduced disease activity scores [$p < 0.01$] and a normalization of immune cell infiltrates (reduced levels of granulocytes [$p < 0.001$], Th1 cells [$p < 0.001$], Th17 cells [$p < 0.001$] and less IFN γ CD8 T cells [$p < 0.001$]).

Furthermore, while low doses of anti-IL12/23 p40 antibody were not able to reduce disease severity as a stand-alone treatment, combination of low-dose anti-IL12/23 p40 with the low dose of the a4b7 inhibitor resulted in amelioration of colitis (normalized endoscopic [$p < 0.001$] and histologic [$p < 0.01$] colitis scores, reduced infiltration of granulocytes, Th1, Th17 and IFN γ CD8 T cells [$p < 0.01$, each], normalization of IFN γ , TNF α and IL-1b protein and mRNA levels in the intestine).

Conclusion: Our results demonstrate that small molecule inhibitors for a4b7 and IRAK4 were efficient in reducing colitis in a model of spontaneous immune-cell driven intestinal inflammation. Combination of the a4b7 inhibitor with low doses of the IRAK4 inhibitor or sub-optimal doses of an anti-IL12/IL23 antibody was effective to relieve the disease in the IL-10-KO model. This indicates that combination treatment of a4b7 inhibition with other immune-modulatory drugs, such as IL12/23 neutralization or IRAK4 inhibition might be a promising approach for patients that do not respond to single therapies.

Furthermore, our results indicate that combination therapy is able to induce significant disease-relieving effects when the drugs are administered in low concentrations what could minimize side effects without interfering with treatment response.

Disclosure: Nothing to disclose.

PP0370

TACROLIMUS OPTIMIZES OXIDATIVE METABOLISM OF COLONOCYTES IN EXPERIMENTAL COLITIS

W. Lv¹, L. Liu¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: lvweieg@163.com

Introduction: It has emerged that the energy metabolism of colonocytes shapes the gut microbiota, and loss of epithelial hypoxia accompanied by respiration-dependent dysbiosis is observed in experimental colitis^{1,2}.

The inhibitory effect of tacrolimus on inducible nitric oxide synthase (iNOS), a vital protein in nitrate respiration, was reported in human colonic epithelial cell lines³.

Our previous study reported that tacrolimus significantly alleviated colitis in mice and induced beneficial alterations of the gut microbiome⁴. However, the mechanism of how tacrolimus improves the gut microbiota in colitis remains to be elucidated.

Aims & Methods: In this study, we aim to explore the effects of tacrolimus on colonocyte metabolism in colitis. Male C57BL/6J mice aged 8 to 10 weeks were employed. Solutions of 2.5% dextran sulfate sodium (DSS) were prepared in the drinking water to induce colitis for 7 consecutive days. Tacrolimus (Tacro) at a dose of 10 mg/kg was administered via gavage, while aminoguanidine hydrochloride (AG), the selective iNOS inhibitor, was given intraperitoneally at a dose of 100 mg/kg per day. The body weight was observed daily. For hypoxia detection, mice were treated with 60 mg/kg of pimonidazole HCl intraperitoneally 1 hour before euthanasia. Colon lengths were measured, and the colon samples were fixed in 4% paraformaldehyde for subsequent hematoxylin and eosin staining and hypoxia staining. Total RNA and protein were extracted from the isolated colonocytes for the measurement of iNOS expression. For the *in vitro*

study, the human colorectal adenocarcinoma cells (Caco-2) were incubated with 10 µg/mL tacrolimus or 0.1% DMSO for 4 hours, then the oxygen consumption rates were measured on the Seahorse XFe24 Analyzers according to the manufacturer's protocols.

Results: Hypoxia in the colonic epithelium was significantly disrupted in DSS-induced colitis mice, which was partially restored by tacrolimus treatment. The iNOS expression on both mRNA and protein levels was significantly upregulated by DSS and downregulated after tacrolimus administration, while the addition of AG enhanced the effects of tacrolimus.

Compared with the individual tacrolimus intervention, the combined treatment of tacrolimus and AG achieved a better remission in weight loss, colonic shortening, and colonic pathological changes including the disruption of crypt-villus structure, goblet cell loss and immune cell infiltration. *In vitro* measurement of mitochondrial oxidative phosphorylation showed that tacrolimus significantly enhanced oxygen consumption, and promoted ATP production and spare respiratory capacity in Caco-2 cells.

Conclusion: Our results indicated that tacrolimus improved the oxidative metabolism of colonocytes in experimental colitis, which could be an important contributor to the alterations in the gut microbes induced by tacrolimus. The observed effect of tacrolimus in colonocytes may be associated with the inhibition of iNOS.

References: 1. Litvak Y, Byndloss MX, Bäuml AJ. Colonocyte metabolism shapes the gut microbiota. *Science* 2018;362.

2. Cevallos SA, Lee JY, Velazquez EM, et al. 5-Aminosalicylic Acid Ameliorates Colitis and Checks Dysbiotic *Escherichia coli* Expansion by Activating PPAR-γ Signaling in the Intestinal Epithelium. *mBio* 2021;12.

3. Hämäläinen M, Lahti A, Moilanen E. Calcineurin inhibitors, cyclosporin A and tacrolimus inhibit expression of inducible nitric oxide synthase in colon epithelial and macrophage cell lines. *Eur J Pharmacol* 2002;448:239-44.

4. Lv W, Zhang D, He T, et al. Combination of *Lactobacillus plantarum* improves the effects of tacrolimus on colitis in a mouse model. 2023;13.

Disclosure: Nothing to disclose.

PP0371

A NOVEL PEPTIDE CAN SIGNIFICANTLY IMPROVE PRECLINICAL OUTCOMES IN A MURINE DEXTRAN SULFATE SODIUM MODEL OF COLITIS

S. D' Alessio¹, J.H. Griffin², S. Danese³

¹Phoenixlab srls, Lodi, Italy, ²The Scripps Research Institute, Department of Molecular Medicine, La Jolla, California, United States of America, ³Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal Immunopathology, Milan, Italy

Contact E-Mail Address: silviadalebis@gmail.com

Introduction: Most current approaches for therapy for Inflammatory Bowel Disease (IBD) focus on inhibition of excessive inflammation. However, with clinical remission rates for IBD plateauing, new approaches, are needed. The protease, Activated Protein C (APC), can exert a broad range of cytoprotective actions including inhibition of inflammation, stabilization of endothelial and epithelial barriers and suppression of apoptosis. APC shows therapeutic effects in various inflammatory diseases, and its cytoprotective functions often require biased cleavage of protease-activated receptor (PAR)1 and PAR3.

Biparetide is a bivalent PAR1:PAR3-derived peptide formed by covalent linkage of PAR1-residues 47-55 to PAR3-residues 51-65 via a 10-mer oligo-Gly peptide. Biparetide *in vitro* mimics APC's anti-inflammatory activity.

Aims & Methods: Aim: Our objective was to assess the *in vivo* therapeutic benefits of intrarectal and intraperitoneal administration of biparetide in a murine preclinical 40kDa dextran sulfate sodium (DSS) model of colitis. Methods: Eight-week-old female C57Bl/6N mice were given 2% (weight/volume) DSS in drinking water for three 7-day cycles followed by 7 days of regular drinking water to induce colitis. Both biparetide (1, 10 and 50 mg/kg) and scrambled biparetide (peptide with randomized amino acid sequence) were given daily from day 18 to day 41 by concomitant intrarectal (half volume) and intraperitoneal (IP) injection (half volume).

Anti-TNFα was administered IP 15mg/kg 3 times per week from day 18 to day 41. Prednisolone was administered IP (1mg/kg) once daily from day 18 to day 42. Control groups included healthy mice and DSS-treated animals receiving only vehicle. Colitis severity was monitored using a disease activity score (DAI) based on daily evaluation of weight, stool consistency, and presence of blood; at study end, endoscopic scoring was performed. Colon length and weight were measured, and histological analysis on formalin-fixed paraffin sections was performed by a blinded pathologist.

Results: DSS effectively induced chronic colitis. Biparetide dose-dependently reduced body weight loss compared to vehicle-dosed DSS-treated mice from day 24 ($p<0.01$). Biparetide at both 10 and 50 mg/kg significantly improved body weight loss compared to prednisolone ($p<0.01$) and anti-TNF-α from day 31 ($p<0.01$), and it was associated with a dose-dependent, significant reduction in DAI score compared with vehicle-dosed DSS-treated mice, e.g., from day 24 (for 10 mg/kg, $p<0.01$). Biparetide significantly reduced DAI compared with prednisolone ($p<0.01$) and reduced DAI similar to anti-TNF-α. The peptide's protective effects against chronic colitis observed at both 10 and 50 mg/kg were accompanied by improvements in colon length shortening and in colon weight/length ratio ($p<0.01$), with effects comparable to anti-TNF-α. Amelioration of histological and endoscopic parameters of colitis was seen with anti-TNF-α and biparetide (10 and 50mg/kg) treatments.

Conclusion: In this DSS-induced colitis model, biparetide gave dose-dependent improvement in clinical signs and symptoms, reducing body weight loss and improving DAI score. These significant improvements were seen at 10mg/kg and 50mg/kg peptide. Similar improvements were observed during endoscopy and upon histological assessment.

Here we demonstrate proof of concept that biparetide is a novel anti-inflammatory peptide that mimics APC's previously reported *in vivo* benefits for DSS-induced colitis. Moreover, these data suggest that biparetide merits further evaluation for clinical translation for inflammatory pathologies.

Disclosure: Nothing to disclose.

PP0372

TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) MODULATES ENTERIC NERVOUS SYSTEM (ENS)-CELL EXPRESSION PATTERNS AND INTESTINAL BARRIER IN CHRONIC DSS COLITIS

J.J. Wiese¹, F. Weiß¹, S. Manna¹, S. Krug¹, M. Bubeck², C. Günther², J. Patankar², B. Siegmund¹, M. Prüß¹, N. Hering¹, M. Schumann¹

¹Charité – University Medicine Berlin, Department of Gastroenterology - Infectious Diseases and Rheumatology, Berlin, Germany, ²University Hospital Erlangen, Dept. of Internal Medicine 1, Erlangen, Germany

Contact E-Mail Address: michael.schumann@charite.de

Introduction: Chronic visceral pain is a clinical challenge in >50% of Inflammatory Bowel Disease (IBD) cases (Morrison et al., 2013). A randomized controlled trial (RCT) demonstrated that transcranial direct current stimulation (tDCS) can modulate brain activity and effectively alleviate chronic abdominal pain associated with IBD (Neeb et al., 2019).

To elucidate the underlying mechanism of tDCS, we implemented this technique in a mouse model of inflammatory, chronic DSS colitis.

Aims & Methods: The tDCS protocol, including a total of 10 stimulations, was designed based on established human tDCS studies. An anodal direct current (0.5 mA, 20 min) was administered to both primary motor cortices over two separate periods with each period consisting of five consecutive days of stimulation, separated by a two-day break. The study was controlled by including a sham-treatment-group (0.5-minute sham stimulation).

For histology, H&E stained FFPE-sections of colon were assessed by scoring (Koelink et al., 2018). Barrier integrity was analysed by Ussing chamber experiments. To confirm that tDCS was affecting murine activity, mice were tracked in home cages using subcutaneously injected RFID-chips. Myenteric plexus (MP) cells of the murine small intestine, primarily the terminal ileum, were isolated and cultivated for 10 days.

Staining with beta3-tubulin and S100B was performed confirming neuronal cell identity. Bulk-RNA sequencing was conducted using the NovaSeq Xplus system (read length 150 bp, read depth 30 million copies/run).

Results: The distal colon of DSS-treated mice revealed significantly stronger inflammation in the H&E scores compared to control mice (mean±SEM: Ctrl: 0.14±0.08; DSS: 1.52±0.19; MWU: p=0.0005). Only a tendency towards less inflammation was observed in tDCS-treated mice compared to sham-tDCS.

The DSS caused an inflammation-driven thickening of the colon wall, resulting in an increased transmural resistance. This effect was ameliorated by the tDCS-treatment (mean±SEM: DSS+sham-tDCS: 72.2±8.2 Ω·cm²; DSS+tDCS: 48.1±2.1 Ω·cm²; MWU: p=0.007).

DSS colitis was associated with a reduced activity, which was partially recovered by tDCS (mean±SEM: DSS+sham-tDCS: 70.7±15.2 relative distance units/day; DSS+tDCS: 205.9±40.4 relative distance units/day; MWU: p=0.029).

Neuronal cell identity was confirmed in isolated murine MP cells by immunostaining (beta3-tubulin, S100B). Bulk-RNAseq revealed a clear separation of tDCS and sham-tDCS treated colitis mice by PCA. Subsequently, 739 differentially expressed genes (DEGs) were identified in tDCS-treated DSS colitis mice compared to a sham-tDCS-treatment (622 upregulated, 117 downregulated genes; log₂(fold-change)≥1.5; padj<0.05), *Table 1*.

Analysis of KEGG and GO pathways revealed involvement in several biological processes, comprising neuroactive ligand-receptor interaction (p=7.94·10⁻³), gated channel activity (p=2.4·10⁻⁷), substrate-specific channel activity (p=1.99·10⁻⁷), and leukocyte migration (p=3.99·10⁻⁷).

Gene name	Differential expression	Log ₂ (fold-change)	Adjusted p-value
Nos1, Nitric oxide synthase 1	upregulated	2.68·10 ⁻¹⁴	5.32·10 ⁻⁰⁸
Fos, FBJ osteosarcoma oncogene	upregulated	2.21·10 ⁻¹³	4.04·10 ⁻⁰⁷
Ncam2, Neural cell adhesion molecule 2	upregulated	2.29·10 ⁻¹⁴	2.66·10 ⁻⁰⁴
Chrb4, Cholinergic receptor, nicotinic, beta polypeptide 4	upregulated	1.69·10 ⁻¹⁴	3.69·10 ⁻⁰⁴
Cend1, Cell cycle exit and neuronal differentiation 1	upregulated	1.67·10 ⁻¹⁴	6.71·10 ⁻⁰³

Table 1 Selection of neurologically relevant DEGs.

Conclusion: In colitis, transcranial direct current stimulation (tDCS) has the capacity to modulate activity of DSS-treated mice and alters gene expression in MP cells. This reveals another layer of evidence for the impact of central pathways on the gut / brain-gut-axis.

References: Morrison, G. et al., *Inflamm. Bowel Dis.*, 2013. 19(6): 1210-7: *Inflammatory Bowel Diseases* publishes original basic science, translational, and clinical research regarding pathogenesis, epidemiology, evaluation, and treatment of IBD.

Neeb, L. et al., *Brain Stimulation*, 2019: *BMJ* 2019; 364 doi: Comparative efficacy and acceptability of non-surgical brain stimulation for the acute treatment of major depressive episodes in adults: systematic review and network meta-analysis.

Koelink, P. J. et al., *JCC* 2018: *Journal of Crohn's and Colitis*, Volume 12, Issue 7, July 2018, Pages 794–803, Development of Reliable, Valid and Responsive Scoring Systems for Endoscopy and Histology in Animal Models for Inflammatory Bowel Disease.

Disclosure: Nothing to disclose.

PP0373

DOES A TRANSCRIPTIONAL SIGNATURE COMPOSED OF TWELVE METALLOPROTEINASES PREDICT THE RESPONSE TO ANTI-TNF THERAPY IN PATIENTS WITH ULCERATIVE COLITIS?

L. Arosa-Garcia¹, M. Camba-Gomez¹, I. Bastón-Rey^{2,1}, R. Ferreiro-Iglesias^{1,2}, C. Calviño-Suarez^{2,1}, M.d.S. Porto-Silva³, L. Nieto-García³, J.E. Domínguez Muñoz^{2,1}, M. Barreiro de Acosta^{1,2}, J. Conde-Aranda¹

¹Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ²University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Failure of anti-TNF therapy contributes to the socio-economic burden of inflammatory bowel disease (IBD). This is particularly relevant when new drugs targeting α4β7 integrin, IL-12/IL-23, Janus kinases or sphingosine-1 are added to the IBD therapeutic armamentarium. Anti-TNFs are the usual first-line biologic agents and, therefore, pre-treatment discrimination of patients who will be refractory to these therapies is important to prevent IBD patients from being exposed to multiple therapeutic failures. Many studies have reported predictive biomarkers for response to anti-TNF therapy.

However, the implementation of easily readable biomarkers in daily clinical practice is an unmet need. Due to the active role of the metalloproteinase (MMP) family in the development of intestinal inflammation, we wanted to isolate robust and reproducible transcriptional markers capable of specifically predicting response to anti-TNF therapy by comprehensive analysis of these proteases.

Aims & Methods: We analysed the expression of twelve MMPs in publicly available microarray and RNAseq datasets from the Gene Expression Omnibus and the European Bioinformatics Institute: GSE12251, GSE16879,

GSE73661 and E-MTAB-7845 for colon biopsies from ulcerative colitis (UC) patients before anti-TNF or vedolizumab therapy. The R package was used for differential expression analysis and receiver operating characteristic (ROC) calculation. Cytoscape software and Morpheus (broadinstitute.org) were used for network data integration and visualisation.

In addition, we evaluated the expression of these twelve MMPs by RT-qPCR in peripheral blood mononuclear cells and polymorphonuclear cells from a local cohort of UC patients (n=21).

Results: We isolated a colonic transcriptional signature consisting of twelve MMPs that is highly associated with disease activity. Most of the transcripts of this signature were significantly up-regulated in colon biopsies of non-responders to anti-TNFs before treatment in three different microarray datasets, but not in vedolizumab-treated patients. ROC curves of the twelve MMPs showed variability in correlation with anti-TNF response in all datasets analysed.

However, the combination of MMP2, MMP3, MME and PHEX efficiently discriminated patients who failed anti-TNF therapy (ROC AUC = 84%). Interestingly, this four-gene signature was not able to predict the response to vedolizumab (ROC AUC = 63%).

For completeness, we observed that of the twelve MMPs analysed, only MME showed increased expression in peripheral mononuclear cells from patients refractory to anti-TNF therapy, confirming that this MMP could be a feasible biomarker in both colonic tissue and peripheral blood.

Conclusion: Overall, our study reveals a novel and robust colonic transcriptional signature consisting of four MMPs associated with anti-TNF, but not vedolizumab, therapy response.

Furthermore, MME levels in peripheral blood cells emerge as a novel, easily readable predictive biomarker of anti-TNF response. Nevertheless, our results should be confirmed in independent cohorts of UC patients to test their efficacy and sensitivity in the clinical setting.

Disclosure: Nothing to disclose.

PP0374

PATIENTS WITH ULCERATIVE PROCTITIS ON ADVANCED THERAPY EXPERIENCE SIMILAR DISEASE BURDEN AS THOSE WITH LEFT-SIDED COLITIS AND PANCOLITIS

M. Fumery¹, V. Ghestem², I. Redondo², I. Jamonneau², N. Esquerre², R. Altwegg³

¹Amiens University Hospital, Gastroenterology department, Amiens, France, ²Eli Lilly France SAS, Neuilly Sur Seine, France, ³Hospital Saint-Eloi, University Hospital of Montpellier, Department of Gastroenterology, Montpellier, France

Contact E-Mail Address: mathurin@hotmai.fr

Introduction: Ulcerative colitis (UC) is a chronic, idiopathic inflammatory bowel disease (IBD), with mucosal inflammation affecting the rectum (proctitis, E1), left side of the colon (E2), or whole colon (pancolitis, E3). Proctitis is considered a mild disease, and often excluded from clinical trials due to heterogeneity in accessing the affected area of the colon. Proximal extension of the disease is associated with a more severe clinical course. We compared the disease burden of patients with UC according to disease extent.

Aims & Methods: THEFAR is a cross-sectional, observational, multicentre study, including adult patients with UC treated with advanced therapy (AT; biologics or Janus kinase inhibitors). Gastroenterologists across 41 centres included consecutive patients during routine clinic visits. They completed medical and therapeutic management data, including disease activity (partial Mayo score) using an electronic case report form (eCRF). Patients completed self-reported quality of life (EQ-5D-5L), dis-

ability (IBD-Disk), incontinence (Wexner score), bowel urgency (Urgency Numeric Rating Scale, UNRS), and Work Productivity and Activity Impairment UC (WPAI:UC) questionnaires.

Results: 293 patients with UC (mean age 44 ± 16 years; 50% [147/293] male) were enrolled, with 292 self-reported questionnaires returned for analysis; 45 (15%) patients had proctitis (E1), 117 (40%) left-side colitis (E2), and 131 (45%) extensive colitis (E3). Former smokers were more common in E2 (25%) and E3 (28%) than E1 (11%) subgroups (p=0.01). Comorbidities, including chronic rheumatological disease and cardiovascular diseases, were similar across all subgroups (p>0.05). Disease duration was related to the extent of disease: mean duration of 5.3 years (E1) to 8.8 years (E3) (p=0.02). Age at diagnosis was lowest in E3 (33 years) compared to E1 and E2 (38 years each) subgroups (p=0.02). Regardless of subgroup, there was a similar incidence of flares over the past year, presence of extra-intestinal manifestations, and disease activity per partial Mayo score (all p>0.05). There was no proof of difference in current treatment allocation, duration or lines of advanced therapies, or corticosteroid use (p>0.05 for all [except golimumab]) between subgroups. The proportions of hospitalized patients were significantly different in subgroups: E1 (11%), E2 (21%), and E3 (46%) (p<0.0001).

There was no between-group difference for EQ-5D-5L, IBD-Disk, or WPAI:UC scores (all p>0.05). UC-related patient-reported outcomes were similar across subgroups according to both the Wexner score (p>0.05) and UNRS (p>0.05; Table).

Conclusion: In this cohort of patients with UC treated with AT, there was no association between the extent of disease and quality of life, disability, treatment allocation, work impairment, incontinence, or bowel urgency. However, the extent of disease was associated with hospitalizations. Patients with proctitis treated with AT experience similar disease burden and require a comparable level of treatment as those with left-sided colitis and pancolitis.

Demographics and disease characteristics of study participants	E1	E2	E3	p-value
EQ-5D-5L Utility, mean (SD)	0.871 (0.162)	0.893 (0.147)	0.889 (0.174)	0.38
UNRS, mean (SD)	3.5 (3.3)	3.1 (2.9)	2.8 (2.9)	0.46
Wexner Score, mean (SD)	8.4 (4.9)	7.4 (5.1)	8.2 (4.3)	0.35
Total IBD-Disk Score, mean (SD)	36.4 (24.8)	33.5 (25.0)	32.6 (26.1)	0.69
WPAI:UC scores (on people employed*)				
Absenteeism, mean % (SD)	11.1 (29.9)	8.1 (17.6)	7.7 (21.7)	0.52
Work impairment (loss of productivity), mean % (SD)	26.7 (27.1)	22.8 (26.5)	19.4 (26.1)	0.51
Activity impairment, mean % (SD)	27.2 (25.7)	20.1 (23.6)	22.3 (27.0)	0.47

*44 patients in E1, 117 in E2 and 131 in E3 completed the WPAI:UC questionnaire. E1, proctitis; E2, left-sided colitis; IBD, inflammatory bowel disease; UNRS, Urgency Numeric Rating Scale; WPAI-UC, Work Productivity and Activity Impairment-UC; SD, standard deviation. Utility was calculated using the French value set for EQ-5D-5L.

Disclosure: M.F. has received lecture/consultant/travel support fees from Abbvie, MSD, Ferring, Tillots, Takeda, Sandoz, Fresenius, Arena, Pfizer, Amgen, Biogen, Gilead, Galapagos, Janssen

V.G., I.R., and I.J. are employees and minor shareholders of Eli Lilly and Company Ltd.

N.E. is an employee and minor shareholder of Eli Lilly and Company Ltd and reports previous employment and minor shareholdings with AbbVie and Gilead Science.

R.A. has no conflicting interests to declare.

PP0375

ML-DERIVED, QUANTITATIVE HISTOLOGIC FEATURES OF THE INFLAMMATORY MICROENVIRONMENT AFTER ADALIMUMAB INDUCTION TREATMENT ALLOW PREDICTION OF RESPONSE IN PATIENTS WITH ULCERATIVE COLITIS

J. Shamshoian¹, F. Najdawi¹, S. Degryse¹, C. Jayson¹, J. Brosnan-Cashman¹, K. Kolahi², A. Shrotre², H. Guay², F.S. Laroux²
¹PathAI, Boston, United States of America, ²AbbVie, South San Francisco, United States of America

Contact E-Mail Address: john.shamshoian@pathai.com
Introduction: Ulcerative colitis (UC) is a chronic disease characterized by inflammation. Despite the advent of anti-inflammatory biologics, most patients do not achieve a deep response to therapy. Furthermore, predicting response to therapy is challenging. Quantitative histologic features of the inflammatory microenvironment in UC have potential to inform treatment selection and maintenance efficacy once a regimen has started. To address this hypothesis, we compared such features derived from machine-learning (ML) models with endoscopic response status (Mayo endoscopic score; MES<2) in patients with UC treated with adalimumab (ADA). **Aims & Methods:** A retrospective analysis of a phase III clinical trial of ADA (NCT02065622) was performed. A suite of ML models, collectively known as IBD Explore™ (PathAI, Boston¹)* previously trained to quantify tissue regions (e.g., granulation tissue) and cells (e.g., goblet cells) were deployed on 345 hematoxylin and eosin (H&E)-stained whole slide images (WSI) of biopsies from the rectum and sigmoid colon at ADA end-of-induction (week 8). Human interpretable features (HIFs) were extracted from each WSI. Features were then correlated with end-of-maintenance (week 52) region-level endoscopic response status (MES<2) using univariate logistic regression. Multivariable logistic regression predictive models were also developed on a subset of the samples (277 WSIs). Predictive accuracy was assessed on a held-out test dataset (66 WSIs). **Results:** Of the 657 model-derived HIFs assessed at end-of-induction, 251 were associated (p<0.05) with end-of-maintenance region level MES response status after applying Benjamini-Hochberg (BH) false discovery rate correction. Some example HIFs and their associated odds ratio with end-of-maintenance MES response are noted in Table 1.

Feature	Odds ratio	BH p-value
Median density of goblet cells in crypts	2.85	< 1e-10
Median area ratio of goblet cell mucin to epithelium + crypt abscess in crypts	2.50	< 1e-9
Proportion of neutrophils within 20 µm of goblet cells	2.40	< 1e-8
Proportion of inflamed crypts	0.46	< 1e-7
Proportion of plasma cells + intraepithelial lymphocytes in mucosa	0.66	< 1e-3
Area proportion of granulation tissue in mucosa	0.72	0.032
Heterogeneity of crypt area	0.71	0.01

Table 1: Example HIFs taken at end-of-induction and associated odds ratio to end-of-maintenance MES response.

To develop predictive models of region-specific end-of-maintenance endoscopic response, 5-fold cross validation was used. Biopsies from each subject were placed in a single split to minimize data leakage. The selected model (L1 penalized, class balance weighted) achieved a sensitivity and specificity of 0.64 and 0.67, respectively, on WSI not seen during predictive model development. **Conclusion:** A quantitative understanding of the histologic changes in the colonic microenvironment shortly after treatment initiation is critical to advance our collective knowledge of UC and may aid in the prediction of a patient's response. Here, quantitative features of goblet cells and gob-

let cell mucin were especially predictive of endoscopic response from end-of-induction. ML-derived quantitative histology features have the potential to guide therapeutic decisions in UC that leverage mechanistic rationale derived from histology, contributing to precision medicine in immunology. **References:** *Gaitan et al., 2023. Machine learning-based prediction of Geboes score and histologic improvement and remission thresholds in ulcerative colitis. Digestive Disease Week 2023 Poster Presentation **Disclosure:** ¹PathAI Employee and owner of stock options ²AbbVie Employee and owner of stock options.

PP0376

THE CAUSAL EFFECTS OF INFLAMMATORY BOWEL DISEASE ON SKIN CARCINOMA: A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

L. Luo¹, X. Zhong¹, X. Tang¹, X. Hu¹, L. Li¹, J. Xu¹
¹Affiliated Hospital of Southwest Medical University, Luzhou, China

Contact E-Mail Address: luolian5309@163.com
Introduction: Observational studies have indicated that inflammatory bowel disease (IBD) patients have higher incidence of skin carcinoma (SC), including melanoma skin carcinoma (MSC) and nonmelanom skin carcinoma (NMSC) than healthy people. However, whether the correlation is causal remains unclear. The purpose of this study was to evaluate the causality of IBD on SC using the mendelian randomization (MR) analysis. **Aims & Methods:** We performed a two-sample MR analysis with public genome-wide association studies (GWAS) data. Eligible instrumental variables (IVs) were selected according to the three assumptions of MR analysis. The inverse-variance weighted (IVW) method was the main method. Complementary methods included the MR-Egger regression, the Weighted Median, the Weighted Mode and MR pleiotropy residual sum and outlier (MR-PRESSO) methods. **Results:** Genetically predicted IBD (IVW OR = 1.07, 95% CI: 1.02-1.13, P = 0.011) and ulcerative colitis (UC; IVW OR = 1.09, 95% CI: 1.03-1.16, P = 0.003) was associated with an increased risk of MSC. Results of complementary methods were consistent with those of the IVW method except Weighted mode. In addition, Crohn's disease (CD; IVW OR = 1.04, 95% CI: 0.99-1.08, P = 0.128) had not a causal effect on MSC. Moreover, IBD (IVW OR = 1.03, 95% CI: 1.00-1.07, P = 0.034) and CD (IVW OR = 1.03, 95% CI: 1.00-1.06, P = 0.045) were associated with a higher risk of NMSC. However, UC (IVW OR = 1.00, 95% CI: 0.97-1.04, P = 0.803) was not associated with NMSC. **Conclusion:** Our study revealed genetically predicted associations of IBD on MSC and NMSC in European populations. Additionally, UC increased the risk of MSC, and CD increased the risk of NMSC. But the influence of the use of immunosuppressive agents or biologics cannot be ruled out. **References:** 1.Cushing KC, Du X, Chen Y, et al. Inflammatory Bowel Disease Risk Variants Are Associated with an Increased Risk of Skin Cancer. Inflamm Bowel Dis. 2022 Nov 2;28(11):1667-1676. 2.Narous M, Nugent Z, Singh H, Bernstein CN. Risks of Melanoma and Non-melanoma Skin Cancers Pre- and Post-Inflammatory Bowel Disease Diagnosis. Inflamm Bowel Dis. 2023 Jul 5;29(7):1047-1056. 3. Burgess S, Davey Smith G, Davies NM, et al. Guidelines for performing mendelian randomization investigations. Wellcome Open Res (2019) 4:186. 4. Smith GD, Ebrahim S. Mendelian randomization: prospects, potentials, and limitations. Int J Epidemiol (2004) 33(1):30-42. 5. Burgess S, Scott RA, Timpson NJ, Davey Smith G, Thompson SG, Consortium E-I. Using published data in Mendelian randomization: a blueprint for efficient identification of causal risk factors. Eur J Epidemiol (2015) 30:543-552.

6. Bowden J, Davey SG, Haycock PC, et al. Consistent estimation in Mendelian randomization with some invalid instruments using a weighted median estimator. *Genet. Epidemiol.* 2016;40(4):304–314.

7. Verbanck M, Chen CY, Neale B, Do R. Detection of widespread horizontal pleiotropy in causal relationships inferred from mendelian randomization between complex traits and diseases. *Nat Genet* (2018) 50(5):693–698.

Disclosure: There is no conflict of interest.

PP0377

IMPACT OF ENDOMETRIOSIS ON THE EVOLUTION OF INFLAMMATORY BOWEL DISEASES: A MULTICENTER RETROSPECTIVE STUDY

L. Méheut¹, O. El Oumami², P. Seksik³, G. Le Cosquer⁴, V. Abitbol⁵, S. Nancey⁶, A. Buisson⁷, A. Amiot⁸, M. Vidon⁹, L. Caillio¹⁰, B. Caron¹¹, A. Benezech¹², C. Atanasiu¹³, G. Savoye¹⁴, A. Nuzzo¹⁵, C. Le Berre¹⁶, A. Bourrier¹⁷, C. Reenaers¹⁸, J. Labreuche², C. Rubod², M. Serrero¹⁹, L. Guillo¹, P. Wils²

¹APHM, Marseille, France, ²CHU Lille, Lille, France,

³Gastroenterology & Nutrition Department, Gastroenterology and Nutrition Unit, Paris, France, ⁴CHU Toulouse, Toulouse, France,

⁵Hopital Cochin Gastroentérologie AP-HP, Paris Cedex 14, France,

⁶HCL, Dept. de Gastroenterologie, Pierre Benite, France, ⁷CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France,

⁸Henri Mondor Hospital, APHP Dept. of Gastroenterology, Dept. of Gastroenterology, Creteil, France, ⁹APHP, Créteil, France,

¹⁰CHU DE NIMES, Gastro enterology, Nîmes, France, ¹¹Hôpital de Haute-pierre, Strasbourg, France, ¹²CH Avignon, Avignon, France,

¹³HIA Begin, Gastroenterology, Paris, France, ¹⁴Hopiaux de Rouen, Hépto Gastro Entérologie, Rouen, France, ¹⁵Beaujon Hospital, Intestinal Stroke Center unit, Department of Gastroenterology, IBD, Intestinal Failure, Paris, France, ¹⁶CHU de Nantes Hôtel

Dieu, Gastro-entérologie, Nantes, France, ¹⁷APHP St Antoine, Paris, France, ¹⁸Assistants en formation gastro, réseau Ulg - CHU Sart Tilman, Assistants en formation gastro, réseau, CHU Sart Tilman, Lantremange, Belgium, ¹⁹Hopital Nord, Gastroenterology, Marseille, France

Contact E-Mail Address: lucas.guillo690@gmail.com

Introduction: Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), and endometriosis are two nosological frameworks affecting young women. They share a spectrum of abdominal symptoms and partially common pathophysiological mechanisms involving immune system dysregulation. It is described that women with endometriosis have a higher risk of developing IBD. However, the impact of endometriosis on IBD is poorly understood.

The aim of our study was to evaluate the impact of the coexistence of both diseases on the phenotype and evolution of IBD.

Aims & Methods: We conducted a retrospective cohort study in 18 GETAID (Groupe d'Étude Thérapeutique des Affections Inflammatoires du tube Digestif) centers between June 2022 and March 2023. Any patient with both endometriosis and IBD was eligible for inclusion. They were then randomly matched to 1 or 2 patients with IBD without endometriosis, according to the following criteria: type of IBD (CD or UC), year of birth (± 5 years), year of IBD diagnosis (± 4 years), and date of the last consultation (± 2 years). Data from non-exposed patients (IBD alone) were collected from a single center (CHU de Lille).

The evolution of IBD was assessed using a composite severity criterion including intestinal damage (stenosis, fistula, or intra-abdominal abscess) or the need for intestinal resection surgery. The use of immunosuppressants and biologics was also recorded.

Results: In total, 207 patients with both endometriosis and IBD (149 CD

and 58 UC) were included and matched to 409 patients with IBD alone. The median age of patients at the diagnosis of IBD was 23 years [IQR 18; 29]. The median follow-up duration for IBD was 10 years [5.75; 17]. For patients with CD, there was no difference between the two groups regarding disease location, disease phenotype, and anoperineal involvement. For patients with UC, there was a difference in disease extent with more rectal involvement in the endometriosis group (29.3% vs 12.6%; $p=0.03$). Patients exposed to endometriosis had significantly less use of immunosuppressive treatments (UC $p < 0.01$; CD $p < 0.001$) and biologics (UC $p < 0.01$; CD $p < 0.001$), both anti-TNF (UC $p=0.01$; CD $p < 0.001$) and non-anti-TNF (UC $p=0.04$; CD $p=0.001$). In the actuarial analysis according to the composite severity criterion, patients exposed to endometriosis had a more favorable evolution of their CD than non-exposed patients (HR=0.68; 95% CI [0.50; 0.92]; $p=0.011$). In the subgroup of patients with CD who underwent surgery for their endometriosis during follow-up ($n=72$), a less severe progression was also observed (HR=0.65; 95% CI [9.42; 1]; $p=0.05$). The luminal surgery rate for CD in these patients was lower (32.2% vs 43.9%; $p=0.01$) in the "exposed" group.

No difference was observed for anoperineal manifestations ($p=0.16$) and the use of anoperineal surgery ($p=0.82$). For the UC group, those with endometriosis seemed to have a less favorable disease course, according to the composite severity criterion (HR=1.73; 95% CI [0.74; 4.00]; $p=0.20$). However, the rate of colectomy was not significantly higher for exposed patients (19.0% vs 11.5%; $p=0.20$).

Conclusion: Although patients with endometriosis are at a higher risk of developing IBD, it does not negatively influence the course of IBD. On the contrary, patients with CD appear to have a less severe progression, with significantly less exposure to immunosuppressants and biologics. However, both conditions have a major impact on patients, requiring multidisciplinary follow-up to ensure symptom control and improve their quality of life.

Disclosure: Nothing to disclose.

PP0378

ALTERED EXPRESSION AND ENZYMATIC ACTIVITY OF XANTHINE OXIDASE IN INFLAMMATORY BOWEL DISEASE

A. Di Petrillo¹, S. Onali¹, N. Raho¹, A. Favale¹, D. Murtas¹, C. Maxia¹, E. Grecu¹, A. Fais¹, B. Era¹, P. Caboni¹, V. Sogos¹, C. Porcedda¹, M.C. Fantini¹

¹Università degli Studi di Cagliari, Monserrato, Italy

Contact E-Mail Address: amalia.dip@unica.it

Introduction: Xanthine oxidase (XO) is involved in the last steps of purine metabolism; indeed, it catalyzes the oxidation of hypoxanthine to xanthine and xanthine to uric acid (UA) with the production of superoxide anion. The accumulation of UA has been shown to initiate the inflammatory process through NLRP3 inflammasome and the production of reactive oxygen species (ROS) contributes to inflammation-related tissue damage. In murine models of colitis, XO inhibitors, allopurinol or febuxostat, reduced the expression of proinflammatory cytokines supporting the involvement of XO in the intestinal inflammatory process.

Aims & Methods: This study aims to conduct a thorough investigation of the role XO plays in IBD pathogenesis and to explore the potential of XO inhibition as a therapeutic strategy.

Biopsies from the sigmoid colon of 15 Healthy Controls (HC), 20 Ulcerative Colitis (UC), and 15 Crohn's Disease (CD) patients, as well as from the ileum of 10 HC and 10 CD patients, were collected at the University Hospital of Cagliari. Disease activity was assessed using Mayo and SES-CD scores. XO expression levels were evaluated using Real-Time PCR and validated by GEO database (GSE11223, GSE117993). XO enzymatic activity was

quantified spectrophotometrically in protein extracts from the biopsies. XO and NLRP3 inflammasome activation pathway, including NLRP3, ASC, and CASPASE1, was investigated using immunohistochemistry (IHC). Biopsies samples were lysed in RIPA buffer and Capillary Western analyses were performed with ProteinSimple Jess System utilizing 1:10 dilution for XO, NLRP3, ASC, and Caspase 1; 1:100 dilution for Beta-actin as primary antibodies. Ex-vivo organ culture were assayed with Intestinal biopsies from UC and CD patients. Briefly, the biopsies were cultivated with or without XO inhibitors, allopurinol and febuxostat, for 24 hours in a 24-well plate with 250 μ L RPMI at 37°C with 95% O₂ /5% CO₂ atmosphere. After 24h the biopsies were used for IHC analysis of NLRP3 pathways.

Results: Increased XO mRNA expression was found in UC and CD sigmoid colon mucosa compared to HC in the GEO database. This finding was further confirmed by Real-Time PCR in our patients, with a Relative Quantification (RQ) of 1.93 vs. 0.99 ($p=0.004$) for UC and CD sigmoid colon, and RQ of 2.72 vs. 1.26 ($p=0.004$) for CD ileum. XO activity was higher in UC and CD sigmoid colon (3.86 nmol UA/min/mg in UC, 4.82 in CD vs. 1.03 in HC, $p<0.001$) and CD ileum (8.41 vs. 1.83 in HC, $p<0.001$). IHC and Western analysis confirmed that XO and the NLRP3 inflammasome pathway are more expressed in IBD patients than in HC, predominantly within epithelial cells. The ex-vivo organ culture of CD patients, and UC patients, showed a reduced UA levels and reduced NLRP3 pathways activation after treatment with XO inhibitors.

Conclusion: XO expression was higher in UC and CD patients than in HC individuals. Alongside this increase in XO activity, there was a concurrent hyperactivation of the NLRP3 inflammasome. The inhibition of XO activity in ex-vivo organ culture resulted in reduced activation of the NLRP3 inflammasome pathway. These findings support the hypothesis that XO plays a critical role in the pathogenesis of IBD and highlight its potential as a therapeutic target.

Disclosure: I declare that there are no conflicts of interest.

PP0379

LIMITED PREDICTIVE VALUE OF THE GUT MICROBIOME AND METABOLOME FOR RESPONSE TO BIOLOGICAL THERAPY IN INFLAMMATORY BOWEL DISEASE

F. Prins¹, I.J. Hidding¹, M.A.Y. Klaassen¹, V. Collij¹, H.-P.D. Schultheiss², B.H. Jansen¹, EAM Festen¹, A. Vich Vila³, B. Oldenburg², R. Gacesa¹, R.K. Weersma¹

¹University of Groningen, University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands, ³Rega Institute for Medical Research, Department of Microbiology and Immunology, Leuven, Belgium

Contact E-Mail Address: f.m.prins@umcg.nl

Introduction:

The complexity of Inflammatory Bowel Diseases (IBD) presents challenges for the management of these diseases. Predicting treatment outcomes remains difficult, leading to suboptimal outcomes and high costs. Emerging evidence suggests the potential of the gut microbiome in predicting response to biologic treatments (1,2). In this prospective study we aimed to predict treatment response to vedolizumab and ustekinumab in 79 IBD patients by integrating clinical data, gut microbiome profiles and fecal metabolites and validating these findings in a replication cohort of 47 IBD patients.

Aims & Methods: Treatment response was defined as either continuation or discontinuation of biologic therapy after six months. We performed whole genome metagenomic shotgun sequencing on the baseline fe-

cal samples to identify microbial and functional profiles. Additionally, abundances of over 1000 metabolites were captured through untargeted metabolomic profiling. Baseline diversity, dissimilarity and differential abundance analyses compared responder and non-responder groups. The prediction tool CoDaCoRe was used to identify predictive log-ratio biomarkers. We tested the identified ratios in an external cohort and attempted to replicate the microbiome-based signals of previous studies. Finally, we used a neural-network framework to model the relationship between metabolites and microbes, comparing identified clusters in responders and non-responders and tested our approach with different definitions of response.

Results: We identified 7 differentially abundant metabolites between responders and non-responders ($FDR < 0.05$), and no significant differences in bacterial species or pathways. Our prediction analysis indicated only marginal predictive utility of the gut microbiome and fecal metabolites for treatment response, when compared to a clinical model using fecal calprotectin, disease duration and disease activity, among other factors (AUC only clinical features: 0.71 ± 0.13 , AUC microbial and clinical features: 0.73 ± 0.12). The main predictive features of these models were the high abundance *Phocaeicola vulgatus*, *Bacteroides uniformis* and *Alistipes onderdonkii*, and low abundance of *Ruminococcus gnavus* and *Faecalibacterium prausnitzii*. Testing our identified ratio of 10 species in an external cohort of 47 IBD patients reinforced the lack of predictive power of the microbiome. No replication of previously published predictive signals of the microbiome was observed. Additionally, we identified two metabolite and one microbiome cluster associated with response, and observed that predictors were highly dependent on the definition of response.

Conclusion: While previous studies of similar size have shown that microbial features can predict response to either vedolizumab (VedoNet, 1), or vedolizumab, ustekinumab and anti-TNF (2), our comprehensive study found no significant differences in the gut microbiome at baseline between responders and non-responders among IBD patients treated with ustekinumab or vedolizumab. Microbial features added no predictive power to drug response in our IBD patient cohort or an independent replication cohort. Addition of metabolite features did not improve predictive power. These findings suggest minimal impact of the gut microbiome on treatment outcomes with these medications in IBD patients at this disease stage. Generalizability beyond initial study cohorts is limited, leaving predictors for individualized IBD-medication selection unidentified, but based on this work, likely do not lie in the fecal microbiome.

References:

1. Ananthakrishnan AN, Luo C, Yajnik V, et al. Gut Microbiome Function Predicts Response to Anti-integrin Biologic Therapy in Inflammatory Bowel Diseases. *Cell Host Microbe*. 2017;21(5):603-610.e3. doi:10.1016/j.chom.2017.04.010
2. Caenepeel C, Falony G, Machiels K, et al. Dysbiosis and Associated Stool Features Improve Prediction of Response to Biological Therapy in Inflammatory Bowel Disease. *Gastroenterology*. 2024;166(3):483-495. doi:10.1053/j.gastro.2023.11.304

Disclosure:

EAMF is supported by a ZonMW Clinical Fellowship grant (project number 90719075) and has received an unrestricted research grant from Takeda. RG received funding by Janssen Pharmaceuticals (for unrelated research projects), received consulting funding from Esox Biologics (for unrelated research projects). RKW has received unrestricted Research Grants from Takeda, Johnson & Johnson, Ferring and Tramedico and speakers fees from Abbvie, MSD and Boston Scientific and has acted as a consultant for Takeda Pharmaceuticals. BO has received grants from MSD, AbbVie, Takeda, Cablon, Ferring, Falk, and Pfizer.

PP0380

PROTECTIVE EFFECT OF FOOD EMULSIFIERS
CARBOXYMETHYLCELLULOSE (CMC) ON MICE COLITIS MODEL IN HIGH-
MILK-FAT DIET

L. Shao¹, J. Liu¹, L. Liu¹

¹West China Hospital, Sichuan University, Department of
Gastroenterology and hepatology, Chengdu, Sichuan, China

Contact E-Mail Address: m18267952034@163.com

Introduction: Inflammatory bowel disease (IBD) is a complex chronic and relapsing inflammatory disorder of the gastrointestinal tract with unclear pathogenesis. Accumulating evidence suggests food emulsifiers as a risk factor for the development of IBD. It is indicated that food emulsifiers carboxymethylcellulose (CMC) can alter gut microbiota and promote intestinal inflammation in IBD under normal diet. Since high-fat diet is the main life scenario for CMC use, little is known about the effect of CMC on colitis model in different high-fat diet.

Aims & Methods: C57/BL6 mice (3-5 weeks old) were randomly divided into three high-fat diet (HFD) groups, which only differed by fat composition (40 %), derived from corn oil (HCO, n-6 polyunsaturated fatty acids), olive oil (HOO, monounsaturated fatty acids) and milk fat (HMF, saturated fatty acids), and exposed to CMC (1.0% w/v) in drinking water for 4 weeks before the establishment of dextran sulfate sodium (DSS) induced acute colitis mice model. Colon inflammation severity was evaluated using survival rate, HE staining, colon length, body weight change and DAI score. Ki67 and TUNEL assays were performed to detect proliferation and apoptosis.

Results: Compared with the CMC+DSS group, the HMF+CMC+DSS group markedly increased survival rate ($P=0.013$), colon length ($P=0.027$) and body weight (day4, day5, day6 and day7, $P<0.05$, respectively), and relieved DAI score (day4 and day6, $P<0.05$, respectively) and histological damage ($P<0.0001$). The HOO+CMC+DSS group seemed to have no significant difference from the CMC+DSS group. In contrast, the HCO+CMC+DSS group developed more aggressive colitis with increased DAI score (day5, $P<0.01$) and decreased body weight (day1, day2, day5 and day6, $P<0.05$, respectively). In terms of maintaining homeostasis of the intestinal barrier, the HMF+CMC+DSS group showed the highest Ki67 ($P=0.012$, $P=0.0002$, $P=0.042$, respectively) and TUNEL positive cells ($P=0.324$, $P<0.0001$, $P<0.0001$, respectively) compared with the CMC+DSS, HOO+CMC+DSS or HCO+CMC+DSS group. Between CMC+DSS and HOO+CMC+DSS or HCO+CMC+DSS group, there was no difference in Ki67 positive cells, while TUNEL positive cells significantly decreased ($P=0.002$, $P=0.008$, respectively).

Conclusion: The function of CMC on DSS colitis varies in different high-fat. Unexpectedly, CMC protects against the development of high-milk-fat related colitis by maintaining homeostasis of proliferation and apoptosis.

References: The function of CMC on DSS colitis varies in different high-fat. Unexpectedly, CMC protects against the development of high-milk-fat related colitis by maintaining homeostasis of proliferation and apoptosis.

Disclosure: None.

PP0381

A NOVEL MULTIOMIC APPROACH TO UNRAVEL THE MECHANISMS OF
ACTION OF BIOLOGICS AND TOFACITINIB IN INFLAMMATORY BOWEL
DISEASE

M. Baldan Martin¹, M. Azkargorta², A.M. Aransay³, R. Gil-Redondo⁴, I. Moreno-Indias⁵, I. Iloro², I. Soletto¹, M. Orejudo del Río¹, C. Ramírez¹, A.J. Lucendo⁶, C. Rodríguez Gutiérrez⁷, A. Gutiérrez-Casbas⁸, E. Martín-Arranz⁹, L. Bujanda Fernández de Piñola¹⁰, I. Rodríguez-Lago¹¹, R.M. de Francisco García¹², E. Iglesias-Flores¹³, F. Bermejo¹⁴, M. Van Domselaar¹⁵, M.J. García¹⁶, L. Fernández-Salazar¹⁷, Á. De Prado¹⁸, X. Calvet Calvo¹⁹, L. Torrealba Medina²⁰, I. Bastón-Rey²¹, H. Pallares Manrique²², Y. Ber Nieto²³, E. Leo-Carnerero²⁴, M.J. Casanova¹, O. Millet⁴, F. Elortza², J. Mato⁴, F.J. Tinahones⁵, M. Chaparro^{*1}, J.P. Gisbert^{*1}, *co-last authors

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Proteomics Platform, CIC bioGUNE, BRTA (Basque Research & Technology Alliance), CIBERehd, Derio, Spain, ³Genome Analysis Platform, CIC bioGUNE, Basque Research and Technology Alliance (BRTA), CIBERehd, Derio, Spain, ⁴Precision Medicine and Metabolism Lab, CIC bioGUNE, Derio, Spain, ⁵Virgen de la Victoria University Hospital, Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y la Nutrición (CIBEROBN), Instituto de Salud Carlos III, Department of Endocrinology and Nutrition, Madrid, Spain, ⁶Hospital General de Tomelloso, Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), CIBERehd, Ciudad Real, Spain, ⁷Hospital Universitario de Navarra, Pamplona, Spain, ⁸Hospital General Universitario Alicante, CIBERehd and Instituto de Investigación Sanitaria y Biomédica de Alicante, Gastroenterology, Alicante, Spain, ⁹Hospital Universitario La Paz and Instituto de Investigación Sanitaria La Paz (IdiPaz) and UAM, Madrid, Spain, ¹⁰Hospital Universitario Donostia and Instituto Biodonostia and Universidad de País Vasco (UPV/EHU), San Sebastián, Spain, ¹¹Hospital Universitario de Galdakao, Biocruces Bizkaia HRI, Vizcaya, Spain, ¹²Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ¹³Hospital Universitario Reina Sofía, Córdoba, Spain, ¹⁴Hospital Universitario de Fuenlabrada, Madrid, Spain, ¹⁵Hospital Universitario de Torrejón and Universidad Francisco de Vitoria, Madrid, Spain, ¹⁶Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology and Hepatology Unit, Santander, Spain, ¹⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ¹⁸Hospital Universitario Río Hortega, Valladolid, Spain, ¹⁹Consorci Corporació Sanitaria Parc Taulí, CIBERehd, Sabadell, Spain, ²⁰Hospital Universitario Dr. Josep Trueta, Girona, Spain, ²¹Hospital Clínico Universitario de Santiago, Gastroenterology and Hepatology, Santiago de Compostela, Spain, ²²Hospital Juan Ramón Jiménez, Huelva, Spain, ²³Hospital San Jorge, Huesca, Spain, ²⁴Hospital Universitario Virgen del Rocío, Sevilla, Spain

Contact E-Mail Address: mbaldanm@gmail.com

Introduction: Inflammatory bowel diseases (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), are complex and heterogeneous diseases characterized by a multifactorial etiology. IBD prevalence is increasing worldwide. The availability of diverse treatments with different mechanisms of action have revolutionized the ability to achieve clinical

remission and endoscopic healing. The aim of this study was to achieve a deeper understanding of the mechanism of action and response to different IBD treatments using a multiomic approach.

Aims & Methods: We analysed the metabolome of serum and urine, metagenome of stool samples and transcriptome and proteome of mucosal biopsies from 53 patients with moderate-to-severe CD and 50 UC patients initiating biologic therapy (anti-TNF, ustekinumab or vedolizumab) or tofacitinib. Patients were assessed at 14 weeks for endoscopic remission and were categorized into responders or non-responders. The methodologies employed in this study were RNA-seq analysis, liquid chromatography-mass spectrometry, nuclear magnetic resonance, and 16S rRNA gene sequencing.

Results: The multiomic analyses revealed substantial alterations in the transcriptome, proteome, metabolome and metagenome of both responders and non-responders IBD patients before and after treatment (14 weeks) to different biologics and tofacitinib. Gene enrichment analysis showed noteworthy differences in all study comparisons, except for patients with CD and UC who did respond to anti-TNF and tofacitinib. Functional enrichment analysis of differentially expressed proteins indicated several processes that could be potentially involved in the mechanisms of action of different treatments. More differences were observed in lipoproteins than in serum and urine metabolites in the different study comparisons. Finally, metagenomic findings indicated changes in the composition of gut bacteria communities among CD patients treated with ustekinumab and UC patients treated with tofacitinib (responders vs non-responders at 14 weeks).

Conclusion: The present study provides novel insights into the mechanisms of action of different IBD treatments from a multiomic approach. Nonetheless, multiomic data integration and validation studies are needed to confirm these findings within a more extensive and independent cohort of patients.

Disclosure: Nothing to disclose.

PP0382

NOVEL BIOMARKERS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

M. Baldan Martin¹, I. Iloro², M. Azkargorta², M. Orejudo del Río¹, C. Ramírez¹, I. Soletto¹, J. Mercado¹, F. Suarez-Trujillo¹, C. Sánchez Sánchez¹, C.H Gordillo³, R.M. de Francisco García⁴, M. Rivero⁵, A. Gutiérrez-Casbas⁶, I. Rodríguez-Lago⁷, L. Fernández-Salazar⁸, D.S. Ceballos Santos⁹, J.M. Benítez¹⁰, M. Aguas¹¹, I. Bastón-Rey¹², F. Bermejo¹³, M.J. Casanova¹, R. Lorente¹⁴, Y. Ber Nieto¹⁵, V. Royo Escosa¹⁶, M. Esteve Comas¹⁷, F. Elortza², J.P. Gisbert^{*1}, M. Chaparro^{*1}, *co-last authors
¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM) and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Proteomics Platform, CIC bioGUNE, BRTA (Basque Research & Technology Alliance), CIBERehd, Derio, Spain, ³Hospital Universitario de La Princesa, Anatomía Patológica, Madrid, Spain, ⁴Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ⁵Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology, Santander, Spain, ⁶Hospital General Universitario Alicante, CIBERehd and Instituto de Investigación Sanitaria y Biomédica de Alicante, Gastroenterology, Alicante, Spain, ⁷Hospital Galdakao-Usansolo, Vizcaya, Spain, ⁸Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ⁹Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain, ¹⁰Hospital Universitario Reina Sofía and IMIBIC, Córdoba, Spain, ¹¹Hospital Universitari i Politecnic La Fe and Health Research Institute (IISLaFe), Valencia, Spain, ¹²Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain, ¹³Hospital Universitario de Fuenlabrada, Madrid, Spain, ¹⁴Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, ¹⁵Hospital San Jorge, Huesca, Spain, ¹⁶Hospital Universitari Son Espases, Palma de Mallorca, Spain, ¹⁷Hospital Universitari Mutua Terrassa and CIBERehd, Barcelona, Spain

Contact E-Mail Address: mbaldanm@gmail.com

Introduction: Inflammatory bowel disease (IBD) is a chronic multi-factorial disease characterized by inflammation of the gastrointestinal tract. Currently, the mechanisms underlying the disease are far from being elucidated. Thus, the study of proteins involved in its pathogenesis would allow further insights into the molecular mechanisms underlying IBD.

Aims & Methods: The serum and intestinal mucosa (ileum and left colon) proteomic profiles of patients with Crohn's disease (CD) and ulcerative colitis (UC) and healthy controls (HC) were analyzed through label-free relative quantitative proteomic profiling using nLC MS/MS. Data mining and pattern recognition techniques were performed to identify hidden relationships that are not detectable using classical linear classifiers, and thus identify potential markers able to discriminate between the different study groups. Six candidate biomarkers were selected for further validation using enzyme-linked immunosorbent assay (ELISA) and immunohistochemistry (IHC) in serum and intestinal tissue samples, respectively.

Results: Comparison of serum proteins between UC patients and HC revealed statistically lower levels of protein 1 and 2 and higher levels of protein 3. The comparison of potential biomarkers between CD and HC group showed lower levels of protein 1 and higher levels of protein 3. In addition, protein 4 was differentially upregulated in CD patients compared to UC. Regarding the intestinal biopsies, protein 5 showed higher intensity in the

IHC staining of ileum from CD patients compared to HC, whereas protein 6 was significantly decreased in left colon and ileum from CD and UC patients compared to HC. These proteins are involved in thyroxine transport, regulation of chemotactic chemokine activity, inflammatory processes, triglyceride homeostasis, oxidative stress and regulation of NF-kappa-B activation in the cytosol.

Conclusion: In this study, we have identified a panel of six potential biomarkers that could help to elucidate mechanisms involved in IBD pathogenesis. Their roles in the pathophysiology need to be clarified in further experiments.

Disclosure: Nothing to disclose.

PP0383

WITHDRAWN

PP0384

WITHDRAWN

PP0385

FETAL THIOPURINE SENSITIVITY IN A MOUSE MODEL BASED ON NUDT15 GENE POLYMORPHISM

T. Imai¹, S. Nakao¹, Y. Yokota¹, S. Shintani¹, M. Ohno¹, A. Nishida¹, O. Inatomi¹

¹Shiga University of Medical Science, Otsu, Japan

Contact E-Mail Address: ryukou1984@gmail.com

Introduction: Thiopurines are vital therapeutic agents for inflammatory bowel diseases but often cause severe myelosuppression. The NUDT15 polymorphism, particularly p.Arg139Cys (NUDT15R139C), is strongly linked to severe leukocytopenia and is prevalent in Asian populations. Despite thiopurine use during pregnancy, it remains unclear if NUDT15R139C affects fetal thiopurine sensitivity.

Aims & Methods: The human and murine NUDT15 proteins share 89% homology with the preservation of arginine at codon 139 of human NUDT15 in codon 138 of murine Nudt15. We established a knock-in mouse model with a point mutation (c.412C>T) generating p.Arg138Cys (Nudt15^{R138C}), mimicking the human phenotype. In the current study, we investigated offspring generated from Nudt15^{+/R138C} or Nudt15^{+/+} female mice that were mated with Nudt15^{+/R138C} male mice and simultaneously administered with mercaptopurine (MP). To evaluate the effects of thiopurine on the fetus, we evaluated the number of hematopoietic stem cells in the fetal liver, which is the center of fetal hematopoiesis.

Results: In administration with the tolerable MP dose (0.5 mg/kg) for adult Nudt15^{+/R138C} mice, genotypes of the neonatal mice born from breeding between Nudt15^{+/R138} male mice and Nudt15^{+/R138} female mice were 35 (37.2%) Nudt15^{+/+}, 59 (62.8%) Nudt15^{+/R138C}, and 0 Nudt15^{R138C/R138C}. On embryonic day 14.5, Nudt15^{+/R138C} fetal mice showed shorter body lengths and fewer hematopoietic stem cells in the fetal liver than Nudt15^{+/+} fetal mice. The number of fetal HSCs was not altered in any of the Nudt15 genotypes without MP treatment. However, it was significantly reduced by MP treatment in Nudt15^{+/R138C} fetal mice ($p < 0.01$, mean number 1104 in DMSO and 577 in MP) and in Nudt15^{R138C/R138C} fetal mice ($p < 0.01$, mean number 927 in DMSO and 402 in MP), but not in Nudt15^{+/+} fetal mice ($p = 0.39$, mean number 1004 in DMSO and 820 in MP). The number of HSCs in Nudt15^{R138C/R138C} fetal livers was significantly reduced to less than 50% of that in Nudt15^{+/+} fetal livers by MP treatment during gestation ($p = 0.0089$). In administration with the tolerable MP dose (1.0 mg/kg) for Nudt15^{+/+} adult mice, genotypes of neonatal mice born from breeding between

Nudt15^{+/R138} male mice and Nudt15^{+/+} female mice were 23 Nudt15^{+/+} and 0 Nudt15^{+/R138C}. Without MP administration, neonatal mice were born in a Mendelian fashion.

Conclusion: Fetal toxicity may arise if the fetus has more NUDT15 R139C alleles than the mother, despite safe thiopurine doses for the mother. Analysis of the father's NUDT15 genotype may enable safer thiopurine use during pregnancy, emphasizing the importance of considering parental genotypes in therapeutic decisions.

Disclosure: Nothing to disclose.

PP0386

LOSS OF UNCULTURED BACTERIA AND BILE ACID DYSMETABOLISM IN INFLAMMATORY BOWEL DISEASE

S. Hussain¹, A. Lavelle^{2,3,4}, S. Nancey⁵, J.-M. Reimund⁶, D. Laharie⁷, P. Marteau⁸, X. Treton⁹, M. Allez¹⁰, X. Roblin¹¹, G. Malamut¹², C. Oeuvray^{2,3}, N. Rolhion^{2,3}, X. Dray¹³, D. Rainteau^{2,3}, A. Lamaziere^{2,3}, J. Kirchgesner^{3,14}, L. Beaugerie^{3,15}, P. Seksik^{2,3}, L. Peyrin-Biroulet^{16,17,18}, H. Sokol^{2,3,19}

¹University College Cork, Cork, Ireland, ²Sorbonne University, INSERM, Centre de Recherche Saint-Antoine, CRSA, AP-HP, Saint Antoine Hospital, Gastroenterology, Paris, France, ³Paris Centre for Microbiome Medicine FHU, Paris, France, ⁴APC Microbiome Ireland, University College Cork, Cork, Ireland, ⁵University Claude Bernard Lyon 1 Hospices Civils de Lyon, Gastroenterology, Lyon, France, ⁶Hôpital de Hautpierre, CHU de Strasbourg, Service d'Hépatogastroentérologie et Assistance Nutritive, Strasbourg, France, ⁷CHU de Bordeaux, Hôpital Haut-Lévêque, Université de Bordeaux, Service d'Hépatogastroentérologie et Oncologie Digestive, Bordeaux, France, ⁸Sorbonne University, INSERM, Centre de Recherche Saint-Antoine, CRSA, AP-HP, Tenon Hospital, Gastroenterology, Paris, France, ⁹MICU et Assistance Nutritive, DMU DIGEST, Hôpital Beaujon, Gastroentérologie, Clichy, France, ¹⁰Hôpital Saint-Louis, Hepato-Gastroenterology, Paris, France, ¹¹CHU de Saint-Étienne - Hôpital Bellevue, Gastroenterology, Saint Etienne, France, ¹²Hôpital Européen Georges-Pompidou, Gastroenterology, Paris, France, ¹³Sorbonne University, Endoscopy Unit, AP-HP, Hôpital Saint-Antoine, Paris, France, ¹⁴Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Assistance Publique - Hôpitaux de Paris, Hôpital Saint-Antoine, Gastroenterology, Paris, France, ¹⁵Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Assistance Publique - Hôpitaux de Paris, Hôpital Saint-Antoine, Gastroenterology, Paris, France, ¹⁶Nancy University Hospital, Gastroenterology, Nancy, France, ¹⁷Inserm NGERE, Université de Lorraine, Vandœuvre-Lès-Nancy, France, ¹⁸FHU Cure, Nancy, France, ¹⁹INRA, UMR 1319 Micalis & AgroParisTech, Jouy en Josas, France

Contact E-Mail Address: saabiq.hussain@gmail.com

Introduction: The gut microbiome has been implicated in inflammatory bowel disease (IBD), with functional defects leading to disturbances in important classes of metabolites, including bile acids. Bile acids are molecules produced by the liver that help aid in the digestion of dietary fats. While most are reabsorbed in the small intestine, approximately 5% escape into the colon and are metabolized by bacteria in the colon. Bile acids are important signalling molecules and have been implicated in both inflammation and colorectal cancer. More information is needed to understand how dysbiosis modifies bile acid profiles in patients with IBD.

Aims & Methods: This is a bioinformatic analysis of whole metagenomic sequences that searched for bacteria and genes involved in the transformation of primary bile acids into secondary bile acids. The population

consisted of 215 IBD patients who were previously recruited from France. The faecal samples and metagenome sequences were obtained for each patient. The data was processed through a metagenomic pipeline using HUMAnN 3.0 and MetaPhlAn 3.

Results: Cluster analysis previously revealed 3 distinct patient groups based on their gut microbiome composition, one of which, cluster 3, was strongly associated with bile acid dysmetabolism. *Firmicutes* CAG:103 and *Firmicutes* CAG:83, previously uncultured co-abundance groups, most strongly positively correlated with secondary bile acid levels in the dataset. *Firmicutes* CAG:103 has previously been identified as a potential dominant secondary bile acid producer in metagenomic surveys. Notably, these bacterial groups were almost completely absent in cluster 3 subjects, implicating them as potential actors in secondary bile acid depletion in IBD patients.

Conclusion: This study suggest loss of *Firmicutes* CAG:103 and *Firmicutes* CAG:83 could be a driving factor for bile acid dysmetabolism in IBD patients. Further research is underway to validate these findings using metagenome-assembled genomes.

References: Lavelle, A., Nancey, S., Reimund, J. M., Laharie, D., Marteau, P., Treton, X., ... & Sokol, H. (2022). Fecal microbiota and bile acids in IBD patients undergoing screening for colorectal cancer. *Gut Microbes*, 14(1), 2078620.

Lavelle, A., & Sokol, H. (2020). Gut microbiota-derived metabolites as key actors in inflammatory bowel disease. *Nature reviews Gastroenterology & hepatology*, 17(4), 223-237.

Disclosure: Nothing to disclose.

PP0387

THE TRANSCRIPTION FACTOR HEPATOCYTE NUCLEAR FACTOR 4A IN THE SMALL INTESTINE PROTECTS AGAINST ACUTE INFLAMMATORY STIMULI

D. Pupo Gomez¹, V. Reyes¹, G. Marrero², N. Perreault¹, A. Menendez², F. Boudreau¹

¹Université de Sherbrooke, Immunology and Cell Biology, Sherbrooke, Canada, ²Université de Sherbrooke, Microbiology and Infectious Disease, Sherbrooke, Canada

Contact E-Mail Address: dianne.pupo.gomez@usherbrooke.ca

Introduction: Inflammatory bowel disease (IBD), are characterized by chronic inflammation of the intestine, and affects millions of people worldwide. There are two main classifications of IBD: Crohn's disease and ulcerative colitis with different mechanisms and etiology of disease progression. IBD is multifactorial; the incidence of this disease may be associated with a dysregulated immune response, genetics, environment, and interactions with the host microbiome. The gastrointestinal epithelium acts as a barrier against harmful stimuli, and defects in its integrity are a precursor for the development of IBD. Our laboratory has shown that the conditional deletion of the Hepatocyte nuclear factor 4A (HNF4A) in the mouse intestinal epithelium (*Hnf4a*) leads to chronic intestinal inflammation. However, the functional impact of HNF4A on epithelial barrier integrity is still controversial.

Aims & Methods: To evaluate the impact of *Hnf4a* deletion on barrier integrity during acute inflammation.

We used a tamoxifen-inducible Cre^{ER}-loxP system to delete *Hnf4a* in the adult intestinal epithelium. Intestinal permeability was assessed in *Hnf4a*^{ΔIEC-ind} and control littermate mice in the collected serum after oral gavage of FITC-dextran. Mice were infected with an invasion-attenuated strain of *Salmonella* Typhimurium (SB103 (invA::strep)). *S. Typhimurium* loads were scored in the feces, liver, and spleen by plating homogenates on LB agar supplemented with streptomycin. Histological assessment was

performed by various staining. In addition, we used a model of T-cell-induced enteropathy triggered by a T-cell activating monoclonal anti-CD3 Ab. Control and *Hnf4a*^{ΔIEC-ind} mice received an intraperitoneal injection of 50 µg monoclonal antiCD3ε Ab (145-2C11). Mice were assessed for clinical signs of enteropathy and sacrificed 1-, 3-, and five days post-injection. Gene expression levels of selected targets were measured by RT-qPCR. Also, Ki67+ staining was performed in the small intestinal tissue

Results: FITC-dextran assay showed a significant increase of intestinal permeability in uninfected *Hnf4a*^{ΔIEC-ind} mice compared to controls. In contrast, an oral infection with an invasion-deficient *Salmonella* Typhimurium strain did not differentially impact tissue bacterial loads or epithelial damage between groups. Likewise, the loss of epithelial HNF4A led to increased Muc2 transcripts expression in the ileum of infected *Hnf4a*^{ΔIEC-ind} mice. Histological examinations at four days post-infection showed an elevated number and size of goblet cells in the ileal crypts of *Hnf4a*^{ΔIEC-ind} mice. Bacterial localization using the general bacterial probe EUB388-cy3 (red) staining showed that infected *Hnf4a*^{ΔIEC-ind} mice tended to enhance barrier mucus layer thickness compared to the controls. On the contrary, acute T cell activation with anti-CD3 mAb induced a significant increase of *Cxcl1* transcripts in the small intestine of *Hnf4a*^{ΔIEC-ind} mice. H&E staining showed elongated ileal crypts in *Hnf4a*^{ΔIEC-ind} mice compared to controls after anti-CD3 injection. Moreover, five-days after inflammatory stimulus, the ki67+ staining showed a proliferative phenotype located in the hyperplastic crypts of *Hnf4a*^{ΔIEC-ind} mice.

Conclusion: Altogether, these results support that HNF4A could play a crucial adaptive role in modulating the small intestine epithelial barrier function and controlling the immune system during acute inflammatory stress.

Disclosure: No conflict of interest in the text.

PP0388

ABLATION OF THE COLONIC EPITHELIAL MUSCARINIC RECEPTOR 3 INDUCES SEX SPECIFIC MODULATION OF INTESTINAL STEM CELLS AND RESPONSE TO INTESTINAL INJURY

M. Ragab¹, J. Wieland², C.M. Waldherr Ávila de Melo¹, T. Agibalova¹, A. Ermolova¹, A. Hempel¹, F. Heindl¹, I.E. Demir³, B. Kohnke-Ertel¹, M. Quante⁴, R.M. Schmid¹, M. Middelhoff¹

¹Klinikum rechts der Isar, Technical University of Munich, Munich, Germany, ²Klinikum rechts der Isar, Technical University of Munich, München, Germany, ³Klinikum Rechts Der Isar, Technical University of Munich, Department of Surgery, Munich, Germany, ⁴Universitätsklinikum Freiburg, Department of Internal Medicine II, Freiburg, Germany

Contact E-Mail Address: mohab.ragab@tum.de

Introduction: Intestinal stem cells (ISCs), located at the intestinal crypt base, are exposed to diverse signals that contribute to their proliferation and differentiation. These signals originate from the stem cell niche, which is comprised of epithelial cell types, enteric neurons, myofibroblasts or endothelial cells. Acetylcholine (ACh) is an important neurotransmitter of the enteric nervous system (ENS), which activates muscarinic (mAChRs) and nicotinic receptors (nAChRs). Mammalian mAChRs consist of five main subtypes (M1–M5) which are coupled to G-proteins. In addition to cells of the ENS, mAChRs are prominently expressed by intestinal epithelial cell (IEC) types including Lgr5-positive ISC. We could previously show that the modulation of mAChRs altered small intestinal differentiation and the cellular activity of Lgr5+ ISCs.

Aims & Methods: We investigated the role of mAChRs in colonic epithelial homeostasis and regeneration by utilizing male and female Vil-Cre×M3R fl/fl mice with epithelial ablation of M3R. The colonic *Lgr5*-expressing ISC

number was assessed in Vil-Cre×M3R fl/fl and C57bl/6 mice by *in situ* hybridization (ISH). Intestinal inflammation was induced by treating C57bl/6 and Vil-Cre×M3R fl/fl mice with 1% (v/v) DSS in drinking water for 7 days, followed by 5 days of normal drinking water. Epithelial cell proliferation rate and numbers of Lgr5+ ISC were assessed in colonic organoids treated with 250 nM bethanechol (Beth), a muscarinic agonist, for 4 days.

Results: Epithelial deletion of M3R *in vivo* revealed sex-based differences in colonic Lgr5- expressing ISC cell numbers. While male Vil-Cre×M3R fl/fl mice exhibited a severe reduction in colonic Lgr5-expressing ISCs, female mice showed the opposite phenotype with a moderate expansion of Lgr5-expressing cells. This translated into exacerbated DSS-induced colitis in male Vil-Cre x M3R fl mice as compared to very mild inflammation in female Vil-Cre x M3R fl mice normalized to respective age- and gender matched C56BL WT controls. *In vitro*, pharmacologic muscarinic agonism using Bethanechol similarly induced sex-specific changes to epithelial proliferation as well as Lgr5-positive ISC counts employing murine colonic organoids. Interestingly, Bethanechol treatment induced increased proliferation and an expansion of Lgr5-positive ISC *in vitro* in colonoids from female mice, which did not occur in treated organoids from male mice.

Conclusion: In summary, our study highlights the significant role of mAChRs, particularly M3, in ISCs and colonic health. The sex-based disparities observed in Lgr5+ ISC populations and responses to inflammatory stimuli emphasize the potential intricate interplay between mAChRs and sex hormones in intestinal physiology. These findings suggest potential therapeutic targets for intestinal disorders, emphasizing the importance of understanding sex-specific mAChR signaling for personalized treatments.

Disclosure: Nothing to disclose.

PP0389

LONG-TERM FOLLOW UP OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED FOR CYTOMEGALOVIRUS COLITIS

G. Singh¹, C. Rentsch¹, W. Beattie^{1,2}, B. Christensen^{1,3}, F. Macrae^{1,3}, J. Segal^{1,3}

¹The Royal Melbourne Hospital, Gastroenterology and Hepatology, Melbourne, Australia, ²University Hospital Geelong, Gastroenterology and Hepatology, Geelong, Australia, ³The University of Melbourne, Department of Medicine, Parkville, Australia

Contact E-Mail Address: gurtej.singh@hotmail.com.au

Introduction: Inflammatory bowel disease (IBD) describes two chronic inflammatory intestinal diseases: Ulcerative Colitis (UC) and Crohn's Disease (CD). Treatment of these conditions is often through immunosuppression to induce remission then maintenance. Cytomegalovirus (CMV) is a virus commonly found latent in all humans with seroprevalence rates existing between 40-100% depending on geographical location (1). Pathological reactivation of CMV is triggered by inflammation and immunosuppression; both present in the pathogenesis and treatment of IBD respectively (2). Consequentially, CMV reactivation occurs in IBD flare-ups around a rate of 25% (2) and greater than 30% in steroid-refractory patients (1, 3). Whether CMV reactivation is associated with escalating medical therapy, further hospital admissions, and worse clinical outcomes such as toxic megacolon or colectomy when compared to non-CMV associated flare-ups remains controversial. As such, the aims of this study were to follow up patients with IBD following an index episode of CMV colitis and analyse disease progression, relapse of CMV colitis, and clinical outcomes.

Aims & Methods: As such, the aims of this study were to follow up patients with IBD following an index episode of CMV colitis and analyse disease progression, relapse of CMV colitis, and clinical outcomes.

A retrospective study of patients treated at Royal Melbourne Hospital, Parkville, Australia treated between 2018-2023 was completed. Patients were included if they had a diagnosis of IBD, had positive immunohistochemistry for CMV on biopsy, and were treated with Ganciclovir or Valganciclovir for CMV colitis. Data collected included demographic details and laboratory investigations at time of first episode of CMV colitis. Data regarding treatment for IBD and CMV colitis at time of CMV colitis was also collected. Outcome results were collected at 6-month and 12-month time points after first episode of CMV colitis. Fourteen patients were included in this study; 13 with UC and 1 with CD.

Results: Recurrence of CMV colitis occurred in 21% of cases at 6 months and 29% at 12 months. Additional courses of corticosteroids remained constant at 21% of cases at 6 and 12 months. Forty-three percent of patients had changed their biologic at 6 months and this stayed constant at 12 months. Similarly, 29% of patients had escalated their biologic dose at 6 months which was the same at 12 months. At 6 months, 43% of patients had been re-hospitalised due to IBD or CMV including 2 colectomies. At 12 months, these figures increased to 36% and 3 respectively. Disease remission was only achieved by 7% of patients at 6 months, increasing to 29% at 12 months.

Conclusion: While a descriptive study, our results when compared with previous studies (4) suggest that CMV colitis is a negative prognostic marker in patients with IBD, resulting in higher rates of hospitalisation, failed medical therapy requiring medication change or dose escalation, and colectomy. These risks may be greater at <6 months from index episode of CMV colitis. Further research regarding effective management of CMV colitis is needed to minimise poor outcomes in these patients.

References: 1. Maher MM, Nassar MI. Acute cytomegalovirus infection is a risk factor in refractory and complicated inflammatory bowel disease. *Digestive diseases and sciences*. 2009;54:2456-62.

2. Kandiel A, Lashner B. Cytomegalovirus colitis complicating inflammatory bowel disease. *Official journal of the American College of Gastroenterology* | ACG. 2006;101(12):2857-65.

3. Cottone M, Pietrosi G, Martorana G, Casa A, Pecoraro G, Oliva L, et al. Prevalence of cytomegalovirus infection in severe refractory ulcerative and Crohn's colitis. *The American journal of gastroenterology*. 2001;96(3):773-5.

4. Zhang M, Bai X, Zhang H, You Y, Lv H, Li Y, et al. The role of cytomegalovirus colitis on short- and long-term outcomes for patients with ulcerative colitis. *Scandinavian Journal of Gastroenterology*. 2022;57(3):282-9.

Disclosure: Nothing to disclose.

PP0390

PREDICTION OF ENDOSCOPIC FEATURES OF DISEASE FROM SINGLE-CELL RNA SEQUENCING DATA IN SIGMOID COLON OF PATIENTS WITH ULCERATIVE COLITIS

K. Kohl^{1,2}, A. Riva^{1,2}, C. Primas¹, M. Gerstorfer^{1,2}, M. Wiekowski³, S. Badalamenti³, W. Reinisch¹, G. Busslinger^{1,2}

¹Medical University of Vienna, Dep.of Internal Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria, ²CeMM - Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria, ³Sanofi Pharmaceuticals, New Jersey, United States of America

Contact E-Mail Address: Georg.Busslinger@meduniwien.ac.at

Introduction: Patients suffering from ulcerative colitis (UC) have reduced life qualities and an increased risk of developing cancer. Current treatment options are limited and have a ceiling effect with remission rates of ~35%. A possible reason is the multi-factorial aetiology, which are as-

sociated with an overactivation of the immune system and a dysbiosis of the gut microbiome. An important step towards a better understanding is the characterization of epithelial lesions. Their severity is classified by the Mayo score system based on their macroscopic appearance. While previous studies analysed cellular changes within the colon in UC patients, a detailed characterization of different UC-associated lesions are still missing, which is the aim of our study in collaboration with Sanofi Pharmaceuticals.

Aims & Methods: We recruit patients with active disease at our endoscopy unit and collect different biopsies from multiple regions within these patients to compare the reproducibility of single cell RNA sequencing (scRNAseq) results of similar appearing lesions within and between patients. For the sample preparation, we performed a cellular enrichment step for immune, epithelial and stromal cells before performing 10x scRNAseq to obtain equal numbers for each cell fraction from every sampled area. Additionally, we collected stool samples and endoscopic brushes to determine the associated microbial communities by 16S rRNA sequencing.

Results: Our cellular isolation strategy allows successful recovery of fibroblast, epithelial and immune cell fractions from each lesion. All expected epithelial cell types as previously described are detected in our dataset as well. Moreover, our experimental setup to obtain comparable numbers of fibroblasts, epithelial and immune cells enables us now to investigate cell-cell communication differences within different Mayo score lesions. For example, CXCL signals increased with the severity of macroscopic lesions and involves multiple cell types.

Additionally, we are in the middle of correlating microbial diversity with the corresponding disease conditions.

Conclusion: Our results provide exciting insights into cell-cell communications at an unprecedented depth, which identifies aberrant signalling pathway that may contribute to treatment failure in the clinics.

Disclosure: We have nothing to disclose.

PP0391

LACK OF DNA METHYLTRANSFERASE DNMT3A IN FIBROBLASTS IMPAIRS CELL GROWTH AND WOUND HEALING

C. Escudero-Hernández¹, E. Hübner¹, S. Núñez-Torvisco¹, A. Rodríguez-Peña¹, J. Montague¹, P. Rosenstiel²

¹University Hospital Schleswig-Holstein / Institute of Clinical Molecular Biology (IKMB), Cell Biology, Kiel, Germany, ²Kiel University, University Hospital Schleswig-Holstein, Institute of Clinical Molecular Biology (IKMB), Kiel, Germany

Contact E-Mail Address: celia.escher@gmail.com

Introduction: Fibrosis in Crohn's disease (CD) is a complication of chronic inflammatory processes that may result in impaired gastrointestinal function and bowel strictures. However, exact pathomechanisms leading to intestinal fibrosis in CD are not fully understood. Since the de novo DNA methyltransferase DNMT3A is involved in cellular differentiation processes and genetic variants have been associated with increased risk for CD, we sought to characterize how DNMT3A loss might affect fibroblasts, the key mesenchymal cells involved in fibrosis.

Aims & Methods: We stably deleted Dnmt3a in 3T3 fibroblast cell line using CRISPR-Cas9 technology and subsequently selected GFP-positive clones using FACS sorting. Cell cultures were performed in cell culture plates with or without 0.2% gelatin coat. Reverse transcription quantitative PCR, western blot, and immunofluorescence were used to confirm Dnmt3a gene deletion and characterize wild-type (WT) and knockout (KO) cells. Cell adhesion was evaluated by fluorescence levels of calcein acetoxymethyl ester (CAM)-labelled cells that attached to cell culture plates

after 1h of culture and subsequent wash. Collagen lattice assays in presence of proinflammatory and profibrotic stimuli served to assess fibroblast contractibility.

Results: 3T3 fibroblasts lacking Dnmt3a acquire an activated myofibroblast phenotype (increased alpha-SMA expression) that also overexpress tissue remodeling matrix metalloproteinase Mmp3, and the inflammation-induced necroptosis marker RIPK3 when compared to their WT counterparts. In addition, Dnmt3a-depleted 3T3 cells adhere more strongly to cell culture plates. In presence of transforming growth factor (TGF)-beta, cells embedded in a 3D collagen matrix and lacking Dnmt3a build an interconnected cellular network and contract up to a 77.78% (compared to interconnected cells that reach up to 13.73% contraction by WT cells). This contraction was independent of the presence of interleukin (IL)-11. Profibrotic factors such as bleomycin prevent intercellular network formation in both WT and KO cells; hence, incapacitating cells to contract the collagen matrix.

Conclusion: We conclude that Dnmt3a is crucial for fibroblast homeostasis, including cell activation and functionality. Furthermore, TGF-beta induces higher fibroblast contractibility when Dnmt3a is lacking. Thus, additional characterization of Dnmt3a depletion in fibroblasts will deepen the understanding of fibrosis and may point towards new therapeutic approaches for this untreatable complication.

References: 1. Hampe J, Franke A, Rosenstiel P, et al. A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. *Nat Genet.* 2007;39(2):207-211. doi:10.1038/ng1954

2. Fazio A, Bordoni D, Kuiper JWP, et al. DNA methyltransferase 3A controls intestinal epithelial barrier function and regeneration in the colon. *Nat Commun.* 2022;13(1):6266. doi:10.1038/s41467-022-33844-2

Disclosure: Nothing to disclose.

PP0392

HIGH SERUM LIPOCALIN-2 EXPRESSION AT THE DIAGNOSIS IN CHILDREN WITH ULCERATIVE COLITIS: A PILOTSTUDY

G. D'Arcangelo¹, C. Petrella², M. Fiore², M. Distante¹, F. Zucconi¹, S. Rotulo¹, A. Gravina¹, M. Aloï¹

¹Sapienza University of Rome, Pediatric Gastroenterology Unit, Rome, Italy, ²Institute of Biochemistry and Cell Biology (IBBC-CNR), Rome, Italy

Contact E-Mail Address: giuliadarcangelo87@gmail.com

Introduction: Lipocalin-2 (LCN2) is a pleiotropic mediator of various inflammatory processes. Upon gastrointestinal damage, bacterial infection, or intestinal inflammation, LCN-2 is strongly upregulated, resulting in high concentrations of this molecule.

Aims & Methods: We determined the serum levels of LCN-2 in a cohort of newly diagnosed UC children, and we compared them with healthy controls.

We conducted a prospective cross-sectional observational study conducted at the Pediatric Gastroenterology Unit of the Umberto I Hospital and at the IBBC – Institute of Biochemistry and Cell Biology – CNR in Rome. All children aged 6-18 years of age, newly diagnosed with UC were consecutively enrolled. Blood withdrawal was conducted upon diagnosis. Human serum LCN-2 (Cat. No. DY1757) was measured using a sandwich enzyme-linked-immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA), according to the protocols provided by the manufacturer. Clinical, demographic, biochemical and endoscopic data were recorded.

Results: Thirty-two children with a new diagnosis of UC [11 (34%) female, mean age 12.7 ± 4] and 38 age- and sex-matched healthy control [21 (55%) females, mean age 11.71 ± 4] were consecutively enrolled. Serum LCN-2

levels were significantly higher in cases compared to controls (280 ± 152 ng/mL vs 66 ± 55 ng/mL), $p < 0.001$]. Among UC children, significantly higher LCN2 levels were measured in pancolitis (363.7 ± 155.2 ng/mL) compared to proctitis, left-sided and extensive colitis (184.9 ± 74.65 ng/mL; $P = 0.0003$). A significant inverse correlation was observed between LCN-2 and albumin levels at the diagnosis by the Spearman coefficient correlation ($r = -0.455$; $P = 0.03$) and a significant direct correlation was observed between LCN-2 and CRP values at the diagnosis ($r = 0.44$; $P < 0.05$).

Conclusion: Serum LCN-2 levels are significantly higher in children with UC compared to the healthy control group, with the highest levels observed in children with the most extensive disease. Such results as well as its correlation with the actual disease monitoring tool, make this protein an interesting candidate biomarker.

Disclosure: Nothing to disclose.

PP0393

OCTN1 VARIANTS SHAPE INNATE IMMUNITY AND PREDICT INDIVIDUAL RESPONSE TO VEDOLIZUMAB IN ULCERATIVE COLITIS PATIENTS: AN EXPLORATORY STUDY

P. Puca¹, I. Capobianco¹, L. Masi¹, V. Petito¹, A. Poscia¹, G. Coppola¹, M. Fidaleo², F. Del Chierico³, I. Palucci¹, E. Schiavoni¹, D. Napolitano¹, V. Amatucci¹, L. Turchini¹, D. Pugliese¹, L. Laterza¹, L. Putignani³, L.R. Lopetuso¹, G. Cammarota¹, A. Gasbarrini¹, G. Pani⁴, F. Scaldaferri¹

¹Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ²Università La Sapienza, Rome, Italy, ³Ospedale Bambino Gesù, Rome, Italy, ⁴Università Cattolica del Sacro Cuore, Rome, Italy

Contact E-Mail Address: pgpuca@gmail.com

Introduction: Limited evidence is available about predictors of response to specific medications for ulcerative colitis (UC). OCTN1, an organic cation transporter, with its variants, could modulate the inflammatory response and potentially predict individual response to immune-modulatory therapy (anti-TNF α and vedolizumab).

Aims & Methods: We first confirmed the ability of OCTN1 to differentially modulate IL1 β secretion under different stimuli in a human leukemia monocytic cell line (THP-1) and in human peripheral blood mononuclear cells. We therefore prospectively enrolled a cohort of UC patients starting either anti-TNF α or vedolizumab, determined their OCTN1 genotype and evaluated their clinical features at baseline and clinical response to therapy after six months, as well as two years therapy persistence.

Results: OCTN1-deficient THP1 cells showed reduced IL-1 β secretion in response to peptidoglycan (PGN) and *Fusobacterium nucleatum* (Fn), whilst primary monocytes bearing OCTN1 503F variant displayed an increased production of IL-1 β in response to PGN and live bacteria. We therefore enrolled 90 patients, of which 50 starting anti-TNF α and 40 vedolizumab. At the multivariate analysis, an overall better response to therapy was observed with the mutated 503F variant (OR=16.72, $p=0.011$) in comparison to wild type (503L) and heterozygous variants; nevertheless, a significant reduction of clinical response after six months was observed in patients with 503F variant treated with vedolizumab (OR=0.02, $p=0.04$). Furthermore, the same trends were observed the two years steroid free therapy persistence was taken into consideration.

Conclusion: Mutated OCTN1 genotype (503F) could favor an increased IL1 β secretion from human leukocytes, thus suggesting a worse disease course and lower response to vedolizumab as compared to homozygous 503L and heterozygous.

Disclosure: Nothing to disclose.

PP0394

ENDOTHELIAL AND SUBCLINICAL CARDIAC DYSFUNCTION IN INFLAMMATORY BOWEL DISEASE

H. Telaprolu¹, H. Bhujade², P. Panda³, V. Jearth¹, H. Mandavdhare¹, V. Sharma¹, Y.P. Sharma³, U. Dutta¹, A.K. Singh¹

¹Postgraduate Institute of Medical Education and Research, Department of Gastroenterology, Chandigarh, India,

²Postgraduate Institute of Medical Education and Research, Department of Radiodiagnosis and Imaging, Chandigarh, India,

³Postgraduate Institute of Medical Education and Research, Department of Cardiology, Chandigarh, India

Contact E-Mail Address: harshavardhan.telaprolu@gmail.com

Introduction: Endothelial dysfunction is seen in chronic inflammatory diseases and also associated with inflammatory bowel disease (IBD). (1-3) Similarly, subclinical cardiac dysfunction has also been seen in children with IBD. (4) This has not been studied in adults with IBD.

Aims & Methods: This study aims to assess the prevalence of endothelial and subclinical cardiac dysfunction among patients of IBD.

Adult patients with active IBD, IBD in remission and healthy control (age and sex matched) were recruited. Diagnosis of IBD was based on clinical, endoscopic, and histological findings. Ulcerative colitis (UC) severity was evaluated with Total Mayo Score (MS) and Crohn's Disease (CD) with Crohn's Disease Activity Index (CDAI). All participants underwent investigations to assess disease severity, presence of anemia and dyslipidemia. Conventional 2D and speckled echocardiography was done to assess subclinical cardiac dysfunction. Endothelial dysfunction was detected using endothelium dependent flow mediated dilation (FMD). Vascular doppler ultrasound of brachial artery was done to assess FMD.

Group comparisons of numerical data were done with one-way ANOVA test or Kruskal-Wallis test, depending on the normality of the data. Holm-Sidak test was used as post hoc test for multiple assessment. Proportions were compared using the chi-square test. Statistical significance was determined when the p-value was less than 0.05.

Results: 90 subjects were analyzed in the study (30 with active IBD, 30 IBD in remission and 30 healthy controls). 55 patients had UC and 5 patients had CD. The median duration of disease was 24 (48.3) months and was similar in both active IBD and IBD in remission.

The median FMD was 13.7 %, 22.9% and 23.3% in active IBD, IBD in remission and controls respectively. FMD was significantly lower in patients with active IBD as compared to controls ($p=0.025$) and IBD in remission ($p=0.048$). There was no difference in FMD between controls and IBD in remission ($p=0.707$). There was no correlation between impaired FMD and disease duration (Pearson's $r = -0.104$, $p=0.21$). Cardiac evaluation revealed comparable ejection fraction (EF) among different groups. The global longitudinal strain (GLS) was significantly lower in active IBD [-18.0 (5.73)%] ($p=0.002$) and IBD in remission [-18.0 (3.30)%] ($p=0.034$) as compared to controls [-20.2 (1.95)%]. GLS was similar in IBD in remission and active IBD ($p=0.933$). The prevalence of subclinical cardiac dysfunction based on GLS was 4% (4/30) in controls, 14.4% (13/30) in IBD in remission and 15.6% (14/30) in active IBD. The difference among the groups was significant ($p=0.011$). FMD was not different between subjects with normal and abnormal GLS ($p=0.936$).

Outcome Median (IQR)	Active IBD	IBD in remission	Controls	p Value	p1	p2	p3
FMD (%)	13.7 (16.3)	22.9 (15.1)	23.3 (6.4)	0.017	0.048	0.025	0.707
GLS	-18.0 (5.73)	-18.0 (3.30)	-20.2 (1.95)	0.003	0.99	0.002	0.003

Comparison between: p1 –Active IBD and IBD in remission; p2 –active IBD and controls, p3 – IBD in remission and controls

Conclusion: Endothelial dysfunction was more in active IBD compared to IBD in remission and controls. It was similar in IBD in remission and controls. Subclinical cardiac dysfunction was also more in IBD patients. Endothelial dysfunction did not correlate with disease duration. We also found no correlation between Endothelial Dysfunction and presence of subclinical cardiac dysfunction.

References:

1. Principi M, Mastrodonato M, Scicchitano P, Gesualdo M, Sassara M, Guida P, et al. Endothelial function and cardiovascular risk in active inflammatory bowel diseases. *J Crohns Colitis*. 2013 Nov;7(10):e427-433.
2. Kocaman O, Sahin T, Aygun C, Senturk O, Hulagu S. Endothelial dysfunction in patients with ulcerative colitis. *Inflamm Bowel Dis*. 2006 Mar;12(3):166-71.
3. Roifman I, Sun YC, Fedwick JP, Panaccione R, Buret AG, Liu H, et al. Evidence of endothelial dysfunction in patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2009 Feb;7(2):175-82.
4. Hensel KO, Abellan Schneyder FE, Wilke L, Heusch A, Wirth S, Jenke AC. Speckle Tracking Stress Echocardiography Uncovers Early Subclinical Cardiac Involvement in Pediatric Patients with Inflammatory Bowel Diseases. *Sci Rep*. 2017 Dec;7(1):2966.

Disclosure: Nothing to disclose.

PP0395

TRANSCRIPTOMIC ANALYSIS REVEALS DIFFERENTIAL EXPRESSION OF OXIDATIVE STRESS PATHWAYS IN CROHN'S DISEASE PATIENTS

J. Bouvet¹, H.P. Pham², C. Polcar³, M. Ngollo⁴, S. Nancey⁵, M. Nachury⁶, X. Treton⁷, M. Fumery⁸, A. Buisson⁹, N. Barnich¹⁰, S. Demignot¹, M. Bezault⁴, L. Le Bourhis⁴, R. Study group⁴, M. Allez⁴, P. Seksik^{11,1}

¹Sorbonne University, CRSA Team : Microbiota Intestin & Inflammation, Paris, France, ²Parean Biotechnologies, Saint-Malo, France, ³Ecole Normale Supérieure, PSL university, CNRS, Laboratoire des biomolécules, Département de chimie, Paris, France, ⁴Gastroenterology, Hopital Saint-Louis, APHP, INSERM U1160, Université Denis Diderot, Gastroenterology, Paris, France, ⁵Université Claude Bernard, Dept. de Gastroentérologie, Pierre Benite, France, ⁶CHRU Lille, Gastroenterology, Courbevoie Cedex, France, ⁷Institut des MICI, Gastroenterology, Neuilly sur Seine, France, ⁸Amiens University Hospital, Gastroenterology department, Amiens, France, ⁹CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France, ¹⁰Université Clermont Auvergne, M2iSH, Clermont-Ferrand, France, ¹¹Gastroenterology & Nutrition Department, Gastroenterology and Nutrition Unit, Paris, France

Contact E-Mail Address: philippe.seksik@aphp.fr

Introduction: Crohn's disease (CD) poses a clinical challenge due to its unpredictable post-operative recurrence and the necessity for effective therapeutic interventions. The molecular mechanisms governing recurrence are poorly understood, although oxidative stress (OS) has been implicated in CD pathogenesis. However, its specific role in recurrence remains elusive. This study aimed to analyze the gene expression signatures regarding OS and their implications for CD recurrence using transcriptomic analysis.

Aims & Methods: Ileal mucosa samples were obtained from the prospective multicentric cohort of CD patients undergoing surgery. They were collected from ileal resection margins (n = 196) at the time of surgery (M0) and in the neo-terminal ileum (n = 121) 6 months after surgery (M6) while patients were classified as in remission (Rem) or recurrence (Rec) based on the Rutgeerts score. Endoscopic recurrence was defined as a Rutgeerts score ≥ 2 . Gene data sets (Affymetrix microarrays) were issued on a principles paper*. Pathway analysis was conducted to identify significant OS pathways using the Ensemble of Gene Set Enrichment Analyses (EGSEA) method and through unsupervised signature generation (Independent Component Analysis) from M0 and M6 genes dataset. Statistical analyses were carried out to assess differential gene expression and pathway enrichment between Rem and Rec patients at M0 and M6.

Results: No significant genes were differentially expressed between Rem and Rec groups at M6 and M0. However, using EGSEA at M6, of the 1766 significant pathways, 40 were related to OS and predominantly overexpressed in the Rec group, indicating a potential association between OS resolution and pressure relief. At M0, of the 2556 significant pathways, 40 were related to OS and equally distributed between the Rem and Rec groups, and therefore did not predict recurrence at M6. Applying unsupervised signature generation, 140 signatures were identified and 8 were annotated as OS pathways. These OS pathways were upregulated at M6 in the Rec group and at M0 in the Rem group.

Conclusion: The study highlights the role of OS in CD progression and post-operative relapse. The significant increase in OS pathways at M6 in relapsed patients and at M0 in patients who remain in remission suggests that resolution of OS is necessary to counteract CD relapse. Further research is needed to delineate the role of oxidative stress in CD recurrence and to identify new therapeutic targets tailored to individual patient profiles.

References:

- *Ngollo et al. Identification of Gene Expression Profiles Associated with an Increased Risk of Post-Operative Recurrence in Crohn's Disease *JCC* 2022;16(8):1269-1280. doi: 10.1093/ecco-jcc/jjac021.

Disclosure: There is no conflict of interest regarding this abstract

PP0396

THE E3 UBIQUITIN LIGASE RNF31 MEDIATES THE DEVELOPMENT OF ULCERATIVE COLITIS BY REGULATING NLRP3 INFLAMMASOME ACTIVATION

C. Zeng¹, P. Wang¹, C. Tang¹, J. Li¹, Y. Chen¹, Peng Wang, ChaoTao Tang, Jun Li, Youxiang Chen

¹Jiangxi Provincial Key Laboratory of Digestive Diseases, Jiangxi Clinical Research Center for Gastroenterology, Digestive Disease Hospital, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University,, Gastroenterology, Nanchang, China

Contact E-Mail Address: zcy896@163.com

Introduction: The NLRP3 inflammasome is a multiprotein complex consisting of the receptor protein NLRP3, the linker protein ASC, and the effector protein caspase-1. Activation of NLRP3 can lead to increased production of proinflammatory cytokines, which disrupt intestinal barrier function and induce the development of ulcerative colitis.

Aims & Methods: Whether RNF31 regulates the expression of the NLRP3 inflammasome is not known. In this study, we examined the expression of RNF31, and NLRP3 in ulcerative colitis tissues by GEO database analysis and immunohistochemical assays, and subsequently determined that RNF31 can regulate NLRP3 inflammasome expression by constructing an RNF31-deficient cell model, and elucidated the role of RNF31 in the development of ulcerative colitis.

Results: We found that the expression of NLRP3 decreased after the addition of MG132 inhibited the level of ubiquitination. A cycloheximide (CHX)-chase analysis showed that RNF31 was able to make NLRP3 more stable, which was most likely due to the fact that RNF31 changed the level of ubiquitination on NLRP3. Multiple co-immunoprecipitation (CO-IP) assays showed that there was an interaction between RNF31 and NLRP3 and that this interaction increased the level of ubiquitination on NLRP3. And CO-IP experiments using truncated RNF31 plasmids showed that the RBR structural domain interacted with NLRP3, increasing the level of ubiquitination on NLRP3 and making NLRP3 more stable. By constructing a cell model with RNF31 deletion as well as overexpression and using CO-IP experiments we found that the K63 ubiquitination chain plays an important role in stabilizing NLRP3.

Finally, we constructed RNF31-deficient mouse models using adenovirus and showed that the expression of NLRP3 and inflammatory factors IL-18 and IL-1 β were reduced in the absence of RNF31.

Conclusion: Our study shows that RNF31 can interact with NLRP3 through the RBR structural domain and increase the level of the K63 ubiquitin chain on NLRP3 thereby making NLRP3 more stable and activating the assembly of the inflammasome, elucidating how RNF31 is involved in the mechanism of colitis development.

References: 1. D. Oikawa, et al., Linear Ubiquitin Code: Its Writer, Erasers, Decoders, Inhibitors, and Implications in Disorders, *Int. J. Mol. Sci.* 21 (9) (2020) 3381.

2. F. Humphries, et al., The E3 ubiquitin ligase Pellino2 mediates priming of the NLRP3 inflammasome, *Nat. Commun.* 9 (1) (2018) 1560.

3. X. Wu, et al., MyD88-Dependent Signaling Is Required for HOIP Deficiency Induced Autoinflammation, *J. Immunol.* 207 (2) (2021) 542–554.

4. K. Bulek, et al., Epithelial-derived gasdermin D mediates nonlytic IL-1 β release during experimental colitis, *J. Clin. Invest.* 130 (8) (2020) 4218–4234.

5. P. Wan, et al., Cullin1 binds and promotes NLRP3 ubiquitination to repress systematic inflammasome activation, *FASEB J* 33 (4) (2019) 5793–5807.

Disclosure: Nothing to disclose.

PP0397

EXPLORING BIOMARKERS OF SYSTEMIC OXIDATIVE STRESS AND PLACENTAL INSUFFICIENCY IN PREGNANT WOMEN WITH INFLAMMATORY BOWEL DISEASES

H.J. Holstein¹, D.G. Bouwknegt¹, M.C. Visschedijk¹, M.L.C. Bulthuis², M. Reinders-Luinge², M.H. Schoots², H. van Goor², S.J. Gordijn³, G. Dijkstra¹, A.R. Bourgonje^{1,4}

¹University of Groningen, University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands,

²University of Groningen, University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands,

³University of Groningen, University Medical Center Groningen, Gynecology and Obstetrics, Groningen, Netherlands, ⁴Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America

Contact E-Mail Address: H.j.holstein@umcg.nl

Introduction: Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), often manifests around the fertile age. It is known that disease activity affects pregnancy outcomes. However, little is known about how IBD affects pregnancy outcomes and vice versa. Both IBD and pregnancy complications, particularly those in which placental insufficiency is implicated, are accompanied by oxidative stress. Oxidative stress is defined as an imbalance between reactive oxy-

gen species (ROS) production and antioxidant availability. Free thiols (FT) are circulating biomarkers of oxidative stress since they readily scavenge ROS. Previous research has shown reduced levels of FT in both IBD¹ and pregnancy complications². Classical biomarkers of placental insufficiency include soluble FMS-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PLGF), and their ratio is reflective of maternal pregnancy complications². However, the behavior of these biomarkers in pregnant women with IBD remains unclear.

Aims & Methods: In this study, we aimed to investigate the relationship between FT, sFlt-1, and PLGF and the occurrence of pregnancy complications in patients with IBD, and to assess their dynamics before, during, and shortly after pregnancy.

In this retrospective clinical pilot study, we investigated a cohort of pregnant women with IBD and healthy pregnant controls who were pregnant between 2000 and 2023. Serum samples taken before (IBD n=41), during (IBD n=33, controls n=14), and after (IBD n=25) pregnancy were analyzed for PLGF, sFlt-1 and FT levels. FTs were measured using a colorimetric detection method. sFlt-1 and PLGF were measured using an immunofluorescent assay. Extensive clinical data were collected, including data about pregnancy complications such as pre-eclampsia, fetal growth restriction, and gestational diabetes, and IBD disease parameters, including fecal calprotectin and clinical disease scores.

Results: In total, 40 patients (n=32 CD, n=7 UC, and n=1 IBD-U) with 47 pregnancies and 14 non-IBD control pregnancies were included. Comparing patients with IBD to controls during pregnancy, serum FT levels were significantly reduced in patients, even after adjustment for gestational age (p=0.043). FT levels significantly decreased during pregnancy compared to preconception (p=0.001), suggesting increased systemic oxidative stress during pregnancy. The sFlt-1/PLGF ratio was significantly higher in IBD compared to controls (p=0.011), which was partially due to a difference in gestational age (median (IQR): controls 32.6 weeks (29.4–33.1) vs. 15.4 weeks (7.0–22.7) in IBD). In total, 32 patients (56%) and 3 controls (21%) developed pregnancy complications. The sFlt-1/PLGF ratio was higher in those developing maternal complications, almost reaching significance (p=0.053), while FT showed a trend towards decreased levels in those developing maternal complications (mean (SD): 368.9 μ M (38.7) without vs. 349.1 μ M (21.9) with maternal pregnancy complications, p=0.082).

Conclusion: This study provides evidence for increased systemic oxidative stress (reflected by lower systemic FT levels) during pregnancy in IBD, when compared to both healthy controls and their own pre-conceptual levels. These results suggest a difference in redox status between pregnant women with IBD compared to those without. Further research is necessary to substantiate these findings and evaluate the utility of these biomarkers in predicting pregnancy complications and guiding clinical decision making in IBD pregnancy.

References: 1. Bourgonje AR, Gabriëls RY, de Borst MH, Bulthuis MLC, Faber KN, van Goor H, Dijkstra G. Serum Free Thiols Are Superior to Fecal Calprotectin in Reflecting Endoscopic Disease Activity in Inflammatory Bowel Disease. *Antioxidants (Basel)*. 2019 Sep 1;8(9):351. doi: 10.3390/antiox8090351.

2. Schoots MH, Bourgonje MF, Bourgonje AR, Prins JR, van Hoorn EGM, Abdulle AE, Muller Kobold AC, van der Heide M, Hillebrands JL, van Goor H, Gordijn SJ. Oxidative stress biomarkers in fetal growth restriction with and without preeclampsia. *Placenta*. 2021 Nov;115:87–96. doi: 10.1016/j.placenta.2021.09.013.

Disclosure: Nothing to disclose.

PP0398

INCIDENCE OF CHRONIC END-STAGE RENAL DISEASE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED COHORT STUDY FROM THE FRENCH NATIONAL HEALTH INSURANCE DATABASE

C. Prothe¹, A. Boitel², B. Martin³, V. Clairet⁴, L. Juif⁵, S. Koch⁵, S. Lang⁶, D. Ducloux⁷, M. Desmarests², L. Vuitton⁸

¹CHU Minjoz, Gastroenterology, Besançon, France, ²CHU Minjoz, Centre d'Investigation Clinique (CIC-1431), Unité de Méthodologie en Recherche Clinique Epidémiologie et Santé Publique (uMETH, Besançon, France, ³CHU Minjoz, Centre d'Investigation Clinique (CIC-1431), Unité de Méthodologie en Recherche Clinique Epidémiologie et Santé Publique (uMETH), Besançon, France, ⁴CHU Minjoz, Gastroenterology, Besançon, France, ⁵Chru Minjoz Besançon, Gastroenterology Unit, Besançon, France, ⁶CHU Minjoz, Nephrology, Besançon, France, ⁷Chru Minjoz, Nephrology, Besançon, France, ⁸Besançon university hospital gastroenterology, Dept. of Gastroenterology, Besançon, France

Contact E-Mail Address: carole.prothe@gmail.com

Introduction: Renal disorders are among the extra-intestinal manifestations of inflammatory bowel disease (IBD), and treatments may also lead to renal failure. However, the incidence of end-stage renal disease (ESRD), defined as the need for renal replacement therapy (dialysis and/or renal transplantation (RT)), is poorly known. The primary objective of our study was to assess the incidence of ESRD in IBD patients, and to compare it with the general health insurance scheme population.

Aims & Methods: We conducted a prognostic cohort study based on data from the French National Health Insurance Database (SNDS). Prevalent cases of IBD affiliated to the general health insurance scheme during the period 2011-2020 were identified on the basis of declarations long-term diseases ALD 24 or the presence of 2 hospital stays for IBD with ICD-10 codes or a single stay with reimbursement of specific treatments. Incident cases of ESRD were identified on the basis of a stay with a RT or a period with dialysis sessions for at least 45 days. Crude incidence rates of ESRD were calculated over the period for the IBD and the non-IBD population, with their 95% confidence intervals.

Results: A total of 280,283 IBD patients were included in the study over the period 2011-2020, 134,567 with ulcerative colitis (UC) and 145,716 with Crohn's disease (CD). The mean age at study inclusion was 39.8 (± 17.1) years. The M/F sex ratio was 0.9. The mean age at incidence of ESRD in the non-IBD population was 65.0 (± 17.0) years, the M/F sex ratio cases was 1.7. Among IBD patients, 534 patients began replacement therapy by dialysis or RT, they were younger than non-IBD patients (60.3 (± 16.7) years, $P < 0.001$). The mean incidence rate of ESRD over the period was 26.4 per 100,000 person-years (IC95% 23.1-29.6), 480 (89.9%) patients entered ESRD by dialysis, and 54 (10.1%) by preemptive RT. In the non-IBD population the mean rate of ESRD was 15.9 per 100,000 person-years (IC95% 14.8-17.1; $P < 0.0001$ compared with IBD): 79,606 (94.5%) patients entered ESRD by dialysis, and 4,634 (5.5%) by RT (as compared with IBD, $P < 0.001$). In subgroup analysis, the mean incidence rate of ESRD was 22.8 per 100,000 person-years (IC95% 18.9-26.7) in UC patients and 29.5 (IC95% 25.3-33.6) in CD patients ($P < 0.0001$). The rates of preemptive RT were 12.4% in UC patients (87.6% dialysis) and 8.6% in CD patients (91.4% dialysis).

Over a median follow-up of 6.8 years, the survival rate after ESRD was 40.8% in ESRD-IBD patients VS 34.2% in ESRD non-IBD patients ($P < 0.001$). This difference remained significant for patients under 65 ($p < 0.0073$).

No significant difference for the risk of re-hospitalization after RT ($p = 0.84$), of retransplantation during the follow-up period in RT patients ($p = 0.67$), or for the risk of hospitalization for severe infection ($p = 0.97$) after RT in patients from the general population compared with IBD patients. The same was true for the type of severe infections after RT ($p = 0.068$) and for

the risk of solid and haematological cancer after RT ($p = 0.48$). However, there was a significant difference in the type of first severe infection after RT ($p = 0.003$), but we are waiting for the results to tell us which one.

Conclusion: The incidence of ESRD is significantly higher in IBD than in the general data base population, confirming the need for regular monitoring of renal function in our patients.

Survival after ESRD onset, is higher in IBD patients.

The high incidence of RT in the IBD population confirms that access to transplantation is not restricted in this population.

References: Kirchgessner et al, Gastroenterology 2018

Meyer et al, Aliment Pharmacol Ther. 2020

Tuppin et al, Nephrol Ther 2016

Disclosure: Nothing to disclose.

PP0399

TISSUE-DIRECTED GENE THERAPY FOR INFLAMMATORY BOWEL DISEASE

K.A. Toth¹, Z.H. Lu¹, M. Iticovici¹, M. Lee¹, T. Rhie¹, G. Oliva Escudero¹, I. Dmitriev¹, D.T. Curiel¹, M. Ciorba¹

¹Washington University School of Medicine, Saint Louis, United States of America

Contact E-Mail Address: mciorba@wustl.edu

Introduction: There is an unmet need for new therapies to promote mucosal healing and restoration of epithelial barrier function in the inflammatory bowel diseases (IBD). The development of novel approaches to specifically deliver a therapy to the gut has the theoretical advantage of optimizing benefit while limiting side effects. Adenoviral (Ad) gene therapy has been successful in treating cancer and has recently been used in clinical trials as a vaccine for SARS-Cov2. Ad vectors can be modified to target specific tissues and therefore may be more effective vehicles for gene therapy for diseases like IBD than other systemic therapeutics. We propose that gene therapy using adenovirus has promise to achieve these goals in IBD. As a proof of concept, we developed an approach to deliver IL-22 via Ad gene therapy. IL-22 plays an important role in maintaining the epithelial barrier at mucosal sites like the skin, airway, and intestine. Epithelial cells are the primary target of IL-22 signaling, where it activates transcription of genes involved in cell proliferation and promotes antimicrobial functions.

Aims & Methods: We hypothesize that gene therapy with Ad vectors to deliver IL22 directly to the intestine could be an effective therapeutic for IBD by promoting intestinal wound healing and microbial homeostasis. To test this hypothesis, we injected human adenovirus serotype 5 (huAd5) expressing *IL22* (Ad-CMV-IL22) intravenously into 6-week-old C57BL/6 mice.

Results: IL-22 protein levels in the serum, liver, ileum, and colon were increased with Ad-CMV-IL22 compared to the empty vector control (Ad-CMV-GFP). We analyzed transcription of genes downstream of IL-22 signaling and found Ad-CMV-IL22 increased relative expression of *Lcn2* in the liver, ileum, and colon, as well as increased expression of *Mt1* and *Mt2* in the liver and colon. Ad-CMV-IL22 induced increased crypt depth and goblet cell count in the ileum and colon, and increased villus length in the ileum compared to Ad-CMV-GFP. Changes to the stool microbiome included increased abundance of the pro-tolerogenic family Lachnospiraceae-Ruminococcaceae with Ad-CMV-IL22 in both colon and ileum. It is known that huAd5 has liver tropism and gene therapy with hAd5 has been associated with liver toxicity. We also observed higher levels of IL-22 in the liver than in the serum, ileum, or colon after Ad-CMV-IL22 treatment. To reduce liver tropism, we modified the vector to incorporate myeloid-binding peptide (MBP) on the virus fiber, which re-targets the virus to the intestine and

vascular endothelium. Incorporation of MBP significantly reduced IL-22 protein levels in the liver by nearly 10-fold. The ratio of IL-22 protein levels in the ileum and colon was 1.35 and 1.81 times higher with the targeted vector compared to untargeted virus. Increased colon and ileal crypt depth (45%) as well as villus length (9%) were seen with Ad-CMV-MBP-IL22 as compared to the untargeted virus.

Conclusion: Together, these data suggest that IL-22 gene therapy in the intestine can promote cell proliferation and microbial homeostasis. In the future, this adenoviral gene therapy could be modified further to increase *IL22* gene delivery specifically to intestinal tissues.

Disclosure: D.T.C. is a consultant for Ocugen, Circero, Asgard, Accession and Tome Biosciences.

PP0400

IMPACT OF PHYSICAL ACTIVITY ON THE QUALITY OF LIFE OF PATIENTS WITH IBD: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

S. Mechhor¹, M. Cherkaoui Malki², H. El Bacha¹, N. Benzoubeir², I. Errabih²

¹Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ²Ibn Sina Hospital, Department of Gastroenterology, Hepatology and Proctology « Medicine B »; Ibn Sina University Hospital, Rabat, Morocco, Rabat, Morocco

Contact E-Mail Address: salmamechhor@gmail.com

Introduction: Chronic inflammatory bowel diseases (IBD) are chronic conditions that profoundly affect the quality of life (QoL), and their evaluation has become essential during IBD follow-up. Regular and tailored physical activity (PA) can contribute to improving QoL; however, engaging in PA may be limited during these diseases.

The aim of this study was to describe the factors associated with PA practice and its impact on QoL.

Aims & Methods: This was a descriptive and analytical prospective study conducted on a sample of 85 patients followed in IBD consultations. We collected data regarding the disease and assessed PA intensity using the International Physical Activity Questionnaire (IPAQ), which distinguishes between three activity levels: light, moderate, and vigorous. We assessed QoL using the Inflammatory Bowel Disease Questionnaire (IBDQ), calculating sub-scores for digestive symptoms, systemic symptoms, emotional disorders, social function, and overall score. Statistical analysis was performed using SPSS 20.0 software. Qualitative variables were compared using the Chi-square test and McNemar's test. Factors associated with PA practice were identified using a binary logistic regression model in univariate and multivariate analysis.

Results: We collected data from 85 patients. The mean age was 35 +/- 3.4 years. The female-to-male ratio was 1.23. Crohn's disease was reported in 65 (76.47%) patients, while 20 (23.53%) had ulcerative colitis. 68 (80%) patients were in remission. Two patients (3.3%) were smokers. The prevalence of joint manifestations was 13.3%. 12 patients (14.1%) had undergone surgery as part of their disease management. 51 (60%) patients were on biologic therapy with a mean treatment initiation of 3.5 +/- 1.2 years; 13 (15.29%) patients were on thiopurines alone, 19 (22.3%) were on salicylates, and 2 (2.35%) were on corticosteroids. Among our patients: 58 (80%) engaged in light PA, 18 (21.1%) in moderate activity, and 9 (10.58%) in vigorous activity. The mean sub-score for digestive symptoms was better in patients engaging in moderate to vigorous activity compared to those engaging in light activity, with respective values of 31.3 +/- 1.16 vs. 29.15 +/- 2.11, $p < 0.001$. The mean sub-score for systemic symptoms was also better in patients engaging in moderate to vigorous activity: 34.6 +/- 3.61 vs. 28.52 +/- 1.21 in cases of light PA, $p = 0.003$. In multivariate analysis, en-

gaging in moderate to vigorous PA was associated with clinical remission (OR 1.06; [1.02; 3.15]; $p = 0.002$) and absence of joint manifestations (OR 2.93; [1.24 - 3.05], $p < 0.001$). Smoking and a history of digestive surgery did not influence PA. Patients engaging in moderate to vigorous activity had a better quality of life than those engaging only in light activity, with mean overall IBDQ scores of 198.3 +/- 21.3 vs. 151.11 +/- 25.3, $p = 0.0003$. The emotional sub-score was better with moderate to vigorous activity: 33.7 +/- 5.1 vs. 31.05 +/- 4.51 in patients with light PA, $p = 0.002$. Similarly, the social function sub-score was better with moderate to vigorous activity: 29.04 +/- 7.16 vs. 26.23 +/- 4.61, $p < 0.001$.

Conclusion: In our study, engaging in moderate to vigorous PA among patients with IBD was associated with better quality of life. Certain factors limit its practice, notably disease flare-ups and joint manifestations. The importance of physical activity should therefore be evaluated during consultations, and patients with IBD should be encouraged to engage in regular and tailored PA according to their disease profile

Disclosure: Nothing to disclose.

PP0401

THROMBOEMBOLIC ACCIDENTS IN IBD: IS THERE A GENDER EFFECT?

A. Asmaa¹, S. Mechhor², M. Cherkaoui Malki³, H. El Bacha⁴, N. Benzoubeir¹, I. Errabih⁵

¹Mohammed V, Rabat, Morocco, ²Ibn Sina Hospital, Medecine B, Rabat, Morocco, ³University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ⁴Hopital Ibn Sina / Université Mohamed V / Faculté de Medecine, Gastroenterologie et Hépatologie, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: asmaa.aboullait@gmail.com

Introduction: Chronic inflammatory bowel disease (IBD) is at high risk of thromboembolic events (TEA), which are a significant cause of morbidity and mortality.

They are attributed to a pre-thrombotic state caused by the inflammatory activity of this disease.

The objective of our study was to evaluate the prevalence and risk factors (FDR) of ATEs in patients with IBD, to determine their clinical and evolutionary particularities while specifying the existence or not of a gender effect.

Aims & Methods: This is a retrospective descriptive and analytical study carried out at the hepato-gastroenterology and proctology department "Médecine B" CHU Ibn Sina Rabat, between January 2001 and July 2023, including all patients who presented during their follow-up with an ATE confirmed by imagery (thoracic angioscanner/ cerebral angio MRI/ doppler ultrasound).

We collected demographic, clinical and paraclinical data.

The Chi-2 test was used to compare categorical variables.

Results: During the study period, among the 1643 IBD cases collected in the department, we recorded 21 cases of IBD complicated by ATE, a prevalence of 1.27%.

The mean age was 42.7 years (23-61 years), with a male predominance of 12 men (57%) and 9 women (43%), with a sex ratio of M/F : 1.3.

Among the 12 men, 7 (58%) had Crohn's disease and 5 (42%) UC, with a mean disease duration of 8 years and 4 months. Among the 9 women, 6 (67%) were being followed for Crohn's disease and 3 (33%) for UC.

The occurrence of a thrombo-embolic complication during hospitalization for a disease exacerbation was more frequent in men than in women (8 (67%) Vs 5 (55%); $p=0.3$).

Deep vein thrombosis (DVT) was more common in women than in men (6(67%) Vs 1(8%); $p=0.003$).

Cerebral thrombophlebitis was found in 2 men (17%) and 2 women (22%). Budd Chiari syndrome was found in 1 woman (11%). Pulmonary embolism was found in 3 men (25%), portal thrombosis in 3 men (25%), renal artery thrombosis in 2 men (17%), superior mesenteric vein thrombosis in 1 man (8%). None of the women had these manifestations.

Thrombophilia testing revealed decreased anti-thrombin activity in women, associated with protein C deficiency in 2 patients (22%). In the men, we noted protein C deficiency in 1 patient (8%) and 1 case (8%) of protein S deficiency.

Hyperhomocysteinemia was positive in one patient (11%), with no cases in men.

All patients were treated with anti-coagulants for curative purposes.

The absence of thrombosis and good revascularization was confirmed by follow-up imaging after 6 months of treatment in 5 men (42%) and 3 women (33%); $p=0.4$.

A complication in the form of extensive cerebral ischemic necrosis of thrombosed vessels was noted in 1 man (8%).

A single case of death was reported in 1 man (8%) following a severe pulmonary embolism. No cases of death were recorded in women.

Conclusion: Patients with chronic inflammatory bowel disease have a non-negligible risk of developing TEA, particularly during the active phase of the disease, underlining the importance of preventing thromboembolic disease when managing patients during relapses.

Disclosure: Nothing to disclose.

PP0402

CANDIDA YEASTS IN CROHN'S DISEASE: PREVALENCE, ASSOCIATED FACTORS, AND IMPACT ON DISEASE PROGRESSION

M. Sabbah¹, F. Kahlaoui¹, A. Bouratbine², M. Ben Abid², N. Bibani¹, H. Jlassi¹, S. Soua¹, K. Aoun², D. Gargouri¹

¹Habib Thameur Hospital, Gastro-entérology, Tunis, Tunisia,

²Pasteur institute, Parasitology, Tunis, Tunisia

Contact E-Mail Address: meriam_sabbah@yahoo.fr

Introduction: Crohn's disease (CD) has a complex etiopathogenesis involving the intestinal fungal microbiota which appears to have a significant impact on the development and progression of the disease.

Aims & Methods: The objectives of our study were to investigate the prevalence of *Candida* yeasts and the factors associated with their presence, as well as their impact on the course of CD. A prospective study involving patients with CD [June 2020 - March 2021] was conducted at the gastroenterology department of HHT in collaboration with IPT. A mycological examination of stool samples was performed to identify *Candida* yeasts.

Clinical and laboratory follow-up was conducted to assess disease progression. Unfavorable evolution was defined in the presence of flare-ups, complications (abscesses, collections, surgical intervention for CD), and therapeutic escalation.

Results: Fifty-two patients with a mean age of 40.7 years [18-67] and a gender ratio (M/F) of 1.59 were included. Yeasts were detected in 71.2% of patients, with *Candida* genus present in 55.8%.

The isolated species were *Candida albicans* (45%), *Candida parapsilosis* (32%), *Candida glabrata* (10%), *Candida tropicalis* (6%), and *Candida krusei* (7%).

Two patients harbored two *Candida* species simultaneously: *C. krusei* and *C. parapsilosis*, and *C. albicans* and *C. parapsilosis*, respectively.

The presence of *Candida* was associated with a history of diabetes ($p=0.001$), ileal ($p=0.018$) and ileocolonic ($p=0.017$) disease locations, and clinical disease activity as assessed by CDAI ($p=0.03$).

C. albicans was associated with both stenosing and fistulizing phenotypes of CD ($p=0.04$) and a CRP > five mg/L ($p=0.005$). *C. glabrata* was associated with ileal localization ($p=0.01$), and *C. tropicalis* was associated with the occurrence of collections ($p=0.049$) and therapeutic escalation ($p=0.01$).

Conclusion: *Candida* genus yeasts are common in CD and are associated with disease activity and an unfavorable disease course. We suggest their systematic investigation during MC, although their treatment is not consensual.

- References:** 1. Sokol H, Leducq V, Aschard H, Pham HP, Jegou S, Landman C, et al. Fungal microbiota dysbiosis in (IBD). Gut. 2017 Jun;66(6):1039-48. 2. Imai T, Inoue R, Kawada Y, Morita Y, Inatomi O, Nishida A, et al. Characterization of fungal dysbiosis in Japanese patients with inflammatory bowel disease. J Gastroenterol. 2019 Feb;54(2):149-59. 3. Sartor RB, Wu GD. Roles for intestinal bacteria, viruses, and fungi in pathogenesis of inflammatory bowel diseases and therapeutic approaches. Gastroenterology. 2017 Feb;152(2):327-39. 4. Zuo T, Ng SC. The gut microbiota in the pathogenesis and therapeutics of inflammatory bowel disease. Front Microbiol. 2018 Sep;9:2247. 5. World Health Organization. A healthy lifestyle: (WHO) recommendations [En ligne]. OMS [cité le 27/12/2023]; Consultable à l'URL: <https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle--who-recommendations> 6. Best WR, Beckett JM, Singleton JW, Kern F. Development of a Crohn's disease activity index. National cooperative Crohn's disease study. Gastroenterology. 1976 Mar;70(3):439-44. 7. Harvey RF, Bradshaw JM. A simple index of Crohn's disease activity. Lancet. 1980 Mar;1(8167):514. 8. Rutgeerts P, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. Gastroenterology. 1990 Oct;99(4):956-63.

Disclosure: Nothing to disclose.

PP0403

CHARACTERISTICS OF LEISHMANIA INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

L. Madero¹, J.M. Benítez², A. MÍNGUEZ SABATER³, L. Mayorga Ayala⁴, J.J. Ramirez Palanca⁵, N. Moreno Sánchez⁶, C. Amorós García⁷, M.Á. Nieto Vitoria⁸, R. Mena Sánchez⁹, L. Gimeno Pitarch¹⁰, N. Maroto Arce¹¹, C. Suria Bolufer¹², F. Rodríguez-Moranta¹³, I. Ordás¹⁴, L. Ruiz Sánchez¹⁵, M. García-Brenes¹⁶, A. Martín-Cardona¹⁷, C. Rubín de Célix¹⁸, D. Ginard¹⁹, K. Cárdenas-Jaén²⁰, L. Medina Prados²¹, N. Pedrero Leparmentier²², M.d.R. Plaza Santos²³, R. Salmoral Luque²⁴, T.d.J. Martínez Perez²⁵, V. Algara Soriano²⁶, Y. Zabana²⁷, A. Gutiérrez Casbas²⁸

¹Hospital General Universitario Doctor Balmis, Alicante. ISABIAL., Alicante, Spain, ²Hospital Universitario Reina Sofía, IMIBIC (Córdoba), Córdoba, Spain, ³Hospital Universitari i Politècnic la Fe, Valencia, Valencia, Spain, ⁴Unitat d'Atenció Crohn-Colitis, Servei d'Aparell Digestiu, Hospital Universitari Vall d'Hebron, Barcelona, Spain, ⁵Hospital Lluís Alcanyis (Xativa), Gastroenterology, Algemesí, Spain, ⁶Hospital Doctor Peset de Valencia., Valencia, Spain, ⁷Hospital Arnau de Vilanova, Valencia, Valencia, Spain, ⁸Hospital Reina Sofía, Murcia., Murcia, Spain, ⁹Consorti Sanitari de Terrassa, Terrassa, Spain, ¹⁰Hospital General Universitario de Castellón, Castellón, Spain, ¹¹H. de l'horta-manises, Manises, Spain, ¹²Hospital Clínico Universitario de Valencia., Servicio Medicina Digestiva, Valencia, Spain, ¹³Unidad de EII del Servicio de Gastroenterología, Hospital Universitario Bellvitge, IDIBELL, Hospitalet de Llobregat, Barcelona, Spain, ¹⁴Hospital Clinic of Barcelona, Gastroenterology, Barcelona, Spain, ¹⁵Hospital General Universitario de Valencia. Gastroenterología., Valencia, Spain, ¹⁶Inflammatory Bowel Disease Unit, Gastroenterology Department, Hospital Clínico San Carlos and Instituto de Investigación del Hospital Clínico San Carlos [IdISSC], Madrid, Spain., Madrid, Spain, ¹⁷Hospital Universitari Mútua Terrassa, Centro de Investigación biomédica en red de enfermedades hepáticas y digestivas (CIBERehd), Gastroenterology Department, Terrasa (Barcelona), Spain, ¹⁸Hospital Universitario de La Princesa, Madrid, Spain, ¹⁹Hospital Universitario Son Espases, Palma de Mallorca, Spain, ²⁰Hospital Virgen de Los Lirios., Gastroenterology, Alcoy, Spain, ²¹Hospital Marina Baixa, Villajoyosa, Alicante, Spain, ²²Hospital General Universitario Santa Lucía, Cartagena, Murcia, Cartagena, Murcia, Spain, ²³H. Infanta Leonor, Madrid, Spain, ²⁴Hospital General Universitario de Toledo, Toledo, Spain, ²⁵Hospital Virgen de Luz, Cuenca, Spain, ²⁶Hospital Vinalopó, Elche, Alicante, Spain, ²⁷Hospital Universitari Mútua Terrassa. entro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Gastroenterology, IBD Unit, Terrassa, Spain, ²⁸Hospital General Universitario Doctor Balmis, Alicante. ISABIAL. CIBERehd, Alicante, Spain

Contact E-Mail Address: luciamv_20@hotmail.com

Introduction: Infection by Leishmania spp. in patients diagnosed with inflammatory bowel disease (IBD) is an uncommon infectious complication. The use of anti-TNF- α is well known risk factor for Leishmania infection (LI), particularly in some endemic areas, but only a few case series have been reported in the literature, mainly in the Mediterranean basin.

Aims & Methods: Aim: To evaluate the main demographic, IBD-disease features and risk factors as well as LI disease characteristic and required treatment among IBD patients who develop LI.

Methods: This is a retrospective, observational, multicenter study conducted in twenty-five Spanish hospitals, promoted by the Young Group of GETECCU, including patients diagnosed with IBD and subsequent diagnosis of LI.

Results: We collected a total of 73 patients, 48 of them were men (65.8%) with a mean age of 48 ± 15.06 years. 92% of patients resided in the Mediterranean basin, an endemic area of Leishmania. Only 1 patient was born outside of Spain. Nineteen percent of patients were smokers and 16.4% had some comorbidities.

Fifty patients had Crohn's disease (CD) (68.5%) with ileocolonic involvement (30.1%) and inflammatory behaviour (45.2%) and 42.9% had perianal disease. 94% of CD patients were on clinical remission at the time of LI diagnosis. In addition, 23 patients had ulcerative colitis (UC) (31.5%), being extensive colitis the most frequent extent (78.3%), and all of them were on clinical remission or had mild disease activity. 69 patients (94.5%) were under immunosuppressive and/or biologic treatment during the 6 months prior to the LI. 6.8% were on immunosuppressants monotherapy, 42.5% in combination and 38.4% under biologic monotherapy. Regarding biological treatment, 97% of patients were under AntiTNF and only 2 patients were under treatment with Ustekinumab.

Regarding the characteristics of LI, 62 patients presented cutaneous involvement (85%), 9 visceral (12%) and the rest presented mucocutaneous involvement.

Symptoms associated to LI were fever (9.6%), abdominal pain (4.1%) and constitutional syndrome (8.2%), moreover 24.7% required hospital admission. Regarding the location of the skin lesions, the most frequent were the upper limbs (35.6%) followed by lower limbs (30.1%).

The treatment used for LI was systemic amphotericin in 60.3% of patients and pentavalent antimonials in 35.4%; the remaining patients were treated with other treatments, including miltefosine. LI solved at one month in 33 patients (45.2%) and at one year in 95.3% of patients, and only 11% of patients had recurrent LI.

Treatment was stopped temporarily in 38.4% of patients and definitively in 27.4%, starting Ustekinumab (36.8%), Vedolizumab (15.8%) and anti-TNF (10.6%) and the rest of the patients remained without biological treatment after the LI.

Conclusion: The usage of antiTNF is associated to LI in IBD patients, but LI could also happen under immunosuppressants or ustekinumab therapy. Although cutaneous involvement is the most frequent manifestation, 12% of patients have visceral involvement or LI recurrences. This infectious complication should be considered in IBD patients in endemic areas.

Disclosure: No Conflict of Interest.

PP0404

INTERLEUKIN-8 AS A POSSIBLE PREDICTIVE MARKER OF LONG-TERM RESPONSE IN ULCERATIVE COLITIS PATIENTS TREATED WITH VEDOLIZUMAB

A. Mínguez Sabater¹, P. Ripoll¹, A. Aguerri², V. Argumáñez Tello¹, I. Navarrete¹, A. Garrido¹, M. Aguas¹, M. Iborra¹, E. Cerrillo Bataller¹, P. Nos Mateu¹, G. Bastida¹

¹La Fe University and Politecnical Hospital, Valencia, Spain,

²Universidad Católica de Valencia, Valencia, Spain

Contact E-Mail Address: alejandrosab11@gmail.com

Introduction: Vedolizumab has demonstrated efficacy in moderate-severe Ulcerative Colitis (UC). To date, few tools are available to predict medium- and long-term response to the drug. The aim of the study is to characterise the profile of circulating cytokines associated with the pathophysiology of inflammatory bowel disease (IBD) to identify markers of immune response to vedolizumab in UC patients. As a secondary objective,

we analysed the possible involvement of baseline characteristics such as smoking and disease duration until drug initiation, previous exposure to other biologics, and baseline faecal calprotectin (FCP) and C-reactive protein (CRP) values in the response to the drug.

Aims & Methods: Retrospective single-centre cohort study including 28 patients diagnosed with UC with inflammatory activity objectified by clinical and biochemical data who started treatment with vedolizumab in the period from 2015 to 2022. Participants consented and authorised the collection of biological samples. Plasma samples were collected prior to drug initiation and response to treatment was assessed at the end of follow-up.

Response to treatment was based on clinical remission (pMAYO < 3 with no subscore >1) together with a biochemical response (reduction in FCP and/or CRP > 50%) at the end of follow-up. In patients where colonoscopy was available, endoscopic response was defined as an endoscopic Mayo of 0 or 1. Cytokines were determined by Magpix® Luminex using a Milliplex® Human High Sensitivity T Cell Magnetic Bead Panel containing 12 proteins.

The cytokines studied were (interferon-gamma, interleukin 10, interleukin 12, interleukin 13, interleukin 17A, interleukin 10, interleukin 2, interleukin 21, interleukin 23, interleukin 7, interleukin 8, TNF-alpha).

Results: Twenty-eight patients with UC (100% pancolitis or left colitis) and S2+S3 94.7% were included in the study. 85.2% were bioexposed (infliximab in 75%). 50% of patients received concomitant corticosteroid therapy at the start of vedolizumab.

Vedolizumab response was seen in 13 patients (46.4%) after a median overall treatment duration in both cohorts of 2.79 years (IQR 7.55). The responder group was on vedolizumab treatment for a median of 5.58 (IQR 6.9) years vs 1.17 (IQR 5.13) years in the non-responder group, $p=0.005$. There were no baseline differences between responders in pMayo or in FCP and CRP values. Active smoking, disease duration until vedolizumab initiation and previous exposure to other biologics were not associated with response/non-response to vedolizumab treatment.

Vedolizumab responders had significantly lower median interleukin 8 (IL8) levels at baseline than vedolizumab non-responders (median IL8 1.67 pg/mL versus 3.03 pg/mL, $p=0.016$). No statistically significant differences in baseline concentrations were found in any of the other interleukins analysed.

Conclusion: In our series of UC patients treated with vedolizumab, patients with long-term response to the drug show lower plasma IL8 levels than non-responders at baseline. Therefore, IL8 could serve as a predictive marker of long-term response to vedolizumab in UC patients. These results should be confirmed in prospective studies with larger sample sizes.

Disclosure: Nothing to disclose.

PP0405

CAUSAL ASSOCIATION BETWEEN CIRCULATING IMMUNE CELL COUNTS AND INFLAMMATORY BOWEL DISEASE: A BIDIRECTIONAL TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

C. Liang¹, Z. Wang¹, Y. Yuan¹, M. Wang¹, Y. Liu¹, W. Zhang¹, Y. Li¹, X. Lu¹, Z. Lin¹, J. Li¹, T. Mao¹

¹Dongfang hospital, Beijing University of Chinese Medicine, Beijing, China

Contact E-Mail Address: maotangyouqun@126.com

Introduction: Inflammatory bowel disease (IBD) is a chronic recurrent inflammatory bowel disease, whose cause involves the interaction between genetic and environmental factors. At present, the pathogenesis

of IBD has not been fully understood. Although there is a recognized link between immune response and IBD, the causal relationship between circulating immune cell counts and IBD remains controversial.

Aims & Methods: This study aimed to elucidate the causal relationship between genetically predicted circulating immune cell counts and IBD. We conducted a bidirectional two-sample Mendelian randomization (MR) study using aggregated statistics from genome-wide association studies. The causal relationship between five circulating leukocytes cells (monocytes, lymphocytes, eosinophils, basophils and neutrophils) counts and IBD, including Ulcerative colitis (UC) and Crohn's disease (CD) was analyzed. Inverse variance weighting (IVW) was used as the primary MR analysis method, and horizontal pleiotropy test and heterogeneity test were used to ensure the stability of the results.

Results: Our findings indicated that monocytes, lymphocytes, eosinophils, and basophils count were not significantly associated with IBD, however, elevated circulating neutrophils count was significantly associated with higher risk of IBD [odds ratio (OR): 1.002; 95% confidence interval (CI): 1.001–1.003; $p = 0.009$] and UC [OR: 2.465; 95%CI: 1.236–4.916; $p = 0.01$].

In addition, we also found that IBD [OR: 12.07; 95% CI: 1.909–76.316; $P = 0.008$] and UC [OR: 2.465; 95% CI: 1.236 - 4.916; $P = 0.01$] were significantly associated with higher circulating neutrophils count in reverse MR.

Conclusion: This MR study provides genetic evidence for the causal relationship between the genetically predicted increase in circulating neutrophils count and the risk of IBD (UC and CD). This finding stresses the need for further exploring physiological functions of neutrophils in order to develop effective strategies against IBD.

Disclosure: The authors state that the study was conducted in the absence of any business or financial relationships that could be interpreted as potential conflicts of interest.

PP0406

THE EFFECT OF VEDOLIZUMAB ON THE LEVEL OF ADHESIVE MOLECULES ICAM-1, ICAM-2, SL-SELECTIN IN ULCERATIVE COLITIS

V. Pavlenko¹, A. Pavlenko¹

¹» Stavropol State Medical University of the Ministry of Health of the Russian Federation, Chair of Propaedeutics of Internal Diseases, Stavropol, Russian Federation

Contact E-Mail Address: pavlenkovv@yandex.ru

Introduction: A deeper understanding of the pathogenesis of UC has led to the emergence of new therapeutic strategies. One of them consists of targeted exposure with biological drugs to certain molecules that regulate the interaction between leukocytes and endothelial cells in the inflammatory zone (mainly leukocyte integrins and endothelial cell adhesion molecules of the immunoglobulin superfamily).

Aims & Methods: Purpose of the study: To study the content of adhesion molecules ICAM-1, ICAM-2 and L-selectin in the peripheral blood of patients with ulcerative colitis (UC) and the effect of vedolizumab (Intivio) on their levels.

We examined 12 patients with moderate and severe forms of UC and the ineffectiveness of previous standard therapy. The severity of the UC attack was calculated according to the Mayo index. Antivio® 300 mg was administered to patients intravenously according to the attached instructions. The content of adhesion molecules in the peripheral blood was studied before and 6 weeks after the first injection of vedolizumab. The control group consisted of 15 healthy volunteers. The content of ICAM-1, ICAM-2 and L-selectin in blood serum was determined by multilayer ELISA analysis (Bender med.Systems, Austria). Statistical processing of the obtained results was carried out using SPSS 13.0 software.

Results: It was found that the initial levels of ICAM-1 (461.9 ± 28.4 ng/ml), ICAM-2 (323.3 ± 18.4 ng/ml) and sL-selectin (1650 ± 12.25 U/ml) in the peripheral blood of patients with UC were increased ($P < 0.05$ with control), the Mayo index was 9 points. After four infusions of Vedolizumab (week 14), the levels of soluble molecules decreased in 4 patients, with a predominant decrease in sL-selectin (201 ± 9.32 ng/ml, 197 ± 8.54 pg/ml and 1008 ± 15.3 U/ml respectively). The Mayo index was 5 points. In 8 patients, by the 6th week of treatment, the levels of the studied adhesive molecules did not change, although the Mayo index decreased by 3 points.

Conclusion: The initial level of ICAM-1, ICAM-2 and sL-selectin in the peripheral blood of patients with severe forms of UC is increased. The dynamics of the synthesis of adhesive molecules by immunocompetent cells under the influence of the fourth administration of Vedolizumab may predict the possibility of continuing the administration of the drug.

Disclosure: Nothing to disclose.

PP0407

EPIDEMIOLOGY AND THERAPEUTIC MANAGEMENT OF INFLAMMATORY BOWEL DISEASE USING DATA FROM THE FRENCH NATIONAL HEALTH DATA SYSTEM 2014- 2021 – THE EPITHERA STUDY

L. Vuitton¹, L. Peyrin-Biroulet², S. Chaalal³, L. Gautier³, K. Sosnowiez³, L. Clevy⁴, H. Omichessan⁴, P. Rabiega⁵, G. Bizouard⁵, T. Nishikawa⁵, J. Kirchgesner⁶

¹UMR Right Inserm, Besançon university hospital, Dept. of Gastroenterology, Besançon, France, ²Inserm U1256, Nancy University Hospital, Gastroenterology, Vandoeuvre-les-Nancy, France, ³Janssen-Cilag, Medical Affairs, Issy-les-Moulineaux, France, ⁴Janssen-Cilag, Market Access, Issy-les-Moulineaux, France, ⁵IQVIA, Courbevoie, France, ⁶Institut Pierre Louis d'Epidémiologie et de Santé Publique, Sorbonne University, Hôpital Saint Antoine, Gastroenterology, Paris, France

Contact E-Mail Address: julien.kirchgesner@gmx.com

Introduction: Inflammatory bowel disease (IBD) prevalence is steadily increasing worldwide, particularly in developed countries. In parallel, the medical treatment of IBD evolved significantly with the marketing approval of advanced therapies over the last decade. The aim of this study was to describe the epidemiology of IBD and to assess treatment patterns in real-life management in France.

Aims & Methods: This was an observational study using the French National Health Databases (SNDS) including all adult patients diagnosed with Crohn disease (CD) or ulcerative colitis (UC) meeting at least one of the following criteria between 2014 and 2021: i) long term disease (LTD) related to IBD ii) at least 2 hospital stays for IBD iii) one hospital stay for IBD and 3 or more IBD treatment deliveries. A look-back period of at least 5 years prior to index date was considered to assess epidemiology and patients' characteristics, and a follow-up period of at least 12 months to describe treatment patterns.

Results: In the study period, 274,694 IBD patients were identified: 139,001 CD patients (including 45,939 (33.0%) incident patients), and 135,693 UC patients (including 53,939 (39.8%) incident patients). CD prevalence varied from 193.5 per 100,000 person-years (py) in 2014 to 234.4 per 100,000 py in 2021, while incidence varied from 12.1 to 9.7 per 100,000 py respectively. UC prevalence and incidence varied respectively from 173.1 to 229.2 per 100,000 py and from 13.7 to 11.8 per 100,000 py.

Prevalent CD patients were 56.7% female, median age was 42 years (IQR 31-56) and median follow-up was 8.0 years (IQR 4.6-8.0). Among patients with at least 1 year of follow up, 42.3% were exposed to at least one biologic: 96.9% received an anti-TNF in first line, 1.6% an anti-interleukin, 1.4% an anti-integrin and 36.4% received a concomitant immunosuppressant.

Among incident CD patients (54.6% female, median age of 37 years (IQR 26-53) and median follow-up of 3.9 years (IQR 2.0-5.9)), 50.8% of patients with at least 1 year of follow-up were exposed to at least one biologic. The treatment distribution in first line was similar to prevalent patients. Prevalent UC patients were 50.8% male, median age was 49 years (IQR 36-62) and median follow-up was 8.0 years (IQR 3.9-8.0). Among patients with at least 1 year of follow up, 20.3% were exposed to at least one biologic: 94.0% received an anti-TNF in first line, 5.3% received an anti-integrin, 0.4% an anti-interleukin, 0.3% a JAK inhibitor (JAKi) and 34.5% received a concomitant immunosuppressant. Among incident UC patients (50.9% male, median age of 43 years (IQR 31-58) and median follow-up of 3.8 years (IQR 1.9-5.8)), 23.5% of patients with at least 1 year of follow-up were exposed to at least one biologic, with comparable treatment distribution in first line as in prevalent patients.

After a switch or a swap from an anti-TNF in first line for CD, the use of anti-TNF in second line tends to decrease (from 92.8% in 2014 to 36.2% in 2020) in favor of anti-integrins (from 2.3% to 16.7%) and anti-interleukins (from 4.9% to 47.1%). The same trend is observed for UC, for anti-TNF (from 93.8% to 30.0%), mostly in favor of anti-integrins (from less than 5.6% to 57.0%).

Conclusion: This study reports an increase in prevalence and a slight decrease in incidence of IBD in France between 2014 and 2021. Treatment patterns evolved with an increased use of advanced therapies and a swap out of class in the second line.

Disclosure: LV received fees from abbvie, amgen, MSD, Ferring, Takeda, Pfizer, Janssen, Lilly, Galapagos, Celltrion, Viartis

LPB received fees from Abbvie, Abivax, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, Connect Biopharm, Cytokine Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, Hac Pharma, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD

Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par' Immune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance, Thermo Fischer, Tigenix, Tillots, Viartis, Vifor, Vectivbio, Ventyx, Ysopia

JK received fees from Janssen, Takeda, Lilly, Abbvie, Pfizer, Tillots, Amgen, Celltrion, Roche, Gilead, Galapagos

SC, HO, LG, KS, LC works for Janssen-Cilag

PR, GB, TN works for IQVIA.

PP0408

OUTPATIENT CARE FOR CROHN'S DISEASE IN BRAZILIAN HEALTHCARE PUBLIC SYSTEM: FROM COST TO REFUND

L. Rosevics¹, E. Lima Júnior¹, O. Ramos Júnior¹

¹Complexo Hospital de Clínicas - Universidade Federal do Paraná, Curitiba, Brazil, ²Universidade Federal do Paraná, Curitiba, Brazil

Contact E-Mail Address: le.rosevics@yahoo.com.br

Introduction: Crohn's disease (CD) is characterized by a rare, chronic disease that requires lifelong treatment, representing a burden on healthcare systems. Considering that in Brazil, through the Unified Health System (SUS), patients have access to all treatment, it is important to know how the costs are being distributed in these patients, to better plan their care.

Aims & Methods: The present study aims to evaluate the costs for the hospital and SUS reimbursement for outpatient treatment of patients with CD. This is a retrospective cohort of patients with CD followed between 2006 and 2020 in a Brazilian public tertiary hospital. Patients over 18 years of age and with complete information in their medical records were included.

cluded. Through medication and exams carried out during follow-up, SUS reimbursement values were calculated using the SIGTAP-SUS table and hospital costs using the table provided by the hospital. The values for the acquisition of medications were provided by the State Health Department. Conversion to dollars was carried out each year, as well as correction for inflation. The statistical difference was evaluated across disease phenotypes according to the Montreal classification using the ANOVA test and the Scheffe post hoc test.

Results: One hundred and ninety-one patients were included, 50.26% being female. The SUS reimbursement cost was \$6741.40 ± 2526.87, the hospital cost was \$7162.88 ± 2732.30, and adjusted for inflation was \$11274.36 ± 5806.85. In post hoc analysis, there was a statistical difference between groups A2 and A3 (age at disease onset between 16 and 40 years and over 40 years) in the reimbursement group, and between the inflammatory and fistulizing phenotypes in the cost and reimbursement groups.

Conclusion: In Brazil, the treatment of CD has lower costs but maintains differences between phenotypic profiles similar to international studies. Showing the difference in cost, reimbursement and inflation, questions are raised about the updating of SIGTAP-SUS tables and the credibility of cost studies and its management planning.

Disclosure: Nothing to disclose.

PP0409

WITHDRAWN

PP0410

INCIDENCE AND NEOPLASTIC RISK ASSOCIATED WITH COLONIC STRICTURE IN PEDIATRIC-ONSET CROHN'S DISEASE: A POPULATION-BASED STUDY

N. Richard¹, A. Leroyer^{2,3}, C. Dupont-Lucas⁴, D. Turck^{5,3}, V. Bertrand⁶, P. Wils^{7,3}, C. Gower-Rousseau⁸, N. Guillon², G. Savoye¹, D. Ley^{3,5}, H. Sarter², M. Fumery⁹

¹University Rouen Normandie, INSERM, ADEN UMR1073, "Nutrition, Inflammation and microbiota-gut-brain axis", CHU Rouen, Department of Gastroenterology, Rouen, France, ²Lille University Hospital, Department of Public Health, Epidemiology, and Economic Health, EPIMAD Registry, Regional House of Clinical Research, Lille, France, ³Lille University Hospital, INSERM U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France, ⁴Caen University Hospital, Pediatrics, Caen, France, ⁵Lille University Hospital Faculty of Medicine, Pediatrics, Lille, France, ⁶Le Havre Hospital, Department of Paediatrics, 76600, France, ⁷Lille University Hospital, Department of Gastroenterology, Lille, France, ⁸Reims University Hospital, Research and Public Health Unit, Reims, France, ⁹Amiens University Hospital, Gastroenterology department, Amiens, France

Contact E-Mail Address: mathurin@hotmai.fr

Introduction: The identification of colonic stricture in patients with Crohn's disease (CD) often leads to surgery due to concerns about associated neoplasia. Nevertheless, information regarding the neoplastic risk associated to colonic stricture is still limited.

Aims & Methods: The objective of this study was to assess both the incidence of colonic stricture in pediatric-onset CD and the associated neoplastic risk at the population-based level. All patients diagnosed with CD before age 17 between 1988 and 2011, and included in a population-based registry, were followed until 2013. Colonic stricture was defined as a narrowing of the digestive lumen observed on endoscopic or radiological examination. Excluded were stricture in the ileocaecal valve, anal canal,

or low rectum. Univariate risk factors for colonic stricture were explored using Cox proportional hazards models with time-dependent variables, and a multivariable Cox model analysis was performed.

Results: A total of 1,007 patients diagnosed with CD between 1988 and 2011 were included. Median age at diagnosis was 14.5 years [IQR: 12.0-16.1]. Throughout the follow-up period (median follow-up, 8.8 years [4.6-14.2]), patients were predominantly exposed to 5-aminosalicylates (88.1%), immunosuppressants (70.6%), and biologics (47.9%). Colonic stricture was diagnosed in 52 patients, including 11 at CD diagnosis. The cumulative incidence of colonic stricture in CD was 2.9% [1.8%-4.0%] at 5 years. The overall incidence rate of colonic stricture in CD was 5.4 cases/1000 person-years, 95% CI [4.1-7.1]. In multivariable analysis, an increased risk of colonic stricture was observed during periods of active disease (HR = 2.62, [1.40-4.89], p<0.01).

Conversely, the absence of colonic involvement at diagnosis (HR = 0.18, [0.04, 0.80], p<0.05) or treatment with aminosalicylates (HR = 0.39, [0.19-0.79], p<0.05) was associated with a lower risk of colonic stricture. After a median follow-up of 6.4 [2.4-12.7] years, colonic stricture surgical resection was performed in 29 patients (55.8%). Colon adenocarcinoma was detected in one patient (1.9%) within 6 months after the diagnosis of colonic stricture.

Conclusion: In this population-based study of pediatric-onset Crohn's disease, 52 patients (5%) experienced colonic stricture, with a 2.9% incidence rate observed after 5 years of follow-up. Additionally, one patient (2%) presented with an associated adenocarcinoma.

Disclosure: M.F. has received lecture/consultant fees from AbbVie, Ferring, Tillotts, MSD, Biogen, Amgen, Fresenius, Hospira, Sandoz, Pfizer, Celgene, Gilead, Boehringer, Galapagos, Janssen, and Takeda. C.D. has received consultant fees from AbbVie. N.R. has received lecture/consultant fees from AbbVie and Takeda. The other authors state that they have no competing interests regarding this work to disclose.

PP0411

SPINE AND SACROILIAC JOINT INVOLVEMENT IN NEWLY DIAGNOSED PATIENTS WITH INFLAMMATORY BOWEL DISEASE - SYMPTOMS, CLINICAL AND MAGNETIC RESONANCE IMAGING FINDINGS FROM A POPULATION-BASED COHORT STUDY

N. Vladimirova¹, M. Attauabi², G. Madsen³, J. M. Møller⁴, S. Bay Hansen⁵, H. Roman Siebner⁵, F. Bendtsen⁶, J.B. Seidelin², J. Burisch⁷, M. Østergaard¹

¹COPECARE (Copenhagen center for arthritis research), Center for Rheumatology and Spine Diseases, Rigshospitalet-Glostrup, Glostrup, Denmark, ²Copenhagen University Hospital, Herlev Hospital, Gastrounit, Herlev, Denmark, ³COPECARE (Copenhagen center for arthritis research), Gastrounit, medical section, Copenhagen, Denmark, ⁴Copenhagen University Hospital, Herlev Hospital, Department of Radiology, Herlev, Denmark, ⁵Copenhagen University Hospital - Amager and Hvidovre, Copenhagen, Denmark, Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Hvidovre, Denmark, ⁶Hvidovre Hospital, Gastrounit, Medical Division, 3 Dept. of Gastroenterology, Hvidovre, Denmark, ⁷Hvidovre University Hospital, Gastrounit, medical section, Copenhagen, Denmark

Contact E-Mail Address: mohamed.attauabi.02@regionh.dk

Introduction: Axial spondyloarthritis (axSpA), characterised by chronic inflammation of the sacroiliac joints (SIJs) and spine, is a common extraintestinal manifestation in Inflammatory Bowel Disease (IBD). It is associated with poor outcomes and a substantial impact on quality of life. Thus,

early detection is important to optimally tailor treatment and suppress the inflammation in all disease domains. However, the prevalence and pattern of axial involvement have not been described in early IBD.

Aims & Methods: We aimed to describe the prevalence and distribution of axial symptoms, clinical findings and MRI-determined inflammatory and structural lesions in the spine and SIJs of patients with newly diagnosed IBD. Patients with newly diagnosed IBD from a prospective population-based inception cohort were consecutively included. Structured rheumatological interview collecting data on peripheral and axial symptoms and clinical evaluation were performed. MRI assessment for spine and SIJ inflammation and structural lesions was based on validated and widely applied scoring systems [1,2]. Further, an expert assessment of the MRIs as +/- indicative of axSpA applying standardized definitions was performed [3,4].

Results: Of 110 included patients (mean age 42 years, 40% male, 40 with Crohn's disease (CD), 70 with ulcerative colitis (UC)), 74 had active IBD. At the time of evaluation, 4 patients received treatment with systemic glucocorticoid and one received TNF-inhibitor. Nine patients were HLA-B27 positive. None were previously diagnosed with SpA.

Back and/or buttock pain was reported by 48(44.9%) patients and inflammatory back pain by 10(9.1%). In 23(21.5%) patients the pain could not be better explained by competing conditions (for example degenerative disc disease, nerve root compression, osteoporosis or fibromyalgia) according to the assessing rheumatologist. The axial symptoms were accompanied by peripheral joint and/or enthesal symptoms in 30(62.5%) patients and 33(68.8%) had tender and/or swollen joints and/or entheses.

According to the MRI expert, MRIs of 17(16.7%) patients were indicative of axSpA (spine and SIJs evaluated together), while 11(10.8%) of the spine-MRIs and 13(12.7%) of the SIJ-MRIs were indicative of axSpA. Only 10 of the 17 patients with typical axSpA MRI findings had axial symptoms. There was no difference in symptoms or MRI findings between patients with UC and CD, or between patients with active and inactive IBD.

Spine bone marrow oedema (BME) in ≥ 1 slice was present in 30(30.3%) patients. SIJ BME in ≥ 1 slice was found in 27(26.5%) patients, erosion was present in 24(23.5%) patients, fat lesions in 12(11.8%) and ankylosis in 3(2.9%). The definition of positive MRI for sacroiliitis was fulfilled in 12 (11.8%) patients of whom six had axial symptoms. The Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axSpA were met in 11 cases.

Conclusion: One out of six patients with newly diagnosed IBD had findings indicative of axSpA on spine and SIJs MRI. Since only 60% of these patients were symptomatic, we conclude that axSpA may be an underdiagnosed early-occurring condition among IBD patients. Our results indicate a low threshold for performing MRI of the spine and SIJs and a need for multidisciplinary collaboration to ensure early detection of axial involvement to enable an optimal therapeutic strategy and prevent future structural damage and disability.

References:

1. Maksymowych et al., *Art Rheum*, 2005, 53(5) and 53(4)
2. Maksymowych et al., *Journal of rheum*, 2014
3. Lambert et al., *Ann Rheum Dis* 2016
4. Maksymowych et al., *Rheumatology* 2021

Disclosure: Nothing to disclose.

PP0412

INNOVATIONS IN HEALTHCARE: AI'S IMPACT ON INFLAMMATORY BOWEL DISEASE AND DIGESTIVE HEALTH

R. Rammohan¹, M. Joy¹, S.G. Magam¹, D. Natt¹, W. Lau¹, S.R. Magam¹, L. Pannikodu¹, A. Tadikonda¹, J. Desai¹, K. Subramani¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rrammoha@numc.edu

Introduction: Artificial Intelligence (AI) has significantly changed the landscape of healthcare, particularly in the diagnosis and treatment of Inflammatory Bowel Disease (IBD) and various digestive conditions. Key AI tools like ChatGPT and Google Gemini have the ability to decode endoscopic images, examine various samples, streamline administrative tasks, and aid in the evaluation of medical imagery and device automation. These AI solutions improve the management of digestive diseases by tailoring treatments and predicting potential adverse reactions. The incorporation of AI into healthcare allows patients to make informed decisions through the assessment of personalized treatment options.

Aims & Methods: The aim of the study was to assess the accuracy of two popular chatbots, ChatGPT and Google Gemini, in addressing medical management inquiries. Each chatbot was given a set of questions to answer, with their responses rated on a 1-10 Likert scale, where 1 represented a low score and 10 was high. To ensure fair evaluation, two neutral evaluators examined the responses of each bot. The research sought to highlight the abilities of these chatbots by methodically evaluating their performance in terms of accuracy and reliability. The use of two evaluators and the Likert scale method was instrumental in reducing potential biases, thereby validating the results.

Results: Our research evaluated the effectiveness of ChatGPT and Google Gemini in the realm of medical management. ChatGPT outperformed, attaining a 71% accuracy rate compared to Google Bard's 39% ($p = 0.032$), and surpassed in information reliability with 58% against Google Bard's 29% ($p = 0.021$). This study emphasizes the critical role of accuracy and reliability in the development of chatbots for managing IBS. ChatGPT's impressive performance suggests its potential as a reliable tool, yet it also points to the continuous need for research and improvement in this area.

Conclusion: AI has profoundly transformed healthcare, especially in the diagnosis and management of IBD. ChatGPT and Google Bard stand out as crucial AI instruments for interpreting medical imagery, evaluating samples, and enhancing efficiency. Our study assessed the accuracy and reliability of these chatbots within medical management contexts. ChatGPT outshone Google Bard by achieving 71% accuracy and a 58% reliability rate in information. ChatGPT demonstrates significant promise as a dependable AI tool for IBD care, yet our findings also underline the ongoing need for further research and development in the field.

References:

1. Okagawa Y, Abe S, Yamada M, Oda I, Saito Y. Artificial Intelligence in Endoscopy. *Dig Dis Sci*. 2022 May;67(5):1553-1572. doi: 10.1007/s10620-021-07086-z. Epub 2021 Jun 21. PMID: 34155567.
2. Goma S, Posey J, Bashir B, Basu Mallick A, Vanderklok E, Schnoll M, Zhan T, Wen KY. Feasibility of a Text Messaging-Integrated and Chatbot-Interfaced Self-Management Program for Symptom Control in Patients With Gastrointestinal Cancer Undergoing Chemotherapy: Pilot Mixed Methods Study. *JMIR Form Res*. 2023 Nov 10;7:e46128. doi: 10.2196/46128. PMID: 37948108; PMCID: PMC10674151.

Disclosure: Nothing to disclose.

PP0413

BRIDGING THE GAP: ETHNIC VARIATIONS IN IBS OUTCOMES AFTER BARIATRIC SURGERY

R.m. Ram mohan¹, S.G. Magam¹, M. Joy¹, D. Natt¹, S.R. Magam¹, W. Lau¹, A. Tadikonda¹, L. Pannikodu¹, R. Jiyan¹, S. Sheikh¹, J. Desai¹, K. Subramani¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rrammoha@numc.edu

Introduction: Bariatric surgery emerges as a powerful intervention for obesity, promoting enhanced metabolic health. However, substantial evidence indicates a rise in Irritable Bowel Syndrome (IBS), primarily following such surgical interventions. The effect of race on the occurrence of IBS after surgery has yet to be investigated. Given the widespread occurrence of IBS and its confirmed connection to bariatric surgery, examining the effect of racial disparities is crucial. This study seeks to ascertain whether racial differences impact the probability of an individual developing IBS post-bariatric surgery. Revealing this relationship is vital for improving patient results and optimizing postoperative care.

Aims & Methods: We executed a retrospective study to analyze patients who underwent bariatric surgery at our facility between 2009 and 2022. Data about comorbidities, insurance statuses, surgical techniques, colonoscopy and pathology reports, and initial patient attributes were collected through ICD and CPT codes. Patients who developed IBS post-surgery were monitored until 2023 and categorized by gender, race, and duration post-surgery. We used propensity score matching to balance baseline characteristics. Participants with a previous diagnosis of IBS were excluded from the study. Kaplan-Meier survival analysis and Cox proportional hazards models were leveraged to examine the onset of IBS among different racial groups. Additionally, odds ratios were employed to discern independent variables influencing the study outcomes

Results: Between 2009 and 2022, 960 bariatric surgeries were performed at our institution. Of these, 39 patients, equating to 0.04%, were diagnosed with IBS, typically around 40±9.2 months post-surgery. The subjects' average age was approximately 39±8.7 years, with females constituting 51.2% of the participants. Regarding racial breakdown, 29.2% were African Americans, 33.5% were Whites, 21.8% were Hispanics, and 15.5% were Asians. Notably, White patients manifested symptoms of IBS significantly earlier compared to other racial groups (23±5vs 36±7, 31±8, 29±6) (Breslow: 12.46, p=0.015). Additionally, a heightened risk of IBS was observed among individuals with lower educational attainment (OR: 1.25, P=0.025).

Conclusion: This research aims to bridge the prevailing knowledge void relating to the influence of race on the emergence of IBS following bariatric surgery. Our retrospective analysis of 960 surgeries from 2009 to 2022 highlighted a 0.04% occurrence of IBS, generally identified around 40 months after surgery. Notably, White patients experienced the onset of IBS in considerably less time than other racial groups, with individuals with lower educational levels exhibiting increased risks. These insights emphasize the importance of considering racial and other sociodemographic elements in refining postoperative care

References: 1. Turner PL, Oyetunji TA, Gantt G, Chang DC, Cornwell EE, Fullum TM. Demographically associated variations in outcomes after bariatric surgery. *Am J Surg.* 2011 Apr;201(4):475-80. doi: 10.1016/j.amjsurg.2010.08.035. PMID: 21421101.

Disclosure: Nothing to disclose.

PP0414

SHORT-TERM EXPOSURE TO ENVIRONMENTAL AIR POLLUTION AND INFLAMMATORY BOWEL DISEASE FLARES: A TIME-STRATIFIED CASE CROSS-OVER STUDY

D. Noviello¹, L. Fedrizzi², E. Fracas¹, T. Pessarelli¹, F. Conforti³, P.M. Mannucci⁴, A.C. Pesatori², M. Vecchi¹, M. Carugno⁵, F. Caprioli¹

¹University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ²Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Epidemiology Unit, Milan, Italy, ³Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Milan, Italy, ⁵University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Contact E-Mail Address: noviellodaniele@gmail.com

Introduction: Some epidemiological studies suggest that long-term exposure to environmental air pollutants, such as particulate matter (PM), could have a role in inflammatory bowel disease (IBD) incidence and pathogenesis. However, less is known about the potential effect of short-term air pollution exposure. The aim of this study is to investigate whether short-term exposure to environmental air pollution is associated with the occurrence of IBD flares.

Aims & Methods: Anonymized hospital discharge records (HDR) with ICD-9-CM codes 555 (Crohn's disease) and 556 (ulcerative colitis) for years 2002-2009 from all hospitals of the Lombardy region were collected. All HDR of adult patients (18-75 years) resident in Milan were included, except for recurrent hospitalizations within 6 months.

Each record was assigned daily PM ≤10 µm (PM10) concentrations at municipality level by averaging PM10 levels of the day of admission with the levels of the day before (lag01) and of each preceding day up to six days before (lag06).

To evaluate the association between PM10 and IBD-related hospitalizations, a time-stratified case-crossover study design was applied. Conditional logistic regression models, calculating Odds Ratios (OR) and 95% Confidence Intervals (95%CI) per increments of 10 µg/m³ of PM10, were performed.

Results: Overall, 2,176 hospital admissions (males=1,137, Crohn's disease=1,264, ulcerative colitis=912) were included. In the entire population no clear association between PM10 and IBD-related hospitalization was identified, notwithstanding a small risk increase for males (OR: 1.03; 95%CI: 0.99-1.08 at lag04).

When further stratifying for ICD code, an increased risk of hospitalization for "left-sided ulcerative colitis" (ICD code: 556.5) was found in males only, for exposures in all days preceding hospitalization up to lag04 (1.28; 1.05-1.28; 59 cases, 207 controls) (Figure 1). In females, the association was weaker, although positive (1.14; 0.91-1.42; 49 cases, 164 controls). No relevant findings emerged when looking at other ICD codes.

Conclusion: We observed an increased risk of IBD-related hospitalization in male patients with left-sided ulcerative colitis per increasing levels of air pollution in the days preceding hospital admission. Although preliminary, our findings suggest the possible role of sex as an effect modifier of the influence that air pollution might exert on IBD flares.

Further studies are needed to better comprehend the complex framework characterizing the interplay between environmental and individual factors contributing to IBD.

Disclosure: DN received unrestricted research grants from Pfizer, consulting fees Dr. Falk, and lecturer fees from Ferring. MV served as a consultant for Abbvie, MSD, Takeda, Janssen-Cilag, and Celgene. He received lecturer

fees from Abbvie, Ferring, Takeda, MSD, Janssen-Cilag, and Zambon. MA received consulting fees from Nikkiso Europe, Mundipharma, Janssen, Abbvie, Ferring, Galapagos, and Pfizer. FCA has served as consultant for Mundipharma, AbbVie, MSD, Takeda, Janssen, Roche, and Celgene; received lecture fees from AbbVie, Ferring, Takeda, Allergy Therapeutics, and Janssen; and received unrestricted research grants from Giuliani, SOFAR, MS&D, Takeda, Pfizer, and AbbVie.

PP0415

TESTING MACHINE LEARNING WITH FINNISH REGISTER DATA TO PREDICT NON-RESPONSE TO CONVENTIONAL TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

T. Kovalainen¹, J. Mehtälä¹, K. Elomaa², H. Lopenen¹, P. Kamble³, T. Ylisaukko-oja¹, P. Szolovits⁴

¹MedEngine Oy, Helsinki, Finland, ²Takeda Oy, Helsinki, Finland,

³Takeda Pharmaceuticals Inc., Global Evidence and Outcomes-Gastroenterology, Marlborough, United States of America,

⁴Massachusetts Institute of Technology, Computer Science and Artificial Intelligence Laboratory, Cambridge, United States of America

Contact E-Mail Address: kaisa.elomaa@takeda.com

Introduction: Inflammatory bowel disease (IBD), including both Crohn's disease (CD) and ulcerative colitis (UC), are difficult to diagnose due to a broad symptoms spectrum.^{1,2}

If symptoms remain uncontrolled with conventional therapy (CT), patients are transitioned to biologics. Little is understood about which CD and UC patients will respond to CT and which patients may have a more aggressive disease progression, and therefore should be treated with biologic therapies sooner.

Aims & Methods: We aimed to develop and evaluate machine learning (ML) models to identify non-responders to CT based on patients' demographic characteristics and on data available before their treatment with CT. The study cohort included all Finnish patients ≥18 years of age, with a diagnosis for CD or UC between 1.1.2000–31.12.2019. Data were collected from electronic health records and national healthcare and prescription registers. CT drugs included corticosteroids (CS), immunomodulators and 5-aminosalicylic acids. CT failure outcomes are defined in *Table 1*.

A set of 6,782 predictive features including demographic and clinical characteristics, comorbidities, healthcare visits, procedures, laboratory measurements, and medication were created for three different baseline periods. A Lasso model was run both separately and in combination for each period, splitting the data into training and testing subcorpora ten different times to estimate the error bounds.

Results: After applying specific attrition criteria, the final analysis cohort included 12,818 CD and 30,178 UC patients. In total, 64.2% of CD and 61.1% of UC patients experienced CT failure (*Table 1*).

For CD, CS at baseline and young age (0–18 and 18–30 years) were the highest predictors of CT failure. For UC, the model selected 78 predictive features, the strongest being: baseline CS use, age (0–18, 18–30, and 65+ years), gastrointestinal and schizoaffective disorders, and secondary care visits to rheumatology, general medicine, and emergency.

The key findings of the Lasso model were:

- 1) The performance of CD-models was slightly better than the UC-models (median test accuracy was 0.65 [CD] and 0.62 [UC]);
- 2) a slight discrepancy between test and training statistics suggested overfitting, and;
- 3) most features appeared in all ten splits indicating their relevance.

CT failure outcomes	CD, n	CD, %	UC, n	UC, %	Total, n	Total, %
Prescription for biologics ¹	718	5.6%	828	2.7%	1,546	3.6%
IBD-related surgery	803	6.3%	728	2.4%	1,531	3.6%
90-day gap in CT medication (5-ASA ² , IM ³)	2,339	18.2%	5,325	17.6%	7,664	17.8%
≥2 corticosteroid ⁴ prescriptions	6,347	49.5%	14,302	47.4%	20,649	48.0%
IBD-related inpatient stay	1,339	10.4%	2,160	7.2%	3,499	8.1%
IBD-related ED visit	193	1.5%	398	1.3%	591	1.4%
Any of the above	8,223	64.2%	18,453	61.1%	26,676	62.0%

¹adalimumab, vedolizumab, infliximab, golimumab, ustekinumab, and tofacitinib; ²mesalazine, olsalazine, and sulfasalazine; ³methotrexate, mercaptopurine, azathioprine, cyclosporine, and metronidazole; ⁴prednisolone, hydrocortisone, budesonide, methylprednisolone, prednisone, and dexamethasone. Abbreviations: CD, Crohn's disease; CT, conventional therapy; ED, emergency department; IBD, intestinal bowel disease; IM, immunomodulators; UC, ulcerative colitis; 5-ASA, 5-aminosalicylic acid

Table 1. CT failure outcomes (within one year from CT initiation) for CD, UC, and combined cohorts.

Conclusion: Data quality is critical to build high-performance models. Even though Finnish registries provide access to comprehensive longitudinal data allowing the generation of relatively large analysis cohorts, our ML model demonstrated a weak predictive potential, with low AUCs and accuracies (0.6 range), in line with previous findings.³ Due to scarcity of information on additional clinical variables available in the Finnish IBD registry, their use did not improve prediction of CT failure.

Additional prediction difficulty is introduced by non-standardized data recording practices. Confounding factors and random chance affect complicated outcomes, such as CT failure, making them especially difficult to predict.

References: 1. Wang, R., Li, Z., Liu, S. & Zhang, D. Global, regional and national burden of inflammatory bowel disease in 204 countries and territories from 1990 to 2019: a systematic analysis based on the Global Burden of Disease Study 2019. *BMJ Open* 13, e065186 (2023).

2. Yantiss, R. K. & Odze, R. D. Diagnostic difficulties in inflammatory bowel disease pathology. *Histopathology* 48, 116–132 (2006).

3. Chen, I. et al. PGI27 Applying Machine Learning to Large Databases to Predict Nonresponse to Conventional Treatment in Patients with Ulcerative Colitis. *Value Health* 24, S99 (2021).

Disclosure: This study was sponsored by Takeda Oy. TK, JM, and HL are employees by MedEngine Oy. TY is the CEO and founder of MedEngine Oy. KE and PK are employed by Takeda and hold Takeda stocks/stock options. Mónica Ferreira (PhD) from MedEngine Oy is acknowledged for medical writing support.

PP0416

IMPACT OF COVID-19 INFECTION ON INFLAMMATORY BOWEL DISEASE COURSE: A SYSTEMATIC REVIEW AND META-ANALYSIS

E.S. Vitus¹, S. Mann², C.W. Lees^{3,4}, T. Jess^{5,1}, R. Elmahdi^{1,5}

¹Aalborg University, Center for Molecular Prediction of Inflammatory Bowel Disease, PREDICT; Department Of Clinical Medicine, Copenhagen, Denmark, ²St Peter's Hospital, Ashford and St Peter's NHS Trust, Surrey, United Kingdom, ³University of Edinburgh, Center for Genomics and Experimental Medicine, Edinburgh, United Kingdom, ⁴The Western General Hospital, Department of Gastroenterology and Hepatology, Edinburgh, United Kingdom, ⁵Aalborg University Hospital, Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: esvi@dcm.aau.dk

Introduction: Several viral respiratory infections have been implicated in the exacerbation of immune mediated inflammatory diseases (IMID)¹⁻³. There has however been limited investigation and conflicted findings of the long-term outcomes in inflammatory bowel disease (IBD) following COVID-19⁴. We therefore performed a systematic review and meta-analysis of the long-term impact of SARS-CoV-2 infection on the disease course of IBD.

Aims & Methods: To understand the impact of early SARS-CoV-2 variants and to be better prepared for future variants, we aimed to carry out a meta-analysis of the available evidence. We searched MEDLINE and EMBASE for studies investigating the risk of adverse IBD-related outcomes (IBD flares, change in disease activity, change in medication, IBD-related hospitalization, and surgery) following a SARS-CoV-2 infection, compared to IBD patients without a SARS-CoV-2 infection. ROBINS-E for observational studies was used to assess the risk of bias in the included studies. We used random effects model (REM) meta-analysis to calculate pooled hazard ratios (HR) for the risk of adverse IBD outcomes following the acute phase of COVID-19 infection. Subgroup meta-analysis was carried out to assess the risk of the outcomes by IBD subtype (Crohn's disease (CD) and ulcerative colitis (UC)). Meta-regression was undertaken to assess whether sex or duration of follow-up were significant predictors of IBD-related outcomes.

Results: A total of 3119 studies were identified of which 5 studies were eligible for inclusion after screening using the pre-defined inclusion criteria. The studies were based on cohorts from Denmark, Italy, the US, and a pan-European consortium including a total of 34,977 SARS-CoV-2 positive IBD patients and 53,270 IBD patients without a recorded SARS-CoV-2 infection.

Two studies were assessed as having a high risk of bias. REM meta-analysis did not show an increased risk of adverse IBD-related outcomes in IBD patients with a recorded SARS-CoV-2 infection compared to those without (HR:1.05, 95% CI:0.75-1.46) and substantial between-study heterogeneity was identified in the included studies ($I^2=91\%$, $p<0.01$).

There was no significant difference in adverse IBD-related outcomes between CD and UC patients (CD HR: 0.91, 95% CI: 0.82-1.02; UC HR: 0.83, CI: 0.75-0.90). Following meta-regression, neither sex nor duration of follow-up were found to be significant predictors of individual study effect size.

Conclusion: In this systematic review and meta-analysis, we find that SARS-CoV-2 infection does not increase the risk of long-term adverse IBD-related outcomes. High-quality studies with longer follow-up periods are required to understand the long-term impact of SARS-CoV-2 infection on IBD outcomes.

References: 1. Khan RR, Lawson AD, Minnich LL, Martin K, Nasir A, Emmett MK, et al. Gastrointestinal Norovirus Infection Associated With Exacerbation of Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr.* 2009 Mar;48(3):328.

2. Ozdemir B, Atay A, Kayhan MA, Ozin YO, Gokce DT, Altunsoy A, et al. Tissue quantitative RT-PCR test for diagnostic significance of cytomegalovirus infection in patients with inflammatory bowel disease and treatment response: Cytomegalovirus infection in patients with inflammatory bowel disease. *Medicine (Baltimore).* 2023 Aug 4;102(31):e34463.

3. Dimitroulia E, Pitiriga VC, Piperaki ET, Spanakis NE, Tsakris A. Inflammatory Bowel Disease Exacerbation Associated With Epstein-Barr Virus Infection. *Dis Colon Rectum.* 2013 Mar;56(3):322.

4. Zollner A, Koch R, Jukic A, Pfister A, Meyer M, Rossler A, et al. Postacute COVID-19 is Characterized by Gut Viral Antigen Persistence in Inflammatory Bowel Diseases. *Gastroenterology.* 2022;163(2):495-506.

Disclosure: Professor Charlie Lees has acted as a speaker and/or consultant to AbbVie, Janssen, Takeda, Pfizer, Galapagos, GSK, Gilead, Vifor Pharma, Ferring, Dr Falk, BMS, Boehringer Ingelheim, Novartis, Sandoz, Celltrion, Cellgene, Amgen, Samsung Bioepis, Fresenius Kabi, Tillotts, Trelus Health and Iterative Health.

Study	Country	Source Population	Study Period	COVID-19 cohort	Reference cohort	Summary estimates with 95% CI: type of relative estimate	Adverse IBD-outcome	ROBINS-E overall Risk of Bias (RoB) [‡]
Papa et al., (2022)	Italy	IBD patients from 5 Italian treatment centers	Oct 2020 - Mar 2021 (6)	95	190	0.42 (0.08-2.15): HR	Need for therapy intensification	High RoB
Hadi et al., (2022)	USA	TriNetX (40+ US Health Care Organizations)	Jan 2020 - Mar 2021 (3)	4310	22508	1.33 (1.18-1.51): RR	Inpatient hospitalisation along with a collection of stool studies, intravenous methylprednisolone requirement or flexible sigmoidoscopy	High RoB
Hong et al., (2022)	USA	5 academic medical centers within New York's Crohn's & Colitis Organization	Feb 2020 - Dec 2021 (11)	251	251	0.84 (0.44-1.42): HR	IBD-related hospitalisation/surgery	Low RoB
Bezzio et al., (2022)	Italy	IG-IBD Italian cohort	Mar 2020 - Dec 2020(7)	219	219	1.48 (0.90-2.42): OR	Change in HBI or PMS	Some concerns
Nørgård et al., (2023)	Denmark	Danish National IBD Cohort	Mar 2020 - Jul 2022(6)	30102	30102	0.85 (0.79-0.91): IRR	Corticosteroid prescription	Some concerns
Amiot et al., (2022)	EU I-CARE cohort [†]	I-CARE European prospective longitudinal multicenter cohort	Apr 2020 - Dec (9)	233	5224		Change in HBI or SCCAI	Some concerns
Lukin et al., (2021)	USA	I-CARE European prospective longitudinal multicenter cohort	(6 months)	118	118		Change in HBI or PMS	Some concerns

Table.

Abbreviations: HR- Hazard Ratio, RR - Relative Risk, OR - Odds Ratio, IRR - Incidence Rate Ratio, HBI - Harvey Bradshaw Index, SCCAI - Simple Clinical Colitis Activity Index, PMS - Partial Mayo Score.

[†] Belgium, Denmark, France, Germany, Greece, Hungary, Ireland, Israel, Italy, the Netherlands, Poland, Portugal, Spain, Sweden and the United Kingdom.

[‡] The studies are rated as having a high risk of bias, some concerns or low risk of bias.

PP0417

FATIGUE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN REMISSION (THE IBSEN III STUDY)

K.I.A. Holten^{1,2}, T. Bernklev^{3,4}, V.A. Kristensen^{5,1}, R. Opheim^{6,7}, B.C. Olsen^{1,8}, I. Johansen^{7,9}, C. Lund^{1,6}, G. Perminow¹⁰, R. Boyar¹¹, R. Torp¹², P. Ricanek¹³, T.E. Detlie¹⁴, Ø. Hovde^{1,15}, Ø. Asak¹⁶, M.-B. Bengtson¹⁷, T.B. Aabrek¹⁸, S.O. Frigstad¹⁹, M. Henriksen², G. Huppertz-Hauss²⁰, M.L. Høivik^{6,1}, L.-P. Jelsness-Jørgensen^{21,2}

¹Institute of Clinical Medicine, University of Oslo, Oslo, Norway,

²Østfold Hospital Trust, Department of Gastroenterology,

Sarpsborg, Norway, ³Vestfold Hospital Trust, Research and

Development Department, Sandefjord, Norway, ⁴Institute of

Clinical Medicine, Oslo, Norway, ⁵Oslo University Hospital,

Department Of Gastroenterology, Oslo, Norway, ⁶Oslo University

Hospital, Department of Gastroenterology, Oslo, Norway,

⁷University of Oslo, Institute of Health and Society, Department of

Public Health, Oslo, Norway, ⁸Telemark Hospital Trust, Department

of Gastroenterology, Skien, Norway, ⁹Østfold University College,

Faculty of Health, Welfare and Org., Fredrikstad, Norway,

¹⁰Oslo University Hospital, Pediatric Department, Oslo, Norway,

¹¹Diakonhjemmet Hospital, Department of Medicine, Oslo,

Norway, ¹²Innlandet Hospital Trust, Department of Medicine,

Hamar, Norway, ¹³Lovisenberg Diaconal Hospital, Department of

Gastroenterology, Oslo, Norway, ¹⁴Akershus University Hospital,

Department of gastroenterology, Lørenskog, Norway, ¹⁵Innlandet

Hospital Trust, Department of Medicine, Gjøvik, Norway,

¹⁶Innlandet Hospital Trust, Department of Gastroenterology,

Lillehammer, Norway, ¹⁷Vestfold Hospital Trust, Department of

Gastroenterology, Tønsberg, Norway, ¹⁸Vestfold Hospital Trust,

Department of Medicine, Tønsberg, Norway, ¹⁹Vestre Viken Hospital

Trust, Department of Medicine, Bærum, Norway, ²⁰Telemark

Hospital, Dept. of Gastroenterology, Skien, Norway, ²¹Østfold

University College, Department of Health Sciences, Fredrikstad,

Norway

Contact E-Mail Address: lars.p.jelsness-jorgensen@hiof.no

Introduction: Chronic fatigue (CF) is prevalent among patients with ulcerative colitis (UC) and Crohn's disease (CD), but the influence of the disease activity is not established.

Aims & Methods: The primary aim of this study was to evaluate the prevalence and probability of chronic fatigue (CF) in patients with CD and UC one year after diagnosis, stratified by different measures for disease remission (symptomatic, biochemical, endoscopic, and histological). Additionally, we aimed to evaluate factors associated with chronic fatigue among patients in endoscopic/radiological remission.

Patients ≥18 years with CD and UC were recruited from the Inflammatory Bowel Disease South-Eastern Norway (IBSEN III) study, a population-based, observational inception cohort. Fatigue was assessed using Fatigue Questionnaire (FQ), and CF was defined as a dichotomized score of ≥4 with a duration of ≥6 months. Only patients with complete FQ data, without history of colectomy, were eligible for inclusion. Binary logistic regression analyses were used to examine the probability of CF for various indicators of remission, including i) symptomatic remission (Harvey-Bradshaw index score <5 for CD and Simple Clinical Colitis Activity Index score <3 for UC), ii) biochemical remission (Fecal calprotectin ≤ 250 µg/g), iii) endoscopic/radiological remission (Mayo endoscopic score 0 in UC, and endoscopically verified absence of inflammation combined with normal intestinal MRI/CT in CD), and iv) histological remission (normal histology in all mucosal biopsies). Additionally, in patients with endoscopic/radiological remission, associations between CF and selected clinical factors were evaluated using binary logistic regression analysis.

Results: In total, 711/1416 patients with CD or UC diagnosis were included (CD: 33.8%, UC: 66.2%). Among them, 619 (87.1%) underwent colonoscopy, intestinal MRI/CT and/or fecal calprotectin testing. Prevalence of CF stratified by different indicators of remission is presented in table 1. In univariate binary logistic regression analysis regarding measures for disease remission, the probability of CF was only significantly reduced in patients with UC in symptomatic remission (OR: 0.48 (0.30, 0.77), p=0.003). Among patients with CD and UC in endoscopic/radiological remission (n=181), CF was independently associated with current biological treatment (OR: 2.92 (1.002, 8.49), p=0.05) and sleep disturbance (OR: 6.23 (2.03, 19.14), p=0.001) in multivariate logistic regression.

	CD (% (n/n total))	UC (% (n/n total))
Symptomatic remission	33.6 (51/152)	30.0 (85/283)
Biochemical remission	33.3 (25/75)	34.6 (62/179)
Endoscopic/radiological remission	40.4 (21/52)	33.3 (33/99)
Histological remission	36.8 (14/38)	35.0 (28/80)

Abbreviations and table legends: CD: Crohn's disease. UC: Ulcerative colitis. Symptomatic remission: Simple Clinical Colitis Activity Index (SCCAI) score <3 for UC / Harvey-Bradshaw index (HBI) score <5 for CD. Biochemical remission: Fecal calprotectin ≤ 250 µg/g. Endoscopic/radiological remission: Mayo endoscopic score 0 in UC and absence of intestinal disease on endoscopy and/or intestinal MRI/CT in CD. Histological remission: normal histology in all mucosal biopsies.

Table 1: Prevalence of chronic fatigue among CD and UC patients with different measures for remission one year after diagnosis.

Conclusion: The probability of CF one year after diagnosis was not associated with either low fecal calprotectin level, normal endoscopic/radiological examinations, or normal histology. Among patients with UC, but not CD, symptomatic remission was associated with a reduced probability of CF. For patients in endoscopic/radiological remission, CF was independently associated with sleep disturbances and current biological treatment.

Disclosure: Nothing to disclose.

PP0418

ADHERENCE TO MEDITERRANEAN DIET AND DIET QUALITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SINGLE CENTER, OBSERVATIONAL, CASE-CONTROL STUDY

M. Cadoni¹, A. Favale¹, M. Demurtas², P. Soddu¹, A. Usai¹, I. Ibba², M.C. Fantini³, S. Onali¹

¹University of Cagliari, Italy, Dep. of Medical Science and Public Health, Cagliari, Italy, ²Azienda Ospedaliero-Universitaria di Cagliari, Italy, Cagliari, Italy, ³University of Cagliari, Department of System Medicine - Gastroenterology, Monserrato, Italy

Contact E-Mail Address: AGNESEFAVALE@ICLOUD.COM

Introduction: The nutritional status of patients affected by inflammatory bowel disease (IBD) is often impaired. Although a link between inflammation-related pathophysiologic mechanisms and malnutrition in IBD has been proposed, the role of dietary regimen and adherence to Mediterranean diet, known to have anti-inflammatory properties, is under investigated.

The aim of this study was to assess quality of diet and adherence to Mediterranean diet in a cohort of Sardinian IBD patients.

Aims & Methods: We conducted a case-control study in which IBD patients, both Crohn's disease (CD) and ulcerative colitis (UC), were compared with healthy controls matched for age, sex and BMI at a 1:2 ratio. Diet Quality Index (DQI) and Medi-Lite questionnaires were collected from IBD patients and controls to assess individual diet quality and adherence to Mediterranean diet, respectively. Subgroup analysis by disease phenotypic characteristics and use of biologic or small molecules as proxy of

disease severity was also performed. Differences between groups were analyzed by descriptive statistics and non-parametric tests were used to assess statistical significance of the observed differences.

Results: Fifty CD and an equal number of UC were matched each with 100 healthy control subjects. Both DQI and Medi-Lite scored significantly lower in IBD patients as compared to controls (DQI: CD 34.5 [IQR 33-37] vs CTRL 40 [IQR 38.5-43] $p<0.0001$; UC 34.5 [IQR 33-37] vs CTRL 42 [IQR 40-44] $p<0.0001$; Medi-Lite CD 7.5 [IQR 7-9] vs CTRL 9 [IQR 7-10] $p=0.0379$; UC 8 [IQR 7-10] vs CTRL 9 [IQR 8-10.5] $p=0.0046$). In CD, DQI was consistently lower than controls independently of disease localization and behavior. However, Medi-Lite score was significantly lower in patients with stricturing phenotype and ileo-colonic localization. In UC patients, DQI was consistently lower as compared to controls independently of disease extent. Among these patients, Medi-Lite score was significantly lower only in those with extensive colitis.

Finally, DQI was lower in both CD and UC independently of the use of concomitant biologic or small molecules, while Medi-Lite resulted significantly lower in UC but not CD patients undergoing major therapies.

Conclusion: IBD was associated with an overall low quality of diet independently of disease type and phenotype.

However, Medi-Lite score detected a lower adherence to Mediterranean diet in patients affected by ileo-colonic stenosing disease and in UC patients with extensive colitis suggesting that the potential benefit of Mediterranean diet may be deemed by low acceptance in specific IBD patient subgroups.

Disclosure: Nothing to disclose.

PP0419

CURRENT STATUS OF LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN JAPAN

N. Tsuruoka¹, H. Takedomi¹, Y. Sakata¹, S. Fujioka², R. Sakemi³, S. Ashizuka⁴, N. Nishimata⁵, T. Kinjyo⁶, Y. Furuta⁷, S. Yoshioka⁸, A. Takamori⁹, M. Esaki¹

¹Saga University, Department of Internal Medicine, Saga, Japan, ²Kyushu University Hospital, Department of Endoscopic Diagnostics and Therapeutics, Fukuoka, Japan, ³Tobata Kyoritsu Hospital, Center for Gastroenterology, Kitakyushu, Japan, ⁴Fukuoka University Faculty of Medicine, Fukuoka, Japan, ⁵Junaikai Medical Corporation Sameshima Hospital, Kagoshima, Japan, ⁶University of the Ryukyus, Okinawa, Japan, ⁷Kumamoto University, Department of Gastroenterology and Hepatology, Kumamoto, Japan, ⁸Kurume University School of Medicine, Division of Gastroenterology, Department of Medicine, Kurume, Japan, ⁹Saga University Hospital, Clinical research center, Saga, Japan

Contact E-Mail Address: nana.tsuruoka@gmail.com

Introduction: When starting immunosuppressive therapy in patients with inflammatory bowel disease (IBD), screening test for latent tuberculosis infection (LTBI) and subsequent preventive treatment for positive patients are recommended to reduce the risk of tuberculosis reactivation especially in moderate-burden countries like Japan. However, the prevalence of LTBI and TB in patients with IBD and its influence in the selection of immunosuppressive therapy remain uncertain.

Aims & Methods: Our multicenter study group (IBD-Quality team; IBD Q-shu all institutional study team) conducted a retrospective study to clarify the prevalence of LTBI and the difference in therapeutic management according to the LTBI status in Japanese patients with IBD. Electronic clinical records of each institution during the period between July 2010 and June 2020 were reviewed to assess patients' clinical profile and subse-

quent medication after screening test of LTBI. LTBI was defined as positive when interferon γ release assays (IGRAs) or tuberculin test was positive with normal chest X-ray.

Results: This retrospective study included 10 institutions of IBD-Quality team, where 4257 IBD patients (Crohn's disease: CD 1646, Ulcerative colitis: UC 2611) were treated during the study period. LTBI was diagnosed in 69 patients (1.62%), and their mean ages of the diagnosis of IBD and LTBI were 40.9 ± 2.2 years and 51.8 ± 2.1 years, respectively. Of the 69 patients, 47 patients (68%) were having clinically active IBD, 3 patients (4.4%) had been treated for TB before the diagnosis of IBD, and 5 patients (7.3%) had a family history of TB.

After the diagnosis of LTBI, 57 patients (82.6%) were treated for LTBI (LTBI treatment group), whereas the remaining 12 patients were followed up without treatment of LTBI (non-LTBI treatment group). In LTBI treatment group, patients were treated with anti-TNF α antibody in 40 cases (70.2%), JAK inhibitors in 3 cases (5.2%), ustekinumab in 12 cases, and vedolizumab in 5 cases.

During the observation period, two patients (1 CD and 1 UC) developed TB 9 and 18 months after completing LTBI treatment, and they were treated with anti-TNF α antibody and JAK inhibitor, respectively. On the other hand, patients in non-LTBI treatment group were treated with ustekinumab in 2 cases, vedolizumab in 1 case, and other drugs in 9 cases, however, neither anti-TNF α antibody nor JAK inhibitors were used. No patient developed TB in the non-LTBI treatment group during the observation period.

Conclusion: The prevalence of LTBI was 1.62% (95% CI; 1.28-2.05) and the rate of developing TB during IBD treatment was 0.05% (95% CI; 0.013-1.17). No cases of TB were observed in the LTBI-negative group during the study period. Although rare, TB can develop in patients with IBD treated with immunosuppressive treatment even after LTBI treatment. Careful follow-up with imaging modalities for TB seems to be mandatory, and further research is required to determine the possible influence of immunosuppressive therapies for the development of TB in patients with IBD.

Disclosure: Nothing to disclose.

PP0420

IBD IN THE ELDERLY POPULATION: LONG-TERM DISEASE COURSE, SURGERY RATES AND BIOLOGICAL USE IN CROHN'S DISEASE AND ULCERATIVE COLITIS – A POPULATION-BASED STUDY FROM HUNGARY BETWEEN 1977–2020

L. Goncz¹, D. Angyal¹, F. Balogh¹, L. Lakatos², P.A. Golovics³, T. Pandur⁴, Z. Erdelyi², G. David², I. Szita², Á. Iliás¹, P.L. Lakatos^{5,1}
¹Semmelweis University, First Department of Internal Medicine, Budapest, Hungary, ²Csolnoky F. County Teaching Hospital, Internal Medicine, Veszprem, Hungary, ³Central Hospital of Northern Pest-Military Hospital, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Internal Medicine, Pápa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgoncz@gmail.com

Introduction: There is a scarcity of population-based studies investigating therapeutic strategies and the long-term disease outcomes in inflammatory bowel diseases (IBD) amongst the elderly. This is a population population-based cohort from Veszprem Province, Hungary, with a follow-up of the incidence and disease course for over 40 years.

Aims & Methods: Our aim was to analyze long-term disease course, surgery rates, medication exposures (especially biological therapy) in a prospective population-based cohort of incident, elderly onset Crohn's disease and ulcerative colitis patients.

Patient inclusion was between January 1, 1977 and December 31, 2018. Patient follow-up ended December 31, 2020. Elderly-onset IBD was defined if diagnosis was established at more than 60 years of age. Disease outcomes and surgery rates were compared based on time of diagnosis: 'pre-biological era', 1977-2008; vs. 'biological era', 2009-2018. Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up.

Results: Data of 840 CD and 1,295 UC patients were analyzed, 58 and 183 of which were elderly-onset IBD patients, respectively. Proportion of patients with colonic (L2) disease location and stenosing behavior (B2) at diagnosis were higher in the elderly population compared to adult-onset CD ($p=0.014$ and $p=0.017$, respectively). In UC, the prevalence of extensive colitis was less amongst the elderly ($p=0.001$).

In time dependent analysis, the probability of biological therapy was $0.0\pm0\%$ and $3.2\pm3.2\%$ at 1 and 5 years from diagnosis in elderly CD patients, $7.8\pm3.3\%$ and $16.6\pm4.8\%$ among elderly UC patients, respectively. Biological therapy was significantly lower in elderly patients compared to adult-onset disease in CD [$p\text{LogRank}=0.003$], but similar exposure was seen amongst UC patients [$p\text{LogRank}=0.770$].

The cumulative probability of resective surgery in the elderly CD population was $31.1\pm6.1\%$, $32.9\pm6.2\%$, and $35.3\pm6.4\%$ after 1, 5 and 10 years. There were no statistically significant differences in resective surgery rates between the elderly and adult-onset cohorts in CD [$p\text{Log Rank}=0.838$]. The cumulative probability of colectomy in elderly UC patients was $2.2\pm1.1\%$, $3.4\pm1.4\%$, and $3.4\pm1.4\%$ after 1, 5 and 10 years, respectively. Colectomy rates in the elderly and adult-onset cohorts were similar [$p\text{Log Rank}=0.435$].

The probability of disease behavior progression in CD patients with luminal (B1) behavior into stenosing or penetrating phenotype (B2/B3) was lower among elderly patients, compared to adult-onset CD. [$p\text{LogRank}=0.015$]. Similarly, disease extent progression ($E1/2\gg E2/3$) in elderly UC patients was also lower [$p\text{LogRank}=0.022$].

Logistic regression model showed that male gender (OR 0.22; 95%CI 0.07-0.72; $p=0.013$) stenosing or penetrating disease (B2/B3) behavior (OR 8.69; 95%CI 2.17-34.85; $p=0.001$) and ileal or ileo-colonic (L1/L3) location (OR 9.71; 95%CI 2.41-39.13; $p=0.001$) were predictors of resective surgery in elderly CD patients. Whereas, extensive colitis (E3) (OR 7.17; 95%CI 1.63-31.52; $p=0.011$), continuous disease activity (OR 11.07; 95%CI 2.28-53.77; $p=0.010$), and anaemia (OR 10.13; 95%CI 1.97-52.13; $p=0.004$) were predictors of colectomy in elderly UC.

Conclusion: Elderly patients represent an increasing proportion of the IBD population. Biological therapy use was lower in elderly CD, however no different in elderly UC compared to adult-onset populations. There were no significant differences in resective surgery and colectomy rates between the elderly and adult-onset cohorts, whereas disease phenotype progression was slower in the elderly.

References: .

Disclosure: PLL has been a speaker and/or advisory board member: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Gilead, Janssen, Eli Lilly, Merck, Organon, Pendopharm, Pfizer, Roche, Sandoz and Takeda and has received unrestricted research grant: AbbVie, Gilead and Pfizer.

PP0421

IBD HEALTH EQUITY SUMMIT: A CALL TO ACTION

M. Doyle-Scharff¹, C. Jimenez¹

¹Pfizer Inc, Institute of Translational Equitable Medicine, New York, United States of America

Contact E-Mail Address: maureen.doyle-scharff@pfizer.com

Introduction: Pfizer's Institute for Translational Equitable Medicine and our Chief Medical Officer, Aida Habtezion, MD, hosted an IBD Health Equity Summit at DDW 2023 in Chicago, Illinois on May 5, 2023 with a group of 22 key opinion leaders in the gastroenterology field. The purpose of the Summit was to uncover health equity research gaps and quality of care gaps that will enable Pfizer and our partners to determine future directions in IBD research and contribute to achieving healthcare equity by providing opportunities to improve patient outcomes, as well as address practice-based disparities.

Aims & Methods: A full day Summit was designed and developed, bringing together thought leaders and experts (representing research, HCPs and patients) to discuss health disparity gaps and possible solutions. The day was split into two parts: a morning session focused on research, with IBD researchers presenting different facets of the research construct with follow-on discussion with the audience. The afternoon was dedicated to clinical care and also included IBD experts addressing Health Equity concerns and opportunities. A follow-on summary report was developed, distributed and serves as the basis for current and future strategies aimed at closing disparity gaps among IBD patients.

Results: Several overarching themes emerged, highlighting IBD as a global affliction, and challenges that transcend geographical borders. Addressing these challenges will require solutions tailored to local and regional contexts that consider factors such as race, ethnicity, socio-economic status, culture, diets, and sexual orientations. It was also recognized that many of the challenges posed by IBD are not unique to this disease, and that valuable insights can be gained by examining other complex disease states to improve the quality of care and address health disparities in patients with IBD.

Conclusion: IBD Research

Key gaps include low clinical trial participation of patients from diverse communities due to lack of healthcare literacy, low historical representation, bias in recruitment, lack of diversity in providers.

Strategies to address these gaps include improving health literacy, workforce development and educating providers, adequate compensation for time, flexibility for participating in trials, and incorporation of digital health tools for follow-ups.

Clinical Care

There are groups of patients in several regions that lack any care, and addressing healthcare disparities in IBD care for these patients cannot be done online but will need to be done on a local and regional level on the ground.

When addressing health inequities, the heterogeneities within underserved populations like Black and Hispanic patients need to be considered.

Gaps in data on the effectiveness of therapies in specific patient populations (ie, response to anti-TNFs in black patients and patients with comorbidities).

Sponsorship is lacking to establish efforts in underserved communities on a global level; There is an opportunity to provide connection for minority physicians to resources.

By identifying gaps and potential strategies to close them, the participants have provided Pfizer and our partners a roadmap to address health disparities among IBD patients worldwide. These data and information have served as the basis for a go-forward plan to support and invest in

change initiatives to close gaps. Our desire is to enlist additional partners and collaborators through a Call to Action to identify solutions at the local level that can accelerate improved IBD care and outcomes for some of the most vulnerable populations in the world.

Disclosure: Employee of Pfizer Inc.

PP0422

PATIENT AND FAMILY INSIGHTS ON PREDICTION AND PREVENTING INFLAMMATORY BOWEL DISEASE – A WORLDWIDE SURVEY

A.C. Bravo¹, S.G. Christensen², M. Julsgaard^{2,3}, I. Rodriguez-Lago⁴, D. Ginard⁵, P. Juillerat⁶, H.G. Sørensen⁷, G. Fiorino⁸, A. Buisson⁹, N. Stemmer¹⁰, N. Queiroz¹¹, A. Ribas¹², V. Parra Izquierdo¹³, C. Siegel¹⁴, K. Croitouru¹⁵, E. Spencer¹⁶, I. Peter¹⁷, J.-F. Colombel¹⁸, M. Agrawal^{18,3}, R. Ungaro¹⁸, C.A. Fidalgo¹, B. Morão¹⁹, L. Avedano²⁰, S. Leone²⁰, L. Exposito²¹, J. Torres^{1,18,22}

¹Hospital Beatriz Ângelo, Division of Gastroenterology, Loures, Portugal, ²Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ³Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark, ⁴Hospital Universitario de Galdakao, Department of Gastroenterology, Galdakao, Spain, ⁵Hospital Universitario Son Espases, Department of Gastroenterology, Palma, Spain, ⁶Intesto Gastroenterologische Praxis & Crohn-Colitis-Zentrum Bern, Centre Fribourgeois de Gastroentérologie, Bern, Switzerland, ⁷Gjødstrup Hospital, Department of Medicine, Gjødstrup, Denmark, ⁸Vita Salute San Raffaele University, Department of Gastroenterology and Digestive Endoscopy, Milan, Italy, ⁹Université Clermont Auvergne, Inserm, CHU Clermont-Ferrand, 3iHP, Service d'Hépatogastro-Entérologie, Clermont-Ferrand, France, ¹⁰Städtisches Klinikum Lüneburg, Department of Internal Medicine, Gastroenterology and Hepatology, Lüneburg, Germany, ¹¹Health Sciences Graduate Program, Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba, Brazil, ¹²Bahia State University UNEB, Department of Life Science, Salvador, Bahia, Brazil, ¹³Hospital Internacional de Colombia, Bucaramanga, Gastroenterology and Rheumatology, Bucaramanga, Colombia, ¹⁴Center for Digestive Health, Dartmouth Hitchcock Medical Center, Section of Gastroenterology and Hepatology, Lebanon, New Hampshire, United States of America, ¹⁵University of Toronto and Zane Cohen Centre for Digestive Diseases, Mount Sinai Hospital, Department of Medicine, Toronto, Canada, ¹⁶Icahn School of Medicine at Mount Sinai, Division of Pediatric Gastroenterology & Nutrition, Department of Pediatrics, New York, United States of America, ¹⁷Icahn School of Medicine at Mount Sinai, Department of Genetics and Genomic Sciences, New York, United States of America, ¹⁸Icahn School of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division of Gastroenterology, New York, United States of America, ¹⁹Hospital Beatriz Ângelo, Division of Gastroenterology, Loures, Portugal, ²⁰European Federation of Crohn's & Ulcerative Colitis Association (EFCCA), Brussels, Belgium, ²¹ACCU España - Confederación de Asociaciones de Enfermos de Crohn y Colitis Ulcerosa de España, Madrid, Spain, ²²Hospital da Luz Lisboa, Division of Gastroenterology, Lisbon, Portugal

Contact E-Mail Address: catarina.bravoo@gmail.com

Introduction: Significant advances have been made in identifying biomarkers to predict IBD onset. With the use of predictive testing to identify individuals at risk of developing the disease, it would be possible to inter-

vene and try to mitigate that risk. However, the feasibility of such strategy would depend on whether individuals at risk of developing IBD would be willing to undergo predictive testing and preventive interventions.

Aims & Methods: An anonymized electronic survey was created in eight different languages and disseminated by clinicians and patient's associations; patients with IBD, patients with an at-risk first-degree relative (offspring), and their first-degree relatives were invited to provide their feedback.

The survey had four main sections – participants' characterization, knowledge of disease, predictive tests and preventive interventions. Univariate and multivariate logistic regression were used to assess factors associated to acceptance of predictive testing and preventive interventions.

Results: Overall, 2034 participants (73% women, mean age of 43±13 years old) from 66 different countries (80% from Europe), participated. Most participants (52%) were parents with IBD with healthy at-risk children. 51% of individuals with IBD had Crohn's disease, 56% were undergoing treatment with biologics, 28% had a history of surgery, and 61% reported a significant impact on their quality of life caused by disease. 73% recognized IBD as a disease with no defined genetic transmission, but with an increased risk among FDR of affected patients.

Most participants (82%) would be willing to undergo, predictive testing, or to have their children undergo them, mainly with minimally-invasive blood (91%), stool (90%) or saliva tests (78%), or intestinal ultrasound (68%); 46% would accept a colonoscopy.

The main benefits recognized with predictive testing were the possibility of starting preventive interventions to minimize the risk of developing IBD (69%) and to obtain an earlier diagnosis (58%). The main disadvantage was anxiety generated from a positive result (57%).

Overall, 97% of participants were willing to accept preventive interventions. The most accepted were dietary modification (82%), physical exercise (79%) and probiotics (71%). Overall, 40% and 34% would accept oral or intravenous/subcutaneous immunosuppressive treatment, respectively; provided that the risk of minor adverse events was negligible to acceptable (23%), while 44% considered that the risk of major adverse events should be <1% to be acceptable. In multivariate analysis, factors associated with less acceptance of predictive testing were older age ($p<0.001$) and treatment with thiopurine ($p<0.001$).

Factors only associated with less acceptance of preventive interventions were having ulcerative colitis ($p=0.004$) or undetermined colitis ($p<0.001$) and being treated with mesalazine ($p<0.001$). Having a disease with low impact in their/their family members' quality of life were associated with less acceptance of both predictive testing and preventive interventions ($p<0.001$).

Conclusion: The vast majority of parents with children at-risk for IBD, or first-degree relatives at risk for IBD development would accept minimally-invasive predictive testing for IBD. The vast majority expressed acceptance of non-pharmacological interventions, however, more than one-third would be willing to accept immunosuppressive medications, particularly if associated with a low risk of minor and major adverse events. This data provides useful and important information for the development of prediction and prevention strategies.

Disclosure: Nothing to disclose.

PP0423

FINANCIAL IMPLICATIONS OF FIXED DOSING OF SUBCUTANEOUS INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

M. Jang¹, H. Yoo¹, T. Kwon¹

¹Celltrion, Incheon, South Korea

Contact E-Mail Address: minyoung.jang@celltrion.com

Introduction: In Australian patients receiving intravenous (IV) infliximab (IFX) treatment, 44% of patients do not respond to standard regimen and require dose escalation within a year. The REMSWITCH (6-month evaluation) and REMSWITCH-LT (18-months evaluation) investigated the effectiveness of switching from IV to subcutaneous (SC) IFX in patients with inflammatory bowel disease (IBD) who received standard and dose-escalated IV regimen.

The two studies concluded that a fixed dose of 120 mg Q2W is feasible, safe and well-accepted leading to a low risk of long-term relapse in patients with escalated IV doses except for those on 10mg/kg/4weeks regimen. In this study, we developed a model to estimate the financial implications of switching.

Aims & Methods: Clinical efficacy parameters were derived from the REMSWITCH and REMSWITCH-LT studies and applied to the Australian context. Number of Australian patients who are on IFX, the proportion of patients on dose escalated regimen, and cost parameters were identified from the published literature or publicly available resources. A financial model was developed based on the assumption that a cohort of patients will receive either IV or SC IFX, and the analysis concluded with the cost difference.

Results: The model assumes that a total of 5.6K patients are receiving IV IFX, with 44.2% of them receiving dose escalation and/or shortened interval of IV IFX. The model produced 6 months and 12 months results, suggesting savings between 582 and 882 AUD per patient, respectively, and equates to a yearly societal savings of 5 million AUD.

Conclusion: IFX SC deserves premium over IFX IV, given that the novel formulation offers tangible and intangible benefits that originator Remicade and biosimilars cannot provide. There is a concern regarding the affordability of SC IFX because it is generally priced higher than IV IFX, which has many biosimilars on the market.

However, this study asserts that fixed dosing of 120mg of IFX is cost-saving for society, considering highly prevalent practice of dose escalation and/or shortened intervals of IFX regimen.

Disclosure: Nothing to disclose.

PP0424

INDOOR RADON LEVELS AND ITS ASSOCIATION WITH THE DIAGNOSIS AND EVOLUTION OF INFLAMMATORY BOWEL DISEASES

M.V. Mauriz Barreiro^{1,2}, A. Ruano-Raviña^{3,4}, R. Ferreiro-Iglesias^{1,2}, I. Bastón-Rey^{1,2}, C. Calviño Suarez^{1,2}, L. Nieto-García⁵, M.d.S. Porto-Silva⁵, X. Martinez-Seara⁵, J. Peon-Gonzalez³, J.E. Domínguez Muñoz^{1,2}, M. Barreiro-de Acosta^{1,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³University of Santiago de Compostela, Preventive Medicine and Public Health, Santiago de Compostela, Spain, ⁴CIBER de Epidemiología y Salud Pública, CIBERESP, Santiago de Compostelaspp, Spain, ⁵Health Research Institute of Santiago de Compostela (IDIS), Gastroenterology and Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Environmental factors have only been partially implicated in the aetiopathogenesis of inflammatory bowel disease (IBD). The role of indoor radon, a radioactive gas, has not been formally studied and may play a role in the pathogenesis of the disease.

Aims & Methods: The aim of this study is to analyse the role of individual residential radon exposure on the incidence of IBD in a radon-prone area, also characterised as a high incidence IBD region, and whether this exposure is associated with the development of the disease.

Methods: A case-control study was developed in the health area of Santiago de Compostela (Galicia, Spain) between June 2020 and September 2023, including all consecutive incident cases with IBD. Controls were selected by frequency matching based on sex and age and without IBD. All participants had to have lived in the same home for at least 5 years. All cases were followed up for one year to assess disease progression. Endoscopic index, imaging techniques and analytical parameters were collected. In patients with IBD, hospitalisations related to the disease and the number and severity of flares (measured by Partial Mayo Score and Harvey-Bradshaw) were recorded. Radon levels measured in participants' homes over three months were compared between cases and controls, and between different types of IBD. Each individual was provided with a home radon meter (an RSKS trace detector), which was delivered and read by the Galician Radon Laboratory, a certified radon laboratory. Radon concentrations were categorised into three groups: 0-99 Bq/m³, 100-299 Bq/m³ and >299 Bq/m³. The results are expressed as odds ratios with their 95% CIs obtained by logistic regression.

Results:

RADON LEVELS (Bq/m ³)	IBD PATIENTS (%)	CONTROLS (%)	OR (95%CI)
0-99	34.3	19.8	1
100-299	45.2	55.8	0.5 (0.3-0.8)
>299	20.5	24.4	0.5 (0.3-0.9)

*OR = Odds Ratio; CI = Confidence Interval.

178 incident cases and 178 controls were included, with a median age of 51 years (IQR 40-59.5). 51.7% were female. 136 IBD patients completed one year of follow-up (78 ulcerative colitis, 52 Crohn's disease and 6 unclassified colitis). The median radon level in the homes of the IBD patients was 144.5 (IQR 83 - 260) and the median radon level in the homes of the controls was 189.5 (IQR 112 - 292.5). After adjustment for age and sex, high radon levels showed a negative association with the development of IBD (taking levels of 0-99 Bq/m³ as reference, OR 100-299 Bq/m³ is 0.5 (95%CI 0.3-0.8) and OR >299 Bq/m³ is 0.5 (95%CI 0.3-0.9). The results are shown in Table 1. Taking into account the different types of IBD, radon levels show

the same negative association, but without statistical significance. There were no statistically significant differences in radon levels, taking levels of 0-99 Bq/m³ as reference, between hospitalised and non-hospitalised patients (OR 0.8 95%CI 0.3-2.1 for 100-299 Bq/m³, OR 1.7 95%CI 0.6-5.0 for >299 Bq/m³), nor in patients with a flare compared with patients without a flare during the follow-up year (OR 0.4 95%CI 0.0-4.5 for 100-299 Bq/m³, OR 5.4 95%CI 0.8-34.3 for >299 Bq/m³). Radon levels were also not associated with the number of flares (OR 0.6 95%CI 0.3-1.7 for 100-299 Bq/m³, OR 1.5 95%CI 0.5-4.5 for >299 Bq/m³). Stratification by type of IBD did not alter the results.

Conclusion: High radon levels may be a protective factor against the development of IBD, and indoor radon levels do not appear to be associated with the development of IBD in terms of hospitalisations or flares.

Disclosure: Nothing to disclose.

PP0425

IMPACT OF THE FASTING MONTH OF 'RAMADAN' ON DISEASE ACTIVITY IN EMIRATI PATIENTS WITH INFLAMMATORY BOWEL DISEASE AT A TERTIARY REFERRAL CENTER IN ABU DHABI, UNITED ARAB EMIRATES: RESULTS OF RETROSPECTIVE COHORT STUDY

K. Altenajji¹, S.W. Khan², H.A. Ahmed², M.N. Alzaabi², A. Alali³, T. Swaid², M. Alahmad⁴, K.K. Kumar², Y. Ghoris⁵, T.A. Malik⁶

¹Sheikh Shakhbout Medical City, Abu Dhabi, United Arab Emirates,

²Sheikh Shakhbout Medical City, Gastroenterology, Abu

Dhabi, United Arab Emirates, ³Sheikh Shakhbout Medical City,

Abudhabi, United Arab Emirates, ⁴Sheikh Shakhbout Medical City,

Gastroenterology, Abudhabi, United Arab Emirates, ⁵Arizona State

University, Arizona, United States of America, ⁶Mayo Clinic, Arizona, United States of America

Contact E-Mail Address: Dr.khalifa14@gmail.com

Introduction: Current Literature examining how Ramadan affects gastrointestinal disorders indicates that individuals with inflammatory bowel disease (IBD) generally face a low likelihood of worsening symptoms, although older men with ulcerative colitis (UC) are more susceptible to exacerbations during fasting. Moreover, individuals with duodenal ulcers have a heightened risk of experiencing bleeding following fasting during Ramadan (1).

Aims & Methods: **Aim:** To study the impact of 'Ramadan' on Inflammatory bowel disease (IBD) activity in an Emirati cohort.

Methods: We designed a retrospective cohort study of adults (> 16 years) with IBD seen at our tertiary care IBD referral center in Abu Dhabi, the United Arab Emirates (UAE) for IBD related emergencies, IBD related hospitalizations and in-person clinic visits during Ramadan, the Islamic lunar calendar month of fasting vs. during the preceding month of Shaban in the year 2023. Exposure of interest was the month (30 days) of 'Ramadan' and the unexposed cohort was the month (30 days) of 'Shaban'. Chi-square testing was used to compare emergency department (ED) visits and hospitalizations.

Logistic regression was used to assess the impact of Ramadan vs. Shaban on the risk of active clinical disease during in-person clinic visits. Statistical analysis was performed using R (version 4.0.2) and a p-value of <0.05 was considered statistically significant. IRB approval was in place for this study.

Results: A total of 294 encounters in the cohort (130 in Ramadan vs. 164 in Shaban) During Ramadan, 12 of 130 (9%) IBD encounters were ED visits for an IBD related emergency vs. 4 of 164 (2%) patients during Shaban ($X^2 = 5.25$, 95%CI 0.06-0.13, $P=0.02$). During Ramadan, 16 of 130 (12%) IBD encounters led to hospitalization vs. 16 of 164 (10%) during Shaban ($X^2=0.26$, 95%CI -0.054-0.1, $P=0.61$). In Ramadan, during 33/77 (43%) in-person clin-

ic visits, patients had active disease vs. 24/106 (23%) in Shaban ($X^2=7.59$, 95%CI 0.055-0.35, $P=0.006$). Logistic regression model adjusted for age and gender demonstrated that during Ramadan, the risk (likelihood) of active clinical disease was approximately 3 times higher compared to during Shaban (OR 2.70, 95% CI 1.41-5.25, $P=0.003$).

Conclusion: This is the first study examining the effect of the fasting month of 'Ramadan' on disease activity among Emirati patients with IBD. We found that during Ramadan, there was higher likelihood of ED visits, hospitalizations and active clinical disease when compared to during Shaban. This risk was profound and statistically significant regarding ED visits and likelihood of active clinical disease. There may be several factors underlying these significant findings.

For example, in the UAE during Ramadan, there are limited meal and drink options during the day, there occurs a sudden drastic change in diet patterns and there are limited working hours that reduce access to the IBD Clinic. IBD practices in the UAE could try to mitigate the risk of flares during Ramadan by increased dietary and lifestyle counseling of patients in preparation for the month, encourage patients to hydrate adequately and perhaps by increasing access when needed to the IBD clinic during Ramadan.

References: 1. Tibi S, Ahmed S, Nizam Y, et al. (March 31, 2023) Implications of Ramadan Fasting in the Setting of Gastrointestinal Disorders. *Cureus* 15(3): e36972. doi:10.7759/cureus.36972

Disclosure: Nothing to disclose.

PP0426

INFLAMMATORY BOWEL DISEASE AND CONCOMITANT ENDOMETRIOSIS: FREQUENCY AND CHARACTERISTICS IN A MULTIDISCIPLINARY APPROACH

M. Fiorillo¹, B. Neri¹, F. Iacobini², R. Mancone¹, S.C. Schiavone¹, C. Russo², M. Franchin¹, C. Exacoustos², L. Biancone¹

¹Università degli Studi di Roma Tor Vergata, Medicina dei

Sistemi, Rome, Italy, ²Università degli Studi di Roma Tor Vergata, Gynecological Unit, Rome, Italy

Contact E-Mail Address: fiorillo93@gmail.com

Introduction: Inflammatory bowel disease (IBD) and endometriosis are both immuno-mediated chronic inflammatory diseases, sharing some common clinical manifestations (i.e. abdominal pain). A possible association between IBD and endometriosis has been suggested but is currently still undefined.

Aims & Methods: In a multidisciplinary prospective single-center study, we aimed to assess the frequency of undiagnosed endometriosis in IBD patients by searching for symptoms compatible with this condition (dysmenorrhea, dyschezia, dyspareunia, dysuria, heavy menstrual bleeding, HMB).

Secondary end point was to compare symptoms compatible with endometriosis in IBD patients with vs without a subsequent diagnosis of endometriosis. In a prospective study, all female IBD patients in childbearing age with symptoms compatible with endometriosis, as revealed by filling a questionnaire during a scheduled visit at our IBD center, were enrolled. After informed consent, gynecological evaluation and transvaginal ultrasonography (TVUS) was performed by our referral dedicated gynecologist, in order to search for pelvic endometriosis.

Inclusion criteria:

- 1) female gender;
- 2) age ≥ 18 and ≤ 50 years;
- 3) well-defined diagnosis of IBD;
- 4) ≥ 1 symptom compatible with endometriosis;
- 5) written informed consent.

Exclusion criteria:

- 1) pregnancy;
- 2) menopause.

Characteristics of endometriosis and adenomyosis were reported according to standard classifications. Data were expressed as median [range].

Results: The study population included 51 IBD patients (age 37 [23-53] years, body mass index 21.6 [17.3-41.6]). In IBD, there were 24 (47.05%) Crohn's Disease (CD) and 27 (52.9%) Ulcerative Colitis (UC) patients.

At enrollment, questionnaires revealed dysmenorrhea in 43 (84.3%), dyschezia in 18 (35.3%), dyspareunia in 31 (60.8%), dysuria in 4 (7.8%), HMB in 33 (64.7%) patients. At TVUS, endometriosis in any form was observed in 35 (68.6%) IBD patients, adenomyosis in 26 (51%).

Both diseases were concomitantly detected in 22 patients (43.1%). In patients showing endometriosis, deep infiltrating endometriosis was diagnosed in 33 (94.3%) IBD patients, and 7 out of these 33 (21.2%) patients showed rectal endometriosis.

Among the 35 patients with endometriosis, IBD included CD in 16 (45.7%) and UC in 19 (54.3%).

The frequency of the tested 5 symptoms compatible with endometriosis were then compared between IBD patients with vs without a subsequent diagnosis of endometriosis. Dysmenorrhea (32 [91.4%] vs 11 [68.75.4%]; $p=0.04$) and HMB (26 [74.3.%] vs 7 [43.75%]; $p=0.04$) were more frequent in IBD patients with endometriosis.

Differently, the other considered symptoms were comparable between IBD patients with vs without endometriosis: dyspareunia (24 [68.6%] vs 7 [43.75.%]; $p=0.09$), dyschezia (11 [31.4%] vs 7 [43.7%]; $p=0.39$), dysuria (3 [8.6%] vs 1 [6.25%]; $p=0.77$).

No significant differences were observed between UC and CD patients in terms of characteristics of endometriosis, when excluding a higher frequency of endometriosis involving the uterosacral ligament in UC vs CD (16 [84.2%] vs 6 [36.5%]; $p=0.005$).

Conclusion: Findings from a prospective multidisciplinary study suggest that endometriosis may be highly underestimated in IBD and that specific symptoms, particularly dysmenorrhea and HMB, should be carefully searched in young patients. In IBD, endometriosis was mostly represented by deep infiltrating endometriosis and a higher frequency of rectal endometriosis, potentially leading to rectal bleeding was observed.

References:

[1] J. Satsangi, MS Silverberg, S. Vermeire, and J-F. Colombel. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006; 55(6): 749–753.

[2] American Society for Reproductive Medicine. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 1997;67:817–821.

Disclosure: Nothing to disclose.

PP0427

HIGHER FREQUENCY OF PERIANAL DISEASE AND FAILURE OF BIOLOGICS IN OVERWEIGHT AND OBESE CROHN'S DISEASE PATIENTS: A PROSPECTIVE STUDY

B. Neri¹, R. Mancone¹, M. Fiorillo¹, G. Fioravanti¹, L. Putzu¹, S. Migliozi¹, S.C. Schiavone¹, L. Biancone¹

¹Università degli Studi di Roma Tor Vergata, Medicina dei Sistemi, Rome, Italy

Contact E-Mail Address: benedettoneri@gmail.com

Introduction: The relationship between obesity and inflammatory bowel disease (IBD) is currently undefined. The clinical outcome of obese and non-obese IBD patients is apparently comparable. However, evidences at this regard are conflictual.

Aims & Methods: Primary aim was to compare, in a prospective study, IBD characteristics between overweight or obese and non-obese consecutive IBD patients. Secondary aim was to compare the frequency of immunomodulator therapies, IBD-related surgery and hospitalizations between overweight or obese and non-obese patients.

In a prospective, single-center study, consecutive IBD patients undergoing scheduled outpatients visit between September 2022 and January 2023 were enrolled. Demographic and clinical data including body mass index (BMI) were recorded. Inclusion criteria: 1) defined diagnosis of IBD; 2) age ≥ 18 years; 3) regular follow up (≥ 2 visits/year). Exclusion criteria: 1) BMI < 18.5 kg/m^2 , 2) incomplete data. Data were expressed as median [range]. Normal distribution of continuous variables tested by the Kolmogorov-Smirnov test. Comparisons assessed by Student-t test, Mann-Whitney u-test and Chi-squared test.

Results: Out of 300 IBD patients assessed, 284 were enrolled (141 [49.6%] Crohn's Disease (CD); 143 [50.4%] UC). The median age of IBD group was 51 [20-87] and male gender was observed in 157 (55.3%) patients. The median IBD duration was 13.5 [1-57] years. Overall, 170 (59.8%) IBD patients were normal-weight and 114 (40.2%) were overweight or obese.

Among the 141 CD patients enrolled, 89 (63.1%) normal-weight patients and 52 (36.9%) overweight or obese patients were observed. Lesions distribution and behavior was comparable between normal-weight and overweight or obese patients (L1: 62 [70%] vs 35 [67.3%], $p=0.77$; L2: 8 [9%] vs 4 [7.7%], $p=0.79$; L3: 19 [21%] vs 13 [25%], $p=0.61$; L4: 7 [7.9%] vs 2 [3.8%], $p=0.34$; B1: 24 [27%] vs 13 [25%], $p=0.79$; B2: 44 [49.4%] vs 32 [61.5%], $p=0.16$; B3: 21 [23.6%] vs 7 [13.5%], $p=0.74$, respectively). Perianal disease was more frequently observed in overweight or obese vs normal-weight patients (9 [10.1%] vs 12 [23%], $p=0.03$). Immunosuppressive (ISS) or biologic use was comparable between groups (ISS: 33 [37%] vs 19 [36.5%], $p=0.94$; biologics: 23 [25.8%] vs 17 [32.7%], $p=0.38$). Lack of response to biologics was more frequently observed in overweight and obese vs normal-weight patients (0 [0%] vs 4 [23.4%], $p=0.01$). Loss of response and adverse events were comparable between groups (11 [47.8%] vs 5 [29.4%], $p=0.23$; 13 [56.5%] vs 8 [47.1%], $p=0.55$).

Among the 143 UC patients enrolled, 81 (56.6%) normal-weight patients and 62 (43.4%) overweight or obese patients were observed. Proctitis and extensive UC were more frequently reported in overweight or obese vs normal-weight patients (E1: 18 [29%] vs 11 [13.6%], $p=0.02$; E3: 35 [56.4%] vs 31 [38.3%], $p=0.03$). Left-sided UC were more frequent in normal-weight than in overweight or obese patients (E2: 39 [48.1%] vs 19 [30.6%], $p=0.03$). ISS use was comparable between groups (14 [17.3%] vs 7 [11.3%], $p=0.31$) while biologics were more frequent in normal-weight than in overweight or obese patients (15 [18.5%] vs 4 [6.4%], $p=0.03$). Lack of response, loss of response and adverse events were comparable between groups (6 [40%] vs 1 [25%], $p=0.58$; 5 [33.3%] vs 1 [25%], $p=0.75$; 6 [40%] vs 0 [0%], $p=0.12$).

Conclusion: In the tested population, overweight or obese CD patients showed a higher frequency of perianal disease and refractoriness to biologics than normal weight patients. These preliminary findings in CD suggest that BMI and phenotype may influence responsiveness to biologics.

Disclosure: Nothing to disclose.

PP0428

INSIGHTS INTO MICROSCOPIC COLITIS: A COMPREHENSIVE ANALYSIS FROM LONDON'S PREMIER TEACHING HOSPITAL IN THE UNITED KINGDOM

S. Hoque¹, J. Kottwitz¹, K. Giaslakitiotis¹¹Barts Health NHS Trust, Gastroenterology, London, United Kingdom**Contact E-Mail Address:** samihoque@nhs.net

Introduction: Microscopic colitis is a cause of chronic watery, non-bloody diarrhoea diagnosed mainly on histology after taking biopsy from macroscopically normal colonoscopy. Thereby mainly two subtypes can be identified: Lymphocytic and collagenous colitis. So far, no biomarkers for the diagnosis of microscopic colitis have been identified. Here, we looked at, risk factors and treatment outcome of microscopic colitis in a large series of cases.

Aims & Methods: In this study, we analysed all cases of microscopic colitis diagnosed from 2018-2022 in the Northeast London from 5 different teaching hospitals in the UK. 225 cases (121, Lymphocytic, 124 cases are collagenous colitis) were identified and their electronic health record from hospital and from the primary General Practitioner (GP) were manually reviewed.

Results: In this cohort, 32% male, 68% female with ratio of (1:3, $P < 0.036$) with mean age of 64years. Thirty three percent were active or ex-smoker, Disease symptoms were significantly different compared to non-smoker ($p < 0.007$). PPI uses were associated with in 81% cases. While NSAIDs and statin were associated in 57% and 49% cases, respectively. We also found that SSRI use was associated in about 31% cases.

Painless watery diarrhoea was the main cause for referral in 90% of cases, while complaint of abdominal pain noted in only 39% cases. Thirty-five (25%) cases noted to have history of weight loss. Forty-eight (48%) patients received treatment with Budesonide, 46% treated with loperamide, 5% with Immunomodulator or Biologics and 1% Bismuth Subsalicylates respectively. Other autoimmune disease was associated in 6% cases and 2% cases were associated with Coeliac disease. In Nineteen (19%) of cases symptoms improved immediately after stopping above associated drugs without any specific therapy.

Twenty-five (25%) percent relapses 6 months after stopping of therapy. Patients present with abdominal pain, and arthralgia were significantly ($p < 0.001$) higher risk of relapsing compared to patients with other symptoms.

Conclusion: In this large series of microscopic colitis, we found that in addition to associated drug use is not only risk, but patient also presents with abdominal pain and arthralgia have higher risk of relapse, after stopping of therapy of microscopic colitis. Further studies are needed to identify biomarker of this frustrating disease which has significant impact on patients of quality of life.

References: nil**Disclosure:** Nothing to disclose.

PP0429

SLEEP, ILLNESS PERCEPTION AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE – SHOULD WE BE CONCERNED?

M.J. Temido¹, C. Costa Cardoso², P. Rocha¹, J. Pereira³, N.P. Almeida^{1,2}, P. Narra Figueiredo^{2,1}, F. Silva Portela^{2,1}¹Unidade Local de Saude de Coimbra, Gastroenterology, Coimbra, Portugal, ²University of Coimbra, Faculty of Medicine, Coimbra, Portugal, ³Unidade Local de Saude de Coimbra, Serviço de Farmácia Hospitalar, Coimbra, Portugal**Contact E-Mail Address:** mariajosetemido@hotmail.com

Introduction: The management of inflammatory bowel disease (IBD) has traditionally focused on controlling symptoms and reducing or even clearing inflammatory burden. However, the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE)-II statements have expanded the targets to include health-related quality of life (HRQoL) as a long-term outcome. Despite this, the predictive factors for worse HRQoL have yet to be fully completely determined. Alongside psychosocial status, it has been hypothesized that illness perception may also influence HRQoL. Additionally, a bidirectional relationship between sleep quality and IBD has been observed.

Aims & Methods: We thus aim to investigate the potential association between self-reported sleep quality and HRQoL in patients with IBD and to identify other predictors of HRQoL to so that these factors can be integrated into the evaluation of IBD patients. We conducted a prospective single-center cohort study at a tertiary center. From January 2024 to March 2024, patients previously diagnosed with IBD were invited to complete a comprehensive questionnaire assessing HRQoL using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), self-reported sleep quality using the Pittsburgh Sleep Quality Index (PSQI), and illness perception using the revised version of the Illness Perception Questionnaire. Demographic, clinical (including history of psychopathology), and symptomatology (evaluated using the Harvey Bradshaw Index (HBI) and Partial Mayo Score), as well as analytical parameters (fecal calprotectin), were assessed at the time of questionnaire completion. Clinical remission was defined as HBI $\leq$ 3 or Partial Mayo Score $\leq$ 1. Poor HRQoL was defined as SIBDQ $<$ 50 and poor sleep quality defined as PSQI $>$ 5. Logistic regression was used to performed both univariate and multivariable analysis. Predictors with $p < 0.1$ in the univariate analysis were included in the multivariable analysis.

Results: A total of 272 patients were included, with 53.3% being male. The median age was 48 years (interquartile range [IQR] 38-58). Ulcerative colitis was present in 184 (68%) patients, while the remaining patients had Crohn's disease. A history of psychopathology was noted in 35 (12.9%) patients. The majority of patients were in clinical remission (245 (90.1%) patients). Poor QoL was reported by 87 (32.7%) and poor sleep quality was reported in 185 (70.1%). Univariate analysis revealed a statistically significant association between female gender, Crohn's disease, absence of clinical remission, self-reported poorer sleep quality, and illness perception (higher scores in four components: timeline cyclical, illness consequences and coherence, and emotional representation of IBD) and worse HRQoL. Multivariable analysis confirmed younger age, absence of clinical remission, worse sleep quality, and illness perception (illness consequences, coherence, and emotional representation of IBD) as independent predictors of poor HRQoL.

Conclusion: HRQoL in IBD is influenced by factors beyond disease activity. Sleep quality emerges as a significant determinant of HRQoL, alongside the patient's illness perception. Therefore, integrating sleep quality assessment into patient clinical evaluation is paramount. Moreover, addressing patients' understanding of their disease, perspective on consequences, and emotional response to the condition is crucial for improving HRQoL.

References: Khan S, Sebastian SA, Parmar MP, et al. Factors influencing the quality of life in inflammatory bowel disease: A comprehensive review. *Dis Mon.* 2024;70(1S):101672. doi:10.1016/j.disamonth.2023.101672

Knowles SR, Graff LA, Wilding H, Hewitt C, Keefer L, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses-Part I. *Inflamm Bowel Dis.* 2018;24(4):742-751. doi:10.1093/ibd/izx100

Knowles SR, Keefer L, Wilding H, Hewitt C, Graff LA, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses-Part II. *Inflamm Bowel Dis.* 2018;24(5):966-976. doi:10.1093/ibd/izy015

Mitropoulou MA, Fradelos EC, Lee KY, et al. Quality of Life in Patients With Inflammatory Bowel Disease: Importance of Psychological Symptoms. *Cureus.* 2022;14(8):e28502. Published 2022 Aug 28. doi:10.7759/cureus.2850

Qazi T, Farraye FA. Sleep and Inflammatory Bowel Disease: An Important Bi-Directional Relationship. *Inflamm Bowel Dis.* 2019 Apr 11;25(5):843-852. doi: 10.1093/ibd/izy334. PMID: 30388243.

Disclosure: FP received speaker fees from Abbvie, Falk, Ferring, Janssen, Pfizer, Pharmakern, Takeda and Tillotts.

independent risk factors for depression (OR=15.169, $p<0.001$; OR=5.577, $p=0.042$ respectively). The only independent risk factor for anxiety was clinical disease activity (OR=3.437, $p=0.049$). A significant correlation was noted between the IBD-Disk global score, the anxiety score and the depression score (respectively $r=0.511$ and $r=0.524$, $p<0.001$).

Conclusion: IBD patients tend to have a higher prevalence of depression and anxiety disorders than the general population. The IBD disk is an easy tool that correlates well with HADS scores. Its utilisation in clinic allows holistic assessment, particularly in patients with active disease.

Disclosure: Nothing to disclose.

PP0431

WITHDRAWN

PP0430

CAN THE IBD DISK ADEQUATELY ASSESS PSYCHOLOGICAL BURDEN IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE?

R. Limam¹, N. Elleuch¹, H. Kallel¹, W. Dahmani¹, A. Hammami¹, A. Ben Slama¹, A. Braham Ep Krifa¹, H. Jaziri¹, M. Ksiaa¹
¹Sahloul Gastroenterology Departement, Sousse, Tunisia

Contact E-Mail Address: limamrihab33@gmail.com

Introduction: Inflammatory bowel disease (IBD) is often diagnosed in early adulthood and can lead to a substantial decline in quality of life. It has been suggested that patients with IBD are at increased risk of depression and anxiety disorders.

The IBD Disk is a validated 10-question, self-administered visual questionnaire that includes characterisation of psychosocial disease burden. Whether scores in these domains correlate with traditional measures, such as the Hospital Anxiety and Depression Scale (HADS), is not known.

Aims & Methods: The aim of this study was to assess the prevalence of anxiety and depression in IBD patients, and the correlation between IBD-Disk and traditional measures.

We conducted a cross-sectional study over 3 months between April and June 2023. IBD patients responded to the IBD-Disk and HADS questionnaires.

HADS Scores are out of 21; with 0–7 normal, 8–10 mild, 11–15 moderate and 16–21 severe.

Results: We enrolled 57 patients (50.9% men) with a median age of 38 years [31–48].

Thirty-eight patients (66.7%) had Crohn's disease (CD). It was ileal in 14 patients (36.8%), ileocolic in 15 (39.5%), and colonic in 9 (23.7%). Ano-perineal involvement was present in 36.8% of cases. Nineteen patients (33.3%) had ulcerative colitis. Pancolic involvement was noted in 13 patients (68.4%).

Thirteen patients were depressed (22.8%) and 16 patients were anxious (28.1%).

In univariate analysis, depression was significantly associated with clinical disease activity ($p=0.002$), hospitalization at the time of interview ($p<0.001$), anemia ($p=0.01$), elevated CRP ($p=0.015$), hypoalbuminemia ($p=0.016$) and corticoresistance profile ($p=0.01$).

Anxiety was significantly associated with clinical activity ($p=0.043$), hypoalbuminemia ($p=0.023$) and high CRP ($p=0.043$). In multivariate analysis, only hospitalization at the time of interview and corticoresistance were

PP0432

CLINICOPATHOLOGIC FEATURES AND PROGNOSIS OF COLITIS-ASSOCIATED COLORECTAL CANCER IN ULCERATIVE COLITIS PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS: A NATIONWIDE COHORT STUDY IN JAPAN

K. Komatsu¹, T. Shinagawa¹, M. Uchino², H. Ikeuchi², K. Okabayashi³, S. Oka⁴, K. Futami⁵, M. Itabashi⁶, K. Watanabe⁷, M. Shibutani⁸, Y. Okita⁹, T. Wakai¹⁰, Y. Mizuuchi¹¹, K. Okamoto¹², K. Yamada¹³, Y. Sato¹⁴, T. Ogino¹⁵, H. Kimura¹⁶, K. Takahashi¹⁷, K. Hida¹⁸, Y. Kinugasa¹⁹, F. Ishida²⁰, J. Okuda²¹, K. Daito²², T. Yamamoto²³, S. Yamamoto²⁴, F. Koyama²⁵, T. Hanai²⁶, K. Komori²⁷, D. Shida²⁸, J. Arakaki²⁹, Y. Akagi³⁰, S. Yamaguchi³¹, H. Ueno³², K. Matsuda³³, A. Maemoto³⁴, R. Nezu³⁵, S. Sasaki³⁶, E. Sunami³⁷, T. Noguchi¹, K. Sugihara³⁸, Y. Ajioka³⁹, S. Ishihara¹, the Study Group for Inflammatory Bowel Disease Associated Intestinal Cancers by Japanese Society for Cancer of the Colon and Rectum

¹The University of Tokyo, Department of Surgical Oncology, Tokyo, Japan, ²Hyogo Medical University, Department of Inflammatory Bowel Disease Surgery, Nishinomiya, Japan, ³Keio University School of Medicine, Department of Surgery, Tokyo, Japan, ⁴Graduate School of Biomedical and Health Sciences, Hiroshima University, Department of Gastroenterology, Hiroshima, Japan, ⁵Fukuoka University Chikushi Hospital, Department of Surgery, Chikushino, Japan, ⁶Tokyo Women's Medical University, Department of Surgery, Division of Inflammatory Bowel Disease Surgery, Tokyo, Japan, ⁷Tohoku University Graduate School of Medicine, Department of Surgery, Sendai, Japan, ⁸Osaka Metropolitan University Graduate School of Medicine, Department of Gastroenterological Surgery, Osaka, Japan, ⁹Institute of Life Sciences, Mie University Graduate School of Medicine, Department of Gastrointestinal and Pediatric Surgery, Tsu, Japan, ¹⁰Graduate School of Medical and Dental Sciences, Niigata University, Division of Digestive and General Surgery, Niigata, Japan, ¹¹Graduate School of Medical Sciences, Kyushu University, Department of Surgery and Oncology, Fukuoka, Japan, ¹²Tokyo Yamate Medical Center, Department of Coloproctology, Tokyo, Japan, ¹³Coloproctology Center Takano Hospital, Department of Surgery, Kumamoto, Japan, ¹⁴Toho University Sakura Medical Center, Department of Surgery, Chiba, Japan, ¹⁵Graduate School of Medical, Osaka University, Department of Gastroenterological Surgery, Osaka, Japan, ¹⁶Yokohama City University Medical Center, Inflammatory Bowel Disease Center, Yokohama, Japan, ¹⁷Tohoku Rosai Hospital, Department of Colorectal Surgery, Sendai, Japan, ¹⁸Kyoto University Hospital, Department of Surgery, Kyoto, Japan, ¹⁹Tokyo Medical and Dental University, Department of Gastrointestinal Surgery, Tokyo, Japan, ²⁰Showa University Northern Yokohama Hospital, Digestive Disease Center, Kanagawa, Japan, ²¹Osaka Medical and Pharmaceutical University, Department of General and Gastroenterological Surgery, Takatsuki, Japan, ²²Faculty of Medicine, Kindai University, Department of Surgery, Osaka, Japan, ²³Yokkaichi Hazu Medical Center, Inflammatory Bowel Disease Center, Yokkaichi, Japan, ²⁴Tokai University School of Medicine, Department of Gastroenterological Surgery, Tokyo, Japan, ²⁵Nara Medical University, Department of Surgery, Nara, Japan, ²⁶Fujita Health University, School of Medicine, Department of Surgery, Aichi, Japan, ²⁷Aichi Cancer Center Hospital, Department of Gastroenterological Surgery, Aichi, Japan, ²⁸IMSUT Hospital, The Institute of Medical Science, The University of Tokyo, Department of Surgery, Tokyo, Japan, ²⁹Urasoe General Hospital, Center for

Gastroenterology, Department of Surgery, Okinawa, Japan, ³⁰Kurume University Hospital, Department of Surgery, Kurume, Japan, ³¹Saitama Medical University International Medical Center, Department of Gastroenterological Surgery, Saitama, Japan, ³²National Defense Medical College, Department of Surgery, Tokorozawa, Japan, ³³The Fraternity Memorial Hospital, Department of Surgery, Tokyo, Japan, ³⁴Sapporo Higashi Tokushukai Hospital, Inflammatory Bowel Disease Center, Sapporo, Japan, ³⁵Nishinomiya Municipal Central Hospital, Department of Surgery, Nishinomiya, Japan, ³⁶Japanese Red Cross Medical Center, Department of Coloproctological Surgery, Tokyo, Japan, ³⁷Kyorin University, Department of Surgery, Tokyo, Japan, ³⁸Tokyo Medical and Dental University, Tokyo, Japan, ³⁹Niigata University, Department of Pathology, Niigata, Japan

Contact E-Mail Address: kk783work@gmail.com

Introduction: The prevalence of primary sclerosing cholangitis (PSC) among ulcerative colitis (UC) is known to be lower in Eastern Asia, including Japan, than in Western countries. There have been few studies describing the details of ulcerative colitis-associated colorectal cancer (CAC) in UC with PSC (PSC-UC) in Japan so far, owing to its rarity.

Aims & Methods: This retrospective study aimed to evaluate the clinicopathologic features and prognosis of CAC in PSC-UC in the largest nationwide cohort of its kind in Japan. A total of 797 eligible patients diagnosed with CAC from 1983 to 2020 were categorized into those with PSC (PSC-UC group, n = 26) and those without PSC (UC-alone group, n = 771). Clinicopathologic features, 10-year overall survival (OS) and 10-year cancer-specific survival (CSS) were compared between the two groups.

Results: In PSC-UC group, duration of UC was shorter (12.8 vs 17.0 year, p=0.042), and age at CAC diagnosis was younger (47.8 vs 53.4 years old, p=0.042) compared to UC-alone patients. Right-sided colon cancer was significantly more common in PSC-UC group than in UC-alone group (34.6% vs 15.5%, p=0.032). Left-sided colon cancer (38.5%) and rectal cancer (26.9%) accounted for a similar proportion with right-sided colon cancer in PSC-UC group. There were no differences between the two groups in terms of sex, age at UC diagnosis, disease extent of UC, medical therapies for UC, diagnostic opportunity for CAC, histological types, and pathological stages of CAC. PSC-UC group showed a comparable 10-year OS (70.6% vs 83.1%, p=0.072) and 10-year CSS (84.1% vs 87.6%, p=0.50) as UC-alone group.

Conclusion: Our study highlighted the differences and the similarities of CAC between UC with PSC and without PSC patients. In patients with PSC-UC, it may be beneficial to start surveillance colonoscopy earlier because of the shorter duration of UC before the CAC diagnosis.

Disclosure: Nothing to disclose.

PP0433

PREVALENCE AND TREND OF ANEMIA IN A LARGE COHORT OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE

G. D'Arcangelo¹, M. Brecciaroli¹, G. Gagliostro¹, D. Auletta¹, S. Pellegrino², S. Arrigo³, F. Graziano⁴, E. Miele⁵, M.T. Illiceto⁶, P. Alvisi⁷, D. Dilillo⁸, C. De Giacomo⁹, P. Lionetti¹⁰, M. Pastore¹¹, M. Cananzi¹², M. Bramuzzo¹³, R. Pancieri¹⁴, L. Norsa¹⁵, M. Aloï¹
¹Sapienza University of Rome, Pediatric Gastroenterology Unit, Rome, Italy, ²University of Messina, Pediatric Gastroenterology and Cystic Fibrosis Unit, Department of Human Pathology in Adulthood and Childhood G. Barresi, Messina, Italy, ³IRCCS Istituto Giannina Gaslini, Gastroenterology Unit, Genova, Italy, ⁴Villa Sofia Cervello Hospital, Pediatric Unit, Palermo, Italy, ⁵University of Naples "Federico II", Napoli, Italy, ⁶Santo Spirito Hospital, Azienda Sanitaria Locale, Pescara, Italy, ⁷Maggiore Hospital, Pediatrics, Bologna, Italy, ⁸Vittore Buzzi Children's Hospital, University of Milan, Milan, Italy, ⁹ASST GOM Niguarda Milano, Milan, Italy, ¹⁰Università Firenze, Osp. Meyer, Firenze, Italy, ¹¹Scientific Institute "Casa Sollievo della Sofferenza", Foggia, Italy, ¹²University Hospital of Padova, Padova, Italy, ¹³IRCCS "Burlo Garofolo", Trieste, Italy, ¹⁴Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, ¹⁵ASST Papa Giovanni XXIII, Bergamo, Pediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy

Contact E-Mail Address: giuliadarcangelo87@gmail.com

Introduction: Anemia is a common extraintestinal manifestation of inflammatory bowel disease (IBD) with an important impact on patients' quality of life. The prevalence is uncertain (6% to 74% depending on the definition and on the subgroup of patients examined). In Italy a prevalence of anemia at the diagnosis of 13.6% among the adult IBD outpatients is reported.

Aims & Methods: We aimed to determine the prevalence of anemia and its characteristics at the diagnosis in children with IBD and to investigate its trend during follow-up.

This was an observational, multicenter cohort study including data of IBD children with anemia at the diagnosis prospectively enrolled in the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP) IBD registry. Data were collected at the diagnosis and anemia trend was evaluated at 1-year follow-up. Anemia was diagnosed based on the WHO criteria and classified as mild, moderate, and severe accordingly. Based on serum ferritin and CRP level and/or transferrin saturation (TNSat), anemia was defined as iron deficiency anemia (IDA), anemia of chronic disease (ACD) or inflammatory IDA (InflIDA).

Results: Five hundred eighty-nine [295 CD (50%) and 294 UC/IBDU (50%)] out of 1634 children with IBD presented with anemia, resulting in a prevalence of 36%. Anemia rate was higher in CD than in UC (39% vs 33%, $p = 0.009$) and most patients had moderate anemia (55%). Iron deficiency anemia and InflIDA were diagnosed equally in 42% of children, while only 15.4% presented with ACD. Children with CD showed higher rates of mild anemia (38% vs 33%, $p < 0.0001$) and a higher frequency of ACD compared to UC patients (26.5% vs. 4.5%, $p < 0.0001$). A severe form of anemia was more common in UC (13% vs 6%, $p = 0.001$) as well as the IDA (53% vs 31%, $p < 0.0001$). Younger age and lower albumin levels significantly correlated with the severity of the anemia in CD. In UC, females were more likely to experience severe anemia (69% vs 47%, $p = 0.02$) and an extensive disease was prevalent in children with moderate and severe anemia than in those with mild anemia ($p = 0.01$ and $p = 0.03$, respectively).

At 1 year, 99 children (17%) were still anemic. At the multivariable logistic regression analysis, baseline wPCDAI and SES-CD significantly correlated with the risk of the persistence of anemia at 1 year in CD. No variables correlated with the persistence of anemia in UC.

Conclusion: More than one-third of pediatric patients presents with anemia at the diagnosis of IBD, most commonly moderate. A severe anemia is most common in UC compared to CD. IDA (alone or in its form of ACD) is the most common cause of anemia in children with IBD. One out of five is still anemic after 1 year from the diagnosis.

Disclosure: Nothing to disclose.

PP0434

EVALUATION OF THE RELATIONSHIP BETWEEN PAIN, PSYCHOLOGICAL PROFILE AND DYSAUTONOMIA IN NEWLY DIAGNOSED IBD PATIENTS USING THE EXPERIENCE SAMPLING METHOD

I. Aurangzeb¹, I. Khwaja¹, E. Ul Haq^{1,1}, R. Idrees¹, D. Bulmer², H. Sokol³, N. Vergnolle⁴, N. Guadenzio⁴, A. Hart⁵, P. James Lindsay¹, C. Norton⁶, M. Parkes⁷, D. Keszthelyi⁸, R. Margalit Yehuda¹, Q. Aziz¹
¹Wingate Institute, Queen Mary University, London, United Kingdom, ²Cambridge University, School of Biological Sciences, Cambridge, United Kingdom, ³Saint-Antoine Hospital, Gastroenterology Department, Paris, France, ⁴INSERM UMR-1220, Digestive Health Research Institute (IRSD), Toulouse, France, ⁵St Mark's The National Bowel Hospital, London, United Kingdom, ⁶King's College London, Clinical Nursing Research, London, United Kingdom, ⁷Inflammatory Bowel Disease Research Group, Addenbrooke's Hospital, Cambridge, UK, Cambridge, United Kingdom, ⁸Maastricht University Medical Center, Gastroenterology-Hepatology, Maastricht, Netherlands

Contact E-Mail Address: ismaeel.aurangzeb1@nhs.net

Introduction: Chronic abdominal pain (CAP) occurs in up to 50% of patients with Inflammatory Bowel Disease (IBD), even in remission¹. Previous studies demonstrate that CAP is associated with fatigue, depression and reduced quality of life in IBD patients².

These studies, however, are mostly retrospective questionnaire based which are subject to recall bias.

The Experience Sampling Method (ESM) is a digital patient reported outcome measure (PROM) allowing real-time assessment of current symptoms and reduces recall bias compared to end of day or end of week surveys^{3,4}. ESM has not been used in IBD patients to evaluate the relationship between pain, psychological profile and autonomic symptoms.

Aims & Methods: 69 patients with newly diagnosed IBD within the last 12 months were included in the analysis. Patients completed an ESM-based PROM (with a maximum of 10 buzz questionnaires per day) for 7 consecutive days. Within each of the ESM questionnaires, patients reported on current abdominal pain, anxiety, mood, and autonomic symptoms on a scale from 0 (not at all) to 10 (very much). The mean score across the 7 days was calculated for each of the symptoms. Only patients who had completed >25% of the ESM questionnaires (18/70) were included in the analysis.

Results: 63 patients completed >25% of the ESM questionnaires (age range 18-62, 34 male, 29 female) and were included in the analysis. 39 patients (62%) had no abdominal pain (mean pain score 0-1), 15 patients (24%) had mild pain (mean pain score 1-4), whilst 9 patients (14%) had moderate/severe pain (mean pain score 4-10).

The mean scores for low mood (2.35, 95% CI 1.69-3.00) and anxiety (1.57, 95% CI 0.78-2.37) were higher in the mild pain group compared to the mean scores for low mood (1.25, 95% CI 0.75-1.76) and anxiety (1.01, 95% CI 0.59-1.43) in the no pain group ($p < 0.01$). Likewise, the mean scores for low mood (4.59, 95% CI 2.93-6.25) and anxiety (3.59, 95% CI 1.64-5.53) were higher in the moderate/severe pain group compared to the mild pain group ($p < 0.05$).

There was a higher mean score for palpitations and dizziness in both the mild pain and moderate/severe pain groups compared to the no pain group ($p < 0.01$). The mean score for dyspnea was higher in the moderate/severe pain group compared to no pain group ($p < 0.05$), however it was similar between the mild pain and no pain groups ($p = 0.39$).

Finally, the mean score for sweating was similar between the three groups ($p = 0.34$).

A strong positive correlation ($r = 0.84$) between pain intensity and low mood intensity was found ($p < 0.01$).

Similarly, there was also a strong positive correlation ($r = 0.82$) between pain intensity and anxiety intensity ($p < 0.01$).

Conclusion: Newly diagnosed IBD patients experiencing moderate to severe abdominal pain are more likely to have lower mood, higher levels of anxiety as well as more symptoms of dysautonomia.

Further evaluation of the ESM data will provide a greater insight into the course of symptoms as well as potential triggers for the abdominal pain.

Acknowledgements: Ismaeel Aurangzeb, Iman Khwaja & Ebad Ul Haq are joint first authors.

Reuma Margalit Yehuda & Qasim Aziz are joint senior authors.

References:

- 1: A Rezazadeh Ardabili, et al. *DOP07 Chronic Abdominal Pain in IBD Patients in Remission: Real-World Data on Contributing Factors*. Journal of Crohn's and Colitis, 2022. 16(1): p. 56-58.
- 2: Schirbel, A., et al., *Impact of pain on health-related quality of life in patients with inflammatory bowel disease*. World journal of gastroenterology, 2010. 16(25): p. 3168-3177.
- 3: Vork, Lisa, et al. *The Experience Sampling Method—Evaluation of Treatment Effect of Escitalopram in IBS with Comorbid Panic Disorder*. Neurogastroenterology & Motility, 2019. 31 (1): p. e13515.
- 4: Klaassen, Tim, et al. *Psychometric Evaluation of an Experience Sampling Method-Based Patient-Reported Outcome Measure in Functional Dyspepsia*. Neurogastroenterology and Motility, 2021. 33(9): p. e14136.

Disclosure: Nothing to disclose.

PP0435

FACTORS ASSOCIATED WITH CHRONIC PAIN IN INFLAMMATORY BOWEL DISEASE: A LARGE CROSS-SECTIONAL QUESTIONNAIRE-BASED STUDY

R. Idrees¹, P. Luthra¹, M. Dean¹, R. Margalit Yehuda¹, E. Haq¹, I. Aurangzeb¹, I. Khwaja¹, Q. Aziz², J.O. Lindsay¹, M. Parkes³, H. Sokol⁴, A.L Hart⁵, N. Vergnolle⁶, D.C. Bulmer⁷, N. Gaudenzio⁸, C. Norton⁹

¹The Wingate Institute of Neurogastroenterology, Queen Mary University of London, London, United Kingdom,

²Wingate Institute for Neurogastroenterology - Centre for Neuroscience and Trauma, Centre for Neuroscience, Surgery and Trauma, London, United Kingdom, ³Inflammatory Bowel Disease Research Group, Addenbrooke's Hospital, Cambridge, UK, Cambridge, United Kingdom, ⁴Saint-Antoine Hospital, Gastroenterology Department, Paris, France, ⁵St Mark's Hospital and Academic Institute, Gastroenterology, Harrow, United Kingdom, ⁶INSERM UMR-1220, Digestive Health Research Institute (IRSD), Toulouse, France, ⁷Cambridge University Hospital, Cambridge, United Kingdom, ⁸Toulouse Institute for Infectious and Inflammatory Diseases (Infinity), Toulouse, France, ⁹King's College London, Clinical Nursing Research, London, United Kingdom

Contact E-Mail Address: pavit12@gmail.com

Introduction: Up to half of inflammatory bowel disease (IBD) patients experience chronic pain despite disease remission. The factors affecting the development of chronic pain are poorly understood and pain-directed therapies are scarce.

Our study aimed to compare the clinical features and psychological characteristics of patients with and without chronic abdominal pain (CAP). The current analysis focuses on patients with IBD in remission and used REDCap to capture electronic data [1].

Aims & Methods: This is a cross-sectional online questionnaire-based study of 2381 IBD patients aged 16 years and above. The Rome IV questionnaire was used to diagnose irritable bowel syndrome (IBS). Remission was defined as Harvey Bradford Index (HBI) < 5 for patients with Crohn's disease (CD) or Simple Colitis Activity Index (SCAI) < 3 for patients with ulcerative colitis (UC) [2]. Participants in remission with at least weekly abdominal pain for at least three months were defined as the cohort with chronic abdominal pain, and the rest were categorised as the pain-free cohort.

The independent samples t-test was used to compare mean Body Mass Index (BMI) and age at diagnosis, and the independent samples Mann Whitney U test to compare the non-parametric scale data of the two cohorts. Spearman's correlation was used to compare the pain intensity and pain interference scores from the Brief Pain Inventory with scale data from the following scales: Big Five Personality Questionnaire (BFPQ), Highly Sensitive Person Scale (HSPS), General Anxiety Disorder-7 (GAD7), Patient Health Questionnaire 9 (PHQ9), and Cognitive and Behavioural Response Questionnaire (CBRQ). Cronbach's alpha was used to assess the reliability of these scales.

Results: 1191 participants in remission were studied. Their ages ranged from 17 to 92, with a mean age of 51, and 52.6% were male. Eighty-eight percent were of White British ethnic origin and 40% were current or previous smokers.

25.9% (308) of those in remission reported CAP, with a mean age of 47 years, and 41.6% of them were males. The mean age at diagnosis of IBD was 35 years in those with CAP in remission, versus 30 in those without CAP ($t = -4.548$, $p < 0.001$, 95% CI -6.598 to -2.621). In the CAP group, the prevalence of IBS was 73.1% compared to the total prevalence of 18.9% in

the remission cohort. The prevalence of CD and UC were 72.4% and 27.6% respectively in the CAP in remission cohort, compared to 61.3% and 38.7% in all remission participants. 34.4% of people with CAP in remission had previous surgery.

There was a significant difference between the CAP and non-CAP cohort median scores with p values < 0.001 for neuroticism from the BFPQ, Ease of Excitation (EoE) from the HSPS, GAD7, PHQ9. The CBRQ components of fear avoidance, embarrassment avoidance, symptom focusing, all-or-nothing behaviour score, and avoidance/resting behaviour score also showed differences between the CAP and non-CAP groups ($p < 0.001$, 95% confidence interval).

Pain intensity and pain interference scores showed positive correlations significant at the 0.01 level with neuroticism, EoE, GAD7, PHQ9, and all components of the CBRQ except catastrophisation score within the CAP in remission group.

Conclusion: Our results demonstrate that an older age at diagnosis, IBS prevalence, Crohn's disease, neurotic personality type, and certain behavioural and psychological profiles are significant features of IBD patients with chronic abdominal pain in remission. Further studies will help to develop management strategies and to establish causality.

References:

- Farrokhyar, F., et al., *Functional gastrointestinal disorders and mood disorders in patients with inactive inflammatory bowel disease: Prevalence and impact on health*. Inflammatory Bowel Diseases, 2006. **12**(1): p. 38-46.
- Srinath, A.I., et al., *Predictors of abdominal pain in depressed pediatric inflammatory bowel disease patients*. Inflamm Bowel Dis, 2014. **20**(8): p. 1329-40.
- Harris, P.A., et al., *Research electronic data capture (REDCap)—a meta-data-driven methodology and workflow process for providing translational research informatics support*. J Biomed Inform, 2009. **42**(2): p. 377-81.
- Teruel, C., E. Garrido, and F. Mesonero, *Diagnosis and management of functional symptoms in inflammatory bowel disease in remission*. World J Gastrointest Pharmacol Ther, 2016. **7**(1): p. 78-90.

*Dr Ruqaya Idrees and Dr Pavit Luthra are joint first authors on this abstract.

Disclosure: Nothing to disclose.

PP0436

EXPLORING THE RELATIONSHIP BETWEEN HORMONAL CONTRACEPTIVE USE AND ULCERATIVE COLITIS FLARES: A LONGITUDINAL ANALYSIS

B. Gros^{1,2}, C. Frutos¹, J.M. Benítez¹, P. Soto¹, S. Marin¹, E. Iglesias-Flores¹

¹Reina Sofía University Hospital, Gastroenterology and Hepatology, Cordoba, Spain, ²Maimónides Institute of Biomedical Medicine, IMIBIC, Cordoba, Spain

Contact E-Mail Address: begrosal@gmail.com

Introduction: Numerous studies have implicated hormonal contraceptive therapy (HCT) as a potential trigger for IBD onset. However, data regarding disease flares in hormonal contraceptive users are limited in ulcerative colitis (UC). This study aims to explore this association.

Aims & Methods: Female patients who were diagnosed with UC after 1st January 2014, and born between 1966-2008 were included. The Andersen-Gill extension of the Cox proportional hazards model was used to account for recurrent events within the same subjects. Two models were employed: the first included each patient corresponding to only one cohort, while in the second one those who initiated HCT after diagnosis, were included twice, one from diagnosis to HCT as non-exposed and as exposed thereafter.

Results: Among 2359 patients in our local database, 545 were women with UC, of whom 132 met the inclusion criteria for analysis. The majority had UC proctitis 57 (43.2%) with 24 (18.2%) were smokers. The median age was 32.5 (23.3-42) years.

Of the cohort, 52 (39.1%) women exposed HCT, with a median exposure duration of 1.5 (0.5-5.0) years. Of these, 33 (25%) were exposed to HCT during follow-up.

Over 518 person-years of follow up, 178 flares and 198 courses of steroids were observed with 56 admissions and one colectomy, differences were observed among the incidence rates between groups Table 1.

Additionally, there were 24 pregnancies documented.

No differences in time to first flare (log-rank test $p=0.83$). However, the Cox proportional hazard model showed that HCT was associated with higher cumulative risk of flares in both models (HR 1.53, 95%CI 1.05-2.22, $p=0.029$) and (HR 1.47, 95%CI 1.019-2.11, $p=0.039$), Figure 1A and 1B. No adverse events associated to HCT occurred during follow-up.

N=132	All N=132	No OCP n=99	HCT n=33	Incidence rate ratio (95%CI)	p
Age at diagnosis, median (IQR)	32.5 (23.3-42)	36 (27-45)	25 (20.5-32)		0.0001
UC extent, n (%)					
E1	57 (43.2)	40 (40.4)	17 (51.5)		0.38
E2	40 (30.3)	33 (33.3)	7 (21.2)		
E3	35 (26.5)	26.3 (26.3)	9 (27.3)		
Time to 1 st flare	493 (182-1187)	481 (177-1210)	522 (184-1226)		0.83
Person-year follow-up	517	458	56		N/A
Flare rate (n°event/person- year follow-up)	167/518=0.34	132/458=0.29	35/56=0.63	0.46 (0.32-0.69)	<0.0001
Hospitalization rate	56/518=0.11	39/458=0.09	17/56=0.3	0.28 (0.16-0.53)	<0.0001
Surgery rate	1/518=0.002	1/458=0.002	0	0.002 (-0.01-0.01)	0.73
Steroid courses rate	198/518=0.38	158/458=0.35	40/56=0.72	0.48 (0.34-0.70)	<0.001

Conclusion: Our study suggests that HCT is associated with an increased cumulative risk of flares, steroid prescription and hospitalization rates in ulcerative colitis patients. Furthermore, no safety signals were observed with the use of HTC in this cohort.

Disclosure: Beatriz Gros has served as consultant to Galapagos and Abbvie and as speaker for Abbvie, Jansen, Takeda, Pfizer and Galapagos.

PP0437

WITHDRAWN

PP0438

PRIORITIZING PATIENT PERSPECTIVES: IDENTIFYING KEY SYMPTOMS IN CROHN'S DISEASE AND ULCERATIVE COLITIS TO ENHANCE CLINICAL TRIAL DESIGN

C. Carmichael¹, L. Lucats², E. Brown Hajdukova², K. Jones², S. McKee¹, T. Hemrika²
¹Clarivate, Boston, United States of America, ²Sanofi, R&D, Paris, France

Contact E-Mail Address: Tessa.Hemrika@sanofi.com

Introduction: Due to the diverse symptoms experienced by patients living with Crohn's Disease (CD) and Ulcerative Colitis (UC), it can be challenging to understand how best to assess the benefit of new therapeutics for these conditions. Identifying priority symptoms that significantly impact patient's well-being and functioning is essential to inform the development of new therapies that truly improve their quality of life. Qualitative interviews with patients are a fundamental step in collecting this critical data, ensuring patient-focused drug development.

This study aimed to identify the most pertinent concepts (signs, symptoms, and impacts) from the patient perspective to provide an in-depth understanding of what aspects of their condition they prioritize.

Aims & Methods: A total of 24 qualitative interviews were conducted with US adult patients with UC or CD. Concept elicitation was conducted remotely using an IRB-approved, semi-structured guide. Participants rated the bothersomeness on a 10-point scale from 0 (no bother) to 10 (greatly bothersome); the average rating of bothersomeness for each symptom was calculated and combined with the total number of incidence reports to assess the saliency of each identified concept.

Data were analyzed in Atlas.ti and then visualized in a graphical format using Microsoft Excel. Saliency was assessed for the present time ('at the interview') and at worst.

Results: Twelve UC adults (mean age: 39.5 years, 7 female, 7 white, 4 with only high school education) participated. The average time since UC diagnosis was 5.3 years, with 10 receiving one UC treatment at the time of the interview. Patients with UC most frequently reported rectal bleeding (N=12), fatigue (n=9/12), abdominal pain (n=9/12), bowel urgency (n=9/12), and diarrhea (n=8/12).

The symptoms identified as most bothersome in a ranking task were abdominal pain (n=7/12), bowel urgency (n=5/12), rectal bleeding (n=4/12), and diarrhea (n=4/12). In symptom saliency tasks 'at its worst', rectal bleeding (bothersomeness, 8.7/10) and bowel urgency (bothersomeness, 9.3/10) were identified as most salient. Most frequently reported UC impacts were diet change (N=12), worrying (n=10/12) and increased need for rest (n=10/12).

Twelve CD adults (mean age: 40.3 years, 8 female, 10 white, 4 with only high school education) participated. The average time since CD diagnosis was 10.3 years, with 11 receiving one CD treatment at the time of the interview. Patients with CD most frequently reported fatigue (n=11/12), bowel urgency (n=9/12), abdominal pain (n=8/12), and diarrhea (n=7/12).

The symptoms identified as one of the most bothersome to patients in a ranking task were fatigue (n=8/12), frequent bowel movements (n=6/12), diarrhea (n=4/12), bowel urgency (n=4/12) and abdominal pain (n=8/12). In symptom saliency tasks 'at its worst', fatigue (bothersomeness, 8.3/10) was identified as most salient. Most frequently reported CD impacts were inability to leave home (n=10/12), low mood (n=10/12) and planning around bathroom use (n=10/12).

Conclusion: The UC and CD patients reported priorities and concerns that may not be adequately assessed by the Mayo score (fatigue, abdominal pain and bowel urgency are not assessed) and CD Activity Index (CAI) (fatigue, bowel urgency and diarrhea are not assessed) currently used in UC and CD clinical trials, respectively.

This underlines a need to increase patient experience data collection and to investigate whether inflammatory bowel disease (IBD) drugs in development (as well as those already approved) adequately address patients' priorities.

Disclosure: Nothing to disclose.

PP0439

CLOSTRIDIODES DIFFICILE INFECTION IN ADMITTED PATIENTS WITH ULCERATIVE COLITIS: ANALYSIS OF 23 YEARS THROUGH PROPENSITY SCORE MATCHING

B. Gros¹, P. Alañon¹, B. Carrillo¹, S. Marin¹, P. Soto¹, E. Iglesias-Flores¹, J.M. Benitez Cantero²
¹Reina Sofia University Hospital, Gastroenterologist, Cordoba, Spain, ²Hospital Universitario Reina Sofia, Gastroenterology, Cordoba, Spain

Contact E-Mail Address: begrosal@gmail.com

Introduction: Clostridioides difficile infection (CDI) represents the leading cause of nosocomial diarrhea in the Western world. Patients with ulcerative colitis (UC) have a higher risk of developing this infection, which has been associated with an increased risk of flare-ups, need for surgery, and mortality. The aim of the present study was to evaluate the impact of this infection in patients hospitalized for a UC flare-up.

Aims & Methods: Retrospective case-control study including all patients hospitalized for a UC flare-up at Reina Sofia Hospital in Córdoba between January 2000 and January 2023. To avoid potential selection biases, Propensity Matching Score (PMS) adjusted for age, gender, duration, and extent of the disease, with a 1:2 ratio was used. Primary objective was to assess the need for treatment intensification (initiation or dose escalation of biologics/small molecules or immunosuppressant). Secondary endpoints included readmission rate, colectomy, mortality, and CDI risk factors identification.

	All patients				PMS		
	Overall N=419	CDI n=46	NO CDI n=373	p	CDI n=46	NO CDI n=92	p
Length of admission, days, median (IQR)	11 (7-16)	11 (8-15)	11 (7-17)	0.79	11 (8-15)	8 (5-15)	0.107
Albumin <3.5gr/L, n (%)	145 (34.6)	17 (37)	128 (34.3)	0.83	17 (37)	31 (33.7)	0.848
Need for blood transfusion, n (%)	45 (10.7)	9 (19.6)	36 (9.7)	0.042	9 (19.6)	10 (10.9)	0.203
Therapy intensification, n (%)							
- During admission	225 (53.7)	19 (41.3)	206(55.7)	0.065	19 (41.3)	46 (50)	0.366
- Within 3 months	59 (14.1)	8 (17.4)	48 (14.6)	0.49	9 (20.9)	14 (15.2)	0.655
- Within 3-12 months	59 (14.1)	11 (23.9)	48 (12.4)	0.035	11 (27.5)	7 (7.6)	0.004
Readmission within 12 months, n (%)	80 (19.1)	17 (37)	63 (16.9)	0.001	17 (37)	16 (17.4)	0.009
Complications during admission, n (%)	66 (15.3)	5 (10.9)	61 (16.4)	0.34	5(10.9)	17 (17.7)	0.39
- Toxic megacolon	26 (6)	3 (6.3)	23 (6.2)		3 (6.3)	7 (7.3)	
- Bowel perforation	5 (1.2)	0	5 (1.3)		0	1 (1)	
- Severe bleeding	7 (1.6)	1 (2.1)	6 (1.6)		1 (2.1)	2 (2.1)	
- Other	26 (6)	1 (2.1)	25 (6.5)		1 (2.1)	7 (7.3)	
Colectomy, n (%)	49 (11.7)	3 (6.3)	46 (12.3)	0.25			
- During admission	14 (3.2)	3 (6.3)	10 (2.7)	0.19	3 (6.3)	11 (12)	0.385
- Within 1 st year	11 (2.5)	3 (6.3)	8 (2.1)	0.09	6 (13)	6 (6.6)	0.214
Death within 12 months, n (%)	8 (1.9)	3 (6.5)	5 (1.3)	0.047	3 (6.5)	1 (1.1)	0.108

Table 1. Hospitalisation characteristics, evolution and complications

Results: During the study period, 419 patients were hospitalized for a UC flare-up, of whom 251 (59.9%) were men, with a median age of 41 (IQR 28-55) years and disease duration of 0.89 (0-5.8) years. Of all admissions, 46 (11%) had CDI. After PMS, CDI was associated with increased therapeutic intensification between 3-12 months after discharge (27.5% vs. 11.7%, p = 0.004) and a higher risk of readmission at 12 months (37.5% vs. 13.7%, p = 0.009) but not to risk of colectomy or mortality (Table 1). Infection recurrence was detected in 8 (16.7%) patients.

Classical risk factors for CDI were not found to increase the risk of CDI

among UC patients, however antiTNF therapy was associated to CDI in both models: full cohort (OR 3.52, 95%CI 1.46-8.49) and PMS (OR 4.63, 95%CI 1.32-16.31).

Chi-square test or Fisher test were used to compare categorical variables. U-Mann Whitney test was used to compare continuous variables.

PROPENSITY SCORE MATCHING ANALYSIS: Cohort matched adjusting for: age, gender, disease duration and disease extension.

Conclusion: CDI in UC was associated with a greater need for therapeutic intensification and a higher readmission rate at one year. There was no evidence of an increased risk of colectomy or mortality in these patients. Classical risk factors for CDI were not identified but patients on antiTNF were at higher risk of CDI.

Disclosure: Beatriz Gros has served as a consultant for Galapagos and Abbvie and as a Speaker for Abbvie, Janssen, Takeda, Pfizer and Galapagos.

PP0440

GENE-ENVIRONMENT INTERACTIONS IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW OF HUMAN EPIDEMIOLOGIC STUDIES

J. Bai¹, D.G. Bouwknegt¹, R.K. Weersma¹, G. Dijkstra¹, K. van der Sloot¹, E.A.M. Festen^{1,2}

¹University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands,

²University Medical Center Groningen, Department of Genetics, Groningen, Netherlands

Contact E-Mail Address: j.bai@umcg.nl

Introduction: While genetic susceptibility and environmental exposures are known contributors to the pathophysiology of Inflammatory Bowel Disease (IBD), their complex gene-environment interactions (GXE) remain elusive. This systematic review aims to summarize the current evidence of GXE in IBD.

Aims & Methods: PubMed, EMBASE, Web of Science and Scopus were systematically searched from inception through July 20, 2022 to identify publications examining the interaction effect of genetic variants and environmental factors in IBD. All eligible studies were graded using the STREGA guideline.

Results: 4,305 publications were identified and screened, resulting in 36 eligible studies. 17 studies reported statistically significant interactions. *NOD2*-smoking interaction was most frequently investigated and showed variant-specific effects at rs2066847 regarding the risk of Crohn's disease. Gene-smoking interactions were further identified in other IBD risk genes (*ATG16L1*, *IL23R*, and *CALM3*), detoxification genes (*GSTP1* and *HMOX1*), smoking-associated genes (*CHRNA3*, *CHRNA5*, *PPP1R3C*, and *BDNF*), and the inflammatory cytokine (*IL1B*) through a candidate gene approach. Immunochip-wide interaction analyses yielded 64 smoking interacting variants. Gene-diet interactions were observed across multiple nutritional measures, including fatty acid intake with *CYP4F3* and *FADS2*, serum selenium with *SEPHS1* and *SEPSECS*, potassium intake with *IL21*, alcohol consumption with *IL12B*, heme iron intake with *FCGR2A* and serum vitamin D with *VDR*.

Conclusion: Although previous studies have provided valuable insights into potential roles of GXE in the etiology of IBD, current evidence is sparse and inconclusive due to limited statistical power and lack of replication. Further studies, including genome wide environment interaction studies (GWEIS) and genotype-based nutrition/lifestyle clinical trials, are needed to unravel the missing heritability influenced by environmental exposures, and to construct personalized recommendations of lifestyle/dietary modification based on an individual genetic background.

Disclosure: Nothing to disclose.

PP0441

PREVALENCE AND RISK FACTORS OF GALLSTONE DISEASE IN KOREAN PATIENTS WITH ULCERATIVE COLITIS: A RETROSPECTIVE STUDY

K. Nam¹, J.Y. Lee², S.H. Park², H.W. Hwang², H.-S. Lee³, K. Oh², H.S. Hong², K. Kim², J.H. Park², S.W. Hong², S.W. Hwang², D.-H. Yang², B.D. Ye², J.-S. Byeon², S.-J. Myung², S.-K. Yang²
¹Dankook University Hospital, Dankook University College of Medicine, Gastroenterology, Cheonan, South Korea, ²Asan Medical Center, Department of Gastroenterology, Seoul, South Korea, ³University of Ulsan College of Medicine, Seoul, South Korea

Contact E-Mail Address: nambag1108@gmail.com

Introduction: The prevalence of gallstone disease in patients with ulcerative colitis (UC) is higher than in the general population. However, risk factors of gallstone disease in these patients remain unclear. Thus, we investigated the prevalence and risk factors of gallstone disease in Korean patients with UC.

Aims & Methods: Patients diagnosed with UC who underwent abdominal imaging between 1997–2020 were investigated using a well-established referral center-based large volume inflammatory bowel disease cohort. The prevalence and clinical characteristics of patients with gallstone disease were evaluated and compared with those without gallstone disease.

Results: Overall, 2811 patients with UC were enrolled. During the follow-up period (mean 5.7 years), 198 (7.0%) patients were diagnosed with gallstone disease and compared with those without gallstone disease (n = 2613). The proportion of extensive colitis at maximum extent, primary sclerosing cholangitis (PSC), history of cytomegalovirus, corticosteroid use, immunomodulatory use, colectomy, and appendectomy were significantly higher in the gallstone group (all $P < 0.05$). In multivariate analyses, age ≥ 60 years at gallstone evaluation (odds ratio [OR] 1.027; 95% confidence interval [CI] 1.002–1.052; $P = 0.033$), PSC (OR 6.304; 95% CI 3.162–12.565; $P < 0.001$), and history of colectomy (OR 2.494; 95% CI 1.222–5.087; $P = 0.012$) were significant risk factors for gallstone disease in patients with UC.

Conclusion: The prevalence of gallstone disease in Korean patients with UC was 7.0%, and age ≥ 60 years at gallstone evaluation, PSC, and history of colectomy were significant risk factors for UC patients with gallstone disease.

References: 1. Zhang FM, Xu CF, Shan GD, Chen HT, Xu GQ. Is gallstone disease associated with inflammatory bowel diseases? A meta-analysis. *J Dig Dis* 2015;16:634-641.

2. Ha JH, Park YS, Seon CS, et al. Increased risk of asymptomatic gallstones in patients with ulcerative colitis. *Intest Res* 2015;13:122-127.

3. Jeong YH, Kim KO, Lee HC, et al. Gallstone prevalence and risk factors in patients with ulcerative colitis in Korean population. *Medicine (Baltimore)* 2017;96:e7653.

Disclosure: Nothing to disclose.

PP0442

TRANSITION OF INFLAMMATORY BOWEL DISEASE PATIENTS FROM PEDIATRIC TO ADULT CARE: A SINGLE-CENTER TEN-YEARS EXPERIENCE

G. Mocci¹, G. Orrù², F.M. Onidi¹, W. Elisei³, M. Corpino⁴, A. Marongiu⁴, G. Argiolas⁵, M. Runfola⁶, G. Locci⁷, E. Tamponi⁷, T. Zolfino¹, P. Usai Satta¹, A. Muscas⁸, M. Congia⁴, S. Savasta⁴
¹ARNAS "G. Brotzu" Cagliari, Division of Gastroenterology, Cagliari, Italy, ²University of Cagliari, Italy, ³Department of Medical Sciences and Public Health, Cagliari, Italy, ⁴A.O. "S. Camillo Forlanini", Division of Gastroenterology, Rome, Italy, ⁵Microcitemic Asl8, Pediatric Clinic and Rare Disease, Cagliari, Italy, ⁶ARNAS "G. Brotzu" Cagliari, Division of Radiology, Cagliari, Italy, ⁷ARNAS "G. Brotzu" Cagliari, Division of Surgery, Cagliari, Italy, ⁸ARNAS "G. Brotzu" Cagliari, Unit Pathologic Anatomy, Cagliari, Italy, ⁹ARNAS "G. Brotzu" Cagliari, Division of Pediatric, Cagliari, Italy

Contact E-Mail Address: giorgiaorru1996@tiscali.it

Introduction: Transition of adolescents with inflammatory bowel disease (IBD) to adult care is a challenge for patients, families, and healthcare providers. Considering that ~ 25% of IBD patients are diagnosed before the age of 16 years, and that these patients are at higher risk for poorer clinical disease outcomes, interest in the transition of care has been increasing considerably in the last decade. To assess the main clinical and epidemiological features of a single centre pediatric population of IBD patients at diagnosis and at the time of transition to the adult center

Aims & Methods: From June 2014 to June 2023 we performed a multi-center, observational, cross-sectional study that included pediatric patients with IBD enrolled in the only pediatric IBD reference center in Sardinia. Data were obtained from the patients' medical records and from a questionnaire administered at the inclusion visit.

Results: Sixty-five IBD patients were enrolled (UC 40, CD 25, M 32, F 33). Median age at diagnosis was 13 years (IQR 2-18). After a median disease duration of 8 years (IQR: 1-25), no UC patients experienced proximal extension of proctitis or left-sided colitis, and no CD patients experienced new localizations of disease. Fifteen patients developed extraintestinal manifestations. No significant difference was found in median diagnostic delay (DD) between UC [4 months (IQR: 1-84)] and CD patients [4,5 months (IQR: 1-48)]. At the transition visit, overall, twenty-nine patients (44,6%) were exposed to one biologic agent (vs 3% at baseline; $p < 0.02$); 0 patients (0%) were exposed to two biologic agents. 4,6% of patients (3/ 65) underwent surgery

Conclusion: Our results provide important insights into the clinical and epidemiological features of paediatric IBD population, and while waiting for a nation Italian registry, present eligible data on the IBD population in Sardinia

Disclosure: Nothing to disclose.

PP0443

IMPACT OF VITAMIN D LEVEL ON OUTCOMES IN ULCERATIVE COLITIS IN THE EMIRATI PATIENT POPULATION AT A TERTIARY CARE CENTER IN ABU DHABI, UNITED ARAB EMIRATES: RESULTS OF A RETROSPECTIVE COHORT STUDY

S.W. Khan¹, J.S. Mattackal¹, N.A. Almarzooqi¹, A. Alakberi², Y.A. Ghoris³, M. Alahmad⁴, T.A. Malik⁵
¹Sheikh Shakhboub Medical City, Gastroenterology, Abu Dhabi, United Arab Emirates, ²Khalifa University, Abu Dhabi, United Arab Emirates, ³Arizona State University, Arizona, United States of America, ⁴Sheikh Shakhboub Medical City, Gastroenterology, Abudhabi, United Arab Emirates, ⁵Mayo Clinic, Arizona, United States of America

Contact E-Mail Address: drshaima.khan@gmail.com

Introduction: Vit D is a known immunomodulator and is essential in maintaining immune balance as well as controlling processes observed in inflammatory disorders like ulcerative colitis (UC) [1,2].

Aims & Methods: Aim: We previously completed a study looking at the effect of vitamin-D on Crohn's disease activity and noted a marginal beneficial effect. In this study, we sought to investigate the association between Vitamin D (VitD) levels and Ulcerative Colitis (UC) activity in the Emirati patient population of the United Arab Emirates (UAE).

Methods: We designed a retrospective cohort study using a sample population of patients (16-85 years) with UC, who were followed for at least one year in the Division of Gastroenterology at our tertiary care center in Abu Dhabi, between January 2021 and October 2023.

Demographics were collected on patients retrospectively identified in the EMR. Eligibility criteria were applied that included patients who had their VitD levels recorded at baseline and whose disease outcomes were measured between 1-12 months post-baseline visit. VitD was documented as a continuous variable and dichotomized into low vs. adequate level categories.

The primary outcome was clinical disease activity measured dichotomously. Summary statistics were calculated. Unadjusted logistic regression analysis was employed to examine the association between VitD level as a continuous variable and when categorized into low vs. adequate levels on clinical disease activity in UC.

Multivariable logistic regression looked at the independent effect of VitD levels by adjusting for covariates of effect size >20%. Statistical analysis was performed using R (version 4.0.2) and a p-value of <0.05 was considered statistically significant. IRB approval was in place for this study.

Results: We identified 89 patients with UC. Of these, 75 met our eligibility criteria, out of which 47 had their Vit D levels recorded at baseline, and 18 were noted to be deficient. 34 (45%) were women. The mean age of the cohort was 36 years. Detailed summary statistics were done. Unadjusted logistic regression analysis revealed that VitD did not appear to impact disease activity.

However, in the multivariable logistic regression analysis, when the model was adjusted for variables with an effect size of greater than 20% (age, BMI, duration of disease, steroid use), a marginal association between VitD as a continuous variable and active clinical disease was observed (OR 0.96 95%CI 0.93-0.99 $P = 0.039$).

Conclusion: This is the first study looking at the impact of VitD on Emirati patients with UC. While there are previous studies in other cohorts that have suggested an association between VitD level and disease activity in UC, it appears that having adequate VitD levels, similar to our experience with Emirati patients with CD has a positive effect. The results of this study highlight the need for IBD practices in the UAE to consider VitD level sampling at baseline and replacement when necessary but discourage the frequent use or overuse of VitD testing in the UC population in the UAE.

References: 1. Gubatan, J., Mitsuhashi, S., Longhi, M. S., Zenlea, T., Rosenberg, L., Robson, S., & Moss, A. C. (2018). Higher serum vitamin D levels are associated with protective serum cytokine profiles in patients with ulcerative colitis. *Cytokine*, 103, 38–45. <https://doi.org/10.1016/j.cyto.2017.12.023>

2. Dash, K. R., Panda, C., Das, H. S., Mishra, D., Behera, S. K., Parida, P. K., & Mohapatra, D. (2021). Association of Vitamin D Level With Disease Severity and Quality of Life in Newly Diagnosed Patients of Ulcerative Colitis: A Cross-Sectional Analysis. *Cureus*, 13(7), e16481. <https://doi.org/10.7759/cureus.16481>

Disclosure: Nothing to disclose.

PP0444

UTILITY OF CANCER GENOME ANALYSIS USING BIOPSY TISSUES FROM COLORECTAL NEOPLASIAS DEVELOPING FROM ULCERATIVE COLITIS MUCOSA

N. Yamamoto¹, Y. Urabe¹, K. Takasago¹, A. Ishikawa², A. Tsuboi¹, H. Tanaka¹, K. Yamashita¹, Y. Hiyama³, H. Takigawa¹, T. Kuwai⁴, K. Arihiro⁵, F. Shimamoto⁶, S. Oka¹

¹Hiroshima University Hospital, Department of Gastroenterology, Hiroshima, Japan, ²Hiroshima University Hospital, Department of Molecular Pathology, Hiroshima, Japan, ³Hiroshima University Hospital, Clinical Research Center in Hiroshima, Hiroshima, Japan, ⁴Hiroshima University Hospital, Department of Gastrointestinal Endoscopy and Medicine, Hiroshima, Japan, ⁵Hiroshima University Hospital, Department of Anatomical Pathology, Hiroshima, Japan, ⁶Hiroshima Cosmopolitan University, Faculty of Health Sciences, Hiroshima, Japan

Contact E-Mail Address: d211116@hiroshima-u.ac.jp

Introduction: Colorectal neoplasias developing from ulcerative colitis mucosa (CRNUCs) can be divided into ulcerative colitis-associated neoplasias (UCANs) and sporadic neoplasias (SNs); however, it is often difficult to distinguish between UCAN and SN from biopsy.

We previously reported the utility of cancer genomic analysis for differentiating UCAN from SN in post-resection CRNUC samples (Inflamm Bowel Dis. 2021).

Aims & Methods: This study investigates whether genomic analysis can differentiate UCANs from SNs using CRNUC biopsy tissues. In the first step, of the 36 early-stage CRNUCs (high-grade dysplasias and T1 carcinomas) resected at Hiroshima University Hospital between June 1998 and July 2018, and examined for genetic landscapes in the resection specimens, 14 CRNUC samples that underwent biopsy before endoscopic or surgical resection were analyzed.

The genomic landscape of the biopsy and resection specimens was examined for concordance. In the second step, the relationship between the genomic status and pathological diagnosis was investigated using biopsy specimens from 26 CRNUC cases, not included in the first step, which provided sufficient DNA for genomic analysis.

A custom panel of 27 genes, previously identified as mutated in CRNUC studies, was used for deep sequencing analysis of the cancer genome. In the evaluation of biopsy specimens, UCAN diagnosis using p53 immunostaining (IHC) was defined as cases exhibiting strongly positive p53-IHC results, and UCAN diagnosis based on *TP53* mutations was defined as cases with pathogenic mutations. UCAN diagnosis, combining hematoxylin and eosin (HE) staining with p53-IHC or *TP53* mutation analysis, was defined as follows: cases diagnosed with UCAN based solely on HE staining of the biopsy specimen, or cases with strongly positive p53-IHC or a pathogenic *TP53* mutation when HE staining alone was insufficient for a UCAN or non-UCAN diagnosis.

Results: After the first step of analysis, 14 out of the 27 candidate genes were found to be mutated. The concordance rate for pathogenic mutations across all 14 genes between the biopsy and resected specimens was 29% (4/14), whereas that for pathogenic mutations in *TP53* and *KRAS* was 79% (11/14). After the second step of analysis, the accuracy of diagnosing UCAN/non-UCAN using only HE staining of biopsy specimens was 38% (10/26), whereas p53-IHC achieved an accuracy of 73% (19/26, $p=0.026$), and *TP53* mutation analysis achieved an accuracy of 77% (20/26, $p=0.012$). The combination of HE pathology with other methods improved UCAN diagnosis. Specifically, combining HE pathology with p53-IHC in biopsy specimens achieved a sensitivity of 73% and an accuracy of 85% (22/26), while combining HE pathology with *TP53* mutation analysis resulted in a sensitivity of 87% and an accuracy of 88% (23/26).

Conclusion: Both p53 immunohistological staining and *TP53* mutation analysis of biopsy tissue were found to be useful for diagnosing UCAN, with *TP53* mutation analysis demonstrating comparable accuracy to p53 immunohistological staining for UCAN diagnosis.

Disclosure: Nothing to disclose.

PP0445

UTILIZING PATIENT-DERIVED COLON ORGANOIDs TO EXPLORE THE EFFECT OF GENETICALLY DETERMINED ERAP2-PROFICIENCY UPON PROINFLAMMATORY STIMULATION

S. Sæterstad¹, A.E. Østvik², M. Doré Hansen³, T. Bruland², A. van Beelen Granlund⁴

¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Department of Gastroenterology and Hepatology, Clinic of Medicine (St. Olav's University Hospital), Trondheim, Norway, ³Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Clinic of Laboratory Medicine (St. Olav's University Hospital), Trondheim, Norway, ⁴Norwegian University of Science and Technology, Centre of Molecular Inflammation Research, Department of Clinical and Molecular Medicine, Department of Gastroenterology and Hepatology, Clinic of Medicine (St. Olav's University Hospital), Department of Pathology (St. Olav's University Hospital), Trondheim, Norway

Contact E-Mail Address: siri.saterstad@ntnu.no

Introduction: Most immune-mediated disorders display a degree of heritability, with specific genetic variants linked to disease susceptibility. Variants in Endoplasmic Reticulum Amino-peptidase 2 (*ERAP2*) have been associated with numerous inflammatory conditions, including Inflammatory Bowel Disease (IBD). As several species (rodents included) lack the *ERAP2* gene, functional studies have been relatively limited. Several immunological functions of *ERAP2* beyond peptide trimming have been proposed, yet most of these findings have been reported in immune cell populations. As the epithelial involvement in IBD pathogenesis is getting increasingly recognized, we set out to explore the impact of epithelial *ERAP2* presence during inflammatory encounter using human-derived colonoids as a model system. To investigate the effect of genotype on *ERAP2* expression in different disease states, patient material from a IBD cohort was used to correlate genotype to *ERAP2* expression in inflamed and noninflamed colonic biopsies.

Aims & Methods: Two single nucleotide polymorphisms (SNPs) linked to *ERAP2* expression (rs2910686/rs2248374) were analyzed in a cohort of IBD patients. Genotypes for both SNPs were correlated with colonic *ERAP2* expression levels in noninflamed and inflamed biopsies. Based on rs2910686

genotype, ERAP2-proficient ($n=4$) and ERAP2-deficient ($n=4$) colon organoids were established to study differential expression between proficient and deficient donors after proinflammatory stimulation.

Results: Conditioning on genotype reveals upregulation of *ERAP2* in the inflamed colon of IBD patients. ERAP2 expression proficiency correlates with rs2910686 genotype. IFN γ induces colonic epithelial ERAP2 expression. Western blot confirms that mechanisms independent of the frequently studied SNP rs2248374 can cause ERAP2-deficiency. A total of 586 genes involved in various molecular mechanisms are differentially expressed between ERAP2-proficient and -deficient colonoids upon proinflammatory stimulation, including *AOC1*, *CPE*, *ANPEP* and *MEP1A* (catalytic activity), *TNFSF9*, *MDK*, *GDF15*, *ILR6A*, *LGALS3* and *FLNA* (regulator activity), *SLC40A1* and *SLC5A1* (transmembrane transporter activity), *FGL2*, *HMCN2*, and *MUC17* (extracellular matrix structural constituents).

Conclusion: Our findings demonstrate that ERAP2 expression is significantly upregulated in the inflamed colon of IBD patients, and expression levels correlates with rs2910686 genotype. Although rs2248374 is commonly used to assess ERAP2 expression proficiency, our findings confirm that mechanisms independent of rs2248374 can lead to ERAP2-deficiency. We further demonstrate that stratifying organoid donors based on genotype is a useful way of exploring the impact of genetic variants. Our data support that ERAP2 play a multifaceted role in modulating the inflammatory response in epithelial cells.

Disclosure: Nothing to disclose.

PP0446

EVALUATION OF DIET-DERIVED MICROBIOME-ASSOCIATED METABOLITES ON GUT INFLAMMATION IN ORGANOID MODELS OF INFLAMMATORY BOWEL DISEASE

I. Aleknaviciene¹, D. Tilindė¹, R. Ramonaite², R. Inciuraite¹, J. Kupcinskas¹, V. Kiudelis², G. Kiudelis², L.V. Jonaitis², J. Skieceviciene¹

¹Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ²LUHS Dept. of Gastroenterology, Kaunas University of Medicine, Department of Gastroenterology,, Kaunas, Lithuania

Contact E-Mail Address: indre.aleknaviciene@lsmu.lt

Introduction: Maintaining intestinal homeostasis relies on the interplay between individuals and their unique gut microbiota. Disruptions may result in chronic inflammation and Inflammatory Bowel Disease (IBD) [1]. This study delves into this interplay, emphasizing the characterization of diet-derived microbiome-associated metabolites and prioritizing them based on their effects on epithelial barrier integrity and inflammatory status.

Aims & Methods: Diet-derived microbiome-associated metabolites – epigallocatechin-gallate, gallic acid (GA), protocatechuic acid (PCA), ellagic acid (EA), and urolithins (Uro-A, B, C, D) – were selected through extensive literature research. In the commercial colon cell model (Caco-2) and 3D epithelial organoids from primary adult intestinal-epithelial stem cells, inflammation was induced with TNF- α and IFN- γ (25ng/ml and each) to mimic IBD conditions. The expression of inflammatory cytokines genes (TNF- α , CXCL-9, MCP-1, IL-8) and epithelial barrier integrity markers (ZO-1 and OCLN) were evaluated by qRT-PCR. Epithelial barrier integrity was visualized using FITC-dextran assay.

Results: The induction of inflammation significantly increased in key inflammatory markers by an average 7.5-fold change (± 1.8 SD) in Caco-2 and 3D IBD organoid models. Metabolite analysis in Caco-2 cells showed that GA exhibited a 1.24-fold increase in TNF- α ($p=0.036$) and a -7.22-fold decrease in MCP-1 ($p=0.049$) gene expressions. EA decreased the expres-

sion of TNF- α and MCP-1 genes by -1.59-fold ($p=0.045$) and -3.59-fold ($p=0.036$) respectively, whereas IL-8 was reduced by -7.62-fold ($p=0.01$). Uro-A uniquely decreased MCP-1 gene expression by -7.16-fold ($p=0.004$) but increased IL-8 by 8-fold ($p=0.01$). PCA demonstrated a statistically significant decrease in all tested inflammatory markers ($p<0.05$). Analysis of 3D IBD organoids highlighted unique effects in restoring the epithelial barrier and expression of inflammatory marker genes.

Conclusion: Our findings demonstrate the anti-inflammatory properties of gallic acid, ellagic acid, protocatechuic acid, and urolithin-A in both Caco-2 and 3D organoid models. This research elucidates the complex interrelationships within the nutrition-microbiome-metabolome axis and its consequential impact on gut health.

References: 1. Zheng, D., Liwinski, T. & Elinav, E. Interaction between microbiota and immunity in health and disease. *Cell Res* **30**, 492–506 (2020). <https://doi.org/10.1038/s41422-020-0332-7>

Disclosure: No conflict of interest to declare.

PP0447

CLINICAL SYMPTOM TRAJECTORIES ARE SUPPORTED BY DIFFERENTIAL REGULATION OF MUCOSAL TRANSCRIPTOMES IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH FILGOTINIB: A POST HOC ANALYSIS OF THE SELECTION STUDY

S. Schreiber¹, M. Randall², J. Halfvarson³, F. Rieder^{4,5,6}, P. Irving^{7,8}, B.G. Feagan^{9,10}, L. Cougnard¹¹, A. Oortwijn¹², Y. Bauer², W. Reinisch¹³

¹University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel University, Kiel, Germany, ²Galapagos GmbH, Basel, Switzerland, ³Örebro University, Department Gastroenterology, Faculty of Medicine and Health, Örebro, Sweden, ⁴Cleveland Clinic, Department of Inflammation and Immunity, Lerner Research Institute, Cleveland, United States of America, ⁵Cleveland Clinic, Department of Gastroenterology, Hepatology and Nutrition, Digestive Disease Institute, Cleveland, United States of America, ⁶Cleveland Clinic, Center for Global Translational Inflammatory Bowel Disease Research, Cleveland, United States of America, ⁷Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, ⁸King's College London, School of Immunology and Microbial Sciences, London, United Kingdom, ⁹Alimentiv Inc., London, ON, Canada, ¹⁰Western University, London, ON, Canada, ¹¹Open Analytics NV, Antwerp, Belgium, ¹²Galapagos NV, Leiden, Netherlands, ¹³Medical University of Vienna, Division of Gastroenterology and Hepatology, Vienna, Austria

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: The SELECTION trial (NCT02914522) demonstrated that filgotinib (FIL), a once-daily, oral, Janus kinase 1 preferential inhibitor, was effective at inducing and maintaining clinical remission in patients with moderately to severely active ulcerative colitis (UC).¹

A *post hoc* analysis of FIL responders identified five unique patient groups with different trajectories of response modelled from partial Mayo Clinic Score (pMCS) data, ranging from sustained improvement to rebound of symptoms.²

Aims & Methods: We investigated the underlying biology associated with these pre-defined symptomatic trajectories using colon biopsies collected during SELECTION; the trial design has been reported previously.¹ Using group-based trajectory modelling, FIL responders (defined as patients treated with FIL who were in clinical remission or with a Mayo Clinic Score response at week 10) were clustered into trajectories based on similar changes in pMCS from baseline to week 58.² RNA was extracted from colonic mucosal biopsies collected at baseline and week 10, and RNA

sequencing was performed as per standard protocols. Trajectory-specific transcriptional changes were assessed at baseline by differentially expressed gene (DEG) analysis.

Key comparisons were:

- Each trajectory at baseline versus the average of the other trajectories and
- The change from baseline to week 10, assessed separately for each trajectory group.

Results: Comparison of DEGs between each trajectory group demonstrated minimal transcriptional differences between the groups at baseline. However, the number of DEGs from baseline to week 10 differed between the trajectory groups (Table). Interestingly, trajectories associated with greater symptomatic improvement beyond week 10 had higher numbers of DEGs.

Conclusion: We identified transcriptional differences in the change from baseline to week 10 in DEGs between trajectory groups, aligning with symptomatic improvement beyond week 10 in patients receiving FIL. A qualitative analysis of DEGs is under investigation, for which preliminary results support the potential for personalized medicine in UC, by identifying differences in underlying pathophysiology associated with differential response to targeted therapy. These findings could further help to identify blood biomarkers that predict treatment outcomes in patients with UC on FIL.

	Group A	Group B	Group C	Group D	Group E
n (%)	4683 (8.85%)	4356 (8.23%)	1306 (2.47%)	14 690 (27.76%)	14 677 (27.73%)

Table. Change in number of significantly differentially expressed genes from baseline to week 10 for each trajectory

References:

- Feagan BG *et al.* *Lancet* 2021;397:2372–84
- Schreiber S *et al.* [MP443] Poster presented at the United European Gastroenterology Week (UEGW), 8–11 October 2022, Vienna, Austria.

Disclosure: The SELECTION trial was sponsored by Gilead Sciences Inc (Foster City, CA, USA). Galapagos NV (Mechelen, Belgium) was a collaborator for the SELECTION trial and funded this analysis.

Medical writing support for the development of this abstract was provided by Annika Pecchia-Bekkum, PhD, of PharmaGenesis London, London, UK, and was funded by Alfasigma S.p.A.

SS and MR contributed equally.

MR and AO are employees of Alfasigma S.p.A at the time of abstract submission.

SS reports personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos/Gilead Sciences, Hikma Pharmaceuticals, I-Mab, Janssen Pharmaceuticals, Morphic Therapeutic, MSD, Mylan, Pfizer, Protagonist Therapeutics, Provention Bio, Sandoz/Hexal, Takeda, Theravance Biopharma and Ventyx Biosciences.

MR and AO are former employees and shareholders of Galapagos NV, and are employees of Alfasigma S.p.A.

JH reports speaker and/or consulting fees from AbbVie, Aqilion, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma and the Falk Foundation, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Hospira, InDex Pharmaceuticals, Janssen Pharmaceuticals, MEDA Pharmaceuticals, Medivir, Medtronic, MSD, Novartis, Pfizer, Prometheus Laboratories Inc., Sandoz, Shire, Takeda, Thermo Fisher Scientific, Tillotts Pharma, Vifor Pharma and UCB; and grants from Janssen Pharmaceuticals, MSD and Takeda.

FR reports consulting fees from Adiso, Adnovate, Agomab, Allergan, AbbVie, Arena, Astra Zeneca, Bausch & Lomb, Boehringer-Ingelheim, Celgene/BMS, Celltrion, CDISC, Celsius, Cowen, Eugit, Ferring, Galapagos, Galmed,

Genentech, Gilead, Gossamer, Granite, Guidepoint, Helmsley, Horizon Therapeutics, Image Analysis Limited, Index Pharma, Landos, Janssen, Koutif, Mestag, Metacrine, Mirum, Mopac, Morphic, Myka Labs, Organovo, Origo, Palisade, Pfizer, Pliant, Prometheus Biosciences, Receptos, RedX, Roche, Samsung, Sanofi, Surmodics, Surrozen, Takeda, Techlab, Teva, Theravance, Thetis, Trix Bio, UCB, Ysios and 89Bio.

PI reports lecture fees from AbbVie, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, MSD, Pfizer, Sandoz, Sapphire Medical, Shire, Takeda, Tillotts Pharma, and Warner Chilcott; grants from Celltrion, Galapagos, MSD, Pfizer and Takeda; and advisory fees from AbbVie, Apriso, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Genentech, Gilead Sciences, Hospira, Janssen Pharmaceuticals, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor Pharma and Warner Chilcott.

BGF reports grants and personal fees from AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Janssen Biotech/Centocor, Johnson & Johnson/Janssen, Pfizer, Receptos and Takeda; and personal fees from Ablynx, ActoGenix, AdMIRx, Akebia Therapeutics, Allergan, Atlantic Pharmaceuticals, Avaxia Biologics, Avir Pharma, Baxter Healthcare Corporation, Biogen, BiomX Israel, Biora Therapeutics (formerly Progenity), Boehringer Ingelheim, Boston Pharmaceuticals, Calypso Biotech, Celgene, Elan/Biogen, Eli Lilly, enGene, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, glCare Pharma, Gilead Sciences, Given Imaging, Gossamer Bio, GSK, Inception IBD, Ironwood Pharmaceuticals, Japan Tobacco Company, Kyowa Hakko Kirin, Lexicon Pharmaceuticals, Lycera, Mesoblast, MSD, Nestlé, Nextbiotix, Novartis, Novo Nordisk, ParImmune, Prometheus Therapeutics and Diagnostics, Protagonist Therapeutics, Qu Biologics, Salix Pharmaceuticals, Shire, Sienna Biopharmaceuticals, Sigmoid Pharma, Synergy Pharma, Takeda Oncology (formerly Millennium Pharmaceuticals), Teva Pharmaceuticals, TiGenix, Tillotts Pharma, UCB, Vertex Pharmaceuticals, VHSquared, Vivelix Pharmaceuticals, Wyeth, Zealand Pharma and Zyngenia.

LC is an employee of Open Analytics.

YB is an employee and shareholder of Galapagos NV.

WR reports speaker fees from AbbVie, Celltrion, Ferring Pharmaceuticals, Galapagos, Janssen Pharmaceuticals, Medice, MSD, Pfizer, Roche, Sobi and Takeda; consulting fees from AbbVie, Amgen, AOP Health (formerly AOP Orphan), Boehringer Ingelheim, Bristol Myers Squibb, Calyx, Celltrion, Eli Lilly, Galapagos, Gilead Sciences, InDex Pharmaceuticals, Janssen Pharmaceuticals, MedAhead, Microbiotica, Pfizer and Takeda; advisory board fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Galapagos, Janssen Pharmaceuticals and Pfizer; and research funding from AbbVie, Janssen Pharmaceuticals, Sandoz, Sanofi and Takeda.

PP0448

GENOME WIDE ANALYSES UNRAVEL NOVEL INTERACTIONS BETWEEN TOBACCO SMOKING AND GENETIC VARIANTS IN CROHN'S DISEASE AND ULCERATIVE COLITIS

J. Bai¹, R.K. Weersma¹, G. Dijkstra¹, K. van der Sloot¹, E.A. Festen^{1,2}

¹University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands,

²University Medical Center Groningen, Department of Genetics, Groningen, Netherlands

Contact E-Mail Address: j.bai@umcg.nl

Introduction: The divergent impact of tobacco smoking in Crohn's disease (CD) and ulcerative colitis (UC) has been widely observed, but it's not completely understood whether the effect of smoking may be modified by genetic makeup.

Our present study aims to systematically identify the genetic modifiers of tobacco smoking in relation to CD and UC disease risk based on genome wide screening.

Aims & Methods: We performed a case-only genome wide association meta-analysis to examine the multiplicative interaction effect between tobacco smoking and single nucleotide polymorphisms (SNPs) in two independent IBD cohorts, the 1000IBD cohort (N=990) and the Dutch Parelsoer-IBD cohort (N=2540). Imputed Global Screening Array genotype datasets combined with classical HLA alleles were used to compare the genotype frequencies between ever versus never smokers, current versus never smokers, and former versus never smokers in patients with IBD. We further separated entire analyses for CD and UC to characterize interactions where opposite direction was observed.

Functional mapping and annotation of smoking interaction variants were conducted using FUMA, including positional mapping, eQTL mapping and chromatin interaction mapping.

Results: A total of 572 lead SNPs showed consistent evidence of interaction with tobacco smoking between two independent cohorts (meta-analysis $P < 5 \times 10^{-5}$, heterogeneity Q test > 0.05). Thirty SNPs exhibited opposite associations with smoking behaviors between CD and UC. (Effect size ratio > 5 or < 0.1) An HLA Class II haplotype (HLA-DRB1*03:01~HLA-DQA1*05:01~HLA-DQB1*02:01) showed lower frequency in IBD smokers than never smokers.

Functional mapped genes were significantly overrepresented in various immune-response regulation pathways as well as collagen metabolic processes and showed enrichment in specific cell types, such as fetal intestine myeloid cells and midbrain neurotypes. These implicated genes also significantly overlapped with the risk genes for mental disorders, including autism spectrum disorders, schizophrenia, and major depressive disorders.

Conclusion: Our findings indicate that the influence of smoking behaviors on IBD risk depends on individual genetic background. Genetic modifiers of tobacco smoking with opposite directions may explain the differential impact of smoking on the susceptibility to CD and UC. Overrepresentation of these mapped genes in multiple mental disorders reflected complex pleiotropy.

Disclosure: Nothing to disclose.

PP0449

EARLY VEDOLIZUMAB DRUG LEVELS PREDICT ENDOSCOPIC IMPROVEMENT IN BIOLOGICAL-NAIVE PATIENTS: A SINGLE-CENTER EXPERIENCE

B. Smolović¹, M. Lukic², O. Sekulić², T. Antunović³, M. Jakšić⁴

¹Faculty of Medicine, University of Montenegro; Clinical

Center of Montenegro, Internal Clinic, Department of Gastroenterohepatology, Podgorica, Montenegro, ²Clinical

Center of Montenegro, Internal Clinic, Department of Gastroenterohepatology, Podgorica, Montenegro, ³Clinical

Center of Montenegro, Center for Clinical-Laboratory Diagnostic, Podgorica, Montenegro, ⁴Institute for Children's Diseases, Clinical Center of Montenegro, Department of Laboratory Diagnostics, Podgorica, Montenegro

Contact E-Mail Address: petar.s@t-com.me

Introduction: Inflammatory bowel diseases (IBD) are chronic gastrointestinal diseases that include ulcerative colitis (UC) and Crohn's disease (CD). IBD is a major public health concern, affecting approximately 6 million people globally (2). Although more common in industrialized countries, the prevalence of IBD is rising in emerging countries as a result of lifestyle changes.

Unfortunately, there is no official data on the occurrence of IBD in Montenegro, either for children or adults. Vedolizumab is a humanized monoclonal antibody that selectively targets $\alpha 4\beta 7$ integrin and was approved for the treatment of adult patients with moderately to severely active UC and CD. The effects of therapeutic drug monitoring or a target serum concentration for vedolizumab are not fully established at this time. It is assumed that higher serum concentrations of vedolizumab lead to a higher probability of clinical response or remission.

Aims & Methods: The aim of the study was to investigate the relationship between vedolizumab serum concentrations (measured at week 6th after beginning of treatment) and clinical and endoscopic responses in IBD patients (evaluated at week 14th). The trial included 22 biologic-naïve IBD patients (15 - UC, 7 - CD), who received vedolizumab as a first-line treatment. We evaluated endoscopic scores (Mayo Score for UC and Simple Endoscopic Score (SES) for CD) as well as the clinical disease activity scores (Ulcerative Colitis Disease Activity Index (CDAI), Partial Mayo Score (PMS) for UC, and Harvey Bradshaw Index (HBI) for CD). Endoscopic response was defined as a 50% decrease in SES-CD score from the baseline value and Mayo endoscopy subscores of 0 or 1 were considered satisfactory. Clinical remission was defined as an HBI < 5 , Mayo Score ≤ 2 , and no individual subscore > 1 . Clinical response was defined as a decrease in HBI ≥ 3 , a decrease in Mayo Score $\geq 30\%$, and ≥ 3 points from the induction baseline, with a rectal bleeding subscore of 0 or 1.

Results: In the 14th week of therapy, a statistically significant clinical and endoscopic response was achieved, surpassing the overall response of patients with UC and CD ($p < 0.001$). Furthermore, a statistically significant reduction in individual clinical scores (CDAI, HBI, and PMS) was observed in the 14th week of drug application ($p = 0.004$; $p = 0.026$, $p = 0.005$, respectively). The endoscopic response was statistically significant in patients with UC (Mayo endoscopic score, $p = 0.003$) in the 14th week, but not in patients with CD ($p = 0.176$).

The difference in vedolizumab concentration was statistically significant between patients who achieved an endoscopic response in the 14th week and those who did not ($p = 0.02$). Additionally, the difference in drug concentration was close to statistical significance ($p = 0.088$) between patients with UC (28.6 ± 13.6) and CD (21 ± 9.7).

In biologic-naïve IBD patients, a vedolizumab serum concentration of 25.6 mcg/mL or greater at week 6th demonstrated a sensitivity of 88.9% and a specificity of 100% in predicting an endoscopic response at week 14th.

Conclusion: Early determination of vedolizumab serum concentration in biologic-naïve IBD patients, primarily UC, can be a promising predictor of endoscopic improvement in these patients.

References:

1. Osterman MT, Rosario M, Lasch K, et al. Vedolizumab exposure levels and clinical outcomes in ulcerative colitis: determining the potential for dose optimisation. *Aliment Pharmacol Ther.* 2019;49(4):408-418
2. Sandborn WJ, Feagan BG, Rutgeerts P, et al; for the GEMINI 2 Study Group. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med.* 2013a;369(8):711-721
3. Dreesen E, Verstockt B, Bian S, et al. Evidence to support monitoring of vedolizumab trough concentrations in patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol.* 2018;16(12):1937-1946
4. Liefverinckx C, Minsart C, Cremer A, et al. Early vedolizumab trough levels at induction in inflammatory bowel disease patients with treatment failure during maintenance. *Eur J Gastroenterol Hepatol.* 2019;31(4):478-485
5. Scribano ML. Vedolizumab for inflammatory bowel disease: From randomized controlled trials to real-life evidence. *World J Gastroenterol.* 2018;24(23):2457-2467

Disclosure: This abstract was presented at the 1st International Congress of Gastroenterohepatologists of Montenegro, held from June 9-11, 2023 in Budva, Montenegro.

PP0450

THE ULTRASOUND MEASUREMENT OF PSOAS MUSCLE AS AN INDEX OF SARCOPENIA IN A COHORT OF PATIENTS AFFECTED BY INFLAMMATORY BOWEL DISEASE: CORRELATIONS WITH THEIR CLINICAL HISTORY AND VARIABLES

F.M. Stalla¹, G. Pecorella², M. Mendolaro¹, E. Morello¹, D. Stradella¹, R. Rocca¹, M. Daperno¹

¹Mauriziano Hospital, Gastroenterology Unit, Torino, Italy,

²University of Turin, Department of Medical Science, Torino, Italy

Contact E-Mail Address: francesco.stalla@gmail.com

Introduction: Sarcopenia is a progressive disorder characterized by reduced musculoskeletal mass leading to reduced strength and poor physical performance. Nutritional status is critical to therapeutic success in Crohn's Disease (CD) and Ulcerative Colitis (UC) but it is clear how traditional weight and body mass index (BMI) scores are poorly representative of these.^[1,2]

Sarcopenia could better reflect the degree of malnutrition.^[3]

In inflammatory bowel disease (IBD) sarcopenia has been associated with refractory to medical treatment, prolonged hospitalization, increased rate of surgery and increased frequency of post-operative complications.^[4-6] Recently the measurement of the psoas muscle (PM) by ultrasound (US) has been proposed as a surrogate of sarcopenia obtaining an high concordance with the reference standard CT scan.^[7]

Aims & Methods: Our preliminary prospective study aims to identify correlations between US measurement of PM in a cohort of 57 patients with IBD and their clinical history and variables. The transverse area of the PM in cm² (US-TPA) and the same divided the square height in cm²/m² (US-PMI) were measured in the right iliac fossa using a low frequency probe: General Electric Logiq P8 (Boston, USA) for outpatients whereas Esaote MyLab One/Touch (Genova, Italia) for inpatients.

Results: Normal weight patients have significantly higher US-TPA and US-PMI values (p=0.032 and 0.031) than underweight (BM<18.5 kg/m²) or overweight (BMI>25 kg/m²). CD patients have significantly lower US-TPA (p=0.03) than UC patients. Patients with history of fistulizing perianal disease or who have at least two surgeries have significantly lower US-TPA

and US-PMI values than the rest of the population (p=0.02). Patients with severe disease activity (Mayo Partial 5 or Harvey-Brashaw Index>8) have lower US-TPA and US-PMI (p = 0.0003 and 0.0004) than those in clinical remission or mild-moderate activity. As well as for patients with disease activity of any degree (Mayo Partial >2 or HBI>5) compared to remission (p= 0.001 and 0.002). With due caution, we have empirically applied the US-PMI cut-offs proposed by Kobayashi^[8] in their cirrhotic cohort of 1.89 cm²/m² for males and 1.81 cm²/m² for females: 13 (23%) of our patients were found to be sarcopenic.

Of these, 46% of patients were admitted at the time of inclusion, 50% clinically active and 77% clinically severe. The higher frequency of sarcopenia observed in these groups was statistically significant with OR 5.42 (IC 95% 1.4-21.8) and p=0.017, OR 5.4 (IC 95% 1.4-21.2) and p=0.02 and OR 19.3 (IC 95% 3.2-116) and p=0.0002 respectively. Underweight and overweight subjects (BMI <18.5 kg/m² or >25 kg/m²) were more frequently sarcopenic according to the same cut-off than normal weighted with OR 3.97 (95% IC 1.08 - 14.53) and p=0.037.

Conclusion: US is a simple and reproducible method of measuring the PM as a surrogate for sarcopenia, an independent nutritional index that could affect therapeutic responses and outcome in IBD. Our study has found a correlation between the so quantified sarcopenia and the disease activity and clearly demonstrates how such a state of malnutrition is linked to both underweight and overweight. The widening of the population will allow us in future to emphasize associations and differences. The impact and predictive role of sarcopenia on IBD outcomes will be investigated. It will be necessary to identify PM US cut-off for IBD, validated and related by nutritional parameters or other quantitative or qualitative methods.

References:

- 1 Bryant R V. et al. Systematic review: body composition in adults with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; 38: 213–225.
- 2 Dhaliwal A, Quinlan JI, Overthrow K, Greig C, Lord JM, Armstrong MJ, Cooper SC. Sarcopenia in Inflammatory Bowel Disease: A Narrative Overview. *Nutrients* 2021, Vol 13, Page 656 2021; 13: 656.
- 3 Adams DW et al. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. *Inflamm Bowel Dis* 2017; 23:1182–1186.
- 4 Sigurdsson GV et al. Altered body composition profiles in young adults with childhood-onset inflammatory bowel disease. 2020; 55: 169–177.
- 5 Bryant R V. et al. Low muscle mass and sarcopenia: common and predictive of osteopenia in inflammatory bowel disease. *Aliment Pharmacol Ther* 2015; 41: 895–906.
- 6 Pedersen M et al. Sarcopenia is a Predictor of Surgical Morbidity in Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2017; 23: 1867–1872.
- 7 Takai Y. et al. Ultrasound method for estimating the cross-sectional area of the psoas major muscle. *Med Sci Sports Exerc* 2011; 43: 2000–2004.
- 8 Kobayashi K et al. Application of transcutaneous ultrasonography for the diagnosis of muscle mass loss in patients with liver cirrhosis. *J Gastroenterol* 2018; 53: 652–659

Disclosure: Francesco Maria Stalla hosted to congresses: Giuliani s.p.a.

MONITORING STRUCTURAL BOWEL DAMAGE IN PATIENTS WITH CROHN'S DISEASE: CAN IT BE REVERSED BY BIOLOGICAL TREATMENT?

S. Albert Palomares¹, P. Marqués García¹, M. Fiqui Chetouani¹, J.R. Lorente Montoro¹, J. Torrente Sánchez¹, A.A. Pérez Ibáñez¹, E. Peiró García¹, A. Rabadán Mata¹, J.M. Paredes Arquiola¹
¹Hospital Universitario Dr Peset, Gastroenterology, Valencia, Spain

Contact E-Mail Address: saraalbert44@gmail.com

Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease, characterized by a progressive course that leads to structural bowel damage (SBD). There is no clear definition of SBD. The Lémann index has been proposed, but it's too complicated to calculate. However, the presence of detectable complications through imaging techniques, such as strictures, fistulas or abscesses is widely accepted to describe SBD. Their presence is strongly associated with the severity of the disease and predicts the risk of hospitalization and surgery. Therefore, reversing structural bowel damage is an emerging medical goal in the time of biological treatments.

Aims & Methods: The main objective of this study was to assess the ability of biological treatments to reverse structural bowel damage monitored by intestinal ultrasound (IUS) and compare the disease course of patients with CD with inflammatory behaviour vs complicated behaviour (stricturing or penetrating -abscesses and fistulas-).

This was a longitudinal observational study, which included patients with CD who started a biological treatment in our center and that were monitored with IUS. Clinical, laboratory and ultrasound variables were collected at the beginning of biological treatment, after 12 weeks and after one year of treatment in order to study the evolution of the disease.

To achieve our objective, we compared the transmural healing (TH) at 12 weeks and one year after starting biological treatment. TH is defined as intestinal parietal thickness ≤ 3 mm, with no detectable Doppler signals and absence of complications.

As a secondary objective, we compared the need for medical treatment, hospital admission and surgery during the first year of biological treatment

Results: A total of 137 patients with CD were included in this study. Their characteristics and treatments are shown in Table 1.

Variables		Absolute frequency (%)
Male		67 (48.9%)
Initial bowel damage	Stricturing	31 (22.6%)
	Abscesses	11 (8%)
	Fistula	21 (15.3%)
Montreal Classification	Age	≤ 16 years: 12 (8.8%) 17-40 years: 79 (57.7%) ≥ 41 years: 46 (33.6%)
	Location	Ileal: 75 (54.7%) Colonic: 19 (13.9%) Ileocolonic: 43 (31.4%) Upper disease: 1 (0.7%)
	Behaviour	Inflammatory: 53 (38.7%) Stricturing: 30 (21.9%) Penetrating: 54 (39.4%)
Indication for initiating biologic treatment	Stenotic complication	25 (18.2%)
	Penetrating complication	22 (16.1%)

Table 1.

At the beginning of biological treatment, 50 patients (36.5%) exhibited a complicated behaviour (strictures, abscesses, and fistulas).

After 12 weeks of treatment, TH was achieved in 22.9% of all evaluated patients. By groups, 8.2% of patients with complicated CD and 31.3% with an inflammatory behavior achieved TH, being the last difference statistically

significant ($p 0.02$). After one year of treatment, TH on IUS was achieved in 46% of all evaluated patients. 31.8% of these patients had a complicated EC and 45.1% presented an inflammatory behavior, without reaching statistical significance ($p 0.159$).

Furthermore, the group with complicated behavior exhibited a significantly higher need for corticosteroid therapy, hospital admission, and surgery.

Conclusion: Patients with SBD showed a significantly lower rate of TH compared to patients with an inflammatory behaviour after 12 weeks of biological treatment.

Additionally, the need for corticosteroid therapy, hospital admission, and surgery was significantly higher in patients with a complicated CD. However, after one year, the TH rate showed no differences between groups. This suggests that reversing structural bowel damage is possible but that the treatment of these patients is more complex.

References:

1. Wilkens, Rune et al. Relevance of monitoring transmural disease activity in patients with Crohn's disease: current status and future perspectives. *TherapAdvGastroenterol*. 2021 Apr 16;14:17562848211006672.
2. Paredes, José María et al. Clinical Impact of Sonographic Transmural Healing After Anti-TNF Antibody Treatment in Patients with Crohn's Disease. *Dig Dis Sci*. 2019 Sep;64(9):2600-2606
3. Muñoz, Fernando et al. Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on the use of abdominal ultrasound in inflammatory bowel disease. *Gastroenterol-Hepatol*. 2021 Feb;44(2):158-174.
4. Calabrese, Emma et al. Ultrasonography Tight Control and Monitoring in Crohn's Disease During Different Biological Therapies: A Multicenter Study. *ClinGastroenterolHepatol*. 2022 Apr;20(4):e711-e722
5. Fraquelli, Mirella et al. Impact of intestinal ultrasound on the management of patients with inflammatory bowel disease: how to apply scientific evidence to clinical practice. *Dig Liver Dis*. 2020 Jan;52(1):9-18.
6. Wilkens, Rune et al. Relevance of monitoring transmural disease activity in patients with Crohn's disease: current status and future perspectives. *TherapAdvGastroenterol*. 2021 Apr 16;14:17562848211006672
7. Roda, Giulia et al. Crohn's disease. *Nat Rev Dis Primers*. 2020 Apr 2;6(1):22
8. Fiorino, Gionata et al. Impact of therapies on bowel damage in Crohn's disease. *United European Gastroenterol J*. 2020 May;8(4):410-417

Disclosure: Nothing to disclose.

PP0453

TYPE 2 DIABETES AND INFLAMMATORY BOWEL DISEASE: IS THERE A POSSIBLE LINK?

M. Mtir¹, M. Ayari¹, A. Chehaider¹, I. Abdelaali¹, M.H. Douggui¹, J. Mohamed Taieb¹

¹Internal Security Forces Hospital, Gastroenterology department, La Marsa, Tunisia

Contact E-Mail Address: mtirmaha@gmail.com

Introduction: Nowadays, it is widely recognized that the gastrointestinal tract plays an important role in the homeostasis of glycemic metabolism. Some studies suggest that the presence of chronic intestinal inflammation is associated with an over-risk of type 2 diabetes (T2D), due to dysbiosis (1).

However, the impact of diabetes on chronic inflammatory bowel disease (IBD) has been insufficiently studied.

The aim of our study was to compare the clinical and therapeutic features as well as the evolutionary character of IBD according to the presence or not of T2D.

Aims & Methods: We conducted a monocentric retrospective study, including patients with Crohn disease (CD) or ulcerative colitis (UC) IBD, over a 7-year period [2014 - 2021]. Clinico-biological data, disease severity as well as the long-term therapeutic and evolutionary data were collected. Patients were compared according to the presence or absence of diabetes. They were divided into two groups:

- Group 1 (N=21): diabetic patients with IBD

- Group 2 (N=79): non-diabetic patients with IBD.

The statistical study was carried out by using SPSS V23 software.

Results: We enrolled 100 patients with IBD: 50% with CD and 50% with UC. The mean age was 46.5 years [extremes: 11 - 82], with a noticeable male predominance (M/F sex ratio of 2.5). The prevalence of T2D in our population was 21%, essentially affecting patients with UC in two-thirds of cases (N=14) versus seven diabetic patients with CD.

The comparison of these two groups showed no significant difference in terms of sex ratio ($p=0.961$), smoking habits ($p=0.731$), duration of disease progression ($p=0.744$) or association with extraintestinal manifestations. However, the mean age was higher in cases of diabetes ($p=0.017$), with a cut-off of 51 years. Among diabetic patients, we observed a higher rate of complications such as acute severe colitis in 38.1% versus 15.2% of non-diabetic patients ($p=0.020$).

The number and severity of IBD flare-ups were not associated with diabetes. Nevertheless, bacterial or viral superinfection during relapses was significantly more frequent in case of diabetes (38.1% versus 15.2%, $p=0.020$). It was mainly due to superinfection with *Escherichia Coli*. Thromboembolic complications also occurred more frequently in diabetic patients (14.3% versus 1.3%, $p=0.028$). As for the therapeutic component, there was no significant difference between the two groups regarding the use of systemic corticosteroid therapy ($p=0.458$), immunosuppression ($p=0.101$) or biotherapy ($p=0.803$). Nonetheless, we found that side effects of corticosteroids were more important among diabetic patients (21.4% versus 2.3%, $p=0.013$). The risk of undergoing surgery was similar in both groups (33.3% versus 34.2%, $p=0.944$).

In multivariate studies, type 2 diabetes was an independent factor in the occurrence of superinfection during relapses (OR=4.8; 95% CI [1.096 - 21.747]; $p=0.038$), as well as the side effects of corticosteroid therapy (OR=17.6 95% CI [1.281 - 243.006]; $p=0.032$) among IBD patients.

Conclusion: In our study, type 2 diabetes seems to have a negative impact by increasing the risk of superinfections and cortico-induced side effects during IBD, justifying increased surveillance in these patients. However, it does not appear to have a significant effect on the prognosis and long-term course of the disease.

References: 1. Jess T, Jensen BW, Andersson M, Villumsen M, Allin KH. Inflammatory Bowel Diseases Increase Risk of Type 2 Diabetes in a Nationwide Cohort Study. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2020 Apr;18(4):881-888.e1.

Disclosure: Nothing to disclose.

PP0454

PREDICTIVE VALUE OF THE MOBILE HEALTH INDEX IN DIFFERENT RISK GROUPS IN INFLAMMATORY BOWEL DISEASES: SIX-MONTH OUTCOMES OF A PROSPECTIVE COHORT STUDY

L.J. Koppelman¹, N.M. Althuis¹, J.P. Maljaars¹, P.W. Voorneveld¹, R.J. Jacobs², A.E. Van Der Meulen - De Jong¹

¹Leiden University Medical Centre, Gastroenterology and Hepatology, Leiden, Netherlands, ²Alrijne Hospital, Gastroenterology and Hepatology, Leiderdorp, Netherlands

Contact E-Mail Address: l.j.m.koppelman@lumc.nl

Introduction: Patients with inflammatory bowel disease (IBD) require long-term, intensive care. To optimise future healthcare delivery, identifying patients suitable for remote monitoring is crucial. Patient-reported outcome measures integrated within eHealth systems, such as the 4-item Mobile Health Index (mHI)¹, offer potential for predicting disease activity. This study explores the predictive value of the mHI within the e-health system DEARhealth² at a Dutch university medical centre.

Aims & Methods: This multi-centre prospective cohort study tracked IBD patients within the e-health system. Patients were categorised into high-, intermediate-, and low-risk groups based on current and past biochemical disease activity. High-risk patients had current biochemical disease activity (FCP > 150 µg/g and/or CRP > 5 mg/L), intermediate-risk patients were in remission but experienced a biochemical flare within the last three years, while low-risk patients had been in biochemical remission for at least three years.

A personalised care pathway, considering both risk group and medication usage, dictated the frequency of outpatient visits and lab tests. Over a 24-month period, patients are monitored according to standard of care (biochemical disease activity; endoscopic disease activity) and with mHI scores at both pre-defined time points and patient-initiated moments. These preliminary results focus on assessing the predictive value of the mHI, above a validated cut-off value¹, at baseline for predicting a flare within six months. Sensitivity, specificity, and predictive values are calculated alongside simple logistic regression and Kaplan-Meier analyses.

Results: Out of 319 patients (56.7% Crohn's Disease (CD), median age 43 years, median disease duration 15 years), 89 exhibited biochemical disease activity at baseline and were excluded from the current analysis. Among the 230 patients in remission at baseline, 51 (21.3%) scored above the mHI cut-off point at baseline and 79 (34.3%) experienced a biochemical flare-up within six months of follow-up. The relative risk of experiencing a disease flare in Ulcerative Colitis (UC) patients with a baseline mHI score above the cut-off point was 2.44 ($p=0.04$) with sensitivity of 42.1%, specificity of 82.4%, positive predictive value of 40.0%, and negative predictive value of 83.6%. In CD patients, this relative risk was 1.62 ($p=0.39$) with sensitivity of 38.5%, specificity of 73.4%, positive predictive value of 14.7%, and a negative predictive value of 90.9%. Logistic regression analysis revealed a significant association between a mHI score above the cut-off point and disease flares in UC patients (OR = 3.394, 95% CI: 1.110-10.330, $p=0.03$), whereas in CD patients, such an association was not significant (OR = 1.724, 95% CI: 0.487-5.603, $p=0.37$). Similarly, Kaplan-Meier analysis demonstrated a longer flare-free survival in UC patients with a baseline mHI score below the cut-off point ($p=0.03$), while no significant difference was observed in CD patients ($p=0.14$).

Conclusion: This study indicates that the mHI could be a valuable tool for predicting disease activity, and particularly quiescent disease, in UC patients. However, this predictive capability was not observed in patients with CD. These results underscore the potential utility of mHI in enhancing the management of IBD patients, with implications for personalised care and resource allocation within healthcare systems.

Further research should explore repeated mHI measurements in combination with biomarkers like calprotectin for a more comprehensive approach.

References: ¹Van Deen, W. K., van der Meulen-de, A. E., Parekh, N. K., Kane, E., Zand, A., DiNicola, C. A., ... & Hommes, D. W. (2016). Development and validation of an inflammatory bowel diseases monitoring index for use with mobile health technologies. *Clinical gastroenterology and hepatology*, 14(12), 1742-1750.

²DEARhealth: Software as a medical device using Dynamic & Risk-based care pathways and Smart Decision Support Recommendations. DEARhealth. (n.d.). <https://dearhealth.com/hospital/>

Disclosure: PWJM reports consulting fees from Abbvie and Takeda, and payment for presentations from Galapagos and Takeda. PWV reports consulting fees from Abbvie, Galapagos, BMS, Janssen, Lilly, and Takeda, and payment for presentations from Galapagos and Takeda. AEvdMdJ received research grants from Nestle, Norgine, Cablon, Galapagos, and Zon-Mw, including speaker's fees from, Tramedico, Janssen Pharmaceuticals, Takeda, Galapagos, Vedanta, Ferring, and AbbVie. These are not related to this work. All other authors have no conflicts of interest to declare.

This study has received funding from Galapagos/Alfasigma.

PP0455

WITHDRAWN

PP0456

CLINICAL RECURRENCE AFTER ILEOCOLIC RESECTION FOR CROHN'S DISEASE: INTEREST OF THE REMIND GROUP'S ENDOSCOPIC SCORE

J. Amal¹, N. Abdelwahab¹, B. Sonia¹, M. Ayari², Z. Benzarti¹, N. Hemdani¹, B. Bouchabou¹, J. Mohamed Taieb², R. Ennaifer³, M.H. Dougui²

¹Mongi Slim Hospital University Of Tunis El Manar, Gastroenterology, Tunis, Tunisia, ²Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia, ³Mongi Slim Hospital University Of Tunis El Manar, Hepatology, Tunis, Tunisia

Contact E-Mail Address: amal.jerbi@etudiant-fmt.utm.tn

Introduction: The Rutgeerts score is the most commonly used score for assessing endoscopic recurrence after ileocolic resection in Crohn's disease. However, a significant drawback of this score is that it combines lesions localized to the anastomosis with those in the neo-terminal ileum in the same category, assigning them equal prognostic significance.

Aims & Methods: The aim of this study was to evaluate the performance of the REMIND score in predicting postoperative recurrence of Crohn's disease and compare its performance with the Rutgeerts score.

We conducted a monocentric, retrospective, evaluative study of patients operated for Crohn's disease. All patients had a follow-up colonoscopy within one year of surgery.

The REMIND score was derived from endoscopic details documented in the colonoscopy reports. Clinical relapse was defined by the Crohn's disease related symptoms or complications, such as intra-abdominal collection or occlusion, or subsequent surgery Postoperative. Statistical analysis was performed using SPSS.25 for Windows.

Results: Eighty patients were included, with a mean age of 35.7 years, and a gender ratio H/F=2,2. Median follow-up was 5 years from surgery. Clinical recurrence-free survival was significantly shorter in patients with ileal lesions whatever their severity was I(1,2,3,4)A(x), compared with patients without ileal lesions I(0)A(x): p<0,001 and not significantly different between patients without anastomotic lesions I(x)A(0) and patients with anastomotic lesions whatever their severity was I(x)A(1,2,3): p=0,2.

However, patients with at least semicircumferential anastomotic ulcerations A(2,3) had more anastomotic occlusive complications than patients classified A0 or A1: A0 VS A2 p=0,01 A0 VS A3 p<0,001 A0 VS A1 p=0,9. The I(x) score, compared with the Rutgeerts and A(x) scores, had the best values in terms of discriminative capacity (Area under the curve= 0,83 VS 0,73 VS 0,61), monotonicity (linearity test χ^2 of 26,77 VS 12,36 VS 3,89), and homogeneity (likelihood ratio χ^2 of 33,91 vs 18,45 VS 5,49).

Conclusion: In contrast to the Rutgeerts and A(x) scores, the I(x) score seems to exhibit superior performance in predicting postoperative recurrence. Therefore, the use of a score describing separately ileal and anastomotic lesions might be more appropriate to define postoperative endoscopic recurrence.

References:

Hammoudi N, Auzolle C, Tran Minh ML, Boschetti G, Bezault M, Buisson A, et al. Postoperative endoscopic recurrence on the neoterminal ileum but not on the anastomosis is mainly driving long-term outcomes in crohn's disease. *Am J Gastroenterol*. 2020 Jul;115(7):1084-93.

Disclosure: Nothing to disclose.

PP0457

EPITHELIAL AND NOT LAMINA PROPRIA NEUTROPHIL LOCALIZATION AND INTESTINAL BARRIER PROTEIN EXPRESSION ARE INNOVATIVE OUTCOME PREDICTORS IN INFLAMMATORY BOWEL DISEASE

I. Zammarchi¹, G. Santacroce¹, M. Puga-Tejada^{1,2}, B. Hayes^{3,4}, R. Crotty³, E. O'Driscoll³, S. Majumder¹, W. Kaczmarczyk³, Y. Maeda¹, J. McCarthy⁵, K. Sugrue⁵, C. O'Sullivan⁵, L. Burke^{3,4}, S. Ghosh¹, M. Iacucci¹

¹University College Cork, APC Microbiome Ireland, College of Medicine and Health, Cork, Ireland, ²Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ³Cork University Hospital, Department of Histopathology, Cork, Ireland, ⁴University College Cork, Department of Pathology, Cork, Ireland, ⁵Mercy University Hospital, Department of Gastroenterology, Cork, Ireland

Contact E-Mail Address: irene.zammarchi01@universitadipavia.it

Introduction: Patients with inflammatory bowel disease (IBD) in clinical and endoscopic remission may still experience disease relapse. Therefore, there is an unmet need for reliable predictors of outcomes to enable a personalized therapeutic approach. Recently, a novel histological score has highlighted the pivotal role of neutrophils in predicting disease outcomes in Ulcerative Colitis (UC)¹. Furthermore, the impairment of the intestinal barrier plays a key role in forecasting disease outcomes in UC and Crohn's disease (CD). Hence, this study aims to assess the predictive role of neutrophils according to their tissue localization and intestinal barrier protein expression in IBD patients.

Aims & Methods: IBD patients in clinical remission who underwent colonoscopy between January 2020 and June 2022 at two tertiary referral centres were enrolled. Patients with a Mayo Endoscopic Score ≤ 1 for UC and a Simple endoscopic score of ≤ 6 for CD were included. The histological activity was assessed using the Robarts Histopathology Index, Nancy Histological Index, and PICaSSO Histological Remission Index. Neutrophil localization in the epithelium and lamina propria was carefully evaluated

by experienced pathologists. Additionally, the immunohistochemical expression of barrier proteins, such as Claudin-2 and JAM (junctional adhesion molecule)-A, was assessed to evaluate the integrity of the intestinal barrier.

Results: Out of 60 UC and 76 CD patients, 60% were in histological activity. 25.8% of patients developed an adverse outcome within 12 months. Only neutrophils in the epithelium and not in lamina propria could predict adverse outcomes for UC (HR 5.20, $p=.01$) and CD (HR 4.38, $p=.03$) patients in endoscopic remission.

Moreover, epithelial Claudin-2 expression correlated with endoscopic and histological disease activity and predicted outcomes in UC. Combining neutrophils in the epithelium or Claudin-2 expression significantly predicted outcomes in UC patients (HR 3.23, $p=.035$). Similar results were found for JAM-A in CD despite this protein showing less specificity as a barrier predictor of outcome.

	Ulcerative colitis	Crohn's disease
Neutrophils in epithelium		
Study sample	5.20 (1.46 - 18.46; .01)	1.86 (0.72 - 4.81; .20)
Endoscopic remission	2.5 (0.6 - 11.04; .24)	4.38 (1.16 - 16.55; .03)
Endoscopic mild inflammation	Inf (0 - Inf; .999)	0.32 (0.07 - 1.44; .14)
Neutrophils in lamina propria, not epithelium		
Study sample	3.02 (0.85 - 10.72; .09)	1.59 (0.6 - 4.25; .35)
Endoscopic remission	1.75 (0.39 - 7.83; .46)	4.36 (0.94 - 20.21; .06)
Endoscopic mild inflammation	Inf (0 - Inf; .999)	0.32 (0.07 - 1.44; .14)
Claudin-2 expression		
Study sample	2.12 (1.62 - 43.18; .01)	1.28 (0.001 - 1368.4; .94)
Endoscopic remission	2.08 (0.46 - 9.36; .34)	1.45 (0.44 - 4.76; .54)
Endoscopic mild inflammation	1.07 (0.21 - 5.29; .94)	0.27 (0.06 - 1.36; .11)
JAM-A expression		
Study sample	1.20 (0.44 - 3.32; .72)	3.18 (1.22 - 8.30; .02)
Endoscopic remission	1.32 (0.30 - 5.9; .71)	1.98 (0.58 - 6.78; .27)
Endoscopic mild inflammation	1.16 (0.29 - 4.63; .84)	6.88 (1.23 - 38.43; .03)

Conclusion: This multicentre study highlights the potential role of *epithelial* neutrophil localization and Claudin-2 'leaky gut' protein expression as practical clinical tools for predicting outcomes in IBD and potentially guiding patient-tailored therapy.

References: ¹Gui X et al., *Gut*. 2022;71(5):889-898.

Disclosure: Nothing to disclose.

PP0458

THE URGENCY NUMERIC RATING SCALE: PSYCHOMETRIC EVALUATION IN ADULTS WITH CROHN'S DISEASE

M. Dubinsky¹, A. Vadhariya², S. Su², X. Zhou³, F. Durand², C. Clucas⁴, L. Stassek⁴, A. Kawata⁴, S. Travis⁵

¹Icahn School of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division of Gastroenterology, New York, United States of America,

²Eli Lilly and Company, Indianapolis, United States of America,

³Syneos Health, Morrisville, United States of America, ⁴Evidera, Bethesda, United States of America, ⁵University of Oxford, Kennedy Institute, Translational Gastroenterology Unit and Biomedical Research Centre, Oxford, United Kingdom

Contact E-Mail Address: marla.dubinsky@mssm.edu

Introduction: Bowel urgency is one of the symptoms that patients with Crohn's disease (CD) frequently experience and consider most important to control. Bowel urgency often has a substantial negative impact on quality of life. The Urgency Numeric Rating Scale (NRS) is a single-item patient-reported outcome assessing severity of bowel urgency in the previous 24 hours on an 11-point scale (0–10), with higher scores indicating more severe bowel urgency. The Urgency NRS was initially developed to assess the urgency to have a bowel movement in ulcerative colitis due to

lack of appropriate existing instruments.

Aims & Methods: This work aimed to evaluate the psychometric properties of the Urgency NRS in CD and to estimate thresholds for meaningful change and remission for bowel urgency. Pooled data from VIVID-1 (NCT03926130), a Phase 3, multicentre, randomised, placebo- and active-controlled study of mirikizumab in adults with moderately to severely active CD were analyzed.

The measurement properties (reliability, validity, and responsiveness) of the Urgency NRS were evaluated using weekly average scores at Weeks 0 (Baseline), 4, 12, and 52, which were calculated by averaging the most recent 7 days in the 12 days prior to the visit.

These analyses used other measures administered in VIVID-1, including the Patient Global Rating of Severity (PGRS), Patient Global Impression of Change (PGIC), Inflammatory Bowel Disease Questionnaire (IBDQ), and Crohn's Disease Activity Index (CDAI). PGRS and PGIC were used as primary anchors to establish the Urgency NRS score thresholds for meaningful change and remission of bowel urgency. Data from VIVID-1 treatment arms were pooled for these analyses.

Results: The analysis population comprised 1065 adults (mean age 36.2 years [standard deviation: 13.0]; 55% male, 71% White). The Urgency NRS weekly average score decreased during the trial (from 6.6 at Baseline to 2.9 at Week 52), indicating a reduction in bowel urgency severity. Test-retest reliability was good for patients who were stable between Baseline and Week 4 based on the PGRS (intraclass correlation coefficient [ICC] 0.86) and the PGIC (ICC 0.78).

At Weeks 12 and 52, the Urgency NRS showed moderate correlations ($0.30 \leq r < 0.70$) with the PGRS, IBDQ Bowel Symptom domain, IBDQ total score, and CDAI score; as expected, correlations with clinical and laboratory assessments were weak ($r < 0.30$), demonstrating discriminant validity. The Urgency NRS could differentiate between groups of participants known to be distinct based on PGRS and IBDQ Bowel Symptom domain scores.

Improvement in the Urgency NRS average score from Baseline to Weeks 12 and 52 was statistically significantly different between most PGRS change groups and PGIC groups, as well as groups based on IBDQ Bowel Symptom domain, IBDQ response and remission, and clinical response/remission by CDAI, indicating that the Urgency NRS was able to detect change. Anchor-based analysis indicated that clinically meaningful improvement could be represented by a 3–5-point reduction in the Urgency NRS score and that an Urgency NRS score of ≤ 2 could represent bowel urgency remission.

Conclusion: These results support the reliability, validity, responsiveness of the Urgency NRS and provide definitions of clinically meaningful improvement (reduction of 3–5 points in the Urgency NRS score) and remission of bowel urgency (Urgency NRS score of ≤ 2) in adults with moderately to severely active CD. These findings confirm the Urgency NRS as suitable for assessing treatment benefits in patients with CD during clinical trials.

Disclosure: MD reports being a consultant for AbbVie, Arena, BMS, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Gilead, Janssen, Merck, Pfizer, Prometheus Laboratories, Takeda, and UCB; and received research grants from Janssen, AbbVie, and Prometheus Laboratories. AV, SS, and FD are employees and shareholders of Eli Lilly and Company. XZ is an employee of Syneos Health, which received funding from Eli Lilly and Company in connection with this study. CC, LS, and AK are employees of Evidera, which received funding from Eli Lilly and Company in connection with this study. ST has received grants from AbbVie, BUHLMANN Diagnostics, ECCO, Eli Lilly and Company, Ferring Pharmaceuticals, International Organization for the Study of Inflammatory Bowel Disease, Janssen, Merck Sharp & Dohme, Norman Collison Foundation, Pfizer, Procter & Gamble, Schering-Plough, Takeda, UCB Pharma, Vifor Pharma, and Warner Chilcott; and reports other disclosures from Abacus Pharma, AbbVie, Actial

Farmaceutica, ai4gi, Alcimed, Allergan, Amgen, Aptel, Arena Pharmaceuticals, Asahi Kasei Pharma, Aspen Pharmacare, Astellas, AstraZeneca, Atlantic Pharmaceuticals, Barco, Biocare Medical, Biogen, BL Pharma, Boehringer Ingelheim, Bristol Myers Squibb, BUHLMANN Diagnostics, Calcico Therapeutics, Celgene, Cellerix, Cerimon Pharmaceuticals, ChemoCentryx, Chiesi, Cisbio, Comcast, Coronado Biosciences, Cosmo Pharmaceuticals, Dr. Falk Pharma, Ducentis BioTherapeutics, Dynavax Technologies, Elan Pharma, Eli Lilly and Company, Enterome, Equillium, Ferring Pharmaceuticals, Galapagos NV, Genentech/Roche, Genzyme, Gilead Sciences, GlaxoSmithKline, Glenmark Pharmaceuticals, Grünenthal, GW Pharmaceuticals, Immunocore, Indigo Biosciences, Janssen, Lexicon Pharmaceuticals, Medarex, MedTriX, Merck, Merrimack Pharmaceuticals, Mestag Therapeutics, Millennium Pharmaceuticals, Neovacs, Novartis, Novo Nordisk, NPS Pharmaceuticals/Nycomed, Ocera Therapeutics, OPTIMA Pharma, Origin Pharma, Otsuka, Palau Pharma, Pentax Medical, Pfizer, PharmaVentures, Phesi, Phillips Pharma Group, Procter & Gamble, Pronota, Proximagen, Resolute Pharma, Robarts Clinical Trials, Sandoz, Santarus, Satisfai Health, Sensyne Health, Shire, Sigmoid Pharma, Sorriso Pharmaceuticals, Souffinez, SynDermix, Synthon, Takeda, Theravance Biopharma, TiGenix, Tillotts Pharma AG, Topivert, Trino Therapeutics with Wellcome Trust, TxCell SA, UCB Pharma, Vertex Pharma, VHSquared, Vifor Pharma, Warner Chilcott, and Zeria Pharmaceutical.

PP0459

A PATIENT-REPORTED OUTCOME MEASURE COMPRISING THE STOOL FREQUENCY AND ABDOMINAL PAIN ITEMS FROM THE CROHN'S DISEASE ACTIVITY INDEX: PSYCHOMETRIC EVALUATION IN ADULTS WITH CROHN'S DISEASE

S. Schreiber¹, A. Vadhariya², S. Su², X. Zhou³, F. Durand², A. Kawata⁴, L. Stassek⁴, C. Clucas⁴, J. Lewis⁵

¹University Hospital Schleswig-Holstein, Christian-Albrechts-University, Department of Internal Medicine I, Kiel, Germany, ²Eli Lilly and Company, Indianapolis, United States of America, ³Syneos Health, Morrisville, United States of America, ⁴Evidera, Bethesda, United States of America, ⁵University of Pennsylvania, Division of Gastroenterology and Hepatology, Philadelphia, United States of America

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: The Crohn's Disease Activity Index (CDAI) is an 8-item disease activity measure with three patient-reported items that cover stool frequency, presence of abdominal pain, and patient's general well-being. Absolute scores of the Stool Frequency (SF) and Abdominal Pain (AP) items, together referred to as the Patient Reported Outcome (PRO), have been used separately in the VIVID-1 study.

Both PRO items have recall periods of 24 hours; the SF item measures the number of liquid or very soft stools per day and the AP item measures abdominal pain severity on a 4-point scale (0=none, 1=mild, 2=moderate, and 3=severe).

Aims & Methods: This study aimed to evaluate the measurement properties of the SF and AP items and estimate thresholds for remission. Pooled data from VIVID-1 (NCT03926130), a Phase 3, multicentre, randomized, placebo- and active-controlled study of mirikizumab in adults with moderately to severely active Crohn's Disease (CD) were analysed.

The measurement properties (reliability, validity, and responsiveness) of the PRO items were evaluated separately using average weekly scores of the SF and AP items at Weeks 0 (Baseline), 4, 12, and 52. Patient Global Rating of Severity (PGRS) and Patient Global Impression of Change (PGIC) were used as primary anchors to estimate the remission thresholds. Exit interviews were conducted in a subgroup of participants to support the

remission thresholds.

Results: Data from 1065 participants (mean age: 36.2 years [standard deviation: 13.0], 55% males, 71% White) were analysed. During the trial, average weekly scores decreased for both items: SF from 5.7 (Baseline) to 1.9 (Week 52) and AP from 2.1 (Baseline) to 0.8 (Week 52). Both PRO items demonstrated moderate to good test-retest reliability for participants who were stable between Baseline and Week 4 based on PGRS (intraclass correlation coefficient [ICC] 0.85 for SF and 0.82 for AP) and PGIC (ICC 0.79 for SF and 0.69 for AP). SF had moderate ($0.30 \leq r < 0.70$) correlations with Inflammatory Bowel Disease Questionnaire (IBDQ) item 1–stool frequency (Baseline and Weeks 12 and 52) as well as with IBDQ total score, IBDQ Bowel Symptoms domain score, and PGRS (Weeks 12 and 52 only). AP had moderate to large correlations ($0.30 \leq r \leq 0.90$) with PGRS, IBDQ total score, IBDQ item 13–abdominal pain, 36-item Short Form Health Survey (SF-36) Bodily Pain domain, and EQ-5D-5L Pain/Discomfort (Baseline and Weeks 12 and 52).

As anticipated, both PRO items had weak correlations ($r < 0.30$) with the Simple Endoscopic Score for Crohn's Disease (SES-CD), demonstrating discriminant validity. The PRO items could differentiate between groups of participants known to be distinct based on PGRS (for SF and AP), IBDQ Bowel Symptom domain score (for SF), and EQ-5D-5L Pain/Discomfort (for AP).

The PRO items were able to detect change, as score changes in both items between Baseline and Weeks 12 and 52 were statistically significantly different between most PGRS change groups and PGIC groups. Anchor-based analyses combined with results from the exit interviews suggested that an SF score of ≤ 3 and an AP score of ≤ 1 could represent remission.

Conclusion: These psychometric evaluation results support the reliability, construct-validity, and responsiveness of the PRO items when administered to adults with moderately to severely active CD. A combination of an SF score of ≤ 3 and an AP score of ≤ 1 could represent clinical remission by PRO.

Disclosure: SS has been a consultant for AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Dr Falk Pharma, Ferring, Fresenius, Galapagos, Genentech, GSK, Gilead, I-MAB Biopharma, Janssen, Eli Lilly and Company, Merck, Novartis-Sandoz, Pfizer, Protagonist, Takeda, and Theravance. AV, SS, and FD are employees and shareholders of Eli Lilly and Company. XZ is an employee of Syneos Health, which received funding from Eli Lilly and Company in connection with this study. AK, LS, and CC are employees of Evidera, which received funding from Eli Lilly and Company in connection with this study. JL has received personal fees from Johnson & Johnson Consumer Inc; grants, personal fees, and other from Takeda Pharmaceuticals and Pfizer; personal fees and nonfinancial support from AbbVie; grants and personal fees from Janssen Pharmaceuticals, Nestle Health Science; personal fees from Eli Lilly and Company, Samsung Bioepis, UCB, Bristol-Myers Squibb, Bridge Biotherapeutics, Celgene, Merck, Gilead, Arena Pharmaceuticals, and Protagonist Therapeutics.

PP0460

PSYCHOMETRIC EVALUATION OF THE FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY-FATIGUE IN ADULTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE

V. Jairath¹, S. Su², A. Vadharaya², X. Zhou³, F. Durand², L. Stassek⁴, A. Kawata⁴, C. Clucas⁴, M. Regueiro⁵

¹Western University, Division of Gastroenterology, Department of Medicine, London, Canada, ²Eli Lilly and Company, Indianapolis, United States of America, ³Syneos Health, Morrisville, United States of America, ⁴Evidera, Bethesda, United States of America, ⁵Cleveland Clinic, Department of Gastroenterology, Hepatology and Nutrition, Cleveland, United States of America

Contact E-Mail Address: vjairath@uwo.ca

Introduction: In Crohn's disease (CD), fatigue is a common symptom that affects ~40% of patients [1] and often has a major impact on their quality of life. The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) is a 13-item patient-reported outcome assessing fatigue over the previous week on a 5-point scale. In the FACIT-Fatigue, scores for all items are summed to give a total score between 0 and 52, with a higher score indicating less fatigue. The psychometric properties of the FACIT-Fatigue have been assessed in multiple chronic illnesses, including CD.

Aims & Methods: The objective of this study was to provide further evidence on the measurement properties of the FACIT-Fatigue and to determine thresholds for meaningful improvement in fatigue for patients with moderately to severely active CD. Pooled data from VIVID-1 (NCT03926130), a Phase 3, multicentre, randomised, placebo- and active-controlled study of mirikizumab in adults with moderately to severely active CD were analysed. The measurement properties (reliability, validity, and responsiveness) of the FACIT-Fatigue were evaluated at Weeks 0 (Baseline), 12, and 52. Other assessments completed in the trial were used for these analyses, including the Patient Global Rating of Severity (PGRS), Patient Global Impression of Change (PGIC), Inflammatory Bowel Disease Questionnaire (IBDQ), Crohn's Disease Activity Index (CDAI), and 36-Item Short Form Health Survey (SF-36). PGRS and PGIC were used as primary anchors to estimate the FACIT-Fatigue total score change that would constitute meaningful improvement.

Results: Analyses included 1065 adults (mean age 36.2 years [standard deviation: 13.0], 55% males, 71% White). The mean FACIT-Fatigue total score improved during the study (Baseline: 31.5; Week 12: 37.1; Week 52: 40.0). The measure demonstrated internal consistency across visits (Cronbach's alpha: 0.92–0.94); correlations between individual items and the total score were moderate ($0.30 \leq r < 0.70$) to large ($r \geq 0.70$). Across visits, the FACIT-Fatigue total score showed moderate to large correlations with the PGRS; IBDQ Bowel Function domain, item 2 (fatigue), and total score; CDAI score; and SF-36 Vitality domain score. However, correlations with clinical measures were weak ($r < 0.30$), demonstrating discriminant validity. The FACIT-Fatigue could differentiate between groups of participants known to be distinct based on the PGRS, IBDQ total score, and IBDQ item 2. The FACIT-Fatigue was able to detect change, as FACIT-Fatigue total score improvements from Baseline to Weeks 12 and 52 were statistically significantly different between most PGRS change groups and PGIC groups, as well as between groups based on IBDQ response/remission, IBDQ item 2, SF-36 Vitality domain, and clinical response/remission by CDAI. Anchor-based analyses suggested that a 6–9-point increase in the FACIT-Fatigue total score could represent meaningful improvement.

Conclusion: These findings expand on previous research supporting the internal consistency, reliability, construct validity, and responsiveness of the FACIT-Fatigue. Analyses suggest an improvement range of 6–9 points for FACIT-Fatigue as clinically meaningful in the VIVID-1 trial population of adults with moderately to severely active CD.

References: [1] D'Silva A, Fox DE, Nasser Y, Vallance JK, Quinn RR, Ronksley PE, Raman M. Prevalence and risk factors for fatigue in adults with inflammatory bowel disease: A systematic review with meta-analysis. *Clin Gastroenterol Hepatol.* 2022 May;20(5):995-1009.e7. doi: 10.1016/j.cgh.2021.06.034. Epub 2021 Jun 30. PMID: 34216824.

Disclosure: VJ has received fees or grant and/or research support and/or served as a consultant and/or speaker for AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Flagship Pioneering, Fresenius Kabi, Galapagos NV, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Metacrine, Mylan, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Sorriso Pharmaceuticals, Takeda, Teva, Topivert, Ventyx Biosciences, and Vividion Therapeutics. SS, AV, and FD are employees and shareholders of Eli Lilly and Company. XZ is an employee of Syneos Health, which received funding from Eli Lilly and Company in connection with this study. LS, AK, and CC are employees of Evidera, which received funding from Eli Lilly and Company in connection with this study. MR serves on advisory boards for AbbVie, Janssen, UCB, Takeda, Pfizer, BMS, Organon, Amgen, Genentech, Gilead, Salix, Prometheus, Eli Lilly and Company, TARGET Pharma Solutions, and Trellus.

PP0461

CLINICAL USEFULNESS OF IMMUNE PROFILING FOR DIFFERENTIAL DIAGNOSIS BETWEEN CROHN'S DISEASE, INTESTINAL TUBERCULOSIS, AND BEHCET'S DISEASE

J.S. Soh¹

¹University of Hallym College of Medicine, Department of Internal Medicine, Anyang, South Korea

Contact E-Mail Address: jssoh@hanmail.net

Introduction: It is important to make a differential diagnosis between inflammatory diseases of the bowel with similar clinical and endoscopic features. Misdiagnosis or delayed diagnosis can affect patients' therapeutic outcomes and prognosis. The profiling of immune cells is helpful for accurately diagnosing inflammatory diseases.

Furthermore, evaluating differences of immune marker expression between Crohn's disease (CD), intestinal Behcet's disease (BD), and intestinal tuberculosis (TB) could be useful in differentiating the diseases.

Aims & Methods: This study aimed to compare the expression levels of immune markers between CD, intestinal BD, and intestinal TB and evaluate the usefulness of immune profiling in differential diagnoses using this advanced imaging system. Biopsy specimens were acquired around ulcerations on the terminal ileum or cecum from five patients with each disease.

Panel 1 included multiplexed immunohistochemistry staining for CD8, CD4, Foxp3, CD20, programmed death-1, and granzyme B. CD56, CD68, CD163, CD11c, and HLA-DR were analyzed in panel 2. Cell density was used to compare the expression levels of immune cells.

Results: The expression of immune cells in panel 1 was not different between diseases. Differences in cytotoxic T cells, helper T cells, and regulatory T cells identified by the double-positivity method were also not significant. However, the expression of CD68⁺ cells in panel 2 was the highest in intestinal BD among bowel diseases (Table 1).

In the co-expression method, the expression levels of M1 macrophages (CD56⁺CD68⁺CD163⁺HLA-DR⁺) and dendritic cells (CD56⁺CD68⁺CD163⁺CD11c⁺HLA-DR⁺) were significantly different ($P = 0.001$, $P = 0.012$, respectively).

	Crohn's disease	Intestinal Behcet's disease	Intestinal tuberculosis	p-value
CD56 ⁺ , median cells/mm ² (range)	199 (63-263)	75 (44-335)	160 (14-602)	0.582
CD68 ⁺ , median cells/mm ² (range)	530 (508-840)	1828 (1648-3366)	1224 (508-1404)	<0.001
CD163 ⁺ , median cells/mm ² (range)	63 (17-228)	154 (89-408)	114 (69-167)	0.165
CD11c ⁺ , median cells/mm ² (range)	362 (20-1160)	19 (0-616)	304 (36-649)	0.252
HLA-DR ⁺ , median cells/mm ² (range)	258 (193-451)	152 (3-640)	890 (168-1147)	0.208

Table 1. Comparison of immune cell densities in panel 2 between Crohn's disease, intestinal Behcet's disease, and intestinal tuberculosis.

Conclusion: The expression of immune cells, including M1 macrophages and dendritic cells, was different between CD, intestinal BD, and intestinal TB. Immune profiling can be helpful for differential diagnoses of inflammatory bowel diseases.

References:

1. de Souza, H. S.; Fiocchi, C. Immunopathogenesis of IBD: current state of the art. *Nat Rev Gastroenterol Hepatol* 2016, 13 (1), 13-27.
2. Lee, S. H.; Kwon, J. E.; Cho, M. L. Immunological pathogenesis of inflammatory bowel disease. *Intest Res* 2018, 16 (1), 26-42.
3. Tiwari, V.; Kedia, S.; Garg, S. K.; Rampal, R.; Mouli, V. P.; Purwar, A.; Mitra, D. K.; Das, P.; Dattagupta, S.; Makharia, G.; et al. CD4⁺ CD25⁺ FOXP3⁺ T cell frequency in the peripheral blood is a biomarker that distinguishes intestinal tuberculosis from Crohn's disease. *PLoS One* 2018, 13 (2), e0193433.
4. Soh, J. S.; Jo, S. I.; Lee, H.; Do, E. J.; Hwang, S. W.; Park, S. H.; Ye, B. D.; Byeon, J. S.; Yang, S. K.; Kim, J. H.; et al. Immunoprofiling of Colitis-associated and Sporadic Colorectal Cancer and its Clinical Significance. *Sci Rep* 2019, 9 (1), 6833.
5. Limsrivilai, J.; Shreiner, A. B.; Pongpaibul, A.; Laohapand, C.; Boonanutwat, R.; Pausawasdi, N.; Pongprasobchai, S.; Manatsathit, S.; Higgins, P. D. Meta-Analytic Bayesian Model For Differentiating Intestinal Tuberculosis from Crohn's Disease. *Am J Gastroenterol* 2017, 112 (3), 415-427.

Disclosure: Nothing to disclose.

PP0462

USEFULNESS OF NOVEL IMAGE-ENHANCED ENDOSCOPY FOR PREDICTING MAINTENANCE OF CLINICAL REMISSION IN ULCERATIVE COLITIS

Y. Mamiya¹, T. Taida¹, Y. Ozeki¹, Y. Koshibu¹, N. Shu¹, M. Furuya¹, Y. Oyama¹, H. Nakazawa¹, R. Horio¹, S. Takahashi¹, A. Kurosugi¹, M. Sonoda¹, T. Kaneko¹, T. Ishikawa¹, Y. Ohta¹, K. Okimoto¹, T. Matsumura¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Gastroenterology, Chiba, Japan

Contact E-Mail Address: yukiyo0311@icloud.com

Introduction: Clinical remission and mucosal healing have been advocated as treatment goals for patients with ulcerative colitis (UC). Novel molecularly targeted drugs for the treatment of UC have enabled to target not only clinical remission but also endoscopic remission and even histologic remission.

Recently, the usefulness of novel image enhanced endoscopy (IEE) such as texture and color enhancement imaging (TXI) and red dichromatic imaging (RDI) have been reported in endoscopic evaluation of UC. We aimed to verify the usefulness of the novel IEE in prediction of maintenance of clinical remission in UC patients.

Aims & Methods: Patients with UC in clinical remission who underwent colonoscopy with IEE from March 2021 to December 2023 at our hospital were enrolled in this prospective study.

Disease activities in six segments (cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum) were assessed using white-light imaging (WLI), TXI and RDI. Endoscopic evaluation of disease activity using WLI was performed using Mayo endoscopic score (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). IEE evaluation was performed using predefined TXI score (0-2: 2 indicates maximum severity) and RDI score (1-4: 4 indicates maximum severity) for UC. MES of ≤1 and UCEIS of ≤1 were defined as endoscopic remission. With IEE, TXI score 0-1 and RDI score 1 were defined as endoscopic remission in accordance with previous reports.

We evaluated the correlation of those scores by Spearman's rank correlation coefficient. Moreover, relationships between endoscopic remission of WLI, TXI and RDI, and maintenance of clinical remission were evaluated by Kaplan-Meier analysis. Relapse was defined as worsening of clinical symptoms that required additional medical therapies for UC.

Results: Total 117 patients with UC were enrolled. Of these, 17 were excluded because adequate images could not be obtained. Therefore, total 100 patients were assessed. The median MES, UCEIS, TXI, and RDI scores were 1 (range 0-3), 1 (range 0-5), 2 (range 1-3) and 2 (range 1-4), respectively. The average follow-up period was 10.1 months, and 8 cases showed clinical relapse during the observation period.

Evaluation of endoscopic images at each colonic site revealed that UCEIS (P<0.001), TXI score (P<0.001), and RDI score (P<0.001) were significantly associated with MES, respectively. In addition, scores at the most inflamed area showed a positive correlation between MES and UCEIS (r=0.91, P<0.001), MES and TXI (r=0.73, P<0.001), and MES and RDI (r=0.77, P<0.001).

In Kaplan-Meier analysis, MES remission (log-rank, P=0.245), UCEIS remission (log-rank, P=0.701), and RDI remission (log-rank, P=0.827) were not significantly associated with subsequent maintenance of clinical remission. On the other hand, TXI remission (log-rank, P=0.045) was significantly associated with subsequent maintenance of clinical remission.

Conclusion: TXI score and RDI score were significantly associated with existing endoscopic score. In particular, TXI remission was significantly associated with subsequent maintenance of clinical remission. Novel IEE may be useful option in prediction of maintenance of remission in UC patients.

Disclosure: Nothing to disclose.

PP0463

PREVALENCE OF SARCOPENIA IN A COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE: OBSERVATIONAL STUDY IN A TERTIARY CARE CENTRE

C.M. Palmisano¹, P. Dell'Aquila², S. Cormio², A.V. Borraccino², F. Savino², D. Forastiere², F. Squeo², D. Novielli², A. Di Lorenzo³, A. Moschetta¹, A. Di Leo², M.R.D. Principi²

¹Internal Medicine Unit "C. Frugoni", Department of Interdisciplinary Medicine, University of Bari "Aldo Moro", Bari, Italy, ²Section of Gastroenterology, DiMePre-J, University of Bari "Aldo Moro", Bari, Italy, ³Hygiene Unit - Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", Bari, Italy

Contact E-Mail Address: chiarapalmi8@gmail.com

Introduction: Malnutrition is a common condition of patients with inflammatory bowel disease (IBD) and could be associated with sarcopenia i.e. a reduced muscle mass and strength. Recent data suggest that the prevalence of sarcopenia is, respectively, 52% and 37% in Crohn's disease (CD) and ulcerative colitis (UC). It is well demonstrated that sarcopenic IBD patients have two to three times higher risk of lost of response to biotechnology drugs than non-sarcopenic patients.

Aims & Methods: Consecutive IBD patients accessing the IBD outpatient service were enrolled. Detailed data regarding the characteristics of MC and CU populations, current therapy and disease activity are reported. Each patient was interviewed about the frequency (none, low, high) and the kind (aerobic or anaerobic) of the physical activity they were practicing.

At the enrolment, nutritional assessments were performed by body mass index (BMI) evaluation according with the World Health Organization recommendations, global subjective assessment by the MUST (Malnutrition Universal Screening Tool) index according with the European Society for Clinical Nutrition and Metabolism and the Global Leadership Initiative on Malnutrition [GLIM]. Moreover, the SARC-F questionnaire, recommended by the scientific consensus EWGSOP 2 to identify individuals at risk for sarcopenia was administered. A SARC-F value ≥ 4 was significant of sarcopenia. Finally, the quality of life was assessed using the inflammatory bowel disease questionnaire (IBDQ). Univariate and multivariate analysis was conducted between BMI, MUST, SARC-F and IBDQ values and patient characteristics (age, current therapy, disease activity and physical activity).

Results: A total of 321 IBD patients (158 CD and 163 UC), 56.07% male, with a mean age of 44.78 years were enrolled. Sixty-seven patients (20.87%) reported a current smoking habit. A mean BMI of 70.37 kg, was calculated. Regarding malnutrition, 199 patients (61.99%) were considered at low risk (MUST=0), 75 subjects (23.36%) at medium risk (MUST=1), 47 (14.64%) at high risk (MUST ≥ 2). A SARC-F value ≥ 4 was evaluated in 50 patients (15.58%). A reduction in quality of life, understood as IBDQ < 209, was found in 45 (14.02%) patients. Females and males presented a significantly different prevalence of sarcopenia (χ^2 : 9.69; p-value: 0.002). Univariate analysis shows a significant protective role of male sex (OR vs. female sex: 0.33; p-value: 0.018) in the risk of sarcopenia; older subjects had a slightly higher sarcopenic risk (OR: 1.04; p-value < 0.001). The risk was associated with corticosteroid therapy (OR 1.03, p-value < 0.001), with increasing MUST (OR 1.65, p-value < 0.001) and with the IBDQ decreases (OR 2.1; p-value < 0.001).

Multivariate analysis confirmed an higher incidence of sarcopenia in female subjects of advanced age with active-stage disease (R^2 : 0.88, p-value < 0.0001), furthermore female patients with active-stage disease who did not engage in physical activity had a greater impairment in quality of life, regardless of age (R^2 : 0.75, p-value < 0.0001). Aerobic and anaerobic physical activity played a protective role in the onset of sarcopenia regardless of sex and age (R^2 : 0.82, p-value < 0.0001).

Conclusion: In our cohort of patients, sarcopenia was present in only 18.94%. Male sex was found to be a protective factor for sarcopenia. Disease status is firmly linked to the risk of sarcopenia. Regular physical activity has been shown to have a protective role for good quality of life and it was related with a lower risk of sarcopenia. This study will continue to expand the cohort taken into account.

Disclosure: Nothing to disclose.

PP0464

TRANSMURAL HEALING ON INTESTINAL ULTRASOUND IS ASSOCIATED WITH IMPROVED LONG TERM OUTCOMES IN ULCERATIVE COLITIS

C.T. Lim^{1,2}, C. Teichert¹, M. Pruijt¹, F. de Voogd¹, G.R. D'Haens¹, K.B. Gecse¹

¹Amsterdam University Medical Centre, Amsterdam, Netherlands,

²Singapore General Hospital, Singapore, Singapore

Contact E-Mail Address: thomson.lim.c.t@singhealth.com.sg

Introduction: Recently, endoscopic healing (EH) has been recognized as a long term treatment goal for ulcerative colitis (UC)¹. It has been demonstrated that UC does not often remain limited to the mucosa but affects all layers of the bowel². Intestinal ultrasound (IUS) is a useful tool to assess transmural disease in UC³.

Aims & Methods: We performed a retrospective study on UC patients in remission and on stable maintenance treatment with EH (endoscopic Mayo score of ≤ 1) who had an IUS performed between 2 weeks before and 6 months after endoscopic evaluation and had clinical follow up data available for at least 6 months. Patients were identified from 4 prospective cohorts (January 1, 2017 up till December 31, 2023). Clinical follow up data were analysed from date of endoscopy till December 31, 2023.

Transmural healing (TH) measured with IUS was defined as bowel wall thickness (BWT) ≤ 3 mm and modified Limberg Doppler score of ≤ 1 on all colonic segments except for rectum. Histology data (healing defined as absence of granulocytes) was also obtained.

Primary outcome was occurrence of any UC related event: documented relapse, initiation of corticosteroids, intensification/change of medical therapy, hospitalization and/or surgery. Patients were censored at first event and time to event analyses with Cox regression was used to determine the association between TH, EH, histological healing and UC related event.

Characteristic	Transmural Healing (n=30)	Non Transmural Healing (n=18)	Overall (n=48)	p value
Gender (male, %)	15 (50.0)	8 (44.4)	23 (47.9)	0.71
Duration of disease (years, median, IQR)	8.6 (3.2, 11.7)	7.6 (4.1, 16.7)	7.9 (3.6, 17.1)	0.77
Age at baseline (years, median, IQR)	33 (27, 46)	42 (27, 55)	38 (27, 50)	0.37
C-Reactive Protein (mg/L, median, IQR)	0.6 (0.3, 0.9)	1.3 (0.4, 4.4)	0.7 (0.3, 9.0)	0.22
Number of prior biologics used (%)				
0	12 (40.0)	1 (0)	13 (27.1)	0.09
1	8 (26.7)	9 (50.0)	17 (35.4)	
2	5 (16.7)	5 (27.8)	10 (20.1)	
≥ 3	5 (16.7)	3 (16.7)	8 (16.7)	
Previous anti-TNF use (%)				
Yes	16 (53.3)	14 (77.8)	30 (62.5)	0.09
No	14 (46.7)	4 (22.2)	18 (37.5)	
Current Medications (%)				
5-Aminosalicylate				0.88
Thiopurines / Methotrexate	7 (23.3)	5 (27.8)	12 (25.0)	
Anti-TNF (Infliximab / Adalimumab)	2 (6.7)	1 (5.6)	3 (6.3)	
Vedolizumab	7 (23.3)	4 (22.2)	11 (22.9)	
Ustekinumab	7 (23.3)	0 (0)	7 (14.6)	
Jak Inhibitors	0 (0)	2 (11.1)	2 (4.2)	
UC Extent (Montreal classification) (%)				
E1 Ulcerative proctitis	13 (43.3)	11 (61.1)	24 (50.0)	0.82
E2 Left-sided UC	2 (6.7)	2 (11.1)	4 (8.3)	
E3 Pancolitis	12 (40.0)	6 (33.3)	18 (37.5)	
Endoscopic Mayo Score (%)				
0	16 (53.3)	10 (55.6)	26 (54.2)	0.64
1	12 (40.0)	6 (33.3)	18 (37.5)	
	18 (60.0)	12 (66.7)	30 (62.5)	

Table 1.

Results: There were 48 patients available for the current analysis. Baseline characteristics are shown in Table 1. The mean duration of follow up was 38.1±13.1 months. Primary outcome occurred in 18/48 patients (37.5%; TH=5, no TH=13). All patients had a clinical relapse as the first UC related event. Subsequently, 4 patients were initiated with corticosteroids, 13 patients had intensification/change of medical therapy and 1 patient had a colectomy. The mean time to event was numerically shorter in patients without TH than in those with TH (67.9±46.4 weeks vs 92.4±61.2 weeks; $p=0.370$)

Univariate Cox regression showed that TH (HR 0.17, 95% CI 0.06-0.48), endoscopic Mayo score of 0 (HR 0.52, 95% CI 0.18-1.48) and histological healing ($n = 31$, HR 0.96, 95% CI 0.26-3.59) were associated with absence of UC related event. However, in multivariate analysis adjusting for age, gender, duration of disease and number of previous biologics and anti-TNF exposure, only TH remained a significant factor ($p=0.025$) associated with event-free long term outcome. Similar results were observed in analysis involving BWT ≤ 3 mm with modified Limberg Doppler score 0.

Conclusion: TH is an independent predictor of favorable long-term outcome for UC patients with EH. This novel finding is currently undergoing validation in larger cohorts.

References: 1. Turner, Dan et al. "STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD." *Gastroenterology* vol. 160,5 (2021): 1570-1583. doi:10.1053/j.gastro.2020.12.031

2. Maaser, Christian et al. "Intestinal ultrasound for monitoring therapeutic response in patients with ulcerative colitis: results from the TRUST&UC study." *Gut* vol. 69,9 (2020): 1629-1636. doi:10.1136/gutjnl-2019-319451

3. Ilvemark, Johan F K F et al. "Defining Transabdominal Intestinal Ultrasound Treatment Response and Remission in Inflammatory Bowel Disease: Systematic Review and Expert Consensus Statement." *Journal of Crohn's & colitis* vol. 16,4 (2022): 554-580. doi:10.1093/ecco-jcc/jjab173

Disclosure: Chong-Teik Lim: None.

Christoph Teichert: None.

Maarten Pruijt: None.

Floris de Voogd: received speaker or honoraria fees from AbbVie, Janssen, Galapagos, Pfizer and Takeda.

Geert D'Haens: received research grants from Abbvie, Alimentiv, BMS, J&J, Pfizer, Takeda; consulting fees from Abbvie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom Biosciences, Galapagos, Index Pharmaceuticals, Kaleido, Glaxo Smith Kline, Gossamerbio, Pfizer, Immunic, Johnson and Johnson, Polpharma, Proclis Diagnostics, Prometheus laboratories, Prometheus Biosciences, Progenity, Protagonist, and Ventyx; speaker's fees from Abbvie, Arena, Boehringer Ingelheim, Celltrion, Galapagos, Gilead, Pfizer, BMS, and Takeda; data monitoring board: Galapagos, AstraZeneca, Seres Health.

Krisztina Gecse: received grants from Pfizer Inc, Celltrion, and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, ImmunicTherapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis, and Takeda; and speaker's honoraria from Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda, and Tillotts.

PP0465

ANTI-INTEGRIN $\alpha\text{V}\beta 6$ AUTOANTIBODIES PREDICT RESPONSE TO ADVANCED THERAPY IN ULCERATIVE COLITIS

S. Shibui¹, K. Asonuma², S. Kuronuma³, A. Nogami², M. Komatsu², K. Serizawa², S. Umeda², S. Sagami¹, G. Berman⁴, O. Takeuchi³, M. Nakano², T. Hibi¹, N. Maharshak⁴, T. Kobayashi¹

¹Kitasato University Kitasato Institute Hospital, Center for Advanced IBD Research and Treatment, Tokyo, Japan, ²Kitasato University Kitasato Institute Hospital, Department of Gastroenterology, Tokyo, Japan, ³Kitasato University Kitasato Institute Hospital, Department of Research, Tokyo, Japan, ⁴Tel Aviv Medical Center, Department of Gastroenterology and Liver Diseases, affiliated to the Faculty of Medicine and Health Sciences, Tel Aviv University, Tel Aviv, Israel

Contact E-Mail Address: s_shunsuke1116@yahoo.co.jp

Introduction: Precision medicine relies on accurate prediction of treatment response. Anti-integrin $\alpha\text{V}\beta 6$ autoantibodies serve as a serum diagnostic biomarker for ulcerative colitis (UC) and associated with adverse UC-related outcomes.¹

Aims & Methods: We aimed to investigate the association between anti- $\alpha\text{V}\beta 6$ autoantibody titers and treatment outcomes of advanced therapies. This study was conducted as a part of the prospective biobank in two centers in Japan and Israel. Patients with active UC who received advanced therapies between June 2017 and February 2023 were prospectively included and followed up for 1 year.

The primary and secondary outcomes were treatment persistence rate for 1 year and clinical remission rate at week 6 in the anti- $\alpha\text{V}\beta 6$ autoantibody low-titer versus high-titer groups, respectively. Treatment persistency was defined as continuation without switching to another advanced therapy or UC-related surgery, and clinical remission was defined as a two-item patient-reported outcome of ≤ 1 (rectal bleeding = 0 and stool frequency ≤ 1).

The cumulative treatment persistence rate was analyzed using the log-rank test. Cox proportional hazards models adjusted for confounders were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for treatment persistence.

Week 6 remission rate was presented as numbers (%) and differences were analyzed using the Chi square test. Logistic regression models adjusted for confounders were used to estimate odds ratios (ORs) and 95% CIs for Week 6 remission.

Results: A total of 102 patients were enrolled in the cohort (median age, 41 years; male, 55.9%; median disease duration, 78.5 months; proctitis, 1%, left-sided colitis, 12.7%, extensive colitis, 86.3%; prior use of advanced therapies, 56.9%, median modified Mayo score, 7). The median observation period was 10 months (interquartile range [IQR]: 2-12 months), with treatment discontinuation occurring in 49 (48.0%) patients.

The cumulative treatment persistence rate was significantly lower in the high-titer (>128 U/mL) compared to the low-titer (≤ 128 U/mL) group ($p = 0.03$).

Multivariate Cox proportional hazards model analysis indicated that anti- $\alpha\text{V}\beta 6$ autoantibodies were the sole independent predictor of treatment persistence (HR, 2.03 [95% CI, 1.04-3.95], $p = 0.04$) (Table).

Clinical remission at Week 6 was achieved more frequently in the low-titer group than in the high-titer group (48.8% versus 18.2%, respectively, $p = 0.04$). Multivariate logistic regression analysis also showed that anti- $\alpha\text{V}\beta 6$ autoantibody titer (OR, 3.52 [95% CI 1.08-11.47], $p = 0.04$) was a significant predictor associated with Week 6 remission, in addition to the modified Mayo score (OR, 0.35 [95% CI 0.14-0.90], $p = 0.03$).

	Crude analyses		Multivariable adjusted analyses	
	HR (95% CI)	p value	HR (95% CI)	p value
Disease duration				
3 years	1.00 (reference)		1.00 (reference)	
>3 years	0.99 (0.53-1.84)	0.97	0.77 (0.38-1.53)	0.46
Disease extent				
Proctitis or left side colitis	1.00 (reference)		1.00 (reference)	
Extensive colitis	0.60 (0.24-1.52)	0.28	0.85 (0.32-2.29)	0.75
History of advanced therapies use				
Advanced therapy-naïve	1.00 (reference)		1.00 (reference)	
Prior use of advanced therapies	0.70 (0.39-1.27)	0.24	0.71 (0.38-1.34)	0.29
Modified Mayo score				
Moderate	1.00 (reference)		1.00 (reference)	
Severe	0.55 (0.30-1.00)	0.05	0.58 (0.31-1.08)	0.09
CRP (per 1mg/dL increase)	1.00 (0.89-1.15)	0.98	1.02 (0.91-1.21)	0.69
Anti- $\alpha\text{v}\beta 6$ autoantibody titer				
128 U/mL	1.93 (reference)		1.00 (reference)	
>128 U/mL	1.00 (reference)	0.03	1.00 (reference)	0.04

The multivariable Cox proportional hazards analysis included 5 likely confounders: disease duration, disease extent, history of advanced therapies use, modified Mayo score, and CRP.

Abbreviations: CI, confidence interval; CRP, C-reactive protein; HR, hazard ratio.

The modified Mayo score is the sum of the Mayo stool frequency, rectal bleeding, and endoscopic subscores, with a maximum total score of 9. On the modified Mayo scoring system, a score of 4 to 6 indicates moderate ulcerative colitis, and a score of 7 to 9 severe ulcerative colitis.

Table. Predictors of treatment persistence by Cox proportional hazards model analysis.

Conclusion: Anti- $\alpha\text{v}\beta 6$ autoantibodies are valuable for predicting the outcomes of advanced therapy in active UC.

References:

1. Livanos AE, Dunn A, Mehandru S, et al. Anti-Integrin $\alpha\text{v}\beta 6$ Autoantibodies Are a Novel Biomarker That Antedate Ulcerative Colitis. *Gastroenterology*. 2023;164(4):619-629

Disclosure: S. Sagami has served as a speaker for AbbVie, Eli Lilly, Janssen Pharmaceutical K.K., Gilead Sciences, Inc., JIMRO Co., Ltd., KISSEI Pharmaceutical Co., Ltd., Kyorin Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corporation, EA Pharma Co., Takeda Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., and Zeria Pharmaceutical Co., Ltd. He has also held endowed chairs sponsored by AbbVie, JIMRO Co., Ltd.; Zeria Pharmaceutical Co., Ltd., Kyorin Pharmaceutical Co., Ltd., Mochida Pharmaceutical Co., Ltd., and EA Pharma Co., Ltd., and has received research grants from Bristol-Myers Squibb and Ferring Pharmaceuticals.

M. Nakano has served as a speaker or a consultant in Covidien, Mochida Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical, Kyorin Pharmaceutical, and Nippon Kayaku, received research funding from Mitsubishi Tanabe Pharma and Japanese foundation for research and promotion of endoscopy.

T. Hibi has received Lecture fees from, Abbvie GK, EA Pharma, Janssen, JIMRO, Mitsubishi-Tanabe Pharma, Mochida Pharmaceutical, Pfizer, Takeda Pharmaceutical, Zeria Pharmaceutical Co., Ltd., advisory/consultancy fees from Abbvie GK, Celltrion, EA Pharma, Eli Lilly, Gilead Sciences, Janssen, Mitsubishi-Tanabe Pharma, Nichi-Iko Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical and research grants from Abbvie GK, Activaid, Alfresa Pharma Corporation, JMDC Inc., Gilead Sciences, Inc., Eli Lilly Japan K.K., Mochida Pharmaceutical Co., Ltd., Janssen Pharmaceutical K.K., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., Ferring Pharmaceuticals and Bristol-Myers Squibb; received scholarship contributions from EA Pharma, Mitsubishi Tanabe Pharma Corporation, Zeria Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd.; Pfizer Japan Inc. belonged to study group sponsorship by Alfresa Pharma Corporation, JIMRO Co., Ltd., Kyorin Pharmaceutical Co., Ltd., and Mochida Pharmaceutical Co., Ltd. Miyarisan Pharmaceutical Co., Ltd. Zeria Pharmaceutical Co., Ltd.

N. Maharshak has received speaking and/or consulting fees from Pfizer, Abbvie, Lilly, Takeda, Janssen, Ferring, BiomX, BMS, Nestle, Trobix Innovation, Teva and grant support from Takeda, Janssen, Abbott, Abbvie, Pfizer, BMS, and Nestle.

T. Kobayashi served as an advisory board member, consultant, or speaker for AbbVie, Activaid, Alfresa Pharma, Alimentiv, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical, and has received research funding from AbbVie, Alfresa Pharma, Bristol Myers Squibb, EA Pharma, Gilead Sciences, Kyorin Pharmaceutical, Mochida Pharmaceutical, Nippon Kayaku, Otsuka Holdings, Pfizer, Sekisui Medical, Takeda, and Zeria Pharmaceutical.

PP0466

INADEQUATE VACCINATION RATES AGAINST HEPATITIS B AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN GREECE: A SINGLE-CENTER STUDY

S. Rellou¹, D. Manou¹, S. Efstathiou¹, S. Lamprou¹, A. Pagoni¹, A. Spyrtantis¹, T. Sdonas¹, A. Tasovasili¹

¹General Oncology Hospital of Kifisia, Gastroenterology Department, Athens, Greece

Contact E-Mail Address: s_r_1235@hotmail.com

Introduction: Although there is a childhood vaccination program against hepatitis B virus (HBV) in Greece, vaccination rates are thought to be sub-optimal both in general population and in inflammatory bowel disease (IBD) patients^{1,2}.

Wide use of new immunosuppressant and biologic therapy could lead to an opportunistic infection. As it is recommended by European Crohn's and Colitis Organisation (ECCO) for prevention of HBV infection, patients should be serologically screened at baseline, before and during an immunosuppressive therapy³ and be appropriately vaccinated. Vaccination is until now the most effective way in order to protect from HBV offering longtime protection. Lower successful immunization rates are seen after induction of immunosuppressant therapy carrying a higher risk of a current HBV infection and complications. There are limited epidemiological data about successful immunization, among Greek patients with inflammatory bowel disease, prior to immunosuppressant therapy initiation¹.

Aims & Methods: The aim was to detect the vaccination rate against HBV among IBD patients who are going to be treated with immunosuppressant therapy. Retrospectively collected data from medical records of IBD patients in a single referral IBD center between 2017 and 2023 were analyzed. Inclusion criteria were IBD patients prior to immunosuppressant therapy initiation with no natural immunity to HBV, absence of hepatitis B surface antigen (HBsAg), absence of isolated hepatitis B core antibody (anti-HBc) and any status of hepatitis B surface antibody (anti-HBs).

Results: In total 126 patients were included in the study with average age 46 years old (+/- 28 years old). 42.86% (54/126) of them were women and 57.14% (72/126) were men. 52.38% (66/126) had been diagnosed with Crohn's disease and 47.61% (60/126) with ulcerative colitis. In total 40.48% (51/126) had positive anti-HBs, because of successful immunization against HBV and 59.52% (75/126) were seronegative.

Conclusion: Our study confirms inadequate immunization results against hepatitis B among IBD patients in Greece. Intensive care should be given in vaccination protocols and serology testing especially in IBD patients that are going to start immunosuppressive agents. Primary care and IBD specialist should be well informed about serology testing and appropriate vaccination against hepatitis B, carefully advise and strongly recommend vaccination in IBD patients.

References: Fousekis FS, Katsanos KH, Theopistos VI, Baltayiannis G, Kosmidou M, Glantzounis G, Christou L, Tsianos EV, Christodoulou DK. Hepatobiliary and pancreatic manifestations in inflammatory bowel dis-

eases: a referral center study. *BMC Gastroenterol.* 2019 Apr 3;19(1):48. doi: 10.1186/s12876-019-0967-3. PMID: 30943899; PMCID: PMC644630

Tsiligianni I, Bouloukaki I, Papazisis G, Paganas A, Chatzimanolis E, Kalatharas M, Platakis I, Tirodimos I, Dardavesis T, Tsimtsiou Z. Vaccination coverage and predictors of influenza, pneumococcal, herpes zoster, tetanus, measles, and hepatitis B vaccine uptake among adults in Greece. *Public Health.* 2023 Oct 9;224:195-202. doi: 10.1016/j.puhe.2023.09.002. Epub ahead of print. PMID: 37820537.

T Kucharzik, P Ellul, T Greuter, J F Rahier, B Verstockt, C Abreu, A Albuquerque, M Allocca, M Esteve, F A Farraye, H Gordon, K Karmiris, U Kopylov, J Kirchgessner, E MacMahon, F Magro, C Maaser, L de Ridder, C Taxonera, M Toruner, L Tremblay, M Scharl, N Viget, Y Zabana, S Vavricka, on behalf of the European Crohn's and Colitis Organisation [ECCO], ECCO Guidelines on the Prevention, Diagnosis, and Management of Infections in Inflammatory Bowel Disease, *Journal of Crohn's and Colitis*, Volume 15, Issue 6, June 2021, Pages 879-913

Disclosure: Nothing to disclose.

PP0467

NEW BLOOD-BASED TEST, 7-ALPHA-HYDROXY-4-CHOLESTEN-3-ONE (7ALPHAC4), FOR BILE ACID MALABSORPTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE OR UNSPECIFIED DIARRHEA

J. Yang¹, D. Alfego², K.Y. Chun³

¹Labcorp, Specialty Medicine, Calabasas, United States of America, ²Labcorp, Center for Excellence in Data Science, Artificial Intelligence and Bioinformatics, Burlington, United States of America, ³Labcorp, Esoterix Specialty Medicine, Calabasas, United States of America

Contact E-Mail Address: yangj5@labcorp.com

Introduction: Serum 7AlphaC4 (7-alpha-hydroxy-4-cholesten-3-one) is a diagnostic test for bile acid (BA) malabsorption (BAM) or bile acid diarrhea (BAD) and the only available blood-based test for BAM/BAD. Concentrations >48 ng/mL have a high positive predictive value (PPV) of 82% for BAD and high likelihood of responding to BA sequestrants.¹

In BAM, less BAs re-enter enterohepatic circulation and more BAs spill into the colon increasing motility and secretion. Less reabsorbed BA means less negative feedback and an ensuing increase in hepatic BA synthesis. As BA synthesis increases, blood levels of 7AlphaC4, a BA precursor, also increase.

This 7AlphaC4 test performed on a random blood collection as a surrogate measure of stool BA aims to simplify the investigation and thereby, improve recognition of BAM/BAD which may often be overlooked in IBD and other patients with more than one possible etiology of diarrhea.

Aims & Methods: We assessed the distribution of numeric serum 7AlphaC4 results (in ng/mL) in 712 patient samples using an in-house developed method utilizing protein precipitation followed by liquid chromatography with tandem mass spectrometry. Reference range of this validated assay is 1.8 – 57 as determined using sera of 120 non-disease individuals.

Results: Analysis of 712 patient samples yielded a mean (± standard deviation) 7AlphaC4 of 36.2 ± 50.1 ng/mL (range, undetectable (<0.5) to 549); 37.6% were low at <15 (associated with a NPV of 85%); 21.3% were high at >48. Most 7AlphaC4 was ordered in the general or urgent medical setting (42.8%), by gastroenterologists (27.8%) or infectious disease specialists (9.3%).

Other testing in order of frequency included: tTG IgA or other celiac tests, fecal calprotectin, fecal pancreatic elastase, stool PCR for 22 GI pathogens, fecal fat, *C. difficile* toxin, *Giardia*, *H.pylori*, *C.* and stool lactoferrin. Most common International Classification of Diseases (ICD) codes were: diarrhea unspecified, noninfectious gastroenteritis and colitis, abdominal

distension, unspecified abdominal pain, irritable bowel syndrome with diarrhea (IBS-D), change in bowel habit, other fatigue, gastroesophageal reflux, functional diarrhea.

ICD codes are not known for all samples. However, of 50 patients with the highest 7AlphaC4 levels (>100), at least 20% had CD (ileal resection status unknown). In 86 patients with known diagnoses, those with CD with small intestine involvement had the highest mean 7AlphaC4 of 83.9 ± 77.1 (n=27) compared to 46.1 ± 83.7 in functional diarrhea (n=20), 37.3 ± 58.9 in unspecified diarrhea (n=191), 31.4 ± 22.3 in IBS-D (n=31), and 22.1 ± 10.8 in UC (n=8).

Serum 7AlphaC4 concentration (ng/mL)	Percentage of total patient results	Interpretation
< 15	37.6%	Low; Associated with 85% NPV for BAM/BAD
15 – 48	41.1%	Normal; Does not help rule in/out BAM/ BAD
> 48	21.3%	High; Associated with 82% PPV for BAM/BAD

Table 1. Distribution of All Serum 7AlphaC4 Results

Conclusion: More than half (58.9%) of all 7AlphaC4 results were low (< 15) or high (>48) and as such, potentially diagnostic, carrying a high NPV or high PPV for bile acids contributing to diarrhea. BAM/BAD may account for 30% of all chronic diarrhea cases, thereby, affecting 1-2% of the general population. Disruptions in BA homeostasis and reabsorption occur more frequently in IBD (up to 40%, with or without ileal resection).

We observed that many of the highest 7AlphaC4 levels occurred in Crohn's patients. In summary, 7AlphaC4 is a new blood-based marker that provides quantitative evidence of the contribution of colonic BA toward diarrhea (and hence, a higher likelihood of responding to BA sequestrants), especially in patients with persistent diarrhea of more than one possible etiology.

References: 1. Walters JRF. Making the Diagnosis of Bile Acid Diarrhea. *Am J Gastroenterol.* 2020 Dec;115(12):1974-1975.

Disclosure: Nothing to disclose.

PP0468

CHARACTERIZATION OF CARDIOVASCULAR RISK, LIVER STEATOSIS AND FIBROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A. Bargas Bárbara¹, C. Moreira-Barbosa¹, A. Guedes¹, A.C. Bravo¹, B. Abreu¹, J. Revés², C. Gouveia¹, C. Frias-Gomes¹, L.M. Roque Ramos¹, M. Canhoto¹, M.L. Gloria¹, C. Palmela¹, J. Torres¹

¹Hospital de Loures, Gastroenterology, Lisboa, Portugal, ²Hospital Beatriz Angelo, Gastrenterology, Lisboa, Portugal

Contact E-Mail Address: bargasandre2@gmail.com

Introduction: Recent studies have indicated an increased prevalence of steatosis and liver fibrosis(LF), obesity and cardiovascular diseases among inflammatory Bowel disease(IBD) patients. We aimed to characterize these conditions and risk factors associated.

Aims & Methods: Cross-sectional study on patients with IBD. Pregnancy or known cause of chronic liver disease were excluded. All patients underwent transient elastography, clinical and laboratorial assessment. International Physical Activity Questionnaire(IPAQ) classified activity as low, moderate, or high. Presence of steatosis and fibrosis was defined as Controlled Attenuated Parameter(CAP) measurement of >248dB/m and Liver Stiffness Measurement(LSM) >8kPa, respectively. Fibrosis-4 score (FIB4) was also calculated. For cardiovascular risk (CVR), SCORE2 was calculated according to European Society of Cardiology (if >40 years).

Results: 79 consecutive patients were enrolled [53 Crohn's disease (CD), 24 Ulcerative colitis (UC)]. Baseline characteristics and CVR factors are presented in table 1. Median SCORE2 was 4 (IQR3-10) and 5 (IQR2-10),

($p=0.83$), conferring low cardiovascular risk; 36% of CD and 70% of UC patients had liver steatosis ($p=0.04$) and 11% of CD and 25% of UC had LF ($p=0.13$). Median LSM and CAP was 4.7, IQR (4-6) kPa vs 4.6, IQR (3.6-8.6) kPa ($p=0.86$) and 234, IQR (171-284) vs 217, IQR (179-294) dB/m ($p=0.86$), for CD and UC respectively. We found a moderate correlation between FIB4 and LSM in CD ($r=0.66$, $p<0.001$), but not in UC ($r=0.37$, $p=0.37$).

Comparison between patients with and without fibrosis in IBD showed significant differences in terms of age (47, IQR [45-66] vs 36, IQR [29-54]), $p=0.01$); body mass index (BMI) (31.01, [26.54-37.83] vs 24.61, [20.61-28.05], $p=0.03$), and history of thromboembolic diseases (23% vs 3%, $p=0.007$). In a multivariate regression, adjusting for clinically relevant variables, only higher BMI showed higher risk of fibrosis (OR 1.25, CI [1.05-1.48], $p=0.01$).

	CD	UC	p
Male, %	53%	46%	0.57
Age, median, IQR	55, (31-54)	45, (29-56)	0.42
Low IPAQ, %	87%	71%	0.13
Dyslipidemia, %	11%	8%	0.13
Diabetes, %	4%	4%	0.93
Smoker/Previous smoker, %	44%	65%	0.93
BMI, median, IQR	25.5, (21-29)	26.53, (21-29)	0.93

Conclusion: In our population, IBD patients had a low cardiovascular risk, and 11% of CD and 25% of UC had liver fibrosis. A potential factor linking both conditions is a higher BMI, was independent risk factor for the development of fibrosis.

Disclosure: Nothing to disclose.

PP0469

ASSESSMENT OF INTESTINAL ULTRASOUND IN THE DIAGNOSIS OF POST-OPERATIVE RECURRENCE IN CROHN'S DISEASE

C. Amor Costa¹, C. Suárez Ferrer^{1,2}, J. Poza Cordón^{2,1}, J.L. Rueda García^{2,1}, M. Sanchez-Azofra^{2,1}, E. Martín-Arranz^{2,1}, K. Silva², C. Amiana Roig¹, I. González Díaz¹, L. García Ramírez², M.D. Martín-Arranz^{1,2,3}

¹Hospital La Paz, Gastroenterology and Hepatology, Madrid, Spain, ²Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain, ³School of Medicine. Universidad Autónoma de Madrid, Madrid, Spain

Contact E-Mail Address: carmenamorcc@gmail.com

Introduction: Ileocolonoscopy and Rutgeerts endoscopic score (RS) remains the gold standard to evaluate post-operative recurrence (POR) in Crohn's disease (CD). Intestinal ultrasound (IUS) is proposed as a non-invasive alternative for the diagnosis of POR, with a sensitivity of 89%, specificity of 86% and area under curve (AUC) of 0.93 (1).

Bowel wall thickness (BWT) alone has a high accuracy in the diagnosis of POR and it is proposed that the association of other parameters such as hyperemia, loss of bowel wall stratification, involvement of mesenteric fat (i-fat) or ultrasound scores, increases sensitivity and specificity in the diagnosis of POR (2).

Aims & Methods: The aim of this study is to assess whether IUS parameters and ultrasound scores correlate with endoscopy in the diagnosis of POR. A unicentric retrospective study was performed. There were included patients with CD with both an ileocolonoscopy and intestinal ultrasound performed for the detection of POR, the time between tests was less than 6 months or there was no therapeutic change between tests. Endoscopic POR was evaluated with Rutgeerts score (RS), RS i0 and i1 was considered no POR and RS $\geq$ i2a was POR. The IUS parameters were: BWT, Limberg Score, bowel wall stratification, inflammation of mesenteric fat, Simple US Score, SUS-CD and IBUS-SAS score.

Results: 129 patients were included, baseline characteristics are in Table 1. In 108 patients (83.7%) the time between test was <6 months and in 21 (16.3%) >6 months without therapeutic changes. 38 (29.7%) were classified as endoscopic POR (RS i0 – i1) and 90 (69.8%) as POR: 28 (21.2%) i2a, 17 (13.3%) i2b and 45 (35.1%) severe (RS i3 – i4). With IUS, 42 patients (32.6%) were classified as no POR and 87 (67.4%) as POR. The mean BWT by IUS in patients without endoscopic POR was 2.6 mm (SD $\pm$ 1.2) versus 4.8 (SD $\pm$ 1.6) in patients with RS $\geq$ i2a (p 0.001). BWT $\geq$ 3 had a sensitivity of 86.6%, specificity 78.9% and AUC of 0.83 in the diagnosis of POR. Hyperemia (Limberg $\geq$ 1) was present in 75 patients (84.3%) with RS $\geq$ i2a versus in 8 patients (21.1%) without endoscopic POR (p 0.001). 21 patients (23.9%) of patients with RS $\geq$ i2a presented loss of bowel wall stratification versus 0 (0%) with i0-i1 (p 0.001). I-fat was present in 16 patients (12.4%), all of them RS $\geq$ i2a (p 0.02).

The mean results of IUS scores were: Simple US score 5.6 (SD $\pm$ 2.9), SUS-CD 2.1 (SD $\pm$ 1.8) and IBUS-SAS 31.6 (SD $\pm$ 23.3). In patients without endoscopic POR the mean result of Simple US Score was 3.0 (SD $\pm$ 2.0) versus 6.7 (SD $\pm$ 2.4) in RS $\geq$ i2a ($p>0.05$). The mean result of SUS-CD without POR was 0.5 (SD $\pm$ 1.0) versus 2.8 (SD $\pm$ 1.5) in POR ($p>0.05$). In IBUS-SAS the mean result in RS i0-i1 was 13.4 (SD $\pm$ 10.8) versus 39.2 (SD $\pm$ 22.9) in RS $\geq$ i2a ($p>0.05$). Simple US Score showed an AUC of 0.85 in the diagnosis of POR (95% CI 0.78 – 0.92), SUS-CD of 0.87 (95% CI 0.81 – 0.93) and IBUS-SAS of 0.85 (95% CI 0.77 – 0.92).

Variable	n 129
Men (%)	65 (50.4)
Active smoking (%)	32 (25.4)
Montreal classification (%)	
- L1	59 (45.7)
- L2	2 (1.5)
- L3	60 (46.5)
- L4	8 (6.2)
- B1	19 (14.7)
- B2	49 (38.0)
- B3	61 (47.3)
- p	8 (6.2)
Preventive treatment (%)	
- None	35 (27.1)
- Immunomodulator	39 (30.2)
- Biological therapy	33 (25.6)
- Immunomodulator + biological	21 (16.3)
C-reactive protein (mg/L) (mean, SD)	16.3 (127.7)
Fecal calprotectin (μ g/g) (mean, SD)	192.1 (391.6)
Bowel wall thickness (mm) (mean, SD)	4.1 (1.8)
Limberg score (0-3) (mean, SD)	1.5 (1.2)
Loss of bowel wall stratification (%)	21 (16.5)

Conclusion: In our experience, IUS parameters such as BWT, Limberg score, loss of wall stratification, i-fat and IUS scores (IBUS-SAS, SUS-CD and Simple US Score), have a high accuracy in the diagnosis of POR.

References: 1. Barchi, Alberto et al. "Recent advances in the use of ultrasound in Crohn's disease." *Expert review of medical devices* vol. 20,12 (2023): 1119-1129. doi:10.1080/17434440.2023.2283166

2. Yung, Diana E et al. "Capsule Endoscopy, Magnetic Resonance Enterography, and Small Bowel Ultrasound for Evaluation of Postoperative Recurrence in Crohn's Disease: Systematic Review and Meta-Analysis." *Inflammatory bowel diseases* vol. 24,1 (2017): 93-100. doi:10.1093/ibd/ixx027

Disclosure: Nothing to disclose.

PP0470

ASSESSMENT OF DISEASE ACTIVITY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE USING INTESTINAL ULTRASOUND: A COMPARATIVE DIAGNOSTIC ANALYSIS

S. Massironi¹, G. Mulinacci², G. Zuin³, L. Pirola¹, R. Panceri³, M. Calia³, N. Zucchini⁴, M.E. Dinelli², M. Maino²

¹Fondazione IRCCS San Gerardo Hospital Monza, Gastroenterology and Endoscopy, Monza, Italy, ²Fondazione IRCCS San Gerardo Hospital Monza, Interventional Endoscopy, Monza, Italy, ³Fondazione IRCCS San Gerardo Hospital Monza, Department of Pediatrics, Monza, Italy, ⁴Fondazione IRCCS San Gerardo Hospital Monza, Department of Pathology, Monza, Italy

Contact E-Mail Address: sara.massironi@libero.it

Introduction: Intestinal ultrasound (IUS) is increasingly used as a point-of-care tool for patients with ulcerative colitis (UC). The non-invasive monitoring of pediatric patients with UC is crucial in managing disease progression and therapeutic intervention. The Milan Ultrasound criteria (MUC), the Intestinal Bowel Ultrasound Segmental Activity Score (IBUS-SAS), and the Civitelli score are promising tools for evaluating disease activity in real-time, offering a potential alternative to invasive procedures like endoscopy.

Aims & Methods: The study aimed to assess the correlation and efficacy of MUC, IBUS-SAS, and the Civitelli score in evaluating disease activity in pediatric UC patients, using endoscopic findings and histological parameters as comparative benchmarks.

A prospective cohort of 16 pediatric UC patients underwent IUS and colonoscopy to assess disease activity using the MUC, IBUS-SAS, and Civitelli scores in relation to endoscopic findings and histological evaluation using the Nancy Index. Endoscopy and ultrasound examinations were performed within a 7-day interval, without any change in therapy between assessments. The diagnostic accuracy was evaluated through receiver operating characteristic (ROC) analysis, considering endoscopy as the reference standard.

Results: The study population consisted of 16 pediatric patients with UC (average age 12 years, 56% male), presenting a range of disease severities and durations. The area under the curve (AUC) for MUC was 0.615, IBUS-SAS was 0.667, and Civitelli was 0.603, indicating moderate diagnostic accuracy. Although no significant differences were observed in ROC curve comparisons among these scores, IBUS-SAS demonstrated the highest accuracy. Regarding histological parameters, the AUC was 0.500 for MUC, 0.579 for Civitelli, and 0.563 for IBUS-SAS.

Conclusion: Although potentially less effective than in adult populations, both MUC, Civitelli score, and IBUS-SAS provide reasonable diagnostic accuracy in the assessment of pediatric UC, compared to traditional endoscopic and histologic evaluations. IBUS-SAS, in particular, may offer superior sensitivity in pediatric contexts due to its focus on vascularization and wall patterns. These features are particularly significant in pediatric cases where the disease is recent and the wall often is not very thickened, yet highly vascularized.

References: 1. van Wassenae EA, van Rijn RR, Zwetsloot SLM, et al. Intestinal Ultrasound to Assess Ulcerative Colitis Disease Activity in Children: External Validation and Comparison of 2 Intestinal Ultrasound Activity Indices. *Inflamm Bowel Dis.* 2023;29:1217-1222.

2. Allocca M, Dell'Avallè C, Cravioito V, et al. Predictive value of Milan ultrasound criteria in ulcerative colitis: A prospective observational cohort study. *United European Gastroenterol J.* 2022;10:190-197.

Disclosure: Nothing to disclose.

PP0471

THE BURDEN OF PSYCHIATRIC MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASES: A SYSTEMATIC REVIEW WITH META-ANALYSIS

S. Massironi¹, A. Pigioli², E.A.M. Vegni³, L. Keefer⁴, M.C. Dubinsky⁵, P. Brambilla⁶, G. Del Vecchio², S. Danese⁷

¹Fondazione IRCCS San Gerardo Hospital Monza, Gastroenterology, Monza, Italy, ²Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy, Department of Neurosciences and Mental Health, Milan, Italy, ³Department of Mental Health, ASST Santi Paolo e Carlo Milan, Italy, Department of Health Sciences, University of Milan, Milan, Italy, Milan, Italy, ⁴Icahn School of Medicine, Gastroenterology & Hepatology, New York, United States of America, ⁵Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ⁶Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Università degli Studi di Milano, Milan, Italy, Department of Neurosciences and Mental Health, Milan, Italy, ⁷Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy

Contact E-Mail Address: sara.massironi@libero.it

Introduction: Psychiatric manifestations in individuals with inflammatory bowel disease (IBD) have been the subject of extensive research. Still, uncertainties remain regarding its precise magnitude, its impact on intestinal disease, and the whole burden of psychiatric manifestations.

Aims & Methods: This systematic review aims to synthesize available evidence on the prevalence and impact of psychiatric symptoms, including depression, anxiety, bipolar disorders, and schizophrenia in IBD patients. A systematic search was conducted in the PubMed/MEDLINE, EMBASE and SCOPUS databases to identify relevant studies published between January 2010 and January 2023. Cross-sectional, case-control, cohort, registry and population studies were selected that addressed the prevalence of depression, anxiety, bipolar disorder, and schizophrenia in people with IBD compared to the general population. A meta-analysis was also conducted to assess the strength of the association. Data extraction and quality assessment were performed.

Results: The search yielded a total of 3209 articles. Although 193 met the inclusion criteria, only 26 studies provided complete data. Overall, the prevalence of psychiatric comorbidities was found to be significantly higher in IBD patients compared to the general population. The analysis revealed a moderate but significant association between IBD and depression, with a calculated pooled odds ratio (OR) of 1.42 ($p < .0001$).

Also, anxiety disorders emerged as a prevalent comorbidity in IBD with a calculated pooled OR of 1.3 ($p < .0001$). Evidence for the association between bipolar disorders and IBD was limited but significant, with a pooled OR of 1.64 ($p < .0001$), despite a substantial heterogeneity ($I^2 = 94.01\%$). Only 3 studies examined the association between schizophrenia and IBD, providing widely heterogeneous results, with an inconclusive OR (0.93, $p = 0.73$).

Conclusion: This systematic review with meta-analysis highlights that psychiatric comorbidities such as depression, anxiety, and bipolar disorders are more prevalent in IBD than in the general population. Depression and anxiety are particularly prevalent. Bipolar disorder is still an under-researched area in the context of IBD. Data on the association between schizophrenia and IBD is sparse and inconclusive and requires further research.

Given the findings of this systematic review, there is a need for a deeper understanding of these associations and early detection in order to develop tailored mental health interventions for patients with IBD.

References: 1. Jairath V, Feagan BG. Global burden of inflammatory bowel disease. *Lancet Gastroenterol Hepatol.* 2020;5(1):2-3.

2. Barberio B, Zamani M, Black CJ, Savarino EV, Ford AC. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(5):359-70.

3. Piovani D, Armuzzi A, Bonovas S. Association of Depression With Incident Inflammatory Bowel Diseases: A Systematic Review and Meta-Analysis. *Inflamm Bowel Dis*. 2023.

Disclosure: Nothing to disclose.

PP0472

WITHDRAWN

PP0473

INFLAMMATORY BOWEL DISEASE IN REMISSION IS ASSOCIATED WITH MINOR COGNITIVE IMPAIRMENT COMPARED TO HEALTHY CONTROLS

D. Compare¹, C. Sgamato¹, S. Minieri¹, S.A. Marchitto¹, S. Cinque¹, C. Ambrosio¹, F. Cascella¹, A. Rocco¹, G. Nardone¹

¹University Federico II, Clinical Medicine and Surgery, Gastroenterology Unit, Naples, Italy

Contact E-Mail Address: Costa.sgamato@gmail.com

Introduction: Compelling evidence suggests that inflammatory bowel disease (IBD) can affect the brain. IBD can increase the risk of developing mood and behavioural disorders or neurological diseases. However, few studies assessed cognitive function in such patients, yielding inconsistent results.

Aims & Methods: To evaluate minor cognitive impairment in IBD patients compared with age, sex, and education-matched healthy controls (HC). We enrolled adult (18-65 years) IBD patients referred to our tertiary centre. Clinical remission was defined as Harvey-Bradshaw Index <5 for Crohn's disease (CD) and Partial Mayo score <2 for Ulcerative colitis (UC), respectively. Healthy subjects were recruited from friends and relatives of physicians involved in the study. Exclusion criteria were psychiatric or neurologic diseases, language difficulties, sleep disorders, ileostomy or colostomy, severe comorbidities, alcohol abuse, and use of corticosteroid or other medications with known effects on neuropsychological functions in the three months before enrolment. Cognitive function was assessed by using the Montreal Cognitive Assessment (MoCA) test. A MoCA score greater than 26 was considered normal. To rule out the potential impact on cognitive abilities of conditions such as anxiety and depression, we screened patients using the Hospital Anxiety and Depression Scale (HADS) test. A score equal to or greater than 8 on either HADS-D or HADS-A is considered a 'possible case', and above 11 a 'probable' case. Demographic and clinical data were also recorded. The Mann-Whitney rank-sum or t-test and Chi-square or Fisher's exact test were used to compare continuous or categorical variables, respectively.

A univariate analysis was performed to establish whether baseline clinic psychometrics parameters contributed to predicting MoCa score below the lower limit of normal. Multivariate analysis was then performed by logistic regression with the calculation of odds ratio (OR) and a confidence interval (CI) of 95%.

Results: Ninety-four IBD patients [48 CD and 46 UC] and 68 HC were finally considered for statistical analysis. No significant differences in terms of sex ($p=0.224$), age ($p=0.243$), and years of schooling ($p=0.279$) were observed between patients with IBD and HC. A significantly higher percentage of IBD patients had MoCA scores below the lower limit of normal in comparison to HC (57% vs 42%, $p=0.037$). A similar result was obtained also after excluding patients with probable anxiety and depression as assessed with HADS (42% vs 25%, $p=0.025$). UC patients had significantly

lower mean scores in the memory domain than HC (3.1 ± 1.4 vs 2.5 ± 1.5 , $p=0.041$). Age ($p=0.036$), years of schooling ($p=0.002$), and UC ($p=0.037$) were significantly associated with a MoCA score below the lower limit of normal. At multivariate analysis, age (OR 1.04, 95%CI 1-1.1, $p=0.017$) and UC (OR 2.2, 95%CI 1.4-5.3, $p=0.047$) were the only variables that independently predicted a MoCA score below the lower limit of normal.

Conclusion: IBD patients had minor cognitive impairment in a percentage significantly higher than controls as assessed by MoCA. UC patients showed deterioration of the memory domain. Our data support the existence of a gut-brain axis and suggest that colonic rather than small bowel inflammation could be the pathogenetic link for cognitive impairment in IBD. A multidisciplinary approach is required for IBD patients, which should also include cognitive function assessment.

Disclosure: Nothing to disclose.

PP0474

EVALUATION OF THE RESULTS OF A MICROLEARNING PROGRAMME FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN IMPROVING THERAPEUTIC ADHERENCE. THE ADEII PROJECT

L. De Castro Parga¹, V. Hernández Ramírez¹, J. Martínez-Cadilla¹, L. Sanromán Álvarez¹, J.I. Rodríguez Prada¹

¹Hospital Alvaro Cunqueiro. Complejo Hospitalario Universitario de Vigo (CHUVI), Gastroenterology, Vigo, Spain

Contact E-Mail Address: maria.luisa.de.castro.parga@sergas.es

Introduction: Information and communication technologies (ICTs) represent a novel approach to chronic disease management. However, their use in Inflammatory Bowel Disease (IBD) is scarce as no specific tools are available. Our aim was to develop a microlearning programme for IBD patients and to evaluate their outcomes with respect to adherence, medication beliefs and perception of the disease.

Aims & Methods: Prospective cohort study in adult IBD patients (18-70 years) who underwent a microlearning programme over 2 months, through 4-minute videos organised into individualised video pathways that were sent via mobile phone using a Telegram bot. All patients received the main pack of 4 videos, consisting of 2 videos with information about their disease (ulcerative colitis or Crohn's disease), 1 video on adherence and 1 video on corticosteroid treatment. We then add a video for each medication used by the patient in the management of their IBD. Before starting the programme and at 6 months, patients completed the BMQ (Beliefs Medicines Questionnaire) and Brief Illness Perception Questionnaire (BIPQ). We checked the medication possession rate (MPR) at these same intervals, considering a $MPR \geq 80\%$ as adequate adherence.

Results: Between June and October 2022, 1226 videos were sent to 200 IBD patients: 51.5% female (103), Ulcerative colitis 52.5% (105), median age 46.1 (13.2) years (Table 1). The median of videos per patient was 6 (6-7). Attendance to the ADEII programme ranged from 78% to 90%. Baseline non-adherence in this cohort was 29.8% (59 patients), decreasing significantly to 18.1% (36) after the programme ($p=0.02$). Likewise, in the BMQ scales, we found significant decreases in the median and IQR of the BMQ scores: Medication Abuse: 8 (7-9) vs 8 (6-9) ($p=0.001$), BMQ-Medication Harm 10 (8-12) vs 9.5 (7-11) ($p=0.002$) and BMQ-Treatment Concern 13.5 (11-16) vs 13 (10-16) ($p=0.001$), with no change in BMQ-Treatment Need. Regarding illness perception, on the post-intervention BIPQ scale there were significant decreases in P8 Negative Emotions 6 (3-8) vs 5 (3-7) ($p=0.003$) and P5 Identity 6 (4-8) vs 5 (3-7) ($p=0.003$), as well as a significant increase in P7 Understanding of illness 7 (5-9) vs 8 (7-9) ($p=0.003$).

	Ulcerative colitis (105)	Crohn's Disease (95)	IBD (200)
Male / Female	59 (56,2%) 46 (43,8%)	38 (40%) 57 (60%)	97 (48,5%) 103 (51,5%)
Age	47 (12,7)	45,1 (13,7)	46,1(13,2)
Studies: Primary school/ Secondary / University	25 (24%) 57 (54,8%)	23 (24,2%) 49 (51,6%)	48 (24,1%) 106 (53,3%) 45 (22,6%)
Years from diagnosis	10,8 (8,2)	15,2 (11,2)	13(10)
UC E1/ E2/ E3	21 / 47 / 36		
CD A1/ A2/ A3		5 / 77 / 13	
CD: L1/ L2/ L3		52 /13 / 30	
CD: B1/ B2/ B3		49 / 27 / 19	
EIMs	9 (8,6%)	19 (20%)	28 (14%)
Perianal disease	7 (6,7%)	22 (23,2%)	29 (14,5%)
Surgery No	101 (96,2%)	68 (71,6%)	169 (84,5%)
One / ≥2	4 (3,8%)	19 (20%) 8 (8,4%)	23 (11,4%) 8 (4%)

Conclusion: The ICT-based ADEII educational programme was widely accepted by patients, demonstrating an improvement in adherence to treatment with a decrease in negative beliefs about medication and negative emotions and representations, improving the understanding of the disease.

Disclosure: Nothing to disclose.

PP0475

HEAD TO HEAD COMPARISON OF A RAPID AND A CONVENTIONAL FECAL CALPROTECTIN KIT AS PREDICTOR OF CLINICAL SCORE IN ULCERATIVE COLITIS AND CROHN'S DISEASE

J. Florholmen¹, E. Lindi², S.B. Gaup², S. Hegge², H. Kitt², K.-M. Johnsen¹, S.U. Johansen¹

¹Inst Clinical Medicine, Gastroenterology, Tromsø, Norway, ²Sami Klinikkha, Hospital of Finnmark HF, Norway, Internal medicine, Hammerfest, Norway

Contact E-Mail Address: jon.florholmen@unn.no

Introduction: Measurements of fecal (fe) calprotectin as a surrogate biomarker of gastrointestinal inflammation have great clinical impact in the judgement of clinical activity in inflammatory bowel disease. There is no accepted standardization procedure of ELISA-based calprotectin kits, but several commercial kits use of a combined pioneering polyclonal calprotectin antibody (CA) (1) and a monoclonal CA.

Aims & Methods: To evaluate the accuracy of a new rapid fe-calprotectin kit (RFC) including a polyclonal-based CA to predict clinical activity in comparison to a standard commercial (SCFC) kit in patients with ulcerative colitis (UC) and Crohn's disease (CD) with special focus on clinical remission.

Included were 16 UC and 20 CD patients on ongoing treatment from May 2022 to March 2024 (5ASA, azathioprine, biological therapy). The degree of illness was evaluated at regularly visits every three months using the clinical scoring system- Ulcerative Colitis Clinical Score (UCCS), and Harvey-Bradshaw index (HBI). From the same fe-sample RFC analyses were performed at the Sami Klinikkha, Finnmark Hospital and the SCFC analyses at the University Hospital Tromsø, Norway, both with an upper normal level of 50 µg/g.

Statistical evaluation was done by correlation and limits of agreement analysis; cut-off levels were explored by Receiver Operating Characteristic (ROC) analysis against clinically defined remission

Results: The intra-assay variation of the RFC was 5.3% at a level of 133 µg/g.

Mean calprotectin values (µg/g) with 95 % confidential interval (CI) are shown at various degrees of clinical activities during the observation time (remission, slight and mild), Table 1. In general, the RFC measured lower

means and CI levels compared to the SCFC. In clinical remission, the upper RFC CI interval were in proximity to the upper normal level, whereas the corresponding SCFC CI levels were almost three times higher than the upper normal level.

A ROC curve was performed for prediction of clinical remission. Both assays had significant area under the curve (AUC) in both UC and CD patients (p<0.0001). The RFC kit predicted endoscopic remission with 100% specificity at cut-off levels 139 µg/g in both UC and CD. The specificity of the SCFC kit was lower applying the same cut-off levels. Increasing the cut-off to 246 µg/g in the SCFC kit (Youden's J index 0.68 in the UC group and 0.49 in the CD group), the specificity increased to 96.3 and 96.4% in the UC and CD group, respectively.

On the other hand, the test sensitivity decreased (71.4% in UC and 52.2% in the CD patient group).

	Remission UC n=27	Slight UC 10	Moderate UC 8	Remission CD 28	Slight CD 27	Moderate CD 10
RFC	60 (mean) 45-69 (CI)	202 170-232	365 161-569	69 54-84	206 175-236	433 283-583
SCFC	104 69-139	325 187-436	677 143-1209	110 82-138	234 183-286	558 314-801

Table 1.

Conclusion: The rapid fe-calprotectin test is an accurate test and predicts remission in UC and CD patients better than a conventional commercial fe-calprotectin kit

References:

Røseth A, Fagerhol MK, et al. Assessment of the neutrophil dominating protein calprotectin in feces. A methodologic study. Scand J Gastroenterol 1992, 27, 793-8.

Disclosure: Nothing to disclose.

PP0476

BOWEL URGENCY IN ULCERATIVE COLITIS PATIENTS: PREVALENCE AND ITS ASSOCIATION WITH CLINICAL, ENDOSCOPIC DATA, AND DISABILITY IN A REAL-WORLD SETTING

O.M. Nardone¹, G. Calabrese², M. Allocca³, F. Caprioli⁴, M.C. Fantini⁵, S. Onali⁶, A. Orlando⁶, E.V. Savarino⁷, A. Soriano⁸, A. Variola⁹, A. La Mantia², A. Rispo², A. Testa², F. Castiglione²

¹University of Naples Federico II, Gastroenterology, Department of Public Health, Naples, Italy, ²University of Naples Federico II, Gastroenterology, Department of Clinical Medicine and Surgery, Naples, Italy, ³IRCCS Hospital San Raffaele and University Vita-Salute San Raffaele, IBD Center, Milano, Italy, ⁴University of Milan, Department of Pathophysiology and Transplantation, Milano, Italy, ⁵University of Cagliari, Department of Medical Science and Public Health, Monserrato, Italy, ⁶A.O. Ospedali Riuniti "Villa Sofia Cervello", IBD Unit, Palermo, Italy, ⁷University of Padua, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁸IRCCS of Reggio Emilia Arcispedale S. Maria Nuova, Department of Internal Medicine-Gastroenterology Division and IBD Center, Reggio Emilia, Italy, ⁹IRCCS Ospedale Sacro Cuore Don Calabria, IBD Unit, Negrar di Valpolicella, Italy

Contact E-Mail Address: Olga.nardone@libero.it

Introduction: Bowel Urgency (BU), identified as the sudden need for bowel movements, is increasingly being recognized as an impactful symptom in patients with Ulcerative Colitis (UC), distinct from Stool Frequency (SF) and Rectal Bleeding (RB).

Aims & Methods: We aimed to assess the association of bowel urgency (BU) with Patient-Reported Outcomes (PRO), including stool frequency (SF) and rectal bleeding (RB), along with endoscopic findings in a real-world setting. Additionally, we investigated its impact on disability and quality of life.

A cross-sectional multicenter study, which consecutively enrolled UC patients aged ≥ 18 years, was conducted between February 2023 and October 2023 using data from the 'IBD-Disk: Italian translation and validation study. Demographic, clinical and endoscopic data were collected. Clinical remission was defined as partial Mayo score ≤ 1 and endoscopic activity as MES ≥ 2 . All patients completed the following questionnaire for disability IBD-Disk and IBD Questionnaire-32 (IBDQ-32) for quality of life. BU was assessed using the question about regulating defecation in the past 7 days using a 10-point NRS ranging from 0 (absolutely disagree) to 10 (totally agree) from the IBD-Disk. RB was measured from question 22 of IBDQ and SF from question 1 of IBDQ-32, both using a 7-point NRS ranging from 0 (always) to 7 (never).

Results: 209 UC patients with a median age of 37 (IQR 28-52) were enrolled, 111 (53.1%) being female. Overall, 31 (14.8%) had proctitis, 91 (45.5%) had left colitis and 87 (41.6%) had extended/pancolitis. The median pMAYO score was 4 (IQR=2-6), while the median MES was 2 (IQR=1-2). 75% patients (35.9%) reporting BU were more likely to have moderate clinical (pMAYO=5; IQR=3-6) and endoscopic activity of disease (median MES=2; IQR=1-2) compared to those without urgency ($p<.0001$). Additionally, BU was associated with a higher median rate of hospitalizations in the previous 12 months ($\Delta=1$; $p<0.001$). Patients with BU reported a higher degree of RB (33.3%) and SF (50.7%) than patients without BU ($p<.0001$). Noteworthy, individuals with BU had higher median IBD-Disk total score (29; IQR=9-52) and lower scores for IBDQ-32 (168; IQR=138-196) compared to patients without BU [median IBD-Disk=17 (IQR=5-39); median IBDQ-32=181, IQR=158-202], $p<0.001$. In the univariate analysis, BU was associated with a higher IBD-Disk total score (OR=1.04, CI=1.02-1.06; $p<0.001$) and SF (OR=0.59, CI=0.45-0.78; $p=0.001$), without being associated with RB ($p=0.57$) and IBD-Q32 total score ($p=0.84$).

	BU (n=75)	No-BU (n=134)	OR (CI 95%)	p value
pMAYO score, median (IQR)	5 (3-6)	1 (0-3)		$p<0.001$
pMAYO >1 , n (%)	60 (80.0%)	62 (46.3%)	4.6 (2.4-9.0)	$p<0.001$
MES, median (IQR)	2 (1-2)	1 (1-2)		$p<0.001$
MES ≥ 2 , n (%)	53 (70.7%)	54 (40.3%)	3.6 (1.9-6.5)	$p<0.001$
Relapses in prev 12 months, median (IQR)	1 (0-1)	0 (0-1)		$p<0.001$
RB, n (%)	25 (33.3%)	9 (6.7%)	6.9 (3.0-15.9)	$p<0.001$
SF, n (%)	38 (50.7%)	12 (8.9%)	10.4 (4.9-22.0)	$p<0.001$
IBD Disk, median (IQR)	29 (9-52)	17 (5-39)		$p<0.001$
IBDQ-32, median (IQR)	168 (138-196)	181 (158-202)		$p<0.001$

Conclusion: BU can be a surrogate marker for UC clinical and endoscopic activity. Our findings suggest that BU is an independent factor from RB and it is associated with disability. Hence, it can be considered as an additional key PRO in UC. However, a systematic standardized approach for BU definition and assessment is strongly awaited to incorporate it as treat-to-target endpoint.

References: 1. Dubinsky M, Am J Gastroenterol. 2023 Nov 1;118(11):1940-1953. doi: 10.14309/ajg.0000000000002404. .

2. Caron B, Clin Gastroenterol Hepatol. 2023 Jun;21(6):1403-1413.e27. doi: 10.1016/j.cgh.2023.02.029..

3. Ghosh S, Inflamm Bowel Dis. 2017 Mar;23(3):333-340. doi: 10.1097/MIB.0000000000001033. .

Disclosure: Nothing to disclose.

PP0477

EXTERNAL VALIDATION OF THE ELIAKIM SCORE IN CAPSULE PANENDOSCOPY: AN EFFECTIVE TOOL FOR DIAGNOSIS AND MONITORING OF CROHN'S DISEASE

J. Carlos Goncalves^{1,2,3}, A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, B. Rosa^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Unidade Local de Saúde do Alto Ave, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: joaogoncalves92@gmail.com

Introduction: Capsule panendoscopy is increasingly used in Crohn's disease (CD), particularly in patients with extensive small bowel and colonic involvement. It offers a non-invasive, one-step evaluation of both segments, making it appealing for disease monitoring and treatment response. However, there is a need for validated scoring systems that objectively assess inflammatory activity in both the small bowel and the colon.

Aims & Methods: The aim of this study was to externally validate the Eliakim Score (Elk-S), developed to assess mucosal inflammation in CD by capsule panendoscopy. Patients referred for PillCam™ Crohn's examination at our institution were selected, and procedure data were collected retrospectively to calculate the Elk-S.

Results: A total of 72 patients were included, 62.5% female, with a mean age of 42 ± 15 years. In 52 (72.2%) individuals, the indication for the procedure was suspected CD. Among them, the diagnosis was rejected in 38 cases, while in 14 cases, the diagnosis was established. There was a significant difference in mean Elk-S between the two groups (5.3 ± 1.5 vs. 21.8 ± 5.3 , respectively; $p<0.001$). Capsule panendoscopy was used to evaluate inflammatory activity in 20 (27.8%) patients with CD. Treatment remained unchanged in 10 cases, while therapy was intensified in 10 patients, and there was a significant difference in mean Elk-S between the two groups (2.2 ± 0.5 vs. 17.1 ± 2 , respectively; $p<0.001$). The Elk-S demonstrated an area under the ROC curve of 0.979 for the diagnosis of CD and 0.875 for predicting therapeutic escalation. An Elk-S ≥ 7 (Table 1) had a Sensitivity, Specificity, Negative Predictive Value, and Positive Predictive Value of 100%, 89.5%, 100%, 77.8%, respectively, for the diagnosis of CD. To determine the need for therapeutic intensification in patients with established CD, the same cut-off value showed a Sensitivity, Specificity, Negative Predictive Value, and Positive Predictive Value of 90%, 70%, 87.5%, 75%, respectively.

Elk-S cutoff: ≥ 7	Sensitivity	Specificity	NPV	PPV
CD Diagnosis	100%	89.5%	100%	77.8%
Treatment intensification	90%	70%	87.5%	75%

Table 1: Performance of the Elk-S for diagnosing CD and predicting therapeutic escalation.

Conclusion: The Elk-S exhibited high accuracy in establishing the diagnosis of CD and was equally useful in predicting the need for therapeutic intensification in cases of established CD. The present study represents the first external validation of the Elk-S, demonstrating its effectiveness for assessing inflammatory activity via capsule panendoscopy of both the small bowel and colon.

References: Eliakim R, Yablecovitch D, Lahat A, et al. A novel PillCam Crohn's capsule score (Eliakim score) for quantification of mucosal inflammation in Crohn's disease. *United Eur Gastroenterol J*. 2020;8(5):544-551. doi:10.1177/2050640620913368

Disclosure: Nothing to disclose.

PP0478

WITHDRAWN

PP0479

A PREDICTIVE MODEL FOR HISTOLOGICAL RESPONSE TO THERAPY GUIDING THERAPEUTIC STRATEGIES IN ULCERATIVE COLITIS: A POST-HOC DATA ANALYSIS FROM A PHASE-II MIRIKIZUMAB CLINICAL TRIAL

M. Iacucci¹, M. Puga-Tejada¹, J. Eckenberger¹, G. Santacroce¹, K.T. Gottlieb², C. Owen², W.J. Eastman², U. Chaudhari³, R. Del Amor⁴, I. Ditunno¹, B.B. Kolawole³, Y. Maeda¹, P. Meseguer^{4,5}, V. Vadori³, I. Zammarchi¹, S. Ghosh¹, V. Naranjo⁴, E. Grisan³

¹APC Microbiome Ireland, College of Medicine and Health, University College of Cork, Cork, Ireland, ²Eli Lilly and Company, Indianapolis, United States of America, ³School of Engineering, London South Bank University, London, United Kingdom, ⁴Instituto Universitario de Investigación e Innovación en Tecnología Centrada en el Ser Humano, HUMAN-tech, Universitat Politècnica de València, València, Spain, ⁵ValgrAI – Valencian Graduate School and Research Network of Artificial Intelligence, Valencia, Spain

Contact E-Mail Address: iacuccim@yahoo.it

Introduction: Clinical trials are ongoing to develop novel therapies for ulcerative colitis (UC), aiming to break the existing therapeutic ceiling. Mirikizumab, a monoclonal antibody targeting the p-19 subunit of IL-23, was evaluated in a phase-II clinical trial for the treatment of moderate-to-severe UC. Identifying predictive variables for response to therapy is still an unmet need and would serve as a valuable asset in clinical trials and clinical practice to guide therapeutic strategies.

Aims & Methods: This post-hoc data analysis aimed to identify variables predicting response to mirikizumab in UC patients from a phase II clinical trial. One-hundred and six randomly selected patients from the induction phase were considered: 26 (24.5%) were assigned to receive mirikizumab 50mg IV Q4W, 37 to 200mg IV Q4W (34.9%), 30 to 600mg IV Q4W (28.3%) and 13 to placebo (12.3%). In the maintenance phase, 44 received 200mg SC Q12W (42.3%), 47 received 200mg SC Q4W (45.2%), and 13 received placebo (12.5%). Patients who did not achieve clinical remission (14, 13.2%) were excluded from the analysis related to the maintenance phase.

A stepwise analysis was conducted, initially using a principal coordinate analysis (PCoA) with permutational multivariate analysis of the variance (PERMANOVA), followed by a univariate analysis (Fisher's or Wilcoxon signed-rank test) to select significant variables ($p < .05$).

Further, a country-nested, three-visit repeated-measured generalized mixed ordinal logistic regression model (GLM) using significant PCoA variables was conducted. For both models the endpoint was histological remission at weeks 12 and 52, defined as Geboes score < 2 .

Results: At week 12, histological remission was achieved in 34 patients (32.1%) while at week 52 in 42 patients (39.6%). PCoA, PERMANOVA and univariate analysis considered histological remission to be significantly predicted by faecal calprotectin, endoscopic remission (Mayo 0, UCEIS ≤ 1) and induction therapy at weeks 12 and 52 ($p < .05$). Also, at week 52, the 32-IBD Questionnaire (systemic symptoms and social function), Physician Global Assessment, partial and total Mayo scores, and maintenance treatment were significant.

Considering these as explanatory variables for the GLM, we confirmed the following as significant predictors of histological remission: faecal calprotectin $< 250 \mu\text{g/g}$ (Odds Ratio 0.26; 95% CI 0.12-0.58; $p < .001$), endoscopic remission (OR 0.16; 95% CI 0.04-0.57; $p = .005$), induction treatment with mirikizumab 200mg IV Q4W (OR 0.09; 95% CI 0.02- 0.45; $p = .004$), 600 mg

IV Q4W (OR 0.09; 95% CI 0.01-0.50; $p = .006$) and maintenance with 200 mg SC Q4W (OR 0.05; 95% CI 0.01-0.30; $p = .001$). A more severe Physician Global Assessment predicted histological activity (OR 2.29; 95% CI 1.03- 5.11; $p = .043$).

Conclusion: Our predictive model identified faecal calprotectin, endoscopic remission, and Physician Global Assessment as predictive factors for response to therapy. Notably, our model identified the most effective therapeutic strategies to achieve histological remission during induction and maintenance phases, showing promising ability to guide therapeutic choices in clinical trials and clinical practice.

Additional investigation utilizing a larger clinical dataset would further enhance the ability of this model to identify variables predictive of response to therapy.

Disclosure: Nothing to disclose.

PP0480

CORRELATION BETWEEN PSOAS INDEX AND DIAPHRAGMATIC INDEX ULTRASOUND IN THE EVALUATION OF SARCOPENIA IN A COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A STUDY IN A TERTIARY REFERRAL CENTER

C.M. Palmisano¹, P. Dell'Aquila², S. Cormio², A.V. Borraccino², F. Savino², D. Forastiere², F. Squeo², D. Novielli², A. Di Lorenzo³, A. Moschetta¹, A. Di Leo², M.R.D. Principi²

¹University of Bari 'Aldo Moro', Internal Medicine Unit 'C. Frugoni', Department of Interdisciplinary Medicine, Bari, Italy, ²University of Bari 'Aldo Moro', Section of Gastroenterology, DiMePre-J, Bari, Italy, ³University of Bari 'Aldo Moro', Hygiene Unit - Interdisciplinary Department of Medicine, Bari, Italy

Contact E-Mail Address: chiarapalmi8@gmail.com

Introduction: Sarcopenia is prevalent in patients with inflammatory bowel disease (IBD) and impacts surgical and therapeutic outcomes; thus, effective diagnostic tools are needed to assess muscle mass and function in IBD population. The ileo-psoas muscle (IP) muscle has already been used in the literature for the assessment of sarcopenia, however, as it is a deep muscle and it needs experienced operators for a proper measurement. Therefore, diaphragm muscle (DM) more superficial and easily assessed, was examined to check its correlation with IP.

Aims & Methods: The aim of this work was to evaluate the correlation of positivity SARC-F score with ultrasound (US) measure of the IP and DM. A total of 50 IBD patients with significant suspected sarcopenia with SARC-F score positive ≥ 4 , were enrolled. IP and DM US were detected in the enrolled patients. The transverse diameter of the right IP was evaluated.

We defined "reliable" the measurements of the IP that fulfilled all of the following criteria: all anatomical boundaries could be clearly identified (superior margin of the iliac crest and lumbar vertebrae); the maximum diameter of the psoas between each of the three measurements did not deviate from the other two by more than 5 mm. Moreover, we calculated the US psoas/height ratio as the average of the psoas diameter divided by the patient's height (mm/m). For DM, an extended space between the axillary line and the hemi clavicular line was used, in the diaphragmatic thickness between the hyperechogenic limiting. Diameters during expiration and during inspiration were assessed, then diaphragmatic expansion was evaluated.

We calculated the diaphragm/height ratio (mm/m) as well. The correlation between IP and DM ratio was researched by using the Pearson correlation test. Age and sex were taken into consideration as confounders in a linear regression model, using the psoas/height ratio and these confounders as independent variables and the diaphragm index as dependent variable.

Results: The mean of the three US IP measured diameters was 30.37 mm, the psoas/height ratio was 17.92 mm/m. The mean maximum inspiration DM diameter was 20.4 mm (± 5 mm), the mean minimum expiration DM diameter was 10.7 mm (± 35 mm). The mean difference between the two diameters was 9.7 mm ($\pm 3,4$ mm). The diaphragm/height ratio was 0.59 mm/m (± 0.21 mm/m).

A significant correlation was identified between IP and DM ratio, with a Pearson coefficient $r = 0.3568$ (p -value < 0.05). A consistent association was found between the two indices, with diaphragm/height ratio increasing linearly with the psoas/height ratio (OR: 0.018; p -value: 0.008). Multivariate analysis showed that age and sex were not significantly associated with the diaphragm/height ratio (p -value > 0.05).

Conclusion: The findings of this study emphasize the potential of muscle US as a reliable diagnostic tool for assessing sarcopenia in IBD patients. IP US is confirmed to correlate with sarcopenia. DM can be used more easily and correlates with IP. This research could take a significant implications for disease management in IBD patients and underscores the importance of further investigations to validate these findings in larger cohorts. This study will continue to expand the cohort under evaluation.

Disclosure: Nothing to disclose.

PP0481

PREVALENCE OF SEXUAL DYSFUNCTION IN INFLAMMATORY BOWEL DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS

O.M. Nardone¹, G. Calabrese², L. Bertin³, A.C. Ford⁴, F. Castiglione², F. Zingone³, E.V. Savarino³, B. Barberio³

¹University of Naples Federico II, Gastroenterology, Department of Public Health, Naples, Italy, ²University of Naples Federico II, Gastroenterology, Department of Clinical Medicine and Surgery, Naples, Italy, ³University of Padua, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁴St. James's University Hospital, Department of Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: Olga.nardone@libero.it

Introduction: Patients with inflammatory bowel disease (IBD) can face various challenges, including sexual dysfunction, which refers to any physical or psychological perturbation of sexual health. This can manifest through symptoms such as reduced libido, erectile dysfunction, discomfort during intercourse, and other psychosocial issues that negatively impact patients' quality of life. However, uncertainties remain about the magnitude of this problem

Aims & Methods: Therefore, we aimed to assess prevalence of sexual dysfunction in adult patients with IBD. We conducted a systematic review and meta-analysis examining this issue. MEDLINE EMBASE, EMBASE Classic (from inception to 30th March 2023) were searched to identify observational studies that reported prevalence of sexual dysfunction in adult patients with IBD based on validated screening instruments (Female Sexual Function Index (FSFI) and International Index of Erectile Function (IIEF) for women and men respectively). Data were extracted from published study reports, and pooled prevalence, odds ratios (OR), and 95% confidence intervals (CIs) were calculated.

Results: Of 1017 citations evaluated, 18 articles fulfilled eligibility criteria, containing 2,694 patients with IBD recruited from 13 different countries. The pooled prevalence of sexual dysfunction in patients with IBD, was 50.6% (95% CI 40.8% to 60.5%; $I^2=96.3\%$). The OR for sexual dysfunction in patients with IBD versus healthy controls was 2.94 (95% CI 1.99 to 4.35, $I^2=73.4\%$). When we considered UC or CD separately, the pooled prevalence of sexual dysfunction was 64.8% (95% CI 45.1% to 82.1%; $I^2=88.8\%$) in patients with UC, and 58.3% (95% CI 36.0% to 79.0%; $I^2=95.3\%$) in pa-

tients with CD. When we conducted subgroup analyses based on sex, the pooled prevalence of sexual dysfunction was higher in females with IBD compared with males (62.7% versus 34.0%), with a four-times higher odds of sexual dysfunction. Similar trends were observed when analysing CD and UC patients separately by sex, although limited data were available for this subgroup analysis.

Finally, the pooled prevalence of sexual dysfunction was higher in patients with IBD with active disease compared with inactive disease (75.1% vs 34.2%), with a nine-fold higher odds of sexual dysfunction.

Conclusion: We demonstrated a high prevalence of symptoms of sexual dysfunction in patients with IBD, especially in women with CD. Encouraging gastroenterologists to screen for, and treat, these disorders with a holistic approach might improve quality of life of patients with IBD.

Disclosure: Nothing to disclose.

PP0482

COMBINING ULTRA-HIGH MAGNIFICATION ENDOCYTOSCOPE WITH AUTOMATED SPATIAL MULTISPECTRAL INTESTINAL BARRIER PROTEIN IMAGING FOR ASSESSMENT OF HEALING AND OUTCOMES IN ULCERATIVE COLITIS

M. Iacucci^{1,2,3}, S. Majumder^{2,3}, G. Santacroce³, I. Zammarchi³, Y. Maeda³, M. Puga-Tejada³, I. Dittonno³, B. Hayes⁴, R. Crotty⁴, E. Fennell⁵, U.N. Shivaji^{1,2}, Z. Abdawn⁶, R. Hejmadi⁶, P. Murray⁵, L. Burke⁴, S. Ghosh³

¹Gastroenterology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom,

²Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom, ³APC Microbiome Ireland, College of Medicine and Health, University College Cork, Cork, Ireland, ⁴Department of Histopathology, Cork University Hospital, Cork, Ireland, ⁵Health Research Institute, University of Limerick, Limerick, Ireland, ⁶Department of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Contact E-Mail Address: iacuccim@yahoo.it

Introduction: Endoscopic and histologic remission are key therapeutic targets in Ulcerative Colitis (UC). Recently, intestinal barrier healing has demonstrated superiority in predicting clinical adverse outcomes. It is promising, especially in patients with primary sclerosing cholangitis (PSC) colitis, which has more aggressive disease behaviour and a higher risk of colorectal cancer.¹

Hence, novel real-time and in-vivo tools for the intestinal barrier are pivotal.

Aims & Methods: This study aimed to assess intestinal barrier healing in UC using ultra-high magnification endocytoscope (ECS) and automated multispectral imaging. Thirty-four UC patients, 68% with PSC, in clinical remission undergoing surveillance colonoscopy, and 3 healthy controls were prospectively enrolled from two tertiary university referral centres. Ileal, ascending and descending colonic mucosa were evaluated with high-definition, virtual chromoendoscopy, and ECS, with biopsies taken from each segment.

Endoscopic remission was defined as MES ≤ 1 , UCEIS ≤ 1 , PICA ≤ 3 , while histological remission as RHI ≤ 3 without lamina propria or epithelial neutrophils, NHI ≤ 1 and PHRI = 0. A novel ECS score was applied to assess ileal and colonic intestinal barrier (Table 1).

Furthermore, the barrier was deeply characterised through automated multiplex immunofluorescence (inForm® Akoya Biosciences), quantifying tight junctions (TJs). Specifically, the cell density and mean expression of Claudin-2, Occludin and JAM-A were assessed in all intestinal segments.

Patients were followed up for a median of twelve months, and adverse outcomes, including flare-ups, hospitalisation, colectomy and changes in medication, were recorded.

ECS Ileum		ECS Colon	
Normal	0	Crypts architecture	
Break	1	Normal, elongated	1
		Irregular	2
		Necrosis	3
Few gaps / drop-out	2	Infiltration of the cell between the crypts	
Multiple gap / dropout	3	≤ 50%	1
		> 50%	2
Total Score	0 – 3	Distance between crypts	
		Normal (≥ 3 crypts in a VF)	1
		Elongated (< 2 crypts in VF)	1
		Intermediate (2-3 crypts in a VF with infiltrating cells in LP)	2
		Drop-out / necrosis	3
		Visibility of superficial microvessels	
		Not visible	0
		Visible	1
		Total score	3 – 9

Table 1. ECS score for barrier assessment.

Results: The ECS score moderately correlated with endoscopic scores ($r=0.48$ for MES, $r=0.66$ for UCEIS and $r=0.63$ for PICaSSO) and strongly with histological scores ($r=0.69$ for RHI, $r=0.71$ for NHI and $r=0.84$ for PHRI). Seven patients experienced adverse outcomes, with an ECS score <5 in the colon and <3 in the ileum predicting them (HR 2.35; $p<0.01$ and HR 5.78; $p=0.05$, respectively). All TJs were less expressed in UC patients than controls, with Claudin-2 and Occludin predominantly expressed in the epithelium and JAM-A mainly in the lamina propria. Notably, Claudin-2 cell density predicted outcomes (3370 vs 1290; $p=0.01$) and the ECS score in both colon and ileum correlated with Claudin-2 mean expression and cell density ($p=.15$; $p=0.02$ and $p=.48$, $p<0.01$, respectively). The combined intestinal barrier assessment by ECS and Claudin-2 cell density and mean expression significantly predicted outcomes in both colon and ileum (log rank test $p<0.01$).

Conclusion: ECS demonstrated promising ability to assess intestinal barrier in UC, positively correlating with TJ expression. Moreover, the novel barrier assessment through ECS complemented automated multispectral imaging in predicting adverse outcomes. These innovative tools hold promise in clinical practice for assessing barrier healing and guiding therapeutic management in UC and PSC colitis.

References: ¹ Han IS, Baek DH, Hong SM, et al. Incidence and adverse clinical events of primary sclerosing cholangitis with ulcerative colitis. *Int J Colorectal Dis.* 2023;38:175. doi:10.1007/s00384-023-04464-z

Disclosure: Nothing to disclose.

PP0483

IMPACT OF SICKLE CELL DISEASE ON THE COURSE OF INFLAMMATORY BOWEL DISEASE AND DRUG SAFETY PROFILE: A MULTICENTER STUDY

P. Freiha¹, J. Kirchgessner², A. Nuzzo³, I. Sobhani⁴, P. Bartolucci⁵, M. Uzzan⁶

¹Henri Mondor Hospital, Assistance Publique -Hopitaux de Paris, Department of Gastroenterology, Creteil, France, ²Saint-Antoine Hospital, Assistance publique-Hopitaux de Paris, Department of Gastroenterology, Paris, France, ³Beaujon Hospital, Assistance publique-Hopitaux de Paris, Intestinal Stroke Center unit, Department of Gastroenterology, IBD, Intestinal Failure, Paris, France, ⁴Henri Mondor Hospital, Assistance publique-Hopitaux de Paris, Department of Gastroenterology, Creteil, France, ⁵Henri Mondor Hospital, Assistance publique-Hopitaux de Paris, Genetic red blood cell diseases unit, Creteil, France, ⁶Henri Mondor Hospital, Assistance publique -Hopitaux de Paris, Department of Gastroenterology, Creteil, France

Contact E-Mail Address: Pamela.freiha@hotmail.com

Introduction: While patients with Sickle Cell Disease (SCD) often exhibit digestive manifestations, the underlying pathophysiology remains poorly understood. SCD could notably affect the intestinal mucosa through microvascular phenomena. Co-occurrence of SCD and Inflammatory Bowel Diseases (IBD) has been reported in a very limited number of cases. Our aim was to explore the intersection between SCD and IBD, particularly focusing on the impact of SCD on the natural course of IBD and the safety profile of drugs in this high-risk population.

Aims & Methods: We conducted a multicenter retrospective case-control study involving all adult patients diagnosed with both IBD and concomitant SCD and followed in 3 tertiary university hospitals. Each IBD patient with SCD was matched with up to 4 IBD patients without SCD, based on disease phenotype (UC or CD), sex, date of birth (± 3 years), length of disease follow-up (± 2 years), and year of diagnosis (± 3 years). The primary outcome was a complicated disease course, defined by a composite outcome including intestinal resection, perianal surgery, and/or the need for advanced therapy.

Results: Overall, 125 patients with IBD were studied, including 24 with concomitant SCD and 101 controls. Of the 24 SCD patients, 5 (20.8%) had Crohn's disease (CD), 17 (70.8%) had ulcerative colitis (UC) and 2 (8.3%) had indeterminate colitis. 23/24 (95 %) had colonic involvement. Of note, 8 of 24 (33.3%) SCD patients had concomitant primary sclerosing cholangitis (PSC) compared to 1% of patients in the control group ($p<0.001$). Survival without a complicated course of the disease was estimated at 58.7 % (IC95[49.6-69.5]) at 5 years and at 38.9% (IC95[29.9-50.4]) at 10 years, for non-SCD patients, and at 63.3% (IC95[45.7-87.6]) and 52.7% (IC95[34.9-79.6]) at 5 and 10 years, respectively, for patients with SCD and IBD ($p=0.36$, Log-rank test). The survival without the need of advanced therapy was estimated at 66.1% (IC95[57.3-76.2]) at 5 years for non-SCD patient, and at 78.2% (IC95[63-97.2]) in patients with SCD patients ($p=0.45$). Regarding the safety profile, 26.3% (5/19) of patients with SCD and 13.5 % (14/104) of controls experienced adverse events with advanced therapies ($p=0.17$, Fisher's exact test). There was one reported vaso-occlusive crisis associated with the use of thiopurines. No death occurred during follow-up.

Conclusion: While patients with SCD and IBD displayed a distinctive phenotype characterized by nearly constant colonic involvement and a high prevalence of associated PSC, the disease natural history of IBD did not differ from that of patients without SCD. Given the notable prevalence of PSC, systematic screening with cholangio-MRI should be considered. Furthermore, no significant safety signal regarding the use of immunomodulator or advanced therapy was raised.

Disclosure: Nothing to disclose.

PP0484

SEXUAL FUNCTION IN PATIENTS WITH ACTIVE PERIANAL FISTULIZING CROHN'S DISEASE

M.T. Bak¹, A.C. de Vries¹, L.P. Stassen², C.J. Buskens³, A.J. Pronk³, J. van der Bilt^{4,3}, K.B. Gecse⁵, N.K. de Boer⁶, C.D. Witjes^{7,8}, C. Fitzpatrick⁹, L. Nissen¹⁰, E.G. Verdaasdonk¹¹, M. Pierik¹², S.O. Breukink², L. Gilissen¹³, J.G. Bloemen¹⁴, R. West¹⁵, R.T. Kortekaas¹⁶, W. Mares¹⁷, G.M. de Jong¹⁸, S. Jansen¹⁹, A.L. Bloemendaal²⁰, M. Sikkema²¹, D. Zimmerman²², K.C.M.J. Peeters²³, F. Van Schaik²⁴, M.C. Richir²⁵, K. van Dongen²⁶, M. Duijvestein²⁷, F.J. Hoogenboom²⁸, M.C. Visschedijk²⁹, M.M. ter Kuile³⁰, A.E. Van Der Meulen - De Jong³¹, O. van Ruler^{7,8}, on behalf of the Dutch Initiative on Crohn and Colitis and the Dutch Initiative on Crohn and Colitis - Surgery

¹Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Maastricht University Medical Center, Surgery, Maastricht, Netherlands, ³Academic University Medical Center, Surgery, Amsterdam, Netherlands, ⁴Flevoziekenhuis, Surgery, Almere, Netherlands, ⁵Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁶Academic University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁷IJsselland Hospital, Surgery, Capell a/d IJssel, Netherlands, ⁸Erasmus University Medical Center, Surgery, Rotterdam, Netherlands, ⁹IJsselland Hospital, Gastroenterology and Hepatology, Capelle aan den IJssel, Netherlands, ¹⁰Jeroen Bosch Hospital, Gastroenterology and Hepatology, 's Hertogenbosch, Netherlands, ¹¹Jeroen Bosch Hospital, Surgery, 's Hertogenbosch, Netherlands, ¹²Maastricht University Medical Centre, Gastroenterology and Hepatology, Maastricht, Netherlands, ¹³Catharina Hospital, Gastroenterology and Hepatology, Eindhoven, Netherlands, ¹⁴Catharina Hospital, Surgery, Eindhoven, Netherlands, ¹⁵Sint Franciscus Gasthuis, Gastroenterology and Hepatology, Rotterdam, Netherlands, ¹⁶Sint Franciscus Gasthuis, Surgery, Rotterdam, Netherlands, ¹⁷Gelderse Vallei, Gastroenterology and Hepatology, Ede, Netherlands, ¹⁸Gelderse Vallei, Surgery, Ede, Netherlands, ¹⁹Reinier de Graaf Group, Gastroenterology and Hepatology, Delft, Netherlands, ²⁰Reinier de Graaf Group, Surgery, Delft, Netherlands, ²¹Elisabeth-TweeSteden Ziekenhuis, Gastroenterology and Hepatology, Tilburg, Netherlands, ²²Elisabeth-TweeSteden Ziekenhuis, Surgery, Tilburg, Netherlands, ²³Leiden University Medical Center, Surgery, Leiden, Netherlands, ²⁴University Medical Centre Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands, ²⁵University Medical Centre Utrecht, Surgery, Utrecht, Netherlands, ²⁶Pantein Hospital, Surgery, Boxmeer, Netherlands, ²⁷Radboudumc, Gastroenterology and Hepatology, Nijmegen, Netherlands, ²⁸University Medical Center Groningen, Surgery, Groningen, Netherlands, ²⁹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ³⁰Leiden University Medical Center, Obstetrics and Gynaecology, Leiden, Netherlands, ³¹Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands

Contact E-Mail Address: m.bak@erasmusmc.nl

Introduction: Sexual function is an important determinant of quality of life (QoL) and may be affected in patients with perianal fistulizing Crohn's disease (pCD). However, the literature on this topic is limited in patients with pCD.

Aims & Methods: Aims: This study aimed to evaluate the sexual function, the correlation between sexual function and quality of life and to identify potential risk factors for SD in patients with active pCD in a national prospective multicenter cohort study.

Methods: Patients with active pCD were identified from a prospective multicenter cohort study in 41 Dutch hospitals. Respondents on the sexual function (FSFI [female patients] or IIEF-5 [male patients]) and HR-QoL questionnaires (CAF-QoL scale and sIBDQ) were included in this study. Primary outcome was the prevalence of SD (FSFI<26.55, IIEF-5<22). Correlation for SD with HR-QoL was assessed with Spearman's correlation test. Potential risk factors for SD were identified using multivariable logistic regression.

Results: 214 patients with active pCD were included. Median age of the study cohort at inclusion was 37 years (IQR 30 – 51) and 52% of the patients were female. The median CD duration and median pCD duration comprised 8 years (3 – 17) and 4 years (2 – 8). The median FSFI and the median IIEF-5 scores were 19 (IQR 3.0 – 27) and 19 (IQR 9 – 24). Overall SD was reported by 69% of the patients and was more prevalent in female patients (75%) as compared to male patients (63%) without reaching significance ($p=0.07$). A significant higher CAF-QoL score (i.e. decreased pCD-related QoL)(median score 54 points vs. 35 points, $p<0.01$) and significant lower sIBDQ (i.e. decreased IBD-related QoL)(median score 46 points vs. 52 points, $p<0.01$) were observed in patients with SD. In addition, SD patients reported significantly more depressive symptoms (49% vs. 27%, $p<0.01$) as compared to patients with no SD. Higher rates of fatigue were reported in patients with SD, but did not reach significance. A weak correlation of SD with the CAF-QoL scale ($r=0.25$) and sIBDQ ($r=-0.24$) was observed. Multivariable analysis identified an older age (aOR 1.0; 95% CI 1.0 – 1.1), a longer pCD duration (aOR 0.9; 95% CI 0.8 – 0.9) and a decreased pCD-related QoL (aOR 1.0; 95% CI 1.0 – 1.1) were independently associated with SD (Table 1).

Variable	aOR	95% CI
Female sex	1.7	0.8 - 3.3
Age at baseline*	1.0	1.0 - 1.1
pCD duration*	0.9	0.8 - 0.9
Low educational level	1.7	0.6 - 5.3
Active luminal disease	1.3	0.7 - 2.7
Seton in situ	0.8	0.4 - 1.6
Ostomy in situ	0.9	0.4 - 2.7
Self-reported depressive symptoms	1.2	0.5 - 2.9
Self-reported fatigue	1.1	0.4 - 2.8
CAF-QoL scale*	1.0	1.0 - 1.1
sIBDQ	0.9	0.9 - 1.1

Table 1. Multivariable logistic regression

Abbreviations. aOR = adjusted odds ratio; CI = confidence interval; pCD = perianal fistulizing Crohn's disease; CAF-QoL = Crohn Anal Fistula - Quality of Life; sIBD = short Inflammatory Bowel Disease Questionnaire

Conclusion: Sexual dysfunction is highly prevalent in both male and female patients with pCD. A weak correlation between HR-QoL and SD was observed. An older age and a decreased pCD-related QoL were identified as risk factors for SD. Reversely, a longer pCD duration was identified as protective factor. Due to the high prevalence, the sexual function should be evaluated routinely by the treating team. When necessary, a referral to an expert may be considered.

Disclosure: Nothing to disclose.

PP0485

QUALITY OF CARE IN INFLAMMATORY BOWEL DISEASE THROUGH PATIENTS' EYES: VALIDATION OF THE PORTUGUESE VERSION OF IQCARO-QOC QUESTIONNAIRE

S. Ramos Lopes¹, M. Teixeira¹, D. Tomás¹, C. Sequeira¹, C. Teixeira¹, E. Gamito¹, A.L. Alves¹

¹Unidade Local de Saúde da Arrábida - Hospital São Bernardo, Gastroenterology Department, Setúbal, Portugal

Contact E-Mail Address: saramarlobes@gmail.com

Introduction: As a chronic disease, patients' perspectives of the quality of care (QoC) provided are increasingly recognized as an essential aspect of inflammatory bowel disease (IBD) management and an essential standard for units that manage patients with IBD¹.

Aims & Methods: Aims:

- Primary: Translation and validation of the Portuguese version of the IQCARO-QoC decalogue².

- Secondary: identify factors associated with a perception of better QoC.

Methods: A unicentric cross-sectional study was conducted in an IBD unit in a non-tertiary hospital. All consecutively evaluated IBD patients in the outpatient setting between January and December 2023 were included. Demographic and disease characteristics were collected.

The original version of IQCARO-QoC decalogue was translated and adapted into Portuguese (independent forward and back-translation).

Validity was assessed through correlation between IQCARO-QoC and visual analogue scale (VAS). Reliability was assessed through internal consistency, test-retest and intraclass correlation. Test-retest (4-week repeat) was used for measuring reliability.

Factors associated with QoC were analyzed.

Results: A total of 114 patients were included (51% female; mean age: 44±15 years), of whom 63% had Crohn's disease. 69% of patients were receiving biological therapy. Among the patients, 24% were solely in clinical remission and 48% in both clinical and endoscopic remission. 31 patients (27%) perceived their disease to be in remission.

The mean IQCARO score was 9.3±1.9. Construct validity analyses demonstrated moderate-to-strong correlations between the IQCARO-QoC and VAS. The IQCARO-QoC exhibited high internal consistency (Cronbach's $\alpha = 0.703$) and intraclass correlation (intraclass correlation coefficient = 0.622).

In univariate analysis, concerning patients' self-assessment of disease activity, those who considered their disease to be in remission reported higher IQCARO scores ($p=0.02$). Individuals with higher educational levels tended to perceive higher QoC ($p=0.037$). Disease duration, previous surgeries, hospitalizations, and number of outpatient appointments did not exhibit a statistically significant impact on QoC perception. Regarding quality of life, as assessed by the SIBDQ³ with a mean score of 50.7±12.1, a statistically significant positive correlation was observed between QoC and the SIBDQ ($r=0.276$, $p=0.004$).

Multivariate analysis revealed that education significantly influenced the perception of QoC provided ($\beta = -0.284$ [-1.490; -0.340], $p=0.002$).

Relationship between clinical outcomes and IQCARO-QoC	IQCARO-QoC
Treatment (Conventional vs Biological/ Advanced therapies)	$p=0.099$
Previous intestinal surgery	$p=0.296$
Hospitalization related to IBD	$p=0.346$
Clinical remission	$p=0.877$
Clinical and endoscopic remission	$p=0.624$
Patient-reported disease activity	$p=0.02$
Education	$p=0.037$
Disease duration	$r=0.112$ ($p=0.256$)
Quality of life (SIBDQ-PT)	$r=0.276$ ($p=0.004$)

Conclusion: The Portuguese version of the IQCARO-QoC is a simple, valid, and reliable tool for assessing the QoC perception among patients with IBD in clinical practice.

Furthermore, these observational data suggest an association between patients' perspectives of QoC and their evaluations of disease activity and quality of life. In our cohort, education emerged as an independent predictor influencing the perception of QoC received.

References:

1 - Fiorino G, et al. Quality of Care Standards in IBD: a ECCO Position Paper. J Crohns Colitis. 2020 Sep 7; 14(8):1037-1048.

2 - Calvet X, Saldaña R, Carpio D, Minguez M, Vera I, Juliá B, Marín L, Casellas F. Improving Quality of Care in Inflammatory Bowel Disease Through Patients' Eyes: IQCARO Project. Inflamm Bowel Dis. 2020 Apr 11;26(5):782-791.

3 - Roseira J, Sousa HT, Marreiros A, Contente LF, Magro F. Short Inflammatory Bowel Disease Questionnaire: translation and validation to the Portuguese language. Health Qual Life Outcomes. 2021 Feb 18;19(1):59.

Disclosure: Nothing to disclose.

PP0486

TAILORING CROHN'S DISEASE SURVEILLANCE AFTER ILEOCOLIC RESECTION: THE IMPORTANCE OF INFLAMMATORY BIOMARKERS

A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, J. Carlos Goncalves^{1,2,3}, C. Arieira^{1,2,3}, S. Xavier^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²School of Medicine, University of Minho, Life and Health Sciences Research Institute (ICVS), Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: joaogoncalves92@gmail.com

Introduction: Recurrence of Crohn's disease (CD) after ileocolic resection is common. However, reliable non-invasive monitoring methods are lacking, for instance, the use of faecal calprotectin (FC) has showed inconsistent results in this subgroup of patients.

Aims & Methods: The aim of this study was to evaluate clinical and biochemical factors associated with post-operative endoscopic recurrence in CD patients.

Retrospective single-center study including patients with CD who underwent ileocolonoscopy for CD surveillance, after ileocolic resection. The patients' clinical status was evaluated through Harvey-Bradshaw index (HBI), with clinical remission considered as ≤ 4 points. Biochemical parameters included erythrocyte sedimentation rate (ESR), c-reactive protein (CRP) and FC.

Clinical and biochemical parameters were evaluated in the 6 months prior to ileocolonoscopy. Post-operative endoscopic recurrence was defined as a Rutgeerts score $\geq$ i2b.

Results: A total of 81 patients and 121 ileocolonoscopies were included. Most patients were female (55.6%), with a mean age of 48±13 years. Regarding the Montreal classification, 37 patients had ileal disease (45.7%) and 44 ileocolonic disease (54.3%); 9 patients had nonstricturing, nonpenetrating disease (11.1%), 35 stricturing (43.2%) and 37 penetrating disease (45.7%). Nineteen patients had perianal disease (23.5%). The mean time between the surgery and the endoscopic evaluation was 135±79 months. Post-operative endoscopic recurrence was observed in 52 ileocolonoscopies (43.0%).

Symptomatic patients (HBI > 4 points) were 11 times more likely to have post-operative endoscopic recurrence (OR 10.686, 95%CI 2.930-38.974, $p<0.001$). Those with post-operative endoscopic recurrence had a significantly higher FC values (median 189 vs 69 μ g/g, $p<0.001$) and higher ESR

values (median 14 vs 9 mm, $p=0.002$). In fact, patients with FC values ≥ 150 $\mu\text{g/g}$ and those with ESR values > 12 mm were 4 and 3 times more likely to have post-operative endoscopic recurrence (OR 3.654, 95%CI 1.605-8.316, $p=0.002$ and OR 3.059, 95%CI 1.397-6.696, $p=0.005$, respectively). The presence of post-operative endoscopic recurrence was not associated with CRP values (median 2.9 vs 2.9 mg/L, $p=0.466$), and neither with mean time between the surgery and the endoscopic evaluation (mean 126 ± 83 vs 142 ± 75 months, $p=0.263$).

Conclusion: The presence of symptoms (HBI > 4 points), FC values ≥ 150 $\mu\text{g/g}$ and ESR values > 12 mm was associated with post-operative endoscopic recurrence in CD. Therefore, the HBI, FC and ESR values can be used to monitor CD patients after ileocolic resection, and prompt endoscopic evaluation should be performed in those with HBI > 4 points, FC values ≥ 150 $\mu\text{g/g}$ and/or ESR values > 12 mm.

Disclosure: Nothing to disclose.

PP0487

ASSESSMENT OF A REMOTE CALPROTECTIN MONITORING TOOL IN IBD: A COMPARATIVE AGREEMENT ANALYSIS OF A CLASSICAL LAB-BASED ASSAY AND A MOBILE PHONE-BASED QUANTITATIVE PATIENT SELF-TEST

H. Solhaug¹, A. Qamar¹, K. Sikorski¹, M. Schartum¹, L. Tommerup¹, E. Moerk¹

¹Calpro AS, Lysaker, Norway

Contact E-Mail Address: Ali.Qamar@svarlifescience.com

Introduction: Several treatment guidelines and published clinical consensus studies recommend using fecal Calprotectin as a monitoring tool for IBD. Available analysis methods range from well-established laboratory analysis methods to more recently developed rapid methods for remote monitoring and point of care.

Since there is no international reference for calprotectin, an established agreement between different assay platforms is needed to use them interchangeably. Ideally the assays from the same manufacturers should measure fecal calprotectin equally, although this is not always the case.

This study compares fecal calprotectin measurements from two different assay platforms from the same manufacturer.

Aims & Methods: 131 fecal samples from IBD patients were measured using CalproLab ELISA ALP (CALP0170) and CalproSmart Self-Test for remote monitoring of IBD. All fecal samples were extracted and analysed in parallel according to the kit-specific instructions given by the manufacturer, requiring individual sample collection and extraction methods for both assays. 64 samples covered the linear range for the assays and were included in the method comparison analysis.

Results: When comparing the two analysis methods, the slope and intercept values of 0.92 and 4.44 respectively suggest that there is no significant difference between the two methods within their common linear range. This includes all relevant clinical cut-off values for the two methods. Furthermore, the relative difference between the two assays ranges from -1.9% to -6.8% at selected calprotectin values.

Calprotectin values [mg/kg]	Relative difference [%]
77	-1.9%
100	-3.2%
200	-5.5%
250	-5.9%
500	-6.8%

Table 1: The relative difference between CalproSmart and CalproLab ELISA at selected calprotectin values.

Conclusion: CalproSmart and CalproLab ELISA measures fecal calprotectin equally and can be used interchangeably.

Disclosure: All authors are employees at Calpro AS. Experiments performed at Calpro R&D lab.

PP0488

EARLY MONITORING TREATMENT RESPONSE IN ULCERATIVE COLITIS: A MULTICENTER STUDY

F. Zorzi¹, F. Castiglione², A. Rispo², M. Fraquelli³, C. Bezzio⁴, M. Allocca⁵, E. Cuccagna¹, F. Furfaro⁵, F. Caprioli³, M. Ventura⁶, A. Testa², S. Saibeni⁷, G. Maconi⁸, E. De Cristofaro¹, G. Monteleone⁹, E. Calabrese¹⁰

¹University of Rome Tor Vergata, Gastroenterology Unit, Department of Systems Medicine, Roma (Rm), Italy, ²Federico II University, Naples, Italy, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁴IBD Centre, IRCCS Humanitas, Research Hospital, Rozzano,, Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy, ⁵IRCCS Hospital San Raffaele and University Vita-Salute San Raffaele, IBD Center, Milano, Italy, ⁶National Institute for Health, Migration and Poverty (INMP), Rome, Italy, ⁷ASST Rhodense, Gastroenterology Unit, Rho, Italy, ⁸Luigi Sacco University Hospital Gastroenterology Unit Biomed and Clinical Sciences, Department Of Biomedical And Clinical Sciences - L.Sacco University Hospital - Milan Italy, Milan, Italy, ⁹University Tor Vergata, Dept. of Systems Medicine, Rome, Italy, ¹⁰University of Rome Tor Vergata, Gastroenterology, Department of Systems Medicine, Rome, Italy

Contact E-Mail Address: emma.calabrese@uniroma2.it

Introduction: Data on using Intestinal Ultrasonography (IUS) for monitoring colonic lesions and treatment response in ulcerative colitis (UC) are still limited and most results are from single-center units usually performed in centers with a special expertise in IUS.

Aims & Methods: Our multicenter study aimed to identify predictive factors and monitor early response after different therapies in UC.

Methods: From July 2022 to Oct. 2023, we conducted a multicenter study at 5 IBD centers. UC pts starting biological therapies or small molecules were included, and underwent colonoscopy (CS), IUS, clinical assessments at baseline and at 12 weeks. All pts received standard of care therapy according to ECCO guidelines.

Exclusion criteria were disease limited to the rectum, active infections, and inability or contraindication to perform CS and/or IUS within the time intervals established by the study. Colonic wall thickening (CWT), vascularization (CWF), Milan Ultrasound Criteria (MUC), Mayo endoscopic score (MES), total/partial Mayo score were evaluated.

Results: Eighty-four UC patients were enrolled and eligible for starting biological therapy or small molecules. Forty-nine out of 84 pts (58.4%) were male, 40 pts (47.6%) had extensive colitis and 44 pts (52.4%) had left colitis, with a disease duration of 20 months (1-336); 53 pts (63%) were steroid-dependent/refractory.

Forty-one pts (48.9%) started anti-TNFs, 14 pts (16.6%) anti-IL12/23 or anti IL 23, 16 pts (19%) vedolizumab, and 13 pts (15.5%) JAKi. After 12 weeks, 39 out of 84 patients (46.4%) had partial Mayo score ≤ 2 , 31 patients (36.9%) 2-4, 10 patients (11.9%) 5-7, and 4 patients (4.76%) > 7 .

Forty-three out of 84 patients (51.2%) had MES=0-1, while 41 out of 84 patients (48.8%) had MES=2-3. Fifteen out of 84 patients (17.9%) had ultrasonographic response (defined as CWT < 3 mm) and 26 out of 84 patients (30.1%) had MUC < 6.2 (1). Logistic regression was performed to evaluate the relationship between clinical/endoscopic and ultrasonographic

characteristics and early IUS response at 3 months. Univariable analysis showed that active smoking ([RR], 1.9; 95% CI, 1.2–3.1, $p<0.005$), appendectomy ([RR], 2.5; 95% CI, 1.9–3.2, $p<0.0001$), partial Mayo score <2 ([RR], 2.18; 95% CI, 1.5–3, $p<0.001$) were associated with higher risk of response at 3 months. Inversely, severe endoscopic lesions (MES 3) (RR, 0.3; 95% CI, 0.2–0.6; $p<0.0001$), presence of lymph-nodes, mesenteric hypertrophy and vascularization ($p<0.001$, RR 0.36, 0.28, 0.45 respectively) were associated with a lower risk of response at 3 months. CWT was associated with a lower risk of response at 3 months (RR 0.66, 95% CI, 0.53–0.81, $p<0.0001$) and every increased mm was associated with a 34% reduction of IUS response. MUC was associated with a lower risk of response at 3 months (RR 0.78, 95% CI, 0.7–0.87) and every increased of one point was associated with a 22% reduction of IUS response.

In the multivariable analysis, CWT and MUC were the only predictive factors associated with IUS response at 3 months (RR 0.70, 0.78 respectively, $p<0.04$). A CWT <5.5 mm showed a 2.5 risk of treatment response at 3 months.

Conclusion: Our multicenter study demonstrated that IUS allows close monitoring of treatment in UC. MUC, and in particular CWT, are valuable parameters to predict early response in UC.

References: 1) Allocca M, et al. Predictive value of Milan ultrasound criteria in ulcerative colitis: a prospective observational cohort study. *United European Gastroenterol J.* 2022; 10:190–7.

Disclosure: Nothing to disclose.

PP0489

EVALUATION OF THE IMPACT OF AN IBD NURSE IN AN INFLAMMATORY BOWEL DISEASE CENTER

A. Rachart¹, V. Cluzeau¹, C. Martins², X. Hebuterne¹, A. Nicolau¹
¹Hospital Archet 2, Nice, Department of Gastroenterology and Clinical Nutrition, Nice, France, ²APHP, Gastroenterology, Paris, France

Contact E-Mail Address: nicolau.a@chu-nice.fr

Introduction: In some European countries, IBD nurse is not a recognized status. IBD nurses are general care nurses who wants to improve their knowledges and get involved in the « Care and Support » of IBD patients. An increasing number of IBD centers are using the services of IBD nurse. It seems important to evaluate the role and impact of IBD nurse.

Aims & Methods: The aim of this study was to evaluate prospectively the activity and impact of IBD nurse on the management of IBD patients in an IBD center. From March 13th to June 13th, 2023, all patients having interacted with IBD nurse in an expert center, were prospectively recorded. The main points were, the number and characteristics of patients, means and reasons of contact, actions implemented, follow-up and, finally, patient satisfaction assessed using a standardized questionnaire (visual analog scale from 0 to 10).

Results: During three months, 132 patients, 69 women and 63 men (47% Ulcerative Colitis, 52% Crohn's disease and 1% indeterminate colitis), with a median age of 40 years (16 to 87), had contacted the IBD nurse. Contact were made by phone call: $n=131$ (42%), text messages: $n=25$ (8%), e-mail: $n=69$ (22%), face-to-face consult: $n=86$ (27.5%) and teleconsultation: $n=1$ (0.5%).

The reasons for contact were: advices/questions/information: $n=121$ (39%), a scheduling/organization appointment issue: $n=60$ (19%), care-providing (biological check-up + starting treatment): $n=77$ (25%), emergency: $n=22$ (7%), request for an appointment/Information with IBD nurse: $n=19$ (6%), request for a patient education session (PE): $n=13$ (4%).

The 312 contacts had led to 315 actions divided into seven groups:

Action realized	Number of patients (n)	Percentage (%)
Explanation/Reinsurance	166	53%
Implementations or renewing prescription /administrative documents	55	17%
Scheduled visit (doctor, dietician, Nurse, Patient education program, outpatient unit, ...)	40	132%
Nursing care/learning self-care	25	8%
Referral to Patient Education Program	19	6%
Referral to emergency department or another department	7	2%
Patient hospitalization	3	1%

Over this period, IBD nurse was contacted 22 times by 19 patients for a real or perceived emergency. These situations were managed by a multidisciplinary team, and resulted in reinsurance (68%), referral to others medical specialist (18%) or hospitalization (14%).

Overall satisfaction with the IBD nurse intervention has been evaluated at 10/10 for 78% of patients and 9/10 for 11%. To the question: “do you think that the intervention of the IBD nurse improves disease management?”: 78.5% agreed at 10/10 and 7% at 9/10. To the question: “do you think contact with the IBD nurse improves access to care: 67.5% agreed at 10/10 and 3.5% at 9/10.

The main patients’ advice / reviews to improve care were: to adjust levels of follow-up according to the patient and his/her needs, to strengthen the IBD Nurse coordination team to limited days off, to have explanation sheets and reports of IBD Nurse intervention, to develop more workshops for patients in the Education program.

Conclusion: This pilot study showed the importance of the IBD Nurse activity in an expert center. The patients who benefited from this care were very enthusiastic about it.

Disclosure: This study has been funded by Janssen Pharmaceuticals.

PP0490

METAGENOMIC SEQUENCING IN DE NOVO PEDIATRIC INFLAMMATORY BOWEL DISEASE VERSUS CONTROLS WITH AND WITHOUT GASTROINTESTINAL SYMPTOMS

F. Prins¹, E. Vermeer², I.J. Hidding¹, J. Jagt³, R. Gacesa¹, R.K. Weersma¹, N.KH de Boer⁴, T.G. de Meij⁵
¹University of Groningen, University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ²Emma Children's Hospital, Amsterdam UMC, Department of Paediatric Gastroenterology and Nutrition, Amsterdam, Netherlands, ³Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Department of Pediatric Gastroenterology, Amsterdam, Netherlands, ⁴Amsterdam University Medical Center Location Vrije Universiteit Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁵VU University Medical Centre, Department of Pediatric Gastroenterology, Amsterdam, Netherlands

Contact E-Mail Address: f.m.prins@umcg.nl

Introduction: Inflammatory bowel disease (IBD), including Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U), often manifests in adolescence or young adulthood, with a trend towards decreasing age at presentation. Current diagnostic protocols for pediatric IBD involve an invasive colonoscopy under general anesthesia to differentiate between IBD and other conditions, such as functional abdominal pain and irritable bowel syndrome.

Previous microbiome research indicates significant differences in microbial composition of pediatric IBD patients compared to healthy controls (HC), illustrating its potential as non-invasive biomarker for pediatric IBD,

but an IBD-specific microbial signature has not yet been defined(1). This study aims to profile the microbiome in de novo pediatric IBD patients compared to controls with gastrointestinal symptoms (CGI), and HC.

Aims & Methods: We collected baseline fecal samples and clinical data from a cohort of de novo pediatric IBD patients and CGI. Consecutively, we matched all included patients from this cohort to a HC cohort from the Dutch Microbiome Project, based on age and sex. Metagenomic sequencing was performed to obtain data on bacterial species and functional pathway abundances. Diversity, dissimilarity and differential abundance analyses were conducted for bacterial species and pathways across various group comparisons.

Additionally, prediction analysis using Coda4Microbiome was performed to differentiate IBD from HC, IBD from CGI, and to predict treatment outcomes based on both microbial features and clinical features, including disease activity scores and inflammatory markers.

Results: We included 99 de novo IBD patients (66 CD, 27 UC, 6 IBD-U) and 74 CGI, matched to 341 HC. Microbial composition differed significantly across HC, CGI and IBD groups. Alpha-diversity decreased progressively from HC to CGI ($p<0.001$), further decreasing in IBD patients ($p=0.0056$). Disease status significantly explained a part of microbiome composition variance (beta-diversity, $p<0.001$, $R^2=0.045$), with distinct clustering patterns between HC, CGI and IBD samples. Differential abundance analysis revealed 116 differential abundant species between HC and IBD, and 30 species between CGI and IBD. We observed an increase in *F. prausnitzii* ($p<0.001$) in IBD compared to HC. Prediction models accurately distinguished IBD from HC using microbiome features (microbiome: $AUC=0.96\pm0.02$, clinical + microbiome: $AUC=0.96\pm0.02$) based on high abundance of *G. pamelaeae* and low abundance of *A. communis*, and IBD from other diseases (microbiome: $AUC=0.72\pm0.10$, clinical + microbiome: $AUC=0.83\pm0.09$), based on high abundance of *E. coli* and low abundance of a *Clostridia* species. Prediction of response to diet-based induction of remission in CD patients using baseline microbiome features yielded an AUC of 0.67 ± 0.13 , suggesting a potential effect of the gut microbiome, possibly limited by our non-responder numbers.

Conclusion: This study confirmed previous findings of profound microbiome differences between de novo pediatric IBD patients and HC. Additionally, we observed distinct microbiome compositions between CGI and IBD. Although clinical and biochemical models are often effective in distinguishing IBD from other diseases, our prediction models demonstrated that microbiome features have predictive power as well, including for predicting responses to nutrition-based treatments. Given the non-invasive nature of fecal sample collection, integrating microbiome features into future clinical diagnostics shows promise for improving diagnostic and therapeutic precision.

References: 1. Fitzgerald, Rachel S et al. "Paediatric Inflammatory Bowel Disease and its Relationship with the Microbiome." *Microbial ecology* vol. 82,4 (2021): 833-844. doi:10.1007/s00248-021-01697-9

Disclosure: RG received funding by Janssen Pharmaceuticals (for unrelated research projects), received consulting funding from Esso Biologics (for unrelated research projects). RKW has received unrestricted Research Grants from Takeda, Johnson & Johnson, Ferring and Tramedico and speakers fees from Abbvie, MSD and Boston Scientific and has acted as a consultant for Takeda Pharmaceuticals. TGJdM has received an unrestricted grant from Nutricia Benelux Corporation unrelated to this work. NKHdB has served as a speaker for AbbVie and MSD, as consultant and/or principal investigator for TEVA Pharma BV and Takeda and received a (unrestricted) research grant from Dr Falk, TEVA Pharma BV, MLDS and Takeda.

PP0491

IS TRANSMURAL HEALING BETTER THAN MUCOSAL HEALING IN PEDIATRIC CROHN'S DISEASE?

G. D'Arcangelo¹, L. Carnevale¹, S. Oliva¹, F. Maccioni², G. Russo¹, L. Busato², M. Aloï¹

¹Sapienza University of Rome, Pediatric Gastroenterology Unit, Rome, Italy, ²Sapienza University of Rome, Rome, Italy

Contact E-Mail Address: giuliadarcangelo87@gmail.com

Introduction: Data on the long-term benefit of transmural healing (TH) are scarce in children.

Aims & Methods: We investigated the outcomes of pediatric Crohn's disease (CD) patients with TH comparing them to those with mucosal healing (MH) and with "no healing".

We conducted a prospective, single-center, observational study conducted at the Pediatric Gastroenterology Unit of Sapienza University of Rome. Children with an established diagnosis of CD and under biological therapy undergoing an MRE and an ileocolonoscopy within a 3-month interval were consecutively enrolled. TH was defined as the complete healing of both the mucosa at endoscopy and of the bowel layers at the MRE. In the presence of a normal colonoscopy but an active MRE children were deemed as MH. The group "no healing" (NH) included children with an active endoscopy, regardless of the MRE classification. At 6, 12, and 24 months number disease flares, CD-related hospitalization, CD-related surgery, need for step-up treatment, and occurrence of complications were collected.

Results: 93 children were included (mean age 11.2 ± 3.8). Twenty-three (25%) were classified as TH, 27 (29%) as MH and 43 (46%) as NH. The risk of any unfavorable outcome was lower in both TH and MH patients compared to NH (Log Rank $p<0.0001$ and $p=0.002$). Children with TH were at lower risk of hospitalization ($p=0.02$), and complications ($p=0.007$) compared to those with NH.

No difference was found between MH and NH children for the same outcomes. Both TH and MH children were at lower risk of step-up treatment ($p<0.0001$ and $p=0.0002$, respectively) compared to NH. TH and MH patients were comparable for all the outcomes evaluated.

Conclusion: Achieving TH in pediatric CD is associated with better outcomes, although the additional benefit over MH alone does not appear significant. However, the persistence of inflammation is associated with worse outcomes in all patients.

Disclosure: Nothing to disclose.

PP0492

A COMPREHENSIVE ASSESSMENT OF FECAL INCONTINENCE, SEXUAL FUNCTION, AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASES

J. Vastarella¹, S. Camera¹, A. Di Domenico¹, L. Ruggiero¹, N. Sica¹, M. Angiuoni¹, A. Santonicola¹, P. Iovino¹

¹University of Salerno, Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", Salerno, Italy

Contact E-Mail Address: josephinevastarella@gmail.com

Introduction: Inflammatory bowel diseases (IBD) are chronic systemic conditions that affect patients' lives in various ways. To date, there is a scarce evidence correlating fecal incontinence, sexual dysfunctions, disease activity, and quality of life (QoL) in these patients.

This study aimed to evaluate the impact of fecal incontinence on sexual functions such as erectile and prostatic function in a cohort of IBD patients; and to analyse the relationship among fecal incontinence, sexual function and QoL.

Aims & Methods: IBD patients were enrolled from IBD clinic of the Gastroenterology Unit of the University Hospital of Salerno. Demographic characteristics, anthropometric data, and usage of immunosuppressive drugs were collected. Patients underwent a physical examination, and laboratory tests, including C-reactive protein (CRP) and fecal calprotectin (FC). A standardized questionnaire was used to assess gastrointestinal (GI) symptoms such as abdominal pain and fecal incontinence. For the latter, we also used the Wexner score. Crohn's Disease Activity Index (CDAI) and Mayo score as well as FC levels, and endoscopic findings were used to classify IBD patients as in active or in remission phase. Patients with perianal manifestations were excluded. Hormonal values (FSH, LH, Prolactin, 17-betaestradiol, testosterone) were measured. Sexual function was evaluated using the International Index of Erectile Function (IIEF), Male Sexual Health Questionnaire (MSHQ), Ejaculatory Dysfunction (EJD), prostatic dysfunction using the National Institute of Health - Chronic Prostatitis Symptom Index (NIH-CPSI) and International Prostatic Symptoms Score (IPSS). QoL was assessed by FiQoL domains (lifestyle, coping behaviour, self-perception and depression, embarrassment).

Results: Eighty-five male IBD patients (47 Crohn's disease [CD] and 38 ulcerative colitis [UC]), were enrolled. Mean age was 43.7 ± 15.9 years; mean BMI was 36.4 ± 25.5 Kg/m². Twenty-four CD patients had an active disease and 23 were in remission, while 20 UC patients had an active disease and 18 were in remission. UC patients showed significantly higher fecal incontinence and Wexner scores compared to CD patients (1.0 ± 1.9 vs 0.4 ± 1.2 , $p=0.05$ and 2.84 ± 4.2 vs 2.3 ± 1.1 , $p=0.01$, respectively). Only the Mayo score significantly correlated with Wexner score ($R_s=0.578$; $p<0.001$), and fecal incontinence ($R_s=0.584$; $p<0.001$).

Sexual function, evaluated by erectile and prostatic scores, nicely correlated each other's ($p<0.05$ in all cases). However, no association was found between fecal incontinence and all sexual function scores. The FiQoL domain self-perception and depression was significantly associated with IIEF ($p=0.01$).

Conclusion: This study highlighted the prevalence of fecal incontinence is higher in UC than CD patients. However, fecal incontinence did not impact on sexual function, evaluated by erectile and prostatic scores. QoL influenced erectile function.

Disclosure: Nothing to disclose.

PP0493
CAPSULE ENDOSCOPY AND ILEOCOLONOSCOPY FOR ILEAL CROHN'S DISEASE MONITORING, A COMPARATIVE ANALYSIS. PRELIMINARY RESULTS FROM A RETROSPECTIVE STUDY

L. Vergés Aleix¹, M. Marqués¹, M. Martínez², G. Torres³, A. Elosua González⁴, N. Torres¹, A. Carpio¹, D. Vázquez Gómez¹, I. Pascual¹, E. Sesé¹, B. Michans¹, R. Palau¹
¹Hospital Arnau de Vilanova, Gastroenterology, Lleida, Spain, ²Institut de Recerca Biomèdic de Lleida, Lleida, Spain, ³Hospital General de Granollers, Granollers, Spain, ⁴Hospital García Orcoyen | Hospital Universitario de Navarra, Gastroenterology and Hepatology, Pamplona, Spain

Contact E-Mail Address: vergeslaia@gmail.com
Introduction: The terminal ileum stands out as the most frequently affected segment of the gastrointestinal tract in Crohn's disease (CD). However, ileocolonoscopy (IC) may occasionally fail to fully explore this area. Notably, there is a lack of standardized quality criteria for IC in the context of ileal CD. Additionally, assessing inflammation activity only in the terminal ileum may lead to an underestimation of the overall ileal involvement. Capsule endoscopy (CE) offers a complete examination of both the entire terminal ileum and the remaining ileal segment.

Aims & Methods: This study presents the preliminary analysis of a retrospective study conducted at a single center. The primary outcome is the correlation between the total ileal activity, as assessed by CE, and the activity in the terminal ileum, as evaluated by IC. Furthermore, we explored the correlation between the results of these two examinations specifically concerning the evaluation of the terminal ileum. Patient inclusion criteria permitted a maximum time interval of 3 months between the two examinations. Activity measurement for CE was graded with the Lewis score of the third segment of the small intestine (Lewis-3S) and the Lewis score of the terminal ileum (Lewis-TI). For IC, the SES-CD index of the terminal ileum was collected. The study also includes an analysis of the correlation of endoscopic scores with biochemical markers (PCR, fecal calprotectin). Clinical, blood tests, and therapeutic data from medical records were systematically collected. **Results:** A total of 18 patients with ileal CD underwent CE and IC. CE revealed terminal ileum activity in 14 out of 18 patients (78%), whereas IC detected activity in only 4 out of 18 patients (22%). Notably, no significant correlations between CE and IC scores were observed. A moderate to strong correlation was, however, identified between the two CE scores, Lewis-3S and Lewis-TI (ρ 0.72 [0.31-0.94], $p=0.001$). The median length explored by IC was 15 [15-20] centimeters. Importantly, no correlation between endoscopic scores and biochemical parameters was observed, and no adverse events were documented.

Correlation SESD terminal ileum and Lewis 3rd segment p	0,391 (p>0,05%)
Correlation SESD terminal ileum and Lewis terminal ileum p	0,545 (p<0,05%)
Correlation Lewis third tercer segment and Lewis terminal ileum p	0,719 (p<0,05)

Table 1: Correlation between analytical data and between the two explorations.

Conclusion: In this preliminary analysis, despite the limited sample size, our findings indicate an underestimation of global ileal activity when measured by IC in comparison to CE examination.
Disclosure: Nothing to disclose.

PP0494
IN HINDSIGHT, DID WE OVERREACT? INSIGHTS ON COVID19 VACCINATION RESPONSE FROM A LARGE, REAL-WORLD IMID-PATIENT COHORT EVALUATED DURING SEQUENTIAL PHASES OF THE PANDEMIC

J. Geldof¹, M. Truyens², J. Sabino³, M. Ferrante³, J. Lambert⁴, H. Lapeere⁴, T. Hillary⁵, A. Van Laethem⁵, K. de Vlam⁶, P. Verscheuren⁶, E. Padalko⁷, T. Lobaton Ortega¹, S. Vermeire³, BELCOMID
¹Ghent University Hospital, Gastroenterology, Ghent, Belgium, ²IBD Research Unit UZ Ghent, Gastroenterology, Ghent, Belgium, ³University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ⁴Ghent University Hospital, Dermatology, Ghent, Belgium, ⁵University Hospitals Leuven, Dermatology, Leuven, Belgium, ⁶University Hospitals Leuven, Rheumatology, Leuven, Belgium, ⁷Ghent University Hospital, Laboratory Medicine, Ghent, Belgium

Contact E-Mail Address: jeroengeldof@gmail.com
Introduction: The BELCOMID study recruited immune mediated inflammatory disease (IMID) patients during the COVID19 pandemic. Patients were evaluated before vaccination, after onset of the vaccination campaign and after onset of booster vaccinations. Clinical data, Nucleocapsid(N)-antibodies and Spike(S-) antibodies were assessed.

Aims & Methods: Current subgroup analysis aimed to firstly, explore factors associated with N-/S-antibody response in IMID patients with different COVID19 vaccination status. Five patient groups were identified. G1: no vaccination before the vaccination campaign, G2: complete baseline vaccination, G3: 1 booster, G4: 2 boosters, G5: patients refusing every vaccine even after the booster campaign. We report on influence of IMID treatment and smoking status.

Secondly, we explored influence of SARS-CoV2 infection and vaccination on IMID flare-up.

Results: Demographics of 2165 recruited IMID patients are shown in Table. After baseline vaccination (G2) odds of N-seroconversion were higher in patients treated with combined IMM/TIMT (OR2.52, $p=0.023$). No other association with N-seroconversion was found.

Mean S-antibody titre increased progressively from G2 to G4. After completed baseline vaccination (G2), odds of S-antibody seroconversion were lower in those treated with TIMT (OR0.28, $p=0.0079$) particularly rituximab (OR0.0354, $p<0.001$), IMM (OR0.276, $p<0.001$), combined IMM/TIMT (OR0.156, $p<0.001$) and systemic steroids (OR0.183, $p<0.001$). IMID flare prior to vaccination was associated with lower risk of S-seroconversion (RR0.94, $p<0.001$). By contrast, mean S-titre was higher for those treated with antiIL23 (mean ratio 2.17, $p=0.011$) and vedolizumab (mean ratio 1.84, $p<0.001$) in G2.

After 1 booster (G3), lower odds of S-seroconversion remained with rituximab (OR0.0368, $p<0.001$), IMM (OR0.222, $p=0.0014$), combined IMM/TIMT (OR0.15, $p<0.001$) or systemic steroids (OR0.0637, $p<0.001$). Vedolizumab was associated with lower odds of being in the lowest S-titer quartile (OR0.206, $p<0.001$). Odds for S-antibody seroconversion with anti-TNF were higher compared to rituximab both for patients in G2 (OR26.3, $p<0.001$) and G3 (OR27.5, $p<0.001$).

Patients who received 2 boosters (G4) all had S-seroconversion and no IMID treatment modality was associated with higher odds of being in the lowest quartile.

After baseline vaccination (G2) smokers had higher risk of being in the lowest S-antibody titer quartile (RR1.45, $p=0.0098$). This observation persisted after 1 booster (G3) (RR1.42, $p=0.0122$) but was no longer noticed after 2 boosters (G4).

After start of booster vaccinations, 25.17% of patients had experienced IMID flare-up in the previous months. No significant association between IMID flare-up rate and previous SARS-CoV2 infection was found. There was no increased risk of IMID flare-up with additional booster vaccination. However, patients who received 2 booster vaccines showed a lower RR for IMID flare-up compared to those who only received 1 booster (RR0.70, $p=0.0067$).

	G1 (N: 2144)	G2 (N: 1532)	G3 (N: 1283)	Group 4 (N: 147)	Group 5 (N: 40)
Mean age (SD)	44.6 (35.5)	46.9 (30.8)	46.6 (32.7)	51.0 (15.7)	39.4 (14.4)
Male/female	1088 (51.0%) /1047 (49.0%)	794 (51.9%) /737 (48.1%)	661 (51.6%) /621 (48.4%)	80 (54.4%) /67 (45.6%)	24 (60.0%) /16 (40%)
Active smoker	369 (17.2%)	261 (17.0%)	201 (15.7%)	24 (16.3%)	12 (30.0%)
TIMT (targeted treatment)	1580 (73.7%)	1232 (80.4%)	1073 (83.6%)	119 (81.0%)	38 (95.0%)
IMM (immunomodulator)	456 (21.3%)	311 (20.3%)	225 (17.5%)	39 (26.5%)	8 (20.0%)
IMM+TIMT combined	263 (12.3%)	197 (12.9%)	152 (11.8%)	24 (16.3%)	8 (20.0%)
Recent systemic steroids	229 (10.7%)	91 (5.94%)	59 (4.60%)	6 (4.08%)	4 (10.0%)

Conclusion: Certain immune-modulating treatment modalities and smoking may blunt serologic COVID19 vaccination responses. However, this is overcome by repeated booster vaccination without increased risk of IMID flare-up.

Disclosure: The BELCOMID study group received research grants from following pharmaceutical companies: Almirall, Roche, Janssen, Pfizer, Eli Lilly, Amgen, Biogen, Mylan, LEO Pharma. These companies had no role in study design, conduct nor reporting of results.

PP0495

IBD-DISK AS A PREDICTIVE TOOL FOR INSOMNIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

R. Limam¹, N. Elleuch¹, H. Kallel¹, W. Dahmani¹, A. Hammami¹, A. Ben Slama¹, A. Braham Ep Krifa¹, H. Jaziri¹, M. Ksiai¹

¹Sahloul Gastroenterology Departement, Sousse, Tunisia

Contact E-Mail Address: limamrihab33@gmail.com

Introduction: The IBD-Disk is a validated 10-question, self-administered visual questionnaire used to assess the inflammatory bowel disease (IBD) related disability. Insomnia is common in IBD, and is often associated with a decline in patients' quality of life. The Insomnia Severity Index (ISI) is a validated tool that assesses the severity of insomnia in individuals.

Aims & Methods: The aim of this study was to evaluate the role of IBD Disk in the predilection of sleep disorders.

We conducted a cross-sectional study over 3 months between April and June 2023. IBD patients responded to the IBD-Disk and ISI questionnaires. Insomnia and severe insomnia were defined by a "Sleep" sub-score > 5 and > 7 respectively. The correlation between IBD-Disk and the ISI was analyzed using Pearson's correlation coefficient.

Results: We enrolled 57 patients with a mean age of 40.37 years [20-69] and a M/F sex ratio of 1.03.

Two-thirds of patients had Crohn's disease (CD). It was ileal in 14 patients (24.6%), ileocolic in 15 (15.8%), and colonic in 9 (26.3%). Ano-perineal involvement was present in 38.2% of cases. Nineteen patients (33.3%) had ulcerative colitis. Severe disease activity was noted in 14 patients (24.6%).

According to the ISI, insomnia was present in 24 patients (42.1%), distributed as follows: Mild insomnia in 19.3% of cases, moderate insomnia in 17.5% and severe insomnia in 1.8%. Insomnia was associated only with disease activity ($p=0.003$). According to the IBD Disk "Sleep" sub-score, insomnia was present in 29.8% of patients, distributed as follows: Moderate insomnia in 12.3% and severe insomnia in 17.5%.

A significant correlation was noted between the ISI, the IBD-Disk global score and the "Sleep" sub-score (respectively $r=0.506$ and 0.609 , $p<0.001$).

Conclusion: The IBD Disk is a psychometric tool that predicts the presence and severity of insomnia in IBD patients.

Disclosure: Nothing to disclose.

PP0496

VIRTUAL CHROMOSCOPY AND AUTOFLUORESCENCE FOR ASSESSMENT OF INFLAMMATION DEGREE IN IBD PATIENTS

M. Teberdieva¹, Y. Buzunova¹, E. Lomakina¹, A. Budzinskaya², A. Levitskaya¹

¹Moscow Regional Clinical Research Institute named after M.F. Vladimirovsky (MONIKI), Gastroenterology, Moscow, Russian Federation, ²Moscow Regional Scientific and Research Institute named M.F. Vladimirovsky, Department of Endoscopy, Moscow, Russian Federation

Contact E-Mail Address: atitaeva@inbox.ru

Introduction: Currently, most IBD clinics are equipped with endoscopic devices with virtual chromoscopy (VC) and autofluorescence imaging (AFI) screening functions.

These functions allow the mucosa and various neoplasms of the gastrointestinal tract to be examined in more detail and allow a presumptive conclusion to be made about the origin and histological nature of the changes detected.

Aims & Methods: To determine the potential of virtual chromoscopy (VC) and autofluorescence (AFI) for the assessment of inflammation in ulcerative colitis (UC) and Crohn's disease (CD).

151 patients with IBD (51 with CD, 100 with UC) were examined by ileocolonoscopy using the Olympus CF FH260AZL endoscope system EVIS LUCERA ELITE CLV-290SL with narrow-spectrum function and autofluorescence function with biopsy. Similar examinations were performed on 45 controls without bowel disease.

Results: Minimal UC showed the absence of venules in VC ($p < 0.05$), as well as green staining with purple foci in AFI ($p < 0.05$). Moderate inflammation was characterised by visualisation of submucosal venules ($p < 0.001$) and violet staining of the mucosa with green foci, which was significantly higher than this colour with minimal activity ($p < 0.001$).

Autofluorescence diffuse purple staining occurred significantly more often in patients with severe inflammation than in those with less severe inflammation, in those in remission and in controls ($p < 0.001$), and two types of vascular patterns were absent in VC ($p < 0.001$).

In CD, the infiltration phase was characterised by a statistically significant higher frequency ($p = 0.033$ and $p = 0.006$) of the visualisation of two types of green staining in the autofluorescence mode in comparable amounts than other colour options.

In the ulcer-fissure phase of VC, we observed predominantly capillary or venous visualization in the same amount ($p < 0.001$). In the scar phase, the frequency of the different types of staining was comparable to that in the remission phase and to that in the control group. In the VC, both types of vascular patterns were detected with a significantly higher frequency ($p = 0.001$).

Conclusion: Based on the results of our study, VC and AFI are additional methods in diagnosing the degree of activity of IBD and can be used in difficult cases to clarify the severity of inflammation in patients with UC and CD.

Disclosure: Nothing to disclose.

PP0497

THE VALUE OF FAECAL CALPROTECTIN TESTING IN PATIENTS PRESENTING WITH LOWER GASTROINTESTINAL SYMPTOMS; A RETROSPECTIVE PRIMARY CARE STUDY

N. Umar¹, P. Harvey², N. Harvey³, S. Haroon³, N. Trudgill⁴

¹Sandwell and West Birmingham Hospitals NHS Trust/University of Birmingham, Gastroenterology, West Bromwich, United Kingdom, ²The Royal Wolverhampton NHS trust, Gastroenterology, Wolverhampton, United Kingdom, ³University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom, ⁴Sandwell and West Birmingham Hospitals NHS Trust, Gastroenterology, West Bromwich, United Kingdom

Contact E-Mail Address: nosheen.umar@nhs.net

Introduction: Faecal calprotectin (FC) is of value in differentiating Inflammatory Bowel Disease (IBD) from other causes of lower gastrointestinal (GI) symptoms and is recommended in national guidance. This study aims to examine its role and factors associated with faecal calprotectin requesting in primary care.

Aims & Methods: Retrospective open cohort study using Clinical Practice Research Datalink (CPRD Aurum) of adults aged over 18 years with lower GI symptoms between 2015 and 2019. FC requested 30 days before to 3 months after a lower GI symptom record in primary care were included. Logistic regression analysis explored patient level factors associated with FC testing. Referral pathways and outcomes (IBD diagnoses) of patients with and without FC testing were also examined.

Results: Of 741,190 symptomatic patients, only 18,320 (2.5%) had FC requested in primary care: median age 38.3 (IQR 28.9-50.7); 51.4% female. The rate of FC requesting in symptomatic patients increased from 0.02% in 2010 to 4.4% in 2019 ($p = 0.001$).

FC value of < 50 ug/g and 50-200 ug/g were predominantly seen in patients with abdominal pain (42.1% and 37.9% respectively), while FC > 200 ug/g was predominantly seen in patients with diarrhoea (45.3%). Factors associated with FC requesting included: increasing age (> 70 years adjusted Odds Ratio 0.16 (95% CI 0.15-0.18)); female (0.89 (0.86-0.92); Black (0.61(0.56-0.66) or Asian (0.75 (0.70-0.80) ethnicity; obesity (0.89(0.85-0.93); lower socioeconomic status (0.91(0.86-0.98); comorbidity score > 2 (0.73(0.68-0.79); current smoking (0.89(0.85-0.92)); change in bowel habit (7.31(6.90-7.75), rectal bleeding (2.04(1.95-2.13) or diarrhoea (2.88(2.78-2.99) compared to abdominal pain; and ex-smokers (1.06(1.03-1.11).

IBD was diagnosed in 21.5% of patients referred with a FC > 200 ug/g, but only 2.9% of referred patients with a FC 50-200 ug/g. The only patients with a significant risk of IBD with FC 50-200ug/g were patients with rectal bleeding (8%), with the risk in all other patients only 1.7%. 27.8% patients with a normal FC test result were still referred to secondary care, of which only 0.4% had IBD.

Conclusion: Despite an increase in FC requests in recent years, only 4.4% of patients with relevant lower GI symptoms had an FC requested in primary care as recommended. Despite a negative FC test, a third of patients were still referred to secondary care, with very few diagnosed with IBD. Patients with an FC between 50 ug/g and 200 ug/g without rectal bleeding have a low risk of IBD and can be safety netted in primary care.

Disclosure: Nothing to disclose.

PP0498

CLUSTERING OF PATIENT-REPORTED OUTCOMES IN INFLAMMATORY BOWEL DISEASES – FINDINGS FROM A DANISH POPULATION-BASED INCEPTION COHORT

M. Attauabi^{1,2,3}, G. Roager Madsen^{2,3}, F. Bendtsen^{2,3,4}, J.B. Seidelin^{4,1}, J. Burisch^{2,3,4}

¹Copenhagen University Hospital, Herlev Hospital, Department of Gastroenterology and Hepatology, Herlev, Denmark, ²Copenhagen University Hospital - Hvidovre Hospital, Gastroint, Medical Section, Hvidovre, Denmark, ³Hvidovre Hospital, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents, and Adults, Hvidovre, Denmark, ⁴Faculty of Health and Medical Sciences, University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark

Contact E-Mail Address: mohamed.attauabi.02@regionh.dk

Introduction: Patient-reported outcomes (PROs) are pivotal in assessing treatment efficacy, delivering patient-centered care, and estimating the burden for inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD).

Aims & Methods: We aimed to investigate PROs at IBD diagnosis, including associated factors.

Since May 1st, 2021, all adult and pediatric patients with incident IBD within a catchment area encompassing 20% of the Danish population were enrolled in the prospective population-based Copenhagen IBD Inception Cohort.¹

Upon diagnosis, all adult patients diagnosed between May 2021 and May 2023 were asked to report PROs including Short inflammatory Bowel Disease Questionnaires (SIBDQ), IBD-Disability Index (IBD-DI), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Symptoms were evaluated using Memorial Symptom Assessment Scale, IBD Symptom Inventory, and Mayo Assessment of Functional Gastrointestinal

Disease. Multivariable logistical analysis adjusting for gender, age, and disease phenotype was conducted (adjusted odds ratio, aOR (95% confidence interval)).

Results: The population consisted of 203 and 116 patients with UC and CD (66% and 58% of the original cohort), respectively, who completed the PROs questionnaires within a median of 1.2 (IQR 0.3–3.0) months from diagnosis. The only baseline difference between participants and non-participants was a higher proportion of females with UC in the former group (60% vs. 44%, $p<0.01$).

In total, 160 (79%) and 99 (85%, $p=0.18$) patients with UC and CD, respectively, reported moderate to severe affection of at least one PRO, while 44% and 64% ($p<0.01$), respectively, reported moderate to severe affection of at least two PROs.

Specifically, a higher proportion of patients with CD reported moderately to severely impaired quality of life (QoL) (96 (82.8%)) compared to UC (141 (69.5%), $p<0.01$). Of those, 33 (82.5%) and 41 (56.9%), respectively, reported simultaneously moderate to severe fatigue and disability ($p=0.48$), while 19 (19.8%) and 27 (19.1%, $p=0.90$), respectively, reported moderate to severe QoL and fatigue but not disability. In addition, among 71 (35.0%) and 52 (44.8%) with UC and CD, respectively, reporting moderate to severe fatigue ($p=0.08$), all but three patients with UC had moderate to severe QoL, while 57.6% and 63.5%, respectively, reported moderate to severe disability. Accordingly, FACIT-F correlated strongly with SIBDQ in both UC (Pearson correlation coefficient (PCC) 0.76 (0.70–0.82) and CD (PCC 0.84 (0.78–0.89)).

The most frequent symptoms of UC were bloody stool (88%), lack of energy (82%), and abdominal pain (78%), whereas those of CD were lack of energy (86%, $p=0.36$) and abdominal pain (84%, $p=0.17$). These symptoms as well as bowel urgency (46% vs. 43%, $p=0.60$) were equally common in UC and CD, while bloody stool was less frequent in CD (54%, $p<0.01$). Finally, bowel urgency was linked to moderate to severe disability in UC (aOR=4.01 (1.11;14.51)), but not QoL or fatigue, which was confirmed in sensitivity analysis of proctitis.

Conclusion: Our prospective population-based inception cohort study highlights a considerable burden of UC and CD at the time of diagnosis, with moderate to severe impairment of PROs in most patients. In addition, we observed a clustering of impaired PROs in half of the patients, underscoring the interconnectedness of PRO metrics and symptoms. These findings emphasize the importance of tight monitoring of PROs and symptoms in clinical practice, allowing timely interventions.

References: 1. Attauabi M, Madsen GR, Bendtsen F, et al. Influence of Genetics, Immunity and the Microbiome on the Prognosis of Inflammatory Bowel Disease (IBD Prognosis Study): the protocol for a Copenhagen IBD Inception Cohort Study. *BMJ Open*. 2022;12(6):e055779. doi:10.1136/bmjopen-2021-055779

Disclosure: Mohamed Attauabi: None

Gorm Roager Madsen: Personal fees from Tillotts

Flemming Bendtsen: Tillotts, Ferring

Jakob Benedict Seidelin: has received research grants from Takeda, Janssen, the Danish Research Council, and the Capital Region Denmark, and is national coordinator of studies from AbbVie, Arena Pharmaceuticals, Ely Lilly, and Boehringer Ingelheim.

Johan Burisch: reports grants and personal fees from AbbVie, grants and personal fees from Janssen-Cilag, personal fees from Celgene, grants and personal fees from MSD, personal fees from Pfizer, grants and personal fees from Takeda, grants and personal fees from Tillotts Pharma, personal fees from Samsung Bioepis, grants and personal fees from Bristol Myers Squibb, grants from Novo Nordisk, personal fees from Pharmacosmos, personal fees from Ferring, personal fees from Galapagos, outside the submitted work.

PP0499

RAMAN SPECTROSCOPY AS A PROMISING EXPLORATORY MOLECULAR TOOL FOR DIAGNOSIS, PHENOTYPING AND ASSESSMENT OF MUCOSAL HEALING IN INFLAMMATORY BOWEL DISEASE

G. Santacroce¹, D.M. Ghauri^{2,3}, S. Maryam², I. Zammarchi¹, K. Komolibus², B. Hayes⁴, R. Crotty⁴, Y. Maeda¹, S. Majumder¹, M. Puga-Tejada¹, I. Ditunno¹, C. Prendiville¹, M. Hurley¹, A.-M. O'Keefe¹, J. McCarthy⁵, L. Burke⁴, R. Gautam², S. Ghosh¹, S. Andersson-Engels², M. Iacucci¹

¹APC Microbiome Ireland, College of Medicine and Health, University College Cork, Cork, Ireland, ²Tyndall National Institute, University College Cork, Cork, Ireland, ³University College Cork, Department of Engineering and Food Sciences, Cork, Ireland, ⁴Cork University Hospital, Department of Histopathology, Cork, Ireland, ⁵Mercy University Hospital, Department of Gastroenterology, Cork, Ireland

Contact E-Mail Address: giovanni.santacroce01@universitadipavia.it

Introduction: Diagnosing and assessing Inflammatory Bowel Disease (IBD) requires invasive procedures such as endoscopy and intestinal biopsies. However, reliable and accurate non-invasive tools for assessing and monitoring inflammation in IBD patients are in an exciting phase of early development. Raman spectroscopy (RS), which provides molecular vibrational spectra, can characterise human biofluids and intestinal samples, offering the potential for non-invasive molecular assessment, characterisation and monitoring in IBD.

Aims & Methods: This study aims to explore the potential of RS applied to saliva, blood and intestinal biopsies from IBD patients for molecular characterisation and development of new biomarkers enabling a reliable and accurate non-invasive diagnosis of IBD, phenotyping between Crohn's disease (CD) and Ulcerative Colitis (UC) and predicting mucosal healing (MH). IBD patients undergoing advanced endoscopy, i.e. ultra-high magnification endocytoscopy or probe-based confocal laser endomicroscopy, for disease assessment or surveillance and healthy controls were prospectively enrolled from two university hospitals in Cork, Ireland. Peripheral blood, saliva, and biopsies from the most representative bowel areas were collected. All matching samples were processed through a novel waveguide-enhanced RS technique, enabling sensitive detection of metabolites and other biochemical components.

Additionally, MH from matching biopsies was assessed as RHI $\leq$ 3 without lamina propria or epithelial neutrophils, NHI $\leq$ 1 and PHRI=0. RS data processing was performed using Matlab®. Spectral markers matched for saliva, blood and biopsies and differentiating IBD vs controls, CD vs UC and MH vs active inflammation were identified. A machine learning model based on linear discrimination analysis was used to assess the classification accuracy.

Results: A cohort of 16 IBD patients (median age 39, 11:5 M: F), comprising 9 UC and 7 CD, and 4 healthy controls (median age 43.5, 3:1 M: F) was enrolled, with matching saliva, blood, and biopsies. MH was found in 4 IBD patients. When comparing IBD patients with controls, differences in 3 wavenumbers were observed in all samples, corresponding to decreased tyrosine and lipids signals and increased carotenoids signal in IBD. Similarly, differences in spectral markers were found in CD vs UC, with increased lipids signal in CD and increased signals for carotenoids, nucleic acid, and amide proteins in UC.

Interestingly, 5 matching differences in saliva, plasma and biopsies spectra were found in patients with MH compared to those with active inflammation, including an increase in nucleic acids and amide proteins and a decrease in phosphate, lipids, and carotenoids. The machine learning model showed promising accuracy (above 82%) of RS-aided biofluids analysis in diagnosing IBD and predicting phenotype and MH.

Conclusion: The combination of spectral markers from saliva and plasma, confirmed at tissue level, showed promise in accurately diagnosing IBD and distinguishing CD from UC. Notably, RS non-invasive biomarkers could predict MH with promising accuracy, identifying metabolites involved in IBD-associated inflammation, particularly lipids, carotenoids, and nucleic acids. Therefore, RS holds potential as a monitoring and predictive tool for inflammation and healing in IBD, with intriguing translational implications. Further studies are required to validate these preliminary findings and shed light on molecular mechanisms.

Disclosure: Nothing to disclose.

PP0500

THE PREDICTIVE VALUE OF INTESTINAL ULTRASOUND FOR TREATMENT RESPONSE IN IBD: A SYSTEMATIC REVIEW

C. Teichert^{1,2}, J.M. Vos^{3,2}, F. de Voogd¹, G.R. D’Haens¹, B. Koot³, K.B. Gecse¹

¹Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands,
²Amsterdam Gastroenterology Endocrinology Metabolism (AGEM) Amsterdam University Medical Center, Amsterdam, Netherlands,
³Emma Children’s Hospital Amsterdam University Medical Center, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Contact E-Mail Address: c.teichert@amsterdamumc.nl

Introduction: Selecting the right treatment in the early stages of inflammatory bowel disease (IBD) is essential for preventing disease progression and modifying disease course. Intestinal ultrasound (IUS) is a promising tool in predicting early treatment response. We aimed to systematically review current literature on the predictive value of IUS for treatment response.

Aims & Methods: A literature search was performed on the 24th of October and updated on the 26th of March 2024 using PubMed, Medline, Embase, Cochrane Library and Cinahl. We included articles in paediatric and adult IBD patients where IUS was used for the assessment of treatment. Studies were grouped based on timing of IUS after start of treatment. In acute severe ulcerative colitis (ASUC) timing included within 5 days or between 6-14 days. In ulcerative colitis (UC) or Crohn’s disease (CD) baseline, 0-3 weeks, 4-8 weeks, 12-16 weeks and >16 weeks were used. Additional response assessments included clinical or endoscopic disease activity scores and adverse events (e.g. surgery, hospitalization, treatment escalation).

Results: Out of 1739 unique articles, 27 were included with 17 in CD, 6 in UC and 4 in ASUC. Baseline IUS parameters were not predictive of treatment response in CD, UC or ASUC. In CD, most studies investigated response to anti-TNF (n=12), though multiple therapies were evaluated (n=5). For anti-TNF, IUS was predictive of response to therapy at all time points from 2 weeks onward. IUS at week 4 to 8 showed conflicting results in studies using multiple treatments. After 12 weeks, IUS predicted clinical and endoscopic outcomes as well as adverse events in all studies regardless of treatment. Lastly, an IUS several months after starting treatment predicted clinical response, adverse events and endoscopic response in the follow years. A variety of medical treatments were included in most UC studies (n=3). IUS within 3 weeks of treatment initiation was able to predict both short- and long-term clinical response in UC. Endoscopic response could be predicted by IUS after 6 weeks. The combination of BWT and colour Doppler signal (CDS) measured at 3 and 9 months of therapy predicted endoscopic activity after 9 and 15 months, respectively.

In ASUC, bowel wall thickness (BWT) significantly differed between responders and non-responders of intravenous steroid treatment when measured 1-3 days after treatment initiation.

	IUS time point	Drug*	Clinical outcomes	Adverse outcomes**	Endoscopic outcomes
CD	<3 weeks	Anti-TNF MT	Yes	No	Yes
	4-8 weeks	Anti-TNF USTE MT	Yes	Inconclusive	Yes
			Yes		Yes
	12-16 weeks	Anti-TNF USTE MT	Yes	Yes	Yes
					Yes
ASUC	1-5 days	CS	Yes	Yes	
	6-21 days	CS	Yes	Yes	
UC	<3 weeks	CYTA MT	Yes		No
	4-8 weeks	MT			Yes
	12-16 weeks	CS MT			Yes
					Yes
	>16 weeks	CS			Yes

* CS=corticosteroids | MT=multiple treatments |CYTA=cytapheresis | USTE=Ustekinumab
**Hospitalization, surgery, treatment escalation or no discontinuation of corticosteroids

Conclusion: IUS performed at 1-3 days, 2 weeks and 6 weeks was predictive of treatment response in ASUC, CD and UC, respectively. Further data is needed to characterize IUS response kinetics of the individual therapies.

Disclosure: J.M.B.W. Vos: None

C. Teichert: None

F.A.E. De Voogd: received speaker or honoraria fees from AbbVie, Janssen, Galapagos, Pfizer and Takeda

G.R.A.M. D’Haens: received research grants from Abbvie, Alimentiv, BMS, J&J, Pfizer, Takeda; consulting fees from Abbvie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom Biosciences, Galapagos, Index Pharmaceuticals, Kaleido, Glaxo Smith Kline, Gossamerbio, Pfizer, Immunic, Johnson and Johnson, Polpharma, ProCise Diagnostics, Prometheus laboratories, Prometheus Biosciences, Progenity, Protagonist, and Ventyx; speaker’s fees from Abbvie, Arena, Boehringer Ingelheim, Celltrion, Galapagos, Gilead, Pfizer, BMS, and Takeda; data monitoring board: Galapagos, AstraZeneca, Seres Health.

B.G.P. Koot: None

K.B. Gecse: received grants from Pfizer Inc, Celltrion, and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, ImmunicTherapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis, and Takeda; and speaker’s honoraria from Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda, and Tillotts.

PP0501

PHYSIOLOGIC AND ANATOMIC CHARACTERISTICS OF PELVIC FLOOR DISORDERS IN INFLAMMATORY BOWEL DISEASE PATIENTS

M. Livne Margolin¹, R. Yehuda Margalit¹, C. Maradey¹, A. Levartovsky¹, U. Kopylov¹, D. Carter¹

¹Sheba Medical Center, Gastroenterology, Ramat Gan, Israel

Contact E-Mail Address: Moranlivne@gmail.com

Introduction: With the expansion of treatment options available for inflammatory bowel disease (IBD), the emphasis on refractory functional disorders grows along with new treatment targets, aiming at quality-of-life improvement. Pelvic floor disorders such as fecal incontinence (FI) and obstructive defecation syndrome (ODS) are considered as disabling conditions and are a source of embarrassment and suffering for IBD patients. Reluctance to complain and feeling of incompetence leads to a delay in diagnosis and treatment.

Aims & Methods: Aim: To characterize the etiology and the physiological characteristics of pelvic floor disorders in a cohort of IBD patients as compared with non IBD patients.

Methods: Data was collected from the medical files of IBD patients who went through a workup due to defecation disorder during 2015-2024. All patients completed either an anorectal manometry, trans anal ultrasound (TRUS) or evacuation proctography. Data was compared to that of a control group, that included patients with defecation disorders without IBD, that went through a similar medical workup.

Results: 67 IBD patients were included, 44 patients (66%) with Crohn's disease (CD) and 23 with ulcerative colitis (34%). Perianal involvement was diagnosed in 25% of the CD group. The control group consisted of 140 patients. Gender and age did not differ significantly between the groups. The median number of deliveries in the IBD group was 2.5 (IQR=1) versus 2 births (IQR=1) in the control group ($P=0.38$). The prevalence of pelvic floor surgery was higher in the control group (36%, VS. 18%, $p=0.01$).

Pelvic floor dyssynergy was diagnosed in 75% of the patients in the control group compared with 59% of the patients in the IBD group ($p=0.03$). Rectal hyposensitivity was found in 44% of the patients in the control group compared with 46% of patients in the IBD group ($p=0.06$), and rectal hypersensitivity was diagnosed in 13% of the patients in the control group versus 33% of the IBD group, $p=0.003$. (Table 1)

		IBD	Non-IBD	P value
Dyssynergia		34 (59%)	75 (75%)	$P=0.03$
Anal compliance	normal	12 (25%)	51 (39%)	$P=0.07$
	low	36 (75%)	79 (61%)	
Balloon explosion		11 (21%)	22 (16%)	$P=0.56$
	hyposensitive	24 (46%)	58 (44%)	$P=0.06$
	hypersensitive	17 (33%)	17 (13%)	$P=0.003$
TRUS	Internal sphincter tear	6 (16%)	24 (17%)	0.84
	External sphincter tear	10 (26%)	23 (16%)	0.16
	fistula	4 (11%)	1 (0.7%)	0.0009

Conclusion: Pelvic floor disorders in IBD patients may be associated with higher prevalence of rectal hypersensitivity compared with non-IBD patients. Dyssynergy is common in IBD patients and is associated with FI. Understanding the mechanisms of pelvic floor disorders in IBD patients is essential for choosing the best treatment modalities in this group of.

Disclosure: Nothing to disclose.

PP0502

CPA9-HNE: A NEUTROPHIL-DERIVED FRAGMENT OF CALPROTECTIN MEASURED IN SERUM CAN MONITOR ENDOSCOPIC AND CLINICAL DISEASE ACTIVITY IN ULCERATIVE COLITIS

M. Sorokina Alexdóttir¹, A. Poulsen², M. Pehrsson¹, M.A. Karsdal¹, A.-C. Bay-Jensen¹, J. Burisch³, J.B. Seidelin⁴, J.H. Mortensen¹

¹Nordic Bioscience A/S, Biomarkers and Research, Herlev, Denmark, ²Bispebjerg Hospital, Digestive Disease Center, København N, Denmark, ³Hvidovre University Hospital, Gastrounit, Medical Section, Virum, Denmark, ⁴Herlev Hospital, Gastroenterology and Hepatology, Herlev, Denmark

Contact E-Mail Address: mara@nordicbio.com

Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) presenting in remitting ulcerations of the colonic mucosa and submucosa. Mucosal healing is therefore an important treatment target for optimal disease management. While fecal calprotectin is a common biomarker used to monitor mucosal healing in UC, patient compliance is low due to a preference for serological markers over fecal ones.

Aims & Methods: This study aimed at investigating the association of serum calprotectin [CPa9-HNE], a non-invasive neo-epitope biomarker of neutrophil activity, with both clinical and endoscopic disease activity in UC. The cohort included 49 patients with active UC and 50 and healthy controls (HC). Endoscopic and clinical disease activity was assessed using the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and the full Mayo score. Serum calprotectin [CPa9-HNE] was measured, reflecting a human neutrophil elastase-derived fragment of calprotectin. Spearman's rank correlation was applied. Group differences were evaluated using Kruskal-Wallis with Dunn's test, bonferroni corrected for MCP. Diagnostic and discriminative capabilities were assessed using receiver operating characteristic (ROC) statistics with area under the curve (AUC).

Results: CPa9-HNE was significantly elevated in patients with UC compared to HC (ng/ml [IQR]: 32.4 [29.0–52.3] vs. 26.0 [22.6–29.0], $p<0.0001$) and presented acceptable discriminative capabilities (AUC [95% CI]: 0.77 [0.67–0.87], $p<0.0001$). CPa9-HNE showed a moderate positive correlation to UCEIS and Mayo ($p=0.42$; $p=0.48$, both $p<0.01$). When patients were stratified according to endoscopic disease activity (UCEIS), CPa9-HNE was significantly elevated in patients with severe disease compared to those with mild disease (ng/ml [IQR]: 55.6 [40.9–66.4] vs. 28.9 [24.6–31.1], $p<0.01$) and could accurately discriminate between the two groups. Similarly, when patients were grouped according to the full Mayo score, CPa9-HNE was significantly elevated in patients with mild vs. severe disease (29.1 [24.3–32.4] vs. 62.9 [55.2–67.5], $p<0.01$) and moderate vs. severe disease (32.0 [29.2–39.2] vs. 62.9 [55.2–67.5], $p<0.01$), and could accurately discriminate between the groups.

Conclusion: CPa9-HNE was elevated in patients with UC compared with healthy subjects. Furthermore, CPa9-HNE accurately discriminated between patients with mild and severe endoscopic disease based on the UCEIS score, as well as between patients with mild, moderate, and severe clinical disease activity according to the full Mayo score. These findings highlight the potential use of CPa9-HNE as a non-invasive tool to monitor both endoscopic and clinical disease activity in UC, with the potential of guiding treatment decisions and better aligning with patient preferences.

Disclosure: MSA, MPE, MAK, ACBJ, and JHM are employees of NB.

L. Oldenburg¹, B. Hens², M. Hollenberg¹, G.R. D'Haens¹¹Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²UZ Brussel, Gastroenterology, Jette, Belgium**Contact E-Mail Address:** l.oldenburg@amsterdamumc.nl**Introduction:** A small but significant proportion of patients with Crohn's disease (CD) will ultimately require a permanent ileostomy. (1-3) The natural history and treatment success in these patients remain unclear and studies on endoscopic recurrence are lacking.

The aim of this study was to investigate the endoscopic recurrence rate, possible risk factors, and treatment outcomes with current biological agents.

Aims & Methods: We performed a retrospective study of CD patients with a permanent ileostomy in a tertiary referral center. Inclusion criteria were CD adults (≥ 16 years) and the presence of an ileostomy for at least 12 months. Ileal postoperative recurrence was defined as the presence of ulcerations during ileoscopy.Traditional risk factors historically associated with postoperative recurrence (age at diagnosis ≤ 16 years, active smoking, penetrating phenotype, and inflammation at resection margin) were evaluated. (4,5) The probability of developing post-operative ileitis was examined by cox regression and Kaplan Meier analysis.

	All patients (N=166)	Endoscopic surveillance (N=115)
Female, n (%)	105 (63.3)	77 (67.0)
Median age at diagnosis, years (IQR)	22.0 (16.8-31.0)	22.0 (16.0-30.0)
Median disease duration at time of surgery, years (IQR)	7.0 (2.0-15.0)	7.0 (2.0-13.0)
Smoking status at time of surgery, n (%)		
Never	89 (53.6)	68 (59.1)
Former	29 (17.5)	26 (22.6)
Current	36 (21.7)	16 (13.9)
Unknown	12 (7.2)	5 (4.3)
Disease location and behaviour at diagnosis, n (%)		
L1, ileal	13 (7.8)	11 (9.6)
L2, colonic	95 (57.2)	67 (58.3)
L3, ileocolonic	42 (25.3)	30 (26.1)
Unknown location	16 (9.6)	7 (6.1)
B1, inflammatory	71 (42.8)	54 (47)
B2, stricturing	13 (7.8)	7 (6.1)
B3, penetrating	28 (16.9)	20 (17.4)
Unknown behaviour	54 (32.5)	34 (29.6)
Perianal disease at time of surgery, n (%)	74 (44.6)	51 (44.3)
Previous intestinal resection, n (%)	86 (51.8)	55 (47.8)
Previous immunomodulator, n (%)	109 (65.7)	79 (68.7)
Previous biological therapy, n (%)	125 (75.3)	88 (76.5)
Previous anti-TNF	102 (61.4)	71 (61.7)
≥ 2 prior biologicals	32 (19.3)	23 (20)
≥ 1 traditional risk factor*, n (%)	138 (83.1)	95 (82.6)
Endoscopic recurrence, n (%)		46 (40)
Endoscopic remission after treatment, n (%)		
Infliximab		4/13 (20.8)
Adalimumab		7/13 (53.8)
Vedolizumab		6/8 (75)
Ustekinumab		4/12 (33.3)

Table 1.

*Defined as age at diagnosis ≤ 16 years, active smoking, penetrating phenotype, history of IBD-surgery and inflammation at resection margin.**Results:** 166 patients were identified (median age 34 years (IQR 24-46), 63% female) (Table 1). Median follow-up after surgery was 5.5 years (IQR 2-14) and 37% had a loop ileostomy without resection. 115/166 (69%) underwent endoscopy during follow-up. Indications for ileoscopy were symptoms of flare (50%), planning for ostomy closure (14%) and other indications (21%). Endoscopic lesions were observed in 40% of patients, with a cumulative risk at 1-, 3- and 5-years of 13%, 27% and 36%, respectively. Controlling for traditional risk factors, patients with preoperative anti-TNF treatment were at higher risk (HR 2.18, 95% CI 1.11-4.28), with 17%, 41%, and 44% recurrence rates at 1, 3, and 5 years respectively (log rank $P = 0.01$). Other traditional risk factors for postoperative recurrence were not predictive of endoscopic disease recurrence in this cohort. Ileal recurrence was treated with biological therapy, including infliximab, adalimumab, vedolizumab, or ustekinumab. Patients treated with vedolizumab had the highest rate of remission (6/8 patients) and longest treatment persistence (54 months, IQR 19-102.8) (Table 1).**Conclusion:** This retrospective study showed that 40% of ileostomy patients developed endoscopic recurrence. Patients with previous anti-TNF exposure were at higher risk of recurrence. Vedolizumab was the most effective treatment, although this finding needs to be confirmed in larger cohorts.**References:**

1. Cosnes, J., Gower-Rousseau, C., Seksik, P., & Cortot, A. (2011). Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology*, 140(6), 1785–1794. <https://doi.org/10.1053/j.gastro.2011.01.055>
2. Ma, C., Almutairdi, A., Tanyingoh, D., Seow, C. H., Novak, K. L., Lu, C., Panaccione, R., Kaplan, G. G., & Kotze, P. G. (2019). Reduction in surgical stoma rates in Crohn's disease: a population-based time trend analysis. *Colorectal disease: the official journal of the Association of Colorectal Surgery of Great Britain and Ireland*, 21(11), 1279–1287. <https://doi.org/10.1111/codi.1473>
3. Everhov, Å. H., Kalman, T. D., Söderling, J., Nordenvall, C., Halfvarson, J., Ekblom, A., Ludvigsson, J. F., Olén, O., & Myrelid, P. (2022). Probability of Stoma in Incident Patients With Crohn's Disease in Sweden 2003-2019: A Population-based Study. *Inflammatory bowel diseases*, 28(8), 1160–1168. <https://doi.org/10.1093/ibd/izab245>
4. Gionchetti P, Dignass A, Danese S, Magro Dias FJ, Rogler G, Lakatos PL, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 2: Surgical Management and Special Situations. *J Crohns Colitis*. 2017;11(2):135-49.
5. Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*. 2019;68(Suppl 3):s1-s106.

Disclosure: Geert D'Haens has served as advisor and/or speaker for Abbvie, Alimentiv, Astrazeneca, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Ferring, Eli Lilly, Galapagos, Glaxo Smith Kline, Immunicon, Index Pharmaceuticals, Johnson and Johnson, Polpharm, Prometheus biosciences, Prometheus laboratories, ProCise diagnostics, Protagonist, Sandoz, Takeda, Tillotts, Ventyx.

PP0504

EARLY INTESTINAL ULTRASOUND IN ULCERATIVE COLITIS PATIENTS TREATED WITH FILGOTINIB: PRELIMINARY DATA FROM THE STEER STUDY

M. Pruijt¹, C. Teichert¹, F. de Voogd¹, M. Lowenberg¹, R. Goetgebuer¹, G.R. D'Haens¹, K.B. Gecse¹

¹Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: m.j.pruijt@amsterdamumc.nl

Introduction: Intestinal ultrasound (IUS), in particular bowel wall thickness (BWT), is accurate in determining endoscopic disease activity in ulcerative colitis (UC). Reduction of BWT six weeks into advanced anti-inflammatory treatment predicted endoscopic response and clinical remission. Filgotinib is a preferential JAK1-inhibitor effective in UC. Currently, there is no data on IUS-kinetics or early prediction of treatment response with filgotinib.

Aims & Methods: In this study, we aimed to identify early IUS predictors of treatment response to filgotinib in patients with moderate to severe UC. This prospective observational study included UC patients with active endoscopic disease (i.e. endoscopic MAYO score (EMS) ≥ 2) starting with filgotinib. Clinical scores (UCEIS, Lichtiger), biochemical parameters and IUS parameters of the sigmoid were assessed at baseline, after 4 weeks (W4) and at the time of the second endoscopy (between W8 and W23). Endoscopic remission (i.e. EMS=0), endoscopic response (i.e. decrease in EMS ≥ 1 compared to baseline) and clinical remission (SCCAI ≤ 2 or Lichtiger score ≤ 3) were assessed. IUS response (i.e. defined as a reduction in BWT of $>25\%$ or >2.0 mm, or >1.0 mm and one colour Doppler signal) was assessed at week 4. All normally distributed data were reported in mean $\pm$ standard deviation [SD] and non-normally distributed in median and interquartile range [IQR]. Mann-Whitney U tests were used to compare continuous non-parametric variables, chi square tests for dichotomous variables.

Results: A total of 20 patients were included. 13 patients underwent second endoscopy, 2 refused a follow-up endoscopy and 5 patients were still in follow-up. At baseline, 9 patients (9/20, 45%) had received ≥ 2 biologicals, 16 patients (16/20, 80%) had previous anti-TNF exposure, and no patients were exposed to other JAK-inhibitors. 8 patients (8/20, 40%) had severe endoscopic disease at baseline (i.e. EMS=3). 5 patients (5/13, 38%) were endoscopic responders at W8-23, and no patient reached endoscopic remission. BWT was significantly lower in the sigmoid colon from W4 onwards for patients reaching endoscopic response (Table 1). Decrease in BWT compared to baseline was statistically greater in endoscopic responders from W4 onwards (Table 1). IUS response was seen at W4 in 6 patients, of which 5 were endoscopic responders (83%, $p=0.002$). Decrease in BWT from W4 onwards was statistically greater in patients reaching clinical remission at W8-23 (-45% (-55% to -36.6%) vs -9% (-25% to +8%), $p=0.014$).

Time point	Endoscopic response (n=5)	Endoscopic non-response (n=8)	p-value
Median BWT (IQR) at baseline	4.5 mm (3.2-6.2)	5.1 mm (3.6-6.5)	$p=0.61$
Median BWT (IQR) at W4	1.9 mm (1.8-3.8)	4.7 mm (3.3-5.9)	$p=0.019$
Median BWT (IQR) at W8-23	2.2 mm (1.8-3.7)	5.3 mm (4.3-6.7)	$p=0.008$
Median decrease in BWT (IQR) W4	-42% (-53% to -38%)	-3% (-16% to +9%)	$p=0.003$
Median decrease in BWT (IQR) W8-23	-45% (-51% to -35%)	-10% (-1% to +24%)	$p=0.003$

Conclusion: On IUS, UC patients treated with filgotinib have significantly lower BWT from week 4 onwards compared to baseline, which could predict endoscopic response.

Disclosure: MP received speakers fees from Janssen and Tillotts
CT received speakers fees from Tillotts

FV received speaker or honoraria fees from AbbVie, Janssen and Tillotts
ML received consultancy/lecturefees from Abbvie, Bristol Myers Squibb, Eli Lilly, Galapagos, Janssen-Cilag, Johnson & Johnson, Medtronic, Pfizer, Takeda and Tillotts.

RG Received speakers fee from Janssen and Tillotts

GD has served as a consultant and/or received speaker's fees from AbbVie, Alimentiv, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion Healthcare, Cytoki Pharma, Eli Lilly, Ferring, Galapagos, Glaxo SmithKline, Gossamer Bio, Immunic, InDex Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Takeda, Tillotts, Ventyx Biosciences.

KG has received grants from Pfizer Inc, Celltrion and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunic Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis and Takeda and speaker's honoraria from Abbvie, Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda and Tillotts.

PP0505

ARTIFICIAL INTELLIGENCE-ASSISTED DIGITAL PATHOLOGY IS COMPARABLE TO EXPERT PATHOLOGISTS AND OUTPERFORMS NON-EXPERTS IN INFLAMMATORY BOWEL DISEASE: A NETWORK META-ANALYSIS

M. Puga-Tejada¹, S. Majumder¹, Y. Maeda¹, I. Zammarchi¹, I. Ditonno¹, G. Santacroce¹, S. Ghosh¹, M. Iacucci¹

¹APC Microbiome Ireland, College of Medicine and Health, University College of Cork, Cork, Ireland

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Histological diagnosis and assessment of Inflammatory Bowel Disease (IBD) face significant intra- and inter-observer variability, even among expert pathologists (1). Artificial intelligence (AI)- assisted digital pathology models have been developed to address this challenge (2). However, their comparative accuracy with pathologists remains uncertain.

Aims & Methods: This is the first meta-analysis comparing performance metrics among IBD-related AI models and expert and non-expert pathologists. A systematic search identified papers investigating AI-digital pathology in IBD, published from inception to March 2024. Using the online EPPI-reviewer platform duplicates among PubMed and Scopus were automatically excluded. Consequently, four experienced IBD researchers conducted blind manual screening and excluded studies lacking sufficient data. We computed the pooled diagnostic accuracy metrics, including sensitivity or recall, positive predictive value (PPV) or precision, observed agreement or accuracy, F1 score and Matthew's correlation coefficient (MCC). Data were meta-regressed and network meta-analysed using the "meta" and "netmeta" libraries from R v4.0, respectively (R Foundation for Statistical Computing; Vienna, Austria).

Results: Among 223 studies retrieved after the systematic search strategy, only 23 were selected for full-text evaluation, and 12 were included for final analysis (Table 1).

The included studies were published between 2022 to 2024. According to the random effect model, pooled sensitivity, PPV, accuracy, F1 score and MCC of AI models were 0.85 (0.81; 0.88; $I^2=94.9\%$), 0.88 (0.85; 0.90; $I^2=91.1\%$), 0.88 (0.85; 0.90; $I^2=96.3\%$), 0.85 (0.82; 0.88; $I^2=96.4\%$), and 0.71 (0.60; 0.82; $I^2=100.0\%$), respectively. Although high heterogeneity was found, accuracy sub-analysis showed no significant difference between CD vs UC (.88 vs.87) or disease diagnosis vs disease assessment (.89 vs .87). Expert pathologists reached the highest pooled accuracy (.91), fol-

lowed by AI models (.88) and non-expert pathologists (.82), being significantly different according to the meta-regression ($p<.01$). Network meta-analysis revealed no significant difference between the performance of AI vs expert pathologists, while AI outperformed non-experts in accuracy (OR 2.68; 95% CI 1.08-.66), F1 score (OR 2.52; 95% CI 1.03-6.16), and MCC (OR 4.53; 95% CI 2.08-9.88).

Studies included		n (%)
Inflammatory Bowel Disease (IBD) phenotype*, n (%)	Ulcerative colitis (UC)	9/12 (75%)
	Crohn's disease (CD)	3/12 (25%)
	Not specified	1/12 (8%)
Aim of the study, n (%)	IBD diagnosis	2 (17%)
	Disease assessment	10 (83%)
Observer, n (%)	Artificial intelligence (AI)	12 (100%)
	Expert pathologist	2 (17%)
	Non-expert pathologist	1 (8%)

Table 1. Studies included in the network meta-analysis.
*Not-mutually exclusive variables.

Conclusion: AI-assisted digital pathology exhibits promising potential in IBD diagnosis and disease activity assessment, comparable to expert pathologists and superior to non-experts. These findings support the integration of AI models to expedite central reading in clinical trials and hold promise for future application in clinical practice. Nonetheless, standardisation efforts are pivotal to reducing heterogeneity and facilitating widespread AI implementation.

References: 1. Rymarczyk D, Schultz W, Borowa A, Friedman JR, Danel T, Branigan P, Chałupczak M, Bracha A, Krawiec T, Warchoł M, Li K, De Hertogh G, Zieliński B, Ghanem LR, Stojmirovic A. Deep Learning Models Capture Histological Disease Activity in Crohn's Disease and Ulcerative Colitis with High Fidelity. *J Crohns Colitis*. 2024 Apr 23;18(4):604-614. doi: 10.1093/ecco-jcc/ijad171. PMID: 37814351; PMCID: PMC11037111.

2. Gui X, Bazarova A, Del Amor R, Vieth M, de Hertogh G, Villanacci V, Zardo D, Parigi TL, Røyset ES, Shivaji UN, Monica MAT, Mandelli G, Bhandari P, Danese S, Ferraz JG, Hayee B, Lazarev M, Parra-Blanco A, Pastorelli L, Panaccione R, Rath T, Tontini GE, Kiesslich R, Bisschops R, Grisan E, Naranjo V, Ghosh S, Iacucci M. PICaSSO Histologic Remission Index (PHRI) in ulcerative colitis: development of a novel simplified histological score for monitoring mucosal healing and predicting clinical outcomes and its applicability in an artificial intelligence system. *Gut*. 2022 May;71(5):889-898. doi: 10.1136/gutjnl-2021-326376. Epub 2022 Feb 16. PMID: 35173041; PMCID: PMC8995819.

Disclosure: Nothing to disclose.

PP0506
ASSOCIATION OF ULTRASONOGRAPHIC INFLAMMATORY ACTIVITY PARAMETERS WITH FUTURE DRUG FAILURE IN CROHN'S DISEASE PATIENTS DURING MAINTENANCE ANTI-TNF THERAPY

D. Carter¹, S. Haj², I. Veisman³, L. Dr³, S. Ben-Horin⁴, O. Regev⁵, U. Kopylov⁴, A. Albshesh⁴
¹Sheba Medical Center and Faculty of Medical & Health Science, Tel Aviv University, Gastroenterology, Tel Hashomer, Israel, ²Sheba Medical Center, Internal Medicine C, Ramat Gan, Israel, ³Sheba Medical Center, Gastroenterology, Ramat Gan, Israel, ⁴Sheba Medical Center and Faculty of Medical & Health Science, Tel Aviv University, Gastroenterology, Tel Hashomer, Israel, ⁵Joyce & Irving Goldman Medical School, Faculty of Health Sciences, Ben-Gurion-University of the Negev, Beer Sheva, Israel

Contact E-Mail Address: ahmad.albshesh@gmail.com

Introduction: Intestinal ultrasound (IUS) is effective for monitoring treatment efficacy in Crohn's disease (CD). Bowel wall thickness (BWT) is used as a surrogate of inflammatory activity. However, the added value of other IUS parameters ((bowel wall flow (BWF), stratification (BWS), lymph node enlargement, mesenteric fat hypertrophy, and complications)) for monitoring and predicting treatment failure during anti-TNFs' maintenance therapy is still poorly defined and was the goal of this study.

Aims & Methods: This was a retrospective cross-sectional study. The study population included patients treated on infliximab or adalimumab maintenance treatment who had undergone an index intestinal ultrasound examination. We examined the added value of various ultrasonographic activity signs, in addition to bowel wall thickness, for their association with subsequent treatment failure. Treatment failure was defined as the need for CD-related surgery, hospitalization, corticosteroid use, dose escalation, and drug discontinuation.

Variable	Treatment Failure				Drug Discontinuation		
	Adjusted Odds Ratio (aOR)	95% CI	P-Value		Adjusted Odds Ratio (aOR)	95% CI	P-Value
BWT	≥3	3.25	1.30-8.12	0.012	2.3	0.94-5.60	0.068
	≥3.5	2.7	1.07-6.78	0.035	1.78	0.73-4.35	0.209
	≥4	2.47	0.93-6.51	0.068	2.68	1.04-6.89	0.042
High BWF	2.93	1.16-7.39	0.023		1.5	0.63-3.59	0.361
Enlarged lymph nodes	1.41	0.32-6.34	0.651		0.68	0.15-3.07	0.62
Mesenteric fat hypertrophy	4.44	1.15-17.07	0.03		5.29	1.61-17.44	0.006
Disturbed BWS	4.64	0.93-23.20	0.062		2.73	0.71-10.44	0.143
IUS Complications	6.04	0.69-52.59	0.104		4.66	0.80-27.05	0.086

Table 1: Sonographic Characteristics Associated with Treatment Failure and Drug Discontinuation.
Abbreviation: BWT - bowel wall thickness; BWF - bowel wall flow; BWS - bowel wall stratification; IUS - intestinal ultrasound.

Results: The study included 103 CD patients treated with anti-TNF therapy (67% adalimumab and 33% infliximab) who underwent an IUS at a median of 10 months (IQR 6-18) after starting therapy. Of 103 patients, 59.2% experienced treatment failure at a median of 5 months (2-12.5) after the index IUS examination. Among the failure group, bowel thickness at preceding index IUS was significantly higher compared with patients without failure (3.9 vs 3mm, respectively, $P= 0.007$), BWF was higher (49.2% vs.

23.8%, $P=0.009$), and mesenteric hypertrophy was more prevalent (20.4% vs 7.1%, $P=0.006$). Logistic regression identified increased BWT and mesenteric hypertrophy as having a significant association with therapy failure.

A sensitivity analysis with the outcome of therapy discontinuation revealed that mesenteric fat hypertrophy was a significant predictive factor along with increased BWT (Table 1).

Conclusion: Our study highlights the significance of BWT, BWF, and mesenteric fat hypertrophy as key sonographic markers associated with anti-TNF treatment failure in Crohn's disease. Integrating these indicators into scoring systems may enhance predictive accuracy, providing a quantitative tool for evaluating disease severity and treatment response.

Disclosure: Nothing to disclose.

PP0507

NON-INVASIVE DIAGNOSTICS OF ULCERATIVE COLITIS REMISSION

A. Zubova¹, G. Tarasova¹

¹Rostov State Medical University, Gastroenterology, Rostov-on-Don, Russian Federation

Contact E-Mail Address: doctor-gastro@yandex.ru

Introduction: Studies using a variety of diagnostic techniques confirm the importance of the gut microbiota in the pathogenesis of ulcerative colitis (UC), as well as its possible influence on the effectiveness of drug therapy and the prognosis of the disease. In different phases of the UC course, structural and quantitative changes in the gut microbiota suggest its use as a non-invasive diagnostic tool and the tool predicting the achievement of clinical and endoscopic remission of the disease.

Aims & Methods: The objective of the study was to determine the taxonomic diversity of the gut microbiota in patients with UC in various phases of the disease and to identify microorganisms that are predictors of remission. The study included 21 patients (age from 20 to 41 years, 13 men and 8 women) in the relapse phase of UC - left-sided UC with mild to moderate activity (Truelov-Witts scale, Mayo index); and 20 patients (age from 26 to 52 years, 10 men and 10 women) in the phase of clinical endoscopic remission. The gut microbiota was assessed by NGS sequencing of the bacterial 16S ribosomal RNA gene structure using the IlluminaMiSeq platform. After the normality test, we performed statistical analysis using the nonparametric Mann-Whitney test, the analysis is presented by median and quartiles.

Results: We predicted clinical and endoscopic remission of UC using a logistic regression model, including microorganisms, the number of which in absolute values changed more significantly. In cases of achieving clinical and endoscopic remission of the disease, we recorded a statistically significant increase in the levels of Streptococcus, NK4A214_group and Pelomonas and a decrease in Enterococcus and Actinomyces. The developed logistic regression model is statistically significant and statistically reliable using evaluation criteria: chi-square ($p=0.002$), Cox & Snell's pseudo R-squared is 0.556, Nagelkerk is 0.741, which allows its use in wide gastroenterological practice to make decisions on modifying the course of drug therapy for UC (Table 1).

Genus	Coefficient	Odds ratio	p
Enterococcus	-117,244	$1.2 \cdot 10^{-51}$	0,011
Streptococcus	1,117	3,06	0,045
NK4A214_group	2,335	10,33	0,008
Pelomonas	67,529	$2.1 \cdot 10^{29}$	0,011
Actinomyces	-55,947	$5.0 \cdot 10^{-25}$	0,008
Constant	-0,528	0,59	0,201

Table 1. Results of modeling the gut microbiotope in patients with UC using logistic regression.

Conclusion: The study results provide a prognostic model for non-invasive diagnosis of achieving UC remission. Predictors of achieving clinical and endoscopic remission of UC are high levels of Streptococcus, NK4A214_group and Pelomonas, as well as a decrease in the number of Enterococcus and Actinomyces.

Disclosure: Nothing to disclose.

PP0508

ADHERENCE TO QUALITY PERFORMANCE MEASURES FOR ENDOSCOPY IN IBD: A NATIONWIDE ITALIAN SURVEY

A. Cassinotti¹, I.M. Luppino², R. Pumpo³, L. Ceccarelli⁴, R. Vassallo⁵, S. Segato¹, M. Soncini⁶, M.C. Di Paolo⁷

¹ASST Sette Laghi, Varese, Italy, ²Annunziata Hospital Cosenza, Gastroenterology, Cosenza, Italy, ³P.O. Santa Maria del Loreto Nuovo, Endoscopy Unit, Napoli, Italy, ⁴AOU Pisa, Pisa, Italy, ⁵Ospedale "Buccheri la Ferla" Fatebenefratelli, Gastroenterology, Palermo, Italy, ⁶ASST Lecco, Lecco, Italy, ⁷Azienda Ospedaliera Complesso Ospedaliero San Giovanni Addolorata, Roma, Italy

Contact E-Mail Address: andreacassinotti@libero.it

Introduction: The quality of gastrointestinal endoscopy in inflammatory bowel disease (IBD) patients has been recently identified as a major priority being associated with better outcomes.

Aims & Methods: We aim to assess the adherence of Italian gastroenterologists to current international recommendations on quality performance measures for IBD endoscopy.

From March to July 2023 a total of 178 Italian consultants were invited to participate to an online questionnaire-based survey, which included questions on their demographics, professional characteristics and clinical behaviour as well as structural features of their affiliations. Four clinical domains were analysed: A) the first endoscopy for suspected IBD; B) assessment of endoscopic activity; C) post-operative Crohn's disease; and D) surveillance endoscopy for patients at high risk of colorectal neoplasia. Recommendations from three consensus on quality performance measures for IBD endoscopy (BRIDGE, ECCO, ESGE) were used as reference standards. A p value ≤ 0.05 was considered statistically significant.

Results: Overall, responders paid low attention to perform ileal biopsies in case of the first colonoscopy for suspected IBD (67% vs standard of care 80%) as well as to the use of the Paris (70%) and mucosal pattern classifications (60%) for lesion characterization of endoscopic visible lesions. Ileal intubation (97%) and colonic biopsies (80%) during the first colonoscopy for suspected IBD, adequate tissue samples management (96%), post-operative schedule within 1 year (94%), implementation of surveillance plans (96%) and use of endoscopic index of activity (95%) were highly reported. No significant regional differences were observed, while significantly lower performances were reported for many outcomes by small centers (<100 IBD patients in follow-up and/or no more than 2 physicians for each IBD unit) or physicians spending <50% of their clinical activity for IBD. Young doctors <35 years old had a significantly higher use of modern classifications for lesion characterization (Paris: 89% vs 68%; Kudo: 82% vs 56%).

Conclusion: In Italy, the adherence to current standards of care for IBD endoscopy is generally good, with some practices to be improved. There is a need to support the endoscopic activity of small centers and doctors less engaged in IBD.

Disclosure: Nothing to disclose.

PP0509

SERUM BIOMARKERS OF PROTEOLYTIC TISSUE DESTRUCTION, FORMATION AND MACROPHAGE ACTIVITY CAN DISCERN PATIENTS WITH IBD ACCORDING TO INFlixIMAB TREATMENT NON-RESPONSE OR RESPONSE

M. Pehrsson¹, E. Aighobahi¹, M. Sorokina Alexdóttir¹, C.S. Steenholdt², T.L. Boye², M. Karsdal¹, A.-C. Bay-Jensen¹, M.A. Ainsworth³, J.H. Mortensen¹

¹Nordic Bioscience A/S, Immunoscience, Herlev, Denmark,

²Herlev Hospital, Herlev, Denmark, ³Odense University Hospital, Gastroenterology, Odense, Denmark

Contact E-Mail Address: eai@nordicbio.com

Introduction: Characterized by chronic inflammation, patients with Inflammatory Bowel Disease (IBD) experience detrimental remodeling of their intestinal extracellular matrix (ECM). Treatment with anti-inflammatory drugs can reduce inflammation, leading to remission and tissue healing. However, adequate monitoring of patients is critical to ensure and maintain treatment response. As potential surrogate markers of ECM remodeling, we investigated blood-based biomarkers of type III and -VII collagen and posttranslational modifications of vimentin in patients with IBD.

Aims & Methods: By quantifying biomarkers of intestinal tissue destruction (C3M), tissue formation of type VII collagen (PRO-C7), and the macrophage activity biomarker, VICM, we aimed to determine the value of these biomarkers for identifying and monitoring response to infliximab (IFX).

160 IBD patients initiating IFX treatment at visit 1 were included, having blood drawn at visits 1, 2, and 3, with treatment response evaluated at visit 3 using the Physicians Global Assessment (PGA) score. The response was defined as a PGA of 0 at Visit 3. Measuring the biomarkers C3M (MMP-9 degraded type III collagen), PRO-C7 (pro-peptide of type VII collagen), and VICM (citrullinated and MMP-degraded vimentin) in the blood, we evaluated their ability to identify responders (n=141) and non-responders (n=19) to IFX induction therapy. The biomarker levels between responders and non-responders were statistically assessed using a stepwise logistical regression model and DeLong et al. receiver operating characteristics.

Results: Using logistical regression, the combination of serum C3M and PRO-C7 measured at visit 1 could discern non-responders and responders with an AUC of 0.717 (p=0.001, sens: 61.1%, and spec: 80.2%). At visit 2, serum VICM provided an AUC of 0.684 (p=0.006, sens: 57.9%, and spec: 78.9%), whereas measuring C3M at visit 3 discerned patients with an AUC of 0.695 (p=0.009, sens: 60.0%, and spec: 74.4%). Finally, we performed a stepwise logistical regression model combining all the biomarkers for a composite score. Measuring PRO-C7 at visit 1, VICM at visit 2, and C3M at visit 3 identified non-responders to IFX treatment with an AUC of 0.797 (p<0.001, sens: 80.0%, and spec: 74.5%).

Conclusion: Quantifying specific fragments of MMP-degraded type III collagen reflecting tissue destruction, the formation of type VII collagen, and the macrophage activity biomarker VICM in patients treated with IFX could, with a moderate to good AUC, identify patients who at visit 3 would be determined a non-responder or responders to IFX treatment based on their PGA. Our data suggest differences in the proteolytic tissue destruction and formation biomarkers, in combination with macrophage activity, can discriminate between responders and non-responders to IFX treatment.

Disclosure: Martin Pehrsson, Marta Alexdottir, Morten Karsdal, Anne-Christine Bay-Jensen, and Joachim Mortensen are employed at Nordic Bioscience A/S

The remaining authors have nothing to declare.

PP0510

BACTERIAL PROFILE OF THE GUT IN PATIENTS WITH ULCERATIVE COLITIS IN DIFFERENT PHASES OF DISEASE PROGRESSION

A. Zubova¹, G. Tarasova¹

¹Rostov State Medical University, Gastroenterology, Rostov-on-Don, Russian Federation

Contact E-Mail Address: doctor-gastro@yandex.ru

Introduction: Numerous studies show that changes in the composition of the gut microbiota constitute an important factor influencing both the development of ulcerative colitis (UC) and the prognosis of the disease, drug metabolism and effectiveness of treatment. The growing global prevalence of UC necessitates continued advances in diagnostics and treatment. Gut microbiota can be considered as a promising dynamic biomarker for non-invasive assessment of the severity of UC and the effectiveness of treatment.

Aims & Methods: The purpose of the research was to study the taxonomic diversity of the gut microbiota in patients with UC at different stages of the disease. The study included 21 patients (ages from 20 to 41, 13 men and 8 women) in the relapse stage of UC - left-sided UC with mild to moderate activity (Truelov-Witts scale, Mayo index); and 20 patients (ages from 26 to 52, 10 men and 10 women) in the stage of clinical endoscopic remission. The study of the coprofiltrate microbiota was carried out by NGS sequencing of the structure of the bacterial 16S ribosomal RNA gene using the Illumina MiSeq platform. Statistical analysis was preceded by testing of the distribution for normality using the Kolmogorov-Smirnov (with Lilliefors significance correction) and Shapiro-Wilk tests. Hypotheses about the distribution corresponding to normal were rejected, and therefore the calculation of descriptive statistics is presented by median and quartiles. Group comparisons were made using the nonparametric Mann-Whitney test.

Results: Statistically significant differences between the relapse and remission groups were identified for 15 genera of microorganisms. In the relapse group, higher levels of Enterococcus, Streptococcus, Granulicatella, Pelomonas, TM7x, Actinomyces, Gemella, Corynebacterium, Bradyrhizobium, and lower levels of NK4A214_group, Pseudoscardovia, Family_XIII_UCG-001, Anaerofilum, Candidatus_Soleaferrea, DNF00809 were found (Table 1).

Genus	Me (Q25%; Q75%)		U Mann-Whitney	p
	Relapse (n=21)	Remission (n=20)		
Enterococcus	0.03 (0.00; 0.26)	0.00 (0.00; 0.00)	24.00	0.012
Streptococcus	1.22 (0.78; 6.27)	0.28 (0.18; 1.15)	25.00	0.035
NK4A214_group	0.07 (0.00; 0.48)	0.87 (0.07; 1.53)	25.50	0.036
Granulicatella	0.08 (0.00; 0.82)	0.00 (0.00; 0.02)	21.00	0.013
Pelomonas	0.08 (0.03; 0.30)	0.01 (0.01; 0.02)	19.50	0.012
TM7x	0.11 (0.01; 0.23)	0.00 (0.00; 0.02)	18.00	0.007
Actinomyces	0.27 (0.07; 0.38)	0.00 (0.00; 0.03)	14.00	0.003
Gemella	0.03 (0.00; 0.37)	0.00 (0.00; 0.01)	21.50	0.013
Pseudoscardovia	0.00 (0.00; 0.01)	0.04 (0.00; 0.14)	25.50	0.028
Family_XIII_UCG-001	0.00 (0.00; 0.01)	0.02 (0.01; 0.03)	25.00	0.025
Corynebacterium	0.01 (0.00; 0.05)	0.00 (0.00; 0.00)	25.00	0.008
Bradyrhizobium	0.01 (0.00; 0.03)	0.00 (0.00; 0.00)	20.00	0.003
Anaerofilum	0.00 (0.00; 0.02)	0.02 (0.01; 0.04)	28.00	0.048
Candidatus_Soleaferrea	0.00 (0.00; 0.00)	0.01 (0.00; 0.01)	24.00	0.009
DNF00809	0.00 (0.00; 0.00)	0.01 (0.00; 0.02)	30.00	0.027

Table 1. Comparison results of the remission and relapse groups of UC (statistically significant differences).

Conclusion: Data obtained demonstrates taxonomic differences at the genus level in patients in the relapse phase and in clinical and endoscopic remission of UC. The identified structural changes in the gut microbiota allow for implementation as a non-invasive method for monitoring the course of progression the disease.

Disclosure: Nothing to disclose.

PP0511

SYSTEMIC OXIDATIVE STRESS ASSOCIATES WITH CLINICAL AND BIOCHEMICAL DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE DIAGNOSTIC VALIDATION STUDY

S. Geertsema¹, H. Holstein¹, M.L.C. Bulthuis², K.N. Faber¹, H. van Goor², G. Dijkstra¹, A.R. Bourgonje^{3,1}

¹University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands, ³Icahn School of Medicine at Mount Sinai, The Henry D. Janowitz Division of Gastroenterology, New York, United States of America

Contact E-Mail Address: s.geertsema@umcg.nl

Introduction: Inflammatory bowel disease (IBD), consisting of Crohn's disease (CD) and ulcerative colitis (UC), are characterized by chronic inflammation of the intestines. This is accompanied by oxidative stress, which plays an important role in the pathophysiology of IBD. Oxidative stress-related biomarkers can serve as potential biomarkers for disease activity monitoring. Systemic free thiols (FT) are found to accurately reflect oxidative stress brought on by inflammation and have shown promise as a biomarker for inflammatory disease activity in IBD.

However, the clinical significance of this marker warrants validation. This prospective diagnostic study aimed to compare FT to other validated biomarkers and investigate the link between FT and endoscopic disease activity in patients with IBD.

Aims & Methods: An interim analysis was conducted in 52 patients. FT were measured using a colorimetric detection method. Clinical disease activity was quantified by the Harvey-Bradshaw Index (HBI) for CD and Simple Clinical Colitis Activity Index (SCCAI) for UC. Biochemical disease activity was determined by measuring blood C-reactive protein [CRP] and fecal calprotectin [fCal] levels. Endoscopic disease activity was quantified with the Mayo endoscopic sub score for UC and the Simple Endoscopic Score (SES-CD) for CD. Serum FT levels were assessed for correlations with disease activity parameters using linear and logistic regression analyses. Discriminative capacity of FT as biomarker was assessed by calculating receiver operating characteristics (ROC) statistics.

Results: Serum FT levels demonstrated a significant inverse correlation with clinical parameters, such as the HBI ($r=-0.53$, $p<0.05$). Additionally, other inflammatory biomarkers, including CRP, exhibited a negative correlation with serum FT levels ($r=-0.43$, $p<0.05$), which were decreased in patients with active IBD. Discrimination between clinically quiescent (HBI<5) and active disease based on serum FT levels was accurate (AUC=0.80, $p=0.02$) with a value numerically higher than that of fCal (AUC=0.55, $p=0.83$). Serum FT levels did not significantly differ between biochemically quiescent and active disease based on CRP (AUC=0.69, $p=0.20$). Both endoscopic scores demonstrated a tendency toward negative associations with serum FT levels.

Patients with moderate and severe disease activity had lower FT levels compared to those with mild disease activity (estimated marginal means [EMM] 497.2 vs 529.5 μ M, $p=0.43$) and 447.1 vs 529.5 μ M, $p=0.06$, respectively).

Conclusion: The interim analysis of this study indicates that plasma FT levels inversely correlate with IBD activity and may surpass traditional markers like fCal in detecting disease states. Plasma FT demonstrates potential as a sensitive biomarker for both clinical and endoscopic disease activity in IBD. Further patient inclusion and longitudinal data are essential to validate FT's utility fully. Continued research could establish FT as a key tool for personalized treatment strategies, improving patient outcomes in IBD management.

Disclosure: S. Geertsema, A.R. Bourgonje, H. van Goor, G. Dijkstra, and K.N. Faber are supported by a research grant from Janssen Research & Development LLC. A.R. Bourgonje received speaker fees from AbbVie. G. Dijkstra received research grants from Royal DSM, Takeda, and Janssen Pharmaceuticals and speaker fees from AbbVie, Pfizer, Takeda, and Janssen Pharmaceuticals.

PP0512

MICRO VS MACROSCOPY IN PEDIATRIC COLONOSCOPIES: A PROSPECTIVE CLINICAL STUDY

D. Narayanan M.J¹, D Kesavelu², S. Sankaranarayanan², S. K³

¹Apollo Hospitals, Chennai, Pediatrics, Chennai, India,

²Apollo Hospitals, Chennai, Pediatric Gastroenterology, Chennai, India,

³Apollo Hospitals, Chennai, Pathology, Chennai, India

Contact E-Mail Address: devnarayanan1995@gmail.com

Introduction: Inflammatory bowel disease (IBD) is a growing cause for concern and often missed or not thought of among pediatric population in developing economies. It is reported that about 25% of IBDs present before the age of 20.

Growing plethora of investigations have not been able to replace the role of direct visualisation of intestinal mucosa in various colorectal issues. Macroscopic findings may or may not help in clinching the diagnosis of IBD, hence "Biopsy" remains the Elixir of diagnosis. In this article, we review and attempt to correlate colonoscopic (macroscopy) and histological (microscopy) findings of colonoscopies in pediatric population, done over a period of 1 year.

Aims & Methods: To compare macroscopic findings versus histopathology findings of colonoscopies in pediatric population in suspected IBD.

To study the correlation of macroscopic findings with histopathologic findings of colonoscopies in pediatric population and to assess the frequency and pattern of microscopic impressions of colonoscopies in our cohort.

A prospective observational study carried out in a tertiary referral centre in children who underwent colonoscopies, aged 1 month to 17 years over a period of 12 months.

All children whose parents consented were included in the study. Inclusion and Exclusion criteria were formulated. Informed consent was obtained from the parents. Clinical details, colonoscopy findings and histopathology reports were. A total of 135 cases were enrolled during our study period. Results were collated using Microsoft Excel™.

©Ethical clearance was obtained from the institutional ethical committee.

Results: We found that the diagnosis of IBD was much more specific than expected with good sensitivity when data was matched between Macroscopy and Microscopy

	Colonoscopy Finding Marked "Normal"	Colonoscopy -Moderate to Severe inflammation	Histopathology Moderate-Severe inflammation	Sensitivity	Specificity	P value
RECTUM	81%	19%	26%	68.18	94.87	0.028
COLON	86%	14%	27.4%	45.83	96.05	0.019
ILEUM	57%	17%	19%	85.71	94.19	0.021

Conclusion: It is our standard practice to do colonoscopic biopsies from 7 areas (terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum) of the colon to exclude microscopic colitis which may be missed by the endoscopist or marked as 'normal'. Microscopic findings are considered as 'Gold standard' in the diagnosis of IBD and we envisage that it will remain the gold standard in the many next decades to come

Our data of sensitivity and sensitivity of the microscopic findings inclined the relevance of colonic mucosal biopsies in children with a normal-appearing mucosa and also the need to analyse every segment of the colon to diagnose IBD that may masquerade as “normal” in children which will add burden to the family, society and health care system and more importantly to the child’s quality of life.

References:

1. Manfredi, Michael A et al. “Good agreement between endoscopic findings and biopsy reports supports limited tissue sampling during pediatric colonoscopy.” *Journal of pediatric gastroenterology and nutrition* vol. 58,6 (2014): 773-8.
2. Altamimi, Eyad & Odeh, Yousef & Al-Quraan, Tuka & Mohamed, Elmi & Rawabdeh, Naif. (2022). Diagnostic and therapeutic outcomes of pediatric colonoscopies in Jordanian children. *Journal of Pediatric and Neonatal Individualized Medicine*. 11.

Disclosure: Nothing to disclose.

PP0513

METABOLOMIC PROFILING FOR IBD DIAGNOSIS: SEARCH FOR OPTIMAL SETS OF METABOLOMIC IBD MARKERS

N. Zakharzhevskaya¹, O. Shagaleeva¹, A. Silantiev¹, D. Kardonsky¹, E. Vorobyeva¹, V. Kozakova¹, D. Kashatnikova¹, E. Belousova², E. Korsunskiy², T. Kalachnuk¹, B. Efimov¹
¹LOPUKHIN FRCC PCM, Moscow, Russian Federation, ²Department of Gastroenterology of the M.F. Vladimirovskiy Moscow Regional Research and Clinical Institute, Moscow, Russian Federation

Contact E-Mail Address: natazaha@gmail.com

Introduction: Crohn’s disease (CD) and ulcerative colitis (UC) are the most common types of IBD. CD and UC are practically indistinguishable at early stages, which makes its diagnostics difficult. Various molecular methods are designed to carry out for global search of the most informative markers for IBD types verification and CD and UC differential diagnosis. Among omics technologies, metabolomics, as one of the promising tools that can contribute to the search and rapid implementation of informative markers. Today, various options are available for the assessment of low molecular weight compounds, such as HPLC-MS/MS, GC-MS/MS, etc. In this study, we combined the search for metabolomic markers using HPLC-MS/MS and HS GC-MS/MS methods for analyzing such groups of metabolites as lipids, volatile metabolites and hydrophilic metabolites in serum and stool samples from Crohn’s disease and ulcerative colitis patients.

Aims & Methods: The study was conducted for groups of patients with a verified diagnosis of Crohn’s disease and ulcerative colitis. Serum and stool samples were obtained from patients in a hospital. Informed consent for the study was obtained from all patients. The total number of serum and stool samples was 160 samples (CD and UC combined). The samples were provided by the Department of Gastroenterology of the M.F. Vladimirovskiy Moscow Regional Research and Clinical Institute, Moscow, Russia., as well as the Department of Gastroenterology of the LOPUKHIN FRCC PCM. Lipid and hydrophilic fractions of metabolites extracted from serum was carried out using HPLC-MS TripleTOF 6600+ System. Stool samples were analyzed using a Shimadzu QP2010 Ultra GC/MS with a Shimadzu HS-20 headspace extractor.

Results: Stool samples analysis shown that isovaleric acid is one of the markers for the IBD and the ratio of valeric and isovaleric acids using the logistic regression method allows us to obtain a risk coefficient for the IBD development. Analysis of the serum hydrophilic fraction demonstrated quantitative difference for the following compounds: Sphingosine, Urocanic Acid, N-Acetylcytidine, 5'-S-Methylthioadenosine, Adenine, -Hydroxyanthranilic acid, Acetylcarnitine, O-Acetyl-L-carnitine, Nicotinamide,

Phenylalanine, Isoleucine, Choline chloride, Proline, Cholic acid_CA, Chenodeoxycholic acid, Inosine, Glycoursodeoxycholic acid. Mentioned markers contributed to the IBD verification, while O-Acetyl-L-carnitine contribute to the differentiation between Crohn’s disease and ulcerative colitis. When analyzing the lipid fraction, differences were identified for a limited range of lipids, however, such lipids as Cer 37:0;3O|Cer 20:0;2O|17:0;O, PE P-36:2|PE P-18:0_18:2 and PC 36:2|PC 18:1_18:1 were detected only in CD samples.

Conclusion: The obtained metabolomic differences in the hydrophilic fraction and volatile components make it possible to reliably verify inflammatory bowel diseases, since separate lipid markers and O-Acetyl-L-carnitine contribute to the CD detection.

Disclosure: Nothing to disclose.

PP0514

APPLICATION OF ICCE CRITERIA FOR PATIENTS UNDERGOING SMALL BOWEL CAPSULE ENDOSCOPY FOR SUSPECTED CROHN’S DISEASE AND ITS DIAGNOSTIC YIELD

G. Madders¹, R. Grainger², C. Costigan², D. McNamara¹
¹Tallaght University Hospital, Gastroenterology, Dublin, Ireland,
²Tallaght University Hospital, Dublin, Ireland

Contact E-Mail Address: gillianmadders@gmail.com

Introduction: Small bowel capsule endoscopy (SBCE) is a recommended modality to investigate suspected small bowel Crohn’s disease (CD). The International Conference on Capsule Endoscopy (ICCE) set forward criteria to optimize patient selection and diagnostic yield. Capsule candidates should meet one criterion from group A (GI symptoms) along with 1 other criterion from group B/C/D (extraintestinal symptoms/ inflammatory markers /abnormal radiology).

Aims & Methods: The aim of this study is to evaluate the diagnostic performance when ICCE criteria are satisfied in those referred for SBCE with suspected CD. We performed a retrospective single-center study of patients referred for SBCE with suspected CD between March 2021 and March 2024. Demographics, clinical and capsule data were assessed from our hospital’s database and recorded. Patients with incomplete data were excluded. A positive SBCE was defined as a Lewis Score (LS) ≥ 135 . Patients were grouped according to ICCE criteria: ICCE+ were those who satisfied ≥ 2 ICCE criteria and ICCE- were those who did not fulfil criteria. Where available, histopathological results, MDT outcomes and treatment decisions were analyzed to determine CD diagnosis.

Results: A total of 335 of 433 capsules for suspected Crohn’s disease were included (58.5% female, mean age 42 years). In all, 82 capsules (24.5%) had clinically significant enteritis (median LS= 266, range 135-6600). 119 patients (35.5%) satisfied ICCE criteria; ICCE A+B (n=3, 2%), ICCE A+C (n=82, 69%), ICCE A+D (n=19,16%), ICCE x3 (n=15, 13%). Of those, 48 patients (40%) had a positive capsule (average LS = 917.46). As expected ICCE + cases were statistically more likely to have significant enteritis compared with ICCE – cases; 48/119 (40%) versus 34/216 (16%) respectively, OR 3.49, p< 0.0001, 95%CI 2.0892 to 5.8508.

Of note the diagnostic yield was similar for ICCE category B,C &D (p=0.6356). On follow up a histological diagnosis of CD was made in 25 (30%) cases and was similar in both the ICCE + and ICCE – groups, 17/ 48 versus 8/34 (p=0.09).

Conclusion: ICCE criteria in our cohort predicted significant enteritis and CD. Each of the secondary ICCE categories performed similarly. Of interest is the significant rate of enteritis in patients not meeting the criteria, with similar rates of confirmed CD to the ICCE + cohort, suggesting these patients still warrant investigation with capsule and that the clinical features and presentation of small bowel CD is varied.

References: Mergener K, Ponchon T, Gralnek I et.al. Literature review and recommendations for clinical application of small bowel capsule endoscopy, based on a panel discussion by international experts. Consensus statements for small bowel capsule endoscopy. 2006/2007, Endoscopy 2007; 39: 895-909.

Disclosure: Nothing to disclose.

PP0515

THE ACE (ALBUMIN, CRP, ENDOSCOPY) SCORE IN ACUTE ULCERATIVE COLITIS

B. Soukaina¹, A. Said¹, F.Z. Elrhaoussi¹,
M. Tahiri Joutei Hassani¹, F. Haddad², W. Hliwa¹, B. Ahmed¹,
W. Badre¹

¹Hospital University Center IBN ROCHD, Gastroenterology, Casablanca, Morocco, ²Hospital University Center IBN ROCHD, Hépatogastro-Entérologie, Casablanca, Morocco

Contact E-Mail Address: bannanisoukaina@gmail.com

Introduction: Patients with acute severe ulcerative colitis (ASUC) have a lifetime risk of an acute flare requiring hospital stay. The diagnosis of acute severe ulcerative colitis is based on Truelove and Witts criteria and the treatment by intravenous steroids showed improved clinical remission and reduced mortality. However, some patients respond poorly to systemic steroids and need a medical treatment by of anti TNF agents or a surgical treatment by colectomy.

The aim of our work is to study the ACE score as a predictive factor of surgery in acute severe ulcerative colitis.

Aims & Methods: We conducted a retrospective study on the Hepato gastro enterology department in IBN Rochd University Hospital of CASABLANCA, including all the admissions of patients with acute severe ulcerative colitis between 2016 and 2023. Demographic (sex, age, smoking habits, age of the diagnosis, prior episodes of severe ulcerative colitis, extent of the disease according to Montreal classification, maintenance medication prior to hospital admission), clinical (lichtiger score at admission and 3 days after IV steroid, laboratory (albumin, CRP) at day 1 and day 3 during hospital stay and endoscopic (Mayo score and UCEIS) characteristics of the patients were collected from medical records.

The primary outcome was to calculate the ACE score and determine the association between a high score and a major risk of surgery.

The score ACE was calculated following this formula: $\text{albumin} \leq 30 \text{ g/L} \{-\text{score}=1\} + \text{CRP} \geq 50 \text{ mg/L} \{\text{score}=1\} + \text{increased endoscopic severity} \{\text{score}=1\}$ predicting 78.1% of no responders.

Results: 97 patients were included in the study. The median age was 28 years with interquartile range (IQ) [15, 64]. The sex ratio was 1.22, 7% had a history of smoking. For 53 patients, acute severe ulcerative colitis was inaugural. At day1, the median C-reactive protein (CRP) was 84 mg/dl and the mean of albumin level was 29.9+/-6.28. The evolution at day 5 was marked by the persistence of a high Lichtiger score in 21 patients. 10 were treated with anti TNF alpha and 11 underwent colectomy.

Younger age (<20 years) and inaugural acute severe ulcerative colitis was significantly associated with a higher risk of colectomy ($p=0.019$; $p=0.001$). Elevated C-reactive protein (>45) at day 3 ($p=0.004$), decreased albumin level ($<30\text{g/L}$) ($p=0.02$) and positive oxford criteria ($p<0.01$) was also significantly associated with colectomy risk. The ACE (Albumin, CRP, Endoscopic) score was calculated in our patients, and a higher score of 3 was significantly associated to a major risk of colectomy.

Conclusion: Multiple biomarkers have been used to predict a non-response to steroids in the situation of acute severe ulcerative colitis. The most used is Travis score at day 3. The ACE score has been used recently in many studies, and confirm its ability to predict non responders to first line

medical therapy. Further research and validation of these scoring systems are warranted to enhance their accuracy and reliability in predicting the need for a second line therapy or surgery.

References:

1. Dinesen LC, Walsh AJ, Protic MN, Heap G, Cummings F, Warren BF, et al. The pattern and outcome of acute severe colitis. J Crohns Colitis. oct 2010;4(4):431-7.
2. Ho GT, Mowat C, Goddard CJR, Fennell JM, Shah NB, Prescott RJ, et al. Predicting the outcome of severe ulcerative colitis: development of a novel risk score to aid early selection of patients for second-line medical therapy or surgery. Aliment Pharmacol Ther. 15 mai 2004;19(10):1079-87
3. Corte C, Fernandopulle N, Catuneanu AM, Burger D, Cesarini M, White L, et al. Association between the ulcerative colitis endoscopic index of severity (UCEIS) and outcomes in acute severe ulcerative colitis. J Crohns Colitis. mai 2015
4. Travis SP, Farrant JM, Ricketts C, Nolan DJ, Mortensen NM, Kettlewell MG, et al. Predicting outcome in severe ulcerative colitis. Gut. juin 1996;38(6):905-10.
5. Grant RK, Jones GR, Plevris N, Lynch RW, Jenkinson PW, Lees CW, et al. The ACE (Albumin, CRP and Endoscopy) Index in Acute Colitis: A Simple Clinical Index on Admission that Predicts Outcome in Patients With Acute Ulcerative Colitis. Inflamm Bowel Dis. 15 mars 2021;27(4):451-7.

Disclosure: Nothing to disclose.

PP0516

THE INFLUENCE OF THE BODY MASS INDEX ON THE COURSE OF INFLAMMATORY BOWEL DISEASES

H. Hassine¹, S. Monastiri¹, R. Khemiri¹, H. Dabbebi¹, H. Yacoub¹,
D. Cherif¹, H. Kchir¹, N. Maamouri¹

¹La Rabta Hospital, Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: nadiamaamouri1939@yahoo.com

Introduction: The role of nutritional status, as indicated by the body mass index (BMI), in inflammatory bowel diseases (IBD) is encountered at various levels: etiopathogenic, therapeutic, and prognostic.

Aims & Methods: The aim of this study was to assess the impact of the BMI on the disease course of IBD patients.

Methods: This was an 8-year study period [January 2016-December 2023] of patient records followed for IBD. We collected clinical, biological, radiological, endoscopic, therapeutic, and follow-up data. Patients were divided into three groups based on body mass index (BMI) at diagnosis: group 1: overweight or obese patients ($\text{BMI} \geq 25 \text{ kg/m}^2$), group 2: patients with normal BMI ($18.5 \leq \text{BMI} < 25 \text{ kg/m}^2$), and group 3: patients with malnutrition ($\text{BMI} < 18.5 \text{ kg/m}^2$). A comparison of the three groups was performed through univariate logistic regression.

Results: We enrolled 126 patients, with a mean age of 37.3 years [14-75] and a gender ratio (M/F) of 1.5. The median BMI at inclusion was 20.98 kg/m^2 [13-33]. Malnourishment was observed in 24.6% of patients at the disease first diagnosed. Obesity or overweight were noted in 18.25% of patients, while 57.14% had normal BMI. Patients with malnutrition mostly had Crohn's disease (96.77%) with ileal, colonic, and ileocolonic localization in 3, 13, and 14 cases respectively. Comparison of these groups showed no significant differences in terms of age ($p=0.09$), sex ratio ($p=0.06$), smoking history ($p=0.54$), disease duration ($p=0.25$), disease phenotype ($p=0.64$), perianal ($p=0.67$) or upper digestive tract involvements ($p=0.4$).

However, a significant association was observed between normal BMI and clinical and biological remission compared to other BMIs ($p=0.013$). After a mean follow-up of 56 months [6 - 90], there was no significant difference

between the three groups regarding the occurrence of CD complications ($p = 0.78$), the use of immunosuppressive therapies ($p = 0.49$), biotherapies ($p = 0.24$), or surgical intervention ($p = 0.12$).

Conclusion: According to our study, a normal BMI seems to be associated with better control of IBD, highlighting the importance of nutritional status in these patients. This findings need to be confirmed by large-scale studies.

Disclosure: Nothing to disclose.

PP0517

LIVER FIBROSIS PREDICTS RESPONSE TO ADVANCED THERAPY IN INFLAMMATORY BOWEL DISEASE: A NEW PERSONALIZED TREATMENT APPROACH?

F. D'Amico¹, S. Bencardino¹, R. Barà¹, M. Allocca¹, A. Zilli¹, F. Furfaro¹, T.L. Parigi¹, F. Ungaro², G. Fiorino³, L. Peyrin-Biroulet⁴, L. Massimino², S. Danese¹, A. Moschetta⁵

¹IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ²IRCCS Ospedale San Raffaele, Experimental Gastroenterology Unit, Division of Immunology, Transplantation and Infectious Disease, Milan, Italy, ³San Camillo-Forlanini Hospital, IBD Unit, Department of Gastroenterology & Digestive Endoscopy, Rome, Italy, ⁴Nancy University Hospital, Department of Gastroenterology, Vandœuvre-lès-Nancy, France, ⁵University Hospital of Bari, Department of Internal Medicine, and Rare Diseases Centre "C. Frugoni", Bari, Italy

Contact E-Mail Address: damico_ferdinando@libero.it

Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are chronic and progressive inflammatory bowel diseases (IBD). It is estimated that up to 30-50% of patients with IBD develop intestinal fibrosis leading to complications such as strictures. Liver fibrosis occurs up to 16.7% of patients with IBD. However, the impact of liver fibrosis on the response to therapy in patients with IBD is unknown.

Aims & Methods: Our aim was to investigate the association between liver fibrosis before starting an advanced therapy and response to treatment in IBD. We conducted a retrospective analysis of data that were prospectively gathered from consecutive patients with a confirmed diagnosis of UC or CD, spanning from November 2021 to December 2023. All patients who started an advanced therapy and had transaminase concentrations, body mass index (BMI), history of diabetes, and platelet counts available were eligible. Several scores of liver fibrosis were measured including AST/ALT ratio (AAR), AAR platelet ratio index (AARPRI), AST to platelet ratio index (APRI), body mass index AST/ALT ratio and diabetes mellitus score (BARD), fibrosis index based on four factors (FIB -4), and modified FIB-4 (m-FIB4).

All available clinical (partial Mayo score for UC and Harvey-Bradshaw index for CD), biochemical (fecal calprotectin, FC), and endoscopic (endoscopic Mayo score for UC and simple endoscopic score for Crohn's Disease (SES-CD) and Rutgeert's score for CD) data at 6 months were collected. A logistic regression multivariate analysis was performed to identify any correlation between scores of liver fibrosis at baseline and response to advanced therapies. Analyses were subjected to correction using the false discovery rate (FDR) method.

Results: In total, 122 patients were included in the analysis (73 UC (59.8%), 65 female (53.3%), median age of 42.8 years). Approximately half of the patients were biologic naïve (60, 49.2%), while among biologic-experienced subjects 23/62 (37.1%) had been treated with more than one advanced therapy. Patients were treated with ustekinumab (46, 37.8%), infliximab (33, 27.0%), vedolizumab (16, 13.1%), adalimumab (15, 12.3%), upadacitinib (6, 4.9%), tofacitinib (4, 3.3%), golimumab (1, 0.8%), filgo-

tinib (1, 0.8%). A small proportion of patients (16/122, 13.1%, 2 CD and 14 UC) discontinued treatment at 6 months. Clinical remission at 6 months was achieved in approximately half of CD (23/49, 46.9%) and UC patients (39/73, 53.4%). Similarly, half of CD patients (25/49, 51.0%) and one third of UC patients (22/73, 30.1%) had FC normalization ($<150\mu\text{g/g}$). A quarter of CD patients (4/16, 25.0%) and UC patients (9/28, 32.1%) achieved endoscopic remission at 6 months. Two UC patients (2.7%) were hospitalized. Five patients (4.1%) underwent surgery (2 UC-related and 3 CD-related). No cases of neoplasia or death occurred. In the multivariate analysis, mFIB-4 at baseline was a predictor of clinical activity at 6 months in CD (FDR=0.08), while AARPRI and AAR at baseline predicted clinical activity at 6 months in UC (FDR=0.08 and FDR=0.06, respectively).

Conclusion: Patients with IBD and concomitant liver fibrosis have a lower rate of clinical remission after 6 months of advanced therapy. Scores of liver fibrosis could predict the response to therapy. Further prospective studies are warranted to implement their use in clinical practice.

Disclosure: Nothing to disclose.

PP0518

COMPLETE ENDOSCOPIC HEALING ASSOCIATED WITH BETTER OUTCOMES THAN PARTIAL ENDOSCOPIC HEALING IN PATIENTS WITH CROHN'S DISEASE: RESULTS OF A PROSPECTIVE MULTICENTER STUDY

C. Yzet¹, F. Brazier², E. Derval², P. Vanelslander³, V. Dejour³, D. Pricope⁴, M. Diouf², M. Fumery⁵

¹Amiens university hospital, Gastroenterology, Amiens, France, ²Amiens university hospital, Amiens, France, ³Clinique Saint Claude, Saint Quentin, France, ⁴Compiègne hospital, Compiègne, France, ⁵Amiens University Hospital, Gastroenterology department, Amiens, France

Contact E-Mail Address: clara.yzet@gmail.com

Introduction: The STRIDE II guidelines recognize endoscopic healing (EH), defined by an SES-CD score ≤ 2 or a CDEIS score < 3 , as one of the main therapeutic targets in Crohn's disease (CD). Nevertheless, complete EH could reduce the risk of long-term complications in CD. The aim of this study was to assess the risk of long-term complications in CD according to the degree of EH achieved.

Aims & Methods: We conducted a prospective multicenter study that included all patients with CD undergoing colonoscopy for EH assessment between September 2019 and September 2022 in three centers and were compared outcomes of patients with complete EH (CDEIS = 0) vs partial EH (CDEIS greater than 0 but less than 4). The primary endpoint was therapeutic failure, defined as the need for drug intensification and/or corticosteroid initiation and/or CD-related hospitalization and/or development of a luminal strictures/fistula and/or perianal CD and/or the need for intestinal resection.

Results: A total of 128 patients were included with a median disease duration of 10 (IQR, 4-18) years. Fifty-six (43%) patients had ileocolonic location and 79 (62%) an inflammatory (B1) behavior. Patients had been on treatment for a median of 12 months (8.3-24.3) prior to colonoscopy and 81 (63%) patients had complete EH. After a median follow-up of 22.5 months [IQR, 19.3-23.7], therapeutic failure was observed in 40 patients (31%). The risk of therapeutic failure was significantly higher among patients with partial EH group (25% vs. 43% $p = 0.036$, HR = 1.90; IC95% = [1.02 - 3.53]; $p = 0.043$). The risk of CD-related hospitalizations (2.5% vs. 17%), $p = 0.005$, HR = 7.09; IC95% = [1.51 - 33.4]; $p = 0.013$) was significantly higher in patients with partial EH. The risk of intestinal resection, steroid initiation and drug intensification among patients with complete and partial EH, were 0% vs. 4.3% ($p = 0.13$), 2.5% vs. 11% ($p = 0.1$) and 22% vs. 36% ($p = 0.088$), respectively.

Conclusion: This prospective multicenter study confirms that complete endoscopic healing is associated with better long-term outcomes than partial endoscopic healing in patients with CD, as well as fewer hospitalizations and an overall decreased risk of treatment failure.

Disclosure: Nothing to disclose.

PP0519

A PROSPECTIVE, PILOT, REAL-WORLD STUDY TO ASSESS THE PRESENCE AND SEVERITY OF URGENCY IN PATIENTS WITH CROHN'S ILEITIS

G.J. Mantzaris¹, A. Loukou¹

¹White Cross Hospital, The Athens Clinic, Gastroenterology, Athens, Greece

Contact E-Mail Address: gjmantzaris@gmail.com

Introduction: Urgency is not an IBD Patient Reported Outcome (PRO) in the STRIDE II but it has been assessed at baseline and as an outcome measure in recent pivotal RCTs with newer biologicals and targeted synthetic small molecules in both Crohn's disease (CD) and ulcerative colitis (UC). However, although it is reasonable to assume that UC patients or CD patients with rectal involvement may complain for severe urgency, urgency has been assessed even in patients with Crohn's ileitis (iCD).

Aims & Methods: The aim of this study was to assess whether urgency is reported by iCD patients with flares or quiescent disease in a Real-World (RW) setting. This prospective, pilot, RW study included CD patients with solely L1 phenotype. L1 location was documented by ileocolonoscopy, histology and, imaging (MRE, US, or capsule endoscopy). Patients with colonic and/or rectal disease, perianal involvement and complicated ileal disease were excluded. Patients were interviewed by office visits during disease flare [HBI>5, CRP <5mg/dl, faecal calprotectin (FC)>250µg/g faecal tissue and SES-CD for terminal ileum >3 if colonoscopy was performed within a month prior to the visit) and during clinical remission (HBI<5, CRP <5mg/dl and FC <200µg/g and ileal SES-CD=0, in a recent ileocolonoscopy). The presence of and severity of urgency was recorded by a Symptom Rating Score of 0-10 (absent to very severe). The presence and severity of abdominal pain, the number and consistency of stools, nocturnal stools, blood and/or mucus in the stools, and the feeling of inadequate evacuation were sought by a structured questionnaire.

Results: During a 15-month period, 85 iCD patients [45 males, median age (range) 33 (18-65) years, median (range) disease duration 9 (0.6-25) years] were enrolled in the study. Patients were receiving a wide range of treatments, including anti-TNF agents (n=35), ustekinumab (N=25), vedolizumab (N=5), azathioprine (n=10), budesonide (n=5) and mesalazine (n=15). Fifty patients had a flare, 65 were in remission and 30 patients were interviewed sequentially in flare and remission of disease.

All patients in disease flare reported abnormal classical PROs of CD. Moderate to severe urgency [median score 5, range 4-8] was reported by 5/50 (10%) patients with disease flare, 8/65 (12%) patients with disease remission and 2/30 (6.5%) patients who were interviewed during flare and remission of disease. 3/50 patients with urgency during a flare of CD did not report urgency during disease remission. Six of the 8 patients who were interviewed only with iCD in remission and reported urgency had concurrently typical Irritable Bowel Symptoms (IBS, abdominal pain relieved by defecation, alternating diarrhoea/constipation, inadequate bowel emptying).

Conclusion: This prospective, pilot, real-world study shows that the reliability of urgency as classical PRO in patients with iCD is questioned and raises doubts whether urgency should be included in the spectrum of PROs for patients with iCD both in RCTs and in RW studies. Validation of the terminology in different ethnic languages may also pose additional barriers in patient understanding and reporting the symptom in the pres-

ence of additional IBS-type symptoms. Large studies are needed to assess if urgency is present in patients with iCD and how reliably is reported especially in multinational RCTs.

Disclosure: Dr GJ Mantzaris: Research grants: AbbVie, Genesis, Merck Sharp & Dohme, Takeda; advisor/speaker: AbbVie, Aenorasis, Dr Falk, Ferring, Hospira, Janssen, Merck Sharp & Dohme, MYLAN, Pfizer, Takeda, Vianex.

Dr A Loukou: Nothing to declare.

PP0520

FAECAL PAI-1 LEVEL IS A NEW TOOL FOR DISEASE MONITORING IN INFLAMMATORY BOWEL DISEASES - RESULTS OF THE LDN-051 PROJECT

B. Jójárt^{1,2,3,4}, T. Resál², D. Kata⁵, T. Molnár^{2,3}, P. Bacsur^{2,6}, V. Szabó^{3,2,4}, L. Kajári³, A. Varga^{2,3,4}, K. Szántó², P. Pallagi^{1,2,3,4}, I. Földesi⁵, T. Molnár², J. Maléth^{1,2,3,4}, K. Farkas^{2,6}

¹Ladon Therapeutics Ltd, Szeged, Hungary, ²University of Szeged, Albert Szent-Györgyi Medical School, Department of Medicine, Szeged, Hungary, ³University of Szeged, ELKH-USZ Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ⁴University of Szeged, HCEMM-USZ Molecular Gastroenterology Research Group, Szeged, Hungary, ⁵University of Szeged, Albert Szent-Györgyi Medical School, Institute of Laboratory Medicine, Szeged, Hungary, ⁶University of Szeged, HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary

Contact E-Mail Address: jojart.boldizsar@gmail.com

Introduction: Crohn's disease and ulcerative colitis, two forms of inflammatory bowel disease (IBD) require lifelong treatment and patient monitoring. Current predictors of relapse and therapeutic success have limitations, therefore there is a high unmet need to identify novel biomarkers in IBD. Monitoring approaches for IBD are mostly invasive, time-consuming, and expensive. Therefore, a simple, rapid, and non-invasive test, with the ability to differentiate IBD from other gastrointestinal conditions and to monitor disease activity, will have important clinical implications. Our previous mucosal cytokine profiling identified that Plasminogen activator inhibitor type 1 (PAI-1) is expressed in IBD patients with active disease, but not in control.

Aims & Methods: Therefore, we aimed to assess the utility of PAI-1 in monitoring disease activity and therapeutic response of IBD patients in different biological samples.

Serum, biopsy, and faecal samples were collected from more than 160 IBD patients and controls without IBD. ELISA method was used to define the level of PAI-1 in the mucosa, serum, and faecal samples and the serum CRP levels were also determined. For the mucosal gene expression analysis qRT-PCR was used. The correlation and ROC analyses were applied to observe the relationship between the disease activity and PAI-1 level.

Results: The applied screening approach detected significantly higher expression of PAI-1 in active IBD compared to the control. We demonstrated that the serum, mucosal, and faecal PAI-1 concentration was significantly elevated in IBD patients showing clinical and endoscopic activity. Additionally, the initial PAI-1 level decreased significantly upon successful therapy in responder patients, whereas it remained unchanged in non-responders. qRT-PCR analysis of the mucosa showed same results of PAI-1 expression pattern as the ELISA. We also showed that faecal PAI-1 selectively increases in active IBD patients, but not in other organic gastrointestinal diseases. In addition, the stability analysis of faecal PAI-1 showed that the protein was detectable for up to one week at room temperature and 4°C. The serum, mucosal, and faecal PAI-1 levels showed positive correlation to the endoscopic activity. ROC curves demonstrated that faecal

PAI-1 showed a relatively high power to distinguish between active and control patients. However, the serum CRP level reflected to the disease activity, but no to the therapeutic response. Correlation between the serum CRP and faecal PAI-1 level was not observed.

Conclusion: Our results suggest that serum, mucosal and faecal PAI-1 expression reflects to the disease activity in IBD, which could be used to disease monitoring and possibly therapeutic response. The correlation between the faecal PAI-1 level and the endoscopic activity promotes that it could be used as a novel non-invasive disease specific faecal biomarker in the IBD diagnosis.

Disclosure: LDN-051 is owned by Ladon Therapeutics Ltd.

PP0521

PAIN IN INFLAMMATORY BOWEL DISEASE: A FUNCTION OF DISEASE ACTIVITY OR CENTRAL SENSITIZATION?

L. Fayad¹, R. Burns², L. Chaaban², R. Chowdhury², S. Dudley-Brown², M. Lazarev², A. Parian², F. Selaru², H.M. Yu², D.E. Peters², B. Slusher², J. Melia²

¹Johns Hopkins Medical Institution, Endoscopy, Baltimore, United States of America, ²Johns Hopkins Medical Institution, Baltimore, United States of America

Contact E-Mail Address: leafayad@gmail.com

Introduction: Chronic abdominal pain is prevalent in individuals with inflammatory bowel diseases (IBD). However, the determinants and phenotypes of IBD-associated pain are not well-characterized, frustrating effective pain management and mitigation strategies

Aims & Methods: Aims: This is an ongoing descriptive, cross-sectional study aimed at phenotyping the types of pain experienced by patients with IBD, the impact on health-related quality of life (HRQoL) and psychological health, and relationship to disease activity assessed by clinical metrics and endoscopy. Methods: Fifty-eight adult patients diagnosed with IBD were prospectively enrolled at a single academic medical center between October 17, 2022 and November 7, 2023. Patients completed a set of online patient-reported outcome measures (PROM)-based standardized and validated questionnaires (Table 2) just prior to a scheduled colonoscopy. Endoscopically active disease was defined as Mayo Endoscopic Score ≥ 1 for ulcerative colitis (UC) and SES-CD ≥ 3 for Crohn's Disease.

Results: A total of 58 patients (28 UC/30 Crohn's, 24 male/34 female, median age 44.5 $\pm$ 14.5 years) were included. An initial analysis examined relationships based on endoscopic disease activity. Interestingly, there was no significant difference between those with endoscopically active disease and those without on metrics of pain, HRQoL, or impact on psychological health ($p>0.05$). However, those with endoscopically inactive disease had significantly higher scores on central sensitization (CS) (31.1 $\pm$ 11.5 vs. 23 $\pm$ 12.1, $p<0.05$). Using a validated score threshold of 40 on the central sensitization inventory (CSI), the cohort was then stratified into two new groups (those with and without evidence of CS).

Overall, 12/58 patients met diagnostic criteria for CS. Table 1 summarizes the baseline characteristics of the two groups. As detailed in Table 2, those with CS had higher scores on abdominal pain (severity and interference, including catastrophizing), visceral hypersensitivity, lower scores on HRQoL questionnaires, and greater scores on depression and anxiety scales ($p<0.05$). There was no significant difference in neuropathic pain ($p=0.85$).

Conclusion: Central sensitization affected at least 20% of this cohort of IBD patients, which is consistent with prior studies. Interestingly, there was a trend towards more central sensitization in those with quiescent disease. CS was associated with worse pain, HRQoL, and psychosocial distress across a broad range of outcomes measured. These data support

enhanced attention to contribution of CS to pain in IBD patients, particularly those with persistent pain in remission, as therapies emerge for the treatment of CS.

Disclosure: Nothing to disclose.

PP0522

PREDICTIVE ACCURACY OF FECAL CALPROTECTIN IN ASSESSING CLINICAL ACTIVITY AND DISEASE SEVERITY IN PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE

S. Gopal¹, A. Jain¹, S. Shenoy¹, A. Shetty¹, B.V. Tantry¹

¹Kasturba Medical college Hospital, Mangalore, Manipal Academy of Higher Education(MAHE),Manipal, Gastroenterology, Mangalore, India

Contact E-Mail Address: sandeep.gopal@manipal.edu

Introduction: Inflammatory bowel disease is an idiopathic disorder characterized by repeated relapses and remissions. Endoscopy, the gold standard for diagnosis and monitoring, is time consuming, expensive and invasive. Fecal calprotectin has been suggested as a surrogate marker to assess intestinal inflammation and predict disease relapse. Published evidence regarding the utility of fecal calprotectin as an indicator of clinical activity and endoscopic severity in patients with inflammatory bowel disease is not unambiguous.

Aims & Methods: The aim of this study was to determine the use of fecal calprotectin as a predictor of clinical activity and endoscopic severity in patients with inflammatory bowel disease.

Methods: Patients fulfilling selection criteria were recruited for the study. Clinical examination findings, laboratory investigations and fecal calprotectin levels were documented as per proforma. Endoscopic and clinical severity were measured by Simple Endoscopic Score and Crohn's Disease Activity Index for Crohn's disease and by Ulcerative Colitis Endoscopic Index of Severity score and Simple Clinical Colitis Activity Index for Ulcerative Colitis. Lab investigations and calprotectin were repeated after six months and compared with endoscopic and clinical activity indices.

Results: Fecal calprotectin correlated with Crohn's Disease Activity Index both at first visit and follow up ($r=0.689$, $p=0.016$) ($r=0.425$, $p\text{-value}<0.05$). The sensitivity and specificity of calprotectin in detecting active disease and remission at first visit were 93.8% and 80% respectively (AUC-0.869). At follow up, the sensitivity and specificity were 80% and 93.3% respectively (AUC-0.867). In Ulcerative colitis, Simple Clinical Colitis Activity Index score correlated with fecal calprotectin levels at first visit and follow up. ($r=0.231$ / 0.387 , $p\text{-value}$ 0.001/0.001). The sensitivity of calprotectin in detecting active disease and remission in ulcerative colitis was 92.6% and specificity was 83.3%. AUC was 0.88. At follow up, the sensitivity of fecal calprotectin in detecting active disease and remission was 89.9% and the specificity was 87.0% ; AUC was 0.879.

Conclusion: Fecal calprotectin levels show significant correlation with clinical and endoscopic activity indices in patients of inflammatory bowel disease. Therefore, calprotectin levels in stool could be used as a surrogate marker for monitoring mucosal status as well as predicting endoscopic remission in these patients.

References: 1.Sturm A, Maaser C, Calabrese E, et al. ECCO-ESGAR guideline for diagnostic assessment in ibd part 2: Ibd scores and general principles and technical aspects. J Crohns Colitis. 2018;13(3):273-284.

2. Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? Gut. 2006;55:426-431

3. Denis MA, Reenaers C, Fontaine F, Belaiche J, Louis E. Assessment of endoscopic activity index and biological inflammatory markers in clinically active Crohn's disease with normal C-reactive protein serum level. Inflamm Bowel Dis. 2007;13:1100-5.

4. Yui S, Nakatani Y, Mikami M. Calprotectin (S100A8/S100A9), an inflammatory protein complex from neutrophils with a broad apoptosis inducing activity. *Biol Pharm Bull.* 2003;26:753–60.
5. Daperno M, Castiglione F, Ridder L, et al. Results of the 2nd part Scientific Workshop of the ECCO. II: measures and markers of prediction to achieve, detect, and monitor intestinal healing in inflammatory bowel disease. *J Crohns Colitis.* 2011;5:484–98.
6. Canani RB, de Horatio LT, Terrin G, et al. Combined use of noninvasive tests is useful in the initial diagnostic approach to a child with suspected inflammatory bowel disease. *J Pediatr Gastroenterol Nutr.* 2006;42:9–15.
- Disclosure:** Nothing to disclose.

PP0523

FISTULA DRAINAGE ASSESSMENT IS CORRELATED WITH IMPROVEMENT IN QUALITY OF LIFE AFTER 26 WEEKS OF TREATMENT IN PERIANAL FISTULIZING CROHN'S DISEASE

L.G.M. Mulders¹, K. Beek², J. Tielbeek³, C.J. Buskens⁴, J. Stoker², R. van Hulst⁵, G.R. D'Haens¹, K.B. Gecse¹, AMFIBIO Study Group

¹Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Department of Radiology and Nuclear Medicine, Amsterdam, Netherlands, ³Spaarne Gasthuis, Department of Radiology and Nuclear Medicine, Haarlem, Netherlands, ⁴Amsterdam UMC, Department of Surgery, Amsterdam, Netherlands, ⁵Amsterdam UMC, Department of Anesthesiology, Amsterdam, Netherlands

Contact E-Mail Address: l.mulders@amsterdamumc.nl

Introduction: Perianal fistulizing Crohn's disease (pfCD) is a debilitating phenotype that severely impacts quality of life (QoL). pfCD frequently implies a stepwise, combined medical and surgical treatment approach. Treatment goals are ideally individual and include improvement of QoL, however precise outcomes are not determined yet. Currently, most commonly used outcomes are clinical response/remission, and radiological healing, the latter most relevant to long-term disease remission.

Aims & Methods: The aim of this study was to evaluate QoL in pfCD and compare it with clinical and radiological outcomes after 26 weeks of treatment.

In this prospective exploratory, observational cohort (AMFIBIO), we included patients with pfCD starting on anti-TNF- α therapy, mesenchymal stem cell injection (MST), or hyperbaric oxygen therapy (HBOT) combined with surgical closure. We collected patient-reported IBD-specific (IBDQ-32) and fistula-specific (CAF-QoL) QoL outcomes. MAGNIFI-CD (remission defined as MAGNIFI-CD ≤ 6), perianal disease activity index (PDAI; response defined as ≤ 4) and fistula drainage assessment (FDA) were evaluated at baseline and week 26. Paired T tests were used to analyze changes in QoL, clinical and radiological scores. Pearson's correlation coefficients were used to correlate changes between the outcomes.

Results: Twenty-one patients were analyzed at week 26 (Table 1). Mean change between baseline and week 26 in CAF-QoL and IBDQ-32 was 13 (95%CI 3 – 23) and 9 (95%CI -5 – 24) respectively. FDA correlated moderately with improvement in CAF-QoL ($p=0.59$; 95%CI 0.19 – 0.82), and moderately with improvement in IBDQ-32 ($p=0.49$; 95%CI 0.04 – 0.77). Improvement in CAF-QoL ($p=0.31$; 95%CI -0.20 – 0.69) and IBDQ-32 ($p=0.35$; 95%CI -0.16 – 0.72) did not correlate with improvement in PDAI, nor with PDAI response (resp. $p=0.38$; 95%CI -0.009 – 0.71, and $p=0.40$; 95%CI -0.08 – 0.72). No correlation was seen between changes in CAF-QoL and MAGNIFI-CD ($p=0.08$; 95%CI -0.39 – 0.52), or MRI remission ($p=0.22$; 95%CI -0.26 – 0.61).

Age (years) at baseline, mean (95%CI)	34.7 (28.5 – 40.9)
Female, n (%)	16 (76)
Caucasian, n (%)	16 (76)
Crohn's disease duration (years), mean (95%CI)	8.8 (3.3 – 14.3)
Perianal disease duration (years), mean (95%CI)	37.1 (3.3 – 10.8)
Perianal fistula classification (Geldof et al.), n (%)	2a: 11 (52) 2b: 8 (38) 2c-ii: 2 (10)
Therapy during study, n (%)	anti-TNF: 10 (48) MST: 6 (29) HBOT: 5 (24)
SES-CD at baseline, median [IQR]	2 [0 – 7.5]
CAF-QoL at baseline, mean (95%CI)	58.1 (51.0 – 65.2)
IBDQ-32 at baseline, mean (95%CI)	145.1 (130.7 – 159.4)

Table 1. Patient and fistula characteristics (n=21)

Conclusion: IBD- and fistula-specific Quality of Life scores improve after therapy at week 26 in patients with pfCD. This improvement correlates with fistula drainage assessment, however it does not correlate with PDAI and MRI outcomes.

Disclosure: LM, KB, JT and RvH have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this abstract. CB has received grants from Boehringer Ingelheim and Roche; speakers honoraria from AbbVie, Janssen, Galapagos, Takeda, and Tillotts. JS is President-elect of the European Society of Gastrointestinal and Abdominal Radiology. GD has served as consultant for AbbVie, Astrazeneca, Alimentiv, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion, Cosmo, Eli Lilly, Galapagos, GSK, Johnson and Johnson, Takeda, Pfizer Inc, Polpharma, Prometheus Biosciences, Tillotts and Ventyx; received speaker fees from AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly, Johnson and Johnson, Takeda, Pfizer Inc and Tillotts. KG has received grants from Pfizer Inc, Celltrion and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunic Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis and Takeda and speaker's honoraria from Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda and Tillotts.

PP0524

THE IMPACT OF STRESS ON INFLAMMATORY BOWEL DISEASE PATIENTS' CONDITION AND THEIR QUALITY OF LIFE

F. Barker¹, I. Mohamed¹, Y. Ntuli¹, T. Naughton¹, K. Okuwobi¹, M. Hanna¹

¹University Hospital Lewisham, Gastroenterology, London, United Kingdom

Contact E-Mail Address: florence.barker@nhs.net

Introduction: It has long been hypothesised and increasingly proven that stress (both acute and chronic) can have a significant impact on inflammatory bowel disease (IBD) patient's condition in terms of relapses and worsening disease.¹ It is also understood that patients with IBD are at a higher risk of developing depressive disorders than the healthy population. ² As such ongoing work into the bidirectional gut brain axis and its association with the inflammatory response in the gut is important in understanding how reduction in stress can assist in managing IBD. ³

Aims & Methods: Our study aim was to assess the impact of stress on our IBD patients' self-reported symptoms, to understand how our IBD patients' managed their stress levels and to assess how their inflammatory bowel disease affects their quality of life.

101 IBD patients attending University Lewisham Hospital completed an anonymous structured paper questionnaire between December 2023 and January 2024. Data was analysed for age, gender, IBD subtype and medications, the impact of stress on their condition, their methods of stress

reduction as well as the impact of IBD on their social, work and sexual life.

Results: 101 patients completed the survey. 55% were female and the median age was 42 years (IQR 30-58). 45% had ulcerative colitis (UC), 48% had Crohn's disease (CD) and 8% had IBD-unspecified (IBD-U). 5.6% of patients were not on treatment, 29.7% on mesalazine, 10.9% on azathioprine and 75% were on a biologic therapy.

Of the 101 patients surveyed 76.2% (77/101) felt that stress triggers flares in their condition. 26.7% (27/101) felt that stress directly led to their IBD developing, while 23.8% (24/101) felt it was a contributing factor. 40.6% (41/101) felt that controlling stress was more important than their medications. 62.4% (63/101) employed methods of stress reduction.

The most common methods were: exercise/sports/yoga (41.5%), walking (30.7%), reading (26.7%), socialising (22.8%), alcohol (10.9%) smoking (5.9%) and recreational drugs (3.0%).

32.7% (33/101) felt their condition made them exhausted all of the time. 63.4% (64/101) reported avoiding social events due to their IBD. 48.5% (49/101) reported their condition affected their sex life. 25.6% (26/101) felt their relationship with their partner was affected because of their condition.

Over half of patients surveyed (57.4%, 58/101) felt that their condition affected their mental health, but only 24.8% (25/101) felt they had received sufficient NHS mental health support.

19.8% (20/101) of patients felt their condition had stopped them from getting promoted at work, and 47.5% (48/101) attended work whilst in a disease flare for fear of losing their job. 14.9% (15/101) reported feeling discriminated against because of their condition.

Conclusion: Over three quarters of IBD patients surveyed felt that stress is a significant trigger for flares, however surprisingly over a quarter of IBD patients perceive stress as a direct factor for their disease developing. IBD significantly impacts patients social, work, and sexual life with a significant impact seen on mental health. This survey found that although a good proportion of patients used commonly perceived healthy methods of stress reduction, almost 20% of patients relied on unhealthy methods (smoking, alcohol/recreational drugs). This data presents a clear argument for a holistic approach to IBD patient care and integrating psychological support within an IBD service. Further work should follow on the relationship between patient perceived stress levels and disease outcomes and failed treatments.

References: 1) Mikocka-Walus A, Pittet V, Rossel JB, von Känel R; Swiss IBD Cohort Study Group. Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol*. 2016 Jun;14(6):829-835

2) Sun Y, Li L, Xie R, Wang B, Jiang K, Cao H. Stress Triggers Flare of Inflammatory Bowel Disease in Children and Adults. *Front Pediatr*. 2019 Oct 24;7:432.

3) Ge L, Liu S, Li S, Yang J, Hu G, Xu C, Song W. Psychological stress in inflammatory bowel disease: Psychoneuroimmunological insights into bidirectional gut-brain communications. *Front Immunol*. 2022 Oct 6;13:1016578

Disclosure: Nothing to disclose.

PP0525

NON-ALCOHOLIC FATTY LIVER DISEASE AND LIVER FIBROSIS IN INFLAMMATORY BOWEL DISEASE: A FIBROSCAN-BASED ASSESSMENT

R. Saidani¹, D. Cherif¹, H. Dabbebi¹, H. Yacoub¹, H. Hassine¹, H. Kchir¹, N. Maamouri¹

¹La Rabta Hospital, Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: raouia.saidani@etudiant-fmt.utm.tn

Introduction: Non-alcoholic fatty liver disease (NAFLD) prevalence is elevated in patients with inflammatory bowel disease (IBD) in Western nations. Both intestinal inflammation and metabolic factors contribute to IBD-associated NAFLD. However, the burden of NAFLD in non-Western populations remains unclear.

Aims & Methods: This study aimed to evaluate the prevalence of NAFLD and liver fibrosis in a cohort of Tunisian IBD patients.

Methods: This cross-sectional, single-center study enrolled 84 consecutive IBD patients followed up at our department from April to December 2023. All participants underwent FibroScan examination for hepatic steatosis and fibrosis assessment using liver stiffness measurement (LSM) and controlled attenuation parameter (CAP). Patients with excessive alcohol consumption or recent steroid use were excluded. Univariate and multivariate analyses were performed. Hepatic fibrosis was defined by transhepatic elastography exceeding 7 kPa.

Results:

A total of 84 patients (37 ulcerative colitis, 47 Crohn's disease) were included. The median age was 39 years, with a median disease duration of 10 years. Body mass index (BMI) distribution was: normal weight (38.9%), underweight (11.1%), overweight (41.3%), and obese (8.7%). Mean CAP values increased progressively with BMI: 143.52 dB/m (underweight), 198.77 dB/m (normal weight), 269.3 dB/m (overweight), and 278.51 dB/m (obese). NAFLD was diagnosed in 28.57% of patients, with 1.19% exhibiting significant fibrosis. Increased BMI (odds ratio [OR] 2.03, 95% confidence interval [CI] 1.1–2.62) and older age at IBD diagnosis (OR 1.34, 95% CI 1–1.61) were significantly associated with NAFLD presence. Patients with CD and UC did not differ significantly in terms of hepatic steatosis. The median stiffness in IBD patients was normal. Hepatic fibrosis was detected in 7 (8.3%) of all IBD patients, predominantly in Crohn's disease (6/7). Most patients (7.14%) had an F2 grade, 1.2% had an F3 grade and no patient had an F4 grade.

Conclusion: This study demonstrates a 28.57% prevalence of NAFLD in Tunisian IBD patients. Higher BMI and older age at IBD diagnosis were associated with NAFLD. Hepatic fibrosis occurred predominantly in Crohn's disease patients. Further longitudinal studies are warranted to elucidate the impact of IBD on hepatic complications.

Disclosure: Nothing to disclose.

PP0526

VALIDATION OF THE PORTUGUESE VERSION OF IBD-CONTROL QUESTIONNAIRE AND COMPARISON WITH IBD-DISK

T. Carvalho¹, J. Franco², A. Guimarães¹, J. Damasceno¹, J. Neves¹, B. Arroja¹, A. Rebelo¹, S. da Silva Mendes¹, A.C. Caetano¹, D. Fernandes¹, T. Leal¹, R. Gonçalves¹, J.B. Soares¹

¹ULS de Braga, Gastroenterology, Braga, Portugal, ²Escola de Medicina da Universidade do Minho, Braga, Portugal

Contact E-Mail Address: taniacarvalho1994@gmail.com

Introduction: IBD-Control questionnaire and IBD-Disk are two easy-to-use IBD-specific patient-reported outcome measures aimed to measure the impact of IBD in the different health domains. Contrary to IBD-Disk, there is no fully published validated Portuguese version of IBD-Control. Additionally, the two instruments have not yet been compared.

Aims & Methods: The authors aimed to translate and validate the IBD-control in Portugal and to compare it with IBD-Disk. Acceptability was verified in a pilot patient group (n = 10) after the forward-backward translation of the IBD-control (Figure 1). Prospective validation involved completion of the IBD-Control, EQ-5D, short IBDQ, IBD-Disk and disease activity measurement by PRO2. Test-retest (2-week repeat) was used for measuring reliability. We compared user-friendliness (through 3 questions) and the ability to identify good disease control (through ROC analysis) of IBD-Control and IBD-Disk.

Results: Questionnaires were completed by 142 IBD patients (108 Crohn's disease, 34 ulcerative colitis). The mean completion time was 168s. Internal consistency (Cronbach's alpha) was 0.796 for the sub-group of 8 questions (IBD-control-8). Construct validity analyses demonstrated moderate-to-strong correlations of the IBD-control-8 and the other instruments (0.55-0.82) (Table 1).

Test-retest reliability for stable patients (n=54) was high (intraclass correlation coefficient - 0.861). The IBD-control-8 showed good discriminant ability between well-controlled and insufficient/poor-controlled disease (15±2 vs 11±4; p<.001). No significant differences were noted between IBD-Control and IBD-Disk regarding user-friendliness and AUC (0,79 vs 0,76) for identification of good disease control.

Conclusion: The Portuguese IBD-control is a rapid, reliable, and valid instrument for measuring disease control from an IBD patient's perspective, with no significant difference in terms of user-friendliness and measurement ability when compared to IBD-Disk.

Disclosure: Nothing to disclose.

PP0527

COMPARISON BETWEEN THE BOWEL ULTRASOUND SCORE AND INTERNATIONAL BOWEL ULTRASOUND SEGMENTAL ACTIVITY SCORE BASED ON ILEOCOLONOSCOPY IN PATIENTS WITH CROHN'S DISEASE

I. Yuksel^{1,2}, Y. Cagir¹, M.B. Durak³, A. Atay¹, M. Ergul¹, O. Ozturk¹, E. Keskin¹, A.B. Fedai¹, M.M. Ince¹, K. Kenarli¹, E. Deniz¹

¹Ankara Bilkent City Hospital, Gastroenterology, Ankara, Turkey, ²Ankara Yildirim Beyazit University, Faculty of Medicine., Gastroenterology, Ankara, Turkey, ³Hacettepe University, Faculty of Medicine, Gastroenterology, Ankara, Turkey

Contact E-Mail Address: yukselilhami@hotmail.com

Introduction: Intestinal ultrasound (IUS) has proven to be a valuable tool for accurately detecting intestinal damage and characterizing disease behavior in Crohn's disease (CD). IUS scoring systems for CD activity

have been developed, however all the studies had methodological flaws. Therefore, studies comparing and validating the existing IUS scores in CD patients are required.

Aims & Methods: In this study, we aimed to compare two main existing scores, Bowel Ultrasound Score (BUSS) and International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) in patients with ileal CD using the simplified endoscopic activity score for CD (SES-CD).

An observational cross-sectional study was performed to evaluate the disease activity in adult CD patients with ileal involvement between November 2019 and February 2024. All patients had undergone ileocolonoscopy and IUS, the time interval between the two procedures was lower than 10 days. Receiver operating characteristic (ROC) curve analyses was performed for BUSS and IBUS-SAS to predict SES-CD ≤2 for CD.

Results: Total 56 adult patients with ileal CD were included in the study, 38 patients (67.9%) were male, the median age was 40.5 (IQR 26-46.75) years and the median duration of the disease was 8.4 (IQR, 4.93-10.29) years. In the endoscopically remission (SES-CD ≤2) group; the median BUSS was 2.63 (IQR 2.12-3.45) and the median IBUS-SAS was 14 (IQR, 11.3-18.4), while in the endoscopically active (SES-CD >2) group; the median BUSS was 5.67 (IQR, 3.47-7.76) and the median IBUS-SAS was 49.7 (IQR, 23.3-72.65). The median BUSS and median IBUS-SAS in the endoscopically remission group were significantly lower than those of the endoscopically active group (p< 0.001, for both).

The cut-off value for BUSS to determine endoscopic remission (SES-CD ≤2) was 3.9 (AUC: 0.839, 95% CI: 0.737-0.941, sensitivity: 92%, specificity: 73%, p < 0.001), while the cut-off value for IBUS-SAS to establish endoscopic remission (SES-CD ≤2) was 24.4 (AUC: 0.871, 95% CI: 0.780-0.962, sensitivity: 100%, specificity: 73%, p < 0.001).

There was a very high positive correlation between BUSS and IBUS-SAS (r=0.914, p<0.001), a high positive correlation between BUSS and SES-CD (r=0.659, p<0.001), a moderate positive correlation between BUSS and CRP (r=0.577, p<0.001). There was a high positive correlation between IBUS-SAS and SES-CD as well as IBUS-SAS and CRP (r=0.728, p<0.001 and r=0.657, p<0.001 respectively).

Conclusion: In this study, we found that the most accurate cut-off value for BUSS was 3.9 and the most accurate cut-off value for IBUS-SAS was 24.4 in CD patients with endoscopic remission (SES-CD ≤2) group. Also, we have confirmed that both BUSS and IBUS-SAS significantly correlate with endoscopic activity in a real-world cohort.

Disclosure: Nothing to disclose.

PP0528

ASSESSING VISCERAL ADIPOSITY WITH CT ENTEROGRAPHY COULD HELP PREDICT RESPONSE TO BIOLOGIC THERAPY IN PATIENTS WITH CROHN'S DISEASE OF THE SMALL BOWEL

P. Kevrekidou¹, E. Xinou², G. Georgiadou¹, E. Athanasiadou¹, B. Mollagiousoufoglou¹, G. Lazaraki¹, D. Tzilves³, K. Soufleris¹
¹Theagenio Cancer Hospital of Thessaloniki, Gastroenterology Department, Thessaloniki, Greece, ²Theagenio Cancer Hospital of Thessaloniki, Department of Diagnostic Radiology, Pefka - Thessaloniki, Greece, ³Theagenio Cancer Hospital of Thessaloniki Greece, Gastroenterology Department, Thessaloniki, Greece

Contact E-Mail Address: eftychiaath1@gmail.com

Introduction: Recent studies implicate visceral adiposity in various bad outcomes of Inflammatory Bowel Disease. Patients with moderate to severe Crohn's Disease involving the small bowel are especially difficult to treat. The study aimed to seek any correlation between visceral fat and response to biologic therapy in this group of patients with the use of computed tomography enterography (CTE).

Aims & Methods: This was a retrospective cohort of patients with Crohn's Disease of the small bowel who underwent baseline assessment with CTE before the start of a new biologic therapy. Repeat imaging assessment with CTE was performed 6 to 12 months post new treatment initiation. Examinations were performed in a 16-slice CT scanner.

A single cross sectional CT slice at the L3 level was used for the segmentation of visceral and subcutaneous adipose tissue with syngo via dedicated software. We measured the ratio of visceral to subcutaneous adipose tissue (VAT/SAT).

The primary outcome was radiologic response: disease worsening vs complete response, partial response or stable disease. Secondary outcomes were clinical response, treatment persistence, Crohn's related surgeries and hospitalizations.

Results: A total of 114 exams from 62 patients were included in the study. Baseline disease characteristics were: median age 40 years (23-76), median disease duration 15 years (1-40), median BMI 24 (18-46), median body weight 71 Kg (45-160), stricturing disease 72%, previous surgery 56%, smokers 30%.

Most patients received anti-TNF agents: infliximab 40%, adalimumab 40%, ustekinumab 15%, vedolizumab 5%. Visceral fat > 12 was recorded in 65.8% of patients. VAT/SAT was associated with radiologic response (p=0,03), clinical response (p=0,02) and treatment persistence (p=0,03), but not with surgeries or hospitalizations.

Multivariate analysis confirmed the statistical correlation of VAT/SAT with radiologic response. Interestingly enough, no specific type of biologic therapy or disease characteristic showed any association with the primary outcome. Baseline BMI, weight and visceral fat volume also failed to correlate with response to therapy.

Conclusion: The use of visceral to subcutaneous adipose tissue ratio to quantify visceral adiposity helped to predict response to biologic therapy in Crohn's Disease patients with disease of the small bowel. This might confer an added value of enterography to other imaging modalities as for example intestinal ultrasound. Visceral fat seems to play an important role in inflammatory bowel disease and its accurate assessment may aid to risk stratify patients and plan therapy accordingly.

Disclosure: Nothing to disclose.

PP0529

THE INTESTINAL ULTRASOUND SCORE IBUS-SAS SIGNIFICANTLY CORRELATES WITH ENDOSCOPY AND HISTOLOGY IN ULCERATIVE COLITIS

S. Fischer^{1,2}, D. Fischmann¹, J. Wilde¹, M. Vetter^{1,2}, L. Wolf^{1,2}, C. Geppert³, R. Atreya^{1,2}, M. Waldner^{1,2}, D. Strobel^{1,2}, M.F. Neurath^{1,2}, S. Haberkamp^{1,2}, S. Zundler^{1,2}
¹Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Medicine 1, Erlangen, Germany, ²Deutsches Zentrum Immuntherapie, Erlangen, Germany, ³Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Pathology, Erlangen, Germany

Contact E-Mail Address: Sarah.Fischer@uk-erlangen.de
Introduction: Intestinal ultrasound (IUS) is widely recognised in the monitoring of inflammatory bowel diseases (IBD) and the resolution of bowel wall thickening (transmural healing) is currently investigated as treatment goal in IBD.¹
The international bowel ultrasound- segmental activity score (IBUS-SAS) was developed to guarantee high inter-observer reliability in Crohn's disease (CD) and data aiming to validate it are promising.²⁻⁴ Regarding IUS in ulcerative colitis studies remain scarce. We aimed to validate IBUS-SAS in UC-patients in comparison to the established Limberg-score.⁵

Aims & Methods: Patients with established diagnosis of UC were eligible for inclusion. The IBUS-SAS in the sigmoid colon was quantified according to the IBUS-groups guidelines.² Data regarding clinical (Mayo clinical score [MCS]), endoscopic (Mayo endoscopic score [MES]; ulcerative colitis endoscopic index of severity [UCEIS]), histologic (Nancy index) and biomarker (C-reactive protein [CRP], faecal calprotectin [FC]) activity were registered. The correlations between IBUS-SAS and these parameters were analysed using Spearman's rank test. All p-values <0,05 were considered to be statistically significant.

Results: We enrolled 51 UC patients (31 female), with a median IBUS-SAS (individual factors see table 1) of 41.6 (IQR 24.0; 62.3). The IBUS-SAS was significantly correlated with every individual parameter (p<0.001, r=0.48, 95% CI 0.22–0.67 for MCS; p<0.01, r=0.53, 95% CI 0.25–0.73 for MES; p<0.001, r=0.53, 95% CI 0.24–0.73 for UCEIS; p=0.03, r=0.36, 95% CI 0.02–0.73 for Nancy index; p<0.001, r=0.52, 95% CI 0.26–0.70 for CRP; p=0.03, r=0.61, 95% CI 0.07–0.87 for FC).

The Limberg-score showed a significant correlation to the clinical (p=0.01, r=0.36, 95% CI 0.08–0.59), endoscopic (p=0.001, r=0.50, CI 95% 0.21–0.71 for MES and p=0.001, r=0.50, 95% CI 0.21–0.71 for UCEIS) activity and CRP (p=0.02, p=0.44 95% CI 0.02–0.65), but not for histologic activity (p=0.27) and FC (p=0.14).

Overall, the correlations of the IBUS-SAS with the various disease activity parameters were stronger than their correlation with the Limberg score regarding clinical disease activity (r=0.48 vs. 0.36), the endoscopic picture (r=0.53 vs. 0.50 for MES; r=0.53 vs. 0.50 for UCEIS), histological activity (r=0.36 vs. 0.19) and the biomarkers of inflammation (r=0.52 vs. 0.44 for CRP; r=0.61 vs. 0.43 for FC).

IBUS-SAS features				
Bowel wall thickness (MM)		median 5.0 (IQR 4.0 – 5.9)		
Color Doppler signal	0	n =	20	(39.2 %)
	1	n =	19	(37.3 %)
	2	n =	10	(19.6 %)
	3	n =	2	(3.9 %)
Intestinal fat	0	n =	22	(44.0 %)
	1	n =	8	(16.0 %)
	2	n =	20	(40.0 %)
Bowel wall stratification	0	n =	33	(66.0 %)
	1	n =	10	(20.0 %)
	2	n =	2	(4.0 %)
	3	n =	5	(10.0 %)
IBUS-SAS		median 41.6 (IQR 24.0 – 62.3)		

Table 1: The distribution of the individual IBUS-SAS parameters in this UC-cohort.

Conclusion: We conclude that the IBUS-SAS shows a better correlation to established objective read-outs of disease activity in UC than previously established IUS scores and therefore seems a promising candidate for further validation as a tool for real-world disease monitoring and future clinical trials.

References: 1. Neurath, M. F. & Vieth, M. Different levels of healing in inflammatory bowel diseases: mucosal, histological, transmural, barrier and complete healing. Gut 72, 2164–2183 (2023).
2. Novak, K. L. et al. Expert Consensus on Optimal Acquisition and Development of the International Bowel Ultrasound Segmental Activity Score [IBUS-SAS]: A Reliability and Inter-rater Variability Study on Intestinal Ultrasonography in Crohn's Disease. J. Crohns. Colitis 15, 609–616 (2021).
3. Wang, L. et al. External validation and comparison of simple ultrasound activity score and international bowel ultrasound segmental activity score for Crohn's disease. Scand. J. Gastroenterol. 58, 883–889 (2023).
4. Xu, C., Li, L., Zhang, Y., Wang, R. & Zhang, H. Diagnostic accuracy of different cross-sectional imaging techniques for disease location and activity in Crohn's disease and external validation and comparison of MARIAS and IBUS-SAS. Abdom. Radiol. (New York) 48, 821–832 (2023).

5. Limberg, B. [Diagnosis of chronic inflammatory bowel disease by ultrasonography]. *Z. Gastroenterol.* 37, 495–508 (1999).
6. Lewis, J. D. et al. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. *Inflamm. Bowel Dis.* 14, 1660–6 (2008).

Disclosure: Nothing to disclose.

PP0530

NATURAL HISTORY AND MRI PREDICTIVE FACTORS OF RADIOLOGICAL HEALING IN FISTULIZING PERIANAL CD

V. Delmotte¹, E. Defraigne-Peigneur², P. Meunier³, E. Louis⁴, R. Gillard², C. Reenaers⁵

¹CHU Liège, Gastroenterology, Liège, Belgium, ²CHU Liege, Radiology, Liege, Belgium, ³CHU Liege, Radiology, Liège, Belgium, ⁴CHU Liege, Gastroenterology, Liege, Belgium, ⁵CHU Liege, Gastroenterology, Liège, Belgium

Contact E-Mail Address: catherine.reenaers@chuliege.be

Introduction: Fistulizing perianal Crohn's disease (CD) is a disabling condition affecting up to 30 % of patients. While mucosal healing is associated with a better clinical outcome in luminal CD, the objective of the management of perianal CD is less clear. Radiological parameters are rarely considered as an outcome in perianal CD. Some studies have suggested that a high degree of fibrosis of the fistula tract was associated with a better clinical outcome.

The aim of this study was to describe the natural history of perianal CD including MRI parameters and to identify clinical and radiological factors of perianal CD relapse and radiological healing.

Aims & Methods: All pelvic MRI performed for fistulizing perianal CD in the CHU of Liège, Belgium, between 2018 and 2023 were collected. MRI examinations were performed according to the protocol of the institution, using a 1.5-T [Siemens Aera ou Sola] or 3-T [Siemens Vida] machine, including T2 turbospin-echo, T2 TSE fat-saturated, T1 TSE FS before contrast in the axial plane and T1 TSE FS after gadolinium. The MAGNIFI-CD index and the Van Assche index were evaluated for each patient. The degree of fibrosis of the fistula tract was evaluated by two radiologists, blinded for the clinical history. The first MRI was evaluated in all patients. Patients with perianal flare had only one MRI included in the analysis. The first and the last MRI performed during the study period were analyzed, if available, in patients without perianal flare. Perianal flare was defined by the drainage of an abscess or a stoma for active perianal CD. Radiological remission was defined by a fibrosis of the fistula tract of $\geq 80\%$ or a MAGNIFI CD score of 0.

Results: Seventy-five pelvic MRI from 60 patients were included in the study. The median age of the patients was 37.0 (30.0 - 48.5) years old, 37 (62%) patients were male, the median duration of perianal CD was 36.00 (0.60 - 123.00) months, 19 (31.7%) had a seton at the time of the first MRI, 23 patients (40%) were on anti-TNF. Nineteen (32%) patients, required abscess drainage in the follow-up period. Sixty-three % were on anti-TNF at the time of the drainage. No clinical nor radiological factors at baseline were predictive of perianal flare.

Fifteen patients without perianal flare had a second MRI during the follow-up. Seven patients (46.7%) had radiological healing at the end of the follow-up. One patient (6.7%) had radiological healing at the first MRI but not at the last MRI, 2 patients (13.3%) had radiological healing at both MRI 1 and 2 (13.3%), 5 patients (33.3%) had no radiological healing at MRI 1 but had radiological healing at MRI 2. Longer duration of perianal CD was associated with higher rates of radiological healing at the last MRI whereas high VA hyperintensity T2 (OR=0.13, p=0.099) and hyperintensity on postcontrast T1 (OR=0.11p=0.071) at the first MRI were predictive of absence of mucosal healing during the follow-up.

Conclusion: One third of the patients with perianal CD required abscess drainage whereas about half of the patient had radiological healing at the end of the follow-up. No clinical predictive factors were associated with perianal flare and few radiological factors were predictive of radiological healing. Predicting the outcome of perianal disease remains challenging in clinical practice. Radiological factors are promising and should be validated in a prospective cohort.

Disclosure: Speaking fees, consulting fees, travel fees, grant from: Abbvie, Alfa Sigma, Takeda, Janssen, BMS, Pfizer, Lilly, Roche, Fresenius Kabi, Biogen, celltrion, ferring.

PP0531

ENDOSCOPIC SKIPPING AND PENETRATING COMPLICATIONS IN CROHN'S DISEASE ON TANDEM ILEO-COLONOSCOPY AND CROSS-SECTIONAL IMAGING: A RETROSPECTIVE COHORT STUDY

V. Solitano¹, S.K. Vuyyuru², A. Aruljothy³, M. Alkhattabi³, M. Beaton⁴, J. Gregor⁴, Z. Kassam⁵, R. Sedano⁶, H. Marshall⁵, D. Ramsewak⁵, M. Sey⁶, V. Jairath³

¹Università Vita-Salute San Raffaele, Gastroenterology, Milan, Italy, ²Alimentiv Inc., London, Canada, ³Western University, Division of Gastroenterology, Department of Medicine, London, Canada, ⁴Division of Gastroenterology, Western University, London, Ontario, Canada, ⁵Western University, London, Ontario, Canada, ⁶Western University, London, Ontario, Canada, Division of Gastroenterology, Department of Medicine, London, Canada

Contact E-Mail Address: virginiasolitano@gmail.com

Introduction: Crohn's disease (CD) is characterized by discontinuous inflammation. Failure to identify skipping lesions of the terminal ileum (TI) or transmural changes can lead to incorrect management.

Aims & Methods: Eligible adult patients with CD undergoing ileo-colonoscopy and computed tomography enterography (CTE) or magnetic resonance enterography (MRE) within six months. We determined the prevalence of endoscopic skipping (normal ileum on colonoscopy but proximal small bowel inflammation on cross-sectional imaging), skip lesions (discontinuous inflammation along the gastrointestinal tract identified on cross-sectional imaging), and penetrating complications.

Clinical Characteristics	Active Crohn's Disease and Normal TI (n = 81)	Active Crohn's Disease and Abnormal TI (n = 121)	P value
Age, median (range), years	44.00 (15.91)	46.00 (16.55)	P = 0.88
Sex			
Male	34 (41.98)	45 (37.19)	P = 0.50
Female	47 (58.02)	76 (62.81)	
Smoking history, n (%)			
Former smoker	7 (8.64)	13 (10.74)	P = 0.50
Smoker	17 (20.99)	18 (14.88)	
Non-smoker	57 (70.37)	90 (74.38)	
Duration of Crohn's Disease			
≤5 years	35 (43.21)	49 (40.50)	P = 0.74
>5 years	46 (56.79)	71 (58.68)	
Previous Perianal Surgery, n (%)	13 (16.05)	8 (6.61)	P = 0.03
Previous resection, n (%)	30 (37.04)	47 (38.84)	P = 0.80
C-reactive protein, mean (SD), mg/L	4.31 (5.17)	8.00 (10.43)	P = 0.005

Results: Among 202 patients, 45 (22.3%) had endoscopic skipping proximal to TI intubation. Fifty patients (24.5%) had small bowel skip lesions, primarily in the ileum. Strictures were identified in 34 patients (16.8%) through both imaging and ileo-colonoscopy, in 21 patients (10.4%) solely through cross-sectional imaging, and in 3 patients (1.5%) solely through

ileo-colonoscopy. Approximately 63.8% of stricturing cases would be missed without cross-sectional imaging. Penetrating complications, including abscesses (2.5%) and various fistula types (4.9%), were detected in 15 (7.4%) patients.

Conclusion: Ileo-colonoscopy missed detection of active CD in approximately one-fifth of cases due to more proximal disease location. Stricturing disease would be missed in more than half of cases if cross-sectional imaging was not performed.

Disclosure: Virginia Solitano no conflict of interests.
Sudheer Kumar Vuyyuru has received consultancy fees from Alimentiv Inc.
Achuthan Aruljothy no conflict of interests.
Maan Alkhatabi has received consulting fees from Janssen. Speaker's fees from Janssen, Takeda & Pfizer.
Melanie Beaton has received advisory board fees from AbbVie, Astra Zeneca, Gilead,
Janssen, Novo Nordisk, Lupin, Pfizer and Takeda.
Jamie Gregor has no conflict of interests.
Zahra Kassam has received Bayer Pharmaceuticals speaker honorarium and research grant, Fusion MD speaker fees, Alimentiv Inc consulting fees.
Rocio Sedano has received consultancy fees from Alimentiv Inc.
Harry Marshall has no conflict of interests,
Darryl Ramsewak has no conflict of interests.
Michael Sey has received consultant fees from Medtronic; Research grants and speaker fees from Pendopharm; Educational grant from Cook Medical.
Vipul Jairath has received consultancy/advisory board fees from AbbVie, Alimentiv Inc., Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, GlaxoSmithKline, Genentech, Gilead, Janssen, Merck, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Topivert, Ventyx, and Vividion; and speaker's fees from, Abbvie, Ferring, Galapagos, Janssen Pfizer Shire, Takeda, and Fresenius Kabi.

PP0532
THE ROLE OF ULTRASOUND IN EVALUATING RESPONSE TO THERAPY IN ACTIVE ULCERATIVE COLITIS: RESULTS FROM A PROSPECTIVE COHORT STUDY

A.C. Bravo¹, J. Revés¹, B. Abreu¹, A. Bargas Bárbara¹, D. Abrantes¹, S. Bragança², M.A. Rafael², A. Guedes³, L. Glória¹, L. Roques Ramos¹, C. Palmela¹, J. Torres^{1,4}, C. Frias-Gomes¹
¹Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal,
²Hospital Prof. Doutor Fernando da Fonseca, Gastroenterology, Amadora, Portugal, ³Hospital Beatriz Ângelo, Loures, Portugal,
⁴Hospital da Luz, Gastroenterology, Lisbon, Portugal

Contact E-Mail Address: catarina.bravoo@gmail.com
Introduction: Intestinal ultrasound is emerging as a non-invasive method of monitoring patients with ulcerative colitis (UC). Our goal was to prospectively evaluate the association between ultrasound and endoscopic response and remission.
Aims & Methods: This is a prospective cohort of patients with left-sided UC (E2) or extensive UC (E3) with active disease (defined by SCCAI≥5), proposed to initiate/optimize therapy. Clinical activity (PRO2/SCCAI), biochemical activity (fecal calprotectin (FCaI)/CRP), ultrasound (wall thickening (BWT)/Milan-Ultrasound Criteria (MUC) score) was assessed at week 0 (W0), 2 (W2), 6 (W6), 14 (W14), and 30 (W30), and endoscopic (Mayo endoscopic sub-score (sMayo)) at W0, W14, and W30. Ultrasound response was defined as: 1-reduction in BWT >25%, 2-reduction in BWT >2mm, or 3-decrease in BWT >1mm + decrease in Modified Limberg score ≥1. Endoscopic

response was defined as a decrease in sMayo ≥1. Ultrasound remission was defined as MUC <6.2, and endoscopic remission as sMayo = 0.
Results: Twenty patients with UC were included (65% male, median age 54 (28-67) years, 50% E3, 60% on biologic therapy). Clinical, biochemical, ultrasound, and endoscopic activity characterization is found in Table 1. Clinical, biochemical, ultrasound, and endoscopic remission was achieved at W30 in 56%, 57%, 40%, and 33%, respectively. Patients with ultrasound response at W2 or ultrasound remission at W6 showed more endoscopic remission at W14 (p=0.032 and p=0.014, respectively). The presence of ultrasound remission at W14 was associated with endoscopic response at W30 (p=0.011).

Variables, median (IQR)	W0	W2	W6	W14	W30
SCCAI	7 (6-10)	3 (1-5)	3 (0-6)	3 (0-5)	1 (0-6)
FCaI (ug/g)	858 (705-2050)	750 (111-2110)	452 (69-1760)	162 (26-1092)	170 (36-580)
BWT (mm)	4.79 (4.13-5.40)	4.30 (3.84-4.91)	3.93 (3.23-4.50)	3.85 (2.65-4.53)	3.80 (2.20-4.70)
MUC	8.4 (7.4-9.6)	7.8 (6.5-8.9)	7.2 (4.9-8.2)	5.7 (3.7-8.0)	7.1 (4.6-8.6)
sMayo	3 (2-3)	---	---	2 (1-3)	1 (0-3)

Table 1 - Clinical, biochemical, ultrasound, and endoscopic activity characterization.

Conclusion: The presence of ultrasound response at W2 and ultrasound remission at W6 was associated with endoscopic remission at W14. Additionally, ultrasound remission at W14 was associated with endoscopic response at W30. Ultrasound response in active ulcerative colitis appears to be early, allowing its use as a non-invasive tool for tight control, enabling early optimization of therapy.
Disclosure: Nothing to disclose.

PP0533
BEYOND THE SCOPE: UTILITY OF INTESTINAL ULTRASOUND FOR PREDICTING CLINICAL OUTCOMES IN ULCERATIVE COLITIS IN CLINICAL REMISSION

R. Vaughan¹, J. Zhou¹, L. Chen¹, N. Mingos¹, J. Segal¹, B. Christensen¹
¹Royal Melbourne Hospital, Gastroenterology, Melbourne, Australia

Contact E-Mail Address: jessiezhoumd@gmail.com
Introduction: Intestinal Ultrasound (IUS) is a point-of-care tool that is increasingly utilised in the management of ulcerative colitis (UC) as a marker of active disease and response to medical therapy. IUS has the advantage of being non-invasive, non-irradiating, well tolerated, cost-effective with good reproducibility when compared to ileo-colonoscopy and magnetic resonance enterography.
There is however limited evidence that sonographic remission on IUS predicts UC disease course.
Aims & Methods: This study aimed to examine the relationship of IUS and clinical outcomes in UC patients in clinical remission and determine if presence of sonographic inflammation was associated with medication escalation, corticosteroid use, hospitalisation or surgery.
A retrospective study at The Royal Melbourne Hospital included all UC patients who underwent IUS for IBD between 2017 and 2022 in clinical remission (Simple Colitis Clinical Activity score ≤2) at the time of IUS and followed up for at 6 months. Patients with rectum-confined disease (E1), a stoma, or suboptimal IUS were excluded. Sonographic healing, defined as BWT ≤3 mm without hyperemia, inflammatory fat, or disrupted bowel wall stratification was the combined endpoint.

Kaplan-Meier analysis was performed to compare medication-escalation-free survival, corticosteroid-free survival, hospitalisation-free survival and surgery-free survival in those with and without sonographic healing. Univariate and multivariate Cox proportional hazard regression analyses were performed to identify predictors of these clinical outcomes.

Results: 2,113 ultrasound reports were assessed for eligibility, and 394 patients had a confirmed UC diagnosis. Of 149 consecutive patients in clinical remission met inclusion criteria (43% male), sonographic inflammation was present in 45%.

During mean follow-up of 634 days, medication escalation occurred in 40%, corticosteroid use in 27%, hospitalisation in 13% and UC related surgery in 2%.

Sonographic inflammation did not emerge as a predictive factor for these outcomes; the only factor predictive of significant outcomes was the baseline Montreal classification (Table 1). Patients with sonographic inflammation on the whole had worse outcomes however.

Variable	Univariate (n=149)			Multivariate (n=149)		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender	1.25	0.64, 2.46	0.5	1.41	0.65, 3.13	0.4
Smoker	1.02	0.63, 1.63	> 0.9	0.95	0.55, 1.61	0.8
Montreal	2.23	1.28, 4.03	0.006	2.43	1.30, 4.78	0.007
Steroid	2.77	1.27, 7.39	0.020	1.93	0.86, 5.20	0.14
Immunomodulator	1.07	0.81, 1.40	0.6	0.84	0.59, 1.17	0.3
Biologic	1.06	0.92, 1.22	0.4	1.02	0.87, 1.20	0.8
Hyperaemia	8.24	1.28, 160	0.057	7.30	0.80, 174	0.12
US Inflammation	0.90	0.46, 1.74	0.8	0.51	0.13, 1.84	0.3

Table 1: Univariate and multivariate predictors of medical escalation in patients with ulcerative colitis. Data is shown as hazard ratio (95% confidence intervals)

OR = Odds Ratio, CI = Confidence Interval

Conclusion: This study is the first to examine the predictive utility of IUS in the setting of clinical remission and interestingly demonstrates that IUS does not appear to predict clinical complications. The role of IUS in UC has been slower to be established compared to Crohn's disease due to concerns about poor rectal views and lower sensitivity to detect mild mucosal inflammation.

This retrospective study challenges the utility of intestinal ultrasound in predicting clinical outcomes in UC patients in clinical remission, highlighting the need for further research to establish its role in guiding real time treatment decisions.

Disclosure: Nothing to disclose.

PP0534

BOWEL PREPARATION OPTIMIZATION OF DOUBLE BALLOON ENTEROSCOPY AND MAGNETIC RESONANCE OF SMALL INTESTINE IN PATIENTS WITH CROHN'S DISEASE IMPROVES PATIENTS' SATISFACTION

J. Wang¹, P. An¹, A. Yin¹, W. Wang²

¹Renmin Hospital of Wuhan University, Department of Gastroenterology, Wuhan, China, ²Xiangyang Central Hospital, Department of Gastroenterology, Xiangyang, China

Contact E-Mail Address: anping_05@163.com

Introduction: Double balloon enteroscopy (DBE) and Magnetic resonance enterography (MRE) are routine examination to detect lesions in the small intestine of Crohn's disease (CD). However, twice bowel preparation within several days reduces patients' satisfaction and compliance.

Aims & Methods: This study combined these two examinations on the same day with only one bowel preparation was required and compared the quality of DBE and MREC with two bowel preparations. This is a retrospective study collected 243 CD patients received both DBE and MREC within three days between April 2023 and April 2024. Patients in OBP group took bowel cleansing medication the night before two examinations. They underwent MREC and DBE in the order the next day: received MRMC in the morning and had DBE in the afternoon. Patients in TBP group underwent twice bowel preparations, MRMC and DBE as scheduled time within three days. Overall sex- and age-adjust analysis was performed.

Results: A total of 123 patients was in one bowel preparation (OBP) group and 120 in twice bowel preparation (TBP) group. 115(95.83%) patients qualified for bowel preparation at both examinations, 1(0.83%) only qualified for bowel preparation at MREC, and 4(3.33%) only qualified for bowel preparation at DBE in OBP group. While in TBP group, 116(94.31%) patients had bowel preparations qualified in both examinations, 2(1.63%) patients had bowel preparations only qualified in MRE, and 5(4.06%) patients had bowel preparations only qualified in DBE (P=0.81).

The average depth of insertion was 255.00±70.52 cm in OBP and 255.59±95.83 cm in TBP for the antegrade approach from the pylorus (P=0.98) and 144.70±75.40cm vs. 155.06±98.35cm for the retrograde procedures beyond the ileocecal valve (P=0.41). Complications of hypoglycemia was observed in 7(5.83%) patients in OBP group and 17(13.82%) patients in TBP group (P=0.037). The questionnaire results showed that 82.50% (99/120) of patients in OBP group while 68.29% (84/123) of patients in TBP group were satisfied with the process of examination (P=0.01). The mean intervention depth of OBP and TBP was 255.00±70.52 cm and 255.59±95.83 cm (P=0.98), and the mean intervention depth of OBP and TBP was 144.70±75.40 cm and 155.06±98.35 cm (P=0.41). In this paper, we discuss the relationship between the mechanism and the relationship between the mechanism. The results showed that the patients were satisfied with the inspection process of OBP group and the patients were satisfied with the inspection process of OBP group, and the patients were satisfied with the inspection process of TBP group.

Conclusion: One bowel preparation for DBE and MRE has similar effect as split-dose bowel preparation, and increases the compliance and tolerance of patients.

Disclosure: None.

PP0535

ARTIFICIAL INTELLIGENCE (AI) ASSISTED INTESTINAL ULTRASOUND: DEVELOPMENT AND EVALUATION OF AN AI MODEL FOR BOWEL WALL SEGMENTATION AND MEASUREMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS

B.L. Møller¹, B. Lo^{2,3}, J.H. Karrer¹, J. Ruiz-Molgaard¹, G. Madsen^{2,3}, M.G. Tolsgaard⁴, K. Theede^{2,3}, J. Fremberg Ilvemark⁵, I. Vind^{2,3}, F. Bendtsen^{2,3}, J. Burisch^{2,3}, C. Igel¹, B. Ibragimov¹, T. Boysen^{2,3}

¹University of Copenhagen, Department of Computer Science, Copenhagen, Denmark, ²Copenhagen University Hospital – Amager and Hvidovre, Hvidovre, Gastro Unit, Medical Section, Hvidovre, Denmark, ³Copenhagen University Hospital – Amager and Hvidovre, Hvidovre, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre, Denmark, ⁴Rigshospitalet, Copenhagen Academy of Medical Education and Simulation (CAMES), Copenhagen, Denmark, ⁵Herlev University Hospital, Gastroenterology, Copenhagen, Denmark

Contact E-Mail Address: bobby.lo@regionh.dk

Introduction: Intestinal ultrasound (IUS) is increasingly used to assess inflammatory bowel disease (IBD). It provides physicians with detailed insights into transmural inflammation. Measurements of bowel wall thickness (BWT) based on IUS have proven to be a strong detector of active disease in both ulcerative colitis and Crohn's disease. However, the result of IUS relies heavily on the skill of the operator. To address this problem, we aim to develop an artificial intelligence (AI) model to assist operators in accurately identifying the inner and outer bowel walls, thereby facilitating AI-assisted BWT measurements.

Aims & Methods: We extracted 600 ultrasound frames from 231 ultrasound cine loops (videos) of IBD patients. Each frame was segmented, and the inner and outer bowel walls were labelled by four International Bowel Ultrasound Group (IBUS) certified experts from Denmark, with each expert annotating 150 frames. The annotated frames were split 80/10/10 into training-validation-test sets. There was no overlap in the video between the different splits. An AI model was trained to segment the inner and outer bowel walls in the frames. A postprocessing step was employed to refine the segmentations and perform automated BWT measurement, rejecting any segmentations considered too poor (e.g. a distance measure > 35 pixels).

The model's segmentations were evaluated against the reference expert segmentations using the rejection rate, absolute pixel difference, and Dice Similarity Coefficient (Dice score).

Results: A total of 30 frames were discarded due to poor visibility, leaving 570 annotated frames. In the test set (unseen data), the rejection rate was 4.2%. The mean pixel difference in BWT measurements was 3.712 (SD: 3.979). The AI model achieved a Dice score of 0.42 when compared with expert annotations. These results indicate that the model tended to match the distances measured by experts, albeit with slight shifts in the exact points of measurement.

Conclusion: Our preliminary findings suggest that the AI-assisted IUS model has the potential to aid operators by providing reliable, expert-level approximations of BWT with a low rejection rate. It may become a useful tool in clinical practice for consistent IBD assessments. Further training and refinement of the framework could enhance its accuracy and facilitate its application in real-time diagnostic assessments.

Disclosure: Nothing to disclose.

PP0536

ENHANCING CALPROTECTIN'S PREDICTIVE POWER AS A BIOMARKER OF ENDOSCOPIC ACTIVITY IN ULCERATIVE COLITIS: A MACHINE LEARNING USE CASE

M. Dranga¹, C. Mihai², O. Gavrilescu², C. Cijevschi Prelipcean³, I.V. Popa¹

¹University Of Medicine And Pharmacy Gr. T. Popa, Iasi, Romania,

²UMF "Grigore T. Popa", Center of Gastroenterology and Hepatology, University Hospital "Sf. Spiridon", Iasi, Romania, ³"St. Spiridon" Emergency Hospital, Gastroenterology, Iasi, Romania

Contact E-Mail Address: mihaela_dra@yahoo.com

Introduction:

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by periods of exacerbation and remission, making disease monitoring and management challenging. Endoscopy, the gold standard for assessing disease activity and severity, involves invasive procedures and is associated with patient discomfort and risks. Using machine learning (ML) to combine fecal calprotectin with other clinical or biological tests can significantly enhance the non-invasive prediction of endoscopic disease activity (EDA) in UC.

Aims & Methods: Aim: To prove that by fusing fecal calprotectin with other clinical data into an ML model, the performance of the non-invasive prediction of EDA can be significantly improved. Methods: We conducted a prospective, observational, single-center study encompassing 103 patients diagnosed with UC. We employed multilayer perceptron models as the core ML algorithm for predicting EDA. For the constructed models, we utilized the varImp function from the caret library in R to assess the significance of each variable in predicting the outcome.

Results: Calprotectin as a sole predictor obtained an accuracy of 70% and an area under the curve (AUC) of 0.68. Combining calprotectin with the list of selected predictors that were fed to the MLP models improved accuracy and the AUC. The accuracy of the algorithm on the test set was 85%. Similarly, the AUC increased to 0.93. This is the first study to propose the use of calprotectin as a predictor in an ML model to estimate UC endoscopic disease activity.

Conclusion: The deployment of this ML model can furnish doctors and patients with valuable evaluation of endoscopic disease activity which can be highly beneficial for individuals with UC who need long-term treatment.

Disclosure: Nothing to disclose.

PP0537

LEVELS OF FATTY ACIDS IN ERYTHROCYTE MEMBRANES AND BLOOD SERUM AS EXACERBATION PREDICTORS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

M.V. Kruchinina^{1,2}, A.I. Valuyskikh¹, E.Y. Valuyskikh^{2,3}, I.O. Svetlova², A.A. Gromov¹, A.S. Sokolova⁴

¹Research Institute of Internal and Preventive Medicine - Branch of the Institute of Cytology&Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation, ²Novosibirsk State Medical University, Novosibirsk, Russian Federation, ³LLC Novosibirskiy Gastrocenter, Clinical Research, Novosibirsk, Russian Federation, ⁴Vorozhtsov Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation

Contact E-Mail Address: kruchmargo@yandex.ru

Introduction: Unclear etiology of IBD, the frequent similarity of their clinical and endoscopic manifestations, lack of a gold standard in diagnosing diseases, which complicates the choice of targeted therapy, urgently require improving the efficiency of currently available diagnostic technologies [1]. Significant efforts are being made to search for biomarkers that can be used to identify patients at high risk of IBD relapse who need more intensive monitoring and therapy in the early stages of these diseases, in remission to prevent long-term irreversible structural damage [2].

Aims & Methods: The purpose of the research was to study the levels of fatty acids (FAs) in red blood cells (rbc) membranes and blood serum in patients with IBD examined under follow-up control as possible predictors of disease exacerbation.

During our study, 44 patients with IBD have been monitored, in the course of that period, the average age was equal to 36.3 ± 5.2 . The first examination has been performed in remission of the diseases, the second one 6 to 12 months after the first step, and it has been done in the acute stage of IBD. The composition of the FAs has been studied using gas chromatography-mass spectrometry (Agilent 7000B (USA)).

Results: Predictors of exacerbation progress in patients with IBD have been found to be reduced levels of such FAs as C20:5 n-3 ($p=0.002$), C18:3 n-3 ($p=0.039$), C20:2 n-6 ($p=0.002$), C16:2 n-6 ($p=0.006$), C22: 4 n-6 ($p=0.008$), and on the contrary, increased content of FA C18:0 ($p=0.005$), SFAs/USFAs ($p=0.039$), SFAs/PUFAs ($p=0.03$) in rbc membranes and FA C20:0 in blood serum ($p=0.008$). The diagnostic model created was able to predict the exacerbation progress with a sensitivity of 87.2%, specificity of 91.3% (AUC 0.936), incorporating the above-described fatty acids with respect to their degree of contribution. We have found correlations of rbc C18:0 with haemoglobin level ($r=-0.344$, $p<0.001$), erythrocyte sedimentation rate ($r=0.480$, $p=0.012$), fibrinogen level ($r=0.352$, $p=0.004$); rbc C18:3n-3 - with level of C-reactive protein ($r=-0.472$, $p=0.023$), fibrinogen ($r=-0.420$, $p=0.022$), faecal calprotectin ($r=-0.391$, $p=0.044$). The content of rbc C16:2n-6 was directly correlated with the level of fecal calprotectin ($r=0.407$, $p=0.028$), ratio of SFAs/USFAs was depending on the number of leukocytes ($r=0.411$, $p=0.046$). The function of elevated levels of SFAs as predictors of exacerbation of IBD is probably determined by the fact that they potentially regulate inflammatory reactions by acting on the pathways of the PPAR- γ and retinoid X receptors (RXR) [3].

Reduced levels of C18:3n-3 as a predictor of exacerbation may be related to the ability of this FA to reduce the activity of ionised calcium-binding adaptor molecule 1-positive macrophages [4] and to reduce the expression of proinflammatory genes IL-8, COX2 and inducible nitric oxide synthase to reduce intestinal inflammation [5].

The significance of C20:5n-3 for prediction of the active stage of IBD is due to the fact that it inhibits the inflammatory pathways of transforming growth factor beta-1/epidermal growth factor receptor P-EGFR and NF-

κ B, and it also modulates redox balance and mitigates the progression of UC [6]. Reduced levels of several omega-6 PUFAs may be related to their increased consumption during elongation, desaturation, including in the arachidonic cascade associated with the synthesis of proinflammatory cytokines [7].

Conclusion: The use of fatty acids of rbc membranes and blood serum is promising and pathogenetically justified, namely as biomarkers for predicting the exacerbation progress in patients with IBD.

References:

1. Seyedian SS, Nokhostin F, Malamir MD. A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. *J Med Life*. 2019 Apr-Jun;12(2):113-122. doi: 10.25122/jml-2018-0075.
2. Tibble J.A., Sigthorsson G., Bridger S. et al. Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. *Gastroenterology*. 2000; 119: 15-22. doi:10.1053/gast.2000.8523
3. Mozaffarian D. Trans fatty acids effects on systemic inflammation and endothelial function. *Atheroscler Suppl* (2006) 7(2):29-32. doi: 10.1016/j.atherosclerosis.2006.04.007
4. Kim J, Ahn M, Choi Y. et al. Alpha-linolenic acid alleviates dextran sulfate sodium-induced ulcerative colitis in mice. *Inflammation* (2020) 43(5):1876-83. doi: 10.1007/s10753-020-01260-7
5. Reifen R, Karlinsky A, Stark AH. et al. A-linolenic acid (Ala) is an anti-inflammatory agent in inflammatory bowel disease. *J Nutr Biochem* (2015) 26 (12):1632-40. doi: 10.1016/j.jnutbio.2015.08.006
6. El Mahdy RN, Nader MA, Helal MG. et al. Eicosapentaenoic acid mitigates ulcerative colitis-induced by acetic acid through modulation of nf-kb and tgf-B/egfr signaling pathways. *Life Sci* (2023) 327:121820. doi: 10.1016/j.lfs.2023.121820
7. Ajabnoor SM, Thorpe G, Abdelhamid A, Hooper L. Long-term effects of increasing omega-3, omega-6 and total polyunsaturated fats on inflammatory bowel disease and markers of inflammation: a systematic review and meta-analysis of randomized controlled trials. *Eur J Nutr*. 2021 Aug;60(5):2293-2316. doi: 10.1007/s00394-020-02413-y.

Disclosure: Nothing to disclose.

PP0538

CORRELATION OF BOWEL ULTRASONOGRAPHY AND ENDOSCOPY IN CHRONIC INFLAMMATORY BOWEL DISEASE (IBD)

T. Waal¹, C. Thon¹, R. Rosania¹, A. Afifi¹, V. Keitel-Anselmino¹, U. von Arnim¹, A. Link¹

¹Otto-von-Guericke University, Clinic for Gastroenterology, Hepatology and Infectiology, Magdeburg, Germany

Contact E-Mail Address: alinkmail@gmail.com

Introduction: Accurate assessment of disease activity and prediction of treatment response and prognosis are challenges in the management of chronic inflammatory bowel disease (IBD). Due to the invasiveness of colonoscopy, non-invasive methods are of high clinical relevance. Bowel ultrasonography (B-US) is establishing itself as a non-invasive, cost-effective method in daily clinical practice.

Aims & Methods: The aim of this study is to evaluate the correlation between B-US and endoscopy in relation to inflammatory activity and severity of IBD. Patients were retrospectively selected for comparison between B-US and endoscopy.

A total of 473 patients were included, of whom (n=274) had Crohn's disease (CD) and (n=199) had ulcerative colitis (UC). The examination results were divided into four sections (terminal ileum, proximal colon, distal colon and rectum) and systematically analyzed. Inflammatory activity was classified according to intestinal wall thickness in mm:

none (0): 0-2.9, mild (1): 3.0-4.9, moderate (2): 5.0-7.9, severe (3): >8.0. Endoscopic evaluation was performed according to simplified Mayo and SES-CD criteria.

Results: Based on endoscopy, patients were divided into groups with inflammatory activity (274 CD, 175 UC) and remission (34 CD, 24 UC). Comparison of B-US and endoscopy showed a significant correlation regarding inflammatory activity ($r=0.44$, $p<0.001$). The correlation was more significant in UC ($r=0.5548$, $p<0.001$) than in CD ($r=0.3665$), except in the ileum in UC ($r=-0.1050$, $p<0.4822$). The best correlation in MC was found in the ileum ($r=0.4783$, $p<0.001$) and in the distal colonic segments ($r=0.5217$, $p<0.001$), while in UC the best correlation was found in the proximal ($r=0.5586$, $p<0.001$) and in the distal colonic segments ($r=0.6250$, $p<0.001$). Localization of rectal inflammation was associated with lower diagnostic accuracy. Compared to endoscopy, B-US showed a sensitivity of 82.2%, a specificity of 51.7% and a positive predictive value of 92.4%.

Conclusion: B-US shows reliable diagnostic accuracy compared to endoscopy in assessing inflammatory activity in IBD patients and can be considered as a complementary non-invasive diagnostic tool.

Disclosure: AL received research funding from the European Regional Development Fund (Project ID: ZS/2018/11/95324) and the German Federal Ministry of Education and Research (BMBF) (FKZ 01GM2204A). AL has received speaker fees from Janssen, Ferring and Luvos.

PP0539

COMPARATIVE EFFICACY AND SAFETY OF ENDOSCOPIC MODALITIES FOR COLORECTAL CANCER SCREENING IN INFLAMMATORY BOWEL DISEASE: A NETWORK META-ANALYSIS USING GRADE METHODOLOGY

G. Nigam¹, V. Sinopoulou², M. Ganeshan², M.R. Tokonyai², A. Wilson³, M. Iacucci⁴, S. Dolwani⁵, V. Subramanian⁶, M. Gordon², J.E. East⁷

¹Oxford University NHS Hospitals, Gastroenterology, Oxford, United Kingdom, ²University of Central Lancashire, Preston, United Kingdom, ³St. Marks Hospital, Wolfson Unit for Endoscopy, London, United Kingdom, ⁴University College of Cork and APC Microbiome, Cork, Ireland, College of Medicine and Health, Cork, Ireland, ⁵Cardiff University, Population Medicine, Cardiff, United Kingdom, ⁶Leeds Teaching Hospitals NHS Trust, St. James University Hospital, Molecular Gastroenterology, Leeds, United Kingdom, ⁷John Radcliffe Hospital, Translational Gastroenterology Unit, Oxford, United Kingdom

Contact E-Mail Address: gaurav.nigam@nhs.net

Introduction: Long-standing Inflammatory bowel disease (IBD) increases the risk of colonic neoplasia, necessitating effective screening strategies. Various endoscopic modalities are used for surveillance colonoscopy in IBD patients, yet their comparative effectiveness and safety remain unclear. Previous guidelines have supported using both dye-based and virtual chromoendoscopy as equivalent¹; however, their additional benefit in the era of high-definition (HD) white light remains controversial.

Aims & Methods: This network meta-analysis (NMA), part of the British Society of Gastroenterology's initiative to update IBD surveillance guidelines, aims to compare the efficacy and safety of different endoscopic techniques to inform clinical practice and guidelines. We searched CENTRAL, ClinicalTrials.gov, Embase via Ovid, MEDLINE via Ovid, WHO ICTPR for randomised controlled trials (RCTs), and reference lists of relevant studies up to February 2024 for RCTs comparing endoscopic modalities for screening colonoscopy in patients with IBD. The primary outcome for efficacy was the detection of any dysplastic lesion (Vienna classification 2-5) per patient and, for safety, serious adverse events. Review authors independently screened and extracted data and assessed the risk of bias using

the Cochrane tool. We conducted an NMA under a frequentist framework to estimate the relative effectiveness and safety of the interventions. The GRADE approach was employed to assess the certainty of the evidence for each outcome.

Results: A total of 27 RCTs involving 4,159 participants were included. The network comprised 6 endoscopic modalities: HD white light endoscopy (HD-WLE), HD virtual chromoendoscopy (HD-VCE), HD dye-based chromoendoscopy (HD-DCE), HD-WLE with segmental re-inspection (SR), auto-fluorescence imaging (AFI), and full-spectrum endoscopy (FUSE). There were no RCTs comparing HD to standard definition (SD) WLE/DCE; thus, the SD modalities could not be connected to the main network. HD-DCE may be more effective for detecting dysplasia, with a risk ratio (RR) of 1.42 (95% CI: 1.02-1.98) and low-GRADE certainty compared to HD-WLE. All other modalities had very low-GRADE certainty to draw conclusions about them, with RRs of 0.99 (95% CI: 0.69-1.43) for HD-VCE; 1.35 (95% CI: 0.66-2.77) for HD-WLE with SR; 3.24 (95% CI: 0.66-15.87) for FUSE; and 1.18 (95% CI: 0.55-2.57) for AFI. A similar trend was noted in sensitivity analyses, excluding studies reporting on serrated lesions (RR for HD-DCE: 1.91, 95% CI: 1.36-2.69) and excluding single endoscopist studies (RR for HD-DCE: 1.57, 95% CI: 1.10-2.26) compared to HD-WLE. Similar performances were noted for HD-VCE subtypes and varying concentrations of dye used in HD-DCE. Data on serious adverse events were limited, precluding any meta-analysis. In studies that reported this outcome, 2 serious adverse events were reported out of 2164 patients; however, this outcome had very low-GRADE certainty.

Conclusion: HD DCE is suggested over other modalities for surveillance in IBD, considering its potential to detect a small number of additional patients with dysplastic lesions compared to HD WLE. HD-VCE was not supported as an equivalent alternative to HD-DCE. However, the certainty of this recommendation is low due to the limited evidence. When choosing the surveillance modality, clinicians should also consider patient preferences, resource availability, and individualised risk assessments.

References: 1 Murthy et al. *Gastroenterology* 2021

Disclosure: Nothing to disclose.

PP0540

INTESTINAL ULTRASOUND IDENTIFIES HISTOPATHOLOGICAL APPENDICEAL INFLAMMATION IN ULCERATIVE COLITIS

M. Pruijt¹, E. Visser², F. de Voogd¹, M. Reijntjes², W.A. Bemelman², G.R. D'Haens¹, A. Mookhoek³, C.J. Buskens², K.B. Gecse¹

¹Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Department of Surgery, Amsterdam, Netherlands, ³University of Bern, Department of Pathology, Bern, Switzerland

Contact E-Mail Address: m.j.pruijt@amsterdamumc.nl

Introduction: Growing evidence points to appendectomy as an alternative treatment for ulcerative colitis (UC). Histopathological appendiceal inflammation might be correlated with response to appendectomy. Intestinal ultrasound (IUS) is a non-invasive diagnostic modality used to visualize appendiceal inflammation.

Aims & Methods: We aimed to investigate appendiceal IUS's relationship with histopathology findings in appendix resection specimens. Therapy-refractory UC patients undergoing appendectomy in single center clinical trials were included. IUS parameters included appendix diameter, wall thickness, submucosal layer thickness and submucosal hyperechogenicity. Submucosal layer hyperechogenicity was quantified using the mean aerial grayscale intensity which is a numerical scale 0-255, with zero corresponding to black. To adjust for variations in depth and gain, we measured the Δ grayscale intensity using the difference between the sub-

mucosa and muscularis propria in a perpendicular fashion. The Robarts Histopathology Index (RHI) was used to measure mucosal histological disease activity in the appendix ranging from 0-33. Appendiceal inflammation was defined as RHI >3, with at least subscores of lamina propria neutrophils or epithelium neutrophils ≥ 1 , or presence of ulcers or erosions.

Results: 37 of 55 (67.3%) included patients had a visualized appendix on IUS. The median RHI was 6 (IQR 0-12) and histopathological appendiceal inflammation was present in 21/37 (57%). Submucosal layer thickness was significantly higher, and the submucosal layer hyperechogenicity was significantly enhanced in microscopically inflamed appendices (Table 1). Submucosal hyperechogenicity predicted histopathological appendiceal inflammation (OR 1.03, 95% CI 1.0-1.05; $p=0.035$). Submucosal thickness ≥ 0.75 mm diagnosed histopathological appendiceal inflammation with 66.7% sensitivity, 81.3% specificity and an AUC of 0.69 ($p=0.046$). Submucosal hyperechogenicity >110.20 diagnosed histopathological appendiceal inflammation with 57.1% sensitivity, 81.3% specificity and an AUC of 0.69 ($p=0.046$).

IUS characteristic	Total N=37	RHI $\leq$ 3 N=16	RHI>3 N=21	p-value
Diameter (mm)	4.3 (3.7-5.8)	4.3 (3.5-5.6)	4.4 (3.9-6.0)	0.24
Wall thickness (mm)	1.9 (1.5-2.3)	1.9 (1.4-2.1)	1.9 (1.5-2.4)	0.36
Mucosa (mm)	0.6 (0.4-0.8)	0.7 (0.4-0.8)	0.6 (0.4-0.8)	0.72
Submucosa (mm)	0.7 (0.5-0.9)	0.6 (0.4-0.7)	0.9 (0.6-1.0)	0.04
Muscularis propria (mm)	0.5 (0.3-0.6)	0.5 (0.3-0.6)	0.5 (0.3-0.7)	0.5
Submucosal hyperechogenicity (Δ grayscale value, 0-255)	99.5 (83.4-133.3)	95.4 (76.2-108.1)	113.5 (87.7-151.7)	0.02

Table 1. Ultrasound characteristics of the visible appendices.

Conclusion: IUS is able to identify patients with histopathological appendiceal inflammation who may benefit from appendectomy as treatment for UC.

Disclosure: MP received speakers fees from Janssen and Tillotts
EV has Nothing to disclose.

FV received speaker or honoraria fees from AbbVie, Janssen and Tillotts
MR has Nothing to disclose.

WB has Nothing to disclose.

GD has served as a consultant and/or received speaker's fees from AbbVie, Alimentiv, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion Healthcare, Cytokine Pharma, Eli Lilly, Ferring, Galapagos, Glaxo SmithKline, Gossamer Bio, Immunic, InDex Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Takeda, Tillotts, Ventyx Biosciences.

AM has Nothing to disclose.

CB has Nothing to disclose.

KG has received grants from Pfizer Inc, Celltrion and Galapagos; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunic Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis and Takeda and speaker's honoraria from Abbvie, Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda and Tillotts.

PP0541

INTER-RATER AGREEMENT FOR BOWEL WALL COLOUR DOPPLER SIGNAL ASSESSMENT USING INTESTINAL ULTRASOUND IN CROHN'S DISEASE PATIENTS

P. Cacic¹, S. Pelajic¹, M. Masic², V. Tomasic¹, Z. Jovicic³, D. Ogresta-Kordej¹, I. Burcul⁴, F. Babic¹, Z. Dorosulic¹, D. Hrabar^{1,5}, A. Biscanin^{5,1}, D. Kralj¹

¹University Hospital Center Sestre milosrdnice, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ²Children's Hospital Zagreb, Referral Center for Pediatric Gastroenterology, Hepatology and Nutrition, Zagreb, Croatia, ³University Clinical Centre of Vojvodina, Department of Gastroenterology and Hepatology, Novi Sad, Serbia, ⁴General Hospital Karlovac, Karlovac, Croatia, ⁵University of Zagreb, School of Medicine, Zagreb, Croatia

Contact E-Mail Address: petra.cacic@gmail.com

Introduction: Intestinal ultrasound (IUS), a non-invasive, point-of-care method, is increasingly emerging as a cornerstone technique for the diagnosis and follow-up of patients with inflammatory bowel disease (IBD). The importance of IUS is even more evident in Crohn's disease (CD) patients where activity of disease doesn't frequently correlate with the symptoms. One of the key assessment parameters in intestinal ultrasound is the Colour Doppler signal (CDS), semiquantified according to the Limberg score (LS).

Although, simple and user friendly, its reliability and reproducibility in CD are not well established. Therefore, we aimed to assess the inter-rater agreement among IUS experienced (E) and IUS non-experienced (NE) group of physicians.

Aims & Methods: The inter-rater agreement among 8 physicians (3 experienced, each with more than 300 procedures, and 5 non-experienced, each with up to 50 procedures) from 3 different IBD centers was assessed. They independently scored 317 de-identified CDS IUS images, including both colon and small intestine views in transverse and longitudinal perspectives, using non-modified LS. All images were recorded using GE Logiq s8 linear probe. CDS was optimized for slow flow with a maximum velocity scale of 5-7 cm/s. Initially, the scale was increased to its maximum, then gradually decreased until noise dissipated. LS was treated as an ordinal variable and Kendall coefficient of concordance was calculated. Additionally Cohen's kappa was used in order to assess agreement between normal (LS 0 and 1) and pathological findings (LS>1).

Results: The test database comprised 36.3% (115) transverse view images and 63.7% (202) longitudinal view images. Overall inter-rater agreement was $W = .73$, $p < .01$, with higher concordance among E group $W = .85$, $p < .01$ compared to NE group $W = .73$, $p < .01$. No difference in inter-rater agreement was found among the three most experienced physicians, regardless of the view modality (transverse vs longitudinal view), $W = .85$, $p < .01$ for both categories. Agreement for the binary outcome (normal vs pathological finding) among most experienced physician was substantial $\kappa = .74$.

Conclusion: Our results showed that assessment of colour doppler signaling in CD patients is reliable even between physicians of varying experience, regardless of probe perspective. Further analyses on cine-loops are warranted.

Disclosure: Nothing to disclose.

PP0542

LONG-TERM, REAL-WORLD TREATMENT PERSISTENCE, MUCOSAL HEALING AND CORTICOSTEROID-FREE CLINICAL REMISSION RATES WITH VEDOLIZUMAB IN PATIENTS WITH ULCERATIVE COLITIS: SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

M. Chaparro¹, A. Armuzzi^{2,3}, P. Biedermann⁴, M. Meyer⁵, E. Robertshaw⁶, C. Shaw⁶, S. Schreiber⁷, S. Vermeire⁸

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid, and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Gastroenterology, Madrid, Spain, ²IBD Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy, ³Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Milan, Italy, ⁴Takeda Pharmaceuticals International AG, Zurich, Switzerland, ⁵Takeda Pharma AG, Zurich, Switzerland, ⁶Putnam Associates, Newcastle upon Tyne, United Kingdom, ⁷Institute of Clinical Molecular Biology and Clinic for Internal Medicine, Kiel University, Kiel, Germany, ⁸University Hospital Leuven, Department of Gastroenterology and Hepatology, Leuven, Germany

Contact E-Mail Address: mariachs2005@gmail.com

Introduction: Vedolizumab (VDZ) is approved in Europe and the USA for the treatment of moderately to severely active ulcerative colitis (UC). Real-world evidence is needed to assess the effectiveness and benefit-risk profile of VDZ for UC outside clinical trial settings. A systematic literature review (SLR) and meta-analysis published in 2018 confirmed the real-world effectiveness and positive benefit-risk profile of VDZ treatment for up to 1 year in patients with inflammatory bowel disease.¹ Further real-world evidence is required to support the long-term (> 1 year) effectiveness of VDZ in patients with UC.

Aims & Methods: The aims of the current meta-analysis based on the SLR were to evaluate the rates of treatment persistence at 1 and at 2 years and of mucosal healing and corticosteroid-free clinical remission at 1 year (overall and stratified by biologic-naïve versus biologic-experienced patients). Literature searches identified studies published from 2014 to 2022. For the SLR overall, outcomes of interest included clinical remission, mucosal healing, treatment patterns (including treatment persistence) and safety. Data on adults with UC treated with vedolizumab in a real-world setting were extracted for meta-analysis if there were at least 2 studies for each timepoint and population. Weighted proportions and corresponding 95% confidence intervals (CIs) were calculated using the DerSimonian-Laird random-effects model to account for between-study heterogeneity.

Results: Data from 68 studies of 21 774 patients with UC had at least one outcome of interest for analysis. The mean age ranged from 34.0–53.0 years (16 studies), the mean disease duration ranged from 4.9–10.4 years (5 studies) and the mean partial Mayo score ranged from 4.1–6.1 (6 studies). In the 28 and 9 studies that assessed treatment persistence at 1 and at 2 years, the rates of treatment persistence were 72.4% (95% CI 68.7–75.8) and 64.2% (95% CI 55.3–72.2), respectively. Similar treatment persistence rates at 1 year were observed among biologic-naïve vs biologic-experienced patients, but at 2 years higher rates were observed for biologic-naïve patients vs overall (Table). The overall mucosal healing rate at 1 year (assessed in 29 studies) was 42.6% (95% CI 37.0–48.3), and similar rates were observed in biologic-naïve vs biologic-experienced patients (Table). The corticosteroid-free clinical remission rates at 1 year were 42.7% (95% CI 38.4–47.1; 22 studies) and at 2 years 43.4% (95% CI 27.9–60.2; 5 studies); higher rates were observed among biologic-naïve vs biologic-experienced patients at 1 year (Table).

	Overall		Biologic-naïve		Biologic-experienced	
	Patients ^a (studies)	Rate, % (95% CI) ^b	Patients ^a (studies)	Rate, % (95% CI) ^b	Patients ^a (studies)	Rate, % (95% CI) ^b
1-year VDZ treatment persistence	5642 (28)	72.4 (68.7–75.8)	1666 (7)	74.5 (66.8–80.9)	1368 (5)	73.1 (62.4–81.6)
2-year VDZ treatment persistence	1735 (9)	64.2 (55.3–72.2)	449 (2)	77.6 (70.8–83.2)	— ^c	— ^c
1-year mucosal healing	1851 (29)	42.6 (37.0–48.3)	376 (3)	45.7 (31.4–60.7)	316 (5)	40.9 (30.9–51.8)
1-year corticosteroid-free clinical remission ^d	2797 (22)	42.7 (38.4–47.1)	465 (7)	45.5 (37.9–53.3)	580 (8)	36.6 (30.3–43.5)

^aNumber of patients assessed.

^bEvents per 100 patients.

^cNo meta-analysis because only one study reported this outcome.

^dResolution of symptoms or clinical measures of disease activity without the use of corticosteroids.

Table.

Conclusion: This meta-analysis of real-world studies of VDZ demonstrated high rates of long-term treatment persistence, mucosal healing and corticosteroid-free clinical remission in patients with UC, indicating effective disease management for these outcomes. However, the assessment of mucosal healing rates may not have been systematically conducted across all studies.

This study was funded by Takeda Pharmaceuticals International AG, Zurich, Switzerland.

Writing assistance provided by E Sugrue, PhD, of Oxford PharmaGenesis.

References: Schreiber S et al. *J Gastroenterol.* 2018;53:1048–64.

Disclosure: MC has served as a speaker or consultant, or has received funding for research or education, from AbbVie, Biogen, Dr Falk Pharma, Eli Lilly, Ferring, Gilead, Hospira, Janssen, MSD, Pfizer, Shire Pharmaceuticals, Takeda and Tillotts Pharma.

AA has received advisory board/lecture fees from AbbVie, Amgen, Arena, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr Falk Pharma, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, Lion Health, MSD, Nestlé, Novartis, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda, Teva Pharmaceuticals and Tillotts Pharma.

PB is an employee and stockholder of Takeda Pharmaceuticals International AG, Zurich, Switzerland.

MM is an employee and stockholder of Takeda Pharma AG, Zurich, Switzerland.

ER is an employee of Putnam Associates, which received funding for this study from Takeda Pharmaceuticals International AG, Zurich, Switzerland. CS is an employee of Putnam Associates, which received funding for this study from Takeda Pharmaceuticals International AG, Zurich, Switzerland. SS has received personal fees from AbbVie, Amgen, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr Falk Pharma, Fresenius, Galapagos/Gilead, Hikma, I-Mab, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, ProventionBio, Takeda, Theravance Biopharma and Ventyx. SV has received financial support for research from AbbVie, Galapagos, J&J, Pfizer and Takeda, and speakers' and/or consultancy fees from AbbVie, Abolera, AboleraSPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Cytokine Pharma, Dr Falk Pharma, Eli Lilly, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma AG, VectivBio, Ventyx and Zealand Pharma.

PP0543

CRP/ALBUMIN RATIO: A NEW PREDICTOR OF DISEASE COURSE IN ACUTE SEVERE ULCERATIVE COLITIS

W. Khemiri¹, N. Ben Mustapha¹, N. Ben Safta¹, S. Laabidi¹, D. Gouiaa¹, M. Serghini¹, A. Labidy¹, M. Fekih¹

¹La Rabta Hospital, Gastroenterology "A", Tunis, Tunisia

Contact E-Mail Address: Khemiri.wafa00@gmail.com

Introduction: Acute Severe ulcerative colitis (ASUC) is a life-threatening medical emergency of colonic inflammatory bowel disease (IBD). Corticosteroids remain the primary initial therapy, although one-third of patients do not respond to treatment. In this perspective, early identification of steroid non-responsive ASUC patients is the key to an effective management and thus, a better prognosis.

Aims & Methods: The aim of our study was to evaluate the impact of CRP/albumin ratio measured on day 3 on treatment outcomes and disease course in ASUC. We conducted a retrospective descriptive study including patients who presented with ASUC over a 10-year period [January 2010 - December 2019]. The diagnosis of ASUC was established on Truelove and Witts criteria and supported by endoscopic findings. Patients demographics were collected; C-reactive protein (CRP) and albumin levels were recorded at baseline and during admission. Data were entered and analyzed by SPSS software version 26.

Results: We included 54 patients with a sex ratio of M/F=0.71. The mean age at diagnosis of IBD was 41.48 years [12-58]. A family history of IBD was noted in 13% of the patients. Twenty-seven patients had Ulcerative Colitis and 27 patients had Crohn's disease. ASUC was inaugural of the disease in 35% of the patients. For the diagnosis of ASUC, the median number of bloody stools was 7 and the mean CRP level was 91 mg/L. At day 3 of first-line treatment with corticosteroids, the median number of bloody stools was 1 and the mean CRP level was 49 mg/L. First-line treatment failure was noted in 40% (n=20) of the patients with a mean duration of 8 days [3-20]. The mean level of the CRP/albumin ratio on day 3 was 1.8 [0.8-2.9]. Area under the receiver operating characteristic curve analysis showed that this ratio measured on day 3 was highly predictive of steroid non-responsiveness (AUROC=0.69, p=0.02). The optimal cutoff value was 1.6 (sensitivity, 80%; specificity, 57%). There was no significant linear association (Spearman r=-0.11, p=0.64) between this ratio and the timeframe of corticosteroids failure. A significant association was noted between this ratio and the urge to a rescue medical therapy (p=0.015) without being predictive of response (p=0.327). If on day 3, the ratio was higher than 1.6 and bloody stool frequency was beyond 3, the relative risk of steroid non-response was significantly raised at 3.85 (p<0.001) versus 1.7 if only a ratio above 1.6 was considered. As for longer prognosis, this ratio was higher in patients who underwent colectomy within a year of ASUC, without a significant association (n=13, p=0.07), and no correlation was noted with ASUC recurrence (p=0.23).

Conclusion: Our study showed that CRP/albumin ratio on day 3 is not only an effective predictor of non-response to steroids in ASUC, but also predicts the disease course beyond this severe flare-up.

Disclosure: Nothing to disclose.

PP0544

THE INCIDENCE OF ACTIVE TUBERCULOSIS AND IMPACT OF PROPHYLACTIC TREATMENT AMONG PATIENTS WITH LATENT TUBERCULOSIS, IN THE PHASE 3 ELEVATE UC 52 AND ELEVATE UC 12 TRIALS

N.SF Queiroz¹, S. Dighe², D. Branquinho³, J. Wu⁴, M. Keating³, A. McDonnell⁵, K. Lazin⁶, G. Solano⁷, S. Danese⁸
¹Santa Cruz Hospital, IBD Center, Curitiba, Brazil,
²Pfizer Ltd, Mumbai, India, ³Pfizer Inc, New York, NY, United States of America, ⁴Pfizer Inc, Cambridge, MA, United States of America, ⁵Pfizer Ltd, Sandwich, United Kingdom,
⁶Pfizer AG, Zürich, Switzerland, ⁷Pfizer Inc, San José, Costa Rica,
⁸IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Division of Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: sdanese@hotmail.com

Introduction: Tuberculosis (TB) is a prevalent disease, especially in developing countries.¹ The TB medication isoniazid (INH) has known hepatotoxic and drug-drug interaction (DDI) potential.²

With the increasing prevalence of ulcerative colitis (UC) in newly industrialised countries,³ more patients (pts) are expected to take UC medications concomitantly with INH.

Therefore, the likelihood of DDIs is an important UC treatment consideration. Etrasimod is an oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active UC.

Aims & Methods: This post hoc analysis aimed to evaluate the incidence of active TB in pts receiving etrasimod 2 mg QD or placebo and the impact of concomitant INH on safety outcomes in pts receiving etrasimod 2 mg QD. This analysis pooled data (≤52 weeks) from phase 3 trials, ELEVATE UC 52 (NCT03945188) and ELEVATE UC 12 (NCT03996369). Pts with latent TB infection (LTI; at enrolment or historically) who received/were receiving adequate treatment were allowed to enrol in both studies. We report the incidence of active TB in pts receiving etrasimod 2 mg QD or placebo and in those with an LTI history.

We also report liver enzyme elevations (irrespective of treatment-emergent adverse event [TEAE] classification) in pts taking concomitant etrasimod + INH. Data are summarised descriptively.

Results: Of the 527 and 260 pts receiving etrasimod and placebo, respectively, 17 (3.2%) and 3 (1.2%) had history of LTI. No pts receiving etrasimod experienced active TB and one event of active TB was reported in a pt receiving placebo (without history of LTI).

Overall, 9/20 pts with history of LTI were taking etrasimod + INH per protocol. Most of these pts were White (7/9) and originated from Georgia (2/9), India (2/9), Poland (2/9), Romania (2/9) and South Africa (1/9).

No liver-associated TEAEs were reported during etrasimod + INH use.

One pt had elevated alanine transaminase (ALT; >1 to ≤2 × upper limit of normal [ULN]), aspartate transaminase (AST; >1 to ≤2 × ULN) and γ-glutamyl transferase (GGT; events of >1 to ≤2 and >2 to ≤3 × ULN) while receiving etrasimod + INH concomitantly (Table).

Additionally, post-baseline, two pts had transiently elevated ALT and AST (all >1 to ≤2 × ULN), and two pts had transiently elevated GGT (>1 to ≤2 × ULN) while receiving etrasimod + INH concomitantly (Table).

These were not considered by the investigator to be TEAEs. None of these pts with liver enzyme elevations discontinued treatment or met drug-induced liver injury criteria; all pts continued etrasimod in the open-label extension study (NCT03950232).

The incidence of elevated liver enzymes was generally similar in those receiving etrasimod + INH vs the overall ELEVATE UC cohort.

Pts, n	Pts receiving etrasimod 2 mg QD (N=527)
With a history of LTI	17
With active TB	0
Liver enzyme elevations recorded any time post-baseline, n	Pts receiving concomitant etrasimod 2 mg QD + INH (N=9)
ALT >1 to ≤2 × ULN	3 ^a
ALT >2 × ULN	0
AST >1 to ≤2 × ULN	3 ^a
AST >2 × ULN	0
GGT >1 to ≤2 × ULN	3 ^b
GGT >2 to ≤3 × ULN	1 ^b
GGT >3 × ULN	0

aOne pt receiving etrasimod 2 mg QD was excluded in the count as elevated AST and ALT were experienced after the discontinuation of concomitant etrasimod + INH.

bOne pt had elevation of GGT >1 to ≤2 × ULN and GGT >2 to ≤3 × ULN.

ALT, alanine transaminase; AST, aspartate transaminase; GGT, γ-glutamyl transferase; INH, isoniazid; LTI, latent tuberculosis; n, number of patients with event; N, number of patients in analysis set; pt, patient; QD, once daily; TB, tuberculosis; TEAE, treatment-emergent adverse event; UC, ulcerative colitis; ULN, upper limit of normal.

Table. Incidence of active TB in pts with a history of LTI receiving etrasimod and the proportion of pts receiving etrasimod with liver enzyme elevations (irrespective of TEAE classification) in ELEVATE UC 52 and ELEVATE UC 12 (pooled).

Conclusion: No pts receiving etrasimod experienced active TB, regardless of LTI history, and in the limited population of pts receiving etrasimod + INH, there was no increased risk of liver injury or abnormal liver function.

References:

1. Glaziov P et al. Cold Spring Harb Perspect Med 2014; 5: a017798.
2. FDA. Isoniazid tablets, USP. 2016. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/008678s028lbl.pdf. Accessed January 2024.
3. Desai D et al. Indian J Gastroenterol 2023; 43(1):15-17.

Disclosure: NSFQ is an advisory/committee board and speakers bureau member for Janssen, Takeda and Pfizer. SD is an employee of Pfizer Ltd. DB, JW, MK and GS are employees and shareholders of Pfizer Inc. AM is an employee of Pfizer Ltd and shareholder of Pfizer Inc. KL is an employee of Pfizer AG and shareholder of Pfizer Inc. SD has received lecture/ speaker fees from AbbVie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer and Takeda; consultancy/advisory fees from AbbVie, Allergan, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Gilead Sciences, Hospira, Janssen, Johnson & Johnson, MSD, Mundipharma, Pfizer Inc, Roche, Sandoz, Takeda, TiGenix, UCB, and Vifor; and has directorship/ownership of Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele.

PP0545

TO WHAT EXTENT ARE PHYSICIANS CYCLING THROUGH MORE THAN ONE TNFI (TUMOR NECROSIS FACTOR INHIBITOR) IN ULCERATIVE COLITIS (UC) TREATMENT?

J. Godfrey¹, S. Brown^{1,1}, H. Parfitt¹, C. O’Kane¹, L. Wen¹, R. Spencer¹, J. Singh Mann¹

¹Research Partnership, London, United Kingdom

Contact E-Mail Address: sarah.brown@researchpartnership.com

Introduction: With the wider availability of non-TNFi treatments in Ulcerative Colitis (UC), the long-established treatment approach to cycle through two TNFi treatments (such as adalimumab and infliximab) is changing.

Aims & Methods: Objectives: The purpose of this study was to evaluate to what extent TNFi cycling is occurring in the EU5 management of UC, and how this has changed over the last 3 years. More specifically, the data is used to demonstrate which types of patients are likely to cycle through 2 TNFi products, and which are likely to be prescribed a non TNFi after one TNFi treatment choice.

Methodology: In Q3 of 2023, 205 gastroenterologists from France, Italy, Germany, Spain, and the UK contributed 1430 anonymous patient record forms for individuals receiving advanced therapy for UC. All the forms were collected through the Therapy Watch IBD (UC and Crohn’s) survey by Research Partnership. The survey has been conducted with similar numbers of gastroenterologists for 3 years at regular intervals. Informed consent from physicians was obtained. Where relevant, statistical comparisons were performed using a pairwise z-test.

Results: UC patients who require an advanced treatment (biologic or JAKi) are most likely to be prescribed a TNFi first-line. From our Q3 23 data, 81% of EU5 UC patients received a TNFi (most commonly adalimumab or infliximab) as first-line. The integrin blocker vedolizumab, IL12/23 inhibitors (such as ustekinumab) and JAK inhibitors are more likely to be prescribed at 2nd or 3rd+ line; at 2nd line, TNFi were prescribed to 37% of patients.

In Q3 23, of the 485 UC patients who were currently on their 2nd line of advanced treatment, 32% had a TNFi in both 1st and 2nd line (i.e. cycling TNFi) and 59% had a TNFi in 1st line and a non TNFi in their 2nd line of treatment. In Q1 21, 41% were cycling TNFi, and 50% were not. This represents a statistically significant reduction in TNFi cycling between Q1 21 and Q3 23 (p<0.05).

Certain patient characteristics are more prevalent amongst patients who switch to a non TNFi at 2nd line, compared with those who cycle to a second TNFi, as follows (all represent a statistically significant difference, p<0.05):

- More likely to be younger (51% under 40, compared with 41% among TNFi cyclers)
- Less likely to have any comorbidities (44% no comorbidities, compared with 27% among TNFi cyclers)
- More likely to have blood in stool and bowel incontinence (45% compared with 20% among TNFi cyclers)
- More likely to have an increasing rate of UC flares (29% compared with 15% among TNFi cyclers).

Conclusion: Our findings confirm that there has been a statistically significant reduction in TNFi cycling over the past 3 years, with an increase in the proportion of UC patients who are prescribed a non TNFi in 2nd line. TNFis remain the main 1st line advanced treatment choice for UC.

At this point, our data suggests that physicians are making decisions between TNFi cycling and switching directly to a non-TNFi, based on certain patient characteristics or disease status.

References: Data from Therapy Watch IBD survey (UC and Crohn’s) conducted by Research Partnership.

Disclosure: Nothing to disclose.

PP0546

EFFECTIVENESS OF USTEKINUMAB FOR PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: A MULTI-CENTER REAL-WORLD CANADIAN STUDY (IMPACT STUDY)

V. Solitano^{1,2}, N. Narula³, T. Bessissow⁴, A. Nanayakkara⁵, K.E. Suarez⁶, A. Zoughlami⁷, L. Guizzetti⁸, C. Ma⁹, V. Jairath²
¹Università Vita-Salute San Raffaele, Gastroenterology, Milan, Italy, ²Western University, Division of Gastroenterology, Department of Medicine, London, Canada, ³McMaster University, Medicine, Hamilton, Canada, ⁴McGill University Health Center, Dept. of Gastroenterology, Montreal, Canada, ⁵McMaster University, Department of Medicine, Division of Gastroenterology, Farncombe Family Digestive Health Research Institute, Hamilton, Canada, ⁶University of Calgary, Division of Gastroenterology and Hepatology, Cumming School of Medicine, Calgary, Canada, ⁷McGill University Health Center, Division of Gastroenterology, Department of Medicine, Montreal, Canada, ⁸Independent Researcher, London, Canada, ⁹University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada

Contact E-Mail Address: virginiasolitano@gmail.com

Introduction: We aimed to evaluate the real-world effectiveness and safety of ustekinumab for the treatment of both bio-naïve and bio-exposed ulcerative colitis (UC) patients in a real-world setting.

Aims & Methods: Retrospective, Canadian multicenter cohort study. Standardized data collection was performed on consecutive adult UC outpatients treated with ustekinumab in 4 large IBD centers. The primary outcomes were clinical remission and endoscopic remission. Key secondary outcomes included composite clinical and endoscopic response, safety, and persistence. A multivariable Cox proportional hazards model was used to explore associations between baseline factors and endpoints. For multivariable model selection, backwards elimination was used with a threshold $P < 0.05$.

Results: A total of 198 patients were included, of whom 47.5% were female and 85.9% under 65 years. The majority had severe endoscopic activity at baseline (47.5%, $n=87$) and were bio-exposed (88.8%, $n=176$; 33%, $n=66$ prior failure of 3 or more biologics. Patients were followed for a median of 12.8 (IQR 8.2 to 22.1) months after induction. Clinical remission rates were 43.7% (69/198), 43.8% (56/128), and 62.4% (58/93) at 3, 6 and 12 months respectively. Endoscopic remission rates were 11.3% (7/62), 24.7% (23/93), and 23.4% (11/43) at 3, 6 and 12 months respectively. Bio-naïve patients were more likely to achieve clinical and endoscopic remission compared to bio-exposed (HR=1.71, 95% CI: 1.02–2.88, and HR=7.33, 95% CI: 2.15–25.01, respectively). Adverse events were reported in 14.1% (18/198), with colectomies exclusively observed in bio-exposed individuals (8.6%; 17/198).

Conclusion: In a highly refractory and largely bio exposed population more than half of patients with UC treated with ustekinumab achieved clinical remission and one-third achieved endoscopic remission. Prior biologic exposure was independently associated with clinical and endoscopic remission. Safety profile was consistent with interleukin (IL)-12-23 blockade.

Disclosure: VS, AN, KES, AZ, LG have no conflict of interest

NN has been a speaker or advisor for Janssen, Abbvie, Takeda, Pfizer, Merck, Sandoz, Fresenius Kabi, Innomar, Iterative Scopes, Bristol Myers Squibb, Viatris and Ferring

TB has received consulting or speaker fees for Abbvie, Alimentiv, Amgen, Bristol Myers Squibb, Ferring, Janssen, Merck, Pfizer, Roche, Sandoz, Takeda, Gilead, Viatris, Fresenius, Kabi

CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius

Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Ferring, Janssen, Takeda, and Pfizer; research support from Ferring, Pfizer VJ consulting/advisory board fees from AbbVie, Alimentiv Inc, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, SCOPE, Second Genome, Sorriso, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; speaker's fees from, Abbvie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi.

PP0547

EFFICACY AND SAFETY OF ETASIMOD IN PATIENTS WITH ULCERATIVE COLITIS STRATIFIED BY BODY MASS INDEX: A POST HOC ANALYSIS FROM THE ELEVATE UC CLINICAL PROGRAMME

A.J Yarur¹, M. Long², J. Torres^{3,4,5}, N. Nandi⁶, R. Cross⁷, A.M. Abbateamarco⁸, D. Blanco⁹, W. Niezychowski⁹, C.M Crosby¹⁰, J. Wu¹¹, G. Pradeep¹², M. Goetsch¹³, R. Panaccione¹⁴
¹Cedars-Sinai Medical Center, Inflammatory Bowel Disease Center and Division of Gastroenterology and Hepatology, Los Angeles, United States of America, ²University of North Carolina, Center for Gastrointestinal Biology and Disease, Chapel Hill, United States of America, ³Hospital Beatriz Ângelo, Division of Gastroenterology, Loures, Portugal, ⁴Hospital da Luz, Division of Gastroenterology, Lisbon, Portugal, ⁵Universidade de Lisboa, Faculdade de Medicina, Lisbon, Portugal, ⁶Penn Presbyterian Medical Center, University of Pennsylvania, Division of Gastroenterology and Hepatology, Philadelphia, United States of America, ⁷University of Maryland School of Medicine, Division of Gastroenterology and Hepatology, Baltimore, United States of America, ⁸Pfizer Inc, New York, United States of America, ⁹Pfizer Inc, Collegeville, United States of America, ¹⁰Pfizer Inc, La Jolla, United States of America, ¹¹Pfizer Inc, Cambridge, United States of America, ¹²Pfizer Healthcare India Private Ltd, Chennai, India, ¹³Pfizer AG, Zürich, Switzerland, ¹⁴University of Calgary, Division of Gastroenterology and Hepatology, Department of Medicine, Calgary, Canada

Contact E-Mail Address: joanatorres00@gmail.com

Introduction: A high body mass index (BMI) may negatively impact treatment efficacy in patients with ulcerative colitis (UC) treated with advanced therapies, such as biologics,¹ which is relevant due to the prevalence of obesity and UC increasing substantially over the past decades.^{2,3} Etrasimod is an oral, once-daily (QD), selective sphingosine 1-phosphate (S1P)_{1,4,5} receptor modulator for the treatment of moderately to severely active UC.

Aims & Methods: This post hoc analysis of ELEVATE UC 52 and ELEVATE UC 12 investigated the impact of BMI on the efficacy and safety of etrasimod in patients with UC. ELEVATE UC 52 (NCT03945188) and ELEVATE UC 12 (NCT03996369) were phase 3, randomised, placebo-controlled trials.⁴ ELEVATE UC 52 had a treat-through design consisting of a 12-week (wk) induction and 40-wk maintenance period; ELEVATE UC 12 comprised a 12-wk induction period. Patients who received ≥ 1 dose of etrasimod 2 mg QD or placebo were stratified by baseline BMI: <25 kg/m², 25–30 kg/m² and >30 kg/m². Efficacy outcomes (aligned to the predefined outcomes for the ELEVATE UC 52 and ELEVATE UC 12 trials) included the primary endpoint (clinical remission) and selected secondary endpoints at Wk 12

(data pooled for both trials) and Wk 52 (ELEVATE UC 52 only). Safety outcomes assessed the proportions of treatment-emergent adverse events (TEAEs).

Results: Of the 787 patients enrolled in the ELEVATE UC clinical programme, 443 (56.3%) had baseline BMI <25 kg/m², 217 (27.6%) had baseline BMI 25–30 kg/m² and 127 (16.1%) had baseline BMI >30 kg/m². In the BMI <25 kg/m² and BMI 25–30 kg/m² subgroups, significantly more patients (*p*<0.05) receiving etrasimod vs placebo achieved all efficacy endpoints at Wks 12 and 52. In the BMI >30 kg/m² subgroup, significantly more patients receiving etrasimod vs placebo achieved clinical remission at Wk 52 (*p*<0.0001; Wk 12: *p*=0.05), endoscopic improvement and clinical response at Wks 12 and 52, and corticosteroid-free clinical remission at Wk 52 (all *p*<0.05; *Table*). The proportions of patients with the most common TEAEs were generally consistent between BMI subgroups receiving etrasimod. Incidence of serious AEs was generally similar across BMI subgroups receiving etrasimod (<25 kg/m²: 17/308 [5.5%]; 25–30 kg/m²: 8/137 [5.8%]; >30 kg/m²: 1/82 [1.2%]).

	BMI <25 kg/m ²			BMI 25–30 kg/m ²			BMI >30 kg/m ²		
	Placebo QD	Etrasimod 2 mg QD	% Difference (95% CI)	Placebo QD	Etrasimod 2 mg QD	% Difference (95% CI)	Placebo QD	Etrasimod 2 mg QD	% Difference (95% CI)
Clinical remission, ^b Wk 12, n (%)	18 (13.3)	86 (27.9)	15.0 (7.4, 22.7)***	8 (10.0)	39 (28.5)	18.6 (8.2, 29.0)***	3 (6.7)	18 (22.0)	12.7 (0.0, 25.4)
Clinical remission, ^b Wk 52, n (%)	7 (10.0)	48 (30.8)	22.7 (12.6, 32.9)***	3 (6.3)	27 (33.3)	26.3 (13.7, 38.9)***	1 (3.9)	19 (36.5)	33.3 (17.3, 49.4)***
Endoscopic improvement, ^c Wk 12, n (%)	28 (20.7)	111 (36.0)	15.2 (6.7, 23.8)***	14 (17.5)	49 (35.8)	18.5 (6.8, 30.1)***	4 (8.9)	26 (31.7)	19.7 (6.0, 33.5)***
Endoscopic improvement, ^c Wk 52, n (%)	11 (15.7)	56 (35.9)	23.2 (12.3, 34.0)***	6 (12.5)	32 (39.5)	25.4 (11.2, 39.6)***	2 (7.7)	25 (48.1)	43.2 (25.5, 60.8)***
Clinical response, ^d Wk 12, n (%)	55 (40.7)	195 (63.3)	22.2 (12.3, 32.1)***	28 (35.0)	88 (64.2)	28.5 (15.2, 41.9)***	17 (37.8)	50 (61.0)	25.4 (7.3, 43.6)***
Clinical response, ^d Wk 52, n (%)	15 (21.4)	72 (46.2)	26.8 (14.6, 38.9)***	13 (27.1)	44 (54.3)	26.4 (10.1, 42.8)***	7 (26.9)	27 (51.9)	24.7 (1.9, 47.5)***
CS-free clinical remission* with CS use at baseline, Wk 52, n/N1 (%)	3/24 (12.5)	19/64 (29.7)	19.9 (2.1, 37.6)	0/9 (0.0)	7/18 (38.9)	40.5 (16.6, 64.4)***	0/9 (0.0)	3/11 (27.3)	38.8 (4.8, 72.9)

****p*<0.001; ***p*<0.01; **p*<0.05.
 Population size assessed for each subgroup and time point were: BMI <25 kg/m²: placebo QD, N=135 (Wk 12) and N=70 (Wk 52) and etrasimod 2 mg QD, N=308 (Wk 12) and N=156 (Wk 52); BMI 25–30 kg/m²: placebo QD, N=80 (Wk 12) and N=48 (Wk 52) and etrasimod 2 mg QD, N=137 (Wk 12) and N=81 (Wk 52); BMI >30 kg/m²: placebo QD, N=45 (Wk 12) and N=26 (Wk 52) and etrasimod 2 mg QD, N=82 (Wk 12) and N=52 (Wk 52). Difference (95% CI) and 2-sided *p* value are based on the Cochran-Mantel-Haenszel method adjusting to reported randomisation stratification of (1) naïve to biologic or Janus kinase inhibitor therapy at study entry, (2) baseline CS use (yes or no), (3) baseline disease activity (MMS: 4–6 or 7–9) and (4) study identifier (ELEVATE UC 52 and ELEVATE UC 12).
 *Data were pooled at Wk 12 for both trials (ELEVATE UC 52 and ELEVATE UC 12); Wk 52 is ELEVATE UC 52 only.
^bClinical remission was defined as SFS=0 (or =1 with a ≥1-point decrease from baseline), RBS=0 and ES ≤1 (excluding friability).
^cEndoscopic improvement was defined as ES ≤1.
^dClinical response was defined as a ≥2-point and ≥30% decrease from baseline in MMS, and a ≥1-point decrease from baseline in RBS or an absolute RBS ≤1.
 *CS-free clinical remission was defined as the proportion of patients with clinical remission at Wk 52 who had been receiving CS at baseline but had not been receiving CS for ≥12 wks immediately prior to Wk 52.
 BMI, body mass index; CI, confidence interval; CS, corticosteroid; ES, endoscopic subscore; MMS, Modified Mayo score; n, number of patients; N, number of patients in the subgroup; N1, number of subjects in each baseline BMI subgroup category; QD, once daily; RBS, rectal bleeding subscore; SFS, stool frequency subscore; UC, ulcerative colitis.

Table. Primary and select secondary efficacy endpoints at Wk 12 in ELEVATE UC 52 and ELEVATE UC 12 (pooled)^a and Wk 52 in ELEVATE UC 52, stratified by baseline BMI.

Conclusion: In the ELEVATE UC clinical programme, significant improvements in efficacy were observed for patients receiving etrasimod 2 mg QD vs placebo, regardless of baseline BMI. The safety profile of etrasimod was consistent between BMI subgroups and with the overall ELEVATE UC population.

References: 1. Kurnool S et al. *Aliment Pharmacol Ther* 2018; 47: 1472–1479.
 2. Molodecky NA et al. *Gastroenterology* 2012; 142: 46–54 e42; quiz e30.
 3. Ng M et al. *Lancet* 2014; 384: 766–781.
 4. Sandborn WJ et al. *J Crohns Colitis* 2023; 17: 338–351.

Disclosure: AJY has received consultancy fees from AbbVie, Pfizer Inc, Arena, Takeda and Bristol Myers Squibb; and lecture/speaker fees from Bristol Myers Squibb. MDL is a consultant for AbbVie, Janssen, Pfizer Inc, Takeda, Bristol Myers Squibb, Target PharmaSolutions, Prometheus, Lilly, Salix, Valeant, Genentech, Roche, Calibr and Theravance; and has received research support from Pfizer Inc and Takeda. JT has received advisory board fees from AbbVie, Arena, Bristol Myers Squibb, Galapagos, Janssen and Pfizer Inc; research grants from AbbVie and Janssen; and speaker fees from AbbVie, Galapagos, Janssen and Pfizer Inc. NN is a consultant and advisory board member for AbbVie, Bristol Myers Squibb, Janssen, Lilly and Pfizer Inc; and has received research support from Ferring, Janssen, Pfizer Inc and Seres. RKC has received consultancy and advisory board fees from AbbVie, Adiso, Bristol Myers Squibb, CorEvitas, Fresenius Kabi, Fzata, IBD Education Group, Janssen, Magellan Health, Option Care, Pfizer Inc, Sandoz, Samsung Bioepis, Sebela and Takeda; and research grant/support from Janssen. AMA is an employee and shareholder of Pfizer Inc. DB and WN are employees of Pfizer Inc. CMC and JW are employees and shareholders of Pfizer Inc. GP is an employee of Pfizer Healthcare India Private Ltd. MG is an employee and shareholder of Pfizer AG. RP is a consultant for Abbott, AbbVie, Abbvax, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Lilly, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda, Theravance Biopharma, Trellus, Viatrix, Ventyx and UCB; has received speaker fees for AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Lilly, Merck, Organon, Pfizer, Roche, Sandoz, Shire and Takeda; is an advisory board member for AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Lilly, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda and Ventyx; and has received research support from AbbVie, Janssen, Takeda and Pfizer.

UNDERSTANDING GASTROENTEROLOGIST PREFERENCES AT THE TIME OF TREATMENT ESCALATION TO FIRST-LINE ADVANCED THERAPIES IN ULCERATIVE COLITIS: A DISCREET CHOICE EXPERIMENT IN FIVE EUROPEAN COUNTRIES

S. Schreiber¹, A. Walsh², P. Hur³, L. Panattoni⁴, B. Hauber³, G. Gahlon⁴, J. Coulter³, K. Wosik¹¹, J.C Cappelleri⁵, N. Prood⁴, X. Guo⁹, A. Buisson^{6,7}

¹University Hospital Schleswig-Holstein, Kiel University, Department of Internal Medicine I, Kiel, Germany, ²Oxford University Hospital, Translational Gastroenterology Unit, Oxford, United Kingdom, ³Pfizer Inc, New York, United States of America, ⁴PRECISIONheor, New York, United States of America, ⁵Pfizer Canada, Kirkland, Canada, ⁶Pfizer Inc, Groton, United States of America, ⁷Pfizer Inc, Collegeville, United States of America, ⁸University Hospital Estaing, Clermont-Ferrand, France, ⁹Clermont Auvergne University, Inserm U1071, M2iSH, USC-INRA 2018, F-63000 Clermont-Ferrand, France

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: As the number of advanced treatment options for moderately to severely active ulcerative colitis (UC) increases, it is necessary to understand the factors driving gastroenterologist (GE) choice when escalating patients from conventional to advanced therapy.

Aims & Methods: We completed a quantitative analysis of GE therapy attribute preferences when choosing to escalate patients to their first advanced UC therapy. We conducted an online, cross-sectional survey using a discrete choice experiment (DCE) design.

Attribute and level selection was informed by a targeted literature search and formative qualitative research with patients and clinicians. Survey responders were practising GEs experienced in treating patients with moderately to severely active UC, recruited from France, Germany, Italy, Spain and the United Kingdom (UK).

Preference weights were estimated using a random parameters logit model for varying levels of seven attributes: time to symptom improvement, probability of remission at one year, difference between probability of remission and CS-free remission, five-year risk of malignancy, annual risk of serious infection, annual risk of major adverse cardiovascular events and mode and frequency of administration.

Relative importance (RI) was calculated using the difference in preference weights between the most and least preferred level of each attribute, scaled from 0 to 100%. An additional survey section was included to understand GE treatment and prescribing practices.

Results: A total of 397 GEs were included (France n = 140; Germany n = 40; Italy n = 40; Spain n = 47; UK n = 130). The most common GE-reported barriers to prescribing advanced therapies were concerns about contraindications and risks/side effects from patients (54.9%) and GEs (39.8%), perceived patient concerns about receiving injections or infusions (35.5%) and concerns about cost or insufficient reimbursement (32.2%). All DCE attributes factored into GE treatment decisions (see Table for RI and preference weights).

The three most impactful attributes were probability of remission at one year (RI 48.4%), followed by 5-year risk of malignancy (RI 11.4%) and time to symptom improvement (RI 11.1%; Table).

	Time to symptom improvement	Probability of remission at one year	Difference between probability of remission and CS-free remission	Five-year risk of malignancy	Annual risk of serious infection	Annual risk of MACE	Mode and frequency of administration
Attribute RI,* % (95% CI)*	11.1 (8.9, 13.4)	48.4 (45.7, 51.1)	8.0 (6.1, 10.0)	11.4 (9.5, 13.2)	6.7 (4.9, 8.5)	6.8 (5.0, 8.6)	7.5 (5.4, 10.1)
Preference weight level (95% CI)*							
Level 1	2 weeks 0.50 (0.31, 0.69)	20% probability -2.11 (-2.42, -1.81)	0% difference 0.27 (0.13, 0.41)	1/1000 patients 0.49 (0.35, 0.62)	1/100 patients 0.27 (0.14, 0.40)	1/1000 patients 0.27 (0.14, 0.40)	Oral pill 1-2 times daily with potential dose change 0.15 (-0.02, 0.33)
Level 2	4 weeks 0.22 (0.09, 0.34)	35% probability 0.26 (0.18, 0.34)	5% difference 0.12 (0.03, 0.21)	3/1000 patients -0.04 (-0.13, 0.05)	3/100 patients 0.02 (-0.07, 0.10)	3/1000 patients 0.01 (-0.08, 0.10)	Oral pill 1-2 times daily with the same dose throughout 0.23 (0.10, 0.35)
Level 3	8 weeks -0.31 (-0.44, -0.18)	45% probability 1.85 (1.65, 2.06)	15% difference -0.39 (-0.48, -0.29)	5/1000 patients -0.45 (-0.54, -0.35)	5/100 patients -0.28 (-0.38, -0.19)	5/1000 patients -0.28 (-0.38, -0.19)	Injection every 1-2 weeks 0.01 (-0.12, 0.14)
Level 4	12 weeks -0.41 (-0.55, -0.27)	N/A	N/A	N/A	N/A	N/A	Infusion every 4-8 weeks -0.39 (-0.52, -0.26)

The DCE model included seven attributes, each with several preference weight levels.
*RI is calculated as the difference in preference weights between the most preferred and least preferred level divided by the sum of the differences across all attributes; estimates sum to 100%.
*95% CIs that do not include zero indicate a statistically significant RI of an attribute. All seven attributes were statistically significantly important when selecting an advanced therapy. 95% CIs that do not overlap for pairs of attributes indicate a statistically significant difference in importance between attributes. Probability of remission at one year was statistically significantly more important than all other attributes.
*Preference weight levels are effects coded; zero indicates the mean effect across all attribute levels.

CI, confidence interval; CS, corticosteroid; DCE, discrete choice experiment; MACE, major adverse cardiovascular events; N, total number of patients; N/A, not applicable; RI, relative importance; UC, ulcerative colitis.

Table. Preference weights and RI of attributes influencing advanced UC therapy choice (N = 397).

Conclusion: All attributes factored into the trade-offs GEs consider when escalating patients with moderately to severely active UC to their first advanced therapy. Whereas risk of side effects was the most stated GE barrier to prescribing advanced therapy, probability of remission outweighed all other DCE attributes.

Disclosure: SS has received lecture/speaker fees from AbbVie, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Falk, Fresenius, Janssen, MSD, Pfizer Inc and Takeda; and consultancy/advisory fees from AbbVie, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Falk, Fresenius, Gilead Sciences, IMAB, Janssen, MSD, Mylan, Pfizer Inc, Protagonist, Provention Bio, Takeda, Theravance and Ventyx Biopharma. AW has received grant/research support from AbbVie, Pfizer, Lilly, Janssen, Buhlmann, BMS and Takeda. PH is an employee and shareholder of Pfizer Inc; shareholder of Liquidia, Idorsia, Clene Nanomedicine, Proctor Gamble, Longboard Pharmaceuticals and Haleon; and has IP/Patents for US 2022/0257594 A1. LP is an advisory/review panel member for ISPOR Planning Committee; a consultant, employee and shareholder of PrecisionAQ; and has received grant/research support from American Cancer Society, NIH, NCI, Fred Hutchinson Cancer Research Center, Microsoft, AHRQ, Gordon and Betty Moore Foundation. BH, JC, JCC and XG are employees and shareholders of Pfizer Inc. GG and NP are consultants for PRECISIONheor. KW is an employee and shareholder of Pfizer Canada Inc. AB has received lecture and consulting fees for AbbVie, Amgen, Arena, Biogen, Janssen, MSD, Mayo-ly-Spindler, Norgine, Pfizer, Roche, Takeda and Tillots.

IMPACT OF OZANIMOD ON TYPE IV COLLAGEN BIOMARKERS AND THE ASSOCIATION WITH OZANIMOD EFFICACY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 TRUE NORTH STUDY

G. D'Haens¹, R. Maddux², C. Wu², Y. Hu², B.E. Sands³,

J.H. Mortensen⁴, J. Zhang², A. Petersen², S. Harris²

¹Amsterdam University Medical Center, Amsterdam, Netherlands,

²Bristol Myers Squibb, Princeton, United States of America, ³Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁴Nordic Bioscience, Herlev, Denmark

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Ozanimod was efficacious and well tolerated for up to 52 weeks in patients with moderately to severely active ulcerative colitis (UC) in the phase 3 True North study (NCT02435992). Type IV collagen, a major component of the intestinal basement membrane, is thought to be involved in the pathogenesis of UC.

Aims & Methods: This analysis assessed the effect of ozanimod on type IV collagen biomarkers and their association with ozanimod efficacy in True North. Patients in Cohort 1 were randomized to ozanimod (n=429) or placebo (n=216) and patients in Cohort 2 received open-label ozanimod (n=367) through Week 10. Ozanimod patients with clinical response at Week 10 were rerandomized to ozanimod (ozanimod/ozanimod, n=230) or placebo (ozanimod/placebo, n=227) through Week 52; placebo patients with clinical response at Week 10 continued placebo through Week 52 (n=69). Levels of biomarkers for type IV collagen formation (type IV collagen propeptide [PRO-C4]), degradation (granzyme B-degraded [C4G] and matrix metalloproteinase-degraded [C4M] type IV collagen), and turnover (PRO-C4/C4M ratio) were assessed at baseline, Week 10, and Week 52. Baseline and Week 10 disease activity scores, including rectal bleeding, stool frequency, Physician Global Assessment (PGA), and endoscopy subscores, and partial and total Mayo scores, were correlated to biomarker levels. Associations between type IV collagen biomarkers and disease activity were assessed using Spearman's *rho* correlation.

	Induction (Week 10)			Maintenance (Week 52)	
	Placebo: Cohort 1	Ozanimod: Cohort 1	Ozanimod: Cohort 2	Ozanimod/ placebo	Ozanimod/ ozanimod
PRO-C4	0.07 (-2.40, 2.60) n=162	-3.38* (-5.05, -1.67) n=346	-2.06 (-3.82, -0.26) n=298	-2.46 (-5.13, 0.29) n=112	-6.71* (-8.91, -4.45) n=157
C4G	0.04 (-4.53, 4.84) n=151	-8.60** (-11.60, -5.50) n=315	-6.41* (-9.52, -3.20) n=282	-3.75 (-9.14, 1.96) n=103	-18.30*** (-22.12, -14.28) n=154
C4M	-1.37 (-5.24, 2.66) n=165	-10.53*** (-13.02, -7.96) n=346	-11.67*** (-14.22, -9.03) n=299	-16.85 (-20.57, -12.96) n=112	-20.40 (-23.50, -17.18) n=157
PRO-C4/ C4M	1.80 (-1.78, 5.50) n=162	8.02** (5.35, 10.76) n=346	10.71*** (7.86, 13.63) n=298	17.32 (12.72, 22.10) n=112	16.88 (12.90, 21.00) n=157

*P<0.05, **P<0.01, ***P<0.001 vs placebo: Cohort 1 for induction or ozanimod/placebo for maintenance.

Table. Adjusted mean percent change from baseline in type IV collagen biomarker levels (95% CI).

Results: At Week 10, significant decreases in PRO-C4, C4G, and C4M and significant increases in PRO-C4/C4M were seen with ozanimod vs placebo (Table). C4M decreases and PRO-C4/C4M increases with ozanimod at Week 10 were significantly greater in patients with vs without Week 10 clinical response. Baseline C4M was significantly positively correlated and PRO-C4/C4M was significantly negatively correlated with all baseline disease activity scores except rectal bleeding. In ozanimod-treated patients, changes in PRO-C4 and C4M at Week 10 were significantly positively correlated with changes in all disease activity scores at Week 10 except rectal bleeding and PGA for PRO-C4, while changes in C4G and PRO-C4/

C4M at Week 10 were significantly negatively correlated with changes in all disease activity scores at Week 10. Decreases in PRO-C4 and C4G continued through Week 52 and were significantly greater in ozanimod/ozanimod than ozanimod/placebo patients; decreases in C4M and increases in PRO-C4/C4M continued at Week 52 at similar levels in ozanimod/ozanimod and ozanimod/placebo patients (Table).

Conclusion: Ozanimod decreased type IV collagen degradation and increased turnover, which are effects associated with disease activity. The T-cell activity marker C4G showed the strongest, but delayed, decrease at Week 52, which is aligned with the mechanism of action of ozanimod. These findings support ozanimod involvement in modulating key molecules in intestinal epithelial barrier function, extracellular matrix remodeling, and T-cell activity in UC.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Anny Wu, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

GD: served as an advisor for AbbVie, Agomab, Alimentiv, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Cytoki, Eli Lilly, Exelium Biosciences, Galapagos, GlaxoSmithKline, Immunic, Johnson & Johnson, Pfizer, Polpharma, ProCiseDx, Progenity, Takeda, Tillotts, and Ventyx; received speaker fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Galapagos, Johnson & Johnson, Pfizer, Takeda, and Tillotts.

RM, CW, YH, JZ, AP, and SH: employees and/or shareholders of Bristol Myers Squibb.

BES: received consulting fees from AbbVie, Alimentiv, Amgen, Arena, Artugen, AstraZeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Enthera, Equillum, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphic Therapeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, and Ventyx Biosciences; received consulting and speaker fees from Abivax; received consulting and speaker fees and other support from Eli Lilly; received research grants, consulting and speaker fees, and other support from Bristol Myers Squibb, Janssen, Pfizer, and Takeda; received research grants and consulting fees from Theravance Biopharma; received stock options from Ventyx Biosciences.

JHM: employed at Nordic Bioscience A/S, a company involved in the discovery and development of biochemical biomarkers.

MIRIKIZUMAB EFFECT ON BOWEL URGENCY RESOLUTION IN A
RANDOMISED CONTROLLED PHASE 3 TRIAL OF PARTICIPANTS WITH
CROHN'S DISEASE

V. Jairath¹, B.E. Sands², M. Chaparro³, M. Chen⁴,
G.R. D'Haens⁵, M.C. Dubinsky⁶, M. Ferrante⁷, L. Peyrin-Biroulet⁸,
S. Schreiber⁹, S. Travis¹⁰, H. Carlier¹¹, Z. Lin¹¹, R. Moses¹¹,
M. Protic¹¹, A. Vadhariya¹¹, K. Tsilkos¹¹, S. Ghosh¹²

¹Western University, Department of Medicine, Division
of Gastroenterology, London, Canada, ²Icahn School
of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division
of Gastroenterology, New York, United States of America,
³Hospital Universitario de La Princesa, Instituto de
Investigación Sanitaria Princesa, Madrid, Spain, ⁴First
Affiliated Hospital of Sun Yat-sen University, Division of
Gastroenterology, Guangzhou, China, ⁵AMC Amsterdam
Inflammatory Bowel Disease Centre - Academic Medical
Center, AMC Amsterdam Inflammator, Academic Medical
Center, Amsterdam, Netherlands, ⁶Mount Sinai Hospital,
Mount Sinai, Department of Pediatrics, Susan and Leonard
Feinstein IBD Center, New York City, United States of
America, ⁷University Hospitals Leuven, Department of
Gastroenterology and Hepatology, Leuven, Belgium,
⁸Nancy University Hospital, Department of Gastroenterology,
INFINY Institute, FHU-CURE, INSERM NGERE,, Vandoeuvre-
les-Nancy, France, ⁹Kiel University, Department of Internal
Medicine, Kiel, Germany, ¹⁰University of Oxford, Translational
Gastroenterology Unit, Nuffield Department of Experimental
Medicine, Oxford, United Kingdom, ¹¹Eli Lilly and Company,
Indianapolis, United States of America, ¹²University College
Cork, APC Microbiome Ireland, College of Medicine and
Health, Cork, Ireland

Contact E-Mail Address: vjairath@uwo.ca

Introduction: Bowel urgency (BU), the sudden or immediate need to have
a bowel movement, is an impactful symptom of Crohn's disease (CD) that
varies in intensity¹. We report the efficacy of the IL-23 p19 inhibitor, miriki-
zumab (miri) in improving BU among patients with moderately-to-severe-
ly active CD from the phase 3 VIVID-1 trial (NCT03926130). VIVID-1 co-pri-
mary and gated endpoints, including comparison with ustekinumab, are
already reported².

Aims & Methods: Adult patients (N=1065) were randomised to placebo
(PBO) or miri 900mg intravenously at weeks (W) 0, 4, and 8, then 300mg
subcutaneously every 4 weeks (Q4W) from W12 to W52. At W12, PBO re-
sponders continued PBO to W52, non-responders received the blinded
miri regimen per protocol. BU was assessed at W12 and W52 using the Ur-
gency Numeric Rating Scale (UNRS)³.

We evaluated the proportion of patients with baseline (BL) UNRS ≥3 and
≥6 who achieved BU Clinically Meaningful Improvement (CMI; >3 change
in UNRS) and BU remission (UNRS ≤2). Treatment comparisons used Co-
chran-Mantel-Haenszel tests with non-responder imputation for missing
values.

Results: Study population: 55.1% male. Mean (SD) age 36.2 (13.0) years.
Disease duration 7.4 (7.9) years. At BL, median (Q1, Q3) UNRS 6.9 (5.2, 8.1),
94.5% patients achieved UNRS ≥3 and 66.0% patients achieved ≥6. In pa-
tients with BL UNRS ≥3, nominally significantly higher proportions of miri
versus PBO patients achieved BU CMI and BU remission at both W12 and
W52 (Table).

A nominally significantly greater proportion of miri-treated patients
achieved W52 BU CMI-composite and BU remission-composite (Table).
Similar results were seen with BL UNRS ≥6.

		W12 PBO	W12 Miri	W12 p-value	W12 95% CI	W52 PBO	W52 Miri	W52 p-value	W52 95% CI
	UNRS ^a CFB (LSM ±SE)	-1.58 (0.168)	-2.44 (0.099)	0.00011	-1.24, -0.48	-1.23 (0.180)	-3.24 (0.106)	<0.0001	-2.42, -1.60
Patients with BL UNRS ≥3	BU CMI-TT	50/186 (26.9)	227/547 (41.5)	0.0004	6.7, 22.0	38/186 (20.4)	301/547 (55.0)	<0.0001	28.0, 42.1
	BU CMI- composite ^a					38/186 (20.4)	251/547 (45.9)	<0.0001	18.5, 32.8
	BU Remission- TT	29/186 (15.6)	134/547 (24.5)	0.01	2.3, 15.0	21/186 (11.3)	209/547 (38.2)	<0.0001	21.0, 33.2
	BU Remission- composite					21/186 (11.3)	180/547 (32.9)	<0.0001	15.7, 27.8
Patients with BL UNRS ≥6	BU CMI-TT	38/137 (27.7)	180/376 (47.9)	0.0001	9.8, 28.2	31/137 (22.6)	229/376 (60.9)	<0.0001	30.1, 47.3
	BU CMI- composite					31/137 (22.6)	188/376 (50.0)	<0.0001	18.4, 36.0
	BU Remission- TT	11/137 (8.0)	70/376 (18.6)	0.007	3.8, 15.8	13/137 (9.5)	126/376 (33.5)	<0.0001	17.1, 31.1
	BU Remission- composite					13/137 (9.5)	111/376 (29.5)	0.0002	13.2, 27.0

PBO, N=199; Miri, N=579. Data are N (%) unless otherwise stated. ^aUNRS
scale: 0 (no urgency)-10 (worst possible urgency)³. ^bComposite=Clinical re-
sponse by PRO (2 of the patient-reported items of the CDAI, AP and SF) at
W12 and W52 parameter (CMI or Remission). ^cBU remission=no to minimal
BU (UNRS≤2).

Treatment comparison: CFB used a mixed model for repeated measures
model containing treatment, BL value, visit, stratification factors and in-
teraction of BL value by visit and treatment by visit. Response rates used
Cochran-Mantel-Haenszel tests with non-responder imputation. AP=ab-
dominal pain; BL=baseline; CFB=change from BL; CI=confidence inter-
val; CMI=clinically meaningful improvement; LSM=least squares mean;
PBO=placebo; PRO=Patient Reported Outcome; SD=standard deviation;
SE=standard error; SF=stool frequency; TT=treat-through; UNRS=Urgency
Numeric Rating Scale; W=week.

Conclusion: BU is one of the most unrecognised symptoms in patients
with CD. Patients enrolled in VIVID-1 had high BU scores at BL. Compared
to PBO-treated pts, miri-treated pts achieved nominally significantly high-
er rates of BU CMI and remission at W12 and W52.

References: 1. Dulai PS, et al. *Aliment Pharmacol Ther* 2020; 51(11): 1047-
66.

2. Ferrante, M et al. (2024). *Journal of Crohn's and Colitis*, 18(Supple-
ment_1), i7-i9.

3. Dubinsky MC, et al.. *Qual Life Res* 2023; 32(12): 3403-15.

Disclosure: VP consulting/advisory board fees from AbbVie, Alimentiv
Inc., Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zene-
ca, Avoro Capital, Bristol Myers Squibb, Celltrion, Lilly, Endpoint Health,
Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde
Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Jans-
sen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist,
Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz,
SCOPE, Second Genome, Sorriso, Takeda, TD Securities, Teva, Topivert,
Ventyx, and Vividion; speaker's fees from, Abbvie, Ferring, Bristol Myers
Squibb, Galapagos, Janssen Pfizer Shire, Takeda, and Fresenius Kabi.

BES consulting fees from Abbvie, Alimentiv, Amgen, Arena Pharmaceuti-
cals, Artugen Therapeutics, Astra Zeneca, Boehringer IngelheSim, Boston
Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, En-
thera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead
Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Inno-
vation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morpich Ther-
apeutics, MRM Health, Progenity, Prometheus Biosciences, Prometheus
Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen,
Target RWE, Teva, TLL Pharmaceutical, and Ventyx Biosciences; consult-
ing/speaking fees from Abivax; consulting/speaking fees/other support
from Lilly, Bristol Myers Squibb, Janssen, Pfizer, and Takeda; research
grants and consulting fees from Theravance Biopharma; stock options
from Ventyx Biopharma.

MC speaker, consultant, or has received research/education funding from MSD, AbbVie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr Falk Pharma, Tillotts Pharma, Biogen, Gilead, and Lilly.

MChen provided educational activities for AbbVie, China Medical System, IPSEN, Janssen, and Takeda; advisory board for Boehringer Ingelheim and Janssen; support for clinical research from Janssen and Takeda.

GD'H adviser and/or speaker for AbbVie, Alimentiv, Amgen, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Ferring, Lilly, Engene, Galapagos, Glaxo Smith Kline, Immunic, Index Pharmaceuticals, Johnson and Johnson, Merck, Polpharm, Prometheus biosciences, Prometheus Laboratories, ProCise diagnostics, Protagonist, Sandoz, Takeda, Tillotts, and Ventyx.

MD consultant for AbbVie, Arena, Astra Zeneca, Boehringer Ingelheim, Celgene, Lilly, Gilead, Janssen, Merck, Pfizer, Prometheus Laboratories, Takeda, and UCB; research grants from Janssen, AbbVie, and Prometheus Laboratories.

MF research grants from AbbVie, Biogen, EG, Janssen, Pfizer, Takeda, and Viartis; consultancy fees from AbbVie, AgomAb Therapeutics, Boehringer Ingelheim, Celgene, Celltrion, Lilly, Janssen-Cilag, MRM Health, MSD, Pfizer, Takeda, and ThermoFisher; speakers' fees from AbbVie, Biogen, Boehringer Ingelheim, Falk, Ferring, Janssen-Cilag, MSD, Pfizer, Takeda, Truvion Healthcare, and Viartis.

LP-B personal fees from Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillotts, Celltrion, Takeda, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Inotrem, Allergan, MSD, Roche, Arena, Gilead, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius Kabi, OSE Immunotherapeutics, Entera, Theravance, Pandion Therapeutics, Gossamer Bio, Viartis, and Thermo Fisher Scientific; grants from AbbVie, MSD, Takeda, and Fresenius Kabi; holds stock options in Clinical Trials Mobile Application.

SS consultant/speaker fees from AbbVie, Allergosan, Amgen, Arena, BMS, Celltrion, Falk Pharma, Ferring, Galapagos, Gilead, Genentech (Roche), GSK, IMAB, Janssen, Lilly, MSD, Pfizer, Shire, Takeda, and Ventyx.

ST consultancy from Biogen, Bristol-Myers Squibb, Celgene, ChemoCentryx, Cosmo, Enterome, Ferring, Giuliani, GlaxoSmithKline, Genentech, Immunocore, Immunometabolism, Janssen, Lilly, MSD, Merck, Neovacks, Novonordisk, Novartis, NPS Pharmaceuticals, Pfizer, Proximagen, Receptos, Roche, Shire, Sigmoid Pharma, Takeda, Topivert, UCB, VHSquared, Vifor, Zeria, Sensyne, Satisfai, Bioclinica, Equillium, Mestag, Sorriso, Protagonist; research support from AbbVie, the International Organization for the Study of Inflammatory Bowel Diseases, Lilly, UCB, Vifor, Norman Collisson Foundation, Pfizer, UK-India Education and Research Initiative, ECCO Health Care, the Helmsley Trust; honoraria from AbbVie, Amgen, Biogen, Ferring, Takeda, Lilly; travel expenses covered or reimbursed from AbbVie, Lilly, Johnson & Johnson, Pfizer, Takeda, Ferring, Amgen, and Biogen.

HC, ZL, RM, MP, AV and KT are employees and stockholders of Lilly.

SG speaking commitments with AbbVie, Takeda, Janssen, Pfizer, Gilead, Galapagos, Ferring, Lilly and Company, and Celltrion; drug monitoring committees with Janssen; advisory committees with Janssen, AbbVie, Takeda, Gilead, Galapagos, Lilly, Pfizer, Celltrion, and Ferring; steering committees with Janssen, Bristol Myers Squibb, and AbbVie.

PP0551

THROUGH THE LENS OF INFLAMMATORY BOWEL DISEASE: IMPACT OF RHEUMATOLOGICAL INVOLVEMENT ON DISEASE COURSE

W. Khemiri¹, M. Ayari¹, A. Chehaider¹, H. Bettaieb², M. Boudokhane², I. Abdelaali¹, M.H. Douggui¹, M.T. Jomni¹

¹FSI hospital, Gastroenterology department, La Marsa, Tunisia, ²FSI hospital, Rheumatology department, La Marsa, Tunisia

Contact E-Mail Address: Khemiri.wafa00@gmail.com

Introduction: Inflammatory bowel diseases (IBD) are systemic disorders that may be associated with extraintestinal manifestations in up to 40% of patients. Recognizing the recurrent emergence of these manifestations in IBD, with a particular emphasis on rheumatological aspect, becomes a pivotal focal point for a holistic therapeutic approach.

Aims & Methods: The aim of this study was to evaluate the impact of ankylosing spondylitis in IBD on disease course. We conducted a retrospective and comparative study, including patients followed for IBD over an 8-year period [2014 - 2022]. Clinico-biological data, disease severity, and long-term outcomes (surgery and disease course) were collected. IBD patients with ankylosing spondylitis (group1) and patients without (group2) were compared. Data were entered and analyzed via SPSS 26 software.

Results: One-hundred IBD patients were enrolled with a sex ratio of M/F=2.44 and a mean age of disease diagnose of 37.26 ± 13.46 years. Eighteen patients had ankylosing spondylitis (18%). The two groups were comparable in terms of age at disease onset, gender, smoking status and family history of IBD ($p=0.65$; $p=0.9$, $p=1$ and 0.1 respectively). In Crohn's disease, there was no difference between the two groups regarding the extent of the disease ($p=0.71$), the presence of upper gastro-intestinal tract involvement ($p=0.11$) and perineal manifestations ($p=0.7$). Inflammatory, structuring, and penetrating phenotypes were also comparable between the two groups ($p=0.67$; $p=0.3$; $p=1$ respectively). However, the occurrence of acute intestinal obstruction was significantly more common in ankylosing spondylitis patients (G1:54% vs. G2:10%; $p=0.004$). As for ulcerative colitis, extensive presentation (G1:28% vs. G2:41%; $p=0.66$) and the occurrence of disease extension during follow-up was comparable between the two groups ($p=0.78$). None of the patients with or without rheumatological involvement had any dermatological or ophthalmological involvement related to IBD, but there was a more significant prevalence of hepatic manifestations in ankylosing spondylitis group (G1:16% vs. G2:2%, $p=0.01$). The mean number of flare-ups was not significantly different between the two groups (G1:3.21 $\pm$ 1.47 vs. G2:2.53 $\pm$ 1.4; $p=0.06$). Regarding treatment, recourse to methotrexate (G1:16% vs. G2:2%; $p=0.01$) and the use of anti-TNF agents (G1:77% vs. G2:22%; $p<0.001$) was more frequent in group 1, with no difference in the occurrence of adverse events ($p=1$), the use of corticosteroids ($p=0.22$) or azathioprine ($p=0.1$). Surgical treatment was more frequently indicated in ankylosing spondylitis patients (G1:51% vs. G2:30%; $p=0.06$). Post-operative relapse of Crohn's disease was comparable between the two groups ($p=1$).

Conclusion: In our study, rheumatological involvement was not likely responsible of a more severe clinical phenotype of IBD.

Disclosure: Nothing to disclose.

PP0552

COMPARATIVE STUDY OF THE EFFICACY OF TWO BIOLOGIC THERAPY SEQUENCES IN INFLAMMATORY BOWEL DISEASE

J. Damasceno e Costa¹, B. Arroja¹, T. Carvalho¹, A. Guimarães¹, J. Neves¹, D. Costa¹, J.B. Soares¹, R. Gonçalves¹

¹Braga Hospital, Gastroenterology Department, Braga, Portugal

Contact E-Mail Address: jpdcosta.93@gmail.com

Introduction:

Vedolizumab (VED) and ustekinumab (UST) are valid options for ulcerative colitis (UC) and Crohn's disease (CD) patients who fail anti-tumour necrosis factor (TNF) therapy. However, there are conflicting data on which drug should be preferred as second-line.

Aims & Methods:

UC and CD patients who received VED or UST after anti-TNF failure or intolerance were included, and treatment groups were compared. The primary outcome of clinical remission (CR) was evaluated at 6 and 12 months of therapy, as were the secondary outcomes of corticosteroid-free CR and biochemical remission (BR). Endoscopic remission (ER) was evaluated at 12 months. Predictors of these outcomes were assessed using Cox regression.

Results: A total of 72 patients were included, 21 with UC (14 UST | 7 VED) and 51 with CD (35 UST | 16 VED). There were no significant differences in the various remission rates between both treatment groups, in UC and CD. In CD, multivariate analysis revealed baseline Harvey-Bradshaw index (HBI) as an independent predictor of failed CR ($p < 0.001$, HR 1.42, IC 95% 1.18-1.71) and corticosteroid-free CR ($p < 0.001$, HR 1.43, IC 95% 1.19-1.72) at 12 months. Anti-TNF discontinuation due to primary or secondary failure (vs. adverse event) was an independent predictor of BR at 12 months ($p = 0.028$, HR 2.33, IC 95% 1.09-4.98). Interestingly, subanalysis of 16 patients who advanced to a third-line therapy with the opposite drug revealed a tendency for lower CR rates with VED (40.0%), when compared to UST (72.73%), albeit not statistically significant ($p = 0.299$).

Conclusion:

In this study, clinical, biochemical and endoscopic remission rates in UC and DC were not significantly different between patients treated with VED or UST as second-line therapy. HBI and reason for anti-TNF withdrawal were independent predictors of failed CR and BR, respectively. There may be a tendency for larger differences in CR when comparing VED and UST as third-line agents, with better results for the latter.

References:

- García MJ, Rivero M, Fernández-Clotet A, De Francisco R, Sicilia B, Mesonero F, et al. Comparative Study of the Effectiveness of Vedolizumab Versus Ustekinumab After Anti-TNF Failure in Crohn's Disease (Versus-CD): Data from the ENEIDA Registry. *Journal of Crohn's and Colitis*. 2024 Jan 27;18(1):65–74.
- Onali S, Pugliese D, Caprioli FA, Orlando A, Biancone L, Nardone OM, et al. An Objective Comparison of Vedolizumab and Ustekinumab Effectiveness in Crohn's Disease Patients' Failure to TNF-Alpha Inhibitors. *Am J Gastroenterol*. 2022 Aug;117(8):1279–87.
- Hyun HK, Zhang HS, Yu J, Kang EA, Park J, Park SJ, et al. Comparative effectiveness of second-line biological therapies for ulcerative colitis and Crohn's disease in patients with prior failure of anti-tumour necrosis factor treatment. *BMC Gastroenterol*. 2022 Dec;22(1):143.
- Singh, Amandeep MD; Khan, Freeha MD; Lopez, Rocio MS, MPH; Shen, Bo MD, FACG. Ustekinumab versus Vedolizumab for Moderate to Severe Crohn's Disease: 713. *American Journal of Gastroenterology* 112(0):p S393-S394, October 2017.

Disclosure: Nothing to disclose.

PP0553

ANTI-TUMOUR NECROSIS FACTOR DRUG CONCENTRATION IS NOT ASSOCIATED WITH DISEASE OUTCOMES IN POUCHITIS: A RETROSPECTIVE, INTERNATIONAL, MULTI-CENTRE, CROSS-SECTIONAL STUDY

S. Honap^{1,2}, B. Caron^{3,4,5,6}, J. Ollech⁷, M. Fischman⁸, K. Papamichael⁹, D. De Jong¹⁰, K.B. Gecse^{10,11}, A. Centritto¹¹, M. Samaan¹¹, P. Irving^{1,11}, M.P. Sparrow^{12,13}, K. Karmiris¹⁴, T. Chateau¹⁵, I. Dotan⁷, L. Peyrin-Biroulet^{3,4,5,6,16,17}

¹King's College London, School of Immunology and Microbial Sciences, London, United Kingdom, ²St George's University Hospitals NHS Foundation Trust, Department of Gastroenterology, London, United Kingdom, ³Nancy University Hospital, INFINY Institute, Nancy, France, ⁴Nancy University Hospital, Department of Gastroenterology, Nancy, France, ⁵Nancy University Hospital, FHU-CURE, Nancy, France, ⁶University of Lorraine, INSERM, NGERE, Nancy, France, ⁷Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ⁸Hebrew University of Jerusalem, Department of Military Medicine, Faculty of Medicine, Jerusalem, Israel, ⁹Beth-Israel Deaconess Medical Center - Harvard Medical School, Center for Inflammatory Bowel Diseases, Division of Gastroenterology, Boston, United States of America, ¹⁰Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹¹Guy's and St. Thomas' NHS Foundation Trust, IBD Centre, Department of Gastroenterology, London, United Kingdom, ¹²Alfred Health, Gastroenterology Department, Melbourne, Australia, ¹³Monash University, Faculty of Medicine, Nursing and Health Sciences, Melbourne, Australia, ¹⁴Venizeleio General Hospital, Gastroenterology, Heraklion, Greece, ¹⁵Grenoble Alpes University Hospital, Department of Hepato-Gastroenterology and Digestive Oncology, Grenoble, France, ¹⁶Groupe Hospitalier privé Ambroise Paré - Hartmann, Paris IBD Center, Paris, France, ¹⁷McGill University Health Centre, Division of Gastroenterology and Hepatology, Montreal, Canada

Contact E-Mail Address: honap@hotmail.co.uk

Introduction: Therapeutic drug monitoring is an important tool for optimising anti-tumour necrosis factor- α (TNF- α) therapy in inflammatory bowel disease. However, the exposure-response relationship has never been assessed in patients with pouchitis.

Aims & Methods: The aim was to explore the association between anti-TNF- α drug concentration and pouchitis disease activity in patients with a background of ulcerative colitis. A retrospective, international, multicentre, cross-sectional study was conducted in adult patients with pouchitis requiring anti-TNF- α treatment.

Rates of clinical remission (≤ 1 on a 4-point Physician's Global Assessment scale) and endoscopic remission (lack of friability or ulceration) were calculated, and drug concentrations during maintenance therapy were compared between remission and non-remission cohorts.

Results: Sixty-three patients were included; median age, 48 years (IQR 36-59), male 28 (44%), median time since pouchitis diagnosis, 7 years (IQR 2-13). Patients received infliximab, $n = 27$ (43%), adalimumab, $n = 29$ (46%), or both $n = 7$ (11%). Thirty-two (51%) patients received concomitant immunomodulation.

Median infliximab trough concentrations (mg/ml) were similar between patients in clinical remission ($n = 21$) vs non-remission ($n = 11$), 5.3 vs. 4.4, $p = 0.73$, although patients with moderate-to-severely active endoscopic pouchitis ($n = 19$) had significantly higher trough concentrations than those in endoscopic remission ($n = 13$), 10.6 vs. 3.5, $p = 0.04$. For adalimumab, median drug concentrations did not significantly differ between remission/

non-remission groups based on clinical ($n=18/18$), 11.4 vs 7.6, $p=0.32$, or endoscopic assessment, ($n=7/29$), 9.0 vs. 7.8, $p=0.78$. Four patients had positive anti-drug antibodies with undetectable drug concentration.

Conclusion: In a cohort of patients with pouchitis, higher anti-TNF- α drug concentrations were not associated with more clinical or endoscopic remission.

Disclosure: SH served as a speaker, a consultant, an advisory board member, and/or has received travel grants from Pfizer, Janssen, AbbVie, Takeda, Ferring, Pharmacosmos, Galapagos.

BC has received lecture and/or consulting fees from Abbvie, Amgen, Celltrion, Ferring, Galapagos, Janssen, Lilly, Pfizer, Takeda.

JEO reports institutional research grants from Pfizer.

KP received lecture/speaker fees from Physicians Education Resource LLC and Grifols; scientific advisory board fees from ProCiseDx Inc and Scipher Medicine Corporation; and serves as a consultant for Prometheus Laboratories Inc.

DJ has received speaker fee from Johnson and Johnson.

KBG has received grants from Pfizer Inc., Galapagos, and Celltrion; consultancy fees from AbbVie, Arena Pharmaceuticals, Galapagos, Gilead, Immunix Therapeutics, Janssen Pharmaceuticals, Novartis, Pfizer Inc., Samsung Bioepis, and Takeda; and speaker's honoraria from Celltrion, Ferring, Janssen Pharmaceuticals, Novartis, Pfizer Inc, Samsung Bioepis, Takeda, and Tillotts, all outside the submitted work.

MAS has received personal fees from Takeda, Janssen, Sandoz, MSD, Falk, Samsung Bioepis, Galapagos, and Bristol Myers Squibb.

PMI reports research grants from Celltrion, Pfizer Inc, Takeda Pharmaceutical Company, and Galapagos; consulting fees from AbbVie Inc, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Elasmogen Ltd, Gilead Sciences Pty Ltd, Janssen Pharmaceuticals, Eli Lilly and Company, Pfizer Inc, Prometheus, and Sandoz; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from AbbVie Inc, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Galapagos, Gilead Sciences Inc, Janssen Pharmaceuticals, Eli Lilly and Company, Pfizer Inc, Takeda Pharmaceutical Company, and Tillotts Pharma AG; and support for attending meetings and/or travel from AbbVie and Tillotts Pharma AG.

MPS has received educational grants or research support from Ferring, Orphan and Gilead; speaker's fees from Janssen, AbbVie, Ferring, Takeda, Pfizer, and Shire; and served on advisory boards for Janssen, Takeda, Pfizer, Celgene, AbbVie, MSD, and Emerge Health.

KK has served as speaker, consultant and advisory board member for AbbVie, Amgen, Ferring, Galenica, Genesis, Janssen, MSD, Pfizer, Takeda and Vianex

ID has received consultation fees, research grants, or honoraria from Janssen, Pfizer, AbbVie, Takeda, Genentech/Roche, Ferring, Iterative Scopes, Integra Holdings, Eli-Lilly, Falk Pharma, Gilead, Galapagos, Celgene/BMS, Arena, Sublimity, Sangamo, Sandoz, Celltrion, Abbott, Prometheus, Altman, Athos, Shareholder: Harp Diagnostics, GUTREAT.

LPB reports fees received from: AbbVie, Adacety, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytokine Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morpich, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillotts, Viatrix, Vifor, Ysopia, Abivax, Samsung, Ventyx, Roivant, Vectivbio.

The remaining authors have no conflicts to disclose.

PP0554

COST-EFFECTIVENESS AND COST-UTILITY OF OPTIMIZED MERCAPTOPYRINE TREATMENT VERSUS PLACEBO IN ULCERATIVE COLITIS PATIENTS: THE RANDOMIZED CONTROLLED OPTIC TRIAL

M. Lowenberg¹, M. van Barneveld^{2,1}, A. Volkers¹, S. van Gennep³, M. Duijvestein⁴, A. van Bodegraven^{5,6}, D. van Asseldonk⁷, R. West⁸, K. (.) de Boer⁹, G.R. D'Haens¹⁰, M.G.W. Dijkgraaf¹¹

¹Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam UMC, Amsterdam, Netherlands, ³Amsterdam UMC, University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁴Radboudumc, Gastroenterology and Hepatology, Nijmegen, Netherlands, ⁵Zuyderland, Sittard Geleen, Netherlands, ⁶Maast, Sittard, Netherlands, ⁷Noordwest Ziekenhuisgroep, Gastroenterology and Hepatology, Alkmaar, Netherlands, ⁸Sint Franciscus Gasthuis, Dept. of Gastroenterology, Rotterdam, Netherlands, ⁹VU University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹⁰AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands, ¹¹Amsterdam UMC, Department of Epidemiology and Data Science, Amsterdam, Netherlands

Contact E-Mail Address: m.lowenberg@amsterdamumc.nl

Introduction: The randomized controlled OPTIC trial reported that optimised mercaptopurine treatment was superior to placebo in achieving clinical, endoscopic and histological outcomes at one year in ulcerative colitis (UC) patients failing 5-aminosalicylates after receiving induction treatment with corticosteroids.

Aims & Methods: We aimed to assess cost-effectiveness and cost-utility of therapeutic drug monitoring (TDM)-guided mercaptopurine treatment in UC. Data were collected during the OPTIC trial to perform a health economic evaluation for mercaptopurine treatment versus placebo in UC patients. The economic evaluation was performed from a health care and societal perspective using a cost-effectiveness and cost-utility analysis with a time horizon of one year. Volumes and costs of in-hospital care, out-of-hospital care, out-of-pocket expenses and productivity loss were assessed. Main outcomes were the costs per patient who achieved combined corticosteroid-free clinical remission and endoscopic improvement at one year and the costs per quality-adjusted life-year (QALY).

Results: In total, 59 patients were randomized to the intervention ($n = 29$) and control ($n = 30$) group. Patients on mercaptopurine treatment showed a non-significant gain in QALYs of 0.047 (-0.024 to 0.117) ($P=0.184$) corrected for baseline health utility. Non-significant differences in costs were €63 (-€1267 to €1434; $P=0.927$) in favour of placebo from a health care perspective and -€742 (-€3683 to €2016; $P=0.644$) in favour of mercaptopurine from a societal perspective, including patients' out-of-pocket expenses and employers' productivity loss. The probability of optimised mercaptopurine treatment being cost-effective was 0.80 at a willingness to pay per additional QALY of €20,000.

Conclusion: Optimised mercaptopurine treatment in UC patients failing 5-aminosalicylates is a cost-effective strategy from a societal perspective.

References:

1. de Boer NKH, Peyrin-Biroulet L, Jharap B, et al. Thiopurines in inflammatory bowel disease: new findings and perspectives. *J Crohns Colitis* 2018;12:610–20.
2. Löwenberg, M., Volkers, A., van Gennep, S., Mookhoek, A., Montazeri, N., Clasquin, E., Duijvestein, M., van Bodegraven, A., Rietdijk, S., Jansen, J.,

van Asseldonk, D., van der Zanden, E., Dijkgraaf, M., West, R., de Boer, N., & D'Haens, G. (2023). Mercaptopurine for the Treatment of Ulcerative Colitis: A Randomized Placebo-Controlled Trial. *Journal of Crohn's & Colitis*, 17(7), 1055–1065.

Disclosure: NA.

PP0555

COMPARISON OF REAL-WORLD TREATMENT PERSISTENCE AND SAFETY OF VEDOLIZUMAB AND ANTI-TUMOUR NECROSIS FACTOR-ALPHA TREATMENT IN BIOLOGIC-NAIVE PATIENTS WITH ULCERATIVE COLITIS: SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

S. Vermeire¹, S. Schreiber², P. Biedermann³, M. Meyer⁴, E. Robertshaw⁵, C. Shaw⁵, A. Armuzzi^{6,7}, M. Chaparro⁸

¹University Hospital Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ²Institute of Clinical Molecular Biology and Clinic for Internal Medicine, Kiel University, Kiel, Germany, ³Takeda Pharmaceuticals International AG, Zurich, Switzerland, ⁴Takeda Pharma AG, Zurich, Switzerland, ⁵Putnam Associates, Newcastle upon Tyne, United Kingdom, ⁶IBD Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy, ⁷Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Milan, Italy, ⁸Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid, and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Gastroenterology, Madrid, Spain

Contact E-Mail Address: severine.vermeire@uzleuven.be

Introduction: Vedolizumab (VDZ) is approved in Europe and the USA for the treatment of moderately to severely active ulcerative colitis (UC). A previous systematic literature review (SLR) and meta-analysis published in 2018 demonstrated the real-world effectiveness and positive benefit-risk profile of VDZ treatment for up to 1 year in patients with inflammatory bowel disease.¹ There is limited real-world evidence on the long-term (> 1 year) treatment persistence and safety of VDZ compared with anti-tumour necrosis factor-alpha (TNF α) treatment in biologic-naive patients with UC. **Aims & Methods:** The aims of this meta-analysis were to assess the real-world effectiveness and treatment persistence of VDZ in patients with UC. We report an exploratory analysis of treatment persistence and serious adverse events (SAEs) among biologic-naive patients with UC treated with VDZ compared with anti-TNF α treatment at 1 and at 2 years. Literature searches were conducted to identify studies published from 2014 to 2022. For the primary analysis, outcomes of interest included clinical remission, mucosal healing, treatment patterns (including treatment persistence) and safety. Data on adults with UC treated with VDZ or anti-TNF α treatment in a real-world setting were extracted if there were at least 2 studies for each timepoint and population. Weighted proportions and corresponding 95% confidence intervals (CIs) were calculated using the DerSimonian-Laird random-effects model to account for between-study heterogeneity. No formal statistical significance testing between treatments was applied.

Results: Among comparative studies of VDZ and anti-TNF α treatment, 8 studies were identified (10 486 biologic-naive patients with UC). Of these, 5 and 2 studies, respectively, reported the rates of treatment persistence in biologic-naive patients at 1 and at 2 years. The rate of treatment persistence at 1 year was 74.9% with VDZ (95% CI 64.3–83.3) and 59.0% with anti-TNF α treatment (47.2–69.8). Similarly, the rate of treatment persistence at 2 years was 77.6% with VDZ (70.8–83.2) and 60.0% with anti-TNF α treatment (48.3–70.7). Three retrospective cohort studies of 775 biologic-naive patients with UC treated with VDZ (n=465) versus anti-TNF α

treatment (n=310) reported SAEs. In the first study, safety outcomes were followed from treatment initiation up to five half-lives after treatment discontinuation; 6.8% treated with VDZ experienced SAEs compared with 19.2% with anti-TNF α treatment.² In the second study, the rate of SAEs was similar between patients treated with VDZ (4.5%) and anti-TNF α treatment (5.0%).³ In the third study that reported SAEs within the first year of treatment; the rates of SAEs were 14.3% and 10.9% among patients who received VDZ and anti-TNF α treatment, respectively.⁴

Conclusion: This analysis of comparative studies in biologic-naive patients with UC suggested that treatment persistence rates were higher with VDZ than with anti-TNF α treatment both at 1 and at 2 years. In addition, these data support a comparable safety profile, with similar rates of SAEs between VDZ and anti-TNF α treatment.

This study was funded by Takeda Pharmaceuticals International AG, Zurich, Switzerland.

Writing assistance provided by E Sugrue, PhD, of Oxford PharmaGenesis.

References:

- Schreiber S et al. *J Gastroenterol*. 2018;53:1048–64.
- Bressler B et al. *J Crohn's Colitis*. 2021;15:1694–706.
- Helwig et al. *BMC Gastroenterol*. 2020;20:211.
- Moens et al. *Inflamm Bowel Dis*. 2022;28:1135–1142.

Disclosure: SV has received financial support for research from AbbVie, Galapagos, J&J, Pfizer and Takeda, and speakers' and/or consultancy fees from AbbVie, Abivax, AboleroISPharma, AgomAb, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Cytokine Pharma, Dr Falk Pharma, Eli Lilly, Ferring, Galapagos, Genentech-Roche, Gilead, GSK, Hospira, Imidomics, Janssen, J&J, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MrMHealth, Mundipharma, MSD, Pfizer, Prodigest, Progenity, Prometheus, Robarts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillots Pharma AG, VectivBio, Ventyx and Zealand Pharma.

SS has received personal fees from AbbVie, Amgen, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr Falk Pharma, Fresenius, Galapagos/Gilead, Hikma, I-Mab, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, ProventionBio, Takeda, Theravance Biopharma and Ventyx. PB is an employee and stockholder of Takeda Pharmaceuticals International AG, Zurich, Switzerland.

MM is an employee and stockholder of Takeda Pharma AG, Zurich, Switzerland.

ER is an employee of Putnam Associates, which received funding for this study from Takeda Pharmaceuticals International AG, Zurich, Switzerland. CS is an employee of Putnam Associates, which received funding for this study from Takeda Pharmaceuticals International AG, Zurich, Switzerland. AA has received advisory board/lecture fees from AbbVie, Amgen, Arena, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr Falk Pharma, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, Lion Health, MSD, Nestlé, Novartis, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda, Teva Pharmaceutical and Tillots Pharma.

MC has served as a speaker or consultant, or has received funding for research or education, from AbbVie, Biogen, Dr Falk Pharma, Eli Lilly, Ferring, Gilead, Hospira, Janssen, MSD, Pfizer, Shire Pharmaceuticals, Takeda and Tillots Pharma.

PP0556

TARGET ACHIEVEMENT AFTER 32 WEEKS OF VEDOLIZUMAB TREATMENT IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: AN INTERIM ANALYSIS FROM THE VERDICT TRIAL

V. Jairath^{1,2,3}, G. Zou^{2,3,4}, S. Adsul⁵, L. Peyrin-Biroulet^{6,7,8,9,10}, J.-F. Colombel¹¹, G.R. D'Haens¹², M. Freire⁵, G.W. Moran^{13,14}, W.J. Sandborn¹⁵, S. Sebastian¹⁶, S. Travis¹⁷, S. Vermeire¹⁸, J. Hanžel^{3,19}, C. Ma^{3,20,21}, R. Sedano^{1,2,3}, P. Sheridan³, N. Arya²², M. Beaton¹, P. Bossuyt²³, S. Danese²⁴, D. Green²⁵, W. Harlan III²⁶, M. Horynski²⁷, J. Kierkus²⁸, A. Kopon²⁹, M. Klopocka^{30,31}, F. Magro³², R. Petroniene³³, M.S. Silverberg³⁴, L. Wolanski³⁵, B.G. Feagan^{1,2,3}

¹Western University, Department of Medicine, Division of Gastroenterology, London, Canada, ²Western University, Department of Epidemiology and Biostatistics, London, Canada,

³Alimentiv Inc, London, Canada, ⁴Western University, Robarts Research Institute, Schulich School of Medicine and Dentistry, London, Canada, ⁵Takeda Pharmaceuticals, Cambridge, United States of America, ⁶Nancy University Hospital, Department of Gastroenterology, F-54500 Vandoeuvre-lès-Nancy, France,

⁷INSERM, NGERE, University of Lorraine, F-54000, Nancy, France, ⁸INFINY Institute, Nancy University Hospital, F-54500 Vandoeuvre-lès-Nancy, France, ⁹FHU-CURE, Nancy University Hospital, F-54500 Vandoeuvre-lès-Nancy, France, ¹⁰Groupe Hospitalier Privé Ambroise Paré - Hartmann, Paris IBD Center, 92200 Neuilly sur Seine, France, ¹¹Icahn School of Medicine at Mount Sinai, Division of Gastroenterology, New York, United States of America, ¹²Amsterdam University Medical Centers, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ¹³University of Nottingham, Nottingham Digestive Diseases Biomedical Research Centre, Nottingham, United Kingdom, ¹⁴Nottingham University Hospitals NHS Trust, NIHR Nottingham Biomedical Research Centre, Nottingham, United Kingdom, ¹⁵University of California San Diego, Division of Gastroenterology, La Jolla, United States of America, ¹⁶Hull University Teaching Hospitals, IBD Unit, Hull, United Kingdom, ¹⁷University of Oxford, Kennedy Institute and Biomedical Research Centre, Oxford, United Kingdom, ¹⁸University Hospitals Leuven, KU Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ¹⁹University of Ljubljana, Department of Gastroenterology, Faculty of Medicine, Ljubljana, Slovenia, ²⁰University of Calgary, Division of Gastroenterology & Hepatology, Cumming School of Medicine, Calgary, Canada, ²¹University of Calgary, Department of Community Health Sciences, Cumming School of Medicine, Calgary, Canada, ²²ABP Research Services Corp., Oakville, Canada, ²³Imelda General Hospital, Imelda GI Clinical Research Center, Bonheiden, Belgium, ²⁴Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastroenterology and Gastrointestinal Endoscopy Unit, Milan, Italy, ²⁵Taunton Surgical Centre, Department of Gastroenterology, Oshawa, Canada, ²⁶Asheville Gastroenterology Associates, Asheville, United States of America, ²⁷Endoskopia Sp. z o.o., Sopot, Poland, ²⁸The Children's Memorial Health Institute, Warsaw, Poland, ²⁹Toruńskie Centrum Gastrologiczne Gastromed, Department of Gastroenterology, Toruń, Poland, ³⁰Nicolaus Copernicus University, Department of Gastroenterology and Nutritional Disorders, Collegium Medicum, Bydgoszcz, Poland, ³¹Dr. Jana Biziel University Hospital n 2 in Bydgoszcz, Gastroenterology Clinic, Bydgoszcz, Poland, ³²CINTESIS@RISE, Departmento, Faculty of Medicine of the University of Porto, Porto, Portugal, ³³Barrie GI Associates Inc., Barrie, Canada, ³⁴Toronto

Immune and Digestive Health Institute, Toronto, Canada,

³⁵Samodzielny Publiczny Zakład Opieki Zdrowotnej w Łęcznej, Gastroenterological Department, Łęcznej, Poland

Contact E-Mail Address: vipul.jairath@robartsinc.com

Introduction: The primary objective of the VERDICT study, a continuing randomized controlled trial (NCT04259138),^{1,2} is to determine the optimal treatment target in moderately-to-severely active ulcerative colitis (UC). Patients are allocated to Group 1 (corticosteroid-free [CSF] symptomatic remission), Group 2 (CSF symptomatic remission + CSF endoscopic remission), and Group 3 (CSF symptomatic remission + CSF endoscopic remission + CSF histologic remission, also termed disease clearance). Patients follow treatment algorithms involving early introduction of vedolizumab (VDZ), without week 10 dosing, nor dose escalation before week 16. Here we report target achievement at weeks 16 and 32 amongst groups.

Aims & Methods: VDZ 300 mg was administered intravenously following a treatment algorithm related to baseline UC treatment until assigned treatment target was reached at week 32, with an escalation step between week 16 and 32 as indicated. CSF symptomatic remission was defined as Mayo rectal bleeding subscore=0, CSF endoscopic remission was defined as Mayo Endoscopic Score [MES]≤1, and CSF histologic remission was defined as Geboes score<2B.0.

Results: As of 29 Feb 2024, 612 patients were enrolled with 154, 198, and 260 patients assigned to target Groups 1, 2, and 3, respectively. Baseline age and disease duration were similar amongst groups, with respective percentages of patients having baseline MES=3 given by 60.4%, 61.6%, and 64.2%, and receipt of concomitant corticosteroids given by 42.9%, 40.9%, and 50.4% (median dose 25.4, 25.3, and 23.7 mg). There were 71.4%, 75.3%, and 83.5% of patients who were bionaiive, respectively. At time of analysis, 63.6%, 71.2%, and 80.8% of randomized patients in the groups had completed the week 32 visit.

	Group 1 Bionaiive N=86	Group 1 Bio- exposed N=12	Group 1 Total N=98	Group 2 Bionaiive N=116	Group 2 Bio- exposed N=25	Group 2 Total N=141	Group 3 Bionaiive N=183	Group 3 Bio- exposed N=27	Group 3 Total N=210
CSF remission, n (%)	72 (83.7)	8 (66.7)	80 (81.6)	74 (63.8)	13 (52.0)	87 (61.7)	101 (55.2)	11 (40.7)	112 (53.3)
Non-CSF remission, n (%)	3 (3.5)	0 (0.0)	3 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)
Remission target not achieved, n (%)	11 (12.8)	3 (25.0)	14 (14.3)	40 (34.5)	12 (48.0)	52 (36.9)	81 (44.3)	16 (59.3)	97 (46.2)
Remission target status missing, ^b n (%)	0 (0.0)	1 (8.3)	1 (1.0)	2 (1.7)	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)

^aWeek 32 completer analysis set includes all patients who reached the week 32 visit. Group 1 is defined as CSF symptomatic remission; Group 2 is defined as CSF symptomatic remission + CSF endoscopic remission; and Group 3 is defined as CSF symptomatic remission + CSF endoscopic remission + CSF histologic remission.

^bRemission target status missing includes patients who ended the study before the week 32 visit, those who had not reached the week 32 visit, and those who reached the week 32 visit but had no status, as of 29 FEB 2024.

Abbreviation: CSF, corticosteroid-free.

Table 1. Summary of Target Achievement by Week 32^a.

In patients with observed data and a week 16 visit, 64.1% (75/117), 42.2% (73/173), and 40.2% (94/234) in Groups 1, 2, and 3, respectively, achieved CSF remission at week 16. In patients with observed data and a week 32 visit, 81.6% (80/98), 61.7% (87/141), and 53.3% (112/210), respectively, achieved CSF remission by week 32, with higher proportions in bionaiive (83.7%, 63.8%, and 55.2%) compared to bio-exposed (66.7%, 52.0%, and 40.7%) (Table 1). In the intention-to-treat population, 48.7%, 36.9%, and 36.2% of patients, respectively, achieved CSF remission at week 16, with higher proportions in patients who were bionaiive (56.4% [62/110], 38.3%

[57/149], and 38.2% [83/217]) compared to bio-exposed (29.5% [13/44], 32.7% [16/49], and 25.6% [11/43]). By week 32, 51.9%, 43.9%, and 43.1% of the intention-to-treat population achieved CSF remission, with higher proportions in bionave (65.5% [72/110], 49.7% [74/149], and 46.5% [101/217]) compared to bio-exposed (18.2% [8/44], 26.5% [13/49], and 25.6% [11/43]). For patients not achieving target at week 16, treatment escalation occurred in 22.7%, 49.5%, and 53.5% of patients; after escalation, proportions achieving CSF remission by week 32 were 41.9% (13/31), 27.0% (20/74), and 19.0% (23/121), respectively.

Conclusion: These interim week 32 results provide evidence of improvement from week 16 to 32 across all endpoints and continue to support the efficacy of VDZ in achieving the stringent endpoint of CSF disease clearance.

References: ¹Jairath V, Zou G, Wang Z, et al. Determining the optimal treatment target in patients with ulcerative colitis: rationale, design, protocol and interim analysis for the randomised controlled VERDICT trial. *BMJ Open Gastroenterol.* 2024;11:e001218. Doi:10.1136/bmjgast-2023-001218
²Jairath V, Zou G, Adsul S, et al. DOP11 Disease clearance after 16 weeks of treatment with vedolizumab in patients with moderate to severe Ulcerative Colitis: An interim analysis from the VERDICT trial. *J Crohns Colitis.* 2024;18 (Suppl 1):i92-i93. Doi: 10.1093/ecco-jcc/jjad212.0051

Disclosure: VJ has received consulting/advisory board fees from Alimentiv Inc. (formerly Robarts Clinical Trials) and Takeda; and received speaker's fees from Takeda.

GZ has received consulting fees from Alimentiv Inc.

SA and MF are employees of Takeda Pharmaceuticals.

LPB has received personal fees from Alimentiv Inc. and Takeda.

JFC reports receiving research grants, payment for lectures, and consulting fees from Takeda.

GRD has served as a consultant and/or received speaker fees from Alimentiv Inc. and Takeda.

GWM is a consultant for Alimentiv Inc.

WJS reports receiving consulting fees from Alimentiv Inc.

SS reports receiving research grants from Takeda; and receiving personal fees for speaker role and advisory board meetings from Takeda outside the submitted work.

ST has received grants/research support, consulting fees, and speaker fees from Takeda,

SV has received grants from Takeda; and received consulting and/or speaking fees from Alimentiv Inc. and Takeda.

JH has received consulting fees from Alimentiv Inc. and speaker's fees from Takeda.

CM has received consulting fees from Alimentiv Inc. and has received consulting fees and speaker's fees from Takeda.

RS has received consulting fees from Alimentiv Inc.

PS is an employee of Alimentiv Inc.

NA reports no conflicts of interest.

MB has received honoraria and advisory board fees from Takeda; and reports clinical trials with Takeda.

PB reports receiving research grants, lecture fees, and consulting fees from Takeda.

SD reports consultancy fees from Alimentiv Inc. and reports consultancy fees and lecture fees from Takeda.

DG has received advisory board fees from Takeda.

WH reports no conflicts of interest.

MH reports no conflicts of interest.

JK reports no conflicts of interest with Alimentiv Inc. or Takeda

AK reports no conflicts of interest.

MK has received personal fees from Shire, a Takeda company, during the conduct of the study, and received personal fees and non-financial support from Takeda.

FM has received fees from Takeda.

RP reports no conflicts of interest with Alimentiv Inc. and Takeda.

MSS has received consulting, speaker, and advisory board fees from Takeda.

LW reports no conflicts of interest.

BGF is a scientific advisory board member for Takeda; has received consulting fees, lecture fees, and grant support from Takeda; and is the Senior Scientific Officer of Alimentiv Inc.

PP0557

LONG-TERM OUTCOMES FOLLOWING WITHDRAWAL OF ANTI-TUMOUR NECROSIS FACTOR TREATMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS IN REMISSION: THE EXIT LONG-TERM STUDY OF GETECCU

M.J. Casanova¹, C. Rubín de Célix¹, S. Riestra², A.J. Lucendo³, J.M. Benítez⁴, M. Navarro-Llavat⁵, J. Barrio⁶, V.J. Morales-Alvarado⁷, M. Rivero⁸, D. Busquets⁹, E. Leo-Carnerero¹⁰, O. Nantes-Castillejo¹¹, P. Navarro¹², M. Van Domselaar¹³, A. Gutiérrez-Casbas¹⁴, I. Alonso-Abreu¹⁵, M. Barreiro-de Acosta¹⁶, L. Fernández-Salazar¹⁷, M. Iborra¹⁸, M.D. Martín-Arranz¹⁹, N. García-Morales²⁰, J. Guardiola²¹, A. Bouhmid-Assakali²², M. Esteve²³, C. Muñoz-Villafranca²⁴, I. Rodríguez-Lago²⁵, D. Ceballos²⁶, I. Guerra²⁷, M. Mañosa²⁸, I. Marín-Jiménez²⁹, I. Vera-Mendoza³⁰, A. Garre¹, M. Chaparro^{*1}, J.P. Gisbert^{*1}, EXIT LONG-TERM Study group of GETECCU, *co-last authors
¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Gastroenterology, Madrid, Spain, ²Hospital Universitario Central de Asturias, e Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Gastroenterology, Oviedo, Spain, ³Hospital General de Tomelloso, CIBEREHD, Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Gastroenterology, Tomelloso, Spain, ⁴Hospital Universitario Reina Sofía, Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Gastroenterology, Córdoba, Spain, ⁵Hospital de Sant Joan Despí Moisès Broggi, Gastroenterology, Sant Joan Despí, Spain, ⁶Hospital Universitario Río Hortega, Gerencia Regional de Salud de Castilla y León (SACYL), Gastroenterology, Valladolid, Spain, ⁷Hospital General de Granollers, Gastroenterology, Granollers, Spain, ⁸Hospital Universitario Marqués de Valdecilla, Instituto de Investigación Sanitaria Valdecilla (IDIVAL), Gastroenterology, Santander, Spain, ⁹Hospital Universitari Girona Dr. J. Trueta, Gastroenterology, Girona, Spain, ¹⁰Hospital Universitario Virgen del Rocío, Gastroenterology, Sevilla, Spain, ¹¹Hospital Universitario de Navarra, Gastroenterology, Pamplona, Spain, ¹²Hospital Clínico Universitario de Valencia, Gastroenterology, Valencia, Spain, ¹³Hospital Universitario de Torrejón, Universidad Francisco de Vitoria, Gastroenterology, Madrid, Spain, ¹⁴Hospital General Universitario Dr. Balmis, Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), CIBEREHD, Gastroenterology, Alicante, Spain, ¹⁵Hospital Universitario de Canarias, Gastroenterology, Santa Cruz de Tenerife, Spain, ¹⁶Complejo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain, ¹⁷Hospital Clínico Universitario de Valladolid, Universidad de Valladolid, Gastroenterology, Valladolid, Spain, ¹⁸Hospital Universitari y Politecnia La Fe, Gastroenterology, Valencia, Spain, ¹⁹Hospital Universitario La Paz, Facultad de Medicina, Universidad Autónoma de Madrid, Instituto de Investigación Hospital Universitario La Paz (IdiPAZ), Gastroenterology, Madrid, Spain, ²⁰Complejo

Hospitalario Universitario de Vigo, Research Group In Digestive Diseases, Galicia Sur Health Research Institute, SERGAS-UVIGO, Gastroenterology, Vigo, Spain, ²¹*Hospital Universitario de Bellvitge, Gastroenterology, L'Hospitalet de Llobregat, Spain,* ²²*Hospital de Santa Bárbara, Gastroenterology, Puertollano, Spain,* ²³*Hospital Universitari Mutua Terrassa, and CIBEREHD, Gastroenterology, Barcelona, Spain,* ²⁴*Hospital Universitario de Basurto, Gastroenterology, Bilbao, Spain,* ²⁵*Hospital Universitario de Galdakao, Instituto de Investigación Sanitaria Biobizkaia, Gastroenterology, Galdakao, Spain,* ²⁶*Hospital Universitario de Gran Canaria Dr. Negrín, Gastroenterology, Las Palmas de Gran Canaria, Spain,* ²⁷*Hospital Universitario de Fuenlabrada, Gastroenterology, Madrid, Spain,* ²⁸*Hospital Universitari Germans Trias i Pujol and CIBEREHD, Badalona, Spain,* ²⁹*Hospital Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón (IISGM), Facultad de Medicina, Universidad Complutense, Gastroenterology, Madrid, Spain,* ³⁰*Hospital Universitario Puerta de Hierro, Gastroenterology, Madrid, Spain*

Contact E-Mail Address: mjcasanova.g@gmail.com

Introduction: The EXIT trial showed there is no difference between inflammatory bowel disease (IBD) patients who were in remission and withdrew anti-TNF therapy, and those who maintained anti-TNF therapy with respect to the percentage of sustained remission at 12 months. However, data of the long-term outcomes are crucial.

Aims & Methods: Aims: To compare long-term risk of relapse in IBD patients in remission who withdrew anti-TNF therapy versus those who maintained anti-TNF therapy, to analyse the response to anti-TNF resumption in those patients who relapsed after anti-TNF withdrawal, and to evaluate the overall success of the anti-TNF resumption strategy.

Methods: This study is an extension of the follow-up from the EXIT trial. Patients included in EXIT trial were IBD patients who have achieved clinical remission for ≥ 6 months at standard anti-TNF dosage, with absence of significant endoscopic/radiological lesions, no previous IBD-related surgery, and ongoing immunomodulatory treatment. Patients were randomised either to maintain or to withdraw the anti-TNF therapy¹. The long-term outcomes of patients in sustained clinical remission who have completed the follow-up of EXIT trial per-protocol were analysed at the end of the EXIT trial. After that, patients were managed at the discretion of their physicians. Patients who were randomised in EXIT trial to continue with the anti-TNF comprised the maintenance arm (MA). For these patients, follow-up continued until either the anti-TNF resumption, or until the initiation of another biologic treatment or until the small molecule therapy (due to relapse or electively) or until the last visit (if no relapse occurred). Patients who were randomised in EXIT trial to withdraw the anti-TNF comprised the withdrawal arm (WA). For these patients, follow-up ended either at the time of relapse, at the withdrawal of anti-TNF treatment (electively, due to relapse, or adverse events), or at the last visit. The success of the anti-TNF resumption strategy was defined as the achievement and maintenance of clinical remission after restarting the anti-TNF therapy due to relapse, without experiencing adverse events or major complications (such as the need for surgery for IBD or the appearance of new perianal fistulas) that led to treatment withdrawal.

Results: 125 patients were included, 63 in MA and 62 in WA. Median follow-up was 12 and 26 months in MA and in WA, respectively ($p < 0.05$). The main characteristics of the study population are detailed in table 1. In MA, the cumulative incidence of relapse was 8% at 12 months, 47% at 24 months, and 65% at 36 months, whereas in the WA was 16% at 12 months, 39% at 24 months and 43% at 36 months of follow-up, ($p = 0.3$). The incidence rate of relapse was 22% (95% CI 14-31) and 19% (95% CI 13-26) per patient-year of follow-up in MA and WA, respectively. In the multivariate

analysis, having a fecal calprotectin at baseline of the EXIT trial $> 250 \mu\text{g/g}$ was the only variable associated with a higher risk of relapse ($\text{HR} = 3.94$, 95% CI = 1.92-8.06; $p < 0.0001$). Of the 29 patients of WA who relapsed, 26 patients (90%) resumed the same anti-TNF and 69% of them achieved clinical remission.

At the end of the follow-up, 16 out of 26 patients (62%) who restarted anti-TNF maintained remission, while 10 out of 26 patients (38%) discontinued anti-TNF: 4 due to non-response, 2 due to loss of response, and 4 due to adverse events. The proportion of adverse events was similar in the MA and the WA, 69% and 68%, respectively ($p > 0.05$).

Conclusion: In the long-term analysis of the outcomes of patients included in EXIT trial, the withdrawal of anti-TNF therapy in patients with IBD in remission was not associated with higher risk of relapse. Resumption of anti-TNF after relapse recapture remission in the majority of patients. The anti-TNF withdrawal approach was safe.

Variables	Maintenance arm N=63	Withdrawal arm N=62	P
-Mean age at inclusion, years (range)	41 (18-65)	42 (20-68)	0.5
-Mean age at diagnosis, years (range)	31 (10-58)	32 (12-65)	0.9
-Median time under current anti-TNF (years), IQR	2.8 (1.8-4.9)	2.6 (1.2-5.7)	0.7
-Median time in remission with current anti-TNF at standard dose (months), IQR	23.2 (13-41)	21.9 (9.2-37.4)	0.9
-Median disease duration at inclusion (months), IQR	77.2 (39-163)	100.8 (36.5-188)	0.4
Male gender, n (%)	36 (57)	42 (68)	0.2
Current smoker, n (%)	10 (16)	10 (16%)	0.9
Crohn's disease, n (%)	29 (46)	25 (40)	0.5
-L1, n (%)	9 (31)	7 (28)	
-L2, n (%)	9 (31)	6 (24)	0.7
-L3, n (%)	11 (38)	12 (48)	
-L4, n (%)	1 (3)	1 (3)	0.3
-B1, n (%)	20 (69)	23 (92)	
-B2, n (%)	7 (24)	2 (8)	0.09
-B3, n (%)	2 (7)	0 (0)	
-Perianal, n (%)	2 (6)	2 (6)	1
Ulcerative colitis, n (%)	39 (56)	39 (56)	
-Extensive, n (%)	25 (73)	20 (54)	1
-Left-sided, n (%)	8 (24)	16 (43)	
-Proctitis, n (%)	1 (3)	1 (3)	
Extraintestinal manifestations	13 (21)	8 (13)	0.2
Type of anti-TNF, n (%)			
-Adalimumab, n (%)	9 (14)	9 (15)	0.9
-Infliximab, n (%)	54 (86)	53 (85)	
Indication for the anti-TNF, n (%)			
-Refractoriness to immunomodulators, n (%)	18 (29)	20 (32)	
-Steroid-dependency, n (%)	22 (35)	19 (31)	0.7
-Steroid-refractoriness, n (%)	13 (21)	12 (19)	
-Top-down strategy, n (%)	1 (2)	4 (7)	
-Others, n (%)	9 (14)	7 (11)	
Prior intensification of current anti-TNF, n (%)	11 (18)	9 (15)	0.7
Median C-reactive protein, IQR	0.1 (0.1-0.3)	0.1 (0.1-0.4)	0.1
Faecal calprotectin $> 250 \text{ mg/g}$, n (%)	4 (7)	8 (15)	0.35

IQR, interquartile range; TNF, tumour necrosis factor

Table 1. Characteristics of the study population at baseline.

References: 1.

Chaparro M., Donday MG., Barreiro-de Acosta M., Domènech E., Esteve M., García-Sánchez V., et al. Anti-tumour necrosis factor discontinuation in inflammatory bowel disease patients in remission: study protocol of a prospective, multicentre, randomized clinical trial. *Therap Adv Gastroenterol* 2019;12. Doi: 10.1177/1756284819874202.

Disclosure: Manuel Barreiro-de Acosta has served as a speaker, consultant and advisory member for or has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, GALAPAGOS, Pfizer, Sandoz, Biogen, Fresenius, Lilly, Ferring, Faes Farma, Dr. Falk Pharma, Chiesi, Gebro Pharma, Adacety and Vifor Pharma.

María José Casanova, has received education funding from Pfizer, Takeda, Janssen, MSD, Dr. Falk, Shire, Ferring, Galápagos and Abbvie.

María Chaparro has served as speaker, consultant or research or educa-

tion funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Biogen, Gilead and Lilly.

Javier P. Gisbert has served as speaker, consultant, and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene/Bristol Myers, Gilead/Galapagos, Lilly, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Norgine and Vifor Pharma.

Ana Gutiérrez-Casbas has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Kern Pharma, Takeda, Janssen, Ferring, Faes Farma, Shire Pharmaceuticals, Tillotts, Pharma, Chiesi and Otsuka Pharmaceutical.

Marisa Iborra reports grants and personal fees from MSD, Janssen, Abbvie, Takeda, Kern and Chiesi, during the conduct of the study.

Eduardo Leo has received grants or honoraria for scientific activities, presentations or as a scientific advisor for MSD, Pfizer, Abbvie, Takeda, Janssen, Tillotts Pharma, Shire Pharmaceuticals, Ferring, Dr. Falk Pharma, Adacyte and Otsuka Pharmaceutical

Montserrat Rivero has served as a speaker or advisory member from Takeda, Janssen, Galapagos, Ferring and Pfizer.

Iago Rodríguez-Lago has received financial support for traveling and educational activities from or has served as an advisory board member for Abbvie, Adacyte, Celltrion, Chiesi, Danone, Ferring, Faes Farma, Janssen, Galapagos, MSD, Pfizer, Roche, Takeda, and Tillotts Pharma. IRL-L is supported by a research grant from Gobierno Vasco-Eusko Jaurlaritz [Grant No 2020111061] and by a research grant from Biobizkaia Bizkaia HRI [Grant No BCB/I/LIB/22/008].

Cristina Rubín de Céliz has received education funding from Ferring, Tillotts Pharma, Abbvie, Norgine, MSD, Pfizer, Takeda and Janssen.

Manuel Van Domselaar has received educational funding from Janssen, Kern Pharma, and Takeda.

Rest of authors have nothing to declare.

PP0558

THE REAL-WORLD TREATMENT PATTERNS AND CLINICAL OUTCOMES OF 5-AMINOSALICYLIC ACID TREATMENT IN KOREAN PATIENTS WITH ULCERATIVE COLITIS: A POPULATION-BASED RETROSPECTIVE STUDY

S.J. Park¹, S.W. Park², J.H. Cheon³

¹Yonsei University College of Medicine, Department of Internal Medicine and Institute of Gastroenterology, Seoul, South Korea,

²Ferring Pharmaceuticals Korea Co., Ltd., Seoul, South Korea,

³Yonsei University College Of Medicine, Department of Internal Medicine and Institute of Gastroenterology, Seoul, South Korea

Contact E-Mail Address: sjpark@yuhs.ac

Introduction: This retrospective study analysed the real-world use patterns and clinical outcomes of 5-aminosalicylic acid (5-ASA) treatment in Korean patients with ulcerative colitis (UC) based on the records from national health insurance claims database (NHICD).

Aims & Methods: The records of individuals aged ≥15 years, first diagnosed as having UC between 1 January 2009 and 30 September 2018, were considered eligible for the study if 5-ASA was prescribed for ≥30 days within six months after the diagnosis.

The data were extracted until the events of interest, patient's death, or 31 March 2019, whichever occurred earlier. The events of interest were defined as UC-related hospitalisation, UC-related surgery, and 5-ASA non-response, the latter corresponding to the prescription of steroids, immunosuppressants, and/or biological medications during the follow-up period. The yearly proportions of patients in each average daily dose (ADD) group,

i.e., rectal monotherapy (RM), oral low dose (<2 g/day) monotherapy (OML), oral standard-to-high dose (2 g/day to ≥3 g/day) monotherapy, oral low dose combination(oral+rectal) therapy (OCL), and oral standard-to-high dose combination(oral+rectal) therapy (OCSH) group, were presented. Odds ratio for prescribing high dose 5-ASA was calculated from a logistic regression model.

The incidence of the events of interest was expressed per 1000 person-years (PY). Hazard ratios for 5-ASA insufficient-response and UC-related hospitalisation in each ADD group were obtained from a Cox proportional hazard model, with OML as a reference group. Treatment adherence was expressed as a proportion of days covered (PDC) within the first 12 months from the prescription index date.

Results: The analysis included the data of 11,338 patients (mean age 42.15 years, 59.53% of males).

During a median observation period of 1,720 days, a tendency to a decrease in RM proportion was observed, along with an increase in the proportions of oral + rectal combination therapies. The odds of prescribing high-dose 5-ASA increased significantly since 2013.

The proportion of OCSH increased from 18.1% in 2009 to 39.5% in 2018, whereas OML and OCL proportions decreased from 17.5% to 6.6% and from 11.6% to 6.6%, respectively. Incidence rates of 5-ASA insufficient-response and UC-related hospitalization were significantly lower in the RM group than in the OML group, with no significant differences between the OML group and other ADD groups. Mean PDC in overall population was 0.70, ranging from 0.65 to 0.76 across the ADD groups. 82.4% of patients responded to 5-ASA, and Mean PDC in overall population was 0.70, ranging from 0.65 to 0.76 across the ADD groups.

Conclusion: A tendency to a more frequent prescription of standard to high-dose 5-ASA as combination therapy was observed in 2009-2018, along with a decrease in RM prescription frequency, which is consistent with the current guidelines.

Disclosure: Nothing to disclose.

PP0559

MIRIKIZUMAB PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIPS IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE IN PHASE 2 AND 3 STUDIES

L. Chua¹, Y. Otani¹, S. Friedrich¹, F. Durand¹, X. Zhang¹

¹Eli Lilly and Company, Indianapolis, United States of America

Contact E-Mail Address: otani_yuki@lilly.com

Introduction: Mirikizumab (MIRI) is a humanized anti-interleukin-23-p19 monoclonal antibody (mAb) approved for ulcerative colitis (UC) with demonstrated efficacy for Crohn's disease (CD) in Phase 2 (AMAG, NCT02891226) and Phase 3 (VIVID-1, NCT03926130) trials.^{1,2} This analysis characterized MIRI pharmacokinetic (PK) properties and exposure-response (ER) relationships in adults with moderately to severely active CD using data from 2 trials.

Aims & Methods: Patients received 12-week MIRI induction (200, 600 or 1000 mg [AMAG] or 900 mg [VIVID-1] intravenously [IV] every 4 weeks [Q4W]), followed by MIRI maintenance (200, 600 or 1000 mg IV [AMAG], or 300 mg administered subcutaneously (SC) [AMAG and VIVID-1] Q4W) up to Week (W)52. PK parameters were estimated by non-linear mixed-effects modeling. Covariate effects on MIRI exposure were evaluated using simulation-based estimations. The exposure efficacy model included data from participants who had model-predicted average drug concentration during multiple dosing. Clinical efficacy at W12 was compared with AMAG graphically and models were conducted on primary endpoints. ER for patients achieving endoscopic response by Simple Endoscopic Score for CD (SES-CD) at W12 and W52 were assessed using logistic regression models.

Results: MIRI PK was best described by a linear two-compartment model with first-order absorption. Population (PopPK) model-estimated parameters were consistent across AMAG and VIVID-1 (Table). AMAG indicated a near-maximal efficacy for doses between 600 and 1000 mg IV for endoscopic response by SES-CD at W12, suggesting that 900 mg IV in VIVID-1 would produce near-maximal effect for W12 endpoints. Linear relationships between exposure and W12 endoscopic response by SES-CD best described observed data in VIVID-1. In AMAG, model-based analyses of the relationships between exposure and W52 efficacy measures showed no ER trend across MIRI maintenance doses, supporting 300 mg SC Q4W for VIVID-1 Maintenance Period. Linear relationships between exposure and endoscopic response by SES-CD on a logistic scale best described observed data in VIVID-1 at W52. None of the covariates evaluated in PK or ER modelling were considered clinically relevant.

	CL (L/h)	Albumin effect on CL	Q (L/h)	BLBW effect on CL and Q	V _c (L)	V _p (L)	BLBW effect on V _c and V _p	F ² %	BL BMI effect on F
VIVID-1 Population estimate	0.0197 ^a	-0.0200	0.00921 ^b	0.268	2.78 ^b	1.61 ^b	0.445	38.8	-0.0354
[95% CI, % SEE]	[0.0179 to 0.0230, 4.53]	[-0.0228 to -0.0173, 7.25]	[0.00529 to 0.0252, 26.6]	[0.150 to 0.378, 23.1]	[2.71 to 2.82, 0.978]	[1.13 to 2.85, 16.5]	[0.372 to 0.517, 9.53]	[33.8 to 45.8, 5.62]	[-0.0469 to -0.0263, 13.9]
AMAG Population estimate	0.0217 ^a	-0.754	0.00884 ^c	0.538	3.31 ^d	1.75 ^d	0.543	0.334 ^e	-0.0318
[95% CI, % SEE]	[0.0203 to 0.0306, 6.27]	[-0.976 to -0.598, 12.0]	[0.00605 to 0.0202, 42.3]	[0.348 to 0.745, 19.7]	[3.08 to 3.45, 2.21]	[1.49 to 5.67, 18.2]	[0.330 to 0.721, 18.1]	[0.296 to 0.445, 8.44]	[-0.0434 to -0.0206, 18.2]

^aEstimated using bootstrap; ^bCL=CL*(BLBW/65.0)^{0.288}*(1+Albumin-44.57)*0.02*(BL CRP/7.41)^{0.085}; Q₀=Q*(BLBW/65.0)^{0.288}; ^cV_c=V_c*(BLBW/65.0)^{0.445}; V_p=V_p*(BLBW/65.0)^{0.445}; ^dEstimate is on the logit parameter for bioavailability; ^eCL=CL*(BLBW/71.8)^{0.538}(BL SES-CD/12)^{0.227}(Albumin/44.0)^{0.754}; CL₀=CL*(BLBW/71.8)^{0.538}; V_{c0}=V_c*(BLBW/71.8)^{0.543}; V_{p0}=V_p*(BLBW/71.8)^{0.543}; F₀=F*(1+(VL BMI -24.75)^{0.0318})

BL=baseline; BW=body weight; BMI=body mass index; CI=confidence interval; CL=clearance; CV=geometric coefficient of variation; F=bioavailability; i=individual; L/h=Liters per hour; Q=intercompartmental clearance; SEE=standard error of the estimate; SES-CD=Simple Endoscopic Score for CD; V_c=volume of distribution of the central compartment; V_p=volume of distribution of the peripheral compartment

Conclusion: MIRI PK characteristics in AMAG and VIVID-1 were consistent with UC studies and typical of mAbs.³ ER analyses showed MIRI induction dose of 900 mg IV at W0, W4, and W8 followed by maintenance dose of 300 mg SC Q4W resulted in near-maximal efficacy in VIVID-1. These findings support MIRI dosing regimen proposed for patients with moderately to severely active CD. PK and ER data suggested that no adjustments based on patient factors are warranted.

References:

- 1. Sands B, et al. *Gastroenterology*. 2022;162:495-508.
 - 2. Ferrante M, et al. *J Crohns Colitis*. 2024;18:i7-i9.
 - 3. Chua L, et al. *Clin Pharmacokinet*. 2023;62:1479-1491.
- Disclosure:** L. Chua, Y. Otani, F. Durand and X. C. Yang are current employees of and shareholders: Eli Lilly and Company; S. Friedrich is a former employee of: Eli Lilly and Company.

PP0560
EFFECTS OF MIRIKIZUMAB VERSUS PLACEBO ON HISTOLOGIC INFLAMMATION EVALUATED BY COMPREHENSIVE ASSESSMENT IN 5 INTESTINAL SEGMENTS IN A RANDOMIZED CONTROLLED PHASE 3 TRIAL OF PARTICIPANTS WITH CROHN’S DISEASE

V. Jairath¹, F. Magro², G. De Hertogh³, B.G. Feagan⁴, N. Harpaz⁵, T. Hisamatsu⁶, G. D’Haens⁷, R. Pai⁸, Z. Lin⁹, N. Morris⁹, M. Protic⁹, E. Hon⁹, C. Owen⁹, R. Escobar⁹, W. Reinisch¹⁰
¹Western University, Department of Medicine, Division of Gastroenterology, London, Canada, ²Centro Hospitalar São João, Gastroenterology, Porto, Portugal, ³Faculty of Medicine, KU, Department of Imaging and Pathology, Leuven, Belgium, ⁴The University of Western Ontario, Gastroenterology, London, Canada, ⁵Icahn School of Medicine at Mount Sinai, Departments of Pathology and Gastroenterology, New York, United States of America, ⁶Kyorin University School of Medicine, Tokyo, Japan, ⁷Inflammatory Bowel Disease Centre, Amsterdam University Medical Centers, Amsterdam, Netherlands, ⁸Mayo Clinic, Department of Laboratory Medicine and Pathology, Phoenix, United States of America, ⁹Eli Lilly and Company, Indianapolis, United States of America, ¹⁰Medical University of Vienna, Dep. of Internal Medicine IV, Division of Gastroenterology and Hepatology, Wien, Austria

Contact E-Mail Address: vjairath@uwo.ca
Introduction: Histologic inflammation persists in up to one quarter of patients with Crohn’s Disease (CD) despite endoscopic mucosal healing. Responsiveness of histologic inflammation to treatment is an evolving outcome measure in CD. Mirikizumab (MIRI) increased histologic response (H-Res) and remission (H-Rem) relative to placebo (PBO) in the Phase 2 SERENITY trial.¹

Aims & Methods: We compared the effect of MIRI on H-Res and H-Rem at week (W)12 and W52 to PBO by composite endpoints of response (clinical response by Patient-Reported Outcome [PRO] at W12 and W52 H-Res) and of remission (clinical response by PRO at W12 and W52 H-Rem) at W52. The overall population of patients with moderately to severely active CD, patients without prior biologic failure (non-BF), and patients with prior BF were assessed, using data from the Phase 3 VIVID-1 trial (NCT03926130). Two biopsy specimens from each of 5 intestinal segments (1 ileal and 4 colonic) were obtained from the edge of the ulcers, or the most inflamed mucosa from randomized patients at screening, W12, and W52. Criteria for H-Res were the absence of epithelial neutrophils and epithelial damage, erosions, and ulceration or ≥50% decrease in either the sum of the 5 segments of Robarts Histopathology Index or the Global Histologic Disease Activity Score. H-Rem was defined as complete absence of mucosal neutrophils (in epithelium and lamina propria), and no epithelial damage, erosions, and ulcers; these criteria had to be met in all biopsy specimens. Clinical response by PRO was defined as ≥30% decrease in stool frequency and/or abdominal pain with neither score worse than baseline. H-Res, H-Rem, composite H-Res, and composite H-Rem in all patients were pre-specified, non-multiplicity-controlled endpoints. Analyses in non-BF and BF patients were post hoc.

Results: At W12, treatment with MIRI resulted in nominally statistically significantly higher rates of H-Res in all three patient groups analyzed (p<.001) (Table). At W12, differences between MIRI vs PBO were nominally significant in achieving H-Rem in all patients (p<.01) and in non-BF and BF patients (both p<.05). For W52 composite H-Res, differences between MIRI vs PBO were nominally statistically significant in all patient groups examined (p<.001). For W52 composite H-Rem, nominally statistically significant differences between MIRI vs PBO were observed in all patients (p<.001), in non-BF patients (p<.05), and in BF patients (p<.001).

	All patients			Without Prior Biologic failure			With Prior Biologic Failure		
	PBO (N=199)	MIRI (N=579)	Difference (95% CI)	PBO (N=91)	MIRI (N=273)	Difference (95% CI)	PBO (N=88)	MIRI (N=255)	Difference (95% CI)
W12 H-Res	30.7	52.7	22.2 (14.6-29.7)***	37.4	58.6	21.2 (9.7-32.8)***	22.7	47.8	25.1 (14.4-35.8)***
W12 H-Rem	12.1	22.1	10.2 (4.7-15.7)**	14.3	27.5	13.2 (4.3-22.1)*	4.5	12.2	7.6 (1.7-13.5)*
W52 Composite H-Res	16.1	44.4	28.2 (21.6-34.7)***	26.4	46.5	20.1 (9.3-31.0)***	6.8	45.9	39.1 (31.0-47.1)***
W52 Composite H-Rem	8.5	23.3	14.7 (9.5-19.9)***	14.3	24.9	10.6 (1.8-19.5)*	2.3	21.6	19.3 (13.4-25.2)***

Data are %; *p<.05; **p<.01; ***p<.001 vs PBO

"Without prior biologic failure" and "With prior biologic failure" were subgroups of all patients with active histologic disease at baseline. P-values for "All patients" were from the Cochran-Mantel-Haenszel test adjusting for baseline covariates. P-values for the "Without prior biologic failure" and "With prior biologic failure" subgroups were from the Fisher's exact test.

CI=confidence interval; H=histologic; MIRI=mirikizumab; PBO=placebo; Rem=remission; Res=response; W=week

Conclusion: Based upon strict definitions that applied to all 5 intestinal segments, MIRI achieved nominally significantly higher rates of H-Res and H-Rem compared to PBO in all patients at W12 and W52. The statistical difference was more pronounced in the BF population after 1 year of treatment.

References:

1. Magro F, et al. *Clin Gastroenterol Hepatol*. 2023;S1542-3565(23)00948-5.

Disclosure: V. Jairath received fees or grant and/or research support and/or served as a consultant and/or speaker for: AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Flagship Pioneering, Fresenius Kabi, Galapagos NV, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Metacrine, Mylan, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Sorriso Pharmaceuticals, Takeda, Teva, Topivert, Ventyx Biosciences, Vividion Therapeutics; F. Magro served as a speaker for: AbbVie, Arena, Biogen, Bristol Myers Squibb, Eli Lilly and Company, Falk, Ferring Pharmaceuticals, Hospira, Janssen, Laboratórios Vitoria, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, UCB, Vifor; G De Hertogh received fees for clinical trial activities with Centocor Inc; and received consultancy fees from: Eli Lilly and Company, MRM Health; B. Feagan was a consultant for: AbbVie, AbolierS Pharma, Agomab Therapeutics, Alliantera, Amgen, AnaptysBio, Applied Molecular Transport, Arena Pharmaceuticals, Avoro Capital Advisors, Atomwise, BioJamp, Biora Therapeutics, Boehringer Ingelheim, Boxer, Celgene/BMS, Celsius Therapeutics, Connect BioPharma, Cytoki Pharma, Disc Medicine, Duality, EcoR1, Eli Lilly and Company, Equillium, Ermium Therapeutics, First Wave BioPharma, First Word Group, Galapagos NV, Galen Atlantica, Genentech/Roche, Gilead Sciences, Gossamer Pharma, GlaxoSmithKline, Hinge Bio, Hot Spot Therapeutics, InDex Pharma, Imhotex, Immunic Therapeutics, JAKAcademy, Janssen, Japan Tobacco, Kaleido Biosciences, Landos Biopharma, Ladiant, L.E.K. Consulting, Lenczner Slaght, LifeSci Capital, Lument AB, Millennium Pharmaceuticals, MiroBio, Morgan Lewis, Morpich Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Play to Know AG, Progenity, Protagonist Therapeutics, PTM Therapeutics, Q32 Bio, Rebiotix, Redx Pharma, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen Inc., Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared, Viatrix, Ysios, YSOPIA Bioscience, and Zealand Pharma; was on the speaker's bureau for: AbbVie, Janssen, and Takeda; a member of the Scientific Advisory Board, DSMB for: AbbVie, Amgen, AMT, AnaptysBio, Axio Research, Boehringer Ingelheim, Celgene/

BMS, Ecor1Capital, Eli Lilly and Company, Genentech/Roche, GlaxoSmithKline, InDex Pharma, Janssen, MiroBio, Morpich, Origo BioPharma, Pfizer, Progenity, Prometheus, Redx Pharma, Sanofi, Takeda, Tillotts Pharma, and Teva; a stock shareholder of: Gossamer Pharma; and an employee as Senior Scientific Director of: Western University and Alimentiv; N. Harpaz served as an advisory board member and/or consultant for: AbbVie, Bristol Meyers Squibb, Eli Lilly and Company, PathAI Inc; T. Hisamatsu received lecture fees from: AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceutical K.K., JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; has received honoraria as an advisory board member or consultant for: AbbVie, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Pfizer, Takeda; and has received pharmaceutical/research grants from: AbbVie, Alfresa Pharma, Daiichi Sankyo, EA Pharma, JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nichi-Iko Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, Zeria Pharmaceutical; G. D'Haens has been an advisor for: AbbVie, AgomAb Therapeutics, AstraZeneca, Avaxia Biologics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, Celltrion, Eli Lilly and Company, Exelium Biosciences, Galapagos NV, GlaxoSmithKline, Immunic Therapeutics, Johnson & Johnson, Merck Sharp & Dohme, Pfizer, ProciseDx, ProDigest, Progenity, Samsung Bioepis, Sanofi, Takeda, Tillotts Pharma AG, Ventyx; and received speaker's fees from: AbbVie, Johnson & Johnson, Takeda, Pfizer, Tillotts Pharma AG; R. Pai received consulting fees from: Alimentiv Inc, Allergan, BRACCO. Z. Lin, N. Morris, M. Protic, E. Hon, C. Owen, and R. Escobar are employees and shareholders of: Eli Lilly and Company; W. Reinisch received lecture and consulting fees from and/or served as an advisory board member for: AbbVie, Actelion, Alpha Wasserman, AstraZeneca, Cellerix, Cosmo Pharmaceuticals, Ferring Pharmaceuticals, Genentech, Grunenthal, Johnson & Johnson, Millennium, Merck, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos, Schering-Plough, Salix Pharmaceuticals, Takeda, UCB Pharma, Vifor Pharma.

PP0561

EVALUATION OF AN EXERCISE PROGRAM FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PILOT STUDY

E. Visser¹, N. van de Pol², D. Leemreis- van Noord³, V. de Jonge⁴, C.J. van der Woude⁵, A.C. de Vries⁶, R. West⁷

¹Franciscus Gasthuis & Vlietland, Gastroenterology, Rotterdam, Netherlands, ²Erasmus MC, Gastroenterology and Hepatology, Rotterdam, Netherlands, ³Franciscus Gasthuis & Vlietland, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁴Albert Schweitzer Ziekenhuis, Gastroenterology and Hepatology, Dordrecht, Netherlands, ⁵Erasmus Medisch Centrum, Gastroenterology, Rotterdam, Netherlands, ⁶Erasmus MC University Medical Center, Gastroenterology And Hepatology, Rotterdam, Netherlands, ⁷Sint Franciscus Gasthuis, Gastroenterology, Rotterdam, Netherlands

Contact E-Mail Address: e.visser6@franciscus.nl

Introduction: Patients with inflammatory bowel disease (IBD) tend to be less physical active, whilst maintaining an active lifestyle has been associated with enhanced disease control, diminished fatigue, and improved quality of life (1,2,3).

Aims & Methods: This study aims to evaluate the feasibility and potential impact of a specially designed exercise program for IBD patients. Patients with IBD participated in a 16-week exercise program based on their individual fitness level, between March and June 2023. All outcomes were measured before and after the program. Body composition included, BMI, muscle mass and fat percentage. Physical fitness was based on

performance of the Fundamental Motor Skills. Effect on quality of life, fatigue and disease control was assessed using validated questionnaires. For statistical analyses, a paired t-test or Wilcoxon matched paired rank test was used.

Results: In total 32 patients were included in the exercise program. Mean age was 50.1 years (SD 12.3), 37.5% were male, and 50% had Crohn's disease (Table 1).

The full program was completed by 84.4% of all patients, and average rating of the program was 8.6 out of 10. After 16 weeks, muscle mass improved compared to baseline ($P=0.020$) and fat percentage decreased ($P=0.003$). Physical fitness improved significantly; lower body strength and coordination ($P=0.006$), flexibility ($p=0.002$), speed and endurance ($P<0.001$). Quality of life improved with on average 8 points on the Inflammatory Bowel Disease Questionnaire. The program significantly improved fatigue scores ($P=0.013$). Disease control showed no significant improvement after the program.

		Overall (n=32)
Mean age, y (SD)		50.1 (12.3)
Male		12 (37.5)
Smoking	Current	3 (9.4)
Physical activity, d (IQR) ^{a,b}	Light / Moderate / High	4 (2-7) / 2 (1-4) / 1 (0-2)
Diagnosis	Crohn's disease	16 (50)
	Ulcerative Colitis	16 (50)
Median diagnosis age, y (IQR)		34.5 (25-47.3)
Abdominal surgery (Yes)		10 (31.1)
Stoma (Yes)		2 (6.3)

Table 1. Baseline characteristics

Note: data are described as numbers (percentages) unless stated otherwise.
Abbreviations: CD, Crohn's disease; d, days; IQR, interquartile range; n, number; SD, standard deviation; UC, ulcerative colitis; y, year.
^a Physical activity is based on the patients who filled in the questionnaire (n=25)
^b Physical activity is categorized in light, moderate and high. Light is walking. Moderate is cycling, exercising at a low intensity level. High exercise is working out or dancing.

Conclusion: This pilot study shows that a specially designed exercise program is feasible and has a positive effect on IBD patients. These findings underline the importance of physical activity in IBD patients and can be used as an initial step towards integrating an exercise program in standard IBD care.

References:

1. Fagan G, Osborne H, Schultz M. Physical Activity in Patients with Inflammatory Bowel Disease: A Cross-Sectional Study. *Inflamm Intest Dis*. 2021;6(2):61-9.
2. Agrawal T, Acquah I, Dey AK, Glassner K, Abraham B, Blankstein R, et al. Prevalence of cardiovascular risk factors in a nationally representative adult population with inflammatory bowel disease without atherosclerotic cardiovascular disease. *Am J Prev Cardiol*. 2021;6:100171.
3. Mareschal J, Douissard J, Genton L. Physical activity in inflammatory bowel disease: benefits, challenges and perspectives. *Curr Opin Clin Nutr Metab Care*. 2022;25(3):159-66.

Disclosure: Conflicts of interest: N. Van de Pol, E.H. Visser, D. Leemreis-van Noord, and V. de Jonge have nothing to declare; C.J. van der Woude has received grants from ZonMW, Falk and Pfizer, has received consulting fees from Janssen, Galapagos, and Pfizer, has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Ferring and AbbVie and had leadership roles in the European Crohn's & Colitis organisation, United European Gastroenterology council and the Dutch Association for Gastroenterology (NVGE); A.C. de Vries has served on advisory boards for Takeda, Janssen, Bristol Myers Squibb, Abbvie, Pfizer, and Galapagos and has received unrestricted research grants from Takeda, Janssen, and Pfizer outside the submitted

work; R.L. West has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Ferring, Pfizer, Galapagos, AbbVie and Janssen.

PP0562
IMPACT OF MIRIKIZUMAB ON CLINICALLY MEANINGFUL IMPROVEMENTS IN FATIGUE AS MEASURED BY FACIT-F IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

P. Bossuyt¹, M. Regueiro², M. Fischer³, K. Traxler⁴, G. Yu⁴, M. Protic⁴, K. Tsilkos⁴, A. Vadharaya⁴, T. Hisamatsu⁵, P. Juillerat⁶
¹Imelda General Hospital, Bonheiden, Belgium, ²Cleveland Clinic, Cleveland, United States of America, ³IUPUI, Gastroenterology, Indianapolis, United States of America, ⁴Eli Lilly and Company, Indianapolis, United States of America, ⁵Kyorin University School of Medicine, Tokyo, Japan, ⁶Intesto Crohn's and Colitis Center, Bern and Fribourg, Switzerland

Contact E-Mail Address: peter.bossuyt@imelda.be
Introduction: Fatigue is a debilitating multifactorial symptom experienced by many patients with Crohn's disease (CD).¹ Topline efficacy data of mirikizumab (MIRI), an anti-interleukin-23p19 antibody, vs. placebo (PBO) and ustekinumab (UST) in patients with moderately to severely active Crohn's disease in the Phase 3 VIVID-1 study were previously reported.²⁻⁴

Aims & Methods: This analysis assesses the impact of MIRI vs. PBO in improving fatigue and the correlation of patient variables with fatigue severity at baseline (BL) in the VIVID-1 study. Participants were randomized 6:3:2 to MIRI (900 mg intravenous at Week [W]0, W4, and W8, then 300 mg subcutaneous every 4W from W12-W52), UST or PBO. Fatigue was assessed via the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire (scale 0-52, higher scores indicating less fatigue,⁵ meaningful within-patient change identified as a 6-9 point [pt] increase). At W12 we report the proportion of PBO (N=199) and MIRI (N=579) patients achieving FACIT-F ≥6- or ≥9-pt increase from BL. Comparisons with PBO at W52 used composite (C) endpoints: clinical response by Patient-Reported Outcome at W12 (≥30% decrease in stool frequency [SF] or abdominal pain [AP], and neither worse than BL), and FACIT-F increase of either ≥6-pts (C≥6) or ≥9-pts (C≥9) by W52. *p*-Values were calculated via Cochran-Mantel-Haenszel test adjusted by biologic-failed status (yes/no); BL Simple Endoscopic Score for CD (SES-CD) total score (<12, ≥12); either BL SF ≥7 and/or AP ≥2.5 (yes or unknown/no).

The pooled population of patients randomized to PBO or MIRI at BL, excluding those with missing data, with a range of patient variables was analyzed by the random forest method to assess the correlation with fatigue severity. Variables were ranked by importance by the random forest method and Pearson correlation coefficients (*r*) calculated for continuous variables.

Results: At W12, 31.2% (PBO) and 43.0% (MIRI) patients achieved FACIT-F ≥6-pt increase ($p<0.005$) and 22.1% (PBO) and 32.6% (MIRI) patients achieved FACIT-F ≥9-pt increase ($p<0.01$). At W52, 20.1% (PBO) and 34.9% (MIRI) patients met C≥6 ($p<0.0005$) and 15.6% (PBO) and 28.5% (MIRI) patients met C≥9 ($p<0.0005$). A strong association ($r>0.5$) was found between fatigue severity and Inflammatory Bowel Disease Questionnaire (IBDQ), and with the emotional functioning domain of IBDQ and Mental Component Summary (MCS) of Short Form (SF)-36 (Table).

There was a weak association ($r=0.1-0.3$) with AP score, SF score, and Urgency Numeric Rating Scale, and insubstantial association ($r<0.1$) with objective markers of inflammation, including SES-CD, C-reactive protein, and fecal calprotectin.

Variable	Importance value based on random forest	Pearson correlation coefficient	Association based on Pearson correlation
IBDQ-systemic symptoms score	56.756	0.784	Strong
SF-36 Mental Component Summary	18.816	0.654	Strong
IBDQ-emotional functioning score	12.299	0.686	Strong
SF-36 Physical Component Summary	10.423	0.577	Strong
Inflammatory Bowel Disease-Disability Index score	5.951	-0.567	Strong
IBDQ-social functioning score	3.529	0.602	Strong
IBDQ-bowel symptoms score	1.510	0.538	Strong
Patient Global Rating of Severity score	0.472	-0.307	Moderate
Urgency Numeric Rating Scale	0.342	-0.136	Weak

Table: Correlation of highest ranked BL variables with FACIT-F

Conclusion: MIRI showed a nominally clinically significant improvement in fatigue vs. PBO at W12 and a nominally statistically higher improvement in composite endpoints vs. PBO at W52. At BL, fatigue was not associated with objective inflammatory markers of disease severity or with typical CD symptoms. The observed strong association between fatigue and MCS of SF-36 and the emotional functioning domain of IBDQ implies bidirectional effects of brain-gut interactions that are not well understood.

References:

1. D'Silva A, et al. *Clin Gastroenterol Hepatol.* 2022;20:995-1009.
2. Ferrante M, et al. *J Crohn's Colitis.* 2024;18:i7-i9.
3. Jairath V, et al. *J Crohn's Colitis.* 2024;18:i62-i64.
4. Travis S, et al. *J Crohn's Colitis.* 2024;18:i21-i23.
5. Tinsley A, et al. *Aliment Pharmacol Ther.* 2011;34:1328-1336.

Disclosure: P. Bossuyt has received financial support for research from: AbbVie, Amgen, Janssen, Pfizer, and Viartis; lecture fees from: AbbVie, Bristol Myers Squibb, CAG, Celltrion, Eli Lilly and Company, EPGS, Galapagos NV, Globalport, Janssen, Materia Prima, Pentax, Scope, and Takeda; and advisory board fees from: AbbVie, Bristol Myers Squibb, Celltrion, CIRC, Dr. Falk Pharma Benelux, Eli Lilly and Company, Galapagos NV, Janssen, Pentax, PSI-CRO, Roche, Takeda, and Tetrameros; M. Regueiro has served as an advisor and/or consultant for: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Genentech, Gilead Sciences, Janssen, Organon, Pfizer, Prometheus Therapeutics and Diagnostics, Salix Pharmaceuticals, Takeda, and UCB Pharma; M. Fischer has received consulting fees from: AbbVie, Bristol Myers Squibb, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Pfizer, Rebiotix, Scioto Biosciences, and Seres Therapeutics; K. Traxler, G. Yu, M. N. Protic, K. Tsilkos, and A. Vadhariya are employees and shareholders of: Eli Lilly and Company; T. Hisamatsu has received lecture fees from: AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceutical K.K., JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; has received honoraria as an advisory board member or consultant for: AbbVie, Bristol Myers Squibb, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Pfizer, and Takeda; and has received pharmaceutical/research grants from: AbbVie, Boston Scientific, Daiichi Sankyo, EA Pharma, Kissei Pharmaceutical, JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nichi-Iko Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical; P. Juillerat has received fees for lectures and consulting/advisory board from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly and Company, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Merck Sharp & Dohme, Pfizer, Pierre Fabre, Sandoz, Takeda, Tillotts Pharma AG, and UCB Pharma.

PP0563

PSYCHOLOGICAL INTERVENTIONS IMPROVE MENTAL HEALTH-RELATED OUTCOMES IN PATIENTS WITH INFLAMMATORY DIGESTIVE DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

D.-E. Floria^{1,2}, B. Teutsch³, B. Fogarasi¹, E. Tari⁴, L. Szabó¹, D.S. Veres^{1,5}, A.S. Bognár¹, B. Sikó¹, D. Dohos^{6,7}, B. Eross¹, M.F. Juhász^{3,7}, K. Ocskay¹, P. Hegyi^{6,1}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, ³Medical School, University of Pécs, Institute for Translational Medicine, Pécs, Hungary, ⁴Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁵Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁶Institute for Translational Medicine, University of Pécs, Medical School, Department of Medicine, Pécs, Hungary, ⁷Heim Pál National Pediatric Institute, Budapest, Hungary

Contact E-Mail Address: iovdiana95@gmail.com

Introduction: Inflammatory digestive diseases can have a major impact on the physical and mental wellbeing of affected patients. Psychosocial factors can alter the behaviour linked to disease and influence treatment outcomes.

Aims & Methods: The aim of this systematic review and meta-analysis was to assess the efficacy and safety of psychological interventions on depression, anxiety, and stress in patients with inflammatory digestive diseases. The study protocol was prospectively registered on PROSPERO (CRD42021282965). The systematic search was conducted on April 1st, 2023 in three medical databases (PubMed, CENTRAL, Embase). Randomized controlled trials (RCTs) that investigated the effects of various psychological interventions on mental and physical health in patients with all types of inflammatory digestive diseases were included. Outcomes were assessed at the end of therapy and at various timepoints during the follow-up period (short-, mid- and long-term follow-up). Owing to the differences in scales and questionnaires, the standardised mean difference (SMD) was used to pool effect sizes, with its corresponding 95% confidence interval (CI). Higgins and Thompson's I^2 statistics were used to assess heterogeneity.

Results: We included 24 RCTs that investigated the effect of psychological interventions on depressive symptoms, totalling 1572 participants. The pooled analysis found that psychological interventions resulted in a moderate reduction of depression compared to controls (SMD -0.46; 95% CI: -0.75; -0.18; I^2 87%). Data from 19 RCTs with 1593 patients also demonstrated a moderate reduction in anxiety symptoms in subjects undergoing psychological interventions (SMD -0.58; 95% CI: -0.94; -0.22; I^2 90%). The pooled analysis of 13 RCTs totalling 772 participants found that psychological therapy was associated with a moderate decrease in stress (SMD -0.53; 95% CI: -1.04; -0.03; I^2 85%). Additional analysis of follow-up data showed that benefits resulting from treatment gradually decrease, showing no significant difference at the end of the long-term follow-up period.

Conclusion: Psychological interventions effectively improve mental health-related outcomes in patients with inflammatory digestive diseases. Since benefits from therapy seem to decrease during the follow-up period, repeated interventions may be necessary.

Disclosure: Nothing to disclose.

PP0564

HOSPITALIZATION AND EMERGENCY DEPARTMENT VISITS AMONG INDIVIDUALS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH INFLIXIMAB: PRELIMINARY DATA FROM CAN-AIM

M. Birck¹, L. Lukusa¹, A. Neville¹, L. Wilhelm², W. Afif^{3,4}, N. Narula⁵, Y. Leung⁶, H. Singh⁷, S. Bernatsky^{1,4}

¹Research Institute of the McGill University Health Centre, Montreal, Canada, ²Canadian Arthritis Patient Alliance, Kings Country, Canada, ³McGill University Health Center, Gastroenterology, Montreal, Canada, ⁴McGill University, Montreal, Canada, ⁵McMaster University, Medicine, Hamilton, Canada, ⁶University of British Columbia, Vancouver, Canada, ⁷University of Manitoba, Max Grady College of Medicine, Winnipeg, Canada

Contact E-Mail Address: waqqas.afif@mcgill.ca

Introduction: Infliximab is used to treat inflammatory bowel disease (IBD) but may be associated with adverse events such as infections. We describe hospitalization and emergency department (ED) visits among IBD patients using infliximab bio-originator (INF-O) or biosimilar (INF-B).

Aims & Methods: We used data from Canadian IBD Research Consortium (CIRC) cohorts contributing to CAN-AIM's biosimilar registry, a pan-Canadian clinical registry of biosimilar/bio-originator users. We included people diagnosed with IBD who initiated infliximab between 2019-2023. Our outcome was self-reported hospitalization or ED visits, any time from INF initiation until outcome, treatment discontinuation or last information available. Categorical variables are presented as absolute numbers (percentage) and continuous as median (interquartile range, IQR). Kaplan-Meier curves with log-rank test and Cox regression model were used for time to event analyses for first hospitalization or ED - adjusted for sex and age at INF initiation.

Results: Of 158 individuals (78% INF-B), 53% had Crohn's and 47% ulcerative colitis. Individuals were 54% male, 85% Caucasian, age at INF initiation at 37 years; 28% were using prednisone at enrolment. 16% were hospitalized at least once (first hospitalization within a median follow-up of 17 months (IQR 7-25) and 25% had at least one ED visit (first ED occurred at a median of 13 months, IQR 5-26). A total of 45 hospitalizations and 61 EDs were recorded. Most ED visits were due to IBD flare (n=33), infections (n=9), and other reasons (n=15). Most hospitalizations were for IBD-related surgery (n=19), IBD flare (n=16), and infections (n=7). Time from treatment initiation to first hospitalization or first ED was similar for INF-B and INF-O. Compared to INF-O, aHR for first hospitalization was 0.64 (95%CI 0.27-1.50) and ED was 0.72 (0.36-1.43) for INF-B.

Conclusion: In this real-world dataset, almost one-third of infliximab users for IBD had hospitalization or ED visits, often due to IBD flare, IBD-related surgery, and infections. We noted no clear differences between biosimilars and bio-origins, though limited sample size precluded precision.

Disclosure: Author disclosures (speaker, advisory board and/or grants): WA (Abbvie, Amgen, BMS, Dynacare, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Prometheus, Sandoz, Sanofi, Takeda); NN (Janssen, Abbvie, Takeda, Pfizer, Merck, Sandoz, Novartis, Fresenius Kabi, Amgen, Celltrion, Viatris, Innomar Strategies, Iterative Health, and Ferring); YL: (BMS; Janssen, Abbvie, Frenius Kabus; Amgen; Takeda, Pfizer, Lilly, Pendopharm; BioJamp); HS (Amgen Canada, Roche Canada, Sandoz Canada, Takeda Canada, Pendopharm Inc and Guardant Health, Inc); MGB, LL, AN, LW, SB: nothing to disclose.

PP0565

DISEASE CHARACTERISTICS ASSOCIATED WITH BOWEL URGENCY IN CROHN'S DISEASE; RESULTS FROM THE PHASE 3 VIVID-1 TRIAL

G.R. D'Haens¹, B.E. Sands², V. Jairath³, S. Travis⁴, M. Chaparro⁵, L. Peyrin-Biroulet⁶, M. Chen⁷, M.C. Dubinsky⁸, M. Ferrante⁹, S. Schreiber¹⁰, K. McGinnis¹¹, A. Vadhariya¹¹, G. Yu¹¹, M. Protic¹¹, R. Moses¹¹, S. Ghosh¹²

¹AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands, ²Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States of America, ³Western University & London Health Sciences Centre, London, Canada, ⁴University of Oxford, Kennedy Institute and Translational Gastroenterology Unit, Oxford, United Kingdom, ⁵Hospital Universitario de La Princesa, Gastroenterology Unit, Madrid, Spain, ⁶Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ⁷First Affiliated Hospital of Sun Yat-sen University, Division of Gastroenterology, Guangzhou, China, ⁸Mount Sinai Hospital, Mount Sinai, New York City, United States of America, ⁹University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ¹⁰University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ¹¹Eli Lilly and Company, Indianapolis, United States of America, ¹²University College Cork, Institute of Translational Medicine, Cork, Ireland

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Data on bowel urgency (BU) in Crohn's disease (CD) are limited, and associated factors are not well identified. Here we evaluate the association of BU with baseline (BL) disease characteristics in patients with moderately to severely active CD in the randomized, double-blind, double-dummy, treat-through design Phase 3 VIVID-1 trial (NCT03926130).

Aims & Methods: BU was assessed using the average Urgency Numeric Rating Scale (UNRS) (range 0-10) from 7 days prior to the visit. Adult patients as previously described¹, that had an UNRS ≥ 3 and no missing values at BL were included in this analysis.

The association of UNRS with Crohn's Disease Activity Index (CDAI), abdominal pain (AP), stool frequency (SF), Simple Endoscopic Score for CD (SES-CD) total score, disease location, count of inflamed intestinal segments, rectal involvement, presence of narrowing, presence of perianal fistulae, number of bowel resections and inflammatory biomarkers were analyzed.

Other factors explored included sex, age, age at diagnosis, duration of CD, BL corticosteroid and immunomodulator use, and prior biologic failure. Random forest method (RFM) was applied to rank variables by importance associated with BU score at BL. Pearson correlation coefficients (r-value) were calculated for continuous baseline variables.

Results: At BL, 73.4% (782/1065) patients randomized to placebo (n=141), MIRI (n=433), or ustekinumab (n=208) reported a UNRS ≥ 3 with a median UNRS of 7.0 Among BL disease characteristics, CDAI total score and AP were the top two important factors based on RFM (CDAI=0.701; AP=0.398) and had moderate positive correlations (CDAI=0.479; AP=0.384) with UNRS (Table). Notably, disease characteristics such as SF (RFM=0.236; r=0.286), SES-CD total score (RFM=0.056; r=0.118), age at diagnosis (RFM=0.037; r=-0.018), age (RFM=0.033; r=-0.022), faecal calprotectin (RFM=0.029; r=0.031), C-reactive protein (RFM=0.028; r=0.050), count of inflamed segments (RFM=0.021; r=0.069), duration of CD (RFM=0.015; r=-0.007), presence of perianal fistula (RFM=0.009; r=0.090), and number of bowel resections (RFM=0.000; r=-0.036) all had weak correlations with

UNRS. BL corticosteroid (RFM=0.015) and immunomodulator (RFM=0.007) use, disease location (RFM=-0.005), rectal involvement (RFM=0.011), presence of narrowing (RFM=0.007), prior biologic failure (RFM=0.003), and sex (RFM=0.007) had weak correlations with UNRS implied by RFM.

Patient baseline variables	Importance value based on random forest	Pearson correlation coefficient (r)
CDAI Total Score	0.701	0.479
Abdominal pain score	0.398	0.384
Stool frequency score	0.236	0.286
SES-CD total score	0.056	0.118
Age at diagnosis	0.037	-0.018
Age	0.033	-0.022
Faecal calprotectin	0.029	0.031
C-reactive protein	0.028	0.050

Correlation strength defined as: $r > 0.5$ = strong, $0.5 \geq r \geq 0.3$ = moderate, $0.3 > r \geq 0.1$ = weak, $r < 0.1$ = insubstantial²

RFM is used to rank the relative importance of the patient baseline variables to UNRS. The higher values mean more important with a stronger association with UNRS.

Abbreviations: CDAI=Crohn's Disease Activity Index; CI=confidence interval; RFM = random forest method; SES-CD=Simple Endoscopic Score for Crohn's Disease; UNRS = Urgency Numeric Rating Scale

Conclusion: Most patients reported BU ≥ 3 at BL. The only moderate positive correlations were observed between BU, clinical disease severity (CDAI), and AP. Even though the association of BU with other disease characteristics such as extent and severity of endoscopic inflammation, rectal involvement, presence of active perianal disease, disease location, previous resection, and duration of CD were weak, they potentially interact and contribute together resulting in BU.

References:

1. M Ferrante, S Danese, M Chen, G D'Haens, S Ghosh, T Hisamatsu, V Jairath, J Kierkus, L Peyrin-Biroulet, B Siegmund, S M Bragg, W Crandall, T Hunter Gibble, Z Lin, M Ugolini Lopes, N Morris, H Carlier, B Sands, VIVID Study Group, OP05 Primary efficacy and safety of mirikizumab in moderate to severe Crohn's Disease: results of the treat-through VIVID 1 study, *Journal of Crohn's and Colitis*, Volume 18, Issue Supplement_1, January 2024, Pages i7–i9, <https://doi.org/10.1093/ecco-jcc/jjad212.0005>
1. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Routledge; 1988

Disclosure: GD-H: has served as adviser and/or speaker for. ie, Alimientiv, Amgen, BristolMeiersSquibb, BoehringerIngelheim, Celltrion, Ferring, Lilly, Engene, Galapagos, GlaxoSmithKline, Immunic, IndexPharmaceuticals, JohnsonandJohnson, Merck, Polpharm, Prometheusbiosciences, PrometheusLaboratories, Procisediagnostics, Protagonist, Sandoz, Takeda, Tillotts, and Ventyx.

BES: reports consulting fees from Abbvie, Alimientiv, Amgen, ArenaPharmaceuticals, ArtugenTherapeutics, Astra eneca, BoehringerIngelheim, BostonPharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Evommune, FreseniusKabi, Galapagos, Roche, GileadSciences, GlaxoSmithKline, GossamerBio, IndexPharmaceuticals, InnovationPharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, MorphticTherapeutics, MRM Health, Progenity, PrometheusBiosciences, PrometheusLaboratories, ProtagonistTherapeutics, Q32Bio, SunPharma, Surrozen, TargetRWE, Teva, TLL Pharmaceutical, VentyxBiosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from BristolMyersSquibb, Janssen, Pfizer, Takeda; research grants and consulting fees from TheravanceBiopharma; and stock options from VentyxBiopharma.

VJ: has received fees or grant and/or research support and/or served as a consultant and/or speaker for: AbbVie, Alimentiv, ArenaPharmaceuticals, AsahiKaseiPharma, AsierisPharmaceuticals, AstraZeneca, BristolMyersSquibb, Celltrion, EliLillyandCompany, FerringPharmaceuticals, FlagshipPioneering, FreseniusKabi, GalapagosNV, Genentech, GileadSciences,

GlaxoSmithKline, Janssen, Merck, Metacrine, Mylan, PandionTherapeutics, Pendopharm, Pfizer, PrometheusTherapeuticsandDiagnostics, ProtagonistTherapeutics, ReistoneBiopharma, Roche, Sandoz, SecondGenome, SorrisoPharmaceuticals, Takeda, Teva, Topivert, VentyxBiosciences, and VividionTherapeutics

ST: has received grants from: AbbVie, BUHLMANNDiagnostics, ECCO, EliLillyandCompany, FerringPharmaceuticals, InternationalOrganizationfortheStudyofInflammatoryBowelDisease, Janssen, MerckSharp&Dohme, NormanCollisonFoundation, Pfizer, Procter&Gamble, Schering-Plough, Takeda, UCBPharma, ViforPharma, and WarnerChilcott; and reports other disclosures from: AbacusPharma, AbbVie, ActialFarmaceutica, ai4gi, Alcimed, Allergan, Amgen, Aptel, ArenaPharmaceuticals, AsahiKaseiPharma, AspenPharmacare, Astellas, AstraZeneca, AtlanticPharmaceuticals, Barco, BiocareMedical, Biogen, BL Pharma, BoehringerIngelheim, BristolMyersSquibb, BUHLMANNDiagnostics, CalcicoTherapeutics, Celgene, Cellerix, CerimonPharmaceuticals, ChemoCentryx, Chiesi, Cisbio, Comcast, CoronadoBiosciences, CosmoPharmaceuticals, Dr.FalkPharma, DucentisBioTherapeutics, Dynavax Technologies, ElanPharma, EliLillyandCompany, Enterome, Equillium, FerringPharmaceuticals, GalapagosNV, Genentech/Roche, Genzyme, GileadSciences, GlaxoSmithKline, GlenmarkPharmaceuticals, Grünenthal,

GWPharmaceuticals, Immunocore, IndigoBiosciences, Janssen, LexiconPharmaceuticals, Medarex, MedTrix, Merck, MerrimackPharmaceuticals, MestagTherapeutics, MillenniumPharmaceuticals, Neovacs, Novartis, NovoNordisk, NPSPPharmaceuticals/Nycomed, OceraTherapeutics, OPTIMAPharma, OriginPharma, Otsuka, PalauPharma, PentaxMedical, Pfizer, PharmaVentures, Phesi, PhillipsPharmaGroup, Procter&Gamble, Pronota, Proximagen, ResolutePharma, RobartsClinicalTrials, Sandoz, Santarus, SatisfaiHealth, SensyneHealth, Shire, SigmoidPharma, SorrisoPharmaceuticals, Souffinez, SynDermix, Synthon, Takeda, TheravanceBiopharma, TiGenix, TillottsPharmaAG, Topivert, TrinoTherapeutics with WellcomeTrust, TxCellSA, UCBPharma, VertexPharma, VHSquared, ViforPharma, WarnerChilcott, and ZeriaPharmaceutical

MCha: has served as a speaker, as a consultant, or has received research or education funding from MSD, AbbVie, Hospira, Pfizer, Takeda, Janssen, Ferring, ShirePharmaceuticals, DrFalkPharma, TillottsPharma, Biogen, Gilead, and EliLilly

LP-B: Reports the following: personal fees from Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillotts, Pharmacosmos, Celltrion, Takeda, BoehringerIngelheim, Pfizer, IndexPharmaceuticals, Sandoz, Celgene, Biogen, SamsungBioepis, Alma, Sterna, Nestle, Inotrem, Enterome, Allergan, MSD, Roche, Arena, Gilead, Hikma, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, FreseniusKabi, OppilanPharma, SublimityTherapeutics, AppliedMolecularTransport, OSEImmunotherapeutics, Enthera, and Theravance; grants from Abbvie, MSD, and Takeda; and stock options from CTMA

M-HC: provided educational activities for AbbVie, ChinaMedicalSystem, IPSEN, Janssen, and Takeda; served on an advisory board for BoehringerIngelheim and Janssen; and has support for clinical research from Janssen and Takeda.

MD: has received honoraria as a consultant for: AbbVie, ArenaPharmaceuticals, BoehringerIngelheim, BristolMyersSquibb, Celgene, EliLillyandCompany, F.Hoffmann-LaRoche, Genentech, GileadSciences, Janssen, Pfizer, PrometheusTherapeuticsandDiagnostics, Takeda, and UCBPharma; has been contracted for research by: AbbVie, Janssen, Pfizer, and PrometheusBiosciences; has stock interest in: TrellusHealth; and has received licensing fees from: Takeda;

MF: has received fees for grants and/or contracts from: AbbVie, Amgen, Biogen, JanssenCilag, Pfizer, Takeda, and Viatrix; consulting fees from: AbbVie, BoehringerIngelheim, Celltrion, Lilly, JanssenCilag, Medtronic, MerckSharp&Dohme, Pfizer, Regeneron, Sandoz, Takeda, and ThermoFisherScientific; lecture fees or honoraria from: AbbVie, Amgen, Biogen, BoehringerIngelheim, Celltrion, Dr.FalkPharma, Lilly, FerringPhar-

maceuticals, Janssen, Lampro, Medtronic, MerckSharp&Dohme, Mylan, Pfizer, SamsungBioepis, Sandoz, Takeda, and ThermoFisher; support to attend meetings from: AbbVie, BoehringerIngelheim, Celltrion, Dr.Falk-Pharma, Janssen, Pfizer, and Takeda; and data safety monitoring fees from: AbbVie, BoehringerIngelheim, Celltrion, Lilly, Janssen, Medtronic, MerckSharp&Dohme, Pfizer, Sandoz, Takeda, and ThermoFisherScientific SS: has been a consultant for AbbVie, Amgen, ArenaPharmaceuticals, BristolMyersSquibb, BoehringerIngelheim, Celltrion, DrFalkPharma, Ferring, Fresenius, Galapagos, Genentech, GSK, Gilead, I-MABBiopharma, Janssen, Lilly, Merck, Novartis-Sandoz, Pfizer, Protagonist, Takeda, and Theravance.

KM, AV, GY, MP, RM: Employees and shareholders of EliLillyandCompany SG: has received research grants and consultancy from: EliLillyandCompany; served on steering committees for: AbbVie and BristolMyersSquibb; received consultancy fees from: AbbVie, Celltrion, FerringPharmaceuticals, GalapagosNV, Janssen, Pfizer, and Takeda.

PP0566

EXIT INTERVIEWS EXPLORING PATIENTS' EXPERIENCE OF CHANGES IN THEIR FATIGUE DURING THE PHASE 3 CLINICAL TRIAL OF MIRIKIZUMAB FOR TREATMENT OF MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

T.H. Gible¹, J. Macey², H. Makin², R. Rosu¹, K. Mellor², H. Kitchen², E. Hon¹, A. Vadhariya¹, S. Su¹, M. Regueiro³

¹Eli Lilly and Company, Indianapolis, United States of America, ²Clinical Outcomes Assessment, Clarivate, London, United Kingdom, ³Division of Gastroenterology, Hepatology, and Nutrition, Cleveland Clinic Foundation, Cleveland, Ohio, United States of America

Contact E-Mail Address: su_sylvia@lilly.com

Introduction: Fatigue is a common and debilitating symptom of Crohn's disease (CD), associated with functional impairment and reduced quality of life.^{1,2}

Aims & Methods: Here we qualitatively explore change in fatigue in participants with moderately to severely active CD who completed the phase 3, randomised, double-blind, placebo- and active-controlled, mirikizumab clinical trial (VIVID-1/NCT03926130). Qualitative, web-assisted, semi-structured, 90-minute exit interviews were conducted in 62 trial participants within 3 weeks of completing the final trial visit (May 2022–July 2023). Clinical trial arms were blinded for this study. A sub-set of participants from either mirikizumab, ustekinumab or placebo arms were asked open-ended questions to explore changes in fatigue (N=31). Interview audio recordings were transcribed verbatim and analysed using a directed content analysis approach in ATLAS.ti v9.

Results: Among the 31 participants who were asked about fatigue (61.3% male [n=19], 90.3% White [n=28]), median age was 42 (n=30; range: 24–75) years and median CD duration was 5.9 (n=30; range: 1.4–54.3) years. Overall, 31.0% (n=9/29) participants had a college degree or higher and 41.4% (n=12/29) participants were employed full-time. Participants were from the United States (n=15), Czech Republic (n=5), Germany (n=5), Poland (n=3), Australia (n=2) and Canada (n=1).

At the start of the trial, participants reported that they had difficulty in performing daily activities (n=7), walking or climbing stairs (n=3), completing outdoor tasks and activities (n=2), concentrating or focusing (n=2) and were unable to feel well-rested from sleep (n=3), lacked energy (n=2), felt exhausted (n=1), dozed off in evening (n=1) and took breaks during the day (n=1) due to fatigue. They also reported socialising less (n=1) and feeling worried (n=3), demotivated (n=2), grumpy (n=1), frustrated (n=1) and depressed (n=1).

Although it was unknown which treatment the participants had received, most participants reported experiencing an improvement in fatigue (74%, n=23/31) during the trial. Seven participants reported experiencing no change in fatigue (23%, n=7/31). Of these, four participants reported experiencing no or little fatigue at the start of the trial, which did not change until their last visit. One participant reported worsening of fatigue (3%, n=1/31) during the trial which impacted their daily activities as they needed to sleep more often during the day.

Among participants who experienced an improvement in fatigue, 11 reported an improved emotional well-being such as feeling more relaxed, confident, independent, and motivated. Overall, 9 participants reported that their physical function improved, and they were able to walk further, had more energy and felt stronger. Eight participants reported being able to function more day-to-day. Improvement in fatigue resulted in better friendships or relationships (n=4), being more successful in work or school (n=3), sleeping better (n=2), napping less (n=2), being able to exercise more (n=2), go out for longer duration (n=2), being able to work (n=1), and gaining more enjoyment in life (n=1). When participants were asked about meaningful improvement in fatigue, 10 out of 13 participants reported a meaningful improvement.

Conclusion: Exit interview results showed that irrespective of the treatment received, most interviewed participants with moderately to severely active CD experienced an improvement in fatigue by end of the trial, resulting in better energy levels, physical function, daily functioning, and emotional well-being.

References:

1. Nocerino A, et al. (2020) *Adv Ther.* 37(1):97–112.
2. Regueiro M, et al. (2023) *J Patient Rep Outcomes.* 7(1):75.

Disclosure: Theresa Hunter Gible: Employee and stockholder of Eli Lilly and Company

Jake Macey: Employee and stockholder of Clarivate

Harriet Makin: Employee and stockholder of Clarivate

Rodica Rosu: Employee and stockholder of Eli Lilly and Company

Katie Mellor: Employee of Clarivate

Helen Kitchen: Employee and stockholder of Clarivate

Emily Hon: Employee and stockholder of Eli Lilly and Company

Aisha Vadhariya: Employee and stockholder of Eli Lilly and Company

Sylvia Su: Employee and stockholder of Eli Lilly and Company

Miguel Regueiro: Advisory Boards and Consultant (both) for Abbvie, Janssen, UCB, Takeda, Pfizer, BMS, Organon, Amgen, Genentech, Gilead, Salix, Prometheus, Lilly, Celgene, Boehringer Ingelheim Pharmaceuticals Inc. (BIPI), Celltrion, Roche

PP0567

THE IMPACT OF BODY MASS INDEX ON TREATMENT RESPONSE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: RESULTS OF THE PROSPECTIVE DUTCH INITIATIVE ON CROHN AND COLITIS (ICC) REGISTRY

D. Oomkens¹, Z. Mujagic², A.C. de Vries³, A.E. Van Der Meulen - De Jong⁴, T. Straatmijer⁴, M. Lowenberg⁵, S. van der Marel⁶, R. West⁷, A. Bodelier⁸, F. Van Schaik⁹, M.C. Visschedijk¹⁰, M. Duijvestein¹, Initiative on Crohn and Colitis

¹Radboud University Medical Centre, Gastroenterology and Hepatology, Nijmegen, Netherlands, ²Maastricht University Medical Center, Gastroenterology & Hepatology, Maastricht, Netherlands, ³Erasmus MC University Medical Center, Gastroenterology And Hepatology, Rotterdam, Netherlands, ⁴Leiden University Medical Center, Gastroenterology, Leiden, Netherlands, ⁵Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁶HMC, Gastroenterology, Den Haag, Netherlands, ⁷Sint Franciscus Gasthuis, Gastroenterology, Rotterdam, Netherlands, ⁸Amphia Hospital, Gastroenterology, Eindhoven, Netherlands, ⁹University Medical Centre Utrecht, Utrecht, Netherlands, ¹⁰Groningen University Medical Center, Gastroenterology and Hematology, Groningen, Netherlands

Contact E-Mail Address: dorien.oomkens@radboudumc.nl

Introduction: To examine the effect of Body Mass Index (BMI) on treatment response in patients with inflammatory bowel disease (IBD).

Aims & Methods: Patients ≥ 16 years old with IBD, a documented baseline BMI and starting thiopurines, intravenous (iv) vedolizumab, subcutaneous (sc) vedolizumab, ustekinumab, ozanimod, filgotinib, or tofacitinib were selected from the Initiative on Crohn and Colitis (ICC) registry in the Netherlands. Patients with a current follow-up shorter than 24 weeks were excluded. Some of the patients in the registry started vedolizumab sc electively whilst in remission after being treated with vedolizumab iv. Therefore, patients with vedolizumab sc were excluded if they were in steroid-free clinical remission (SFCR) (i.e. Simple Clinical Colitis Activity Index (SCCAI) ≤ 2 for ulcerative colitis and Harvey Bradshaw Index (HBI) < 5 for Crohn's disease) at baseline. Patients who discontinued treatment were classified as non-responders at all timepoints after treatment discontinuation. SFCR at baseline, week 12 and week 24 was compared between patients with normal weight (BMI < 25 kg/m²), overweight (BMI 25-30 kg/m²) and obesity (BMI ≥ 30 kg/m²) using Chi-Square tests. SFCR rates over time in the three groups were analysed using generalized linear mixed modelling.

Results: 1101 patients with IBD (631 Crohn's disease, 470 ulcerative colitis) were included, 636 had normal weight, 313 were overweight and 152 were obese. Generalized linear mixed model demonstrated that the course of SFCR over time after initiating treatment was significantly different between the three groups ($p = 0.038$). Chi-Square tests showed significant differences in SFCR between the normal weight, overweight and obese patients at week 12 (40.1%, 49.8%, 42.9%, respectively, $p = 0.027$) and week 24 (48.2%, 49.4%, 34.7%, respectively, $p = 0.015$). No significant difference in SFCR was found between groups at baseline.

Conclusion: Obesity was associated with a lower SFCR rate at week 24. Surprisingly, at week 12, overweight was associated with a higher rate of SFCR. Although overweight patients have shown a faster treatment response, this advantage had vanished at 24 weeks. The week 12 results could possibly be explained by the protective effect of excess bodyweight during illness, which is an hypothesis of the 'obesity paradox', concerning the finding of lower mortality rates in overweight and obese patients with cardiovascular diseases and malignancies^{1,2}.

References:

1. Tutor AW, Lavie CJ, Kachur S, Milani RV, Ventura HO. Updates on obesity and the obesity paradox in cardiovascular diseases. *Prog Cardiovasc Dis*. 2023 May-Jun;78:2-10. doi: 10.1016/j.pcad.2022.11.013. Epub 2022 Dec 5. PMID: 36481212.
 2. Hahn AW, Venkatesh N, Msaouel P, McQuade JL. The Influence of Obesity on Outcomes with Immune Checkpoint Blockade: Clinical Evidence and Potential Biological Mechanisms. *Cells*. 2023 Oct 31;12(21):2551. doi: 10.3390/cells12212551. PMID: 37947629; PMCID: PMC10649394.
- Disclosure:** Dorien Oomkens: none. Zlatan Mujagic: reports grants from MLDS, Niels Stensen Fellowship, and Galapagos, and has served as speaker for Galapagos, adviser for Johnson and Johnson, all outside the submitted work. Annemarie C de Vries: has served on advisory boards for Takeda, Janssen, Bristol Myers Squibb, Abbvie, Pfizer, and Galapagos and has received unrestricted research grants from Takeda, Janssen, and Pfizer outside the submitted work. Andrea E. van der Meulen-de Jong has served as speaker for: Galapagos, Janssen-Cilag, Takeda, Tramedico. She has received research grants from Cablon, Galapagos, Nestle, Norgine and ZonMW. Tessa Straatmijer: none. Mark Lowenberg: Abbvie, Alimentiv, Bristol Myers Squibb, Celgene, Covidien, Dr. Falk, Ferring Pharmaceuticals, Galapagos, Gilead, GlaxoSmithKline, Janssen-Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Protagonist therapeutics, Receptos, Takeda, Tillotts, Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, Dr Falk, Achmea healthcare, Galapagos and ZonMW. Sander van der Marel: none. Rachel West: has participated in advisory board or as speaker for Jansen, Abbvie and Pfizer. Alexander Bodelier: has served on the advisory board of Takeda, Abbvie, and Janssen outside the submitted work. Fiona van Schaik: served as adviser for Takeda, Galapagos, and Dr Falk. LPLG has served as a speaker for AbbVie and Boston, and received a grant from Ferring to develop e-learning about therapeutic drug monitoring. Marijn C Visschedijk: received speaker fees from Janssen-Cilag, Galapagos, and Ferring B.V. Marjolijn Duijvestein: reports advisory fees from Echo Pharma and Robarts Clinical Trials, Inc., speaker fees from Janssen, Merck & Co., Inc., Pfizer, Takeda and Tillotts Pharma, and nonfinancial support from Dr. Falk Pharm.

PP0568

PATIENT-REPORTED OUTCOMES WITH USTEKINUMAB FOR CROHN'S DISEASE IN REAL-LIFE CLINICAL PRACTICE IN GREECE: FINAL RESULTS FROM THE PROSPECTIVE 'REASSURE' STUDY

G. Bamias¹, G.J. Mantzaris^{2,3}, C. Gkamaloutsos⁴, K. Thomopoulos⁵, M. Tzouvala⁶, I. Koutroubakis⁷, C. Liatsos⁸, S. Vradelis⁹, T. Sdonas¹⁰, G. Papatheodoridis¹¹, D.K. Christodoulou¹², K.D. Paraskeva¹³, I. Goulis¹⁴, K.H. Katsanos¹⁵, G. Germanidis¹⁶, A. Protopapas¹⁷, K. Soufleris¹⁸, I. Pachiadakis¹⁹, E. Zampeli²⁰, V. Ntelis²¹, E. Papathanassiou²⁰, M.-L. Chatzinikolaou¹, K. Chalakatevaki¹, G. Theocharis⁵, A. Trikola²², E. Beka²³, G. Tribonias²⁴, M. Palatianou⁶, K. Foteinogiannopoulou⁷, A. Machaira⁷, N. Kyriakos⁸, M. Giakoumis⁹, E. Giannakouloupoulou¹⁰, A. Tasovasili¹⁰, P. Karatzas²⁵, N. Mathou¹³, G. Kokkonis²⁶, G. Kalopitas¹⁶, G. Michalopoulos²¹, P. Giannelis²⁷, A. Protopapas¹⁷, K. Fasoulas¹⁸, A. Mpoumponaris¹⁹, A. Nakos¹⁹, C. Taloumtzis¹⁹, E. Karamintziou²¹, E. Stergiou¹⁸, A. Mpartsea⁴, I. Kanistras⁴, S. Michopoulos²⁰

¹National and Kapodistrian University of Athens, GI-Unit, 3rd Academic Dpt. of Internal Medicine, Athens, Greece, ²Hygeia Hospital, Dept. of Gastroenterology, Athens, Greece, ³White Cross Clinic, Dept. of Gastroenterology, Athens, Greece, ⁴Janssen-Cilag, Athens, Greece, ⁵University Regional Hospital of Patras, Gastroenterology Clinic, Patras, Greece, ⁶General Hospital of Nikaia, Dept of Gastroenterology, Nikaia, Greece, ⁷University General Hospital of Heraklion, Gastroenterology Clinic, Heraklion, Greece, ⁸401 Army General Hospital of Athens, Dept. of Gastroenterology, Rafina-Pikermi, Greece, ⁹Democritus University Hospital, Dept of Endoscopy, Alexandroupolis, Greece, ¹⁰General Oncology Hospital "Agioi Anargyroi", Dept of Gastroenterology, Kifissia, Greece, ¹¹Univ. Medical School Hippokratia Hospital - Academic Dept. of Gastroenterology, Univ. Medical School, Academic Dept. of Gastroenterology, Athens, Greece, ¹²Gastroenterology Unit University Hospital, 1st Division Of Internal Medicine And Hepato-Gastroenterology Unit, Ioannina, Greece, ¹³General Hospital "Agia Olga", Gastroenterology, Athens, Greece, ¹⁴Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece, ¹⁵Medical School of Ioannina, Division of Internal Medicine, Ioannina, Greece, ¹⁶AHEPA University General Hospital, A' University Internal Medicine Clinic, Thessaloniki, Greece, ¹⁷AHEPA University General Hospital, 1st Propaedeutic Internal Medicine Clinic, Thessaloniki, Greece, ¹⁸Theagenion Anticancer Hospital of Thessaloniki, Dept of Gastroenterology, Thessaloniki, Greece, ¹⁹424 Military General Hospital of Thessaloniki, Gastroenterology and Hepatology, Thessaloniki, Greece, ²⁰Alexandra General Hospital, Dept of Gastroenterology, Athens, Greece, ²¹"G. Genimatas" General Hospital, Dept of Gastroenterology, Athens, Greece, ²²Naval Hospital of Athens, Gastrointestinal Department, Athens, Greece, ²³Evangelismos Hospital, Gastroenterology and Hepatology, Athens, Greece, ²⁴Red Cross Hospital, Gastroenterology Clinic, Athens, Greece, ²⁵Hygeia Hospital, Gastroenterology Clinic, Athens, Greece, ²⁶Bioclinic Hospital, Dept of Gastroenterology, Thessaloniki, Greece, ²⁷"Tzaneio" General Hospital, Gastroenterology Clinic, Piraeus, Greece

Contact E-Mail Address: michosp5@gmail.com

Introduction: Due to lack of published data on ustekinumab (UST) use in Greece, REASSURE study aimed to generate real-world evidence (RWE) on treatment persistence, and patient-reported outcomes (PROs) in patients with Crohn's Disease (CD).

Aims & Methods: REASSURE was a non-interventional, 24-month prospective study of adult (18-80 years old) CD patients newly initiated on UST as 1st, 2nd, or 3rd biologic therapy per the approved label in Greece. Data were collected by routine assessments, including Harvey-Bradshaw Index (HBI), and PROs at baseline (start of UST) and at 4 follow-up visits at 6-month intervals, with a final visit at Month 24 (±2 months) or at treatment discontinuation (whichever occurred first). PROs included the validated Greek version of the Inflammatory Bowel Disease Questionnaire (IBDQ), the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale and the Work Productivity and Activity Impairment Questionnaire in Crohn's Disease (WPAI:CD). PROs at 24 months are presented herein.

	Overall (N=169)	Bio-naïve (1L) (N=60)	Bio-experienced (N=109)
Time from CD diagnosis to UST initiation, median (IQR), years	7.0 (1.8, 13.0)	1.3 (0.3, 6.2)	10.1 (5.9, 15.9)
Baseline characteristics, % (n/N)			
Age ≤50 years	62.7 (106/169)	51.7 (31/60)	68.8 (75/109)
Females	50.9 (86/169)	41.7 (25/60)	56.0 (61/109)
Employed (full-time or part-time)	43.4 (72/166)	55.9 (33/59)	36.4 (39/107)
At least 1 comorbidity	55.0 (93/169)	55.0 (33/60)	55.0 (60/109)
Strictureing and/or penetrating disease	43.2 (70/162)	33.3 (19/57)	48.6 (51/105)
Extraintestinal manifestations	36.5 (61/167)	31.7 (19/60)	39.3 (42/107)
Starting UST maintenance dosage: 90 mg SC Q8W	89.9 (152/169)	83.3 (50/60)	93.6 (102/109)
IBDQ at month 24			
Response (change ≥16 points), % (n/N), as observed	56.8 (63/111)	60.5 (26/43)	54.4 (37/68)
Response (change ≥16 points), % (n/N), imputed	44.2 (73/165)	49.2 (29/59)	41.5 (44/106)
Median/mean change from baseline (IQR/SD), as observed	24.0 (5.0, 52.0)*	33.0 (39.6)*	25.7 (35.6)*
Median change from baseline (IQR/SD), imputed	9.0 (0.0, 36.0)*	14.0 (-1.0, 47.0)*	8.0 (0.0, 36.0)*
FACIT-F at month 24			
Significant improvement (≥4 points), % (n/N), as observed	59.3 (67/113)	62.8 (27/43)	57.1 (40/70)
Significant improvement (≥4 points), % (n/N), imputed	47.9 (80/167)	53.3 (32/60)	44.9 (48/107)
Median/mean change from baseline (IQR/SD), as observed	6.0 (0.0, 15.0)*	9.1 (14.3)*	7.2 (12.1)*
Median/mean change from baseline (IQR/SD), imputed	2.0 (0.0, 12.0)*	4.0 (0.0, 14.5)*	1.0 (0.0, 10.0)*
Activity impairment at month 24 (based on WPAI:CD)			
Median change from baseline (IQR), as observed	-20.0 (-40.0, 0.0)*	-20.0 (-40.0, 0.0)*	-20.0 (-40.0, 0.0)*
Patients completing WPAI:CD at both baseline and 24 months	N=113	N=43	N=70
Median change from baseline (IQR), imputed	-10.0 (-40.0, 0.0)*	-10.0 (-30.0, 0.0)*	-5.0 (-40.0, 0.0)*
Patients completing WPAI:CD at baseline	N=166	N=60	N=106
Work productivity loss at month 24 (WPAI:CD)			
CMI (decrease of ≥7 points), % (n/N), as observed	68.4 (26/38)	77.8 (14/18)	60.0 (12/20)
CMI (decrease of ≥7 points), % (n/N), imputed	53.8 (28/52)	63.6 (14/22)	46.7 (14/30)
Median change from baseline (IQR), as observed	-20.0 (-56.8, 0.0)*	-20.0 (-60.0, -10.0)*	-10.0 (-35.8, 0.0)*
Median change from baseline (IQR), imputed	-10.0 (-30.0, 0.0)*	-20.0 (-56.9, 0.0)*	0.0 (-21.6, 0.0)*

Data imputation was performed using last observation carried forward analysis. For change from baseline, median (IQR) or mean (SD) is displayed, depending on p-value of normality (< or ≥0.05, respectively). Abbreviations: 1/2/3L: First/Second/Third Line; CD: Crohn's Disease; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; IBDQ: Inflammatory Bowel Disease Questionnaire; IQR: Interquartile Range; IV: intravenous; N: number of patients with available data; n: number of patients with variable; ns, not statistically significant; PRO: Patient Reported Outcome; Q8W: every 8 weeks; SC: subcutaneous; SD: Standard Deviation; T: T-test p-value of change <0.01, indicating statistical significance; UST: ustekinumab; W: Wilcoxon signed-rank test p-value of change <0.01, indicating statistical significance; WPAI:CD: Work Productivity and Activity Impairment Questionnaire in Crohn's Disease; CMI: Clinically meaningful improvement.

Table 1: Baseline characteristics and 24-month PROs.

Results: Between Apr/2019 and Feb/2021, 169 eligible patients were enrolled in 19 Gastroenterology Clinics in Greece. The median (IQR) age at baseline was 45.0 (35.0-54.0) years; of the evaluable patients, 17.5% were overweight, 49.0% had tertiary level of education, and 68.5% were ever-smokers. In terms of employment, 43.4% (72/166) of patients were employed, 29.5% (49/166) unemployed (due to CD in 21.6%; 8/37), 16.3% (27/166) retired (due to CD in 24.0%; 6/25), and 10.8% (18/166) reported other status. Among UST treated patients, 35.5% were bio-naïve (BN) and 64.5% were bio-experienced (BE).

Median (IQR) duration of study participation was 23.9 (18.3-24.7) months (median treatment duration: 24.0 months). At 24 months, 72.8% (123/169) [BN: 76.7% (46/60); BE: 70.6% (77/109)] remained on treatment with UST, while 21.9% (37/169) had discontinued UST after a mean (SD) of 10.2 (6.4) months mainly due to lack/loss of response (15/37), safety issues (10/37), or loss to follow-up (6/37). The proportion of evaluable patients in remission (HBI score 0-4) at 24 months was 87.7% (100/114) [BN: 90.7% (39/43); BE: 85.9% (61/71)].

Baseline median IBDQ (170.0), FACIT-F (34.0), WPAI:CD work productivity loss (WPL) (30.0) and activity impairment scores (30.0) significantly improved ($P<0.01$) at 24 months, with median changes of 24.0, 6.0, -20.0, and -20.0, respectively, among paired observations. Significant improvements were also noted based on imputed data and in both bio-naïve and bio-experienced patients. At 24 months, among patients with paired ob-

servations, 56.8% achieved an IBDQ response (≥ 16 -point increase), 59.3% a significant FACIT-F improvement (≥ 4 -point increase) and 68.4% a clinically meaningful improvement in WPL (≥ 7 -point decrease) from baseline. Further details on baseline characteristics and 24-month PROs are shown in Table 1.

Conclusion: These data provide RWE on the beneficial effect of UST on health-related quality of life, fatigue, and work productivity in both bio-naïve and bio-experienced CD patients in Greece.

Disclosure: This study was sponsored by Janssen - Cilag, Greece.

Giorgos Bamias Advisor/lecturer for Janssen, Pfizer, Takeda, Abbvie, MSD, Mylan, Genesis Pharma, Adacyte Therapeutics, Amgen, Ferring, Cooper, BMS; Funding (Grants/Honoraria): Pfizer, Takeda, Abbvie, Aenorasis; Research/Clinical Trials: Abbvie, Takeda, Janssen.

Gerassimos J. Mantzaris has received consultant and/or speaker fees from AbbVie, MSD, Celtrion, Ferring, Aenorasis, Janssen, Pfizer, Takeda, Falk Pharma, and Vianex and research support from AbbVie, Ferring, MSD, and Vianex

Maria Tzouvala has received clinical research funding from Janssen-Cilag Pharmaceuticals SACI, Takeda HELLAS SA, AbbVie Pharmaceuticals S.A. Consulting and/or speaking fees MSD Sharp& Dohme, Janssen-Cilag Pharmaceuticals SACI, Takeda, AbbVie Pharmaceuticals S.A, Pfizer, Amgen. Advisory boards: Janssen-Cilag Pharmaceuticals SACI, Takeda, AbbVie Pharmaceuticals S.A, Pfizer, Amgen

Dimitrios Christodoulou has received consulting and speaking fees for Janssen, MSD, Galenica. Advisory Board for Galenica

Ioannis Koutroubakis has received clinical research funding: Abbvie, Faran, Ferring, Pfizer, Viatrix, Vianex, Vifor, Unipharm. Consulting and/or speaking fees Abbvie, Genesis, Janssen, MSD, Takeda, Vianex. Advisory boards: Abbvie, Janssen, MSD, Pfizer, Takeda, Vianex

Christos Liatsos has received clinical research funding from: Janssen, and consulting and/or speaking fees from: MSD, Pfizer, Boston SCI, Amgen, Galenica.

Georgios Papatheodoridis Clinical research funding: Abbvie, Gilead, Takeda, Vianex. Consulting and/or speaking fees: Abbvie, Astra-Zeneca, BioARS Therapeutics, Elpen, Genesis, Gilead, GlaxoSmithKline, Ipsen, Novo Nordisk, Roche, Sobi. Advisory boards: Abbvie, Astra-Zeneca, Albireo, Amgen, Galenica, Genesis, Gilead, GlaxoSmithKline, Ipsen, Janssen, Novo Nordisk, Roche, Takeda

Dr Katsanos Konstantinos received honoraria for consulting services (educational services, scientific articles, participation in Advisory Boards, clinical trials, lecture fees, other) from the companies as follows: AbbVie, AMGEN, ENORASIS, Epsilon Health, Ferring, Genesis, Grifols S.A., JANSSEN, MSD, Mylan, Shire and Takeda.

Evanthia Zampeli has received clinical research funding: Janssen, TAKEDA, ABBVIE. Consulting and/or speaking fees: Janssen, TAKEDA, BMS, AMGEN, MYLAN. Advisory boards: BMS, GALENICA

Georgios Germanidis has received clinical research funding from Janssen. Konstantinos Soufleris Consulting and/or speaking fees: AbbVie, Janssen, MSD, Pfizer, Takeda. Clinical research funding: Pfizer. Advisory board: BMS, Galenica.

Matina-Lydia Chatzinikolaou has received consulting fees from Abbvie, Takeda, Amgen, Ferring, Janssen

George Kokkonis has received clinical Research funding from Janssen and speaking fees from Janssen and Amgen

Alexandros Boubonaris has served as advisory board member for Amgen, Takeda

Marios Giakoumis has received clinical research funding from Janssen

Artemis Trikola has received clinical research funding from Janssen

George Michalopoulos has received speaker fees: Takeda, MSD, , Abbvie, Janssen, Pfizer, Amgen

Vasileios Delis, Konstantina Paraskeva, Theodosios Sdonas, Athanasia Tasovasilis, Evgenia Papathanasiou, Maria Palatianou, Andreas Nakos, Ni-

koletta Mathou, George Kalopitas, Panagiotis Giannelis, Kalliopi Foteinogiannopoulou, Konstantina Chalakatevaki, Eleni Beka, Evmorfia Karamintziou, Eleftheria Giannakouloupoulou have no conflicts to disclose.

Konstantinos Thomopoulos, Stergios Vradelis, Andreas Protopapas, Ioannis Pachiadakis, Ioannis Goulis, Pantelis Karatzas, George Theocharis, George Tribonias, Angeliki Machaira, Nikolaos Kyriakos, Adonis Protopapas, Konstantinos Fasoulas, Evdoxia Stergiou and Charilaos Taloumtzis have not disclosed any conflicts

Spyridon Michopoulos has received clinical research funding from Janssen, Takeda, BMS, consulting and/or speaking fees from Takeda, and has served as advisory board member for Takeda.

Christos Gkamaloutsos, Ioannis Kanistras and Aikaterini Mpartsea are employees of Janssen - Cilag, Greece

PP0569

EXPLORING THE CHARACTERISTICS OF CROHN'S DISEASE (CD) PATIENTS WHO HAVE BEEN TREATED WITH ADVANCED THERAPY FOR MORE THAN 6 MONTHS

M. Thoo¹, D. Baldock², P. Robinson²

¹Ipsos, Kuala Lumpur, Malaysia, ²Ipsos, London, United Kingdom

Contact E-Mail Address: denise.baldock@ipsos.com

Introduction: The Crohn's Disease Activity Index (CDAI) is a widely used research tool used to quantify CD patient's symptoms, evaluate the severity of CD and to determine treatment outcomes.

Aims & Methods: The objective of this study was to assess any nuances in treating CD patients with active disease (CDAI score >150), who have remained on the same advanced therapy (biologics/ novel oral molecules) for more than 6 months.

The Ipsos CD Therapy Monitor, a multi-centre online medical chart review study of patients with CD was conducted between July – September 2023 among UK, FR, DE, IT & ES gastroenterologists practicing across hospital and private practices.

Physicians were screened for practice duration and patient volume. Charts of patients prescribed with advanced therapy were included in the analysis.

Results: 208 sampled physicians collectively reported 373 CD patients who were recorded as being on the same advanced therapy for more than 6 months. 286 reported patients were deemed in remission (CDAI score ≤ 150) and 87 patients recorded with active disease (CDAI score >150). Looking at reported CD patient co-morbidities, metabolic conditions were more common in patients with active disease vs those in remission (24% vs 19%)

When looking at extra-intestinal manifestations (EIMs) between the two patient groups, patients with active disease were more likely to experience EIMs vs those in remission.

CD patients	Patients with active disease (CDAI >150)	Patients in remission (CDAI ≤ 150)
% experienced anaemia	21%	11%
% experienced arthritis	9%	7%
% experienced osteoporosis	6%	2%

Table 1: EIMs in reported CD patients (% patients)

A higher proportion of patients with active disease activity were currently receiving non-tumour necrosis factor (TNF) therapy vs those in remission (37% vs 24%) and reported higher steroid usage (% reported patients currently on steroids – 11% vs 3%).

When analysing reasons for prescribing selected advanced therapy between the two patient groups, a greater proportion of patients with active disease had the following reasons specified more frequently by the sampled physicians, vs the patients in remission: 'To achieve steroid-free remission' (51% vs 43%), 'Good safety profile' (40% vs 35%), and 'Low incidence of side-effects' (35% vs 21%).

Conclusion: Comparisons in this study cohort highlighted that active disease in CD patients, as determined by the CDAI score, is associated with a higher number of patient co-morbidities and a greater likelihood of extra-intestinal manifestations; this indicates a more severe or complicated disease burden.

As additional development products with new mechanisms of action become available in gastroenterology, non-TNF therapy usage may grow over time to provide more holistic and individualised treatment strategies for CD patients. Further investigation using comparator cohort is warranted.

References: [1] Use of the Crohn's disease activity index in clinical trials of biological agents, Hugh James Freeman <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725371/>

Disclosure: Nothing to disclose.

PP0570

ROAD TO EXIT STRATEGY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: READY OR NOT?

A. Todeschini¹, R. Ciccocioppo², M. Bernuzzi², A. Geccherle¹, P. Signoretti¹, N. Colaci¹, G. Barugola³, A. Variola¹

¹IRCCS Sacro Cuore - Don Calabria, IBD Unit, Negrar di Valpolicella, Italy, ²AQUI Policlinico GB Rossi & University of Verona, Department of Medicine, Verona, Italy, ³IRCCS Sacro Cuore - Don Calabria, General Surgery, Negrar di Valpolicella, Italy

Contact E-Mail Address: ale_tode@hotmail.com

Introduction: Whereas there is an emerging consensus on the optimal approach to initiation of a range of therapies in inflammatory bowel disease (IBD), there remains greater uncertainty about the risks, benefits, and timing of stopping treatment when patients are in stable remission on therapy. When planning an exit strategy for drug withdrawal, the risk of disease relapse must be balanced against the risk of drug-related adverse events and healthcare costs.

Aims & Methods: Our study evaluated the risks of disease relapse associated with withdrawal of the biologic therapy in both ulcerative colitis (UC) and Crohn's disease (CD). In this is a retrospective observational study, the exit strategy was proposed to 60 patients regularly followed in two IBD referral centre from 2015 to 2023. The exit strategy was performed as: (i) discontinuation without de-escalation, (ii) progressive de-escalation and (iii) azathioprine as monotherapy. Data on medical history were collected from electronic health records. Chi-square test was used to compare categorical variables. Logistic regression was used to assess the relationship between disease-related characteristics and the onset of disease relapse after the withdrawal.

Results: 60 IBD patients were enrolled, 46 patients withdrawal their biologic therapy and 14 patients were in a de-escalation strategy. These 46 patients (15 UC and 31 CD) performed discontinuation without de-escalation (65%), progressive de-escalation (26%) and azathioprine as monotherapy (9%). They withdraw anti-TNF (82%) or other biologics (18%). Most of patients (71%) were on first line of biologic therapy. The median follow-up period after drug withdrawal was 29 months. A disease relapse occurred in 14 patients with a median period of 12 months. A good recapture of previous therapy was observed in 57% of patients. Logistic regression analysis revealed a trend of significance between biologic therapy duration (p 0.05) and absence of flare-up after exit strategy. No correlation was noticed with duration of endoscopic or clinical remission before starting the drug withdrawal.

Conclusion: There are no specific factors related to a successful exit strategy. Biologic drug discontinuation is something best considered on a case-by-case basis and determined by patient preferences and disease features. We need more specific study in order to identify patients who can stop therapy without undue risk of poor outcomes.

Disclosure: Nothing to disclose.

PP0571

THE IMPACT OF DISEASE STATUS AFTER BIOLOGIC INDUCTION THERAPY ON LONG-TERM OUTCOMES IN PERSONS WITH CROHN'S DISEASE

P. Tandon¹, G. Brar¹, M. Haque², N. Butt¹, M. Sanon³, D. Naessens³, E. Pone⁴, L. Targownik¹

¹University of Toronto, Gastroenterology, Toronto, Canada,

²University of Saskatchewan, Medicine, Regina, Canada, ³Janssen Global Services, Horsham, United States of America, ⁴Janssen Inc. Canada, Toronto, Canada

Contact E-Mail Address: mhparul@gmail.com

Introduction: Despite the increase in the therapeutic armamentarium of the treatment of Crohn's disease (CD), historically less than 50% of patients achieve partial response after induction, and less than 20% achieve clinical remission. It remains unknown how response to biologic induction therapy influences disease behavior, treatment patterns, and healthcare utilization in those patients who are maintained on biologic therapy for the treatment of their CD.

Aims & Methods: Aims: To determine the impact of achieving clinical remission after induction therapy for CD on post-induction outcomes.

Methods: A retrospective chart review of all persons with CD, age 18 or above, followed at Mount Sinai Hospital, Canada who were dispensed an approved biologic therapy for IBD between April 1st, 1996, and June 30th, 2021, and completed a complete course of induction was conducted. We stratified patients into those who were in clinical remission as per the physician global assessment at completion of biologic induction ("remitters") and those who were not ("non-remitters"). The start of follow-up was the completion date of biologic induction and patients were followed until end of last follow-up date. We extracted data on IBD symptoms, decisions on biologic therapy (such as discontinuation), healthcare utilization such as hospitalizations and emergency department (ED) visits, need for CD surgery, and endoscopic assessments. Endoscopic remission was defined based on a SES-CD score of ≤ 4 when available, or on the endoscopists' impression of absence of mucosal inflammation.

Results: A total of 160 patients were eligible for data extraction; 60.0% were male, 35.6% and 25.0% had stricturing and penetrating complications respectively, 28.9% had perianal disease and 34.3% had a history of a CD surgery. The index biologic included Infliximab in 24.4% patients, adalimumab in 32.5% patients, vedolizumab in 25.0% patients, and ustekinumab in 11.9% patients. Fifty-five (34.4%) patients were remitters and 105 (65.6%) were non-remitters after completion of biologic induction. Those in clinical remission at induction were less likely to have upper gastrointestinal CD (3.6% vs. 10.5%), have penetrating complications (18.2% vs. 28.6%), and perianal disease (16.4% vs. 35.2%) at time of biologic start.

Remitters were more likely to be in sustained clinical remission throughout follow-up compared to non-remitters (47.2% vs. 27.6%, $p=0.01$), be in clinical remission at last follow-up date (87.2% vs. 69.5%, $p=0.04$), and appeared to have a lower likelihood of discontinuing the index biologic (7.2% vs. 16.1%, $p=0.06$).

Similarly, remitters were less likely to undergo a CD-related intestinal resection during follow-up (3.6% vs. 13.3%, $p=0.05$).

There appeared to be no significant differences between remitters and non-remitters in proportion of patients being hospitalized for IBD (10.9% vs. 19.0%, $p=0.14$) or non-IBD (5.4% vs. 7.6%, $p=0.62$) reasons and visiting the emergency department (7.2% vs. 13.3% $p=0.26$). Of the 160 patients, 117 (73.1%) underwent a colonoscopy or sigmoidoscopy during follow-up. There were no differences in the rates of ulcer persistence (51.6% vs. 53.5%, $p=0.63$) or achievement of endoscopic remission (58.9% vs. 48.7%, $p=0.76$) between remitters and non-remitters at induction.

Conclusion: Achieving clinical remission after biologic induction is associated with sustained clinical remission in follow-up but not endoscopic remission.

Disclosure: Nothing to disclose.

PP0572

IMPACT OF NON-REMISSION IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS

H. Knight¹, A. Russnak¹, E. Pone², M. Sanon³

¹Adelphi Real World, Bollington, United Kingdom, ²Janssen Inc Canada, Montreal, Canada, ³Janssen Global Services, Horsham, United States of America

Contact E-Mail Address: msanon@its.jnj.com

Introduction: Current treatments for Crohn's disease (CD) and ulcerative colitis (UC) are associated with loss of treatment response. However, studies assessing the real-world burden of non-response in Canada are scarce and the clinical and humanistic burden remains unknown. We aimed to describe the burden of active disease on symptom prevalence and work impairment by describing patients with CD and UC according to remission status.

Aims & Methods: Data were drawn from the Adelphi Real World Inflammatory Bowel Disease Specific Programme™, a real-world, cross-sectional survey of gastroenterologists (GEs) and their consulting patients with CD and UC in Canada from June 2023 to January 2024. Data included physician-reported patient demographics and clinical characteristics. Descriptive analyses were conducted.

Results: 19 physicians reported data for 144 patients (73 with CD and 71 with UC). Physicians reported 20% of patients not to be in clinical or endoscopic remission (non-remitters), 31% to be in clinical remission only and 49% in both clinical and endoscopic remission. Mean (standard deviation) age was 44.5 (20.5) years among non-remitting patients, 33.5 (13.3) years among those in clinical remission only and 40.4 (17.4) years among patients in those with clinical and endoscopic remission. Among non-remitting patients, 38% were an ex-smoker, versus 14% of clinical remission and 18% of clinical and endoscopic remission patients. The most reported comorbid conditions included anxiety (24% non-remitters, 14% clinical remitters, 18% clinical and endoscopic remitters), depression (14% non-remitters, 0% in clinical remitters, and 14% in clinical and endoscopic remitters) and hypertension (14% non-remitters, 9% clinical remitters, and 14% clinical and endoscopic remitters). Top three current symptoms included fatigue (52% non-remitters, 32% clinical remitters, 15% clinical and endoscopic remitters), abdominal pain (69% non-remitters, 14% clinical remitters, 7% clinical and endoscopic remitters), and non-bloody diarrhea (48% non-remitters, 7% clinical remitters, 6% clinical and endoscopic remitters). Regarding employment, 38% of non-remitters were working full-time versus 48% of clinical remitters, and 58% of clinical and endoscopic remitters.

Conclusion: Patients with CD/UC that had not achieved or maintained remission experienced more symptom burden, comorbid conditions, and were often not in full-time employment than those in disease remission. Notably, non-remitters experienced a high symptom burden, including fatigue, abdominal pain, and diarrhea, which impacted daily living. Patients with both clinical and endoscopic remission experienced fewer symptoms and full-time employment. This highlights the importance of, and significant unmet need for, effective treatment in IBD to manage disease symptoms and decrease inflammation.

Disclosure: Janssen Global Services funded the research and I am an employee of Janssen

5-AMINOSALICYLATES FOR PATIENTS WITH ACTIVE OR QUIESCENT CROHN'S DISEASE: AN UMBRELLA REVIEW OF SYSTEMATIC REVIEWS

A. Alajmi¹, Y. Yuan², F. Magro^{3,4}, M.M. Estevinho^{5,3}, O.M. Nardone⁶, V. Jairath^{2,1,7}

¹Western University, Gastroenterology, London, Canada, ²Lawson Health Research Institute, London, Canada, ³University of Porto, Department of Biomedicine, Unit of Pharmacology and Therapeutics, Faculty of Medicine, Porto, Portugal, ⁴Unidade Local de Saúde de São João, Department of Gastroenterology, Porto, Portugal, ⁵Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal, ⁶Gastroenterology, Porto, Portugal, ⁷University of Naples Federico II, Gastroenterology, Naples, Italy, ⁷Western University, Epidemiology and Biostatistics, London, Canada

Contact E-Mail Address: abdulaziz.alajmi@lhsc.on.ca

Introduction: 5-aminosalicylates (5-ASAs) are commonly used in patients with Crohn's disease (CD), especially in mild-to-moderate disease. Over half of patients receive 5-ASA during their disease course, with up to 30% continuing long-term therapy for either active (induction of remission) or quiescent (maintenance of remission) disease. However, the evidence regarding their efficacy is mixed, with conflicting findings in systematic reviews (SRs). In preparation for the results of the STATIC trial (NCT 03261206)¹, we conducted an umbrella review to consolidate existing knowledge by identifying, evaluating, and synthesizing findings from published SRs on the use of 5-ASA in patients with active or quiescent CD.

Aims & Methods: Following Cochrane guidelines for "Overviews of Reviews" and adhering to the Preferred Reporting Items for Overviews of Reviews (PRIOR), we systematically searched major databases for relevant SRs published in English until February 28, 2024, summarizing data on 5-ASA use in induction, maintenance, or withdrawal trials of CD. We excluded SRs focusing solely on post-surgical patients or studying the chemoprevention effects of 5-ASA. Two independent reviewers screened articles, extracted data, and assessed quality using AMSTAR 2.

Results: Of 795 screened references, 8 SRs met our inclusion criteria, with the number of included RCTs ranging from 2 to 22 (Table). Most SRs included RCTs of patients with mild-to-moderate ileo-colonic CD. Three SRs focused on induction of remission, two on maintenance of medically induced remission, and three included both, while none investigated withdrawal of therapy. Two SRs were network meta-analyses (NMA) comparing 5-ASAs with other active treatments or placebo; four were Cochrane systematic reviews comparing 5-ASAs with placebo, corticosteroids, or thiopurines (AZA or 6-MP). One SR, published in 2017, used the outdated Jadad scale to assess the risk of bias of RCTs; only Cochrane reviews assessed the level of certainty of evidence. The latest NMA in 2017, including 22 RCTs for induction of remission, suggested that high-dose mesalamine was more effective than placebo, ranking higher than low-dose budesonide and sulfasalazine, though lower than systemic corticosteroid and high-dose budesonide. Conversely, the latest Cochrane review in 2016, including 12 RCTs for maintenance of remission, found no evidence of benefit for oral 5-ASAs over placebo for maintaining medically induced remission. No SRs performed subgroup analysis for duration of remission upon enrollment. Only the NMA conducted a sensitivity analysis to evaluate baseline disease activity, indicating that high-dose mesalamine was superior to placebo when restricted to RCTs with an enrollment CDAI between 150 to 450.

Conclusion: The results of this umbrella review of SRs suggest that high-dose mesalamine may be considered for inducing remission in mild-to-moderate CD. However, evidence does not support the role of 5-ASA for maintaining medically induced remission. Updating SRs with new evidence is imperative to provide guidance on patient subsets who

may benefit from 5-ASA use and these results will be updated with the STATIC trial¹.

References: 1. NCT03261206. Stopping Aminosalicilate Therapy in Inactive Crohn's Disease (STATIC) <https://classic.clinicaltrials.gov/ct2/show/NCT03261206>

Disclosure: Nothing to disclose.

Review Type (NMA or SR+MA or SR only)	Author, year	Search date (up to)	Searched database	Number of included studies/ study designs	Study Eligibility	Adults or pediatric	Induction trials, maintenance trials, or both	Intervention (5-ASA) / dose/ treatment duration/follow-up duration (range)	Comparisons (Control regimens, dose)/ duration	Key conclusions related to 5-ASA
NMA	Coward, 2017	Nov 2015	Cochrane reviews, Medline, EMBASE, CENTRAL	22 RCTs (mesalamine =9, sulfasalazine=4)	RCTs comparing budesonide, sulfasalazine, mesalamine, or systemic corticosteroids with placebo in CD	Adults	Induction	Sulfasalazine: 1 g/15 kg /d to 3 g /d; 6 - 17 wk Mesalamine: 1- 4 g /d; 8-16 wk (above and below 2.4 g/d as high vs low dose)	Placebo, systemic corticosteroids, budesonide	Treatment ranking for induction from best to worst: systemic corticosteroid> high dose budesonide > high dose mesalamine > (low dose budesonide = sulfasalazine)> low dose mesalamine > placebo. Mesalamine at doses above 2.4 g/day was more effective than placebo for the induction of remission in CD, this finding was shown in NMA but not the traditional MA. High dose mesalamine may be an option among patients preferring to avoid steroids. Sulfasalazine was not significantly superior to any therapy including placebo.
SR + MA	Chen, 2017	May 2014	Pubmed/Medline, EMBASE, ISI Web of Knowledge, CINAHL, COCHRANE Database of Systematic Reviews, CBM, CNKI, ChiCTR	Total 8 RCTs, but 6 for CD	RCTs of AZA or 6-MP vs 5-ASA	Adults	Both	AZA: 2-3 mg/kg/d; 1-3 yr 6-MP: 50 mg/d; 2 yr	Mesalamine: 3-4 g/d ; 1-3 yr	Thiopurines (AZA/6-MP) are more effective than 5-ASA for the treatment of CD (clinical relapse rate and remission rate).
SR+MA (Cochrane 2016 review)	Akobeng, Jun 2016	Jun 2016	MEDLINE, EMBASE, CENTRAL, Cochrane IBD group specialized register	12 RCTs	5-ASA agents vs either placebo or sulfasalazine in quiescent CD	Both	Maintenance	5-ASA: 1.6 g to 4 g/d; 12-24 mo dose 50 mg/kg/d />6 mo	Placebo	No evidence to suggest that oral 5-ASA preparations are superior to placebo for the maintenance of medically induced remission in patients with CD.
SR+MA (Cochrane 2016 review)	Chande, 2016	Oct 2015	MEDLINE, EMBASE and the two compared vs Cochrane Library	13 RCTs, only 5-ASA	RCTs of AZA and 6-MP for induction of remission in active CD (5-ASA as one of the comparative arms). One study 6-MP vs 5-ASA, one study AZA vs sulfasalazine; the two studies were pooled together	Adults	Induction	AZA and 6MP: NR ;NR	Mesalamine: 3 g/d; 30 wk Sulfasalazine: NR; 17 wk	Overall quality of the evidence for both outcomes was low to very low due to sparse data.
SR + MA (cochrane review)	Lim, 2016	Jun 2015	PubMed, EMBASE, MEDLINE, and the cochrane Central Library	20 RCTs	5-ASA drugs (sulfasalazine & mesalamine) vs placebo, corticosteroids, and other 5-ASA (alone or in combo with corticosteroids) in mild to moderate active CD	Adults	Induction	Mesalamine: 1 - 4.5 g /d; 6-16 wk Sulfasalazine: NR; up to 18 wk	Placebo, corticosteroids, other 5-ASA alone or in combination with corticosteroids	Sulfasalazine is modestly effective compared to placebo and inferior to corticosteroids for the treatment of mild to moderate active CD. Olsalazine and low dose mesalamine (1-2g/d) are not superior to placebo. High dose mesalamine (3.2-4g/d) is not more effective than placebo for inducing response or remission. High dose mesalamine (4-4.5g/d) has conflicting results compared to budesonide.
SR + MA (cochrane review)	Chande, 2015	Jun 2016	MEDLINE, EMBASE, and the Cochrane Library	11 RCTs (only two RCTs included mesalamine or sulfasalazine, published in 2000 and in 1979)	RCTs of AZA and 6-MP for maintenance of remission in active CD (5-ASA was one of the comparative arms). One study compared 6-MP to 5-ASA, one study compared AZA to sulfasalazine- the two studies were pooled together in meta-analysis	Adults	Maintenance	6-MP: 1 mg kg/ d Methotrexate: 10 mg/wk; 76 weeks AZA: 1- 2.5 mg/ kg/ d	5-ASA: 3g/d; 76 wk	Only two RCTs; no statistically significant difference in the proportion of patients who maintained remission between AZA (1.0 to 2.5 mg/kg/day) or 6-MP (1.0 mg/day) and mesalamine (3 g/day) or sulfasalazine (0.5 g/15 kg/day) therapy.
NMA	Moja, 2015	Oct 2014	MEDLINE, EMBASE, the Cochrane library and clinicaltrials.gov	25 RCTs (induction n=11, maintenance n=14)	Budesonide or mesalamine vs placebo or against each other in active or quiescent CD	Adults	Both	Mesalamine: 1 - 4 g/d; 6 wk for induction, 6 mo for maintenance Budesonide: 3 -18 mg/d; 6 wk for induction, 6 mo for maintenance	Placebo or mesalamine or budesonide in different doses	Budesonide 9mg/d or higher for induction of remission in active mild-to-moderate CD and 6mg/d for maintenance of remission appears to be the best treatment choice. Mesalamine is not effective in induction of remission and preventing relapse in mild-to moderate CD.
SR + MA	Ford, 2011	Dec 2011	MEDLINE, EMBASE, Cochrane central register	23 RCTs (active CD n=7, quiescent CD n=13, and quiescent CD=3)	5-ASA drugs (sulfasalazine, olsalazine) vs placebo or no treatment in quiescent or active CD.	Adults	Both	Sulfasalazine: 1 g/15 kg /d to max treatment 5 g/d Mesalamine: 1 - 4 g/d Olsalazine: 2 g /d; 4-12 mo Duration in active CD: 6 wk - 4 mo, in quiescent CD: 6-48 mo	Placebo or no	The role of 5-ASA in inducing remission of active CD and preventing relapse of quiescent CD remains uncertain.

PP0574

DEMOGRAPHIC FEATURES OF ULCERATIVE COLITIS PATIENTS AS PREDICTORS OF RESPONSE TO ADSORPTIVE GRANULOMONOCYTAPHERESIS AS REMISSION INDUCTION THERAPY: A RETROSPECTIVE ASSESSMENT OF TREATMENT OUTCOMES

T. Tanaka¹, D. Hirano¹, S. Ishimaru¹, K. Arataki¹

¹Tsuchiya General Hospital, Gastroenterology, Hiroshima, Japan

Contact E-Mail Address: tomotaka@c.do-up.com

Introduction: Inflammatory bowel disease (IBD) is associated with elevated myeloid lineage leucocytes, which show activation behaviour¹ including the CD14+CD16+DR++ phenotype known as proinflammatory monocytes and a major source of tumor necrosis factor- α .² Accordingly selective depletion of myeloid leucocytes by granulomonocytapheresis (GMA) with an Adacolumn is expected to promote remission and enhance drug efficacy. However, hitherto studies in IBD have reported contrasting efficacy outcomes, ranging from an 85%³ to statistically insignificant.⁴ Patients' demographic features should guide to select responder patients.

Aims & Methods: In ulcerative colitis patients, we were interested to identify relevant demographic features, which potentially could indicate a favourable response to GMA. Therefore, in a retrospective setting, we looked at the baseline clinical and endoscopic features of responders and non-responders to adsorptive GMA in 149 consecutive ulcerative colitis patients who had undergone GMA as remission induction therapy, 76 steroid naïve, 71 steroid dependent, and 2 steroid refractory. Patients had received up to an 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index (CAI) ≤ 4 was defined as remission. Biopsies from endoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.

Results: At entry, the average CAI was 12.8, range 10-17. Ninety-five patients (63.8%) had responded to GMA, 53 of 76 steroid naïve (69.7%), 41 of 71 steroid dependent (57.7%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent cohort. Mucosal biopsies revealed that infiltrating leucocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leucocytes in the biopsies from the responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responders, followed by steroid naïve patients. Further, a short duration of active UC prior to GMA marked a patient as a likely responder.

Conclusion: Patients who responded well to GMA attained a favourable long-term clinical course. GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is favoured by patients for its safety profile and for being a non-drug remission induction option. Patients with extensive deep ulcers, with long duration of UC refractory to multiple pharmacologies are unlikely to benefit from GMA. In therapeutic settings, knowing baseline features, which may identify responder patients should help to avoid futile use of medical resources.

References: 1. McCarthy DA, et al. Peripheral blood neutrophils in inflammatory bowel disease: morphological evidence of in vivo activation in active disease. Clin Exp Immunol 1991; 86: 489-93.

2. Belge KU, et al. The proinflammatory CD14+CD16+DR++ monocytes are a major source of TNF. J Immunol 2002;168:3536-42

3. Cohen RD. Treating ulcerative colitis without medications - look mom, no drugs. Gastroenterology 2005;128:235-36.

4. Sands BE, et al. A randomized, double-blind, sham-controlled study of granulocyte/monocyte apheresis for active ulcerative colitis. Gastroenterology 2008;135:400-09.

Disclosure: Nothing to disclose.

PP0575

PERSISTENCE OF ADVANCED THERAPY IN PATIENTS WITH ULCERATIVE PROCTITIS - ANALYSIS FROM THE POPULATION-BASED REGISTRY CREDIT

O. Hradsky¹, M. Lukas^{2,3}, P. Drastich⁴, T. Vanasek⁵, Z. Serclova^{3,6}, L. Nedbalova^{7,8}, M. Bortlík^{9,10}, D. Duricova^{3,11}

¹Second Faculty of Medicine, Charles University and Motol University Hospital, Paediatric Dpt, Prague, Czech Republic,

²1st Medical Faculty, Charles University in Prague, IBD Research and Clinical Centre, Prague, Czech Republic, ³ISCARE a.s.,

IBD Clinical and Research Center, Prague, Czech Republic,

⁴Institute for Clinical and Experimental Medicine, Department of Hepatogastroenterology, Prague, Czech Republic,

⁵University Hospital Hradec Králové, Czech Republic, Hepato-Gastroenterologie HK, outpatient clinic. 2nd Department of

Internal Medicine, Hradec Králové, Czech Republic, ⁶Faculty Hospital Kralovské Vinohrady, Surgical Department, Prague,

Czech Republic, ⁷Hospital Liberec - Turnov - Frýdlant v Čechách a.s., Clinical Centre for IBD, Liberec, Czech Republic, ⁸Hospital

Liberec - Turnov - Frýdlant v Čechách a.s., Department of Gastroenterology, Liberec, Czech Republic, ⁹Hospital Ceske

Budejovice, IBD Clinical and Research Center, Ceske Budejovice, Czech Republic, ¹⁰First Medical Faculty, Charles University,

Department of Internal Medicine and Institute of Pharmacology, Prague, Czech Republic, ¹¹1st Medical Faculty, Charles University in

Prague, Institute of Pharmacology, Prague, Czech Republic

Contact E-Mail Address: ondrej.hradsky@gmail.com

Introduction: Proctitis, a form of ulcerative colitis, is often highly symptomatic and challenging to manage. Data regarding the outcomes of biologic and small molecule therapy (advanced treatment) for patients with UC proctitis are limited, largely because these patients are usually excluded from randomized controlled trials.

Aims & Methods: Our aim was to evaluate the persistence of advanced treatment in patients with UC proctitis. From the Czech national prospective registry of biologic and innovative therapy of inflammatory bowel disease (CREDIT) which contains 9033 patients with IBD, we identified 200 treatment courses of advanced therapy among 167 patients with UC proctitis and ≥ 3 months follow-up. In this preliminary analysis, we employed mixed-effects Cox regression models to attempt to identify an association between treatment type and time to treatment discontinuation. An individual, medical centre, and time period were added as random effects into the models. To ensure a balance between the groups inverse probability of treatment weighting (IPTW) was used when comparing persistence between anti-tumor necrosis factor inhibitors (anti-TNF) and vedolizumab. We further analysed corticosteroid-free persistence after 6 months of treatment for those observations where this data were available. Missing data of co-variables were imputed using multiple imputation.

Results: Among 200 treatment courses, 78 were with infliximab (39%), 39 with adalimumab (20%), 59 with vedolizumab (30%), 13 with tofacitinib (7%), three each with filgotinib, golimumab, and ustekinumab, and two with upadacitinib. Most of the treatment courses were given as 1st line (1st 129, 65%; 2nd 46, 23%; $>2^{\text{nd}}$ 25, 13%). Concomitant corticosteroids at the start of advanced treatment course were reported in 119 (60%) of cases. Comparison of different treatment types revealed that persistence on vedolizumab was longer than on infliximab in the final adjusted model (Hazard Ratio [HR] 2.33, 95% CI 1.17 - 4.67, p-value=0.017). Moreover, vedolizumab was also more persistent compared with anti-TNF drugs as a group in the IPTW analysis (HR 8.03, 95% CI 2.60 - 24.84, p-value=0.001). Corticosteroid-free persistence at 6 months was found in 31/50 (62%) courses of vedolizumab and 56/97 (58%) courses of anti-TNF treatment. AI-

though vedolizumab did not show greater corticosteroid-free persistence at 6 months than infliximab (HR 1.50, 95% CI 0.56-3.96, p-value=0.417), IPTW analysis revealed that vedolizumab was significantly more corticosteroid-free persistent compared to anti-TNF drugs as a group (HR 9.55, 95% CI 2.90-31.42, p-value=0.001).

Conclusion: Based on data from real clinical practice, the persistence of advanced treatment in UC proctitis seems to be low. Treatment with vedolizumab appears to be more persistent than anti-TNF therapy. However, efficacy data must also be analysed before vedolizumab can be considered preferable.

Disclosure: OH: Lectures/congress fees/consultancy: MSD, Abbvie, Takeda, Nutricia, Sandoz, Eli Lilly

ML: Lectures/congress fee/consultancy: Johnson&Johnson, Celltrion, Abbvie, Takeda, Biogen, Pfizer

PD: Lecture fee/consultancy: AbbVie, Pfizer, Takeda, Janssen, Eli-Lilly, Sobi, Celltrion

TV: Lecture fee/consultancy: AbbVie, Takeda

ZS: Lecture fee/consultancy: Takeda

LN: Lecture fee/consultancy: Pfizer, Takeda, Janssen (Johnson and Johnson), Ferring

MB: Lecture fee/consultancy: AbbVie, Pfizer, Takeda, Janssen Cilag, Eli-Lilly, Ferring,

Celltrion, Alfasigma, SOBI, PRO.MED.CS

DD: Lecture fee/consultancy: AbbVie, Pfizer, Takeda, Janssen, Eli-Lilly, Ferring

PP0576

MANAGEMENT OF PERIANAL FISTULIZING CROHN'S DISEASE IS NOT IN KEEPING WITH GUIDELINES – RESULTS FROM A MULTI-CENTRE RETROSPECTIVE COHORT STUDY

N. Wan^{1,2}, R.M. Matthias^{3,2}, R.V. Bryant^{3,2}, B. Andrin¹, S.W. Han³, D. Sathananthan^{1,2}

¹Lyell McEwin Hospital, Gastroenterology, Adelaide, Australia,

²University of Adelaide, Faculty of Health and Medical Sciences, Adelaide, Australia, ³The Queen Elizabeth Hospital, Inflammatory Bowel Disease Service, Adelaide, Australia

Contact E-Mail Address: nicholas.wan@sa.gov.au

Introduction: Perianal fistulising Crohn's disease (PFCD) affects up to 20% of patients with Crohn's Disease (CD). PFCD can cause pain, purulent discharge and faecal incontinence, leading to significant morbidity and reduction in quality of life. The use of biologic therapy, antibiotics and surgical intervention remain the mainstay of management of perianal fistulas.

Aims & Methods: This study aims to review current practices in the management of PFCD across two large tertiary IBD centres. This retrospective cohort study assessed adult patients with PFCD between two tertiary Australian hospitals between 2006 to 2024. Patients with PFCD were identified using prescribing data. CD phenotype, therapy and fistula-related data were extracted. Biologic choice and therapeutic drug monitoring, antibiotic choice and duration, surgical intervention, and length of stay in hospital were monitored.

Cross-sectional disease activity of perianal fistulizing disease was assessed at the time of data collection using clinical fistula symptom grade and radiological assessment were available. Clinical remission was defined as fistula symptom grade of 1 or less. Radiological remission was defined by healing fistula tracts or no active inflammation seen on MRI. The study was approved by the Central Adelaide Local Health Network Human Research Ethics Committee (HREC19145).

Results:

Gender	n = 57
Male, n	30
Female, n	27
Age, y, median (IQR)	40 (31-54)
Active Smoker, n (%)	14 (24.5)
Median length of clinical follow up, months, n (IQR)	46.5 (23.8-72.3)
Antibiotics Prescribed	
Metronidazole, n treated (%)	47 (68.1)
Amoxicillin / Clavulanic acid, n treated (%)	13 (27.7)
Others, n treated (%)	9 (4.2)
Duration of Antibiotics	
Metronidazole, median duration, days (IQR)	5 (5-7)
Amoxicillin / Clavulanic acid, median duration, days (IQR)	5 (5-10)
Others, median duration, days (IQR)	14 (7-14)
Biologic therapy	
Total patients on biologic therapy, n (%)	56 (98.2)
Infliximab, n (%)	43 (75.4)
Adalimumab, n (%)	11 (19.3)
Ustekinumab, n (%)	2 (3.5)
Therapeutic Drug Monitoring (Infliximab)	
Infliximab level performed, n (%)	37 (86%)
Subtherapeutic (Infliximab level <10), n (%)	30 (81.1%)
Active disease and subtherapeutic (Infliximab level <10), n (%)	12 (40%)
Remission status	
Clinical Remission, n (%)	
- Defined as Fistula symptom grade of 1 or less	
Radiological Remission, n (%)	48 (84.2)
- Defined as healing fistula tracts or no active inflammation seen on MRI	33 (57.8)
Subtherapeutic Therapeutic Drug Monitoring (All biologic agents)	
In Remission, n (%)	18 (56.2)
Active Disease, n (%)	14 (43.8)

Table 1. Baseline characteristics.

57 patients (median age, 40 years (31-54); 52.6% male) with PFCD were included in the study and followed over a median duration of 46.5 months (23.8-72.3). There were a total of 157 individual surgical procedures over the period, 2.75 per patient, most of which (94.2%) were examination under anaesthesia. Antibiotic therapy was dispensed for either perianal sepsis or an actively draining fistula in 26 patients, 2.65 number of courses per patient. The most common antibiotic prescribed was Metronidazole (68.1%), followed by Amoxicillin / Clavulanic acid (27.7%). The median duration of antibiotic therapy was 5 days (5-7) for Metronidazole and 5 days (5-10) for Amoxicillin / Clavulanic acid. There were 56 (98.2%) patients on biologic therapy. The most common biologic agent was Infliximab (75.4%), followed by Adalimumab (19.3%) and Ustekinumab (3.5%). At the time of analysis, 48 patients (84.2%) were in clinical remission and 33 patients (57.8%) were in radiographical remission. In patients treated with infliximab, 37/43 (86%) had therapeutic drug monitoring performed. Amongst these, 30 (81.1%) had subtherapeutic levels (defined as Infliximab level < 10), with 12/30 (40%) of patients having active PFCD.

Conclusion: Across two tertiary IBD centres, management of PFCD is variable and not in keeping with current guidelines. Short courses of antibiotic therapy were used, and the majority of patients had subtherapeutic drug levels when tested. Optimising outcomes for patients with PFCD requires awareness of best practice and a multidisciplinary team approach.

Disclosure: Nothing to disclose.

PP0577

MEDIUM TERM OUTCOMES AND PREDICTIVE FACTORS OF COLECTOMY IN PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS

N. Wan^{1,1}, B. Tandon^{2,1}, S. Ullah¹, A. Barnes^{2,1}, P. Spizzo^{2,1}

¹Lyell McEwin Hospital, Gastroenterology, Adelaide, Australia,

²Flinders University, College of Medicine and Public Health, Adelaide, Australia, ³Flinders Medical Centre, Gastroenterology, Adelaide, Australia

Contact E-Mail Address: nicholas.wan@sa.gov.au

Introduction: Acute severe ulcerative colitis (ASUC) is a medical emergency associated with a significant mortality rate. The literature amongst medium-term outcomes of ASUC remain limited.

Aims & Methods: This study aims to determine if early medical rescue therapy in patients with ASUC reduces the need for colectomy in the medium-term. This was a retrospective cohort study conducted in an Australian quaternary IBD centre. Adult UC patients admitted between January 2015 and December 2021 that fulfilled the Truelove and Witts' criteria for ASUC were identified and included. Demographic and clinical data was collected including date of colectomy and IBD-related readmission at 6 months. Patients who did not receive Infliximab (IFX) as rescue therapy or following discharge were excluded. Medium term was defined as within 1-3 years. The primary outcome of this study was colectomy (within 1-3 years), secondary outcomes were UC-related hospital re-admissions at 6 months. Kaplan-Meier curves were utilised to investigate colectomy and readmission-free days from the initial flare to the commencement of biologics. Multivariate log binomial models were employed to explore the significant factors related to colectomy and six-month readmission. The study was approved by the Southern Adelaide Local Health Network Ethics Committee LNR/22/SAC/157.

Results:

Baseline Characteristics	Patients (n = 32)
Male / Female, n	17/15
Age, y, median (IQR)	36 (28-48)
Colectomy, n (%)	11 (34.4)
Length of stay in hospital, days, median (IQR)	10 (7.8-13.3)
Flare to IFX commencement, days, median (IQR)	5 (3-7.3)
IFX commencement to colectomy, days, median (IQR)	9 (5-330)
D1 CRP, mg/L, median (IQR)	95 (37.6-157.7)
D3 CRP, mg/L, median (IQR)	29.7 (15.1-98.4)
D1 Albumin, g/L, median (IQR)	29 (23.8-32)
D3 Albumin, g/L, median (IQR)	22 (20.5-27)
Haemoglobin, g/L, median (IQR)	119.5 (110-129.5)
Platelet, 10 ⁹ /L, median (IQR)	400 (306-492.75)
Statistical Analysis - Colectomy	Odds Ratio / p-value
Female	6.59 / 0.2
D1 CRP	1.02 / 0.3
D3 CRP	0.98 / 0.3
D1 Albumin	2.09 / 0.074
D3 Albumin	0.24 / 0.05
Statistical Analysis - Re-admission	Odds Ratio / p-value
Female	1.14 / > 0.9
D1 CRP	1.0 / 0.7
D3 CRP	1.0 / > 0.9
D1 Albumin	0.79 / 0.2
D3 Albumin	0.98 / > 0.9

Table 1. Baseline Characteristics

267 patients with UC flares were identified between the shortlisted timeframes. After exclusions, 32 patients remained (median age, 36 years (18-71); 56.3% male). The median time of admission to the commencement of IFX was 5 days (3-7.3). The overall colectomy rate was 34.4% (11/32); of these patients, 3 needed a colectomy during their index presentation and 8 within the subsequent 3 years. The median time from IFX commencement to colectomy was 9 days (5-330). 9 patients (28.1%) had a UC-related

readmission within 6 months of discharge. Biochemical results (day 1 CRP, day 1 albumin) and demographics such as age and gender were analysed, however we could not find any statistically significant association with the need for colectomy or UC-related readmission. The overall trend and likelihood of undergoing colectomy and having a UC-related admission rose with longer durations between IFX initiation, however the results were not statistically significant.

Conclusion: The need for colectomy remains high in patients with ASUC. We were unable to demonstrate any statistically significant predictors of colectomy in the medium term due to the small sample size. Future larger prospective studies are warranted to obtain statistical significant findings for our current study.

Disclosure: Nothing to disclose.

PP0578

THE INFLAMMATORY DURATION INDEX: A NOVEL SCORE FOR PREDICTING CORTICOSTEROID RESPONSE IN ACUTE SEVERE ULCERATIVE COLITIS

A. Nikolic¹, D. Popovic¹, A. Sokic Milutinovic¹, S. Djuranovic¹, I. Jovicic¹, A. Toplicanin¹, S. Vuksanovic¹, J. Spirić¹, S. Dragasevic¹

¹Clinical Centre of Serbia, Clinic for gastroenterology and hepatology, Belgrade, Serbia

Contact E-Mail Address: andrejanikolic@gmail.com

Introduction: Acute severe ulcerative colitis (ASUC) represents a life-threatening medical emergency¹. Patients with ASUC require hospitalization and instant medical treatment, with corticosteroids remaining the primary initial therapy. One-third of ASUC patients are steroid non-responders². Management of ASUC patients should be based on efficient and fast assessment due to the need for further treatment decisions.

Aims & Methods: Our study aimed to create a new ASUC algorithm to predict corticosteroid response on the first day of hospital admission. A new Inflammatory Duration Index (IDI) was created by multiplying the onset duration of symptoms of UC prior to hospital admission and CRP to Albumin Ratio^{2,3}. A cross-sectional study included 103 newly diagnosed patients with UC hospitalized at the University Clinical Center of Serbia from 2020 to 2023.

Patients included in the study fulfilled the criteria for ASUC according to Truelove's and Witts' severity index (62 male and 41 female, age ranging from 18 to 75 years). Descriptive statistics, Spearman's correlation, logistic regression, and ROC analysis were used to assess the predictive value of the score.

Results: The Inflammatory Duration Index (IDI) showed a significant negative correlation with glucocorticoid response (Spearman's rho = -0.383, p < 0.01). Logistic regression analysis revealed the score's predictive capacity for treatment outcomes. The ROC curve analysis showed an area under the curve (AUC) of 0.722, suggesting a good diagnostic ability to predict the glucocorticoid response. If we were to determine a sensitivity of 91%, this ratio would have to value less than 120 to predict the complete response to glucocorticoids.

Conclusion: The Inflammatory Duration Index (IDI) upon admission can serve as a valuable prognostic tool in UC management. Identifying patients who are less likely to respond to conventional glucocorticoid therapy, facilitates more personalized and effective treatment strategies, but further studies are needed to confirm this.

References:

- Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2:1041-1048.
- Nakase H. Acute Severe Ulcerative Colitis: Optimal Strategies for Drug Therapy. Gut Liver. 2023;17(1):49-57.

3. Gibson DJ, Hartery K, Doherty J, et al. CRP/Albumin Ratio: An Early Predictor of Steroid Responsiveness in Acute Severe Ulcerative Colitis. *J Clin Gastroenterol*. 2018;52(6):e48-e52.
4. Reinisch W, Wang Y, Oddens BJ, Link R. C-reactive protein, an indicator for maintained response or remission to infliximab in patients with Crohn's disease: a post-hoc analysis from ACCENT I. *Aliment Pharmacol Ther*. 2012;35(5):568–76.

Disclosure: Nothing to disclose.

PP0579

TOFACITINIB VERSUS VEDOLIZUMAB AMONG BIO-NAÏVE PATIENTS WITH ULCERATIVE COLITIS: A REAL-WORLD PROPENSITY-WEIGHTED COMPARISON

B. Gros^{1,2}, N. Constantine-Cooke^{3,4}, J. Kennedy², A. Elford^{2,5}, C. O'Hare^{2,6}, C. Noble², G.-R. Jones^{2,7}, I. Arnott², N. Plevris², C.W. Lees^{2,4}

¹Reina Sofía University Hospital, Gastroenterologist, Cordoba, Spain, ²Western General Hospital, Edinburgh IBD Unit, Edinburgh, United Kingdom, ³University of Edinburgh, Centre for Genomics and Experimental Medicine, Institute of Genetics and Cancer, Edinburgh, United Kingdom, ⁴University of Edinburgh, MRC Human Genetics Unit, Institute of Genetics and Cancer, Edinburgh, United Kingdom, ⁵The University of Melbourne, Faculty of Medicine, Melbourne, Australia, ⁶Western General Hospital, Edinburgh Pharmacy Unit, Edinburgh, United Kingdom, ⁷University of Edinburgh, Centre for Inflammation Research, The Queen's Medical Research Institute, Edinburgh, United Kingdom

Contact E-Mail Address: begrosal@gmail.com

Introduction: Over the last decade, treatment options for moderate-to-severe ulcerative colitis (UC) have expanded. However, comparative studies between these agents are limited, especially among biologic naïve patients. We aimed to compare the efficacy, safety and persistence of tofacitinib and vedolizumab as the first advanced treatment for patients with UC.

Aims & Methods: Patients who received either tofacitinib or vedolizumab as their first advanced therapy for UC via the NHS Lothian health board were included. Patients aged 65 years or older were excluded. We used inverse probability of treatment weighting (IPTW). The probability of treatment assignment was calculated via logistic regression using age, gender, IBD duration, Montreal extent, CRP, concomitant corticosteroids, and partial Mayo score at drug commencement. Missing data for these variables were imputed using multivariate imputation by chained equations. Confounder-adjusted survival curves were created using Kaplan-Meier estimates weighted via IPTW. The Pepe and Fleming test was used to compare survival curves.

Results: We included 158 patients of whom 81 (51.2%) received vedolizumab and 77 (48.7%) tofacitinib. Median follow-up for patients on vedolizumab was 3.1 (1.6–4.8) years and for tofacitinib 1.5 (0.34–2.3) years. The cohort was 59.3% male with a median age of 41.1 years (31.5–51.8) and disease duration of 6.21 years (2.56–13.5). At drug commencement there were no differences in steroid prescription, partial Mayo score, CRP or faecal calprotectin.

Vedolizumab persistence was superior to tofacitinib ($p=0.005$). Primary non-response and secondary loss of response were 9.9% and 17.3% for vedolizumab and 23.4% and 13% for tofacitinib respectively. At week 12, steroid free clinical remission was more frequent in the vedolizumab group (69% vs 51.4%, $p=0.030$), Table 1. There were no differences in the frequency of adverse events (11 [13.6%] vedolizumab vs 19 [24.7%] tofac-

itinib, $p=0.629$). However, adverse events resulting in temporary discontinuation of the drug occurred in 1 (1.2%) vedolizumab versus 11 (14.3%) tofacitinib, $p=0.013$.

Conclusion: We found that the persistence and tolerability of vedolizumab was superior to tofacitinib in bio-naïve UC, although the rates of clinical and biomarker remission were comparable. These data may help inform positioning of advanced therapy in UC.

Disclosure: Beatriz Gros has served as consultant to Galapagos and Abbvie and as speaker for Abbvie, Janssen, Takeda, Pfizer and Galapagos. Nikolas Plevris has served as a speaker for Janssen, Takeda and Pfizer. Professor Charlie Lees has acted as a consultant to Abbvie, Janssen, Takeda, Pfizer, Galapagos, Bristol Myers Squibb, B.I., Sandoz, Novartis, GSK, Gilead, ViforPharma, Dr Falk, Trellus Health and Iterative Scopes; he has received speaking fees and travel support from Pfizer, Janssen, Abbvie, Galapagos, MSD, Takeda, Shire, Ferring, Hospira and Dr Falk. Gareth-Rhys Jones has served as a speaker for Takeda, Janssen, Abbvie, Fresenius and Ferring.

PP0580

PREDICTIVE FACTORS OF ADVERSE SKIN REACTIONS DURING BIOLOGIC THERAPY FOR INFLAMMATORY BOWEL DISEASES IN CHILDREN - PRELIMINARY DATA FROM CZECH NATIONAL REGISTRY BASED PROSPECTIVE STUDY

D. Kazeka¹, K. Zarubova¹, I. Copova¹, T. Lerchova^{2,1}, J. Schwarz³, E. Karaskova⁴, M. Hrunka⁵, M. Durilova¹, K. Mitrova¹, E. Vlckova¹, M. Kubat¹, J. Pavelcova¹, J. Bronsky¹, O. Hradsky¹

¹Second Faculty of Medicine, Charles University and Motol University Hospital, Department of Paediatrics, Prague, Czech Republic, ²University of Gothenburg, Sahlgrenska Academy, Department of Paediatrics, Institute of Clinical Sciences, Gothenburg, Sweden, ³Faculty of Medicine in Pilsen, Faculty Hospital, Charles University in Prague, Department of Paediatrics, Pilsen, Czech Republic, ⁴Faculty of Medicine, Palacky University Olomouc and University Hospital Olomouc, Department of Paediatrics, Olomouc, Czech Republic, ⁵Faculty of Medicine, Masaryk University and University Hospital Brno, Department of Paediatrics, Brno, Czech Republic

Contact E-Mail Address: denkazeka@gmail.com

Introduction: No clinical trials have directly compared biologics in children with inflammatory bowel disease (pIBD), with observational studies indicating only modest differences in efficacy [1]. Risk factors for adverse effects of individual preparations are important for treatment personalization. Cutaneous adverse effects of tumour necrosis factor antagonists (anti-TNF) have been widely reported, affecting up to 48% of anti-TNF treated pIBD patients [2]. Identifying patients at risk for developing adverse cutaneous effects may be beneficial for treatment sustainability.

Aims & Methods: The Czech National Prospective Registry of Biologic and Targeted Therapy of Inflammatory Bowel Disease (CREdit) was used to identify the biologic treatment courses. pIBD patients younger than 19 years were considered eligible if they were treated with anti-TNF, vedolizumab, or ustekinumab. Baseline patient characteristics, including anthropological features, disease classification, and the reason for biologic, were collected in the registry. Data on the family and personal history of skin conditions and atopic diseases were collected at enrolment or, if missing, by systematic telephone interview. The occurrence of cutaneous adverse events, including type (atopic, psoriatic, pustulotic or other), distribution and the quality of life as assessed by validated questionnaires were prospectively collected. Observation was defined as one course of

biological therapy in one patient. The primary outcome was defined as time to onset or significant worsening of the skin condition during biological therapy. Cox proportional hazard models with mixed effect were designed for potential predictors. Predictors that were statistically significant in the univariate analysis were used to build the multivariate model. **Results:** Among the 544 included observations of 423 paediatric patients from 4 centres, 208 were treated with adalimumab (38%), 256 with infliximab (47%), 46 with ustekinumab (8%), and 36 with vedolizumab (7%). Most patients had CD (N=311; 74%) and were also treated with an immunomodulator at the time of initiation of biologic therapy (N=478; 78%). The primary outcome was achieved in 108 observations (atopic [9%], psoriatic [34%], pustulotic [13%]), with most of the children treated with adalimumab (50%), 47% with infliximab and 3% with ustekinumab. Female sex (hazard ratio (HR) 1.84, 95% confidence interval (CI) 1.22–2.78), anti-TNF therapy (HR 6.97, 95% CI 2.15–22.59), and family history of atopic diseases (HR 1.77, 95% CI 1.12–2.79) were identified as predictors of the occurrence or progression of the cutaneous adverse events in univariate analysis. These predictors retained their significance in the multivariate model additionally including diagnosis, concomitant immunomodulator use and line of therapy (Table 1).

Predictor	HR (95% CI)	p-value
Female sex	1.82 (1.18–2.81)	0.01
Family history of atopic diseases	1.82 (1.13–2.91)	0.01
anti-TNF therapy	6.84 (1.98–23.63)	<0.01
Crohn's disease	1.33 (0.75–2.36)	0.43
Biologically naïve	0.79 (0.46–1.37)	0.41
Concomitant immunomodulator	1.48 (0.76–2.88)	0.25

Table 1 – Multivariate Cox proportional hazard model of cutaneous adverse effect predictors.

Conclusion: These preliminary data from the prospective multicentre study suggest that when choosing biologic treatment, the female sex, family history of atopic diseases and, in particular, anti-TNF treatment, may be considered as predictors of cutaneous adverse effects in paediatric IBD patients regarding the occurrence of cutaneous adverse reactions.

References:

1. Sands BE, Irving PM, Hoops T, Izanec JL, Gao LL, Gasink C, Greenspan A, Allez M, Danese S, Hanauer SB, Jairath V, Kuehbach T, Lewis JD, Loftus EV Jr, Mihaly E, Panaccione R, Scherl E, Shchukina OB, Sandborn WJ; SEAVUE Study Group. Ustekinumab versus adalimumab for induction and maintenance therapy in biologic-naïve patients with moderately to severely active Crohn's disease: a multicentre, randomised, double-blind, parallel-group, phase 3b trial. *Lancet*. 2022 Jun 11;399(10342):2200-2211. doi: 10.1016/S0140-6736(22)00688-2.

2. Mälkönen T, Wikström A, Heiskanen K, Merras-Salmio L, Mustonen H, Sipponen T, Kolho KL. Skin reactions during anti-TNFα therapy for pediatric inflammatory bowel disease: A 2-year prospective study. *Inflammatory bowel diseases*. 2014;20(8):1309-15. doi: 10.1097/MIB.000000000000088.

Disclosure: DK: Lecture/workshop fee: Takeda, Vitabalans Oy
KZ: Consultancy: Nestlé
IC: Nothing to disclose.
TL: Nothing to disclose.
JS: Lectures/congress fees/consultancy: MSD, Abbvie, Takeda, Nutricia, Nestle
EK: Nothing to disclose.
MH: Lectures/congress fees/consultancy: Nutricia, Nestlé
KM: Lectures/consultancy: Janssen, Eli Lilly
MD: Congress fees: Nutricia
EV: Workshop/congress fee: Biocodex, Ewopharma
MK: Nothing to disclose.
JP: Nothing to disclose.

JB: Lectures/congress fees/consultancy: MSD, Abbvie, Nutricia, Nestlé, Sanofi
OH: Lectures/congress fees/consultancy: MSD, Abbvie, Takeda, Nutricia, Sandoz, Eli Lilly

PP0581
COMPARISON OF THE EFFICACY AND SAFETY OF CORTICOSTEROIDS IN ELDERLY-ONSET ULCERATIVE COLITIS AND NON-ELDERLY-ONSET ULCERATIVE COLITIS

A. Tatsuguchi¹, Y. Shimazu¹, T. Nishimoto¹, K. Iwakiri¹
¹Nippon Medical School, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: tachan@nms.ac.jp

Introduction: Clinical practice guidelines recommend corticosteroids use for remission induction therapy in patients with moderate-severe ulcerative colitis (UC); however, there are limited data on their effectiveness and safety in elderly UC patients. Although comparable outcomes in elderly UC patients have been reported, these patients show higher morbidity, and mortality, than younger patients due to the lower malnutrition and immunocompromised state. It has been reported that elderly onset is associated with a lower effectiveness of intravenous corticosteroids with higher risks of surgery and adverse events in UC. Thus, the efficacy and safety of corticosteroids in elderly UC patients remains to be determined.

Aims & Methods: To compare the clinical characteristics in elderly onset UC patients treated with corticosteroid against non-elderly onset patients. We enrolled 170 UC patients presenting at Nippon Medical School Hospital prior to March 2023. The patients were divided into two groups comprising elderly-onset and non-elderly-onset UC patients, and their clinical characteristics were determined according to medical records. We defined elderly-onset UC as UC initially diagnosed in patients at 65 years or older according to WHO criteria.

Results: Clinical characteristics of UC patients were as follows: 12 patients were categorized as elderly-onset UC including 3 males to 9 females, and 158 were non-elderly-onset UC including 91 males to 67 females. The proportion of females was higher in elderly-onset UC patients than in non-elderly onset UC patients. The rate of patients who underwent corticosteroid induction therapy was significantly higher in elderly-onset UC patients; 9 out of 12 (75%) in elderly-onset UC patients and 81 out of 158 (51%) in non-elderly-onset UC patients, although average prednisone doses were comparable. Adverse events were observed in 3 cases (33%) in elderly-onset UC patients: candidiasis in 2 cases and hyperglycemia in 1 case, and no patients required surgery. While adverse events were 21 cases (26%) in non-elderly-onset UC patients: liver disfunction (n=4), followed by hyperglycemia (n=2), depression (n=2); and one each for cytomegalovirus colitis, clostridioides difficile infection, gastric ulcer and so on. Hemoglobin values were significantly lower (P<0.01), and erythrocyte sedimentation ratio was significantly higher (P=0.04) in elderly-onset UC patients. On the other hand, no significant difference was observed between the two groups regarding; pre-treatment WBC counts, serum albumin concentrations, neutrophil-lymphocyte ratio, CRP values, the rate of patients who achieved clinical remission and steroid-free remission, rate of introduction of immunomodulators, rate of use of biologics, number of hospitalizations, and number of relapses.

Conclusion: There was no difference in responsiveness to steroid therapy between non-elderly and elderly UC patients, and no serious adverse events were observed during the period of steroid therapy in both groups. However, consideration should be given to comorbidity in elderly patients.

Disclosure: The authors declare that they have no competing interests.

PP0582

EXPLORING BIOMARKER OF CORTICOSTEROID THERAPY FOR MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

T. Nishimoto¹, A. Tatsuguchi², N. Akimoto³, J. Omori⁴, Y. Shimazu², R. Inoue², K. Iwakiri²

¹Nippon Medical school, Tokyo, Japan, ²Nippon Medical School, Tokyo, Japan, ³Nippon Medical School, Graduate School of Medicine, Gastroenterology, Tokyo, Japan, ⁴Nippon Medical School Department of Gastroenterology, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: clubman629@gmail.com

Introduction: Ulcerative colitis (UC) is characterized by chronic immune mediated inflammation of the colon and rectum. Corticosteroid (CS) is a common treatment for patients with moderate to severe active UC, but its effect varies among patients, including resistance, response, and dependence. In addition, the longer CS therapy continues, the greater the concern regarding drug-related adverse effects. New immunomodulatory therapies are being developed for the treatment of UC drug showing promise in the treatment of patients with moderate UC refractory to aminosalicylic acid (5-ASA). Thus, the clinical benefit of being able to predict whether certain patients would benefit from CS therapy prior to administration cannot be overestimated.

Aims & Methods: We compared the clinical characteristics of patients with steroid-responder (SR) and steroid-non-responder (SNR) UC and retrospectively evaluated for biomarkers that could predict the efficacy of CS prior to administration in patients with moderate to severe active UC who failed to respond to 5-ASA.

We enrolled 100 UC patients presenting at Nippon Medical School Hospital with a history of CS administration prior to December 2023. The patients were divided into two groups, SR patients and SNR patients, and their clinical characteristics were determined according to medical records. Eosinophil counts were measured in the high-power field using Direct Fast Scarlet staining.

Results: Clinical characteristics of UC patients were as follows: the median age, 48±17 years; height 167±9.2 cm, and weight, 58±14 kg; including 61 males to 39 females. The most common disease extent type was the total colitis (63%), followed by left-sided colitis (32%), and proctitis (5%). Complete SNR was observed in 15 patients (15%), with remaining 85 patients (85%) classified as SR. There was no significant difference found in Mayo Endoscopic Score, first dose of CS, number of hospitalizations, number of relapses, proportion of patients with total-colitis type, or duration of CS treatment between the SR group and the SNR group. The non-remission rate, defined as failure to achieve mucosal healing, was significantly higher in the SNR group (66%) than in the SR group (36%) ($P=0.03$). The proportion of patients treated with azathioprine was significantly higher in the SR group (40%) than in the SNR group (39%). The proportion of patients treated with biologics or small molecular compounds was significantly higher in the SNR group (40%) than in the SR group (22%) ($P=0.03$). We then compared hematological biomarkers in blood samples obtained prior to CS administration between the two groups. There was no significant difference in WBC counts, hemoglobin values, serum albumin concentrations, CRP values, and ESR between the two groups. However, eosinophil profiles (both total count numbers and ratio to white blood cell counts) were significantly higher in the SR group than in the SNR group ($P=0.02$). Neutrophil-lymphocyte ratio tended to be higher in the SR group than in the SNR group ($P=0.06$). The number of infiltrated eosinophils in the inflamed rectal mucosal tissue was not significantly different between the two groups. The number of infiltrated eosinophils in the rectal mucosa tended to decrease in the steroid-response groups ($p = 0.07$). However, there was no difference in the number of infiltrated eosinophils in the ste-

roid-non-response groups.

Conclusion: Both eosinophil in the blood and in the rectal mucosa, and neutrophil-lymphocyte ratio in the blood could be potential biomarkers for steroid responsiveness prior to administration.

References: • British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019; 68: s1–s106

• Severe ulcerative colitis: at what point should we define resistance to steroids? WJG 2008 Sep 28;14(36):5504-7.

• A reproducible grading scale for histological assessment of inflammation in ulcerative colitis: Gut 47 : 404–409. 2000

• Mucosal Eosinophil Abundance in Non-Inflamed Colonic Tissue Is Associated with Response to Vedolizumab Induction Therapy in Inflammatory Bowel Disease : J Clin Med Res,2022

Disclosure: Nothing to disclose.

PP0583

PATIENTS WITH INFLAMMATORY BOWEL DISEASES RECEIVING ESCALATED INFLIXIMAB THERAPY ACHIEVE STEROID-FREE CLINICAL AND BIOCHEMICAL REMISSION WITH HIGHER SERUM TROUGH LEVELS: A CROSS-SECTIONAL STUDY AT A GREEK TERTIARY CENTRE

A. Orfanidou¹, K.H. Katsanos¹, T. Voulgaris², A. Kofinas³, M. Konstandi³, D.K. Christodoulou¹

¹University General Hospital of Ioannina, University of Ioannina, Department of Gastroenterology, Ioannina, Greece, ²Aretaieion University Hospital, 2nd Department of Surgery, Endoscopic Unit, Athens, Greece, ³University of Ioannina, Faculty of Medicine, Department of Pharmacology, Ioannina, Greece

Contact E-Mail Address: dchristodoulou@gmail.com

Introduction: Therapeutic monitoring of infliximab (INF) correlates with improved therapeutic outcomes in inflammatory bowel diseases (IBD).

Aims & Methods: The aim of this cross-sectional study was to assess the relationship between serum INF trough levels (TLs) and positive therapeutic outcomes in patients with ulcerative colitis (UC) and Crohn's disease (CD) in a Greek population. The relationship between adverse events (AEs) and the existence of anti-infliximab antibodies (ADAs) was also investigated. Consecutive adult patients with IBD treated with intravenous INF at maintenance phase in a Greek tertiary centre were included. Investigated therapeutic outcomes included sustained clinical remission (CR), steroid-free clinical remission (SFCR), biomarker remission (CRP <5mg/L, BR) and combined (steroid-free clinical and biochemical) remission (SFCBR). Infliximab TLs and ADAs were assessed using ELISA-based assays.

Results: A total of 77 patients were enrolled (62.3% male, mean age 44 years), 48 (62.3%) with CD, 26 (33.8%) with UC and 3 (3.9%) with unclassified colitis. The mean disease duration was 11.7±8.4 years, while the mean duration of INF infusion was 5.1±4.6 years. Forty-seven (61%) patients had undergone treatment escalation, with a further dose escalation in 7 (9.1%) patients. Concomitant combined therapy was given in 13 (16.8%) patients, 4 (5.2%) of them were receiving azathioprine and 9 (11.7%) corticosteroids. Mean INF-TLs were 7.2±4.9 µg/mL and only correlated with treatment escalation (9.7 vs 3.6 µg/mL, $p<0.001$). Sixty-eight (88.3%) patients had CR, 62 (80.5%) had SFCR, 48 (62.3%) had BR and 43 (55.8%) had SFCBR. Compared to non-responders, mean INF-TLs were numerically higher, although not significantly different, in CR (7.5 vs 5.5 µg/mL, $p=0.254$), SFCR (7.3 vs 6.9 µg/mL, $p=0.761$), BR (7.4 vs 6.9 µg/mL, $p=0.707$) or SFCBR (7.7 vs 6.6 µg/mL, $p=0.349$).

In a subgroup analysis, among patients without treatment escalation, 27 (90%) had CR, 25 (83.3%) had SFCR, 22 (73.3%) had BR and 19 (63.3%) had SFCBR. Mean INF-TLs were significantly increased among patients with BR

(4.2 vs 0.8 µg/mL, p=0.020) and SFCBR (4.3 vs 1.5 µg/mL, p=0.035). In ROC analysis, TLs could significantly predict (p=0.016) with a good accuracy (AUC 0.768, 95% CI: 0.584=0.952) patients with SFCBR, with an optimal TL cut-off at 3.4 µg/mL. Among patients with treatment escalation, 41 (87.2%) had CR, 37 (78.7%) had SFCR, 26 (55.3%) had BR and 24 (51.1%) had SFCBR. In ROC analysis, TLs could significantly predict (p=0.018) with a fair accuracy (AUC 0.653, 95% CI: 0.527=0.755) patients with SFCBR, with an optimal TL cut-off at 11 µg/mL.

Twenty patients had TLs <1 µg/mL, of whom 10 had positive ADAs. Among them, 9 showed combined remission, 4 of whom had positive ADAs. Among 21 (27.3%) patients with reported AEs, 8 (10.4%) had an allergic reaction, which was attributed to INF. Allergic reactions had a tendency of correlation with ADA existence, as 4/5 patients with allergic reaction and TLs <1 µg/mL had positive ADAs, while 4/10 patients with positive ADAs reported allergic reaction, compared to 1/10 patients with negative antibodies (p=0.152).

Conclusion: Infliximab TLs correlate with treatment escalation. Higher TLs appear to result in favourable therapeutic outcomes. It is suggested that patients undergoing treatment escalation could benefit from higher INF-TLs in the achievement of favourable outcomes.

Disclosure: Nothing to disclose.

PP0584

REAL-WORLD EXPERIENCES OF SWITCHING TO SUBCUTANEOUS FORMULATION IN IBD PATIENTS ON MAINTENANCE VEDOLIZUMAB TREATMENT

P. Bacsur^{1,2}, T. Resál^{1,3}, P. Sarlós⁴, Á. Illiás⁵, L.D. Sümegi⁵, D. Kata⁶, A. David¹, B. Farkas¹, E. Iványi¹, A. Balint¹, Z. Bosze¹, A. Fabian¹, R. Bor¹, S. Zoltán¹, W. Afif⁷, T. Bessissow⁷, K. Farkas^{1,2}, P.L. Lakatos⁷, T. Molnár¹

¹University of Szeged, Department of Medicine, Szeged, Hungary, ²HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary, ³Military Hospital-State Health Center, Department of Gastroenterology, Budapest, Hungary, ⁴University of Pécs, First Department of Internal Medicine, Pécs, Hungary, ⁵Semmelweis University, First Department of Medicine, Budapest, Hungary, ⁶University of Szeged, Department of Laboratory Medicine, Szeged, Hungary, ⁷McGill University Health Center, Gastroenterology, Montreal, Canada

Contact E-Mail Address: bacsurp@gmail.com

Introduction: Usability of subcutaneous vedolizumab (SC VDZ) in inflammatory bowel diseases (IBD, ulcerative colitis [UC], Crohn's disease [CD]) have proved via clinical trials, while real-world data collection is ongoing. Experiences of Central-European population and assessment of patient's perspectives are lacking.

Aims & Methods: Our study aimed to evaluate the real-world efficacy, safety and patient's preferences of SC VDZ maintenance treatment after switching from intravenous (IV) formulation in a Hungarian IBD cohort. In this prospective, multicenter cohort study, IBD patients on maintenance IV VDZ treatment were enrolled, who switched to SC administration. Baseline was the day of the switch, while 52-week follow-up was set. Clinical and demographic data were collected, while serum VDZ level and CRP was measured at baseline and at w52. A non-validated questionnaire was filled by patients who were on drug at w12 recording patient's satisfaction. Primary outcome was the drug survival rate at one year, while secondary outcomes were change in corticosteroid-free clinical (CSFR, based on physicians' global assessment score PGA<1), and biochemical remission (BR, 5 mg/l³CRP) rates to w52, safety issues and patients' preferences and change in serum drug levels.

Results: In total, 37 IBD patients were followed (15 CD and 22 UC, male/female ratio 45.9 %, median age 42.0 [IQR 34-49] years). In CD group, 66.7% were in CSFR and 60 % in BR, while in UC group 63.6% were in CSFR and 68.2 % in BR (p=0.55 and p=0.61). Overall, 29.7 % of patients ceased SC VDZ treatment after a median of 20 (IQR 6-26) weeks. Cessation was due to secondary response losing in 3/6 and 4/5 patients in CD and UC group. In case of 2 and one patients, SC treatment was terminated due to local reactions. One patient was fear of needle. Severe adverse event did not occur. Factors associated with discontinuation did not identify. The mean serum VDZ level has higher at w52 compared to baseline in CD and UC patients (CD: 8.9 ±6.9 to 30.6 ±17.8 ug/mL, p = 0.047; UC: 13.6±13.8 to 33.6±17.6 ug/mL, p = 0.001), while disease activity was stable. 84 % of the patients who filled the questionnaire were satisfied with injection, while only one patient found it difficult to inject.

Variables	Total (n = 37)	CD (n = 15)	UC (n = 22)	Sig.
Follow-up duration, weeks, median (IQR)	52 (26-52)	52 (23-52)	52 (46-52)	0.23
Sex, male (%)	17 (45.9)	8 (53.3)	9 (40.9)	0.47
Age at inclusion, years, median (IQR)	42.0 (34-49)	38.0 (35-49)	43.5 (34-52)	0.82
Disease duration at inclusion, weeks, median (IQR)	11.0 (9-17)	11.0 (9-17)	11.5 (8-16)	0.48
IV VDZ treatment duration, weeks, median (IQR)	75.9 (39-106)	86.9 (55-112)	60.3 (32-97)	0.64
Disease activity				
PGA, mean (± SD)	0.5 (0.7)	0.4 (0.6)	0.6 (0.8)	0.75
CSFR, n (%)	24 (64.9)	10 (66.7)	14 (63.6)	0.55
CRP, mg/l, mean (± SD)	7.0 (6.9)	7.3 (6.2)	6.8 (7.4)	0.825

Conclusion: Transition from IV to SC maintenance VDZ treatment is effective at one year, the overall survival rate is high presumably due to the elevated serum drug levels. Severe safety issue did not raise. Satisfaction of switched patients is high, which may improve treatment adherence and save resources.

Disclosure: K.F. has received speaker's honoraria from AbbVie, Janssen, Ferring, Takeda, and Goodwill Pharma. T.M. has received speaker's honoraria from MSD, AbbVie, Egis, Goodwill Pharma, Takeda, Pfizer, Janssen, Sandoz, MundiPharma, Phytotec, Roche, Fresenius, and Teva. Remaining authors have no conflict of interest to declare.

PP0585

EFFECT OF ANTIBIOTIC TREATMENT ON THE FORMATION OF ANTIBODIES AGAINST ANTI-TNFA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CASE - CONTROL STUDY

K. Serra⁴, E. Maristany⁴, F. Rodriguez-Moranta⁴, L. Rodríguez-Alonso⁴, A. Ruiz-Cerulla⁴, N. Padulles¹, M. Alonso¹, S. Castellet⁴, E. Sanchez⁴, S. Anton⁴, J. Orobitg⁴, M. Peñalva Peñas⁴, J. Guardiola⁴
¹Hospital Universitario de Bellvitge, Gastroenterology, L'Hospital de Llobregat (Barcelona), Spain, ²Hospital Universitario de Bellvitge, Pharmacy, L'Hospital de Llobregat (Barcelona), Spain

Contact E-Mail Address: jguardiola@bellvitgehospital.cat

Introduction: Anti- TNFα are the first advanced therapy in inflammatory bowel disease (IBD). However, up to 50% of patients will lose response during treatment. One of the most common mechanisms is immunogenicity. This is associated with obesity, smoking, monotherapy or the presence of HLA-DQA1*05. The gut microbiota appears to play an important role in pathogenesis and response to treatment. This can be altered by several factors, such as antibiotics. Therefore, antibiotics could (potentially) affect immunogenicity and response to treatment.

Aims & Methods: The aim of our study is to evaluate the effect of antibiotic treatment on the development of immunogenicity to anti-TNFα drugs in patients with IBD.

This is a retrospective case – control study of patients with IBD from a tertiary hospital treated with anti- TNF α , with data collected from June 2005 to January 2023. A group of patients who has developed antibodies against the drug (ADA) through a non-tolerant test has been compared. Two controls were selected per case, matched by type of IBD, mono/combotherapy, previous biological treatment, and type of anti- TNF α (infliximab/adalimumab).

The epidemiological variables and their association with the prescription of antibiotics and omeprazole 6 months before and 6 months after the start of biological treatment have been analysed.

Results: 100 patients have been included (30 cases / 70 controls): 50% men, 27% smokers, 55% Crohn's disease, 70% infliximab, 61% associated immunosuppression. 60% required intensification. No differences were found in any baseline characteristics between cases and controls. Anti-TNF withdrawal occurred in 19/30 cases (time until withdrawal: 19.5 $\pm$ 27.52 months).

The use of antibiotics during de 6 months after the start of biological treatment was associated with developing ADA (76.7% vs. 38.6%; $p < 0.0001$). The use of quinolones (33% vs. 11%; $p = 0.009$) and penicillins (17% vs 4%, $p = 0.03$) were associated with de development of ADA. In the multivariate analysis (adjusted for immunosuppressants, tobacco, obesity, number of biologicals), only the use of antibiotics in the first 6 months was associated with the development of ADA (OR 3.95, $p < 0.01$).

Conclusion: Taking antibiotics during the first months after starting anti-TNF α is associated with an increased risk of ADA. The antibiotics that show the greatest association are quinolones and penicillins.

Disclosure: Nothing to disclose.

PP0586

EFFECT OF OZANIMOD AT THERAPEUTIC AND SUPRATHERAPEUTIC DOSES ON ABSOLUTE LYMPHOCYTE COUNT AND HEART RATE IN HEALTHY ADULTS

P. Zhang¹, D.T. Rubin², M. Attanasio¹, S. Walker¹, K. Yu¹, M. Syto¹, M. Thomas¹, B. Murthy¹, G. Lawlor¹, B.E. Sands³, D. Tatosian¹

¹Bristol Myers Squibb, Princeton, United States of America,

²University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States of America, ³Icahn School of Medicine at Mount Sinai, Dr Henry D. Janowitz Division of Gastroenterology, New York, United States of America

Contact E-Mail Address: garrett.lawlor@bms.com

Introduction: Ozanimod (OZA) is an oral selective sphingosine 1-phosphate (S1P) receptor 1 and 5 modulator approved for the treatment of moderately to severely active ulcerative colitis (UC) or relapsing multiple sclerosis. Consistent with the mechanism of action (MOA) of S1P receptor modulators, OZA causes lymphocyte retention in lymphoid organs. S1P receptor modulators also bind to specific receptors in cardiac myocytes, but the associated risk of bradycardia may be mitigated with gradual dose escalation. Evidence from the phase 3 True North study (NCT02435992) suggests that absolute lymphocyte count (ALC) is a pharmacodynamic biomarker but is not predictive or prognostic for clinical response in OZA-treated patients with moderately to severely active UC.

Aims & Methods: We analyzed changes in ALC and heart rate (HR) over 65 d of OZA treatment at the therapeutic dose (0.92 mg) and a supratherapeutic dose (1.84 mg). A phase 1, double-blind, placebo (PBO)-controlled study (NCT04978298) evaluated the pressor effect of oral tyramine in healthy adults receiving OZA. The study included 3 periods; this analysis focuses on Period 2, during which participants (ppts) were randomized to OZA (therapeutic dose group: 7-d dose escalation to 0.92 mg once daily [QD]; supratherapeutic dose group: 10-d dose escalation to 1.84 mg QD)

or matched PBO for 65 d (Day 8–72). Safety endpoints included adverse events (AEs), clinically significant changes in laboratory tests and electrocardiograms, and vital signs.

Results: This study included 27 ppts in the OZA 0.92 mg group (mean [SD] age 36.4 [8.9] y, males 55.6%), 26 ppts in the OZA 1.84 mg group (36.3 [8.4] y, 53.8%), and 25 ppts in the PBO group (40.3 [9.1] y, 52.0%). Mean group level decreases from baseline (BL) in ALC ranged from 0.32 $\times 10^9$ /L to 1.18 $\times 10^9$ /L in the OZA 0.92 mg group and 0.12 $\times 10^9$ /L to 1.37 $\times 10^9$ /L in the OZA 1.84 mg group. ALC decreases were similar in OZA groups. Decreases began to plateau after ~14 d of OZA dosing, with mean group level decreases from BL of 0.82 $\times 10^9$ /L in the OZA 0.92 mg group and 1.09 $\times 10^9$ /L in the OZA 1.84 mg group at Day 21. Two ppts discontinued due to treatment-related lymphopenia: 1 event (3.7%) in the OZA 0.92 mg group was moderate in intensity (0.07–1.02 $\times 10^9$ /L, Period 2); 1 event (3.8%) in the OZA 1.84 mg group was considered mild (0.10–0.88 $\times 10^9$ /L, Periods 2 and 3; reported and discontinued in Period 3). Neither ppt had a reported infection or associated AE. Both events of lymphopenia resolved by end of study. ALC reductions in other ppts were not considered clinically significant. HR was slightly lower with OZA 1.84 mg on Days 8–15 and normalized thereafter, but overall, no clinically meaningful trends in mean HR or change from daily BL occurred across groups (Table).

	PBO			OZA 0.92 mg			OZA 1.84 mg		
	Mean (min, max) predose (BL) HR (bpm)	Mean (min, max) 6-h postdose HR (bpm)	Mean (min, max) change in HR* (bpm)	Mean (min, max) predose (BL) HR (bpm)	Mean (min, max) 6-h postdose HR (bpm)	Mean (min, max) change in HR* (bpm)	Mean (min, max) predose (BL) HR (bpm)	Mean (min, max) 6-h postdose HR (bpm)	Mean (min, max) change in HR* (bpm)
Day 8	63.2 (46, 80)	69.2 (54, 82)	5.9 (–11, 28)	59.8 (50, 80)	62.5 (51, 83)	2.7 (–8, 23)	62.2 (42, 86)	64.1 (51, 78)	1.9 (–15, 18)
Day 12	63.6 (44, 81)	70.4 (56, 94)	6.9 (–3, 16)	56.4 (48, 78)	60.7 (48, 82)	4.3 (–5, 14)	58.3 (39, 75)	61.0 (43, 79)	2.7 (–11, 16)
Day 15	63.8 (48, 80)	69.1 (54, 104)	5.3 (–6, 24)	57.2 (43, 80)	60.9 (45, 71)	3.7 (–12, 17)	58.1 (38, 73)	58.8 (42, 70)	0.7 (–11, 12)
Day 18	60.7 (41, 81)	68.8 (54, 80)	8.2 (–6, 30)	55.9 (44, 70)	59.7 (43, 79)	3.8 (–9, 14)	57.5 (43, 73)	60.8 (44, 73)	3.3 (–4, 20)
Day 21	62.6 (44, 80)	66.5 (48, 82)	3.9 (–7, 17)	58.7 (47, 75)	63.6 (53, 78)	4.9 (–13, 17)	59.5 (42, 79)	64.7 (50, 84)	5.2 (–7, 24)
Day 42	61.9 (45, 72)	68.1 (52, 82)	6.2 (–7, 16)	58.4 (49, 79)	63.0 (51, 77)	4.5 (–12, 14)	59.7 (46, 72)	66.6 (45, 87)	6.9 (–7, 25)
Day 72	58.4 (41, 75)	65.5 (50, 78)	7.1 (–6, 20)	58.1 (47, 73)	64.7 (53, 80)	6.6 (–2, 15)	59.4 (41, 80)	66.4 (46, 84)	7.0 (–4, 17)

*Calculated as the mean change in HR from predose (BL) to 6-h postdose for each day.

Table. Mean predose and 6-h postdose HR and mean change in HR.

Conclusion: In healthy ppts who received OZA at the therapeutic or supratherapeutic dose, ALC decreased as expected given the therapeutic MOA. No clinically significant changes from BL were noted. The ALC decrease was similar across OZA groups and was not dose dependent. No new cardiac safety signals were observed.

Disclosure and acknowledgment: This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Traci Stuve, MA, and Alexandra Stafford, PhD, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb. PZ, MA, SW, KY, MS, MT, BM, GL, and DT: employees and/or shareholders of Bristol Myers Squibb.

DR: received grant support from Takeda; consulted for AbbVie, AltruBio, Aslan Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chronicles, ClostraBio, Connect BioPharma, EcoR1, Eli Lilly, Genentech/Roche, Gilead Sciences, Iterative Health, Janssen, Kaleido Biosciences, Pfizer, Prometheus Biosciences, Reistone, Seres, Syneos, Takeda, Target RWE, and Trellus Health.

BES: received consulting fees from AbbVie, Alimentiv, Amgen, Arena, Artugen, AstraZeneca, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Entera, Evommune, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Morphic Therapeutics, MRM Health, Pro-

genity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, and Ventyx Biosciences; received consulting and speaking fees from Abivax; received consulting and speaking fees and other support from Eli Lilly; received research grants, consulting and speaking fees, and other support from Bristol Myers Squibb, Janssen, Pfizer, and Takeda; received research grants and consulting fees from Theravance Biopharma; received stock options from Ventyx Biosciences.

PP0587

THE IMPACT OF CYTOMEGALOVIRUS INFECTION ON DISEASE RELAPSE IN PATIENTS WITH MODERATE-SEVERE ULCERATIVE COLITIS: A RETROSPECTIVE SINGLE CENTRE STUDY

M. Zanconato¹, C. Cavagna¹, M. Crepaldi¹, C. Mescoli², B. Barberio¹, E.V. Savarino¹, F. Zingone¹

¹University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ²University of Padua, Pathology Unit, Department of Medicine (DIMED), Padua, Italy

Contact E-Mail Address: mirianazanconato45@gmail.com

Introduction: Cytomegalovirus (CMV) infection frequently affects patients with Ulcerative Colitis (UC) and it has been associated with disease relapse and increased severity.

Aims & Methods: Our study aimed to assess clinical and biochemical differences between CMV-positive UC patients with moderate to severe disease relapse and those without CMV infection.

We retrospectively included all patients with UC who were followed for at least one year at the Unit of Gastroenterology of the Azienda Ospedale Università Padova and that were studied for CMV infection at the time of a moderate/severe reactivation (pMayo ≥ 5 and/or fecal calprotectin ≥ 250 and/or endoscopic Mayo ≥ 2) from May 2019 to October 2023. Patients were considered CMV-positive if CMV antigens were revealed by immunohistochemistry (at least 1 CMV intranuclear inclusion body in routine hematoxylin and eosin-stained sections and/or immunohistochemical staining) and/or a positive tissue viral load was detected by qualitative real-time PCR on colonic biopsies. Demographic and clinical features, fecal calprotectin, and previous and ongoing UC therapy were compared between CMV-positive patients and those who tested negative. Finally, the anti-CMV therapy administered was reported. Differences between the two study groups were assessed using the independent-samples t-test, while differences in the categorical analysis were analyzed using the Chi-squared test. A p-value < 0.05 was considered significant. STATA 11 was used for statistical analysis.

Results: We retrospectively included 122 UC patients with moderate-to-severe disease (58.2% females, mean age at study 51 ± 17 years, time from diagnosis 11 ± 10 years). 24 patients (19.7%) were positive for CMV infection; no differences in gender, age, and time from diagnosis were observed between CMV-positive and negative patients. Serum quantitative CMV-DNA was tested in 18 patients and > 1000 copies/ml in 4 patients (22.2%) were detected. Approximately half of the patients were treated with immunomodulatory therapy during disease relapse with a similar distribution between CMV-positive and negative patients ($p = 0.7$). 95.2% of CMV-positive patients had diarrhoea compared to 71.6% of patients without CMV infection ($p = 0.02$), and abdominal pain was present in 71.4% CMV-positive compared to 42.1% CMV-negative patients ($p = 0.015$). In contrast, symptoms like fever and bloody diarrhoea had similar rates in the two groups ($p = ns$). Mean levels of fecal calprotectin were similar between the two groups ($p = 0.07$). Hospitalization was necessary in 91.7% of CMV-positive patients compared to 30.2% of CMV-negative patients. CMV-positive patients were treated with oral or intravenous steroids and

switched to UC biological therapy more frequently than CMV-negative patients ($p < 0.05$). In parallel, 14/24 CMV-positive patients were treated with Ganciclovir for 3-5 days, and 13/14 were subsequently treated with Valganciclovir for another 2-6 weeks. Ten patients were only treated with oral Valganciclovir.

Conclusion: CMV-positive UC patients required systemic steroid therapy and hospitalization more frequently than non-infected patients, suggesting a more challenging management of the disease. Moreover, symptoms such as abdominal pain and diarrhoea emerged as potential indicators of CMV infection when compared to other clinical presentations.

Disclosure: Nothing to disclose.

PP0588

INFLAMMATORY BIOMARKER REDUCTION AND IMPROVEMENT NORMALIZATION AND IN CLINICAL OUTCOMES WITH RISANKIZUMAB VERSUS USTEKINUMAB IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: A POSTHOC ANALYSIS FROM THE PHASE 3 SEQUENCE STUDY

J.-F. Colombel¹, G.R. D'Haens², B. Verstockt³, P. Irving⁴, A. Armuzzi⁵, B.L. Cohen⁶, B. Siegmund⁷, C. Cunneen⁸, A. Garrison⁸, K. Kligys⁸, J. Zambrano⁸, T. Anschutz⁸, L. Peyrin-Biroulet⁹

¹Icahn School of Medicine at Mount Sinai, Gastroenterology, Usa, United States of America, ²AMC Amsterdam Inflammatory Bowel Disease Centre - Academic Medical Center, AMC Amsterdam Inflammator, Academic Medical Center, Amsterdam, Netherlands, ³University Hospitals Leuven and KU Leuven, Translational Research in Gastrointestinal Disorders - IB, Department of Gastroenterology and Hepatology and Department of Chronic Diseases, Metabolism and Aging, Leuven, Belgium, ⁴Guy's and St Thomas' Hospital, Dept. of Gastroenterology, London, United Kingdom, ⁵IBD Center, IRCCS Humanitas Research Hospital, Gastroenterology, Rozzano, Milan, Italy, ⁶Digestive Disease and Surgery Institute, Cleveland Clinic Foundation, Department of Gastroenterology, Hepatology, and Nutrition, Cleveland, United States of America, ⁷Charité - Universitätsmedizin Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ⁸AbbVie, North Chicago, United States of America, ⁹Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France

Contact E-Mail Address: jean-frederic.colombel@mssm.edu

Introduction: Per STRIDE II recommendations, the normalization of high-sensitivity C-reactive protein (hs-CRP) and fecal calprotectin (FCP) should be an intermediate treatment target for patients (pts) with moderate to severe Crohn's disease (CD).¹ The safety and efficacy of risankizumab (RZB), an interleukin (IL)23 p19 inhibitor, and ustekinumab (UST), an IL12/23p40 inhibitor, in pts with CD have been reported previously.²⁻⁴ Using data from the phase 3 SEQUENCE study, we compared RZB versus UST for the achievement of biomarker reduction and normalization (alone or in combination with disease remission).

Aims & Methods: SEQUENCE was an open-label, multicenter, randomized, efficacy assessor-blinded study that directly compared the efficacy and safety of RZB vs UST in pts with moderate to severe CD and prior anti-TNF failure (NCT04524611). Pts were randomized 1:1 to receive recommended induction and maintenance doses of RZB (N=255) or UST (N=265). A mandatory steroid taper began at week (W)2. Randomization was stratified by baseline (BL) steroid use and number of failed anti-TNFs. In this post hoc analysis, pts with elevated FCP (> 250 mg/kg) or hs-CRP (> 5 mg/L) at BL were assessed for achievement of normalized FCP (≤ 250 mg/kg) or hs-

CRP (≤ 5 mg/L) at week W8, week W24, and week W48. At week W24 and W48 week 48, achievement of normalized FCP or hs-CRP in combination with CD activity index (CDAI) clinical remission (CDAI < 150) or with inflammatory bowel disease questionnaire (IBDQ) remission (IBDQ total score ≥ 170), as well as achievement of a 50% reduction in hs-CRP or FCP and CDAI response (reduction of CDAI ≥ 100 points from BL), were examined. Endpoints were analyzed using non-responder imputation, while incorporating multiple imputation to handle missing data due to COVID-19 and/or geopolitical conflict. All *P* values are nominal.

Results:

Endpoint n/N (95% CI)	Risanki- zumab Week 8	Ustekinumab Week 8	Response Rate Difference % (95% CI) P value	Risanki- zumab Week 24	Ustekinumab Week 24	Response Rate Difference % (95% CI) P value	Risanki- zumab Week 48	Ustekinumab Week 48	Response Rate Difference % (95% CI) P value
Normalization of hs-CRP ^a in patients with elevated hs-CRP ^a at BL	58/163; 35.6% (28.2, 42.9)	56/171; 32.7% (25.7, 39.8)	2.8% (-7.3, 13.0) <i>P</i> = 6	72/163; 44.2% (36.6, 51.9)	48/171; 28.1% (21.3, 34.8)	16.2% 28.1% (6.0, 26.3) <i>P</i> < .01	71/163; 43.6% (35.9, 51.2)	38/171; 22.2% (16.0, 28.5)	21.3% (11.5, 31.2) <i>P</i> < .0001
Normalization of FCP ^a in patients with elevated FCP ^a at BL	49/170; 28.8% (22.0, 35.6)	25/180; 13.9% (8.8, 18.9)	14.9% (6.5, 23.4) <i>P</i> < .001	65/170; 38.2% (30.9, 45.5)	35/180; 19.4% (13.7, 25.2)	18.8% 19.4% (9.5, 28.1) <i>P</i> < .0001	72/170 42.4% (34.9, 49.8)	24/180; 13.3% (8.4, 18.3)	29.0 (20.1, 38.0) <i>P</i> < .0001
Normalization of hs-CRP ^a or FCP ^a AND CDAI clinical remission in patients with elevated hs-CRP ^a or FCP ^a at BL				84/211; 39.9% (33.3, 46.5)	53/218; 24.3% (18.6, 30.0)	15.6% 24.3% (6.9, 24.3) <i>P</i> < .001	97/211 46.0% (39.2, 52.7)	54/218; 24.8% (19.0, 30.5)	21.2% (12.4, 30.0) <i>P</i> < .0001
Normalization of hs-CRP ^a or FCP ^a AND IBDQ remission in patients with elevated hs-CRP ^a or FCP ^a at BL				57/211 27.0% (21.0, 33.0)	59/218; 27.1% (21.2, 33.0)	-0.1 22.3% (-8.5, 8.4) <i>P</i> = 1.0	47/211; 22.3% (16.7, 27.9)	34/218; 15.6% (10.8, 20.4)	6.7 (-0.7, 14.1) <i>P</i> = 1.0
$\geq 50\%$ decrease from BL in hs-CRP or FCP AND CDAI clinical response in patients with elevated hs-CRP ^a or FCP ^a at BL				111/211; 52.6% (45.8, 59.3)	74/218 33.9% (27.7, 40.2)	18.6 56.4% (9.4, 27.8) <i>P</i> < .0001	119/211; 56.4% (49.7, 63.1)	68/218; 31.2% (25.0, 37.3)	25.2 (16.1, 34.3) <i>P</i> < .0001

BL, baseline; CD, Crohn's disease; CDAI, CD activity index; CI, confidence interval; FCP, fecal calprotectin; hs-CRP, high-sensitivity C-reactive protein; IBDQ, inflammatory bowel disease questionnaire.

CDAI clinical remission: CDAI < 150 ; IBDQ remission: IBDQ total score ≥ 170 .

^aNormalization of hs-CRP is defined as ≤ 5 mg/L.

^aElevated hs-CRP is defined > 5 mg/L.

^aNormalization of FCP is defined as ≤ 250 mg/kg.

^aElevated FCP is defined > 250 mg/kg.

Efficacy population includes all patients randomized to either ustekinumab (i.e., weight-based induction dose IV followed by maintenance dose 90-mg SC), or the selected dosing regimen for risankizumab (600 mg for induction, 360 mg for maintenance), and who received at least one dose of study drug.

95% CI for response rate is the synthetic result based on Student's *t*-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 and/or geopolitical conflict or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19 and/or geopolitical conflict.

Response rate difference = (risankizumab - ustekinumab); 95% CI for difference is calculated based on normal approximation to the binomial distribution for the comparison of two treatment groups. *P*-value is based on Chi-square test. The calculations are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 and/or geopolitical conflict.

Pooled *p*-value from Chi-square is calculated following Li et al., *Statistica Sinica*, 1991; 1, 68-92.

A greater proportion of pts receiving RZB vs UST achieved normalization of hs-CRP at W24 weeks 24 and W48, as well as normalization of FCP at weeks W8, W24, and 48 (*P* < .01 for all; *Table*). Rates of normalization of FCP or hs-CRP plus CDAI clinical remission were also greater at weeks W24 and W48 in pts receiving RZB vs UST, as were rates of CDAI clinical response and a $\geq 50\%$ reduction in FCP or hs-CRP (*P* < .001 for all; *Table*). Rates of normalization of FCP or hs-CRP plus IBDQ remission were similar between pts receiving RZB vs UST (*Table*). The safety profiles of RZB and UST in CD have been previously reported.²⁻⁴

Conclusion: A greater proportion of pts achieved normalization of biomarkers FCP or hs-CRP with RZB vs UST. Composite endpoints of CDAI clinical remission and biomarker normalization, as well as CDAI clinical response and biomarker reduction ($\geq 50\%$) favored RZB vs UST at weeks 24 and 48.

References: 1 Turner, D et al. *Gastroenterology*. 2021; 160, 1570–1583.

2 D'Haens, G et al. *The Lancet*. 2022; 399, 2015–2030.

3 Ferrante, M et al. *The Lancet*. 2022; 399, 2031–2046.

4 Feagan, BG et al. *N Engl J Med*. 2016; 375, 1946–1960.

Disclosure: Jean-Frederic Colombel: Research grants: AbbVie, Janssen Pharmaceuticals, and Takeda; lecture payments: AbbVie, Allergan, Amgen, Ferring Pharmaceuticals, Shire, and Takeda; consulting fees: AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Ferring Pharmaceuticals, Galmed Research, Genentech, GlaxoSmithKline, Immedex, Immunic, Iterative Scopes, Janssen Pharmaceuticals, Kaleido Biosciences, Lilly, Merck, Microbia, Novartis, PBM Capital, Pfizer, Protagonist Therapeutics, Sanofi, Takeda, TiGenix, and Vifor; and holds stock options in Intestinal Biotech Development.

Geert D'Haens: Adviser: AbbVie, Ablynx, Active Biotech AB, Agomab Ther-

apeutics, Alimentiv, Allergan, Alphabio, Amakem, Amgen, AM Pharma, Applied Molecular Therapeutics, Arena Pharmaceuticals, AstraZeneca, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, DSM Pharma; Echo Pharmaceuticals, Engene, Exeliom Biosciences, Ferring, Dr Falk Pharma, Galapagos, Genentech/Roche, Gilead, GlaxoSmithKline, Gossamerbio, Immunic, Johnson and Johnson, Kintai Therapeutics, Lilly, Lument, Lycera, Medtronic, Merck Sharp & Dome, Mitsubishi Tanabe Pharma, Novo Nordisk, Otsuka, Pfizer, Photopill, ProciseDx, Prodigest, Progenity, Prometheus laboratories/Nestlé, Protagonist, RedHill, Samsung Bioepis, Sandoz, Seres, Setpoint, Shire, Takeda, Teva, Tillotts, Topivert, Versant, and Vifor.

Bram Verstockt: Research support: AbbVie, Biora Therapeutics, Landos, Pfizer, Sosei Heptares and Takeda; speaker's fees: AbbVie, Biogen, Bristol Myers Squibb, Celltrion, Chiesi, Falk, Ferring, Galapagos, Janssen, Lilly, MSD, Pfizer, R-Biopharm, Sandoz, Takeda, Tillotts Pharma, Truvion and ViatriMSD, Pfizer, R-Biopharm, Takeda, Truvion and Viatri.; Consultancy fees: AbbVie, Alfasigma, Alimentiv, Applied Strategic, Atheneum, BenevolentAI, Biora Therapeutics, Boxer Capital, Bristol Myers Squibb, Galapagos, Guidepoint, Landos, Lilly, Mylan, Inotrem, Ipsos, Janssen, Pfizer, Progenity, Sandoz, Sanofi, Santa Ana Bio, Sapphire Therapeutics, Sosei Heptares, Takeda, Tillotts Pharma, Viatri, Alimentiv, Applied Strategic, Atheneum, Biora Therapeutics, Bristol Myers Squibb, Galapagos, Guidepoint, Mylan, Inotrem, Ipsos, Janssen, Pfizer, Progenity, Sandoz, Sosei Heptares, Takeda, Tillotts Pharma and Viatri; stock options: Vagustim.

Peter Irving: Honoraria: AbbVie, BMS, Celgene, Celltrion, Dr Falk Pharma, Ferring, Galapagos, Gilead, MSD, Janssen, Lilly, Pfizer, Takeda, Tillotts, Sapphire Medical, Sandoz, Shire, and Warner Chilcott; advisor: AbbVie, Arena, Boehringer Ingelheim, BMS, Celgene, Celltrion, Connect Biopharma, Genentech, Gilead, Hospira, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor Pharma, and Warner Chilcott.

Alessandro Armuzzi: Consulting/advisory fees: AbbVie, Allergan, Amgen, Arena, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, and Takeda; speaker's fees: AbbVie, Amgen, Arena, Biogen, Bristol Myers Squibb, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda, and Tigenix; research support: MSD, Takeda, Pfizer, and Biogen. Benjamin Cohen: Consultant: AbbVie, Celgene-Bristol Myers Squibb, Lilly, Pfizer, Sublimity Therapeutics, Takeda, and Target RWE; DSMB for Emmes Biopharma Services LLC; educational grant from Pfizer.

Britta Siegmund: Consultant for AbbVie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forga Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; speaker fees: AbbVie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer; grant support: Arena/Pfizer (served as representative of the Charité).

Laurent Peyrin-Biroulet: Personal fees from AbbVie, Adacyte, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytokine Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillotts, Viatri, Vifor, Ysopia, Abivax, Samsung, Ventyx, Roivant, and Vectivbio Colla Cunneen, Andrew Garrison, Kristina Kligys, Javier Zambrano, and Toni Anschutz are full-time employees of AbbVie and may own AbbVie stock or options.

PP0589

EFFICACY OF RISANKIZUMAB VERSUS USTEKINUMAB BY DURATION OF DISEASE IN PATIENTS WITH MODERATE TO SEVERE CROHN’S DISEASE: A POSTHOC ANALYSIS FROM THE PHASE 3 SEQUENCE STUDY

L. Peyrin-Biroulet¹, S. Ben-Horin², C. Ha³, B. Siegmund⁴, F. Aponte⁵, K. Kligys⁵, J. Zambrano⁵, T. Anschutz⁵, A. Garrison⁵, J.-F. Colombel⁶

¹Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 “Inflammation/Cellular Stress and Exposure to Environmental Risks”, Vandoeuvre-les-Nancy, France, ²University of Tel Aviv, Sheba Medical Center, Gastroenterology, Tel-Hashomer, Israel, ³Mayo Clinic, Division of Gastroenterology and Hepatology, Scottsdale, United States of America, ⁴Charité - Universitätsmedizin Berlin, Med. Klinik m.S. Gastroenterologie, Infektiologie und Rheumatologie, Berlin, Germany, ⁵AbbVie, North Chicago, United States of America, ⁶Icahn School of Medicine at Mount Sinai, Gastroenterology, Usa, United States of America

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: Consistent associations between higher remission rates and shorter disease duration have been reported for advanced therapies in Crohn’s disease (CD), but no direct comparisons between newer advanced treatments and efficacy with respect to CD duration have been examined. The efficacy of risankizumab (RZB), an interleukin (IL)23p19 inhibitor, and ustekinumab (UST), an IL12/23p40 inhibitor, in pts with CD have been reported.¹⁻³

Herein, using data from the phase 3 SEQUENCE study, the clinical and endoscopic efficacy of RZB vs UST, stratified by baseline (BL) CD duration, is reported.

Aims & Methods: The SEQUENCE open-label, multicenter, randomized, efficacy assessor-blinded study compared the efficacy and safety of RZB vs UST in pts with moderate to severe CD and prior anti-TNF failure (NCT04524611). Pts were randomized 1:1 to receive recommended induction and maintenance doses of RZB (N=255) or UST (N=265). A mandatory steroid taper began at week (W)2. Randomization was stratified by BL steroid use and number of failed anti-TNFs. This post hoc analysis evaluated CDAI clinical remission and endoscopic remission at W24 and W48, and endoscopic response, steroid-free CDAI clinical remission, and steroid-free endoscopic remission at W48, in pts stratified by disease duration (<2 years [Y], 2-5Y, 5-10Y, >10Y) (endpoints defined in Table footnote). Missing data due to COVID-19 and/or geopolitical conflict was handled using non-responder imputation while incorporating multiple imputation. P values are nominal.

Results: Baseline characteristics were mostly similar across treatments and disease duration subgroups, except total number of pts and proportion of pts failing >1 anti-TNFs (both lower in the <2Y subgroup), and fecal calprotectin (lower with increasing CD duration) (Table). With RZB vs UST, a numerically greater proportion of pts achieved all endpoints, irrespective of disease duration (Table). A greater proportion of pts in all subgroups achieved endoscopic response with RZB vs UST at W48 (<2Y: P<05; 2-5Y, P<001; 5-10Y, P<.05, > 10Y, P<.01), with a similar trend for RZB vs UST observed for most, but not all, disease duration subgroups for W24 endoscopic response and W48 endoscopic remission (Table).

The numerically highest rates of endoscopic response were observed with RZB in pts with a disease duration ≤2Y, and while the numerically greatest treatment differences with RZB vs UST were observed in pts with a disease duration of ≤5Y (Table). The safety profiles of RZB and UST in CD were previously reported.¹⁻³

BL Demographic and Disease Characteristics	Disease Duration at Baseline (BL)											
	<2 years			2-5 years			>5-10 years			>10 years		
	RZB N=36	UST N=43		RZB N=59	UST N=62		RZB N=67	UST N=71		RZB N=93	UST N=89	
Age (years), mean (SD)	36.7 (13.9)	34.2 (13.2)		33.1 (12.6)	36.0 (13.7)		36.3 (13.5)	35.1 (13.8)		43.0 (11.3)	44.3 (12.2)	
Sex (male), n (%)	18 (50)	18 (42)		35 (59)	35 (56)		42 (63)	35 (49)		41 (44)	43 (48)	
Body mass index (kg/m ²), mean (SD)	21.6 (4.2)	22.9 (5.4)		23.1 (5.9)	25.4 (6.6)		24.1 (4.8)	23.3 (5.8)		24.9 (5.9)	26.6 (5.6)	
Average daily stool frequency, mean (SD)	5.1 (2.5)	5.0 (2.6)		5.3 (2.4)	5.6 (2.8)		6.0 (3.2)	5.2 (2.4)		5.5 (2.6)	6.3 (2.3)	
Average daily abdominal pain, mean (SD)	1.9 (0.5)	2.0 (0.6)		2.0 (0.5)	2.0 (0.5)		2.0 (0.5)	1.9 (0.6)		1.9 (0.5)	1.8 (0.6)	
CDAI, mean (SD)	312.5 (58.3)	314.8 (55.3)		318.6 (56.1)	314.6 (63.3)		317.4 (65.1)	304.0 (68.3)		296.8 (62.7)	309.7 (61.3)	
SES-CD, n; mean (SD)	n = 36 14.4 (8.2)	n = 43 15.5 (7.7)		n = 59 12.9 (6.7)	n = 62 15.2 (8.3)		n = 67 14.0 (7.4)	n = 71 13.7 (7.4)		n = 93 13.2 (6.6)	n = 89 13.1 (6.4)	
Fecal calprotectin (mg/kg), median (IQR)	n = 33 1429 (2877)	n = 41 2116 (2811)		n = 47 1453 (2552)	n = 49 1535 (2079)		n = 53 1016 (2217)	n = 57 1515 (2070)		n = 74 593 (1472)	n = 68 1115 (2306)	
hs-CRP (mg/L), n; median (IQR)	n = 35 5 (30)	n = 40 19 (45)		n = 58 10 (22)	n = 60 10 (25)		n = 63 9 (31)	n = 71 8 (15)		n = 90 7 (13)	n = 86 8 (20)	
Anti-TNF failure history (> 1), n (%)	2 (6)	5 (12)		11 (19)	11 (18)		19 (28)	14 (20)		27 (29)	31 (35)	
Corticosteroid use (yes) - n (%)	11 (31)	14 (33)		11 (19)	16 (26)		16 (24)	15 (21)		20 (21)	26 (29)	
Crohn's disease location per SES-CD, n (%)												
Ileal only	6 (17)	9 (21)		9 (15)	12 (19)		9 (13)	10 (14)		18 (19)	14 (16)	
Colonic only	20 (56)	16 (37)		23 (39)	20 (32)		25 (37)	28 (39)		34 (37)	42 (47)	
Ileal-colonic	10 (28)	18 (42)		27 (46)	30 (48)		33 (49)	33 (46)		41 (44)	33 (37)	
	RZB N=36	UST N=43	Difference % (95% CI) P-value	RZB N=59	UST N=62	Difference % (95% CI) P-value	RZB N=67	UST N=71	Difference % (95% CI) P-value	RZB N=93	UST N=89	Difference % (95% CI) P-value
CDAI clinical remission at week 24, n/N; % (95% CI)	23/36 (63.9%)	22/43 (51.2%)	12.7 (-8.9, 34.4) P = 3	30/59 (50.8%)	26/62 (41.9%)	8.9 (-9.9, 26.6) P = 3	40/67 (59.7%)	39/71 (54.9%)	4.8 (-11.7, 21.3) P = 6	59/93 (63.4%)	26/89 (29.2%)	34.2 (-20.6, 47.8) P <.0001
CDAI clinical remission at week 48, n/N; % (95% CI)	23/36 (63.9%)	19/43 (44.2%)	19.7 (-1.9, 33.5) P = 1	33/59 (55.9%)	27/62 (43.5%)	12.4 (-5.3, 30.1) P = 2	39/67 (58.2%)	31/71 (43.7%)	14.5 (-2.0, 31.1) P = 1	60/93 (64.5%)	31/89 (34.8%)	29.7 (-15.8, 40.6) P <.0001
Endoscopic response at week 24, n/N; % (95% CI)	19/36 (52.8%)	14/43 (32.6%)	20.2 (-1.3, 44.5) P = 1	26/59 (44.1%)	12/62 (19.4%)	25.1 (9.0, 41.2) P <.01	33/67 (49.3%)	23/71 (32.4%)	16.9 (0.7, 33.0) P <.05	41/93 (43.9%)	21/89 (23.6%)	16.2 (2.9, 29.5) P <.05
Endoscopic response at week 48, n/N; % (95% CI)	19/36 (52.8%)	11/43 (25.6%)	27.2 (6.3, 48.1) P <.05	24/59 (40.7%)	8/62 (12.9%)	28.7 (12.7, 42.8) P <.001	31/67 (46.3%)	18/71 (25.4%)	20.9 (5.3, 36.6) P <.05	41/93 (44.1%)	21/89 (23.6%)	20.5 (7.1, 33.9) P <.01
Endoscopic remission at week 48, n/N; % (95% CI)	11/36 (30.6%)	8/43 (18.6%)	12.0 (-7.1, 31.0) P = 2	20/59 (33.9%)	19/62 (30.7%)	24.2 (10.1, 38.4) P <.01	19/67 (28.4%)	16/71 (22.5%)	5.8 (-8.7, 20.3) P = 4	31/93 (33.3%)	13/89 (14.6%)	18.7 (6.7, 30.8) P <.01
Steroid-free CDAI clinical remission at week 48, n/N; % (95% CI)	23/36 (63.9%)	19/43 (44.2%)	19.7 (-1.9, 33.5) P = 1	33/59 (55.9%)	26/62 (41.9%)	14.0 (-5.6, 33.6) P = 1	39/67 (58.2%)	31/71 (43.7%)	14.5 (-2.0, 31.1) P = 1	60/93 (64.5%)	31/89 (34.8%)	29.7 (-15.8, 43.6) P <.0001
Steroid-free endoscopic remission at week 48, n/N; % (95% CI)	11/36 (30.6%)	8/43 (18.6%)	12.0 (-7.1, 31.0) P = 2	20/59 (33.9%)	19/62 (30.7%)	24.2 (10.1, 38.4) P <.01	19/67 (28.4%)	16/71 (22.5%)	5.8 (-8.7, 20.3) P = 4	31/93 (33.3%)	13/89 (14.6%)	18.7 (6.7, 30.8) P <.01

BL, baseline; CD, Crohn's disease; CDAI, CD activity index; CI, confidence interval; FCP, fecal calprotectin; hs-CRP, high-sensitivity C-reactive protein; SES-CD, simple endoscopic score for CD; TNF, tumor necrosis factor
CDAI clinical remission: CDAI < 150; endoscopic remission: SES-CD < 4 and ≥ 2 point reduction versus BL and no subscore > 1 in any individual variable, as scored by central reviewer; endoscopic response - decrease in SES-CD > 50% from BL (or for patients with isolated ileal disease and a BL SES-CD of 4, ≥ 2 point reduction from BL), as scored by central reviewer; Steroid-free CDAI clinical remission - CDAI clinical remission without receiving steroids; steroid-free endoscopic remission - endoscopic remission without receiving steroids
Efficacy population includes all patients randomized to either ustekinumab (i.e., weight-based induction dose IV followed by maintenance dose 90-mg SC), or the selected dosing regimen for risankizumab (500 mg for induction, 360 mg for maintenance), and who received at least one dose of study drug.
5% CI for response rate is the synthetic result based on Student's t-distribution from PROC FREQ procedure if there are missing data due to COVID-19 and/or geopolitical conflict or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19 and/or geopolitical conflict.
Response rate difference = (risankizumab - ustekinumab); 95% CI for difference is calculated based on normal approximation to the binomial distribution for the comparison of two treatment groups. P-value is based on Chi-square test. The calculations are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 and/or geopolitical conflict.
Pooled p-value from Chi-square is calculated following Li et al., Statistica Sinica. 1991; 1, 68-92. All P-values are nominal.

Conclusion: At W24 and W48, numerically higher rates of efficacy were observed with RZB vs UST treatment for all endpoints across disease duration subgroups, with notable consistent differences observed for endoscopic response. Endoscopic response rates with RZB were numerically highest in pts with a disease duration of ≤2Y, supporting early intervention for patients with CD.⁴

- References:** 1. D’Haens, G. et al. *The Lancet*. 2022; 399, 2015–2030.
2. Ferrante, M. et al. *The Lancet*. 2022; 399, 2031–2046.
3. Feagan, B. G. et al. *N Engl J Med*. 2016; 375, 1946–1960.
4. Colombel, J.-F. et al. *Gastroenterology*. 2017; 152, 351-361.e5.

Disclosure: Jean-Frederic Colombel received research grants from AbbVie, Janssen Pharmaceuticals, and Takeda; payment for lectures from AbbVie, Allergan, Amgen, Ferring Pharmaceuticals, Shire, and Takeda; consulting

fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Ferring Pharmaceuticals, Galmed Research, Genentech, GlaxoSmithKline, Imedex, Immunic, Iterative Scopes, Janssen Pharmaceuticals, Kaleido Biosciences, Lilly, Merck, Microbia, Novartis, PBM Capital, Pfizer, Protagonist Therapeutics, Sanofi, Takeda, TiGenix, and Vifor; and holds stock options in Intestinal Biotech Development.

Laurent Peyrin-Biroulet received personal fees from AbbVie, Adacyte, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, BMS, Celltrion, CONNECT Biopharm, Cytokine Pharma, Entera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, HAC-Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Norgine, Nordic Pharma, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, Viatrix, Vifor, Ysopia, Abivax, Samsung, Ventyx, Roivant, and Vectivbio

Shomron Ben-Horin has received Advisory Board fees and/or Consulting fees from Janssen, AbbVie, CellTrion, Takeda, Schering Plough, Pfizer, Ferring, Falk Pharma, GSK, BMS, Novartis, Roche, Galmed, Evinature, PredictaMed and Eli Lilly, holds Stocks/options in Galmed, Evinature, PredictaMed and Alma Therapeutics and received research grant support from Janssen, AbbVie, CellTrion, Takeda, Pfizer and Galmed.

Christina Ha has received financial support from advisory board fees from AbbVie, Bristol Myers Squibb, Bausch Health, Roivant, Janssen, Pfizer, and Takeda; consultant fees from AbbVie; educational grant funding from Bristol Myers Squibb, Pfizer, Janssen, AbbVie and the Helmsley Charitable trust

Britta Siegmund has served as consultant for AbbVie, Abivax, Arena, BMS, Boehringer, CED Service GmbH, Celgene, CT Scout, Endpoint Health, Falk, Forge Software, Galapagos, Janssen, Lilly, Materia Prima, Pfizer, Takeda, Pharma Insight, Predictimmune, PsiCro; Speaker fees: AbbVie, BMS, CED Service GmbH, Chiesi, Falk, Ferring, Gilead, Janssen, Lilly, Materia Prima, Takeda, Pfizer and grant support by Arena/Pfizer (served as representative of the Charité).

Fernando Aponte, Kristina Kligys, Javier Zambrano, Toni Anschutz, and Andrew Garrison are full-time employees of AbbVie and may own AbbVie stock or options.

Funding and Acknowledgments: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship. AbbVie and authors thank all the trial investigators and the patients who participated in this clinical trial.

Medical writing support was provided by Stephanie Parsons, PhD, and copy editing support was provided by Angela T. Hadsell, BS, both employees of AbbVie.

PP0590

IMPACT OF EXTRAINTESTINAL MANIFESTATIONS ON DISEASE COURSE IN INFLAMMATORY BOWEL DISEASE

W. Khemiri¹, N. Ben Mustapha¹, N. Ben Safta¹, D. Gouiaa¹, S. Laabidi¹, M. Serghini¹, A. Labidi¹, M. Fekih¹

¹La Rabta Hospital, Gastroenterology "A", Tunis, Tunisia

Contact E-Mail Address: Khemiri.wafa00@gmail.com

Introduction: Inflammatory bowel disease (IBD) represents a group of chronic inflammatory disorders of the gastrointestinal tract. While the hallmark features of IBD involve inflammation and damage to the digestive system, the impact of the disease often extends beyond the gut, manifesting as a spectrum of extraintestinal manifestations (EIM), affecting various organs and contributing to the complexity and heterogeneity of IBD.

Aims & Methods: The aim of this study was to assess the impact of EIM in IBD on disease course. We conducted a retrospective, descriptive and comparative study including patients hospitalized for IBD over a 9-year period [January 2011-January 2020]. Patients with less than 2 years of follow-up were excluded. Clinico-biological data, disease severity, and long-term outcomes (surgery and disease course) were collected. Data were entered and analyzed via SPSS 26 software.

Results: We included 225 men and 227 women. We enrolled 341 patients diagnosed with Crohn's disease (CD) and 111 patients with ulcerative colitis (UC). The mean age at diagnosis was 36.15 ± 12.74 years. One-hundred and sixty-five patients (36.4%) had EIM with respectively: rheumatological manifestations (n=144), dermatological manifestations (n=26), ocular manifestations (n=17) and hepatic manifestations (n=8). We noticed a significant association of EIM with male gender (56.3% vs 45.9%; $p=0.03$). Rheumatological EIM were associated with a significant older age at disease onset (36.7 years vs 32.8 years; $p=0.003$). No significant association was noted between EIM with neither family history of IBD nor the type of IBD ($p=0.33$ and $p=0.3$ respectively). In case of CD, we noted a higher frequency of ileal involvement in patients with EIM, without a significant difference (61.4% vs 51.4%; $p=0.07$). No association was noted between EIM with neither fistulising behaviour nor with extended ileal disease nor with upper gastrointestinal tract involvement ($p=0.1$; $p=0.5$ and $p=0.5$ respectively). In case of UC, no association was noted between EIM and an extensive disease ($p=0.7$). As for treatment, EIM had no impact on corticosteroids' use or immunosuppressive treatment ($p=0.36$ and $p=0.08$), but was associated with a significant higher use of anti-TNF therapy (83.4% vs 27.2%; $p=0.01$). Response to corticosteroids and anti-TNF therapy was similar whether with or without EIM ($p=0.36$ and $p=0.24$ respectively). In the sub-group of ocular EIM, we noted a higher failure of immunosuppressive treatment (70% vs 36.6%; $p=0.04$). We noted that EIM was associated with a rarer urge to surgical treatment (35.7% vs 44.9%; $p=0.05$) with a significant longer timeframe to surgery (47.7 months vs 27.2 months; $p=0.03$). The mean number of years of active disease was significantly higher in patients with EIM (3.3 vs 2.5; $p=0.002$) with a higher number of flare-ups ($p=0.009$) and hospitalizations ($p<0.001$), reflecting a better disease course in patients without EIM.

Conclusion: In our study, EIM were associated with an overall more severe disease course in IBD, thus, emphasizing the importance of comprehensive assessment and management strategies tailored to address both intestinal and extra-intestinal manifestations in the holistic care of IBD patients.

Disclosure: Nothing to disclose.

PP0591

ADHERENCE TO CORTICOSTEROID RECOMMENDATIONS IN IBD PATIENTS: A CRITICAL EVALUATION

V. Coguric¹, B. Smolovic^{1,2}

¹Clinical Center of Montenegro, Internal Clinic, Podgorica, Montenegro, ²University of Montenegro, Faculty of Medicine, Podgorica, Montenegro

Contact E-Mail Address: vidak.coguric@icloud.com

Introduction: Corticosteroid tapering over a period of 6-8 weeks effectively induces remission in inflammatory bowel disease (IBD). However, prolonged corticosteroid use (lasting more than 3 months) is linked to severe side effects.

Aims & Methods: Detecting and mitigating prolonged use is crucial for optimal care. We conducted a prospective study in 2018 involving 116 IBD patients undergoing biologic therapy at an IBD referral center in Montenegro. We utilized the Steroid Assessment Tool (SAT) as described by Selinger et al., 2017, to assess corticosteroid usage in this cohort.

Results: Of the patients, 61% had ulcerative colitis (UC) and 39% had Crohn's disease (CD). 53% of patients received anti TNF biologics (adalimumab or infliximab), and 47% received anti-integrin therapy (vedolizumab) in the current therapy. In the preceding year 32 patients (28%) had used corticosteroids. Most of those patients (78%) received a single course of steroids, while 19% received two courses, and 3% received three. The duration of steroid use was predominantly three months (78% of patients), with the longest duration being nine months (1 patient). Among steroid users, 81% (26/32) did not develop dependency or relapse after three months, while 19% (6/32) were steroid resistant/dependent.

Conclusion: Our study identified corticosteroid excess in 6.0% of patients. While our findings suggest adherence to corticosteroid recommendations in IBD patients undergoing biologic therapy, there's a need to expand routine monitoring of steroid dependency or excess to all IBD patients, regardless of their biologic therapy history.

Disclosure: Nothing to disclose.

PP0592

EARLY APPLICATION OF TIGHT CONTROL IMPROVES THE RATES OF ENDOSCOPIC AND TRANSMURAL REMISSION IN CROHN'S DISEASE

I. Rodrigues^{1,2}, S.R. Fernandes^{1,2}, S. Bernardo¹, S. Saraiva¹, A.R. Gonçalves¹, P.M. Moura dos Santos^{1,2}, A.I. Valente¹, L. Correia^{1,2}, H. Cortez-Pinto^{1,2}, F. Magro^{3,4}

¹ULS Santa Maria, Serviço De Gastroenterologia, Lisboa, Portugal,

²Faculdade de Medicina de Lisboa, Clínica Universitária de Gastroenterologia, Lisboa, Portugal, ³ULS São João, Serviço de Gastroenterologia, Porto, Portugal, ⁴Faculdade de Medicina da Universidade do Porto, CINTESIS@RISE, Departamento de Biomedicina, Porto, Portugal

Contact E-Mail Address: mines.bcrodrigues@gmail.com

Introduction: Increasing evidence support the use of transmural remission as a treatment target in Crohn's disease (CD), but it is seldom achieved in clinical practice. Tight monitoring of inflammation using fecal calprotectin (FC) with reactive treatment escalation may potentially improve these results.

Aims & Methods: We aim to evaluate if treatment escalation based on FC can improve the rates of transmural remission in CD.

Retrospective cohort study including 256 CD patients with 2 consecutive assessments by MRI-enterography and colonoscopy and with regular monitoring using FC. For each occurrence of an elevated FC (≥ 250 ug/g),

we evaluated if a reactive adjustment of medical treatment was performed. The ratio of treatment escalation/elevated FC was correlated with the chances of reaching transmural remission. Early disease was defined as disease duration <18 months without previous exposure to immunomodulators and biologics.

Results: After a median follow-up of 2 years (IQR 1-4), 121 patients (47.3%) reached endoscopic remission and 61 patients (23.8%) reached transmural remission. There was a higher prevalence of early disease (34.4% vs 20.5%, $P=0.038$), non-stricturing non-penetrating phenotype (54.1% vs 37.4%, $P=0.026$) and less biologic use at baseline (13.1% vs 26.7%, $P=0.037$) in patients with transmural remission.

Ratios of escalation $\geq 50\%$ resulted in higher rates of transmural remission (34.2% vs 15.1%, $P<0.001$). The effect was more pronounced in patients with early disease (50.0% vs 12.0%, $P=0.003$). In multivariate analysis, a treatment escalation ratio $\geq 50\%$ (OR 3.46, 95%CI 1.67-7.17, $P=0.001$) and early disease intervention (OR 3.24, 95%CI 1.12-9.34, $P=0.030$) were independent predictors of achieving transmural remission.

Conclusion: Tight-monitoring and reactive treatment escalation increased the rates of transmural remission in CD. Intervention in early disease further improved these results.

Disclosure: Nothing to disclose.

PP0593

PROPOSED USTEKINUMAB BIOSIMILAR Fyb202: PHARMACOKINETIC EQUIVALENCE DEMONSTRATED IN A RANDOMISED, DOUBLE-BLIND, PARALLEL-GROUP, SINGLE-DOSE TRIAL IN HEALTHY SUBJECTS (RUSTIC)

S. Balser¹, K. Nopora¹, J. Körner², M. Anschütz³, R.-S. Wedemeyer⁴, B. Schug³

¹Formycon AG, Martinsried/Planegg, Germany, ²SocraTec R&D GmbH, Erfurt, Germany, ³SocraTec R&D GmbH, Oberursel, Germany, ⁴SocraMetrics GmbH, Erfurt, Germany

Contact E-Mail Address: sigrid.balser@formycon.com

Introduction: Ustekinumab is a recombinant human monoclonal IgG1 antibody targeting the interleukins IL-12 and IL-23. Ustekinumab is approved for treatment of moderately to severely active inflammatory bowel disorders, i.e. Crohn's disease and ulcerative colitis, besides its approved use in moderate-to-severe plaque psoriasis and active psoriatic arthritis.

The presented study provides the basis for the marketing authorisation of the proposed ustekinumab biosimilar Fyb202, together with an extensive analytical characterisation and the results of an efficacy and safety trial in patients with moderate-to-severe plaque psoriasis.

Aims & Methods: The primary objective of the three-arm trial RUSTIC was A) to prove pharmacokinetic (PK) similarity in terms of AUC_{0-inf} and C_{max} of the proposed ustekinumab biosimilar Fyb202 to both EU-approved (EU-Ref) and US-licensed ustekinumab (US-Ref) and B) to prove PK similarity of both reference drugs. PK similarity was concluded if the 90% confidence interval (CI) of the geometric mean ratios was contained within the acceptance interval of 80.00–125.00% (analysis of covariance [ANCOVA] with body weight as covariate).

Treatments included a single 45-mg subcutaneous injection. The multi-centric clinical trial was conducted at four German trial sites. Safety analyses comprised immunogenicity (anti-drug antibodies [ADAs] and neutralising antibodies [NABs]), adverse events (AEs), vital signs, body temperature, 12-lead electrocardiograms, and local tolerability (subject- and investigator-assessed).

Healthy male and female subjects (18–55 years, body weight 60–90 kg, body-mass index 20.5–30.0 kg/m²) were included in the trial and observed for up to 112 days after dosing.

Results: Overall, 491 subjects were randomised (FYB202: n=164, EU-Ref: n=163, US-Ref: n=164); 486 subjects completed the trial, and 478 subjects were included in the PK analysis set. PK similarity was demonstrated for all three comparisons: all 90% CIs of the respective geometric mean ratios for AUC_{0-inf} and C_{max} were contained within the acceptance interval of 80.00–125.00% (Table 1). After administration of FYB202, fewer subjects had at least one positive ADA result at trial end compared to the reference groups (FYB202: 20%, EU-Ref: 42%, US-Ref: 51%). ADA titre levels were similar between all three groups. The percentage of subjects with at least one positive NAb-reactive result at trial end was slightly lower in the FYB202 group compared to the reference groups (FYB202: 11%, EU-Ref: 15%, US-Ref: 18%). More than half of the subjects had at least one treatment-related AE (FYB202: 53%, EU-Ref: 55%, US-Ref: 57%); no treatment-related serious AEs occurred. Local tolerability at the injection site was comparable in all treatment groups.

Parameter	FYB202 vs. EU-Ref	FYB202 vs. US-Ref	EU-Ref vs. US-Ref
AUC_{0-inf}	102.85 (96.84-109.23)	112.05 (105.24-119.30)	109.00 (102.84-115.53)
C_{max}	97.22 (92.05-102.67)	101.65 (96.19-107.42)	104.59 (99.06-110.44)

Table 1: Point estimates and 90% confidence intervals [%] for the primary pharmacokinetic parameters of ustekinumab (PK analysis set; N=478)

Observations: AUC_{0-inf} : n=318 each comparison; C_{max} : n=319 FYB202 vs. EU-Ref, EU-Ref vs. US-Ref; n=318 FYB202 vs. US-Ref

Conclusion: The RUSTIC trial demonstrated bioequivalent PK characteristics between FYB202 and both EU-approved and US-licensed ustekinumab and for the two reference drugs. No clinically meaningful differences with respect to the overall safety, immunogenicity and local tolerability were observed.

Disclosure: The trial is registered in the EU Clinical Trials Register (EudraCT no. 2022-000832-43).

The clinical trial was financed by Formycon AG, Martinsried, Germany and conducted by SocraTec R&D GmbH, Oberursel/Erfurt, Germany (data management: SocraMetrics GmbH, Erfurt, Germany). During conduct of the trial and preparation of the abstract, S.B. and K.N. were employees of Formycon AG. J.K. and M.A. were employees of SocraTec R&D GmbH. R-S.W. was an employee of SocraMetrics GmbH. B.S. was cofounder and managing director of SocraTec R&D GmbH and SocraMetrics GmbH.

PP0594

EUROPEAN AND US PATIENT AND HEALTH CARE PROFESSIONAL PERSPECTIVES ON THE EXPERIENCE OF FATIGUE IN CROHN'S DISEASE AND ULCERATIVE COLITIS: COMMUNICATING NEEDS AND FEATURES OF IBD EXPERIENCES (CONFIDE) SURVEY

R. Panaccione¹, A. Potts Bleakman², S. Schreiber³, S. Travis⁴, M.C. Dubinsky⁵, T. Hibi⁶, T. Hunter Gibble², T. Panni⁷, C. Kayhan², E.J. Flynn², A.D. Favia², C. Atkinson⁸, D.T. Rubin⁹

¹University of Calgary, Calgary, Canada, ²Eli Lilly and Company, Indianapolis, United States of America, ³University Hospital Schleswig-Holstein, Kiel, Germany, ⁴University of Oxford, Oxford, United Kingdom, ⁵Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁶Kitasato University, Kitasato Institute Hospital, Center for Advanced IBD Research and Treatment, Tokyo, Japan, ⁷Eli Lilly and Company, Bad Homburg, Germany, ⁸Adelphi Real World, Bollington, United Kingdom, ⁹University of Chicago, Inflammatory Bowel Disease Center, Chicago, United States of America

Contact E-Mail Address: rpanacci@ucalgary.ca

Introduction: Fatigue is a prevalent and debilitating symptom among patients with Crohn's disease (CD) or ulcerative colitis (UC). However, due to its subjective nature and the lack of effective management strategies in CD/UC, fatigue often goes under-recognized and under-treated.¹ The Communicating Needs and Features of IBD Experiences (CONFIDE) study explored patient and healthcare professional (HCP) perspectives on the experiences and impact of CD/UC-related symptoms in Europe (France, Germany, Italy, Spain, and UK), the United States (US) and Japan.

Aims & Methods: Online, quantitative, cross-sectional surveys were conducted separately among patients with moderate-to-severe CD/UC and HCPs who make prescribing decisions for patients. Moderate-to-severe CD/UC were defined using criteria based on previous treatment, steroid use, and/or hospitalization. Descriptive statistics were used here to summarize the European and US data related to fatigue.

Results: A total of 547 European (55.4% male, mean age: 38.0 years) and 215 US (54.9% male, 40.9 years) patients with CD and 556 European (57.4% male, 38.9 years) and 200 US (61.5% male, 40.4 years) patients with UC completed the surveys. The proportions of patients who received advanced therapies at the time of survey completion were 63.4% and 58.1% among European and US patients with CD. Among patients with UC, the percentages were 54.1% and 76.5% of European and US patients.

Overall, 34.2% European and 35.8% US patients with CD, and 20.9% European and 27.5% US patients with UC reported currently experiencing fatigue (in the past month). Similar results were observed among patients receiving advanced therapies: CD (Europe: 34.3%; US: 36.0%); UC (Europe: 19.9%; US: 25.5%). Fatigue was ranked among the top five symptoms with greatest impact on patients by 44.5% European and 52.9% US patients with CD, and 55.2% European and 37.5% US patients with UC. Among patients who reported currently experiencing fatigue, 29.9% European and 36.4% US patients with CD, and 22.4% European and 40.0% US patients with UC discussed it with their HCPs at every appointment. Among patients who did not discuss fatigue with their HCPs at every appointment, at least two-thirds indicated that they would like to discuss it more frequently: CD (Europe: 75.6%; US: 67.3%); UC (Europe: 74.4%; US: 66.7%). Surveys were completed by 503 European (70.8% male) and 200 US (78.0% male) HCPs, of which 92.5% were gastroenterologists/internal medicine practitioners. A minority of HCPs reported fatigue among the top five symptoms with the greatest impact on patients: CD (Europe: 33.9%; US: 22.0%); UC (Europe: 22.7%; US: 11.5%). More than half of HCPs reported proactively discussing fatigue at a routine appointment with patients: CD (Europe: 69.4%, US: 59.5%); UC (Europe: 64.6%, US: 59.0%). Among HCPs

not proactively discussing fatigue, the most common reason was that they expected patients to bring it up if it is an issue: CD (Europe: 39.0%, US: 30.9%); UC (Europe: 37.1%, US: 32.9%).

Conclusion: For both patients with CD/UC, fatigue was a common and impactful symptom, despite the use of advanced therapies. A substantial proportion of patients experiencing fatigue who did not discuss it at every HCP appointment, reported a desire to discuss fatigue more frequently. Although more than half of HCPs reported proactive discussion of fatigue with their patients, some HCPs expected patients to bring it up. This indicates a communication gap between patients and HCPs and highlights the underappreciation of the impact of fatigue in CD/UC.

References: 1. Farrell D, et al. (2020) Cochrane Database Syst Rev. 4(4), CD012005.

Disclosure: Remo Panaccione, Consultant for: Abbott, AbbVie, AbbVax, Alimentiv (formerly Robarts), Amgen, AnaptysBio, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatrix, Ventyx, UCB; Speaker's Fees for: AbbVie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, Takeda Pharmaceuticals; Advisory Boards for: AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, SandozShire, Sublimity Therapeutics, Takeda Pharmaceuticals, Ventyx.

Stefan Schreiber, Consultancy fees: AbbVie, Arena, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Falk, Fresenius, Gilead Sciences, IMAB, Janssen, Eli Lilly and Company, Hikma, MSD, Mylan, Pfizer Inc, Protagonist, Provention Bio, Takeda, Ventyx, and Theravance.

Simon Travis, Grants: AbbVie, ECCO, Eli Lilly and Company, Helmsley Trust International, International Organization for the Study of Inflammatory Bowel Disease, Norman Collision Foundation, Pfizer, Takeda, UCB Pharma, UKIERI, Vifor Pharma; Honoraria: Ferring Pharmaceuticals, Takeda, Eli Lilly and Company, Bristol Myers Squibb, Janssen, Violicom; Travel grants: AbbVie, Eli Lilly and Company, Janssen, Pfizer, Takeda, Ferring Pharmaceuticals, Amgen, Biogen; Consultancy fees: AbbVie, Allergan, Amgen, Apexian, Bioclinica, Biogen, Bristol Myers Squibb, ChemoCentryx, Cosmo Pharmaceuticals, Endpoint Health, Eli Lilly and Company, Enterome, Equillum, Ferring Pharmaceuticals, Genentech/Roche, GlaxoSmith-Kline, Immunocore, Immunometabolism, Janssen, Merck, Merck Sharp & Dohme, Mestag Therapeutics, Novartis, Pfizer, Protagonist Therapeutics, Proximagen, Receptos, Roche, Sanofi, Satisfai Health, Sensyne Health, Sorriso Pharmaceuticals, Takeda, UCB Pharma, VHSquared, Vifor Pharma. Marla C. Dubinsky, Consultancy fees: AbbVie, Abivax, Astra Zeneca, Boehringer Ingelheim International GmbH, Bristol Myers Squibb, Celgene Corporation, Eli Lilly and Company, F. Hoffman-La Roche Ltd, Genentech Inc., Gilead Sciences, Janssen, LLC, Merck, Pfizer, Prometheus Biosciences, Takeda Pharmaceuticals USA, Inc., and UCB; Stock options: TrellusHealth Inc.; Research support: AbbVie, Janssen, LLC, Pfizer, and Prometheus Lab; and licensing fees: Takeda.

Toshifumi Hibi, Personal fees: Abbvie GK, EA Pharma, Janssen Pharmaceutical K.K, JIMRO, Mitsubishi-Tanabe, Mochida Pharmaceutical, Pfizer Japan, Sandoz K.K, Takeda Pharmaceutical, Zeria Pharmaceutical, Celltrion Healthcare Japan, Eli Lilly Japan, Gilead Sciences, Miyarisan Phar-

maceutical, Alfresa Pharma Corporation, Kyorin Pharmaceutical; Grants: JIMRO, Mochida Pharmaceutical, Zeria Pharmaceutical, Miyarisan Pharmaceutical, Alfresa Pharma Corporation, and Kyorin Pharmaceutical. Christian Atkinson, Employment: Adelphi Real World.

David Rubin, Grant support: Takeda; Consultant: Abbvie, Altrubio, Apex, Avalo Therapeutics, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. Board of Trustees: Crohn's & Colitis Foundation; Board of Directors: Cornerstones Health.

Alison Potts Bleakman, Theresa Hunter Gible, Tommaso Panni, Cem Kayhan, Eoin J. Flynn, and Angelo D. Favia are employees and stockholders of Eli Lilly and Company.

PP0595

USE OF FK-ADA BIOSIMILAR (MSB 11022) IN CONTEXT OF BIOLOGIC SWITCH IN INFLAMMATORY BOWEL DISEASES: BASELINE DATA OF THE REAL WORLD IDEA STUDY

G. Pourcel¹, L. Peyrin-Biroulet², Y. Bouhnik², C. Taxonera Samsó³, S. Howaldt⁴, J. Monnet¹

¹Fresenius Kabi Biopharma, Eysins, Switzerland, ²Groupe Hospitalier Privé Ambroise Paré – Hartmann, Institut des MICI, Neuilly-sur-Seine, France, ³Hospital Clinico, Madrid, Spain, ⁴HaFCEd e.K., Hamburg, Germany

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: Biosimilars offer similar efficacy and safety when compared to their originators, thereby increasing patient access to affordable treatment. FK-ada is an adalimumab biosimilar approved for the treatment of inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC). FK-ada development included 1,234 subjects treated up to 52 weeks (total 420 patients-year). Since first approval, there have been no unexpected safety signals despite more than 115,000 patient-years of exposure. IDEA is an ongoing real-world study in which adult patients with IBD and inflammatory rheumatic diseases (RA, AS, PsA), switching from adalimumab originator, or from adalimumab biosimilar to FK-ada, are followed up to one year. We present here the baseline characteristics of IBD patients, physicians and centres participating to the study.

Aims & Methods: The aim of this study was to identify predictive factors of treatment persistence after switch to FK-ada and to develop a model to predict persistence at 12 months. Data collected include: baseline characteristics of patients, physicians, and the participating centres, reasons for treatment switch, patient clinical status at each follow-up visit including disease activity scores (HBI and Montreal classification), and faecal calprotectin results. Adult patients with either CD or UC were included but those receiving treatment outside of routine clinical care were excluded. Data is presented using descriptive statistics and a logistic regression model will be used to identify possible predictive factors.

Results: IBD patients were recruited in 18 centres (15/18 university or public hospitals, >50% granted incentives to switch to biosimilars, 16/18 secondary and tertiary care level, 12/18 with at least 4 managing physicians in the medical team). All physicians were full time gastroenterologists, (66% over 40 years old, with a median time of 22 years in IBD management and 15 years median time in prescribing biologics). In the past 5 years, 71% have been involved in 6 or more non interventional studies, and 67% in 6 or more clinical trials. 138 IBD patients were recruited (CD: 113, UC: 25 patients were diagnosed with IBD (57% males, median age 43, 90% with secondary or university level of education, median BMI stable at 25.3 [22.2, 28.4] kg/m²). Current smokers were more frequent in CD patients 21.4% vs 8.3 % UC (median 10 pack years). Disease history and current

status at baseline summarized in Table 1. Median fecal calprotectin value: 73.0 [30.0, 299.0] mcg/mg. 54% of patients were switched to FK-ada from the originator, 43% from another adalimumab biosimilar. Main reason for switching was administrative (economic, hospital decision): 88% from originator, 65% from biosimilar; Safety: 1% from originator, 22% from biosimilar.

		CD (N=113)	UC (N=25)	Overall (N=138)
Time since diagnosis (Years)	Median [Q1 - Q3]	11.8 [6.1, 20.1]	7.9 [4.9, 17.4]	11.4 [5.8, 20.1]
Previous surgical procedure	Yes	49/113 (43.4%)	0/24	49/137 (35.8%)
Previous or current non biologic therapy	Yes	75/111 (67.6%)	20/25 (80.0%)	95/136 (69.9%)
Response to steroids	None	26/112 (23.2%)	2/25 (8.0%)	28/137 (20.4%)
Current disease location (Montreal classification)	One location	65/113 (57.5%)	15/25 (60.0%)	80/138 (58.0%)
	>1 location	48/113 (42.5%)	10/25 (40.0%)	58/138 (42.0%)
Current disease activity NA= Not applicable	Clinical remission or mild to moderate (HBI score categorical)	110/113 (97.3%)	NA	NA
	Clinical remission or mild to moderate (Montreal classification)	NA	22/25 (88.0%)	NA

Table 1: Disease history and current status at baseline

Conclusion: FK-ada is a well-known valuable therapeutic option in the treatment of IBD. 52-week IDEA data will support identification of predictive factors of FK-ada treatment persistence after switch.

Disclosure: Pr Laurent Peyrin-Biroulet, Pr Yoram Bouhnik, Pr Stefanie Howaldt, Pr Carlos Taxonera are principal investigators for IDEA study sponsored by Fresenius Kabi.

PP0596

IMPROVED ADHERENCE AND PERSISTENCE IN INFLAMMATORY BOWEL DISEASE PATIENTS TAKING HIGH STRENGTH MESALAZINE TABLETS

H. Wüthrich¹, E. Safroneeva^{1,2}, O. Gerstner¹, J. Kirchgesner³, R. Laoun¹

¹Tillotts Pharma AG, Rheinfelden, Switzerland, ²Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland,

³Saint-Antoine Hospital, Department of Gastroenterology, Paris, France

Contact E-Mail Address: raphaellaoun@yahoo.fr

Introduction: While patients at all stages of ulcerative colitis (UC) are affected by non-adherence, those in symptomatic remission are particularly at risk, often taking less than 70% of their prescribed medication¹, with non-adherent patients being more likely to relapse². Therefore, improving adherence to therapy has become one of the most important goals of patient management of chronic diseases. A high dose formulation of mesalazine was introduced in the French market in May 2020, Fivasa[®] 1600 mg, to reduce the pill burden. However, its impact on treatment compliance has not yet been assessed.

Aims & Methods: This was a retrospective cohort study in French patients using the IQVIA Longitudinal Prescription Data; a patient database based on retail pharmacy claims. An anonymised unique patient ID is assigned to each patient, which enables a longitudinal follow-up of these patients. The French database covers more than 9,600 retail pharmacies (~44% of national coverage). Patients were eligible if they had at least one treat-

ment delivery of oral mesalazine initiated between June 2020 and April 2022, and a pre-observational period of at least 365 days prior to index date. UC and Crohn's disease patients cannot be distinguished in this database.

This study compared the adherence and persistence to oral mesalazine according to the tablet strength (high strength (HS), 1600 mg; standard strength (SS), 800-1000 mg and low strength (LS), 400-500 mg) delivered in the pharmacy.

The primary objective was 1) To compare the adherence to the prescribed dose of oral mesalazine over 1 year between groups of inflammatory bowel disease (IBD) patients in relation to the tablet strength (number of pills per day) provided in retail pharmacy and 2) To compare the persistence to the prescribed dose of oral mesalazine over 1 year between groups of IBD patients in relation to the tablet strength (number of pills per day) provided in retail pharmacy.

Results: The study population is shown in Table 1 and included 9929 patients after exclusion of patients without the pre-observability period, patients <18 years old, patients taking oral granules or patients taking different tablet strengths of mesalazine at index date.

Persistence to medication at 1 month after follow-up was 100%, 73.1% and 64.7% in the HS, SS and LS group, respectively. After 3 months of follow-up, it was 63.7%, 50.9% and 39.7% in the HS, SS and LS group, respectively. After 6 months of follow-up, it was 47.0%, 37.2% and 28.5% in the HS, SS and LS group, respectively. After 1 year of follow-up, it was 24.3%, 17.6% and 11.8% in the HS, SS and LS group, respectively.

Patient adherence to mesalazine tablets was 800/986 (81.1%) patients in the HS group, 5368/6947 (77.3%) patients in the SS group and 1493/1996 (74.8%) patients in the LS group (p<0.001).

At index date	Overall population N=9929	High strength N=986 (9.9%)	Standard Strength N=6947 (70.0%)	Low strength N=1996 (20.1%)
Age, mean (SD)	52.4 (18.6)	46.5 (17.2)	51.3 (18.1)	59.5 (18.6)
Gender, N (%)				
Female	5247 (52.8%)	468 (47.5%)	3693 (53.2%)	1086 (54.4%)
Male	4484 (45.2%)	500 (50.7%)	3107 (44.7%)	877 (43.9%)
Missing data	198 (2.0%)	18 (1.8%)	147 (2.1%)	33 (1.7%)
Number of co-medications, N (%)				
0	3031 (30.5%)	471 (47.8%)	2191 (31.5%)	369 (18.5%)
1	2761 (27.8%)	324 (32.9%)	1987 (28.6%)	450 (22.5%)
2	1663 (16.7%)	119 (12.1%)	1177 (16.9%)	367 (18.4%)
3 or more	2474 (24.9%)	72 (7.3%)	1592 (22.9%)	810 (40.6%)

Table 1: Baseline Characteristics.

Conclusion: These results showed a consistent lower adherence with the increase of pill burden. Both standard and low strength tablets were significantly associated with lower adherence to medication than the high strength tablet group. The impact of pill burden was more prominent on the persistence of medication in patients taking mesalazine and showed significantly/longer persistence in the high strength tablet group.

References:

1. Kane SV, Cohen RD, Aikens JE, Hanauer SB. Prevalence of nonadherence with maintenance mesalamine in quiescent ulcerative colitis. *Am J Gastroenterol.* 2001;96(10):2929-33
2. Kane S, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *Am J Med.* 2003;114(1):39-43.

Disclosure: HW, ES, OG and RL are employees of Tillotts Pharma AG.

PP0597

A FOUR-STRAIN PROBIOTIC EXERTS A POSITIVE EFFECT ON SYMPTOMS OCCURING IN IBD IN THE ABSENCE OF INFLAMMATION (IBD/IBS OVERLAP)

A. Fennessy¹, M. Doyle¹, A. Boland¹, R. Bourke¹, Y. Gammell¹, I. Warnock¹, A. O'Connor²

¹Tallaght University Hospital, Gastroenterology, Dublin, Ireland, ²Tallaght University Hospital/Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: anne.m.fennessy@gmail.com

Introduction: Irritable Bowel Syndrome (IBS) is common in patients with inflammatory bowel disease, with a systematic review and meta-analysis of observational studies reporting an overall pooled prevalence of 39% and 35% in patients in clinical remission [1].

This subset of IBD patients report a reduced quality of life and increased anxiety and depression [2].

These patients are usually excluded from randomised clinical trials of treatments for IBS and therefore the evidence base for treatment strategies is small. A multi-strain probiotic (Symprove™, Symprove Ltd, Farnham, United Kingdom) has been shown to lead to improvement in overall symptom severity in patients with IBS and associated with decreased intestinal inflammation in patients with UC, but not in CD and is well tolerated in both populations [3,4].

Aims & Methods: Aim: To assess the efficacy of a liquid, multi-strain probiotic (Symprove) in patients with IBD whose disease is in remission as evidenced by the absence of inflammation but have ongoing IBS symptoms. Methods: A single-centre double-blind, placebo controlled trial. Baseline demographic and clinical data; IBS symptom severity scores (IBS-SSS), IBD scores, bloods and faecal calprotectin were collected at week 0 and participants will receive either placebo or probiotic. At week 12 we repeated assessment of symptoms, repeat CRP and faecal calprotectin. Participants must be considered in remission from IBD as evidenced by a C-reactive Protein (CRP) <5mg/L and faecal calprotectin (FC) < 250ng/ml at recruitment but with ongoing gastrointestinal symptoms and meeting Rome IV criteria for the diagnosis of IBS.

Primary Outcome: 100-point drop in IBS-SSS post treatment

Secondary Outcomes: Change in IBS-SSS. Negative IBD outcomes including biochemical flare, steroid treatment or escalation of maintenance therapy.

	PLACEBO (N=21)	SYMPROVE (N=40)
MEAN AGE	45 years	41 years
GENDER	71% Female 29% Male	70% Female 30% Male
DIAGNOSIS	38% UC, 62% CD	23% UC, 77% CD
MEDIAN DURATION OF DIAGNOSIS	17.5 years	11 years
PREVIOUS RESECTION	38.1%	20%
STOMA	0	0
BIOLOGIC USE CURRENTLY	57%	70%

Results: 61 patients were enrolled in the study, 40 of whom received active agent and 21 of whom received placebo. The average age of patients was 42 years and 71% of patients were female. 28% (n=17) had Ulcerative Colitis and 72% (n=44) had Crohn's Disease, demographics are outlined in Table 1. Overall 45% of patients receiving the active agent achieved the end point compared to 33% of those receiving placebo (P=0.423). Separating patients with Crohn's Disease from those with UC, 50% of patients with UC receiving placebo achieved the endpoint compared to 44% of those receiving the active agent (p=1.000), however in Crohn's Disease 45% of those receiving the active agent achieved the endpoint compared to 29% of those receiving placebo (p=0.340). 23.8% (n=5) of those receiving placebo experienced a biochemical flare or steroid prescription or Escalation of

Therapy compared to 12.5% of those receiving the active agent (p=0.266). In Crohn's Disease the mean IBS-SSS declined by 55 points in the placebo group (SD, -86) compared to 74 points in the active group (SD, -125).

Conclusion: A tendency among patients with Crohn's Disease towards improved IBS-SSS scores as well as fewer adverse IBD outcomes was noted in the probiotic group. Although this did not reach statistical significance this pilot study allows us to adequately power larger studies addressing this question.

References:

1. Halpin SJ and Ford AC. *Am J Gastroenterol* 2012; 107:1474–1482
2. Gracie DJ et al. *Clinical Gastroenterology and Hepatology* 2017;15:376–384
3. Sisson G et al. *Aliment Pharmacol Ther.* 2014;40(1):51-62.
4. Bjarnason I, et al. *Inflammopharmacology* 2019;27(3):465–73.

Disclosure: Active agent and Placebo were provided by Symprove Ltd, Farnham, United Kingdom.

PP0598

MANAGEMENT OF COMPLICATIONS IN PATIENTS WITH AN ILEOSTOMY: AN UMBRELLA REVIEW OF SYSTEMATIC REVIEWS FOR THE ENDOTRIAL CONSORTIUM

V. Solitano^{1,2}, S.K. Vuyyuru³, Y. Yuan⁴, S. Singh⁵, N. Narula⁶, C. Ma⁷, M. Hutton⁸, J. Ann Van Koughnett⁹, F. Rieder¹⁰, V. Jairath¹¹

¹Universita Vita-Salute San Raffaele, Gastroenterology, Milan, Italy, ²Western University, Division of Gastroenterology, London, Ontario, Canada, ³Alimentiv Inc., London, Canada, ⁴Lawson Health Research Institute,, London, Canada, ⁵Division of Gastroenterology, Department of Medicine, University of California, San Diego, La Jolla, United States of America, ⁶McMaster University, Medicine, Hamilton, Canada, ⁷University of Caglar, Division of Gastroenterology and Hepatology, Calgary, Canada, ⁸Nursing Practice Excellence and Innovation, London Health Sciences Centre, London, Canada, ⁹Division of General Surgery, Department of Surgery, University of Western Ontario, London, Canada, ¹⁰Cleveland Clinic Foundation, Lerner Research Institute Dept. of Pathobiology - NC22, Cleveland Heights, United States of America, ¹¹Division of Gastroenterology, Western University, London, Ontario, Canada, London, Canada

Contact E-Mail Address: virginiasolitano@gmail.com

Introduction: Ileostomies, whether temporary or permanent, may be required in patients with Crohn's Disease (CD) due to medically refractory disease or penetrating complications. However, standardized clinical care processes for patients with CD and a permanent ileostomy (PI) are lacking. The EndoTrial consortium aims to address this gap by developing pathways for care.

This umbrella review sought to consolidate existing knowledge by identifying, evaluating, and synthesizing findings from published systematic reviews on various aspects of clinical care for ileostomy patients, including managing high stoma output, disease recurrence, peristomal skin care, stoma pouching system and adhesives, behavioral interventions, mental health, and dietary management.

Aims & Methods: Following Cochrane guidelines for "Overviews of Reviews" and adhering to Preferred Reporting Items for Overviews of Reviews (PRIOR), we systematically searched major databases for relevant systematic reviews (SRs) or scoping reviews (ScR) published in English until January 5, 2024. Two independent reviewers screened articles, extracted data, and assessed quality using AMSTAR 2. Data synthesis was conducted narratively.

Results: Of 1349 screened papers, we selected 24 reviews, including 22 SRs (8 with meta-analysis) and 2 ScRs. None exclusively focused on PI. Furthermore, nine reviews did not mention patients with inflammatory bowel disease (IBD), and only two reviews included patients with high-output ileostomy, highlighting a large evidence gap. The identified reviews covered eleven types of interventions, including ostomy care pathways, clinical management of high-output stoma, peristomal skin care, dietary management, nurse specialists, post-discharge continuous care, telemedicine, patient education, self-management interventions, management of parastomal varices, and chewing gum for postoperative ileus. Notably, none of the reviews exclusively examined stoma pouching system and adhesives, behavioral interventions, or mental health.

Interventions	SR	SR+MA	ScR	Key Findings
Ostomy care pathways	1	0	0	Ostomy care pathways (including preoperative education and counseling, postoperative education and discharge planning, and outpatient home visits and telephone follow-ups), may contribute to patient satisfaction and decrease in both hospital length of stay and hospital readmission rates
Clinical management of high-output stoma	1	1	0	No significant effect of common agents on stoma output. Variation in management strategies and discrepancies in recommendations were noted. Magnesium may benefit hypomagnesemia
Peristomal skin care	1	1	0	Systemic steroids and combination therapies are crucial for peristomal pyoderma gangrenosum, and adjunctive techniques showed no significant benefit in peristomal skin condition compared standard care
Dietary management	1	1	1	Dietary management findings from various reviews and guidelines indicate a range of strategies with inconsistent effects. Low fiber and fat diets seem generally beneficial, while alcohol intake is detrimental. Distal feeding shows promise in reducing complications and improving outcomes. For lower GI surgery, early enteral nutrition reduces hospital stay without added risks
1. Nursing care 2. Post-discharge continuous care	3	2	1	Importance of stoma care nurse specialists. Nursing interventions mitigate stoma-related quality of life issues. Validated HRQOL measurement instruments (QOLS, CO-HQOL-O, Stoma-QOL) identified for research use. Continuing care improved health outcomes and care satisfaction for patients with stomas compared with routine care
Telemedicine	1	1	0	Telemedicine reduced the incidence of stoma and peristomal complications. Technologies-based interventions (e.g., sensor-based wearable technologies and computer-based) created a positive effect on the management of an ostomy, provided opportunities for enhancing self-efficacy, self-care, and self-management
1. Patient Education 2. Self-management interventions	4	1	0	Patient education interventions for individuals with stomas, have the potential to positively impact various aspects of patients' lives, including quality of life, psychosocial skills, and self-management. Self-management interventions showed positive effects on self-efficacy and self-reported self-management skills but had mixed outcomes for quality of life and objective measures of self-management. Nurse involvement and post-operative contact improved outcomes, leading to the development of a leaflet with a traffic light system for self-monitoring
Parastomal varices management	1	0	0	TIPS had superior efficacy in preventing recurrent hemorrhage from parastomal varices compared to local measures, surgical or non-operative, which were less effective
Prevention of postoperative ileus	1	1	0	Gum chewing after ostomy was found to significantly reduce the time to pass flatus and stool; it may reduce the time to resolution of postoperative ileus and length of hospital stay

Conclusion: Evidence for best practice interventions to help improve the quality of life for patients living with an ileostomy is limited and heterogeneous. Notably, systematic reviews have largely overlooked interventions for patients with PI. There is an urgent need for standardized clinical care processes and pathways tailored to the unique needs of this patient population, which is a key workstream of the EndoTrial Consortium

Disclosure: VS, YY, MH, JAVK have none to disclose.

SKY is an employee of Alimentiv Inc.

SD has received research grants from Pfizer.

NN has received speaking/advisor fees from Janssen, Abbvie, Takeda, Pfizer, Merck, Sandoz, Fresenius Kabi, Innomar, Iterative Scopes, Bristol Myers Squibb, Viatris, and Ferring.

CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius

Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche, Sanofi; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Ferring, Fresenius Kabi, Janssen, Takeda, Pendopharm, and Pfizer; royalties from Springer Publishing; research support from Ferring, Takeda, Pfizer.

FR is consultant to Agomab. Allergan, AbbVie, Boehringer Ingelheim, Celgene, Cowen, Falk Pharma, Genentech, Gilead, Gossamer, Guidepoint, Helmsley, Index Pharma, Janssen, Koutif, Mestag, Metacrine, Morphic, Origo, Pfizer, Pliant, Prometheus, Receptos, RedX, Roche, Samsung, Takeda, Techlab, Theravance, Thetis, UCB and received funding from the National Institute of Health, Helmsley Charitable Trust, Crohn's and Colitis Foundation, Rainin Foundation, UCB, Boehringer-Ingelheim, Pliant, Morphic, BMS, 89Bio.

VJ has received consultancy/advisory board fees from AbbVie, Alimentiv Inc., Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, GlaxoSmithKline, Genentech, Gilead, Janssen, Merck, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Topivert, Ventyx, and Vividion; and speaker's fees from, Abbvie, Ferring, Galapagos, Janssen Pfizer Shire, Takeda, and Fresenius Kabi.

PP0599

A SINGLE CENTER COHORT STUDY ON THE USE OF BIOLOGIC THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND CANCER

P. Kevrekidou¹, D. Lazou¹, S. Mamalis¹, S. Kallinikidis¹, A. Andreadou², G. Lazaraki³, K. Soufleris¹, D. Tzilves¹

¹Theagenio Cancer Hospital of Thessaloniki, Gastroenterology Department, Thessaloniki, Greece, ²Theagenio Cancer Hospital of Thessaloniki, Third Department of Medical Oncology, Thessaloniki, Greece, ³Theaghenion Cancer Hospital, Gastrointestinal Oncology, Thessaloniki, Greece

Contact E-Mail Address: dimitris.tzilves@gmail.com

Introduction: In the years to follow we anticipate a rise in the prevalence of an aging population of inflammatory bowel disease (IBD) patients and a rise in cancer incidence. We are in urgent need of data to help us manage these patients.

We therefore followed a cohort of patients from a referral oncology hospital with prior and active cancer who received biologic therapy to control their IBD.

Aims & Methods: We first recorded data regarding inflammatory bowel disease characteristics: disease type, disease duration, disease severity, previous surgery or hospitalization and received therapy: type and duration of biologic therapy, prior use of immunosuppressants. We also recorded all available data regarding cancer disease: cancer site, stage, virus related cancer, family history of cancer, smoking status and received therapy (curative surgery, chemotherapy, hormone therapy, radiotherapy, immunotherapy). We monitored outcomes of IBD (steroid free clinical remission, IBD-related surgery or hospitalization) and outcomes of cancer (recurrence free survival, progression free survival, overall survival).

A blinded oncologist was asked to retrospectively evaluate all available data regarding cancer prognosis (stage, histology, response to therapy) and to categorize patients in 3 groups: low, intermediate or high risk to recur or progress.

Results: A total of 30 patients were included, 57 % female, median age 60 years, 60% Crohn's Disease, median disease duration 9.5 years, 26% prior IBD surgery, 33% prior azathioprine use, 36% smokers. They were treated with anti-TNF therapy (n=19) anti-integrin therapy (n=8) and anti-IL 12/23 therapy (n=4). The majority (20%) of patients had a history of hematologic

malignancy (lymphomas, myeloproliferative disorders, leukemias), 13% with a virus related cancer and 66% with curative surgery. Patients were classified retrospectively as 63% low risk, 13% intermediate risk and 10% high risk. Four patients) with active cancer (2 with lung cancer and 2 with myeloproliferative disorders) continue to receive biologic therapy for IBD and oncological therapy with no signs of progression from both diseases. All but 3 patients have remained in steroid free clinical remission: 3 had IBD-related surgery. Median follow up under biologic therapy was 5.5 years: only 2 patients showed cancer recurrence: 1 patient with breast cancer developed bone metastases and finally died, and 1 patient with colon cancer developed bladder cancer and died as well. Both patients were classified as high risk.

In both patients biologic therapy was interrupted and that resulted in administration of high-dose steroids and IBD-related hospitalizations and infections (pneumonia, C Difficile colitis).

Conclusion: In this cohort of cancer patients with IBD treated with biologics and followed up for more than 5 years the risk of cancer recurrence was low and not unexpected in oncology terms.

Biologic therapy was successful in the majority of patients and kept them off surgeries and steroids for their underlying IBD. We need more smart and innovative ways to study this particular clinical scenario in the future.

Disclosure: Nothing to disclose.

PP0600

PHASE 1 BIOMARKER ANALYSES OF GS-1427 A NOVEL ORAL $\alpha 4\beta 7$ INTEGRIN INHIBITOR FOR INFLAMMATORY BOWEL DISEASE DEMONSTRATE $\alpha 4\beta 7$ SELECTIVITY AND ONCE DAILY DOSING

X. Shao¹, C. Chang¹, S. Bonne-Annee¹, B.R. Chitteti¹, Y. Wang¹, V. Malkov¹, A. Goddard¹, G. Huang¹, N. Maramreddy¹, J. Zhou¹, F. Hong¹, B. Levesque¹, A. Billin¹, S. Roedder¹

¹Gilead Sciences, Foster City, United States of America

Contact E-Mail Address: silke.roedder@gilead.com

Introduction: GS-1427 is a novel selective small molecule inhibitor of the integrin receptor $\alpha 4\beta 7$ in clinical development for once daily oral dosing in inflammatory bowel disease (IBD). Inhibition of $\alpha 4\beta 7$ is an established efficacious therapeutic option for the treatment of Ulcerative Colitis (UC) and Crohn's Disease, but current treatment requires intravenous or subcutaneous injection. A Phase 1 first-in-human study evaluated the pharmacokinetics, safety, tolerability, and exploratory biomarkers of GS-1427 in healthy subjects. The biomarker objectives in Phase 1 were to confirm preclinical findings of extended $\alpha 4\beta 7$ receptor occupancy (RO) supporting once daily dosing, selectivity for $\alpha 4\beta 7$ and to inform Phase 2 dose selection.

Aims & Methods: Biomarkers were evaluated before and after single (20mg-1000mg fasted, SAD) and multiple (20-500mg fed, once daily for 14 days, MAD) ascending doses GS-1427.

Using fluorescently labeled MadCAM-1, $\alpha 4\beta 7$ RO was assessed in fresh whole blood on CD4+CD45RO+ $\beta 7$ + memory T cells; $\alpha 4\beta 1$ RO was evaluated on CD4+CD45RO+ $\alpha 4\beta 1$ + $\beta 7$ - memory T cells using fluorescently labeled tripeptide leucine aspartic acid valine (LDV). RO was calculated as a percent using the fluorescence intensity values measured post-dose and pre-dose. Changes in the frequency of $\beta 7$ +CD4+ memory T cells by flow cytometry and *CCR9* gene expression by RNAseq in whole blood served to evaluate downstream functional $\alpha 4\beta 7$ pharmacodynamics (PD); absolute lymphocyte counts (ALC) in fresh whole blood and frequencies of CD34+ Hematopoietic stem cells (HSC) in viably frozen PBMC were measured to estimate PD downstream of $\alpha 4\beta 1$.

Results: $\alpha 4\beta 7$ RO analyses post single and multiple once daily doses of GS-1427 demonstrated sustained and prolonged RO $\geq 95\%$ confirming

pre-clinical findings and supporting a once daily dosing regimen. Duration of $\alpha 4\beta 7$ RO $\geq 95\%$ post-dose was dose dependent. Doses ≥ 80 mg GS-1427 demonstrated $\alpha 4\beta 7$ RO $\geq 95\%$ for 24 hours, starting with the first dose on Day 1 and persisted until Day 14.

The highest dose group in the MAD demonstrated extended $\alpha 4\beta 7$ RO $\geq 95\%$ up to 72 hours in 100% of subjects after the last dose on Day 14. Corroborating $\alpha 4\beta 7$ RO findings, analyses of $\beta 7$ +CD4+ memory T cells demonstrated dose and time dependent significant increases from baseline compared to placebo, which reached 40% on average in the highest dose group in the MAD. Dose dependent significant increases of *CCR9* mRNA expression levels compared to placebo were observed for doses ≥ 80 mg GS-1427; up to ~ 2.5 -fold increase on average were measured in the higher dose groups in the MAD.

Unlike $\alpha 4\beta 7$ RO, $\alpha 4\beta 1$ RO was partial and transient across the doses tested, and RO levels returned to baseline within ~ 24 hours post-dose in both SAD and MAD. Individual values of $\alpha 4\beta 1$ RO 24 hours post multiple doses GS-1427 on Day 14 were below the assay's lower limit of quantification. The median maximum $\alpha 4\beta 1$ RO at C_{trough} was estimated to be $\sim 20\%$ in the highest dose group.

Supporting findings for $\alpha 4\beta 1$ RO, percent change of ALC was transient and changes of CD34+ HSC frequencies were highly variable which was expected given the low frequency of this population and were within the natural variation across all GS-1427 doses tested.

Conclusion: In conclusion, the exploratory biomarker results in this Phase 1 study in healthy subjects demonstrating extended $\alpha 4\beta 7$ RO and $\alpha 4\beta 7$ selectivity together with the pharmacokinetics, safety, and tolerability data (abstract in preparation) support further development of GS-1427 with a once daily dosing regimen in a Phase 2 study in IBD.

Disclosure: All authors are employees and shareholders of Gilead Sciences.

PP0601

ADVANCED THERAPY IN PATIENTS WITH ULCERATIVE COLITIS AND MALIGNANT DISEASE: A CASE STUDY

T. Masuda¹, N. Inatsugi², S. Yoshikawa², H. Uchida², S. Terauchi², T. Nakao², M. Inagaki², T. Yokoo², T. Tani², K. Okamoto², Y. Shibata²
¹Ikoma Gastrocoloproctology Clinic, Ikoma, Japan, ²Dongo Hospital, Surgery, Yamatotakada, Japan

Contact E-Mail Address: t-masuda@gaia.eonet.ne.jp

Introduction: Advanced Therapy (AT) should be carefully considered for patients who have both inflammatory bowel disease and a malignancy. The aim of administering AT is to avoid hospitalization and surgery in patients with otherwise intractable inflammatory bowel disease; however, the AT may result in exacerbation or recurrence of the malignancy. After careful consideration, we have been treating patients with both inflammatory bowel disease and a malignancy with AT. We here report the results of AT in patients with ulcerative colitis (UC) and malignant disease.

Aims & Methods: From January 2012 to December 2023, we treated five patients with UC and malignant disease (excluding colitic cancer) at the Ikoma Gastroenterology and Proctology Clinic. Age, sex, disease duration, disease extent, severity, clinical course, intractable or not, use or not of azathioprine, type of AT, duration of AT, curability of malignant disease, type and duration of AT after onset of malignant disease, whether the onset of malignant disease was diagnosed during AT, duration of follow-up after onset of malignant disease, outcome of UC after onset of malignant disease, and outcome of malignant disease.

Results: The results are shown in the Table. Age: range (median) (years) : 45-69(56). Sex: Male/Female: 0/5. Disease duration: range (median) (months) : 114-289 (245). Extent of UC : total colon/left colon: 1/4. Severity

of UC : Severity :severe/moderate : 0/5. Clinical course: chronically persistent/relapsing–remitting: 0/5. Use of azathioprine: yes/no: 0/5. Three patients developed malignant disease during AT (cervical cancer, breast cancer, squamous cell carcinoma of the scalp), the remaining two (breast cancer, thyroid cancer) commencing AT only after the cancer's onset. Four of the patients continued AT, the exception (a patient with squamous cell carcinoma) received adalimumab. After the onset of malignant disease, UC remained in remission in all patients and no new malignant disease developed.

AT	One drug: UST, ADA (2 patients)
	Two drugs: GLM→TOF (1 patient)
	Three drugs: IFX→UST→TOF→UST (1 patient)
	Five drugs: ADA→GLM→VED→TOF→UST (1 patient)
	Duration AT: range (median) (months)
	24–83 (41)
Curability of malignancy: yes/no	5/0
Type and duration of AT after onset of malignant disease (months)	UST(30), VED3→TOF24→UST36 total 63
	UST 30, GLM1→TOF59 total 60
Malignancy first diagnosed during AT: yes/no	Yes: TOF, GLM, ADA (3 patients)/no (2 patients)
Duration of follow-up after onset of malignant disease: range (median)months	30–378 (52)
Outcome of UC after onset of malignant disease: remission/relapse	5/0
Outcome of malignant disease: exacerbation or recurrence/no exacerbation or recurrence	0/5

(AT:Advanced Therapy, UST:Ustekinumab, ADA:Adalimumab,
GLM:Golimumab, TOF:Tofacitinib, IFX:Infliximab, VED:Vedolizumab)

Conclusion: In patients with UC who develop a malignancy before or during AT and achieve cure of that malignancy, continuing AT can prevent progression of the UC without exacerbation or recurrence of the malignant disease.

Disclosure: Nothing to disclose.

PP0602

A NOVEL TREATMENT STRATEGY OPTIMISING MEDICAL AND SURGICAL CARE LEADS TO IMPROVED HEALING OF CROHN'S PERIANAL FISTULAS: A REAL-WORLD PROSPECTIVE COHORT

M. De Gregorio^{1,2}, L.S Winata¹, I. Hartley^{1,2}, C.C Behrenbruch^{1,2}, S.J Connor^{3,4}, B. D'Souza^{2,5}, C. Basnayake^{1,2}, G.R Guerra^{1,2}, M.J Johnston¹, M.A Kamm^{1,2}, J.O Keck¹, M. Lust¹, O. Niewiadomski¹, E.JS Ong¹, J.D Schulberg^{1,2}, A. Srinivasan^{2,6,7}, T. Sutherland^{1,2}, R.J Woods¹, E.K Wright^{1,2}, W.R Connell¹, A.J Thompson^{1,2}, N.S Ding^{1,2}

¹St Vincent's Hospital Melbourne, Fitzroy, Australia, ²University of Melbourne, Parkville, Australia, ³Liverpool Hospital Sydney, Liverpool, Australia, ⁴UNSW Sydney, South West Sydney Clinical Campuses, Sydney, Australia, ⁵Northern Hospital, Epping, Australia, ⁶Austin Health, Heidelberg, Australia, ⁷Eastern Health, Box Hill, Australia

Contact E-Mail Address: mdegregorio@live.com.au

Introduction: Despite best standard care, Crohn's perianal fistula healing rates remain low. We herein evaluated the efficacy of a novel treatment strategy optimising medical and surgical care in Crohn's perianal fistulas.

Aims & Methods: A real-world prospective cohort study evaluated the efficacy of a new treatment strategy in adults with Crohn's perianal fistulas at a single tertiary centre. Sixty patients were sequentially included and followed up for a minimum of 12 months. The treatment strategy implemented structured clinician reviews and a novel treatment algorithm centralised around three dynamic stages of care. The stages of care were directed towards patients' clinical disease activity: stage A, active disease, focused on medical and surgical optimisation; stage B, optimised disease with a seton in situ, focused on definitive surgical management; and stage C, healed disease, focused on treatment maintenance. Endpoints included clinical healing, radiologic remission and response on magnetic resonance imaging, and proportion of patients requiring treatment optimisation.

Results: At baseline, 47% were in stage A, 5% stage B, and 48% stage C. Median age was 40 years (IQR: 32–49), 52% were male, and median perianal disease duration was 9 years (IQR: 2–16). After a median of 22 months follow-up (IQR: 16–25), 83% had clinical healing which was significantly higher than baseline inclusion rates (83 vs 48%, $P < 0.01$). For patients in stage A at baseline, 68% achieved clinical healing with estimated rates of 39% (95%CI: 24–60) and 85% (95%CI: 64–97) at 1 and 2 years, respectively. There was no significant difference in follow-up between patients who achieved clinical healing and those with non-healing fistulas.

	Stage A	Stage B	Stage C	Overall
N	28	3	29	60
Clinical follow-up, median months (IQR)	21.8 (15.9, 25.1)	20.9 (16.5, 22.6)	22.6 (15.9, 24.3)	21.8 (15.8, 24.6)
Clinical outcomes, n	28	3	29	60
Non-healing, n (%)	9 (32.1)	0 (0.0)	1 (3.4)	10 (16.7)
Healing, n (%) *	19 (67.9)	3 (100.0)	28 (96.6)	50 (83.3)
Radiologic outcomes, n	26	2	25	53
Radiologic remission, n (%) #	6 (23.1)	1 (50.0)	20 (80.0)	27 (50.9)
Radiologic response, n (%) †	18 (69.2)	1 (50.0)	6 (24.0)	25 (47.2)

Table 1: Clinical and radiologic outcomes based on baseline stage of care.

*Clinical healing: absence of draining perianal fistula external openings despite gentle finger compression.

#Radiologic remission: VAI=0, VAI_{int}=0, MAGNIFI-CD=0, or FS=6.

†Radiologic response: VAI reduction >3, MAGNIFI-CD reduction >4, or FS increase ≥1.

[FS = Fibrosis Score; MAGNIFI-CD = Magnetic Resonance Index for Assessing Fistulas in Patients with Crohn's Disease; VAI = Van Assche Index; VAI_{int} = VAI-inflammatory subscore].

Overall, radiologic remission was observed in 51% and response in 47%. For patients in stage A at baseline, 23% achieved radiologic remission which was significantly higher than baseline inclusion rates (23 vs 4%, $P<0.05$) and 69% radiologic response (Table 1). Patients who achieved clinical healing had significantly less radiologic disease activity compared to non-healing fistulas. Overall, 53% had biologic dose escalation and 10% switched to an alternative biologic agent with the new treatment strategy. Thirty-seven percent underwent a median of two perianal surgical interventions (IQR: 1-3), 15% had closure or ablative techniques performed, and 15% had seton removal only.

Conclusion: A novel treatment strategy optimising medical and surgical care resulted in high rates of clinical healing and improved radiologic disease activity of Crohn's perianal fistulas. Controlled-matched studies are needed.

Disclosure: MD: served as a speaker for Dr Falk Pharma and Pfizer, received research support from Janssen and St Vincent's Hospital Melbourne, and is a recipient of an Australian Commonwealth Government and University of Melbourne scholarship. CB: served as a speaker for Ferring. JDS: served as a speaker for Dr Falk Pharma and received advisory fees from Abbvie. AS: served as a speaker for Arrotex Pharmaceuticals and Dr Falk Pharma and received advisory fees from Abbvie, Amgen, Arrotex Pharmaceuticals, and Pfizer. EKW: served as a speaker and received consulting fees from Abbvie, BMS, Celltrion, Dr Falk Pharma, Janssen, and Pfizer, and received research support from Abbvie, Ferring, and Janssen. NSD: served as a speaker for Abbvie, Dr Falk Pharma, Janssen, Pfizer, and Takeda. All remaining authors had nothing to disclose.

PP0603

EFFECTIVENESS AND SAFETY OF THIOPURINES IN INFLAMMATORY BOWEL DISEASE PATIENTS HARBORING NUDT15 MUTATIONS: A RETROSPECTIVE ANALYSIS

A. Chatterjee¹, P. Bhatia², S.K Sinha¹, A.K. Singh¹, H. Mandavdhare¹, J. Shah¹, M. Singh³, V. Jearth¹, A. Sasani¹, A. Sekar⁴, U. Dutta¹, J.Y Yang⁵, V. Sharma¹

¹Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Hematology oncology unit, Department of Pediatrics, Chandigarh, India, ³Post Graduate Institute of Medical Education and Research, Pediatric Hematology Oncology, Chandigarh, India, ⁴Post Graduate Institute of Medical Education and Research, Histopathology, Chandigarh, India, ⁵St. Jude Children's Research Hospital, Pharmacy and Pharmaceutical Sciences and Department of Oncology, Memphis, TN, United States of America

Contact E-Mail Address: drabhirup@gmail.com

Introduction: Thiopurines have a well-recognized role as a maintenance therapy in inflammatory bowel disease (IBD). While Nudix hydrolase 15 (NUDT15) polymorphisms are well-known to affect thiopurine metabolism predisposing to leucopenia, especially in Asian population, their appropriate dosing and efficacy are unclear in NUDT15 heterozygous patients.

Aims & Methods: We aimed to study the effectiveness and safety of thiopurine (azathioprine and 6-mercaptopurine) use in NUDT15 mutant patients. We also planned to identify the maximum tolerated dose of the drug among them. We retrospectively analyzed the database of our IBD patients for NUDT15 gene variants (c.415 C>T). Records of those IBD patients who received thiopurine were further studied for dose of the drug at leucopenia, time to develop leucopenia, severity of leucopenia, time to resolution of leucopenia, and maximum tolerated dose of thiopurines.

We also compared them with a historical control of IBD patients with wild variants of NUDT15, and TPMT genes.

Results: Of the 1440 patients of IBD tested for NUDT15 polymorphism, 118 (8.2%) patients were detected to have NUDT15 mutation (5 homozygous, 113 heterozygous). Out of these 118 patients, 51 had information available regarding thiopurine use. The rest were excluded for various reasons like incomplete data, those who never were on azathioprine, or were lost to follow-up. Among these 51 patients, 46 were heterozygous for NUDT15 (c.415 C>T) (90.2%), and 5 patients were homozygous (9.2%). In the NUDT15 heterozygous group, the mean age was 39 ± 13 years (30 males). Ulcerative colitis (UC) and crohn's disease (CD) were diagnosed in 38 and 8 patients. Proctitis, left-sided colitis, and extensive colitis were seen in 3, 11, and 19 patients. Among the CD patients, ileal, colonic, and ileocolonic diseases were seen in 1, 1, and 5 patients, respectively, whereas inflammatory and stricturing phenotypes in 6 and 2 patients, respectively. Twenty-eight patients were on 5-ASA, 14 on corticosteroids, 2 on infliximab, and one patient was on adalimumab. Twenty (43.5%) NUDT15 heterozygous patients developed leucopenia at a mean azathioprine equivalent dose of 81.25 mg (SD 34.3) after 19 weeks (SD 56.9, median 4 weeks). All NUDT15 homozygous patients developed leucopenia at a mean (SD) dose of 65 mg (SD 33.5, median 50 mg) after 1-8 weeks of thiopurine exposure. Concurrent use of 5-aminosalicylate with or without steroids was not significantly different in those with or without leucopenia. Four (8.7%) patients in the heterozygous group and 2 (40%) patients in the homozygous group required hospitalization due to leucopenia. The incidence of cytopenia was significantly higher in the NUDT15 heterozygous group compared to the control group (41.3% vs 7.8%, $p < 0.001$), the maximum tolerated dose of azathioprine was significantly lower in the NUDT15 heterozygous group (mean $\pm$ SD 66.23 ± 33.24 mg vs 93.87 ± 27.12 mg, respectively, $p = 0.02$). The mean duration to develop cytopenia was also earlier in the heterozygous group vs control (19.63 ± 58.43 weeks vs 70.5 ± 63.17 weeks, $p = 0.05$). Seven (35%) heterozygous patients could be maintained at a lower dose of thiopurine (71.43 ± 17.25 mg), and in 13 (65%), it has to be permanently stopped. Twenty-five (78% of available data of 32 patients) underwent remission while on thiopurines.

Conclusion: NUDT15 mutants are more likely to develop thiopurine-induced leucopenia. Thiopurines should be avoided in NUDT15 homozygous patients but can be used cautiously at lower dose with frequent monitoring among heterozygous patients.

References: variant compared with TPMT genotyping in predicting azathioprine-induced leucopenia: prospective analysis of 1014 inflammatory bowel disease patients in India. Aliment Pharmacol Ther. 2020 Dec;52(11-12):1683-94.

2. Grover N, Bhatia P, Kumar A, Singh M, Lad D, Mandavdhare HS, et al. TPMT and NUDT15 polymorphisms in thiopurine induced leucopenia in inflammatory bowel disease: a prospective study from India. BMC Gastroenterol. 2021 Dec;21(1):327.

3. Maillard M, Nishii R, Yang W, Hoshitsuki K, Chepyala D, Lee SHR, et al. Additive effects of TPMT and NUDT15 on thiopurine toxicity in children with acute lymphoblastic leukemia across multiethnic populations. JNCI: Journal of the National Cancer Institute. 2024 Jan 16;djae004.

Disclosure: Nothing to disclose.

PP0604

PHARMACOKINETICS AND TARGET ENGAGEMENT FOLLOWING A SINGLE SUBCUTANEOUS INJECTION OF AN ANTI-TL1A ANTIBODY, TEV-48574, IN CYNOMOLGUS MACAQUES

J. Gill¹, R. Robinson², A. Doyle¹, E. Nir³, T. Angeles²

¹Teva Pharmaceuticals Australia Pty. Ltd, Global Research and Development, Sydney, Australia, ²Teva Branded Pharmaceutical Products R&D, Inc., West Chester, United States of America,

³Teva Pharmaceutical Industries Ltd., Global Research and Development, Netanya, Israel

Contact E-Mail Address: Thelma.Angeles@tevapharm.com

Introduction: Tumor necrosis factor-like ligand 1A (TL1A) is a pleiotropic cytokine involved in immune-mediated pathways leading to inflammation and fibrosis. TEV-48574 is a human IgG1 monoclonal antibody that selectively inhibits TL1A binding to the death receptor 3 (DR3) with greater potency compared to the decoy receptor 3 (DcR3) which could preserve the natural homeostatic mechanism.¹ TEV-48574 has previously been shown to reduce fibrosis, inflammation, and mortality in animal models of asthma and IBD.¹ TEV-48574 is in clinical development as a potential treatment for ulcerative colitis and Crohn's disease.

Aims & Methods: The objectives of the study were to characterize the pharmacokinetic properties of TEV-48574 and evaluate target engagement through analysis of free TL1A concentrations post-dose. Biologic-naïve male cynomolgus monkeys (n = 4) were each administered a single 5 mg/kg dose of TEV-48574 by subcutaneous (sc) injection. Serum samples were collected pre-dose and at selected time points up to last day of the study, Day 42. Serum samples were analyzed using ELISA to determine TEV-48574 concentrations and the presence of monkey anti-TEV-48574 antibodies (ADAs). Pharmacokinetic parameters were determined using non-compartmental methods, and free TL1A levels were measured using a ligand binding assay.

Results: Absorption following sc TEV-48574 administration was consistent, median T_{max} was 1 day with a range from 0.25 to 3 days, mean $\pm$ SD C_{max} was 42.2 ± 10.8 μ g/mL. Mean $t_{1/2}$ was 5.55 ± 4.10 days and $AUC_{0-\infty}$ was 473 ± 134 day* μ g/mL. ADAs were confirmed on day 14 in serum sample for 1 monkey and on Days 21 and 35 for serum samples from all 4 animals. Administration of TEV-48574 resulted in suppressed free TL1A levels immediately post-dosing. Free TL1A remained below the limit of quantitation until Day 21 and below pre-dose baseline values until Day 42.

Conclusion: TEV-48574 demonstrated an acceptable pharmacokinetic profile with maximum serum concentrations observed within 1 day post-dose of a single sc injection of 5 mg/kg TEV-48574 in 4 male cynomolgus monkeys. Target engagement was shown by a rapid and sustained TEV-48574-mediated suppression of free TL1A in serum, supporting further development of TEV-48574 in patients with ulcerative colitis and Crohn's disease.

References: 1. Clarke AW, Poulton L, Shim D, et al. An anti-TL1A antibody for the treatment of asthma and inflammatory bowel disease. *MABs*.2018;10(4):664–677.

Disclosure: All authors are employees of Teva Global Research and Development. TEV-48574 is being developed in a partnership between Teva and Sanofi.

PP0605

COMPREHENSIVE DISEASE CONTROL IN PATIENTS WITH ULCERATIVE COLITIS: REFINEMENT OF AN INDIVIDUAL, MULTI-COMPONENT ENDPOINT USING DATA FROM THE FILGOTINIB SELECTION TRIAL

S. Schreiber¹, B.G. Feagan^{2,3}, S. Vermeire⁴, S. Danese^{5,6}, V. Vyncke⁷, M. Faes⁷, A. Oortwijn⁸, L. Peyrin-Biroulet^{9,10,11,12,13,14}

¹University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel University, Kiel, Germany, ²Alimentiv Inc., London, Canada, ³Western University, London, Canada, ⁴University Hospital Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁵IRCCS Hospital San Raffaele, Department of Gastroenterology and Digestive Endoscopy, Milan, Italy, ⁶Vita-Salute San Raffaele University, Milan, Italy, ⁷Galapagos NV, Mechelen, Belgium, ⁸Galapagos B.V., Leiden, Netherlands, ⁹Nancy University Hospital, Department of Gastroenterology, Vandœuvre-lès-Nancy, France, ¹⁰University of Lorraine, Inserm, NGERE, Nancy, France, ¹¹Nancy University Hospital, INFINY Institute, Vandœuvre-lès-Nancy, France, ¹²Nancy University Hospital, FHU-CURE, Vandœuvre-lès-Nancy, France, ¹³Paris IBD Center, Ambroise Paré – Hartmann Private Hospital Group, Neuilly-sur-Seine, France, ¹⁴McGill University Health Centre, Division of Gastroenterology and Hepatology, Montreal, QC, Canada

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: Ulcerative colitis (UC) treatment requires a patient-centric efficacy endpoint to assess treatment benefits, enabling a shift towards a personalized approach. Comprehensive disease control (CDC) is an individual multi-component endpoint based on findings from a patient and expert Delphi consensus on remission assessment in UC. CDC was defined as IBDQ remission, partial Mayo Clinic Score (pMCS) remission, biomarker (faecal calprotectin [FCP]) remission and endoscopic improvement.

Aims & Methods: We evaluated different definitions of CDC, and the contribution of different CDC components to the net treatment benefit (NTB) of filgotinib 200 mg (FIL200), an oral, once-daily, Janus kinase 1 inhibitor approved for UC treatment following the SELECTION trial (NCT02914522). CDC was assessed at week 58 (W58) of SELECTION in adult patients with active UC treated with FIL200 or placebo (PBO). The CDC definitions evaluated were: 4-component CDC (CDC4) with FCP <150 μ g/g, CDC4-150; CDC4 with FCP <250 μ g/g, CDC4-250; 5-component CDC (with histological remission [CDC5]) with FCP <150 μ g/g, CDC5-150; and CDC5 with FCP <250 μ g/g, CDC5-250. The proportion of patients achieving each combination of components was evaluated. NTB of FIL200 was assessed for each endpoint using generalized pairwise comparisons and is reported here for CDC4-150 (and excluding different components).

Results: At W58, 21.6%, 26.6%, 19.1% and 22.6% of FIL200-treated patients achieved CDC4-150, CDC4-250, CDC5-150 and CDC5-250, respectively. Among patients who did not achieve CDC4-150, 0.5% of patients did not achieve this composite endpoint because they did not achieve pMCS remission; whereas 5.0%, 10.1% and 6.0% did not do so because they did not achieve IBDQ remission, biomarker remission or endoscopic improvement, respectively. Positive overall NTB of FIL200 versus PBO was demonstrated with all CDC definitions, including those with histological remission (CDC5). For CDC4-150 at W58, excluding pMCS remission did not substantially change the NTB (Δ -0.33; *Table*) versus excluding IBDQ or biomarker remission, or endoscopic improvement (Δ 3.87, 6.93 and 3.20, respectively). Similar NTB results were seen for all CDC definitions, with or without histological remission.

Conclusion: CDC is a stringent, patient-level, multi-component endpoint achieved by ~1/5 of FIL200-treated patients at W58. While CDC4-150 could be the optimal operational definition, the addition of histological remission resulted in similar stringency, potentially allowing for the use of dif-

ferent CDC definitions based on context or resources. Additional NTB of FIL200 was identified in patients when IBDQ or biomarker remission or endoscopic improvement were excluded. Overall, CDC appears to be a suitable endpoint to assess individual comprehensive benefit in patients with UC. Prospective validation is needed.

	W10				W58			
	Number of pairs			NTB (Δ NTB)	Number of pairs			NTB (Δ NTB)
	Favourable	Unfavourable	Neutral		Favourable	Unfavourable	Neutral	
CDC4-150	14905	3616	122932	7.98 (-)	3931	1092	14497	14.47 (-)
CDC4-150 excluding IBDQ remission	3204	1760	117968	9.00 (1.02)	900	146	13451	18.33 (3.87)
CDC4-150 excluding pMCS remission	807	898	121227	7.92 (-0.06)	90	155	14252	14.13 (-0.33)
CDC4-150 excluding biomarker remission	6966	5525	110441	9.00 (1.02)	1760	408	12329	21.40 (6.93)
CDC4-150 excluding endoscopic improvement	7685	2538	112709	11.62 (3.64)	1056	432	13009	17.66 (3.20)

CDC4-150 was defined as simultaneous achievement of IBDQ remission (defined as an IBDQ total score ≥ 170), pMCS remission (defined as a pMCS ≤ 2 and no individual rectal bleeding, stool frequency or Physician's Global Assessment subscore >1), biomarker remission (defined as an FCP concentration <150 $\mu\text{g/g}$) and endoscopic improvement (defined as a Mayo endoscopic subscore of 0 or 1). pMCS is the sum of Physician's Global Assessment, rectal bleeding and stool frequency subscores. Generalized pairwise comparisons were used to compare each patient in the FIL200 group with each patient in the PBO group according to each outcome. The number of favourable pairs is the number of superior outcomes of FIL200 compared with PBO. The number of unfavourable pairs is the number of inferior outcomes of FIL200 relative to PBO. The number of neutral pairs is the number of tied outcomes of FIL200 relative to PBO. NTB for CDC4-150 was calculated as the proportion of favourable outcomes minus the proportion of unfavourable outcomes and represents the net probability that a random patient has a better outcome with FIL200 than with PBO. For example, a 10% NTB indicates a 10% greater probability of a positive outcome with FIL200 than with placebo. The NTB for CDC4-150 with excluded outcomes is the NTB for CDC4-150 achievement without including the given outcome in the definition of CDC4-150. The difference (Δ) in NTB is the additive contribution to the NTB of excluding a given component of CDC4-150 relative to achievement of full CDC4-150. CDC4-150, four-component comprehensive disease control with faecal calprotectin <150 $\mu\text{g/g}$; FCP, faecal calprotectin; FIL200, filgotinib 200 mg; IBDQ, Inflammatory Bowel Disease Questionnaire; NTB, net treatment benefit; PBO, placebo; pMCS, partial Mayo Clinic Score; W10, week 10; W58, week 58.

Table. NTB with exclusion of different components of the CDC4-150 endpoint.

Disclosure: We thank Katrien Van Beneden for her contribution to conceptualization, investigation and data interpretation.

The SELECTION trial was sponsored by Gilead Sciences, Inc. (Foster City, CA, USA). Galapagos NV (Mechelen, Belgium) was a collaborator for the SELECTION trial and funded this analysis.

Medical writing support for the development of this abstract was provided by Hannah Stephens, PhD, of PharmaGenesis London, London, UK, and was funded by Alfasisigma S.p.A.

VV and AO are employees of Alfasisigma S.p.A at the time of abstract submission

SS has received personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos/Gilead Sciences, I-Mab, Janssen Pharmaceuticals, MSD, Mylan, Pfizer, Protagonist, Provention Bio, Sandoz/Hexal, Takeda, Theravance Biopharma and UCB. BGF has received grants and personal fees from AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Janssen Biotech/Centocor, Johnson & Johnson/Janssen, Pfizer, Receptos and Takeda; and personal fees from Ablynx, ActoGenix, Akebia Therapeutics, Inc., Allergan, Atlantic Pharmaceuticals, Avaxia Biologics, Inc., Avir Pharma, Baxter Healthcare Corporation, Biogen Idec, BiomX Israel, Boehringer Ingelheim, Boston Pharmaceuticals, Calypso Biotech, Celgene, Elan/Biogen, Eli Lilly, enGene, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, glCare Pharma, Gilead Sciences, Given Imaging, Gossamer Bio, GSK, Inception IBD, Inc., Ironwood Pharmaceuticals, Japan Tobacco Company, Kyowa Hakko Kirin Co. Ltd, Lexicon Pharmaceuticals, Lycera, Mesoblast, Millennium Pharmaceuticals, MSD, Nestlé, Nextbiotix, Novartis, Novo Nordisk, ParImmune, Progenity, Prometheus, Protagonist, Qu Biologics, Q32 Bio (formerly AdMIRx, Inc.), Salix Pharmaceuticals, Shire, Sienna Biopharmaceuticals, Sigmoid Pharma, Synergy Pharma, Teva Pharmaceuticals, TiGenix, Tillotts Pharma, UCB,

Vertex Pharmaceuticals, VHSquared, Vivelix Pharmaceuticals, Wyeth, Zealand Pharma and Zyngenia.

SV receives financial support for research from AbbVie, Galapagos, Johnson & Johnson, Pfizer and Takeda; speaker and/or consultancy fees from AbbVie, Abivax, Abolentis Pharma, AgomAb Therapeutics, Alimentiv, Arena Pharmaceuticals, AstraZeneca, Bior Therapeutics (formerly Progenity), Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cytokine Pharma, Dr Falk Pharma, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Genentech-Roche, Gilead Sciences, GSK, Hospira, IMIDomics, Janssen Pharmaceuticals, Johnson & Johnson, Materia Prima, Mestag Therapeutics, MiroBio, Morphic, MRM Health, MSD, Mundipharma, Pfizer, ProDigest, Prometheus, Roberts Clinical Trials, Surrozen, Takeda, Theravance Biopharma, Tillotts Pharma AG, VectivBio, Ventyx Biosciences and Zealand Pharma.

SD reports personal fees from AbbVie, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring Pharmaceuticals, Gilead Sciences, Hospira, Inotrem, Janssen Pharmaceuticals, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB and Vifor Pharma.

MF is an employee and shareholder of Galapagos NV.

VV and AO are former employees and shareholders of Galapagos NV, and employees of Alfasisigma S.p.A.

LP-B has received consulting fees from Abivax, AbbVie, Alimentiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celltrion, CONNECT Biopharma, Cytokine Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, Gossamer Bio, GSK, HAC Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen Pharmaceuticals, Medac, Mopac, Morphic, MSD, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sandoz, Sanofi, Takeda, Theravance Biopharma, Thermo Fisher Scientific, TiGenix, Tillotts Pharma, VectivBio, Ventyx, Viatrix, Vifor Pharma and Ysopia; grants from Celltrion, Fresenius Kabi and Takeda; and speaking fees from AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Celltrion, Eli Lilly, Ferring Pharmaceuticals, Galapagos, Genentech, Gilead Sciences, Janssen Pharmaceuticals, Medac, MSD, Pfizer, Sandoz, Takeda, Tillotts Pharma, Viatrix and Vifor Pharma.

PP0606

EFFECTIVENESS OF A SECOND-LINE ANTI-TNF α AGENT AFTER FIRST ANTI-TNF α FAILURE COMPARED TO A DIFFERENT MECHANISM OF ACTION IN ULCERATIVE COLITIS: CAMBIACU STUDY

M. López-Vico¹, A. Hernández Martínez², P. Soto-Escribano³, M. Rojas-Feria⁴, A.M Caballero-Mateos⁵, A.M. Traperó-Martínez⁶, A.D. Sanchez Capilla¹, M.J. Cabello Tapia¹, M.M. Martín Rodríguez¹
¹Hospital Universitario Virgen de las Nieves, Gastroenterology Unit, Granada, Spain, ²Hospital Universitario Torrecárdenas, Gastroenterology Unit, Almería, Spain, ³Hospital Universitario Reina Sofía, Gastroenterology Unit, Córdoba, Spain, ⁴Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ⁵Hospital Universitario Clínico San Cecilio, Gastroenterology Unit, Granada, Spain, ⁶Hospital Universitario de Jaén, Gastroenterology Unit, Jaén, Spain

Contact E-Mail Address: leunamlv@gmail.com

Introduction: Ulcerative colitis (UC) is a chronic and relapsing disease for which the number of biological therapies available are increasing over the years. Data comparing the effectiveness of a second anti-TNF α (aTNF) and the switch to a different mechanism of action (MoA) such as Ustekinumab (UST), Vedolizumab (VDZ), Filgotinib or Tofacitinib (JAK) is lacking.

Aims & Methods: We performed a retrospective and multicenter study (6 Andalusian sites). Patients diagnosed of UC who had failed a first biological therapy with an aTNF and started a second-line biological therapy with another aTNF or a different MoA (UST, VDZ, JAK) were included. Clinical response and remission were assessed at weeks 16 and 52. The aim of our study was to evaluate the effectiveness of a second-line biological therapy with aTNF compared to a different MoA after a first aTNF failure.

Results: 185 UC patients were included. There were no differences in the demographic data except for disease duration (9 years with MoA vs 13 years in aTNF, $p=0.02$). As first aTNF, infliximab (IFX) was the most common in both groups (49% MoA group, 56% second aTNF), followed by adalimumab (ADA) (48% MoA group, 33% second aTNF). In the second aTNF group, immunomodulators were significantly more used (60% vs 38%, $p=0.003$). There were no differences in the concomitant use of steroids. 80 patients received a different MoA (37 VDZ, 24 UST, 19 JAK) and 105 a second aTNF (34 IFX, 60 ADA, 11 golimumab). At week 16, 52% of patients were in clinical response (70% with another MoA vs 54% with second aTNF, $p=0.07$; IFX 65%, ADA 53%, VDZ 68%, UST 71%, JAK 74%, $p=0.07$), being 15.6% more likely to achieve response with another MoA. Clinical remission at week 16 was obtained by 36% (39% with another MoA vs 33% with second aTNF, $p=0.6$; IFX 47%, ADA 30%, VDZ 35%, UST 46%, JAK 37%, $p=0.1$). At week 52, 48% achieved clinical response (51% with another MoA vs 45% with second aTNF, $p=0.8$; IFX 50%, ADA 42%, VDZ 49%, UST 54%, JAK 53%, $p=0.5$) and 39% were in clinical remission (40% with another MoA vs 38% with second aTNF, $p=0.53$; IFX 50%, ADA 32%, VDZ 35%, UST 38%, JAK 53%; $p=0.06$). When the effectiveness is analyzed by first aTNF used, independently of the aTNF, subsequent use of a different MoA achieves better results although not significant compared to a second aTNF. Partial Mayo and calprotectin showed a significant decrease at weeks 16 and 52 in both groups. Hemoglobin and albumin levels remained similar during follow-up in both groups.

Conclusion: Second-line biological therapy is effective regardless of biological therapy used in UC, but switching to a different MoA tend to achieve better results in terms of clinical response and remission compared to a second aTNF.

Disclosure: Nothing to disclose.

PP0607

PREVALENCE OF BILE ACID DIARRHOEA IN PATIENTS WITH ACTIVE MICROSCOPIC COLITIS; A PROSPECTIVE STUDY

R. Due Lorentsen¹, C. Borup², A. Poulsen³, E.M. Jørgensen³, U. Rohde¹, S. Høime Hansen⁴, L.K. Munck^{2,5}
¹Hillerød University Hospital, Hillerød, Denmark, ²Zealand University Hospital, Køge, Denmark, ³Bispebjerg University Hospital, Copenhagen, Denmark, ⁴Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, ⁵University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark

Contact E-Mail Address: lkmu@regionsjaelland.dk

Introduction: Coexistence of bile acid diarrhoea (BAD) and microscopic colitis (MC) has been described (1), and treating this with sequestrants could reduce the need for budesonide. Fasting plasma 7 α -hydroxy-4-cholesten-3-one (C4) values >46 ng/mL are specific for BAD but sensitivity is only 47% (37-57%) compared with tauroselcholic [75-Se] acid (SeHCAT) retention <10% (2). C4 values between 33 and 46 are in a diagnostic grey zone. Budesonide directly affects the bile acid homeostasis making the temporal relation between treatment and testing important. Fortunately, unlike SeHCAT testing, C4 may be sampled immediately when a patient presents with a flare of MC.

Aims & Methods: To assess the prevalence of coexisting BAD in patients with active MC.

Consecutive patients with MC and a flare fulfilling the Hjortswang diarrhoea criteria (≥ 3 stools or ≥ 1 watery stool per day) and a negative test for infectious diarrhoea were included. Patients were treated with budesonide 9 mg once daily for 6 weeks. Clinical assessment, Bristol stool charts, and fasting C4 were obtained at baseline, during the last treatment week and 4 weeks after end of treatment. Remission was defined as a daily mean of <1 watery bowel movement and <3 total bowel movements [EudraCT: 2019-002762-12].

Results: 49 patients were included; 26 (53%) with collagenous colitis. Mean age was 60 (range 55-70) years, 22% current smoker, none on NSAIDs. Six (12%; 95%CI: 5-25%) of 49 patients had BAD diagnosed by C4. Another 3 patients had grey zone C4 values. Mean C4 did not change during budesonide treatment, 22 and 23 ng/mL at baseline and at week 6, respectively. SeHCAT was performed outside the study in 26 patients of whom 3 had retention of <10% and 6 of <15%. The mean total number of stools per day declined from baseline 7.9 to 1.9 and watery stools from 3.7 to 0.3 during budesonide treatment. Remission was obtained in 45. Twenty-nine had relapsed four weeks after end of budesonide treatment, 5 of 6 (83%; 95%CI: 36-100%) with MC and BAD, and 24 of 43 (56%; 95%CI: 40-71%) with MC and not BAD.

Conclusion: During an inflammatory flare of MC, 12% (5-25%) had C4-defined BAD. However, C4 only identifies about half of patients with BAD compared with the diagnostic gold standard SeHCAT, meaning about 25% of patients with MC could have coexisting BAD. Screening for BAD may have merit in MC patients with relapse of diarrhoea after budesonide treatment.

References:

- 1 Bjørnbak C, Engel PJH, Nielsen PL, Munck LK. Microscopic colitis: clinical findings, topography, and persistence of histopathological subgroups. *Aliment Pharmacol Ther.* 2011; 34: 1225-34.
2. Borup C, Vinter-Jensen L, Jørgensen SPG, Wildt S, Graff J, Gregersen T, Zaremba A, Andersen TB, Nøjgaard C, Timm HB, Lamazière A, Rainteau D, Hansen SH, Rumessen JJ, Munck LK. Prospective comparison of diagnostic tests for bile acid diarrhoea. *Aliment Pharmacol Ther.* 2024; 59: 39-50.

Disclosure: Budesonide was donated for study use by Tillotts Pharma as an unrestricted scientific grant. Tillotts Pharma had no influence on the planning, conduct, or reporting of the study.

PP0608

RELATIONSHIP BETWEEN INDUCTION SERUM VEDOLIZUMAB CONCENTRATION AND LONG-TERM IBD OUTCOMES : A PROSPECTIVE, MULTICENTRIC, COHORT STUDY (VEDOPREDIRESP)

M. Barrau¹, S. Paul², X. Hebuterne³, M. Fumery⁴, S. Nancey⁵, F. Carbonnel⁶, A.S. Peaucelle¹, L. Bastide¹, A.E. Berger⁷, G. Duru¹, X. Roblin¹

¹Centre Hospitalo-universitaire De Saint Etienne, Saint Etienne, France, ²Hôpital Nord, Immunology, Saint Etienne, France, ³Hospital Archet 2, Nice, Department of gastroenterology and clinical nutrition, Nice, France, ⁴Amiens University Hospital, Gastroenterology department, Amiens, France, ⁵Lyon, Dept. de Gastroenterologie, Pierre Benite, France, ⁶CHU Bicetre - Dept. de Hepato-Gastroenterologie, CHU Bicetre; Le Kremlin Bicetre/FR - Dept. de Hepat, Dept. de Hepato-Gastroenterologie, Le Kremlin Bicetre, France, ⁷Hôpital Nord, Immunology, Saint Etienne, France

Contact E-Mail Address: mathilde.barrau@wanadoo.fr

Introduction: VEDOPREDIRESP is a phase IV, multicentric, prospective, observational study aiming to evaluate the relationship between induction serum trough concentration and treatment outcomes over 52 weeks in IBD patients treated with intravenous (IV) vedolizumab (VDZ)

Aims & Methods: Real-world data from patients with UC or CD treated with IV vedolizumab (300 mg at W0, W2, W6 and e8w) were collected prospectively in five centres. Clinical activity scores were evaluated (CDAI for CD and pMayo score for UC) at every infusion visits; VDZ trough levels were collected at W2, W6 and W14; their results were kept blinded to investigators. VDZ exposure-response relationship was evaluated overall indication by indication and based on baseline characteristics. Three outcomes were defined: (i) group 1: patients in clinical remission under VDZ with no treatment modification until W52, (ii) group 2: patients in clinical remission at W52 with an increased VDZ dose (300mg/4W) and (iii) group 3: patients who stopped VDZ due to loss of response, adverse events or surgery. Clinical remission was defined as CDAI < 150 for CD and pMayo score < 3 for UC.

Results: 115 patients were included (UC, n = 67; CD, n = 48) with a median age of 39 years; (55% men). 87% had prior anti-TNF exposure (46% with two prior anti-TNF). Two resections were performed during the study in CD patients. Severe adverse events were reported in 29% of cases due to loss of response in all cases. 49% of patients were in clinical remission at the end of follow-up (W52) (54% for UC, 47% for CD). 45% of patients had needed a VDZ intensification during follow-up and 50% of these patients were in clinical remission at W52. Mean VDZ serum levels were comparable at W2, W6, and W14 in the three groups (P:NS). These results were similar analyzing Group 1 and 2 all together versus Group 3 (Table 1). The relapse-free survivals were comparable in CD and UC patients (Log-rank test; p=0.45) (Figure 1). In groups 1, 2 and 3, results were similar in CD and UC patients respectively. Finally, mean VDZ serum levels were comparable just before VDZ intensification in patients responders and no responders to optimization. After logistic regression, no factor (clinical characteristics of patients or disease at inclusion, VDZ levels at each time) was significantly associated Group 3.

Conclusion: In this prospective, multicentric cohort study, serum VDZ concentrations during induction were not predictive of outcomes in both UC and CD patients. So, these measurements are not useful in clinical practice.

Disclosure: TAKEDA

PP0609

WITHDRAWN

PP0610

INSIGHTS FROM THE POLISH REGISTRY OF MICROSCOPIC COLITIS: ANALYSIS OF THE FIRST 165 PATIENTS ACROSS NINE ACADEMIC GASTROENTEROLOGY REFERENCE CENTERS IN POLAND

A. Bielski¹, W. Marlicz², E. Malecka-Panas³, J. Regula^{4,5}, A. Mroz⁶, M.M. Zwolinska-Wcislo⁷, D. Wasko-Czopnik⁸, P. Eder⁹, J. Daniluk¹⁰, M. Rosolowski¹¹, G. Rydzewska-Wyszkowska^{1,12}

¹Department of Internal Medicine and Gastroenterology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland, ²Department of Gastroenterology, Pomeranian Medical University, Szczecin, Poland, ³Department of Digestive Tract Diseases, Medical University of Lodz, Lodz, Poland, ⁴Department of Gastroenterology, Hepatology and Clinical Oncology, Centre of Postgraduate Medical Education, Warsaw, Poland, ⁵Department of Oncological Gastroenterology, The Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland, ⁶Department of Pathology, M. Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland, ⁷Department of Gastroenterology and Hepatology, Jagiellonian University Medical College, Krakow, Poland, ⁸Department of Gastroenterology and Hepatology, Medical University of Wroclaw, Wroclaw, Poland, ⁹Department of Gastroenterology, Dietetics, and Internal Medicine, Poznan University of Medical Sciences, Heliodor Swiecicki University Hospital, Poznan, Poland, ¹⁰Department of Gastroenterology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland, ¹¹Department of Hypertension, Gastroenterology, and Internal Medicine, Medical University of Bialystok Clinical Hospital, Bialystok, Poland, ¹²Collegium Medicum of Jan Kochanowski University, Kielce, Poland

Contact E-Mail Address: arkadiusz.bielski95@gmail.com

Introduction: Microscopic colitis (MC) represents a spectrum of chronic inflammatory bowel diseases (IBD) characterized by chronic watery diarrhea and distinctive histologic features. The data concerning the epidemiology of microscopic colitis in Poland are non-existing or scarce.

Aims & Methods: The Polish Registry of Microscopic Colitis was established to better understand the clinical characteristics, treatment patterns, and outcomes of MC patients in Poland.

We present retrospective and prospective data findings from the initial cohort of 165 patients enrolled in the registry, spanning nine academic gastroenterology centers across Poland. Data collection included demographics, clinical presentation, histopathological features, treatment modalities, and clinical outcomes.

Results: The median age at diagnosis was 57 years, with 36% of patients diagnosed before age 45. The majority (80%) had a prior MC diagnosis, with an average delay of approximately 3 years from symptom onset to diagnosis. MC occurred 3.5 times more frequently in women. Lymphocytic colitis (LC) was the most common subtype (66.7%), followed by collagenous colitis (CC) (24.1%) and incomplete colitis (IC) (9.3%). Women were more predisposed to CC. Normal colonoscopy results were observed in 71.5% of patients. Approximately 48% were active or former smokers, with smokers more likely to have CC. Predominant symptoms included watery diarrhea (86.1%), fecal urgency (66.1%), abdominal pain (58.8%), and bloating (62.4%). Weight loss during exacerbation of symptoms was reported in nearly one-fifth of patients. One-third of MC patients reported abdominal pain consistent with Rome IV criteria for irritable bowel syndrome (IBS) during medical interviews. Additionally, nearly half of the patients had a confirmed Covid-19 infection based on authorized testing. Budesonide MMX demonstrated the highest efficacy (92.4% reported improvement), with other treatment modalities showing varied effectiveness. Three patients with severe MC were successfully treated with adalimumab.

	Number of patients using treatment	Number of patients reporting improvement after treatment	Number of patients reporting no improvement after treatment	Improvement after treatment (in percentage)
Budesonide MMX	92	85	7	92.4%
Budesonide	23	21	2	91.3%
Loperamide	34	15	19	44.1%
Mesalazine	18	5	13	27.8%
Rifaximine	40	20	20	50.0%
Probiotics	45	15	30	33.3%

Table 1. Polish Microscopic Colitis Registry. The effectiveness of treatment following therapies.

Conclusion: The Polish Registry of Microscopic Colitis provides comprehensive insights into the clinical features and treatment outcomes of MC in Poland. Budesonide MMX emerged as an effective treatment option, while biologic therapy showed promise in refractory cases. Our findings suggest a potential overlap of symptoms between MC and IBS, highlighting the importance of thorough clinical assessment. Our findings inform evidence-based practice and highlight the importance of multidisciplinary collaboration in MC management. The multicenter nature of the Polish MC Registry provides a comprehensive overview of real-world practices and outcomes, facilitating future research and the development of standardized management strategies for this understudied condition.

References:

- Miehke S., Guagnozzi D., Zabana Y. et al.: European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations. *United European Gastroenterol. J.*, 2021; 9: 13–37.
- Larsson JK, Clarkson S, Sjöberg K: Regional differences in the incidence of lymphocytic and collagenous colitis over time. *Scand J Gastroenterol.* 2023; 58(12):1445–1452.
- Weimers P, Vedel Ankersen D, Lophaven SN et al. Microscopic Colitis in Denmark: Regional Variations in Risk Factors and Frequency of Endoscopic Procedures. *J Crohns Colitis.* 2022; 16(1):49–5

Disclosure: Nothing to disclose.

PP0611

LOW RATES OF TRANSITION FROM SUBCUTANEOUS TO INTRAVENOUS FORMULATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES TREATED WITH VEDOLIZUMAB

K.B. Russ¹, C. Agboton², D. Lindner³, A.M. Wojtowicz², A. Afzali⁴

¹University of Alabama at Birmingham, Division of Gastroenterology and Hepatology, Birmingham, United States of America, ²Takeda, Cambridge, United States of America, ³Takeda, Zurich, Switzerland, ⁴University of Cincinnati College of Medicine, Division of Digestive Diseases, Cincinnati, United States of America

Contact E-Mail Address: christian.agboton@takeda.com

Introduction: Vedolizumab is available in subcutaneous (SC) formulation for maintenance therapy in patients with moderately to severely active ulcerative colitis and Crohn's disease following vedolizumab intravenous (IV) induction therapy. The efficacy and safety of vedolizumab SC maintenance was demonstrated in the pivotal phase 3 VISIBLE clinical studies. Real-world evidence also supports the clinical effectiveness and persistence of vedolizumab SC treatment in patients with IBD; however, some patients transition back from vedolizumab SC to IV maintenance.

Aims & Methods: We aimed to describe current real-world evidence regarding the transition from vedolizumab SC maintenance to IV maintenance treatment. EMBASE and MEDLINE publication databases were

searched (date 13 March 2024) for real-world studies, excluding single case reports, that reported vedolizumab-treated patients who transitioned from SC back to IV maintenance. Data on patient proportions and reasons for the SC-IV transition were extracted.

Results: There were 11 publications meeting prespecified search criteria, which included 2 retrospective studies,^{1,2} 7 prospective studies,^{3–9} 1 case series of 7 patients¹⁰ and 1 report of 31 patients who were transitioned from IV to SC administration during the COVID-19 pandemic.¹¹ Patient numbers in retrospective and prospective studies ranged from N=19⁷ to N=168.³ Excluding the case series,¹⁰ reported rates of transitioning from SC maintenance back to IV maintenance ranged from 3.2% (1/31) among patients in the UK during the COVID-19 pandemic¹¹ to 12.9% (12/93) in a 2023 Italian cohort⁹, with the overall rate in these 10 publications of 7.4%. The most commonly reported reasons for SC to IV transition were injection site reactions (reported in 1/2⁷, 3/5⁸, 6/12⁹ and 7/7¹⁰ patients who transitioned back to IV maintenance), unspecified AEs (8/8⁴ and 9/12⁶), allergic reaction (1/5²), fear of needles (3/12⁶) and preferred route of administration (2/5⁸ and 2/12⁹). Four of 12 patients who transitioned back to IV in a 2023 Italian cohort did so due to disease flare.⁹ Additionally, among 31 patients from the UK who transitioned to SC during the COVID-19 pandemic, 1 transitioned back to IV administration due to disease flare.¹¹ In a 2023 Italian cohort, 24/168 patients experienced disease relapse following IV to SC transition, 10 of whom transitioned back to IV treatment and 8 then recaptured clinical remission.³ A 2022 UK study reported that 12/164 patients transitioned from SC back to IV, 4 of whom at an escalated dose, and 1 patient experienced an anaphylactic reaction upon restarting IV.⁵ Additionally, a 2023 case series reported that 7 patients experienced allergic manifestations including urticaria, hypotension and lip swelling following the transition from SC to IV, which led to vedolizumab discontinuation in 4 patients.¹⁰

Conclusion: Real-world data suggest a low rate of patients transitioning back to vedolizumab IV from SC maintenance, and those that transition back to IV administration do so mainly due to injection site and allergic reactions and preferred route of administration, rather than a loss of response. It is not possible to assess from current published data the extent to which infusion reactions occur when transitioning back to IV maintenance or if transitioning back to IV maintenance may be due to a 'nocebo' effect due to more negative patient expectations or perceptions of SC treatment delivery.

References: 1. Gros B, et al. *Journal of Crohn's and Colitis.* 2024;18(Supplement_1):i1793–5.

2. Kubesch A, et al. *Journal of Clinical Medicine.* 2023;12(24):7657.

3. Ribaldone DG, et al. *Dig Liver Dis.* 2024 Jan;56(1):77–82.

4. Todeschini A et al. *J Crohn's Colitis.* 2023;17:i551–2.

5. Lim S, et al. *J Crohn's Colitis.* 2022;16:i499.

6. Volkers A, et al. *Aliment Pharmacol Ther.* 2022;56(6):1044–54.

7. Nørgaard J, et al. *Journal of Crohn's and Colitis.* 2021 May 1;15(Supplement_1):S547–8.

8. Wiken T, et al. *Scand J Gastroenterol.* 2023 Jul-Dec;58(8):863–873..

9. Parisio L, et al. *J Gastrointest Liver Dis.* 2023 Dec 22;32(4):452–459.

10. Richard N, et al. *Alimentary Pharmacology & Therapeutics.* 2023;57(6):741–2.

11. Maw F, et al. *Gut.* 2021;70(SUPPL 4):A91.

Disclosure: K.B. Russ: Consultant and has served as an advisory board member for Bristol Myers Squibb, Pfizer and Iterative Scopes; C. Agboton, D. Lindner, A.M. Wojtowicz: Employees of and hold stock/stock options in Takeda; A. Afzali: Consultant and has served as an advisory board member for AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Pfizer, and Takeda and received speaker's fees from AbbVie, Bristol Myers Squibb, Janssen, Pfizer, and Takeda.

PP0612

MONITORING THE PSYCHOPATHOLOGICAL PROFILE OF INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH BIOLOGICAL AGENTS AND SMALL-MOLECULES

A.M. D'Onofrio¹, F. Di Vincenzo², L.M. Balzoni¹, G.F. Ferrajoli¹, D. Napolitano², E. Schiavoni², G. Sani¹, A. Gasbarrini³, F. Scaldaferri², G. Camardese¹

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS,

Department of Neuroscience, Section of Psychiatry, Roma, Italy,

²Fondazione Policlinico Universitario "A. Gemelli" IRCCS, IBD Unit-UOS Malattie Infiammatorie Croniche Intestinali, CEMAD, Digestive Diseases Center, Roma, Italy, ³Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Internal Medicine, Gastroenterology and Liver Diseases, Roma, Italy

Contact E-Mail Address: federica.divincenzo30@gmail.com

Introduction: Patients with Inflammatory Bowel Disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), often experience anxiety and depression. A recent meta-analysis revealed that 32.1% of IBD patients suffer from anxiety and 25.2% experience depressive symptoms. Furthermore, previous studies have suggested that biological therapy may alter the psychopathological profile of a subset of patients treated for various diseases, including IBD. However, the lack of comprehensive understanding necessitates a more systematic analysis of this association.

Aims & Methods: The aim of this study is to longitudinally monitor the psychopathological profile of a cohort of IBD patients initiating a new biological treatment at our center, and compare the results with a cohort of IBD patients receiving traditional therapy.

In this prospective longitudinal cohort study, we recruited consecutive adult patients affected by CD and UC treated at Fondazione Policlinico Universitario "A. Gemelli", IRCCS, Rome. Enrolled patients were divided into two cohort: those starting a new biological or small molecules therapy (Cohort 1), and those receiving traditional non-biological therapy (Cohort 2). Hetero-administered scales, including Hamilton Depression Rating Scale [Ham-D], Hamilton Anxiety Rating Scale [Ham-A], Young Mania Rating Scale [YMRS], Brief Psychiatric Rating Scale [BPRS], Partial Mayo Score [PMS] and Harvey-Bradshaw Index [HBI], were utilized to assess psychosomatic symptoms and gastrointestinal at the beginning of the new treatment (or at a random time point in the non-biological group) (baseline, T0), one month (T1), three months (T2) and six months (T3) thereafter. Results obtained at each time point were compared between the two patient groups.

Results: Ninety IBD patients were enrolled, 51 in cohort 1 (26 UC and 25 CD) and 39 in cohort 2 (22 UC and 17 CD). At T0, non-significant differences were found between cohort 1 and cohort 2 in mean scores of Ham-D (5.55 SD±6.16 vs 3.18 SD±3.85, p=0.27), Ham-A (5.84 SD±5.66 vs 4.08 SD±4.77, p=0.79), YMRS (1.10 SD±1.80 vs 0.85 SD±1.42, p=0.679), BPRS (22.43 SD±6.65 vs 20.03 SD±6.52, p=0.210). Statistically significant differences were found in the mean PMS and HBI between T0 and T2 in the 32 patients of cohort 1 who completed T2, and in the 20 patients who completed T3, as well as in cohort 2 between T0, T1 and T2 in the 30 patients who completed T2 and between T0 and T2, as well as T0 and T3 in the 11 patients who completed T3. No statistically significant differences were found in any of the psychiatric scales administered in either cohort at the different time points.

Conclusion: Although a comprehensive understanding of psychosomatic effects of IBD biologic therapy is yet to be defined, our results suggest that they can be safely administered. Close monitoring during the early weeks and months is strongly recommended to assess possible side effects, including psychiatric adverse events.

Disclosure: Nothing to disclose.

PP0613

ACUTE INFUSION REACTIONS DUE TO DIFFERENT BIOLOGIC AGENTS IN A LARGE COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

I. Capobianco¹, S. Colantuono², C. Caruso², G. Rumi², V. Blasi¹, J. Iaccarino¹, F. Di Vincenzo¹, P. Puca¹, F. Termite¹, G. Coppola², V. Calvez², L. Parisio², F. De Biasio², N. Alfieri², I. Mignini², D. Napolitano², E. Schiavoni², L. Laterza², L.R. Lopetuso², D. Pugliese², M. Covino³, A. Gasbarrini², F. Scaldaferri², A. Papa²

¹Università Cattolica Del Sacro Cuore, Rome, Italy, ²Fondazione Policlinico Universitario A. Gemelli IRCCS, CEMAD - Centro Malattie dell'Apparato Digerente, Rome, Italy, ³Fondazione Policlinico Universitario A. Gemelli, IRCCS, Emergency Medicine, Rome, Italy

Contact E-Mail Address: capobianco_ivan@yahoo.it

Introduction: The therapeutic armamentarium for inflammatory bowel disease (IBD) includes several biological agents: infliximab (IFX), adalimumab (ADA), vedolizumab (VED) and ustekinumab (UST). Persistence in therapy with these drugs is not satisfactory, not only due to the loss of clinical response over time but also due to adverse events. Acute infusion reactions (AIRs) occur during or within 24 hours of the infusion. The intensity of AIRs ranges from mild (flushing, dizziness, headache, itching, rash) to severe (anaphylactic).

Aims & Methods: The primary aim of this study was to compare the prevalence rates of AIRs due to the different biological agents in a large cohort of patients with IBD and to assess risk factors for AIRs.

All reports of AIRs occurring from January 2021 to October 2023 in IBD patients treated with different biological agents (IFX, ADA, VED and UST) in a tertiary IBD center were retrospectively reviewed. The electronic records of the identified patients were checked for the type of IBD, whether Crohn's disease (CD) or ulcerative colitis (UC), type of biological agent, route of administration (intravenous or subcutaneous), concomitant immunosuppressive therapies, atopic status. Furthermore, the type of treatment for the AIRs and the subsequent therapy undertaken for IBD were also recorded.

Results: 22 AIRs were recorded out of 1911 patients (1.1%). Of these, 16/550 in patients on IFX biosimilars (2.9 %), 4/590 (0.7%) in patients on ADA biosimilars, 2/318 (0.6%) in patients on VED and 0/453 (0%) in patients on UST (Table 1).

The difference in the prevalence of AIR rates observed with the different biological agents was statistically significant (p<0.01). 7 of 16 post-IFX AIRs were moderate-severe, with two episodes of anaphylaxis occurring in patients with CD.

The two patients treated with VED experienced only mild symptoms, and no anti-reactive treatment has been used; two mild and two moderate AIRs, respectively, have been reported among patients on ADA. 12 of 22 AIRs occurred during the induction period (from the first to the third administration). 7 of 22 patients had previous allergic reactions.

		Infliximab (n=16)	Adalimumab (n=4)	Vedolizumab (n=2)
Type of IBD, n (%)	Ulcerative colitis	8 (50)	2 (50)	2 (100)
Age, y. Median (range)		34.81 (20-62)	47 (42-50)	62.5 (50-75)
Sex, n (%)	Female	7 (43.8)	2 (50)	0 (0)
Duration of IBD, y. median (range)		6.1 (1-22)	12.2 (7-15)	8.5 (6-11)
AIRs' severity	Mild	9 (56.2)	4 (100)	2 (100)
	Moderate-Severe	7 (43.8)	0 (0)	0 (0)
Infusion number, (when AIR occurred) n (%)	1-3	10 (62.5)	1 (25)	1 (50)
	4-7	5 (31.25)	0 (0)	1 (50)
	>7	1 (6.25)	3 (75)	0 (0)

Table 1.

Conclusion: Our real-world data on a large population of IBD patients treated with biologic agents confirm that AIRs are rare and occur mainly in patients treated with IFX biosimilars. Most patients who experienced AIRs were atopic. Almost all patients after AIRs changed biological agents within or out of the same biological class. Further studies are necessary to confirm our results and better characterise the profile of patients at greater risk of AIRs.

Disclosure: Nothing to disclose.

PP0614

SHORT- AND LONG-TERM EFFECTIVENESS AND SAFETY OF CYCLOSPORINE THERAPY IN SEVERE ULCERATIVE COLITIS REFRACTORY TO CORTICOSTEROID TREATMENT

B. Farkas¹, P. Bacsur^{1,2}, E. Ivány¹, A. Bálint¹, M. Rutka¹, Z. Bősze¹, A. Fábián¹, R. Bor¹, Z. Szepes¹, K. Farkas^{1,2}, T. Molnár¹

¹SZTE SZAKK Center for Gastroenterology, Department of Internal Medicine, Szeged, Hungary, ²University of Szeged, HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary

Contact E-Mail Address: farkas.bernie@gmail.com

Introduction: For decades, corticosteroids have been the first-line therapy in patients with severe ulcerative colitis (UC), however 30-40% of patients fail to respond and require second-line rescue therapy with cyclosporine (CsA) or infliximab to avoid colectomy.

Aims & Methods: We conducted a single-center, retrospective study including all patients with active severe, steroid-refractory UC and with at least one year follow-up, to assess the short- and long-term effectiveness and safety of CsA therapy. Disease severity was defined according to Mayo disease activity index. Patients with a pMayo score of ≥ 7 and an eMayo score of ≥ 2 were enrolled, and received 4 mg/kg/day CsA IV for 5-7 days for second- or third-line rescue therapy between 2001 and 2023. IV CsA therapy was followed by oral CsA in case of clinical response. Colectomy-free survival was assessed using Kaplan-Meier analysis. Multivariable logistic regression analyses were performed to identify the predictive value of various factors for therapeutic response to CsA and colectomy during or after CsA treatment.

Results: Ninety-two steroid-refractory UC patients (54.4% male, mean age: 40.0 ± 14.0 years, median disease duration: 4.0 years) were included with the median follow-up time of 14.0 years (IQR: 7-18). Clinical response was achieved in 59/92 (64.1%) patients, and clinical remission was observed in 22/92 (23.9%) patients after the IV phase. During oral CsA therapy (10.4 ± 11.7 months) relapse rate was 42.0%, whereas 33 (40.7%) patients achieved or maintained remission until treatment discontinuation. Remission with oral CsA therapy was significantly higher among those who received concomitant immunomodulator treatment ($p=0.004$, OR: 6.98, 95% CI: 1.9-26.4). 20/92 (21.7%) patients underwent colectomy during CsA therapy, while a total of 45 (48.9%) patients required surgery at the end of follow-up.

Non-response to IV CsA was the only predictor of colectomy during CsA therapy ($p=0.04$, OR: 0.17, 95% CI: 0.03-0.94). No predictors for the effectiveness of the IV CsA could be found. Neither the need for colectomy during CsA therapy ($p=0.33$), nor the rate of remission with oral CsA ($p=0.49$) was influenced by the prior use of biologics.

Remission with oral CsA was found to be the only predictor of colectomy within 3 years after CsA discontinuation. The probability of colectomy-free survival was 74.7%, 62.6%, 57.1% and 45.6% at 1, 3, 5 and 14 years. In 52 patients (64.1%), biological therapy was needed after an average of $7.2 (\pm 6.74)$ months from the start of CsA. Immunomodulators were used in 50 out of 89 patients following CsA discontinuation, as maintenance therapy or as part of combination therapy. Adverse events (AEs) occurred in 53.3%

of patients, 57.2% of them required a dose reduction or treatment discontinuation. AEs were mainly reversible, but 1 patient died of opportunistic infections (acute tuberculous pneumonia). The occurrence of AEs was not associated with the use of concomitant immunomodulators ($p=0.92$). Malignancy was observed in 5 patients during follow-up, mainly melanoma and non-melanoma skin cancer.

Conclusion: CsA is an effective therapeutic option for avoiding colectomy in patients with active severe UC, even in the era of biologics. Moreover, its effectiveness can be enhanced by concomitant immunomodulator therapy without compromising safety. CsA can be used as a "bridge" until the therapeutic effect of immunomodulators or biological therapy is fully developed. However, due to the high occurrence of AEs, tight patient monitoring during CsA therapy is needed.

Disclosure: Nothing to disclose.

PP0615

WHAT FACTORS ARE ASSOCIATED WITH THE NEED FOR DOSE OPTIMISATION OF USTEKINUMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)?

C. Navarro Gerrard¹, I. Bastón-Rey^{1,2}, M. Loureiro-Veira^{1,2}, M. Otero-Iglesias^{1,2}, R. Ferreiro-Iglesias^{1,2}, J. Gonzalez-Lopez³, J.E. Domínguez Muñoz^{1,2}, M. Barreiro-de Acosta^{1,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, ³University Hospital of Santiago de Compostela, Clinical Pharmacology, Santiago de Compostela, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Ustekinumab (USK) is a biological drug that inhibits interleukins 12 and 23. It has been approved for the treatment of inflammatory bowel disease (IBD) as an induction agent, which is administered intravenously, followed by a maintenance subcutaneous therapy at a dose of 90 mg every 8 or 12 weeks. In patients who do not achieve an adequate response with the usual doses, a common clinical practice is to optimise the USK dose.

Aims & Methods: The objective of this study was to evaluate the existence of risk factors associated with the need for this dose optimisation.

Methods: This was a retrospective observational single-centre study which included all adult patients with IBD treated with USK between 2013 and 2023 in the IBD Unit of the Santiago de Compostela Hospital, Spain. The following variables were evaluated: demographic variables (age, sex, BMI, smoking habit), descriptive variables of the disease (type, extension, behaviour, perianal involvement), biomarkers (calprotectin, CRP) and endoscopic characteristics. Furthermore, intestinal ultrasound was conducted in patients with Crohn's disease (CD).

Dose optimization was defined as a reduction in the time interval between USK doses. The chi-square test was employed for qualitative variables, while quantitative variables were analysed using the Shapiro-Wilk test, Student's t-test, and Mann-Whitney U test.

A multivariate logistic regression analysis was conducted to identify factors associated with the need for therapy optimization. Drug persistence measurements were represented using the Kaplan-Meier method.

Results: A total of 189 patients (50.3% men) with a mean age of 51.9 years (SD 16.7) were included in the study. Crohn's disease (CD) was present in 84.7% of the patients, while the remaining patients had ulcerative colitis (UC). The dosage of ustekinumab (USK) was optimised to 90 mg/4 weeks in 67.2% of all patients (69% in CD and 63% in UC). The univariate analysis revealed that BMI ($p=0.023$), disease pattern ($p=0.016$), presence of perianal disease ($p=0.011$), high calprotectin levels ($p=0.039$) and CRP ($p=0.039$) were associated with the need for dose optimisation.

= 0.006) were significantly associated with the need for therapy optimisation. In the logistic regression analysis, BMI was the only significant risk factor for dose intensification of USK (OR 1.093, IC 95% 1.001-1.194). Conversely, an identified protective factor was an inflammatory pattern (OR 0.234, IC 95% 0.069-0.800). The mean time from the commencement of therapy to the necessity for optimisation was 10 months in patients with CD and 5 months in patients with UC.

Conclusion: In more than half of the patients treated with ustekinumab, dose optimization is required. The necessity for dose optimization of ustekinumab in patients with Crohn's disease may be influenced by a higher body mass index value and the non-inflammatory pattern of the disease.

Disclosure: Nothing to disclose.

PP0616

WHAT IS THE PROFILE OF CROHN'S DISEASE PATIENTS WHO ARE IN THE 3RD OR 4TH LINE OF ADVANCED TREATMENT?

J. Godfrey¹, S. Brown¹, H. Parfitt¹, S. Marett¹, R. Spencer¹, L. Wen¹, I. Gadsby¹, C. O'Kane¹, J. SinghMann¹

¹Research Partnership, London, United Kingdom

Contact E-Mail Address: sarah.brown@researchpartnership.com

Introduction: This study looks at the profile of Crohn's patients who have been on at least 3 different advanced treatments, such as tumour necrosis factor inhibitors (TNFi), integrin blockers and IL12/23 inhibitors.

Aims & Methods: Objective: The purpose of this study was to evaluate the profile of Crohn's disease patients who are in the 3rd or 4th line of an advanced treatment and to consider whether patients may be likely to switch to a different treatment.

Methodology: In both Q1 and Q3 2023, ~200 gastroenterologists from France, Italy, Germany, Spain, and the UK contributed ~1200 anonymous patient record forms for individuals receiving advanced therapy for Crohn's Disease. All the forms were collected through the Therapy Watch IBD (UC and Crohn's) online survey by Research Partnership.

The survey has been conducted with similar numbers of gastroenterologists for 3 years at regular intervals. Informed consent from physicians was obtained. Where relevant, statistical comparisons were performed using a pairwise z-test.

In addition, Research Partnership has conducted research with 138 Crohn's disease patients through their Living With Crohn's EU5 survey. Quantitative online interviews were conducted with patients who were currently on an advanced treatment for Crohn's.

Results: Of all the Crohn's disease patient record forms collected in the Therapy Watch survey in 2023, 104 patients were on their 3rd or 4th line of advanced treatment.

The majority of 3rd or 4th line patients were on a non TNFi treatment, such as an integrin blocker or an IL12/ IL23 inhibitor. ~20% of patients were on a TNFi.

The patients were a mix of male and female, at 44% and 56% respectively, and with a wide age range (42% under 40, 30% aged 41-50 and 28% aged over 50). 42% had suffered with Crohn's disease for over 10 years. The majority of patients had an existing co-morbidity, most commonly a CV condition or depression.

At the time of the survey, the current severity of Crohn's was reported by physicians to be: 32% mild, 50% moderate and 18% severe. Approximately a quarter of them also were reported as having flares that are increasing in frequency.

From our Living With Crohn's survey, out of 138 Crohn's patients currently on an advanced therapy*, approximately a quarter stated that their flares had increased in the last 6 months, but they have not requested a differ-

ent treatment from their physician. The reasons for not requesting a new treatment were mainly: patients feel they can still tolerate the symptoms that they experience and they are scared of potential side effects of a different treatment.

* Living With patients include those in any line of advanced treatment, not only 3rd or 4th line.

Conclusion: Our data suggests that the majority of 3rd and 4th line Crohn's patients have moderate or severe disease, and therefore may be candidates for a switch to a new treatment as these become available for Crohn's. 30% of 3rd and 4th line Crohn's disease patients are classified as mild in severity, and this segment appear to have found a level of efficacy at this stage.

Our patient survey (Living With) has shown that even those patients who suffer increasing frequency of Crohn's symptoms do not feel confident in switching to a different therapy; there is a level of fear of switching.

Disclosure: Nothing to disclose.

PP0617

POSTOPERATIVE COURSE OF CROHN'S DISEASE AND THE EFFICACY OF ENDOSCOPIC DILATION: A SINGLE-CENTER RETROSPECTIVE STUDY

S. Nakao¹, T. Imai¹, Y. Yokota¹, S. Shintani¹, M. Ohno¹, A. Nishida¹, O. Inatomi¹

¹Shiga University of Medical Science, Otsu, Japan

Contact E-Mail Address: nakao@belle.shiga-med.ac.jp

Introduction: Crohn's disease (CD), characterized by chronic inflammation, frequently results in complications such as strictures, fistulas, and abscess formation, necessitating surgical intervention. However, the significant rates of postoperative recurrence and reoperation underscore the critical importance of effective postoperative management strategies. Recent advancements in therapeutic agents, particularly biologics, have transformed the management of Crohn's disease by not only achieving clinical remission but also promoting mucosal healing. Endoscopic balloon dilation (EBD) has emerged as a promising option for managing strictures, potentially reducing the necessity for surgery in select cases.

Aims & Methods: We therefore undertook a study to assess the postoperative outcomes of patients with Crohn's disease who had previously undergone surgery and those who underwent endoscopic dilatation for stenosis. We performed a retrospective review of patients with Crohn's disease who underwent surgery and identified factors that contributed to their outcomes. We also evaluated patients who underwent endoscopic dilatation for stenosis.

Results: Of the 87 cases with a history of surgery, initial surgical indications (1979-2019) included strictures in 24 cases, fistulas in 15 cases, abscesses in 18 cases, perforations in 18 cases, bleeding in 5 cases, endoscopic complications in 6 cases, and one case of unknown etiology. A comparison of reoperation rates before and after 2008, when maintenance therapy with biologics and EBD became available, showed a significant decrease in reoperation rates after 2008 ($p = 0.0081$; log-rank test). Multivariate analysis identified biologics and EBD as significant factors associated with reduced reoperation rates (hazard ratios of 0.08 and 0.37, respectively, p -values of 0.000031 and 0.021). Among the cases treated with EBD for strictures (97 cases), an average of 4.3 EBD procedures (431 procedures) were performed, with an average of 2.5 sites dilated per procedure. Before initial dilatation, stricture symptoms included ileus in 35 cases (36.1%), mild symptoms such as abdominal pain or bloating in 32 cases, and no symptoms in 30 cases. Complications observed in the 431 EBD procedures included bleeding requiring prolonged hospitalization in 5 cases, perforation requiring surgery in 4 cases, and local peritonitis in 1 case. During follow-up after the initial EBD, surgery was performed in 22 cases, with

criticisms being the primary cause in 14 cases and abscess formation, perforation (including those caused by complications), or malignancy in the remainder. Analysis of the cumulative reoperation rate specifically for stricture-related cases treated with EBD showed rates of 10.4% at 5 years and 22.2% at 10 years. Logistic regression analysis identified a stricture length of 2 cm or more as a significant factor associated with cases requiring surgery (hazard ratio of 10.2, $p = 0.0036$). Kaplan-Meier analysis comparing groups according to whether initial EBD was performed before or after ileus showed no significant differences in the cumulative rates of ileus or reoperation for strictures.

Conclusion: Since 2008, reoperation rates for Crohn's disease have decreased, probably due to maintenance therapy with biologics and EBD. With EBD, it is important to consider that cases with longer strictures may be difficult to manage without surgery, and complications of EBD may require surgery.

Disclosure: Nothing to disclose.

PP0618

SERUM IMMUNE PROTEIN PROFILING AT BASELINE IN CROHN'S DISEASE PREDICTS ENDOSCOPIC RESPONSE TO USTEKINUMAB

F. Zhou¹, C. Peng¹, X. Zhang¹

¹Nanjing Drum Tower Hospital affiliated with Medical School of Nanjing University, Department of Gastroenterology, Nanjing, China

Contact E-Mail Address: zhoufan24@hotmail.com

Introduction: Dysregulation of the immune response is central to the pathogenesis of inflammatory bowel disease (IBD), including Crohn's Disease (CD) [1].

Serum inflammatory protein profiling emerges as a potential biomarker for diagnosing and predicting treatment efficacy in IBD [2].

This study aimed to identify serum inflammatory proteins that could predict response to ustekinumab in CD patients before therapy initiation.

Aims & Methods: The study cohort included 20 CD patients, divided equally between those who showed an endoscopic response and those who did not after 24 weeks of ustekinumab treatment. Endoscopic response was defined as a reduction of $\geq 50\%$ in the Simple Endoscopic Score for Crohn's Disease (SES-CD). Serum protein profiling was performed using the Olink Target 96 Inflammation assay. Univariate t-test analyses with false discovery rate correction were used to differentiate protein expression between responders and non-responders.

Results: Baseline characteristics were similar across both groups, except for age; non-responders tended to be older, with five diagnosed after age 40. Five proteins—CCL11, OPG, CDCP1, SLAMF1, Flt3L, and CXCL10—were significantly overexpressed in non-responders, while IL-22 RA1 was predominantly found in responders. Functional enrichment analyses demonstrated cytokine-mediated signaling pathway as the most notable biological process, chemokine activity as the most significant molecular function, and extracellular region as the major cellular component. KEGG enrichment also highlighted cytokine-cytokine receptor interaction as the most significant pathway.

Conclusion: This study identifies six serum inflammatory proteins that are differentially expressed at baseline and can predict endoscopic response to ustekinumab in CD. These findings suggest that baseline serum protein profiling could serve as a valuable biomarker for forecasting treatment outcomes in IBD.

References: 1. Adamina M, Bonovas S, Raine T, et al. ECCO guidelines on therapeutics in Crohn's disease: surgical treatment [J]. *J Crohn's Colitis*, 2020, 14 (2): 155-168.

2. Kalla R, Adams A T, Bergemalm D, et al. Serum proteomic profiling at di-

agnosis predicts clinical course, and need for intensification of treatment in inflammatory bowel disease [J]. *J Crohn's Colitis*, 2021, 15(5): 699-708.

Disclosure: Nothing to disclose.

PP0619

VALIDATION OF THE ADMIT-ASC INDEX FOR PREDICTING RESPONSE TO CORTICOSTEROIDS IN ACUTE SEVERE COLITIS

H. Hassen¹, W. Dahmani², N. Elleuch¹, A. Hammami³, A. Ben Slama⁴, A. Braham Ep Krifa⁴, S. Ajmi⁴, H. Jaziri⁴, M. Ksiai⁴
¹Sahloul Hospital, Gastroenterology, Sousse, Tunisia, ²Sahloul University Hospital, Gastroenterology, Ksar Hellal, Tunisia, ³Sahloul University Hospital, Gastroenterology, Sousse, Tunisia, ⁴CHU Sahloul, Gastroenterology, Sousse, Tunisia

Contact E-Mail Address: houssem.hassenn@gmail.com

Introduction: Acute Severe Colitis (ASC) is a medical and surgical emergency that requires prompt and well-coordinated treatment. The initial treatment typically involves intravenous corticosteroids. However, a significant number of patients (around 30-40%) do not respond to corticosteroids and need alternative treatment. Predicting resistance to the first-line treatment early on is a challenge that has not been fully addressed. A new index called ADMIT-ASC (Admission Model for Intensification of Therapy in ASC), which considers biological and endoscopic data, has been developed to predict the failure of steroid treatment.

Our goal is to validate this index's effectiveness in predicting corticosteroid resistance in ASC associated with ulcerative colitis (ASUC).

Aims & Methods: We conducted a retrospective chart review of 210 patients admitted to the gastroenterology department at Sahloul Sousse for ASUC between March 2010 and February 2020. Failure of corticosteroid therapy was defined as the need for second-line medical treatment or colectomy. The ADMIT-ASC score is an index ranging from 0 to 4, calculated by adding points based on specific parameters at admission: CRP ≥ 100 mg/L (1 point), albumin ≤ 25 g/L (1 point), and endoscopic UCEIS score ≥ 4 (1 point) or ≥ 7 (2 points). The area under the ROC curve (AUROC) was calculated to evaluate the accuracy of this score in predicting the failure of corticosteroid therapy.

Results: Two hundred and seventy patients were included in the study, with an average age of 33.5 years and a male-to-female ratio of 0.68. Of these patients, 62.8% had a history of UC, while ASC was the initial episode in 37.2% of cases. Fifty-two point thirty-eight percent (52.38%) of patients did not respond to intravenous corticosteroid treatment. Among them, 34.3% responded to ciclosporin, 2.4% to infliximab, and 5.2% underwent salvage colectomy. The average ADMIT-ASC score was 2.14 ± 0.99 . Patients with scores of 0, 1, 2, 3, and 4 had response rates of 100%, 62.7%, 56%, 43.4%, and 25%, respectively ($p=0.01$). The failure rate of first-line medical treatment was 52.7% for a score ≥ 2 and 62% for a score ≥ 3 (95% CI). The AUROC of ADMIT-ASC in predicting corticosteroid resistance was 0.628 ($p=0.01$, 95% CI [0.552; 0.703]).

Conclusion: The ADMIT-ASC index seems to be a reliable predictor of response to corticosteroid therapy in ASC patients, starting from admission. This could help identify patients early on who would benefit from switching to second-line treatment promptly. However, larger prospective studies are needed to confirm these results.

Disclosure: I confirm that I do not have any conflicts of interest regarding this subject.

PP0620

HISTOLOGICAL AND HISTO-ENDOSCOPIC OUTCOMES WITH ADVANCED TREATMENTS (BIOLOGICS AND SMALL MOLECULES) IN ULCERATIVE COLITIS - A NETWORK METANALYSIS

M.M. Estevinho¹, B. Sousa-Pinto², P. Leão-Moreira³, V. Solitano⁴, P.F. da Silva Mesquita¹, C. Costa¹, L. Peyrin-Biroulet^{5,6}, S. Danese⁷, V. Jairath⁸, F. Magro⁹

¹Unidade Local de Saúde Vila Nova de Gaia Espinho, Gastroenterology, Porto, Portugal, ²Faculty of Medicine, University of Porto, Evidence-Based Decision, Porto, Portugal, ³Unidade Local de Saúde de São João, Clinical Pharmacology, Porto, Portugal, ⁴Western University, London, Division of Gastroenterology, Department of Medicine, London, Canada, ⁵INFINI Institute, FHU-CURE, INSERM NGERE, Nancy University Hospital, Vandœuvre-lès-Nancy, France, Gastroenterology, Porto, Portugal, ⁶INFINI Institute, FHU-CURE, INSERM NGERE, Nancy University Hospital, Vandœuvre-lès-Nancy, Gastroenterology, Nancy, France, ⁷IRCCS Ospedale San Raffaele and Vita-Salute, San Raffaele University, Gastroenterology and Endoscopy, Milan, Italy, ⁸Western University, Division of Gastroenterology, Department of Medicine, London, Canada, ⁹Centro Hospitalar São João, Gastroenterology, Porto, Portugal

Contact E-Mail Address: mmestevinho@gmail.com

Introduction: There is growing awareness of the importance of histological outcomes in ulcerative colitis (UC). However, direct comparisons of histological endpoints are lacking. Thus, we aimed to conduct a network meta-analysis (NMA) to compare the effectiveness of various biologics and small molecules in achieving histological endpoints in UC.

Aims & Methods: We searched four online databases to identify all randomized controlled trials (RCTs) investigating advanced therapies for moderate-to-severe UC that reported histological outcomes. The analysis focused on the proportion of patients achieving histological improvement, histological remission, and histo-endoscopic improvement during induction and maintenance therapy. Using a random-effects frequentist model, we conducted a NMA, presenting the results as odds ratios (OR) with 95% confidence intervals. To evaluate the relative effectiveness of each treatment, we calculated the P-score, which ranges from 0 to 1. We also assessed the risk of bias and evidence certainty using established scoring systems.

Results: Twenty-four RCT were included, comprising 15 different therapies, and enrolling over 8800 patients. Of these trials, 19 provided data on induction therapy, while 10 assessed histological outcomes during maintenance treatment. Outcome definitions were similar among studies. We found that etrasimod 2 mg/day ranked highest in achieving histologic response (P-score 0.98) and remission (P-score 0.90) following induction, while guselkumab ranked first for histoendoscopic improvement. In maintenance trials, upadacitinib 30 mg/day ranked highest in achieving histologic and histo-endoscopic outcomes (P-score 0.88 for both endpoints). Etrasimod 2 mg/day ranked second for histologic remission (P-score 0.70) and histo-endoscopic improvement (P-score 0.73), while mirikizumab 200 mg/month ranked second for histologic response.

Conclusion: Our findings underscore the importance of small molecules in treating moderate-to-severe UC, particularly etrasimod and upadacitinib. Nonetheless, additional head-to-head RCTs are imperative to better inform clinical practice and to address unanswered questions.

Disclosure: Nothing to disclose.

PP0621

NEW OR RECURRENT CANCER OCCURRING IN INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH IMMUNOMODULATORS OR BIOLOGICS AFTER CANCER

R. Mancone¹, B. Neri¹, C. De Francesco², M. Fiorillo¹, S.C. Schiavone¹, A. Galbusera¹, C. Menna¹, S. Migliozi¹, E. Lolli¹, C. Petruzzello¹, S. Festa³, I. Marafini¹, E. Calabrese¹, G. Monteleone¹, W. Fries², L. Biancone¹

¹Università degli Studi di Roma Tor Vergata, Medicina dei Sistemi, Rome, Italy, ²Università degli Studi di Messina, Medicina Clinica e Sperimentale, Messina, Italy, ³Presidio Ospedaliero San Filippo Neri, UOC Gastroenterologia, Roma, Italy

Contact E-Mail Address: roberto.mancone@yahoo.it

Introduction: Whether using immunomodulators (IMM) or biologics after a first cancer in Inflammatory Bowel Disease patients (pts) may increase the risk of new or recurrent cancer is undefined.

Aims & Methods: The primary aim was to assess the frequency of new or recurrent cancer in IBD pts treated with IMM or biologics after a previous diagnosis of cancer. The secondary aim was to evaluate the cancer-related mortality in IBD pts treated with IMM and biologics after the first cancer. In a retrospective, multicentre study, clinical records of all IBD pts treated with IMM or biologics after a previous diagnosis of cancer were reviewed. Inclusion criteria: 1) Diagnosis of Crohn's Disease (CD) or Ulcerative Colitis (UC); 2) Cancer history; 3) IMM or biologics used after a first cancer; 4) IBD and cancer data recorded; 5) Follow-up after cancer ≥ 4 months (mos). Exclusion criteria: 1) IMM used for ≤ 3 mos. Data considered: IBD features, cancer type, IBD duration, age at diagnosis of cancer, follow-up after cancer, cancer-related death. Data expressed as median [range].

First cancer	IMM	Biologics	New cancer	Recurrent cancer
Prostatic	-	UST,VDZ	BCC	Prostatic
Hepatocellular	Tacrolimus	VDZ	SCC	-
Colonic	MTX	VDZ	-	Colonic
BCC	-	ADA	BCC	-
BCC	-	ADA	BCC	-
Urinary tract	MTX	VDZ,TOFA	SCC	-
Melanoma	Thiopurines	UST,VDZ	BCC	Melanoma
Testicular	Thiopurines	IFX,ADA,VDZ	Cardiac Myxoma	-

Table. New and recurrent cancers after IMM/biologics

Results: 75 IBD pts (57 CD, 18 UC) treated with IMM or biologics after a first diagnosis of cancer were enrolled (n [%]: F 36 [48%]; age 61 [26-89] yrs). CD features included (n=): L1 (37); L2 (2); L3 (16); L4 (8); B1 (17); B2 (30); B3 (10). UC extent included: E1 (2), E2 (8), E3 (8). Cancer in IBD pts treated with IMM/biologics included (n [%]): basal cell carcinoma (BCC) 14 (18.4%), breast 9 (12%), colorectal 9 (12%), melanoma 8 (10.7%), prostatic or testicular 7 (9.3%), urinary tract 7 (9.3%), thyroid 6 (8%), squamous cell carcinoma (SCC) 4 (5.3%), endometrial 2 (2.7%), hematopoietic 4 (5.3%), others 7 (9.3%). In 2 (2.7%) pts, ≥ 2 cancers occurred. The median time interval between index cancer and ISS/biologics use was 38 mos [0-428]. IMM after cancer were used for a median of 32.5 [4-131] mos, including: methotrexate (MTX) in 13 (17.3%), thiopurines in 8 (10.7%), mycophenolate mofetil, tacrolimus or everolimus in 3 (4%) pts.

Biologics were used after cancer for a median of 36 [3-194] mos: Ustekinumab (UST) in 24 (32%), Vedolizumab (VDZ) in 31 (41.3%), Adalimumab (ADA) in 17 (22.7%), Infliximab (IFX) in 12 (16%), Tofacitinib (Tofa) in 2 (2.7%), Golimumab in 1 (1.3%) pt. Both IMM and biologics were used after a first cancer in 15 (20%), while ≥ 2 biologics in 16 (%) pts. In a median follow up of 95 [4-509] mos after the first cancer, 8 (10.7%) IBD pts developed a new and/or recurrent cancer after IMM/biologics use.

In particular, cancer recurred in 3 (4%) pts (1 melanoma, 1 prostatic, 1 colonic adenocarcinoma), while new cases of cancer occurred in 6 (8%) pts, all 6 represented by non-melanoma skin cancer (NMSC) (both recurrent and new cancer in 1 pt). A not significant trend for a higher frequency of new vs recurrent cancer ($p=0.47$) was observed. No cancer-related death were observed.

Conclusion: In a retrospective multicentre study, a low frequency of recurrent cancer was observed in IBD pts using IMM or biologics after the first cancer. A not significant trend for a higher frequency of new vs recurrent cancer ($p=0.47$) was observed, being almost all new cancers represented by NMSC.

Disclosure: Nothing to disclose.

PP0622

REAL WORLD VALIDATION OF A PROGNOSTIC CLINICAL INDEX TO PREDICT STEROID RESPONSE IN ACUTE SEVERE COLITIS: A SINGLE TERTIARY CENTER RETROSPECTIVE STUDY

V. Bouillon¹, C. De Terwangne², C. Minsart³, C. Liefferinckx¹, D. Franchimont¹, A. Cremer¹

¹ULB, Gastroenterology-Hepato-Pancreatology and Digestive Oncology, Brussels, Belgium, ²UCL, internal Medecine, Cliniques universitaires Saint-Luc, Brussels, Belgium, ³Université Libre de Bruxelles, Laboratory of Experimental Gastroenterology, Brussels, Belgium

Contact E-Mail Address: vincent.bouillon@ulb.be

Introduction: Acute severe colitis (ASC) is an important cause of morbidity and mortality in Ulcerative Colitis (UC), requiring hospitalisation and, frequently, colectomy. Intravenous corticosteroids (CS) remain the first-line medical treatment. Approximately 40% of episodes of ASC do not respond to this treatment and require rescue therapy with ciclosporin (CIC) or infliximab (IFX)¹. In the past decades, these treatments and protocol-driven management algorithms led to reduced mortality and colectomy rates. A simple clinical scoring system (the Admission Model for the Intensification of Therapy in Acute Severe Colitis (ADMIT-ASC))³, based on CRP, albumin, and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score, was recently developed to predict the steroid response on admission.

Aims & Methods: We aimed to retrospectively assess the steroid non-response during admission with ASC and the usefulness of the new prognostic clinical index ADMIT-ASC at admission to predict steroid response in a Belgian tertiary center. All patients admitted with ASC between 1st January 2015 and 1st April 2023 were identified from our inflammatory bowel disease database at Erasme University Hospital. Inclusion criteria were ASC patients admitted at the hospital, standard treatment with at least 3 days of intravenous CS and endoscopy evaluation upon admission. ASC was defined according to modified Truelove and Witts' criteria as ≥ 6 bloody stools/day with one or more markers of systemic disturbance (tachycardia >90 beats/min, temperature $>37.8^{\circ}\text{C}$, haemoglobin <105 g/L or CRP >30 mg/L). Steroid non-response was defined as the need for medical rescue therapy (CIC or IFX) or colectomy during the admission. ADMIT-ASC index consists of four points: CRP ≥ 100 mg/L (1 point), albumin ≤ 25 g/L (1 point) and UCEIS score ≥ 4 (1 point) or ≥ 7 (2 points).

Results: Out of 127 patients admitted with UC and treated with intravenous CS during three days, 84 (45% male, median age of 31 years old) were included in the study. Admission demographics and clinical characteristics are described in Table 1.

For 17 patients (20%), the admission was their index presentation of UC. Response to CS was seen in 49 patients (58%). Thirty-three patients (39%) received medical rescue therapy (17/33 IFX and 16/33 CIC). Colectomy rate during admission was 13% after a median duration of 18 days (IQR: 16-

54). Admission C reactive protein (CRP) ($p=0.036$), albumin ($p=0.026$) and UCEIS scores ($p=0.022$) were significantly associated with steroid non-response. Patients scoring 0, 1, 2, 3 and 4 had steroid response rates of 90%, 75%, 55%, 19% and 0%, respectively. Scoring of ≥ 3 was 75% (95% CI, 0.43 to 0.95) predictive of steroid failure (OR 5.08, 95% CI 1.38 to 24.5).

	Steroid response (n=49)	Steroid non-response (n=35)	P value
Median disease duration (years) (IQR)	3.6 (0.3-0.9)	2.1 (0.8-5.5)	0.5
Montreal Classification	E1 : 5/49 (10%) E2 : 20/49 (41%) E3 : 24/49 (49%)	E1 : 0/35 E2 : 12/35 (34%) E3 : 23/35 (66%)	0.084
5-ASA, n (%)	22 (45%)	10 (29%)	0.13
Methotrexate or thiopurine, n (%)	6 (12%)	9 (26%)	0.11
Infliximab, n (%)	4 (8.2%)	8 (23%)	0.058
Vedolizumab, n (%)	7 (14%)	5 (14%)	>0.9
Tofacitinib, n (%)	2 (4.1%)	2 (5.7%)	>0.9
Readmission, n (%)	12 (24%)	10 (29%)	0.7
5-ASA, 5-aminosalicylate			
P values from Wilcoxon rank-sum test or Fisher's exact test.			

Table 1 Admission Demographics data (n= 84).

Conclusion: In this tertiary referral cohort study, we confirmed that the ADMIT-ASC index is a simple clinical tool that can be used on the day of admission to predict steroid non-response in ASC with a threshold of ≥ 3 to identify patients who are unlikely to respond to intravenous CS and enabling timely treatment escalation or surgery.

References:

1. Travis S, Satsangi J, Lémann M. Predicting the need for colectomy in severe ulcerative colitis: a critical appraisal of clinical parameters and currently available biomarkers. *Gut* 2011;60:3–9.
2. Travis SP, Farrant JM, Ricketts C, et al. Predicting outcome in severe ulcerative colitis. *Gut* 1996;38:905–10.
3. Adams A, Gupta V, Mohsen W, et al. *Gut* 2023;72:433–442.

Disclosure: VB has no disclosure.

CDT has no disclosure.

CM has no disclosure.

AC has received lecture fees from Galapagos, Abbvie, Janssen, celltrion, Pfizer, Takeda.

DF has received lecture fees from Abbvie, Astrazeneca, Dr.Falk Pharma, Ferring, Janssen, Mundipharma, MSD, Pfizer, Takeda, Amgen, and advisory board fees from Abbvie, Janssen, Takeda, Celltrion, Amgen.

CL has received consultancy fees from Janssen, Abbvie, Takeda and Galapagos and speaker fees from Sandoz, Janssen, Abbvie.

PP0623

EVOLVING MANAGEMENT STRATEGIES IN GASTROINTESTINAL IMMUNOTHERAPY RELATED ADVERSE EVENTS

A. Kerkham¹, C. Chan¹, S. Win², S. Mousa³, J. Chang¹, J. Park²

¹Nepean Hospital, Gastroenterology, Kingswood, Australia,

²Nepean Hospital, Oncology, Kingswood, Australia, ³The University of Sydney, School of Medicine, Camperdown, Australia

Contact E-Mail Address: dr.alice.kerkham@gmail.com

Introduction: The use of Immune Checkpoint Inhibitors (ICI's) have been demonstrated to significantly improve progression free-survival in a number of malignancies ⁽¹⁾.

Immune related adverse effects (IRAEs) are, however, an increasingly prevalent unwanted outcome, and now a widely recognised entity, with a number of guideline based management strategies published. Gastrointestinal IRAEs (GIIRAEs), including colitis and hepatitis are among two of the most reported IRAE's with combination ICI use accounting for 15% and 10% of all IRAE's respectively ⁽²⁾.

Aims & Methods: We aimed to report the rates and severity of Gastrointestinal Immune Related Adverse Effects (GIIRAE's) for patients who had received combination immunotherapy with nivolumab and ipilimumab, and analyse the investigations, treatment regime and response in a single tertiary referral centre. A retrospective cohort analysis was conducted of all patients receiving ipilimumab and nivolumab for melanoma, renal cell carcinoma and mesothelioma between the dates of 2019 to 2023. The local oncology database and electronic hospital records were reviewed. Baseline demographics, incidence, grade and treatment of GIIRAE's were collected.

Results: A total of 99 patients on combination ICI were identified. 26 patients (26%) had a GIIRAE of whom 15% (15/99) had diarrhoea and 11% (11/99) had hepatitis. 47% (7/15) of patients with diarrhoea had radiological or endoscopic confirmation of colitis (5) or enteritis (2). Of the 5 patients with Grade 3-4 diarrhoea, 3 (60%) required escalation to infliximab, all of which only had mild colitis evident at colonoscopy. 7/11 (64%) of patients had Grade 3-4 hepatitis, with only one patient requiring escalation to steroid sparing agent, despite only 57% (4/7) being commenced on high dose intravenous steroids as recommended by current guidelines. 40% (10/26) of Grade 1-2 IRAEs were managed conservatively. Only 50% (13/26) of all identified cases had involvement of a gastroenterologist.

Conclusion: Management strategies for GIIRAEs have and continue to evolve, and our cohort highlights the heterogeneity in investigation and management practice over the course of four years. Based on our findings, symptom-based assessment of severity for diarrhoea associated IRAEs appears to be a better predictor for the need for escalation of therapy rather than severity of investigation findings given only mild colitis was found on endoscopy for all patients who required biologic therapy. For hepatitis associated IRAEs, it would appear that a less aggressive approach to steroid therapy compared to current published guidelines may be adequate. Further prospective studies with larger cohort would be of value to confirm our observations.

References: 1) Sedano R, Cabrera D, Jiménez A, Ma C, Jairath V, Arrese M, Arab JP. Immunotherapy for Cancer: Common Gastrointestinal, Liver, and Pancreatic Side Effects and Their Management. *Am J Gastroenterol*. 2022 Dec 1;117(12):1917-1932. doi: 10.14309/ajg.0000000000001983. Epub 2022 Aug 22. PMID: 36455219.

2) Dahiya DS, Wani F, Guidi JC, Kichloo A. Gastrointestinal Adverse Effects of Immunotherapeutic Agents: A Systematic Review. *Gastroenterology Res*. 2020 Dec;13(6):227-232. doi: 10.14740/gr1340. Epub 2020 Dec 23. PMID: 33447301; PMCID: PMC7781271.

Disclosure: Nothing to disclose.

PP0624

REAL-WORLD DATA ON THE TREATMENT WITH MIRIKIZUMAB IN A MOSTLY BIOLOGICAL-EXPERIENCED ULCERATIVE COLITIS COHORT

A. Kubesch¹, R. Lande¹, K. Farrag¹, A. Dienethal¹, K. Sprinzl¹, S. Zeuzem¹, I. Blumenstein¹

¹Goethe University Frankfurt, University Hospital, Department of Internal Medicine 1, Gastroenterology, Frankfurt a. M., Germany

Contact E-Mail Address: Kubeschalica@gmail.com

Introduction: Mirikizumab was approved for the treatment of Ulcerative colitis (UC) in May 2023. However, real-world data especially in biological-experienced patients, is scarce.

Aims & Methods: We aimed to determine treatment efficacy and persistence on Mirikizumab in mostly treatment-experienced UC patients.

All patients, who were treated for UC in the inflammatory bowel disease (IBD) outpatient clinic of the University Hospital Frankfurt from 07/23-03/23 were retrospectively analyzed. Data on clinical (Simple Clinical Colitis Activity Index (SCCAI)) and biochemical disease activity (fecal calprotectin (FC)) as well as patient history were collected. Patients were followed-up for at least 12 weeks.

Results: Twenty-one patients with UC were included. Eighteen patients had already received at least one biological agent prior to starting Mirikizumab. Thirteen patients were exposed to ≥ 2 biological agents and even 6 patients to ≥ 4 biological agents prior to starting Mirikizumab. Two patients received Mirikizumab as a first line treatment. Eight patients were treated with Ustekinumab prior to the therapy with Mirikizumab. Ten patients received oral steroids as concomitant treatment. The median SCCAI at the start of induction was 7 (1-18). We report a reduction in clinical disease activity to 2 (0-11) at week 12 based on the preliminary data of the SCCAI. Median SCCAI and FC levels are shown in table 1.

Biochemical disease activity was assessed with FC levels. The median FC level at the start of the induction was 642 (14-2100). At week 12 the median FC level was 253 (21-2100) and 330 (9-2100) at week 12. Intravenous induction therapy was extended in 11 patients, with 10 patients receiving 6 infusions. Four patients were re-induced after having previously received Mirikizumab subcutaneously. One patient discontinued treatment after an extended induction due to a primary non-response. One patient reported new nodulous skin lesions after the treatment with Mirikizumab.

Conclusion: We report preliminary real-world data on the treatment with Mirikizumab. In our interim analysis Mirikizumab proves to be an effective and safe treatment in biological-experienced UC patients.

Disclosure: AK reports consulting and lecturer fees and travel grants from Takeda, Janssen-Cilag, Celgene/BMS GmbH, AbbVie, Falk Foundation and Galapagos, RL reports consulting and lecturer fees and travel grants from AbbVie, Janssen-Cilag, KF reports consulting and lecturer fees from Vifor Pharma, Immundiagnostik AG, MSD/Merck, Takeda, BMS GmbH Pharmacosmos, AbbVie, Celgene/BMS, SZ reports consultancy and speaker's bureau fees from AbbVie, Allergan, Biomarin, Gilead, Intercept, Janssen-Cilag, MSD/Merck, Novo Nordisk, SoBi and Theratechnologies and IB reports consulting and lecturer fees from Takeda, AbbVie, Amgen, Biogen, Janssen-Cilag, Celgene/BMS GmbH, Celltrion, Falk Foundation, Fresenius Kabi, Galapagos, Lilly, Pharmacosmos and Pfizer, KS reports consulting fees and clinical studies from Abbvie, BMS, Cymabay, Chemomab, Calliditas, Falk, Ipsen, Janssen-Cilag, Gilead, GDK, MSD, Roche, VIR, MSD, AD none.

PP0625

USTEKINUMAB PROMOTES RADIOLOGICAL FISTULA HEALING IN PERIANAL FISTULIZING CROHN'S DISEASE: RETROSPECTIVE REAL-WORLD ANALYSIS

T. Karakan¹, S. Barutçu², A. Karatas¹, K. Moral¹, M.A. Şahan², B.M. Aykut², V. Sökücü², O.B. Demirbaş³, M. Cindoruk¹

¹Gazi University Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey, ²Gaziantep University Faculty of Medicine, Gastro, Gaziantep, Turkey, ³Gazi University Faculty of Medicine, Department of Public Health, Ankara, Turkey

Contact E-Mail Address: tkarakan@gmail.com

Introduction: Perianal fistula is the most common complication of Crohn's disease (CD), affecting approximately 40% of patients. For patients with perianal abscesses and active draining fistula, seton or fistulotomy should be performed, followed by aggressive medical therapies, including anti-TNF agents. However, a significant proportion of patients are non-responders. There is insufficient evidence to confirm the efficacy of ustekinumab (UST), in promoting fistula closure in perianal fistulizing Crohn's disease (CD) patients.

Aims & Methods: We aimed to evaluate the efficacy of UST in a real-world setting.

The data were retrospectively analyzed. Clinical and endoscopic changes were evaluated. Fistula radiological outcomes were determined using MRI.

Results: A total of 72 patients diagnosed with CD and receiving scheduled UST treatment were enrolled. Of these, 45 patients were excluded due to the absence of perianal fistula based on clinical symptoms and MRI scans, 5 for insufficient follow-up duration, and 5 for incomplete data. A total of 17 eligible patients were finally included, 2 patients did not have follow-up MRI, 65% (n=11) of whom were male, with a mean age of 28.2 ± 2.0 years at diagnosis and a mean disease duration of 3.4 ± 0.6 years. As for the Montreal classification, 62% of the patients were assigned to B1 (non-stricturing, non-penetrating) and 70% to L3 (ileocolonic) phenotypes. Most fistulas were inter-sphincteric (65%). After 58,66 ± 13,48 weeks of UST therapy, fistula closure was shown in 40% (n=6) of patients. In patients with endoscopic remission at 6 months of UST therapy, we did not detect significant difference in fistula closure (57.1% vs 42.9%, p=0.315).

Conclusion: UST is effective in promoting clinical and radiological fistula remission in patients with CD. Intestinal endoscopic remission may not be correlated with fistula outcome. Further research is needed for determining ustekinumab therapy efficacy for perianal fistula.

Disclosure: Nothing to disclose.

PP0626

WITHDRAWN

PP0627

SHORT AND LONG-TERM OUTCOMES AFTER ACUTE SEVERE ULCERATIVE COLITIS IN ADULTS: A 12 YEAR CANADIAN EXPERIENCE IN THE POST BIOLOGIC ERA

S.K. Vuyyuru¹, L. Alphonsus², T.A. De Silva², M. Archer³, V. Solitano^{4,1}, L. Guizzetti⁵, E. Crowley^{6,3}, T. Ponich⁷, M. Beaton⁷, J. Gregor⁷, B. Yan⁷, M. Sey^{7,3}, V. Jairath^{3,8,1}

¹Western University, Medicine, Division of Gastroenterology, London, Canada, ²Western University, Schulich School of Medicine and Dentistry, London, Canada, ³Lawson Health Research Institute, London, Canada, ⁴IRCCS Ospedale San Raffaele, Università Vita-Salute San Raffaele, Division of Gastroenterology and Gastrointestinal Endoscopy, Milan, Italy, ⁵Independent Researcher, London, Canada, ⁶Western University, Children's Hospital, London Health Sciences Centre, Division of Pediatric Gastroenterology, London, Canada, ⁷Western University, Medicine, Division of Gastroenterology, Schulich School of Medicine, London, Canada, ⁸Western University, Epidemiology and Biostatistics, London, Canada

Contact E-Mail Address: svuyyur@uwo.ca

Introduction: Patients with acute severe ulcerative colitis (ASUC) are at increased risk of colectomy following an episode of acute severe exacerbation. Medical rescue therapy in steroid non-responders has reduced the need for emergency colectomy. However, the impact of biologics on longer-term colectomy risk is unclear.

Aims & Methods: A retrospective cohort study of adult patients aged ≥18 years hospitalized with acute exacerbation of UC requiring hospitalization and managed with intravenous corticosteroids between 2010 and 2022 at two regional hospitals in London, Ontario, Canada. Steroid non-response was defined as requirement of medical rescue therapy or colectomy.

Results: A total of 264 adults hospitalized with ASUC were included in the analysis (male: 51.1% [n=136], mean age at admission: 40.8 ± 17.8 years). The majority had extensive colitis (71.3% [n=169]) at the time of diagnosis. 46.3% (n=118/255) presented within one year of disease onset and 23% (n=61) had ASUC as their first presentation with UC. 25.7% (n=66/257) of patients had prior purine analogues and 23.3% (60/257) had previous biologics prior to ASUC presentation. After admission, 55.7% (n=147) responded to intravenous corticosteroids. Of the steroid non-responders, 37.5% (n=99) patients were managed with infliximab rescue therapy and only one patient received tofacitinib rescue therapy. Median CRP, stool frequency and Lindgren index score were statistically significant between steroid responders and non-responders (Table 1). A higher proportion of steroid non-responders had prior exposure to biologics or tofacitinib compared to steroid responders (31.9% vs 16.3%, p<0.01). On multivariate analysis for various factors predicting steroid non-response, assessment by Oxford criteria on day 3 was the only factor that was statistically significant (odds ratio 4.70 [95% CI [1.06-20.8]], p=0.04). Oxford criteria on day 3 had a sensitivity, specificity of 58.6% and 70.8%, respectively for predicting steroid non-response. 8% (n=21) required colectomy during index admission. An additional 13% (n=32) underwent colectomy within 12 months of discharge, for which there was no difference between steroid responders and non-responders (12.2% vs 14.7%). The short term (3 months following discharge) and long-term (3-12 months following discharge) colectomy rates following discharge were 8% (20/245) and 5.4% (12/223) respectively. Hospitalization with UC exacerbation following discharge was 17% (38/223).

Conclusion: 8% of patients admitted for ASUC require colectomy during the same admission and additional 13% required colectomy within 12 months of discharge. Despite a high initial response to corticosteroids, long term colectomy rates and re-hospitalization rates remain high.

Parameter	Overall (n = 264)	Steroid non-responders (n = 117)	Steroid responders (n = 147)	P-value
Extent, n/N (%)				
Proctitis	9 (3.8)	5 (4.9)	4 (3.0)	0.71
Left sided colitis	59 (24.9)	26 (25.5)	33 (24.4)	
Extensive colitis	169 (71.3)	71 (69.6)	98 (72.6)	
Day 1				
Stool frequency (median [IQR])	10.0 (7.0 – 15.0)	10.0 (7.0 – 15.0)	10.0 (7.0 – 15.0)	0.71
CRP (mg/L) (median [IQR])	60.1 (20.2 – 122.6)	61.5 (22.4 – 119.9)	56.2 (16.1 – 132.1)	0.54
Albumin (g/L) (mean [SD])	31.2 (6.0)	31.2 (5.5)	31.2 (6.4)	0.94
CRP/Albumin ratio (median [IQR])	2.0 (0.7 – 3.9)	2.1 (0.8 – 3.9)	1.9 (0.6 – 4.4)	0.25
Seo index (mean [SD])	222.1 (28.6)	220.1 (26.7)	223.3 (29.9)	0.64
Lindgren index (mean [SD])	23.3 (11.9)	22.8 (10.3)	23.7 (13.1)	0.59
Day 3				
Stool frequency (median [IQR])	6.0 (3.0 – 8.0)	7.0 (5.0 – 10.0)	4.0 (3.0 – 7.0)	<0.01
CRP (mg/L) (median [IQR])	32.9 (15.7 – 75.2)	43.4 (19.1 – 86.9)	25.4 (9.9 – 62.2)	0.05
Albumin (g/L) (mean [SD])	29.9 (10.2)	29.2 (7.6)	30.6 (12.2)	0.56
CRP/Albumin ratio (median [IQR])	1.3 (0.5 – 2.3)	1.6 (0.6 – 3.2)	0.8 (0.2 – 1.3)	0.25
Lindgren index (mean [SD])	13.7 (8.5)	16.3 (9.0)	11.4 (7.5)	<0.01
Fulfilling Oxford criteria on day 3 (stool frequency >8 or 3-8/day with CRP>45mg/L)	53/123 (43.1)	34/58 (58.6)	19/65 (29.2)	<0.01
Medical rescue therapy, n/N (%)	102/260 (39.2)	102/117 (87.2)	0/143 (0.0)	<0.01
Colectomy in index admission, n/N (%)	21/259 (8.1)	21/116 (18.1)	0/143 (0.0)	<0.01
Hospital admission with exacerbation between 3-12 months of discharge n/N (%)	38/223 (17.0)	13/94 (13.8)	25/129 (19.4)	0.28
Colectomy between 3-12 months of discharge n/N (%)	12/223 (5.4)	6/94 (6.4)	6/129 (4.7)	0.57
Overall colectomy within 12 months of discharge n/N (%)	32/243 (13.0)	14/96 (14.6)	18/147 (12.2)	0.59

Table 1: Baseline characteristics and outcomes in adult patients with ASUC with comparison between steroid responders and non-responders

CRP: C - reactive protein, IQR: interquartile range, SD: standard deviation.

Disclosure: SKV: None.

LA: None

TADS: None

MA: None

VS: None

LG: None

EC: has received an educational grant and speaker fees from AbbVie, Pfizer, and consulting fees from Alimentiv Inc., Sanofi.

TP: has received Advisory Board/consultant fees from Bristol Myers Squibb, Celltrion, Eli Lilly, Organon and Pfizer recently. He currently serves as an investigator on clinical research studies for Abivax, Alimentiv, Applied Molecular Transport, BristolMyersSquibb, Eli Lilly, Prometheus/Merck and Takeda.

MB: Honoraria: Shire, Allergan, Pfizer, Takeda, Advisory Boards, AbbVie, Takeda, Janssen, Lupin, Gilead, Pfizer, Novo Nordisk, McKesson, Innomar, Clinical Trials: AbbVie, Novo Nordisk, Gilead, Takeda, Boehringer Ingelheim, Janssen, Pfizer, Astra Zeneca, Intercept, Research Publications: Abbvie (2021 – Letter signed)

JG: received speakers fees from AbbVie, Janssen, Takeda, Celltrion, Organon and Ferring

BY: None

MS: None

VJ: has received has received consulting/advisory board fees from AbbVie, Alimentiv Inc, Arena pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Enthera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Gilde Healthcare, GlaxoSmithKline, Genentech, Gilead, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Protagonist, Prometheus Biosciences, Reistone Biopharma, Roche, Roivant, Sandoz, SCOPE, Second Genome, Sorriso, Takeda, TD Securities, Teva, Topivert, Ventyx, Vividion; speaker's fees from, Abbvie, Ferring, Bristol Myers Squibb, Galapagos, Janssen Pfizer Shire, Takeda, Fresenius Kabi

PP0628

TRANSMURAL REMISSION ASSOCIATES WITH A LOWER RISK OF PHENOTYPE PROGRESSION IN CROHN'S DISEASE

L. Rodrigues^{1,2}, S.R. Fernandes^{1,2}, S. Saraiva¹, S. Bernardo¹, A.R. Gonçalves¹, P.M. Moura dos Santos^{1,2}, A.I. Valente¹, L. Correia^{1,2}, H. Cortez-Pinto^{1,2}, F. Magro^{3,4}

¹ULS Santa Maria, Serviço De Gastroenterologia, Lisboa, Portugal,

²Faculdade de Medicina de Lisboa, Clínica Universitária de Gastroenterologia, Lisboa, Portugal, ³Faculdade de Medicina da Universidade do Porto, CINTESIS@RISE, Departamento de Biomedicina, Porto, Portugal, ⁴ULS São João, Serviço de Gastroenterologia, Porto, Portugal

Contact E-Mail Address: mines.bcrodrigues@gmail.com

Introduction: Patients with Crohn's disease (CD) are at risk of progressing from inflammatory to stricturing and penetrating phenotypes. The influence of the type of remission on phenotype progression has not been adequately evaluated.

Aims & Methods: Retrospective cohort study including surgically naïve CD patients with inflammatory or stricturing phenotype evaluated concomitantly by magnetic resonance enterography and colonoscopy. The degree of remission was correlated with the risk of progressing to stricturing and penetrating phenotypes.

Results: 381 CD patients were included, 21.8% with transmural remission, 21.3% with isolated endoscopic remission, 10.5% with isolated radiologic remission, and 46.5% without remission. Patients with transmural remission presented the lowest rates of phenotype progression (1.2%), with a significant difference compared to isolated endoscopic remission (18.3%, $P \leq 0.001$), isolated radiologic remission (17.5%, $P=0.002$), and no remission (36.9%, $P \leq 0.001$). In multivariate regression analysis, transmural remission (OR 0.023 95%CI 0.003-0.171, $P < 0.001$), isolated radiologic remission (OR 0.342 95%CI 0.141-0.826, $P=0.017$), and isolated endoscopic remission (OR 0.441 95%CI 0.220-0.881, $P=0.020$) resulted in lower rates of phenotype progression compared to no remission.

Figure 1 presents the Kaplan-Meier estimates of remaining free of penetrating complication (upper curve) and free of stricturing and/or penetrating complication (lower curve) after the baseline assessment in patients with no remission (A), isolated endoscopic remission (B), isolated radiologic remission (C), and transmural remission (D).

Conclusion: The degree of intestinal remission correlates with the risk of phenotype progression. Patients with transmural remission are at the lowest risk of progressing to stricturing and penetrating phenotypes.

Disclosure: Nothing to disclose.

PP0629

REAL-LIFE EFFECTIVENESS AND SAFETY OF TOFACITINIB AND VEDOLIZUMAB AS A SECOND-LINE THERAPY IN ANTI-TNFS EXPERIENCED ULCERATIVE COLITIS PATIENTS: PRELIMINARY RESULTS OF AN IGBD STUDY (VE2TO-UC)

D. Noviello¹, E.V. Savarino², W. Fries³, M.C. Fantini⁴, F. Conforti⁵, A. Orlando⁶, D.G. Ribaldone⁷, G. Mocci⁸, C. Vigano⁹, S. Festa¹⁰, R. Spagnuolo¹¹, M. Campigotto¹², L. Grossi¹³, A.G. Gravina¹⁴, M.R.D. Principi¹⁵, N. Imperatore¹⁶, A.M. Carvalhas Gabrielli¹⁷, G. Scardino¹⁸, F. Scaldaferrri¹⁹, L. Ceccarelli²⁰, B. Neri²¹, A. Di Sario²², C. De Barba²³, C. De Francesco²⁴, S. Calderone⁶, S. Onali⁴, M. Vecchi²⁵, M. Ventimiglia²⁶, F. Caprioli²⁵

¹University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ²University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And

Gastroenterology, Padua, Italy, ³University of Messina, Dept. of Clinical and Experimental Medicine, Messina, Italy, ⁴University of Cagliari, Department of Medical Sciences and Public Health, Cagliari, Italy, ⁵Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy Unit, Milan, Italy, ⁶"Villa Sofia-Cervello" Hospital, Inflammatory bowel disease Unit, Palermo, Italy, ⁷University of Turin, Department of Medical Sciences, Turin, Italy, ⁸Azienda Ospedaliera ARNAS G. Brotzu, SC Gastroenterologia, Cagliari (CA), Italy, ⁹Division of Gastroenterology- Center for Autoimmune Liver Diseases- Department of Medicine and Surgery- University of Milano-Bicocca, European Reference Network on Hepatological Diseases ERN RARE-LIVER- Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, ¹⁰"San Filippo Neri" Hospital, IBD Unit, Rome, Italy, ¹¹"Magna Graecia" University, Department of Experimental Medicine and Clinic, Catanzaro, Italy, ¹²Azienda Sanitaria Universitaria Giuliano Isontina, Gastroenterologia ed Endoscopia Digestiva/ Clinica Patologie del Fegato, Trieste, Italy, ¹³G d'Annunzio University of Chieti-Pescara, School of Gastroenterology c/o Digestive Physiopathology, Pescara, Italy, ¹⁴Division of Hepatogastroenterology, University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy, ¹⁵University of Bari, Department of Precision and Regenerative Medicine and Ionian Area DiMePre-J- Gastroenterology Unit, Bari, Italy, ¹⁶Santa Maria delle Grazie Hospital, Gastroenterology and Endoscopy Unit, Naples, Italy, ¹⁷ASST Fatebenefratelli-Sacco- Milano, Gastroenterology and Endoscopy Unit, Milano, Italy, ¹⁸"Valduce" Hospital, "Valduce" Hospital, Gastroenterology Department, Como, Italy, ¹⁹Catholic University of Rome Dept. of Internal Medicine Dept. of Gastroenterology, Internal Medicine, Gastroenterology Division, IBD Unit, Roma, Italy, ²⁰AOU Pisa, Pisa, Italy, ²¹University 'Tor Vergata' of Rome, Department of Systems Medicine, Rome, Italy, ²²Polytechnic Marche University, Department of Gastroenterology and Transplantation, Ancona, Italy, ²³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ²⁴University of Messina, Dept. of Clinical and Experimental Medicine, Messina, Messina, Italy, ²⁵University of Milan, Department of Pathophysiology and Transplantation, Milano, Italy, ²⁶Italian Ministry of Health, Directorate General of Medical Device and Pharmaceutical Service, Rome, Italy

Contact E-Mail Address: noviellodaniele@gmail.com

Introduction: Drug positioning in ulcerative colitis (UC) patients refractory to anti-tumor necrosis factor (TNF) is still debated. We aimed to compare the real-life effectiveness and safety of tofacitinib and vedolizumab as second-line therapy in anti-TNFs experienced UC patients.

Aims & Methods: In this Italian multicenter cohort study, we retrospectively included consecutive UC adult patients exposed to ≥ 1 anti-TNF agent starting tofacitinib or vedolizumab. Clinical remission (defined as partial Mayo score (PMS) <3 and no subscore >1) and corticosteroid-free clinical remission (CFREM) were assessed at week 26. Patients who discontinued treatment due to a primary or secondary non-response, adverse events, or intolerance were considered as treatment failure and classified as non-responders. The primary outcome was to compare clinical remission in tofacitinib- and vedolizumab-treated patients at week 26. Propensity score with inverse probability of treatment weighting (IPTW) was used to adjust for confounding, including sex, age at drug initiation, age at diagnosis, smoking habit, disease extension, use of immunosuppressant and steroids at baseline, disease activity at baseline by PMS, reason for anti-TNF discontinuation. Multiple imputation was used for missing data. Venous thromboembolism event, herpes zoster reactivation, major car-

diovascular adverse event, severe lymphopenia, initiation or escalation of cholesterol-lowering drugs, hospitalization, surgery, dysplasia or colorectal carcinoma, and death were assessed for the safety profile.

Results: Overall, 99 tofacitinib- and 230 vedolizumab-treated patients were included. Baseline characteristics are summarized in Table 1. The groups were comparable except that tofacitinib-treated patients were younger and of pediatric onset, with lower comorbidities and cardiovascular risk factors. Of note, 22 patients were excluded due to a lack of sufficient follow-up. After IPTW analysis, no difference between tofacitinib- and vedolizumab-treated patients in terms of clinical remission 1.23 (0.68 – 2.23) and CFREM 1.27 (0.71 – 2.29) was observed at week 26. Similar results in terms of clinical remission 1.13 (0.60 – 2.14) and CFR 1.16 (0.62 – 2.20) were obtained when analyzing patients with a baseline PMS ≥ 2 (Figure 1). Safety was consistent with known tofacitinib and vedolizumab profiles in ulcerative colitis.

	Tofacitinib (n=99)	Vedolizumab (n=230)	p
Age at baseline, y	36 (28.5 – 46)	46 (33 – 57.8)	<0.001
Concomitant steroids	40 (40%)	106 (46%)	0.31
Partial Mayo Score	3 (3 – 6.5)	5 (3 – 6)	0.74
Mayo Endoscopic Subscore			0.56
● 0	1	1	
● 1	6 (8.3%)	8 (5.6%)	
● 2	24 (33%)	58 (41%)	
● 3	41 (57%)	76 (53%)	
Cardiovascular risk factor	13 (13%)	62 (28%)	<0.01

Conclusion: Our preliminary results suggest no difference in terms of clinical remission and CFREM of tofacitinib and vedolizumab as second-line therapy in anti-TNFs experienced UC patients at the 26th week. Safety was consistent with known tofacitinib and vedolizumab profiles in ulcerative colitis.

Disclosure: DN received research grant from Pfizer, consulting fees from Dr. Falk, lecturer fees from Ferring. AO served as an advisory board member for AbbVie, Galapagos, MSD, Janssen, Pfizer, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, Janssen, Pfizer, and Takeda Pharmaceuticals. SO has received speaker fees from AbbVie, Takeda, Janssen, Amgen, Galapagos and Norgin MCF received consultancy fees from Roche, Takeda, Janssen-Cilag, Pfizer, Sandoz, Biogen, Galapagos and research economic support from AbbVie. ES has served as speaker for AbbVie, AGPharma, Alfasigma, EG Stada Group, Fresenius Kabi, Grifols, Janssen, Innovamedica, Malesci, Medtronic, Novartis, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda and Unifarco; has served as consultant for Alfasigma, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Diadema Farmaceutici, Falk, Fresenius Kabi, Janssen, Merck & Co., Reckitt Benckiser, Regeneron, Sanofi, Shire, SILA, Sofar, Synformulas GmbH, Takeda and Unifarco; and has received research support from Reckitt Benckiser, SILA, Sofar and Unifarco. Grants or contracts from any entity AbbVie, Janssen, Kern, Takeda, Galapagos, Pfizer Consulting fees: Janssen. Payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events, AbbVie, Janssen, Takeda, Pfizer. Support for attending meetings and/or travel from Ferring and Janssen. Educational activities research projects scientific meetings or advisory boards sponsored by MSD, Ferring and AbbVie. MV served as a consultant for AbbVie, MSD, Takeda, Janssen-Cilag, and Celgene. He received lecturer fees from AbbVie, Ferring, Takeda, MSD, Janssen-Cilag, and Zambon. FC served as consultant to AbbVie, MSD, Takeda, Janssen, Roche, Celgene, Bristol-Meyers Squibb, Galapagos, Gilead, Pfizer, Mundipharma, Galapagos, Biogen, received lecture fees from AbbVie, Ferring, Takeda, Allergy Therapeutics, Janssen, Pfizer, Biogen, and unrestricted research grants from Giuliani, Sofar, MSD, Takeda, AbbVie.

REDUCED COLONOCYTE HYPERPLASIA IN THE PROXIMAL COLON FOLLOWING ORAL ADMINISTRATION OF EMU OIL IN A MOUSE MODEL OF COLITIS-ASSOCIATED COLORECTAL CANCER

S. Mashtoub^{1,2,3,4,5}, S. Mhlanga^{1,2}, K. Maiolo^{1,2}, L. Chartier^{1,2}, D. Trinder^{5,6}, I. Lawrance^{5,7}, S. Barker^{1,2}, B. Scherer⁸, G. Howarth^{1,2,9}
¹Women's and Children's Hospital, Gastroenterology Department, North Adelaide, Australia, ²University of Adelaide, School of Biomedicine, Faculty of Health and Medical Sciences, Adelaide, Australia, ³The Queen Elizabeth Hospital, Discipline of Surgery, Woodville, Australia, ⁴Flinders University, College of Medicine and Public Health, Bedford Park, Australia, ⁵University of Western Australia, School of Medicine, Perth, Australia, ⁶Harry Perkins Institute of Medical Research, Murdoch, Australia, ⁷Saint John of God Hospital, Centre for Inflammatory Bowel Diseases, Subiaco, Australia, ⁸CSIRO Health and Biosecurity, Adelaide, Australia, ⁹University of Adelaide, School of Animal and Veterinary Sciences, Roseworthy, Australia

Contact E-Mail Address: suzanne.mashtoub@adelaide.edu.au

Introduction: Ulcerative colitis, a type of inflammatory bowel disease, is characterised by chronic colonic inflammation often resulting in uncontrolled crypt lengthening and the development of colitis-associated colorectal cancer (CA-CRC). Orally administered Emu Oil, derived from Emu adipose tissue, has demonstrated protective and reparative properties in preclinical models of bowel disease, including CA-CRC. However, its long-term potential to reduce colonocyte proliferation and inhibit CA-CRC progression remains undetermined. Protein Ki-67 has been used widely as a proliferation marker for human tumour cells and may serve as a potential predictive biomarker for cancer progression.

Aims & Methods: We hypothesized that orally administered Emu Oil would reduce colonocyte proliferation, evidenced by decreased Ki-67 expression, in a mouse model of CA-CRC. Female C57BL/6 mice were injected with saline or azoxymethane (7.4mg/kg; intraperitoneal), followed by *ad libitum* access to either water or three dextran sulphate sodium (DSS)/water cycles (each cycle comprising seven days DSS [2%w/v] and 14 days water). Mice (n=9/group) were orally administered either water (80µL) or Emu Oil (low 80µL or high 160µL dose) thrice weekly for nine weeks. Proximal and distal colonic sections were stained with haematoxylin and eosin for crypt depth, cell count and size measurements and stained immunohistochemically to detect and quantify the proliferation marker Ki-67 in upper and lower colonocyte crypt zones. p<0.05 was considered statistically significant.

Results: In the proximal colon, numbers of Ki-67-positive cells in the upper and lower crypt regions of CA-CRC mice were increased by up to 100% compared with normal controls; low dose Emu Oil significantly decreased numbers of Ki-67-positive cells by 47% (p<0.05) compared with CA-CRC controls. Numbers of Ki-67-positive cells in the distal colon increased only in the upper crypt region in CA-CRC controls compared with normal mice (157%), with no further impact following Emu Oil administration (p>0.05). The overall percentage of Ki-67-positive cells remained unchanged in proximal and distal colonic crypts across treatment groups (p>0.05). Proximal and distal colonic crypt depth increased in mice with CA-CRC (20% and 37%, respectively; p<0.01), with greater distal colonocyte count, compared with normal controls (37%; p<0.05). Emu Oil did not impact proximal and distal colonic crypt depth nor cell counts in normal or CA-CRC mice (p>0.05). Furthermore, proximal colonocyte count, proximal and distal colonic cell diameter, and number of cells per 100µm remained unchanged among treatment groups (p>0.05).

Conclusion: Crypt lengthening in CA-CRC was primarily attributed to crypt cell hyperplasia, determined by increased cell numbers with no

change in cell size. Low-dose Emu Oil administration in mice with CA-CRC resulted in attenuation of proximal colonic crypt cell proliferation, with no impact on crypt depth or cell size. Importantly, crypt depth and proliferation in normal mice remained unchanged following Emu Oil treatment, supporting its safety for long-term use to treat intestinal disorders. Future studies would benefit from an assessment of Emu Oil and its impact on expression of the oncogene *Kras*, tumour suppressor genes *p53* and *Apc*, and inflammatory cytokines, including interleukin-6, tumor necrosis factor-alpha and interferon-gamma, which are implicated in colorectal cancer progression.

Disclosure: Nothing to disclose.

PP0631

EMU OIL-MODULATED FAECAL MICROBIOTA TRANSPLANTATION AMELIORATES CLINICAL INDICATORS OF DISEASE IN A MOUSE MODEL OF CROHN'S-LIKE COLITIS

S. Mashtoub^{1,2,3,4,5}, S. Ndukwe^{3,4}, K. Wanner^{3,4}, S. Mhlanga^{3,1}, C. Mitchell^{3,6}, L. Chartier^{3,1}, G. Howarth^{3,1,6}
¹University of Adelaide, School of Biomedicine, Faculty of Health and Medical Sciences, Adelaide, Australia, ²The Queen Elizabeth Hospital, Discipline of Surgery, Woodville, Australia, ³Women's and Children's Hospital, Gastroenterology Department, North Adelaide, Australia, ⁴Flinders University, College of Medicine and Public Health, Bedford Park, Australia, ⁵University of Western Australia, School of Medicine, Perth, Australia, ⁶University of Adelaide, School of Animal and Veterinary Sciences, Roseworthy, Australia

Contact E-Mail Address: suzanne.mashtoub@adelaide.edu.au

Introduction: Crohn's disease (CD), a variant of inflammatory bowel disease, is a complex, debilitating, chronic and relapsing disorder of the gastrointestinal tract. If poorly controlled, patients are at risk of intestinal obstruction and infection due to the formation of strictures, fistulae and narrowing of the intestinal lumen, often requiring surgical intervention. As the precise aetiology remains unclear, current treatments for CD are limited. An altered composition of native gut microbiota may play a role in CD pathogenesis, with recent faecal microbiota transplantation (FMT) studies revealing variable therapeutic efficacy in CD management. Orally administered Emu Oil, derived from Emu adipose tissue, has demonstrated anti-inflammatory and reparative properties in models of intestinal disease.

Aims & Methods: The current study aimed to determine whether Emu Oil-modulated FMT could reduce disease severity and modulate the gut microbiota in a mouse model of trinitrobenzene sulfonic acid (TNBS)-induced Crohn's-like colitis. Female ARC(s) mice were assigned to FMT donor (n=5/group) and recipient (n=10/group) groups. Donor mice were orally administered either Water (80µl), Olive Oil (OO) or Emu Oil (160µl) daily (days -7 to 0); fresh faeces were collected (days -1 to 3) and pooled per group. Recipient mice were administered TNBS (3mg; day 0) and donor faecal supernatant (120µl; day 3) intrarectally and euthanised on day 6. Daily bodyweight and disease activity index (DAI), colonoscopically-assessed disease severity, organ weights, intestinal permeability (fluorescein isothiocyanate [FITC]-dextran uptake), histologically-assessed colonic damage (disease severity, crypt depth), intestinal barrier function (mucin-secreting cells), acute inflammation (myeloperoxidase [MPO]) and faecal microbiome (16S rRNA amplicon sequencing) were assessed. p<0.05 was considered statistically significant.

Results: TNBS induced bodyweight loss in all groups, which normalised to day 0 values on the final day of the experimental period. Daily DAI remained elevated throughout the trial in all groups; only Emu Oil FMT normalised DAI on day 6 compared with day 0 (p<0.05). TNBS increased colonoscopically-assessed disease severity scores (p<0.05), with no significant

Emu Oil nor OO FMT effect. Emu Oil FMT decreased liver weights and increased small intestinal weights relative to bodyweight, reduced histologically assessed disease severity and increased colonic mucin counts compared with Water and OO FMT ($p < 0.05$). The most abundant genera across all groups were *Muribaculaceae*, *Eisenbergiella* and *Bacteroides*; while alpha and beta diversity, taxonomic profiles, FITC-dextran, crypt depth and MPO activity remained unchanged in all treatment groups ($p > 0.05$).

Conclusion: Emu Oil-modulated FMT improved histologically-assessed indicators of intestinal disease and barrier function, compared with Water FMT and OO FMT. Interestingly, Emu Oil-modulated FMT affected liver and small intestinal organs weights, suggesting a systemic effect in this setting of disease. Importantly, key genera across taxonomic profiles were identified, however, the microbiome and remaining disease indicators were largely unchanged between treatments. Overall, Emu Oil-modulated FMT demonstrates therapeutic potential in CD management. Future studies would benefit from a deeper assessment of the gastrointestinal microbiome through long-read whole genome sequencing to further determine the role of the microbiome in EO FMT efficacy compared with conventional FMT.

Disclosure: Nothing to disclose.

PP0632

EVALUATING THE EFFICACY AND SAFETY OF ZASOCITINIB (TAK-279), A HIGHLY SELECTIVE ORAL TYROSINE KINASE 2 INHIBITOR, IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: STUDY DESIGN FOR A PHASE 2B RANDOMIZED CLINICAL TRIAL

V. Jairath^{1,2}, V. Goh³, L. Zaru³, V.A. Nguyen³, O. Ayodele³, A.N. Desch³, F. Nordio³, T. Freney³, L. Sears³, N. Singh³

¹Department of Medicine, Division of Gastroenterology, Western University, London, Canada, ²Western University, Department of Epidemiology and Biostatistics, London, Canada, ³Takeda Development Center Americas, Inc., Cambridge, United States of America

Contact E-Mail Address: vjairath@uwo.ca

Introduction: Tyrosine kinase 2 (TYK2) mediates cytokine signalling in immune-mediated inflammatory diseases, including Crohn's disease (CD). Zascotinib (TAK-279) is a highly selective, oral, allosteric TYK2 inhibitor with efficacy and acceptable safety shown in patients with psoriasis and psoriatic arthritis.^{1,2} This phase 2b study (NCT06233461) aims to assess the efficacy and safety of zascotinib in patients with moderately to severely active CD.

Aims & Methods: This is a multicentre, randomized, double-blind induction, placebo-controlled, dose-ranging, treat-through study in patients (18–75 years) with moderately to severely active ileal, ileocolonic or colonic CD (CD Activity Index [CDAI] score 220–450 and ulcerations characteristic of CD defined by ileocolonoscopy at screening and Simple Endoscopic Score for CD [SES-CD] ≥ 6 or ≥ 4 for isolated ileitis). Eligible patients must have inadequate/loss of response or intolerance to ≥ 1 of oral aminosalicylates, corticosteroids, immunosuppressants, biologics, JAK inhibitors (JAKi) or sphingosine-1-phosphate (S1P) receptor modulators. Patients who have also failed < 3 classes of advanced therapies will be included. After screening (30 days), approximately 268 patients will be randomized 1:1:1:1 to receive low-, medium- or high-dose zascotinib or placebo orally once daily for 12 weeks (induction phase), followed by a 40-week maintenance period and a 4-week safety follow-up. At or after Week 12, patients receiving placebo with disease worsening based on PRO2 score will receive active zascotinib treatment. Study doses are expected to provide $\geq 90\%$ TYK2 inhibition over the 24-hour dosing interval, and were associated with efficacy in preclinical models.³ Randomization will be stratified

based on previous biologic, JAKi or S1P receptor modulator therapies, and steroid use at baseline. The number of patients who received previous biologic, JAKi, S1P receptor modulator, anti-interleukin (IL)-23p19 or anti-IL-12/23p40 therapy will be capped.

Primary endpoint analysis will be conducted using a Cochran–Mantel–Haenszel (CMH) test. Binary secondary endpoints will be analysed similarly to primary endpoints. Longitudinal continuous secondary endpoints up to Week 12 will be analysed using a mixed-effects model with repeated measures. Safety data will be presented by treatment group and assessment period.

Results: The study is actively enrolling with the first patient randomized in March 2024. An open-label extension is planned for zascotinib responders. The primary efficacy endpoint is the achievement of endoscopic response at Week 12 ($> 50\%$ decrease in SES-CD from baseline [for patients with isolated ileal disease: SES-CD ≤ 4 or ≥ 2 -point reduction]). Secondary efficacy endpoints at Week 12 include: clinical remission (CDAI < 150), clinical response (CDAI reduction from baseline of ≥ 100), endoscopic remission (SES-CD ≤ 4 or ≤ 2 for patients with ileal disease, no subscore > 1), patient-reported symptoms and disease-specific health-related quality of life (HRQoL). Safety and tolerability will be assessed by treatment-emergent adverse events (AEs), serious AEs and AEs of special interest throughout the study. Intestinal ultrasound measurements, using the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS), will be assessed at Weeks 4, 12 and 52 in a subset of patients.

Conclusion: Alongside evaluating the efficacy and safety of zascotinib in patients with moderately to severely active CD, this unique 52-week treat-through study design will assess the impact of treatment on HRQoL, an area of significant unmet need in this population.

References: 1. Armstrong A *et al.* AAD 2023.

2. Kivitz A *et al.* *Arthritis Rheumatol* 2023;75(Suppl 9).

3. Kong KF *et al.* *J Crohns Colitis* 2024;18(Suppl 18).

Disclosure: VJ has received: consulting/advisory board fees from AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris, AstraZeneca, Avoro Capital, Bristol Myers Squibb, Celltrion, Eli Lilly, Endpoint Health, Entera, Ferring, Flagship Pioneering, Fresenius Kabi, Galapagos, Genentech, Gilde Healthcare, Gilead, GlaxoSmithKline, Innomar, JAMP, Janssen, Merck, Metacrine, Mylan, Pandion, Pendopharm, Pfizer, Prometheus Biosciences, Protagonist, Reistone Biopharma, Roche, Roivant, Sandoz, Second Genome, Sorriso, Synedgen, Takeda, TD Securities, Teva, Topivert, Ventyx and Vividion; and speaker fees from AbbVie, Bristol Myers Squibb, Ferring, Fresenius Kabi, Galapagos, Janssen, Pfizer, Shire and Takeda. VG, LZ, VN, OA, AND, FN, TF, LS and NS are employees and equity holders of Takeda.

PP0633

DISEASE CLEARANCE IS AN ACHIEVABLE TARGET IN PATIENTS WITH UC: PRELIMINARY RESULTS

L. Bertin¹, C. De Barba¹, L. Frasson², B. Barberio³, F. Zingone¹, E.V. Savarino¹
¹University of Padua, Department of Gastroenterology, Surgery and Oncology, Padova, Italy, ²University of Padua, Padova, Italy, ³Azienda Ospedaliera Di Padova, Surgery, Oncology and Gastroenterology, Padova, Italy

Contact E-Mail Address: luluisa92@gmail.com

Introduction: Recent delineations by experts from the IOIBD organization have emphasized disease clearance as a comprehensive outcome in ulcerative colitis (UC), incorporating concurrent clinical, endoscopic, and histologic remission [1]. However, real-world data regarding disease clearance following biologic therapy remain scarce.

Aims & Methods: We conducted a retrospective observational cohort study at our academic tertiary care institution in Padova, comprising 119 patients receiving treatment with biologic drugs, totaling 142 treatments. Patient data encompassed demographics, disease phenotype, treatment history, and concomitant medications. Categorical variables underwent comparison using the Chi-Squared exact test, Mann-Whitney U test, and McNemar test, while continuous variables were assessed via either the Student's t-test or the Wilcoxon test, based on their distribution. Propensity score matching was employed to analyze outcomes between patients administered Vedolizumab and Infliximab. Furthermore, conditional logistic regression was utilized to estimate the odds of outcomes. All data analyses were conducted using the JASP 0.18.3 statistical software package, DATAtab: Online Statistics Calculator (DATAtab e.U. Graz, Austria), and XLSTAT 2024 (Assinsoft, Paris, France).

Results: In total, 142 treatments were administered to 119 adult patients diagnosed with UC. Of these patients, 67 (47.1%) presented with pancolitis, 63 (44.4%) had left-sided colitis, and 12 (8.4%) had rectal involvement at the onset of biologic therapy. At initiation, 75 (52.8%) were biologic therapy naïve. The median duration of biologic therapy was 48 months (IQR 35-71). Following Infliximab therapy, disease clearance was achieved by 9 out of 43 patients (20.9%), by 4 out of 47 patients (8.5%) with Vedolizumab, 4 out of 25 patients (16.0%) with Adalimumab, 1 out of 7 patients (14.3%) with Ustekinumab, 4 out of 15 patients (26.7%) with Golimumab, and 1 out of 5 patients (20.0%) with Tofacitinib. Upon applying propensity score matching to the cohorts treated with Infliximab and Vedolizumab, Vedolizumab demonstrated an odds ratio of 0.26 (95% CI 0.04 - 1.56, p = 0.139) compared to Infliximab. Additionally, the log-rank test showed no significant difference in the time to event occurrence among various biologic therapies (p = 0.41).

Conclusion: Attaining disease clearance is an attainable goal for UC patients undergoing biologic therapy. Future data will shed light on whether specific medications facilitate reaching this target more effectively. Continued research endeavors are essential to validate and enhance these findings.

References: 1. D'Amico, F.; Magro, F.; Siegmund, B.; Kobayashi, T.; Kotze, P.G.; Solitano, V.; Caron, B.; Al Awadhi, S.; Hart, A.; Jairath, V.; et al. Disease Clearance as a New Outcome in Ulcerative Colitis: A Systematic Review and Expert Consensus. *Inflammatory Bowel Diseases* **2023**, izad159, doi:10.1093/ibd/izad159.

Disclosure: Nothing to disclose.

PP0634

OPTIMISM MAY OUTWEIGH DISEASE ACTIVITY IN MITIGATING MEDICAL TRAUMA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

A. Fuss^{1,2}, C. Jagielski³, T. Taft⁴
¹Harvard Medical School, Boston, United States of America, ²Massachusetts General Hospital, Boston, United States of America, ³University of Michigan Medicine, Ann Arbor, United States of America, ⁴The Rome Foundation, Oak Park, United States of America

Contact E-Mail Address: afuss@mgh.harvard.edu

Introduction: Recent research finds 25%-30% of IBD patients experience chronic post-traumatic stress due to their disease (IBD-PTS) and IBD-PTS is associated with poorer outcomes. Post-traumatic growth (PTG) is defined as “positive psychological changes that occur as a result of one’s struggle to cope with trauma or a major life crisis.” PTG can reduce the negative impacts of IBD-PTS, which may be moderated by disease activity in IBD.

Aims & Methods: We aim to examine the relationship between remission status, patient expectations regarding if they can achieve and sustain remission, and PTG among patients with IBD. Adults (18+) with IBD were recruited via social media IBD support groups, and flyers posted in gastroenterology clinics and community bathrooms with additional snowball sampling methods. Surveys were completed online via Qualtrics and included demographics, Patient Simple Clinical Colitis Activity Index (P-SCCAI), Post-Traumatic Growth Inventory (PTGI), and PTSD Checklist for DSM-5 (PCL-5). Participants reported if they were in remission or experiencing a flare of symptoms, and their expectations of experiencing a flare in the next 2 months on a 4-Point Likert scale.

Results: 313 adults with IBD: UC (n=140, 44.7%), CD (n=173, 55.3%). Age 18-70 years (M=33, SD=11), 75.1% female. Scores for PTGI, P-SCCAI, and PCL-5 are in Table 1. Participants tended to have active disease and high levels of IBD-PTS. No significant correlation existed between P-SCCAI score and PTG (r= -.09 p=.127).

Those in a current IBD flare (n=133,42.4%) reported lower confidence in the longevity of their remission over the next 2 months compared to participants who were in remission (X²=114.01,p<.001), with no difference in PTG levels between groups (p=.310). However, participants who demonstrated optimism about sustained remission had higher levels of PTG (F(3,309)=4.688,p=.003).

Participants who endorsed “I am positive I will experience a flare up in the next two months” had much lower levels of PTG (M=65.91,SD=25.33) than participants who endorsed “I am positive I will not experience another flare up in the next two months” (M=81.52,SD=25.58;p=.004).

Those who endorsed “I am at least 50% positive I will experience another flare up” had lower rates of PTG (M=69.99, SD=22.95) than those who endorsed “I am positive I will not experience another flare up in the next 2 months” (M=65.91,SD=25.33;p=.026). A linear regression found the extent of the differences in the levels of confidence in maintaining remission influenced levels of PTG (F(3,309)=4.688 p=.003). Participants who were the least confident in their remission scored 15.61 points lower for PTG than for participants who were the most confident. Participants who were at least 50% sure they would experience another flare in the next two months scored 11.53 points lower for PTG than participants who were the most confident in their remission.

Outcome Measure	Mean (SD)	Maximum Score	Cutoff
PTGI	72.81 (24.36)	105	> 45
PCL-5	45.99 (16.28)	80	> 35
P-SCCAI	5.56 (3.51)	27	> 4

Conclusion: Our findings suggest IBD patients who expect to achieve disease remission are more likely to have higher levels of PTG than those who are more pessimistic about their disease course, independent of current symptom activity. However, those in an IBD flare are less likely to believe they can attain remission. Due to the unpredictable nature of IBD, patients are chronically exposed to risks for medically traumatic experiences. Patients with confidence in their remission longevity may conceptualize remission as an “end” to the threat of IBD-PTS, thus allowing PTG to occur. Conversely, if remission is seen as a temporary reprieve before the next inevitable flare, it may limit patients’ abilities to cultivate PTG. Providers can help patients move towards a PTG mindset by assessing patients’ expectations of remission, modeling optimism in a patient’s prognosis, and providing evidence for ongoing hope.

References: Fuss, A., & Lease, S. (2023). Moderating the Relationship Between Ulcerative Colitis and Crohn’s Disease and Symptoms of PTSD: The Role of Remission. *Journal of Clinical Gastroenterology*, 57(8), 816-823. Purc-Stephenson, R. J. (2014). The posttraumatic growth inventory: Factor structure and invariance among persons with chronic diseases. *Rehabilitation Psychology*, 59, 10–18. <https://doi.org/10.1037/a0035353>

Disclosure: The authors have no disclosures

PP0635

A NOVEL MONOCLONAL ANTIBODY DRUG CANDIDATE SPY001 TARGETING INTEGRIN $\alpha 4\beta 7$ FOR THE TREATMENT OF IBD: IN VITRO PROPERTIES AND NON-HUMAN PRIMATE PHARMACOKINETICS AND SAFETY

E. Zhu¹, D. Rios¹, R. Vaz¹, J. Friedman², D. Nguyen², A. Spencer², M. Rose², O. Ballew², J. Oh¹, H. Shaheen¹

¹Paragon Therapeutics, Waltham, United States of America, ²Spyre Therapeutics, Waltham, United States of America

Contact E-Mail Address: mark.rose@spyre.com

Introduction: Antagonism of the interaction between the cellular adhesion integrin $\alpha 4\beta 7$ and endothelial ligand mucosal addressin cell-adhesion molecule-1 (MAdCAM-1) has proven to be relatively safe and effective in the treatment of Crohn’s disease (CD) and ulcerative colitis (UC). Additional benefit may be gained from an $\alpha 4\beta 7$ antagonist given via the subcutaneous (SC) route at extended intervals (eg, every 8 to 12 weeks) during maintenance therapy.

Aims & Methods: The humanized monoclonal IgG1 antibody SPY001 binds to the same $\alpha 4\beta 7$ epitope as vedolizumab and includes a YTE modification within the Fc region to increase its serum half-life via increased affinity for the neonatal Fc receptor (FcRn), thereby favoring recycling into the circulation over degradation. The binding affinity of SPY001 to $\alpha 4\beta 7$ was determined by kinetic exclusion assay (KinExA), surface plasmon resonance, and flow cytometry. In vitro functional activity was determined by inhibition of MAdCAM-1-mediated cell adhesion. In vivo half-life extension was evaluated via pharmacokinetic analysis in Tg276 transgenic mice (hemizygous for human FcRn) and in non-human primates (NHP). PK simulations in humans were based on allometric scaling of SPY001 clearance observed in NHP. Safety was assessed via a good laboratory practice toxicity (GLP-tox) study in NHP.

Results: SPY001 binds specifically to $\alpha 4\beta 7$ and not to the related integrins $\alpha 4\beta 1$ and $\alpha E\beta 7$. In cell-based binding assays, SPY001 binds $\alpha 4\beta 7$ expressed on the surface of RPMI-8866 cells with an affinity matching that of vedolizumab, but does not bind to Ramos cells expressing $\alpha 4\beta 1$. It demonstrates high affinity for $\alpha 4\beta 7$, with a K_D of <1 nM.

Functionally, SPY001 potently inhibits MAdCAM-1-mediated cell adhesion with an IC_{50} comparable to that of vedolizumab but has no inhibitory activity for VCAM-1-mediated cell adhesion.

In Tg276 mice, the half-life of SPY001 was approximately 12 days compared to approximately 4 days for vedolizumab. In cynomolgus monkeys, the half-life of SPY001 was approximately 22 days following a single SC infusion, substantially longer than the half-life of vedolizumab (~6 days) in the same study. Based on allometric scaling of SPY001 clearance observed in this study, predictive simulations of SPY001 PK in humans suggest that Q8W-Q12W SC dosing will achieve therapeutic exposure in patients across a wide range of body weights and albumin concentrations. In a repeat-dose GLP toxicity study in NHP no adverse or dose limiting toxicities were observed even at the highest dose tested. Both SC and IV administration were well-tolerated and observations related to the administration procedure were similar across doses including controls.

Conclusion: SPY001 is a novel humanized monoclonal IgG1 with an extended half-life relative to that of vedolizumab in Tg276 mice and cynomolgus monkeys. Repeat-dose toxicity studies at doses up to 160 mg/kg showed no SPY001-related adverse events and a safety profile supportive of progression into clinical development. SPY001 offers the potential for effective and safe treatment of CD and UC with the advantage of infrequent SC dosing. Clinical studies are warranted to demonstrate this potential.

Disclosure: EZ, DR, RV, JO, and HS are employees of Paragon Therapeutics.

JF, DN, AS, MR, and OB are employees of Spyre Therapeutics.

PP0636

COMPARISON OF THE EFFICACY AND SAFETY OF GLUCOCORTICOIDS AND BIOLOGICS IN THE TREATMENT OF MODERATE TO SEVERE ULCERATIVE COLITIS

C. Zeng¹, X. Cai¹, S. Long¹, W. Liao¹, X. Shu¹, Z. Yin¹, Y. Chen¹, Xuesheng Cai, Shunhua Long, Wangdi Liao, Xu Shu, Yin Zhu and Youxiang Chen

¹Jiangxi Provincial Key Laboratory of Digestive Diseases, Jiangxi Clinical Research Center for Gastroenterology, Digestive Disease Hospital, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University,, Gastroenterology, Nanchang, China

Contact E-Mail Address: chenyx102@126.com

Introduction: Currently, biologics are widely used in patients with moderate to severe ulcerative colitis (UC), while there is limited research directly comparing the efficacy of biologics and traditional corticosteroid therapy in patients with moderate to severe UC.

Aims & Methods: This study aims to analyze whether the efficacy and safety of biologics (such as infliximab, IFX, or vedolizumab, VDZ) in patients with moderate to severe UC are superior to corticosteroids. A retrospective analysis was conducted on patients diagnosed with moderate to severe UC at the First Affiliated Hospital of Nanchang University from July 2014 to January 2023. Patients were divided into two groups based on prescription treatment: biologics and corticosteroids. A comparison was made between the two groups at 14 weeks for endoscopic remission (ER), clinical remission (CR), clinical response rate, and the difference in survival rates without UC-related events (relapse, discontinuation of medication, surgery, malignancy, death) at 52 weeks. Factors influencing endoscopic remission, clinical remission, and clinical response within 14 weeks in both treatment groups were analyzed. The incidence of adverse events in both treatment groups was also analyzed.

Results: This analysis demonstrates that after IPTW adjustment, the endoscopic remission rate at 14 weeks in the biologics group was significantly higher than in the corticosteroids group (biologics group vs corticosteroids group: OR: 4.14, 95% CI 1.20-15.3; $P=0.001$). However, there were no statistically significant differences between the two groups in terms of

clinical response rate at 14 weeks (OR: 1.26, 95% CI 0.36-2.05; $P=0.754$) and clinical remission rate (OR: 1.46, 95% CI 0.46-4.75; $P=0.700$). Furthermore, the 52-week survival rate without any UC-related events in the biologics group was significantly higher than in the corticosteroids group (biologics group vs corticosteroids group: HR: 0.26, 95% CI 0.12-0.59; $P<0.001$). In addition, biologic therapy ($P=0.031$), disease severity ($P=0.019$), and baseline high-sensitivity C-reactive protein (CRP) levels ($P=0.010$) were independently associated with endoscopic remission at 14 weeks in UC patients. Baseline high-sensitivity CRP levels were independently associated with clinical remission at 14 weeks in patients with ulcerative colitis ($P=0.045$). Regarding adverse events, there were no statistically significant differences between the two groups, including adverse events (OR: 1.52, 95% CI 0.52-4.50; $P=0.444$) and the incidence of severe adverse events (OR: 0.34, 95% CI 0.03-3.89; $P=0.364$).

Conclusion: Biologic therapy (IFX or VDZ) for severe ulcerative colitis shows higher endoscopic remission rates at 14 weeks and higher survival rates without UC-related events at 52 weeks compared to corticosteroid treatment. Despite baseline imbalances between the two treatment groups, similar conclusions were drawn after adjusting for confounding factors with IPTW. It is hoped that these findings will be further confirmed in prospective randomized trials.

References: 1.Fumery M, Singh S, Dulai PS, et al. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. *Clin Gastroenterol Hepatol* 2018;16:343-356.e3.

2.Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology* 2021;160:1570-1583.

3.Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol* 2019;114:384-413.

4.Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology* 2020;158:1450-1461.

5.Meserve J, Aniwan S, Koliani-Pace JL, et al. Retrospective Analysis of Safety of Vedolizumab in Patients With Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol* 2019;17:1533-1540.e2.

6.Targownik LE, Bernstein CN, Benchimol EI, et al. Trends in Corticosteroid Use During the Era of Biologic Therapy: A Population-Based Analysis. *Am J Gastroenterol* 2021;116:1284-1293.

7.Xu F, Liu Y, Greenlund K, et al. Trends and demographic patterns in biologic and corticosteroid prescriptions for inflammatory bowel disease: findings from electronic medical records, 2011-2020. *J Investig Med* 2022;70:1771-1776.

Disclosure: Nothing to disclose.

PP0637

ENDOSCOPIC BALLOON DILATION ASSOCIATED WITH BIOLOGICAL THERAPY IN CROHN'S DISEASE STRICTURES: A SINGLE CENTER EXPERIENCE

L.R. Lopetuso¹, G. Coppola², N. Alfieri¹, C. Morretta², D.V. Federica³, P. Puca³, L. Parisio³, C. Marmo¹, L. Laterza³, D. Pugliese³, M.E. Riccioni¹, G. Cammarota⁴, A. Papa¹, A. Gasbarrini⁵, F. Scaldaferri³

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Surgical and Medical Sciences Department, Roma, Italy, ²Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, CEMAD - IBD Unit, Rome, Italy, ³Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD - IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ⁴Catholic University, Fondazione Policlinico Gemelli, Internal Medicine and Gastroenterology, Rome, Italy, ⁵Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy

Contact E-Mail Address: gcoppa@gmail.com

Introduction: Symptomatic luminal stricture in Crohn's Disease (CD) occurs in up to 20% of patients at the diagnosis and in more than 50% during their lifetime. A considerable percentage of patients often require further surgery for post-operative CD recurrence, with a consequent increased burden of short bowel syndrome. In this scenario, combining biological therapy with endoscopic balloon dilation (EBD) could potentially reduce this risk.

Aims & Methods: Our study aimed to evaluate the efficacy of EBD combined with biologic therapy in symptomatic gastrointestinal strictures in CD patients. We conducted a retrospective study including consecutive CD patients who underwent EBD for low gastrointestinal strictures from December 2015 until November 2022 at our tertiary IBD Center. Subsequent subocclusive/occlusive episodes, the need for steroids, and surgery due to CD stenosis were evaluated during a follow-up period of 6, 12 months, and 24 months.

Results: A total of 52 patients treated with EBD with an overall number of 55 strictures were included. The mean age was 46,8 (18-77) years. The median of disease duration was 9 (0-42) years. Among the total of 55 studied strictures: 14 (25%) in patients with active smoking, 21 (38%) with increased CRP values at the time of dilation, 43 (78%) had evidence of moderate or severe endoscopic disease activity with ulcerative lesions at stricture site. Anastomotic strictures accounted for 26 (47%) of all 55 strictures. The remaining 29 (53%) were de novo stricture: 8 (15%) ileal, 11 (20%) at ileocecal valve, 4 (7%) colonic, and 6 (11%) anal. Forty-two patients (76%) were under biologic therapy at the time of EBD and 2 (4%) started after EBD. EBD technical success was reported in 60% of the procedures, and no adverse events were recorded. After 6 months from EBD, at univariate analysis, increased CRP at the time of dilation resulted in a risk factor for the need for steroids (OR 14,63, IC 2,690 to 71,50; p-value = 0,0006, Table 2). Concomitant biological therapy, active smoke, and the presence of ulcerative lesions did not show a significant correlation with considered outcomes. After 12 and 24 months from EBD, concomitant biological therapy resulted in being a protective factor for surgery (OR 0,06; IC 0,005 to 0,502; p-value=0,0047), while subocclusive and occlusive events were less frequent in anastomotic strictures than ileal stenosis (OR 0,07; IC 0,005 to 0,651; p-value=0,0152).

Conclusion: In patients with CD undergoing EBD for intestinal CD stricture, concomitant biological therapy reduces the risk of surgery for CD stenosis recurrence. Further prospective and controlled studies are underway to confirm these observations.

Disclosure: Antonio Gasbarrini reports personal fees for consultancy for Eisai S.r.l., 3PSolutions, Real Time Meeting, Fondazione Istituto Danone, Sinergie S.r.l. Board MRGE, and Sanofi S.p.A, personal fees for acting as a speaker for Takeda S.p.A, AbbVie, and Sandoz S.p.A, and personal fees for acting on advisory boards

for VSL3 and Eisai. Daniela Pugliese received speaker fees from AbbVie, MSD, Takeda and Janssen, Pfizer; advisory board fees from Pfizer. Franco Scaldaferri: advisory board for Abbvie, Janssen, MSD, Sanofi and Takeda; All the other authors have no conflict of interest to declare.

PP0638

PHARMACOKINETIC COMPARABILITY OF ABP 654 ADMINISTERED EITHER VIA PREFILLED SYRINGE OR AUTOINJECTOR IN HEALTHY ADULT SUBJECTS: RESULTS FROM A RANDOMIZED, OPEN-LABEL, PARALLEL-GROUP STUDY

V. Chow¹, P. Winkle², D.T. Mytych¹, J. Cao¹, C. Barragan¹, W. Radziszewski¹, J. Franklin¹

¹Amgen Inc, Thousand Oak, United States of America, ²Anaheim Clinical Trials, Anaheim, United States of America

Contact E-Mail Address: vchow@amgen.com

Introduction: ABP 654 is a biosimilar to ustekinumab reference product that is supplied in a prefilled syringe (PFS). The ABP 654 autoinjector (AI) is in development as a single-use, disposable, handheld, latex-free, mechanical injection device that aims to offer additional convenience for patients and healthcare professionals.

Aims & Methods: This clinical study was designed to evaluate the comparability, based on exposure (maximum observed serum concentration [C_{max}] and area under the serum concentration-time curve from time 0 extrapolated to infinity [AUC_{inf}]), of ABP 654 after a single subcutaneous (SC) injection delivered by PFS or AI in healthy male and female adults. The study also assessed additional pharmacokinetics (PK) parameters, safety, tolerability, and immunogenicity.

A total of 156 subjects (78 subjects in the PFS group and 78 subjects in the AI group) were randomized in a 1:1 ratio to receive a single 90 mg SC injection of ABP 654 administered either via PFS or AI. Serum concentrations of ABP 654 were determined using a validated electrochemiluminescent assay. PK variables were calculated from the serum concentration data using noncompartmental methods and actual sampling times. Blood samples for antidrug antibody (ADA) assessments were collected at various times. Samples testing positive for binding ADAs were also tested for neutralizing ADAs. Adverse events (AEs) were graded by severity according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

Results: Mean ($\pm$ SD) serum ABP 654 concentration-time profiles show a high degree of similarity between the PFS and AI groups with overlapping profiles over the course of the study. PK comparability was established between the PFS and AI groups based on the 90% CIs of the geometric mean ratios (GMR) for the primary PK endpoints of AUC_{inf} and C_{max} being contained within the prespecified margin of 0.8 to 1.25. Exposure was comparable between the 2 groups. Peak concentrations were observed on average about 8 days following injection. After achieving peak ABP 654 concentrations, levels declined in a monophasic manner with a $t_{1/2}$ of about 23 days. The estimated $t_{1/2}$ was comparable for both groups. The mean percentage of AUC_{inf} due to extrapolation from the last quantifiable concentration observed to infinity ($AUC\%Extrap$) was 5.13% and 4.53% for the PFS and AI groups, respectively, confirming the adequacy of the duration of PK sampling for the evaluation of AUC_{inf} . The frequency, type, and severity of AEs were comparable between the groups and consistent with the safety profile of ustekinumab. Through the end of the study, 10 (12.8%) subjects in the PFS group and 16 (20.5%) subjects in the AI group

tested positive for the development of binding ADAs. This numerical difference is not considered clinically impactful, based on demonstrated PK comparability and similarity of safety profiles between treatment arms.

Treatment	AUC _{inf} (90% CI)	GMR (90% CI)	C _{max} (µg/mL) GM (Geo CV [%])	T _{max} (h) Median (range)	AUC _{last} (h*µg/mL) GM (Geo CV [%])	AUC _{inf} (h*µg/mL) GM (Geo CV [%])	t _{1/2} (h) Mean (SD)	AUC% Extrap (%) Mean (SD)
ABP 654 PFS			9.79 (31.7)	191.93 (48.00, 599.62)	9040 (35.1)	9660 (36.6)	575.75 (155.38)	5.13 (3.48)
	1.0069 (0.92, 1.10)	1.0503 (0.97, 1.14)						
ABP 654 AI			10.30 (32.8)	191.09 (48.00, 291.92)	9300 (34.8)	9720 (36.8)	556.11 (143.34)	4.53 (2.87)

Table 1. Summary of ABP 654 PFS and ABP 654 AI PK Parameters

Conclusion: PK comparability was established between the PFS and AI groups. Both treatments were safe and well-tolerated. Overall, the results support conclusions of PK comparability and similar safety and immunogenicity profiles between ABP 654 administered via PFS and AI.

Disclosure: V. Chow, D. Mytych, J. Cao, C. Barragan, W. Radziszewski and J. Franklin are Amgen employees and shareholders. P. Winkle has no conflicts.

PP0639

EFFECTIVENESS AND SAFETY OUTCOMES BEYOND FIVE YEARS OF IBD PATIENTS TREATED WITH VEDOLIZUMAB. THE LONG-LIVE IG-IBD STUDY

D. Pugliese¹, G. Privitera², A. Armuzzi³, IG-IBD LIVE Study Group
¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ²Università degli Studi di Milano, Milan, Italy, ³IBD Center, IRCCS Humanitas Research Hospital, Gastroenterology, Rozzano, Milan, Italy

Contact E-Mail Address: gpp.privitera@icloud.com

Introduction: Long-term real-life data on vedolizumab (VDZ) are scarce. In this study, we aim to evaluate the long-term outcomes of patients (pts) with inflammatory bowel disease (IBD) who received VDZ.

Aims & Methods: The LONG-LIVE is the long-term extension (LTE) of the LIVE study, including IBD pts who had started VDZ from 04 to 06/2017 at 47 Italian centres affiliated with IG-IBD, prospectively followed-up to 06/2019. For this study, data on therapy withdrawal, clinical and endoscopic activity, need for surgery/hospitalizations, deaths, and serious adverse events (SAEs) were retrospectively extracted from 07/2019 up to the last available follow-up (fup).

Results: Seven hundred eighty-two (70% of the original cohort) pts were enrolled in the LTE (394 CD, 388 UC), 316 (40%) of whom had already definitively discontinued VDZ; 43% were female, mean age was 53 $\pm$ 16 years, mean disease duration was 17 $\pm$ 9 years, 76% of patients were bioexposed to anti-TNF α therapy. Among the remaining 466 still receiving VDZ, 204 (44%) subsequently suspended VDZ permanently and 9 (2%) temporarily: mean VDZ therapy duration was 113 $\pm$ 92 weeks and 311 $\pm$ 60 weeks among those who suspended and those who continued VDZ, respectively. Mean therapy duration was 177 $\pm$ 124 weeks (172 $\pm$ 124 weeks for CD and 182 $\pm$ 125 weeks for UC, with no significant differences); longer mean persistence was observed in bionative vs bioexposed CD pts (197 $\pm$ 123 vs 182 $\pm$ 122 weeks, $p < 0.05$), while no such difference was observed in UC pts (193.1 $\pm$ 126 vs 190 $\pm$ 122. week, $p = ns$). Among CD pts who continued VDZ throughout the entire LTE, 74% and 54% were in clinical and endoscopic remission, respectively, at the last fup; among UC pts who continued VDZ throughout the entire LTE, 79% and 50% were in clinical and endoscopic remission, respectively, at the last fup. During the LTE, CD pts had a higher

risk of IBD-related hospitalizations (Hazard Ratio, HR, 1.37, 95% Confidence Interval, CI, 1.04-1.72, $p=0.027$). Specifically, 153 (20%) pts (83 CD, 70 UC) were hospitalized to receive IBD-related surgery after a mean time of 136 ± 87 weeks from VDZ start (for CD vs UC comparison, HR 1.17, 95% CI 0.85-1.60, $p=ns$); 85 (11%, 54 CD, 31 UC) pts underwent IBD-related hospitalization for non-surgical reasons (CD vs UC, HR 1.71, 95% CI 1.21-2.62, $p=0.015$). New or recurrent cancers were reported in 17 pts (the most common localization being 4 breast cancers and 3 gastrointestinal cancers): mean interval between first VDZ administration and cancer diagnosis was 214 (± 95) weeks; 20 non-oncological SAEs were recorded in pts receiving VDZ, the most common being infections ($n=7$), mostly pneumonia ($n=4$). Finally, 15 deaths were reported (of which 9 occurred in patients still receiving VDZ); the most common causes of death were infections ($n=5$), cardiovascular diseases ($n=5$) and cancer ($n=3$).

Conclusion: About one-third of pts were still receiving VDZ after a follow-up of more than 6 years, with the majority of them being in clinical remission and more than 50% also having quiescent endoscopic activity at the last observation; bio-naïve CD patients had longer persistence compared to bio-exposed ones. During the LTE, CD pts had higher rates of IBD-related hospitalizations; most hospitalizations were due to the necessity of surgery. SAEs were observed in a minority of patients and predominantly consisted of infections; the rates of cancer diagnosis are seemingly in line with those of the general population. Overall, our study strengthens the notion that vedolizumab is associated with a long-term real-life durability in terms of both effectiveness and safety.

Disclosure: Daniela Pugliese received speaker fees and/or advisory board from AbbVie, Galapagos, MSD, Takeda and Janssen, Pfizer. Giuseppe Privitera received consultancy fees from Alphasigma and Janssen. Alessandro Armuzzi: consulting and/or advisory board fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Arena, Biogen, Bristol-Myers Squibb, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mitsubishi-Tanabe, Novartis, Pfizer, Roche, Sandoz, Samsung Bioepis, Takeda; and research grants from MSD, Pfizer, Takeda and Biogen.

PP0640

LONG TERM FOLLOW-UP OF PATIENTS WITH ULCERATIVE COLITIS AFTER WITHDRAWAL OF INFLIXIMAB FOR DEEP AND STABLE REMISSION

N. Dussias¹, L. Melotti¹, N. Vanigli¹, P. Gionchetti¹, F. Rizzello¹

¹Alma Mater Studiorum - Università di Bologna; IRCCS AOU Bologna, Policlinico Sant'Orsola-Malpighi, DIMEC, Bologna, Italy

Contact E-Mail Address: nikolas.dussias@studio.unibo.it

Introduction: Infliximab (IFX) is the first anti-TNF biologic drug approved for treating moderate to severe ulcerative colitis (UC). While IFX is effective in inducing mucosal healing and enhancing quality of life, concerns persist about the long-term safety and cost-effectiveness of extended immunosuppression. Current guidelines lack clarity on when to discontinue treatment after achieving stable deep remission. Moreover, existing literature is limited to studies characterized by small sample sizes and heterogeneous criteria for defining remission. Our study aimed to evaluate the rate of remission maintenance in UC patients who discontinued IFX after achieving stable deep remission, to identify predictors of relapse post-discontinuation, and to examine clinical outcomes in those who experienced a relapse.

Aims & Methods: In this single-center, retrospective, observational study, we analyzed UC patients at our tertiary IBD Referral Center who discontinued IFX due to sustained deep remission, defined as the combination

of partial Mayo subscore ≤ 1 and endoscopic Mayo score = 0, and who had at least 1 year of follow-up post treatment withdrawal. We assessed the relapse rates at intervals of 6 months, 1 year, 2 years, and beyond 2 years post-IFX discontinuation. For those who relapsed, we recorded the therapeutic strategy and its effectiveness, including the necessity for colectomy. Additionally, we performed univariate and multivariate analyses to identify relapse predictors post-treatment suspension.

Results: From 2006 to 2022, 790 UC patients received IFX treatment at our center; 113 suspended IFX due to stable deep remission with at least 1 year of follow-up and were included in this study. Of these, 41.6% maintained remission over a median of 5.17 years. Flare rates were 14.2%, 23.9%, and 35.5% within 6, 12, and 24 months, respectively, with 58.4% experiencing a flare overall. Multivariate analysis showed that longer treatment duration reduced relapse risk ($p=0.001$), while steroid use during IFX treatment and early IFX initiation post-diagnosis increased relapse risk ($p=0.004$ and $p=0.043$, respectively). Most cases of disease relapse were successfully managed medically either with a course of steroids, restarting IFX, or initiation of a different type of biologic/small molecule, whereas the rate of colectomy was 7.1%.

Conclusion: This study is one of the largest to date with the longest follow-up that evaluates outcomes post-IFX discontinuation in UC patients in deep remission. Our findings suggest that withdrawal of IFX treatment can be considered in carefully selected cases. In patients who relapse after IFX suspension, medical treatment is often effective, while the rate of colectomy is low. Further studies are warranted to better identify ideal candidates for treatment withdrawal.

Disclosure: Nothing to disclose.

PP0641

FRAILITY IS DYNAMIC OVER TIME AND ASSOCIATED WITH ALL-CAUSE AND ACUTE HOSPITALIZATIONS DURING 18 MONTHS FOLLOW-UP IN OLDER PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A.B. Fons¹, VER Asscher^{1,2}, RJL Stuyt², AMC Pronk³, S van der Marel⁴, RJ Jacobs⁵, JJJ Haans⁶, AE van der Meulen-de Jong¹, SP Mooijaart^{7,8}, KJ Kalisvaart⁹, PWJ Maljaars¹
¹Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²HagaZiekenhuis, Department of Gastroenterology and Hepatology, The Hague, Netherlands, ³Groene Hart Ziekenhuis, Department of Gastroenterology and Hepatology, Gouda, Netherlands, ⁴Haaglanden Medical Centre, Department of Gastroenterology and Hepatology, The Hague, Netherlands, ⁵Alrijne Hospital, Department of Gastroenterology and Hepatology, Leiden and Leiderdorp, Netherlands, ⁶Maastricht University Medical Centre, Department of Gastroenterology and Hepatology, Maastricht, Netherlands, ⁷Leiden University Medical Center, Gerontology and Geriatrics, Leiden, Netherlands, ⁸Leiden University Medical Center, LUMC Center for Medicine for Older People, Leiden, Netherlands, ⁹Spaarnse Gasthuis, Department of Geriatric Medicine, Haarlem, Netherlands

Contact E-Mail Address: a.b.fons@lumc.nl

Introduction: Frailty is prevalent among older patients with Inflammatory Bowel Disease (IBD). A geriatric assessment is a method to assess the presence of frailty and its course over time. However, the predictive value of the geriatric assessment and the longitudinal course of frailty have not yet been studied in patients with IBD.

Aims & Methods: The primary aim was to evaluate the course of frailty and to identify factors associated with changes in level of frailty over 18 months follow-up in older patients with Inflammatory Bowel Disease (IBD). The second aim was to study the association of frailty with hospi-

talizations during follow-up. A prospective multicenter cohort study was conducted in IBD patients (≥ 65 years). At baseline, a geriatric assessment was performed in all 405 patients, assessing impairment in five domains: the somatic domain, (instrumental) activities of daily living, physical capacity, mental and social domain. Follow-up was conducted after 18 months. Part of the patients were seen for a second, follow-up geriatric assessment. The rest of the patients was contacted by phone for a follow-up assessment. Primary outcome was change in the level of frailty, defined as a change in the number of impaired domains at follow-up compared to baseline (an increase in number of impaired domains suggests an increase in level of frailty, a decrease in number of impaired domains suggests a decrease in level of frailty). Secondary outcomes were all-cause, acute and IBD-related hospitalizations during 18 months. Logistic regression was performed to identify factors associated with changes in level of frailty, adjusted for age, sex, type of IBD and educational level. Cox regression analyses were performed to study the association of frailty with adverse outcomes, adjusted for age, sex and biochemical disease activity (C-reactive protein ≥ 10 mg/L and/or fecal calprotectin ≥ 250 μ g/g).

Results: Out of 405 patients (median age: 70 years) with a geriatric assessment at baseline, 160 (39.5%) patients had 2 or 3 impaired domains and 32 patients (7.9%) had 4 or 5 impaired domains. Follow-up was conducted in 356 patients (87.9%), of which 154 (43.3%) patients were seen for a geriatric assessment and 202 patients (56.7%) were contacted by phone. In the geriatric assessment, 32.5% had increased and 26.0% decreased ≥ 1 in number of impaired domains compared to baseline. Use of systemic corticosteroids at or three years prior to baseline associated with an increase in impaired domains (adjusted odds ratio (aOR) 3.00; 95% confidence interval (95% confidence interval (CI)) 1.11-8.08; p-value=0.030), while initiation of biological therapy associated with a decrease in impaired domains (aOR 4.92, 95%CI 1.41-17.15, p-value=0.013). Over 18 months, all-cause hospitalizations occurred 136 times in 96 patients (23.7%). Of all hospitalizations, 103 (75.7%) were acute occurring in 74 patients and 41 were IBD-related (30.1%) occurring in 28 patients. Frailty was independently associated with both all-cause (adjusted hazard ratio (aHR) 1.28, 95% confidence interval [CI] 1.05-1.56, p-value=0.016) and acute hospitalizations (aHR 1.30, 95% CI 1.04-1.61, p-value=0.020). No association was found for IBD-related hospitalizations.

Conclusion: The level of frailty is dynamic in 58.5% of the older patients with IBD over 18 months. In addition, frailty at baseline is independently associated with all-cause and acute hospitalizations. Future studies should establish how interventions targeting frailty could improve health outcomes.

Disclosure: Nothing to disclose.

PP0642

A RETROSPECTIVE COHORT STUDY TO DEMONSTRATE MAINTENANCE OF REMISSION RATES FOR SUBCUTANEOUS COMPARED TO INTRAVENOUS VEDOLIZUMAB IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

D. Al-Zarrad¹, N. Fernandes², N. Kamperidis¹, F. Aslam¹, A. Chana¹, S. Radhakrishnan¹, L. Dyall^{1,2}, N. Arebi^{1,2}

¹St Marks National Bowel Hospital, London Northwest University Healthcare NHS Trust, Department of IBD, London, United Kingdom, ²Imperial College, Dept of Metabolism, Digestion & Reproduction, London, United Kingdom

Contact E-Mail Address: dania.al-zarrad@nhs.net

Introduction: Vedolizumab (VDZ) is an anti $\alpha 4\beta 7$ integrin antibody therapy that inhibits migration of T-lymphocytes to the gastrointestinal epithelium through mucosal addressin cell adhesion receptor¹. As a licensed treatment for inflammatory bowel disease (IBD), it is now available as a subcutaneous (SC) formulation. The efficacy and safety of SC VDZ was comparable to intravenous (IV) therapy in two randomised controlled trials (VISIBLE 1 and 2) in ulcerative colitis (UC)² and Crohn disease (CD)³. SC biologic preparations offer patients flexibility to self-administer therapy and reduce hospital visits.

Aims & Methods: Objective is to evaluate the efficacy of SC to IV VDZ in IBD and to assess impact on costs.

Patients receiving IV VDZ infusions at a single tertiary centre were assessed for eligibility to switch to SC formulation. Between February 2021 to February 2023, all patients switch and remaining on IV were included. Baseline data was collected with follow-up at 6 and 12 months. The primary outcome was maintenance of clinical remission, defined as HBI ≤ 4 for CD and SCCAI ≤ 3 for UC at 6 and 12 months. Secondary outcomes included serum CRP, faecal calprotectin (FCP), drug persistence at 6 and 12 months and potential savings calculated using the drug price and bed costs.

Results expressed as rates and odds ratio (OR) were analysed with GraphPad prism using one-way ANOVA, mixed-effect analyses (q value) and chi-squared test. Benjamini-Hochberg false discovery rate (FDR) adjustment was used for P value correction

Results: 246 patients on IV VDZ were identified. 29 were not suitable to switch: 20/29 due to disease phenotype remained in the IV group, 11 patients on escalated dose regimen were excluded from both groups.

Of the 195 included patients, 175 were eligible to switch: 80/175 declined SC treatment due to preferences and continued IV therapy. In the SC switch group (n=95, 54%) median age was 54.5 years, 43% (n=41) were females, 63% (n=60) had UC, 37% (n=35) had CD. The commonest CD phenotype was ileal disease (N=15/35). Compared to the IV group (n=100, 51%) median age was 46 years, 42% (n=42) were females, 63% (n=63) had UC, 37% (n=37) had CD. The commonest CD phenotype was ileocolonic disease (N=11/37).

The primary outcomes are shown in Table 1 which demonstrated statistical significance in maintenance of remission with SC VDZ. The odd for remission with SC VDZ at 6 and 12 months were 1.1 [CI] (p0.7) and 3.6 [CI] (p0.006) at 12 months.

There were no statistically significant differences in CRP and FCP between baseline, 6, or 12 months for the IV and SC groups. For CRP, 80% and 75% of patients maintained biochemical remission 6 and 12 months and for FCP 78% at 6 and 81% at 12 months.

Drug persistence for SC at 6 and 12 months were 93% and 87%, respectively. 4% (N=4) patients switched to a different drug due to loss of response, 8% (n=8) switched back to IV VDZ due to adverse events, issues with homecare or symptom control.

Based on this cohort of patients, an expected reduction of £ 72,010 per annum is likely to be achieved.

	SC		IV	
Baseline	81% (n=77)		77% (n=77)	
6 months	82% (n=78)	q=0.2979 (Baseline vs 6 months)	80 % (n=80)	q=0.894 (Baseline vs 6 months)
12 months	86% (n=82)	q=0.002 (Baseline vs 12 months)	79% (n=79)	q=0.894 (Baseline vs 12 months)

Table 1: Displays baseline, 6-month and 12-month remission rates of VDZ IV and SC in IBD.

Conclusion: Transitioning patients from IV to SC VDZ was associated with low drug discontinuation rate. We observed higher remission rates at 12 compared with 6 months for SC group in comparison to patients who remained on IV VDZ. These findings should be used to encourage uptake of switching strategies.

References:

1. Feagan, B. G., et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2013; 369(8): 699-710.
2. Sandbom WJ, Wolf D, D'haens G, et al. P510 Dose escalation of subcutaneous vedolizumab in patients With ulcerative colitis: A post hoc analysis of the VISIBLE trial data. *Journal of Crohn's and Colitis.* 2020; 14 (Supplement_1): S442-S443

Disclosure: None.

PP0643

COMBINING IL-23 BLOCKADE WITH ANTI- α 4 β 7 OR ANTI-TL1A FOR THE TREATMENT OF IBD IS SUPPORTED BY IN VITRO AND MOUSE IBD MODEL EXPERIMENTS

D. Rios¹, M. Alam¹, J. Vidal¹, J. Friedman², D. Nguyen², A. Spencer², J. Oh¹, H. Shaheen¹

¹Paragon Therapeutics, Waltham, United States of America, ²Spyre Therapeutics, Waltham, United States of America

Contact E-Mail Address: deanna.nguyen@spyre.com

Introduction: Despite the discovery of advanced treatments for IBD, placebo-adjusted clinical remission rates during induction therapy are typically only 10%-25%, and loss of response is common even among those who initially benefit. Monoclonal antibodies targeting IL-23 or α 4 β 7 are both relatively safe and effective treatments for Crohn's disease (CD) and ulcerative colitis (UC), while antibodies to the cytokine TL1A have shown promise in phase 2 clinical trials. The combined use of targeted biologic agents may improve efficacy by inhibiting multiple pathways while avoiding the risks associated with broad immunosuppression. Pre-clinical studies are needed to assess the potential benefit of combining IL-23 antagonism with α 4 β 7 or TL1A blockade.

Aims & Methods: IL-17 production in response to IL-23 and/or TL1A by human peripheral blood mononuclear cells (PBMC) and mouse splenocytes was assessed in the presence of anti-IL-23 and/or anti-TL1A. The ability of anti-IL-23 and anti- α 4 β 7 as monotherapies or in combination to prevent colitis was assessed by transferring CD4⁺ CD45RB^{high} T cells into *Rag2*^{-/-} mice. Survival, body weight, disease activity, histology, and colon IL-17 levels were measured.

Results: IL-23 and TL1A had a synergistic effect on IL-17 production by human PBMC and mouse splenocytes, extending previous findings in CD patient-derived lamina propria T cells¹. Both anti-IL-23 and anti-TL1A inhibited IL-17 production, with the greatest inhibition occurring with combined IL-23 and TL1A blockade.

In the mouse T-cell transfer colitis (TCT) model, the anti-IL-23 and anti- α 4 β 7 combination at high doses resulted in improved body weight relative to either monotherapy. The monotherapies and the combination of anti-IL-23 and anti- α 4 β 7 (both high and low doses) resulted in similar

improvements in survival, disease activity index, and histology score. The combination resulted in greater reductions in colonic IL-17 protein than either monotherapy alone.

Conclusion: IL-23 and TL1A have a synergistic effect on promoting IL-17 secretion from human and mouse immune cells. The combination of anti-IL-23 and anti-TL1A suppresses IL-17 secretion more effectively than either agent alone. In the TCT model of IBD, combination therapy with anti-IL-23 and anti- α 4 β 7 improves body weight and reduces colonic IL-17 levels relative to monotherapy with less obvious effect on other disease measures.

References: Kamada, N. et al. TL1A produced by lamina propria macrophages induces Th1 and Th17 immune responses in cooperation with IL-23 in patients with Crohn's disease. *Inflamm. Bowel Dis.* 16, 568-575 (2010).

Disclosure: DR, MA, JV, JO, and HS are employees of Paragon Therapeutics.

JF, DN, and AS are employees of Spyre Therapeutics.

PP0644

EXPLORING THE MOLECULAR TARGETS AND MECHANISM OF TARAXASTEROL IN THE TREATMENT OF ULCERATIVE COLITIS BASED ON NETWORK PHARMACOLOGY AND EXPERIMENTAL VALIDATION

C. Zeng¹, J. Li², Y. Chen², Jun Li, Youxiang Chen
¹Digestive disease Hospital, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang China, Department of Gastroenterology, Nanchang, China, ²Jiangxi Provincial Key Laboratory of Digestive Diseases, Jiangxi Clinical Research Center for Gastroenterology, Digestive Disease Hospital, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University,, Gastroenterology, Nanchang, China

Contact E-Mail Address: zcy896@163.com

Introduction: Ulcerative colitis (UC) is a chronic, non-specific inflammatory disease of the bowel of unknown etiology. This disease is characterised by high difficulty in cure, high recurrence and cancer rates, which seriously endangers the lives and health of our population. Taraxasterol (TA), a major constituent of the traditional Chinese medicine dandelion, has been reported in several studies to have good anti-inflammatory and antioxidant activities as well as anti-tumour effects.

Aims & Methods: However, the molecular targets and mechanisms of action of TA against UC have not been fully elucidated. The Swiss Target Prediction, PharmMapper databases were used to obtain relevant targets for the drug TA. Targets for UC were obtained from GeneCards, OMIM, PharmGkb, DrugBank databases. Targets of TA anti-UC identified by intersection of drug target and disease target.

The relevant targets of TA anti-UC were uploaded to the String database and the resulting data were imported into Cytoscape 3.9.1 software to construct a protein-protein interaction (PPI) network of drug-disease targets. At the same time, the top 10 hub targets were screened using CytoHubba software.

Gene ontology (GO) and Kyoto Encyclopedia of Genomes (KEGG) pathway enrichment analyses were performed on TA anti-UC targets using R software, and molecular docking was performed by Autodock Vina 1.1.2. The GEO dataset was used to analyze the differential mRNA expression of the TA anti-UC top 10 hub gene in UC patients and the normal population. Lipopolysaccharide (LPS)-induced intestinal epithelial cells (NCM460) were used to construct an in vitro cellular inflammation model and a Dextran Sulfate Sodium Salt (DSS) induced acute mouse colitis model. The pivotal targets and key signaling pathways were also validated by RT-qPCR and Western blotting.

Results: A total of 129 relevant targets of TA against UC were obtained, of which the top 10 hub targets were GRB2, PTPN11, SRC, PIK3R1, LCK, EGFR, MAPK1, IGF1, ESR1 and JAK2. The PI3K-Akt pathway was significantly associated with TA treatment of UC as identified by KEGG enrichment analysis. GEO dataset analysis demonstrated that EGFR and GRB2 were upregulated in UC patients, while SRC, PIK3R1 and JAK2 were down-regulated. In vitro experiments revealed that TA treatment reversed the expression of EGFR, GRB2, PIK3R1 and JAK2 differential genes.

Furthermore, TA was able to up-regulate the mRNA expression of pro-inflammatory factor IL-10 and decrease the mRNA levels of anti-inflammatory factors IL-6, IL-1 β and TNF- α in LPS-induced NCM460 cells. In vivo assay confirmed that TA significantly alleviated DSS-induced colonic inflammation in mice, including reversal of weight loss and shortening of colon length, reduction of DAI score in mice, and improvement of intestinal barrier disruption. In vivo and in vitro experiments have confirmed that TA also inhibits the activation of the PI3K/Akt pathway, thus exerting an anti-inflammatory effect.

Conclusion: TA may play a therapeutic role in UC by inhibiting the PI3K-Akt pathway. EGFR, GRB2, PIK3R1 and JAK2 may be the most relevant potential therapeutic targets for TA in the treatment of UC.

Disclosure: Nothing to disclose.

PP0645

THE VALUE OF TOFACITINIB FOR THE TREATMENT OF MODERATE TO SEVERE ULCERATIVE COLITIS: TWO-YEARS DATA FROM TOFA-UC, A SN-IBD STUDY

F.S. Macaluso¹, E. D'Antonio², W. Fries³, A. Viola³, O. Ksissa³, M. Cappello⁴, S. Muscarella⁴, N. Belluardo⁵, E. Giangreco⁵, F. Mocciano⁶, R. Di Mitri⁶, C. Ferracane⁷, A. Vitello⁸, M. Grova⁹, S. Calderone¹, S. Renna¹, A. Casà¹, M. Ventimiglia¹⁰, A. Orlando¹, Sicilian Network for Inflammatory Bowel Disease (SN-IBD)

¹"Villa Sofia-Cervello" Hospital, IBD Unit, Palermo (Pa), Italy, ²"S. Anna e S. Sebastiano" Hospital, Gastroenterology Unit, Casera, Italy, ³University of Messina, "G. Martino" Hospital, IBD Unit, Messina, Italy, ⁴University of Palermo, Gastroenterology & Hepatology Section, PROMISE, Palermo, Italy, ⁵"Guzzardi" Hospital, Gastroenterology Unit, Vittoria, Italy, ⁶Arnas Civico-Di Cristina-Benfratelli Hospital, Gastroenterology and Endoscopy Unit, Palermo, Italy, ⁷"Vittorio Emanuele" Hospital, Gastroenterology Unit, Catania, Italy, ⁸"S. Elia- Raimondi" Hospital, Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ⁹"Villa Sofia-Cervello" Hospital, Digestive Endoscopy Unit, Palermo, Italy, ¹⁰Italian Ministry of Health, Directorate General of Medical Device and Pharmaceutical Service, Rome, Italy

Contact E-Mail Address: fsmacaluso@gmail.com

Introduction: Real-world evidence is becoming increasingly important to determine the value of drugs in clinical practice. We have recently reported one-year data on safety and effectiveness of tofacitinib (TOFA) for the treatment of moderate to severe ulcerative colitis (UC) in Sicily, Italy.

Aims & Methods: TOFA-UC is a multicenter, observational, 2-year study performed among the Sicilian Network for Inflammatory Bowel Disease (SN-IBD). All consecutive patients with moderate to severe UC starting TOFA from June 2021 to June 2023 (24 months) were enrolled. The primary outcome was the assessment of safety, in terms of rate of adverse events (AEs). Secondary outcomes included the rates of clinical response and steroid-free clinical remission (based on partial Mayo score) after 8 and 52 weeks, the rate of loss of response, and treatment persistence.

Results: 171 patients were included [median follow-up: 12.0 (IQR 6.0, 19.0) months]. Only 9 patients (5.3%) were naïve to biologics, while most had previous failures to one (39.2%), two (25.1%), three (24.6%), or four (5.8%) biologics.

Thirty adverse events were reported (17.5%; incidence rate: 15.85 per 100 patient-years), with hypercholesterolemia being the most frequent one (13 cases). No herpes zoster reactivation was reported, while one case of pulmonary embolism occurred. At week 8, the rates of clinical response and steroid-free clinical remission were 76.6% and 51.5%, respectively.

At week 52, the rates of clinical response and steroid-free clinical remission were 63.6% and 58.3%, respectively. Forty patients experienced a loss of response after successful induction (38.8%; incidence rate: 108.3 per 100 patient-years).

Sixty-seven patients (39.2%) discontinued TOFA over time, of whom 9 due to AEs, and 58 due to primary non response or loss of response. By multiple regression analysis model, being former smoker (hazard ratio=2.05; 95% CI=1.02-4.13; p=0.043) and a higher partial Mayo score at baseline (hazard ratio=1.20; 95% CI=1.04-1.38; p=0.011) were the variables associated with a higher risk of treatment discontinuation.

Conclusion: After two years of use in clinical practice, our multicenter study confirmed the safety and effectiveness of TOFA for the treatment of patients with moderate to severe UC and multiple previous failures to biological therapies.

Disclosure: Funded by Pfizer. The protocol of this investigator-sponsored study was selected in the context of the "Local Competitive Grant Program RE-CUP 2021 (Global Medical Grants system ID #71844083)", a competition between Italian projects promoted by Pfizer.

PP0646

DESIGN OF A PHASE 2 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF THE HIGHLY SELECTIVE ORAL TYROSINE KINASE 2 INHIBITOR ZASOCITINIB (TAK-279), IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

L. Peyrin-Biroulet^{1,2,3,4,5,6}, S. G. Rajendra⁷, L. Zaru⁷, V.A. Nguyen⁷, O. Ayodele⁷, A.N. Desch⁷, F. Nordio⁷, T. Freney⁷, L. Sears⁷, N. Singh⁷

¹INFINY Institute, Nancy University Hospital, Vandœuvre-lès-Nancy, France, ²Department of Gastroenterology, Nancy University Hospital, Vandœuvre-lès-Nancy, France, ³INSERM, NGERE, University of Lorraine, Vandœuvre-lès-Nancy, France, ⁴FHU-CURE, Nancy University Hospital, Vandœuvre-lès-Nancy, France, ⁵Groupe Hospitalier Privé Ambroise Paré – Hartmann, Paris IBD Center, Neuilly-sur-Seine, France, ⁶McGill University Health Centre, Division of Gastroenterology and Hepatology, Montreal, Canada, ⁷Takeda Development Center Americas, Inc., Cambridge, United States of America

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: Tyrosine kinase 2 (TYK2) mediates cytokine signalling pathways involved in immune-mediated inflammatory diseases, including ulcerative colitis (UC). Zascotinib (TAK-279) is a highly selective, oral, allosteric TYK2 inhibitor that has shown efficacy and acceptable safety in psoriasis and psoriatic arthritis.^{1,2}

This phase 2 study (NCT06254950) will assess efficacy and safety of zascotinib in patients with moderately to severely active UC.

Aims & Methods: This is a multicentre, randomized, placebo-controlled, double-blind induction study in adults (18–75 years) with moderately to severely active UC (modified Mayo score of 5–9 points and endoscopic subscore ≥ 2) with a documented diagnosis (endoscopic with histology)

≥30 days before screening. Eligible patients must have inadequate/loss of response or intolerance to ≥1 of oral aminosalicylates, corticosteroids, immunosuppressants, biologics, JAK inhibitors (JAKi), α4 integrin antagonists or sphingosine-1-phosphate (S1P) receptor modulators. Patients who have failed <3 classes of advanced therapies will be included. Approximately 207 patients will be randomized 1:1:1 to receive low- or high-dose zasocitinib or placebo orally once daily for 12 weeks. Study doses were selected to provide ≥90% TYK2 inhibition over the 24-hour dosing interval, and were associated with efficacy in preclinical models.³ Randomization will be stratified based on previous biologic, JAKi, α4 integrin antagonist or S1P receptor modulator therapies, and steroid use at baseline. The study comprises a 30-day screening period, a 12-week double-blind induction treatment period, a 40-week open-label treatment period and a 4-week safety follow-up. After Week 12, all patients will be reassigned to receive active zasocitinib treatment in the open-label maintenance period. Enrolment of patients who have received previous biologic, JAKi, α4 integrin antagonist, S1P receptor modulator, anti-interleukin (IL)-23p19 or anti-IL-12/23p40 therapy will be capped.

Primary endpoint analysis will be conducted using a Cochran–Mantel–Haenszel (CMH) test. Binary secondary endpoints will also be analysed similarly to primary endpoints. A mixed-effects model with repeated measures will analyse longitudinal continuous secondary endpoints. Safety data will be presented by treatment group and assessment period.

Results: The study is actively enrolling. An open-label extension is planned for zasocitinib responders. The primary efficacy endpoint is clinical remission at Week 12, assessed as the proportion of patients achieving a modified Mayo score ≤2, with stool frequency and endoscopic subscores ≤1 and a rectal bleeding subscore of 0. Secondary efficacy endpoints at Week 12 include proportion of patients achieving clinical response (reduction from baseline in modified Mayo score ≥2 and ≥30%, and a decrease in rectal bleeding subscore ≥1 or absolute rectal bleeding subscore ≤1), symptomatic remission (rectal bleeding subscore 0 and stool frequency subscore ≤1), endoscopic improvement (modified Mayo endoscopic subscore ≤1), endoscopic remission (modified Mayo endoscopic subscore 0), patient-reported symptoms and disease-specific health-related quality of life (HRQoL). Safety and tolerability will be assessed by monitoring treatment-emergent adverse events (AEs), serious AEs and AEs of special interest throughout the study.

Conclusion: Alongside evaluating the efficacy and safety of zasocitinib in patients with moderately to severely active UC, this study will assess the impact of treatment on HRQoL, a significant unmet need in this population.

References: 1. Armstrong A *et al.* AAD 2023.

2. Kivit Z *et al.* *Arthritis Rheumatol* 2023;75(Suppl 9).

3. Kong KF *et al.* *J Crohns Colitis* 2024;18(Suppl 18).

Disclosure: LP-B received fees from AbbVie, Abivax, Adacety, Alimemtiv, Alma Bio Therapeutics, Amgen, Applied Molecular Transport, Arena, Biogen, Bristol Myers Squibb, Celltrion, Connect Biopharma, Cytokine Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Gossamer Bio, HAC Pharma, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Nordic Pharma, Norgine, Novartis, OM Pharma, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, ParImmune, Pfizer, Prometheus, Protagonist, Roche, Roivant, Samsung, Sanofi, Sandoz, Takeda, Theravance, Thermo Fisher, Tigenix, Tillots, Vectivbio, Ventyx, Viatrix, Vifor and Ysopia. SGR, LZ, VAN, OA, AND, FN, TF, LS and NS are employees and equity holders of Takeda.

PP0647

JAK INHIBITORS AND S1P RECEPTOR MODULATORS FOR THE TREATMENT OF ANTIBIOTIC REFRACTORY CHRONIC POUCHITIS: AN ECCO CONFER MULTICENTRE CASE SERIES

G. Testa¹, D.G. Ribaldone², B. Verstockt³, T. Molnár⁴, E.V. Savarino⁵, C. Schmidt⁶, S. Vieujeun⁷, N. Teich⁸, M. Corina⁹, P. Juillerat¹⁰, N. Grellier¹¹, T. Lobaton Ortega¹²

¹AOU Città della Salute e della Scienza, Turin, Italy, ²University of Turin, Department of Medical Sciences, Turin, Italy, ³University Hospitals Leuven and KU Leuven, Translational Research in Gastrointestinal Disorders - IB, Department of Gastroenterology and Hepatology and Department of Chronic Diseases, Metabolism and Aging, Leuven, Belgium, ⁴University Of Szeged, Department of Internal Medicine, Szeged, Hungary, ⁵University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁶Fulda Hospital, Medical Clinic II, Fulda, Germany, ⁷CHU Liege Hospital, Gastroenterology, Liège, Belgium, ⁸Friedrich Schiller University, Medical Faculty, Jena, Germany, ⁹Gastroenterology and Hepatology Center, Fundeni Clinical Institute Bucharest, Gastroenterology, Bucharest, Romania, ¹⁰Intesto Gastro-entérologie, Crohn and Colitis Center, Fribourg and Bern, Gastroenterology, Inflammatory Bowel Disease, Bern, Switzerland, ¹¹Poitiers University Hospital, Gastroenterology, Poitiers, France, ¹²Ghent University Hospital, Gastroenterology, Gent, Belgium

Contact E-Mail Address: giulia.testa1493@gmail.com

Introduction: Data regarding effectiveness and safety of JAK inhibitors and S1P receptor modulators in chronic antibiotic refractory pouchitis (CARP) are lacking.¹⁻⁴ This ECCO-CONFER project collected cases of CARP treated with JAK inhibitors or S1P receptor modulators.

Aims & Methods: This retrospective multicentre study collected cases across Europe through the ECCO-CONFER project, including patients with ulcerative colitis (UC) diagnosis who underwent proctocolectomy with ileal pouch anal anastomosis (IPAA), treated with JAK inhibitors or S1P receptor modulators for CARP and at least three months of follow up.

Main outcomes were steroid and antibiotics-free clinical response at three months (T3) for each drug, defined as clinical part of modified Pouchitis Disease Activity Index (mPDAI) reduction by ≥1 points, steroid and antibiotics-free clinical response at 1 year (T12) assessment, defined as mPDAI reduction by ≥2 points, steroid and antibiotics-free clinical remission (mPDAI=0) at T3 and T12, endoscopic response at T12 (improvement in PDAI Endoscopic Inflammation subscore reaching <3) and endoscopic remission at T12 (endoscopic PDAI ≤1). Non-response imputation was applied.

Results: Seventeen treatments with small molecules of CARP in 15 patients were collected from nine centres in seven countries. Eight patients were treated with tofacitinib; steroid and antibiotics-free clinical response at T3 was achieved in six patients (75%) and steroid and antibiotics-free clinical remission was achieved in five patients (62.5%). One patient discontinued tofacitinib for loss of response after eight months. Of the patients with at least 12 months of follow-up, steroid and antibiotics-free clinical response was achieved in 50% of patients, steroid and antibiotics-free clinical remission in one patient (16.7%), endoscopic response in 60%, endoscopic remission in 60%.

One patient was treated with filgotinib, neither steroid and antibiotics-free clinical response nor steroid and antibiotics-free clinical remission were achieved. Six treatments with upadacitinib were collected: at T3 steroid and antibiotics-free clinical response was achieved in 33.3% and steroid and antibiotics-free clinical remission was achieved in 16.7% of cases. Two cases were treated with ozanimod. At T3 steroid and anti-

otics-free clinical response was achieved in one patient (50%) and steroid and antibiotics-free clinical remission was not achieved. No side effects were reported. Main baseline characteristics are summarized in Table 1.

Age at JAK/S1P introduction	38.7 ($\pm$ 11.2)
Mean years (SD)	
Male, n (%)	10 (66.7)
Median years from IPAA (IQR)	50 (4.0-12.0)
Mean years from chronic pouchitis diagnosis (SD)	3.9 ($\pm$ 3.3)
Indication for IPAA, n (%)	Disease refractory to medical treatment, 12 (80.0) Cancer or dysplasia, 3 (20.0)
Target therapies before IPAA, n (%)	
Infliximab	11 (73.4)
Adalimumab	7 (46.7)
Vedolizumab	6 (40.0)
Biologics after IPAA for pouchitis, n (%)	
Infliximab	5 (33.3)
Adalimumab	4 (26.7)
Vedolizumab	9 (60.0)
Ustekinumab	5 (33.3)
Mean score of clinical part of mPDAI, (SD)	3.9 ($\pm$ 1.1)
Mean PDAI endoscopic inflammation subscore, (SD)	4.6 ($\pm$ 0.8)

Conclusion: In a multiple biologic-refractory population, small molecules might be a suitable treatment option for CARP. Based on current limited data, the use of JAK inhibitors should be further investigated.

References: ¹Okano S et al. A case of refractory chronic pouchitis successfully treated with tofacitinib. Clin J Gastroenterol 2020

²Dalal RS et al. Tofacitinib for the Treatment of Pouch-Related Disorders: A Case Series. Inflamm Bowel Dis 2022;

³Akiyama S et al. Treatment of Chronic Inflammatory Pouch Conditions With Tofacitinib: A Case Series From 2 Tertiary IBD Centers in the United States. Inflamm Bowel Dis 2023

⁴Uzzan M et al. Effectiveness and safety of tofacitinib in patients with chronic pouchitis multirefractory to biologics: A multicenter cohort study from the GETAID. Dig Liver Dis 2023

Disclosure: Nothing to disclose.

PP0648

SYSTEMATIC REVIEW WITH META-ANALYSIS OF THE EFFECTIVENESS OF SUBCUTANEOUS BIOLOGICS VERSUS INTRAVENOUS BIOLOGICS IN INFLAMMATORY BOWEL DISEASES

A. Elford^{1,2,3}, R. Heldt², S. Kamal⁴, B. Christensen^{1,2}, J.P. Segal^{1,2}

¹The University of Melbourne, Faculty of Medicine, Melbourne, Australia, ²The Royal Melbourne Hospital, Gastroenterology Department, Melbourne, Australia, ³NHS Lothian, Edinburgh IBD Unit, Edinburgh, United Kingdom, ⁴The Northern Hospital, Gastroenterology Department, Melbourne, Australia

Contact E-Mail Address: alexelford@live.com

Introduction: Biologic therapies are commonly used for inflammatory bowel disease (IBD) patients. Multiple biologic medicines can now be given both intravenously and subcutaneously. The different administration routes present provide different advantages regarding dose escalation, healthcare resource utilisation, pharmacokinetics, convenience, and safety.^{1,2} Comparator effectiveness studies between intravenous and subcutaneous administration are lacking.

Aims & Methods: Our primary outcome was to compare the effectiveness between intravenous (IV) and subcutaneous (SC) biologics in rates of clinical remission. We performed a systematic review and meta-analysis to include all relevant articles from MEDLINE (Ovid), EMBASE, PubMed, and Cochrane central register of controlled trials from January 1st, 1946 to January 28th, 2024. Studies that compared intravenous and subcuta-

neous administration of the same biologic therapy in IBD patients and reported effectiveness outcomes were included. Eligible studies had to include one of the following outcomes: [a] Clinical remission or response with a formalised clinical scoring system as defined by each study; [b] CRP remission; [c] faecal calprotectin remission. This study was registered on PROSPERO (CRD42023442675).

Results: Twenty studies met the inclusion criteria for the systematic review. There were only two randomised controlled trials and therefore were not analysed. There were eighteen cohort studies. One study was a prospective clinical trial switch from IV to SC vedolizumab. Twelve were prospective cohort studies. Five were retrospective cohort studies. Ten studies compared vedolizumab, seven studies compared infliximab and one study compared ustekinumab. We excluded the ustekinumab study given it was the only study evaluating ustekinumab. Of the 17 included studies, 15 were whole cohort switches from IV to SC formulations, with only 2 studies having both IV and SC arms. Nine vedolizumab cohort studies were meta-analysed for clinical remission and no difference was found in clinical remission rates between IV and SC administration (RR 0.99; 95% CI 0.88, 1.11). Six infliximab cohort studies were meta-analysed for clinical remission and no difference was found in rates of clinical remission between IV and SC administration (RR 0.91; 95% CI 0.77, 1.08). Four studies reported CRP remission rates (1 infliximab study and 3 vedolizumab studies), and the vedolizumab studies were meta-analysed. Seventy one percent (159/224) of the SC group and 71% (207/291) of the IV group were in CRP remission. The pooled RR was 0.88 (95% CI 0.88, 1.07; $p=0.09$). We observed a high degree of heterogeneity ($I^2 = 76\%$). Four studies, all studying vedolizumab, reported faecal calprotectin remission, and they were meta-analysed. Seventy six percent (158/207) of the SC group and 76% (140/183) of the IV group were in faecal calprotectin remission. The pooled RR was 0.99 (95% CI 0.90, 1.09). We observed no heterogeneity ($I^2 = 0\%$). The quality of the cohort studies was high, with no studies found to be at a high risk of bias.

Conclusion: There was no difference in the effectiveness between subcutaneous and intravenous administration of infliximab and vedolizumab respectively. However, further high-quality studies, particularly head-to-head studies are required to confirm this finding.

References: 1. Little RD, Ward MG, Wright E, Jois AJ, Boussioutas A, Hold GL, Gibson PR, Sparrow MP. Therapeutic Drug Monitoring of Subcutaneous Infliximab in Inflammatory Bowel Disease-Understanding Pharmacokinetics and Exposure Response Relationships in a New Era of Subcutaneous Biologics. J Clin Med. 2022 Oct 19;11(20):6173. doi: 10.3390/jcm11206173. PMID: 36294494; PMCID: PMC9605309.

2. Heald A, Bramham-Jones S, Davies M. Comparing cost of intravenous infusion and subcutaneous biologics in COVID-19 pandemic care pathways for rheumatoid arthritis and inflammatory bowel disease: A brief UK stakeholder survey. Int J Clin Pract. 2021 Sep;75(9):e14341. doi: 10.1111/ijcp.14341. Epub 2021 Jul 8. PMID: 33963659; PMCID: PMC8236906.

Disclosure: Dr. Alexander Elford is supported by the Australian Commonwealth government via a Research Training Program Scholarship. Dr Shahed Kamal and Miss Rishni Heldt have no conflicts of interest. A/Prof Christensen has received speaking fees from Abbvie, Janssen, Pfizer, Takeda and Ferring; research grants from Janssen and Ferring Pharmaceuticals and served on the advisory board of Gilead and Novartis. A/Prof. Jonathan P. Segal received speaker fees for Takeda and Abbvie, BMS and Falk Pharma and has a non-restricted grant from Tillots.

PP0649

TEDUGLUTIDE FOR THE TREATMENT OF SHORT BOWEL SYNDROME IN CROHN'S DISEASE PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

N.J. Milioli¹, V. Antunes², T. Correa³, O. Martins⁴, A.A. Prata⁵, A.C. Coan⁵, A.M. Reis⁶, E. Bulhões⁷, P. Romeiro⁸, M.V. Fernandes²
¹Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ²Federal University of Health Science of Porto Alegre, Porto Alegre, Brazil, ³Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁴Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁵Federal University of Espírito Santo, Vitória, Brazil, ⁶State University of Campinas, Campinas, Brazil, ⁷College of Higher Education of the United Amazon, Redenção, Brazil, ⁸Department of Medicine, University Center of Maceió, Maceió, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction: Severe Crohn's disease (CD) may progress to short bowel syndrome (SBS). Teduglutide stands as a validated treatment for SBS offering promising results for these patients.

Aims & Methods: This study aims to evaluate the performance of teduglutide in the subgroup of patients with SBS secondary to CD. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies with patients with SBS and CD treated with teduglutide. The primary outcome was the reduction of parenteral support (PS). The secondary outcome was discontinuation of PS. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I² statistics.
Results: The meta-analyses included 4 studies and 77 patients. All studies evaluated PS reduction and teduglutide demonstrated a good performance (PS reduction in 79.94% of the patients; 95% CI 57.97% to 100.00%; I²=85%). Three studies (61 patients) evaluated PS discontinuation and teduglutide demonstrated a good performance too (PS discontinuation in 28.59% of the patients; 95% CI 17.43% to 39.75%; I²=0%).

Conclusion: Teduglutide is a good therapeutic option for patients with SBS in the subgroup of CD patients, improving PS reduction and discontinuation and leading to better quality of life of these patients.

References: 1. Joly F, Seguy D, Nuzzo A, Chambrier C, Beau P, Poullenot F, et al. Six-month outcomes of teduglutide treatment in adult patients with short bowel syndrome with chronic intestinal failure: A real-world French observational cohort study. *Clin Nutr Edinb Scotl.* 2020 Sep;39(9):2856–62.
 2. Kochar B, Long MD, Shelton E, Young L, Farraye FA, Yajnik V, et al. Safety and Efficacy of Teduglutide (Gattex) in Patients With Crohn's Disease and Need for Parenteral Support Due to Short Bowel Syndrome-associated Intestinal Failure. *J Clin Gastroenterol.* 2017 Jul;51(6):508–11.
 3. Sato T, Uchino M, Takeuchi J, Fujihira Y, Shimizu K, Yokoyama K, et al. Short-term clinical evaluation of teduglutide for patients with Crohn's disease on home parenteral support for postoperative short bowel syndrome with intestinal failure. *Clin Nutr Edinb Scotl.* 2023 May;42(5):722–31.
 4. Siu RK, Karime C, Hashash JG, Kinnucan J, Picco MF, Farraye FA. Improved Outcomes Associated With Teduglutide Use in Patients With Both Short Bowel Syndrome and Crohn's Disease. *Crohns Colitis* 360. 2024 Jan;6(1):otae007.

Disclosure: Nothing to disclose.

PP0650

EFFICACY OF LOW-DOSE AZATHIOPRINE ASSOCIATED WITH ALLOPURINOL IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

N.J. Milioli¹, V. Antunes², O. Martins³, T. Correa⁴, A.A. Prata⁵, A.C. Coan⁵, A.M. Reis⁶, E. Bulhões⁷, P. Romeiro⁸, M.V. Fernandes²
¹Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ²Federal University of Health Science of Porto Alegre, Porto Alegre, Brazil, ³Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁴Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁵Federal University of Espírito Santo, Vitória, Brazil, ⁶State University of Campinas, Campinas, Brazil, ⁷College of Higher Education of the United Amazon, Redenção, Brazil, ⁸Department of Medicine, University Center of Maceió, Maceió, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction: Thiopurines are widely used for treating inflammatory bowel disease, either alone or in combination with anti-tumor necrosis factor alpha therapy. However, intolerance to thiopurines is common, leading to discontinuation of treatment in over 30% of individuals.

Aims & Methods: This study aims to evaluate the effectiveness of combined therapy of allopurinol with low-dose azathioprine concerning therapeutic response and improvement of therapy tolerance. We performed a systematic review in PubMed, Embase, Cochrane and Web of Science databases, searching for randomized studies that evaluated low-dose azathioprine therapy plus allopurinol versus azathioprine monotherapy. The primary outcome was clinical remission at weeks 14-16. The secondary outcomes were 6-TGN, 6-MMP and FC (fecal calprotectin) levels and FC lesser than 50ug/g rate. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I² statistics.

Results: The meta-analyses included 3 studies and 237 patients. There was a significant difference favoring low-dose azathioprine plus allopurinol in clinical remission (OR 2.46; 95% CI 1.43 to 4.25; p=0.001; I²=0%) and in 6-MMP levels (MD -2,329.89; 95% CI -3,869.68 to -790.11; p<0.01; I²=94%). There is no difference in 6-TGN levels (p=0.05) and FC levels (p=0.68).

Conclusion:

Patients using allopurinol plus low-dose azathioprine showed improved therapeutic adherence while maintaining superior clinical remission rates compared to azathioprine monotherapy.

References: 1. Kiszka-Kanowitz M, Theede K, Thomsen SB, Bjerrum JT, Brynskov J, Gottschalck IB, et al. Low-dose azathioprine and allopurinol versus azathioprine monotherapy in patients with ulcerative colitis (AAUC): An investigator-initiated, open, multicenter, parallel-arm, randomised controlled trial. *EClinicalMedicine.* 2022 Mar;45:101332.
 2. Kiszka-Kanowitz M, Theede K, Mertz-Nielsen A. Randomized clinical trial: a pilot study comparing efficacy of low-dose azathioprine and allopurinol to azathioprine on clinical outcomes in inflammatory bowel disease. *Scand J Gastroenterol.* 2016 Dec;51(12):1470–5.
 3. Vasudevan A, Con D, De Cruz P, Sparrow MP, Friedman AB, Garg M, et al. Clinical trial: Combination allopurinol-thiopurine versus standard thiopurine in patients with IBD escalating to immunomodulators (the DECIDER study). *Aliment Pharmacol Ther.* 2024 Feb;59(4):504–14.

Disclosure: Nothing to disclose.

PP0651

ROUTINE CARE DATA ANALYZED USING EXPLAINABLE ARTIFICIAL INTELLIGENCE IDENTIFY BEST THERAPEUTIC SEQUENCE OF 2ND LINE BIOLOGIC TREATMENTS AFTER A 1ST LINE WITH ANTI-TNF OR VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE

Y. Bouhnik¹, P. Iriso², B. Malahieude³, C. Stefanescu¹, C. Romdhane², Y. Benhayoun Sadafyine¹, J. Boulahfa², L. Peyrin-Biroulet¹, J. Neuberger³, X. Treton¹, F. Parmentier², M. Afshar²

¹Institut des MICI, Neuilly Sur Seine, France, ²Ariana Pharma, Paris, France, ³Instamed, Paris, France

Contact E-Mail Address: yoram.bouhnik@institutdesmici.fr

Introduction: Inflammatory bowel disease (IBD) includes Crohn's disease and ulcerative colitis, two conditions characterised by chronic inflammation of the gastrointestinal tract, which can damage the bowel and cause serious disabilities in patients' quality of life. Treatments only have a suspensive effect and the therapeutic sequences are currently based on reimbursement criteria or the prescriber's expertise, in a "trial-and-error" approach rather than on validated scientific evidence.

Routine clinical care data from 1,190 IBD patients collected by a private tertiary care centre dedicated to IBD patients, using the customised Instamed® platform, includes comprehensive information on the patient's treatment history, clinical variables and disease activity scores, in particular the Harvey-Bradshaw Index (HBI), Mayo Partial Score (MPS) and Simple Clinical Colitis Activity Index (SCCAI).

KEM® (Knowledge Extraction and Management) is an explainable Artificial Intelligence (xAI) platform using Formal Concept Analysis (FCA) that systematically extracts and evaluates all relations between variables in a database, thus enabling the identification of patient subgroups with greater likelihood of response to treatment sequences.

Aims & Methods: This study addresses the prevalent clinical challenge of uncertainty in treatment selection following the initial administration of anti-TNF or vedolizumab given as first-line therapy for IBD, aiming to identify the most effective second-line treatment options.

Data were aggregated into a consolidated database of 1,190 patients and 1,269 variables within the KEM® xAI Platform. Patients with at least 2 treatment lines were selected. To ensure a strong causality between treatment prescription and response, the maximal number of treatment lines was limited to 3. The outcome used was therapeutic response after three treatment lines, evaluated using HBI, PMS and SCCAI. Within 19,230,463 associations between sequence of the first two treatment lines and the response, 70 associations were retained by KEM® with successful treatment sequence with anti-TNFs, vedolizumab or thiopurine as first treatment line.

Results: 285 patients fulfilled the analysis criteria. We identified hypotheses in favor of a second-line biological treatment (ustekinumab, JAKi, 2nd anti-TNF) after failure of a first-line treatment with anti-TNF or vedolizumab. Ustekinumab was 2 times more likely to be associated with a response to treatment. JAKi was 2 times less likely to be associated with a response to treatment. The 2nd anti-TNF was associated with a response to treatment in a specific subgroup. Moreover, successful treatment sequences with patient count above 10 and up to 30, involved thiopurine as first line of treatment, followed by anti-TNFs or thiopurine repeated as second line of treatment.

Conclusion: We show a powerful setup using routine clinical care data from an initial set of 1,190 IBD patients and the KEM® xAI platform to provide actionable hypotheses supporting therapeutic decisions for disease management. These initial results will be further tested and validated as we accumulate real-life data on new patients and complete the follow-up of patients already included. The flexibility of our

platform will enable us to include more therapeutic sequences and to add all the new treatments available in current clinical practice. This will allow us to offer continuous, up-to-date support for difficult medical decisions, enabling patient management to be guided by results observed in real life and leading de facto to precision medicine.

Disclosure: Nothing to disclose.

PP0652

REAL-LIFE USE OF THE CROHN'S DISEASE EXCLUSION DIET (CDED) IN ADULT PATIENTS WITH MILD-TO-MODERATE CROHN'S DISEASE ACTIVITY: AN OPEN-LABEL, RANDOMIZED CONTROLLED TRIAL

A. Pasta¹, E. Formisano¹, F. Calabrese¹, M. Apollonio¹, L. Pisciotta¹, G. Bodini¹, E.G. Giannini¹

¹University of Genoa, Genoa, Italy

Contact E-Mail Address: andreapasta93@gmail.com

Introduction: The Crohn's Disease Exclusion Diet (CDED) is a dietary approach that exclude specific foods to induce remission in Crohn's disease (CD).

Aims & Methods: We conducted an open-label, randomized controlled trial including adults with mild-to-moderate CD, as determined by the Harvey-Bradshaw Index (HBI). Patients were randomly assigned to either CDED or a control diet (Mediterranean pattern). At enrollment, we collected demographic data and medical histories. We measured weight, body mass index (BMI), HBI, fecal calprotectin, and serum inflammatory markers at baseline, 12 and 24 weeks. Bioelectrical impedance analysis (BIA) evaluated safety for CDED participants. The primary outcome was clinical remission (HBI<5), measured in the intention-to-treat population. This study aims to provide a real-world evidence.

Results: Twenty-four patients were randomized to the CDED diet and 21 to the control group, without significant differences at baseline. Five CDED participants discontinued the diet for intolerance by a median of 5 weeks. After 12 and 24 weeks, CDED patients showed significantly lower HBI and higher remission rates compared to control group (70.8% vs 38.1% at 12 weeks and 79.2% vs 42.9% at 24 weeks; p=0.027 and p<0.0001, respectively). Fibrinogen resulted significantly lower in CDED than control group at week 24. CDED participants reported a median BMI reduction from 25.8 kg/m² to 24.4 kg/m² at 12 weeks and 24.5 kg/m² at 24 weeks (p=0.047), although BIA analysis indicated a reduction in fat mass after 12 and 24 weeks (p<0.001 and p<0.001, respectively) while fat-free mass and body cellular mass significantly increased at 12 weeks (p=0.001 and p=0.042, respectively) and remained stable at 24 weeks (p=0.072 and p=0.120, respectively).

Conclusion: The CDED has proven to be safe and effective for achieving remission in adults with mild-to-moderate CD.

Disclosure: No conflict of interest to disclose.

PP0653

IMPACT OF THE INTRA-OPERATIVE USE OF CORTICOSTEROIDS AND LOCAL ANESTHETICS ON THE POST-OPERATIVE OUTCOME OF INTESTINAL BOWEL DISEASE PATIENTS UNDERGOING SURGERY FOR THEIR CHRONIC DISEASE

A. Cuzzucra¹, R. Rozier¹, M.A. Rahili², A. Nicolau³, O. Perus¹, X. Hebuterne³

¹Hospital Archet 2, Department of Anaesthesia, Nice, France,

²Hospital Archet 2, Department of Visceral Surgery, Nice, France,

³Hospital Archet 2, Nice, Department of gastroenterology and clinical nutrition, Nice, France

Contact E-Mail Address: anthony.cuzzucra@gmail.com

Introduction: Surgical resections are an integral part of the management of patients with inflammatory bowel diseases (IBD). Typically, for patients with complicated or drug-resistant Crohn's disease (CD), ileocecal resection (ICR) is becoming the treatment of choice. In this inflammatory context, post-operative complications affect 15 to 30% of patients.

The aim of this study was therefore to assess the impact of molecules with anti-inflammatory properties, such as local anesthetics (LA) and/or dexamethasone (DXM), used during the surgical period, on the post-operative outcome of CD patients undergoing surgery for their chronic disease.

Aims & Methods: We conducted a retrospective, monocentric study, including all inflammatory bowel diseases (IBD) patients who underwent major surgery related to their disease. We compared patients who received the combination of LA and DXM (LA+DXM group) versus the remaining patients who received only one of the two or neither (non-LA+DXM group). The primary endpoint was overall morbidity within 30 days post-operatively, assessed according to the Clavien-Dindo classification. The secondary endpoints were minor (mC) and major complications (MC), Comprehensive Complication Index (CCI), length of hospitalization, perioperative kinetics of inflammatory markers and pain assessment, and intra- and postoperative morphine consumption.

Results: Between January 2015 and December 2021, a total of 426 patients were operated and were 219 analyzed. Of these, 114 CD were operated on for scheduled ICR. 49 patients received the combination of LA+DXM during surgery and 65 did not (non-LA+DXM). The percentage of complications were 33% vs 60% in the LA+DXM vs non-LA+DXM groups, respectively. In univariate analysis, overall post-operative morbidity was statistically reduced in the LA+DXM group (OR 0.32 [0.15- 0.70], $p = 0.007$), and this result was confirmed after logistic regression (OR 0.26 [0.11-0.63], $p = 0.003$). This reduction in morbidity was also linked to a reduction in mC in the LA+DXM group (OR 0.28 [0.07-0.92], $p = 0.005$), as well as a clear trend towards a reduction in MC. Median length of hospital stay was 8 days for the LA+DXM group vs. 9 days for the non-LA+DXM group ($p = 0.02$). Regarding the post-operative inflammatory syndrome, despite a tendency to decrease in the LA+DXM group, there was no statistical difference in thresholds set at D3, D5 and D7. On the other hand, patients in the LA+DXM group received less intraoperative opioids (83.3mg morphine-equivalent vs. 54.76mg for the LA+DXM group, $p < 0.01$), and the total quantity of opioids titrated in the recovery room was also lower (40.5mg vs. 30mg for the LA+DXM group, $p = 0.01$).

Conclusion: Intraoperative co-administration of LA+DXM in CD patients undergoing scheduled ileocecal resection for chronic disease significantly reduces overall postoperative morbidity. A controlled study is needed to confirm these promising results.

Disclosure: Nothing to disclose.

PP0654

EFFICACY OF USTEKINUMAB IN PREVENTING POST-OPERATIVE RECURRENCE IN A REAL LIFE COHORT OF PATIENTS WITH CROHN'S DISEASE

A. Del Gaudio¹, L.R. Lopetuso¹, G. Cuccia¹, D.V. Federica¹, G. Coppola¹, L. Laterza², L. Parisio¹, D. Pugliese², A. Papa², G. Cammarota², F. Scaldaferri¹

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Roma, Italy, ²Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Rome, Italy

Contact E-Mail Address: delgaudioangelo@gmail.com

Introduction: Prevention of postoperative recurrence (POR) after ileocolonic resection is one of the most relevant issues in the management of Crohn's disease (CD). The role of ustekinumab (UST) especially in the context of real-life studies is still not entirely clear, often due to small sample sizes, thus requiring further investigation and confirmation (1).

Aims & Methods: Our real life single-centre retrospective study aims to evaluate the effect of UST therapy on prophylaxis of endoscopic recurrence after ileo-colonic resection in CD. In the whole cohort UST was used as first-line therapy for prophylaxis of recurrence. All patients (pts) underwent the first endoscopic evaluation within 6-12 months after surgery to assess postoperative recurrence (POR), using the Rutgeerts score and were subsequently evaluated at 22 (+3) months with a second endoscopy. Persistence on therapy ~ two years after the surgery was also evaluated.

Results: 27 pts with a mean age of 51 years old were included. 40% of pts had previously been resected and 45% were active smokers. 93% had already been exposed to one or more biological drugs. The most frequent reason for surgery was the presence of stenosing disease. The first post-operative colonoscopy at 6-12 months, showed severe POR (RS score i3 or i4) in 19% of patients, so 11% changed treatment at this time point. Among patients who continued the drug (24 pts), the second endoscopy performed at 22 (+3) months showed severe POR in 13% of pts, whose treatment was subsequently changed.

At ~ 2 years persistence on therapy in the cohort was 78%, notably endoscopic remission (RS<2) was found in 37%.

No patients discontinued the drug due to adverse effects.

Conclusion: In our real life cohort of complex CD patients, ustekinumab showed high levels of persistence on therapy at the point of time considered, although less than half of the patients achieved endoscopic remission.

References: 1- Tursi A, Mocci G, Picchio M, Elisei W, Maconi G. Letter: ustekinumab for the treatment of post-surgical and refractory Crohn's disease. *Aliment Pharmacol Ther.* 2021 Apr;53(7):859-860. doi: 10.1111/apt.16281. PMID: 33709395.

Disclosure: None/

PP0655

MIRIKIZUMAB PHARMACOKINETICS AND EXPOSURE-RESPONSE IN PEDIATRIC PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 2 SHINE-1 STUDY

Y. Otani¹, L. Chua², W. Komocsar¹, A. Larkin¹, X. Zhang¹

¹Eli Lilly and Company, Indianapolis, United States of America,

²Eli Lilly and Company, Singapore, Singapore

Contact E-Mail Address: otani_yuki@lilly.com

Introduction: Mirikizumab is a p19-directed anti-interleukin-23 antibody approved for treatment of adults with moderately to severely active ulcerative colitis (UC). Here, we report mirikizumab pharmacokinetics and exposure-response in pediatric patients with moderately to severely active UC from the phase-2, multicenter, open-label study SHINE-1 (NCT04004611).

Aims & Methods: Patients aged 2 to <18 years weighing >10kg with a modified Mayo score (MMS) of 4-9 and endoscopic subscore ≥2 received intravenous mirikizumab induction doses (300mg for weight >40kg; 5 or 10mg/kg for weight ≤40kg) every 4 weeks (Q4W) through Week 12. At Week 12, patients achieving MMS clinical response received subcutaneous maintenance doses of mirikizumab 200mg (>40kg), 100mg (>20-≤40kg), or 50mg (≤20kg) Q4W for 36 weeks. Pharmacokinetic parameters were analyzed by nonlinear mixed-effects modeling with fixed allometry for size. Covariate effects on mirikizumab exposure were evaluated using simulation-based estimations. Exposure-response for patients achieving clinical response, remission, and endoscopic response at Weeks 12 and 52 were explored using graphical approaches.

Results: The analysis included 232 samples from 26 patients. Estimated systemic clearance, volume of distribution, and subcutaneous bioavailability were 0.000296 L/hr/kg, 0.069 L/kg, and 49.8%, respectively. Pharmacokinetic model-estimated exposures in all weight groups were similar to those in adult phase-3 studies LUCENT-1 (NCT03518086) and LUCENT-2 (NCT03524092) except for the 10-mg/kg induction dose, which was 2-fold higher (Figure). In the exposure range studied in SHINE-1, exposure-response analysis using post-hoc grouping by average concentration quartile revealed no improvement trend in clinical response, remission, or endoscopic response and showed similar efficacy to that in adults.

Conclusion: Mirikizumab pharmacokinetic exposures and efficacy results at intended phase-3 doses across all pediatric weight groups were similar to those reported in adults. No patient factors other than weight justify dose adjustment. Exposure-matching to the adult exposure data and exposure-response analysis support a phase-3, weight group-divided dosing strategy in pediatric patients.

Disclosure: Y. Otani, L. Chua, W. Komocsar, A. Larkin and X. C. Zhang are employees and shareholders of: Eli Lilly and Company.

PP0656

EFFICACY OF USTEKINUMAB IN THE TREATMENT OF POST-OPERATIVE RECURRENCE IN A REAL LIFE COHORT OF PATIENTS WITH CROHN'S DISEASE

A. Del Gaudio¹, L.R. Lopetuso¹, G. Cuccia¹, D.V. Federica¹, G. Coppola¹, L. Laterza¹, L. Parisio¹, D. Pugliese¹, A. Papa¹, G. Cammarota¹, A. Gasbarrini², F. Scaldaferri¹

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Rome, Italy, ²Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy

Contact E-Mail Address: delgaudioangelo@gmail.com

Introduction: Treatment of post-operative recurrence (POR) after ileocolonic resection is one of the most challenging issues in the management of Crohn's disease (CD). The role of ustekinumab (UST), especially in the context of real-world studies, is still not entirely clear, often due to small sample sizes. Recent studies report encouraging results, with endoscopic remission rates even more than 50% of CD patients, but data are quite heterogeneous (1,2).

Aims & Methods: Our retrospective single-centre real-life study aims to evaluate the effect of UST therapy on the treatment of relapse after ileo-colonic resection in CD. In our cohort, UST was used as second-line therapy in case of recurrence or intolerance of previous therapy.

All patients underwent endoscopic or radiological re-evaluation up to 18 months after the start of therapy. Endoscopic success, defined as a reduction of at least one point in the Rutgeerts score, or radiological success, defined as improvement in the judgement of the radiologist who performed the examination or the multidisciplinary IBD team at our centre, were evaluated. Persistence in therapy ~ two years after surgery was also assessed.

Results: 27 pts with a mean age of 37 years old at surgery were included. 37% of pts had previously been resected and 56% were active smokers. All pts had already been exposed to one or more biological drugs. The most frequent reason for surgery was the presence of stenosing disease. The mean time to start UST therapy since surgery was 21 months.

The reasons for initiation of UST were recurrence of endoscopic and/or radiological disease, or intolerance to previous therapy, Cohort 1 and Cohort 2, respectively.

In Cohort 1 (19 pts) an instrumental re-evaluation was performed after a mean of 14.4 ± 3.3 months following initiation of UST. Endoscopic or radiologic success was reported in 68% 13 of pts, of whom radiologic or endoscopic remission was achieved in 47.3%.

In Cohort 2 (10 pts) an instrumental re-evaluation was performed after a mean of 15.5 ± 3.5 months following initiation of UST, there were no patients who had advanced endoscopic (RS ≥ 3) and/or severe radiological recurrence of disease at the start of UST in this group. Only one patient showed endoscopic worsening of disease since the start of UST and discontinued treatment. 90% of pts had radiological or endoscopic improvement or stability of disease, of which remission was achieved in 50%.

In the entire cohort (27 pts), persistence on therapy at ~ two years was 74%, and radiological or endoscopic remission in 51%.

Conclusion: In our real life cohort of patients with CD, ustekinumab showed high levels of persistence to therapy at time point considered, with a satisfactory result on endoscopic and/or radiological remission of disease.

References:

1-Tursi A, Mocci G, Picchio M, et al. Maconi G. Letter: ustekinumab for the treatment of post-surgical and refractory Crohn's disease. *Aliment Pharmacol Ther.* 2021;53:859-860

2-Macaluso FS, Grova M, Mocciaro F, et al. Sicilian Network for Inflammatory Bowel Disease (SN-IBD). Ustekinumab is a promising option for the treatment of post-operative recurrence of Crohn's disease. *J Gastroenterol Hepatol*. 2023;38:1503–1509.

Disclosure: None.

PP0657

THE PLACE OF ENDOSCOPIC DILATATION IN THE MANAGEMENT OF STENOSES IN STENOSING CROHN'S DISEASE.

F.Z. Mghyly¹, S. Mechhor², M. Cherkaoui Malki², H. El Bacha⁴, N. Benzoubeir¹, I. Errabih⁵

¹Ibn Sina University Hospital, Mohammed V University, Department of Hepato-Gastroenterology and Proctology "Medecine B", Rabat, Morocco, ²Ibn Sina Hospital, Medecine B, Rabat, Morocco, ³University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ⁴Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: mghylyfatimazahra@gmail.com

Introduction: Crohn's disease (CD) is a chronic inflammatory condition of the digestive tract characterized by a cyclical course, the most frequent and feared complication is the formation of stenoses. The management of these stenoses is often multidisciplinary medico-surgical as well as endoscopic.

Endoscopy plays an essential role in the diagnosis, monitoring, and treatment of these stenoses, particularly through endoscopic dilations. The objective of our work is to study the role of endoscopic dilations during stenosing Crohn's disease in addition to medical treatment.

Aims & Methods: This is a single-center descriptive retrospective study carried out within our department over a period of 6 years: from January 2018 to January 2024, including all patients followed for stenosing Crohn's disease who underwent endoscopic dilation. We collected data related to age, history, location, phenotype, clinical symptoms, endoscopic data as well as evolution.

Results: We included 19 patients followed in our training for stenosing Crohn's disease who benefited from endoscopic dilation out of a total of 109 patients followed for Crohn's disease with a stenosing phenotype (17.4%). The average age was 45 years with extremes ranging from 20 to 71, with a male predominance and a M/F sex ratio: 2.8 (14 M and 5 F). Three patients were smokers (15.8%), 6 patients underwent anterior ileocecal resection (31.6%) and a total colectomy ATCD in one patient (5.3%). The median time from diagnosis of Crohn's disease to formation of symptomatic stenosis was 9.3 years.

Clinically, abdominal pain was present in 8 patients (42.1%), Koenig syndrome in 7 patients (36.8%), diarrhea in 3 patients (21%), 4 patients (28.5%) had defecatory pain, evacuation constipation in 3 patients (15.8%) and late postprandial vomiting was present in 1 patient (5.3%). The stenosis was at the last ileal loop in 5 cases (26.3%), 4 (21%) at the rectal level, 1 stenosis respectively at the colonic, anal, esophageal, pyloric and duodenal level (5.3% each) and 5 stenoses at the level of the anastomosis including 4 (21%) at the level of the ileocolic anastomosis and 1 at the level of the ileorectal anastomosis (5.3%).

The average length of the stenoses was 19.2 mm with extremes ranging from 5 to 40 mm. Dilations were carried out using hydrostatic dilation balloons whose caliber varied between 10 and 16.5 mm, 3 (15.8%) patients benefited from dilation to 16.5 mm, 7 (36.8%) at 12mm, 6 (31.6%) at 15mm, and 2 (10.5%) at 11mm.

11 patients benefited (57.9%) from a single dilation session, 7 patients benefited from 2 dilations (36.8%) and 1 patient (5.3%) had recourse to 5 dilations.

Primary success defined by the passage of the endoscope was possible in 15 patients (78.9%). Only one perforation type complication was noted, treated surgically.

The secondary success rate defined by the disappearance of symptoms was in 9 patients (47%). The average follow-up was 31.8 months and the clinical recurrence rate was 37.5% at 6 months. 4 patients (21%) benefited from additional surgery.

Conclusion: Endoscopic dilation is a minimally invasive treatment which constitutes an effective alternative to surgery in the management of stenoses during Crohn's disease; in our study more than half of our patients only had recourse to a single dilation session with a primary success of more than 78.9%, and a disappearance of symptoms at 6 months in almost half of the patients, thus making the use of surgery less frequent.

Disclosure: Nothing to disclose.

PP0658

MANAGEMENT OF ACUTE SEVERE COLITIS IN CROHN'S DISEASE

S. Kaouissi¹, S. Mechhor¹, M. Cherkaoui Malki¹, H. El Bacha¹, N. Benzoubeir¹, I. Errabih¹

¹University Mohamed V, Department of Hepato-Gastroenterology and Proctology Medicine B, Rabat, Morocco

Contact E-Mail Address: S.kaoui@um5r.ac.ma

Introduction: Acute severe colitis (ASC) is a medical-surgical emergency that can occur at any time during the course of chronic inflammatory bowel disease. It most commonly affects UC.

Aims & Methods: Aims: The aim of our work is to describe the particularities of GCA management during Crohn's disease (CD).

Materials and methods: This is a retrospective descriptive and analytical study spread over a 5-year period from January 2018 to January 2023. All patients who developed GAC during the course of Crohn's disease, whether inaugural or progressive, were included in our study. Data collected included age, sex, Crohn's disease location and phenotype, Lichtiger score before and after corticotherapy, second-line treatment, and use of surgery. SPSS 2.0 software was used for the statistical study. A binary logistic regression model was used for univariate analysis.

Results: Of the 424 IBD cases, 267 were being followed for Crohn's disease, of whom 38 (14.2%) patients presented with GAC. Mean age was 44.21 ± 12.7 years (range 19-72 years). The F/H sex ratio was 1.9 (25 women to 13 men). The location of Crohn's disease was pancolic in 28 patients, ileocolic in 9, and ileocolic with high involvement in 1 patient. GCA was inaugural in 10 patients (26.3%), and complicated known Crohn's disease in 28 patients (73.7%). The mean Lichtiger score calculated at D0 was 11.84 ± 1.8. The mean CRP value on admission was 89.8 ± 47. Mean albumin was 27.9 ± 3.6. Emergency abdomino-pelvic CT scans showed no complications such as colectasis, perforation or abscess in our series. All patients received IV methylprednisolone corticosteroids at a dose of 0.8 mg/kg/d, not to exceed 40 mg/d, with close clinico-biological monitoring. 21 patients (55.2%) were corticosteroid sensitive. The mean Lichtiger score calculated at D5 in corticosteroid sensitive patients was 8.7, with a mean CRP value at D3 of 36.8 ± 12.

In univariate analysis, CRP > 45 (on admission) and hypoalbuminemia were predictive factors for failure of IV corticosteroid therapy, with [OR = 3.2 [1.3-5.2]; p = 0.0005] and [OR = 1.31 [1.015-7.], p = 0.002] respectively. Of the 17 (44.8%) corticosteroid-resistant patients, 3 (7.9%) received emergency second-line treatment with Infliximab, and 15 (39.47%) underwent subtotal colectomy with ileostomy. Of these patients, one was scheduled after

failure of second-line treatment. Good outcome was noted in 36 patients (94.7%). 2 cases of death (5.3%) were reported postoperatively. On discharge, 23 patients (63.9%) were treated with immunosuppressive agents or 13 (36.1%) with biotherapy.

Conclusion: Acute severe colitis can reveal or complicate Crohn's disease at any stage of its evolution. Management must be urgent, and requires medical-surgical coordination. The first-line medical treatment is intravenous corticosteroid therapy. Colectomy should be discussed at every stage of management.

Disclosure: Nothing to disclose.

PP0659

EFFICACY OF DIFFERENT MODALITIES OF FAECAL MICROBIOTA TRANSPLANTATION TO INDUCE CLINICAL REMISSION IN PATIENTS WITH ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

J. Chapon¹, J. Scanzi¹, H. Sokol², B. Pereira¹, A. Buisson¹

¹CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-Ferrand, France, ²Saint-Antoine Hospital, Gastroenterology Department, Paris, France

Contact E-Mail Address: a_buisson@hotmail.fr

Introduction: To compare the efficacy of different modalities of FMT to induce clinical remission in patients with ulcerative colitis (UC).

Aims & Methods: We performed a systematic review and network analysis (random effects model) of randomized controlled trials including at least one arm of FMT in adult patients with active UC.

Primary endpoint, i.e. clinical remission (total Mayo score ≤ 2 with Mayo endoscopic score ≤ 1), was assessed between week 6 and 12. Results are expressed as relative risk with 95% confidence intervals, adjusted for bowel cleansing and pre-FMT antibiotics therapy.

Ranking of FMT modalities for clinical remission was calculated as their surface under the cumulative ranking (SUCRA), which represents the percentage of efficacy achieved by an agent compared with an imaginary agent that is always the best without uncertainty. Heterogeneity among studies was evaluated by τ (global statistical heterogeneity across all comparisons).

Results: Among the 12 selected studies, patients were exclusively bio-naïve in 4 studies (4/12), while between 9 and 32% had prior biologics exposure in the other trials. Risk of bias was low across all domains in 7 studies. Global heterogeneity was negligible ($\tau = 0$). After adjustment on bowel cleansing and pre-FMT antibiotics, oral capsule (RR=7.1[1.8-33.3]), lower GI FMT (RR=4.5[1.7-12.5]) and combination of both (RR=12.5[2.1-100]) were more effective than placebo to induce clinical remission contrary to upper GI FMT (RR=1.1[0.2-7.7]) and autologous FMT (RR = 0.8 [0.2-3.8]).

The combination of lower GI FMT and oral capsule was significantly more effective than upper GI FMT to induce clinical remission (RR=10.7[1.1-104.2]). Combination of lower GI FMT and oral capsule ranked highest for the induction of clinical remission (SUCRA=0.93), followed by oral capsule (SUCRA=0.82) and lower GI FMT (SUCRA=0.72). Autologous FMT ranked lower than placebo (SUCRA=0.12 vs 0.22). We performed a sensitivity analysis distinguishing single donor FMT and multi-donor FMT (pooled samples from different donors). Combination of lower GI FMT and oral capsule ranked highest for the induction of clinical remission (SUCRA=0.89), followed by single donor lower GI FMT (SUCRA = 0.70), multi-donor (pooled samples) lower GI FMT (SUCRA = 0.65), multi-donor (pooled samples) oral capsule (SUCRA = 0.61), single donor oral capsule (SUCRA = 0.60).

Conclusion: In this network meta-analysis, we confirmed the efficacy of FMT to induce clinical remission in patients with UC. The combination of lower GI and oral capsule FMT seems to be the best modality of FMT for

patients with UC while upper GI FMT is not suitable. In clinical trials, autologous FMT should be avoided due to a potential detrimental effect.

Disclosure: Anthony BUISSON: Consulting fees for Abbvie, Amgen, Arena, Biogen, Celltrion Healthcare, CTMA, Galapagos/Alfa Sigma, GutyCare/Resilience, Janssen, MSD, Nexbiome, Pfizer, Roche, Sandoz, Takeda, Tillotts. And Viatrix. Lecture fees for Abbvie, Amgen, Biogen, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Mayoli-Spindler, MSD, Nordic Pharma, Norgine, Pfizer, Roche, Takeda, Tillotts and Vifor Pharma. Research grants from: Abbvie, Celltrion Healthcare, Galapagos/Alfa Sigma, Janssen, Lesaffre, Lilly, Pfizer, Takeda.

PP0660

THE PREDICTIVE VALUE OF GAMMA-GLOBULIN AND ALBUMIN LEVELS IN ASSESSING ANTI-TNF RESPONSE IN INFLAMMATORY BOWEL DISEASE

N. Ammar¹, H. Gdoura², S. Mahmoudi¹, M. Moalla², L. Chtourou², M. Boudabous², L. Mnif², A. Amouri², T. Nabil²

¹Faculty of Medicine of Monastir, Monastir, Tunisia, ²Faculty Of Medicine Of Sfax, Sfax, Tunisia

Contact E-Mail Address: ammar.nawrass@gmail.com

Introduction: Loss of response to anti-TNF α therapy is a significant challenge in the management of inflammatory bowel disease (IBD) patients. Identifying predictive biomarkers for this outcome could aid in treatment optimization.

Aims & Methods: This study aimed to evaluate the predictive value of serum γ -globulin and albumin concentrations for treatment failure to anti-TNF α therapy in patients with IBD.

This was a retrospective analytical study conducted at the Gastroenterology Department of Hedi Chaker University Hospital in Sfax. The study spanned a 16-year period from 2007 to 2023. All patients with inflammatory bowel disease (IBD) treated with anti-TNF therapy were included. Patients using anti-TNF therapy for extra-intestinal manifestations of IBD were excluded.

Epidemiological data, characteristics of IBD, biological and endoscopic parameters, as well as fecal calprotectin levels, were collected. Serum albumin and γ -globulin levels were measured as part of the pre-anti-TNF assessment. Therapeutic evaluation followed the STRIDE-II strategy.

Results: The study included a total of 116 patients, among whom 82 had Crohn's disease (CD) and 34 had ulcerative colitis (UC). The mean age at diagnosis was 30.91 ± 12.227 years for all patients, with slightly lower ages observed in CD patients (30.49 ± 13.137 years) compared to UC patients (31.94 ± 9.792 years). 103 patients (88.8%) received infliximab as their first-line anti-TNF therapy while 11.2% patients were initially treated with adalimumab.

The study observed a primary non-response rate of 24.1% (n=28) across all patients with IBD. This rate was significantly higher in patients with UC compared to those with CD (47.1% vs 14.6%; $p < 0.001$).

Secondary loss of response was noted in 47.9% of cases (n=46), with a higher frequency observed among CD patients compared to UC patients (52% vs 33.3%), although this difference was not statistically significant. Regarding specific associations with treatment response, in patients with CD, primary non-response was significantly linked to the presence of hypergammaglobulinemia ($>13.5\text{g/l}$) ($p=0.009$).

In contrast, for patients with UC, secondary loss of response was notably associated with moderately elevated gammaglobulinemia levels ($p=0.039$). Notably, there was no significant association observed between albumin levels and treatment response in either patient group.

Parameter	Total (n=116)	Crohn's (n=82)	UC (n=34)
Age at First Anti-TNF Introduction (years, $\pm$ SD)	36.38 $\pm$ 13.355	35.96 $\pm$ 13.777	37.38 $\pm$ 12.417
Gender Male, n (%)	67 (57.8%)	46 (56.1%)	21 (61.8%)
Albuminemia - Number (%)	95 (81.9%)	65 (79.3%)	30 (88.2%)
- Albuminemia (g/l), Mean $\pm$ SD	33.484 $\pm$ 5.9794	33.269 $\pm$ 5.8248	33.95 $\pm$ 6.3787
- Hypoalbuminemia (<35 g/l), n (%)	26 (27.4%)	20 (30.8%)	6 (20%)
Gammaglobulinemia - Number (%)	87 (75%)	60 (73.2%)	27 (79.4%)
- Gammaglobulinemia (g/l), Mean $\pm$ SD	12.555 $\pm$ 3.902	12.48 $\pm$ 3.635	12.722 $\pm$ 4.5095
- Hypergammaglobulinemia (>13.5 g/l), n (%)	32 (36.8%)	22 (26.7%)	10 (37%)

Table 1: Demographic, Clinical Characteristics, and Biological Parameters of IBD Patients

Conclusion: this study highlights the potential utility of serum biomarkers, particularly gammaglobulinemia, in predicting response to anti-TNF α therapy in IBD patients. Further research in this area could contribute to personalized treatment strategies aimed at improving therapeutic outcomes in this challenging patient population.

Disclosure: No conflict.

PP0661

MEDICAL TREATMENT OF CAPSULE RETENTION IN CROHN'S DISEASE: A SYSTEMATIC REVIEW

P.F. da Silva Mesquita¹, R.T. Pinho², M.M. Estevinho³, C. Costa³, T. Freitas³, A. Ponte³

¹Centro Hospitalar Vila Nova de Gaia/Espinho, Gastroenterology, Vila Nova de Gaia, Portugal, ²Gastreterologia, Centro Hospitalar Vila Nova de Gaia, Senhora da Hora, Portugal, ³Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal, Gastroenterology, Porto, Portugal

Contact E-Mail Address: pedro.filipe.silva.mesquita@gmail.com

Introduction: Capsule retention is the main adverse event of SBCE. Current guidelines support the use of conservative/medical treatment for asymptomatic patients. However, the appropriate duration of conservative and medical therapy, the optimal regimens, and the timing to perform DAE/surgery in asymptomatic patients is still largely undefined.

Aims & Methods: Through a systematic search of multiple electronic databases until November 2023, studies including CD patients undergoing capsule endoscopy (CE) were identified. Capsule retention was defined according to ICCE criteria.

Results: We included 42 studies, totaling 196 capsule retentions in CD patients. Of these, 50 underwent anti-inflammatory therapy, consisting of corticosteroids (n= 34); corticosteroids + antibiotics (n=1), and corticosteroids + infliximab (n= 15). Steroids allowed for spontaneous passage in 44% (n=22): 3 out of 16 asymptomatic patients; 3 out of 5 symptomatic without complete small bowel occlusion (SBO); 2 in 3 with complete SBO. Combination with infliximab solved the retention in further 6 out of 15 patients. Mean time to resolution was 6,9 days (R 15h-21d), which was reported in 6 patients. Steroid administration route was reported in 2 patients (intravenous) and dosage in 3 patients: 100mg for 3 days, 1.2 mg/kg/day for 17 days, 0.5 mg/kg/day for 17 days, the latter being unsuccessful. Conservative treatment only or after failed medical therapy was used in 19 asymptomatic patients, with spontaneous passage in 6. One study reports retention of a capsule for 8.5 years. Of patients undergoing medical treatment 3 underwent urgent and 15 programed surgeries.

Conclusion: Evidence was of low quality. Treatment duration, regimen and time to spontaneous passage was underreported. We were unable to find predictors of the need to perform DAE/surgery in asymptomatic patients. As capsule retentions are increasingly rarer, the available evidence is unlikely to change.

Disclosure: Nothing to disclose.

PP0662

OUTCOMES OF STEM CELL THERAPY FOR ANO-PERINEAL CROHN'S DISEASE : A PROSPECTIVE STUDY

S. Oubaha^{1,2}, O. Nacir¹, F. Aharbil³, K. Krati¹
¹Department of GastroEnterology and Hepatology, Mohammed VI University Hospital Centrre, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco,
²Department of Physiology, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco,
³Department of GastroEnterology and Hepatology, Mohammed VI University Hospital Centrre, Marrakech, Morocco

Contact E-Mail Address: o.nacir@uca.ac.ma

Introduction: Perianal fistulas, which may be difficult to treat, are a common complication of Crohn's disease, which is a chronic disorder that is complex and difficult to control. The purpose of our research was to determine whether or not it would be possible and safe to inject hematopoietic mesenchymal stem cells into these patients' bodies, as well as to investigate the effectiveness of the therapy over a period of forty-eight weeks.

Aims & Methods: Between April 2022 and November 2023, we went through the process of conducting a prospective observational research at our hospital. Twenty-three adult patients who were diagnosed with Crohn's disease and perianal fistulas were included in our study. Hematopoietic stem cells were extracted from the bone marrow of every individual patient and delivered at a dosage of 3x10⁶ cells. The first half of the cells were injected into the entrance of the internal fistula, while the second half was put into the opening of the exterior fistula. The surgery was followed by the administration of an intravenous stem cell infusion to a certain number of individuals.

Results: 36 percent of patients had achieved full closure of all external fistula openings by the 12th week of therapy, and this percentage improved to 52 percent by the 48th week of treatment. The majority of patients who originally presented with more than two external openings showed considerable improvement when at least one of the holes was closed.

It is important to highlight that throughout the follow-up period, one patient had an anal abscess that required further draining, while all other patients did not develop any abscesses. Furthermore, the level of luminal disease activity, as determined by CDAI, remained low throughout the duration of the follow-up period.

Conclusion: In conclusion, the findings of our research indicate that the use of hematopoietic stem cell injections for the treatment of perianal fistulas in patients with Crohn's disease is not only possible but also risk-free. According to the clinical findings, which are consistent with those published in reference studies, the closure rate at one year is fifty percent. In addition, this therapy has been linked to an improvement in patients' perineal activity levels as well as their quality of life.

Disclosure: Nothing to disclose.

PP0663

LAMB-INDUCED ALTERATIONS OF THE MACROPHAGE POLARIZATION EXACERBATE INTESTINAL INFLAMMATION

X. Lu¹, Y. Yuan¹, M. Wang¹, W. Zhang¹, Y. Xing¹, Z. Lin¹, C. Liang¹, T. Mao¹, J. Li¹, L. Wang¹

¹Beijing University of Chinese Medicine, Beijing, China

Contact E-Mail Address: xinyuluu@163.com

Introduction: Ulcerative colitis (UC) is a chronic intestinal inflammatory disease mainly involving the mucosa and submucosa. The pathogenesis of UC has not been clearly elucidated and there are limitations of existing treatment measures. Dietary factors have been implicated closely related to the pathogenesis and clinical outcome of UC. Our team in the early clinical trials observed that UC patients had aggravation or recurrence of their disease after taking in lamb. However, the relationship between them is unclear. Does lamb aggravate the intestinal inflammation of UC patients? What is the mechanism if lamb has a negative impact on intestinal inflammation? It is urgent for us to study further.

Aims & Methods: We aimed to clarify the effect of lamb on intestinal inflammation in UC mice and to reveal the mechanism, so as to provide scientific basis for clinical dietary guidance for UC patients.

Mice were given 2.5% DSS (w/v) solution for 5 days and deionized water for 7 days for 1 cycle, repeated 3 cycles to establish the chronic UC model. Take the start of giving DSS solution as day1, corresponding measures of lamb suspensions at a dose of 0.25, 0.50, 1.00 g/mL or sterile water were administered for 31 days. Then the general condition and the severity of colitis were monitored. Colon tissues were obtained to assess the degree of pathological damage by HE staining and detect the levels of key factors of intestinal barrier by RT-qPCR. Spleen tissues were collected to detect the levels of M1/M2 macrophages and related factors by flow cytometry and RT-qPCR.

Results: Our results showed that lamb aggravated intestinal inflammation of UC mice, as indicated by higher weight loss and DAI, shorter colon and more severe pathological damage. Also, the colonic mechanical barrier-associated factors including *ZO-1*, *Claudin-1*, *Occludin*, *E-cadherin* mRNA and colonic mucosal barrier associated-factors such as *Muc1*, *Muc2*, *Muc3* mRNA showed significant decrease in lamb-treated colitis mice. Moreover, colitis mice with lamb treatment showed significant increased M1 macrophages and reduced M2 macrophages in the spleen, leading to an increased the ratio of M1/M2 macrophage. Meanwhile, the M1 macrophage-associated inflammatory factors gene *TNF-α*, *IL-6* mRNA increased and M2 macrophage-associated inflammatory factors gene *IL-10*, *TGF-β* mRNA decreased significantly in lamb-treated colitis mice.

Conclusion: Our results show that lamb aggravates the intestinal inflammation and damages the mucosal barrier of colitis mice, whose mechanism is related to the promotion of macrophages to M1 cells and inhibition M2 cells differentiation, thereby aggravating the imbalance of M1/M2 macrophages.

Disclosure: Nothing to disclose.

PP0664

TRANSITION FROM INTRAVENOUS TO SUBCUTANEOUS INFlixIMAB: EFFECTIVENESS IN A COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A. Todeschini¹, A. Geccherle¹, P. Signoretto¹, N. Colaci¹, G. Barugola², A. Variola¹

¹IRCCS Sacro Cuore - Don Calabria, IBD Unit, Negrar di Valpolicella, Italy, ²IRCCS Sacro Cuore - Don Calabria, General Surgery, Negrar di Valpolicella, Italy

Contact E-Mail Address: ale_tode@hotmail.com

Introduction: Inflammatory bowel disease (IBD), ulcerative colitis (UC) and Crohn's disease (CD), is a group of chronic inflammatory disorders. Biologics are indicated for patients failing conventional maintenance therapy with moderate to severe activity. Different routes of administration, intravenous (IV), subcutaneous (SC) or oral have been approved. For chronic diseases such as IBD, some patients may prefer self-administered SC dosing to IV dosing as a less time-intensive and more convenient treatment option.

Aims & Methods: This study aims to evaluate the success of infliximab subcutaneous administration after switching from intravenous administration in IBD patients. The transition from IV to SC administration was proposed to 60 IBD patients in clinical remission. Data on medical history and laboratory tests were collected from electronic health records. Moreover, patients filled a paper questionnaire 8 weeks after the switch focused on the level of satisfaction and onset of adverse event (AE).

Results: Overall 60 patients were enrolled for switching from IV to SC therapy. Most of patients (>80%) did not experience any difficulties in handling the device and respected the correct time-table of administration. The switch was a complete success in 50 out of 60 patients (83.3%). Ten patients stopped subcutaneous formulation: five of these switched back to intravenous formulation for adverse event or patient's preference, four swap or swop to other therapy and one withdraw from biologic. No predictor of loss of response was found at multivariate analysis. Faecal calprotectin and C-reactive protein values significantly improve after the switch at 3, 6 and 12 months ($p=0.03$, $p=0.004$, $p=0.01$ and $p=0.06$, $p=0.001$, $p=0.007$ respectively). About 16.7 % of patients had at least one side effect after switching. Local pain and swelling at site of injection were the most common AEs. The vast majority of AE were mild and lasted only a few days. No serious AEs were reported and no patient was hospitalized.

Conclusion: Effectiveness of switching from intravenous to subcutaneous infliximab administration in IBD patients is confirmed in our real world cohort of patients.

Disclosure: Nothing to disclose.

PP0665

ADVANCED THERAPIES, THE BEST COMBINATIONS IN REFRACTORY IBD PATIENTS

M. Vuillemoz¹, M. Martinho^{2,1}, G. Santi², P. Michetti^{3,1},
P. Juillerat^{4,1,2}

¹Crohn and Colitis Center, Beaulieu SA, Gastro-entérologie, Lausanne, Switzerland, ²Gastroenterology Inselspital, Bern University Hospital, Clinic for Visceral Surgery and Medicine, Bern, Switzerland, ³CHUV, Centre Hospitalier Universitaire Vaudois, Gastroenterology, Lausanne, Switzerland, ⁴Intesto, Crohn and Colitis Center, Fribourg and Bern, Gastroenterology, Inflammatory Bowel Disease, Bern, Switzerland

Contact E-Mail Address: juilleratp@intesto.ch

Introduction: The combination of two biological agents or a biological agent with novel small molecules, known as advanced combination therapy (ACT), for inflammatory bowel disease (IBD) has shown promising results in phase II studies as well as in real world studies. We describe the real-world experience of 2 Swiss IBD referral centers.

Aims & Methods: A chart review of all IBD patients on ACT from June 2020 to December 2023 was performed in Bern University hospital and the Crohn and Colitis Center Lausanne (Gastro-entérologie Beaulieu SA). Data on disease duration, extension, previous or concomitant treatments as well as efficacy and safety were collected prospectively.

Results:

Disease	Combination of advanced therapy (number of patients)	Partial or complete Clinical or biological response	Adverse effects, Infections
Ulcerative colitis (N=11)	Vedolizumab / Tofacitinib (5)	2/5 (40%)	none
	Vedolizumab / Anti-TNFs (3)	2/3 (50%)	none
	Vedolizumab / Cyclosporin or Tacrolimus (2) Ustekinumab / Tacrolimus (1)	1/2 (50%) 1/1 (100%)	none
Crohn's disease (N= 17)	ustekinumab (5)/ Anti-TNFs (infliximab (1), adalimumab (4))	5/ 5 (100%)	Eczema, tumefaction left parotide
	ustekinumab (4) / JAK inhibitors Upadacitinib (3) , Tofacitinib (1)	4/4 (100%)	Lymphoma, mycosis, otitis media, lymphopenia, CMV ileitis
	Vedolizumab / Infliximab (1)	0/1 (0%)	none
	Vedolizumab / Tacrolimus	1/1 (100%)	none
	Vedolizumab / Upadacitinib (3)	3/3 (100%)	Acnea, Headache, nausea
	Anti-TNF (adalimumab (2), cimzia (1) / Upadacitinib (3)	2/3 (66%)	Ophthalmic zona
Total		21/28 (75%)	11 events (14%)

A total of 25 IBD patients (48% women, 10 ulcerative colitis, 15 Crohn's disease) received 28 ACT. The indications were extended and refractory luminal disease and/or extraintestinal manifestations. The 25 patients were all steroid dependent or refractory and half of them were either refractory or intolerant to at least two anti-TNF alpha agents.

These treatments were started after a median disease duration of 5 years (range 1-31). The mean duration of ACT was 10 months (range 1-40). Most frequent ACT combinations were vedolizumab or ustekinumab combined with either JAK inhibitors or TNF- alpha inhibitors.

A partial or complete response was observed in 21/28 therapies (75%) with a mean decrease of CRP of 9,4 mg/l (range - 23 to + 59). Among responders, a median decrease of calprotectin by 871 mcg/g (range 0 - 4002; N=8, skewed) was observed.

Concerning safety, 3 infections (ophthalmic herpes zoster, otitis media, cutaneous fungal infection) and 1 case of Non-Hodgkin Lymphoma, were reported. 8 minor adverse events (left parotid gland, tumefaction, eczema, 2 patients with lymphopenia, acne nausea and headaches) were reported, with mostly small molecules implicated. One patient had a successful pregnancy and delivery on combined adalimumab and ustekinumab ACT.

Conclusion: Vedolizumab or ustekinumab combined with either JAK or TNF- alpha inhibitors were the most frequent combinations of ACT in this cohort of severe and steroid-dependent/refractory IBD patients. 75% of patients achieved a clinical /biological response. Small molecules appear to be associated with of lymphopenia, and minor infections. There was one case of Non-Hodgkin Lymphoma while receiving ustekinumab and tofacitinib ACT in the context of previous long exposure to adalimumab.

Disclosure: Marianne Vuillemoz and Maude Martinho Grueber disclose consulting fees from Bristol Myers Squibb. Giulia Santi has nothing to disclose. Pascal Juillerat discloses consulting and speaker fees from AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Merck Sharp & Dohme, Pfizer, Pierre Fabre, Sandoz, Takeda, Tillotts Pharma AG, and UCB Pharma. Pierre Michetti discloses a grant from Iqone and personal fees from Takeda, Ferring, Hospira, Janssen, Pfizer, UCB Pharma, Vifor Pharma, Nestlé Health Sciences, MSD.

PP0666

EFFECTIVENESS AND SAFETY OF ADALIMUMAB BIOSIMILAR IN BIO"NAIVE" PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE GALICIAN EXPERIENCE

C. Regueiro Expósito¹, M.T. Vázquez Rey², I. Bastón-Rey³,
M. Ayude Galego⁴, A. Carmona Campos⁵, A.M. Baz López⁶,
G. Molina Arriero⁷, M.J. Ruiz Barcia⁸, P. Vega⁹

¹Fundación Pública Galega de Investigación Biomédica Galicia Sur, Research Group in Gastrointestinal Oncology, Ourense, Spain, ²Complejo Hospitalario Universitario A Coruña, Gastroenterology Department, A Coruña, Spain, ³Hospital Universitario Clínico de Santiago, Gastroenterology Department, Santiago de Compostela, Spain, ⁴Complejo Hospitalario Universitario de Vigo, Gastroenterology Department, Vigo, Spain, ⁵Hospital Ribera Pavis, Gastroenterology Department, Vigo, Spain, ⁶Complejo Hospitalario Universitario Lucus Augusti, Gastroenterology Department, Lugo, Spain, ⁷Complejo Hospitalario Universitario de Ferrol, Gastroenterology Department, Ferrol, Spain, ⁸Hospital da Costa, Gastroenterology Department, Burela, Spain, ⁹Complejo Hospitalario Universitario de Ourense, Gastroenterology Department, Ourense, Spain

Contact E-Mail Address: cristinaregueiroexpósito@gmail.com

Introduction: Biological drugs has revolutionized the management of inflammatory bowel disease (IBD). However, its use has led to a significant increase in cost that has strained health systems. Biosimilars will reduce cost related to treatment, allowing access to a greater proportion of patients. However, data on the efficacy and safety of the various adalimumab (ADA) biosimilars in IBD patients "naïve" to biologics remains scarce.

Aims & Methods: We performed an observational cohort study in 8 Spanish hospitals located in Galicia. All patients with IBD naïve to biologics who started ADA biosimilar between November 2018 and January 2022 for control of their disease were enrolled. The primary endpoints were efficacy defined as clinical remission at week 8 and long term efficacy defined as persistence on drug treatment at the end of follow-up. The other co-primary endpoint was to determine the incidence of adverse events that lead to suspension or discontinuation of the drug or hospitalization of the patient.

Results: 383 patients (95 CU; 283 CD) with a median age of 47.0 (34.0-59.3) years and a median disease duration of 3.4 (0.8-10.0) years before starting treatment were included. After induction (at 8 weeks) 63.8 % of patients were in clinical remission and 85.3 % achieved clinical response. At this time of follow-up, 14 patients (4.9 %) discontinued treatment mainly due to primary non-response (PNR) (57.1 %) and adverse events (42.9

%). In total, 114 patients discontinued treatment during follow-up. The main reasons for stopping therapy were adverse events (26.3 %), PNR (30.7 %) and secondary loss of response (43.0 %). Clinical remission was maintained in 78.4 % of patients, after a median follow-up of 18 (12-24) months. Drug persistence shown by Kaplan-Meier survival curves were significantly higher in CD patients ($p = 0.012$) and in the group of patients treated with immunomodulators (IMM) ($p = 0.001$). Additionally, the rates of clinical remission and clinical response were higher in CD patients and in IMM-treated patients (Table 1). Adalimumab levels were also measured during follow-up, showing a median of 10.4 (6.7-13.0) $\mu\text{g/mL}$. Significantly, drug persistence was higher in patients with post-induction ADA levels $\geq 7 \mu\text{g/mL}$ ($p = 0.002$). Regarding treatment safety in this population, adverse events that required treatment suspension or discontinuation were reported in 30 patients.

	EC (N = 383)	UC (N = 95)	P	IMM (N = 113)	Non-IMM (N = 252)	P
Clinical remission, n (%)	69.6	63.2	0.243	72.5	65.5	0.161
Clinical response, n (%)	80.6	70.5	0.041	80.2	77.4	0.532
Biochemical remission, n (%)	58.3	58.9	0.912	62.6	57.9	0.378
PNR, n (%)	7.8	13.7	0.086	6.9	10.3	0.267
SNR, n (%)	12.7	13.7	0.809	9.9	14.3	0.225

Table 1. Comparison of the clinical effectiveness at the end of follow-up between EC vs. UC patients and IMM vs. non-IMM treated patients.

Conclusion: ADA biosimilars in usual clinical practice are safe and effective in inducing and maintaining remission in Galician patients with IBD. Drug persistence was significantly higher in patients with CD, treated with IMM and with post-induction ADA levels $\geq 7 \mu\text{g/mL}$.

Disclosure: Nothing to disclose.

PP0667

GUIDELINES SURROUNDING USE OF BIOSIMILARS IN GASTROENTEROLOGY: PERCEPTIONS FROM CLINICAL SOCIETIES

K. Shastri¹, K. Clarke², M. Ainslie-Garcia², N. Ferko²

¹Fresenius Kabi SwissBioSim GmbH, Eysins, Switzerland,

²EVERSANA, Burlington, Canada

Contact E-Mail Address: kunal.shastri@fresenius-kabi.com

Introduction: Since their introduction, biologics have drastically improved management of clinical symptoms in patients with inflammatory bowel disease (IBD); however, historically, biologics have been very expensive medications. Biosimilars provide similar clinical efficacy and safety to reference product (RP) biologics at a reduced cost, which has helped to alleviate undue strain on the healthcare system and improve patient access to biologics treatment. Despite these advantages, uptake remains slow in some regions, which may be due to limited awareness among patients and clinicians. This review sought to understand the recommendations for biosimilar use from government agencies and clinical societies, as they can be an important source for education

Aims & Methods: A literature search was conducted in MEDLINE and Google Scholar focusing on the use of biosimilars in gastroenterology. Search terms included biosimilar and gastroenterology, in combination with position, guidance, recommendation, workshop, or consortium. The literature search was restricted from 2006 (time of biosimilar approval) to present.

Results: Following screening there were 20 position statements/guidelines identified. The use of biosimilars was discussed among gastroenterology societies in Belgium (n = 2), Brazil (n = 1), Canada (n = 2), Italy (n = 2), Korea (n = 2), Mexico (n = 1), Poland (n = 2), Spain (n = 1), and the USA (n

= 1) with regional representation from Europe (eg, ECCO) and Asia (n = 2). Five were published before 2015 and 15 were published in 2015 or later. Although government agencies such as the European Medicines Agency and Food & Drug Administration published positive recommendations for the use of biosimilars, statements from key clinical societies from Canada, Europe, Italy, Poland, and Spain expressed concerns regarding the use of biosimilars for patients with IBD in the early 2010s. The main objection was the extrapolation of biosimilar indications to IBD from clinical studies in patients with rheumatoid arthritis, as statements suggested that clinical trials of biosimilars specific to IBD were necessary before their use. Since then, the efficacy and safety data from real-world observational studies, and the acceptance of indication extrapolation have contributed to positive recommendations from most clinical societies regarding biosimilar use. For example, 2014 guidelines published in Poland was not supportive of biosimilars; however, updated guidelines in 2019 noted that approved biosimilars were not significantly different from originator medicines. Most clinical societies approve biosimilar use for patients with IBD naïve to the molecule as well as those with stable disease, switching from the RP medicine to the biosimilar. One notable exception to this trend is a 2020 Canadian position statement recommending against nonmedical switching from originator to biosimilar in patients with stable IBD. However, several Canadian provinces have since adopted policies that support nonmedical switching, suggesting that medical practices and future Canadian position statements may change.

Conclusion: As real-world efficacy and safety studies continue to demonstrate the clinical value of biosimilars, perceptions surrounding their use have greatly improved among several key clinical societies globally. Notably, most societies expressed the importance of patient consent when deciding to switch to biosimilars. Thus, services that provide education to patients to increase awareness of and confidence in biosimilars are critical to ensure their use and should be optimized to promote expanded patient access.

Disclosure: Kunal Shastri is an employee of Fresenius Kabi, a manufacturer of biosimilars. Kerise Clarke, Margaret Ainslie-Garcia, and Nicole Ferko are employees of EVERSANA who receives consulting fees from Fresenius Kabi.

PP0668

ANTI-JAK EFFICACY IN A REAL WORLD COHORT OF ULCERATIVE COLITIS PATIENTS

L. Melotti¹, N.K. Dussias¹, N. Vanigli¹, P. Gionchetti¹, F. Rizzello¹

¹Alma Mater Studiorum - Università di Bologna; IRCCS AOU Bologna, Policlinico Sant'Orsola-Malpighi, DIMEC, Bologna, Italy

Contact E-Mail Address: laura.melotti2@studio.unibo.it

Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease requiring sustained therapy for both induction and maintenance of remission. Biologics radically changed the natural history of UC patients and are still the cornerstone of treatment, but they have some limitations. The introduction of oral Janus kinase inhibitors (JAKi), recently approved for UC management, presents a novel treatment option. Data are needed to confirm their efficacy in a real world setting.

Aims & Methods: In this retrospective, observational study at the IBD Unit in Bologna, we enrolled consecutive UC patients treated with the JAKi tofacitinib (TOFA) and upadacitinib (UPA). We collected demographic and disease-specific data, assessing clinical activity via the partial Mayo (pMayo) score, biomarker status through C-reactive protein levels, and endoscopic activity via the Mayo endoscopic score at baseline and at 2, 6, and 12 months. Concomitant use of steroids were registered at every time point. We measured clinical response (≤ 3 -point reduction in pMayo or dis-

continuation of steroids) at 2 months, clinical remission rates (pMayo < 2) and endoscopic remission (Mayo score of 0) at each time point. Need for surgery was also recorded.

Results: A total of 50 patients were treated with JAKi between December 2021 and June 2023 (39 TOFA and 11 UPA). Males were 59.57% and median age was 35.5 years. Nobody were bio-naïve and 80.86% were exposed to ≥ 2 biologics/small molecules prior to JAKi initiation. Concomitant steroids were present in 76% of cases at baseline. Clinical response at T2 was obtained in 65.30% of cases. Clinical remission rate was 40% at T2, 32.6% at T6 and 24.4% at T12. Endoscopy was performed at T2 in 24 patients, at T6 in 26 and at T12 in 10 patients; endoscopic remission was observed in 5/24, 9/26 and 4/10, respectively. Treatment optimization was adopted in 52% of cases. A total of 5 patients (10%) underwent colectomy during follow up period. No serious adverse events were observed.

Conclusion: In a cohort of multirefractory UC patients, JAKi demonstrated substantial efficacy in inducing clinical and endoscopic remission, though there was a decline in effectiveness during the maintenance phase. The rate of colectomy remained relatively low, underscoring the potential utility of JAKi in this challenging patient population.

Disclosure: Nothing to disclose.

PP0669

RISK OF ACUTE INFLIXIMAB INFUSION-RELATED REACTIONS IN IBD PATIENTS WITH IMMUNOLOGICAL HYPERSENSITIVITY BACKGROUND

R. Tababi¹, A. Guediche¹, M. Zakhama¹, R. Baklouti¹, I. Jemni¹, M. Ben Abdelwahed¹, A. Sabbek¹, W. Bouhlel¹, N. Ben Chaaben¹, M.H. Loghmani¹, L. Safer¹

¹Fattouma Bourguiba University Hospital, Gastroenterology, Monastir, Tunisia

Contact E-Mail Address: ramzi.tababi@gmail.com

Introduction: Acute infusion-related reactions (IRRs) are common adverse events associated with infliximab, affecting up to 23% of patients. Their etiology involves cytokine release, complement activation, and mast cell degranulation. Consequently, individuals with a history of immunological hypersensitivity reactions are often perceived to be at high risk due to their exaggerated immune responses, and are frequently prescribed premedication.

Aims & Methods: We aimed to determine if patients with immunological hypersensitivity background, receiving infliximab for inflammatory bowel disease (IBD), have an increased risk of IRRs. This retrospective cohort study included all patients diagnosed with IBD who underwent intravenous (IV) infliximab at our centre over a 13-year period. All patients received standard infliximab 2-hour infusion protocol, preceded by premedication with 200mg of IV hydrocortisone. IRRs were defined as any type of mild to severe reaction occurring during infusion or within 2 hours of its completion. Patients were considered to have an allergic predisposition if they had atopic diathesis (such as allergic rhinitis, asthma or atopic dermatitis) or a documented history of allergy to other medications.

Results: Ninety-five patients, with a mean age of 35 ± 13 years at the initiation of infliximab therapy, were included in the study, with females accounting for 52.6%. The majority of patients were diagnosed with Crohn's disease (n=76, 80%), while the remaining 19 patients (20%) had ulcerative colitis. A history of allergy was reported in 20 patients (21.1%) within the cohort.

Over the study period, a total of 258 person-years (PY) of exposure to infliximab were recorded, with a median of 12 infusions per patient (interquartile range: 5-33). In most cases, infliximab therapy was combined with immunomodulators (n=63, 66.3%).

Fourteen IRRs occurred during the follow-up period, resulting in an overall incidence rate of 49.5 per 1000 PY. Patients with and without a history of immunological hypersensitivity showed comparable incidence rates of IRRs (32.5 per 1000 PY and 57.8 per 1000 PY, respectively), as well as similar cumulative incidence (15% and 22.7%, respectively). No statistically significant difference was observed between the two groups (p=0.446).

Conclusion: Having an immunological hypersensitivity background does not appear to increase the risk of developing acute infliximab infusion-related reactions. Consequently, it does not warrant specific premedication or additional precautionary measures.

Disclosure: Nothing to disclose.

PP1248

UNVEILING THE IMPACT ON IN UTERO EXPOSURE TO BIOLOGIC TREATMENTS FOR INFLAMMATORY BOWEL DISEASE (IBD) ON CHILDREN'S PSYCHOMOTOR DEVELOPMENT: INSIGHTS FROM THE DUMBO REGISTRY OF GETECCU

L. Palomino¹, M. Velasco Rodríguez-Belvis¹, Y. Brenes², E. Leo-Carnerero³, C. Calviño Suarez⁴, M. Rivero⁵, M.I. Calvo Moya⁶, M.T. Arroyo-Villarino⁷, A. Fernández-Clotet⁸, I. Pérez-Martínez⁹, A. Masedo Gonzalez¹⁰, V. Hernández¹¹, A. Ruiz Cerulla¹², P. López Serrano¹³, P. Vega¹⁴, I. Rodríguez-Lago¹⁵, R. Vicente Lidón¹⁶, M.Á. De Jorge Turrión¹⁷, I. Guerra¹⁸, L. Arias García¹⁹, G. Molina Arriero²⁰, D. Hervías Cruz²¹, D. Busquets Casals²², A. Gutiérrez-Casbas²³, M. Van Domselaar²⁴, G. Valldosera Gomis²⁵, J.M. Vázquez Morón²⁶, M. Piqueras Cano²⁷, A.J. Lucendo²⁸, M.D. Martín-Arranz²⁹, P. Ramírez de la Piscina Urraca³⁰, M.d.P. Martínez Tirado³¹, V. Robles Alonso³², S. Marín Pedrosa³³, R. Camargo Camero³⁴, E. Armesto Gonzalez³⁵, C. Tardillo Marín³⁶, E. Bernardos Martín³⁷, M.D.C. Rodríguez Grau³⁸, J.M. Huguet³⁹, L. Márquez-Mosquera⁴⁰, P. Sendra Rumbau⁴¹, L. Bujanda Fernández de Piérola⁴², C. Castaño-Milla⁴³, E. Sainz Arnau⁴⁴, L. Hernández Villalba⁴⁵, R. Muñoz Codoceo¹, A. García-Salido¹, J. P. Gisbert², M. Chaparro², On behalf of the DUMBO Project of GETECCU. *co-first authors

¹Hospital Infantil Universitario Niño Jesús, Madrid, Spain,

²Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-IP), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain, ³Hospital Universitario Virgen del Rocío, Sevilla, Spain, ⁴Complejo Hospitalario Universitario de Santiago,

Gastroenterology, La Coruña, Spain, ⁵Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain,

⁶Hospital Universitario Puerta de Hierro Majadahonda, Digestive,

Madrid, Spain, ⁷Hospital Clínico Universitario Lozano Blesa, IIS

Aragón y CIBEREHD, Zaragoza, Spain, ⁸Hospital Clinic, Barcelona,

Spain, ⁹Hospital Universitario Central de Asturias, Oviedo, Spain,

¹⁰Hospital Universitario 12 Octubre, Madrid, Spain, ¹¹Hospital

Álvaro Cunqueiro. Instituto Investigación Sanitaria Galicia Sur,

Gastroenterology, Redondela, Spain, ¹²Hospital Universitari de

Bellvitge, Gastroenterology, Mollet Del Valles, Spain, ¹³Hospital

Universitario Fundación Alcorcón, Madrid, Spain, ¹⁴Complejo

Hospitalario Universitario de Ourense, Gastroenterology, Ourense,

Spain, ¹⁵Hospital Universitario de Galdakao, Gastroenterology,

Bilbao, Spain, ¹⁶H. U. Miguel Servet, Zaragoza, Spain, ¹⁷Hospital

Universitario de Cabueñes, Aparato Digestivo, Oviedo, Spain,

¹⁸Hospital Severo Ochoa, Sección de Digestivo, Madrid, Spain,

¹⁹Hospital Universitario de Burgos, Burgos, Spain, ²⁰Complejo

Hospitalario de Ferrol, Digestive, Ferrol, Spain, ²¹Hospital General

Universitario de Ciudad Real, Ciudad Real, Spain, ²²H. de Girona Dr.

J. Trueta/ICO, Gastroenterology, Girona, Spain, ²³Hospital General Universitario Alicante, Gastroenterology, Alicante, Spain, ²⁴Hospital Universitario de Torrejón, Universidad Francisco de Vitoria, Madrid, Spain, ²⁵Hospital Universitario Joan XXIII, Tarragona, Spain, ²⁶Hospital Universitario Juan Ramón Jiménez, Huelva, Spain, ²⁷Hospital Consorci Terrassa, Terrassa, Spain, ²⁸Hospital General de Tomelloso, Gastroenterology, Madrid, Spain, ²⁹Hospital La Paz, Gastroenterology, Madrid, Spain, ³⁰Hospital Universitario de Álava, Álava, Spain, ³¹Hospital Clínico Universitario San Cecilio, Granada, Spain, ³²H. Vall D'Hebron, Barcelona, Spain, ³³Hospital Universitario Reina Sofía, Córdoba, Spain, ³⁴Hospital Universitario Virgen de La Victoria, Málaga, Spain, ³⁵Hospital Universitario San Agustín, Avilés, Spain, ³⁶Hospital Universitario Nuestra Señora de Candelaria, Tenerife, Spain, ³⁷Hospital Mancha Centro, Ciudad Real, Spain, ³⁸Hospital Universitario del Henares, Madrid, Spain, ³⁹Hospital General Universitario de Valencia, Valencia, Spain, ⁴⁰Hospital del Mar, IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain, ⁴¹Hospital Universitario Son Espases, Gastroenterology and Hepatology, Mallorca, Spain, ⁴²Instituto Bionostia, San Sebastián, Spain, ⁴³Hospital Universitario Rey Juan Carlos, Móstoles, Madrid, Spain, ⁴⁴Hospital Sant Joan de Déu - Althaia, Manresa, Spain, ⁴⁵Santos Reyes, Gastroenterology, Aranda de Duero, Spain

Contact E-Mail Address: laura_palomino_perez@hotmail.es

Introduction: Women with inflammatory bowel disease (IBD) are highly recommended to maintain treatment during pregnancy because discontinuation has been associated with flare-ups, which are linked to a worse prognosis for the mother and the fetus. It is widely known that biologic drugs cross the placenta, but most studies focused on the impact on the risk of infection. Data regarding the impact on psychomotor development are very limited, particularly on non anti-TNF biologics.

Aims & Methods: Our aim was to evaluate the impact of the exposure of biologics in utero on the psychomotor development of children during the first year of life.

Data from children included in the DUMBO registry with complete AQS-3 available up to 12 months of age were analysed. DUMBO is a prospective, observational, and multicentre registry endorsed by GETECCU, which enrolls pregnant women with IBD throughout 5 years in 60 centres in Spain. This subanalysis to evaluate the neurodevelopment of the babies, follows up mothers and babies since the pregnancy diagnosis until delivery during each trimester and then, every 3 months during the first 12 months of babies' life. Normal psychomotor development was defined by ASQ-3 scores above the lower limit of normality (referral zone) in all domains. Serious adverse events (SAE) were defined in accordance with the ICH Topic E 2 A Clinical Safety Data Management.

Results: 352 children born to 343 mothers were included (9 pair of twins). 134 children (38%) had been exposed to biologics in utero; from them, 50 (37%) had been exposed to adalimumab, 44 (32%) to infliximab, 3 (2.2%) to certolizumab, 1 (0.7%) to golimumab, 28 (20%) to ustekinumab, and 10 (7.5%) to vedolizumab. To assess psychomotor development, 2073 ASQ-3 questionnaires were analyzed. No differences were observed in any of the evaluations or domains throughout the first year, except at 12 months, where exposed babies were more likely to achieve normal results in the domain of gross motor skills.

In the univariate analysis between babies with normal development at 12 months and those who did not we only found differences in: Exposure to biologic drugs, which was higher in those who presented a normal ASQ-3. The type of maternal IBD, that babies from mothers with UC had lower likelihood of normal psychomotor development, and prematurity, serious adverse events, and hospitalizations, all of which were more frequent in those who presented abnormal ASQ-3 results. In the multivariate analysis,

to have been born to a mother with CD (vs. UC) was associated with higher likelihood (OR=2, 95%CI=1.1-3.9), while to be premature was associated with lower likelihood (OR=0.3, 95%CI=0.1-0.6) of having ASQ-3 scores above the limit of normality in all domains at 12 months of age.

Conclusion: In the multicenter, prospective DUMBO registry, the exposure to biologics for the treatment of IBD in utero (including anti-TNF and non-anti-TNF agents) did not impair the psychomotor development of the children. Our findings support the safety of these drugs and reinforce the recommendation to continue them during pregnancy.

Disclosure: Nothing to disclose.

PP0670

ISCHEMIC ULCERS DO NOT SIGNIFICANTLY IMPACT THE ENDOSCOPIC RECURRENCE SCORE IN CROHN'S DISEASE: A MULTICENTER COMPARATIVE STUDY AFTER RIGHT-SIDE RESECTIONS FOR CROHN'S DISEASE AND COLORECTAL CANCER

A. Rispo¹, F. Castiglione¹, A. Orlando², G. Solina², A. Fichera³, N. Imperatore⁴, R. Lamanda⁴, E. Di Girolamo⁵, P. Marone⁵, P. Delrio⁵, F.P. Tropeano¹, G. Calabrese¹, M. Cricri¹, S. Calderone², B. Toro¹, A.D. Guarino¹, G. De Palma¹, G. Luglio⁶
¹Federico II University Hospital, Clinical Medicine and Surgery, Naples, Italy, ²Villa Sofia-Cervello Hospital, IBD Unit, Palermo, Italy, ³Baylor University Medical Center, Colon and Rectal Surgery, Dallas, United States of America, ⁴Santa Maria Delle Grazie Hospital, Gastroenterology and Endoscopy Unit, Pozzuoli, Italy, ⁵IRCCS G. Pascale, Gastroenterology and Endoscopy Unit, Naples, Italy, ⁶Federico II University Hospital, Public Health, Naples, Italy

Contact E-Mail Address: giulicalabrese94@gmail.com

Introduction: Post-operative recurrence (POR) is common in patients with Crohn's disease (CD) who have undergone surgery. Endoscopy, mainly based on Rutgeerts' score, is crucial for the diagnosis of POR, showing also high prognostic value. More recently, several studies have suggested that the current endoscopic score system could be affected by the ischemic (not inflammatory) nature of some anastomotic ulcers, particularly at the level of the mucosal inverted stapled line, so overestimating the prevalence of the "real" anastomotic POR.

However, these studies, based on the comparison between CD patients and subjects undergone right-side resection for colon cancer (CRC), included a very small population.

Aims & Methods: Starting from these considerations, we performed a retrospective study aimed to directly compare the prevalence of anastomotic POR in CD with that of patients operated of right-side resection for CRC in a wide population. A retrospective studies was conducted at 4 Italian Institutions (3 with high volume of IBD admissions; 2 with high volume CRC admissions). All patients performed endoscopy within 8 months from surgery. We selected all consecutive CD and CC patients undergone a surgical resection with an anisoperistaltic stapled L-L anastomosis. The diagnosis of POR of CD was made in accordance with the modified Rutgeerts' score (i0, i1, i2A, i2B, 3, 4). The global prevalence of PSR (Rutgeerts's score ≥ 2) was recorded. Furthermore, we directly compared the prevalence of the isolated anastomotic ulcers of CD (Rutgeerts i2A) to that detected in CC patients.

Results: At the end of the study, we enrolled 221 CD patients and 72 CRC subjects. POR was recorded in 127 CD patients (57%). According to the endoscopic grade system, POR was scored as i0: 56 pts (25%), i1: 38 pts (17%); i2A: 42 pts (19%), i2B: 26 pts (12%), i3: 20 pts (9%), i4: 39 pts (18%). In the CRC group, endoscopy detected anastomotic ulcers in 2 out of 72 patients (3%); 1 case (1.4%) of CRC early recurrence was observed. When

comparing the prevalence of isolated anastomotic ulcerations in CD (i2A) vs those in CRC patients, the prevalence of ulcerations was significantly higher in CD patients (19% vs 3%; $p<0.01$; O.R. 6.3).

Conclusion: Our study confirms the high prevalence of early recurrence in CD patients, so confirming the role of early (within 6-8 months) post-operative endoscopy in CD setting. The prevalence of anastomotic (ischemic) ulcers in CRC patients is very low and, as a consequence, this issue should not represent a real diagnostic matter if shifted into the POR setting of CD. Prospective, multicentre and directly comparative studies are needed to confirm our results.

Disclosure: Nothing to disclose.

PP0671

POST-OPERATIVE BMI IN PATIENTS WITH CROHN’S DISEASE UNDERGOING ILEO-COLONIC RESECTION IS DETERMINED BY BASELINE RATHER THAN PERI-OPERATIVE BMI

T. Thurm^{1,2}, G. Berman^{1,2}, H. Leibovitzh^{1,2}, L. Deutsch (Mlynarsky)^{1,2}, R. Anbar^{3,2}, M. Zemel^{4,2}, N. Maharshak^{1,2}
¹Tel-Aviv Sourasky Medical Center, Gastroenterology and Liver Diseases, Tel-Aviv, Israel, ²Tel-Aviv University, Faculty of Health and Medical Sciences, Tel-Aviv, Israel, ³Tel-Aviv Sourasky Medical Center, Nutrition and Dietetic Unit, Tel-Aviv, Israel, ⁴Tel-Aviv Sourasky Medical Center, Surgical Division, Tel-Aviv, Israel

Contact E-Mail Address: tamarth@tlvmc.gov.il
Introduction: Patients diagnosed with Crohn’s disease (CD) often undergo ileo-colonic resection (ICR) due to disease activity and complications. Post-operative weight gain is common, secondary to reduction in inflammatory burden, resolution of strictures and improved nutrition, yet may result in overweight and obesity (oBMI). Recent studies have shown that obesity in CD may lead to disease exacerbation and decreased response to medical treatment.

Aims & Methods: In this retrospective, case control, single tertiary center study, we aimed to identify risk factors for post-ICR oBMI and to explore the association of post-ICR overweight and obesity with disease recurrence in CD patients. All adult patients with CD who underwent ICR between 1/1/2010 to 31/12/2022 were included. Data collected from hospital records included patients and disease characteristics, post-ICR adverse events and endoscopic recurrence (Rutgeerts score), medical treatment before and after ICR. BMI was recorded at 6-12 months prior to disease exacerbation leading to surgery (baseline-BMI), at ICR and at 12-months post-ICR. Patients with (1) protective or end ileostomy, (2) non-CD exacerbation related surgery (e.g. neoplasia, ischemia), (3) lack of in-hospital IBD clinic follow up, and (4) incomplete BMI records, were excluded. The cohort was divided into two groups by post-ICR BMI [non-overweight BMI (nBMI)<25 kg/m² or oBMI≥25 kg/m²]. Logistic regression model was used and two-sided p-value <0.05 was considered significant.

Results: A total of 94 patients met the inclusion criteria and were included in the study. At 12 months post-ICR, 32 (33.7%) patients had oBMI (mean BMI 28.1±2.8 kg/m²) and 62 (66.3%) had nBMI (mean BMI 21.5±2.1 kg/m²). Groups were comparable in baseline characteristics [Table 1]. Mean baseline-BMI and ICR-BMI were higher in oBMI group compared to nBMI group (26.6±3.3 kg/m² vs. 21.4±2.9 kg/m² at baseline and 24.2±4.0 kg/m² vs. 19.6±2.6 kg/m² at ICR, $p<0.001$ for both). oBMI patients had a higher rate of ileocolonic (L3) disease (vs. ileal (L1) disease) compared to the nBMI group (62.5% vs 32.3%, $p=0.005$). No differences were observed in post-operative complications and re-hospitalizations within 12 months of follow up. The rate of endoscopic disease recurrence was comparable within 18 months of ICR (Rutgeerts≥2b 30.8% for oBMI vs 43.1% for nBMI, $p=NS$). A logistic regression analysis adjusted to age, gender, and disease

location, demonstrated that baseline-BMI, but not ICR-BMI was associated with 12 months post-ICR-oBMI (baseline-BMI: OR 1.699, 95%CI 1.242-2.326, $p<0.001$; ICR-BMI: OR 1.208, 95%CI 0.932-1.565, $p=0.153$).

	Post-ICR-nBMI <25kg/m ² (n=62)	Post-ICR-oBMI ≥25kg/m ² (n=32)	p-value
Body Mass Index (kg/m ²), mean±SD			
At baseline	21.4±2.9	26.6±3.3	<0.001
At time of ICR	19.6±2.6	24.2±4.0	<0.001
12 months post-ICR	21.5±2.1	28.1±2.8	<0.001
Male gender, n [%]	36 [58.1]	22 [68.8]	0.313
Age at CD diagnosis, n [%]			
<17 years	7 [11.3]	5 [15.6]	
17-40 years	46 [74.2]	16 [65.6]	0.682
>40 years	9 [14.15]	6 [18.8]	
CD location, n [%]			
Ileal	42 [67.7]	12 [37.5]	0.005
Ileocolonic	20 [32.3]	20 [62.5]	
Disease behavior, n [%]			
Inflammatory	1 [1.6]	1 [3.1]	
Strictureing	26 [41.9]	9 [28.1]	0.400
Penetrating	35 [56.5]	22 [68.8]	
Perianal disease, n [%]	18 [29.0]	9 [28.1]	0.927
Smoking, n [%]			
Never	32 [51.6]	16 [50.0]	
Former	12 [19.4]	11 [34.4]	0.173
Active	18 [29.0]	5 [15.6]	
Disease duration at ICR (years), mean±SD	10.2±8.1	10.5±12.5	0.871
Biologic treatment experienced, n [%]	44 [71.0]	21 [65.6]	0.595

Table 1: Patients’ characteristics
Abbreviations: nBMI – non-overweight body mass index; oBMI – overweight/obese body mass index; SD – standard deviation; ICR – ileo-colonic resection; CD – Crohn’s disease; n – number

Conclusion: BMI≥25 kg/m² prior to CD exacerbation is associated with post-ICR overweight and obesity. Though at short term follow-up, no increase in postoperative complications and endoscopic disease recurrence were observed, longer follow-up may be needed to assess possible effects of post-ICR overweight and obesity on CD’s course.
Disclosure: Nothing to disclose.

PP0672

PRELIMINARY REPORT ON SHORT-TERM POST-OPERATIVE OUTCOMES OF ROBOTIC VERSUS LAPAROSCOPIC APPROACH FOR RESTORATIVE PROCTO-COLECTOMY WITH ILEAL-POUCH-ANAL ANASTOMOSIS IN ULCERATIVE COLITIS: A COMPARATIVE STUDY

E.P. Emma¹, C.V. Palleschi¹, M. Mariatti¹, F. Perna¹, F. Ficari¹, S. Scaringi¹
¹Careggi University Hospital, Digestive and IBD Surgical Unit, Florence, Italy

Contact E-Mail Address: emiliopaolo.emma@unifi.it
Introduction: Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) performed in two or three stages has become the standard surgical treatment in patients with ulcerative colitis (UC) in which the medical management fails. It is a technically complex operation associated with significant morbidity that can be performed with a laparoscopic or robotic approach. Robotic colorectal surgery is gaining popularity because it overcomes many of the mechanical and optical disadvantages of laparoscopy, although limited data are available regarding its safety, efficacy, and costs.
Aims & Methods: This study compares the postoperative short-terms surgical outcomes of the two surgical approaches. Robotic and laparoscopic restorative proctocolectomy procedures with IPAA consecutively per-

formed between June 2015 and May 2023 were retrospectively collected. Inclusion criteria was UC not responders to medical therapy. Exclusion criteria was conversion to open surgery.

Primary analyzed outcome were complications rate in the first month (30 days) according to Clavien Dindo Score and length of hospital stay (days). Statistical analysis was performed with a dedicated software (SPSS).

Results: A total of 54 patients with UC refractory to medical therapy were included, with 31 laparoscopic procedure and 23 robotic procedures.

Demographic data were comparable between two groups in terms of age (48.7 vs 45.7 years; $p=0.62$), BMI (22,0 vs 23,7 Kg/m²; $p=1.311$) and ASA score ($p=0,72$). Short-term complications defined as Clavien Dindo scores 2-3, (compared with score 1) were 13% in the robotic group and 31% in the laparoscopic group (RR= 0.27, 95% conf. interval. 0.11-1.06).

In particular, no high-grade Clavien-Dindo complications occurred in the robotic group while 3 events (grade 3) occurred in the laparoscopic group. No surgical intervention was needed in both groups.

Length of hospital stay was a mean of 7.3 days in lap-group and 6.3 days in rob-group with no statistical significance ($p=0,09$).

Conclusion: This preliminary study concludes that robot-assisted surgery allows a reduction of short-term complications compared to laparoscopic approach. Moreover, robotic surgery allows a reduction of length of hospital stay although not statistically significant. Limits of the study were the retrospective design and the low numerosity of the sample, although comparable with the experiences already published.

Disclosure: Nothing to disclose.

PP0673

THE ENHANCED RECOVERY AFTER SURGERY PROTOCOL TAKE ITS PLACE IN INFLAMMATORY BOWEL DISEASE SURGERY

A. Todeschini¹, E. Bertocchi², G. Masini², A. Geccherle¹, A. Variola¹, G. Barugola²

¹IRCCS Sacro Cuore - Don Calabria, IBD Unit, Negrar di Valpolicella, Italy, ²IRCCS Sacro Cuore - Don Calabria, General Surgery, Negrar di Valpolicella, Italy

Contact E-Mail Address: ale_tode@hotmail.com

Introduction: The enhanced recovery after surgery (ERAS) protocol is an evidence-based standardised multimodal programme formulated to reduce surgical stress and optimise recovery after surgery. The ERAS represents the best care practice for patients undergoing colorectal surgery. To ensure high compliance with active ERAS elements, patients must be educated to actively participate in the perioperative care pathway. ERAS protocols were originally designed to treat patients with CRC, only few studies have assessed this protocol in IBD patients.

Aims & Methods: The aim of this study was to investigate the adherence to ERAS in IBD patients. This retrospective study enrolled adult patients who underwent elective colorectal surgery and the ERAS protocol at our institute between May 2020 and December 2022. The patients were divided into IBD and non-IBD group. Data on medical history were collected from electronic health records. Preoperative, intraoperative, and postoperative data were collected for each procedure using a self-reported mobile application. Adherence was calculated for at least 75% of active ERAS items. Chi-square test was used to compare categorical variables.

Results: 619 patients, 492 non-IBD and 127 IBD, were enrolled. The overall adherence to ERAS protocol items was similar between the two groups (84% vs 82%, $p=0.2$). Adherence was evaluated during the three ERAS phases in the groups: preoperative (92% vs 90%, $p=0.11$), hospitalization (63% vs 62%, $p=0.8$), post-discharge period (96% vs 93%, $p=0.2$). Moreover, focusing on the preoperative ERAS items adherence, there were significant difference between non-IBD and IBD group in nutritional optimization

(84% vs 67%, $p<0.001$) and smart communication (93% vs 89%, $p=0.002$). No difference were reported in the patient's prehabilitation adherence (74% vs 71%, $p=0.4$).

Conclusion: The feasibility of ERAS protocol was good in colorectal surgery as well as in IBD surgery. We need to focus on a tailored nutritional optimization in order to improve adherence and compliance among IBD patient.

Disclosure: Nothing to disclose.

PP0674

ANALYSIS OF COLECTOMY RATES AND ADVANCED THERAPY PRESCRIBING IN ULCERATIVE COLITIS OVER 2 DECADES IN LOTHIAN, SCOTLAND

A. Elford^{1,2}, N. Constantine-Cooke³, P. Jenkinson¹, B. Gros^{1,4}, S. Ong¹, N. Greenlees¹, N. Plevris¹, G.R. Jones^{1,3}, I. Arnott¹, C.W. Lees^{1,3}

¹NHS Lothian, Edinburgh IBD Unit, Edinburgh, United Kingdom,

²The University of Melbourne, Melbourne, Australia,

³University of Edinburgh, Institute of Genetics and Cancer, Edinburgh, United Kingdom, ⁴Reina Sofia University Hospital, Gastroenterologist, Cordoba, Spain

Contact E-Mail Address: alexelford@live.com

Introduction: The impact of increased advanced therapy prescribing on colectomy rates in ulcerative colitis (UC) to date are conflicting. We have previously demonstrated a decrease in the rates of colectomy over time from 2005 to 2018.¹ The influence of the expanding number of available therapies for UC on colectomy rates is unknown.

Aims & Methods: We aimed to describe prescribing trends of all available advanced therapies for UC in the Lothian IBD cohort up until the end of 2023 along with the corresponding colectomy rates. We identified all patients who started an advanced therapy for UC, and all patients who underwent colectomy for UC in the Lothian population from January 1st, 2005, to December 31st, 2023. Incidence and prevalence data of UC in Lothian was obtained from the rigorously validated Lothian IBD Registry.² Prescribing and colectomy rates are presented as a proportion of the prevalent population. Linear and segmental regression analyses were used to identify the annual percentage change and temporal trends in colectomy rates.

Results: From 2005 to 2023, 509 patients with ulcerative colitis underwent colectomy. The median age at colectomy was 42 years old (IQR 29-56). The median time from diagnosis to colectomy was 2.6 years (IQR 0.4-9.7). Colectomy rates per 100 UC patients were 1.47 in 2005, 1.53 in 2010, 0.68 in 2015, and 0.22 in 2023. 68% of colectomies (346/509) were performed for acute severe UC, of which 34% were within 90 days of diagnosis. 3.5% (18/509) of colectomies were for cancer ($n=11$) or dysplasia ($n=7$).

Year	06-07	08-09	10-11	12-13	14-15	16-17	18-19	20-21	22-23
No. of 1st line starts	19	7	20	6	39	67	114	131	199
2nd lines starts	0	1	1	1	7	35	43	83	94
3rd lines starts	0	0	0	0	1	3	14	37	66
4th lines starts	0	0	0	0	0	1	4	17	32
Total no. of new prescriptions of ATs	19	8	21	7	47	106	175	268	391
UC prevalence*	2382	2813	3107	3369	3677	3907	3948	4078	4115
No. of colectomies	71	68	82	63	66	48	28	21	30
Emergency colectomies	49 (69%)	47 (69%)	51 (62%)	39 (62%)	44 (67%)	36 (75%)	18 (64%)	16 (76%)	22 (73%)

AT, advanced therapies. *Prevalence is at the start of the latter year. Prevalence from 2006-2019 is actual prevalence, with 2020-2023 predicted prevalence.

Over the same time period 615 patients received at least one advanced therapy for UC. The median age at first advanced therapy was 40 years old (IQR 28-54). New advanced therapy prescriptions per 100 UC patients increased from 0.67 in 2005, to 0.37 in 2010, 1.01 in 2015, 3.21 in 2020, and 5.15 in 2023. Persistence rates on first line therapy were highest with vedolizumab, followed by infliximab. By the end of 2023, 43% (n=265), 20% (n=121), 9% (n=54), and 3% (n=21), of the 615 patients had received a second, third, fourth, and fifth line of advanced therapy respectively.

Conclusion: The incidence of colectomy for ulcerative colitis has substantially decreased over time and correlates with an increased use, and number of available advanced therapies. However, correlation cannot ascribe causation.

References:

1. Jenkinson PW, Plevris N, Lyons M, Grant R, Fulforth J, Kirkwood K, Arnott ID, Wilson D, Watson AJM, Jones GR, Lees CW. Analysis of colectomy rates for ulcerative colitis in pre- and postbiological eras in Lothian, Scotland. *Colorectal Dis.* 2021 May;23(5):1175-1183. doi: 10.1111/codi.15491. Epub 2021 Feb 17. PMID: 33350054.

2. Jones GR, Lyons M, Plevris N, Jenkinson PW, Bisset C, Burgess C, Din S, Fulforth J, Henderson P, Ho GT, Kirkwood K, Noble C, Shand AG, Wilson DC, Arnott ID, Lees CW. IBD prevalence in Lothian, Scotland, derived by capture-recapture methodology. *Gut.* 2019 Nov;68(11):1953-1960. doi: 10.1136/gutjnl-2019-318936. Epub 2019 Jul 11. PMID: 31300515; PMCID: PMC6839733.

Disclosure: ATE, NCC, PWJ, SO, NG and GRJ have no disclosures. BG has served as consultant to Galapagos and Abbvie and as speaker for Abbvie, Janssen, Takeda, Pfizer and Galapagos. NP has served as a speaker for Janssen, Takeda and Pfizer. IDA has received speaking/consulting fees for Abbvie, Takeda, Dr Falk, Ferring, BMS, Lilley, Galapagos/Alphasigma and Vifor. CWL has acted as a consultant to Abbvie, Janssen, Takeda, Pfizer, Galapagos, Eli Lilly, Bristol Myers Squibb, B.I., Sandoz, Novartis, GSK, Gilead, ViforPharma, Dr Falk, and Iterative Health; he has received speaking fees and travel support from Pfizer, Janssen, Abbvie, Eli Lilly, Galapagos, MSD, Takeda, Shire, Ferring, Hospira and Dr Falk.

PP0675

EVALUATION OF THE EFFECTIVENESS AND SAFETY OF MESENCHYMAL STEM CELL TREATMENT IN FISTULIZING CROHN'S DISEASE – INTERNATIONAL, MULTICENTER, RETROSPECTIVE COHORT STUDY

P. Bacsur^{1,2}, D. Shaham³, T. Resál^{4,1}, B. Farkas¹, P. Sarlós⁵, P. Miheller⁶, N. Maharshak³, M. Zemel⁷, A. Shitrit⁸, A. Balint¹, A. Fabian¹, R. Bor¹, Z. Bosze¹, E. Ivány¹, S. Zoltán¹, K. Farkas^{9,2}, Z. Serclova¹⁰, S. Ábrahám¹¹, T. Molnár¹

¹University of Szeged, Department of Medicine, Szeged, Hungary, ²HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary, ³Faculty of Medicine, Tel Aviv University, IBD Unit, Medical Center, Tel Aviv, Israel, ⁴Military Hospital-State Health Center, Department of Gastroenterology, Budapest, Hungary, ⁵University of Pécs, First Department of Internal Medicine, Pécs, Hungary, ⁶Semmelweis University, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary, ⁷Faculty of Medicine, Tel Aviv University, Colorectal Unit, Surgical Division, Medical Center, Tel Aviv, Israel, ⁸Shaare Zedek Medical Center, IBD and Pregnancy Unit, Jerusalem, Israel, ⁹University of Szeged, Department of Laboratory Medicine, Szeged, Hungary, ¹⁰Surgical Department, NH Hospital, Surgical Department, Horovice, Czech Republic, ¹¹University of Szeged, Department of Surgery, Szeged, Hungary

Contact E-Mail Address: bacsurp@gmail.com

Introduction: Approximately 10-15% of patients with Crohn's Disease (CD) experience penetrating complications during disease course, which significantly burdens patients' lives and impacts the healthcare system. Efficacy and safety of adipose-derived mesenchymal stem cell (MSC) transplantation (darvastrocel) in treating CD complicated by complex perianal fistulas are contradicting and real-world data are lacking.

Aims & Methods: Our study aimed to assess the effectiveness and safety of MSC therapy in managing perianal Crohn's disease. This was a retrospective, multicenter cohort study enrolling CD patients with perianal fistulas. Baseline is defined as the day of MSC treatment while the follow-up is set at 6 to 12 months. Primary outcome was perianal clinical remission at w26 (defined by closure of all external openings), while secondary outcomes were clinical response rate, perianal clinical activity (defined by Perianal Disease Activity Index [PDAI]), and adverse events. Demographic, clinical, and surgical data were recorded at baseline, w12, w26, and at w52. Predictors of treatment failure were analyzed by logistic regression models.

Variables	CD (n = 69)
Follow-up duration, weeks, median (IQR)	52 (48 - 53)
Sex, male (%)	36 (52.2)
Age at inclusion, years, median (IQR)	36 (31 - 44)
Disease duration at inclusion, weeks, median (IQR)	11 (7 - 18)
Disease activity	
CDAI, mean (± SD)	61.2 (53)
PDAI, mean (± SD)	6.9 (3.4)
CRP, mg/l, mean (± SD)	3.8 (5.2)
Number of fistulas, mean (± SD)	2 (1)

Table 1. Baseline demographic and clinical characteristics of enrolled patients.

Results: Overall, data of 69 patients (male/female ratio was 0.52 and median age was 36 [IQR 31-44]) were analyzed with a median follow-up duration of 52 [IQR 48-53] weeks. Perianal clinical remission was achieved in 49.3% until w26 and 44.9% (intention-to-treat) and 53.44% (per protocol) until w52, while baseline PDAI (OR 0.77, p = 0.043) score was associated with treatment failure. Characteristics of perianal fistulas were not linked

to primary outcome. Clinical response rates were 69.6% at w26 and 78.3% (intention-to-treat) and 74.1% (per protocol) at w52. PDAI scores were decreased to w52 (5.2 [$\pm$ 3.1] to 3.2 [$\pm$ 2.8], $p < 0.001$). Worsening of perianal symptoms were not recorded, while improvement was reported in 78.8%, 81.1%, and 85.7% of cases at w12, w26, and w52. Total adverse events occurred in 8.7%, which were needed surgical reintervention. Furthermore, emerging stenosis, anal incontinence and severe infection were not registered.

Conclusion: Efficacy data are consistent with the registration ADMIRE study, more than 80% of patients benefit from the treatment, however the appearance of spontaneous closure is high in the literature. The safety profile is reassuring, and patients' satisfaction is high.

Disclosure: Nothing to disclose.

PP0676

REAL-LIFE EFFECTIVENESS OF ALLOGENEIC EXPANDED ADIPOSE-DERIVED MESENCHYMAL STEM CELL THERAPY FOR PERIANAL FISTULIZING REFRACTORY CROHN'S DISEASE

M. Alonso-Gomez¹, A.-L. Charlois¹, C. Gay¹, E. Malezieux², E. Cotte², R. Altwegg³, G. Boschetti⁴, S. Nancey¹
¹Hôpital Lyon-Sud, Dept. of Gastroenterology, Pierre Benite, France, ²CHU Montpellier, Gastroenterology, Montpellier, France, ³Hopital Saint Eloi, Hepatology Gastroenterology, Montpellier cedex 5, France, ⁴Lyon-Sud Hospital, Dept. of Gastroenterology, Pierre-Benite, France

Contact E-Mail Address: stephane.nancey@chu-lyon.fr

Introduction: Perianal fistulizing Crohn's disease (CD) is frequent (in up to one quarter of patients within two decades of the diagnosis) (1) and represents a chronic, highly debilitating and difficult-to-treat condition. Whereas the efficacy and safety of darvadstrocel (a suspension of expanded human allogeneic, adipose-derived mesenchymal stem cells) have been demonstrated in a phase 3 randomized double-blind placebo-controlled multicenter trial (ADMIRE-CD 1), a second randomized trial (ADMIRE CD 2) was recently reported negative. Real life data about the long-term efficacy of darvadstrocel for treating perianal fistulas in Crohn's disease (CD) remain scarce.

Aims & Methods: Aim: to report the effectiveness and safety of darvadstrocel therapy to close perianal fistula in a real-life cohort of CD patients. Methods: We retrospectively collected data from all CD patients with draining perianal fistulas treated with a single local injection of darvadstrocel. All patients with nonactive or mildly active luminal CD with complex anoperineal fistula who were treated with darvadstrocel were enrolled. Darvadstrocel was locally injected following the standardized procedure of ADMIRE trial. All patients underwent removal of seton, fistula curettage, transanal closure of internal opening(s) by suture followed by local injection of 120 million of mesenchymal stem cells in outpatient surgery.

The primary endpoint was clinical remission (closure of all external openings with no discharge at pressure) at week 24. Combined remission (defined as clinically plus MRI-assessed fistula closure) were also assessed at week 24 and 52. Incidence and time to fistula relapse assessed by Kaplan Meier estimates or new fistula occurrence as well as need for anal surgery were recorded. Short and long-term adverse events were also collected.

Results: A total of 36 refractory CD patients (19 Male, mean age 38.5 years) from 2 referral French IBD centers were included with a median follow up of 16 months. Patients had CD for a mean ($\pm$ SD) of 10.5 $\pm$ 8.5 years and all had received previous immunosuppressants in the past 6 months and were also receiving concomitant immunosuppressive medications. One quarter of them had a history of diverting stomas. The vast majority of

patients had a transphincteric fistula tract (83 %) and only one internal opening (80 %). Clinical remission was achieved in 17 out of 36 patients (47.2 %) and combined remission in 15 out of 36 patients (41.6 %) at week 24. At week 52, clinical and combined remission was achieved in 17 out of 36 patients (47.2 %) and in 15 out of 33 evaluable patients (45.4 %), respectively. The probabilities of relapse-free survival was 87.1 %, 74.2 % and 55.6 % at week 24, 40 and 60. In responders at week 12, fistula relapse occurred in 50 % of patients with a median time of 34 weeks (10-71) and no new fistula was clinically and radiologically evidenced. We failed to detect any predictors of response. No new safety issues, including changes in anal continence, tumorigenicity or ectopic tissue formation were recorded throughout the study period.

Conclusion: This real-life based study shares additional experience on the effectiveness and safety of a single local injection of darvadstrocel for treating complex perianal fistula in a particularly severe and refractory cohort of patients with CD. Clinical remission was achieved in 47.2 % of patients at week 24 and combined remission in one more than 4 out of 10 patients at 52 weeks. Long-term larger studies are needed to better identify predictors of sustained fistula healing using darvadstrocel in perianal fistulizing CD.

Disclosure: Nothing to disclose.

PP0677

WHAT ARE THE INDICATIONS FOR SURGERY IN CROHN'S DISEASE IN THE ERA OF BIOLOGICS?

K. Chahi¹, F. Amri¹, O. Elmqaddem¹, H. Koulali¹, Z. Abdelkrim¹, Z. Ismaili¹, G. Kharrasse¹

¹CHU Mohamed VI Oujda, Hepato-Gastroenterology, Oujda, Morocco

Contact E-Mail Address: kaoutarchahi@gmail.com

Introduction: Despite significant progress in medical therapy, surgery remains a common treatment for Crohn's Disease (CD), particularly in cases with complications such as intestinal obstruction, fistulas, abscesses, or severe bleeding. A substantial proportion of patients require surgery within the first two decades after diagnosis, even with the widespread use of biological therapies.

Aims & Methods: This study is a retrospective, descriptive analysis spanning 8 years, from January 2015 to March 2024, conducted in a gastroenterology department of a university hospital. It includes all patients with Crohn's Disease who underwent surgery during this period. Data were collected from patient records, including demographics, disease characteristics, surgical indications, and treatment history.

This study evaluates the prevalence of surgical interventions and the primary indications for surgery in the era of biological treatments for Crohn's Disease.

Results: The study cohort comprised 292 patients diagnosed with Crohn's Disease, of whom 50 (17.12%) required surgical intervention. The median age at diagnosis among these surgical patients was 30 years, with a range from 9 to 64 years. The mean age at the time of surgery was 32 years (range: 16-64 years). Among the surgical cohort, 28 patients (56%) were male and 22 patients (44%) were female. Additionally, 7 of the 50 surgical patients (14%) had a prior history of appendectomy.

Regarding disease location, 16 patients (32%) had localized ileum involvement, while 42 patients (84%) had ileo-colic involvement. Notably, 13 of the surgical patients (26%) had perineal disease. Concerning the frequency of surgery, 38 patients (76%) underwent a single surgical procedure, 8 patients (16%) had two surgeries, 2 patients (4%) had three surgeries, and 2 patients (4%) required four surgical interventions.

Of the total surgical procedures, 18 (36%) were conducted on an urgent

basis, indicating a significant proportion of acute complications. Regarding medication use prior to surgery, 6 patients (12%) were on corticosteroids, 21 patients (42%) were receiving immunosuppressants, and 5 patients (10%) were undergoing biological therapy.

The primary indications for surgery in this cohort were stenosis, accounting for 35 cases (67.3%), intestinal perforation representing 7 cases (13.5%), fistulation comprising 7 cases (13.5%), and abscess with 1 case (1.9%).

Conclusion: Despite the increasing use of biological therapies, surgery remains necessary for many patients with Crohn’s Disease, with 17.12% of the study cohort requiring surgical intervention. The most common indications for surgery were stenosis, perforation, and fistulation, demonstrating the continued need for surgical management in patients with complex disease profiles. The relatively high rate of urgent surgeries (36%) emphasizes the need for timely and effective treatment strategies. The use of corticosteroids and immunosuppressants prior to surgery indicates that a multi-faceted approach to treatment is crucial. These findings highlight the ongoing importance of surgery in the care of Crohn’s Disease and underscore the need for continued research to improve patient outcomes.

Disclosure: Nothing to disclose.

PP0678

ASSESSMENT OF ADHERENCE TO POSTOPERATIVE ILEOCOLONIC RESECTION GUIDELINES AND IMPACT ON EARLY ENDOSCOPIC RECURRENCE IN CROHN’S DISEASE: AN AUSTRALIAN RETROSPECTIVE STUDY

A. Haig¹, P. Kakkadasam Ramaswamy¹, C. Seng², D. Subhaharan¹, Z. Hong³, L. Lin², G. Walker², A. Dorrington¹, L. White⁴, D. Patrick⁴, M.A. Shahzad³, D. Clark², W. Mohsen¹
¹Gold Coast University Hospital, Gastroenterology and Hepatology, Gold Coast, Australia, ²Royal Brisbane and Women’s Hospital, Gastroenterology, Brisbane, Australia, ³Logan Hospital, Gastroenterology and Hepatology, Meadowbrook, Australia, ⁴Sunshine Coast University Hospital, Buderim, Australia

Contact E-Mail Address: alexmdorrington@gmail.com
Introduction: Recent studies have demonstrated the efficacy of ileocolonic resection in the treatment of ileal Crohn’s disease (CD). Stratification based on risk of recurrence is current standard of care, with international guidelines recommending prophylaxis to high-risk patients. Existing data indicate suboptimal adherence to these guidelines, potentially leading to increased healthcare costs. This study aimed to evaluate (1) guideline adherence in the postoperative setting, and (2) the impact of guideline driven prophylaxis on post-operative endoscopic recurrence (POR).
Aims & Methods: We performed a retrospective cohort study of patients who underwent ileal or ileocolonic resection and anastomosis for CD between 2017 and 2021 in four Australian centres. Adherence to three specific guideline aspects was assessed: (1) colonoscopy within 12 months, (2) documentation of a Rutgeert’s score at colonoscopy, and (3) prophylactic therapy prescription in high-risk patients. High-risk patients were defined as those with one or more of the following risk factors for recurrence: postoperative smoking, prior CD-related intestinal resection, presence of penetrating or perianal disease, or presence of granulomas in the resection specimen. Early POR (defined as a Rutgeert’s score of $\geq$ i2 within 12 months of surgery) was assessed; if this was not documented, it was inferred from the report text and available images.
Results: A total of 180 patients were analysed, with a median age of 46 years, and of whom 55% were female. Disease was confined to the ileum in 59% of patients, and 18% had additional perianal involvement. Disease behaviour was stricturing in 66% and penetrating in 30%. 32% of the

cohort had undergone prior ileocolonic resection, and 25% were smokers. 122 (68%) underwent colonoscopy within 12 months, and 162 (90%) had a colonoscopy during the follow-up period (median 240 days, IQR: 174 – 402 days). A Rutgeert’s score was documented in 89/162 (55%). Of the 142 (79%) patients with at least one risk factor for recurrence, 98 (69%) received prophylactic therapy. Early POR occurred in 54 of 122 patients (44%) who underwent timely colonoscopy (high-risk group 43/94, 46%; low-risk group 11/28, 39%, $p = 0.55$). Prophylactic therapy in the high-risk group did not reduce early POR (28/62, 45% vs 15/32, 47%, $p = 0.87$).

Colonoscopy within 6-12 months	122 (68)
Rutgeert’s score documentation	89 (55)
Prophylaxis in high-risk group	98 (69)
Prophylaxis in low-risk group	20 (53)
Early post-operative recurrence (POR)	
High-risk group (all)	43 (46)*
High-risk group, prophylaxis prescribed	28 (45)
Low-risk group	11 (39)*
* no difference in POR between high-risk and low-risk groups ($p = 0.55$)	

Table 1. Selected Results n (%).

Conclusion: Adherence to guidelines in the management of postoperative Crohn’s is suboptimal, particularly in the documentation of a Rutgeert’s score. Irrespective of prophylactic therapy prescription in our cohort, early POR remains high, and guideline driven prophylaxis did not significantly reduce this rate. Additionally, recurrence was still high in patients without traditional risk factors for recurrence. This invites further investigation into alternative risk-stratification and treatment strategies to reduce POR in Crohn’s disease.

Disclosure: Nothing to disclose.

PP0679

FIRST SURGERY IS DELAYED IN DIFFICULT-TO-TREAT PATIENTS WITH CROHN’S DISEASE

Z. Zelinkova¹, B. Kadlečková², D. Podmanický³
¹Nemnica Bory - Penta Hospitals, Gastroenterology, Bratislava, Slovakia, ²Nemocnica Bory - Penta Hospitals, Gastroenterology, Bratislava, Slovakia, ³Nemocnica Bory - Penta Hospitals, Surgery, Bratislava, Slovakia

Contact E-Mail Address: zdetkova@yahoo.co.uk
Introduction: The majority of patients with Crohn’s disease (CD) undergo surgery at some point of their disease evolution. Timing of surgical procedure is currently at the centre of discussion, with the concept of surgery first showing promising results with regards to short-term quality of life and cost-effectiveness but it is unclear whether this approach can have long-term modifying effect on disease behaviour. With the enlargement of CD therapeutic armamentarium during the past years, the surgical procedure is often being delayed with unclear benefit for the patient.
Aims & Methods: The aim of this study was to determine whether the time to first surgery differ between patients with uncomplicated disease course compared with difficult-to-treat patients. All patients with CD followed at one tertiary IBD centre by March 2024 were identified through automated medical record system and patients with the history of IBD-related surgery were further analysed. Basic demographics, disease phenotype, surgical procedures and biologic use were retrieved from medical records. Surgical procedure of interest for this study purpose was defined as bowel resection of any localisation, stricturoplasty, proctectomy, gastro-entero-anastomosis. Patients with more than one surgical procedure and/or two or more biologics were categorized as difficult-to-treat; patients with one surgical procedure and no or one biologic were considered as patients

with uncomplicated disease course. The differences in basic demographics, disease phenotype and time to surgery between the two groups were analysed statistically.

Results: In total 152 patients with a history of CD-related surgery were included; mean age 40 years (range 19–81), 57 (38%) men, mean duration of the disease 14.9 years (range 1–42), the majority of patients had stenosing or stenosing and penetrating disease behaviour (54% and 33%, respectively) and ileal or colonic localisation (53% and 38%, respectively). Thirty-nine patients (26%) had history of two or more surgeries.

Seventy-seven patients (51%) were considered as difficult-to-treat, there were no differences in disease localisation and behaviour between these patients and patients with uncomplicated disease course. Time to surgery was significantly longer in the difficult-to-treat group ($6.5 \pm \text{SD } 5.6$ yrs) compared with the patients with uncomplicated disease course ($3.8 \pm \text{SD } 5.5$ yrs); $p=0.003$. Among patients with uncomplicated disease course, significantly higher proportion of patients have been operated during the first year after diagnosis compared with difficult-to-treat patients (38 pts, 51% vs. 18 pts, 23%; $p=0.000488$).

Conclusion: Difficult-to-treat patients with Crohn's disease have significantly longer time to surgery than patients with uncomplicated disease course. Considering the finding that these two groups do not differ in disease phenotype as risk factor for difficult-to-treat disease, delayed first surgery might be an independent factor for complicated disease course in these patients at long term.

Disclosure: Nothing to disclose.

PP0680

SECRET-IBD: PRELIMINARY RESULTS OF A MULTICENTRE RETROSPECTIVE OBSERVATIONAL COHORT STUDY ON ONCOLOGICAL OUTCOMES OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE WHO HAVE UNDERGONE SEGMENTAL COLONIC RESECTIONS FOR DYSPLASIA AND CANCER

A. Shamsiddinova^{1,2}, W. Ramadan¹, M. Chitnis³, O. Argyriou¹, S. Davey⁴, A.E. Patel⁵, I. Al Bakir^{6,7}, J. Davies⁸, S. Brown⁴, S. Thomas-Gibson^{1,3}, O. Faiz^{1,2}

¹St Mark's Hospital and Academic Institute, Colorectal Surgery, London, United Kingdom, ²Imperial College London, Surgery and Cancer, London, United Kingdom, ³Imperial College London, Department of Metabolism, Digestion and Reproduction, London, United Kingdom, ⁴Sheffield Teaching Hospitals NHS Foundation Trust, Surgery, Sheffield, United Kingdom, ⁵Cambridge University Hospitals NHS Foundation Trust, Surgery, Cambridge, United Kingdom, ⁶St Mark's Hospital and Academic Institute, Gastroenterology, London, United Kingdom, ⁷Chelsea and Westminster Hospital NHS Foundation Trust, Gastroenterology, London, United Kingdom, ⁸University of Cambridge, Cambridge Biomedical Research Centre, Cambridge, United Kingdom

Contact E-Mail Address: a.shamsiddinova@nhs.net

Introduction: The current international guidelines on the management of dysplasia in Inflammatory Bowel Disease (IBD) recommend proctocolectomy (PC) in cases of endoscopically unresectable dysplasia, multifocal dysplasia and colorectal cancer (CRC), and to consider it in cases of Low Grade (LGD) or Indeterminate dysplasia (IND). However, population-based studies have demonstrated that segmental colectomies (SC) are occurring in 40–70% of patients with IBD-associated CRC. Data on their outcomes is scarce, with only a handful of published articles, as evidenced by a recent systematic review.

Aims & Methods: Our aim is to contribute to this limited body of evidence from English IBD centres. Data of all adult IBD patients undergoing col-

orectal resections in 2004–2019 for dysplasia and CRC were collected from three centres. Primary outcome was oncological and secondary outcome was post-operative. Descriptive statistics were applied to compare outcome between SC (including subtotal colectomy) and proctocolectomy (PC).

Results: Of 131 patients identified, 45 underwent SC, and 86 PC. No statistically significant difference between SC and PC were identified for: gender, age at IBD diagnosis and subsequent surgery, comorbidity status (including Primary Sclerosing Cholangitis), indication for surgery (CRC vs dysplasia), and IBD subtype (CD vs UC) ($p>0.05$). Patients undergoing PC had more extensive and active colitis than those undergoing SC, as well as earlier stage and multifocal cancer. Median follow up time was 86 months (range 0 – 204), and 90 months (range 17 – 211), respectively. Unexpected cancer was found in 41/131 (31%), with no significant difference between SC and PC cohorts (28% vs 33%, $p=0.581$), however only 9/131 (7%) was at a site different to the original neoplasia. Metachronous cancer was found in 1/45 (2%) on completion proctectomy at 125 months post-index extended right hemicolectomy in a patient having completion for High Grade Dysplasia (HGD, SC cohort). Completion surgery occurred in 11/45 (25%) of SC, and only 4/11 were for a neoplastic indication (2/11 LGD, and 2/11 HGD). No significant difference in Overall Survival was observed between SC and PC groups (81% vs 94% at 5 years ($p=0.376$)).

Conclusion: This study failed to identify oncological advantages to proctocolectomy in patients with IBD neoplasia undergoing resection. Although there is potential for type II error with this small cohort, the findings are consistent with those of the published literature and recent systematic review. This study highlights the need for larger prospective studies.

References:

Birch, R.J. *et al.* (2022) 'Inflammatory Bowel Disease-Associated Colorectal Cancer Epidemiology and Outcomes: An English Population-Based Study', *The American journal of gastroenterology*, 117(11), pp. 1858–1870. Available at: <https://doi.org/10.14309/AJG.0000000000001941>.

Bogach, J. *et al.* (2021) 'Extent of Surgical Resection in Inflammatory Bowel Disease Associated Colorectal Cancer: a Population-Based Study', *Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract*, 25(10), pp. 2610–2618. Available at: <https://doi.org/10.1007/S11605-021-04913-6>.

Shamsiddinova, A *et al.* (2024) 'Systematic review: oncological outcome of patients with Inflammatory Bowel Disease undergoing segmental colonic resection for colorectal cancer and dysplasia', accepted for publication in *BJS Open*. doi: 10.1093/bjsopen/zrae052

Disclosure: Nothing to disclose.

PP0681

IMPACT OF SURGERY ON THE PSYCHOLOGICAL PROFILE OF INFLAMMATORY BOWEL DISEASE PATIENTS: A PROSPECTIVE STUDY

H. Oubella¹, M. Cherkaoui Malki², S. Mechhor³, H. El Bacha⁴, N. Benzoubeir¹, I. Errabih⁵

¹Mohammed V university - faculty of medicine and pharmacy, hepato-gastro-enterology and proctology (clinic B) - Ibn Sina university hospital center, Rabat, Morocco, ²University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ³Ibn Sina Hospital, Medecine B, Rabat, Morocco, ⁴Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: hajar-oubella@hotmail.fr

Introduction: Surgery represents an important part of the therapeutic armamentarium for the treatment of IBD, and has been associated with variable effects on the psychological profile of patients with inflammatory bowel disease. However, surgical treatment is often distressingly perceived by these patients as the failure of their therapies, and can be a trigger for anguish, anxiety or depression.

Aims & Methods: The aim of this study is to describe the psychological impact of surgery on operated IBD patients.

This is a prospective descriptive monocentric study, conducted at the Department of Hepato-Gastro-Enterology and Proctology "Medicine B" CHU Ibn Sina Rabat, which collected all patients followed for IBD (Crohn's + UC) and who were operated between August 2021 and August 2023, the psychological impact and apprehension regarding surgery will be addressed in this study. Patients of both sexes who agreed to answer the questionnaire were included, and patients who refused to answer the questionnaire and complicated patients who stayed in intensive care were excluded.

Results: 43 operated patients were included in our study, including 29 (67.4%) in the emergency setting and 14 (32.6%) scheduled. Mean age was 43 ± 16.17 years. The sex ratio was 1.26 (F/H=24/19). 35 patients (81.4%) were being followed for Crohn's disease and 8 patients (18.6%) for ulcerative colitis (UC), of whom 11 patients (25.5%) had a history of previous resection, and 1 patient (2.3%) was being followed for depression.

The surgical indications were GCA in 12 cases (27.9%), stenosis in 18 cases (41.8%), perforation in 1 case (2.3%), abscess in 8 cases (18.6%), and fistula in 4 cases (9.3%).

Our patients underwent ileo-caecal resection in 22 cases (51.2%), hemicolectomy in 6 patients (14%), colectomy in 3 patients (7%), subtotal colectomy in 11 patients (25.6%), of whom 18 patients (41.9%) had an ostomy.

On the announcement of a possible surgical procedure, the thymic symptoms and feelings expressed by patients can be classified as follows: preoperative anxiety in 18 patients (41.9%), fear of death in 7 patients (16.3%), while 24 patients (55.8%) were indifferent.

The main anxiety-generating concern was postoperative pain in 7 patients (14%), potential complications in 7 patients (16.3%), failure of the procedure in 6 patients (14%), fear of dying in 7 patients (16.3%), and 25 patients (58.1%) expressed no anxiety.

The postoperative psychological experience was unremarkable in 37 patients (86%), 3 patients (7%) reported transient postoperative sadness and 3 patients (7%) developed postoperative depression, prompting consultation with a psychiatrist.

Conclusion: The impact of surgery in IBD patients not only concerns the body, but also has an effect on psychological well-being.

This study found that the pre-operative period induces a significant burden of anxiety in these patients, and depression in some.

Disclosure: Nothing to disclose.

PP0682

COLECTOMY INDICATIONS DURING ULCERATIVE COLITIS: A TWENTY-YEAR RETROSPECTIVE FROM A UNIVERSITY HOSPITAL CENTER

O. Nacir¹, F. Lairani¹, A. Ait Errami¹, S. Oubaha^{1,2}, Z. Samlani^{1,1}, K. Krati¹

¹Department of GastroEnterology and Hepatology, Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco, ²Department of Physiology, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco

Contact E-Mail Address: o.nacir@uca.ac.ma

Introduction: Over the past two decades, advancements in medical and surgical therapy have significantly impacted hemorrhagic rectocolitis management. However, it is still not clear what happens in three situations when a colectomy is done during ulcerative colitis (UC): severe acute colitis, an illness that does not get better with medicine, and precancerous lesions.

Aims & Methods: The objective of this study was to evaluate the changes in the reasons and methods for using the UC during the last two decades. This study is an observational retrospective at a university hospital center, examining the progress of operational indicators in patients monitored for colorectal hyperplasia and who underwent segmental or complete colectomy between 2003 and 2023. The primary aim is to compare changes in patient characteristics, compare surgical methods (laparotomy and laparoscopy), and determine the frequencies of early and late post-operative problems based on the Clavien Dindo classification.

Results: The study analyzed 286 patients, with 57% being males and a median age of 40 years. The majority were pancolic and 35% were left-handed. Between 2003 and 2013, 87 patients underwent surgery for refractory chronic colitis (RCH) and 199 patients for severe acute colitis or (pre-) neoplastic lesions. The preoperative clinical features showed similarities between the two groups, particularly in terms of the duration of the course and severity. Over time, there has been a decline in colectomies for refractory chronic colitis, but an increase in colectomies for severe acute colitis or (pre-)neoplastic lesions. The utilization of laparotomy decreased from 52.3% to 18.6%, while the use of laparoscopy increased from 47.7% to 81.4%. An increase in the rate of mechanical ileo-anal anastomosis was detected.

There was no significant difference in the death rate 30 days following colectomy. The incidence of severe early problems following colectomy fell from 12.6% to 5.5%, while the average number of late complications reduced from 1.6 to 0.8. The rate of late recurrence of operation decreased from 38.6% to 19.5%. However, the incidence of infectious complications increased from 27% to 45.7%.

When comparing the two periods, there were notable disparities in the average number of biotherapies received, preoperative exposure to infliximab, and subcutaneous anti-TNFα. The utilization of infliximab considerably increased after 2013 in cases of severe acute colitis.

Conclusion: The study confirms changes in colectomy criteria for chronic ulcerative colitis over the past two decades, with a decrease in treatment-resistant cases and an increase in severe acute colitis or dysplasia/cancer cases, while laparoscopy usage has increased, reducing morbidity despite biotherapies usage.

References: 1/ "Long-term outcome of colectomy for severe ulcerative colitis in patients who failed rescue therapy with cyclosporine." Matsuoka K, et al. Alimentary Pharmacology & Therapeutics, 2015.

2/ "Early predictors of severe clinical events in an Italian cohort of patients with ulcerative colitis in a real-world setting." Danese S, et al. Journal of Crohn's and Colitis, 2021.

3/ “British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults.” Lamb CA, et al. Gut, 2019.

Disclosure: Nothing to disclose.

PP0683

USEFULNESS OF UNDERWATER EMR FOR SPORADIC NEOPLASM IN ULCERATIVE COLITIS

K. Takabayashi¹, Y. Imura¹, S. Murata¹, D. Minezaki², A. Tojo¹, H. Sakurai¹, K. Iwata², K. Miyazaki², T. Masunaga², M. Mizutani¹, T. Akimoto², Y. Takatori², Y. Yoshimatsu³, S. Sugimoto³, H. Kiyohara³, S. Kawasaki¹, Y. Mikami³, N. Matsuura², T. Sujino¹, A. Nakayama², N. Yahagi², M. Kato¹, T. Kanai³

¹Center for Diagnostic and Therapeutic Endoscopy, Keio University School of Medicine, Tokyo, Japan, ²Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Keio University School of Medicine, Tokyo, Japan, ³Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

Contact E-Mail Address: kaoru0902.a2@keio.jp

Introduction: According to Western guidelines, endoscopic resection (ER) is acceptable for neoplastic lesions with clear boundaries, even within areas affected by ulcerative colitis (UC), and this has increased the opportunities for endoscopic resection. However, this procedure is also difficult due to advanced fibrosis of mucosa associated with previous inflammation within areas affected by UC. Underwater endoscopic mucosal resection (UEMR) has become popular in recent years and has been useful for lesions with advanced fibrosis, such as lesions on scars after endoscopic resection. However, there are no reports on lesions on fibrotic mucosa caused by previous inflammation within areas affected by UC.

Aims & Methods: In this study, we verified the safety and usefulness of UEMR for lesions diagnosed as sporadic neoplasms (SN) before ER, among neoplastic lesions that developed within areas affected by UC. We enrolled 35 lesions in 26 patients that underwent UEMR for neoplastic lesions 20 mm or smaller in diameter, which had developed within areas affected by UC, from December 2021 to February 2023 at Keio University Hospital. The primary endpoint was R0 resection rate, while the secondary endpoints were en bloc resection rate, procedure time, and adverse events. Before ER, chromoendoscopy with indigo carmine-dye spraying was performed to confirm the absence of flat type dysplasia around the lesion, then the patients diagnosed with SN were recruited into the study. UEMR was performed on all cases with background mucosa in remission (Mayo Endoscopic Subscore 0 or 1).

Results: The disease types of the subjects consisted of pancolitis in 22 patients (84.6%) and left-sided colitis type in four patients (15.4%), the mean tumor diameter of resected lesions was 11.1 mm, and background mucosa consisted of normal mucosa (regenerated mucosa after inflammation) in nine lesions (25.7%), atrophic mucosa in 20 lesions (57.1%), and atrophic mucosa with ulcer scars in six lesions (17.2%). A total of 34 lesions (97.1%) underwent en bloc resection; of them, 29 lesions (85.3%) underwent R0 resection, while only one (2.9%) underwent piecemeal resection. Median procedure time was 8 minutes. The final pathological diagnosis was SN for all cases: two cases (5.7%) of tubular adenocarcinoma, 21 cases (60%) of tubular adenoma, and 12 cases of sessile serrated lesions (34.3%). In terms of procedural accidents, there were no cases of intraoperative perforation, delayed perforation, post polypectomy coagulation syndrome, and delayed bleeding. Endoscopies performed 1 year later revealed no local recurrence in all cases.

Conclusion: UEMR may be safe and effective endoscopic resection method for SN within areas affected by UC.

References: [1] Yamashina T, Uedo N, Akasaka T, Iwatsubo T, Nakatani Y, Akamatsu T, et al. Comparison of Underwater vs Conventional Endoscopic Mucosal Resection of Intermediate-Size Colorectal Polyps. *Gastroenterology*. 2019;157:451-61.e2.

[2] Takabayashi K, Kato M, Sasaki M, Iwao Y, Ogata H, Kanai T, et al. Underwater endoscopic mucosal resection for a sporadic adenoma located at severe longitudinal ulcer scars in ulcerative colitis. *Endoscopy*. 2022;54:E30-e1.

Disclosure: Nothing to disclose.

PP0684

META-ANALYSIS: REAL-WORLD EFFECTIVENESS AND SAFETY OF DARVADSTROCEL FOR COMPLEX PERIANAL FISTULIZING CROHN'S DISEASE

C. Taxonera^{1,2}, M.A. García-Brenes^{1,2}, D. Olivares^{1,3}, O.N. López-García¹, R. Zapater¹, C. Alba^{1,2}

¹Hospital Clínico San Carlos, IBD Unit, Gastroenterology, Madrid, Spain, ²Instituto de Investigación del Hospital Clínico San Carlos [IdISSC], Madrid, Spain, ³Instituto de Salud Carlos III, Madrid, Spain

Contact E-Mail Address: carlos.taxonera@salud.madrid.org

Introduction: Local injection of darvadstrocel, a suspension of expanded adipose-derived allogenic mesenchymal stem cells with anti-inflammatory and immunomodulatory properties, represents a novel effective treatment for complex perianal fistulas in patients with Crohn's disease (CD).

Aims & Methods: The aim of this systematic review was to summarize reported evidence on the real-world outcomes of darvadstrocel for complex perianal fistulas in CD and to conduct a meta-analysis of effectiveness and safety data.

A comprehensive search was led in electronic databases PubMed, Web of Science, EMBASE, Scopus and ScienceDirect until 15 April 2024 to identify observational studies evaluating darvadstrocel for complex fistulizing CD. Joanna Briggs Institute (JBI) Critical Appraisal tool was used to assess the study quality and the risk of bias. Random-effects meta-analysis model was used to calculate the pooled rates of clinical and safety outcomes. Heterogeneity across studies was assessed with the I² statistic according to Cochrane Handbook.

The primary endpoint was clinical remission (closure of all treated external openings) at months 6 and 12. Adverse events (AE) were reported as incidence rates (IRs) per 100 patients-year (PY) of exposure.

Results: Of the 72 citations identified, 12 studies with 595 patients were eligible for inclusion. According to JBI criteria, 7 and 5 studies showed a low or moderate risk of bias, respectively. The pooled rate of patients achieving clinical remission was 68.1% at month 6 (95% CI 63.4-72.7) and 77.2% (95% CI 70.1-83.8) at month 12 (Table).

Median time to achieve fistula closure was 6 weeks (95% CI 3.8-9.5). Combined remission defined as clinical remission and absence of collections > 2 cm confirmed by magnetic resonance imaging was reported in 60.6% and in 69.7% of patients at month 6 and month 12, respectively. Clinical response was observed in 79.9% and in 81.7% of patients at month 6 and month 12, respectively.

The rate of patients with treatment failure, defined as no clinical remission, at last follow-up (mean 18.7 month; SD 9.9) was 34.5% (95% CI 25.7-43.9). Linear regression analysis indicated that failure rate was independent of follow-up time (R² = 0.001). For all effectiveness outcomes, between-study heterogeneity might not be important (Table).

Pooled IR per 100 PY of AEs and serious AEs were 19.6 and 3.2, respectively. IR per 100 PY of new perianal abscesses and reoperations were 16.9 and 7.1, respectively. For safety analyses, between-study heterogeneity ranged between moderate and substantial (Table).

Effectiveness outcomes	Pooled rate	95% CI	N° studies	Patients	Heterogeneity (I ²)	Risk of heterogeneity
Month 6 clinical remission	68.1%	(63.4-72.7)	7	424	0% (P = 0.78)	Not be important
Month 12 clinical remission	77.2%	(70.1-83.8)	7	191	0% (P = 0.99)	Not be important
Month 6 combined remission	60.6%	(51.0-69.9)	4	111	0% (P = 0.84)	Not be important
Month 12 combined remission	69.7%	(47.6-88.6)	2	25	0% (P = 0.87)	Not be important
Month 6 clinical response	79.9%	(73.1-86.0)	4	370	31% (P = 0.22)	Not be important
Month 12 clinical response	81.7%	(75.2-87.6)	4	177	0% (P = 0.43)	Not be important
Failure at last follow-up	34.5%	(25.7-43.9)	7	191	35 % (P = 0.16)	Not be important
Safety outcomes	Incidence rate/100 PY	95% CI	N° studies	Total PY	Heterogeneity (I ²)	Risk of heterogeneity
AEs	19.6	(10.1-29.1)	7	1245	71 % (P < 0.01)	Substantial
SAEs	3.2	(0.6-5.8)	8	1279	59 % (P = 0.02)	Moderate
Perianal abscesses	16.9	(7.6-26.2)	8	1267	69 % (P < 0.01)	Substantial
Reoperation	7.1	(2.2-12.1)	7	222	44 % (P = 0.09)	Moderate

Table. Pooled rates for effectiveness outcomes and pooled incidence rates per 100 patients-year (PY) for safety outcomes.

Conclusion: Real-world evidence supports the efficacy and safety of darvadstrocel for complex perianal fistulas in CD. Studies reported high fistula healing rates that can be sustained long-term in most patients, with high homogeneity across studies. Darvadstrocel showed a favourable safety profile.

References:

1. Panés J, García-Olmo D, Van Assche G, et al; ADMIRE CD Study Group Collaborators. Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn’s disease: a phase 3 randomised, double-blind controlled trial. *Lancet*. 2016;388:1281-1290.
2. Panés J, García-Olmo D, Van Assche G, et al. Long-term efficacy and safety of stem cell therapy [Cx601] for complex perianal fistulas in patients with Crohn’s disease. *Gastroenterology*. 2018;154:1334–42.e4.

Disclosure: CT has served as a speaker, consultant, and advisory board member for MSD, AbbVie, Pfizer, Takeda, Galapagos, Lilly, Fresenius Kabi, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, and Tillots. MAG, DO, ONL, RZ and CA have no conflicts of interest to declare.

Poster
Lower GI

Lower GI

09:00-18:00 / Poster Exhibition

PP0685

COMPARATIVE EFFECTIVENESS OF VANCOMYCIN AND METRONIDAZOLE ON EVENT-FREE SURVIVAL AFTER INITIAL INFECTION IN PATIENTS WITH *CLOSTRIDIODES DIFFICILE* - A GERMAN MULTICENTRE COHORT STUDY (IBIS)

J. Conrad¹, K. Giesbrecht², R. Cruz Aguilar³, S.K. Gräfe⁴, A. Ullah^{5,6}, K.-P. Hunfeld⁷, C. Lübbert, Lübbert, Lübbert, Lübbert⁸, S. Pützfeld⁹, P.A. Reuken¹⁰, M. Schmitz-Rode¹¹, E. Schalk¹², T. Schmidt-Wilcke^{13,14}, S. Schmiedel¹⁵, P. Solbach¹⁶, M.J.G.T. Vehreschild^{17,18}

¹Johannes Gutenberg University of Mainz, Institute of Medical Biometry, Epidemiology and Informatics, Mainz, Germany,

²Universitätsklinikum Frankfurt, Infectious Diseases, Frankfurt, Germany, ³Department I of Internal Medicine, Division of Infectious Diseases, Medical Faculty and University Hospital Cologne, Cologne, Germany, ⁴University Hospital of Cologne, Department I of Internal Medicine, Faculty of Medicine, ECMM Excellence Centre for Medical Mycology, Cologne Germany, Germany, ⁵Medical Faculty and University Hospital Cologne, Department I of Internal Medicine, Division of infectious Diseases, Cologne, Germany, ⁶Klinikum Leverkusen, Department I of Internal Medicine, Division of Kardiologie und Internistische Intensiv Care, Leverkusenger, Germany, ⁷Northwest Medical Centre, Institute for Laboratory Medicine, Microbiology and Infection Control, Frankfurt/Main, Germany, ⁸University of Leipzig Medical Centre, Division of Infectious Diseases and Tropical Medicine, Department of Medicine I, University of Leipzig Medical Centre, Leipzig, Germany, ⁹Hospital Porz am Rhein, Division of Gastroenterology and Internal Medicine, Cologne, Germany, ¹⁰Jena University Hospital, Department of Internal Medicine IV, Jena, Germany, ¹¹Evangelisches Krankenhaus Kalk, Department of Geriatrics, Cologne, Germany, ¹²University Hospital Magdeburg, 12 Department of Hematology and Oncology, Magdeburg, Germany, ¹³District Hospital Mainkofen, Centre of Neurology, Deggendorf, Germany, ¹⁴St Mauritius Therapieklinik, Meerbusch, Germany, ¹⁵University Medical Center Hamburg-Eppendorf, I. Department of Internal Medicine, Section Infectious Diseases, Hamburg, Germany, ¹⁶University Hospital Schleswig-Holstein, Department of Medicine I, Lübeck, Germany, ¹⁷Universitätsklinikum Frankfurt, Department of Internal Medicine, Infectious Diseases, Frankfurt, Germany, ¹⁸Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt/Main, Germany

Contact E-Mail Address: gieskatharina@gmail.com

Introduction: The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published an update of its guideline in 2021, in which vancomycin or fidaxomicin replaced metronidazole as the preferred first-line treatment option for non-severe *Clostridioides difficile* infection (CDI). This decision was controversially discussed since outcome data in this particular patient group remains limited. The IBIS study aimed to close this evidence gap.

Aims & Methods: The IBIS multicentre cohort enrolled patients with an index episode of CDI between August 2017 and September 2020. The primary endpoint was event-free survival (EFS), defined as response to treatment with metronidazole or vancomycin within ten days of initiation, absence of recurrence and death from any cause up to 90 days post-treatment. A Cox proportional hazards model with inverse probability of treatment weighting was used to investigate the comparative effectiveness of this outcome. Additionally, subgroup analyses were performed based on severe and non-severe infections.

Results: Of the 489 patients included, 118 (24%) received initial treatment with metronidazole and 371 (76%) with vancomycin. Of these, 78/118 (66.1%) and 247/371 (66.6%), respectively, responded to treatment within ten days, neither developed a recurrence nor died within 90 days and thus achieved the outcome of EFS. In the subgroup of non-severe infections, 74/293 patients (25.3%) received metronidazole, and 219/293 (74.7%) received vancomycin. Of these, 33/74 (44.6%) metronidazole patients and 150/219 (68.5%) vancomycin patients survived event-free. The Cox proportional hazards model revealed differences in EFS for the overall population and both sub-groups (reference metronidazole: all severity levels: hazard ratio [HR] 0.46, [95% CI 0.33-0.65]; non-severe: HR 0.39; [95% CI 0.24-0.60]; severe: HR 0.52; [95% CI 0.28-0.95]).

Conclusion: Our analysis confirms current changes in guidelines, as it supports the superiority of vancomycin compared to metronidazole across all severity levels.

References: 1. Khanna S, Pardi DS. The growing incidence and severity of *Clostridium difficile* infection in inpatient and outpatient settings. Expert Review of Gastroenterology & Hepatology. 2010;4(4):409-16.

2. van Prehn J, Reigadas E, Vogelzang EH, Bouza E, Hristea A, Guery B, et al. European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults. Clinical Microbiology and Infection. 2021;27:1-21.

3. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018;66(7):e1-e48.

4. Manthey CF, Eppe H-J, Keller K-M, Lübbert C, Posovszky C, Ramharter M, et al. S2k-Leitlinie Gastrointestinale Infektionen der Deutschen Gesellschaft für

5. Zar FA, Bakkanagari SR, Moorthi KMLST, Davis MB. A Comparison of Vancomycin and Metronidazole for the Treatment of *Clostridium difficile*-Associated Diarrhea, Stratified by Disease Severity. Clinical Infectious Diseases. 2007;45(3):302-7.

6. Debast SB, Bauer MP, Kuijper EJ. European Society of Clinical Microbiology and Infectious Diseases: Update of the Treatment Guidance Document for *Clostridium difficile* Infection. Clinical Microbiology and Infection. 2014;20:1-26.

Disclosure: Nothing to disclose.

PP0686

COMPARATIVE ANALYSIS OF GUT MICROBIOTA CHANGES, DIARRHEA FREQUENCY, AND PROBIOTIC SENSITIVITY DURING *HELICOBACTER PYLORI* ERADICATION IN ELDERLY AND YOUNGER ADULTS

E. Tokunaga¹, J. Inoue¹, N. Asaji¹, K. Oyama¹, Y. Kodama¹
¹Kobe University Graduate School of Medicine, Gastroenterology, Kobe, Japan

Contact E-Mail Address: juninoue@med.kobe-u.ac.jp

Introduction: Antibiotic-associated diarrhea frequently arises due to disruptions in the intestinal microbiome, often becoming severe in elderly individuals. Such instances of diarrhea are also notably prevalent during *Helicobacter pylori* eradication, affecting approximately 26.6% of patients [1]. The composition and diversity of gut microbiota vary with age, suggesting that the frequency of diarrhea associated with antibiotic disruption of the gut flora, as well as sensitivity to probiotics, may differ across age groups.

Aims & Methods: Aims: This study aims to examine the differences in the frequency of diarrhea and disruption of the microbiome during *Helicobacter pylori* eradication between elderly and younger Japanese adults, and to evaluate the effectiveness of the antibiotic-resistant probiotic *Enterococcus faecium* 129 BIO 3B-R in mitigating these effects.

Methods: Seventy-six Japanese adults undergoing *Helicobacter pylori* eradication treatment were enrolled in the study and categorized into two groups: those aged 70 and above (elderly) and those under 70 (younger adults). The diversity of the gut microbiota prior to treatment initiation was assessed using meta 16S sequencing to evaluate differences between the two age groups. Participants were randomly assigned to receive either a resistant lactic acid bacteria preparation (*Enterococcus faecium* 129 BIO 3B-R) or a placebo in a blind manner, and the incidence of diarrhea and changes in microbiota composition were analyzed.

Results: Results: Meta 16S rDNA sequencing analysis revealed distinct microbiota compositions between younger and elderly adults, with significantly higher alpha diversity observed in the elderly. LEfSe analysis showed a higher abundance of the *Lactobacillus* and *Blautia* genera and a lower presence of *Bammaproteobacteria* class in the elderly group. The frequency of antibiotic-induced dysbiosis-related diarrhea was compared between younger and elderly adults, showing a higher tendency in the elderly, although there was no significant difference in the extent of diversity reduction between the age groups. Administration of the resistant lactic acid bacteria preparation, *Enterococcus faecium* 129 BIO 3B-R, resulted in a lower frequency of diarrhea and a tendency to preserve alpha diversity in the microbiota of the elderly compared to the placebo group.

Conclusion: Elderly individuals, with their distinct gut microbiota composition and diversity compared to younger adults, may have different susceptibilities to antibiotic-induced diarrhea. Furthermore, incorporating resistant lactic acid bacteria as a supplementary treatment could be advantageous for managing diarrhea and stabilizing the gut flora in the elderly.

References: [1] Armuzzi A, Cremonini F, Bartolozzi F, et al. The effect of oral administration of *Lactobacillus* GG on antibiotic-associated gastrointestinal side-effects during *Helicobacter pylori* eradication therapy. *Aliment Pharmacol Ther.* 2001;15:163–169.

Disclosure: This work was supported by a research grant from Biofermin Pharmaceutical Co. Ltd.

PP0687

THE SAFETY OF FECAL MICROBIOTA TRANSPLANTATION FOR GASTROINTESTINAL DISEASES: LONG-TERM FOLLOW-UP OF 11025 CASES IN CHINA

H. Tian¹, Q. Chen¹
¹Tongji University School of Medicine, General Surgery of Shanghai Tenth People's Hospital, Shanghai, China

Contact E-Mail Address: kevin_thl@163.com

Introduction: Fecal microbiota transplantation (FMT) has been successfully used in a series of diseases in recent years. Most studies have focused on short-term risks, which are mild and generally associated with delivery methods. There have been no reports of FMT safety in the treatment of multiple diseases and long follow-up periods.

Aims & Methods: We performed a retrospective analysis of 11025 patients who underwent FMT in the Tenth People's Hospital of Tongji University between January 2012 and December 2023. We included patients with various gastrointestinal diseases and patients with extraintestinal diseases that involved intestinal dysfunction.

A questionnaire was administered to the included patients during follow-up (2 weeks, 3 months, 1 year, and 5 years after FMT) via telephone and health portal software Haodaifu app).

Results: Most adverse events during short-term follow-up (2 weeks) were related to the method of delivery. The main adverse events in the nasogastric tube group were tube-related respiratory difficulty (40.6%, include sore throat 14.1%, nasal congestion 8.7%, nasal irritation due to nasogastric intubation 17.8%) and nausea/vomiting (12.6%). In the oral capsules group, nausea and vomiting (8.9%) occurred during oral administration because the capsules are associated with a fecal smell and taste, both of which are difficult to remove completely. For colonoscopy and enema routes, the main adverse events were diarrhea (10.7%, 9.9%) and perianal discomfort (15.3%, 8.4%), respectively.

Two cases in the colonoscopy group and one case in the enema group were complicated with colon perforation, but remission with conservative treatment. The most frequently reported adverse events were mild or moderate in severity and transient. Those symptoms associated with nasogastric tube administration disappeared after tube removal at the completion of treatment. Several other new symptoms were reported during short-term follow-up, although none occurred in >1% of patients. The most common symptom reported was bloating/flatulence. Although more adverse events were reported in the nasogastric tube group, most were mild.

Requirements	Descriptions
Informed consent	Informed consent must be obtained from patients and family members before treatment
Safety of the transplanted bacterial solution	Optimize the quality control of bacterial solution preparation and storage. Ensure that the bacterial solution is used within 1 week.
Assessment of patient suitability for FMT	Ensure normal vital signs, as well as the absence of fever, severe infection, sepsis, SIRS, and other inflammatory diseases. Confirm that the patient can tolerate full oral nutrition or enteral nutrition.
Transplantation route safety	The establishment of transplantation pathways must comply with the requirements of the Chinese guidelines*, including transplantation management, safety assessment, patient tolerance, and individualized selection.
Emergency procedures for suspected adverse events during transplantation	During the transplantation process, if adverse events are suspected, the transplantation should be paused. The cause of the event should be identified; the transplantation can be resumed when the adverse event is resolved.

Table 1.Tongji FMT Requirements.

Additionally, patients are more comfortable with the upper gastrointestinal route because they could use it for enteral nutrition support or gastrointestinal imaging according to their medical needs. Based on our clinical

experience, we proposed the “Tongji FMT Requirements” and implemented them in our clinic (beginning in 2019) to standardize the indications and timing of FMT treatment and to improve FMT safety.

After the implementation of these requirements for 2 years, we compared safety data collected before and after implementation; The application of the requirements has effectively reduced adverse events. The short-term (mainly FMT-related diseases) incidence rate significantly decreased from 32.6% in 2017–2019 to 17.2% in 2019–2021.

Conclusion: FMT appears safe during both short-term and long-term follow-up. The patient group that received FMT did not exhibit an increased incidence of new diseases, and the risk of infection transmission appears to be low. Considering the widespread use of FMT, there is a need for the establishment of a national clinical and patient-reported FMT safety collection system in future.

References:

- 1) Kelly CR, Yen EF, Grinspan AM, et al. Fecal microbiota transplantation is highly effective in real-world practice: initial results from the fmt national registry. *Gastroenterology* 2021;160:183-192
- 2) Mullish BH, Quraishi MN, Segal JP, et al. The use of faecal microbiota transplant as treatment for recurrent or refractory clostridium difficile infection and other potential indications: Joint british society of gastroenterology (BSG) and healthcare infection society (HIS) guidelines. *Gut* 2018;67:1920e41
- 3) Saha S, Mara K, Pardi DS, et al. Long-term Safety of Fecal Microbiota Transplantation for Recurrent Clostridioides difficile Infection. *Gastroenterology* 2021;160:1961-1969
- 4) Zhang S, Chen Q, Kelly CR, et al. Donor Screening for Fecal Microbiota Transplantation in China: Evaluation of 8483 Candidates. *Gastroenterology* 2022;162:966-968
- 5) Parenteral and Enteral Nutrition Branch of Chinese Medical Association, et al. Chinese experts consensus on standardized methodology and clinical application of fecal microbiota transplantation. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23:5-13
- 6) Wang S, Kou C, Liu Y, et al. Rural-urban differences in the prevalence of chronic disease in northeast China. *Asia Pac J Public Health* 2015;27:394-406

Disclosure: Nothing to disclose.

PP0688

VALIDATION OF CLOSTRIDIODES DIFFICILE QPCR METHODS FOR COMPARISON BETWEEN BACTERIAL LOAD AND CONCENTRATION OF TOXIN GENES

R. Smith-Aguasca^{1,2}, N. Camenforte², L. Rodríguez², S. Herrera², K. Vara², D. Lueerssen², F. van Deursen³, C. Camprubí-Font², L. Peñarrubia², O. Vidal¹

¹Universitat de Girona, Biology, Girona, Spain, ²STAT-Dx Life S.L. (A QIAGEN company), Barcelona, Spain, ³QIAGEN Manchester Ltd, Manchester, United Kingdom

Contact E-Mail Address: rebecca.smithaguasca@qiagen.com

Introduction: Adverse outcomes of *Clostridioides difficile* infection (CDI) are derived from toxin presence, thus the gold standard has focused on cell cytotoxin assays (1,2). However, quantitative polymerase chain reaction's (qPCR) cycle threshold values linked to genomic load may be significantly associated with disease outcome, aiding in the distinction between causative pathogens, coinfections and asymptomatic carriage (3). Genes encoding toxins A/B (*tcdA/tcdB*) are usually targeted by PCR diagnostics (3). While most virulent strains produce them simultaneously, both alone can also cause CDI (2,4,5). These genes are located in the genome within the Pathogenicity loci (*PaLoc*), which can be horizontally transferred (4,6).

Recent studies have also discovered extrachromosomal molecules carrying *tcdB* (7). This suggests that the number of cells does not necessarily correlate to the number of toxin genes.

Aims & Methods: The aim was to develop a reliable qPCR method to quantify *C. difficile* toxin A/B genes to compare them to bacterial load by targeting a house-keeping gene (*adK*). Standard curves were validated according to official guidelines and reference publications (efficiency E=90-110%; slope S=(-3.1)-(-3.6); linearity R²≥0.98) (8–11), testing 10 replicates by 9 consecutive 10-fold dilutions starting from copies/mL of 3 quantified dsDNA gBlock stocks. The linear range was validated running 5 dilution points (to copies/mL) in triplicate. The last detected dilution inside the linear range with a coefficient of variation ≤25% was considered limit of quantification. Precision, repeatability and reproducibility were evaluated. Commercially supplied *C. difficile* isolates and retrospective clinical samples confirmed to be *C. difficile* positive were quantified.

Results: All standard curve assays developed showed acceptable qPCR efficiency and qPCR linearity (E=96-103%; S=(-3.2)-(-3.4); R²≥0.99). Four commercially supplied *C. difficile* isolates and 14 clinical samples were tested with all 3 validated methods. For each sample, concentrations resulted in the same order of magnitude but different total numbers for all assays (*adK* to copies/mL; *tcdA* to copies/mL; *tcdB* to copies/mL), except for three samples that presented one order of magnitude less *tcdA* than *adK*. In general, *adK* gene copies resulted in higher numbers than the toxins, with *tcdB* more concentrated than *tcdA*.

Conclusion: Three reliable qPCR standard curve quantification methods were successfully developed and validated to allow for the detection of toxigenic *C. difficile* and quantification of bacterial load. Results indicate that the number of copies for each gene is not the same within one single sample. This raises doubts regarding CDI, such as the possibility of harbouring both toxigenic and nontoxigenic strains (*PaLoc* negative) within one single patient, which would explain the higher concentration of *adK* gene copies in samples. Since multiple copies of the *PaLoc* have not been described, a higher concentration of *tcdB* compared to *tcdA* could suggest either the existence of some *tcdA-tcdB+* organisms or of multiple copies of *tcdB+* extrachromosomal molecules, the percentage of which might have been underestimated. Further studies would be required to elucidate the relevance and implications that these findings might have to CDI diagnosis and treatment.

References:

1. Garvey MJ, et al. Antimicrob Resist Infect Control. 2017 Dec;6(1):127. doi: 10.1186/s13756-017-0283-z
2. Seugendo M, et al. Front Microbiol. 2018 Aug 7;9:1843. doi: 10.3389/fmicb.2018.01843
3. Bonacorsi S, et al. Front Med. 2021 Sep 23;8:711809. doi: 10.3389/fmed.2021.711809
4. Orrell KE, Melnyk RA. Microbiol Mol Biol Rev. 2021 Aug 18;85(3):e00064-21. doi: 10.1128/MMBR.00064-21
5. Marvaud JC, et al. New Microbes New Infect. 2019 Nov;32:100590. doi: 10.1016/j.nmni.2019.100590
6. Di Bella S, et al. Toxins. 2016 May 3;8(5):134. doi: 10.3390/toxins8050134
7. Smits WK, et al. Curr Opin Microbiol. 2022 Feb;65:87–94. doi: 10.1016/j.mib.2021.10.016
8. National Committee for Clinical Laboratory Standards. Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline, EP6-A. 2nd ed. Vol. 23 No. 16. 2003.
9. Broeders S, et al. Trends Food Sci Technol. 2014 Jun;37(2):115–26. doi: 10.1016/j.tifs.2014.03.008
10. Bustin SA, et al. Clin Chem. 2009 Apr 1;55(4):611–22. doi: 10.1373/clinchem.2008.112797
11. Forootan A, et al. Biomol Detect Quantif. 2017 Jun;12:1–6. doi: 10.1016/j.bdq.2017.04.001

Disclosure: QIAGEN provided support in the form of salaries for some authors: RSA, NC, LR, SH, KV, DL, FVD, CCF and LP.

PP0689

HUMAN MICROBIOTA DIVERSITY IN TISSUE SAMPLES OF UPPER AND LOWER GI TRACT

M. Vrško¹, E. Majorova¹, N. Vaňová¹, Š. Mucha¹, J. Krokošová²

¹University of Pavol Jozef Šafárik in Košice, Medical Faculty, Department of Internal Medicine, Košice-Šaca, Slovakia, ²Agellab Slovakia, Clinical Microbiology, Zvolen, Slovakia

Contact E-Mail Address: vrskomartin@gmail.com

Introduction: The microbiota of human gastrointestinal tract is a complex and dynamic population of microorganisms and plays a major role in the maintenance of gut health and disease conditions. The microbial population, structure and function vary considerably throughout the upper and lower gut, but specific population and its diversity for each segment of GI tract is still not well described.

Aims & Methods: Aim: The retrospective evaluation of microorganism population and its diversity separately for upper and lower GI tract by cultivation of tissue samples that were obtained at routine endoscopy of 271 patients indicated to examination for different reasons.

Methods: Biopsies were taken using sterilized standard endoscopic biopsy forceps. Two pieces of tissue were obtained without the removal of forceps from the duodenum, from the antrum of the stomach and in same way from different segments of large intestine. Samples were placed into a 10% glucose solution for microbial cultivation.

Results: Overall, 271 biopsy specimens from the upper and lower GI tract were cultivated, specifically in 235 patients samples were obtained from antrum of stomach and duodenum, in 127 patients from large intestine and in 36 patients from both parts of GI tract. The presence of bacteria in upper GI tract was found in 70,21% and was negative in 29,79% of cases, while in lower GI tract bacteria was found in 93,70% and was negative 6,30% of cases. Tissue samples from both parts of GI tract was obtained from 36 patients and the same genera was found in 44,44%. In upper GI tract *E. coli* was present in 15,74%, followed by *Enterobacter cloacae* in 10,64%, *Pseudomonas aeruginosa* in 8,51%, *Enterococcus species* in 7,66%, *Klebsiella pneumoniae subs pneumoniae* in 5,11%, *Candida albicans* in 4,26%, *Helicobacter pylori* and *Klebsiella pneumoniae* in 2,98%, *Proteus mirabilis* in 2,55%, *Stenotrophomonas maltophilia* in 1,70%, *Neisseria subflava* and *E. coli ESBL positive* in 0,85% and 0,43% belongs to *Klebsiella pneumoniae ESBL positive*, *Streptococcus salivarius*, *Acinetobacter baumannii*, *Staphylococcus warneri*, *Enterococcus faecalis*, *Streptococcus maltophilia*, *Enterococcus hirae* and *Candida complex*. In lower GI tracts *E. coli* was present in 64,57%, followed by *Klebsiella pneumoniae* in 8,66%, *Candida albicans*, *Proteus mirabilis* and *Enterobacter cloacae* in 3,15%, *Enterococcus species* and *Klebsiella pneumoniae subs pneumoniae* in 2,36%, *E. coli ESBL positive*, *Enterococcus faecalis* and *Pseudomonas aeruginosa* in 1,57%, *Candida non albicans* and *Citrobacter koseri* in 0,79%.

The diversity of upper and lower GI tract was measured by Shannon diversity index, and it was 2.48 for upper GI tract and 1.29 for lower GI tract.

Conclusion: Most of studies which reveals fundamental differences between microbiota of upper and lower GI tract is based on examination of luminal content. We are presenting our results of the diversity of microbiota based on cultivation of biopsy samples.

Disclosure: Nothing to disclose.

PP0690

MICROBIOME AWARENESS AND BEHAVIORS AMONG PATIENTS: RESULTS FROM THE INTERNATIONAL MICROBIOTA OBSERVATORY IN 11 COUNTRIES

J. Dore¹, J.-M. Bohbot², H. Stolinska³, P. Kashyap⁴

¹INRAE, Jouy-En-Josas, France, ²Institut Alfred Fournier, Paris, France, ³Dietetyk, Warsaw, Poland, ⁴Mayo Clinic, Gastroenterology and Hepatology, Rochester, United States of America

Contact E-Mail Address: joel.dore@inrae.fr

Introduction: The International Microbiota Observatory aimed to measure awareness, knowledge and behaviors about the microbiome in general populations worldwide and in patients.

Aims & Methods: The survey was conducted among 7,500 individuals aged 18 years old and over in 11 countries (France, Spain, Portugal, Poland, Finland, Morocco, United States of America, Brazil, Mexico, China and Vietnam). Automated selection from the Ipsos online Panel ensured representative samples of general population fit the quotas method based on gender, age, employment status, and country regions. Participants were asked to fill out an online questionnaire with single- or multiple-choice questions. Demographics, microbiome awareness and knowledge, behaviors, information provided by healthcare professionals were documented and analyzed using descriptive statistics. Our focus is a self-reported patients' sub-population that included 4,509 individuals with respiratory (n=888), cardiovascular (n=1,177), digestive (n=1,036), genitourinary and kidney (n=529), neurological (315), autoimmune (n=716), osteoarticular (n=1040), psychiatric diseases (n=652), diabetes (n=745), cancer (n=270) and allergies (n=2,097).

Results: 4,509 people with various chronic diseases from 11 countries completed the questionnaire (52% female, mean 47,7 years). 70% of these patients have heard of the term "microbiome", with 24% knowing exactly what it is. However, patients' awareness varies according to the disease they have: people with diabetes are less aware (65%; (p<0.001) and people with digestive diseases are more aware (79%; (p<0.001) of this term compared to all patients. For patients with cardiovascular disease, awareness is not statistically different compared to all patients (68%). In their daily lives, 61% of patients have changed their behaviors to keep their microbiome as balanced and functional as possible. This proportion varies according to the disease they have: patients with cardiovascular diseases are less likely to change their behaviors (57%; p=0.001) while patients with digestive diseases are more likely to change them (73%; p<0.001). And among patients with diabetes, the proportion who have changed their behaviors (59%) is not statistically different compared to all patients. Only 48% of patients had received from a healthcare professional an explanation of what a microbiome is, its role and function. But, compared to all the patients, people with cardiovascular disease (43%; p<0.001) were the patients the least likely to have received this piece of information and those with digestive diseases were more likely to have received it (61%, p<0.001). Finally, 78% of patients would trust healthcare professionals as the first source of relevant and trustworthy information.

Conclusion: This survey provides insights into the need for additional education in patients. Healthcare professionals could play a crucial role in providing information about the role and functions of the microbiome, more precisely tailored to each chronic disease that patients suffer from.

References: <https://www.biocodexmicrobiotainstitute.com/en/international-microbiota-observatory>

Disclosure: The survey was sponsored by the Biocodex Microbiota Institute.

PP0691

GUT MICROBIOME IN AUTISTIC CHILDREN: THE EFFECT OF OXYTOCIN ON THE GUT MICROBIOME AND THE IMPACT OF LIFESTYLE VARIABLES

M. Evenepoel¹, N. Daniels², M. Derrien³, M. Moerkerke⁴, J. Prinsen², A. Vich Vila³, J. Steyaert⁴, B. Boets⁴, J. Raes³, K. Alaerts²

¹KU Leuven / UGhent, Rehabilitation Sciences / Microbiology, Leuven, Belgium, ²KU Leuven, Rehabilitation Sciences, Leuven, Belgium, ³KU Leuven, Microbiology and Immunology, Leuven, Belgium, ⁴KU Leuven, Neurosciences, Leuven, Belgium

Contact E-Mail Address: margaux.evenepoel@kuleuven.be

Introduction: Gut microbiome has been suggested to play a role in the etiology of autism. Specifically, recent studies have pointed toward altered gut microbiome compositions, resulting in overgrowth of particular bacteria that have been linked to autism symptom severity, increased repetitive behavior, and gastrointestinal problems. However, how variations in the gut microbiome relate to autistic behavioral difficulties remains sparse. Recent autism research points towards alterations in the oxytocinergic system in autistic individuals (1), which have been implicated to form a major mediator of the gut microbiome and his impact on behavior.

However, there have been no studies to date directly addressing whether stimulation of the oxytocinergic system could modulate gut microbiome compositions in autistic children. Furthermore, it is largely unknown how potentially confounding factors may impact the results of this intervention.

Aims & Methods: In the current study we analysed gut microbiome from a previous clinical trial (2). We examined diagnosis-related differences in gut microbiome compositions in autistic versus non-autistic children (8-12 years), and the effects of a 4-week intranasal oxytocin administration on gut microbiome compositions, taking into account confounding variables.

This double-blind randomized placebo-controlled trial consisted of a double-blind phase followed by a 4-week single-blind phase during which all participants received intranasal oxytocin. Effects of oxytocin (12 IU, twice daily) on gut microbiome compositions and behavioral difficulties were assessed immediately after the administration period and 4 weeks after the last administration. Eighty autistic children and 40 typically developing peers were recruited. Note that the collection of stool samples were optional, resulting in 52 autistic children and 27 non-autistic children included in the gut microbiome part of this study.

Behavioral difficulties were assessed using the Social Responsiveness Scale, the Repetitive Behavior Scale-Revised, and the child- and parent-reported version of the Screen for Anxiety Related Emotional Disorders. Gut microbiome was analysed by 16S rRNA sequencing.

Results: No difference in gut microbiome major confounder transit time (Bristol Stool Scale) was observed between autistic and non-autistic children. Diagnosis-related difference analyses in alpha-diversity revealed a significant lower observed richness ($Z = 2.476$, $p = .013$) and a higher microbial evenness ($Z = -2.377$; $p = .017$) in autistic vs non-autistic children after Benjamini-Hochberg correction (BH-correction). Moreover, no significant differences in (CLR-transformed) abundances of bacterial genera were found between the autistic and non-autistic children after BH-correction.

However, examining the overall associations with behavioral difficulties, a significant positive association (q -value (p -value after BH-correction) $< .25$) was evident between *Romboutsia* and parent-reported anxiety-like behavior (Coeff. = 0.048, $q = .06$).

Ongoing analyses will unveil initial findings on oxytocin's effect on the gut microbiome in association to clinical responses at UEG 2024.

Conclusion: Gut microbiome differs modestly between autistic and non-autistic children. The anticipated outcomes of the intervention will allow to advance our understanding of the intricate interplay between the oxytocinergic system and the gut microbiome, offering a foundation for the development of targeted therapeutic interventions.

References:

1. Evenepoel M, Moerkerke M, Daniels N, Chubar V, Claes S, Turner J, et al. Endogenous oxytocin levels in children with autism: Associations with cortisol levels and oxytocin receptor gene methylation. *Transl Psychiatry* [Internet]. 2023 Jun 30 [cited 2023 Jul 3];13(1):235. Available from: <https://pubmed.ncbi.nlm.nih.gov/37391413/>
2. Daniels N, Moerkerke M, Steyaert J, Bamps A, Debbaut E, Prinsen J, et al. Effects of multiple-dose intranasal oxytocin administration on social responsiveness in children with autism: a randomized, placebo-controlled trial. *Mol Autism* [Internet]. 2023 Dec 1 [cited 2023 Oct 23];14(1). Available from: <https://pubmed.ncbi.nlm.nih.gov/37081454/>

Disclosure: Nothing to disclose.

PP0692

STUDY OF THE PREBIOTIC POTENTIAL OF A PREPARATION USED IN FUNCTIONAL GI SYMPTOMS, MARSHMALLOW ROOT EXTRACT, USING THE HIGH THROUGHPUT EX VIVO TECHNOLOGY SIFR

P. Van den Abbeele¹, S. Deyaert¹, K. Bedal², O. Kelber², A. Hensel³, A. Baudot¹

¹Cryptobiotix SA, Ghent, Belgium, ²Steigerwald Arzneimittelwerk GmbH, Phytomedicines Supply and Development Center, Bayer Consumer Health, Darmstadt, Germany, ³University of Münster, Institute of Pharmaceutical Biology and Phytochemistry, Münster, Germany

Contact E-Mail Address: olaf.kelber@bayer.com

Introduction: The extract of the marshmallow (*Althaea officinalis* L.) root is used in gastrointestinal complaints involving irritations of the gastrointestinal mucosa [1]. While the underlying mucosa protective and anti-inflammatory effects have been studied thoroughly over the last years, data on its effect on the gut microbiota are missing.

Aims & Methods: Given that a considerable part of the constituents of the extract can be assumed to be not fully absorbed in the small intestine, its influence on the gut microbiota in the large intestine is worth to be studied.

The impact of marshmallow root extract (STW 42) on the gut microbiome was investigated using the high-throughput, *ex vivo* SIFR[®] technology (Cryptobiotix, Ghent, Belgium). Considering 6 subjects individually, this allowed to cover the broad spectrum of microbial composition that occurs *in vivo*, in line with the so-called enterotypes, thus ensuring representative findings. Simulating a single intake, *Althaea radix* (AR) was dosed at 1.875 g/d and inulin (IN; used as positive control) was dosed at equivalent of 2 g/day.

Results: AR impacted microbial metabolite production as was shown by significantly increased total SCFA and significantly decreased pH. While the extent of the effects of IN was larger, nevertheless, AR significantly increased health-related propionate/butyrate generation, suggesting a health-promoting potential of AR. AR showed a specific effect on butyrate production, which suggests a product-specific impact on the human adult gut microbiome.

In contrast to the major interpersonal differences at family and phylum, potent treatment effects were noted at higher phylogenetic resolution (OTU level): AR exerted effects including the consistent stimulation of an OTU related to *Ruminiclostridium cellulolyticum*.

Conclusion: Overall, the SIFR[®] study demonstrated the prebiotic potential

of marshmallow root extract (AR) based on the impact on microbial metabolite production and microbial composition. This adds to the evidence supporting its use in functional GI symptoms.

References:

1. Committee on Herbal Medicinal Products (HMPC) 2016. European Union herbal monograph on *Althaea officinalis* L., radix. EMA/HMPC/436679/2015
2. Van den Abbeele P, Deyaert S, Thabuis C, Perreau C, Bajic D, Wintergerst E, Joossens M, Firman J, Walsh D, Baudot A. Bridging preclinical and clinical gut microbiota research using the *ex vivo* SIFR[®] technology. *Front Microbiol.* 2023;14:1131662
3. Van den Abbeele P, Grootaert C, Marzorati M, Possemiers S, Verstraete W, Gérard P, Rabot S, Bruneau A, El Aidy S, Derrien M, Zoetendal E, Kleerebezem M, Smidt H, Van de Wiele T. Microbial community development in a dynamic gut model is reproducible, colon region specific, and selective for Bacteroidetes and Clostridium cluster IX. *Appl Environ Microbiol.* 2010;76:5237-46

Disclosure: PVA, SD, and AB are employees of Cryptobiotix SA, Ghent, Belgium. KB and OK are employees of Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany; AH has obtained project support by Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany.

PP0693

ESTABLISHING A STOOL BANK FOR FECAL MICROBIOTA TRANSPLANTATION: A PILOT PROJECT IN CATALONIA

G. Casanova¹, A. Aira², A. Villasanta³, M. Scarpa¹, A. Vergara², M. Ruiz¹, M. Urpi¹, A. Arango¹, E. Rubio², M. Claparols⁴, A. Soriano³, C. Casals², F. Balaguer¹, B. González-Suárez¹

¹Hospital Clínic de Barcelona, Gastroenterology Department, Barcelona, Spain, ²Hospital Clínic de Barcelona, Microbiology Department, Barcelona, Spain, ³Hospital Clínic de Barcelona, Infectious Medicine Department, Barcelona, Spain, ⁴Hospital Clínic de Barcelona, Bank of Blood and Tissues, Barcelona, Spain

Contact E-Mail Address: gscasanova@clinic.cat

Introduction: Faecal microbiota transplantation (FMT) involves the transfer of microbiota from healthy donors to patients with the aim of correcting dysbiosis and restoring intestinal diversity. FMT has been shown to be successful in the treatment of recurrent or refractory *Clostridioides difficile* infection. The main limiting factor to carry out FMT is access to treatments due to the absence of intestinal microbiota banks (IMB), a process that requires a complex structure.

Aims & Methods:

- Define and standardize procedures for the creation of an IMB.
- Fabrication of viable FMT samples.

The project was carried out at the Hospital Clinic of Barcelona. Processes were defined for recruitment donors, collection and processing samples for their later use in clinical practice. A multidisciplinary team was made up with gastroenterologists, microbiologists, infectologists and two clinical nurses.

Results: From May to December 2021, through a questionnaire distributed to the donation unit of the Blood and Tissue Bank (BTB) of Hospital Clinic, 207 potential donors were identified. 52.7% (109/207) of them were considered suitable, but after the a first screening including clinical visit and microbiological analytical studies carried out, only 18.3% (20/109) of them were able to start the donation process. During this period, 79 donations were collected which enabled the processing of 155 stool samples for FMT. After 2 months of quarantine and the second screening, only 73% of the samples (114/155) were ready to be released for clinical use. Two donors were responsible for 40.5% of the donations, while 30% (6/20) did not contribute any samples during the donation period. If we consider

suitable donors those who did not present exclusion criteria in any phase of the established screening, the final number was only 9.1% (10/109).

Conclusion: 1. Correct organization of all processes is essential for the establishment of a IMB.

2. Loyalty of committed donors is essential.

3. This was the first step of a collaborative project currently ongoing at the Clinic Hospital and the Bellvitge Hospital, supported by the Department of Health in Catalonia.

Disclosure: Nothing to disclose.

PP0694

THE IMPACT OF QUALITY IMPROVEMENT PROGRAM ON CLOSTRIDIODES DIFFICILE INFECTION: A QUASI-EXPERIMENTAL STUDY

J.Y. Lee¹, T.-G. Gweon¹, H.S. Kim¹, J.H. Chang¹, T.H. Kim¹, C.W. Kim¹

¹The Catholic University of Korea, College of Medicine, Division of Gastroenterology, Department of Internal Medicine, Seoul, South Korea

Contact E-Mail Address: isabella512@naver.com

Introduction: Clostridioides difficile infection (CDI) is a major cause of nosocomial diarrhea. This study aimed to implement a quality improvement program (QIP) to expedite proper CDI treatment, including discontinuing laxatives and causative antibiotics.

Aims & Methods: Stool test results positive for CDI were automatically sent via text message to the quality improvement team (QIT), specialists in CDI management. The QIT played an advisory role in this treatment. The outcome of this study was the competency of CDI treatment within 24 h of stool test reporting.

Competency was investigated using three different models:

Model 1, initiation of CDI treatment within 24 h of positive stool test report; Model 2, Model 1 criteria met with no concurrent laxative use; and Model 3, Model 2 criteria met with no concurrent causative antibiotics. Competency rates were compared between pre- and post-intervention periods (1 year each). Analyses were performed for all patients with CDI and inpatients with CDI.

Results: In total, 340 patients with CDI (pre-intervention, n=144; post-intervention, n=196) were included in this study. The numbers of inpatients with CDI were 129 and 181, respectively. For the full patient analysis, the rates of competency for Model 1 ($P=0.002$), Model 2 ($P<0.001$), and Model 3 ($P<0.001$) in the post-intervention group were higher to those in the pre-intervention group. In the inpatient analysis, the competency rate was also higher in the post-intervention period in all three models.

Conclusion: QIP enhanced the quality of CDI treatment in terms of prompt treatment and discontinuation of concomitant laxative and causative antibiotics.

References: Berg ML, Baxter C, Ayres AM, et al. The impact of autocancellation of uncollected Clostridioides difficile specimens after 24 hours on reported healthcare-associated infections: A quality improvement intervention. *Infect Control Hosp Epidemiol* 2023;1-6.

Gaffin N, Spellberg B. Sustained reductions in unnecessary antimicrobial administration and hospital Clostridioides difficile rates via stewardship in a nonacademic setting. *Infect Control Hosp Epidemiol* 2023;44:491-493.

Disclosure: Nothing to disclose.

PP0695

DISPARITIES OF CONSUMPTION AND EXPENDITURE ON FIDAXOMICIN AND VANCOMYCIN FOR CLOSTRIDIODES DIFFICILE INFECTION (2012 TO 2023): A LONGITUDINAL STUDY OF 43 COUNTRIES

Z. Yin¹, X. Li¹, E.WY Chan², W.K. Leung¹

¹University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong, ²University of Hong Kong, Department of Pharmacology and Pharmacy, Hong Kong, Hong Kong

Contact E-Mail Address: waikleung@hku.hk

Introduction: While the latest treatment guidelines recommended fidaxomicin and oral vancomycin as first-line treatments for *C. difficile* infections, it is imperative to understand the changes in the use of these medications at the global level, given the disparities on disease prevalence and medication availability.

Aims & Methods: We aim to assess the multinational trends in the consumption and expenditures of fidaxomicin and oral vancomycin for *C. difficile*. This longitudinal trend study used the IQVIA-MIDAS global sales database to analyse data from 2012 to 2023 for fidaxomicin and oral vancomycin in 43 countries. Consumption was quantified in a defined daily dose per year per 100,000 inhabitants (DDD/100K). Expenditure was calculated in dollars per capita per year at manufacture level price, standardised to 2023 US dollars. Changes in consumption and expenditure were estimated using compound annual growth rates (CAGR).

Results: Global consumption of fidaxomicin increased rapidly from 21.68 DDD/100K in 2012 to 126.68 DDD/100K in 2023, with a consumption CAGR of 17.42% and an expenditure CAGR of 14.96%. Oral vancomycin also displayed a slower upward consumption trend from 71.61 to 120.82 DDD/100K between 2012 and 2023 with a CAGR of 4.87 %, but a decreasing trend in expenditure CAGR (-15.16%). Consumption of fidaxomicin and oral vancomycin in high-income countries were substantially higher than in countries of upper- and lower-middle income. At continent level, consumption and expenditure of fidaxomicin was highest in North America, which exceeded the cumulative total of all other continents. However, the most increase in expenditure was seen in Africa continent and lowest in North America.

	Consumption (DDD/100K)			Expenditure (US\$ per capita)		
	2012	2023	CAGR	2012	2023	CAGR
Fidaxomicin (All, n=34)	21.68	126.86	17.42	0.07	0.34	14.96
High income countries (n=31)	24.42	143.86	17.49	0.00	0.39	15.05
Upper middle income (n=2)	0.00	2.72	168.23*	0.00	<0.01	149.43*
Lower middle income (n=1)	0.00	0.00	104.18**	0.00	0.00	99.74**
Oral Vancomycin (All, n=29)	71.61	120.82	4.87	0.20	0.03	-15.16
High income countries (n=22)	203.16	350.79	5.09	0.61	0.10	-14.93
Upper middle income (n=5)	0.11	2.52	37.34	<0.01	<0.01	32.05
Lower middle income (n=2)	1.21	5.70	15.08	<0.01	<0.01	39.62

*2017-2023; **2018-2021

Conclusion: Consumption of fidaxomicin and oral vancomycin continues to increase multi-nationally, with high-income countries and North America consistently being the largest consumers. However, there are marked disparities on increase in expenditure, which was more marked in countries with middle income and African continent. This disparity could jeopardize the optimal delivery of effective medication for patients with *C. difficile* infection in these regions.

Disclosure: Nothing to disclose.

PP0696

DEEP LEARNING-BASED PREDICTION OF CLOSTRIDIODES DIFFICILE INFECTION CAUSED BY ANTIBIOTICS USING LONGITUDINAL ELECTRONIC HEALTH RECORDS

J. Kim¹, J.K. Lee¹, J. Kim², K. Kim³

¹Dongguk University Ilsan Hospital, Internal Medicine, Goyang, South Korea, ²Seoul National University, Interdisciplinary Program in Bioengineering, Seoul, South Korea, ³Seoul National University Hospital, Transdisciplinary Medicine, Seoul, South Korea

Contact E-Mail Address: lastpromise0@hanmail.net

Introduction: *Clostridioides difficile* infection (CDI) is a major cause of antibiotic-associated diarrhea and colitis. It is recognized as one of the most significant hospital-acquired infections. Although CDI can develop severe complications and spores of *Clostridioides difficile* can be transmitted by the fecal-oral route, CDI is occasionally overlooked in clinical settings.

Aims & Methods: Thus, it is necessary to monitor high CDI risk groups, particularly those undergoing antibiotic treatment, to prevent complications and spread. We developed and validated a deep learning-based model to predict the occurrence of CDI within 28 days after starting antibiotic treatment using longitudinal electronic health records. For each patient, timelines of vital signs and laboratory tests with a 35-day monitoring period and a patient information vector consisting of age, sex, comorbidities, and medications were constructed.

Results: When prediction performance of our model was evaluated, the area under the receiver operating characteristic curve was 0.952 (95% CI: 0.932-0.973) in internal validation and 0.972 (95% CI: 0.968-0.975) in external validation. Platelet count and body temperature emerged as the most important features. The risk score, the output value of the model, exhibited a consistent increase in the CDI group, while the risk score in the non-CDI group either maintained its initial value or decreased.

Conclusion: Using our CDI prediction model, high-risk patients requiring symptom monitoring can be identified. This could help reduce the underdiagnosis of CDI, thereby decreasing transmission and preventing complications

Disclosure: Nothing to declare

PP0697

EFFICACY AND SAFETY OF FECAL MICROBIOTA TRANSPLANTATION (FMT) IN RECURRENT C.DIFFICILE INFECTION- RESULTS OF THE ONE-CENTER RETROSPECTIVE STUDY

E.M. Tulewicz-Marti¹, M. Bzdrya¹, A. Przepióra¹, G. Rydzewska Wyszowska¹

¹National Medical Institute of Ministry of Interior and Administration, Department of General Medicine and Gastroenterology, Warsaw, Poland

Contact E-Mail Address: e.tulewicz@gmail.com

Introduction: Many studies have indicated a high effectiveness of fecal microbiota transplantation (FMT) in treatment of recurrent or refractory *Clostridioides difficile* infection (rCDI). Nevertheless, there is still lack of data from subpopulations regarding application of FMT and factors related to its response.

Aims & Methods: The aim of the study was to analyse the data and evaluate retrospectively the efficacy and safety of FMT for recurrent CDI. While working on the task we analysed retrospectively data of characteristics and outcomes of hospitalised patients from tertiary center who received FMT from 2015 to 2022. In all cases FMT was performed through the nasointestinal tube placed during gastroscopy. Frozen donor faces were used for

FMT from unrelated healthy donors. To avoid effect of the single donor, FMT from 2-3 unrelated donors was used. Three days prior FMT vancomycin was applied and preparation with macrogol was administered according to European guidelines. Good response to 1 FMT was considered as improvement, more than 1 FMT as suboptimal response.

Results: FMT was performed for total of 98 patients, out of which 75 patients with recurrent CDI (23 patients needed 2 FMT, 6 - 3FMT and 2 -5FMT). The average age of patients was 68 years. 56 % (42) were women. 41 (54.7%) of patients previously used antibiotics, 2 (2.6%) steroids and 4 (5.3%) proton pump inhibitors (PPI). None of them was under immunosuppressive therapy. After the first FMT procedure clinical improvement was observed in 52 patients (69.3%). What is more 23 out of 30 patients initially non-responding patients had a clinical resolution after a second FMT. Whereas, the remaining 6 patients needed 3 FMT and 1 needed 5 FMT. Though, patients who required more than 1 FMT comorbidity had any cardiovascular disease (CV) such as cardiac insufficiency, diabetes mellitus (DM) or inflammatory bowel disease (IBD). Odds of suboptimal effect of therapy (need of more than 1 FMT) was associated with prior use of metronidazole then vancomycin or fidaxomicin surprisingly. According to our data there was only one irrelevant adverse event documented (abdominal pain). There was no death attributed to CDI in the studied population.

Conclusion: In our study, FMT was effective and safe treatment of recurrent CDI in our population. Nevertheless, at the same time we have identified risk factors of suboptimal response to FMT in our cohort such as CV disease, DM and IBD, as well as use of metronidazole.

References:

1. Cammarota G, Ianiro G, Tilg H, et al. European consensus conference on faecal microbiota transplantation in clinical practice. *Gut*. 2017;66(4):569-580
2. Rao K, Safdar N. Fecal microbiota transplantation for the treatment of *Clostridium difficile* infection. *J Hosp Med*. 2016 Jan;11(1):56-61
3. Ziakas PD, Zacharioudakis IM, Zervou FN, et al. Asymptomatic carriers of toxigenic *C. difficile* in long-term care facilities: A meta-analysis of prevalence and risk factors. *PLoS One* 2015;10:e0117195
4. Hvas CL, Dahl Jørgensen SM, Jørgensen SP, Storgaard M, Lemming L, Hansen MM, Erikstrup C, Dahlerup JF. Fecal Microbiota Transplantation Is Superior to Fidaxomicin for Treatment of Recurrent *Clostridium difficile* Infection. *Gastroenterology*. 2019 Apr;156(5):1324-1332.e3
5. Lee CH, Steiner T, Petrof EO, Smieja M, Roscoe D, Nemataallah A, Weese JS, Collins S, Moayyedi P, Crowther M, Ropeleski MJ, Jayaratne P, Higgins D, Li Y, Rau NV, Kim PT. Frozen vs Fresh Fecal Microbiota Transplantation and Clinical Resolution of Diarrhea in Patients With Recurrent *Clostridium difficile* Infection: A Randomized Clinical Trial. *JAMA*. 2016 Jan 12;315(2):142-9
6. Crobach MJT, Vernon JJ, Loo VG, et al. Understanding *Clostridium difficile* colonization. *Clin Microbiol Rev* 2018;31:e00021-17

Disclosure: Nothing to disclose.

PP0698

PSEUDOMEMBRANOUS COLITIS AS A RISK FACTOR FOR RECURRENT *CLOSTRIDIUM DIFFICILE* INFECTION

R. Jänsch¹, A. Link¹, J. Prestel¹, P. Malfetherheiner^{2,1}

¹Otto-von-Guericke University of Magdeburg, Gastroenterology, Hepatology and Infectious Diseases, Magdeburg, Germany,

²Ludwig-Maximilians-University Munich, Munich, Germany

Contact E-Mail Address: robert.jaensch@med.ovgu.de

Introduction: *Clostridioides difficile* infection (CDI) is one of the most common causes of nosocomial diarrhoea with high morbidity and mortality. Recurrent and refractory courses in particular represent a special

challenge in the management of these patients. The identification of risk factors that lead to recurrent or complicated courses could improve management, e.g. through the use of new and effective therapies in patients with CDI.

Aims & Methods: The aim of this study was to investigate the relationship between pseudomembranous colitis (PMC) and the course of CDI.

In a retrospective, monocentric cohort study of a tertiary centre over a period of 10 years, patients with CDI-related hospitalisations were examined. The study included 336 patients with available information on PMC and CDI history. The patients were systematically evaluated according to concomitant diseases and co-medication. In addition, the presence of ribotype 027 (RT027) in the sub-cohort was investigated using PCR genotyping.

Results: Of the 336 patients included in the study, 210 (62.5%) had an endoscopic evaluation. Of these 210 patients with CDI, 102 (48.57%) had PMC and 108 (51.43%) had no PMC. Patients with endoscopically detected PMC were more likely to have recurrences (OR 3.7 (95%CI 2.05-6.75)). The presence of PMC was associated with older age (71.4 ± 13.41 years PMC+ vs. 61.78 ± 19.42 years PMC-). In contrast, patients with chronic inflammatory bowel disease and patients under immunosuppression were less likely to have PMC (4.90% PMC+ vs. 18.52% PMC- and 16.67% PMC+ vs. 31.48% PMC-, respectively). In patients with PMC, the RT027 ribotype was detected more frequently (44.74% PMC+ vs. 20.00% PMC-). Gender, the other comorbidities analyzed and the use of PPIs played no role in the development of PMC.

Conclusion: Endoscopic detection of PMC is associated with an increased risk of recurrent CDI. Implementation of early assessment of PMC in patients with CDI could potentially lead to improved risk assessment for recurrence.

Disclosure: Nothing to disclose.

PP0699

THE PREDICTIVE FACTORS CONTRIBUTING TO THE RECURRENCE OF *CLOSTRIDIUM DIFFICILE* INFECTION

V. Karpaviciute¹, M. Kriukas², T. Urbonas¹, G. Kiudelis¹, L. Kupcinskas¹, J. Kupcinskas¹

¹Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Department of Gastroenterology, Kaunas, Lithuania,

²Lithuanian University of Health Sciences, Kaunas, Lithuania

Contact E-Mail Address: vita.karpaviciute.0116@gmail.com

Introduction: *Clostridium difficile* infection (CDI) presents a complex challenge in healthcare, particularly within hospitals and long-term care facilities where the use of antibiotics is usually unavoidable. Understanding the factors that contribute to CDI recurrence is crucial for effective treatment and management.

Aims & Methods: This study aimed to assess possible risk factors contributing to the recurrence of CDI. We performed a retrospective analysis of 107 adults diagnosed with CDI who were managed in the tertiary care center during 2018-2020, focusing on variables including demographics, comorbidities, clinical features, history of prior antibiotic and glucocorticoid treatments.

Results: Overall, this study included 63 (58.9%) females, with a median age for all patients of 77 years (IQR 68–82). The cohort comprised a diverse array of comorbid conditions: inflammatory bowel disease (3.7%), diabetes mellitus (10.3%), chronic kidney disease (CKD) (15.9%), with 4 (23.5%) patients requiring haemodialysis, and oncological diseases (21.5%). Obesity/overweight was noted in 28 (26.2%) patients, and a history of stroke was present in 14 (13.1%). Nursing care was required for 41 (38.3%) individuals, while dementia symptoms were reported in 31 (29 %) cases.

There was a common history of prior hospitalization (65.4%), glucocorticoids were used by 14 (13.1%) patients, proton pump inhibitors (PPI) by 23 (21.5%) subjects, and 18 (16.8%) patients had surgeries within 6 months before hospitalization. Antibiotics were administered to 48.6% of patients before the onset of CDI.

During hospitalization, 4 (3.7%) patients died: 3 of whom had oncological history, 2 of them worsened after chemotherapy, and other 2 patients experienced progressive heart failure. Comparative analysis between patients with a first-time CDI diagnosis ($n = 39$), who all remained recurrence-free over a 3-year follow-up, and those with recurrences ($n = 64$), revealed that recurrence was more common in females (73.3% vs. 46.5%, $p = 0.006$), while no significant age differences were observed. Neither surgical history ($p = 0.974$) nor PPI usage ($p = 0.232$) demonstrated a significant influence on CDI recurrence. Moreover, diabetes, oncological history, and CKD did not significantly impact CDI recurrence rates ($p = 0.405$, $p = 0.078$, and $p = 0.974$) either. In contrast, a significant correlation was found between dementia and increased CDI recurrence: 83.3% of patients with dementia experienced recurrence versus 53.4% without dementia ($p = 0.004$). While patients with a history of stroke and those requiring nursing care had higher rates of recurrence, these trends were not statistically significant ($p = 0.533$ and $p = 0.065$, respectively).

Conclusion: While many clinical and demographic factors were assessed, only female sex and dementia showed a significant influence on CDI recurrence. These findings suggest that among the array of potential risk factors, cognitive impairment presents a unique challenge in the management and prevention of CDI recurrence.

Disclosure: Nothing to disclose.

PP0700

UTILITY OF MYCOBACTERIA GROWTH INDICATOR TUBE (MGIT) CULTURE AND XPERT MTB RIF ASSAY IN DIAGNOSING ABDOMINAL TUBERCULOSIS (ATB)

J. Polavarapu¹, H. Chinthala¹, S. Dass¹, L. Patel¹, A. Thomas¹, A. John¹, R. Jaleel¹, R.T. Kurien¹, E. Simon¹, S.D. Chowdhury¹, AJ Joseph¹, A. Pulimood², J.S. Michael³, A.K. Dutta¹

¹Christian Medical College, Dept. of Gastroenterology, Vellore, India, ²Christian Medical College, Dept. of Pathology, Vellore, India, ³Christian Medical College, Dept. of Microbiology, Vellore, India

Contact E-Mail Address: dr.jagadishpolavarapu@gmail.com

Introduction: Diagnosis of abdominal tuberculosis relies on microbiological tests to detect Mycobacterium tuberculosis (MTB) and histopathology. Newer microbiological tests like MGIT (culture test for MTB) and Xpert MTB Rif assay (PCR test for MTB) have an established role in diagnosing pulmonary tuberculosis (TB). This study aimed at assessing the diagnostic accuracy of these tests in abdominal tuberculosis (ATB).

Aims & Methods: We aimed to study the utility of MGIT culture and gene Xpert MTB Rif assay in diagnosing Abdominal Tuberculosis (ATB).

We conducted a retrospective study among patients diagnosed with Abdominal Tuberculosis (ATB) in 2018. The clinical and investigation details were recorded on a data sheet. This included the nature and duration of symptoms and the site of the lesion. The sample of extra-intestinal lesions was acquired under radiological guidance and sent for histopathology, MGIT culture, and Xpert test. The intestinal lesions were detected on colonoscopy or enteroscopy, and the sample was sent for histopathology and microbiological tests - MGIT & Xpert. The final diagnosis of ATB was done using composite reference standard based on the presence of histopathology findings or positive culture or the presence of diagnosed extra-intestinal tuberculosis or response to anti-tuberculosis treatment (ATT). Diagnostic yield of MGIT and Xpert tests were calculated.

Results: A total of 68 patients were studied. Forty patients had intestinal tuberculosis (ITB) and 28 patients had extra-intestinal Abdominal tuberculosis (EIATB).

In patients with ITB, mean age was 37.1 ± 13.4 years, and 30 (70%) were males. The median duration of symptoms was four months (IQR, 2-11.3 months). Abdominal pain (80%) was the commonest symptom. Fever was noted in 37.5% of cases and diarrhea in 17.5%. MGIT culture was positive in 5 (12.5%) cases. Xpert test was positive in two of the five cases with positive MGIT culture report. Another patient had Xpert positive, but MGIT culture was negative. The sensitivity of MGIT culture was 12.5%, and Xpert was 7.5%. The combined sensitivity of the two tests was 15%.

In patients with EIATB, mean age was 47.8 ± 13.6 years and 16 (57.1%) were males. Fever was present in 60.7% of cases, and abdominal pain was present in 35.7% of cases. Tissue sample for diagnosis of TB was obtained from omentum in 16 (57.1%) intra-abdominal lymph node in 7 (25%) and other sites in 5 (17.9%) patients. Histopathology supported a diagnosis of TB in 67.9% of cases. Xpert test was positive in eight (28.6%) cases. MGIT culture was positive in 3 (10.7%), of which two also had a positive Xpert test. The combined sensitivity of the two tests was 32.1%. Six of the seven intra-abdominal lymph node tissue had a positive Xpert test, while none of the omental tissue samples showed a positive result for this test.

Overall, XPERT was positive in 13 cases with a sensitivity of 19.1%. MGIT was positive in 8 cases with a sensitivity of 11.7%. The combined sensitivity of both tests was 28.6%.

Conclusion: Newer microbiological tests (MGIT, Xpert) help in the diagnosis of about one-sixth of cases with ITB and in about one-third of cases of EIATB. The faster availability of results compared to conventional culture is the key advantage, but due to the paucibacillary nature of ATB, its yield is quite low.

Disclosure: Nothing to disclose.

PP0701

ENDOSCOPICALLY-DELIVERED PURASTAT FOR THE TREATMENT OF HAEMORRHAGIC RADIATION PROCTOPATHY IS SAFE, FEASIBLE AND WELL TOLERATED: RESULTS FROM A RANDOMISED FEASIBILITY STUDY

C. Henson¹, P. Collins², A. Wilson³, D.H Vasant⁴, M. Hann⁵, J. McLaughlin⁶

¹Wythenshawe Hospital, Department of Gastroenterology, Manchester, United Kingdom, ²Royal Liverpool University Hospital, Department of Gastroenterology, Liverpool, United Kingdom, ³St. Marks Hospital, Wolfson Unit for Endoscopy, London, United Kingdom, ⁴Manchester University Foundation Trust, Department of Neurogastroenterology, Manchester, United Kingdom, ⁵University of Manchester, Department of Biostatistics, Jean McFarlane Building, Manchester, United Kingdom, ⁶University of Manchester/Salford Royal Hospital, Gastrointestinal Centre, Manchester, United Kingdom

Contact E-Mail Address: caroline.henson77@gmail.com

Introduction: Severe bleeding from radiation proctopathy (RP) affects around 6% of people treated with radiotherapy for pelvic cancer¹. Purastat, a haemostatic agent licensed to treat bleeding from blood vessels in the gut, has been shown to have haemostatic benefit during surgery and endoscopic procedures²⁻⁶. Early case series data for patients with RP have shown improvements in rectal bleeding and endoscopic appearance with no adverse effects⁷, however the effects compared to treatment as usual (TAU, sucralfate enemas) have not previously been studied.

Aims & Methods: In this first clinical trial of Purastat for RP, we investigated the feasibility, acceptability and safety outcomes in comparison to standard treatment (ISRCTN NCT04918758).

Adults with significant bleeding from endoscopically confirmed RP recruited from 3 centres (Manchester University NHS Foundation Trust, Royal Liverpool University Hospital, St Mark's Hospital) were randomised to Purastat (5mls at baseline, week 4 and week 8) or TAU (sucralfate enemas 2g BD for 8 weeks starting at baseline visit).

Significant bleeding was defined as bleeding on an at least weekly basis. Patients with other causes of rectal bleeding, or who had previously been treated with sucralfate enemas or Purastat, were excluded.

Clinical and endoscopic assessments were made at baseline, week 4, week 8 and week 20. Episodes of rectal bleeding were assessed using a patient reported diary 7 days before and after each assessment. Endoscopic grade was recorded at each assessment using the Zinicola score, Rectal Telangectasia Density Score (RTDS) and Vienna Rectoscopy Score. Participant satisfaction was assessed using Client Satisfaction Questionnaire-8 (CSQ8).

Results: 143 patients were screened over 25 months. 26 patients were consented (18%) and 25 started the study. 13 were randomised to the Purastat group. 20 participants completed the study. 5 participants (20%) withdrew (4 TAU, 1 Purastat).

Baseline demographic and clinical outcome data are shown in Table 1.

There were no adverse events relating to Purastat or TAU.

There was an improvement in rectal bleeding episodes, endoscopic grade and number of participants with anaemia in both groups. There is a possible trend towards better outcomes in the Purastat group, but as this is a small feasibility study it is not powered to detect differences between groups.

All participants reported being "very satisfied" or "mostly satisfied" overall (CSQ8).

		Purastat (n=13)	Sucralfate (n=12)
Age (years) [median (range)]		69 (56 to 77)	74.5 (46 to 81)
Gender	Female	2 (15%)	3 (25%)
	Male	11 (85%)	9 (75%)
Tumour site [n (%)]	Bladder	1 (8%)	1 (8%)
	Cervix	0	2 (17%)
	Prostate	10 (77%)	8 (67%)
	Uterine	0	1 (8%)
	Vaginal	2 (15%)	0
Anti-coagulant/ Anti-platelet therapy [n (%)]	Warfarin	0	1 (8%)
	Apixaban	1 (8%)	0
	Aspirin	0	2 (17%)
Previous treatments for RP [n (%)]	Radiofrequency Ablation	0	1 (8%)
	Argon Plasma Coagulation	2 (15%)	0
	Rectal Steroids	0	3 (25%)
Total no. of patient reported bleeding episodes [median (IQR);range]	Prior to Baseline	12 (5, 21); 0 to 34 (n=13)	9 (4, 12); 1 to 50 (n=11)
	Post Week 8	6 (0, 11); 0 to 49 (n=10)	5 (3, 12); 1 to 35 (n=7)
	Prior to Week 20	6 (3, 13); 0 to 23 (n=11)	8 (4.5, 11); 2 to 26 (n=8)
Modal endoscopic grade [Zinicola score; RTDS; Vienna telangectasia density score]	Baseline	C; 3; 3	B,C; 3; 3
	Week 8	A; 2; 2,3	B; 2; 2,3
	Week 20	A; 2; 2	B; 2,3; 2
No. with anaemia [n (%)]	Baseline	7 (54%, n=13)	3 (30%, n=10)
	Week 8	6 (50%, n=12)	1 (13%, n=8)
	Week 20	4 (17%, n=12)	2 (29%, n=7)
Haemoglobin concentration (g/L) [mean (range)]	Baseline	126.3 (80-154)	134.4 (112-159)
	Week 8	128.5 (88-154)	136.8 (126-154)
	Week 20	128.7 (85-153)	141.9 (125-165)

Table 1: Baseline demographic and clinical outcome data

Conclusion: This study shows that the study process and intervention is safe and acceptable. Clinical and endoscopic improvement was seen in both groups. A definitive national, multicentred RCT is required to test the clinical and cost effectiveness of Purastat compared with TAU.

References: 1. Gami B, Harrington K, Blake P, et al. How patients manage gastrointestinal symptoms after pelvic radiotherapy. *Alimentary Pharmacology & Therapeutics*. 2003;18(10):987-994.

2. Masuhara H, Fujii T, Watanabe Y, Koyama N, Tokuhiko K. Novel Infectious Agent-Free Hemostatic Material (TDM-621) in Cardiovascular Surgery. *Annals of Thoracic and Cardiovascular Surgery*. 2012;18(5):444-451.

3. Ellis-Behnke RG, Liang Y-X, Tay DKC, et al. Nano hemostat solution: immediate hemostasis at the nanoscale. *Nanomedicine: Nanotechnology, Biology and Medicine*. 2006;2(4):207-215.

4. Uraoka T, Ochiai Y, Fujimoto A, et al. A novel fully synthetic and self-assembled peptide solution for endoscopic submucosal dissection-induced ulcer in the stomach. *Gastrointestinal Endoscopy*. 2016;83(6):1259-1264.

5. Heller M, Wei C. Self-assembly peptide prevents blood loss. *Nanomedicine: Nanotechnology, Biology and Medicine*. 2006;2(4):216.

6. Luo Z, Wang S, Zhang S. Fabrication of self-assembling d-form peptide nanofiber scaffold d-EAK16 for rapid hemostasis. *Biomaterials*. 2011;32(8):2013-2020.

7. White K, Henson C. Endoscopically-delivered Purastat for the treatment of severe haemorrhagic radiation proctopathy: a case series. *GUT*. 2019;68 (Suppl 2):A195-A196.

Disclosure: Grants received from NIHR and World Cancer Research Fund. Support received from 3D Matrix.

PP0702

CHARACTERISTICS OF POST-EMR COLORECTAL BLEEDING IN THE ELDERLY: FOCUSING ON THE NEED FOR ENDOSCOPIC HEMOSTASIS

H. Nakazawa¹, K. Okimoto², T. Matsumura³, M. Furuya¹, Y. Koshibu¹, Y. Ozeki¹, N. Shu¹, Y. Mamiya¹, Y. Oyama¹, R. Horio¹, S. Takahashi⁴, C. Goto¹, M. Sonoda¹, T. Isikawa¹, Y. Ohta¹, T. Taida¹, J. Kato¹

¹Chiba University Hospital, Chiba, Japan, ²Chiba University Hospital, Department Of Gastroenterology, Graduate School Of Medicine,, Chiba, Japan, ³Chiba University Hospital, Department of Gastroenterology, Chiba, Japan, ⁴Chiba University, Yotsukaido, Japan

Contact E-Mail Address: sunrenz09@gmail.com

Introduction: Bleeding after colorectal endoscopic mucosal resection (EMR) is a relatively frequent complication. Some patients require hemostasis, and some patients can be monitored. Appropriate judgment of which cases are amenable to follow-up is beneficial in avoiding unnecessary invasion, especially in the elderly who are highly complicated. In this study, we aimed to clarify the characteristics of these cases while focusing on age-related factors.

Aims & Methods: Of 2099 colorectal EMR patients with 5744 lesions performed at our hospital between January 2007 and December 2019, 59 patients (M:F=43:16) and 154 lesions in the suspected delayed bleeding (DB) group with hematochezia (including small amounts of blood) or a decrease in Hb of 2 g/dL or more the day after EMR were included in the analysis. The DB group was divided into hemostasis group (H group; endoscopic hemostasis was performed) and no hemostasis group (no-H group; no endoscopy or endoscopy without hemostasis was performed), and the characteristics of patients who could be without hemostasis were identified by comparing patient and lesion's backgrounds. Elderly defined as 75 years and older.

Results: 17 patients (28.8%) in the suspected DB group were elderly, and the mean age of the elderly/nonelderly was 78 (75-92)/ 63 (40-74). Of these, (7 of 17 and 5 of 42 were on antiplatelet drugs, significantly more in the elderly (82.3% vs. 33.3%, p < 0.05). The H/ no-H group was 39/20. The 20 patients in the no-H group consisted of 8 elderly and 12 non-elderly. The elderly were significantly more amenable to no hemostasis than the non-elderly (47.1% vs 28.5%. p < 0.05). Mean lesion diameter (mm) and polypoid (Is, Isp, Ip) were 10 (4-30) /6 (1-50), 36 (78.2%)/33 (82.5%), respec-

tively, with no significant difference. In univariate analysis, the factors that tended to contribute to no-hemostasis were antiplatelet medication (Odds Ratio (OR) 3.66, 95% Confidence Interval (CI) 0.98-13.62, $p=0.053$) and 75 years and older (OR 3.17, CI 0.979-10.264, $p=0.054$).

Conclusion: Many cases of suspected DB in the elderly are amenable to follow-up. It was suggested that antiplatelet drug use leads to small amount of hematochezia that no hemostasis was required. This characteristic should be taken into account when making decisions regarding appropriate endoscopic hemostasis after suspected DB in the elderly.

Disclosure: Nothing to disclose.

PP0703

SIGNIFICANCE OF HB DECREASE IN DELAYED BLEEDING AFTER COLORECTAL ESD

S. Takahashi¹, K. Okimoto¹, T. Matsumura¹, Y. Mamiya¹, Y. Oyama¹, H. Nakazawa¹, C. Goto¹, R. Horio¹, A. Kurosugi¹, M. Sonoda¹, T. Ishikawa¹, T. Kaneko¹, K. Saito¹, Y. Ohta¹, T. Taida¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Chiba, Japan

Contact E-Mail Address: takahashi-satsuki@chiba-u.jp

Introduction: Delayed bleeding (DB) is a major complication of colorectal endoscopic submucosal dissection (ESD). There are several definitions of DB, and one of the main ones is "cases requiring hemostasis with hematochezia or hemoglobin (Hb) decrease ≥ 2 g/dL as compared to the last pre-operative level" [1]. However, it is not clear whether or not cases with Hb decrease actually requires endoscopic hemostasis, and this is sometimes difficult to determine in actual clinical practice.

Aims & Methods: We defined DB as a case requiring hemostasis with hematochezia or a Hb decrease ≥ 2 g/dL after colorectal ESD. The purpose of this study was to clarify the significance of Hb decrease in DB after colorectal ESD. Of the 595 patients (615 tumors) who underwent ESD or hybrid ESD for colorectal tumors at our hospital between June 2009 and April 2022, 145 patients (145 tumors) with suspected DB (suspected DB; with hematochezia or a Hb decrease ≥ 2 g/dL) were analyzed. We compared the hemostasis group (H group; hemostasis performed) and the no-hemostasis group (no-H group; no endoscopy performed or endoscopy performed but no hemostasis performed after hematochezia or Hb decrease) in a retrospective study.

Results: Thirty-two patients with 32 tumors were categorized into the H group, while 113 patients with 113 tumors were in the no-H group. Hematochezia was significantly higher in the H group than in the no-H group (100% vs 83.2%, $p = 0.008$, Fisher's exact test).

On the other hand, the incidence of Hb decrease on postoperative day (POD) 1 was significantly higher in the no-H group than in the H group (26.5% vs 0%, $p < 0.001$, Fisher's exact test). There were 7 cases in the 145 cases who had both hematochezia and a Hb decrease on POD 1, and every 7 cases were in the no-H group. Among the H group, only 8 cases (25%) had a Hb decrease ≥ 2 g/dL on the day of hemostasis compared to the pre-operative level.

On multivariate logistic regression analysis, date from ESD to first hematochezia $\leq$ Day3 (OR 3.57, 95%CI 1.46–8.74; $p = 0.005$) was identified as the significant factor contributing to the no-H group, followed by bleeding duration ≤ 1 day (OR 4.58, 95%CI 1.45–14.43; $p = 0.009$).

Conclusion: The duration and the first date of hematochezia seemed to be important in determining whether to perform hemostasis when DB was suspected. On the other hand, there were no cases in which a Hb decrease ≥ 2 g/dL on POD 1 required hemostasis. This suggests that a Hb decrease may be a low priority factor in DB after colorectal ESD.

References:

1. Tajiri H, Kitano S. Complications associated with endoscopic mucosal resection: Definition of bleeding that can be viewed as accidental. *Dig Endosc* 2004; 16: S134– S136.

Disclosure: Nothing to disclose.

PP0704

UNRAVELING THE CLOTTING CONNECTION: D-DIMER LEVELS AS PREDICTORS OF MESENTERIC ISCHEMIA

R. Rammohan¹, S.G. Magam¹, M. Joy¹, D. Natt¹, W. Lau¹, A. Tadikonda¹, S.R. Magam¹, L. Pannikodu¹, J. Desai¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rrammoha@numc.edu

Introduction: This study investigates the potential link between elevated D-dimer levels and the development of mesenteric ischemia, a severe vascular condition. D-dimer, a fibrin degradation product, is typically elevated in the presence of clot formation and breakdown. Mesenteric ischemia, a life-threatening condition, occurs due to reduced blood flow to the intestines.

This study explores how elevated D-dimer levels could indicate mesenteric ischemia, potentially serving as a valuable diagnostic tool. Through statistical analyses of clinical data, we seek to understand the relationship's nature and its implications for early detection and improved patient outcomes in mesenteric ischemia cases.

Aims & Methods: Our retrospective study, spanning 2009-2023, included all Mesenteric ischemic patients from the Nationwide Inpatient Sample (NIS) database. We collected data on comorbidities, Mesenteric ischemia, D dimer levels, Gender, race insurance, and socioeconomic factors using CPT and ICD codes. The first step involved descriptive analysis, examining the distribution of D-dimer levels and the prevalence of mesenteric ischemia cases. We conducted a Mann-Whitney U test, a non-parametric statistical test suitable for comparing medians between two independent groups.

Spearman's rank correlation coefficient was used to assess the strength and direction of the association between D-dimer levels and mesenteric ischemia. This test provided a measure of correlation, which was moderate and statistically significant in our dataset.

Results: A total of 7854 patients diagnosed with Mesenteric ischemia were included in the study. 4398 (54%) were female. The average age in the study is 58 ± 7 years. The average BMI in the study group was 31 ± 10 . Among the races, The Mann-Whitney U test (10.5 $p < 0.01$) showed a higher D dimer level was associated with Mesenteric ischemia Similarly, the Spearman correlation coefficient of approximately 0.260 ($p < 0.05$) demonstrates a moderate positive correlation between D-dimer levels and mesenteric ischemia, further supporting this association.

Conclusion: The results of our study reveal a noteworthy association between elevated D-dimer levels and mesenteric ischemia. The Mann-Whitney U test indicated significantly higher D-dimer levels in patients with mesenteric ischemia, reinforcing the potential of D-dimer as a marker for this condition.

Furthermore, the Spearman correlation's moderate positive coefficient strengthens the evidence for this link. These findings suggest that monitoring D-dimer levels could aid in the early identification of mesenteric ischemia, potentially improving patient outcomes through timely intervention.

However, the study highlights the need for cautious interpretation and consideration of other influencing factors in clinical settings.

References: 1. Zhang Z, Li GX, Wang XM, Wang D, Han KY, Xu D, Jiang T. [Early diagnosis and treatment of acute mesenteric ischemia for 42 cases in single center]. *Zhonghua Wai Ke Za Zhi*. 2012 Dec;50(12):1068-71. Chinese. PMID: 23336481.

Disclosure: Nothing to disclose.

PP0705

CLINICAL AND ENDOSCOPIC FEATURES OF SOLITARY RECTAL ULCER SYNDROME PRESENTED TO TERTIARY CARE HOSPITAL: MULTICENTER STUDY IN KARACHI, PAKISTAN

G. Mohiuddin¹, N. Butt¹

¹Jinnah Postgraduate Medical Complex, Karachi, Gastroenterology Ward 25, Karachi, Pakistan

Contact E-Mail Address: g.mohiuddinprtoocol@gmail.com

Introduction: Solitary rectal ulcer syndrome (SRUS) is a chronic benign disorder characterized by the presence of an abnormality of the rectum in persons who have a long history of straining during defecation. It is a misnomer as only 3rd of the patients have solitary ulcer, many have no ulcer.

Aims & Methods: This was a retrospective observational longitudinal study, conducted in the department of Gastroenterology at Jinnah Post graduate Medical Center and National Medical Center, Karachi, from 1st March 2017 to till to date . All adult patients of either gender diagnosed with SRUS on basis of clinical history and endoscopic features were included in the study. The data obtained was analyzed on the statistical software SPSS version 26.Descriptive statistics were obtained by frequencies and percentages.

Results: There were total 85 patients in our study out of which 49(58%) were female and 36(42%) were male. Mean age was 35 ±17 years. Most common presentation was per rectal bleed 68(80%) ,Constipation 58 (68.57%) and followed by abdominal pain 32(37.9%).The most common predisposing risk factor was 85 (100%) self-digitation, 51(60%) prolong stay in toilet and rectal prolapse 5 (7.1%). Endoscopically most common finding was of single ulcer 80(95.7%), followed by proctitis 59(70%) and multiple ulcers 12(14.3%) and Histology revealed mucosal ulceration 75(88%) extension of muscular fibers 65 (77%), fibromuscular obliteration of lamina propria 59(70%) and crypt distortion 54 (64.3%). Associated psychological condition among patients were obsessive compulsive disorder 51 (60%) and anxiety disorder 46(52%). Most of the patients were treated through lifestyle modification and biofeedback. Only 4 patients were referred to surgical intervention.

Conclusion: SRUS is a rare disorder with variable clinical presentation. In this study patients commonly presented with bleeding p/r followed by abdominal pain. However, common predisposing factor was self -digitation, in this regard awareness is needed in our region.

References:

1. Felt-Bersma RJF. Solitary rectal ulcer syndrome. *Curr Opin Gastroenterol*. 2021;37(1):59-65.
2. Sadeghi A, Biglari M, Forootan M, Adibi P. Solitary rectal ulcer syndrome: a narrative review. *Middle East J Dig Dis*. 2019;11(3):129-34.
3. Thirumal P, Sumathi B, Nirmala D. A Clinical entity often missed-solitary rectal ulcer syndrome in children. *Front Pediatr*. 2020;8:396.
4. Forootan M, Darvishi M. Solitary rectal ulcer syndrome: a systematic review. *Medicine (Baltimore)*. 2018;97(18):e0565.
5. Abusharifah O, Bokhary RY, Mosli MH, Saadah OI. Solitary rectal ulcer syndrome in children and adolescents: a descriptive clinicopathologic study. *Int J Clin Exp Pathol*. 2021;14(4):399-407.
6. Abreu M, Azevedo Alves R, Pinto J, Campos M, Aroso S. Solitary rectal ulcer syndrome: a paediatric case report. *GE Port J Gastroenterol*. 2017;24(3):142-6

7. Lambin T, Lafeuille P, Rivory J, Rostain F, Fabritius M, Cotte E, et al. Adenocarcinoma arising from a long-standing solitary rectal ulcer syndrome. *Endoscopy*. 2022;54(5):E205-6.

Disclosure: Nothing to disclose.

PP0706

PROSPECTIVE, MULTI-CENTER, COMPARISON OF RISK SCORES FOR THE PREDICTION OF SAFE DISCHARGE FROM THE EMERGENCY DEPARTMENT IN PATIENTS WITH LOWER GASTROINTESTINAL BLEEDING

M. Sey^{1,2}, M. Archer², D. von Renteln³, A. Kohansal⁴, S. Veldhuyzen Van Zanten⁵, H. Singh⁶, M. Edmonds⁷, H. Wiemer⁸, F. Zhou⁴, A. Pedicelli⁹, H. Keshlaf⁶, K. Oakland¹⁰, L. Guizzetti¹¹, A.N. Barkun⁹, V. Jairath¹²

¹Western University, Medicine - Division of Gastroenterology, London, Canada, ²Lawson Health Research Institute, London, Canada, ³University of Montreal, Medicine - Gastroenterology, Montreal, Canada, ⁴Dalhousie University, Medicine - Division of Digestive Care and Endoscopy, Halifax, Canada, ⁵University of Alberta, Medicine - Division of Gastroenterology, Edmonton, Canada, ⁶University of Manitoba, Internal Medicine and Community Health Sciences, Winnipeg, Canada, ⁷Western University, Medicine - Division of Emergency Medicine, London, Canada, ⁸Dalhousie University, Emergency Medicine, Halifax, Canada, ⁹McGill University, Medicine and Health Sciences - Division of Gastroenterology, Montreal, Canada, ¹⁰HCA Healthcare UK, Oxford, United Kingdom, ¹¹Independent Statistician, London, Canada, ¹²Western University, Epidemiology and Biostatistics, London, Canada

Contact E-Mail Address: msey2@uwo.ca

Introduction: Lower gastrointestinal bleeding (LGIB) is usually self-limited, although serious bleeding requiring blood transfusion, surgery, and death can occur in a minority of individuals. Risk scores can differentiate between these patients and identify who can be safely discharged from the emergency department (ED), although which score should be used is unknown.

Aims & Methods: We conducted a prospective cohort study at 8 hospitals across Canada of patients presenting with hematochezia to the ED. Individuals 18 years or older were eligible regardless if they were admitted or discharged from the ED. LGIB risk scores, informed by a prior systematic review and meta-analysis¹, were calculated at presentation for the Oakland, Strate, and BLEED scores.

Two commonly used upper gastrointestinal bleeding risk scores were also included: the Glasgow-Blatchford score (GBS) and the clinical Rockall score (cRockall). All subjects were followed for 28 days. The primary outcome was safe discharge, defined as the absence of rebleeding, readmission, need for blood transfusion, endoscopic hemostasis, radiologic hemostasis, surgery, and death at 28 days.

The performance of each score was evaluated for its overall discriminative ability (c-statistic) in predicting safe discharge. Calibrations were assessed using calibration belt plots as well as grouped calibration plots. The c-statistics of LGIB and UGIB risk scores were separately compared and adjusted for multiplicity with a focus on comparison to the Oakland score. Sensitivities and specificities were determined for each score.

Results: Between Sep 2019 and Feb 2024, a total of 529 subjects were screened, of whom 344 were enrolled. The mean (SD) age was 59.5 years (19.6), 48.5% were female, and 27.4% had a Charlson Comorbidity Index score ≥3. Overall, 39.7% of patients were admitted to hospital. At 28 days

follow-up, 4.6% were readmitted, 10.7% needed blood transfusions, 6.2% had endoscopic hemostasis, 0.3% had radiological hemostasis, 3.3% had surgery, and 1.3% died.

Overall, 79.3% had a composite endpoint of safe discharge within 28 days. Among LGIB risk scores, the AUC (95% CI) was 0.71 (0.63-0.78) for the Oakland score, 0.67 (95% CI 0.57-0.75) for the Strate score, and 0.61 (95% CI 0.53-0.68) for the BLEED score. For UGIB risk scores, the AUC (95% CI) was 0.76 (0.67-0.84) for the GBS and 0.62 (0.54-0.70) for the cRockall score. The sensitivity and specificity for each score were as follows: 23.1% and 92.1% for the Oakland score; 16.7% and 91.7% for the Strate score; 47.4% and 77.8% for the BLEED score; 50% and 88.1% for the GBS; 25.8% and 88.8% for the cRockall, respectively.

Conclusion: The Oakland score can predict safe discharge with a high degree of specificity, but clinical judgment should still be used. If a single risk score for both UGIB and LGIB is desired, then the GBS may be a good alternative although further validation is required.

References:

1. Almaghrabi M, Gandhi M, Guizzetti L, Iansavichene A, Yan B, Wilson A, Oakland K, Jairath V, Sey M. Comparison of Risk Scores for Lower Gastrointestinal Bleeding: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2022;5:e2214253.

Disclosure: HS has been on advisory boards or consulted to Pendopharm, Amgen Canada, Abbvie Canada, Innomar, Sandoz Canada, Takeda Canada, and Guardant Health, Inc. None of this is related to the current work. All other co-authors have no relevant disclosures related to this study.

PP0707

HAEMOCER PLUS IN THE TREATMENT AND PREVENTION OF LOWER GI POST-RESECTIONAL BLEEDING: PROSPECTIVE MULTICENTER REGISTRY

F. Auriemma¹, G. Andrisani², A. Facciorusso³, G. Franchellucci⁴, L. De Luca⁵, F. Calabrese¹, M. Fiacca¹, N. Citterio⁶, D. De Deo⁴, D. Paduano¹, C. Gentile¹, M. Arena⁵, C. Hassan⁴, F. Di Matteo², A. Repici⁴, B.P. Mangiavillano¹

¹Humanitas Mater Domini, Gastroenterology and Digestive Endoscopy, Castellanza, Italy, ²Campus Bio-Medico Of Rome, GI Endoscopy Unit, Roma, Italy, ³University of Foggia, Gastroenterology, Foggia, Italy, ⁴Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ⁵ASST Santi Paolo E Carlo, Digestive Endoscopy Unit, Milano, Italy, ⁶Campus-Bio Medico University, Rome, Italy

Contact E-Mail Address: francesco.auriemma.1987@gmail.com

Introduction: GI bleeding associated to endoscopic procedure is defined as clinical evidence of bleeding and a drop in hemoglobin of ≥ 2 g/dL on the day of the procedure (early bleeding) or up to 14 days after the procedure (delayed bleeding). GI bleeding is a common complication of endoscopic procedures, such as endoscopic mucosal resection (EMR) and endoscopic sub mucosal dissection (ESD). Endoscopic treatments encompass injection therapy (epinephrine, sclerosing agents), mechanical therapy (hemoclipsplacement), and thermaltherapy (monopolar and bipolar coagulation, argonplasma coagulation, or heat probe).

New endoscopic hemostasis modalities (topical hemostatic agents) are emerging as possible alternative endotherapies for primary hemostasis when bleeding is refractory or not amenable to standard endoscopic hemostasis therapies.

Aims & Methods: We aim to establish a multicenter, observational registry to collect data related to the use of HaemoCer PLUS for the primary prevention of delayed bleeding linked to endoscopic resectional procedures of the lower GI tract. Primary aim: prevention of delayed bleeding after

colonic EMR or ESD larger than 30 mm. Secondary aim: evaluation of possible adverse events (AEs) related to the application of the powder.

We enrolled all adults patients undergoing colorectal ESD or EMR for lesions bigger than 30 mm where HaemoCer PLUS has been used will be included.

Results: Preliminary results of first fortytwo enrolled patients: 23 male; mean age 75.2 years old (51-88). Mean diameter of lesions was 63 mm (35-120 mm). During procedure only four major bleeding occurred treated with hemostatic forceps. No mechanical therapy was applied. In all patients hemostatic powder was applied when there was no visible bleeding. Four patients underwent procedure with ongoing antiplatelet therapy.

We encountered only two bleeding, in day 1 post-procedure. Of these, one patient who undergone procedure with ongoing antiplatelet and anticoagulant therapies, due to cardiovascular and hepatic comorbidities; the other had no ongoing or past therapy.

Conclusion: Even if this is a preliminary results report, this hemostatic powder seems to be a valuable additional therapy to prevent bleeding in patients with large colonic endoscopic resection with ongoing antiplatelet therapy. Combined antiplatelet and anticoagulant therapy, conjunct to several comorbidities still remain a difficult to manage situation in daily practice.

Disclosure: Nothing to disclose.

PP0708

RECURRENT ISCHEMIC COLITIS: WHAT RISK FACTORS?

L. Relvas¹, F. Velasco¹, S. Barros¹, I. Malta Carvalho¹, M. Portugal¹, B.M. Santos Peixe¹

¹Unidade Local de Saúde do Algarve, Gastroenterologia, Faro, Portugal

Contact E-Mail Address: isamalta_c16@hotmail.com

Introduction: Ischemic colitis (IC) is the most common form of intestinal ischemia, arising from inadequate blood circulation in the colon. Recurrent ischemic colitis has not been extensively studied.

Aims & Methods: Our study aimed to identify the main risk factors for recurrent ischemic colitis.

An observational, cross-sectional, and descriptive study included all patients diagnosed with IC at our Hospital Center from January 2011 to December 2021. Clinical records of identified patients were analyzed, collecting demographic, clinical, imaging, endoscopic, and histological data, as well as hospitalization duration and mortality. Patients were divided into two groups - recurrent IC and non-recurrent IC - for characterization and statistical analysis.

Results: A total of 142 patients with IC were identified, with recurrence observed in 11 patients (7.7%) during the study period. Smoking was more prevalent in the recurrent IC group compared to the non-recurrent IC group (45.5% vs. 13%; $p=0.014$). Constipation was more frequent in the recurrent IC group (40.0% vs. 4.7%; $p=0.003$). Laparotomy was more common in patients with recurrent IC compared to those with non-recurrent IC (27.3% vs. 6.1%; $p=0.041$). The use of clopidogrel was more prevalent in the recurrent IC group (36.4% vs. 10%; $p=0.029$). Mean hemoglobin levels on hospital admission were lower in the recurrent IC group (11.07 ± 3.67 ; 12.99 ± 2.27 ; $p=0.012$). There was a higher need for blood transfusion in the recurrent IC group compared to the non-recurrent IC group (36.4%; 6.9%; $p=0.01$). Other findings did not show an association with recurrent IC.

Conclusion: Recurrent IC occurred in 7.7% of patients in the study. Smoking, constipation, laparotomy, and the use of clopidogrel were identified as possible risk factors for recurrent IC.

Disclosure: Nothing to disclose.

PP0709

BRAZILIAN TREND IN ANAL CANCER MORTALITY - 2012 TO 2021

C.R. Lazaretti¹, G.C. Meine¹, M.C. Meine²¹Universidade Feevale, Novo Hamburgo, Brazil, ²Pontifical Catholic University of Parana, Curitiba, Brazil**Contact E-Mail Address:** camilarlazaretti@gmail.com

Introduction: Anal cancer accounts for 2% of malignant neoplasms of the gastrointestinal tract. Most cases are squamous cell carcinoma, and the global incidence is increasing alongside the rise in Human Papillomavirus (HPV) incidence.

Individuals infected with HPV, particularly those co-infected with human immunodeficiency virus (HIV), as well as smokers, individuals with more than ten sexual partners, and those who maintain receptive anal intercourse are at increased risk of developing this cancer.

Aims & Methods: Our objective was to analyze the trends in anal cancer mortality rates in Brazil from 2012 to 2021, with a focus on gender and age. This descriptive study of anal cancer deaths (ICD-10 code C21) in Brazil utilized data from the Mortality Information System of the Unified Health System (DATASUS)

Results: In Brazil, from 2012 to 2021, there were a total of 5,955 deaths attributed to anal cancer, with 3,600 deaths in women and 2,355 deaths in men, and most of these deaths occurred after the age of 50. During this period, anal cancer mortality rates increased in both sexes. In 2012, the mortality rate was 0.22 deaths per 100,000 women and 0.13 deaths per 100,000 men, rising to 0.55 deaths per 100,000 women and 0.48 deaths per 100,000 men by 2021.

Furthermore, the average annual percent change (AAPC) in anal cancer mortality rates was higher in males than females across all age groups except for ages 30-39.

In males aged 40 and over, the AAPC of anal cancer mortality rates increased progressively with age, while in females, it remained stable across different age groups.

Notably, among individuals over 80 years old, the AAPC was 11% per year among women and 44% per year among men. As a result, the mortality ratio between women and men decreased from 1.88 (2012-2016) to 1.41 (2017-2021), reaching its lowest value of 1.14 in 2021.

Conclusion: Despite its rarity, anal cancer warrants recognition due to its rising mortality rates.

While initially, mortality rates from anal cancer were significantly higher among women, the accelerated increase in mortality rates among men has led to similar mortality rates between genders by the year 2021.

References:

1. Roberts JR, Siekas LL, Kaz AM. Anal intraepithelial neoplasia: A review of diagnosis and management. *World J Gastrointest Oncol.* 2017;9(2):50-61.
2. Itarat Y, Kietpeerakool C, Jampathong N, Chumworathayi B, Kleeboow P, Aue-Aungkul A, Nhokaew W. Sexual behavior and infection with cervical human papillomavirus types 16 and 18. *Int J Womens Health.* 2019;11:489-494.
3. De Vuyst H, Clifford GM, Nascimento MC, et al: Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: A meta-analysis. *Int J Cancer* 124:1626-1636, 2009.
4. Oliveira CR, Niu YS, Einarsdottir HM, Niccolai LM, Shapiro ED. Disparities in the Epidemiology of Anal Cancer: A Cross-Sectional Time Series. *Health Equity.* 2020 Sep 16;4(1):382-385.
5. Pérez-González A, Cachay E, Ocampo A, Poveda E. Update on the Epidemiological Features and Clinical Implications of Human Papillomavirus Infection (HPV) and Human Immunodeficiency Virus (HIV) Coinfection. *Microorganisms.* 2022;10(5):1047.

6. Kost BP, Hofmann J, Stoellnberger S, Bergauer F, Blankenstein T, Albaladejo I, Stein A, Stuckart C, Weizsäcker K, Mylonas I, Mahner S, Gimgelmaier A. Prevalence of human papillomavirus infection of the anal canal in women: A prospective analysis of high-risk populations. *Oncol Lett.* 2017;13(4):2495-2501.

Disclosure: Nothing to disclose.

PP0710

INCIDENCE OF POST-COLONOSCOPY COLORECTAL CARCINOMA AT THE UNIVERSITY OF SZEGED – RETROSPECTIVE COHORT STUDY

Z. Bosze¹, A. Fabian¹, P. Bacsur^{1,2}, T. Resál¹, A. Balint¹, M. Rutka¹, T. Tóth¹, B. Farkas¹, E. Iványi¹, D. Magyar¹, K. Farkas^{1,2}, T. Molnár¹, Z. Szepes¹, R. Bor¹

¹University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²HCEMM-USZ Translational Colorectal Research Group, Szeged, Hungary

Contact E-Mail Address: bosze.zsafia@gmail.com

Introduction: Colonoscopy and polypectomy reduce the incidence of colorectal carcinoma (CRC), however it does not entirely prevent the emergence of tumours. Post-colonoscopy CRC (PCCRC) is defined when a tumour is detected in a short follow-up period after an index colonoscopy, where no malignancies were found.

This period is hard to define however, as the World Endoscopy Organisation (WEO) does not have a unified decision on this subject, the most widespread period is a five-year long.

Aims & Methods: Our aims were to define the incidence of PCCRC at the University of Szeged, and to identify factors that could influence its detection. Patients diagnosed with CRC between 01.01.2020. and 31.12.2023 were involved. For PCCRC, we used 5-, 3- and 1-year cut-off point. We also investigated the indicators of quality colonoscopy as a predictor and assessed the adherence to guidelines regarding the management of the involved patients.

Results: Overall, 3900 CRCs were diagnosed during the study period, the ratio of PCCRC was 3.82% (N=149), 3.08 (N=120), and 1.13% (N=44) with 5-year, 3-year, and 1-year cut-off, respectively. Regarding PCCRC etiology, 64.5% (N=111) of the cases were missed lesions, 9.4% (N=14) were due to incomplete polypectomy and 16.11% (N=24) were de novo lesions. 40% (N=60) was localized on the right side of the colon, 33% (N=49) was on the left, 30% (N=45) in the rectum. Duplex tumours were detected in 5 cases. From the indicators of quality colonoscopy, coecal intubation was documented in 79% (N=117) of the cases, and adequate bowel preparation was achieved in 76% (N=113), both of which does not reach the required minimum value set by the guidelines. There was no substantial difference between the ratios of CRCs and missed lesion PCCRCs regarding lymph node involvement (grade III) and distant metastases (grade IV) (27.24% vs 23.42% and 26.30% vs 22.52%). Adherence to the adequate follow-up strategy stated by the guidelines currently in effect regarding the results of the index colonoscopy was 60.40% (N=90), negligence of the patients was responsible in 32.20% (N=19) in the non-adherent cases.

Conclusion: The incidence of PCCRC in our institution correlates with the data available worldwide. 75% of PCCRCs are missed lesions, and every third examination was carried out with insufficient bowel preparation and/or without coecal intubation and with inadequate follow-up strategy. The incidence of PCCRC can be lowered with quality colonoscopy and strict adherence to guidelines.

Disclosure: Nothing to disclose.

PP0711

MONITORING OUTCOMES OF COLORECTAL CANCER SCREENING BY ETHNICITY COULD INFORM ALTERNATIVE STRATEGIES TO IMPROVE SCREENING EFFICACY: THE EXAMPLE OF THE NEW ZEALAND NATIONAL BOWEL SCREENING PROGRAM

L. de Jonge¹, D.M.N. van den Berg¹, E. Toes-Zoutendijk¹, C. Whiteside², B. Rendle², S. Parry^{2,3}, I. Lansdorp-Vogelaar¹
¹Erasmus MC University Medical Center Rotterdam, Public Health, Rotterdam, Netherlands, ²Health New Zealand, National Bowel Screening Programme, Wellington, New Zealand, ³University of Auckland, Department of Medicine, Auckland, New Zealand

Contact E-Mail Address: l.dejonge.3@erasmusmc.nl

Introduction: After pilot studies, New Zealand implemented a national colorectal cancer (CRC) screening program in 2017 with a graduate roll out by district health board. The program invites individuals aged 60 to 74 years to perform a fecal immunochemical test (FIT), using a positivity cut-off of 40 microgram Hemoglobin per gram feces. While health disparities exist between Māori and non-Māori populations across various health domains, there has been no systematic assessment of these inequities in the context of CRC screening.

Aims & Methods: This study aimed to assess the differences on key performance indicators of the National Bowel Screening Program between Māori and non-Māori populations in New Zealand and inform policy to improve equity. In this population-based study, we used data from the national population register of invitees for CRC screening between 2017 and 2023, which contained outcomes of up to four screening rounds of the National Bowel Cancer Screening Program in New Zealand. Key performance indicators were the FIT and follow-up colonoscopy participation rate, FIT positivity rate, positive predictive value (PPV) and detection rate of advanced neoplasia (AN; CRC and advanced adenomas). Multivariate logistic regression analyses were used to assess the association between ethnicity and key performance indicators, adjusted for confounding factors such as age, sex and invitation round.

Results: A total of 1,171,205 individuals were invited for CRC screening between 2017 and 2023 for up to four screening rounds. Of these, 675,274 (57.7%) individuals participated (Table 1).

	Participation FIT, % (OR; 95%CI)	FIT positivity rate, % (OR; 95%CI)	Participation follow-up colonoscopy, % (OR; 95%CI)	PPV AN, % (OR; 95%CI)	DR AN, % (OR; 95%CI)
Total	57.7%	4.4%	81.0%	34.0%	1.20%
Ethnicity					
European	62.0%	4.2%	81.2%	36.2%	1.23%
Māori	48.0% (0.60; 0.60-0.61)	6.0% (1.52; 1.46-1.57)	80.4% (0.93; 0.84-1.13)	27.5% (0.67; 0.61-0.73)	1.33% (1.13; 1.04-1.22)
Pacific	37.2% (0.37; 0.37-0.38)	5.0% (1.27; 1.19-1.35)	80.3% (0.97; 0.83-1.13)	22.0% (0.54; 0.45-0.63)	0.89% (0.78; 0.67-0.90)
Asian	45.2% (0.51; 0.51-0.52)	3.9% (0.98; 0.94-1.03)	81.1% (1.02; 0.91-1.15)	26.4% (0.67; 0.60-0.76)	0.84% (0.73; 0.67-0.81)
Mis-sing	27.3% (0.21; 0.19-0.23)	11.5% (2.31; 1.79-2.97)	56.5% (0.27; 0.17-0.44)	41.0% (1.01; 0.53-1.91)	2.66% (1.46; 0.89-2.40)

Abbreviations: FIT, faecal immunochemical test; OR, odds ratio; CI, confidence interval; AN, advanced neoplasia = colorectal cancer + advanced adenomas; DR, detection rate.

Table 1 Multivariate logistic regression analysis: association between ethnicity and key performance indicators in the National Bowel Screening Program in New Zealand between 2017-2023 adjusted for sex-, age- and screening round.

Compared to European descent, the Māori, Pacific and Asian populations were less likely to participate in FIT screening, with odds ratios (OR) of 0.60, 0.37 and 0.51 respectively, while the Māori (OR: 1.52) and Pacific (OR: 1.27) were more likely to have a positive FIT result compared to the European descent population. Participation to follow-up colonoscopy

was not significantly different by ethnicity. Asian, Māori and Pacific people had a significantly lower PPV for AN compared to European descent (OR 0.67, 0.67, 0.54 respectively). The detection rate for AN was significantly higher for Māori individuals compared to the European descent population (OR 1.13), while being significantly lower for Pacific and Asian (0.78 and 0.73, respectively).

Conclusion: CRC screening outcomes in New Zealand differ significantly by ethnicity, in particular for the Māori and Pacific people, with Māori exhibiting the highest yield of CRC screening. These findings highlight the importance of increasing participation in this population subgroup. Given the disparities in screening yield, risk-based screening strategies tailored to ethnicity could also be considered.

References: 1. Hill S, Sarfati D, Blakely T, Robson B, Purdie G, Chen J, et al. Survival disparities in Indigenous and non-Indigenous New Zealanders with colon cancer: the role of patient comorbidity, treatment and health service factors. *Journal of Epidemiology & Community Health*. 2010;64(2):117-23.

Disclosure: Nothing to disclose.

PP0712

WITHDRAWN

PP0713

SHORT-TERM COMBINED IMPACT OF COVID-19 PANDEMIC AND POPULATION-BASED SCREENING ON THE INCIDENCE AND CLINICAL CHARACTERISTICS OF COLORECTAL CANCER – RETROSPECTIVE COHORT STUDY

R. Bor¹, B. Vasas², A. Fabian¹, Z. Bosze¹, M. Szűcs³, M. Rutka¹, D. Magyar¹, T. Tóth¹, A. Balint¹, P. Bacsur¹, T. Resál¹, K. Farkas¹, T. Molnár¹, Z. Szepes¹

¹University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Pathology, Szeged, Hungary, ³University of Szeged, Albert Szent-Györgyi Clinical Centre, Department of Medical Physics and Informatics, Szeged, Hungary

Contact E-Mail Address: bosze.zsofia@gmail.com

Introduction: In Hungary, the population-based colorectal carcinoma (CRC) screening programme was introduced at the end of 2018, shortly before the start of the COVID-19 pandemic.

Aims & Methods: The aim of our retrospective cohort study was to evaluate the impact of two presumably opposing causal factors, COVID-19 pandemic and population-based screening, on the incidence and clinical characteristics of CRC.

All patients with newly diagnosed CRC from 2014 to 2023 were included and categorized into pre-pandemic (confirmed between 2014-2019), pandemic (confirmed in 2020-2021) and post-pandemic (confirmed in 2022-2023) groups.

The extended pre-pandemic period was required to assess the impact of the screening programme, further dividing it into screening-affected (2015, 2016, and 2019) and unaffected (2014, 2017, 2018) subgroups.

Results: A total of 2803 patients were diagnosed with CRC during the study period. The annual number of CRC cases was significantly lower in the pandemic subgroup compared to the pre-pandemic screened and post-pandemic subgroups (254/year, 295/year and 295/year, p=0.009). In addition, in the pandemic subgroup, the incidence rates of CRCs detected at localized stage were significantly lower compared to the other three

groups (36.61%, 50.85%, 46.35% and 49.49%, $p < 0.001$).

Statistically significant difference in the rate of T1 tumors was only observed between the pandemic and the post-pandemic subgroups (7.09% and 12.20%, $p = 0.026$). In the pandemic period, the annual number of colonoscopies decreased by 64.31% compared to the pre-pandemic period overall, however, the post-pandemic period ($n = 4574$) saw a modest 8.70% increase relative to the pre-pandemic period, offering only partial compensation for the shortage experienced during the pandemic.

Furthermore, the annual number of colonoscopies in the extended pre-pandemic subgroup with screening was higher by 20.06% compared to the pre-pandemic subgroup without screening (4591 examinations/year vs 3824 examinations/year) and it was almost the same as the post-pandemic subgroup (4574 examinations/year).

Substantially fewer examinations were required to detect a CRC in the pandemic group compared to the pre-pandemic overall and post-pandemic groups (10.67, 15.56, 13.97 and 15.50 examinations, respectively), but within the extended pre-pandemic group, there was no relevant difference between the two subgroups in the mean number of colonoscopies required to detect a CRC (15.56 vs. 13.97).

Conclusion: Our study confirmed the negative impact of COVID-19 pandemic on the CRC epidemiology. The newly introduced population-based CRC screening has only been able to partially compensate this negative effect during pandemic period, however, was moderately compensated by during the pandemic period, but in the post-pandemic period it caused a favorable change in the clinical features of CRC. Our study demonstrates both the effectiveness of the screening programme and that by introducing non-invasive pre-screening of patients (e.g. iFOBT) in a pandemic situation, it can reduce its negative public health impact.

Disclosure: Nothing to disclose.

PP0714

WITHDRAWN

PP0715

WITHDRAWN

PP0716

WITHDRAWN

PP0717

PEPTIDE TYROSINE TYROSINE IS INCREASED IN INDIVIDUALS WITH BILE ACID DIARRHOEA

A.H. Lange¹, M.L. Kårhus¹, B. Hartmann², J.J. Holst^{2,3}, F.K. Knop^{1,4,5}, A.-M.G. Ellegaard¹

¹Center for Clinical Metabolic Research, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark,

²Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen,

Copenhagen, Denmark, ³Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark,

⁴Clinical Research, Steno Diabetes Center Copenhagen, Herlev, Denmark, ⁵Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Contact E-Mail Address: andreas.holst.lange@regionh.dk

Introduction: Bile acid diarrhoea (BAD) is a socially debilitating disease characterized by chronic and watery diarrhoea due to excess bile reaching the colon resulting in increased water secretion and motility. Since bile acids may stimulate the release of gut hormones, including peptide tyrosine tyrosine (PYY) implicated in diarrhoeal pathophysiology, we investigated fasting as well as postprandial plasma levels of PYY in BAD and healthy controls.

Aims & Methods: Total PYY concentrations were measured in plasma samples from 12 individuals with colesvelam-treated idiopathic or post-cholecystectomy BAD and 12 healthy controls matched on age, sex and body mass index undergoing two 4-hour liquid mixed meal tests on separate days with either the bile acid sequestrant colesvelam (1,875 mg) or placebo performed in a randomized and double-blinded order. Fasting PYY concentrations, area under the curve (AUC) and baseline-subtracted AUC (bsAUC), respectively, were evaluated.

Results: When comparing the two groups on placebo days, individuals with BAD exhibited higher mean fasting PYY concentrations (95.8 [SEM 12.6] pg/ml vs. 51.5 [12.6] pg/ml, $P = 0.0095$) and AUC (27.1 [3.0] ng/ml $\times$ min vs. 16.5 [2.4] ng/ml $\times$ min, $P = 0.0087$) whereas bsAUC was similar between groups (4.1 [1.9] ng/ml $\times$ min vs. 4.1 [1.6] ng/ml $\times$ min, $P = 0.99$). Compared to placebo, colesvelam did not significantly affect PYY levels postprandially in any of the groups.

Conclusion: Here, we demonstrate elevated fasting PYY levels, but normal postprandial PYY responses in individuals with BAD compared to carefully matched healthy controls supporting the notion that bile acids in the gut lumen stimulates the secretion of PYY in individuals with BAD. Whether and how elevated PYY levels contribute to or might counteract BAD pathophysiology remains uncertain.

Disclosure: Filip K. Knop is currently employed by Novo Nordisk A/S, Søborg, Denmark. The remaining authors report no potential conflicts of interest relevant to this abstract.

PP0718

DELTEX E3 UBIQUITIN LIGASE 2 ASSOCIATED WITH DNA DAMAGE REPAIR IN COLORECTAL CANCER

Y. Jia¹, L. Yang¹, J. Yang¹¹West China Hospital of Sichuan University, Chengdu, China**Contact E-Mail Address:** jiaiyifan@stu.scu.edu.cn

Introduction: Different E3 ligases recognize specific substrates and thus can participate in many different cellular processes, such as proliferation, apoptosis, DNA damage repair, immunity, and metabolism, thus playing different roles in the development and progression of tumors. Deltex E3 ubiquitin ligase 2 (DTX2) has been recognized as an E3 ubiquitination ligase and has two main transcripts. However, the role and mechanism of DTX2 in colorectal cancer (CRC) is unclear.

Aims & Methods: The tissue of CRC patients and paired normal tissue (3 cm away from the tumor) were subjected to a quantitative real-time polymerase chain reaction (qRT-PCR) and Western blot (WB). Immunohistochemistry (IHC) was also used to detect the expression of DTX2 proteins in CRC tissues. CRC cell lines HCT-116, SW620, RKO, HCT15, SW480, 174T and human colonic epithelial cells (HCoEpiC) were cultured, and the expression levels of DTX2 mRNA and protein in these cells were compared. The potential substrate proteins of DTX2 in CRC cells were investigated by IP-MS experiment.

Full-length human DTX2 and short human DTX2 were amplified from total RNA by RT-PCR. Full-length and short transcript overexpression plasmids and empty vectors were constructed and transfected into SW480 cells. WB was used to detect the expression level of DTX2 and proteins associated with the DNA damage repair (DDR) pathway.

Results: The results of qRT-PCR and WB showed that the expression level of DTX2 mRNA and protein in CRC tissues was significantly higher than in normal tissues ($p < 0.05$). In addition, the IHC showed that DTX2 was mainly localized in CRC tissue cells. qRT-PCR and WB confirmed the expression of DTX2 mRNA in CRC cells was higher than HCoEpiC. PARP1 was recognized as a key substrate protein of DTX2 in colorectal cancer cells through an IP-MS experiment.

In addition, the expression of DTX2 was positively correlated with the activation of DDR-related pathways ($P < 0.05$). Compared with the control and full-length groups, overexpression of the short DTX2 transcript significantly promoted the DDR in SW480.

Conclusion: In this study, we report that DTX2 is highly expressed in colorectal cancer and associated with PARP1. In addition, the short transcript of DTX2 is implicated in DNA damage repair in colorectal cancer.

Disclosure: Nothing to disclose.

PP0719

WITHDRAWN

PP0720

ATPASE ACTIVITY OF THE SUBCELLULAR FRACTION OF COLORECTAL CANCER SAMPLES UNDER THE ACTION OF BILE ACID

S. Bychkova¹, B. Kyryk², M. Bychkov³

¹Ivan Franko National University of Lviv, Human and Animal Physiology Department, Lviv, Ukraine, ²Lviv Oncology Regional Treatment and Diagnostic Center, Lviv, Ukraine, ³Danylo Halytskyi Lviv National Medical University, Department of Therapy No. 1, Medical Diagnostics and Hematology and Transfusiology, Lviv, Ukraine

Contact E-Mail Address: S.bychkova@gmail.com

Introduction: The development of colorectal cancer is related to genetic mutations, lifestyle, and diet and eating habits. Fat consumption correlates with increased levels of bile acids in the intestinal lumen, where they stimulate the growth and activity of bacteria that convert primary bile acids into secondary bile acids that have pronounced tumorigenic activity. We assumed that one of the mechanisms of the tumor genesis of bile acids may be a violation of the trans-membrane transport of ions in the intestinal mucosa.

Aims & Methods: Therefore, the aim of this work was to study the effect of tauroolithocholic acid 3-sulfate (TLC-S) on the ATPase activity of colorectal cancer samples. The investigation was conducted on colorectal cancer samples of 10 patients. Adjacent samples of healthy tissue served as controls. All patients signed an informed consent to participate in this research. ATPase activity was measured spectrophotometric by the content of P_i in the incubation medium.

Results: We found that the addition of TLC-S to the incubation medium of the subcellular fraction of samples of colorectal cancer patients caused the increase in the specific activity of the Na^+ , K^+ -ATPase by 1.5 times ($P \leq 0.05$; $n=10$) vs to the control (without TLC-S). In healthy samples the activity of this pump did not change under the influence of TLC-S. However, the addition of TLC-S to the incubation medium of healthy samples of the intestinal mucosa caused a statistically significant decrease in the activity of the basal Mg^{2+} -ATPase of the subcellular fraction by 3.6 times vs to the control ($P \leq 0.05$; $n=10$), but in cancer tissue samples the activity of basal Mg^{2+} -ATPase did not change under the influence of TLC-S.

Conclusion: We found that TLC-S causes an increase in the specific activity of the Na^+ , K^+ -ATPase in colorectal cancer samples, and in normal tissue TLC-S reduces the basal Mg^{2+} -ATPase activity

Disclosure: Nothing to disclose.

PP0721

WITHDRAWN

PP0722

CHEMO(RADIO)THERAPY FOR RECTAL ADENOCARCINOMA AND THE RISK OF MULTIPLE PRIMARY GASTROINTESTINAL SQUAMOUS CELL NEOPLASMS

A. Elsayed¹, A. Ellaithy¹

¹Suez Canal University Hospital, Medicine, Ismailia, Egypt

Contact E-Mail Address: UGS.210836@med.suez.edu.eg

Introduction: Rectal cancer represent 30% of colorectal cancer with 46,220 new cases estimated in the United States in 2024. About 98% of rectal cancer patients have rectal adenocarcinoma. Gastrointestinal (GI) squamous cell neoplasm (SCN) is very rare with no enough studies to estimate its incidence and clinical features.

Thus, our aim was to assess the risk of developing second primary GI SCN following chemo(radio)therapy after rectal adenocarcinoma.

Aims & Methods: We used the Surveillance Epidemiology and End Results (SEER) database to obtain the data of 145,789 patients with first primary rectal adenocarcinoma.

We used MP-SIR session to calculate the standardized incidence ratios (SIR) ratio as (observed/Expected) with a latency exclusion period of 0 months, Excess risk (ER) was calculated per 10,000 and 95% Confidence Interval (CI). The results were significant if $P > 0.05$.

Results: Out of 145,789 patients with rectal adenocarcinoma, 4333 patients developed second primary SCN. Among who developed second primary GI SCN, 21.9% received chemotherapy with an O/E of 4.07 ($P < 0.05$, CI: 4.50 - 3.67, ER=74.53) while 3.25% received radiotherapy with an O/E of 2.23 ($P < 0.05$, CI: 2.60- CI: 1.90, ER=42.59).

The group who had no systemic therapy had an O/E of 2.83 ($P < 0.05$, 95%CI: 2.93–2.74, ER=57.27). The group who received combined chemo-radiotherapy had a 2-fold increased risk of developing second primary GI SCN (O/E =2.34, $P < 0.05$, CI:2.44- 2.24, ER=34.88).

There was a significant increase in the 0-11 months interval in the four groups. The group who received chemotherapy O/E was 11.73 ($P < 0.05$, 95 % CI: 13.27– 10.32, ER=233.48) and the group who received radiotherapy had increased O/E to 5.16 ($P < 0.05$, ER=150.85, 95%CI: 6.51–4.03).

Conclusion: Chemotherapy increases the risk of multiple primary GI SCN after the first primary rectal adenocarcinoma, especially in the first year after diagnosis. Chemo(radio)therapy have a significantly high risk second primary GI SCN with different potential and variations across different intervals. Thus, more attention to be given for the screening of second primary GI malignancies after chemo(radio)therapy administration.

Disclosure: Nothing to disclose.

PP0723

UNVEILING THE LANDSCAPE OF SERRATED POLYPS: INSIGHTS FROM A LARGE RETROSPECTIVE COHORT STUDY

R. Taher Natour¹, A. Beshara¹, D. Nicola¹, F. Younis¹, A.-R. Zeina², B. Ovadia¹, O. Gal¹, F. Abu Baker¹

¹Hillel Yaffe Medical Center, Department of Gastroenterology and Hepatology, Hadera, Israel, ²Hillel Yaffe Medical Center, Department of Radiology, Hadera, Israel

Contact E-Mail Address: randataher12@gmail.com

Introduction: Colorectal carcinoma (CRC) screening strategies traditionally focused on conventional adenomas, but reports have highlighted the significance of serrated polyps, particularly sessile serrated polyps (SSP), in CRC pathogenesis.

This study aimed to assess the prevalence, characteristics, and clinical implications of serrated polyps and hyperplastic polyps in our practice.

Aims & Methods: A retrospective analysis covering a decade (2015-2023) of colonoscopy data from our Gastroenterology department was conducted. Inclusion criteria comprised individuals 18 years or older undergoing initial colonoscopies for multiple indications, excluding those with prior colectomies, personal CRC history, or other abdominal tumors. Detailed demographic, procedural, endoscopic, and pathological data were collected and analyzed. Polyp endoscopic characteristics were thoroughly documented, including size, location, type, and pathologic data thoroughly reviewed to identify polyp type and grade of dysplasia.

Results: Among 22,175 colonoscopies reviewed, 5,741 polypectomies with complete histologic and endoscopic data were included. Adenomas comprised the majority, with 3,297 tubular adenomas, 885 tubulo-villous, and 137 villous adenomas. Hyperplastic polyps totaled 1,343, while only 74 were recognized as serrated, primarily located in the proximal colon (90%). Serrated polyps were predominantly sessile (71.6%), flat (24.4%), and pedunculated (4%) in endoscopic report. Reviewing pathology reports revealed 14.6% of serrated polyps exhibiting high-grade dysplasia. Notably, 18% of hyperplastic polyps were proximal to the sigmoid colon, and upon pathological revision, 15.7% were reclassified as serrated polyps.

Conclusion: The prevalence and clinical insights provided shed light on the diagnostic challenges and underscore the importance of accurate identification and management of SSP lesions. Establishing standardized detection metrics for serrated polyps is imperative for enhancing CRC screening efficacy and patient outcomes.

References: 1. US Preventive Services Task Force. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325(19):1965–1977.

2. Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2017; 112:1016.

Disclosure: Nothing to disclose.

PP0724

WITHDRAWN

PP0725

IMPACT OF ARTIFICIAL INTELLIGENCE ON COLONOSCOPIES AT HOSPITAL SÍRIO-LIBANÊS: A RETROSPECTIVE ANALYSIS.

N.A.J. Pinto¹, J.F.M. Loureiro¹, P.A.F.P. Corrêa¹, V. Pfuetszenreiter¹, G.C. Stephanini¹

¹Hospital Sírio-Libanês, Colonoscopy, São Paulo, Brazil

Contact E-Mail Address: nathanjordao1@gmail.com

Introduction: According to the latest statistics, the global estimate for the year 2020 pointed to over 1.9 million new cases of colorectal cancer (CRC) (10.0%), making it the third most incident tumor among all cancers. Among men, there were approximately 1.1 million new cases, with an estimated risk of 23.40 cases per 100,000 men. Among women, there were 865 thousand new cases, making it the second most frequent tumor, with an incidence rate of 16.20 cases per 100,000 women. The highest incidence rates of CRC in men were observed in central, northern, and southern Europe. Among women, the highest incidences were observed in Oceania and northern Europe.

In terms of mortality in Brazil, in 2020, there were 20,245 deaths from CRC (9.56 per 100,000). Among men, there were 9,889 deaths, corresponding to 9.55 deaths per 100,000 men. Among women, there were 10,356 deaths, corresponding to 9.57 deaths per 100,000 women.

Colonoscopy is considered the gold standard for CRC screening as it allows for both diagnosis and resection of lesions. Observational studies

have shown a reduction of up to 77% in the incidence and 29 to 37% in mortality from CRC compared to the group of patients not undergoing prior colonoscopy.

Following successful validation by the Food and Drug Administration (FDA) in 2021, the Computer-Aided Detection (CAdE) system was introduced into clinical practice. Subsequently, it became possible to assess its potential benefit in increasing the adenoma detection rate (ADR) and the rate of adenomas per colonoscopy (APC).

On the other hand, some potential drawbacks were identified, such as the downgrading of the endoscopist's skills or an increase in examination time.

Aims & Methods: The aim was to evaluate the adenoma detection rate (ADR) in a group of patients undergoing colonoscopies with AI assistance and in a group of patients undergoing the procedure without AI assistance at Hospital S rio-Liban s, Bela Vista/SP unit.

The sample size calculation was based on a comparison test of two proportions. At a 5% significance level, minimum power of 80%, considering the values obtained from a previous similar study, 254 individuals were required in each group, totaling n=508.

In the first group, examinations were performed using the Fujifilm processor model VP-7000, with a colonoscope model EC-760ZP-V/M. In this group, throughout the examination period, the CAdE system remained activated and operational, allowing AI assistance in lesion detection. It was at the discretion of the colonoscopist whether to resect the lesion after the alarm emitted by the CAdE.

In the second group, the examinations were performed using the Olympus processor model CV-190, with a colonoscope model CF-HQ190L/I. In this group, no AI assistance was utilized.

Results: The ADR in the entire sample was 37.0%, with a rate of 36.6% among patients whose examinations were performed without the use of AI and 37.4% among those in which the examination was conducted with the use of AI, without statistical difference. The ADR was also stratified by age groups within each gender, showing no significant association with the use of AI in the examination. Within the female gender, a higher ADR was observed in women aged 60 or older compared to those under 60, but without statistical significance (p=0.451).

Conclusion: In this study, after a retrospective analysis of colonoscopies conducted at Hospital S rio-Liban s, Bela Vista/SP unit, the ADR of examinations performed with AI did not show statistically significant superiority compared to examinations performed without AI.

References: Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Pi neros M, Znaor A, et al. Cancer statistics for the year 2020: An overview. *Int J Cancer*. 2021;149(4):778-89.

Dilmaghani S, Coelho-Prabhu N. Role of artificial intelligence in colonoscopy: a literature review of the past, present, and future directions. *Tech Innovations Gastrointest Endoscopy*. 2023;25(3):399-412.

Hassan C, Wallace MB, Sharma P, Maselli R, Craviotto V, Spadaccini M, et al. New artificial intelligence system: first validation study versus experienced endoscopists for colorectal polyp detection. *Gut*. 2020;69(5):799-800.

Mori Y, Kudo SE, Misawa M, Saito Y, Ikematsu H, Hotta K, et al. Real-Time Use of Artificial Intelligence in Identification of Diminutive Polyps During Colonoscopy: A Prospective Study. *Ann Intern Med*. 2018;169(6):357-66.21.

Wang P, Berzin TM, Glissen Brown JR, Bharadwaj S, Becq A, Xiao X, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. *Gut*. 2019;68(10):1813-9.22.

Repici A, Badalamenti M, Maselli R, Correale L, Radaelli F, Rondonotti E, et al. Efficacy of Real-Time Computer-Aided Detection of Colorectal Neoplasia in a Randomized Trial. *Gastroenterology*. 2020;159:512-20.e7.23.

Byrne MF, Shahidi N, Rex DK. Will computer-aided detection and diagnosis revolutionize colonoscopy. *Gastroenterology*. 2017;153:1460-4.e1.

Disclosure: Nothing to disclose.

PP0726

A MULTICENTRE EVALUATION OF FIT LEVELS IN COLORECTAL CANCER PATIENTS

S. Manning¹, E. Hackney¹, R. Bragg¹, C. Taylor², A. Weidner³, D. Stokes⁴, C. Dong⁵, D. Maxfield⁶, L.J. Neilson¹

¹South Tyneside and Sunderland NHS Trust, Gastroenterology, South Shields, United Kingdom, ²North Cumbria Integrated Care NHS Trust, Gastroenterology, Carlisle, United Kingdom, ³Northumbria Healthcare NHS Trust, Gastroenterology, North Tyneside, United Kingdom, ⁴South Tees NHS Trust, Gastroenterology, Middlesbrough, United Kingdom, ⁵Newcastle Hospitals NHS Trust, Gastroenterology, Newcastle upon Tyne, United Kingdom, ⁶North Tees and Hartlepool NHS Trust, Gastroenterology, Stockton, United Kingdom

Contact E-Mail Address: rebecca.bragg@nhs.net

Introduction: NICE recommend FIT (faecal immunochemical test) in almost all suspected colorectal cancer (CRC) cases. FIT-based prediction models perform well [1], but it is unclear how levels change along the adenoma-carcinoma sequence and how lesion type and location affect results.

We previously reported retrospective FIT data from CRC patients at a single site [2]. We have re-evaluated this two years later and, utilising our regional trainee network, have included five more sites.

Aims & Methods: Our aim was to evaluate FIT results at various time points and in different tumour types/locations.

This was a multicentre, retrospective evaluation involving 6 hospital sites. All patients diagnosed with a malignant lesion of colon, rectum or anus in a 6-month period were identified using cancer registries. Data were collected from medical records.

Results: 856 CRC patients were included. Where histology was available, 90% were adenocarcinoma. Referrals were 85% symptomatic, 14% BCSP and 1% surveillance. 492 patients had ≥1 non-BCSP FIT prior to diagnosis. 530 individual results were recorded with a mean of 178 days pre-diagnosis.

Overall, 11% were <10µg/g, however the proportion increased as time from diagnosis increased (≤30 days 5.2%; 31-90 days 7.4%; 91-180 days 22.2%; 181-365 days 21.7%; >366 days 47.2%). When limited to ≤90 days, 6.3% were <10µg/g. This reduced to 5.3% in proven adenocarcinoma. The proportion varied according to lesion location (Table 1).

Location	FIT results	
	Total	<10µg/g
Right colon	113	14 (12.4%)
Left colon	124	2 (1.6%)
Rectum	151	8 (5.3%)

Table 1: Results by lesion location.

Conclusion: Time since FIT is relevant clinically and in research. FITs >90 days old may not be suitable for guiding clinical decisions, however our sample for this time point was small. Prospective, sequential testing would more accurately study the change in FIT along the adenoma-carcinoma sequence. Studies assessing the value of repeat testing at different time points would help guide clinicians. The highest proportion of results <10µg/g was in right colon lesions, consistent with existing literature. However, we identified more false negatives in rectal lesions compared to left colon and recommend further research assessing this.

References: 1. Hampton JS, Kenny RPW, Rees CJ, et al. The performance of FIT-based and other risk prediction models for colorectal neoplasia in symptomatic patients: a systematic review. *EclinicalMedicine* 2023; 64. DOI:10.1016/j.eclim.2023.102204.

2. Manning S, Maxfield D, Bragg R, et al. P241 Is a negative FIT falsely reassuring? A retrospective evaluation. 2022 DOI:10.1136/gutjnl-2022-BSG.295.

Disclosure: Nothing to disclose.

PP0727

STUDY OF INTESTINAL DIFFERENTIATION MARKERS (CDX2 AND SATB2) IN DIGESTIVE NEUROENDOCRINE NEOPLASMS

N.I. Ben Romdhane¹, M. Ayari², A. Dhaoui¹, A. Chehaider², M.H. Dougui², T. Jomni²

¹Internal Security Forces Hospital La Marsa, Pathology, Tunis, Tunisia, ²Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia

Contact E-Mail Address: ayari.myriam@hotmail.fr

Introduction: Digestive neuroendocrine tumors (NETs) are rare and ubiquitous neoplasm of the digestive tract, with an incidence that is increasing significantly in recent years. Special AT-rich sequence-binding protein 2 (SATB2) and the homeotic transcription factor (CDX2) are markers of intestinal differentiation that may be involved in the in the topographic diagnosis of NET and thus orientate towards the site of the primary NET.

Aims & Methods: The aim of our work was to evaluate the immunohistochemical expression of CDX2 and SATB2 in NET according to the topography and the histoprosthetic factors. We conducted a longitudinal and retrospective study including 39 NETs. Epidemiological and anatomopathological data according to the 2019 WHO classification were studied. The study of CDX2 and SATB2 was performed by immunohistochemical method. Positivity was considered in the presence of a nuclear immunoreactivity greater than 10%.

Results: The mean age of patients diagnosed with NETs was 51.4 years with a sex ratio M/F of 0.77. The predilection sites were the small intestine and the appendix, in 33.3% of cases each. CDX2 was expressed in 64% of NETs. It was positive in 90-100% of small intestine, appendix and colon neuroendocrine neoplasms. SATB2 was expressed in 60% of NETs. It was found in 100% of appendicular and colorectal neuroendocrine tumors. A weak staining was observed in 69% of small intestine neuroendocrine tumors. Gastric and pancreatic tumors pancreatic tumors did not express CDX2 nor SATB2. This variation in expression was statistically significant ($p < 0.001$). Grade G1 tumors (67%) were in 70% CDX2+/SATB2+. Grade G2/G3 tumors (33%) were in 68% of cases SATB2- without significant difference. The pT1/pT2 NET (n=19) were CDX2+/SATB2+ in 68%. The pT3/pT4 tumors (n=17) were CDX2- in 35% and SATB2- in 47% without significant difference. Lymph node and distant metastases were found in 28% and 14% of cases respectively. No statistically significant correlation was noted between CDX2 or SATB2 and the presence of lymph node metastases. However, the loss of SATB2 was significantly associated with the metastatic potential ($p < 0.001$).

Conclusion: CDX2 and SATB2 are highly sensitive and relatively specific markers of the digestive tract. They would be useful in the topographic approach of neuroendocrine tumors of unknown origin.

Disclosure: Nothing to disclose.

PP0728

SCREENING COLONOSCOPY IN GREECE: DISCOURAGING PUBLIC AWARENESS

S. Rellou¹, S. Lamprou¹, S. Efstathiou¹, A. Pagoni¹, A. Spyranis¹, D. Manou¹, T. Sdonas¹, A. Tasovasil¹

¹General Oncology Hospital of Kifisia, Gastroenterology Department, Athens, Greece

Contact E-Mail Address: s_r_1235@hotmail.com

Introduction: Colorectal cancer incidence is increasing worldwide. Nowadays it is the third most diagnosed cancer¹. Screening colonoscopy is the gold standard for prevention and often treatment, both economically and efficiently. Hellenic Society of Gastroenterology recommends that screening colonoscopy should starts by 50 years old for average risk population¹. There are limited data about participation in screening colonoscopy in general population in Greece and the existing ones shows discouraging participation rates^{2,3}.

Aims & Methods: The aim of this study was to determinate general population's knowledge about screening colonoscopy in Greece. We created a digital, anonymous questionnaire at Google Forms platform and transferred it via social media in general population that lives in Greece.

Results: In total 711 individuals answered the survey. 65.8% of them(468/711) were woman. 61.5% (437/711) were under 40 years old, 19.7% (140/711) were between 40 and 50 years old and 18.3% (130/711) were between 50 and 75 years old. 40.2% (286/711) did not know if there is an appropriate age for the first screening colonoscopy. 39% (277/711) answered that they thought an appropriate age is at 50 years old, 26.7% (190/711) at 45 years old and 8.2% (58/711) answered that they thought there is not an appropriate age for a screening colonoscopy. Regarding the performance of screening colonoscopy 363 out of 711 (51.1%) are willing to perform it in the future, 20.1% (143/711) answered that they do not know or do not answer the question, 11% (78/711) are not willing to perform it and 2.1% (15/711) are not willing to perform it, because they think it is not necessary for preventing colorectal cancer.

Conclusion: Our study confirms that there is lack of information in general population and unwillingness to screen for colorectal cancer in Greece. General population tends to be uninformed and unwilling about screening colonoscopy¹. Despite the effectiveness of colonoscopy there is not an organized screening program in Greece. Individuals are usually self-referred for screening and usually later than the appropriate age and after symptoms occur¹. Primary health care providers should be well informed and correctly advise individuals about colorectal cancer screening and its privilege, options, and alarm symptoms⁴.

References:

1. Viazis N, Tzouvala M, Theodoropoulou A, Giouleme O, Thomopoulos K, Christodoulou DK, Michopoulos S, Soufleris K, Koutroubakis I, Karamanolis G, Papatheodoridis G, Giotis I, Paspatis G, Mantzaris GJ. Comparison of the Uptake of Screening Colonoscopy between Physicians and the General Population in Greece. *Dig Dis*. 2020;38(1):23-30. doi: 10.1159/000501266. Epub 2019 Jul 9. PMID: 31288225.
2. Kamposioras K, Mauri D, Golfopoulos V, Ferentinos G, Zacharias G, Xilomenos A, Polyzos NP, Bristianou M, Chasioti D, Milousis A, Vittoraki A, Koukourakis G, Chatziioannou I, Papadopoulos P. Colorectal cancer screening coverage in Greece. PACMeR 02.01 study collaboration. *Int J Colorectal Dis*. 2007 May;22(5):475-81. doi: 10.1007/s00384-006-0186-6. Epub 2006 Aug 29. PMID: 16941174.
3. Cardoso R, Guo F, Heisser T, Hoffmeister M, Brenner H. Utilisation of Colorectal Cancer Screening Tests in European Countries by Type of Screening Offer: Results from the European Health Interview Survey. *Cancers (Basel)*. 2020 May 29;12(6):1409. doi: 10.3390/cancers12061409. PMID: 32486077; PMCID: PMC7352919.

4. Mastrokostas A, Gavana M, Gkrizioti M, Smyrnakis E, Cholongitas E, Benos A, Haidich AB. Discrepancies and misconceptions of perceived colorectal cancer screening barriers between primary health professionals and unscreened population. A comparative study in Greece. J BUON. 2018 Dec;23(7):67-76. PMID: 30722114.

Disclosure: Nothing to disclose.

PP0729

WITHDRAWN

PP0730

VIDEO ASSESSMENT OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS SIMILARLY PREDICTS HARD OUTCOMES IN THE ASSESSMENT OF SUBMUCOSAL INVASIVE CANCER RISK COMPARED TO LIVE ASSESSMENT

M. Montori^{1,2}, R. Sofia¹, P.J. Poortmans^{1,3}, S. Smeets¹, M.E. Argenziano^{1,2}, T. Tornai¹, L. Debels^{1,3}, L. Desomer^{1,4}, D.J. Tate¹
¹University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium, ²Università Politecnica delle Marche, Clinic of Gastroenterology, Hepatology, and Emergency Digestive Endoscopy, Ancona, Italy, ³Vrije Universiteit Brussel, Gastroenterology & Hepatology, Jette, Belgium, ⁴AZ Delta Campus Rumbek, Gastroenterology and Hepatology, Roeselare, Belgium

Contact E-Mail Address: pjpoortmans@hotmail.com
Introduction: Cancer in large non-pedunculated colorectal polyps (LNPCs) is poorly discriminated outside expert centres. It is unknown whether video- is comparable to live-assessment for determining submucosal invasion (SMI) in LNPCs. Video-assessment has multiple advantages including collaborative discussion of imaging findings at multi-disciplinary meetings avoiding extra assessment procedures for patients and incorrect decision-making. We compared live LNPC assessment with analysis of high-quality endoscopic videos produced by an expert.
Aims & Methods: Blinded live assessments of LNPCs from consecutive, consenting patients were conducted by 15 endoscopists in a single center. After the live assessment, an expert recorded a standardized video of each LNPC. The remaining endoscopists [who had not assessed the LNPC live] assessed these videos using an online survey. Endoscopists were classified as experienced (>50 EMRs ever and >1000 colonoscopies) or inexperienced. Parameters such as Blink Impression(BI) [1], 6-Blink Features(BF) – namely fold deformation, extra redness, depression, chicken skin mucosa, ulceration and spontaneous bleeding - presence of a Demarcated Area(DA), Vascular Pattern(VP) of any DA, size, location, Paris classification, and morphology were recorded to form the endoscopist's impression of cancer presence in the LNPC. The results were later compared to expert consensus including an external validator. The primary endpoint was to evaluate the accuracy of endoscopists' final impression of cancer and choice of correct treatment between live and video assessments.

Results: 64 live assessments (12 endoscopists) & 96 video assessments (9 endoscopists) of 18 LNPCs were performed. 5 (41.7%) (live) vs 4 (44.4%) (video) endoscopists were inexperienced. The comparison of live versus video assessments revealed no significant difference in the final impression of cancer presence by the endoscopist (sens 80.0% vs 100%, spec 87.0% vs 85.5%), BI (sens 85.7% vs 92.3%, spec 88.6% vs 80.7%) and the presence of ≥2BF (sens 71.4% vs 84.6%, spec 81.8% vs 68.7%) vs histology (P=.77, .34 & .21 respectively). Further the ability of DA & JNET to predict SMI did not differ nor did the rate of correct treatment determination (71.9% live vs 60.4% video, P=.14). Versus expert consensus the determi-

nation of ≥2BF was equally accurate live (82.4%) vs video (76.0%,P=.38). Conversely the exact number of BF vs experts (live 60.4% vs video 37.5%,P=.01), the presence of ≥3 features (location, size, morphology or Paris classification) of COVERT (not visible on the surface) SMI live (81.3%) vs video (65.6%, P=.03) and the correct outcome of a structured algorithm[2] (live 96.9%, video 81.3%,P=.002) were determined differently between the groups.

	LIVE			Video			P
	Sens	Spec	Acc	Sens	Spec	Acc	
Blink pre	85.7% [59.8%-100%]	88.6% [79.3% - 98.0%]	88.2% [79.4% - 97.1%]	92.3% [77.8% - 100%]	80.7% [72.2% - 89.2%]	82.3% [74.7% - 89.9%]	0.345
Blink (vs SMI, ≥2 BF)	71.4% [37.8.0%-100%]	81.8% [70.4% - 93.2%]	80.4% [69.5% - 91.3%]	84.6% [65.0% - 100%]	68.7% [58.7% - 78.7%]	70.8% [61.7% - 79.9%]	0.207
Blink (vs expert, ≥2 BF)	70.0% [41.6%-98.4%]	85.4% [74.6% - 96.2%]	82.4% [71.9% - 92.8%]	63.5% [50.4% - 76.6%]	90.9% [82.4% - 99.4%]	76.0% [67.5% - 84.6%]	0.377
OVERT DA	100.0% [100% - 100%]	75.9% [64.5% - 87.3%]	79.7% [69.8% - 89.5%]	100.0% [100% - 100%]	77.1% [68.1% - 86.2%]	80.2% [72.2% - 88.2%]	0.920
OVERT VascPattern JNET	100.0% [100% - 100%]	70.4% [58.2%-82.6%]	75.0% [64.4% - 85.6%]	100.0% [100% - 100%]	69.9% [60.0% - 79.8%]	74.0% [65.2% - 82.7%]	0.887
Cancer present	80.0% [55.2%-100%]	87.0% [78.1%-96.0%]	85.9% [77.4% - 94.5%]	100.0% [100% - 100%]	85.5% [78.0% - 93.1%]	87.5% [80.9% - 94.1%]	0.777

Conclusion: Final impression of the presence of cancer and determination of correct treatment in LNPCs are predicted equally well from blinded video assessment versus live assessment in a group of similarly experienced endoscopists.

This finding could minimise the need for patients to undergo a repeat procedure to assess their LNPC prior to resection relying instead upon expert assessment of a video.

References:

Debels, L., Smeets, S., Poortmans, P. J., Jorissen, C., Lala, V., Lamiroy, T., Valori, R., Desomer, L., Anderson, J., & Tate, D. (2023). Identification of 6 key features of colorectal polyps increases the sensitivity of cancer detection and ability to discriminate deep submucosal invasion - The basis of the BLINK (first) impression? *Gastrointestinal Endoscopy*, 97(6, Supplement), AB190. <https://doi.org/10.1016/j.gie.2023.04.318>
 GIEQS. Year. "SMIC." Accessed [23/11/2023]. <https://www.gieqs.com/smic>.
Disclosure: Nothing to disclose.

PP0731

QUALITY INDICATORS AND RESULTS OF COLONOSCOPY EXAMINATIONS IN INITIAL FIVE-YEAR PERIOD OF HUNGARIAN POPULATION-BASED COLORECTAL CANCER SCREENING PROGRAM

R. Bor¹, A. Fabian¹, B. Vasas², D. Magyar¹, Z. Bosze¹, T. Tóth¹, A. Balint¹, T. Resál¹, P. Bacsur¹, K. Farkas¹, T. Molnár¹, Z. Szepes¹
¹University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Pathology, Szeged, Hungary

Contact E-Mail Address: magydan02@gmail.com
Introduction: The Hungarian population-based colorectal cancer (CRC) screening program (EFOP-1.8.1-VEKOP-15-2016-00001) was launched in 2019 among asymptomatic individuals between the ages of 50 and 70 with average risk of CRC.
Aims & Methods: Aim of the study was to retrospectively assess the quality indicators and results of screening colonoscopies performed during the initial five-year period of screening program (from 2019 to 2023). Our

non-interventional, observational cohort study retrospectively analyzed clinical records of screening colonoscopies which were prospectively collected in the registry of National Public Health Institute. The quality indicators and results of examinations was determined based on cecal intubation rate, polyp, adenoma and cancer detection rates (PDR, ADR, and CDR), proportion of photo-documentation and sedation.

Results: Total of 27,021 colonoscopies were performed during the initial five-year period of CRC screening program. Cecal intubation rate was 92.54%, from which 66.77% of cases were confirmed by cecal image documentations. The causes of incomplete colonoscopies were inadequate bowel cleansing ($n=172$, 11.48%), anatomical reasons ($n=369$, 24.63%) and malignant colonic obstruction ($n=178$, 11.88%), and only in 191 cases (12.75%), the examination had discontinued due to patients' intolerance. Total of 17,981 patients (66.54%) of participants received some kind of sedation. The result of colonoscopy was non-negative in 80.83% of cases. At least one polyp was found (PDR) in 56.56% ($n=15,282$) of participants among which the largest polyp was located in rectosigmoid colon in 64.92% of cases and the polyp size was higher than 1 cm in 34.69% of cases. Morphological features of polyps could not be assessed due to inappropriate colonoscopy reports in registry. A total of 36,829 polyps were found, of which 30,494 were removed during the registered examinations, becoming polyp-free 82.15% of patients (polypectomy per colonoscopy 1,13). The ADR was 33.53%, where the most relevant lesion histological types were tubular, tubulovillous, villous and serrated in 67.46%, 22.83%, 3.60% and 2.92% respectively. CRC was found in 5.51% of participants from which the most cancers were located in the sigmoid colon ($n=578$, 38.82%) and rectum ($n=458$, 30.76%). The data of registry to description of polyp morphology, usage of advanced imaging assessment, polyp retrieval rate and the image documentation were often missing or inappropriate.

Conclusion: Cecal intubation, polyp and adenoma detection rates of screening colonoscopies of Hungarian CRC screening program are satisfactory according to guideline of European Society of Gastrointestinal Endoscopy, however, the description of polyp morphology, usage of advanced imaging assessment, polyp retrieval rate and the image documentation are inappropriate yet, therefore the evaluation was not possible. The aim for the future is to improve the quality of data input to the register.

Disclosure: Nothing to disclose.

PP0732

PATIENT SATISFACTION MEASUREMENT OF SCREENING COLONOSCOPIES IN THE HUNGARIAN POPULATION-BASED SCREENING PROGRAM - NATIONWIDE, CROSS-SECTIONAL SURVEY STUDY

R. Bor¹, A. Fabian¹, B. Vasas², Z. Bosze¹, D. Magyar¹, T. Tóth¹, A. Balint¹, P. Bacsur¹, T. Resál¹, K. Farkas¹, T. Molnár¹, Z. Szepes¹
¹University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Pathology, Szeged, Hungary

Contact E-Mail Address: fabiananna9@gmail.com

Introduction: In colorectal cancer (CRC) screening programs utilizing colonoscopy, patient satisfaction plays a pivotal role in persistent adherence, thus influencing the program's long-term efficacy. Our study aimed to evaluate patient satisfaction following endoscopic procedures within the Hungarian population-based CRC screening program (EFOP-1.8.1-VEKOP-15-2016-00001) on a national scale.

Aims & Methods: Our study aimed to evaluate patient satisfaction following endoscopic procedures within the Hungarian population-based CRC screening program (EFOP-1.8.1-VEKOP-15-2016-00001) on a national scale. The survey evaluated data from the anonymous, standardized

self-administered questionnaire devised and distributed by the Hungarian National Centre for Public Health and Pharmacy between January 2020 and November 2023. The questionnaire predominantly comprised closed-ended questions. Patient satisfaction was assessed quantitatively by a 5-point scale. Categorical variables were reported as event rates and relative frequencies, and continuous variables as means with standard deviation. Fisher's exact test was used to analyze categorical data.

Results: A total of 4083 questionnaires were evaluated, with a slight male predominance (55.71%) and with 41.96% of patients under 61 years of age. Questionnaire completed by 19.76% of colonoscopy patients (0.46% in 2020, 33.69% in 2021, 27.70% in 2022 and 22.71% in 2023). Respondents were evenly split between county centers/large cities, small towns and villages, but Budapest was under-represented (31.55%, 32.92%, 32.32% and 2.94% respectively). There was considerable variation in the willingness of endoscopic units to cooperate, so that no data at all were available from 4 counties. Sedation was used in 60.40% of patients (analgesia 55.57%, general anesthesia 4.82%), but 493 patients did not answer this question. Patients rated the quality of the colonoscopy units, competence of endoscopy staff and the overall satisfaction with exam execution as 4.68 ± 0.58 , 4.89 ± 0.42 and 4.47 ± 0.77 respectively. They were equally satisfied with the communication of the doctor (4.87 ± 0.41) and the staff (4.87 ± 0.44). Only 1.67% of patients reported that they would prefer to be switched to another doctor in case of a future screening, and the question remained unanswered in 5.44% of cases. Lack of rest room was complained by 9.09% of patients, where it was available, it was rated 4.68 ± 0.67 points, however 7.67% of patients didn't respond to this question. In 33.70% of the cases, colonoscopy was considered to be substantially unpleasant and painful, giving an overall score of 3.85 ± 1.06 . Procedure-related pain and discomfort were rated as significantly less severe in men ($p < 0.001$) and in patients over 61 years of age ($p = 0.001$), as well as in patients who received detailed information from the endoscopist immediately before the endoscopy ($p < 0.001$) and who received sedation ($p < 0.001$). The detailed information provided by the endoscopist ($p < 0.001$), the sedation ($p < 0.001$) and the mild pain experienced during the examination ($p < 0.001$) had a positive influence on patients' overall satisfaction with the colonoscopy.

Conclusion: This is the first large-volume patient satisfaction survey among patients invited to CRC screening program in Hungary. Positive patient feedback indicates high quality of care. Overall satisfaction can be further improved by modulation of procedure-related pain, rate of sedation and quality of postprocedural rest, as well as the quality of information delivered by endoscopists prior to procedures.

Disclosure: Nothing to disclose.

PP0733

ENDOSCOPIC PREDICTORS OF LYMPH NODE METASTASIS IN T1b COLORECTAL CANCER IN THE ABSENCE OF PATHOLOGIC RISK FEATURES: A SINGLE-CENTER STUDY OF 305 LESIONS

D.H. Shin¹, H. Jeong¹, J. Park¹, S.J. Park¹, J.H. Cheon¹, T.I. Kim¹, J.J. Park¹

¹Department of Internal Medicine, Institute of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Seoul, Republic of Korea, South Korea

Contact E-Mail Address: wish40@yuhs.ac

Introduction: There are insufficient data to guide clinical decision-making regarding the implementation of additional surgery following endoscopic therapy in patients with deep submucosal invasive colorectal cancer (T1b CRC) and no additional risk factors for lymph node metastasis (LNM). This investigation sought to identify factors associated with LNM in cases of T1b CRC without other risk factors.

Aims & Methods: Consecutive cases with pathologically proven T1b CRC were retrospectively collected from 2014 to 2023 at a single tertiary hospital in Korea. These patients received either surgical or endoscopic treatment. In patients who received endoscopic treatment alone, no LNM was deemed to exist if there was no recurrence after at least 3 years of follow-up. Excluded were cases with other risk factors, including poor differentiation, lymphovascular invasion, perineural invasion. The cases were compared based on the presence of LNM.

Results: A total of 305 cases were enrolled and LNM was observed in 28 cases (9.18%). In univariate analysis, differentiation, sm3 invasion, tumor growth pattern, and peri-tumoral white spots were related with LNM. Multivariate analysis identified presence of non-polypoid growth parts (odd ratio [OR] 6.39; 95% CI 2.76-14.79), and peri-tumoral white spots (OR 2.85; 95% CI 1.22-6.64) as significant predictive factors for LNM.

Factor	OR	95% CI	P-value
Peri-tumoral white spots	2.85	1.22-6.64	0.015
Non-polypoid growth	6.39	2.76-14.79	0.000

Table. Multivariate analysis

Conclusion: Endoscopic findings including presence of non-polypoid growth and peri-tumoral white spots were related with increased risk of LNM in T1b CRC in the absence of other pathologic risk factors. These findings may be useful in determining further treatment strategy for patients with T1b CRC received endoscopic resection.

References: Liselotte W. Zwager,1,2,3 Barbara A. J. Bastiaansen, et al. Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis. Gut 2022;163:174-189
Chihiro Yasue, Akiko Chino, et al. Pathological risk factors and predictive endoscopic factors for lymph node metastasis of T1 colorectal cancer: a single-center study of 846 lesions. J Gastroenterol(2019) 54: 708-717

Disclosure: Nothing to disclose.

PP0734

IS MODERATELY DIFFERENTIATED ADENOCARCINOMA A RISK FACTOR FOR LYMPH NODE METASTASIS IN T1 COLORECTAL CANCER? A SINGLE-CENTER STUDY OF 881 LESIONS

Y. Niimura¹, S. Kudo¹, K. Ichimasa¹, Y. Kouyama¹, K. Mochizuki², Y. Takashina¹, O. Shiina¹, Y. Morita¹, S. Keisuke¹, K. Wakamura¹, T. Hayashi¹, N. Sawada¹, T. Nemoto³, T. Baba³, H. Miyachi¹, M. Misawa¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²Showa University Northern Yokohama Hospital, Digestive Disease Center, Tokyo, Japan, ³Showa University Northern Yokohama Hospital, Digestive Disease Center, Department of Diagnostic Pathology, Yokohama, Japan

Contact E-Mail Address: nimurayukensyu0620@Gmail.com

Introduction: Several guidelines, including those from the US, Europe, and Japan, recognize “tumor differentiation” as a risk factor for lymph node metastasis (LNM) in T1 colorectal cancer. Surgical resection with lymph node dissection is recommended if poorly differentiated adenocarcinoma, signet-ring cell carcinoma, or mucinous carcinoma are observed in histological findings from endoscopically resected specimens. Recent reports suggest that moderately differentiated adenocarcinoma (tub2) may also be a risk factor for LNM.

Aims & Methods: This study aims to investigate whether tub2 is a risk factor for LNM. We initially evaluated 1,742 patients with T1 colorectal cancer who underwent surgical resection with lymph node dissection at our institution from April 2001 to April 2024. Lesions were assessed based on the worst grade of differentiation. Exclusions were made for patients with (a) metachronous or synchronous advanced cancer, (b) invasion deeper than the muscularis propria, (c) Lynch syndrome, familial adenomatous polyposis, or ulcerative colitis, (d) preoperative chemotherapy or radiotherapy, (e) missing data, or (f) lesions without surgical resection. In addition, after excluding 177 patients with poorly differentiated, mucinous, or signet-ring cell adenocarcinoma, 881 patients were enrolled for analysis. We investigated the sensitivity, specificity, and area under the receiver operating characteristics (ROC) curve of tub2 for predicting LNM, alongside correlations between pathological factors and LNM using multivariate analysis.

Results: LNM was detected in 9.9% (87/881) of patients. The sensitivity, specificity, and area under the ROC curve for tub2 were 78.2%, 42.2%, and 0.60, respectively. In the univariate analysis, tub2 was associated with LNM (p<0.001). Multivariate analysis identified lymphatic invasion, vascular invasion, and tub2 as significant risk factors for LNM, with odds ratios of 7.49, 1.97, and 1.95 (p < 0.01, < 0.01, and = 0.02, respectively).

Conclusion: Moderately differentiated adenocarcinoma (tub2) is a risk factor for LNM in T1 colorectal cancer.

Disclosure: Conflicts of interest: None.

PP0735

USEFULNESS OF COMPUTER-AIDED DIAGNOSIS (CADX) BASED ON NON-MAGNIFIED WHITE LIGHT IMAGES IN THE DIAGNOSIS OF DEEP INVASIVE CANCER IN T1 COLORECTAL CANCER

T. Matsumura¹, K. Okimoto¹, M. Fujie², A. Kurosugi¹, S. Takahashi¹, T. Taida¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Chiba, Japan, ²Chiba University Hospital, Department of Clinical Engineering Center, Chiba, Japan

Contact E-Mail Address: matsumura919@yahoo.co.jp

Introduction: The optical diagnosis of T1 colorectal cancer (CRC) with deep invasion ($\geq$ T1b CRC) is crucial in determining subsequent treatment. Recently, computer-aided diagnosis (CADx) has become available for the diagnosis of deep invasive cancer, but until now, it must be combined with image enhanced endoscopy (IEE) or endocytoscopy. We have developed a CADx system to diagnose deep invasive cancer using non-magnified white light imaging (WLI).

Aims & Methods: This study aimed to compare the diagnostic accuracy of the CADx in T1 CRC diagnosis with that of non-expert endoscopists and expert endoscopists. A total of 365 images of 37 T1 CRCs (16 T1a CRCs and 21 T1b CRCs) from prospectively enrolled consecutive patients were included in the study. Images were independently diagnosed by two non-expert endoscopists and two expert endoscopists; sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of T1b CRC diagnosis by the CAD system were calculated and compared with the endoscopists diagnostic accuracies.

Results: The sensitivity, specificity, PPV, NPV, and accuracy of CAD were 70.2%, 60.4%, 84.2%, 49.3%, and 70.7%, respectively, while those of non-experts were 39.9%, 80.6%, 82.7%, 36.6%, and 51.9%, respectively. The accuracy rate was significantly higher in the CAD group ($p < 0.01$). On the other hand, those of experts were 47.9%, 87.7%, 79.2%, 63.2%, and 67.7%, respectively, which were comparable to the diagnostic accuracy of CAD. The diagnostic time per image was significantly shorter for CAD than for endoscopists (0.49 sec. for CAD, 7.72 sec. for non-expert, and 5.77 sec. for expert, $p < 0.01$, $p < 0.01$, comparison with CAD).

Conclusion: Non-magnified WLI-based CADx is useful for non-expert endoscopists in diagnosing T1 CRC with deep invasion.

Disclosure: This work was supported by JSPS KAKENHI Grant Number 21K07885 and JFE (The Japanese Foundation for Research and Promotion of Endoscopy) Grant.

PP0736

SENSITIVITY OF THE AMINOINDEX CANCER SCREENING FOR EARLY COLORECTAL NEOPLASTIC LESIONS; A PROSPECTIVE COHORT STUDY

H. Takamaru¹, Y. Nakatani^{1,2}, D. Hihara^{1,3}, M. Sekiguchi^{1,4}, M. Yamada¹, T. Sakamoto^{1,5}, T. Yamaji⁶, N. Kobayashi^{1,4}, H. Kitamura⁷, T. Tagami⁷, S. Kikuchi⁸, M. Yamamoto⁷, A. Hagiwara⁷, T. Matsuda^{1,4,9}, Y. Saito¹

¹National Cancer Center Hospital, Endoscopy Division, Tokyo, Japan, ²Noborito Nakatani Gastroenterology and Diabetes Clinic, Tokyo, Japan, ³Toho University Ohashi Medical Center, Division of Gastroenterology and Hepatology, Tokyo, Japan, ⁴National Cancer Center Hospital, Cancer Screening Center, Tokyo, Japan, ⁵University of Tsukuba, Department of Gastroenterology, Institute of Medicine, Tsukuba, Japan, ⁶National Cancer Center Institute for Cancer Control, Division of Epidemiology, Tokyo, Japan, ⁷Ajinomoto Co., Inc., Research Institute for Bioscience Products & Fine Chemicals, Tokyo, Japan, ⁸Ajinomoto Co., Inc., Bioscience Products & Fine Chemicals Division, Tokyo, Japan, ⁹Toho University Omori Medical Center, Division of Gastroenterology and Hepatology, Tokyo, Japan

Contact E-Mail Address: htakamar@ncc.go.jp

Introduction: Screening colonoscopy reduces colorectal cancer (CRC) mortality. However, several studies have reported a lower participation rate of colonoscopy. Now it is important to provide less invasive test for CRC screening.

AminoIndex® Cancer Risk Screening (AICS®) is an examination that measures plasma amino acid concentrations and estimates the risk of existing CRC based on the difference in amino acid balance in patients with CRC and healthy individuals. AICS is calculated from 0.0 to 10.0 with the higher value indicating a higher the risk of existing CRC.

We aimed to conduct a prospective cohort study to evaluate the accuracy of AICS® in detecting the risk probability for early colorectal lesions, such as advanced adenoma (AA), intramucosal neoplasia (Tis), or T1 CRC.

Aims & Methods: Consecutive patients who underwent colonoscopy between 06/02/2017 and 31/03/2021 at the National Cancer Center Central Hospital and endoscopically diagnosed adenoma larger than 20 mm, intramucosal neoplasia (Tis), or submucosal invasive carcinoma (T1) were included as a selection criterion. Patients with endoscopically suspected intramucosal neoplasia or high-grade dysplasia by preoperative colonoscopy, but finally diagnosed with adenoma were also included in the study. We excluded the following patients;

- 1) patients with polyposis such as familial colorectal adenomatosis or inflammatory bowel disease,
- 2) patients with concurrent cancer of other organs,
- 3) patients with obvious bleeding,
- 4) patients with severe defecation disorder, and;
- 5) patients with stenosis of colon or intestine.

We measured plasma amino acid concentrations calculated the AICS score. FIT was also measured at the same time. The lesions were endoscopically resected using EMR or ESD technique. The sensitivity of AICS, FIT, and the combination of FIT and AICS were examined according to the pathological diagnosis.

Results: Two hundred and seventeen patients were included in the primary analysis, and 208 patients excluding 9 patients who did not perform FIT were included in the secondary analysis.

The median age of the 217 patients was 71 years old (range: 32- 91). The mean lesion size was 28.9 mm $\pm$ 12.9. Prevalence of AA, Tis, T1, and advanced lesion was, 63, 118, 30, and 6, respectively. Six lesions were suspected to be T1 carcinoma on preoperative endoscopy, following pathological examination revealed advanced cancer after endoscopic resection.

The sensitivity of AICS for the advanced neoplasia (AN), AA, intramucosal neoplasia (Tis), submucosal invasive carcinoma, and advanced CRC was 28.1%, 30.9%, 25.4%, 23.3%, and 33.3%, respectively.

In the secondary endpoint, the sensitivity of FIT for AN, AA, intramucosal neoplasia (Tis), submucosal invasive carcinoma, and advanced CRC was 47.0%, 35.3%, 49.1%, 46.7%, and 100%, respectively. The sensitivity of the combination of FIT and AICS for AN, AA, intramucosal neoplasia (Tis), submucosal invasive carcinoma, and advanced CRC was 61.1%, 52.9%, 64.0%, 60.0%, 100%, respectively.

Conclusion: Although it was a reasonable value compared to the development data, AICS® has insufficient sensitivity for lesions requiring endoscopic intervention. It could be clinically applicable as a minimally invasive examination to stratify the risk of existing CRC in combination with FIT for colorectal screening.

Disclosure: The primary investigator (Hiroyuki Takamaru) had received research funding from Ajinomoto Co. Ltd.

PP0737

BACK-TO-BACK COLON CAPSULE ENDOSCOPY AND COLONOSCOPY IN BOTH SCREENING AND SYMPTOMATIC POPULATION

E. Gibbons¹, L. Keating¹, R.J Farrell¹, C. Smyth¹, O. Kelly¹, B. Hall¹
¹Connolly Hospital, Gastroenterology Department, Dublin 15, Ireland

Contact E-Mail Address: eimeargibbons@gmail.com

Introduction: Colon capsule endoscopy (CCE) has been demonstrated to be comparable to colonoscopy and better than CT colonography (CTC) for the detection of colonic pathology. Challenges include poor completion rates and high re-investigation rates.

Aims & Methods: The aim of this study was to assess the role of CCE with faecal immunochemical testing (FIT) as a non-invasive, diagnostic tool in symptomatic and screening populations attending Connolly Hospital. Prospective participants were identified from both the central endoscopy waiting list at Connolly Hospital and from our national colorectal screening programme, Bowel Screen. All participants were due to attend Connolly Hospital for a symptomatic or surveillance colonoscopy during the time period of the study.

Consenting participants underwent CCE the day prior to their scheduled colonoscopy. CCEs were read by two expert readers. Participants were sent FIT kits to complete prior to CCE. Primary outcomes were CCE polyp detection rates (PDR). The potential benefit of using FIT as a triage tool to identify low-risk individuals appropriate for CCE over colonoscopy was explored.

Results: 80 back-to-back procedures were completed January 2023-February 2024 (M: F 50:30, mean age 59.6, range 35-78) in a single centre. The most common indications for colonoscopy were surveillance 41.5%, PR bleeding 21% and diarrhoea/ IBD assessment 15%. CCE detected a total of 108 polyps in 45/80 (56%) participants versus 93 polyps in 39/80 (48%) participants at colonoscopy (p= 0.34). When only complete CCE are included, the polyp detection rate increased to 31/45 (68%), p< 0.05. 79% supplied FITs prior to CCE. CCE PDR for all polyps when FIT < 50 ng/ml was 19/33 (57%) versus (20/27) 74% with FIT > 50 ng/ml (p=0.18). There is trend towards significance. A lower FIT cut-off, closer to limit of detection, not available to this study, may have more significant results.

Only one participant had a cancer diagnosed at colonoscopy. It was located on the ileocaecal valve. The cancer was not detected by CCE despite the capsule passing through this region. This, to our knowledge, is only the second missed cancer by CCE documented.

ESGE 2012 guidelines recommend follow up colonoscopy for one polyp

measuring 6mm or more, or if three polyps of any size are detected. 50/80 (62.5%) CCE examinations would have required follow up if they were not part of a study and scheduled for next day colonoscopy. Even when looking at only those CCE examinations that were complete, 17/45 (38%) required further investigation. Reasons for re-investigation included incomplete examination 32/49 (65%), for polypectomy 16/49 (33%) and for biopsy in 1/49 (2%).

False negative CCE rates for polyps greater than 6mm range from 2-15.5% in the literature. In keeping with this, the false negative CCE for all polyps in this study was 8.75%, and 6.25% for polyps greater than 6mm.

There were no adverse events reported. There were technical issues reported in 16% of CCE. These included the capsule not turning on until it was beyond the caecum, participants removing the belt intermittently and one interference which was believed to be secondary to a topical glucose monitor.

Conclusion: The increasing demand on colonoscopy waiting lists raises concerns regarding the ability of health services to deliver traditional endoscopy in a timely fashion. Alternative modalities are necessary and CCE is a viable diagnostic alternative. There is likely a role for FIT testing as a triage tool prior to CCE to reduce re-investigation rates.

Disclosure: Nothing to disclose.

PP0738

CLINICAL FEATURES OF DEPRESSED TYPE COLORECTAL NEOPLASMS - USEFULNESS OF MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY

S. Kudo¹, S. Semba¹, Y. Minegishi¹, K. Kondo¹, K. Sasabe¹, T. Shibuya¹, Y. Ide¹, S. Iwasaki¹, E. Tamura¹, Y. Kouyama¹, T. Sakurai¹, Y. Ogawa¹, K. Ichimasa¹, N. Ogata¹, M. Misawa¹, T. Hayashi¹, N. Sawada¹, K. Wakamura¹, T. Baba¹, F. Ishida¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan

Contact E-Mail Address: kudos@med.showa-u.ac.jp

Introduction: In the carcinogenic pathway of colorectal cancer, the first concept is the “adenoma-carcinoma sequence” and the second concept is the “serrated pathway”. In these concepts, adenomas and serrated lesions gradually progress to cancer. The third concept is the “de novo pathway,” in which cancer develops without adenomas or serrated lesions and is also characterized by high malignancy and rapid progression.

We have endoscopically characterized depressed colorectal cancers considered to be of the “de novo pathway” and validated the usefulness of pit pattern and EC classification.

Aims & Methods: A total of 50119 colorectal neoplasms were resected endoscopically or surgically in our institution from April 2001 to December 2023. They were subjects of this study. Advanced cancers were excluded. Of these, 1633 lesions were submucosally invasive (T1) carcinomas, 6802 lesions were classified as high-grade dysplasia and 38952 lesions as low-grade dysplasia. Morphologically, they were divided into 3 types: depressed, flat, and protruded type comprising 1.1 (%), 45.0 (%), and 54.0 (%), respectively. Specifically, the distinctive features of depressed type neoplasms concerning their pit pattern and EC classification were examined.

Results: Most of the flat (91.5%) and protruded type (94.9%) lesions showed type IIIL or IV pit pattern, which are common findings in adenomas. On the other hand, most of the depressed type lesions (92.3%) classified as type IIIs, VI or VN pit patterns, are typically seen in carcinomas. As for endocytoscopy, most of flat and protruded type lesions were identified as EC2 corresponding to adenomas. In contrast, relatively high rates of depressed type lesions were categorized as EC3a (40.3%) and EC3b (52.3%), consistent with invasive carcinomas.

The proportion of T1 carcinomas in depressed type lesions was 60.0%, whereas in flat and protruded type lesions it was 2.7% and 2.6%, respectively. Additionally, 11.6% of depressed type lesions less than 5mm in diameter were T1 carcinomas, whereas flat and protruded type lesions were 0.01% and 0%, respectively.

Conclusion: This study revealed that depressed lesions were classified as type IIIs, VI or VN pit patterns on magnifying endoscopy and as type EC3a or EC3b on endocytoscopy. Lesions with these features or pit patterns tend to invade the submucosal layer even if they are small size. Despite their high potential for malignancy, depressed lesions are often ignored. However, it is critical to recognize their features and accurately diagnose lesions based on morphology, pit pattern, and EC classification.

Disclosure: Nothing to disclose.

PP0739

CLINICAL VALUE OF FECAL MICRORNA COMBINATION FOR PRECANCEROUS AND CANCEROUS COLORECTAL LESIONS DETECTION

D.A.R. Santos^{1,2,3}, M. Eiras¹, A.C. Pereira^{4,5}, M. Santos^{6,7,8}, L.L. Santos^{1,9}, M. Dinis-Ribeiro^{4,10}, L. Lima¹

¹Research Center of IPO Porto (CI-IPOP), Experimental Pathology and Therapeutics Group, Porto, Portugal, ²University of Porto, Faculty of Medicine of the University of Porto (FMUP), PortoPortugal, Portugal, ³University of Porto, Institute of Biomedical Sciences Abel Salazar (ICBAS), Porto, Portugal, ⁴Research Center of IPO Porto (CI-IPOP), Precancerous Lesions and Early Cancer Management Group, Porto, Portugal, ⁵University of Porto, CINTESIS - Center for Health Technology and Services Research, Porto, Portugal, ⁶Polytechnic Institute of Porto, School of Health, Porto, Portugal, ⁷Instituto Politécnico do Porto, Centro de Investigação em Saúde e Ambiente (CISA), Escola Superior de Saúde, Porto, Portugal, ⁸Research Center of IPO Porto, Molecular Oncology & Viral Pathology, PortoPortugal, Portugal, ⁹Portuguese Oncology Institute of Porto, Department of Surgical Oncology, Porto, Portugal, ¹⁰IPO Porto, Dept. of Gastroenterology, Porto, Portugal

Contact E-Mail Address: daniela.r.santos@ipoporto.min-saude.pt

Introduction: Colorectal cancer (CRC) screening programs can improve patient prognosis and survival rate. However, the Fecal Immunochemical Test based screening has low sensitivity for precancerous lesions and is suboptimal for CRC detection, leading to a high false-negative rate. This limitation increases the number of undiagnosed patients, decreases the overall screening effectiveness, and increases the urgency for the development of new tools. In the past few decades, several molecules have been investigated as potential biomarkers to enhance CRC screening, among them emerged microRNAs (miRs). MiRs play an essential role in the genetic events associated with carcinogenesis. In CRC context, these small molecules have a dysregulated expression that is easily detected in biological samples, such as stool, making them a promising tool for CRC screening.

Aims & Methods: In this respect, we aimed to identify miRs profiles in fecal samples that could potentially serve as biomarkers to improve the early detection of CRC. MiR expression was evaluated using RT-qPCR in stool samples from 96 individuals who underwent colonoscopy with different clinical outcomes, namely, individuals without lesions found on colonoscopy, low-grade dysplasia lesions, high-grade dysplasia lesions, and patients diagnosed with CRC.

Results: Our results showed altered expression of seven miRs in fecal samples from different clinical groups. Of these, miR-451a showed significantly decreased expression in the high-grade dysplasia group, with good performance in distinguishing between this clinical group and individuals

without lesions found on colonoscopy (AUC, 0.706; sensitivity, 63%). Moreover, miR-199a-5p, described for the first time in stool, miR-21-5p, miR-4516, and miR-92a-3p were upregulated in advanced lesions, specifically in CRC and high-grade dysplasia lesions groups. In addition, a panel of three fecal miRs showed high discrimination power between the high-grade dysplasia lesion group and individuals without lesions found in the colonoscopy group (AUC, 0.828; sensitivity, 88%). Also, a panel consisting of two miRs showed moderate performance in identifying the CRC group (AUC, 0.724; sensitivity, 83%).

On the other hand, the use of these two panels in combination improved the performance for CRC detection (sensitivity of 88%) and high-grade dysplasia lesion identification (sensitivity of 92%). Furthermore, regarding the detection of advanced lesions, these panels achieved a sensitivity of 90%.

Conclusion: These findings suggest that the combined use of these miR panels can identify patients with CRC and individuals with high-grade dysplasia lesions and has the potential to be used clinically in combination with the Fecal Immunochemical Test.

Disclosure: The results provided in the abstract are unpublished data, although we have prepared a manuscript that has not yet been submitted. However, these findings will be presented in oral communication at the Porto Cancer Meeting, a Portuguese congress in I3s, Porto.

PP0740

COLORECTAL CARCINOMA IN YOUNG PATIENTS, SINGLE CENTRE STUDY FROM KARACHI, PAKISTAN

G. Mohiuddin¹, N. Butt¹

¹Jinnah Postgraduate Medical Complex, Gastroenterology Ward 25, Karachi, Pakistan

Contact E-Mail Address: g.mohiuddinprtc@gmail.com

Introduction: Colorectal cancer (CRC) is rising among young adults. It is cancer of colon, appendix and rectum. According to GLOBOCON 2018, It is the 4th most common cancer in the world and the third leading cause of cancer mortality. The expected rise of the CRC rate to 60% by year of 2030 globally, will result in 2.2 million new cases and 1.1 million deaths annually. CRC is Heterogeneous, 70% cases of CRCs are sporadic in onset, 10-30% are familial and 5-7% are due to hereditary diseases.

Aims & Methods: To evaluate the clinicopathological features of Colorectal Cancer (CRC) among young adults under the age of 30.

This was cross-sectional Retrospective study conducted at the Gastroenterology and Oncology Department of JPMC, Karachi from Jan. 2018 till Dec. 2022. All patients with CRC under age 30 were included in the study. Diagnosis was made on Colonoscopy and histopathology confirming CRC. The data obtained was analyzed on the statistical software SPSS version 23. Descriptive statistics were obtained by frequencies and percentages.

Results: In this study total 566 patients of CRC and Young patients 117 were analyzed. The majority, 67 (57.3%) patients were male and 50 (42.7%) were female. Most commonly present in Urdu speaking 47(40%) followed by Sindhi 40 (34%) and Pathan and Panjabi 13(11%). Smoking has a strong association, 13(9%) were active smokers followed by Naswar 8 (6%). Most common area was from Orangi Town 8(6%) followed by Korangi 3(4%) Colonoscopy revealed polypoidal growth in 79 (67%) of patients followed by ulcerated lesions in 23 (19.7%). The most common site of CRC was Rectum affecting 48 (41%) followed by Sigmoid colon 46 (39.3%) and the least common site was Ascending colon 7(2.6%). Moderately differentiated Adenocarcinoma was the most common histological type found in 96 (82.5%) and 17 (10%) having signet ring type. The common clinical presentation was abdominal pain 64 (53%) constipation 45 (38.5%) and Bleeding per Rectum 42 (36%).

Conclusion: CRC is the leading cause of mortality. It is on rising pattern among young adults, most commonly involving the left side of the colon. We need more studies to make guidelines for screening and surveillance of CRC in our population.

Disclosure: Nothing to disclose.

PP0741

IMPACT OF SEDATION ON POST COLONOSCOPY COLORECTAL CANCER (PCCRC) DEATHS

D. Penz¹, J. Zessner-Spitzenberg², E. Fuchs³, E. Waldmann⁴, A. Demschik², L.-M. Rockenbauer⁵, M. Trauner⁶, M. Ferlitsch⁷
¹Klinik Floridsdorf, Vienna, Austria, ²Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Wien, Austria, ³St. John of god hospital, 1220, Austria, ⁴Medical University of Vienna, Gastroenterology und Hepatology, Wien, Austria, ⁵Medical University of Vienna, Graz, Austria, ⁶Head of Division of Gastroenterology and Hepatology - Department of Medicine III, Head of Division o, Department of Medicine III, Wien, Austria, ⁷Medical University Vienna, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Wien, Austria

Contact E-Mail Address: daniela.penz1220@gmail.com

Introduction: Use of sedation is associated with a positive effect on endoscopists ADR and a higher proportion of colonoscopies with a withdrawal time > 10. However, the impact of sedation on the risk of post colonoscopy colorectal cancer (PCCRC) deaths remains unclear.

Aims & Methods: Retrospective cohort study within a large population based screening program database in Austria, the association of sedation in screening colonoscopy with post-colonoscopy colorectal cancer death was analysed. Logistic regression was used to estimate the effect of sedation on PCCRC-death.

Results: 407.598 screening colonoscopies were analyzed. In 371.132 (91,1%) sedation was used. 46.8% of sedated patients were men compared to 68,2% in unsedated patients (HR 1.94 (1.60, 2.35), p<0,001). Cecum was reached in 97.3% of sedated and 95.5% of unsedated individuals. (HR 4.22 (3.06, 5.82) p<0,001).

Cumulative incidence of PCCRC in sedated individuals was 0.05 (95% CI 0.05-0.5) after 4 years, 0.07% (0.07-0.07) after 6 years, 0.11% (0.11-0.11) after 8 years, 0.14 (0.14-0.14) after 10 years, 0.18% (0.18-0.18) after 12 years. In unsedated patient, cumulative incidence was 0.1% (0-1-0-1) after 4 years, 0.15% (0.15-0.15) after 6 years, 0.22% (0.21-0.23) after 8 years, 0.25% (0.24-0.26%) after 10 years, 0.27% (0.26-0.28) after 12 years. Hazard ratio was 1.31 (0.94-1.83, p=0.1) for sedation in PCCRC-deaths.

Conclusion: Incidence of PCCRC-death was higher in unsedated patients, however this effect was not significant and probably an effect of lower cecal intubation rate within unsedated patients.

Disclosure: Nothing to disclose.

PP0742

COLONOSCOPY IN ELDERLY VS YOUNG SUBJECTS: WHAT INDICATIONS ARE ASSOCIATED WITH HIGHER RISK LESIONS OF COLORECTAL NEOPLASIA?

L. Mouslim¹, F. Aitiken¹, S. Hdiye¹, R. Chaibi¹, J. Benass¹, A. Benhamdane¹, T. Addajou¹, S. Mrabti¹, R. Berraida¹, E. Ilham¹, F. Rouibaa², H. Seddik¹

¹Mohamed V Military Training Hospital, Rabat, Morocco, ²Military Hospital Mohamed V-Souissi University, Hay Ryad - 10100, Rabat, Morocco

Contact E-Mail Address: imane.mouslim@gmail.com

Introduction: The indications for colonoscopy are clearly defined and its main objective is to look for neoplasia or lesions at high risk of colorectal neoplasia, even if benign lesions are much more frequent. Common indications for young adults < 50 years include rectal bleeding and diarrhea, while for subjects over 50 years, the indications may be larger given the risk of colorectal cancer, despite the recent increase in neoplastic lesions in young adults.

Aims & Methods: A retrospective descriptive and analytical study, including 1518 patients, was carried out over 3 and a half years. The patients were divided into 2 groups: group A for patients aged less than 50 years, and group B for patients aged greater than 50 years. We compared epidemiological, clinical, and endoscopic data between the two groups. Patients known to have inflammatory bowel disease (IBD) were excluded from our study. The statistical analysis was carried out by the JAMOV software.

Our study aims to compare the indications and results of colonoscopy between those under and over 50 years old and to determine the indications associated with a risk of neoplastic lesion.

Results: 65.1% of patients were over 50 years old, and 34.9% were under 50 years old. The average age was 37.5 ± 9 years in group A and 64.4 ± 9 years in group B. The female gender predominated among those under 50 years old (55.3%), while the male gender predominated among those over 50 years old (56.3%) (p<0.001).

History of colorectal cancer predominated among those over 50 years old at 10.5% (vs 4.4%; p<0.001). The indications for colonoscopy were dominated by constipation in patients in group B at 29.1% (vs 22%; p=0.01) and by diarrhea in patients in group A at 33.3% (vs 19.3%; p<0.001).

Colonoscopy was pathological in 49.1% of patients in group B vs 32.9% of patients in group A (p<0.001). It was dominated by colitis or rectocolitis (47.9%) in subjects under 50 years old (vs 11.7%; p<0.001), by polyps (61.5% vs 41.3%; p<0.001) and colorectal neoplasia (16% vs 5%; p=0.002) in older patients.

A higher risk of neoplastic lesions was associated with rectal bleeding and constipation (p < 0.001) in subjects > 50 years old, and with constipation in subjects < 50 years old (p = 0.007).

Conclusion: The presence of neoplastic lesions was strongly associated with the presence of constipation in subjects < 50 years old and with rectal bleeding and constipation in subjects > 50 years old. Early screening with colonoscopy might be beneficial for young individuals with these higher-risk lesions of colorectal cancer.

Disclosure: Nothing to disclose.

PP0743

ANTICOAGULATION IS ASSOCIATED WITH EARLIER GASTROINTESTINAL CANCER DETECTION: A RETROSPECTIVE STUDY

A. Protopapas¹, N. Protopapa¹, A. Filippidis¹, V. Kyritsi¹,
I. Papagiouvanni¹, E.-P. Chamalidou², C. Savopoulos²,
A. Protopapas²

¹Aristotle University of Thessaloniki, AHEPA University Hospital,
First Propedeutic Department of Internal Medicine, Thessaloniki,
Greece, ²Aristotle University of Thessaloniki, Hippokration General
Hospital, Fourth Department of Internal Medicine, Thessaloniki,
Greece

Contact E-Mail Address: adoprot@hotmail.com

Introduction: A significant amount of the population, especially the elderly, are receiving antithrombotic drugs. There is a significant association between antithrombotic therapy (AT) and gastrointestinal bleeding that leads to gastrointestinal cancer detection.

Aims & Methods: The aim of our study is to investigate the possibility that the administration of AT contributes, through the early onset of symptoms, to the early diagnosis of digestive neoplasms. Patients of the department's gastroenterology and oncology units who were followed for gastric or colon neoplasm were analyzed retrospectively. Exclusion criteria included screening colonoscopy, and patients with idiopathic inflammatory bowel diseases or neuroendocrine neoplasms. AT was defined as anticoagulant or antiplatelet therapy.

Results: 152 patients were included, with a mean age of 69.6 ± 10 years, of which 89 were men (58.6%). The majority (84.2%) had colorectal cancer. Forty-nine patients were diagnosed with a bleeding episode (32.2%) and 42 in the context of anemia investigation (27.6%). Fifty-five patients were receiving AT (36.2%). The main reason for receiving AT was the presence of coronary artery disease. Most patients were diagnosed with cancer stage III (45.4%) and II (30.3%). A statistically significant association was observed between the use of AT and an earlier cancer stage at diagnosis ($p=0.001$). 54.5% of patients receiving AT were diagnosed at an early stage (I or II), compared to 30.9% of patients not receiving AT. Patients diagnosed after a bleeding episode or onset of anemia while receiving AT had an earlier stage of disease at diagnosis than the rest of the sample ($p=0.002$). 62.5% of these patients were diagnosed at an early stage (I or II), compared to 32.1 % of patients in other groups.

Cancer Stage	AT	No AT
I	8 (14.5%)	6 (10.9%)
II	22 (40%)	24 (24.7%)
III	22 (40%)	47 (48.5%)
IV	3 (5.5%)	20 (20.6%)
Total	55	97

Table: Cancer stage at diagnosis according to AT use

AT: antithrombotic therapy

Conclusion: Antithrombotic drugs may promote an earlier diagnosis of neoplasms of the digestive tract due to the earlier appearance of bleeding, diffuse or occult. In this subset of patients, a bleeding event, barring significant short term morbidity, may facilitate earlier diagnosis and treatment of the underlying disease..

Disclosure: Nothing to disclose.

PP0744

EFFICACY OF HEMOSTATIC POWDER (UI-EWD) IN REDUCING COAGULATION SYNDROME IN PATIENTS WITH COLONIC NEOPLASMS REMOVED BY ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

J.B. Shin¹, B. Cha¹, J. Hong¹, K.-S. Kwon¹

¹Inha University Hospital, Gastroenterology, Incheon, South Korea

Contact E-Mail Address: shinjongv@naver.com

Introduction: Endoscopic submucosal dissection (ESD) is a widely used and effective treatment modality for colonic neoplasm, such as lateral spreading tumors or early colorectal cancer. However, ESD can cause several procedure-related complications. Coagulation syndrome (CS) is one of the common complications described as localized abdominal pain, fever, and leukocytosis after ESD temporarily.

Aims & Methods: This study aims to evaluate the effect of reducing the incidence of CS by administering UI-EWD after ESD and the practicability and safety of applying UI-EWD to post-ESD ulcer sites. CS occurs more frequently when a tumor size ≥ 20 mm and a lesion located in the left side colon. This study was conducted retrospectively on 79 consecutive patients were treated with ESD between November 2022 and January 2024. We evaluated the rate of CS and the rate of bleeding within 30 days. CS was defined as localized abdominal pain and fever at the ESD site that occurred within 3 days of ESD without perforation.

Results: The total incidence of CS in enrolled patients with CS high risk is large colorectal tumor is 21.5% (14/65). The incidence of CS after ESD was statistically significantly lower in patients who applied UI-EWD. (0% (0/14) vs 27.5% (14/51), $p=0.029$) The rebleeding rate within 30 days was not observed in the UI-EWD application group, but there was no statistically significant difference. (0% (0/14) vs 9.8% (5/51), $p=0.347$) No UI-EWD-related adverse events were observed.

Conclusion: Less CS was observed in the UI-EWD group. It was suggested that the application of UI-EWD after colon ESD in CS high-risk group has a good association with a decrease in CS occurrence. To obtain significant information on the performance of UI-EWD in a decrease of CS, a well-designed, large-scale, randomized control study is needed.

References: 1) Arimoto, Jun, et al. "Risk factors for post-colorectal endoscopic submucosal dissection (ESD) coagulation syndrome: a multicenter, prospective, observational study." *Endoscopy international open* 6.03 (2018): E342-E349.

2) Hong, Mi Jin, et al. "Prevalence and clinical features of coagulation syndrome after endoscopic submucosal dissection for colorectal neoplasms." *Digestive diseases and sciences* 60 (2015): 211-216.

Disclosure: Nothing to disclose.

PP0745

WITHDRAWN

PP0746

IMPACT OF COLORECTAL SCREENING ON THE MANAGEMENT OF T1 COLORECTAL CANCERS

A. Fabian¹, R. Bor¹, Z. Bosze¹, B. Vasas², T. Tóth¹, P. Bacsur^{1,3}, A. Balint¹, B. Farkas¹, K. Farkas^{1,3}, E. Ivany¹, D. Magyar¹, T. Resál¹, M. Rutka¹, T. Molnár¹, Z. Szepes¹

¹University of Szeged, Albert Szent-Györgyi Clinical Center, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²University of Szeged, Department of Pathology, Szeged, Hungary, ³USZ Translational Colorectal Research Group, Hungarian Centre of Excellence for Molecular Medicine, Szeged, Hungary

Contact E-Mail Address: fabiananna9@gmail.com

Introduction: The incidence of early-stage colorectal cancer (CRC) rises with the introduction of colorectal screening programs; there is a shift towards less invasive treatment in screen-detected compared to non-screen-detected CRCs.

Aims & Methods: This retrospective, single-center cohort study aimed to assess the impact of colorectal screening on the incidence of submucosal invasive (pT1) CRC and compare treatment characteristics of screen-detected and non-screen-detected lesions between 2010 and 2023.

Screen-detected pT1 CRC (involving lesions detected with the pilot CRC screening in Csongrád-Csanád county in 2015, and those with the Hungarian population-based screening program [EFOP-1.8.1-VE-KOP-15-2016-00001] initiated in 2019) lesion, patient and treatment characteristics were compared to pT1 lesions detected outside the screening program in average-risk patients aged 50-70 years during the screening period (2015-2016 and 2019-2023). The impact of screening on pT1 CRC incidence was assessed with investigating new pT1 CRC cases throughout the screening period (2015-2016 and 2019-2023) compared to non-screening periods (2010-2014 and 2017-2018).

Results: During the 14-year study period, a total of 182 pT1 CRCs were detected in average-risk patients aged 50-70 years. 81 of these lesions (44.5%) were detected during non-screening periods. During the screening period, 44 lesions were screen-detected (24.2%, 16 of these detected during the pilot screening) and 57 lesions were non-screen-detected (31.3%). Mean pT1 incidence was higher in the screening than in the non-screening periods (14.7 vs. 11.6 lesions/year, $p < 0.01$); with the highest incidence during the pilot screening (2015-2016; 20 lesions/year), and the lowest during the pandemic (2020-2021, 9 lesions/year).

Patient and lesion characteristics were similar in screen-detected and non-screen-detected lesions (mean age: 63.1 vs 63.5 years, male ratio: 62.8% vs 64.3%, follow-up period: 3.85 vs 3.70 years; location: 31.8% vs 33.3% rectal, morphology: 34.1% vs 42.1% pedunculated, mean lesion size: 21.0 vs 24.7 mm).

No difference in histologic prognostic factors were found between the two groups. Treatment choices were similar for both screen-detected, and non-screen-detected lesions: local excision in 65.9% vs 72.2% (incl. ER in 63.6% vs 63.2%, and minimally invasive local surgical resection in 2.3% vs 7.0%), and surgical oncologic resection in 34.1% vs 29.8%, respectively; $p = 0.167$. Screen-detected colon cancers were more likely to be treated with surgical oncologic resection (43.3% vs 28.9%, $p = 0.218$), while screen-detected rectal cancers were preferred to be treated with local excision (85.7% vs 68.4% [ER: 78.6% vs 47.4%], $p = 0.416$) compared to non-screen-detected lesions.

During the follow-up, adverse outcomes (local recurrence and/or dissemination) occurred in two screen-detected, and in one non-screen-detected patient, $p = 0.797$. Lymph node involvement rate was similar in those undergoing surgical oncologic resection in screen-detected, and non-screen-detected patients (6.7% vs 5.9%, respectively; $p = 0.927$).

Conclusion: The incidence of submucosally invasive CRC rises with the implementation of colorectal screening program. There is no difference in the management and outcomes of screen-detected and non-screen-detected pT1 CRCs, but local excision, especially endoscopic resection is preferred for screen-detected rectal lesions.

Disclosure: Nothing to disclose.

PP0747

NEOADJUVANT THERAPY IN RECTAL CANCER - ONE YEAR FOLLOW-UP RESULTS OF STANDARD VERSUS TOTAL NEOADJUVANT STRATEGIES

L. Correia Gomes¹, B. Alves², J. Venâncio², M. Limbert³, J. Maciel³, D. Cavadas³, I. Miguel⁴, A. Luís⁴, J. Oliveira⁴, M. Santos⁴, R. Fonseca⁵, M. Abdulrehman⁶, I. Rosa¹

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, Gastroenterology, Santa Maria da Feira, Portugal,

²Instituto Português de Oncologia de Lisboa Francisco Gentil, Gastroenterology, Lisboa, Portugal, ³Instituto Português de

Oncologia de Lisboa Francisco Gentil, Surgery, Lisboa, Portugal, ⁴Instituto Português de Oncologia de Lisboa Francisco Gentil,

Oncology, Lisboa, Portugal, ⁵Instituto Português de Oncologia de Lisboa Francisco Gentil, Anatomy Pathology, Lisboa, Portugal,

⁶Instituto Português de Oncologia de Lisboa Francisco Gentil, Radiotherapy, Lisboa, Portugal

Contact E-Mail Address: luisfilipe.gomes@outlook.com

Introduction: Locally advanced rectal cancer (LARC) poses a significantly challenge in clinical management, involving multimodal treatment approach.

Among innovative strategies, Total Neoadjuvant Therapy (TNT) has emerged, delivering all planned chemotherapy before surgery.

Aims & Methods: Our aim was to evaluate the real-world application and efficacy of TNT and to compare it with non-TNT strategy.

This retrospective study compared 107 locally advanced rectal adenocarcinoma patients treated with Total Neoadjuvant Therapy (TNT) from 2022 and traditional chemoradiotherapy (CRT) from 2020-2021. Evaluation included primary endpoints of efficacy, tolerability, and completion rates.

Results: Among 107 patients (54.2% male, mean age 62.48 years), non-TNT and TNT follow-ups were 26.66 and 8.19 months, respectively. No differences in gender ($p = 0.163$), staging ($p = 0.707$), or location ($p = 0.727$) were noted. TNT patients received more short-course radiotherapy (42.5% vs 1.5%, $p < 0.001$).

Clinical responses favored TNT ($p = 0.030$) with no significant differences in pathological responses, recurrence rates, or survival. TNT exhibited higher chemotherapy completion ($p = 0.007$) and lower adverse events ($p < 0.001$). Post-surgery events showed no significant differences ($p = 0.470$).

Conclusion: In conclusion, our data add to the body of literature favoring the TNT treatment strategy for locally advanced rectal cancer, aiming to achieve higher complete response rates with less adverse events.

References:

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
2. Oronsky B, Reid T, Larson C, Knox SJ. Locally advanced rectal cancer: The past, present, and future. Semin Oncol. 2020 Feb;47(1):85-92. doi: 10.1053/j.seminoncol.2020.02.001. Epub 2020 Feb 21. PMID: 32147127.
3. Maas M, Beets-Tan RG, Lambregts DM, Lammering G, Nelemans PJ, Engelen SM, van Dam RM, Jansen RL, Sosef M, Leijtens JW, Hulsewé KW, Bui-

Jsen J, Beets GL. Wait-and-see policy for clinical complete responders after chemoradiation for rectal cancer. *J Clin Oncol*. 2011 Dec 10;29(35):4633-40. doi: 10.1200/JCO.2011.37.7176. Epub 2011 Nov 7. PMID: 22067400.

Disclosure: Nothing to disclose.

PP0748

WATCH AND WAIT STRATEGY IN RECTAL CANCER – FOLLOW-UP RESULTS FROM A TERTIARY ONCOLOGY CENTRE

M. Rajão Saraiva¹, G.M. Cancro do Cólon, Reto e Canal Anal¹, I. Rosa²

¹*Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal*, ²*Instituto Portugues de Oncologia de Lisboa, EPE Dept. de Gastroenterologie, Gastroenterology, Lisboa, Portugal*

Contact E-Mail Address: margarida.rsaraiva@gmail.com

Introduction: The treatment of rectal cancer (RC) has been evolving in recent decades, aiming at improving organ preservation. This work evaluates the results of the Watch & Wait (W&W) strategy in a tertiary cancer centre.

Aims & Methods: Patients diagnosed with adenocarcinoma of the rectum up to 6cm from the anal margin, cM0, >cT1N0, with diagnosis and first multidisciplinary consultation between June 2014 and June 2020 were included. All patients received neoadjuvant radiotherapy ± chemotherapy and underwent reassessment at 8-12 weeks. Patients with complete clinical response (cCR), defined by proctological examination, fibrosigmoidoscopy and magnetic resonance imaging, initiated surveillance in the W&W protocol and the other were offered surgery. We present the follow-up of patients until December 2023.

Results: The study included 137 patients, 56% male, mean age 63.7 ±15 years. Stage at diagnosis: III (75%), II (13%) and I (12%). After neoadjuvant treatment, 18 patients (13.6%) had a complete response. Stage I at diagnosis was associated with a higher probability of achieving cCR ($p=0.008$). All patients without CRC (113) underwent surgery: 50.4% abdominoperineal resection and 40.7% anterior resection of the rectum. The operative specimen revealed N+ disease in 23.7% of patients and complete pathological response in 14. Median follow-up time of 44 months ± 26 (3.6 years). In the W&W group, 6/18 patients presented regrowth, between 3 and 35 months (mean at 15.8 months), 4 were treated with surgery (2 refused), 1 of 4 had local recurrence after surgery). None of the patients had distant disease. At the end of follow-up, 15 patients were alive without disease, 2 alive with disease, and 1 died from disease.

Of the remaining 113 patients: 28 (26.4%) patients showed distant recurrence and 3 patients local and distant relapse. At the end of follow-up, 70 (62%) of patients (62 had no disease, 7 had disease, 1 was unknown) and 11.4% had death attributed to disease.

Comparing the two approaches, there is no difference between local recurrence, but there is a higher probability of distant recurrence by the traditional approach ($p<0.009$) as well as death ($p=0.006$).

When comparing patients under WW approach with patients with complete pathological response after traditional approach, there was only a higher probability of local recurrence in WW (0.011), with no statistically significant differences in distant recurrence or mortality.

Conclusion: In this cohort, with a longer follow-up period, the W&W approach continues to be a safe oncological approach, as described internationally.

References:

López-Campos F, Martín-Martín M, Fornell-Pérez R, García-Pérez JC, Die-Trill J, Fuentes-Mateos R, López-Durán S, Domínguez-Rullán J, Ferreiro R, Riquelme-Oliveira A, Hervás-Morón A, Couñago F. Watch and wait

approach in rectal cancer: Current controversies and future directions. *World J Gastroenterol*. 2020 Aug 7;26(29):4218-4239. doi: 10.3748/wjg.v26.i29.4218. PMID: 32848330; PMCID: PMC7422545.

Disclosure: Nothing to disclose.

PP0749

MANAGEMENT OF COLORECTAL CANCER IN PATIENTS WITH LIVER CIRRHOSIS - RETROSPECTIVE STUDY IN A TERTIARY CENTER

C. Anton¹, M. Dimache¹, O. Timofte¹, A. Cemîrtan², E. Gologan¹, D. Andronic³, I. Tocarciuc²

¹*Hospital "St. Spiridon", University of Medicine and Pharmacy "GrigoreT.Popa", Gastroenterology and Hepatology, Iasi, Romania*, ²*Hospital "St. Spiridon", Gastroenterology and Hepatology, Iasi, Romania*, ³*Hospital "St. Spiridon", University of Medicine and Pharmacy "GrigoreT.Popa", Surgery, Iasi, Romania*

Contact E-Mail Address: carmen_ro2008@yahoo.com

Introduction: The actual screening of colorectal cancer (CRC) includes people of 45 years old and patients with alcoholic liver cirrhosis (LC) have an elevated risk of developing colon cancer. Curative treatment of CRC in patients with an existing diagnosis of LC can be a challenge, requiring major surgical resection and may include liver-toxic chemotherapy. Post-operative morbidity and mortality are elevated in patients with LC. For improved survival, optimization of liver function is more important than adjuvant chemotherapy.

Aims & Methods: Our study included 149 hospitalized LC patients Classes Child- Pugh A, B and C, mean age 56 years old, during April 2023-March 2024, of which 13 cases presented lower bleeding, iron deficiency anemia, intestinal transit disorders, abdominal pain, and familial history of CRC. Clinical and paraclinical diagnostic of CRC in LC patients were made by digital rectal examination, hematological samples, rectosigmoidoscopy, total colonoscopy, abdominal ultrasound, computed tomography and magnetic resonance imaging.

Results: Biological tests indicated anemia, trombocitopenia, increased ESR, biochemical liver tests increased, occult bleeding (FIT), and the increase of the tumor markers CA19-9, AFP, CEA that is particularly useful for monitoring treated CRC. Flexible rectosigmoidoscopy detected six cases of rectal cancer, three cases of rectosigmoidian tumors, and total colonoscopy was the "gold standard" imaging investigation that detected two cases of descending colon cancer, one case of hepatic flexure tumor and one patient with ascending colon cancer. Of patients with LC Class Child Pugh A, 6 cases were operated by laparotomy, being referred to Oncology Institute with favorable outcomes, and the rest of seven patients with LC Class Child Pugh B and C had advanced CRC, being treated by chemotherapy. Abdominal ultrasound visualizes liver metastases, abdominal lymph nodes and CT, MRI were the main methods used for staging CRC before surgical and oncological treatment.

Conclusion: Colonoscopy is the exploration of choice in CRC detection with 97% sensitivity, providing histopathological examination by tumor biopsy and also diagnosis of synchronous cancer. Early diagnosis of CRC is essential to prevent complications and increase the survival rate in LC. Men with LC are predominantly affected of CRC. Abdominal ultrasound, CT or MRI are the main imaging investigations recommended in CRC staging before the surgical and oncological treatment. Laparotomy should be preferred in patients with LC. Survival rate is strongly associated with the improvements in liver function. Echoendoscopy, immunoscintigraphy with monoclonal antibodies can be useful in CRC and genetic testing of tumor DNA markers in stool can be recommended in families with genetic syndromes (Turcot, FAP).

Disclosure: Nothing to disclose.

PP0750

OPTIMIZING ENDOSCOPIC MANAGEMENT OF MALIGNANT COLORECTAL POLYPS: INVESTIGATING THE FACTORS HINDERING CURATIVE RESECTION

J. Carlos Goncalves^{1,2,3}, A.I. Ferreira^{1,2,3}, M. Souto^{1,2,3}, S. Xavier^{1,2,3}, P.B. Carvalho^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Unidade Local de Saúde do Alto Ave, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's - PT Government Associate Laboratory, Braga/ Guimarães, Portugal

Contact E-Mail Address: joaogoncalves92@gmail.com

Introduction: Endoscopic recognition of malignant colorectal polyps is challenging, as most do not exhibit obvious signs of submucosal invasion, despite advancements in optical diagnostic techniques. While endoscopic resection might achieve cure, comprehensive data on cure rates and predictive factors are lacking.

Aims & Methods: This study aimed to elucidate the endoscopic predictors associated with achieving cure for malignant polyps. We conducted a retrospective analysis of electronic medical records for patients undergoing colonoscopy with endoscopic mucosal resection at our institution. Patients with confirmed colorectal adenocarcinoma classified as stage T1 were included and those with biopsied and tattooed polyps referred for surgery were excluded. Data regarding polyp size, morphology, location, and indirect signs of submucosal invasion (non-lifting sign; chicken-skin sign; edge retraction; depressed areas; fold convergence; ulceration) were collected. Endoscopic cure was defined by negative margins (>1mm) and favorable histological prognosis factors.

Results: A total of 165 patients were included, 57.6% males, with a mean age of 65 years. A total of 170 malignant polyps were resected with a global cure rate of 33.5%. Pedunculated polyps accounted for 37.1% and exhibited a significant association with endoscopic cure ($p<0.001$, OR 3.4, 95%CI 1.74-6.6) compared to nonpedunculated polyps (Paris classification 0-Is, any 0-II). Most pedunculated polyps were localized in the left colon (87.3%), and 50.8% were resected with cure. Interestingly, neither a large ($p=0.532$) nor a short stalk ($p=0.672$) nor polyp size ($p=0.308$) impacted the likelihood of cure. In contrast, the cure rate for nonpedunculated polyps was 23.4%. The distribution of nonpedunculated polyps was 38.3% in the rectum, 43.9% in the left colon, and 17.8% in the right colon. A "piecemeal" endoscopic resection ($p<0.001$), the presence of indirect signs of submucosal invasion ($p<0.001$) and size (cure: 19.8 ± 7.4 mm, no cure 26.4 ± 12 mm, $p=0.01$) were associated with non-curative resections. However, on multivariate analysis, only *en-bloc* resection emerged as an independent factor associated with cure ($P=0.02$, OR 5.6, 95% CI 1.3-24).

Conclusion: Our data underscores endoscopic resection viability for potentially malignant pediculated polyps, irrespective of size or stalk type. However, sessile/flat polyps present challenges, particularly when large or with endoscopic signs of submucosal invasion. In these scenarios, *en-bloc* removal using advanced techniques might contribute to better outcomes.

References: Saraiva S. Colorectal malignant polyps: a modern approach. *Ann Gastroenterol*. Published online 2021. doi:10.20524/aog.2021.0681
Shaukat A, Kaltenbach T, Dominitz JA, et al. Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. *Off J Am Coll Gastroenterol ACG*. 2020;115(11):1751. doi:10.14309/ajg.0000000000001013

Disclosure: Nothing to disclose.

PP0751

ENDOSCOPIC SUBMUCOSAL DISSECTION OF ANORECTAL JUNCTION: RETROSPECTIVE REVIEW

A. Bargas Bárbara¹, A.C. Bravo¹, J. Revés², B. Abreu¹, L.M. Roque Ramos¹, E. Barjas¹, C. Palmela¹, M.L. Gloria¹, A.O. Ferreira¹

¹Hospital de Loures, Gastroenterology, Lisboa, Portugal, ²Hospital de Loures, Gastreenterology, Lisboa, Portugal

Contact E-Mail Address: bargasandre2@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) of anorectal junction lesions (ARJL) presents technical challenges. This location may be associated to increased risk of adverse events, such as anal stricture, fecal incontinence, and chronic pelvic pain. We aim to identify the safety and effectiveness of the ESD for ARJL.

Aims & Methods: We conducted a retrospective cohort study on consecutive patients undergoing ESD for rectal submucosal lesions between 2018 and 2023 at two centers. Patients without follow-up were excluded. Lesions were categorized as ARJL or proximal rectal lesions (RL). Complications were assessed starting from 12 hours post-procedure.

Results: Our study included 61 patients (54% male; mean age 71 ± 9 years). Forty patients had RL and twenty-one had ARJL. 89% of the patients had an R0 resection. 90% had en bloc resection. On histology 62% of the lesions were low-grade dysplasia adenoma, 16% were high-grade dysplasia adenoma, 7% had intramucosal adenocarcinoma and 15% had adenocarcinoma with submucosal invasion (T1), of which 33% had deep submucosal involvement (sm1), all RL. 3% were submitted to surgery. Mean procedure times were 95 ± 63 and 128 ± 117 minutes ($p=0.21$) with mean sizes of 36.72 ± 16.31 mm and 36.94 ± 25.16 mm ($p=0.96$), for RL and ARJL respectively. Median follow-up time was 18 months (IQR 7-39). In total, only five patients developed complications during follow-up: From the ESD of ARJL, 1 patient developed an asymptomatic stenosis and from the ESD of RL, one also developed an asymptomatic stenosis, two patients developed post-polypectomy syndrome, one had delayed bleeding and one had chronic pelvic pain.

Conclusion: Our study identified a low incidence of adverse effects associated with ESD of the ARJL, being categorized as mild, indicating favorable tolerability and safety of these interventions. Limitations include the retrospective design and small sample size. Further research is needed to validate these findings and to compare ESD and transanal surgery outcomes.

Disclosure: Nothing to disclose.

PP0752

ESD VS EFTR IN SMALL PT1 LESIONS' RESECTION, A COST-EFFECTIVENESS ANALYSIS

A. Gubbiotti¹, G. Corrà², M. Bucci², L. Peraro¹, D. Caroli¹, E. Guido¹, E. Rosa Rizzotto¹

¹Azienda Ospedale-Università di Padova, Padua, Italy, ²University of Padua, Padua, Italy

Contact E-Mail Address: gubbio92@hotmail.it

Introduction: Endoscopic submucosal dissection (ESD) and Endoscopic Full-thickness Resection (EFTR) represent treatments of choice in the endoscopic resection of small gastrointestinal (GI) lesions with superficial submucosal invasion. It is often challenging to assess the best curative option in daily practice, since ESD is thought to be more technical demanding, and requires a longer learning curve.

Aims & Methods: We conducted a monocentric retrospective study, analyzing all GI pT1 lesions < 35 mm resected by either ESD or EFTR in our Unit from 2016 and 2023. All procedures were performed in a Day Hospital setting. As primary endpoints we assessed en bloc resection, R0 resection (clear deep margins) and curative resection (no further need for surgery) rate. As secondary endpoints we analyzed mean procedural time, cost and adverse events that occurred within or after both procedures. Chi-square test, Fisher Test and T-test were performed for categorical variables.

Results: 40 ESD and 37 EFTR were enrolled. En bloc resection was achieved in, respectively, 87.5 % (35/40) and 97% (36/37), without reaching statistical difference (RR 0.9, p=0.74), likewise R0 resection (30/40, 75% vs 36/37, 97%, RR 0.77, p=0.44) and curative resection (22/40, 55% vs 25/37, 67%, RR 0.82, p=0.57). Adverse events analysis showed no statistical difference between the two cohorts (4/40, 12% vs 3/37, 8%, RR 1.5, p=0.79). Mean procedural time appeared significantly lower in EFTR, (69.85 ± 31.94 min vs 48 ± 16.9 min, p=0.0002), whilst mean procedural cost per hospitalization day was lower in ESD than EFTR (2746 € ± 1003 vs 3458 ± 746 €).

Conclusion: ESD and EFTR turned out to be equally successful in terms of resection outcomes in pT1 small lesions. Nevertheless, ESD appeared to be more cost-effective in our study, and therefore should be confirmed as gold standard in daily practice. However, EFTR could allow easier and faster en bloc resection in most challenging procedures, representing a valid alternative in less experienced settings.

Disclosure: Nothing to disclose.

PP0753

WITHDRAWN

PP0754

WITHDRAWN

PP0755

LONG-TERM RESULTS OF THE ENDOSCOPIC RESECTION OF APPENDICEAL LESIONS

L. Gutiérrez-Rios¹, R. Muñoz-González^{1,2}, M. Fraile³, J. Tejedor-Tejada⁴, E. Rojo⁵, J.C. Balboa², B. Oliveras Font⁶, H. Cortés⁷, C. Gutiérrez³, I. Miguel¹, I. Marin¹, A. Calm¹, I. Iborra¹, E. Vayreda¹, M. Rosinach², N. Caballero¹, E. Domenech Morral¹, V. Moreno De La Vega¹, P. Miranda⁵, A. Teran³, E. Rodríguez-De Santiago⁸, H. Uchima^{1,2}

¹Hospital Universitari Germans Trias i Pujol, Endoscopy Unit, Gastroenterology Department, Badalona, Spain, ²Teknon Medical Center, Endoscopy Unit, Barcelona, Spain, ³Marqués de Valdecilla University Hospital, Valdecilla Research Institute (IDIVAL), Gastroenterology and Hepatology Department, Clinical and Translational Research in Digestive Diseases, Santander, Spain, ⁴Hospital Universitario de Cabueñes, Endoscopy Unit, Gastroenterology Department, Gijón, Spain, ⁵Hospital Universitario de La Princesa, Gastroenterology, Madrid, Spain, ⁶Hospital Universitari Doctor Josep Trueta, Endoscopy Unit, Gastroenterology Department, Girona, Spain, ⁷Hospital de Urduliz, Digestive Endoscopy Unit, Vizcaya, Spain, ⁸Hospital Universitario Ramón y Cajal, Endoscopy Unit, Gastroenterology Department, Madrid, Spain

Contact E-Mail Address: laugutri@gmail.com

Introduction: Endoscopic resection of lesions involving the appendiceal orifice is an alternative to surgery. Long term outcomes have not been determined.

Aims & Methods: To determine the long-term efficacy and safety of endoscopic resection of appendiceal lesions.

Retrospective analysis of the endoscopic resection of lesions with appendiceal involvement was performed in seven centers in Spain between January 2016 and July 2022. The technical success rate (complete macroscopic resection at index procedure), recurrence rate and short- and long-term complications were evaluated, including delayed appendicitis with a clinical follow-up of at least 12 months.

The intra-appendicular extension of the lesion was described as superficial (visible appendiceal margin) or deep (if it was not possible to determine the appendiceal margin of the lesion before resection) and the circumferential extension was described according to the affected percentage.

Results: 98 lesions with appendiceal involvement were treated, 73 had a clinical follow-up >12 months with a median follow-up of 26 months ([IQR]16-37 months). There were 35 lesions with deep intra-appendicular involvement and 63 with superficial appendiceal involvement, 64 with a circumferential involvement ≥50%. The median size of the lesions was 20mm([IQR]10-30mm) and 19(19%) had previous manipulation. Underwater endoscopic mucosal resection (UEMR) was performed in 53% of the lesions (24% by underwater cap-suction pseudopolyp formation, CAP-UEMR) with a technical success of 93% (49% en bloc and 51% piecemeal). Among these cases, there were 7 incomplete resection, with 3 patients undergoing surgery and the remaining 4 undergoing endoscopic treatment during a subsequent session.

Within the entire cohort, there were 3 cases of malignant histology: one low-risk pT1 which underwent surgery resulting in no residual cancer and negative lymph nodes, another low-risk pT1a (which chose follow-up and experienced no recurrence), and a third with suspected incomplete resection and pT2 cancer, necessitating surgery.

There were 6 intraprocedural bleeding and 2 delayed bleeding, all managed endoscopically. 45 patients completed at least 12 months of endoscopic follow-up (median 18, [IQR] 8-29months), showing recurrence in 12

cases (6 lesions with deep intra-appendicular extension), 8 (67%) treated endoscopically. There was 1 case of intraprocedural perforation, managed endoscopically.

Surgery was needed during follow-up in 7 additional cases [recurrence=3; pT2 cancer =1; pT1a =1; appendicitis=2 (at 11 months and 56 months post-endoscopic resection)], in total 10 surgeries were needed in the entire cohort.

INTRA-APPENDICULAR EXTENSION	Superficial (n=63)	Deep (n=35)	p-value
Age years(mean+/-SD)	67+/-8.8	71+/-10.6	0.040
Female, n(%)	30(48%)	12(34%)	0.201
Antithrombotic agents	20(32%)	13(37%)	0.588
Lesion size, median mm(median[IQR])	15(8-20)	30(19-45)	<0.001
Circumferential extension			<0.001
<50%	29(46%)	5(14%)	
50-90%	28(44%)	17(49%)	
100%	6(10%)	13(37%)	
Previous manipulation	12(19%)	7(20%)	0.516*
Complete macroscopic resection	60(97%)	31(88%)	0.065*
En bloc resection	39(62%)	9(26%)	<0.001
Clinical follow -up,months(median[IQR])	25(15-34)	27(17-49)	0.154

Table 1- Baseline characteristics of patients and resected lesions
*Fisher's exact test applied.

Conclusion: The endoscopic management of lesions involving the appendix may indeed prove effective and safe after following a minimum follow-up of 12 months, offering a viable alternative to surgery. It is important to note that delayed-onset acute appendicitis, though rare can be observed beyond 11 months post-procedure, although a casual mechanism cannot be proven.

References:

1. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2017 Mar;49(3):270-297. doi: 10.1055/s-0043-102569. Epub 2017 Feb 17. PMID: 28212588.
2. Albéniz E, Pellisé M, Gimeno García AZ, et al; en nombre del Grupo Español de Resección Endoscópica de la Sociedad Española de Endoscopia Digestiva. Clinical guidelines for endoscopic mucosal resection of non-pedunculated colorectal lesions. Gastroenterol Hepatol. 2018 Mar;41(3):175-190. English, Spanish. doi: 10.1016/j.gastrohep.2017.08.013. Epub 2018 Feb 12. PMID: 29449039.
3. Mi Song E, Yang H, Jung Lee H, et al. Endoscopic Resection of Cecal Polyps Involving the Appendiceal Orifice: A KASID multicenter Study. Dig Dis Sci. 2017, 62, 3138–3148, DOI: 10.1007/s10620-017-4760-2.
4. Jacob H, Toyonaga T, Ohara Y, et al. Endoscopic submucosa dissection of cecal lesions in proximity to the appendiceal orifice. Endoscopy, 2016. 48(09): v23-v23. DOI:10.1055/S-0042-110396.
5. Schmidt A. Lesions at the appendiceal orifice- the Achilles'heel of endoscopic resection? Endoscopy, 2022. 54(01): 25-26 DOI: 10.1055/a-1686-8800
6. Patel AP, Khalaf MA, Riojas-barrett M, et al. Expanding endoscopic boundaries: Endoscopic resection of large appendiceal orifice polyps with endoscopic mucosal resection and endoscopic submucosal dissection. World J Gastrointest Endosc 2023, 15(5):386-396. DOI: 10.4253/wjge.v15.i5.386.

Disclosure: Dr Hugo Uchima collaborates as proctor with Erbe Spain and Olympus Iberia. Has received congress registration from Casen Recordati.

PP0756
STOMA-FREE SURVIVAL AFTER PALLIATIVE COLONIC STENTING

I. Mohamed¹, D.H. Dewar¹
¹University Hospital Lewisham, Gastroenterology, London, United Kingdom

Contact E-Mail Address: daviddewar@nhs.net

Introduction: Self-expandable metal stents (SEMS) are the preferred treatment of malignant large bowel obstruction in those individuals who are not likely to have a curative resection (ESGE recommendations 2020). The differentiation between palliative and surgical candidacy may not be possible at presentation. We wished to measure the stoma-free prognosis of palliative patients, who do not have a surgical resection.

Aims & Methods: We analysed all patients undergoing SEMS at our centre over 10 years, collecting data on stoma formation, significant events and survival. Palliative stenting was defined in those who never underwent a resection of their primary obstructing cancer. All patients who had a technically successful SEMS were followed (a stent was placed across the stricture) so cases where there was early clinical failure were included. In our centre, we opt to attempt SEMS in all areas of the colon including the right colon.

Results: 171 patients with malignant large bowel obstruction (mean age 72.6, 57% male, 31% right-sided with obstruction beyond the splenic flexure) were referred for SEMS and no resection of the primary cancer was undertaken (this was 80% of total patients referred for SEMS). In 31% of patients, a stated plan for curative or palliative intent was amended in later decision-making. Where a stent was successfully deployed (150 patients, 88% technical success), 96% of patients avoided a stoma at any time in their palliation and median stoma-free survival was 283 days (9.4 months). Palliative chemotherapy was administered in 38.4% of cases. In those 21 cases where stenting was unsuccessful, 15 had surgery with a stoma formed and 6 were palliated. No procedural perforations occurred. Re-stenting of the primary cancer was required in 15 cases out of 150 (10%) at a median time of 6.5 months. Long term survival showed 33% of patients lived at least 1 year, 16% of patients survived more than 2 years, and 3.6% more than 3 years. Four patients (2.7%) were found to have incidental stent migration on CT to assess response to chemotherapy, but no further intervention (re-stenting or surgery) was required. Three patients may have died prematurely from COVID. Factors associated with significantly lower rate of re-intervention were obstruction in the proximal colon and older age.

Conclusion: In palliative SEMS management of malignant bowel obstruction, 96% of patients can avoid lifetime stoma surgery and can expect a median survival of 283 days.

Disclosure: Nothing to disclose.

PP0757

SURGERY AFTER ENDOSCOPIC REMOVAL OF A MALIGNANT POLYP: IS RESIDUAL DISEASE A REAL ISSUE?

A.I. Ferreira^{1,2,3}, J. Carlos Goncalves^{1,2,3}, M. Souto^{1,2,3}, S. Xavier^{1,2,3}, P.B. Carvalho^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²School of Medicine, University of Minho, Life and Health Sciences Research Institute (ICVS), Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: mariana.souto9@gmail.com

Introduction: The implementation of colorectal cancer screening programmes has been associated with an increase in the incidence of malignant polyps removed endoscopically. In those without endoscopic cure criteria, surgery can be performed to improve oncological outcomes.

Aims & Methods: Evaluate factors associated with the presence of residual malignant disease in the surgical specimen after endoscopic removal of a malignant polyp without endoscopic cure.

Retrospective, cohort study including patients with a malignant polyp endoscopically removed without endoscopic cure, who underwent surgery. The absence of endoscopic cure was defined as positive vertical resection margins (< 1 mm), poorly differentiated grade, depth of submucosal invasion > 1 mm, presence of lymphatic or vascular invasion, or presence of tumour budding. Patients with a synchronous neoplastic lesion and those with a malignant polyp without complete endoscopic removal were excluded.

Results: Included 74 consecutive patients submitted to surgery after the endoscopic removal of a malignant polyp without endoscopic cure. Most patients were male (62.2%), with a mean age of 64 ± 10 years. Regarding the endoscopic mucosal resection (EMR), 45 polyps were removed in one fragment (60.8%) and the other 29 were submitted to piecemeal EMR (39.2%). In 15 cases, snare tip spray coagulation (STSC) was performed at the margins of mucosal defects after EMR, 6 in normal-appearing margins (8.1%) and 9 in margins suspected of residual adenomatous tissue (12.2%). Considering the post-operative outcomes, 7 patients required surgical re-intervention (9.5%), 1 was admitted in the intensive care unit (1.4%), 1 patient died (1.4%), and 2 patients required re-hospitalization in the following 6 months (2.7%).

The presence of residual malignant disease in the surgical specimen occurred in 9 patients (12.2%), 7 had intramural disease (9.5%) and 2 had nodal metastasis (2.7%). Patients with polyps with a flat component were 5 times more likely to have residual disease in the surgical specimen ($p=0.043$). The polyp size and its location in the right colon were not associated with the presence of residual disease in the surgical specimen ($p=0.140$ and $p=0.654$, respectively). Patients with polyps submitted to piecemeal EMR were 7 times more likely to have residual disease in the surgical specimen ($p=0.024$), with 2 patients with residual disease after EMR in one fragment (4.4%) and 7 patients with residual disease from the piecemeal EMR group (24.1%). Those in which STSC was performed were also more likely to have residual disease in the surgical specimen ($p<0.001$). No statistically significant differences were found between the presence of positive margins, lymphatic or vascular invasion or well or moderately differentiated histologic grade, and the presence of residual disease in the surgical specimen ($p=1.000$, $p=0.675$ and $p=0.686$, respectively). Tumour budding was described in 3 patients, none of which had residual disease in the surgical specimen.

Conclusion: A minority of patients had residual malignant disease in the surgical specimen, with a higher risk for those with polyps with a flat component or that were submitted to piecemeal EMR. In fact, with piecemeal EMR almost one quarter of patients had residual disease e less than 5% of

those with EMR in one fragment had residual disease in the surgical specimen, highlighting the need for a careful evaluation of the polyp before endoscopic removal and the importance of removal in one fragment, in case of suspected submucosal invasion.

Disclosure: Nothing to disclose.

PP0758

WITHDRAWN

PP0759

CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR T1 COLORECTAL CARCINOMA - SURVEILLANCE OR SURGICAL TREATMENT?

T. Grega^{1,2}, N. Brodyuk¹, Z. Vackova³, R. Pohnan⁴, E. Traboulsi⁵, J. Bures^{1,2}, P. Urbanek¹, M. Zavoral^{1,2}, S. Suchanek^{1,2}

¹First Faculty of Medicine of Charles University and Military University Hospital, Internal Medicine, Prague 6, Czech Republic, ²Military University Hospital Prague, Gastrointestinal Oncology, Prague, Czech Republic, ³Military University Hospital Prague, Internal Medicine, Prague, Czech Republic, ⁴Military University Hospital Prague, Surgery, Prague, Czech Republic, ⁵Military University Hospital Prague, Pathology, Prague, Czech Republic

Contact E-Mail Address: tomas.grega@uvn.cz

Introduction: Complete endoscopic resection and accurate histological evaluation for T1 colorectal cancer (CRC) is critical to determine subsequent treatment. Endoscopic full-thickness resection (EFTR) and endoscopic submucosal dissection (ESD) are potential curative methods for treatment of T1 CRC.

Aims & Methods: Primary aims were R0 resection rate, histopathological risk-assessment, and curative resections. Secondary aims were short-term outcomes of patients with T1 CRC after endoscopic and surgical resection.

Consecutive EFTR and ESD procedures for T1 CRC at one tertiary endoscopic centre, prospectively recorded in National CRC Registry between 2015 and 2023, were retrospectively analysed. High risk factors included positive resection margin, low-grade differentiation (G3, G4), deep submucosal invasion (DSI) and lymphovascular invasion (LVI).

Results: We analysed 178 procedures: 114 (64 %) ESD and 64 (36 %) EFTR. From all resected lesions, 24 (13 %) were T1 carcinomas, 10 (6 %) subepithelial lesions (GIST/NET), 9 (5 %) T2 carcinomas, 2 (1%) T3 carcinomas, 58 (33 %) intramucosal carcinomas and 75 (42 %) low-grade adenomas. From 24 T1 CRC (54 % men, average diameter of lesion 25 mm) were 15 (63 %) lesions resected by EFTR, 7 (29 %) lesions resected by ESD, and 2 (8 %) lesions resected by hybrid technique ESD/EFTR.

Overall R0 resection was achieved in 18 (75 %) lesions. Seven (29 %) T1 CRC had superficial submucosal invasion ($\leq 1000\mu\text{m}$), 17 (71 %) T1 CRC had deep submucosal invasion, including 1 lesion with lymphovascular invasion. Curative resection rate for resected T1 CRC was 29 % and 71 % after excluding deep submucosal invasion as a risk factor.

Additional oncologic surgery was performed in 9 (38 %) patients, with residual cancer in 1 patient. Endoscopic follow-up was available in 22 (92 %) patients with a median of 3 years and no residual cancer were observed.

Conclusion: EFTR and ESD techniques are effective methods for treatment T1 CRC. Appropriate surveillance without additional surgery may be considered as another option in selected cases after endoscopic resection of T1 CRC.

Supported by programme projects of the Ministry of Health of the Czech Republic with Reg. No. NU22-08-00424, Reg. No. NV18-08-00246, DZVRO - MO1012 and Cooperatio.

Disclosure: Nothing to disclose.

PP0760

THE RELATIONSHIP BETWEEN PRETHERAPEUTIC MALNUTRITION ACCORDING TO GLIM CRITERIA AND CLINICAL OUTCOMES IN PATIENTS WITH COLORECTAL CANCER

S. Zaouga¹, S. Ben Hamida², H. Elloumi Ep Kharrat¹, I. Cheikh¹

¹Habib Bougatfa Hospital, Bizerte, Tunisia, ²University Hospital Bizerte, Gastroenterology, Bizerte, Tunisia

Contact E-Mail Address: zaouga.soumaya@gmail.com

Introduction: Malnutrition is a highly prevalent condition in patients with cancer that has a negative impact on clinical outcomes. The GLIM criteria for malnutrition aim to standardize its diagnosis. In colorectal cancer, poor nutritional status is associated with increased morbidity and mortality and reduce tolerance to treatment.

Aims & Methods: We aimed to assess the prevalence of malnutrition based on the GLIM criteria and to correlate this with patient outcomes and survival in colorectal cancer.

Patients with colorectal cancer diagnosed from January 2015 to December 2022 were included. All of them were screened for malnutrition using the GLIM criteria.

The relationships between GLIM-malnutrition and survival were analyzed.

Results: Sixty patients were included. The mean age was 54 years [35 - 82] with a sex ratio of 1.8 (M/F). Tumors were located in the right colon in 20 patients (33%), the left colon in 22 patients (36%), and the rectum in 15 patients (25%). According to TNM classification, patients were predominantly classified in stages II and III. In terms of treatment, 20 patients received neoadjuvant chemotherapy (30%), 15 patients received neoadjuvant radiotherapy (25%), and 45 patients underwent surgery (75%). Malnutrition, according to GLIM criteria, was present in 40% of patients. It was classified as mild, moderate, and severe in 40%, 45%, and 15% of cases, respectively.

Regarding survival, the difference between the two Kaplan-Meier curves of patients fulfilling GLIM malnutrition criteria versus patients without malnutrition was statistically significant (Log-rank test $p = 0.001$), [HR = 4.35 (95% CI = 2 - 9)], with a mean survival period of 18 ± 4.7 versus 32 ± 5.2 months, respectively ($p = 0.028$). Mild malnutrition was associated with better survival compared to moderate and severe malnutrition: 20 ± 2.3 versus 17 ± 3.2 months, respectively ($p = 0.003$).

Conclusion: Pretherapeutic screening for malnutrition seems to be mandatory due to its negative prognostic impact in patients with colorectal cancer, allowing for better pre-therapeutic stratification.

References: Cederholm T, Jensen GL, Correia MITD, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. *Clin Nutr.* 2019;38(1):1-9.

Disclosure: Nothing to disclose.

PP0761

SURGERY AFTER RESECTION OF MALIGNANT POLYPS: BETTER SAFE THAN SORRY?

M. Souto^{1,2,3}, J. Carlos Goncalves^{1,2,3}, A.I. Ferreira^{1,2,3}, P.B. Carvalho^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, S. Leite^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga/Guimarães, Portugal, ³ICVS/3B's - PT Government Associated Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: mariana.souto9@gmail.com

Introduction: After resection of a malignant colorectal polyp, patients may be proposed for surgical treatment or surveillance, depending on the presence of cure criteria.

Aims & Methods: The aim of this study was to compare the detection of metachronous lesions in patients with malignant polyps undergoing surgery versus surveillance.

Retrospective cohort study including patients with endoscopic removal of malignant polyps. Patients were divided into 2 groups, according to the strategy defined in the oncology group consultation: surveillance (group 1) and surgery (group 2). The diagnosis of metachronous lesions during the follow-up period was the main outcome studied. A metachronous lesion was defined as the detection of adenoma/adenocarcinoma, 6 or more months after index colonoscopy.

Results: 77 patients were included, 55.8% in group 1, 44.2% in group 2. Mean age was 65.2 ± 10.8 years, 45.5% were women.

In group 1, significantly more patients developed metachronous lesions compared to group 2 (66.7% vs 33.3%, $p = 0.036$). The mean time to diagnosis of metachronous lesion was significantly shorter in group 1 (18.6 ± 2.8 vs 36.0 ± 5.6 months, $p = 0.004$).

In group 1, 32.1% of patients developed metachronous lesions in the same colonic segment as the endoscopic resection of the malignant polyp.

In histological characterization, the two groups did not present statistically significant differences: low-grade dysplasia in 92.9% (group 1) and 85.7% (group 2); high-grade dysplasia in 7.1% (group 1) and 14.3% (group 2), $p = 0.457$. No adenocarcinomas were detected during the follow-up period.

Conclusion: Surgical approach was associated with a lower incidence of metachronous lesions, suggesting that a significant proportion of the risk of metachronous lesion occurs in the segment of the index lesion.

Disclosure: Nothing to disclose.

PP0762

THE EFFECTS OF SMALL MOLECULE AXIN-STABILIZER (KYA1797K) IN MONOTHERAPY AND COMBINED TREATMENT WITH CANNABINOID AGONIST (WIN 55,212-2) IN COLORECTAL CANCER CELL LINES

M. Swierczynski¹, A. Makaro¹, Z. Kasprzak¹, M. Salaga¹

¹Medical University of Lodz, Department of Biochemistry, Lodz, Poland

Contact E-Mail Address: mikolaj.swierczynski@stud.umed.lodz.pl

Introduction: Colorectal cancer (CRC) is one of the most common neoplasms world widely. G-protein coupled receptors (GPCR) affect crucial elements of oncogenesis, such as responses to various endo- and exogenous stimuli (e.g. medications), angiogenesis and forming metastases. The magnitude of GPCR signaling is terminated by regulators of G-protein signaling (RGS), which typically possess GTPase activity. AXIN is an atypical RGS without GTPase function. Its main role is stabilization of β -catenin destruction complex in which it cooperates with adenomatous polyposis coli (APC) and glycogen synthase kinase3 (GSK3). Through this complex, AXIN antagonizes prooncogenic canonical Wnt signaling pathway that depends on β -catenin. On the other hand, recently attention has been paid to the potential tumor-suppressive properties of cannabinoids (CB) which are ligands of Gai/o-type GPCR – CB1 and CB2.

Aims & Methods: In this project we aim to test the therapeutic potential of simultaneous targeting of AXIN and CB receptors with KYA1797K and WIN 55,212-2 in CRC cell lines (SW480, Caco-2) and non-cancerous enterocytes CCD 841 CoN as comparator. We hypothesize that KYA1797K is effective in monotherapy and in combination with cannabinoids in CRC. Moreover, we expect that stabilization of AXIN does not to weaken the effect of CB receptor ligands.

Cytotoxicity of KYA1797K (1; 10; 100, 300 μ M) and WIN 55,212-2 (1; 10; 100 μ M) in monotherapies and combined treatment (KYA1797K(10 μ M)+WIN 55,212-2(10 μ M) [K+W10] and KYA1797K(100 μ M)+WIN 55,212-2(10 μ M)) was assessed using MTT test. Relative genes' expression was evaluated using quantitative real-time PCR and Western Blot. Statistical analysis included Shapiro-Wilk test, one-way ANOVA with post-hoc Dunnett's and Tukey's tests.

Results: Caco-2 cells were insensitive to KYA1797K in monotherapy excluding concentration of 300 μ M, for which we observed significant cytotoxicity. Treatment with WIN 55,212-2 in concentration of at least 10 μ M in both mono- and combined therapy significantly reduced viability of this cell line. Similar profile of changes was observed in SW480 line, however the strength of observed effect and sensitivity to KYA1797K were higher. In CCD 841 CoN cells significant additive effect of KYA1797K and WIN 55,212-2 was observed for 100 μ M with no changes observed for 10 μ M. Moreover, we found that treatment with K+W10 causes significant cytotoxicity in cancerous SW480 cells but not in normal enterocytes CCD 841 CoN. Moreover, K+W10 treatment resulted in increased expression of AXIN 1 and 2 in each cell line except AXIN 2 in Caco-2 line, in which opposite effect was observed. The combined treatment decreased CB1 receptors' expression in all examined cell lines, whereas opposing tendency was observed for CB2. Furthermore, K+W10 treatment led to increased expression of RGS2, 11, APC and GSK-3. At the protein level K+W10 treatment surprisingly tended to decrease β -catenin relative expression. CB2 receptors were significantly more expressed in SW480 than in CCD 841 CoN that was consistent with cytotoxicity results.

Conclusion: AXIN stabilization is a promising new approach in CRC treatment. AXIN stabilization does not weaken CB1 and 2-dependent effects. The combined treatment of AXIN stabilizer and CB agonist may be especially important as life-prolonging therapy for patients with advanced CRC.

Disclosure: Nothing to disclose.

PP0763

INVESTIGATION OF THE IN VITRO CYTOTOXIC EFFECT OF PALLADIUM(II) COMPLEXES WITH 2-AMINOTHIAZOLE DERIVATIVES ON MOUSE AND HUMAN COLORECTAL CARCINOMA CELL LINES

M. Maksic^{1,2}, I. Corovic³, M. Jovanovic^{1,2}, D. Radojevic^{1,2}, S. Pavlovic³, I. Stanisavljevic³, T. Veljkovic^{4,5}, I. Jovanovic³

¹Clinical Centre Kragujevac, Clinic for Gastroenterology and Hepatology, Kragujevac, Serbia, ²Faculty of Medical Sciences, Department of Internal Medicine, Kragujevac, Serbia, ³Faculty of Medical Sciences, Center for Molecular Medicine and Stem Cell Research, Kragujevac, Serbia, ⁴Clinical Centre Kragujevac, Pediatric Clinic, Kragujevac, Serbia, ⁵Faculty of Medical Sciences, Department of Pediatrics, Kragujevac, Serbia

Contact E-Mail Address: asussonicmaster95@gmail.com

Introduction: Over the last four decades, metal-based antitumor medications, notably cisplatin, have been extensively utilized in chemotherapy, despite notable side effects. Colorectal cancer, a significant contributor to cancer-related mortality worldwide, has prompted extensive research into innovative treatment methods. Thiazoles and their derivatives constitute integral components of certain cytostatic agents, garnering considerable attention in studies exploring their biological and pharmacological properties.

Aims & Methods: The primary objective of this research is to examine the in vitro cytotoxic effect of newly synthesized palladium(II) complexes with 2-aminothiazole derivatives on colorectal carcinoma cell lines. The cytotoxic effects of newly synthesized palladium(II) complexes (C1, C2) and corresponding ligands (L1, L2) were determined using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay against both mouse (CT26) and human (HCT116) colorectal carcinoma cell lines. Non-tumor cells, specifically mouse mesenchymal stem cells (mMSCs), were employed as controls.

Results: The tested complexes and corresponding ligands reduce the viability of tumor cells in a dose-dependent manner. The C1 complex demonstrated strong cytotoxic activity against all tested tumor cell lines, with the HCT116 cell line being more sensitive to its toxic effects. All tested complexes and corresponding ligands reduced the viability of non-tumor mMSC cells, with mMSC cells being particularly sensitive to the cytotoxic effect of the C2 complex. The IC50 (half maximal inhibitory concentration) value obtained for the C1 complex was higher compared to the gold standard, cisplatin. The C1 complex exhibits the highest cytotoxic capacity towards tumor cells, followed by the highest IC50 values for control.

Conclusion: Palladium(II) complexes with 2-aminothiazole derivatives demonstrate direct antitumor activity in vitro. The C1 complex exhibits a high level of cytotoxicity. Further research is necessary to indicate the potential use of these compounds in experimental tumor therapy.

Disclosure: yes.

PP0764

WITHDRAWN

PP0765

RISK OF PERFORATION OF SELF-EXPANDABLE METAL STENTS WHO RECEIVED BEVACIZUMAB COMPARED TO STENT ALONE OR NON-BEVACIZUMAB CHEMOTHERAPY IN PATIENTS WITH ADVANCED COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

S.-Y. Na¹, S.J. Kim², E.-S. Kim³, Y. Jung⁴¹College of Medicine, The Catholic University of Korea, Internal Medicine, Incheon, South Korea, ²College of Medicine, Chosun University, Internal Medicine, Gwangju, South Korea, ³College of Medicine, Korea University, Internal Medicine, Seoul, South Korea, ⁴College of Medicine, Soonchunhyang University, Internal Medicine, Cheonan, South Korea**Contact E-Mail Address:** umnsy@naver.com

Introduction: Bevacizumab is an anti-angiogenic monoclonal antibody targeting vascular endothelial growth factor used to treat advanced colorectal cancer (CRC). Self-expandable metal stents (SEMS) are employed in cases of advanced obstructive CRC but are linked to adverse events like bleeding, stent migration, and bowel perforation. To date, it is unclear whether bevacizumab-based chemotherapy increases the risk of perforation in patients with SEMS. Therefore, we conducted a systematic review and meta-analysis to evaluate the risk of bevacizumab-related perforation in these patients.

Aims & Methods: We conducted a comprehensive literature search from major databases until December 2023. We identified all potential studies that evaluated the risk of colonic perforation in patients with bevacizumab-based chemotherapy after SEMS insertion. We compared the risk of colonic perforation in patients who received bevacizumab-based chemotherapy with patients who received chemotherapy without bevacizumab or best supportive care. We calculated the odds ratio (OR) and 95% confidence interval (CI) using a M-H random-effects model and I-square method.

Results: Twelve studies, including 1,599 patients, met our inclusion criteria and were included in the meta-analysis. Of 1,559 SEMS patients, 320 received bevacizumab-based chemotherapy, and 1,274 received chemotherapy without bevacizumab or best supportive care. A total of 106 perforations have been reported. The risk ratio for colonic perforation in bevacizumab-based chemotherapy was 2.78 (95% CI: 1.21-6.38, $p=0.02$; $I^2=57\%$) when compared to non-bevacizumab-based therapy. In subgroup analysis, bevacizumab-based chemotherapy showed an increased risk of perforation when compared with chemotherapy without bevacizumab (OR, 3.71; 95% CI: 1.43-93.5; $p=0.007$; $I^2=0$), but no statistically significant difference when compared with SEMS alone (OR, 3.75; 95% CI: 0.64-22.08; $p=0.14$; $I^2=62\%$).

Conclusion: Bevacizumab-based chemotherapy appears to increase the risk of perforation in advanced CRC patients after SEMS compared with non-bevacizumab-based therapy. These results were especially pronounced in chemotherapy without bevacizumab than in SEMS alone.

References: 1. van Hooft JE, Veld JV, Arnold D, et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2020. *Endoscopy* 2020;52:389-407.

2. van Halsema EE, van Hooft JE, Small AJ, et al. Perforation in colorectal stenting: a meta-analysis and a search for risk factors. *Gastrointest Endosc* 2014;79:970-82.

3. Lee JH, Emelogu IE, Kukreja K, et al. Safety and efficacy of metal stents for malignant colonic obstruction in patients treated with bevacizumab. *Gastrointest Endosc* 2019;90:116-124.

Disclosure: Nothing to disclose.

PP0766

ENDOSCOPIC SUBMUCOSAL DISSECTION AS THE PROCEDURE OF CHOICE FOR RESECTION OF LARGE COLORECTAL NEOPLASMS: AN INTERNATIONAL, MULTICENTER STUDY

D. Parekh¹, G. Leung², M. Kim³, Y. Minato⁴, Y. Kimoto⁴, A. Daphale⁵, H. Bapaye⁶, A.A. Pagadapelli⁵, M. Gaidhane⁷, M. Kahaleh⁷, A. Bapaye⁵, K. Ohata⁴¹Mumbai Institute of Gastroenterology, Department of Endoscopy, Mumbai, India, ²University of Pennsylvania, Division of Gastroenterology & Hepatology, Philadelphia, United States of America, ³Saint Louis University School of Medicine, Division of Gastroenterology & Hepatology, Saint Louis, United States of America, ⁴NTT Medical Center Tokyo, Department of Endoscopy, Tokyo, Japan, ⁵Deenanath Mangeshkar Hospital and Research Center, Shivanand Desai Center for Digestive Disorders, Pune, India, ⁶Byramjee Jeejeebhoy Medical College, Department of Internal Medicine, Pune, India, ⁷Rutgers Robert Wood Johnson Medical School, Department of Gastroenterology, New Brunswick, United States of America**Contact E-Mail Address:** dparekh2108@gmail.com

Introduction: Piecemeal endoscopic mucosal resection (EMR) vs endoscopic submucosal dissection (ESD) has been a long standing debate in the endoscopic community worldwide with multiple studies done to evaluate the preferred method to manage large colorectal neoplasms. Piecemeal EMR with thermal ablation of the margin has been strongly advocated and reported by certain groups to be a simple, inexpensive and effective technique and this has been preferred widely due to its perceived ease of performance and shorter learning curve.¹

However, close, repeated surveillance colonoscopy is recommended even when the lesion is thought to have been completely resected² as residual tumors can cause interval cancers.³

Some groups, mainly from east Asian countries, have recommended en bloc resection by ESD due to significantly lower risk of local recurrence and precise pathological diagnosis.⁴

But its usage is limited due to concerns about risk of serious adverse events. With improvement in training and devices, colorectal ESD is now being performed by various centers globally. This study aims to report the outcomes of an international, multicenter study on colorectal ESD.

Aims & Methods: Patients who underwent colorectal ESD for lesions greater than 20mm between January 2022 to April 2024 from centers in USA, Japan, and India respectively were included in this study. Recurrent lesions after endoscopic therapy, neoplasms identified in patients with ulcerative colitis, and non-epithelial lesions were included.

Primary outcomes were en bloc and R0 resection rate, delayed adverse events (bleeding/perforation), and local recurrence rate. Secondary outcomes were procedure time, lesion size, and pathology. Univariate and multivariate analysis were done to identify the risk factors for primary outcomes.

Results: 309 patients (median size, 40(27.5-60)mm; location rectum 52.4%, left colon 26.2%, right colon 21.4%) were involved in this study. The en bloc resection rate was 96.1% and R0 resection rate was 90.3%. 3 patients experienced delayed bleeding which was managed endoscopically. 2 patients underwent surgery for delayed perforation. 6 patients had a local recurrence. 67(23%) patients had intramucosal carcinoma on pathology.

Univariate analysis showed lesser procedure time (median(IQR) 145(80-236.25) vs 270(180-300) minutes, $P=0.005$) and smaller lesion size (median(IQR) 40(26-56.25) vs 60(40-90) mm, $P=0.004$) were significant factors for successful en bloc resection. However, lesser procedure time (median(IQR) 74(29.5-97.5) vs 150(82.5-240) minutes, $P=0.034$) led to an

increased delayed adverse event rate. Multivariate analysis using Cox regression showed en bloc resection (odds ratio 0.038; 95% confidence interval 0.003-0.421; $P=0.008$) was an independent factor preventing local recurrence.

Factors	Variables		P value
En bloc resection rate	<u>En bloc resection</u> (n=297)	<u>Piecemeal resection</u> (n=12)	
	Procedure Time (median (IQR) minutes)	145 (80 – 236.25) 270 (180 – 300)	0.005
	Lesion Size (median (IQR) mm)	40 (26 – 56.25) 60 (40 – 90)	0.004
Recurrence rate	<u>Recurrence</u> (n=6)	<u>No recurrence</u> (n=257)	
	En Bloc resection n (%)	4 (66.7) 246 (98)	0.009
Adverse events	<u>Delayed adverse events</u> (n=5)	<u>No delayed adverse events</u> (n=304)	
	Procedure Time (median (IQR) minutes)	74 (29.5 – 97.5) 150 (82.5 – 240)	0.034

Conclusion: This international, multicenter study with data from three countries shows favorable outcomes for colorectal ESD for large lesions. The high en bloc and R0 resection rate, and low adverse event rate show increased global adaptation to this procedure. Reduced local recurrence is an added benefit. Data from a more centers globally will be valuable to establish ESD as the standard for large colorectal neoplasms.

References:

1. Sidhu M, Shahidi N, Gupta S et al. Outcomes of thermal ablation of the mucosal defect margin after endoscopic mucosal resection: a prospective, international, multicenter trial of 1000 large nonpedunculated colorectal polyps. *Gastroenterology*. 2021 Jul 1;161(1):163-70.
2. Gupta S, Lieberman D, Anderson JC et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. *Gastrointest Endosc* 2020;91:463-485.e5.
3. Rutter MD, Beintaris I, Valori R et al. World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer. *Gastroenterology* 2018;155:909-925.e3.
4. Ohata K, Kobayashi N, Sakai E et al. Long-term outcomes after endoscopic submucosal dissection for large colorectal epithelial neoplasms: a prospective, multicenter, cohort trial from Japan. *Gastroenterology*. 2022 Nov 1;163(5):1423-34.

Disclosure: Nothing to disclose.

PP0767

REAL-WORLD DATA ON PROGNOSIS AND RISK FACTORS FOR LYMPH NODE METASTASIS AND RECURRENCE IN T1 COLORECTAL CANCER TREATED WITH ENDOSCOPIC OR SURGICAL RESECTION: A MULTICENTER RETROSPECTIVE STUDY

H. Tanaka¹, S. Kuribayashi¹, M. Sekiguchi², A. Iwamoto³, Y. Hachisu⁴, Y. Fukai⁵, T. Nakayama⁶, K. Furuya⁷, T. Masuda⁸, K. Takahashi⁹, K. Marubashi¹⁰, Y. Takeuchi¹, T. Uraoka¹, Gunma GI Research Group

¹Gunma University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Maebashi Gunma, Japan, ²Isesaki Municipal Hospital, Internal medicine, Isesaki Gunma, Japan, ³Tomioka General Hospital, Department of Gastroenterology, Tomioka Gunma, Japan, ⁴Saiseikai Maebashi Hospital, Department of Gastroenterology, Maebashi Gunma, Japan, ⁵Maebashi Red Cross Hospital, Department of Gastroenterology, Maebashi Gunma, Japan, ⁶Toho Hospital, Department of Gastroenterology, Midori Gunma, Japan, ⁷National Hospital Organization Shibukawa Medical Center, Department of Gastroenterology, Shibukawa Gunma, Japan, ⁸National Hospital Organization Takasaki General Medical Center, Department of Gastroenterology, Takasaki Gunma, Japan, ⁹Haramachi Red Cross Hospital, Internal medicine, Agatsuma Gunma, Japan, ¹⁰Kusunoki Hospital, Department of Gastroenterology and Hepatology, Fujioka Gunma, Japan

Contact E-Mail Address: h-tanaka@gunma-u.ac.jp

Introduction: According to the European Society of Gastrointestinal Endoscopy (ESGE) guidelines, the curative criteria of endoscopic resection (ER) for T1 colorectal cancer (CRC) are well/moderately differentiated adenocarcinoma or papillary carcinoma, no lympho-vascular invasion, submucosal invasion depth <1000µm, and budding grade (BD) 1. Although an additional surgery is recommended for non-curative ER, the incidence of lymph node metastasis (LNM) is less than 12%. Many reports on lymph node metastasis and recurrence in T1 CRC originate from academic centers, with limited reports of real-world data.

Aims & Methods: The aim of this study was to clarify clinical outcomes in patients with T1 CRC. A total of 686 consecutive patients (Male:447 Female:239) were enrolled from April 2009 to August 2019 at 10 institutions. Exclusion criteria included evidence of familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, or inflammatory bowel disease; presence of active, malignant diseases in any other organs; presence of synchronous or metachronous advanced CRC. Risk factors of LNM and recurrence, and survival were analyzed.

Results: The mean age of patients was 69.3±10.2 years old. The mean tumor size was 20.3±12.4mm. The location of the lesion was 439(64%) and 247(36%) in the colon and rectum, respectively. The histopathological types included 681 cases of differentiated type and 5 cases of undifferentiated type. A number of patients with ER without additional SR (ER alone) were 176(curative resection 86, non-curative resection 90), those with SR (SR alone) were 510, and those with ER and additional SR (ER + additional SR) were 116.

(i) Risk factor of LNM: LNM was found in 13(11.2%) patients with ER + additional SR and in 40(10.6%) patients with SR alone. In multivariate analysis, positive lymphatic invasion and tumor size were significant independent risk factor for LNM (OR 5.9, 95% CI [2.2-16], $p<0.01$, OR 1.04, 95%CI [1.00-1.07] $p=0.028$, respectively).

(ii) Recurrence: During the mean observation period of 45.5±34.3 months, recurrence was found in 27(3.9%) patients. No recurrence was found in the ER curative resection group. Although 43% (90/206) patients with ER non-curative resection did not receive additional SR, there was no signif-

icant difference in recurrence rate between ER alone with non-curative resection and ER + additional SR groups (5.6% (5/90) vs. 2.6% (3/116), respectively; $p=0.3$). In the SR alone group, recurrence was found in 4.8% (19/394). The significant independent risk factor for recurrence was tumor size (OR 1.12, 95% CI [1.05-1.2], $p<0.01$).

(iii) Survival: There were 50 deaths (7.3%, 76.2±6.6 years old) during the observation period of 45.5±34.3 months, but CRC-related death was found in only 6 cases (0.8%); one case was ER alone with non-curative resection and the other cases were SR alone.

Conclusion: This study suggests that the possibility of expanding the indication for ER of T1 CRC, because positive lymphatic invasion and tumor size were the only risk factor for LNM and better long-term outcomes were shown despite including significant number of patients with ER alone with non-curative resection.

Fifty cases of death showed a higher average age and fewer deaths from CRC. Therefore, even in cases of non-curative resection for T1 CRC after ER, avoiding additional SR may be considered due to advanced age or comorbidities.

Disclosure: Nothing to disclose.

PP0768

FEASIBILITY, SAFETY, AND OUTCOMES OF LGI ENDOSCOPIC SUBMUCOSAL DISSECTION FROM UK ESD REGISTRY: A MULTICENTRE PROSPECTIVE STUDY ON WESTERN POPULATION

H. Htet¹, K. Siggins¹, S. Subramaniam¹, A. Haji², B. Hayee², N. Suzuki³, B.P. Saunders³, M. Banks⁴, J.E. East⁵, G. Longcroft-Wheaton¹, F. Thursby-Pelham¹, A.A. Alkandari¹, M. Baker-Moffatt¹, J. White⁶, A. Parra-Blanco⁶, P. Bhandari¹
¹Portsmouth Hospitals University NHS trust, Gastroenterology, Cosham, United Kingdom, ²King's College Hospital NHS Foundation Trust, London, United Kingdom, ³The National Bowel Hospital, London Northwest Healthcare NHS Foundation Trust, London, United Kingdom, ⁴University College London Hospitals NHS Foundation Trust, Endoscopy Unit, Gastrointestinal services, London, United Kingdom, ⁵Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, ⁶Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom

Contact E-Mail Address: heinmyat21@gmail.com

Introduction: The role of EMR in large colonic polyp is already well established whereas the practice and outcomes of ESD are variable depending on the volume and experience, especially in the west.

Aims & Methods: We aim to evaluate practice and outcome of colonic ESD and hence, a multicentre national registry was set up in the UK. This is a prospective observational study for patients undergoing ESD for early GI neoplasia. All technical and outcomes data was prospectively collected onto REDCap.

Results: There were 568 colorectal ESDs from 6 large tertiary referral centres in the UK. Mean age of the patients was 67.3 years (range 37 - 90 years) with male preponderance (341 males vs. 227 females). Majority were in the rectum: 300, 52.8% while 126 (22.2%) in the left colon and 142 (25%) were in the proximal colon. Polyp size ranges from 10 to 210 mm (mean 47 mm). 318 (56%) were flat polyp.

Of 568 ESDs, 128 (22.6%) were hybrid ESDs where more than 80% of submucosal dissection was completed by using a knife before using a snare for completion. Technical success was achieved in 97.7% (555 cases) with en-bloc rate of 83.1%. For Rectal ESDs, 12.0% were hybrid ESDs with overall en-bloc rate of 89.5% whereas, for right colonic ESDs, 38.7% of them were hybrid ESDs with en-bloc resection rate of 71.7%.

Overall, there were 22 (4%) intraprocedural perforation (7 proximal and 15 distal colon) and 7 (1.3%) intraprocedural bleeding (3 proximal and 4 distal colon) which were all managed endoscopically. There were 3 (0.5%) delayed perforation (2 in caecum and 1 in rectum) and out of which, 1 required surgery and 2 were managed conservatively. There were 15 (2.7%) delayed bleeding (6 proximal and 9 distal colon) and 4 of them required blood transfusion while others were managed conservatively/endoscopically. 5 were readmitted with post polypectomy syndrome. Overall, ESD related complication rate was 8.6% (12.0% in right colon and 6.6% in left colon) as shown in Table 1.

Complication rates	All location (%) n= 568	Right sided (%) n= 142	Left sided (%) n= 426
Delayed bleeding	15 (2.7)	6 (4.2)	9 (2.1)
Intraprocedural perforation	22 (3.9)	7 (4.9)	15 (3.5)
Delayed perforation	3 (0.5)	2 (1.4)	1 (0.2)
Post-polypectomy syndrome	5 (0.9)	2 (1.4)	3 (0.7)
Overall (%)	8.6%	12.0%	6.6%

Table 1. Complication rates of colonic ESD.

Post resection histology showed 508 adenomatous neoplasia, 18 sessile serrated lesions (SSLs) with dysplasia, 4 SSLs without dysplasia, 3 hyperplastic polyps, 6 neuroendocrine tumours and 1 squamous cell cancer and 1 melanoma.

Post resection ESD of these adenomatous lesions showed majority (263, 62.2%) was low grade dysplasia with lateral margin R0 rate of 73%. 130 (30.7%) were high grade dysplasia with R0 rate of 88.3%. There were 60 (14.2%) submucosally invasive cancers with deep margin R0 rate of 81.4%.

Conclusion: Our data demonstrates that colonic ESD is feasible and the majority of the lesions were in rectum where ESD has high en-bloc resection rate. It is safe with low complication rate but we observed higher complication rates in right colonic ESD compared to the left. Overall, lateral margin R0 rate of LGD is suboptimal which could be related to very close resection margin which needs improvement.

Disclosure: Professor Bhandari has received research grants or is the advisory board for Fujifilm, Boston, Olympus, Pentax, 3-D matrix, NEC (Japan), Medtronic.

PP0769

EXPLORING UNWARRANTED CLINICAL VARIATION IN THE MANAGEMENT OF EARLY RECTAL CANCER. FINDINGS FROM AN AUSTRALIAN HOSPITAL NETWORK

A. Whitfield^{1,2}, A. Sakiris^{1,2}, J. Gauci¹, C. Kerrison^{1,2}, S. Gupta^{1,2}, O. Cronin^{1,2}, T. O'Sullivan^{1,2}, V. Pernanathan^{1,2}, B. Lam¹, F.V. Mandarino¹, E. Lee^{1,2}, N. Burgess^{1,2}, M.J. Bourke^{1,2}
¹Westmead Hospital, Gastroenterology and Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia

Contact E-Mail Address: brian.lam@health.nsw.gov.au

Introduction: Radical resection in the rectum is associated with significant morbidity and poses a mortality risk, particularly in elderly or comorbid patients. Early or T1 rectal cancer is often curable and can be managed with local endoscopic resection techniques with reduced morbidity and negligible mortality. To establish a pathway for appropriate treatment of these early lesions through the multidisciplinary team (MDT), an early rectal cancer working party (ERCWP) was formed to evaluate management trends and outcomes within our hospital network. The ERCWP was multi-speciality comprising of gastroenterologists, colorectal surgeons and radiation oncologists.

Aims & Methods: A retrospective review was performed across four institutions that make up our network to identify all patients with a new diagnosis of localised (T1-T4,N0,M0) rectal or recto-sigmoid cancer between January 2015 and August 2023. Patients with confirmed adenocarcinoma staged as T1N0M0 or T2N0M0 were included in the analysis. Available electronic medical records from the time of index resection and all encounters for the following 12 months were reviewed. Patients were excluded if their treatment was completed at an outside institution. Patient outcomes were stratified by location of tumour (rectum / recto-sigmoid) and mode of resection (Endoscopic resection, Local surgical excision or Radical surgical resection). Major adverse events included any one of the following: ostomy, deep incisional site infection, abscess, wound dehiscence, pneumonia, sepsis, septic shock, acute renal failure, deep venous thrombosis, pulmonary embolus, stroke/cerebrovascular accident, myocardial infarction, ventilator >48 hours, still in hospital >30 days, cardiac arrest, reoperation, readmission and/or mortality.

Results: A total of 111 localized (T1/T2,N0) and 153 locally advanced (T3/T4,N0) lesions were newly diagnosed during the study period. 95/111 patients with localized disease were included (M=62/95, 65.3% F=33/95, 34.7%). Mean age was 67.8 years in the endoscopy group and 67.0 years in the radical surgical resection group. Mortality was 2.2% in the group of patients who had surgery (1/46). There was no mortality in patients who received endoscopic resection. Major adverse events were recorded in 16/46 (34.8%) of patients who underwent surgery. There were no major adverse events in patients who received endoscopic resection. Mean length of stay was 1.47 days in patients who had endoscopic resection and 10.2 days in patients who had radical resection. Mean length of stay was prolonged where there was a treatment related major adverse event (14.8 days, mean difference 9.8 days, $p < 0.001$). 78.5% (51/65) of the cohort with T1 cancer was low risk (well or moderately well differentiated and no lymphovascular invasion). Of the 16 patients with T1 rectal cancer who underwent definitive surgery, 15 (93.8%) were suitable for cure by en-bloc endoscopic excision. Following establishment of the ERCWP in 2020, there have been no cases of radical resection in the rectum for T1 cancer. For T1 cancer in the rectum, major adverse events were 5/34 (14.7%) pre ERCWP formation and 1/13 (7.7%) post ERCWP formation ($p < 0.001$).

Conclusion: Surgery carries a high risk of morbidity in patients with rectal cancer. Endoscopic resection carries a favourable risk profile and is currently being underutilised. Formation of a local expert group focusing on outcomes in T1 cancer can reduce unwarranted variation and similar groups should be formed at local institutions to optimise patient outcomes.

Disclosure: Nothing to disclose.

PP0770

ENDOSCOPIC SURVEILLANCE OF COLORECTAL CANCER: THE ROLE OF INTENSIFIED ENDOSCOPIC CONTROL

Â. Domingues¹, R.A. Cardoso¹, R. Araújo¹, A.J. Taveira da Silva¹

¹ULS Viseu Dão Lafões, Gastroenterology, Viseu, Portugal

Contact E-Mail Address: angelapintodom95@hotmail.com

Introduction: Endoscopic surveillance after surgery for colorectal cancer (CRC) has the main objectives of early identification of metachronous lesions and neoplastic recurrence. This study aimed to evaluate the possible benefit of intensified endoscopic surveillance compared to standard recommendations.

Aims & Methods: In this retrospective cohort study, all patients who underwent follow-up colonoscopy after CRC surgery over a period of 6 months were included. Patients with endoscopically treated CRC and patients with postoperative complications were excluded. The recommend-

ed follow-up period was considered the 1st year, the 4th year, and the 9th year after surgery and a time period of +/- 6 months to the recommended date was considered. Statistical analysis: Chi-square test; t-student test; Mann-Whitney test.

Results: 102 patients (38 women) were included, aged 72±11 years. Patients were divided into two groups, those who followed the recommended protocol (55.9%; n=57) and those who underwent intensified surveillance (44.1%; n=45). No statistically significant differences were identified between the two groups regarding demographics, location of the neoplasm or type of surgery performed. There was only a higher adenoma detection in the intensive surveillance subgroup in the 1st year after surgery ($p=0.042$), with no differences in the remaining endoscopic controls. None of the advanced adenomas identified in this group required earlier endoscopic surveillance. No advanced adenomas were identified in additional colonoscopies carried out outside the recommended period. The adenoma detection rate didn't show statistically significant differences between the two groups. An excess of 156 colonoscopies were performed over a total of 361 years of follow-up.

Conclusion: Intensified endoscopic surveillance after CRC surgery does not appear to confer benefit and is a significant burden to endoscopy units, in addition to unnecessary risks and discomfort for patients. Adherence to international recommendations should be promoted among referring physicians and a strict colonoscopy vetting process should be enforced.

Disclosure: Nothing to disclose.

PP0771

THE INFLUENCE OF ANTHOCYANINS BLACK RICE BRAN EXTRACT (ABRIBE) ON MRNA EXPRESSION OF THE ABCA1 GENE AND COLORECTAL CANCER CELL PROLIFERATION IN THE HUMAN HT-29 COLORECTAL CANCER CELL LINE

W. Iswanti¹, K. Rahmadia Ekawidyan^{1,2}, - Asmarinah^{3,4},

S. Budijanto⁵, M. Abdullah^{1,6,7,8}

¹Universitas Indonesia, Faculty of Medicine, Department of Nutrition, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, ²IPB University, Faculty of Human Ecology, Department of Community Nutrition, Bogor, Indonesia, ³Universitas Indonesia, Faculty of Medicine, Department of Medical Biology, Jakarta, Indonesia, ⁴Universitas Indonesia, Faculty of Medicine, Integrated Laboratory, Molecular Biology Unit, Jakarta, Indonesia, ⁵IPB University, Faculty of Agricultural Technology, Department of Food Science and Technology, Bogor, Indonesia, ⁶Universitas Indonesia, Faculty of Medicine, Indonesian Medical Education and Research Institute (IMERI), Human Nutrition Research Center (HNRC), Jakarta, Indonesia, ⁷Universitas Indonesia, Faculty of Medicine, Indonesian Medical Education and Research Institute (IMERI), Human Cancer Research Center (HCRC), Jakarta, Indonesia, ⁸Universitas Indonesia, Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterology, Pancreatobiliary and Gastrointestinal Endoscopy, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Contact E-Mail Address: dr.wizaiswanti@gmail.com

Introduction: Anthocyanins decrease the proliferation of colorectal cancer cell and cholesterol regulation via the adenosine triphosphate-binding cassette subfamily A member 1 (ABCA1) protein, which is underexpressed in colon cancer.^{1,2,3} Anthocyanins, which are found in Indonesian native black rice bran, can also promote the outflow of cholesterol from cancer cell.

Aims & Methods: This study aims to explore the influence of Anthocyanins Black Rice Bran Extract (ABRIBE) on mRNA expression of the ABCA1 gene

and colorectal cancer cell proliferation in the human colorectal cancer cell line, HT-29. ABRiBE is thought to suppress the proliferation of HT-29 cell while increasing the expression of the ABCA1 gene. Anthocyanins derived from black rice bran powder using ethanol acidified with citric acid were applied in this experimental work on HT-29 cells. The MTS assay used 12 extract concentrations and control groups to determine the inhibitory concentration (IC₅₀) of 50% cell growth inhibition for 24 and 48 hours. The quantitative Polymerase Chain Reaction (qPCR) method was used to examine the expression of the ABCA1 gene in groups higher than the IC₅₀ value and a control group.

Results: The proliferation of HT-29 cells was lowered by ABRiBE, which had an IC₅₀ of 1.57 and 1.35 mg/mL for incubation of 24 and 48 hours with values of $r=0.97$, $p=0.001$ and $r=0.95$, $p=0.001$, respectively. The expression of the ABCA1 gene was enhanced by 1.16 and 2.32 fold when extract supplementing with 2 doses beyond the IC₅₀ values of 1.7 and 2.0 mg/mL and a control group.

Gene Name	mRNA Relative Expression (fold)	Primary Sequence		Amplicon Size (base pair/ bp)
		Forward	Reverse	
Human HRPT1	1 fold	CCAGTACCAAGACCAGTTTCTC	GGTGGTAGCTGCAGGAATTAT	93 bp
Human ABCA1				
1.7 mg/ mL	1.16 fold	GGTGGTGTTCCTCATTACT	CCGCCTCACATCTTCATCTT	112 bp
2.0 mg/ mL	2.32 fold			

Table 1. The mRNA relative expression of the ABCA1 and HRPT1 (reference) genes as well as their primer pair sequence and amplicon sizes

Conclusion: The ABRiBE decreased the proliferation of the HT-29 cells while increasing the expression of the ABCA1 gene.

References: 1. Mazewski C, Liang K and Gonzalez de Mejia E. 2018. Comparison of the effect of chemical composition of anthocyanin rich plant extracts on colon cancer cell proliferation and their potential mechanism of action using in vitro, in silico, and biochemical assays. Food Chem., 242:378-388. doi:10.1016/j.foodchem.2017.09.086
2. Smith B and Land H. 2012. Anticancer activity of the cholesterol exporter ABCA1 gene. Cell Rep., 2(3):580-590. doi:10.1016/j.celrep.2012.08.011
3. Zhao X, Feng P, He W, Du X, Chen C, Suo L, Liang M, Zhang N, Na A and Zhang Y. 2019. The prevention and inhibition effect of anthocyanins on colorectal cancer. Curr Pharm Des., 25(46):4919-4927. doi:10.2174/1381612825666191212105145

Disclosure: The authors declare no conflict of interest.

PP0772

PLATELETS TO LYMPHOCYTES RATIO: A PROGNOSTIC INFLAMMATION-BASED FACTOR IN COLORECTAL CANCER

W. Khemiri¹, M. Ayari¹, A. Chehaider¹, M.H. Douggu¹, M.T. Jomni¹
¹FSI Hospital, Gastroenterology, La Marsa, Tunisia

Contact E-Mail Address: Khemiri.wafa00@gmail.com

Introduction: Colorectal cancer remains a significant public health concern, with its incidence steadily rising worldwide. Despite notable strides in treatment modalities, predicting disease progression and tailoring therapeutic approaches remains a challenge. In this context, identifying reliable and simple prognostic factors is crucial for optimizing disease outcomes.

Aims & Methods: The aim of this study was to investigate the predictive and prognostic value of platelet-to-lymphocyte ratio (PLR). We conducted a retrospective and descriptive study including patients diagnosed with

primary colon or rectal cancer, over an 8-year period [January 2014-June 2022]. Patient demographics, inflammatory markers, tumor characteristics, treatment and follow-up data were collected. Baseline PLR was calculated for each patient. Data were entered and analyzed by SPSS software version 26.

Results: Eighty-four patients were included, with a mean age at disease diagnosis of 60 ± 12 years and a sex ratio M/F=1.89. The median level of PLR was 169.80 [123.1-269.06]. Smoker patient have significantly higher PLR ($p=0.01$) as well as for patients with older age at diagnosis (Pearson $p=0.001$, $r=0.35$).

No significant association was noted of PLR neither with family history of colorectal cancer ($p=0.47$), nor gender ($p=0.69$), nor tumor localization ($p=0.15$). For biological data, anemia and hypoalbuminemia were significantly associated with a higher level of PLR ($p=0.01$ and $p=0.001$ respectively). Regarding treatment, neither primary surgery, nor adjuvant chemotherapy were associated with PLR ($p=0.36$ and $p=0.97$ respectively).

However, increased PLR was significantly associated with overall survival ($p=0.001$). Area under the receiver operating characteristic curve analysis showed that higher PLR was predictive of a shorter progression-free survival (AUROC = 0.706). The optimal cutoff value was 163.12 (sensitivity, 80%; specificity, 59%).

A total of 48 (57%) patients had a PLR above this threshold. These patients presented more frequently with bowel obstruction (23% vs 6%, $p=0.03$). They also had a higher carcinoembryonic antigen rates ($p=0.007$). Advanced TNM stage 3 or 4 was more common in patients with PLR above this threshold and thus, neoadjuvant chemotherapy was more indicated in this group (29% vs 11%; $p=0.04$). Overall, disease recurrence was similar for PLR above and below 163.12 ($p=0.12$).

Conclusion: Our study demonstrated that PLR has a good predictive value of progression-free survival connected with clinicopathological parameters in patients with colorectal cancer. It is a valuable tool for a simple prognostic assessment during colorectal cancer, contributing to a more personalized treatment decisions.

Disclosure: Nothing to disclose.

PP0773

WITHDRAWN

PP0774

EVALUATION OF THE EFFECTIVENESS OF INCREASED RADIATION DOSE IN NEOADJUVANT THERAPY FOR POTENTIALLY RESECTABLE RECTAL CANCER

I. Malta Carvalho¹, T. Gago¹, S. Barros¹, L. Relvas¹, M. Portugal¹, P. Caldeira¹, B. Peixe¹

¹Unidade Local de Saúde do Algarve - Hospital de Faro, Gastroenterology, Faro, Portugal

Contact E-Mail Address: isamalta_c16@hotmail.com

Introduction: Radiation therapy as part of neoadjuvant treatment for rectal cancer aims to improve local disease control with increased response rates and the possibility of sphincter preservation. The addition of the “watch and wait” (W&W) strategy has increased the efficacy and safety associated with neoadjuvant radiotherapy.

Despite the use of low doses (between 40-50.4 Gy), most studies report complete pathological response rates of 10-27%. However, there is still a lack of studies with higher doses to evaluate effectiveness in terms of clinical and pathological response, versus the toxicity associated with increased radiation dose.

Aims & Methods: The aim was to evaluate the efficacy and tolerance of neoadjuvant therapy for potentially resectable rectal cancer with higher radiation doses.

A retrospective observational preliminary study included 41 individuals with potentially resectable rectal cancer (T2-T4, N0-1, M0), treated with capecitabine (825mg/m² every 12 hours, 5 days a week) and 25 sessions of 54 Gy + 50 Gy to pelvic lymph nodes, considering patients on W&W. Partial response was defined as downstaging of at least 1 level in T and/or N. Complete clinical response was defined as reevaluation by MRI, endoscopy with biopsies, and digital rectal examination without evidence of residual disease. Short- and long-term complications of increased radiation dose were also evaluated.

Results: Out of 41 individuals with potentially resectable disease observed during the study, downstaging was observed in 78% (n=32), with 29% (n=12) showing complete response (clinical and/or pathological). Of the patients with complete clinical response (n=12), 8 underwent total mesorectal excision due to unpassable stenosis affecting adequate visualization of the rectal mucosa (n=1), presence of rectal ulcer with negative biopsies (n=6), and concurrent ulcerative colitis (n=1). All these patients showed complete pathological response. Four patients entered the W&W protocol, 3 of them with residual ulcer and negative biopsies, without recurrence at present (4 years follow-up). Radiation therapy complications were observed in 7% (n=3) of patients, respectively due to rectal stenosis, radiation proctitis, and radiation cystitis.

Conclusion: Our study found higher rates of downstaging and complete response compared to most studies under similar conditions and with lower radiotherapy doses, with a relatively low frequency of adverse effects.

References:

Anter, A., Eladawei, G., & Mosbah, M. (2013). Preoperative capecitabine and pelvic radiation in locally advanced rectal cancer: preliminary results (Mansoura experience). *Translational Gastrointestinal Cancer*, 2(3), 112-117.

Korkolis, D. P., Boskos, C. S., Plataniotis, G. D., Gontikakis, E., Karaitianos, I. J., Avgerinos, K., Katopodi, A., Xinopoulos, D., Dimitroulopoulos, D., Beroukas, K., & Vassilopoulos, P. P. (2007). Pre-operative chemoradiotherapy with oral capecitabine in locally advanced, resectable rectal cancer. *Anti-cancer research*, 27(1B), 541-545.

A. De Paoli, et al. (2006). Capecitabine in combination with preoperative radiation therapy in locally advanced, resectable, rectal cancer: a multicentric phase II study, *Annals of Oncology*, Volume 17, Issue 2, Pages 246-251,

Disclosure: Nothing to disclose.

PP0775

BLUEBERRY INGESTION IMPROVES GASTROINTESTINAL SYMPTOMS AND QUALITY LIFE AND MODULATES PROTECTIVE TIGHT JUNCTION PROTEINS IN PATIENTS WITH DISORDERS OF GUT-BRAIN INTERACTION

C.H. Wilder-Smith¹, A. Materna¹, A. Handberg^{2,3}, S.S. Olesen^{3,4}

¹Brain-Gut Research Group, Gastroenterology Group Practice, Bern, Switzerland, ²Aalborg University, Department of Clinical Biochemistry, Aalborg, Denmark, ³Aalborg University Hospital, Department of Clinical Medicine, Aalborg, Denmark, ⁴Aalborg University Hospital, Department of Gastroenterology, Aalborg, Denmark

Contact E-Mail Address: info@ggpp.ch

Introduction: Changes in intestinal microbiota, stress and inflammation are factors known to be relevant in the pathogenesis of pain and further symptoms in disorders of gut-brain interaction (DGBI), previously designated as functional gastrointestinal disorders (1). The same factors are also implicated in modulating cellular tight junction integrity and thereby also blood-brain and intestinal barrier permeabilities (1,2). Dietary nutrients, especially polyphenols in fruit and vegetables, can beneficially affect cellular tight junction integrity, modulate the gut microbiome and reduce pro-inflammatory effects (3).

Aims & Methods: The effects of blueberries on, 1. GI symptoms (Gastrointestinal Clinical Rating Scale: GSRS), life functioning and quality of life (Outcome Questionnaire OQ45.2), 2. circulating tight junction proteins especially relevant for the integrity of the intestinal and blood-brain barriers and, 3. stool consistency (Bristol stool scale: BSS) were prospectively examined in DGBI. Successive patients with irritable bowel syndrome or functional dyspepsia (Rome 4) received freeze-dried blueberries (equivalent to 180g of fresh blueberries) or sugar and energy-matched placebo for 6 weeks in a double-blind, randomized, cross-over study, with a washout period of 2 to 4 weeks between treatments. Serum concentrations of claudin-3, claudin-5 and zonula occludens-1 (ZO-1) were measured by ELISA and the GSRS, OQ45.2 and BSS scores were collected at baseline and after 6 weeks. The changes in protein concentrations and in GSRS, OQ45.2 and BSS scores from baseline were correlated.

	Blueberry			Placebo		
	Baseline	Week 6	Change (95%CI)	Baseline	Week 6	Change (95%CI)
Questionnaires						
Mean GSRS ± SD	37.7 ± 13.4	33.0 ± 12.9	-4.7 (-8.4 to 1.0) *	38.2 ± 11.3	36.6 ± 12.6	-1.7 (-5.2 to 1.9)
Median BSS (IQR)	3.5 (1.5)	3.5 (1.5)	0 (0 to 1.0)	4.0 (1.5)	4.0 (2.0)	0 (-0.7 to 0.5)
Median OQ-45.2 (IQR)	62.0 (15.0)	61.0 (17)	-3.0 (-5.0 to 0) **	63.0 (21)	66.0 (16)	0 (-3.0 to 3.0)
Serum tight junction protein concentrations						
Median claudin-3 (pg/ml) (IQR)	76.3 (16.3)	77.2 (17.4)	2.1 (1.0 to 4.3) ***	74.5 (16.4)	72.1 (18)	0 (-1.5 to 1.2)
Median claudin-5 (pg/ml) (IQR)	38.5 (15.7)	40.3 (14.9)	1.2 (-1.1 to 4.3)	39.8 (20.2)	40.3 (15.8)	0.1 (-1.6 to 2.1)
Median ZO-1 (pg/ml) (IQR)	81.3 (25.2)	81.3 (12.5)	-1.1 (-3.9 to 1.0)	81.4 (21.3)	80.0 (14.1)	-1.7 (-6.6 to 1.5)

Table. Outcome measures at baseline and after 6 weeks of treatment with blueberry or placebo. Within-group differences (baseline vs. week 6):

*p=0.0129, **p=0.0143,***p=0.00340*

Results: In 43 patients (37 females, mean age±SD 31±12yr) blueberry treatment for 6 weeks increased claudin-3 serum concentrations and improved GSRS and OQ45.2 scores significantly (see Table). Increased serum claudin-5 concentrations correlated with improved GSRS and OQ45.2 scores (Spearman's $r = -0.38$, $p=0.016$; $r = -0.36$, $p=0.024$, resp.), while increased ZO-1 levels correlated with improved OQ45.2 scores ($r = -0.32$,

p=0.046). There were neither significant serum concentration increases in tight junction proteins, changes in clinical outcomes nor correlations between these outcomes during placebo treatment. The median BSS was not significantly changed during either treatment, although constipation was relieved more frequently by blueberries.

Conclusion: Blueberries given for 6 weeks decreased symptoms and improved measures of quality of life and life functioning scores in patients with DGBI. Concomitantly, increased serum concentrations of claudin-3, a tight junction protein important in the regulation of intestinal and other barrier tight junction integrity, were observed. Increases in circulating tight junction protein levels relevant in tightening blood-brain (claudin-5) and other (ZO-1) barrier tight junctions correlated with the improvement in symptoms.*This study was supported by a grant from the US Highbush Blueberry Council.*

References:

1. Martin CR, Osadchiy V, Kalani A, Mayer EA. *Cell Mol Gastroenterol Hepatol.* 2018;6:133-148. (2) Hanning N, Edwinson AL, Ceuleers H, et al. *Therap Adv Gastroenterol.* 2021;14:1756284821993586. (3) Suzuki T. *Anim Sci J.* 2020;91:e13357

Disclosure: Nothing to disclose.

PP0776

THE INADEQUACY OF MALABSORPTION AS A PREDICTOR OF CARBOHYDRATE INDUCED SYMPTOMS: EXPLORING SYMPTOM BURDEN AFTER LACTOSE CONSUMPTION

J. Hammer¹, H.F. Hammer²

¹Medical University of Vienna, Vienna, Austria, ²Medical University of Graz, Dept. Of Internal Medicine, Divison of Gastroenterology and Hepatology, Graz, Austria

Contact E-Mail Address: johann.hammer@meduniwien.ac.at

Introduction: A substantial portion of individuals diagnosed with lactose malabsorption fail to experience significant relief from a lactose-free dietary regimen (1).

The ‘adult Carbohydrate Perception Questionnaire’ (aCPQ) is a simple, test-specific questionnaire for the assessment of gastrointestinal symptoms following a carbohydrate challenge (2). The aCPQ has undergone rigorous validation, it has excellent psychometric properties, and its use has been recommended to replace missing or unvalidated symptom assessments in carbohydrate breath testing (3).

Aims & Methods: Our aim was to assess symptom burden after lactose ingestion by means of the aCPQ with respect to the presence or absence of malabsorption. 753 patients with functional gastrointestinal disorders received a lactose (50 g) intolerance/H₂-breath test (180 min duration), utilizing the aCPQ for test specific, validated symptom assessment and an electrochemical hydrogen detector for quantification of end-expiratory breath hydrogen. Malabsorption (M+) was defined as an increase in end-expiratory H₂ by >20 ppm over baseline (as opposed to M-). The presence of relevant symptoms after lactose ingestion (S+) was defined as an increase of symptom scores by >20 cm in one of the five VAS scales over baseline (as opposed to S-). The maximal rise of symptom severity over baseline was determined (maximal possible rise: 100 for each symptom) and considered the individual symptom burden; the sum of individual symptom burdens was considered the total symptom burden (maximum possible sum of 500).

Results: 308 patients tested M+, 445 M-, and 417 tested S+ vs. 336 S-. 80 patients (26.0%) testing M+ had no clinically relevant symptoms (S-) following the lactose challenge; in contrast, 189 patients (45.3%) testing M- had relevant symptoms after the lactose challenge. Table 1 shows the individual and total symptom burden based on the diagnosis of lactose

intolerance/H₂ breath test: patients with malabsorption who had no clinically relevant lactose-induced symptoms (S-/M+) reported slightly higher intensities of flatulence and diarrhea as compared to S-/M-. Malabsorbers with symptoms had higher symptom burdens as compared to absorbers except for nausea, which was not statistically different between S+/M+ and S+/M-.

mm VAS:	S-/M-	S-/M+	P-value S-/M- vs. S-/M+	S+/M-	S+/M+	P-value S+/M- vs. S+/M+
Abdominal Pain	2.7	3.2	0.4	16.4	32.0	<0.001
Nausea	1.9	2.6	0.2	18.2	16.9	0.5
Bloating	2.8	3.5	0.7	19.9	32.0	<0.001
Flatulence	2.3	3.8	0.02	16.4	34.4	<0.001
Diarrhea	0.8	1.6	0.02	9.4	33.2	<0.001
Total Burden	10.5	14.7	0.02	80.3	148.5	<0.001

Table: Symptom burden after lactose ingestion

Conclusion: Malabsorption may be just one of the factors that lead to the onset of symptoms following lactose consumption. This is crucial regarding both the diagnosis and therapy of lactose intolerance. The aCPQ is the only reliable and valid, test specific instrument to evaluate symptoms triggered by the consumption of carbohydrates. It can be used in conjunction with a breath test, which is necessary if lactose malabsorption is to be detected.

References:

1. Hammer J et al. Carbohydrate induced gastrointestinal symptoms: development and validation of a test-specific symptom questionnaire for an adult population, the adult Carbohydrate Perception Questionnaire aCPQ. *Eur J Gastroenterol Hepatol* 2021;32:171-177
2. Hammer HF et al. European Guideline on indications, performance and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: EAGEN, ESNM and ESPGHAN consensus. *United European Gastroenterol J* 2022;10:15-40
3. Levitt M et al, Clinical implication of lactose malabsorption versus lactose intolerance. *J Clin Gastroenterol* 2013;47:471-480

Disclosure: Nothing to disclose.

PP0777

SYSTEMIC ADVANCED GLYCATION END-PRODUCTS ARE LOWER IN FRUCTOSE INTOLERANT PATIENTS WITH DISORDERS OF GUT-BRAIN INTERACTION (DGBI)

C.H. Wilder-Smith¹, A. Materna¹, S.S. Olesen^{2,3}

¹Brain-Gut Research Group, Gastroenterology Group Practice, Bern, Switzerland, ²Aalborg University Hospital, Department of Gastroenterology, Aalborg, Denmark, ³Aalborg University Hospital, Department of Clinical Medicine, Aalborg, Denmark

Contact E-Mail Address: info@gggp.ch

Introduction: Fructose and fructans/fructooligosaccharides are implicated in the production of advanced glycation end products (AGE), which cause potent oxidative stress and inflammatory responses related to ageing, inflammatory and degenerative diseases (1-3).

It has recently been shown that fructose intolerance is unrelated to fructose malabsorption and more probably to differences in fructose metabolism by the intestinal microbiome (4).

Individual species of the intestinal microbiota can differentially either produce or metabolise AGEs, as well as ferment fructose and fructans (2). DGBI are characterised by a high prevalence of fructose and fructan intolerance, pro-inflammatory markers and changes in gut microbiota (5). The relationships between fructose intolerance, the intestinal microbiome and AGEs are unclear.

Aims & Methods: We examined the association between skin AGEs by autofluorescence (SAGE) as a validated, reproducible and non-invasive marker of metabolically long-acting AGEs (6), exhaled breath hydrogen and symptoms following fructose provocation during breath tests in 1188 patients with DGBI (Rome 4 criteria, 30% male, mean age 40.9 years, mean body mass index 23.6 kg/m²) referred to our Gastroenterology practice. A standardised breath test with fructose 35g was performed after a 24-hour low-FODMAP diet and >8-hour fast. Exhaled hydrogen concentrations and gastrointestinal symptoms (composite symptom index score, 7) were collected every 30 minutes for 5 hours. SAGE was performed with the AGE Reader® (Diagnoptics Technologies B.V., Groningen, NL) before the breath test. Lower SAGE values reflect a lower systemic pro-inflammatory AGE load.

Results: Overall, the SAGE values and hydrogen breath concentrations correlated inversely (Rho= -0.09, p=0.0022, Spearman's rank test). Extensive fructose fermenters, defined by an increase in breath gas concentrations above baseline of >20ppm of hydrogen after fructose ingestion, showed lower SAGE values than poor metabolisers (1.85±0.56 vs. 1.92±0.55; p=0.0221).

Furthermore, patients with an increased symptom index following fructose and thereby classified as fructose intolerant (7), had significantly lower SAGE scores than fructose tolerant patients (1.84±0.55 vs. 1.96±0.57; p=0.0004).

Conclusion: Patients with DGBI and pronounced symptoms and gas production during fructose breath tests appear to have lower systemic AGEs. Metabolism by the intestinal microbiota plays an important role in both fructose intolerance and in modulating the levels of long-acting AGEs. This association may be of crucial relevance in gastrointestinal and extra-gastrointestinal dysfunction in DGBI and requires further investigation. Potential confounders, such as dietary factors, require careful consideration.

References: 1. Kamphuis JBJ et al. *Gastroenterology*. 2020;158:652-663

2. Gugliucci A. *Adv Nutr*. 2017;8:54-62

3. Kamphuis JBJ et al. *FASEB J*. 2022;36:e22297.

4. Wilder-Smith C et al. *Neurogastroenterol Motil*. 2021;33:e14150

5. Spiller R. *F1000Res*. 2016;5:F1000

6. Almengló C et al. *Methods*. 2022;203:103-107

7. Wilder-Smith CH et al. *Aliment Pharmacol Ther*. 2013;37:1074-1083

Disclosure: Nothing to disclose.

We have previously shown that high GABA-producer *L. lactis* CNCM I-5388 exerts antinociceptive properties after 5- and 10-days oral treatment in an IBS-like rat model. We demonstrated, using both mutant *L. lactis* Δ gadB strains and GABA_A receptor antagonist that these antinociceptive properties were dependent on the GAD-enzymatic activity of *L. lactis* and mediated by host's GABA_A receptors. In addition, we have shown that CNCM I-5388 displayed a high cell-bound GAD activity and survival *in vitro* under HCl-mediated acidic stress.

Aims & Methods: In this work, we were interested in studying the GABA-producer *L. lactis* CNCM I-5388 as an active-enzyme postbiotic to relieve visceral hypersensitivity mediated by a psychological stress.

L. lactis CNCM I-5388 was inactivated by ethanol (EtOH) while maintaining its GAD activity. Female Wistar rats were treated orally for 1, 5 or 10 days by the EtOH-treated nonviable *L. lactis* CNCM I-5388 form or the viable *L. lactis* CNCM I-5388 or vehicle. Visceral sensitivity in response to colorectal distension was measured by electromyography before and after partial restraint stress (PRS). GABA levels were quantified by HPLC both in the stomach collected from rats and in the gastric compartment of the TIM-1 human gut model in fed state.

Results: A daily treatment for 5 and 10 days by *L. lactis* CNCM I-5388 both in its viable and nonviable forms counteracted visceral hypersensitivity-induced by PRS in response to colorectal distension. However, after a single administration only viable *L. lactis* CNCM I-5388 tended to reduce visceral hypersensitivity. After 5-days treatment, the production of GABA within the stomach was enhanced in stressed rats treated with the viable or nonviable *L. lactis* CNCM I-5388 form. This increase was confirmed by using the TIM-1 human gut model.

Conclusion: Our results highlight that a postbiotic with an active-GAD of *L. lactis* CNCM I-5388, similarly to its viable psychobiotic form, exerts visceral antinociceptive properties in an IBS-like rat model. These effects are associated with GABA production in the stomach where the low pH promotes GAD activity. From a clinical point of view, this "active GAD-bag" concept offers a new therapeutic perspective in the management of visceral pain in IBS patients with a superior safety profile compared with GABA-producing psychobiotics that could acquire antibiotic resistance and virulence factors in chronic use.

Disclosure: Jonna Koper, Elyse Parent, Nabil Bosco, Nathalie Ballet and Sophie Legrain-Raspaud are full-time employees of Lesaffre. None of the authors have a conflict of interest.

PP0778

LACTOCOCCUS LACTIS CNCM I-5388 AS A GLUTAMATE DECARBOXYLASE (GAD)-ENZYME POSTBIOTIC ALLEVIATES VISCERAL PAIN IN RATS THROUGH GABA PRODUCTION.

P. Gomes^{1,2}, C. Beaufrand¹, V. Laroute², V. Bezirard¹, C. Liebgott¹, J.E. Koper³, E. Parent³, N. Bosco³, N. Ballet³, S. Legrain-Raspaud³, M.-L. Daveran-Mingot², V. Theodorou¹, M. Coccagn-Bousquet^{1,2}, M. Mercier-Bonin¹, H. Eutamene¹

¹UMR 1331, Toxalim INRAE, Université de Toulouse, ENVT, INP-PURPAN, UPS, Toulouse, France, ²Toulouse Biotechnology Institute (TBI), Université de Toulouse, CNRS, INRAE, INSA, Toulouse, France, ³Lesaffre Institute of Science and Technology, Lesaffre International, Marcq-en-Barœul, France

Contact E-Mail Address: helene.eutamene@inrae.fr

Introduction: Irritable Bowel Syndrome (IBS) is a chronic disorder of the gut-brain interaction characterized by visceral hypersensitivity. There is growing evidence underscoring the beneficial impact of probiotics and postbiotics with psychobiotics properties in relieving stress-related gastrointestinal disorders in humans especially in patients suffering from IBS.

PP0779

THE GUT VASCULAR BARRIER IS INVOLVED IN SYMPTOM DEVELOPMENT IN IRRITABLE BOWEL SYNDROME

M.R. Barbaro¹, C. Cremon², G. Marasco³, S. Guglielmetti⁴, A. Di Sabatino⁵, S. Valente³, G. Pasquinelli³, N. Vergnolle⁶, V. Stanghellini⁷, S. Collins⁸, G. Barbara⁷

¹IRCCS AOUBO, Bologna, Italy, ²Internal Medicine and Digestive Pathophysiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy, University of Bologna, Bologna, Italy, ³University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁴Dipartimento di Biotecnologie e Bioscienze, Università degli Studi di Milano Bicocca, Milano, Italy, ⁵IRCCS Policlinico S. Matteo, Pavia, Italy, ⁶INSERM UMR-1220, Digestive Health Research Institute (IRSD), Toulouse, France, ⁷University of Bologna, Bologna, Italy, ⁸Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, ON, Canada, Hamilton, Canada

Contact E-Mail Address: maria.barbaro2@unibo.it

Introduction: Irritable bowel syndrome (IBS) is a multifactorial disorder characterized by recurrent abdominal pain associated with defecation or a change in bowel habits. The pathophysiology of IBS involves alterations in the epithelial barrier, but data on the intestinal vascular barrier are lacking.

Aims & Methods: The aims of this study were to investigate the morpho-functional integrity of the vascular barrier and to correlate barrier dysfunction with IBS symptoms. Forty-eight healthy subjects (AC) and 144 patients with IBS (61 IBS-D, 51 IBS-C and 32 IBS-M) were enrolled in the study. Rome IV criteria, Bowel disease questionnaire, Short Form 12, Hospital Anxiety Depression Scale were used to phenotype patients. Immunohistochemistry, western blot and electron microscopy were used to characterize the vascular barrier. Vascular permeability was evaluated by assessing two markers: plasmalemma vesicle-associated protein-1 (PV1) and vascular endothelial cadherin (VEC). A translational model based on HUVEC was used to evaluate permeability changes induced by mediators spontaneously released by mucosal biopsies, and to highlight the underlying molecular mechanisms. Correlation analyses between experimental and clinical data were performed.

Results: Mucosal vessel density was significantly increased by 1.5 fold in the colonic mucosa of IBS patients compared to AC ($P<0.01$). PV1 expression was increased ($P<0.01$) while VEC expression was decreased in the colonic mucosa of IBS patients compared to AC ($P<0.05$). Compared to AC, IBS mucosal mediators increased permeability in the HUVEC monolayer through the activation of protease-activated receptor (PAR)-2 and histone deacetylase (HDAC)11, resulting in VEC downregulation. PV1 expression significantly correlated with anxiety and depression scores and health-related quality of life reported by IBS patients.

Conclusion: The vascular barrier is impaired in IBS and contributes to clinical manifestations

Disclosure: Nothing to disclose.

PP0780

EVALUATION OF FOOD INTOLERANCE AND FOOD AVOIDANCE IN IRRITABLE BOWEL SYNDROME PATIENTS

J.T.W. Snijkers¹, M. de Graaf¹, B. Winkens², F.A. Zijlstra¹, D. Keszthelyi¹, D.M. Jonkers¹

¹Maastricht University Medical Center, Gastroenterology-Hepatology, Maastricht, Netherlands, ²Maastricht University, Department of Methodology and Statistics, Maastricht, Netherlands

Contact E-Mail Address: daniel.keszthelyi@maastrichtuniversity.nl

Introduction: Many irritable bowel syndrome (IBS) patients report gastrointestinal (GI) symptoms due to various foods, resulting in food avoidance. However, a detailed description of trigger foods and related GI symptoms and avoidance behaviour is lacking. Therefore, we evaluated the extent and nature of food intolerance and avoidance in IBS patients, and its relation to GI symptoms and psychological comorbidities.

Aims & Methods: Food intolerance and avoidance behaviour were evaluated in 124 IBS patients and 113 healthy controls (HC) using a questionnaire with 257 food products of 13 food groups. Per product, participants were asked if they experience symptoms (*i.e.* nausea, constipation, diarrhoea, bloating, abdominal pain) after consumption, and if they consumed this product despite these symptoms. Furthermore, IBS symptom severity and psychological factors were assessed.

Results: IBS patients reported a higher number of food products with perceived intolerance than HC (median of 18.0 (25th-75th percentile 10.0-33.5) vs 1.0 (0.0-8.0), $p<0.001$). A wide variety of trigger foods was reported, with gas-producing foods and fatty/cream-based dairy products most frequently reported by both groups. Predominant symptoms were abdominal pain and bloating. The number of avoided foods was higher in IBS (15.0 (8.0-27.0) vs 1.0 (0.0-7.0), $p<0.001$). Food avoidance was not significantly related to symptom type, but was associated with an IBS diagnosis, female sex, and higher screening scores for somatisation and Avoidant/Restrictive Food Intake Disorder.

Conclusion: Self-reported food intolerance and avoidance is higher in IBS than HC, with a wide variety of trigger foods. Food avoidance was significantly related to psychological factors, but not to symptom type. This warrants individual dietary guidance, as well as attention for psychological factors.

Disclosure: D Keszthelyi: DK reports receiving research funding from Zon-Mw, MLDS, UEG, Rome Foundation, Horizon Europe, Horizon 2020, Grunenthal, Allergan and speaker's fee from Dr Falk (paid to host institute).

DMAE Jonkers: DMAEJ reports receiving a public-private partnership grant of TKI Well on Wheat? and TKI grants from Agri & Food and Health Holland, the Carbokinetics programme as part of the Netherlands Organisation for Scientific Research-Carbohydrate Competence Center partnership, Organic A2BV/Mothersfinest, and Horizon 2020.

PP0781

DEPRESSION, ANXIETY, AND VISCERAL SENSITIVITY IN PATIENTS WITH DIARRHEAL IRRITABLE BOWEL SYNDROME TREATED WITH MULTI-STRAIN PROBIOTICS: A RANDOMIZED STUDY

A. Neverovskyi¹, S. Polishchuk¹, V. Tishchenko¹, K. Linevska¹¹Bogomolets National Medical University, Kyiv, Internal Medicine №1, Kyiv, Ukraine**Contact E-Mail Address:** artemneverovskiy@gmail.com

Introduction: Irritable bowel syndrome (IBS) is considered a disorder of the altered microbiota-gut-brain axis, where gut dysbiosis and impaired central nervous system processing play important roles. The latter, in the form of depression, anxiety, and gastrointestinal-specific anxiety (GSA), frequently coexist and exacerbate IBS. Probiotics might be a promising therapeutic approach to treat IBS and coexisting depression, anxiety, and GSA.

Aims & Methods: The aim of the trial was to compare the impact of standard care combined with multi-strain probiotics with standard care alone on depression, anxiety, and visceral sensitivity in patients with diarrheal IBS (IBS-D). It was a 12-week randomized trial that included 108 patients with IBS-D that were divided into 2 groups: a control group (n = 51) receiving only standard care (diet, peppermint oil) and an experimental group (n = 57) receiving a combination of standard care (diet, peppermint oil) and the study probiotic (based on *Lactobacillus*, *Streptococcus*, *Bifidobacterium*, and *Saccharomyces boulardii* strains). Patient Health Questionnaire-9 (PHQ-9) and Beck's Depression Inventory (BDI) were used to assess depression; the Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression; and the Visceral Sensitivity Index (VSI) was used to assess GSA.

Results: Baseline data were not different between the study groups ($p > 0.05$). After 12 weeks of treatment, PHQ-9, BDI, and anxiety subscale of HADS were not different between the study groups ($p > 0.05$), while the central tendency of the depression subscale of HADS in the control group was higher (3 (2-4)) than in the experimental group (3 (2-3)), $p = 0.046$. VSI was higher in the control group (31±5) compared to the experimental group (29±5.7), $p = 0.032$, after 12 weeks of trial.

Conclusion: In patients with IBS, additional prescribing of a multi-strain probiotic led to a decrease in depression according to HADS, as well as a reduction in GSA and visceral sensitivity assessed by VSI compared to IBS standard care alone.

Disclosure: Nothing to disclose.

PP0782

GUT PERMEABILITY AND ITS ROLE IN PARKINSON'S DISEASE: PRELIMINARY RESULTS FROM A PILOT STUDY

F. Rettura¹, G. Bellini², C. Lambiase¹, N. Bernardini³, C. Pellegrini³, L. Benvenuti⁴, C. Di Salvo⁴, M. Fornai⁴, R. Ceravolo², M. Bellini¹

¹University of Pisa, Gastrointestinal Unit, Department of Translational Sciences and New Technologies in Medicine and Surgery, Pisa, Italy, ²University of Pisa, Neurology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy, ³University of Pisa, Unit of Histology and Embryology, Department of Clinical and Experimental Medicine, Pisa, Italy, ⁴University of Pisa, Unit of Pharmacology and Pharmacovigilance, Department of Clinical and Experimental Medicine, Pisa, Italy

Contact E-Mail Address: rettura.fra@gmail.com

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by both motor and non-motor symptoms, such as gastrointestinal symptoms. Emerging evidence suggests that gut permeability and inflammation play a role in PD pathophysiology via the gut-brain axis. According to Braak's theory, the pathological degeneration associated with PD may originate from the gut and subsequently develop in the brain through the vagus nerve.

Aims & Methods: The aims were to assess the relationship between gut permeability and neuroinflammation in a cohort of patients with PD and REM behavior disorder (RBD), a condition that often precedes the onset of PD. The study prospectively included 28 PD patients and 18 RBD patients both complaining of GI symptoms. No serious organic diseases or therapies potentially affecting GI motility were reported. Relevant demographic and clinical data were collected for all patients. There was the inclusion of 14 healthy controls (HCs). A serum ELISA assay of tumor necrosis factor (TNF), caspase-1, and lipopolysaccharide-binding protein (LBP) was performed in all participants to investigate systemic inflammatory status and gut permeability, respectively.

In a total of 10 PD patients, 4 RBD patients and 9 HCs, multiple colic biopsies were obtained to assay tissue expression of inflammation markers by both western blot (WB) (i.e. caspase-1 and procaspase-1) and immunofluorescence (IF) (i.e. ASC and CD68). Data were expressed as mean ± SD, and ANOVA and Dunnett's tests were used to compare the three groups.

Results: All three groups were comparable in age and sex. Serum assays showed significantly increased LBP, in patients with PD (35.0 ± 0.25 ; $p = 0.002$) and RBD (32.2 ± 1.1 ; $p = 0.009$) compared with HCs. TNF (0.1 ± 0.02 ; $p = 0.03$) and caspase-1 (16.9 ± 9.4 ; $p = 0.04$) were significantly raised only in the PD group in comparison with HCs (Table 1).

WB analysis showed significant differences in the expression of procaspase-1 (157.3 ± 17.8 ; $p = 0.02$) and caspase-1 (168.3 ± 23.3 ; $p = 0.03$) only in PD patients compared with HCs. IF showed a qualitative increase in both CD68+ macrophage infiltration and ASC expression in PD and RBD groups compared with HCs.

	PD	RBD	HCs	P-value
LBP (ng/ml)	35.0 ± 0.25	32.2 ± 1.1	23.1 ± 2.1	0.009 (RBD vs HCs) 0.002 (PD vs HCs)
Caspasi-1 (ng/ml)	16.9 ± 9.4	11.4 ± 2.1	9.9 ± 2.7	0.04 (PD vs HCs)
TNF (pg/ml)	0.1 ± 0.02	0.05 ± 0.02	0.04 ± 0.02	0.03 (PD vs HCs)

Table 1. Serum ELISA assay of TNF, caspase-1, and LBP from HCs and in patients with RBD and PD.

Abbreviations: TNF = tumor necrosis factor; LBP = lipopolysaccharide-binding protein; HCs = healthy controls; RBD = REM behavior disorder; PD = Parkinson's disease.

Conclusion: Our results show a bowel activation of NLRP3 inflammasome in PD, as demonstrated both by the levels of procaspase-1 and caspase-1 on WB analysis and by the increase of CD68+ macrophages and ASC in the lamina propria of colonic mucosa.

Only a qualitative increase in NLRP3 activation at IF could be observed in RBD patients. However, findings from colonic biopsies, if related to elevated serum levels of TNF and caspase-1 in PD patients, and LBP in PD and RBD patients, suggest that bowel inflammation, sustained by increased gut permeability, may represent an early stage in the develop of RBD and PD.

Disclosure: Nothing to disclose.

PP0783

REGULATOR OF G PROTEIN SIGNALING (RGS) 6 BLUNTS THE EFFECT OF CANNABINOIDS IN VITRO AND IN VIVO IN MOUSE MODELS OF INTESTINAL MOTILITY

M. Swierczynski¹, M. Jaczynska¹, Z. Kasprzak¹, A. Makaro¹, M. Salaga¹

¹Medical University of Lodz, Department of Biochemistry, Lodz, Poland

Contact E-Mail Address: macieks100@wp.pl

Introduction: RGS proteins promote silencing of the GPCR responses, e.g. cannabinoid (CB) receptors. In our previous work we showed that RGS6 is highly expressed in the gut and RGS6^{-/-} animals exhibit increased intestinal motility in physiological conditions¹.

Activation of CB receptors cause several well-recognized effects in the GI tract, including smooth muscle relaxation, reduced motility and analgesia. However, little is known about how the effect of those compounds is modulated by RGS6.

Aims & Methods: The aim of this study was to elucidate the function of RGS6 in physiology and pathophysiology of the GI tract. **METHODS:** We used intestinal Caco-2 cells (WT and RGS6^{-/-}) to measure the effect of CB agonist WIN 55,212-2 on the level of intracellular, second messenger cAMP and phosphorylation of extracellular signal-regulated kinase (ERK).

Then in the in vivo conditions we used an RGS6^{-/-} mice to evaluate the effect of this protein on intestinal motility (stress-induced hypermotility) in the course of DSS-induced inflammation in naïve mice as well in the presence of WIN 55,212-2.

Results: WIN 55,212-2 (1 µM) caused significant reduction of both basal and forskolin-stimulated intracellular cAMP in WT and RGS6^{-/-} Caco-2 cells. This effect was dose-dependent and was significantly stronger in the absence of RGS6. Phosphorylation of ERK was significantly increased in RGS^{-/-} Caco-2 cells as compared to WT and stimulation with WIN 55,212-2 (1 µM) diminished this effect in the dose-dependent manner. Previously we observed a significant increase in RGS6 expression in the mouse colon samples during intestinal inflammation¹.

However, we did not see any difference between anti-inflammatory effect of WIN 55,212-2 (1 mg/kg i.p.) in WT vs. RGS6^{-/-} animals in the model of DSS-induced colitis. On the other hand, we observed that in RGS6^{-/-} mice with colitis WIN 55,212-2 (1 mg/kg i.p.) alleviates stress-induced motility significantly stronger than in WT animals.

Conclusion: Serving as a central control point in GPCR signaling cascades, RGS proteins hold great promises as targets for the drug development. Here we present RGS6 protein as a novel candidate for drug targeting in the GI tract.

Our study suggests that loss and perhaps also pharmacological blockade of RGS6 might be used to increase the potency of cannabinoids in the gut.

References: 1. M Swierczynski et al. Regulator of g protein signaling (RGS) protein 6 blunts the effect of cannabinoids on intestinal motility and visceral pain sensation, UEG week 2024, PP1069. Copenhagen, Denmark DOI: 10.1002/ueg2.12461

Disclosure: Nothing to disclose.

PP0784

LOW LEVELS OF FECAL PRIMARY BILE ACIDS ARE ASSOCIATED WITH ALTERED MICROBIOTA AND COLONIC IMMUNE GENE EXPRESSION IN IRRITABLE BOWEL SYNDROME

W. Sjöland¹, T. van Gils², H. Törnblom^{1,2}, P. Patel², K. Sjöberg Jabbar^{1,2}, F. Bäckhed², V. Tremaroli², M. Simrén^{1,2,3}

¹Sahlgrenska University Hospital, Department of Gastroenterology and Hepatology, Gothenburg, Sweden,

²University of Gothenburg, Institute of Medicine, Department of Molecular and Clinical Medicine, Gothenburg, Sweden,

³The University of North Carolina at Chapel Hill, Center for Functional GI and Motility Disorders, Chapel Hill, United States of America

Contact E-Mail Address: wilhelm.sjoland@wlab.gu.se

Introduction: Irritable bowel syndrome (IBS) is a common disorder rooted in a disruption of the gut-brain-axis, characterized by abdominal pain and altered bowel habits.

Altered gut microbiota is reported in IBS, with microbial metabolites, including bile acids, recognized to be potentially involved in the generation of IBS symptoms.

Aims & Methods: This study aims to clarify the potential link between the gut microbiota composition, fecal bile acid levels, colonic gene expression, and IBS symptoms. In patients with IBS (n = 152), and healthy controls without gastrointestinal symptoms (n = 32), we measured fecal bile acids using targeted metabolomics.

We profiled the fecal microbiota by whole-genome metagenomics, and analyzed colonic gene expression patterns by RNA sequencing transcriptomics of mucosal biopsies.

All individuals completed self-reported questionnaires on GI symptom severity and patterns (GSRS-IBS, Bristol Stool Form Scale-based stool diary).

Spearman's correlation with Benjamini-Hochberg multiple testing adjustment was used for correlation analyses, permutational ANOVA for analysis of gut microbial composition on Bray-Curtis dissimilarity, and the Wald test for analysis of differences in colonic gene expression. Differences in bile acid levels were tested with Kruskal-Wallis and post hoc Conover-Iman tests, with Benjamini-Hochberg adjustment.

Results: The levels of the hepatically synthesized primary bile acids, chenodeoxycholic acid and cholic acid, were lower in IBS-C (constipation-predominant IBS) compared to IBS-D (diarrhea-predominant IBS, p = 2.31e⁻⁷), IBS-M (mixed type IBS, p = 0.002) and healthy controls (p = 2.57e⁻⁶, Table 1). In IBS patients, levels of primary bile acids correlated with perceived symptom severity of constipation (negatively, rho = -0.3, p = 0.0002) and diarrhea (positively, rho = 0.26, p = 0.00106).

When dividing IBS patients into quartiles by primary bile acid levels, 95 genes in the lowest quartile showed altered colonic expression. Gene-set enrichment analysis revealed enrichment of immune response-related genes, including those involved in chemokine and cytokine activity. Permutational ANOVA tests revealed altered gut microbiota composition in the two lowest quartiles of primary bile acid levels compared to healthy controls (p = 0.0001, p = 0.0003).

Group	Primary bile acid levels (pmol/mg)
Healthy controls (n = 32)	173.8 (67.3 - 717.4)
IBS-C (n = 57)	25.8 (8.5 - 88.1)
IBS-D (n = 59)	129.4 (63.9 - 1008.8)
IBS-M (n = 36)	86.5 (41.1 - 249.5)

Table 1. Median (interquartile range) of fecal primary bile acid levels in healthy controls and IBS patients.

Conclusion: Alterations in fecal primary bile acid levels were associated with stool consistency in IBS, and lower levels of primary bile acids were linked with altered gut microbiota composition and expression of colonic immune-related genes, suggesting involvement of gut microbiota-bile acid-host crosstalk in symptom generation in IBS.

Disclosure: Nothing to disclose.

PP0785

WITHDRAWN

PP0786

DIAGNOSTIC SCORE OF DYSSYNERGIC DEFECATION IN PATIENTS WITH REFRACTORY CONSTIPATION

T. Geeratragoon¹, T. Chareernboon², P. Chuenprapai¹,

S. Leelakusolvong¹, M. Maneerattanaporn¹

¹Faculty of Medicine Siriraj Hospital, Mahidol University, Division of Gastroenterology, Department of Medicine, Bangkok, Thailand,

²Faculty of Medicine, Thammasat University, Department of Clinical Epidemiology, Bangkok, Thailand

Contact E-Mail Address: tanawat.grtg@gmail.com

Introduction: Dyssynergic defecation (DD) is identified in approximately 30% of patients presenting with chronic constipation. Patients with DD usually poorly responded to standard laxative and biofeedback can be offered as the specific treatment. The diagnostic of DD relies on physiological tests including anorectal manometry (ARM) or defecography, which is not universally accessible. As there are lack of single predictive symptom for DD, hence, we aimed to establish a diagnostic score to help with DD diagnosis.

Aims & Methods: This is a retrospective study conducted at Siriraj Hospital. Derivation cohort included 402 refractory constipation patients who were referred to our center for ARM from 2017-2023. While validation cohort of 100 patients were recruited during 2014-2016. Clinical characteristics and results of physiological tests [ARM, balloon expulsion test (BET), and colonic transit time (CTT)] were collected.

The interpretation of ARM was conducted in accordance with the London classification. Univariable and multivariable logistic regression analyses were utilized and indicative features of DD were identified. The scoring system was formulated from beta-coefficients and simplified into an integer-point format. The diagnostic performance of this score was then assessed using both cohorts.

Results: The derivation cohort had DD prevalence of 52.49%. 82.09% of this cohort were female and the average age of 52.39 years. Logistic regression analysis identified significant associations between DD and the following clinical characters: duration of symptoms less than two years (OR 1.88; 95% CI=1.02-3.49), had three or more bowel movements per week (OR 4.67; 95% CI=2.47-8.86), straining (OR 7.76; 95% CI=3.57-16.90), sensation of incomplete evacuation (OR 1.95; 95% CI=1.02-3.73), sensation of anorectal blockage (OR 3.71; 95% CI=1.75-7.88), and the use of manual maneuvers to facilitate defecation (OR 2.55; 95% CI=1.37-4.78). An 11-point diagnostic scoring system was developed: 3 points are assigned

for straining during defecation; 2 points each for frequent bowel movements, the sensation of anorectal obstruction, and the use of manual maneuvers; 1 point each for a symptom duration of less than two years and the sensation of incomplete evacuation. The diagnostic performance of the score was robust, with an area under the receiver operating characteristic curve (AUROC) of 0.91 (95% CI, 0.88–0.93) in the derivation cohort and 0.88 (95% CI, 0.81–0.95) in the validation cohort. The optimal cutoff was determined to be ≥ 5 points, resulting in a sensitivity of 93.4% (95% CI = 89.1-96.3), a specificity of 72.8% (95% CI = 65.9-79.0), a positive predictive value (PPV) of 79.1% (95% CI = 73.5-84.0), and a negative predictive value (NPV) of 90.8% (95% CI = 85.1-94.9). The score also exhibited excellent calibration performance.

Characteristic	Univariable Analysis		Multivariable Analysis			Score
	Crude OR	p-value	Adjusted OR	p-value	Regression coefficient	
Demographic features						
Age > 35	1.47 (0.85-2.52)	0.165				
Female Sex	1.08 (0.65-1.81)	0.753				
Clinical features						
Duration ≤ 2years	3.72 (2.39-5.79)	<0.001	1.88 (1.02-3.49)	0.044	0.63	1
BM > 3 times/week	10.45 (6.57-16.60)	<0.001	4.67 (2.47-8.86)	<0.001	1.54	2
BSFS > 3	1.65 (1.02-2.66)	0.039	1.31 (0.64-2.66)	0.458		
Straining	17.28 (9.62-31.02)	<0.001	7.76 (3.57-16.90)	<0.001	2.05	3
Incomplete evacuation	7.38 (4.74-11.49)	<0.001	1.95 (1.02-3.73)	0.044	0.67	1
Digital evacuation	7.13 (4.55-11.18)	<0.001	2.55 (1.37-4.78)	0.003	0.95	2
Sensation of blockage	10.55 (5.74-19.38)	<0.001	3.71 (1.75-7.88)	0.001	1.31	2
Present of urge	10.79 (4.99-23.35)	<0.001	2.53 (0.88-7.29)	0.085		
Proctalgia	3.22 (1.26-8.22)	0.014	1.48 (0.43-5.07)	0.529		
Previous anorectal surgery	9.89 (2.28-42.92)	0.002	2.19 (0.39-12.35)	0.374		
Spinal cord disease	2.76 (0.55-13.87)	0.216				
Psychiatric disease	11.38 (0.61-3.16)	0.439				
Medication						
Using of rectal suppository	0.93 (0.53-1.62)	0.793				
Endoscopic features						
SRUS	1.75 (0.73-4.22)	0.213				
Anal fissure	3.72 (0.78-17.76)	0.099	3.03 (0.28-32.73)	0.362		
Hemorrhoid	1.37 (0.77-2.46)	0.286				

Univariable and multivariable analysis of clinical predictors for defecation disorder

Conclusion: We proposed the first diagnostic score for DD diagnosis. As its simplicity and excellent diagnostic performance, this can be served as a practical tool for all physicians to facilitate early identification of DD. Further diagnostic confirmation by standard physiological tests and quicken triaging patients for biofeedback therapy.

References: Carrington EV, Heinrich H, Knowles CH, et al. The international anorectal physiology working group (IAPWG) recommendations: Standardized testing protocol and the London classification for disorders of anorectal function. *Neurogastroenterol Motil.* 2020 Jan;32(1):e13679.

Disclosure: Nothing to disclose.

PP0787

NEW PATHOPHYSIOLOGICAL MECHANISMS OF FUNCTIONAL CONSTIPATION EXAMINED FROM THE PERSPECTIVE OF THE BRAIN GUT AXIS BASED ON RS-FMRI

H. Tian¹, Q. Chen¹
¹Tongji University School of Medicine, General Surgery of Shanghai Tenth People's Hospital, Shanghai, China

Contact E-Mail Address: kevin_thl@163.com

Introduction: Functional constipation (FCon), a highly prevalent functional gastrointestinal disorder (FGID), often accompanies by mental and psychological disorders. Previous neuroimaging studies have demonstrated brain functional and structural alterations in FCon patients. However, little is known about whether and how regional homogeneity (ReHo) is altered in FCon patients. Moreover, the potential genetic mechanisms associated with these alterations remain largely unknown.

Aims & Methods: A total of 73 patients with FCon and 68 healthy controls were recruited, and we conducted ReHo comparison to identify the abnormal spontaneous brain activities in FCon patients. Based on Allen Human Brain Atlas, we further employed partial least squares regression analysis to explore gene expression profiles associated with ReHo alterations in FCon patients.

Results: Compared with healthy controls, FCon patients demonstrated significantly decreased ReHo in both bilateral caudate nucleus, putamen, anterior insula, thalamus and right middle cingulate cortex, supplementary motor area, and increased ReHo in the bilateral orbitofrontal cortex. Genes related to central nervous system development, fatty acid metabolism, and immunity were spatially correlated with abnormal ReHo patterns.

	FCon (N = 73) (Mean ± SD)	HC (N = 68) (Mean ± SD)	FCon vs. HC P value
Age (yrs)	51.14 ± 18.03	53.20±12.24	0.3487
Gender	20M/53F	23M/45F	0.408
BMI (Kg/M2)	21.96 ±4.10	24.78 ± 3.198	< 0.0001
Depression (SDS)	45.54 ± 11.16	37.46 ± 8.15	< 0.0001
Anxiety (SAS)	40.51 ±11.05	35.44± 7.52	0.0019
PAC-QOL	45.16 ± 19.07	N/A	N/A
Wexner constipation score	11.71 ± 3.76	N/A	N/A

Table 1. The demographic and clinical characteristics of FCon and HC.

Conclusion: Our findings showed significant ReHo alterations in FCon patients, and these changes may be related to complex polygenetic and poly-pathway mechanisms, which provides a new perspective to understand the pathophysiology of FCon.

References:

[1]Alame A M, Bahna H. Evaluation of constipation. Clin Colon Rectal Surg. Mar 2012;25(1):5-11.

[2]Drossman D A. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology. Feb 19 2016.

[3]Black C J, Drossman D A, Talley N J, Ruddy J, Ford A C. Functional gastrointestinal disorders: advances in understanding and management. Lancet. Nov 21 2020;396(10263):1664-1674.

[4]Mugie S M, Benninga M A, Di Lorenzo C. Epidemiology of constipation in children and adults: a systematic review. Best Pract Res Clin Gastroenterol. Feb 2011;25(1):3-18.

[5]Barberio B, Judge C, Savarino E V, Ford A C. Global prevalence of functional constipation according to the Rome criteria: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. Aug 2021;6(8):638-648.

[6]Person H, Keefer L. Psychological comorbidity in gastrointestinal diseases: Update on the brain-gut-microbiome axis. Prog Neuropsychopharmacol Biol Psychiatry. Apr 20 2021;107:110209.

[7]Hosseinzadeh S T, Poorsaadati S, Radkani B, Forootan M. Psychological disorders in patients with chronic constipation. Gastroenterol Hepatol Bed Bench. Summer 2011;4(3):159-163.

[8]Martin B C, Barghout V, Cerulli A. Direct medical costs of constipation in the United States. Manag Care Interface. Dec 2006;19(12):43-49.

Disclosure: Nothing to disclose.

PP0788

DOCUMENTATION OF BOWEL, BLADDER AND SEXUAL DYSFUNCTION SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

C. Dell'Oro¹, L. Hicks^{1,2}, E.V. Carrington^{1,2}
¹Imperial College, Department of Surgery and Cancer, London, United Kingdom, ²Imperial College NHS Trust, Gastroenterology and Hepatology, London, United Kingdom

Contact E-Mail Address: chiara.delloro20@imperial.ac.uk

Introduction: Bowel, bladder and sexual dysfunction symptoms are common in patients with Inflammatory Bowel Disease (IBD). Despite significantly impacting on quality of life, few patients proactively seek help for these symptoms. For this reason clinician awareness of these functional symptoms in IBD patients is vital to identifying patients who may benefit from targeted treatment.

Aims & Methods: This study aimed to describe how well clinicians identified bowel, bladder and sexual dysfunction symptoms in IBD patients in the outpatient setting. Clinic letters from consecutive patients attending specialist IBD clinics at a tertiary hospital in the United Kingdom, from 1 January 2024, were reviewed retrospectively for documentation of bowel, bladder and sexual dysfunction symptoms. Patients with unclassified IBD, microscopic colitis, stomas and J-pouches were excluded. Data on patient demographics, IBD disease phenotype and activity were also collected.

Results: One hundred and twenty patients were included, of which 60/120 (50%) were male, 76/120 (63%) had ulcerative colitis (UC), and 44/120 (37%) had Crohn's disease (CD), with median age 45 (range 18-88). Faecal urgency (FU) was the most commonly documented bowel symptom, documented in 26/120 (22%) patients, with 14/120 (12%) documenting the presence of FU and 12/120 (10%) documenting no FU. Faecal incontinence and constipation were each documented in 5/120 (4%) patients, and anorectal pain was documented in 3/120 (2.5%) patients. Urinary symptoms were only documented in one instance: urinary urgency in 1/120 (0.8%) patients. There was no documentation of urinary frequency or voiding dysfunction. Sexual dysfunction symptoms were not documented in any of the 120 letters, nor was impact of bowel symptoms on quality of life. FU was more frequently documented in patients with UC (11/76[14%]) compared to CD (3/44[7%]), whilst all cases of anorectal pain were documented in CD patients 3/44(7%), with no documentation of anorectal pain in any patients with UC. In patients with CD, documentation of FU was similar in remission (Harvey Bradshaw-Index (HBI) <4) and active disease (HBI≥ 4) groups (2/44 vs. 1/44, p=n.s.).

Conclusion: Bowel, bladder and sexual dysfunction symptoms are infrequently documented in patients with IBD. Failure to recognise these symptoms is likely to impair access to appropriate treatment. Introduction of a standardised reporting tool and improving IBD clinician awareness may facilitate best care for this patient group.

Disclosure: Nothing to disclose.

PP0789

STUDY OF FUNCTIONAL CONSTIPATION: IS ANORECTAL MANOMETRY ENOUGH?

A.I. Ferreira^{1,2,3}, C. Arieira^{1,2,3}, S. Xavier^{1,2,3}, P. Campelo^{1,2,3},
B. Rosa^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²School of Medicine, University of Minho, Life and Health Sciences Research Institute (ICVS), Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: pedroncampelo@gmail.com

Introduction: Constipation is a common anorectal symptom that causes significant changes in the patients' quality of life. Anorectal manometry (ARM) and magnetic resonance (MR) defecography are important tools in diagnosing disorders associated with constipation, which are mainly structural and/or functional. Pelvic floor dyssynergia is diagnosed in the presence of alterations in 2 of the following: defecation kinetics in ARM, balloon expulsion test (BET) and/or MR defecography.

Aims & Methods: Compare the findings in ARM and MR defecography, in patients with constipation.

Retrospective cohort study including patients who fulfilled the Roma IV criteria for functional constipation, who were submitted to ARM and MR defecography. The London classification was used to describe the findings in ARM, establishing 3 groups of patients: Group 1 with those who had normal anorectal coordination and normal BET, Group 2 had altered anorectal coordination and altered BET, and Group 3 with those who had inconclusive findings: altered anorectal coordination and normal BET or normal anorectal coordination with abnormal BET. The structural alterations considered significant in MR defecography were those described as moderate to severe, which lead to defecation obstruction.

Results: A total of 51 patients were included, most were female (98.0%), with a mean age of 55 ± 12 years. Regarding the ARM findings, 16 patients were in Group 1 (31.4%), 11 in Group 2 (21.6%) and 24 in Group 3 (47.1%). Forty-three patients had alterations in MR defecography (84.3%), with 42 patients having at least one structural alteration and the most common being rectocele (72.5%) and descending perineum syndrome (66.7%). Pelvic floor dyssynergia was diagnosed by MR defecography in 9 patients (17.6%).

In the group of patients with normal anorectal coordination in ARM and normal BET (Group 1: n=16), 14 had significant structural alterations in MR defecography (87.5%) and 2 patients had no alterations (12.5%). In the group of patients with altered anorectal coordination in ARM and altered BET (Group 2: n=11), 8 also had structural alterations in MR defecography (72.7%). In the group of patients with inconclusive findings in ARM (Group 3: n= 24), 20 had structural alterations (83.3%) and 3 patients had pelvic floor dyssynergia diagnosed by MR defecography (12.5%), 2 of whom had both alterations (8.3%). In this group, 3 patients had no alterations in MR defecography (12.5%).

Patients with pelvic floor dyssynergia, with or without structural alterations, had a significantly lower rectoanal pressure differential than those with solely structural alterations (-25.0 ± 27.1 vs 5.7 ± 30.0 mmHg, $p=0.004$). There were no statistically significant differences in the values of anal pressure at rest and voluntary contraction pressure between patients with pelvic floor dyssynergia and those with solely structural alterations ($p=0.350$ and $p=0.833$), as well as in the values of residual anal pressure, intrarectal pressure and percentage of relaxation during defecation ($p=0.267$, $p=0.257$ and $p=0.348$).

Conclusion: Most patients had alterations in MR defecography, regardless of the ARM findings. Therefore, it is important to interpret the results of the ARM in conjunction with an imaging test capable of identifying struc-

tural alterations that may condition defecation in patients with functional constipation. In addition, those with pelvic floor dyssynergia, with or without associated structural alterations, had a lower rectoanal pressure differential than those with solely structural alterations.

Disclosure: Nothing to disclose.

PP0790

FECAL CONSISTENCY AS A MARKER OF GOOD RESPONSE IN FUNCTIONAL BOWEL DISORDERS TREATMENT AND THE ROLE OF SOLUBLE FIBERS

I. Froehner Junior^{1,2}, J.N. Buzato^{1,2}

¹PELVIA Gastrointestinal Motility and Continence, Curitiba, Brazil,

²Nossa Senhora das Graças Hospital, Gastrointestinal Motility and Continence, Curitiba, Brazil

Contact E-Mail Address: froehnerjr@yahoo.com.br

Introduction: Functional bowel disorders are among the most frequent gastrointestinal complaints. As a first step in clinical therapy, current guidelines are clear in indicating the least invasive, reversible and low morbidity treatments. In this context, soluble dietary fibers are included on some constipation and fecal incontinence guidelines.

A simple way to assess normal intestinal transit is through fecal consistency, commonly demonstrated by the Bristol Stool Scale (BSS). Hard stools (BSS types 1 and 2) can often indicate slowed intestinal transit. Similarly, individuals with normal stools (BSS 3 and 4) tend to have a lower incidence of gastrointestinal symptoms.

Aims & Methods: Objective: To evaluate the clinical response to the use of partially hydrolyzed guar gum and inulin, according to fecal consistency, as the first approach in the treatment of functional intestinal disorders. Methods: Prospective study of 648 patients with functional bowel disorders (functional constipation, functional diarrhea, irritable bowel syndrome and anal incontinence) consecutively treated on an outpatient basis by the same researchers.

Patients were asked to take one measuring spoon (5g) of a mixture composed of partially hydrolyzed guar gum (60%) and inulin (40%) added to water, tea or juice, two times a day for a 30-day period, and to drink it within the first minute.

If BSS was 1 to 2, patients were told to mix the measuring spoon to 250 - 300 mL of water, tea, or juice. If BSS was 5 to 7, to mix it to 50 mL, and finally, if BSS was 3 to 4, to mix the measuring spoon to 200 mL.

Mean BSS, global improvement percentage, complication rate, Constipation Scoring System (CSS) and Cleveland Clinic Incontinence Score (CCIS) were applied by the authors to the patients during the first appointment and during the 30-day follow-up appointment.

All patients accepted to participate by signing the informed consent form.

Results: Of the 648 patients, 61.9% were female, with a mean age of 48.1 years. All patients informed no difficulty in complying with the soluble fiber protocol.

Initial mean CSS was 12,0 (+4,8) and CCIS was 2 (+1). Mean BSS of constipation patients was 2 (+1) of functional diarrhea and fecal incontinence was 5 (+1) and to irritable bowel syndrome was 5 (+1), respectively.

By the time of the 30-day follow-up appointment, 71.7% of the patients had BSS types 3 and 4, associated with 63.1% (+18.4) of overall improvement, while in the patients who presented the other types of fecal consistency (28.3%), the overall improvement was only 21.8% (+14.3). Mean CSS was 6,7 (+3,9) and CCIS was 1 (+1), $p < 0,01$.

Conclusion: Achieving normal fecal consistency is associated with significant overall improvement. Oral soluble fibers use according to fecal consistency are a valid tool in treating functional bowel disorders.

References: 1 Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features, and Rome IV. *Gastroenterology*. 2016; 16: 223-7.

2 Benet LZ, Bowman CM, Koleske ML, Rinaldi CL, Sodhi JK. Understanding drug-drug interaction and pharmacogenomic changes in pharmacokinetics for metabolized drugs. *J Pharmacokinet Pharmacodyn*. 2019; 46: 155-63.

3 Froehner Junior I. Oral soluble fibers as a first approach to low anterior resection syndrome treatment. *Neurogastroenterol Motil*. 2023; 35: 77-8.

4 Froehner Junior I, Buzato JN. Fecal consistency as a marker of good response in the treatment of functional bowel movement disorders and the role of soluble fibers. [Presentation on 8^o Latin American Pelvic Floor International Congress - ALAPP; 2024 fev 21-24; Panamá City, Panamá, onsite]

5 Axelrod CH, Saps M. The role of fiber in the treatment of functional gastrointestinal disorders in children. *Nutrients*. 2018; 10: 1650-66.

6 Ingemansson A, Walter SA, Jones MP, Sjö Dahl J. Defecation symptoms in relation to stool consistency significantly reflect the dyssynergy pattern in high-resolution anorectal manometry in constipated patient. *J Clin Gastroenterol*. 2024; 58: 57-63.

7 Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FEM, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut*. 1992; 33: 818-24.

Disclosure: Nothing to disclose.

PP0791

LIVING WITH FAECAL INCONTINENCE: A QUALITATIVE INVESTIGATION OF PATIENT EXPERIENCES AND PREFERRED OUTCOMES THROUGH SEMI-STRUCTURED INTERVIEWS

S. Assmann^{1,2,3}, D. Keszthelyi^{3,1}, S.O Breukink^{2,3,4}, M. Kimman^{5,6}

¹Maastricht University Medical Center, Department of Gastroenterology-Hepatology, Maastricht, Netherlands,

²Maastricht University Medical Center, Department of Surgery and Colorectal Surgery, Maastricht, Netherlands, ³Maastricht University, Research Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht, Netherlands, ⁴Maastricht University, Research Institute for Oncology and Reproduction (GROW), Maastricht, Netherlands,

⁵Maastricht University Medical Centre, Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht, Netherlands, ⁶Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands

Contact E-Mail Address: s.assmann@maastrichtuniversity.nl

Introduction: Faecal incontinence (FI) is a prevalent and debilitating anorectal problem which can cause embarrassment, anxiety, social isolation and diminishes quality of life (QoL). Currently, there is no optimal treatment option for FI, consequently, treatments primarily focus on symptom reduction and improving QoL. In order to gain a clearer understanding of the challenge's patients encounter, it is essential to actively listen to patients' perspectives and experiences, as well as the specific outcomes they aim to achieve from treatment. This study aims to explore how FI impacts patients' lives and identify important treatment outcomes as part of the development of a Core Outcome Set (COS).

Aims & Methods: Patients with FI were recruited from surgery and gastroenterology outpatient clinics in the Netherlands. Semi-structured interviews were performed, audio recorded, transcribed per verbatim and coded. Thematic analysis was performed to identify (sub)themes and categories relevant to the patients.

Results: Twelve interviews were conducted before saturation was reached (75% female, 25% male, mean age 63, range 39-83 year). Four main themes emerged 'Physical symptoms', 'Impact on daily life', 'Emotional impact' and 'Coping'. Patients expressed how FI severely limits daily activities and emotional wellbeing. Patients' treatment priorities centred on resuming normal activities rather than solely on (physical) symptom reduction.

Conclusion: The impact of FI extends far beyond uncontrolled loss of faeces, affecting psychological, emotional, and social wellbeing. Patients prioritise outcomes focussed on reclaiming normalcy and independence rather than focusing on physical symptoms alone. Integrating these patient-centered outcomes in future studies could enhance treatment satisfaction and patient-perceived treatment success.

Furthermore, outcomes identified through this study will be combined with other outcomes identified through literature review, forming a comprehensive list for a Delphi survey with relevant stakeholders to establish a consensus on a final list of outcomes for a COS for FI.

Disclosure: Nothing to disclose.

PP0792

TOWARDS A CORE OUTCOME SET FOR FAECAL INCONTINENCE – A SYSTEMATIC REVIEW OF OUTCOMES REPORTED IN LITERATURE

S.L Assmann^{1,2,3}, E. Mulders², M. Kimman^{4,5}, D. Keszthelyi^{2,6}, S.O Breukink^{2,1,7}

¹Maastricht University Medical Center, Department of Surgery and Colorectal Surgery, Maastricht, Netherlands, ²Maastricht

University, Research Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht, Netherlands, ³Maastricht University Medical Center, Division

of Gastroenterology-Hepatology, Maastricht, Netherlands,

⁴Maastricht University Medical Centre, Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht,

Netherlands, ⁵Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands, ⁶Maastricht

University Medical Center, Department of Gastroenterology-Hepatology, Maastricht, Netherlands, ⁷Maastricht University,

Research Institute for Oncology and Reproduction (GROW), Maastricht, Netherlands

Contact E-Mail Address: s.assmann@maastrichtuniversity.nl

Introduction: Faecal incontinence (FI) is a prevalent issue which can have a detrimental impact on the patient's quality of life. Current international guidelines lack strong treatment recommendations due to few studies in the field, in combination with the heterogeneity in outcome reporting. To address this, a Core Outcome Set (COS) is proposed to standardize outcome reporting in FI studies, facilitating meta-analyses and enhancing therapeutic recommendations.

This systematic review aims to identify which outcomes have been used in FI intervention studies so far in adult patients as a starting phase for the development of a future COS for FI.

Aims & Methods: Medline, Embase and the Cochrane library were searched to identify all outcomes reported in comparative effectiveness trials assessing one or more treatment option in adult patients suffering from FI. The outcomes were categorized according to the Core Outcome Measurement in Effectiveness Trials (COMET) taxonomy to standardize outcome terminology, assess completeness, and inform subsequent steps in COS development.

Results: A total of 109 studies were included, which revealed 51 unique outcomes which were classified into 38 domains within four core areas. On average four outcomes were reported per study (range 1-11). The most

commonly reported outcomes were ‘Severity of FI’ (83%), ‘Quality of life’ (64%), ‘Number of FI episodes’ (40%), ‘Anorectal motor function’ (39%), and ‘Frequency of bowel movements’ (16%).

Conclusion: This systematic review offers an overview of outcomes reported in FI studies, highlighting the heterogeneity between studies. This heterogeneity emphasises the need for standardising outcome reporting which can be established through the creation of a COS. Outcomes identified through this study will be combined with other outcomes identified through patients interviews, forming a comprehensive list for a Delphi survey with relevant stakeholders to establish a consensus on a final list of outcomes for a COS for FI.

Disclosure: DK and SB have received grant support from UEG and ESCP for the development of a guideline for faecal incontinence. DK has received a grant from ZonMw for the study of the clinical efficacy of anal plugs in faecal incontinence. DK has received research funding from Rome Foundation, MLDS, Horizon 2020, Horizon Europe, Allergan, Grunenthal, and speaker’s fee from Dr Falk (paid to host institute), all outside of submitted work. The other authors declare that they have no conflict of interest.

PP0793

ANORECTAL PAIN IS A PREDICTOR OF DYSSYNERGIC DEFECATION IN PATIENTS WITH REFRACTORY FUNCTIONAL CONSTIPATION

C. Lambiase^{1,2,3}, M. Bellini¹, R. Morganti⁴, F. Rettura¹, S.-L. Popa⁵, G. Chiarioni^{6,7}

¹University of Pisa, Gastrointestinal Unit, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²University of Nottingham, NIHR Nottingham BRC, Nottingham University Hospitals NHS Trust and the University of Nottingham, Nottingham, United Kingdom, ³University of Nottingham, Nottingham Digestive Diseases Centre, Translational Medical Sciences, School of Medicine, Nottingham, United Kingdom, ⁴Azienda Ospedaliero Universitaria Pisana, Clinical Trial Statistical Support Unit, Pisa, Italy, ⁵Iuliu Hațieganu University of Medicine and Pharmacy, 2nd Medical Department, Cluj-Napoca, Romania, ⁶Il Cerchio Med HealthCare, Verona, Italy, ⁷University of North Carolina at Chapel Hill, UNC Center for Functional GI and Motility Disorders, Chapel Hill, United States of America

Contact E-Mail Address: christian.lambiase93@gmail.com

Introduction: Functional Defecation Disorders (FDD) are a frequent cause of refractory functional constipation (FC). The diagnosis of FDD requires anorectal manometry (ARM) and a balloon expulsion test (BET), which are not easily available outside referral centers. FDD often do not respond to conventional treatments, while they respond to biofeedback.

Aims & Methods: The aim of our study was to evaluate if pain reported by patients during defecation or elicited during digital rectal examination (DRE) predicted a FDD diagnosis in a cohort of refractory FC patients. Two-hundred and thirty-eight FC (Rome III Criteria) patients failing a 30-day conservative treatment trial (increased fiber and fluids, tailored laxatives) were enrolled in the study.

The presence of weekly anorectal pain during defecation and the elicited pain/tenderness consequent to a stretching of the levator ani muscle during DRE (DRE-pain) had been evaluated before and after the macrogol trial. Possible causes of organic anorectal pain were excluded.

All patients underwent:

- ARM+BET;
- barium defecography, if ARM and BET were discordant;
- second DRE with evaluation of DRE-pain.

OR and accuracy were calculated for both pain during defecation and DRE-pain in predicting a Rome III FDD.

Results: One hundred and twenty patients (50.42%) showed features of FDD: 82 dyssynergic defecation (DD) and thirty-eight inadequate defecatory propulsion (IDP). Thirty-three structural outlet obstructions (SOO) were identified using barium defecography.

Pain during defecation was strongly associated with DD, with an OR of 7.85 ($p<0.001$) and an accuracy of 75.2% in diagnosing a FDD (Tab.1).

DRE-pain was strongly associated with DD, with an OR of 11.78 ($p<0.001$) and an accuracy of 77.3% in diagnosing DD (Tab.1). Furthermore, DRE-pain showed a very good reproducibility between T0 and T30 (Cohen’s $K=0.87$).

The combination of pain during defecation and DRE-pain showed an even stronger association to DD compared to single items, with an OR of 20.84 and an accuracy of 82.8% in diagnosing DD ($p<0.001$, Tab.1).

Neither pain during defecation nor DRE-pain were predictive of IDP.

		Rome III DD		p-value	OR (95% CI)	Sens.	Spec.	PPV	NPV	Acc.
		No	Yes							
Weekly anorectal pain during defecation	No	121 (77.6%)	24 (29.3%)	<0.001	7.85 (4.2 – 14.68)	70.7%	77.6%	62.4%	83.4%	75.2%
	Yes	35 (22.4%)	58 (70.7%)							
DRE-pain	No	96 (76.8%)	16 (21.92%)	<0.001	11.78 (5.9 – 23.58)	78.1%	76.8%	66.3%	85.7%	77.3%
	Yes	29 (23.2%)	57 (78.08%)							
DRE-pain + Weekly anorectal pain during defecation	No	110 (88%)	19 (26.03%)	<0.001	20.84 (9.83 – 44.17)	73.9%	88%	78.3%	85.3%	82.8%
	Yes	15 (12%)	54 (73.97%)							

Table 1 - Association and diagnostic devaluation of reported pain during defecation and DRE-pain

Abbreviations: DD=dyssynergic defecation; OR=odds ratio; 95% CI=95% confidence interval; Sens.=sensitivity; Spec.=specificity; PPV=positive predictive value; NPV=negative predictive value; Acc.=accuracy; DRE-pain= pain/tenderness consequent to a traction on the levator ani muscles during digital rectal examination

Conclusion: Anorectal pain during defecation or elicited during DRE were shown to be predictive of a DD diagnosis in FC patients. An early referral to anorectal physiology testing may be considered in patients presenting these clinical features, leading to an improvement in their management.

Disclosure: Nothing to disclose.

PP0794

EVALUATION OF A MODIFIED LONDON PROTOCOL INVOLVING ONLY TWO 10-SECOND PUSHES TO DIAGNOSE DEFECATION DISORDERS WITH HIGH-DEFINITION ANORECTAL MANOMETRY

C. Lambiase^{1,2,3}, M. Corsetti^{1,2}, A. Grosso³, R. Tedeschi³, L. Cancelli³, F. Rettura³, A. Bottari³, N. de Bortoli³, M. Bellini³

¹University of Nottingham, NIHR Nottingham BRC, Nottingham University Hospitals NHS Trust and the University of Nottingham, Nottingham, United Kingdom, ²University of Nottingham, Nottingham Digestive Diseases Centre, Translational Medical Sciences, School of Medicine, Nottingham, United Kingdom, ³University of Pisa, Gastrointestinal Unit, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy

Contact E-Mail Address: christian.lambiase93@gmail.com

Introduction: Anorectal manometry (ARM) is one of the required investigations to diagnose defecation disorders according to Rome IV criteria. The International Anorectal Physiology Working Group (IAPWG) introduced into clinical practice a standardized sequence of manoeuvres to perform ARM (London Protocol) (Carrington EV, 2020). IAPWG Protocol suggested the need of performing three push attempts, each of 15s duration, to assess recto-anal coordination, with a consensus <75% between experts.

Aims & Methods: The aim of this study was to assess the diagnostic accuracy, compared to IAPWG recommendations, of simplified ARM protocols featuring:

- only two push attempts (each of 15 seconds);
- three pushes attempts (each of 10s);
- two pushes attempts (each of 10s)

High-Definition ARM (HD-ARM) traces from 150 patients (118 F, mean aged 54 years) who underwent ARM for faecal incontinence (n=37) or constipation (n=105) were retrospectively reviewed. All traces were performed according to the IAPWG Protocol.

Firstly, we evaluated if the mean rectal and anal pressures were different among the three pushes. Subsequently, ARM traces were re-evaluated considering the following modifications to the IAPWG protocol:

- considering only the first two pushes (as if the third had never been performed);
- considering the first ten seconds of each push (as if each push featured only ten seconds);
- considering the first ten seconds of the first two pushes (as if the third had never been performed and the first two featured only ten seconds).

In all three cases, the best push (defined as the most qualitatively normal) among the available pushes was chosen.

New diagnoses were made based on these modified protocols and compared with the standard to evaluate whether these modifications could affect the final diagnosis.

Results: According to the IAPWG London Protocol, the qualitative best pushes were the first, the second or the third in 58, 45 and 47 patients, respectively. No statistically significant differences were found in anal and rectal pressures among the three pushes.

No statistically significant differences were found in anal and rectal pressures comparing the three modified protocols with the IAPWG's one.

Regarding the diagnostic accuracy, all the proposed modified London Protocol showed an almost perfect concordance compared with the standard of practice (K=0.97, Tab.1).

This result was confirmed for the constipated and incontinent patients' subgroup.

		No disorders of rectoanal co-ordination	Normal expulsion with abnormal manometric pattern of rectoanal co-ordination	Abnormal expulsion with normal manometric pattern of rectoanal co-ordination	Abnormal expulsion with poor propulsion	Abnormal expulsion with dyssynergia	Abnormal expulsion with poor propulsion and dyssynergia	Comparison of proportions (Kappa Cohen agreement)
All patients N=150	3 Push 15 sec	5	18	16	25	44	42	-
	2 Push 15 sec	5	18	14	25	45	43	k=0.974
	3 Push 10 sec	5	18	15	25	45	42	k=0.974
	2 Push 10 sec	4	19	15	25	45	42	k=0.966
Constipated patients N=105	3 Push 15 sec	3	15	10	14	30	33	-
	2 Push 15 sec	3	15	9	14	30	34	k=0.975
	3 Push 10 sec	3	15	9	14	30	34	k=0.975
	2 Push 10 sec	3	15	9	14	30	34	k=0.975

Table 1 - Cohen's K concordance according to London Protocol among all patients and in constipated patients

Conclusion: Based on our results, it seems that two pushes of ten second each may be enough to reach an accurate manometric diagnosis of defecation disorders.

Performing only 2 push manoeuvres of 10s each may reduce the examination length of 55s, reducing patient's discomfort and, likely, improving HD-ARM's acceptability.

Disclosure: Nothing to disclose.

PP0795

SHORT-COURSE BIOFEEDBACK THERAPY MAY BE USEFUL IN THE MANAGEMENT OF FUNCTIONAL DEFECATORY DISORDER IN RESOURCE-POOR SETTINGS- A CENTRE PROSPECTIVE OBSERVATIONAL STUDY BASED ON THE LONDON CLASSIFICATION OF ANORECTAL DYSFUNCTION

S. Benny¹, R. Jaleel¹, A. Joseph¹, A.K. Dutta¹, S. Dhar Chowdhury¹, R.T. Kurian¹, N.V. Mathews¹

¹Christian Medical College, Vellore, Gastroenterology, Ranipet, India

Contact E-Mail Address: stenny2.0@gmail.com

Introduction: Dyssynergic defecation constitutes more than half the cases of refractory chronic constipation, and biofeedback therapy is the first-line treatment in the management of functional defecatory disorder (FDD). The studies done by Rao et al¹ and Chiarioni G et al². showed response rates of 79% and 80%, respectively, with the standard protocol of Biofeedback therapy (BFT). However, the need for six to eight sessions of biofeedback therapy once every two weeks can pose economic and logistic challenges to patients.

Aims & Methods: Our study aims to determine whether a short biofeedback course helps manage dyssynergic defecation, especially in a resource-poor setting. We also wanted to know the factors predicting the response to biofeedback therapy.

It was a single-center, prospective observational study. Consecutive patients of age more than 16 years who fulfilled Rome IV criteria for functional defecatory disorder were recruited in the study. Patients with structural and metabolic causes of constipation were excluded. They were classified according to Rao's type of dyssynergia and London classification of anorectal dysfunction. All patients underwent one biofeedback therapy session per day for three consecutive days. Each patient was asked the PAC-SYM questionnaire before initiating biofeedback therapy, and the total score was calculated. The same questionnaire was used after three

months, either in person or via a telephone call. Patients with a reduction in average score by 0.6 points or more at three months were considered to have responded to the biofeedback therapy³.

Results: A total of 70 patients were included in the study. Most patients were males (70%), and the median duration of constipation was 5 (2-10) years. The median PAC- SYM questionnaire score at baseline was 1.33 (1.08- 1.58). Most patients belonged to Rao's Type 1 dyssynergia (91.4%), followed by Type 3 dyssynergia (7.1%). When patients were classified according to the London classification, Anal hypotension with normal contractility was noted in 12.8% patients and anal normotension with hypocontractility was noted in 4.2% patients. Abnormal expulsion with dyssynergia was noted in 78.5% of patients, and abnormal expulsion with poor propulsion and dyssynergia was noted in 21.4%. None of the patients had absent Recto- anal areflexia, abnormal expulsion with normal manometric pattern of recto-anal coordination, abnormal expulsion with poor propulsion, normal expulsion with abnormal manometric pattern of recto-anal coordination, or rectal hyposensitivity.

The study also showed that 52.8% of patients (95% CI 40.5%- 65.9%) responded to biofeedback therapy at the end of three months. However none of the factors like age, sex, duration of illness, and types of anorectal dyssynergia were statistically significant between BFT responders and non-responders (Table-1).

Variables	Responded to BFT	Not responded to BFT	p value
Patients (n, %) (95% CI)	37 (52.8%) (40.5%- 64.9%)	33 (47.1%) (35.1%- 59.4%)	
Age (years)	31 (26-43)	39 (27- 54)	0.12
Sex (%)			0.79
Male	25 (51.0%)	24 (48.9%)	
Female	12 (57.1%)	9 (42.8%)	
Duration of illness (years)	5 (3-10)	4 (2-10)	0.30
Rao's type of Dyssynergia (n,%)			0.38
Type 1	32 (50%)	32 (50%)	
Type 2	1 (100%)	0 (0%)	
Type 3	4 (80%)	1 (20%)	
Type 4	0 (0%)	0 (0%)	
Anal hypotension with normal contractility (n,%)	5 (55.6%)	4 (44.4%)	1.00
Abnormal expulsion with dyssynergia (n,%)	28 (50.9%)	27 (49.0%)	0.39
Abnormal expulsion with poor propulsion and dyssynergia (n,%)	9 (60%)	6 (40%)	0.57

Conclusion: Standard course biofeedback therapy (6- 8 sessions fortnightly) is superior to short course biofeedback therapy in managing dyssynergic defecation. However short course of biofeedback therapy is helpful in the managing dyssynergic defecation in resource-poor setting.

References:

- Rao SS, Valestin J, Brown KC, Zimmerman B, Schulze K. Long-term efficacy of biofeedback therapy for dyssynergic defecation: randomized controlled trial. *Official journal of the American College of Gastroenterology* ACG. 2010 Apr 1;105(4):890-6.
- Chiarioni G, Whitehead WE, Pezza V, Morelli A, Bassotti G. Biofeedback is superior to laxatives for normal transit constipation due to pelvic floor dyssynergia. *Gastroenterology*. 2006 Mar 1;130(3):657-64.
- Yiannakou Y, Tack J, Piessevaux H, Dubois D, Quigley EM, Ke MY, Da Silva S, Joseph A, Kerstens R. The PAC-SYM questionnaire for chronic constipation: defining the minimal important difference. *Alimentary pharmacology & therapeutics*. 2017 Dec;46(11-12):1103-11.

Disclosure: Nothing to disclose.

PP0796

IMPACT OF PUBLISHING A NATIONAL POSITION PAPER ON THE PERFORMANCE AND INTERPRETATION OF ANORECTAL MANOMETRY: ADDRESSING THE GAP BETWEEN INTERNATIONAL RECOMMENDATIONS AND CLINICAL PRACTICE

Y. Mazor¹, A. Mari², J. Lysy³, M. Beer-Gabel⁴, Y. Ron⁵, N. Bar⁶, R. Dickman⁷, D. Carter⁸

¹Rambam Health Care Campus, Department of Gastroenterology, Haifa, Israel, ²Nazareth Hospital EMMS, Gastroenterology Department, Nazareth, Israel, ³Shaare Zedek Medical Center Digestive Disease Institute, Dept. of Gastroenterology, Jerusalem, Israel, ⁴Laniado Hospital, Gastroenterology, Netanya, Israel, ⁵The Tel-Aviv Medical Center, Gastroenterology & Hepatology, Tel-Aviv, Israel, ⁶Tel Aviv Medical Center, Gastroenterology and Hepatology, Tel Aviv, Israel, ⁷Rabin Medical Center, Gastroenterology, Petach Tikva, Israel, ⁸Sheba Medical Center, Gastroenterology, Ramat Gan, Israel

Contact E-Mail Address: dr.dancarter@gmail.com

Introduction: In 2019, an international anorectal physiology working group published a consensus paper ('London') with recommendations for the performance of anorectal manometry (ARM) and balloon expulsion testing (BET)¹. However, little is known on the implementation of these recommendations in the clinical setting.

Aims & Methods: We aimed to (1) evaluate, on a national level, current practice in all aspects of ARM and BET performance and interpretation, (2) identify gaps compared to both updated international recommendations and between testing centers, and if present, (3) jointly draft a national position paper, advocate for its instillation, and examine the impact of the publication on the identified gaps.

Between October and November 2020, gastroenterologists from 20/20 (100%) centres who perform and/or interpret ARM in Israel completed a 61- item online survey encompassing all stages of ARM and BET testing (preparation, testing protocol and reporting).

Results: Major inconsistencies between centres were demonstrated (table 1, baseline survey), especially in reporting, including:

- (1) the use of London classification for description of anorectal dysfunction
- (2) lack of normal values for reference
- (3) selective reporting of anal squeeze pressure and anal slow waves, and;
- (4) report template and language.

High concordance (>90%) between centres in most stages of preparation and testing was noted, consistent with international recommendations, with the exception of testing for anal squeeze endurance, cough, rectoanal inhibitory reflex (RAIR) and BET methodology.

	Baseline survey N=20	Follow up survey N=22	P value for difference
Squeeze endurance testing- n (%)	17 (85%)	20 (91%)	NS
Cough/ Valsalva testing - n (%)	15 (75%)	20 (91%)	NS
RAIR 50 ml, repeat to 100 ml if needed - n (%)	5 (25%)	10 (45%)	NS
BET - on toilet and dedicated expulsion balloon - n (%)	2 (10%)	6 (27%)	NS
BET Balloon fill: water - n (%)	5 (25%)	10 (45%)	NS
Volume of BET balloon: 50 ml - n (%)	15 (75%)	22 (100%)	NS
London classification on report - n (%)	13 (65%)	22 (100%)	<0.01
Anal squeeze pressure on report: absolute and increment - n (%)	6 (30%)	13 (59%)	0.07
Anal slow waves on report- n (%)	4 (21%)	4 (18%)	NS

Table 1. Changes in performing anorectal manometry and balloon expulsion testing following local position paper publication and hands-on educational course.

Following these results, an ARM and BET position paper was endorsed by the Israeli Neurogastroenterology Society (October 2021), followed by a free-of-charge hands-on educational course focused on proper performance of tests (Feb 2022) and publication of the final version of the position paper (Jan 2023)².

One year following publication, in a repeat survey of centres (22/24; 4 new centres), almost all responders (19/22;86%) stated they have changed their clinical practice following publication of the national position paper, and 21/22 (95%) reported now using the published normal values.

Compared to the baseline survey, the following improved (table 1, follow up survey): (1) reporting according to the London classification, and (2) uniform volume of balloon used for BET.

High concordance (>90%) was also demonstrated now for performing squeeze endurance and cough, as well as reporting templates, but not for RAIR or for the use of a dedicated evacuation balloon or sitting position for BET.

Conclusion: The current study highlights major gaps in ARM and BET testing between consensus papers and clinical practice on a national level. Publication of a national position paper along with an educational curriculum can address existing gaps.

References:

- 1. Carrington et al. NGM, 2019
- 2. https://ima-contentfiles.s3.amazonaws.com/Ne201_AnorectalManometry.pdf

Disclosure: Nothing to disclose.

PP0797

DISORDERS OF GUT BRAIN INTERACTIONS FOLLOWING SALMONELLA GASTROENTERITIS: A 30-YEARS LONGITUDINAL AND PROSPECTIVE STUDY

G. Marasco¹, D. Meacci¹, C. Cremon², M.R. Barbaro³, V. Stanghellini¹, G. Barbara¹
¹University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ²St.Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy, ³University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: giovannimarasco89@gmail.com
Introduction: Salmonella Enteritidis, a Gram-negative bacterium, poses a significant threat to gastro-intestinal health, often leading to widespread outbreaks. Acute gastroenteritis increases the likelihood of developing a disorder of gut brain interaction (DGBI), such as irritable bowel syndrome (IBS) and functional dyspepsia (FD). This study investigates the long-term risk of DGBI development 30 years post-Salmonella exposure and explores additional predictive factors.
Aims & Methods: In 1994 a Salmonella Enteritidis outbreak involved 36 schools in Bologna, 1811 individuals tested positive for this bacterium in stool cultures. Following this event, a prospective cohort study was initiated after 30 years. 300 subjects were randomly selected and assessed for DGBI prevalence using Rome III and Rome IV questionnaires, persistent gastrointestinal symptoms via the Gastrointestinal Symptoms Rating Scale (GSRS), anxiety and depression levels with the Hospital Anxiety and Depression Rating Scale (HADS), and quality of life using the SF12 questionnaire (12 item short form). The exposed group comprised 150 people who contracted S. Enteritis infection in 1994, while the control cohort consisted of individuals, matched for sex, age and geographic origin, who had not experienced a bacterial gastroenteritis. The DGBI course was estimated by comparing our results with a previous follow-up carried out in 2009.

Results: Questionnaires were completed by 175 subjects (58,3%, 88 cases and 87 controls). Among the exposed subjects 39.8% developed IBS and 34.1% FD compared to 6.9% IBS and 4.6% FD in the control group ($p<0.001$). Multivariate logistic regression in the study population revealed predictive factors for IBS: S. Enteritidis infection [Odd Ratio (OR) 7.056, 95% CI 2.684-18.554, $p<0.001$] and anxiety level evaluated in 2024 (OR 1.244, 95% CI 1.105-1.400, $p<0.001$).

Similarly, predictors for FD included S. Enteritidis infection (OR 10.218, 95% CI 1.259-82.925, $p=0.03$), anxiety level assessed in 2009 (OR 1.212; 95% CI 1.058-1.390, $p=0.006$), and Mental component summary (MCS) score (OR 0.047; 0.002-0.985; $p=0.049$).

Notably, anxiety level evaluated in 2024 was predictive of IBS development in the exposed group, while anxiety level in 2009, along with MCS score, was predictive for FD. We found an increased IBS and decreased FD occurrence in 2024 compared to 2009 follow-up.

Exposed individuals exhibited a statistically significant higher rates and severity rates of gastrointestinal symptoms in the following areas: abdominal pain, hunger pains, diarrhea, loose stools, urgency, rumbling bloating, constipation, hard stools and incomplete emptying. Psychiatric comorbidities resulted more common in exposed group than in non-exposed one, in particular anxiety evaluated in 2024 (31.8% vs 10.3%, $p=0.002$). The exposed group showed lower scores in all SF12 subcategories compared to the control group.

	OVERALL (n = 175)	CASES (n = 88)	CONTROLS (n= 87)	P
ROME IV				
IBS, n (%)	41 (23.4)	35 (39.8)	6 (6.9)	<0.001
FD, n (%)	34 (19.4)	30 (34.1)	4 (4.6)	<0.001
PDS, n (%)	21 (12.0)	17 (19.3)	4 (4.6)	0.003
EPS, n (%)	19 (10.9)	19 (21.6)	0	<0.001
OVERLAP PDS-EPS, n (%)	6 (3.4)	16 (18.1)	1 (1.2)	<0.001
HADS				
Depression, Mean (SD)	3.68 ± 2.83	3.92 ± 3.01	3.43 ± 2.63	0.433
Anxiety, Mean (SD)	5.33 ± 3.42	6.19 ± 3.92	4.47 ± 2.63	0.001

Conclusion: This study, following a 1994 foodborne culture-proven S. Enteritis outbreak, highlights that a bacterial gastroenteritis is a major risk factor for IBS and for FD even after 30 years from the infection.

Disclosure: Nothing to disclose.

PP0798

TESTING FOR INTOLERANCE TO FRUCTANS, A LONG-ACTING FODMAP, IN 600 PATIENTS WITH DISORDERS OF GUT-BRAIN INTERACTION (DGBI)

C.H. Wilder-Smith¹, A. Materna¹
¹Brain-Gut Research Group, Gastroenterology Group Practice, Bern, Switzerland

Contact E-Mail Address: info@ggpg.ch
Introduction: Fructans or fructooligosaccharides are included in the spectrum of FODMAP (fermented) sugars, which are relevant in the induction of symptoms in patients with disorders of gut-brain interaction (DGBI) and in non-coeliac gluten sensitivity (1). Fructans have been shown to induce visceral hypersensitivity, an increase in mucosal mast cells, and changes in the colonic mucosal barrier in mice, and hypersensitivity associated with an altered gut microbiome in humans (2-5). Breath tests are used in the assessment of intolerances to several FODMAPs, but the test is poorly standardised for fructans (6).

Aims & Methods: A standardised breath test with fructans (10g Orafit[®] HSI) was performed after a 24-hour low-FODMAP diet and >8-hour fast. Exhaled hydrogen and methane concentrations were measured every 30 minutes until 5h, and synchronised symptom assessments performed for 24h (composite symptom index score, SI, 7) in 600 successive male (33%) and female patients of average age 41 years referred to our gastroenterology practice with DGBI (irritable bowel syndrome and/or functional dyspepsia, Rome 4 criteria).

Breath gas concentration thresholds of >20ppm and >8ppm above baseline were used for hydrogen and methane, respectively.

Results: The SI was positive in 61.2% (n=367) of patients within 24 hours of fructan ingestion. The SI peaked in the first 3 hours in 17.5% (n=105) and in the first 5 hours in 42.5% (n=255) of patients. Suprathreshold increases in hydrogen and methane concentrations within 5 hours were seen in 62.7% and 14.9% of patients, respectively. Discordant SI and breath gas results were obtained in 35.1% (hydrogen) and 57.8% (methane) of patients. A negative SI with a suprathreshold hydrogen or methane result occurred in 18.2% and 5.2%, respectively.

A positive SI with a subthreshold hydrogen or methane result occurred in 16.9% and 52.6%, respectively. Suprathreshold concentrations in methane and not in hydrogen were apparent in 4.5%. Main symptoms during tests were excessive flatulence (58.8%), bloating (50.3%), abdominal fullness (49.3%), abdominal cramps (29.0%), nausea (26.7%), GORD (26.7%), diarrhoea (9%) and extra-GI symptoms (16.2%).

Conclusion: Standardised oral provocation with fructans resulted in familiar clinical symptoms in a majority of patients with DGBI, suggesting a high prevalence of fructan intolerance. Due to the slow fermentation of intestinal fructans and the associated delayed symptoms, prolonged data collection over at least 12, preferably 24 hours is recommended. The test duration of 3 hours currently commonly used in test centres is inadequate. Symptom and breath gas concentration results are often divergent, as is known from other FODMAP breath tests, and validation against clinical outcome results is required. Fructans are of interest in DGBI as the current literature suggests they have both protective as well as detrimental effects on intestinal physiology, which may be dependent on the resident microbiota.

References:

1. Gryl et al. *Gastroenterology* 2018;154:529–539
2. Kamphuis JBJ et al. *Gastroenterology* 2020;158:652–663
3. Chen BR et al. *World J Gastroenterol* 2017;23:8321–8333
4. Kamphuis JBJ et al. *FASEB J.* 2022;36:e22297
5. Chumtazi BP et al. *Aliment Pharmacol Ther* 2021;53:499–509
6. Fedewa A et al. *Curr Gastroenterol Rep* 2014;16:370
7. Wilder-Smith CH et al. *Aliment Pharmacol Ther* 2013;37:1074–83

Disclosure: Nothing to disclose.

PP0799

CHARACTERISTICS OF PATIENTS WITH CARBOHYDRATE INTOLERANCE IN DISORDERS OF GUT-BRAIN INTERACTION

H. Mikhael-Moussa¹, C. Desprez^{1,2}, A.-M. Leroi^{1,2}, F. Mion³, G. Gourcerol^{1,2}, C. Melchior^{1,4}

¹Univ Rouen Normandie, INSERM, Normandie Univ, ADEN UMR1073, Nutrition, Inflammation and microbiota-gut-brain axis, Rouen, France, ²Department of Physiology, CHU Rouen, Rouen, France, ³Hospices Civils de Lyon, Digestive Physiology, Lyon, France, ⁴Department of Gastroenterology, CHU Rouen, Rouen, France

Contact E-Mail Address: hiba.mikhael-moussa@univ-rouen.fr

Introduction: Patients with Disorders of Gut-Brain Interaction (DGBI) often experience meal-related symptoms, potentially due to carbohydrate intolerances like fructose and/or lactose. While breath tests are common for exploring carbohydrate malabsorption, assessing intolerances, defined by the onset of gastrointestinal (GI) symptoms after a defined load of carbohydrates, is valuable. The adult carbohydrate perception questionnaire (aCPQ) can be used for detecting carbohydrate intolerances (1).

Aims & Methods: We aimed to determine lactose and fructose intolerance prevalence in DGBI and characterize these patients. DGBI patients who underwent fructose (25g) and lactose (25g) breath tests alongside the aCPQ in our tertiary center between May 2022 and December 2023 were included. Carbohydrate intolerance was a 20 mm increase in any of the five Visual Analog Scales (VAS) scores (for abdominal pain, nausea, diarrhea, bloating, and flatulence) in aCPQ. An increase from baseline of ≥ 20 ppm in exhaled H₂ or ≥ 10 ppm of CH₄ (≥ 20 ppm for fructose) indicated malabsorption. Patients completed questionnaires on irritable bowel syndrome (IBS) symptom severity (IBS-SSS), somatic symptoms (PHQ-15), quality of life (QOL)(GIQLI), anxiety, and depression (HAD).

Results: We included 314 DGBI patients, among them, 124 were lactose intolerant, 138 were fructose intolerant, and 77 were intolerant to both carbohydrates. Lactose intolerant patients were younger (42 ± 15.9 vs 46 ± 15.3 ; $p=0.022$), and more likely to have lactose malabsorption and fructose intolerance, while fructose intolerant patients were more likely to have fructose malabsorption, lactose intolerance, and higher anxiety/depression levels. Both intolerant groups were more likely to be female (81.5% vs 61.6%; $p<0.0001$ for lactose, 77.5% vs 63.1%; $p=0.006$ for fructose), with 2 DGBI or more (63.1% vs 40.7%; $p<0.0001$ for lactose, 57.4% vs 43.5%; $p=0.021$ for fructose), to have a reduced QOL, higher levels of GI symptoms, and somatic symptoms (table).

Variable	Positive Lactose Intolerance (n=124)	Negative Lactose Intolerance (n=190)	P-value	Positive Fructose Intolerance (n=138)	Negative Fructose Intolerance (n=176)	P-value
Positive Lactose Malabsorption	49 (39.5)	29 (15.3)	<0.0001	38 (27.5)	40 (22.7)	0.328
Positive Fructose Malabsorption	36 (29)	45 (23.7)	0.290	49 (35.5)	32 (18.1)	<0.0001
Positive Fructose Intolerance	77 (62.1)	61 (32)	<0.0001			
Positive lactose intolerance				77 (55.8)	47 (26.7)	<0.0001
GIQLI	86 $\pm$ 20.85	95 $\pm$ 19.49	<0.0001	85.1 $\pm$ 19.96	96.4 $\pm$ 19.45	<0.0001
IBS-SSS	252 $\pm$ 100.87	207 $\pm$ 101.53	<0.0001	255.6 $\pm$ 98.48	201.2 $\pm$ 101.06	<0.0001
HAD-Anxiety	7.9 $\pm$ 4.11	7.8 $\pm$ 4.03	0.970	8.4 $\pm$ 3.97	7.4 $\pm$ 4.08	0.032
HAD-Depression	5.7 $\pm$ 3.8	5.2 $\pm$ 3.6	0.233	6 $\pm$ 3.74	4.9 $\pm$ 3.63	0.012
PHQ-15	13 $\pm$ 5.51	10 $\pm$ 4.97	0.0001	13 $\pm$ 5.34	10 $\pm$ 4.98	<0.0001

Table: Comparison of DGBI patients with and without lactose and fructose intolerance.

Values are n (%), or mean $\pm$ SD.

GIQLI, Gastrointestinal Quality of Life Index; IBS-SSS, irritable bowel syndrome symptom severity score; HADS, Hospital Anxiety and Depression Scale; PHQ-15, patient health questionnaire 15.

Logistic regressions showed independent associations of female sex, fructose intolerance, and lactose malabsorption with the lactose intolerance variable, and IBS symptom severity, lactose intolerance, and fructose malabsorption with the fructose intolerance variable.

Conclusion: DGBI patients with lactose and fructose intolerance exhibit severe IBS symptoms and reduced QOL. Interestingly, intolerance to one carbohydrate is associated with malabsorption of this specific carbohydrate and the coexistence of intolerance to the other carbohydrate.

References: 1. Hammer, Johann et al. *European journal of gastroenterology & hepatology* 2021, doi:10.1097/MEG.0000000000001880

Disclosure: CM has served as a consultant/advisory board member for KyowaKirin, Norgine, Biocodex, Mayoly Spindler, Tillots, Ipsen, Nestlé HealthScience and Viatrix.

FM has served as a consultant/speaker for Laborie, Medtronic, Dr Falk Pharma.

GG has served as a consultant/speaker for Laborie, Medtronic, Kyowa Kirin, Lilly and Enterra medical.

PP0800

THE EFFECT OF MICROBIOTA ON ZONULIN EXPRESSION IN FECES IN PATIENTS WITH FUNCTIONAL BOWEL DISEASES

K. Khalaidzheva¹, E. Shikh¹, V. Drozdov¹

¹M. Sechenov First Moscow State Medical University, Ministry of Health of the Russian Federation, 119991, Moscow, Russian Federation, Moscow, Russian Federation

Contact E-Mail Address: Kseniyakhalaidzheva@mail.ru

Introduction: violations of the “gut-brain” axis, changes in intestinal permeability, as well as changes in the qualitative and quantitative composition of the intestinal microbiota.

Zonulin is a protein of intercellular tight contacts capable of reversibly affecting intestinal permeability. It is well known that the main provocateurs of zonulin production are gluten and bacteria. Taking into account the research data indicating differences in the microbial composition in patients with functional intestinal diseases and healthy volunteers, it can also be assumed that their zonulin levels change, as well as its decrease after treatment of such patients with probiotics.

Aims & Methods: To evaluate the relationship between probiotic intake and changes in zonulin levels in patients with functional bowel diseases. We determined zonulin levels in 108 patients with functional bowel diseases, such as functional constipation (FC), functional diarrhea (FD), irritable bowel syndrome with diarrhea (IBS-D) and constipation (IBS-C), before and 4 weeks after taking a multi-strain probiotic containing *Lactobacillus acidophilus* 1.25 x 10⁹ SFU, *Bifidobacterium lactis* - 1.25 x 10⁹ SFU, *Lactobacillus paracasei* - 1.25 x 10⁹ SFU, *Lactobacillus rhamnosus* - 1.25 x 10⁹ SFU.

Zonulin concentration in feces was determined by enzyme immunoassay (Human insulin ELISA kit zonulin, 96 (BlueGene Biotech Shanghai (PRC))). Zonulin levels were assessed as follows:

- within the reference values – less than 83.5 ng/ml
- elevated levels – from 83.5 to 110 ng/ml
- high level – more than 110 ng/ml).

Results: According to the data obtained during our study, the level of zonulin in feces ranged from 13.6 to 458.5 ng/ml, and the median values were 113.5 (98.6-122.9; 95% CI) ng/ml. Zonulin was detected within the reference values in 30 (28%) patients, an elevated level in 24 (22%) patients, and a high level in 54 (50%). When comparing for each of the 4 functional diseases, it was noted that patients with IBS-D were statistically significantly more likely to have an increase in zonulin levels above the reference, compared with IBS-C - 86.0% vs 55.6% (p=0.019; according

to the Fisher criterion) and compared with FC - 86.0% vs 58.0% (p=0.033; according to the Fisher criterion). In patients with FD, there was also a statistically significant difference in the frequency of increased zonulin in feces: 81.0% vs 55.6% (p=0.013; according to Fisher's criterion) between FD and IBS-C and 81% vs 58.0% between FD and FC (p=0.014; according to Fisher's criterion). When comparing IBS-C and FC, as well as IBS-D and FD, there was no statistically significant difference.

Against the background of probiotic therapy for 4 weeks, zonulin levels ranged from 13.6 to 173.7 ng/ml, the median was 82.3(73.9-93.9) ng/ml. In patients with IBS-D, as well as in FD, there was a statistically significant decrease in the level of zonulin in feces: the median values decreased from 121.7 to 67.8 ng/ml (p=0.027) in IBS-D and from 130.7 to 81.1 ng/ml (p=0.039) in FD. In patients with constipation syndrome, a decrease in indicators was also noted, but the results were not statistically significant: in IBS-C, zonulin levels decreased from 89.4 to 79.1 ng/ml (p=0.089), and in FC from 107.6 to 92.8 ng/ml (p=0.077).

Conclusion: Thus, the data of the conducted study show that functional intestinal diseases are associated with an increase in the level of zonulin in feces. The highest values were observed in patients with diarrheal syndrome. Probiotic therapy for 4 weeks had a positive effect on the level of zonulin in the stool.

Disclosure: Nothing to disclose.

PP0801

COLONIC VOLUMES IN IRRITABLE BOWEL SYNDROME AND HEALTHY INDIVIDUALS; THE ASSOCIATIONS WITH SYMPTOMS AND GUT PHYSIOLOGY

T. van Gils¹, E.B. Mark^{2,3}, H. Törnblom¹, A.M. Drewes^{2,3}, C.S. de Jonge^{4,5}, M. Simrén^{1,6}

¹Gothenburg University, Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, Gothenburg, Sweden, ²Aalborg University Hospital, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ³Aalborg University, Department of Clinical Medicine, Aalborg, Denmark, ⁴Amsterdam UMC location University of Amsterdam, Department of Radiology and Nuclear Medicine, Amsterdam, Netherlands, ⁵Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ⁶University of North Carolina at Chapel Hill, Center for Functional Gastrointestinal and Motility Disorders, Chapel Hill, United States of America

Contact E-Mail Address: tom_van_gils@hotmail.com

Introduction: The pathophysiological mechanisms of irritable bowel syndrome (IBS) are complex and incompletely known. Studies investigating the role of colonic volumes and their relation with symptoms and measurements of gut physiology in IBS are sparse.

Aims & Methods: The aim of this study was to explore the associations between colonic volume and symptoms and measurements of gut physiology in IBS and healthy individuals. We included 18 IBS patients (4 IBS-diarrhea, 5 IBS-constipation, 9 IBS-mixed or IBS-unspecified) and 19 healthy individuals. Total and segmental colonic volumes were determined by magnetic resonance imaging (MRI). The GSRS-IBS was used to measure gastrointestinal symptoms and a stool diary (Bristol Stool Form Scale) was completed 14 days before the MRI.

Oro-anal transit time (radiopaque markers) and rectal sensitivity (rectal barostat, including pressure thresholds for first perception, defecation, and discomfort) were measured.

Results: The total colonic volume did not differ between IBS patients and healthy individuals (736 ml [528-903] vs 597 [498-939] (median [IQR]));

$p=0.44$). In the IBS group, there were trends towards inverse associations between total colonic volume and the perceived severity of diarrhea ($r_s = -0.43$; $p=0.08$), as well as the volume of the descending colon and stool frequency ($r_s = -0.48$; $p=0.07$). Other GI symptoms and stool consistency were not associated with colonic volumes. When investigating the physiological parameters in IBS, the total colonic volume was positively associated with oro-anal transit time ($r_s = 0.54$; $p=0.02$) and negatively associated with rectal pressure thresholds for sensations (first perception: $r_s = -0.51$; $p=0.04$, defecation: $r_s = -0.44$; $p=0.09$), Table 1. A similar pattern was seen when investigating individual colonic segments, with tendencies towards positive associations between segmental colonic volumes and oro-anal transit time, and negative associations with rectal sensory thresholds. The associations in healthy individuals between colonic volumes and oro-anal transit time and rectal sensitivity, respectively, were overall weaker (all $p>0.05$).

	Total colonic volume (ml)	
	IBS	Healthy individuals
Oro-anal transit time (days)	0.54*	0.37
Rectal barostat		
First perception (mmHg)	- 0.51*	- 0.21
Defecation (mmHg)	- 0.44	- 0.14
Discomfort (mmHg)	- 0.15	- 0.02

Table 1. Spearman's correlation between total colonic volume measured with magnetic resonance imaging and oro-anal transit time (radiopaque markers) and rectal barostat.

* $p \leq 0.05$

Conclusion: In this pilot study, we have shown that larger colonic volumes, measured with MRI, seem to be associated with slower oro-anal transit and rectal hypersensitivity in IBS. This suggests a potential role for measuring colonic volumes in IBS pathophysiology studies, but larger studies are needed to better appreciate subtype differences and their relevance for symptoms.

Disclosure: Nothing to disclose.

PP0802

DIFFERENCES IN SYMPTOMS AND GUT PHYSIOLOGY BETWEEN IRRITABLE BOWEL SYNDROME SUBGROUPS IDENTIFIED BY MIXTURE MODEL ANALYSIS

T. van Gils¹, J. Algera¹, I. Midenfjord¹, H. Törnblom¹, M. Simrén^{1,2}

¹Gothenburg University, Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, Gothenburg, Sweden, ²University of North Carolina at Chapel Hill, Center for Functional Gastrointestinal and Motility Disorders, Chapel Hill, United States of America

Contact E-Mail Address: tom_van_gils@hotmail.com

Introduction: Irritable bowel syndrome (IBS) is subtyped based on bowel habits. However, an alternative based on combined gastrointestinal (GI), non-GI somatic and psychological symptom profiles has been proposed^{1,2}.

Aims & Methods: This study aimed to validate the novel more comprehensive way to subgroup IBS and investigate differences in symptoms and gut physiology in these groups. In total, 760 IBS patients (Rome III and IV) from six study cohorts were included. Subgroups were based on Gaussian mixture model analysis using 13 single-item GI symptom scores (GSRS-IBS), stool frequency and consistency (Bristol Stool Form Scale), 11 single-item non-GI somatic symptom scores (PHQ-12, excluding menstruation problems), and anxiety and depression scores (HADS). Differences between subgroups were investigated for fatigue (MFI), GI-specific anxiety (VSI), IBS-specific quality of life (IBS-QOL), and measurements of gut physiology, including oro-anal transit time (OATT) assessed by radiopaque

markers, visceral sensitivity assessed by a rectal barostat procedure and lactulose nutrient challenge test (LNCT), and breath hydrogen and methane production during LNCT as markers for microbial fermentation.

Results: Six subgroups based on GI and non-GI symptom profiles were identified: diarrhea with low comorbidities ($n=67$), constipation with low comorbidities ($n=120$), overall mild severity ($n=166$), diarrhea with high comorbidities ($n=231$), constipation with high comorbidities ($n=89$), and mixed GI symptoms with high comorbidities ($n=87$). The groups with high comorbidities had higher levels of fatigue and GI-specific anxiety, and lower QOL compared to the low comorbidities groups, Table 1. OATT was longer in constipation with low comorbidities vs diarrhea with low comorbidities (1.7 [1.0-2.7] vs 0.9 [0.5-1.3] days (median [IQR]), $p<0.01$), but there was no difference in OATT comparing constipation with high comorbidities vs. diarrhea with high comorbidities. Visceral sensitivity and postprandial hydrogen and methane production did not differ between groups, but with a tendency of methane production to be highest in constipation with high comorbidities.

	Diarrhea, Low comorbidities	Constipation, Low comorbidities	Overall mild severity	Diarrhea, High comorbidities	Constipation, High comorbidities	Mixed GI, High comorbidities	p-value
High fatigue (general fatigue score ≥ 13)	61 %	52 %	53 %	69 %	79 %	87 %	<0.001
GI-specific anxiety (VSI), Median (IQR)	45 (36, 54)	41 (31, 53)	40 (27, 51)	45 (32, 56)	47 (34, 58)	53 (41, 62)	<0.001
Quality of life							
IBS-QOL (total) Median (IQR)	70 (62, 79)	65 (56, 79)	71 (65, 83)	65 (54, 75)	55 (47, 65)	56 (38, 68)	<0.001
Gut physiology							
Oro-anal transit time (days), Median (IQR)	0.9 (0.5, 1.3)	1.7 (1.0, 2.7)	1.1 (0.8, 2.0)	1.3 (0.9, 2.0)	1.3 (0.9, 1.9)	1.2 (0.9, 2.2)	<0.01
Rectal barostat (discomfort Z-score*), Median (IQR)	0.22 (-0.22, 0.44)	-0.24 (-0.79, 0.97)	-0.24 (-0.75, 0.47)	-0.16 (-0.75, 0.37)	-0.24 (-0.75, 0.27)	-0.24 (-0.79, 0.09)	0.20
Exhaled hydrogen (LNCT, AUC), Median (IQR)	5415 (3233, 12473)	7388 (5344, 10009)	6758 (3278, 9825)	5708 (4035, 9938)	7155 (3600, 8715)	6210 (3986, 11505)	0.73
Exhaled methane (LNCT, AUC), Median (IQR)	1050 (525, 2220)	1403 (701, 3270)	1320 (743, 2460)	1170 (683, 4073)	2280 (1050, 5535)	1140 (529, 2513)	0.09

Table 1. Symptoms, quality of life and gut physiological parameters.

* Z-scores of rectal barostat discomfort thresholds (mmHg) based on different protocols AUC, area under the curve; IQR, interquartile range; LNCT, lactulose nutrient challenge test; VSI, visceral sensitivity index

Conclusion: We have confirmed previously reported IBS subgroups based on combinations of GI and non-GI symptom profiles. Demonstrated associations with fatigue, GI-specific anxiety, and oro-anal transit time, suggest different pathophysiological mechanisms in these novel subgroups. Our results suggest that the presence or absence of non-GI symptoms could be important when planning IBS treatment strategies.

References: 1. Black CJ, Ng CE, Goodoory VC, Ford AC. Novel Symptom Subgroups in Individuals With Irritable Bowel Syndrome Predict Disease Impact and Burden. *Clin Gastroenterol Hepatol.* 2024;22(2):386-396.e310. 2. Polster A, Van Oudenhove L, Jones M, Öhman L, Törnblom H, Simrén M. Mixture model analysis identifies irritable bowel syndrome subgroups characterised by specific profiles of gastrointestinal, extraintestinal somatic and psychological symptoms. *Aliment Pharmacol Ther.* 2017;46(5):529-539.

Disclosure: Nothing to disclose.

M. Semen¹, O. Lychkovska¹, V. Semen²¹Danylo Halytsky Lviv National Medical University, Department of Propaedeutic Pediatrics and Medical Genetics, Lviv, Ukraine,²Lviv Regional Children's Clinical Hospital "OHMATDYT", Pediatrics Department, Lviv, Ukraine

Contact E-Mail Address: martasemen4@gmail.com

Introduction: In accordance to Rome IV Criteria irritable bowel syndrome (IBS) is classified into four subtypes: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), with mixed bowel habits (IBS-M) or IBS, unsubtyped. Some authors distinguish a post-infectious subtype of IBS, in which an acute episode of infectious gastroenteritis is a trigger of the disorder.

In all the other cases, mostly psycho-emotional stress is the trigger factor, with this variant being defined as stress-associated subtype of IBS.

Aims & Methods: Aim: to study the peculiarities of the formation and course of IBS in children, depending on the trigger factor. A total of 54 patients aged 6-12 years with a verified diagnosis of IBS according to Rome criteria IV have been examined. The trigger factor of the onset of IBS was established by the interrogation of patients and their parents. The levels of trait anxiety and somatization were assessed by Children's Form of the Manifest Anxiety Scale (CMAS) questionnaire and Somatoform Symptom Screening (SOMS) test respectively.

The *Catechol-O-methyltransferase* (COMT) gene val158met polymorphism was estimated by the polymerase chain reaction. Enzyme immunoassay Ridascreen Calprotectin (R-Biopharm AG, Germany) was used for the quantitative determination of calprotectin in stool samples.

Results: We have diagnosed post-infectious subtype of IBS in 30 children. In this group we have found significantly higher concentration of fecal calprotectin (60.0 (35.6; 129.0) vs 31.2 (21.1; 58.7 µg/g)), which is consistent with pathogenesis of this subtype of IBS. On the contrary, we have discovered that psycho-emotional stress was the trigger factor of the onset of IBS in 22 patients (stress-associated subtype of IBS). Children with stress-associated IBS had higher levels of trait anxiety (25.1±5.7 vs. 18.7±6.4) and somatization (11.1 ± 4.0 vs. 8.6 ± 3.1) in comparison to patients with post-infectious subtype of the disorder. Furthermore, the analysis of the COMT gene val158met polymorphism revealed, that almost the half patients (48%) with stress-associated IBS had 472 AA (Met/Met) genotype. Met/Met carriers have genetically determined low enzymatic activity of COMT, which may lead to decreased elimination of catecholamines and is associated with chronic stress. In contrast, only 31% of children with post-infectious subtype of IBS were found to have 472 AA (Met/Met) genotype.

Conclusion: Our study suggests that not only predominant bowel habit, but also trigger factor in the development of IBS determine the heterogeneity of the disorder. This approach may be used for classification of IBS in children, as it dictates treatment strategy.

References: 1. Lacy, B. E., & Patel, N. K. (2017). Rome Criteria and a Diagnostic Approach to Irritable Bowel Syndrome. *Journal of clinical medicine*, 6(11), 99. <https://doi.org/10.3390/jcm6110099>

2. Barbara, G., Cremon, C., Pallotti, F., De Giorgio, R., Stanghellini, V., & Corinaldesi, R. (2009). Postinfectious irritable bowel syndrome. *Journal of pediatric gastroenterology and nutrition*, 48(2), S95–S97. doi:10.1097/MPG.0b013e3181a15e2e

3. Chen, J., Lipska, B. K., Halim, N., Ma, Q. D., Matsumoto, M., Melhem, S., ...& Weinberger, D. R. (2004). Functional analysis of genetic variation in catechol-O-methyltransferase (COMT): effects on mRNA, protein, and enzyme activity in postmortem human brain. *American journal of human genetics*, 75(5), 807–821. doi.org/10.1086/425589

4. Semen, M. O., Lychkovska, O. L., Tyrkus, M. Y., Kaminsky, D. V., & Yelisyeyeva, O. P. (2023). Association between Val158Met polymorphism in the COMT gene with anxiety and heart rate variability in children with irritable bowel syndrome. *Zaporozhye Medical Journal*, 25(5), 439–446. <https://doi.org/10.14739/2310-1210.2023.5.278878>

Disclosure: Nothing to disclose.

PP0804

THE LINK BETWEEN ALEXITHYMIA, PSYCHOLOGICAL COMORBIDITIES
AND THE SEVERITY OF IRRITABLE BOWEL SYNDROMEF. Wuestenberghs^{1,2}, N. Ezratty¹, P. Jouet¹, M. Benallaoua¹, N. Demaré¹, J.-J. Raynaud¹, R. Benamouzig^{1,2}, J.-M. Sabaté^{1,3}¹Sorbonne Paris Nord University, Assistance Publique - Hôpitaux de Paris (AP-HP), Avicenne Hospital, Department of Gastroenterology and Digestive Oncology, Bobigny, France, ²Paris-Saclay University, AgroParisTech, INRAE, UMR 914, Physiology of Nutrition and Eating Behaviour (PNCA), Palaiseau, France, ³Paris-Saclay University, INSERM, UMR 987, Pathophysiology and clinical Pharmacology of Pain Laboratory (LPPD), Boulogne-Billancourt, France

Contact E-Mail Address: fabien.wuestenberghs@hotmail.com

Introduction: Irritable bowel syndrome (IBS) is a disorder of gut-brain interactions that combines abdominal pain and transit disorders in the Rome IV classification. The severity of IBS varies from patient to patient and is influenced by psychological comorbidities such as anxiety and depression. Alexithymia, also called emotional blindness, is the difficulty in identifying and expressing one's own emotions and feelings or those of others, and is present in 2-20% of healthy subjects. It is frequently found in different types of chronic pain disorders and has also been described in IBS (1). The association between alexithymia and pain intensity varies according to the studies and the type of pain, however. The aim of our study was to assess the prevalence of alexithymia in patients with IBS and to look for links between this trait and both the clinical phenotype of the disorder and the levels of anxiety and depression of the patients.

Aims & Methods: This study was carried out, after approval from a local ethics committee, between January and August 2023 in consecutive patients suffering from IBS according to Rome IV criteria assessed in a multidisciplinary day hospital setting (workup by a neurogastroenterologist, a dietician and a psychologist). Clinical characteristics (age, gender, subtype of IBS, disease duration and severity (IBS-SSS)), levels of anxiety-depression (HADS), quality of life (EQ-5D) and alexithymia (TAS-20, a score composed of 20 questions rated from 1 to 5, maximum score of 100, high-level cutoff >60) were recorded.

Results: We included 76 IBS patients (67.1% female; mean age 48.3 ± 16.9 years; BMI 22.1 ± 4.0 kg/m²). The median duration of the disorder was 13 years (IQR 6.7 - 26.4). All subtypes were represented (IBS-D 27.6%, IBS-C 48.7% and IBS-M 17.1%). The majority of patients had a moderate-severe disorder, with a mean IBS-SSS score of 318 ± 107 points (minimal, moderate and severe forms in 1.3%, 34.7% and 58.7% respectively, and remission in 5.3%). Quality of life was impaired, with a median EQ-5D health score of 50 (IQR 35.0-69.5). The HADS-A subscore was 10.8 ± 4.4 points, with 59.7% of patients with definite anxiety (>11), while the HADS-D subscore was 6.2 ± 3.6 points, with 16.4% of patients with definite depression (>11). The total HAD score was 17.0 ± 6.7 points. The severity of IBS was correlated with depression (rho 0.35, p=0.005) and inversely correlated with quality of life (rho -0.28, p=0.02) scores. The mean alexithymia score was 58.7 ± 9.8 points, with 45.4% of patients having a high level of alexithymia (TAS-20 >60). The level of alexithymia was not different between men and women (58.1 ± 9.5 vs 59.8 ± 10.2; p=0.48) and was not influenced by the duration of the disorder (p=0.92). Alexithymia correlated well with

anxiety ($\rho = 0.33$, $p = 0.007$), depression ($\rho = 0.36$, $p = 0.003$) and quality of life ($\rho = -0.31$, $p = 0.016$) scores but not with IBS severity ($\rho = 0.17$, $p = 0.18$). However, the level of IBS severity was greater in the case of high levels of alexithymia (IBS-SSS of 359.2 ± 73.1 vs 298.4 ± 107.7 points for a TAS-20 > 60 vs ≤ 60 ; $p = 0.009$).

Conclusion: In this series of patients with moderate-severe IBS and all subtypes, a high level of alexithymia was found in almost one out of two patients. Alexithymia was linked to the level of anxiety-depression and the deterioration in quality of life. Patients with a high level of alexithymia had more severe IBS. The prognostic value of alexithymia for the response to treatments such as hypnotherapy and cognitive behavioural therapies deserves to be evaluated in patients with IBS.

References: (1) Porcelli et al. Alexithymia and gastrointestinal-specific anxiety in moderate to severe irritable bowel syndrome. *Comprehensive Psychiatry* 2014; 55: 1647-1663.

Disclosure: Nothing to disclose.

PP0805

PSYCHIATRIC DIAGNOSES AND DISEASE BURDEN IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

M. Khadija¹, I. Midenfjord¹, E. Ordell Sundelin¹, I.A. Trindade¹, H. Tjörnblom¹, J. Santos², D. Mulder³, A. Arias Vasquez³, G. Ruesing⁴, A. Reif⁴, M. Aichholzer⁴, M. Van den Houte⁵, L. Van Oudenhove⁶, M. Chiara Matteucci⁷, G. Barbara⁷, M. Bosman⁸, D. Jonkers⁸, J.A. Ramos-Quiroga⁹, E. Jekkel¹⁰, I. Bitter¹⁰, A.-V. Pop¹¹, D.L. Dumitrascu¹¹, C. Alonso Cotoner², A. Rodríguez-Urrutia⁹, M. Simrén¹

¹Institute of Medicine, Internal Medicine and Clinical Nutrition, Gothenburg, Sweden, ²CIBEREHD, Vall d'Hebron Hospital Universitari, Barcelona, Spain, ³Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands, ⁴Johann Wolfgang Goethe-Universität Frankfurt am Main, Frankfurt, Germany, ⁵Laboratory for Brain-Gut Axis Studies (LABGAS), Translational Research Center for Gastrointestinal Disorders (TARGID), Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium, ⁶Laboratory for Brain-Gut Axis Studies (LABGAS), Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium, ⁷University of Bologna and IRCCS Azienda Ospedaliero Universitaria di Bologna, Medical and Surgical Sciences, Bologna, Italy, ⁸NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center, Gastroenterology-Hepatology, Maastricht, Netherlands, ⁹CIBERSAM, Vall d'Hebron Hospital Universitari, Barcelona, Spain, ¹⁰Semmelweis University, Psychiatry and Psychotherapy, Budapest, Hungary, ¹¹Iuliu Hatieganu University of Medicine and Pharmacy, Second Medical, Cluj-Napoca, Romania

Contact E-Mail Address: mahrukh584@gmail.com

Introduction: Psychiatric comorbidity, most commonly measured as severity of anxiety and depression symptoms, has been found to be associated with IBS symptom severity. However, available studies have rarely assessed the importance of formal psychiatric diagnoses on disease burden in IBS. In this analysis from a pan-European project (DISCOVERIE) focusing on the relevance of comorbid mental (anxiety, depression) and/or somatic (fibromyalgia, chronic fatigue syndrome) diagnoses in patients with IBS, we aimed to assess whether presence of psychiatric diagnoses according to the DSM-5 criteria has an impact on overall symptom severity in IBS.

Aims & Methods: We included patients with IBS according to the Rome IV criteria from nine different European centers. Exclusion criteria included the presence of severe psychiatric disease (i.e. bipolar disorder, schizophrenia, autism spectrum disorder, schizoaffective disorder, or organic psychiatric disorder demanding psychopharmacotherapy, psychiatric day-care or inpatient treatment). The patients underwent The Mini International Neuropsychiatric Interview (MINI) to diagnose major psychiatric diagnoses (a total of 17). Fibromyalgia and chronic fatigue were diagnosed by current diagnostic criteria. They also filled in questionnaires assessing Severity of IBS symptoms (IBS-SSS), depression (PHQ-9), anxiety (GAD-7), somatic symptoms (PHQ-15), and fibromyalgia symptoms (FIQ). Severity of symptoms were compared between groups with increasing number of psychiatric diagnoses using One-Way Between-Groups ANOVA with linear trend analysis.

Results: In total, 617 patients with IBS (median age 44 years, 80% females) were included. Among the IBS patients, 269 (44%) had none of the mental (anxiety, depression) or somatic (fibromyalgia, chronic fatigue syndrome) comorbidities (median age 44 y, 75% females), whereas 174 (28%) had comorbid mental disorder only (median age 38 y, 82% females), 49 (8%) had comorbid somatic disorder only (median age 50 y, 86% females) and 124 patients (20%) had mental and somatic comorbidities (median age 47 y, 86% females). The most common psychiatric diagnoses among the IBS patients were depression ($n = 284$), generalized anxiety disorder ($n = 145$) and panic disorder ($n = 38$) followed by agoraphobia ($n = 23$) and social anxiety ($n = 19$). Participants were divided into four groups according to the number of psychiatric diagnoses (0, 1, 2, and ≥ 3). The severity of IBS, depression, anxiety, somatic, and fibromyalgia symptoms all increased gradually with increasing number of psychiatric diagnoses. The effect sizes (partial eta squared) were small for IBS symptoms, medium for somatic symptoms and large for the other severity measures (Table 1).

	No. of psychiatric diagnoses (MINI)				Partial eta squared	P-value
	0 (n=355)	1 (n=83)	2 (n=84)	≥ 3 (n=95)		
IBS symptom severity (IBS-SSS)	230 [170–310]	267 [210–339]	254 [184–348]	282 [232–351]	0.017	0.002
Depression (PHQ-9)	4 [1–8]	8 [4–13]	10 [3–15]	13 [8–17]	0.170	<0.001
Generalized anxiety (GAD-7)	4 [1–7]	5 [3–9]	8 [5–14]	11 [8–15]	0.227	<0.001
Somatic symptoms (PHQ-15)	10 [7–14]	13 [10–16]	13 [8–19]	15.5 [12–21]	0.097	<0.001
Fibromyalgia symptoms (FIQ)	16 [6–29]	31 [17–45]	37 [19–55]	45 [27–62]	0.154	<0.001

Table 1: Symptom severity in groups with increasing number of psychiatric diagnoses

Scores presented as medians with interquartile range.

Conclusion: This multicenter pan-European study shows that psychiatric diagnoses are common among IBS patients and that the overall disease burden in IBS is associated with psychiatric comorbidity. These findings highlight the importance of taking psychiatric comorbidity into consideration and to acknowledge the relevance of gut-brain axis interactions when managing patients with IBS.

Disclosure: Hans Törnblom: Consultant or advisory board member for Allergan, Cinclus Pharma, Medifactia, and VIPUN and as a speaker for Tillotts, Takeda, and Shire.

Daisy Jonkers: Part of the work of DJ, outside the submitted work has been financed by public-private partnership grants of Top Knowledge Institute (TKI) Agri&Food and Health Holland, by the Carbokinetics program as part of the NWO-CCC Partnership Program, by Organic A2BV/Mothersfinest BV.

PP0806

AGREEMENT RATE OF ACUTE FOOD INDUCED MUCOSAL ALTERATIONS VISUALIZED USING CONFOCAL LASER ENDOMICROSCOPY IN IRRITABLE BOWEL SYNDROME PATIENTS

L. Balsiger¹, T. van Gils², Y. Hatem³, A. Blomsten², K. Raymenants^{1,4}, J. Hreinsson², C. Sina^{3,5}, M. Simrén^{2,6}, J. Tack^{1,4}
¹TARGID KU Leuven, Leuven, Belgium, ²Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ³University of Luebeck, Luebeck, Germany, ⁴University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium, ⁵Institute of Nutritional Medicine, University Hospital of Schleswig-Holstein, Campus Luebeck, Luebeck, Germany, ⁶Sahlgrenska University Hospital, Internal Medicine, Gothenburg, Sweden

Contact E-Mail Address: lukas.balsiger@proton.me

Introduction: Confocal laser endomicroscopy (CLE) enables real-time microscopic visualization of the duodenal mucosa during upper endoscopy and has shown acute food-triggered disruption of the epithelial barrier in the duodenum of irritable bowel syndrome (IBS) patients. While this technique offers novel scientific insights, image interpretation is subjective and agreement rates between observers are unknown.

Aims & Methods: We aimed to assess the agreement rate between assessors regarding acute food induced mucosal changes visualized by CLE in IBS. To this end we performed a multicentric, international post-hoc evaluation of CLE recordings. CLE sequences from three centers were blindly assessed. Five investigators from the three participating centers blindly assessed all videos both in real-time and in slow-motion in a random order, including some duplicates.

Mucosa was considered altered if fluorescein leakage AND “cell shedding” were simultaneously present. Outcomes of the global assessment were assessed using the binary outcome “altered” vs. “unaltered”. Agreement was quantified using Fleiss’ kappa for >2 assessors and Cohens’ kappa for 2 assessors – both are reported as κ .

Results: A total of 124 video sequences (94572 frames, 197 minutes of real-time recording) were reviewed. Intraindividual agreement rate was between 90 and 100% ($\kappa=0.74-1.00$). Overall interobserver agreement rate for all assessors and all videos was 86% ($\kappa=0.69$). Agreement rates were not higher when videos were assessed in slow-motion (81%, $\kappa=0.58$). Among the 3 centers, agreement between all blinded assessors and real-time assessment by the endoscopist ranged from 78% ($\kappa=0.55$) to 86% ($\kappa=0.67$). A total of 63 videos were judged the same by all assessors (100% agreement) – here agreement rates with the endoscopist were 97% ($\kappa=0.91$). Using these videos as reference, a cutoff of 2 altered spots in a recording of 5 spots showed a sensitivity and specificity of 100% for the presence or absence of alterations.

Conclusion: We report here for the first time the interobserver agreement rates of acute food induced mucosal alterations as visualized on CLE. The agreement rates were substantial overall – both among blinded assessors and between blinded assessors and real-time judgement by the endoscopist. Slow-motion revision did not increase agreement rates. A cutoff of 2/5 spots was ideal for the detection of acute mucosal alterations.

Disclosure: Nothing to disclose.

PP0807

IMPROVED LIPID AND GLUCOSE PROFILE IN IBS PATIENTS AFTER A DIETARY INTERVENTION WITH SSRD OR LOW FODMAP

B. Roth¹, M. D’Amato², B. Ohlsson³
¹Skane University Hospital, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden, ²Ikerbasque Research Professor Head, Gastrointestinal Genetics Lab CIC bioGUNE - BRTA, Derio, Spain, ³Skane University Hospital, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden

Contact E-Mail Address: Bodil.Ohlsson@med.lu.se

Introduction: Irritable bowel syndrome (IBS) is the most common disorder of gut-brain interaction (DGBI) and associated with other pain syndromes, lifetime stress, and psychological disorders. During the last years, associations have also been described between IBS and overweight and the metabolic syndrome. Low content of fermentable oligo-, di-, and monosaccharides and polyols (FODMAP) and a starch- and sucrose-reduced diet (SSRD) reduce IBS symptoms (1,2). However, concerns have been raised whether a diet may lead to malnutrition when adhered to for a longer time.

Aims & Methods: The aim of the study was to randomize IBS patients according to Rome IV with a total score of IBS-SSS > 175 to either SSRD or low FODMAP and measure nutritional status over time. 155 patients, 131 women (84.5%), age 42 (32-55) years, weight 69.2 (63.0-82.9) kg, BMI 25 (23-28) kg/m² were included. 77 received SSRD (5 dropouts) and 78 low FODMAP (6 dropouts) for 4 weeks, with a second follow-up at week 24. Rome IV, IBS-severity scoring system (IBS-SSS) and visual analog scale-IBS were completed at baseline, and after 4 and 24 weeks. Nutritional status, lipid profile, and glycosylated hemoglobin A1c (HbA1c) were analyzed in blood according to clinical routines at the laboratory. Differences were calculated by Wilxon Signed Ranks with values at week 4 and 24 in comparison with baseline. P<0.05 was considered statistically significant.

Results: There were no differences in baseline values between the groups. All gastrointestinal and extraintestinal symptoms were improved by both diets (p<0.001 in most variables). The weight reduction was most pronounced in SSRD. At week 4, folate was increased (p=0.003), and iron decreased (p=0.001), in the SSRD group, whereas vitamin D was increased in both groups (p=0.004 vs. p=0.017) and HbA1c was decreased (p=0.010 vs. p=0.009). The only negative nutritional measurement at week 24 was lower cobalamin levels in both groups (p=0.009 vs. p=0.002) and lower ferritin in the low FODMAP group (p=0.007). Cholesterol, low-density lipoprotein (LDL) cholesterol, and non-high-density lipoprotein (non-HDL) cholesterol were decreased throughout the study in the SSRD group, but only after 4 weeks in the low FODMAP group (Table).

	SSRD N = 77		Low FODMAP N = 78	
P-Cholesterol (3.3-6.9 mmol/L)	P-value		P-value	
Baseline	5.0 (4.4-5.6)		4.7 (4.4-5.8)	
4 weeks	4.8 (4.0-5.4)	0.007	4.9 (4.2-5.5)	0.003
24 weeks	4.8 (4.3-5.4)	0.009	4.8 (4.2-5.7)	0.166
P-LDL (1.4-4.7 mmol/L)				
Baseline	3.2 (2.7-3.8)		3.1 (2.7-3.8)	
4 weeks	3.0 (2.4-3.7)	0.004	3.0 (2.6-3.6)	0.036
24 weeks	3.0 (2.5-3.6)	0.017	3.0 (2.5-3.8)	0.088
P-non-HDL (1.9-5.1 mmol/L)				
Baseline	3.4 (2.8-4.0)		3.3 (2.8-4.1)	
4 weeks	3.3 (2.6-3.8)	0.015	3.2 (2.7-3.9)	0.002
24 weeks	3.2 (2.6-4.0)	0.008	3.3 (2.8-4.2)	0.164

Conclusion: Both SSRD and low FODMAP decrease gastrointestinal and extraintestinal symptoms. Although some nutritional analyses showed lower values after the intervention, other showed improved values. Metabolic risk factors such as weight, lipid values and HbA1c were improved by

the diets, especially SSRD. Thus, dietary interventions in IBS do not only improve symptoms but also improve lipid and glycemic profiles without any major impact on nutritional status when the IBS patients are followed for 6 months. Reducing carbohydrate intake appears to positively impact bowel symptoms and metabolism in IBS patients, irrespective of the specific carbohydrates targeted by the corresponding diet. Future studies are warranted to identify the individual saccharides most likely to exert therapeutic effects, eventually in relation to their breakdown capacity in individual patients.

References: Mitchell H, Porter J, Gibson PR, Barrett J, Garg M. Review article: implementation of a diet low in FODMAPs for patients with irritable bowel syndrome-directions for future research. *Aliment Pharmacol Ther.* 2019 Jan;49(2):124-139.

Nilholm C, Roth B, Ohlsson B. A Dietary Intervention with Reduction of Starch and Sucrose Leads to Reduced Gastrointestinal and Extra-Intestinal Symptoms in IBS Patients. *Nutrients.* 2019 Jul 20;11(7):1662.

Disclosure: Nothing to disclose.

PP0808

A STARCH- AND SUCROSE-REDUCED DIET HAS SIMILAR EFFICIENCY AS LOW FODMAP IN IBS. A RANDOMIZED NON-INFERIORITY STUDY

B. Roth¹, M. Nseir², H. Jeppsson³, K. Sundquist⁴, M. D'Amato⁵, B. Ohlsson¹

¹Skane University Hospital, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden, ²Lund University, Department of Clinical Sciences, Malmö, Malmö, Sweden, ³Skane University Hospital, Clinical Nutrition, Lund, Sweden, ⁴Lund University/Region Skåne, Centrum för Primärvårdsforskning (CPF), Institutionen för kliniska vetenskaper, Malmö (IKVM), Malmö, Sweden, ⁵Ikerbasque Research Professor Head/LUM University, Casamassima, Italy, Gastrointestinal Genetics Lab CIC bioGUNE - BRTA/Department of Medicine and Surgery, Derio, Spain

Contact E-Mail Address: Bodil.Ohlsson@med.lu.se

Introduction: A diet with low content of fermentable oligo-, di-, and monosaccharides and polyols (FODMAP) are established treatment for irritable bowel syndrome (IBS), with well-documented efficiency. Recently, a starch- and sucrose-reduced diet (SSRD) has shown similar promising effects.

Aims & Methods: This randomized, non-inferiority study aimed to test SSRD against low FODMAP and compare the responder rates to a 4-week dietary intervention of either diet.

The 155 IBS patients were randomized to SSRD (n=77) or low FODMAP (n=78) for 4 weeks, with a follow-up 20 weeks later. The SSRD advice means removal of sucrose and reduction of starch-containing food such as cereals, some vegetables (e.g., potatoes), rice, and pasta, with maintained gluten and lactose. Low FODMAP means reduction of fermentable saccharides and polyols. The questionnaires Rome IV, IBS-severity scoring system (IBS-SSS), and visual analog scale for IBS (VAS-IBS) were completed at baseline and after 2, 4, and 24 weeks. Weight, height, waist circumference, and blood pressures were measured at week 2, 4, and 24. Comparisons were made within the groups and the differences between the changes in the two groups were compared.

Results: The patients were categorized according to the Rome IV criteria as constipation-predominated IBS (IBS-C) (n=26, 16.8%), diarrhea-predominated IBS (IBS-D) (n=44, 28.4%), mixed IBS (IBS-M) (n=54, 34.8%), unspecified IBS (IBS-U) (n=7, 4.5%), and unspecified functional bowel disorder (FBD) (n=24, 15.5%) with weekly abdominal pain but weak association between the pain and bowel habits. There were no differences between the groups at baseline. In the SSRD group, 72 (93.5%) completed the study at

week 4 and 53 (68.8%) at week 24, with corresponding figures 72 (92.3%) and 49 (62.8%) in low FODMAP. The responding rate (RR= Δ Total IBS-SSS ≥ -50) was non-inferior in SSRD compared with low FODMAP at week 2 (84.7% vs. 81.4%; p=0.658), week 4 (84.7% vs. 84.7%; p=1.00), and week 24 (52.8% vs. 68.0%; p=0.159). All gastrointestinal and extraintestinal symptoms were equally improved (p<0.001 in most variables) after the 4-week intervention. This remained at week 24 for all specific abdominal symptoms, total IBS-SSS, total extraintestinal IBS-SSS, and most specific extraintestinal symptoms. The decrease in total IBS-SSS correlated at all time points with the decrease of total extraintestinal symptoms (p<0.001) and improved psychological well-being (p<0.001). At week 4, 26.4% in both groups were considered healthy with <75 in total IBS-SSS. At week 24, around 40-50% had abdominal pain 2-3 times a month, or less, or did have <75 in total IBS-SSS. SSRD rendered more pronounced reductions in weight (p=0.006), body mass index (BMI) (p=0.005), and sugar craving (p=0.05) compared with low FODMAP, whereas waist circumference and blood pressure were equally decreased in both groups. Weight and BMI were regained at follow-up. The decrease in total IBS-SSS at week 24 correlated with the decrease of weight (p=.010) and BMI (p=0.013), and the responders at week 24 in the SSRD group still had lowered weight (-0.7 (-2.5-0.1) vs. 0.2 (-0.7-2.2) kg; p=0.005) and BMI (-0.25 (-0.85-0.03) vs. 0.07 (-0.35-0.77) kg/m²; p=0.009) compared with baseline in contrast to non-responders. Those who had tested both diets preferred SSRD (p=0.032).

Conclusion: The SSRD effect on gastrointestinal and extraintestinal IBS symptoms were not inferior to the low FODMAP effect. Reductions of weight, BMI, and sugar craving were most pronounced following SSRD. Thus, dietary intervention in IBS do not only affect symptoms but also anthropometric parameters.

Disclosure: Nothing to disclose.

PP0809

ONDANSETRON IN DIARRHOEA PREDOMINANT IRRITABLE BOWEL SYNDROME AND FUNCTIONAL DIARRHOEA: OUTCOMES FROM A REAL-LIFE CLINICAL EXPERIENCE

C. Sbarigia^{1,2,3}, C. Lambiasi^{1,2,4}, M.F Butt^{1,2}, R. Spiller^{1,2}, M. Corsetti^{1,2}

¹University of Nottingham, NIHR Nottingham BRC, Nottingham University Hospitals NHS Trust and the University of Nottingham, Nottingham, United Kingdom, ²University of Nottingham, Nottingham Digestive Diseases Centre, Translational Medical Science, School of Medicine, Nottingham, United Kingdom, ³Sapienza University of Rome, Sant'Andrea University Hospital, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy, ⁴University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy

Contact E-Mail Address: cate.sbarigia@gmail.com

Introduction: 5-HT₃ receptor antagonists are a second line treatment for irritable bowel syndrome with predominant diarrhoea (IBS-D), but there is no evidence on their efficacy for functional diarrhoea (FDr) (Savarino, 2022). Randomized controlled trials show that ondansetron seems to be effective in treating IBS symptoms (Garsed 2014, Gunn 2023), but real-life data are lacking.

Aims & Methods: Our aim was to study the clinical response to ondansetron in patients with IBS-D or FDr in a real-life setting. A retrospective analysis on consecutive patients (December 2014 – February 2024) meeting criteria for IBS-D or FDr according to Rome III criteria was conducted in a single Neurogastroenterology outpatient clinic. Only patients prescribed with ondansetron were included. A standardized template was used to

collect clinical data and patient-reported response to treatment. Ondansetron was prescribed at initial dosage of 4mg 1 tablet every other day with the possibility of increasing the dosage up to 6 tablets/daily. Clinical response was defined as (i) an improvement in the number of bowel movements per day vs baseline and (ii) firmer stool consistency (Bristol stool form types 3 and 4, 'normal').

Results: Ninety-four patients (female 68.1%, mean age 45 ±15 years old) were included. Among them, 77 (82%) were diagnosed with IBS-D and 17 (18%) with FDr. The mean follow-up duration was 19.1 months (SD±16.71). Seventy patients (74.5%) achieved a clinical response to ondansetron. Response was maintained with ondansetron at a mean dosage of 2.5 tablets/daily (SD±1.5) for a mean follow-up duration of 23.5±17 months. There was no significant difference between the number of IBS-D and FDr patients who responded to ondansetron (table 1). Patients with IBS-D reported a significantly higher improvement in abdominal pain vs baseline (p<0.01, table 1). Twenty-four patients (25.5%) did not respond to ondansetron. Adverse events were significantly higher in non-responders compared to responders (p=0.02, table 1).

Main characteristics at baseline	Responders, n (%)	Non-responders, n (%)	p-value*
IBS-D	55 (71.4)	22 (28.6)	0.22
FDr	15 (88.2)	2 (11.7)	
Bristol Scale 5	24 (34.3)	8 (33.3)	1
Bristol Scale 6-7	46 (65.7)	16 (66.7)	
Vomit	14 (20)	1 (4.2)	0.07
No vomit	56 (80)	23 (95.8)	
Urgency	29 (41.3)	8 (33.3)	0.63
No urgency	41 (58.7)	16 (66.7)	
Opioids	14 (20)	7 (29.2)	0.39
No opioids	56 (80)	17 (70.8)	
Neuromodulators	22 (31.4)	10 (41.6)	0.45
No neuromodulators	48 (68.6)	14 (58.4)	
Main characteristics post-treatment	Responders, n (%)	Non-responders, n (%)	p-value*
Improvement in pain in IBS-D	40 (72.7)	4 (18.2)	<0.01
No improvement in pain in IBS-D	15 (27.3)	18 (81.8)	
Adverse events	11 (15.7)	10 (41.7)	0.02
No adverse events	59 (84.3)	14 (58.3)	

Table 1. Main characteristics of responders and non-responders at baseline and post-treatment

*Fisher's exact test

Abbreviations: FDr= functional diarrhoea, IBS-D= irritable bowel syndrome with diarrhoea

Conclusion: This is the first real-life study assessing the response to ondansetron in IBS-D or FDr patients showing long-term reduction in the frequency of bowel movements, improvement in faecal consistency, and reduction in abdominal pain. Our data suggest that ondansetron can be used in FDr patients.

References:

1. Savarino E, Zingone F, Barberio B, Marasco G, Akyuz F, Akpinar H, Barboi O, Bodini G, Bor S, Chiarioni G, Cristian G, Corsetti M, Di Sabatino A, Dimitriu AM, Drug V, Dumitrascu DL, Ford AC, Hauser G, Nakov R, Patel N, Pohl D, Sfarti C, Serra J, Simrén M, Suciu A, Tack J, Toruner M, Walters J, Cremon C, Barbara G. Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility. *United European Gastroenterol J.* 2022 Jul;10(6):556-584.

2. Garsed K, Chernova J, Hastings M, Lam C, Marciani L, Singh G, Henry A, Hall I, Whorwell P, Spiller R. A randomised trial of ondansetron for the treatment of irritable bowel syndrome with diarrhoea. *Gut.* 2014 Oct;63(10):1617-25.

3. Gunn D, Topan R, Barnard L, Fried R, Holloway I, Brindle R, Corsetti M, Scott M, Farmer A, Kapur K, Sanders D, Eugenicos M, Trudgill N,

Whorwell P, McLaughlin J, Akbar A, Houghton L, Dinning PG, Aziz Q, Ford AC, Farrin AJ, Spiller R. Randomised, placebo-controlled trial and meta-analysis show benefit of ondansetron for irritable bowel syndrome with diarrhoea: The TRITON trial. *Aliment Pharmacol Ther.* 2023 Jun;57(11):1258-1271.

Disclosure: Nothing to disclose.

PP0810

SYSTEMATIC REVIEW AND META-ANALYSIS: PLANT BASED THERAPY FOR IRRITABLE BOWEL SYNDROME

A. Meyer¹, J. Auer², L. Cascant Ortolano³, N. Schreiber⁴, A. Zimmermann-Klemd⁵, C. Gründemann⁵, P. Busche⁶, M. Fox⁷
¹Ludwig Maximilians-University, Medical Department II, Munich, Germany, ²University Hospital Basel, Clinic of Obstetrics and Gynaecology, Basel, Switzerland, ³Johannes Gutenberg University Mainz, Departmental Library for the University Medical Center, Mainz, Germany, ⁴Martin-Luther-University Halle-Wittenberg, University Medical Center Halle (Saale), Department of Visceral, Vascular and Endocrine Surgery, Halle (Saale), Germany, ⁵University of Basel, Translational Complementary Medicine, Department of Pharmaceutical Sciences, Basel, Switzerland, ⁶Klinik Arlesheim, Department of integrative Gastroenterology, Arlesheim, Switzerland, ⁷Klinik Arlesheim & Zürich University, Gastroenterology and Hepatology, Arlesheim, Switzerland

Contact E-Mail Address: Anselm.Meyer@campus.lmu.de

Introduction: Irritable bowel syndrome (IBS) is characterized by a combination of abdominal pain, bloating, and stool irregularity [1]. Many patients are dissatisfied with the pharmacological treatment of IBS and turn to “complementary and alternative medicine“ (CAM). In particular, plant-based preparations to treat abdominal symptoms are popular [2-4]. **Aims & Methods:** A systematic review and meta-analysis to present the current evidence on phytotherapy for IBS was performed.

A literature search was done using 3 electronic databases (Medline via PubMed, Embase via Ovid, and Web of Science Core Collection) from inception to April 2023. A total of 7894 citations were found. Studies were excluded if they met the following exclusion criteria: (i) were homeopathic medicines, (ii) unpublished or only partially published studies, (iii) patients under 18 years of age, (iv) studies with fewer than ten participants, and (v) publication languages other than German or English. Efficacy was assessed using dichotomous ratings of change in IBS symptoms. To pool data a random effects model with 95% confidence intervals was used. I2 statistics were used to test for heterogeneity of included studies. Scores were 0-24% no-, 25-49% low-, 50-75% moderate- and >75% high heterogeneity.

Results: Through the screening process, 56 eligible studies were identified (6054 patients).

Meta-analysis was performed for fibre (8 studies), peppermint oil (7 studies), aloe vera (3 studies), and Chinese herbal medicine (7 studies). At least one randomized controlled trial (RCT) was performed for the following plant-based products: Ginger, Kiwi fruit, St John's Wort and Aniseed oil; however, there was insufficient data to perform meta-analysis. For 192 of 387 patients fibre was helpful; whereas, placebo intake was beneficial for 127 of 346 patients (RR=1.22; 95% CI: 1.00-1.49). For 144 of 311 patients peppermint oil improved symptoms; whereas, in the control group, 97 of 357 patients experienced a beneficial effect (RR=1.63; 95% CI: 1.33-2.00). For 62 of 155 patients aloe vera relieved symptoms; whereas, the control intervention was helpful for 51 of 144 patients (RR=1.25; 95% CI: 0.76-2.06). In 403 of 731 patients, Chinese Herbal Medicine therapy had a

positive effect; whereas, in the placebo group, 245 of 723 patients found the therapy helpful (RR=1.56; 95% CI: 1.27-1.92. The heterogeneity in the studies ranged from none to moderate. Many studies had some concern of bias in the Risk of Bias 2 (RoB 2) assessment (42/53).

Conclusion: This analysis supports the use of selected plant-based preparations in IBS management. Peppermint oil and Chinese Herbal Medicine preparations demonstrated significant efficacy compared to placebo. Dietary fiber improved stool frequency but had borderline positive effects on IBS scores. The quality of many studies was limited. Additional well-powered RCTs are needed to establish the places of phytotherapy in the management of functional gastrointestinal symptoms.

References:

1. Lacy, B.E., et al., *Bowel Disorders*. Gastroenterology, 2016. 150(6): p. 1393-1407.e5
2. Houghton, L.A., et al., *Age, Gender, and Women's Health and the Patient*. Gastroenterology, 2016. 150(6): p. 1332-1343.e4.
3. Deutsch, J.K., J. Levitt, and D.J. Hass, *Complementary and Alternative Medicine for Functional Gastrointestinal Disorders*. Am J Gastroenterol, 2020. 115(3): p. 350-364.
4. Drossman, D.A., et al., *International survey of patients with IBS: symptom features and their severity, health status, treatments, and risk taking to achieve clinical benefit*. J Clin Gastroenterol, 2009. 43(6): p. 541-50.

Disclosure: Nothing to disclose.

PP0811

INVESTIGATION OF INTESTINAL PERMEABILITY AND MUCUS LAYER IN DIFFERENT COLONIC SEGMENTS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND EFFECT OF A MUCOPROTECTANT FORMULATION

O. Incze¹, P. Pallagi², M. Bagyánszki³, N. Bódi⁴, T. Molnár¹, R. Roka¹

¹University of Szeged, Department of Medicine, Szeged, Hungary,

²Orsolya Incze, Department of Medicine, Szeged, Hungary,

³University of Szeged, Department of Physiology, Anatomy and Neuroscience, Faculty of Science and Informatics, Szeged, Hungary, ⁴University of Szeged, Department of Physiology, Anatomy and Neuroscience, Szeged, Hungary

Contact E-Mail Address: inczeo@gmail.com

Introduction: Irritable bowel syndrome (IBS) is one of the most frequent gastrointestinal disorders with high impact on quality of life and national health systems. Diarrhea predominant IBS (IBS-D) is characterized by abdominal pain and chronic diarrhea. Elevated intestinal permeability is a pathophysiological element of the disease pathogenesis. Mucus layer is a novel target of IBS research.

Aims & Methods: Our aims were to examine the permeability and mucus alterations in IBS-D patients' different colonic segments and the effect of formulation of xyloglucan (XG), pea protein (PP), grape seed extract (GS) and xylo-oligosaccharides (XOS) on pain and intestinal permeability in IBS-D subjects.

Methods: 14 subjects (IBS-D patients and control) were involved. After initial colonoscopy with biopsy sampling XG+PP+GS+XOS was administered to IBS-D patients for 12 weeks. Stool count and pain scores were documented. After treatment, colonoscopy was repeated. Permeability of biopsy samples was measured in Ussing-chambers. Adherent mucus layer thickness and Muc-2 expression were evaluated by histology/immunohistochemistry.

Results: XG+PP+GS+XOS treatment significantly reduced diarrhea and abdominal pain. Intestinal permeability in IBS-D patients was elevated compared to controls, XG+PP+GS+XOS restored permeability in ascendent colon. PAS-stained mucus layer was significantly thinner in IBS-D compared

to controls. XG+PP+GS+XOS therapy caused a further reduction in mucus thickness. After XG+PP+GS+XOS treatment, proportion of Muc-2 positive cells was reduced compared to controls.

Conclusion: The study shows the physiological variance regarding to the adherent mucus thickness and mucus secreting cell count in the different colon segments.

Our study verifies the segmental difference in permeability alteration and shows adherent mucus thickness reduction in IBS-D. These results show the segmentally different pathophysiology in IBS-D. Mucus thickness alteration can be a new therapeutic target for the treatment. In fact, treatment with XG+PP+GS+XOS significantly improved abdominal pain, and diarrhea. Moreover, it was able to restore the permeability in IBS-D patients to a physiological state. Based on this study, XG+PP+GS+XOS can be considered as an effective therapy for IBS-D symptoms.

Funded: by Hungarian National Research, Development and Innovation Office under grant agreement No.116370.

Disclosure: Nothing to disclose.

PP0812

ANTIDEPRESSANTS IN IRRITABLE BOWEL SYNDROME – A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

M.J. Temido¹, M. Cristiano¹, C. Gouveia^{2,3}, B. Mesquita⁴, P. Narra Figueiredo^{1,3}, F. Silva Portela^{3,1}

¹Unidade Local de Saude de Coimbra, Gastroenterology, Coimbra, Portugal, ²Unidade Local de Saude de Coimbra, Psychiatry, Coimbra, Portugal, ³University of Coimbra, Faculty of Medicine, Coimbra, Portugal, ⁴Hospital de Cascais, Departamento de Saúde Mental, Cascais, Portugal

Contact E-Mail Address: mariajosetemido@hotmail.com

Introduction: Irritable bowel syndrome (IBS) is among the most prevalent gastrointestinal conditions. However, its therapeutic management poses challenges, with many current recommendations resting on a low level of evidence.

Aims & Methods: Our objective is to conduct a systematic review with meta-analysis of randomized, double-blind, placebo-controlled trials to assess the efficacy of antidepressants in treating IBS.

Systematic review with meta-analysis performed according to PRISMA guidelines and registered on the PROSPERO platform (CRD42024502427). PubMed, EMBASE, and The Cochrane Library platforms were searched from inception to January 2024. Only randomized, double-blind, placebo-controlled trials, conducted in patients with IBS patients, with a minimum treatment period of 4 weeks, were included. The quality of evidence was assessed using the revised version of the Cochrane tool (RoB 2). A random-effects model was used. Heterogeneity was assessed by the I² statistics. Funnel plots and the Egger test were used to assess publication bias. Statistical analysis was performed using STATA v16.

Results: The search strategy identified 1340 studies, of which 16 were included, totaling 1428 patients. Among these studies, 733 patients were assigned to the antidepressant group and 698 to the placebo group. In the intervention group, 405 (55.3%) patients reported improvement, compared to only 227 (32.5%) patients in the placebo group. The meta-analysis showed that the use of antidepressants in patients with IBS provides a benefit in overall symptom improvement (OR=3.02; 95% CI 2.16-4.2) compared to placebo.

A subgroup analysis of 9 studies, comprising 1008 patients, assessed the efficacy of tricyclic antidepressants (TCAs) in the same setting and revealed similar results (OR=3.39, 95% CI 2.24-5.12), as did the sub-analysis of 6 studies (including 363 patients) evaluating the efficacy of selective serotonin reuptake inhibitors (SSRIs) (OR= 2.39, 95% CI 1.14-5.01). The

efficacy also extends to patients refractory to first-line measures (6 studies including 713 patients) (OR=2.96, 95% CI 1.67-5.25) and to patients without psychopathology (8 studies including 471 patients) (OR=2.92, 95% CI 1.6-5.31). Concerning symptoms, a sub analysis also confirmed the efficacy of antidepressants specifically both in the improvement of abdominal pain (OR=4.33, 95% CI 2.1-8.93) and in abdominal distension (OR=2.68, 95% CI 1.42-5.04).

Only in the sub-analysis assessing the efficacy of SSRIs and of the improvement of abdominal pain, I^2 was slightly >60%, indicating substantial heterogeneity, but <75%. Causes of heterogeneity were searched. Publication bias was detected, and potential sources were identified. Sub-analysis without the studies identified as sources of this bias revealed similar results with lower heterogeneity.

Conclusion: Antidepressants, including both TCAs and SSRIs, demonstrate efficacy in patients with IBS, presenting a validated treatment option supported by evidence. Moreover, these medications can be beneficial to patients resistant to initial treatments and those lacking psychopathological symptoms.

References: Drossman DA, Tack J, Ford AC, Szegedy E, Törnblom H, Van Oudenhoove L. Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction): A Rome Foundation Working Team Report. *Gastroenterology* 2018;154:1140-1171.e1. <https://doi.org/10.1053/j.gastro.2017.11.279>.

Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol* 2021;116:17-44. <https://doi.org/10.14309/ajg.0000000000001036>. Lovell RM, Ford AC. Global Prevalence of and Risk Factors for Irritable Bowel Syndrome: A Meta-analysis. *Clin Gastroenterol Hepatol* 2012;10:712-721.e4. <https://doi.org/10.1016/j.cgh.2012.02.029>.

Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. *Gut* 2021;70:1214-40. <https://doi.org/10.1136/gutjnl-2021-324598>.

Disclosure: FP received speaker fees from Abbvie, Falk, Ferring, Janssen, Pfizer, Pharmakern, Takeda and Tillotts. The other authors have no conflict of interest.

PP0813

EFFECT OF *PEDIOCOCCUS ACIDILACTICI* CECT7483, *LACTOPLANTIBACILLUS PLANTARUM* CECT7484 AND *LACTOPLANTIBACILLUS PLANTARUM* CECT7485: ON PERMEABILITY ALTERATIONS INDUCED BY IRRITABLE BOWEL SYNDROME MEDIATORS: A TRANSCRIPTOMIC AND METABOLOMIC STUDY

M.R. Barbaro¹, E. Bianco¹, C. Cremon¹, G. Marasco², J. Espadaler Mazo³, V. Stanghellini², G. Barbara²

¹IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ²University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ³AB-Biotics SA (Kaneka Group), Department of R&D, Barcelona, Spain

Contact E-Mail Address: francesca.bianco@aosp.bo.it

Introduction: The pathophysiology of irritable bowel syndrome (IBS) is complex and involves several factors including intestinal permeability alterations. The soluble mediators spontaneously released by the colonic mucosa (SUP) of IBS patients increased paracellular permeability in the *in vitro* model based on Caco-2 cells (1).

Aims & Methods: The aims of this study were to evaluate the effect of probiotic blend consisting of *Pediococcus acidilactici* (CECT7483) and *Lactobacillus plantarum* (CECT7484 and CECT7485) on Caco-2 permeability and transcriptomic profile and to correlate these results with the metabolites produced by the probiotic blend.

11 IBS-D, 10 IBS-M and 7 asymptomatic control (AC) were enrolled. IBS patients were diagnosed according to ROMEIV criteria. All subjects enrolled in the study were 18-65 years old and without relevant organic disease or dietary intolerance. IBS/AC SUP were incubated on Caco-2 monolayer with or without the probiotic blend (10^4 and 10^6). Permeability changes were evaluated by assessing the flow of dextran-FITC to the Caco-2 monolayer. At the end of permeability experiments RNA was extracted and used for library preparation for RNAseq analysis. Gene expression was validated by real-time qPCR. Untargeted metabolomics approach was used.

Results: Both doses of probiotic blend significantly recovered permeability changes induced by IBS-SUP. RNAseq results, validated by qPCR showed that the co-incubation of the higher dose of probiotic blend and IBS-SUP compared to IBS-SUP alone induced a significant increase in the expression of Cytochrome P450 Family 1 Subfamily A Member 1 (*CYP1A1*) ($P < 0.05$) and a decrease in the expression of Htra Serine Peptidase 1 (*HTRA1*) gene. On the basis that *CYP1A1* expression is induced by the activation of the aryl hydrocarbon receptor (AhR), we evaluated the production of indoles, natural ligand of AhR, by the strains contained in the probiotic blend. We found that the Indole-3-lactic acid was the most produced one.

Conclusion: This study demonstrated the molecular mechanisms underlying the effect of the probiotic blend containing *Pediococcus acidilactici* CECT7483, *Lactobacillus plantarum* CECT7484, and *Lactobacillus plantarum* CECT7485 on an *in vitro* model of intestinal permeability.

References: 1. Piche T, Barbara G, Aubert P, Bruley des Varannes S, Dainese R, Nano JL, Cremon C, Stanghellini V, De Giorgio R, Galmiche JP, Neunlist M. Impaired intestinal barrier integrity in the colon of patients with irritable bowel syndrome: involvement of soluble mediators. *Gut*. 2009 Feb;58(2):196-201. doi: 10.1136/gut.2007.140806. Epub 2008 Sep 29. PMID: 18824556.

Disclosure: The authors have no conflicts of interest to declare.

PP0814

THE TREATMENT PREFERENCES OF PHYSICIANS REGARDING IRRITABLE BOWEL SYNDROME: A DISCRETE CHOICE EXPERIMENT

R. Sturkenboom¹, B. Essers², D. Keszthelyi¹¹Maastricht University Medical Center, Gastroenterology & Hepatology, Maastricht, Netherlands, ²Maastricht University Medical Center, Clinical Epidemiology and Medical Technology Assessment (KEMTA), Maastricht, Netherlands**Contact E-Mail Address:** roselst@hotmail.com

Introduction: Irritable Bowel Syndrome (IBS) is a highly prevalent, chronic disorder of the Gut-brain interaction which forces increased demands of healthcare facilitations to manage these symptoms. Several treatment options are available, all with comparable clinical efficacy, such as pharmacotherapy, dietary treatment and psychotherapy. Therefore, the guidance of a physician during consultation is essential for effective decision-making. In our previous study, the most-preferred treatment among IBS patients was dietary intervention, subsequently pharmacotherapy and psychotherapy. The preferences of physicians remain unclear, but could be of major importance to give insight in the management strategy of different physicians and to compare with patients' perspective.

Aims & Methods: The aim of this study was to examine these treatment preferences among different types of physicians and evaluate if treatment wishes differ between subgroups of physicians.

Physicians from the Dutch Association of Specialists for Gastroenterology & Hepatology were invited to participate. A labeled discrete choice experiment (DCE) survey was filled in, containing twelve scenarios with each three alternatives (medication, diet, psychotherapy). Each scenario was accompanied by a patient profile differing in predominant symptom and anxiety symptoms. Five attributes were included in the treatment scenario: effectiveness, time until response, cessation of response following discontinuation of therapy, side effects and treatment burden. The preference weights were analyzed using a mixed logit model.

Results: In total, 52 physicians completed the discrete choice experiment (58% female). The majority of these respondents were gastroenterologists (51.9%), followed by gastroenterology trainees (34.7%). A small amount was general practitioner, pediatric gastroenterologist or gastroenterology nurse practitioner. The average work experience with treating IBS patients was 8.5 years (SD 3.5). The discrete choice experiment showed that the most-preferred treatment was pharmacotherapy, which was chosen in 39.71% of the cases. Dietary intervention was chosen 195 times (31.26%) and psychotherapy in 29.02% of the cases. Effectiveness, treatment burden and mild side effect were reported to be important treatment attributes.

Subgroup analysis regarding gender showed that male physicians preferred pharmacotherapy, while female physicians tend to prefer dietary treatment. Important attributes in female physicians were effectiveness, treatment burden, time to response, mild side effects and time until recurrence regarding psychotherapy. Male physicians reported effectiveness, time until recurrence regarding medication and diet and mild side effects, to be important in IBS treatment.

Conclusion: Pharmacotherapy was the most-preferred IBS therapy among physicians. Revealing physicians' preferences regarding the treatment of IBS raises awareness of the important treatment factors which can contribute to improved shared decision-making during consultation.

Disclosure: Nothing to disclose.

PP0815

TRANSIENT COLONIZATION WITH *BLASTOCYSTIS* SPP. AFTER TRANSMISSION VIA FECAL MICROBIOTA TRANSPLANTATIONM.V. Bénard¹, C.M. de Bruijn², S. Matamoros³, E.M. Wentink-Bonnema³, M. Benninga⁴, C.Y. Ponsioen⁵, R. Zonneveld³¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam Gastroenterology Endocrinology Metabolism (AGEM), Amsterdam, Netherlands, ²Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Paediatric Gastroenterology, Amsterdam, Netherlands, ³Amsterdam UMC, Department of Medical Microbiology and Infection Prevention, Section Clinical Parasitology, Amsterdam, Netherlands, ⁴Amsterdam UMC, Emma Children's Hospital, Amsterdam Reproduction & Development Research Institute, AZ Amsterdam, Netherlands, ⁵AMC Amsterdam Gastroenterology and Hepatology - Gastroenterology & Hepatology, AMC Amsterdam Gastroe, Gastroenterology & Hepatology, Amsterdam, Netherlands**Contact E-Mail Address:** m.v.benard@amsterdamumc.nl

Introduction: The pathogenicity of *Blastocystis* spp. is still debated. Guidelines for donor feces screening differ in their advice to screen for *Blastocystis* spp., but when tested, its presence is a common reason for exclusion.¹ *Blastocystis* spp. are correlated to increased bacterial alpha-diversity² and distinct bacterial groups³ and therefore its presence may indicate favorable efficacy of fecal microbiota transplantation (FMT). The latest European consensus report no longer advises to reject feces donors that test positive for *Blastocystis* spp.⁴ Only one paper has been published on human transmission of *Blastocystis* spp. via frozen FMT.⁵

Aims & Methods: We aimed to investigate the long-term effects of the application of *Blastocystis*-positive FMT, prepared with fresh feces.

In a FMT trial on FMT with refractory Irritable Bowel Syndrome (IBS) adolescents (age 16 – 20 years) received two administrations (at baseline and after 6 weeks) of fresh allogeneic FMT via nasoduodenal tube prepared with fecal samples from a *Blastocystis* spp. positive feces donor (NCT03074227). *Blastocystis* spp. presence and subtyping were determined using microscopy, PCR and Sanger sequencing.

Results: Three recipients received FMT from one donor colonized with *Blastocystis* subtype 3 (ST3). Two recipients were negative for *Blastocystis* spp. and one recipient carried ST2 at baseline prior to FMT. After FMT, the two prior-negative recipients tested positive for identical ST3 as the donor after FMT at 12 weeks, but lost carriership of this subtype at week 24 and week 48. The ST2 colonized recipient remained colonized with ST2 and did not acquire ST3 after FMT. Transient adverse events did occur, but did not differ from patients treated with *Blastocystis* spp.-negative FMT. No FMT-related serious adverse events occurred.

Recipient	Baseline	Before FMT 1	Donor		Before FMT 2	Donor		
			FMT 1	FMT 2		FMT 2		
	Week -2	Week 0	Week 0	Week 6	Week 6	Week 12	Week 24	Week 48
1 Woman, 18 y	negative	negative	ST3	ST3	+, no seq	ST3	negative	negative
2 Woman, 20 y	negative	negative	ST3	+, no seq	ST3	ST3	ST3	ST3
3 Woman, 16 y	ST2	ST2	ST3	+, no seq	ST3	ST2	ST2	ST2

Table 1: Sanger PCR sequencing results of frozen feces samples from three adolescents with IBS and one healthy donor.

Samples were collected before, during and after the FMT treatment schedule with follow-up unto week 48. Light blue cells indicate a different sequence order of *Blastocystis* ST3 than the *Blastocystis* ST3 indicated in the dark blue cells. Grey cells indicate columns representing donor samples. Abbreviations: FMT; fecal microbiota transplantation, ST; subtype, seq; sequence, y; years.

Conclusion: We present the first long-term results of *Blastocystis* spp. transmission by fresh FMT in three cases. Transient colonization with *Blastocystis* spp. did occur without the occurrence of FMT-related serious adverse events.

References: 1. Benard MV, de Bruijn CMA, Fenneman AC, Wortelboer K, Zeevenhoven J, Rethans B, et al. Challenges and costs of donor screening for fecal microbiota transplantations. *PLoS One*. 2022;17(10):e0276323. 2. Tito RY, Chaffron S, Caenepeel C, Lima-Mendez G, Wang J, Vieira-Silva S, et al. Population-level analysis of *Blastocystis* subtype prevalence and variation in the human gut microbiota. *Gut*. 2019;68(7):1180-9. 3. Nieves-Ramirez ME, Partida-Rodriguez O, Laforest-Lapointe I, Reynolds LA, Brown EM, Valdez-Salazar A, et al. Asymptomatic Intestinal Colonization with Protist *Blastocystis* Is Strongly Associated with Distinct Microbiome Ecological Patterns. *mSystems*. 2018;3(3). 4. Keller JJ, Ooijsaar RE, Hvas CL, Terveer EM, Lieberknecht SC, Hogenauer C, et al. A standardised model for stool banking for faecal microbiota transplantation: a consensus report from a multidisciplinary UEG working group. *United European Gastroenterol J*. 2021;9(2):229-47. 5. Terveer EM, van Gool T, Ooijsaar RE, Sanders I, Boeije-Koppenol E, Keller JJ, et al. Human Transmission of *Blastocystis* by Fecal Microbiota Transplantation Without Development of Gastrointestinal Symptoms in Recipients. *Clin Infect Dis*. 2020;71(10):2630-6.

Disclosure: CYP has received research grants from Gilead and Perspectum, consultancy fee from Chemomab and NGM, and speaker's fee from Tillotts. The other authors disclose no conflicts.

PP0816
MELATONIN FOR FUNCTIONAL ABDOMINAL PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

P. Santo¹, A. Nau², E.C. Barbosa³, S. Baraldo⁴, M. Meine⁵, G. Meine⁶
¹Federal University of São Carlos, São Carlos, Brazil, ²Jaraguá Hospital, Jaraguá do Sul, Brazil, ³Evangelical University of Goiás - UniEVANGÉLICA, Anápolis, Brazil, ⁴Barretos Cancer Hospital, Barretos, Brazil, ⁵Pontifical Catholic University of Parana, Curitiba, Brazil, ⁶Feevale University, Novo Hamburgo, Brazil

Contact E-Mail Address: mcmeine@gmail.com

Introduction: Functional abdominal pain is a common disorder for which pharmacological strategies are still inadequate. Melatonin has many direct and indirect effects on the gastrointestinal tract and seems to have an important influence on the brain-gut axis.

Aims & Methods: We aimed to assess the efficacy of melatonin versus placebo for treating patients with functional abdominal pain, performing subgroup analyses by age range, dosage of melatonin, and follow-up time. We systematically searched PubMed, Embase, and Cochrane Library databases until March 31, 2024. The primary outcome was the improvement of abdominal pain severity. The secondary outcomes were reduction in abdominal pain frequency and improvement in quality of life. We analyzed continuous outcomes using the standardized mean difference (SMD) with 95% confidence interval (CI). We used random-effects model, and statistical significance was regarded at p-value <0.05. Between-study heterogeneity was assessed using Cochran's Q test and I² statistics. Statistical analyses were performed using R statistical software. We assessed the certainty of evidence for each outcome using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool.

Results: Five randomized controlled trials (including 236 patients) were included. The summary of findings for the primary and secondary outcomes is shown in **Table 1**. Melatonin was associated with greater improvements in abdominal pain severity (SMD 1.18; 95% CI 0.75, 1.61), abdominal pain frequency (SMD 1.19; 95% CI 0.62, 1.75), and quality of life

(SMD 0.47; 95% CI 0.05, 0.88) compared to placebo. The subgroup analysis of adult patients showed that melatonin had a significantly greater decline in pain severity (SMD 1.13; 95% CI 0.57, 1.69) and pain frequency than placebo (SMD 1.30; 95% CI 0.51, 2.09). In the subgroup analysis based on the lowest dosage of melatonin (3 mg), the intervention showed a greater decline in pain severity scores compared to placebo (SMD 1.14; 95% CI 0.58, 1.69). When analyzing only studies with longer follow-up (≥8 weeks), melatonin improved pain severity (SMD 0.56; 95% CI 0.04, 1.07), pain frequency (SMD 0.89; 95% CI 0.04, 1.76), and quality of life (SMD 0.56; 95% CI 0.003, 1.11) compared to placebo.

Outcome	Pooled effect. SMD [95% CI]	p-value	I ²	Certainty of evidence
Abdominal pain severity	1.18 [0.75 - 1.61]	< 0.001	0%	High
Abdominal pain frequency	1.19 [0.62 - 1.75]	<0.001	60%	Moderate
Quality of life	0.47 [0.05 - 0.88]	0.027	0%	High

Table 1. Results from the pooled analyses.
CI, confidence interval; SMD, standardized mean difference.

Conclusion: In patients with gastrointestinal functional disorders, melatonin was associated with a statistically significant decline in abdominal pain severity and frequency when compared to placebo, as well as greater improvement in quality of life. The subgroup analyses suggest that the improved outcome can be achieved even with low melatonin dosage, may be sustained over a longer follow-up time, and is effective in adult patients.

- References:**
1. Dipasquale V, Palermo L, Barbalace A, et al. Randomised controlled trial of melatonin for paediatric functional abdominal pain disorders. *J Paediatr Child Health* 2023; 59: 458–463.
 2. Lu WZ, Gwee KA, Mochhalla S, et al. Melatonin improves bowel symptoms in female patients with irritable bowel syndrome: a double-blind placebo-controlled study. *Aliment Pharmacol Ther* 2005; 22: 927–934.
 3. Saha L, Malhotra S, Rana S, et al. A preliminary study of melatonin in irritable bowel syndrome. *J Clin Gastroenterol* 2007; 41: 29–32.
 4. Song GH, Leng PH, Gwee KA, et al. Melatonin improves abdominal pain in irritable bowel syndrome patients who have sleep disturbances: a randomised, double blind, placebo controlled study. *Gut* 2005; 54: 1402–1407.
 5. Faghhi Dinevari M, Jafarzadeh F, Jabbaripour Sarmadian A, et al. The effect of melatonin on irritable bowel syndrome patients with and without sleep disorders: a randomized double-blinded placebo-controlled trial study. *BMC Gastroenterol* 2023; 23: 135.
- Disclosure:** Nothing to disclose.

PP0817
WITHDRAWN

PP0818

PREDICTIVE CT FINDINGS TO BETTER RISK-STRATIFY RECURRENCES IN THE OUTPATIENT MANAGEMENT OF UNCOMPLICATED ACUTE DIVERTICULITIS

D. Carlomagno¹, S. Lanciotti¹, S. Simonetti¹, A. Schirinzi¹, P. Ricci¹, C. Severi¹, G. Galardo¹

¹Sapienza Università di Roma, Rome, Italy

Contact E-Mail Address: dominga.carlomagno@uniroma1.it

Introduction: Among the different clinical phenotypes of diverticular disease, acute diverticulitis (AD) and its recurrences represent the most significant economic burden for healthcare systems. As indicated by current guidelines, AD care programs have been organized for outpatient management of acute uncomplicated diverticulitis to contain costs. This approach resulted in safe and economically efficient but to improve the quality of patient care, it would be useful to establish the risks of early and late AD recurrence.

Aims & Methods: The aim of the study was to identify possible CT findings predictive of AD recurrence to better risk-stratify the management of outpatients after the 1st episode. Over the past year, 66 patients referred to the Emergency Department of Policlinico Umberto I Hospital (Rome) for uncomplicated AD, defined as modified Hinchey stages 1a and 1b, were included. 33 of these patients were those enrolled in the outpatient AD care program with 1 year-follow-up without recurrence (NR-pts) and 33 patients, matched per gender and age, were patients admitted for a recurrent AD (R-pts) within 12 months from the previous 1st access for AD to the Emergency Department. 1st episode CT images were analyzed for known parameters of disease severity by two radiologists and compared with χ^2 and Student t-tests. Data are expressed as mean $\pm$ SD. Univariate and multivariate Cox regression models and Hazard Ratio (HR) were used to identify risk factors predictive of AD recurrence.

Results: No statistically significant differences were found regarding gender and age distribution between NR-pts (F 36%, ages 58.0 $\pm$ 12.2) and R-pts (F 39%, ages 61.0 $\pm$ 14.0). Among the analyzed CT parameters, at univariate analysis, R-pts showed significantly greater parietal thickness compared to NR-pts (16.0 $\pm$ 4.2mm vs 11.5 $\pm$ 2.6 mm, p <0.001) and grade 4 peridiverticular inflammation (40% R-pts vs 12% NR-pts, p =0.014), with HR of 1.25 (1.15-1.36, p <0.001) and 3.44 (1.50-18.71 p =0.004) respectively. At multivariate analysis, only parietal thickness was confirmed as a significant risk factor, with Kaplan-Meier plots showing a 6-fold increase in recurrence probability with a wall increase >15 mm. For early recurrence within 90 days from first discharge, further risk factors were a longer inflamed segment length (9.0 $\pm$ 2.3 mm < 90 days vs 8.0 $\pm$ 2.3 mm >90 days; p <0.001) and the onset Hinchey stage, recurrence being more frequent in Hinchey Ib than Hinchey Ia (54% vs 16%, p =0.011).

Conclusion: The use of CT predictive factors could represent useful tools in clinical practice to tailor a personalized follow-up and appropriate treatment for outpatient management of acute uncomplicated diverticulitis.

Disclosure: Nothing to disclose.

PP0819

A PROSPECTIVE STUDY ON THE INTERRELATIONSHIP BETWEEN CLINICAL, MANOMETRIC, AND IMAGING FINDINGS IN FAECAL INCONTINENCE

C. Borges Chaves¹, C. Correia¹, M. Cristiano¹, P. Rocha¹, D. Feijó¹, C. Agostinho¹, P. Souto¹, P. Narra Figueiredo^{1,2}

¹Unidade Local de Saúde de Coimbra, Gastroenterology Department, Coimbra, Portugal, ²Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal

Contact E-Mail Address: carlosbchaves123@gmail.com

Introduction: Faecal incontinence (FI) is prevalent, being associated with a high biopsychosocial burden and considerable health costs. The pathophysiology of FI is varied and often multifactorial, representing a diagnostic and therapeutic challenge. Anorectal manometry is the first recommended diagnostic method, although its utility is debatable due to overlapping findings between healthy individuals and patients.

Aims & Methods: The aim of this study is to establish a relationship between FI clinical presentation, manometric findings, and imaging.

We prospectively included all patients undergoing high-resolution anorectal manometry, according to the London protocol, at a tertiary centre, who agreed to respond to a questionnaire to characterize their FI, between August 2021 and March 2023. Clinical records were consulted, in order to access demographic data and past imaging reports. Statistical analysis was performed using IBM SPSS Statistics version 26[®].

Results: Forty-seven patients were included with a mean age of 63.5 $\pm$ 11.6 years, 87.2% women, of whom 73.2% had an obstetric history. Depressive/anxious symptoms were described in 59.6%, previous perineal surgery in 38.3%, and concomitant urinary incontinence in 40.0%. Mean FI duration was 5.4 $\pm$ 5.2 years, with 51.1% reporting daily complaints and a bowel movement median of 2.0 (IQR 3.0). Males tended to have more bowel movements than females (3.5 (IQR 5.0) vs 2.0 (IQR 2.0); p -value 0.03). FI for flatus and faeces was present in 57.4%, for faeces alone in 34.0%, and for flatus alone in 8.5%. Urgency FI was verified in 37.0%, passive FI in 37.0%, and mixed FI in 26.1%. Mean Wexner score was 10 $\pm$ 5. Rectal examination revealed hypotonicity in 15.9%. Mean resting pressure on anorectal manometry was 55.9 $\pm$ 22.5 mmHg, dyssynergy was identified in 16.7% and altered balloon expulsion in 19.5%. The mean value of first sensation, first urge to defecate, and maximum tolerated volume were within the normal range. Imaging was performed in 19 patients (40.4%), with external anal sphincter injury in 15.8% and internal sphincter injury in 10.5%. Mean thickness of the internal anal sphincter (IAS) was 2.3 $\pm$ 1.0 cm. Patients with hypotonicity in rectal examination had lower anal resting pressure (35.7 $\pm$ 16.0 mmHg vs 60.3 $\pm$ 22.4 mmHg; p -value 0.09) and lower IAS thickness (1.6 $\pm$ 0.8 mm vs 2.6 $\pm$ 0.9 mm; p -value 0.07), although not statistically significant. Patients with depressive/anxious symptoms showed lower maximum incremental pressure (56.6 $\pm$ 34.0 mmHg vs 81.2 $\pm$ 46.2 mmHg; p -value 0.045), as well as females when compared to males (60.0 $\pm$ 34.9 mmHg vs 108.7 $\pm$ 53.2 mmHg; p -value 0.005). No other statistically significant results were found, especially correlating clinical findings with manometry or imaging.

Conclusion: Our study showed, as previously replicated, that clinical, manometric and imaging findings have low correlation in the assessment of FI, reflecting its pathophysiological complexity.

Disclosure: Nothing to disclose.

PP0820

UNRAVELLING SOLITARY RECTAL ULCER SYNDROME:
INSIGHTS
FROM A CASE SERIESN.S. Malhi¹, R. Grover¹, J.S. Dhingra¹¹Advanced Gastroenterology Institute (A.G.I.)-The GASTROCITI,
Ludhiana, India**Contact E-Mail Address:** doctorjasmeet@gmail.com**Introduction:** Solitary rectal ulcer syndrome (SRUS), often mistakenly classified as a rectal motility disorder, arises from defecatory irregularities and presents with diverse clinical manifestations. This prospective study conducted at a leading medical center aims to elucidate the spectrum of clinical presentations, potential risk factors, colonoscopic findings, histopathological characteristics, and therapeutic approaches in individuals affected by SRUS.**Aims & Methods:** The prospective analysis included all patients diagnosed with SRUS at the Advanced Gastroenterology Institute (AGI) - The GASTROCITI, Ludhiana, over 48 months from March 2020 to February 2024. Cases were identified using the comprehensive database of the Endoscopy Department. Data retrieval from medical records provided insights into clinical symptoms, endoscopic observations, and histopathological features.**Results:** From approximately 7000 diagnostic sigmoidoscopies & colonoscopies, a meticulous identification of 48 patients with SRUS was achieved. The average age was 48.5 years (± 18.5), with 75% (36) being males. Rectal bleeding was reported by 77% (37) of patients, 64.5% (31) experienced constipation, and 50% (24) described bowel movement difficulties, with an average symptom duration of 13.7 months.

Associated factors included constipation (75%), digital rectal manipulation (43.75%), high-pressure water jet usage (25%), prior rectal surgeries (10.5 %), and rectal prolapse (10.5%). Endoscopic findings revealed solitary ulcers in 64.5% of cases, multiple ulcers in 27 %, and polypoid appearance in 10.5%. Two patients presented with a proliferative mass-like anomaly (pseudotumor) and two had a circumferential rectal stricture.

The finding of difficult-to-take endoscopic biopsies due to underlying submucosal fibrosis showed a robust positive predictive value (PPV) exceeding 90% for SRUS diagnosis. Histopathological analysis revealed surface ulceration (90%), lamina propria fibrosis (70%), architectural distortions (60%), and increased muscle hypertrophy with mucin production (50%). Conservative interventions were effective in all cases, without the need for surgical intervention.

Conclusion: SRUS, often misinterpreted as a rectal motility disorder, presents with diverse manifestations. Management strategies including high-dose laxatives, avoidance of digital evacuation and high-pressure water jet usage, adoption of a fiber-rich diet, and localized application of mesalamine/sucralfate and biofeedback therapy have shown efficacy. This study highlights the complex nature of SRUS and emphasizes the importance of a comprehensive approach to diagnosis and management.**References:****Disclosure:** Nothing to disclose.

PP0821

INSIGHTS INTO RESULTS OF GLOBAL AUDIT FOR FECAL INCONTINENCE
ON BEHALF OF THE EUROPEAN SOCIETY OF COLOPROCTOLOGY (ESCP)
COLLABORATING GROUPA. Dulskas^{1,2}, D. Cerkauskaitė^{1,2}, A. El-Hussuna³, J. Glasbey⁴,
D. Dardanov⁵, T. Pinkey⁴, S. Svagzdys⁶, G. Gallo⁷, C. Knowles⁸,
D. Morton⁴¹National Cancer Institute, Department of Abdominal and General
Surgery and Oncology, Vilnius, Lithuania, ²Vilnius University,
Vilnius, Lithuania, ³Aalborg University Hospital, Aalborg,
Denmark, ⁴Institute of Applied Health Research, Birmingham,
United Kingdom, ⁵University Hospital Lozenetz, Sofia Bulgaria,
General Surgery, Sofia, Bulgaria, ⁶Lithuanian University of
Health Sciences Kaunas Clinics, Kaunas, Lithuania, ⁷University
of Catanzaro, Department of Medical and Surgical Sciences,
Catanzaro, Italy, ⁸Barts and the London School of Medicine and
Dentistry, London, United Kingdom**Contact E-Mail Address:** audrius.dulskas@gmail.com**Introduction:** Faecal incontinence (FI) is a common problem, affecting about 9% of Western populations. However, only a few patients seek consultation and the number of such patients reaching hospital care is unknown. Current treatment pathways are poorly evidence based and are thought to vary greatly between different countries.**Aims & Methods: Background:** The aim of this study was to evaluate the incidence of fecal incontinence (FI) in patients attending colorectal clinics in a global setting, treatment choices and accessibility to diagnostic and treatment tools.**Methods:** An international, multi-center snapshot audit was performed in an 8-week period between January 9, 2023 and March 28, 2023. All eligible cross-sectional data was recorded. Data was entered and saved in a RED-Cap secured database. Two physician- and center-level surveys were filled for current practice evaluation.**Results:** 1,813 outpatients with FI from 110 hospitals, from 35 countries were included in this audit. Majority of patients with FI were females, parous, and in age range 50-70. Patients most commonly waited 1 to 3 years until seen in outpatient clinic. Etiology skewed toward anal injury and rectal prolapse. Stress incontinence was diagnosed more common than urge incontinence (36% vs 23% respectively). Majority of patients received previous treatment (n=222 (61%)), which mostly included pelvic floor physiotherapy (n=149), bowel retraining with biofeedback (n=114), and nurse-led continence support (n=90). Sacral nerve stimulation was the most commonly performed procedure (n=114/395) for FI in outpatient clinics, followed by sphincteroplasty (n=87/395). Endoanal ultrasound (n=206/1,226) as well as anorectal manometry (n=185/1,226) are the basic diagnostic tools used to diagnose FI in outpatient settings. More than a half (56%) of clinics have access to pelvic floor MDT. The majority of physicians offer surgical treatment (colostomy or sphincter repair) for FI.**Conclusion:** Patients FI wait 1-3 years until attending colorectal clinics. Anal injury and rectal prolapse are the main causes of FI. FI treatment consists of conservative and surgical treatment, and there has not been a single best treatment option.**Disclosure:** Nothing to disclose.

PP0822

HIGH ANAL HR-HPV PREVALENCE AND ABNORMAL ANAL CYTOLOGY IN MEN HAVING SEX WITH MEN WHO USE PREP: ARE THEY A DISTINCT RISK GROUP FOR ANAL CANCER?

M. Surmont¹, M. Verheyden², M. Goossens³, J. Brunetta⁴, S. Sahebali⁵, J. Gutermuth², S. Allard⁶

¹UZ Brussel, Gastroenterology, Jette, Belgium, ²UZ Brussel, Department of Dermatology and Venereology, Jette, Belgium, ³VUB, Department of Oncology, Jette, Belgium, ⁴MLMC, Toronto, Canada, ⁵UZ Brussel, Pathology, Jette, Belgium, ⁶UZ Brussel, Internal Medicine and Infectious Diseases, Jette, Belgium

Contact E-Mail Address: magalimarie@hotmail.com

Introduction: Persistent High-Risk Human Papillomavirus (HR-HPV) infection can lead to an anal high-grade squamous intraepithelial lesion (HSIL), the precursor lesion to anal squamous cell carcinoma (SCC). Anal cytology and HR-HPV testing are strategies used for anal SCC screening. Anal HR-HPV prevalence in HIV-negative MSM and in MSM living with HIV (MSM-HIV) is 41% and 74%, respectively. The use of Pre-Exposure Prophylaxis (PrEP) in HIV-negative MSM to prevent HIV contraction created a new Sexual Minority Group among MSM, i.e. MSM using PrEP (MSM-PrEP). The aim of this study was to determine the prevalence of anal HR-HPV infection and abnormal anal cytology in MSM-PrEP and MSM-HIV.

Aims & Methods: MSM-PrEP and MSM-HIV were enrolled in this mono-centric study during consultations at the S-clinic and the HIV-reference centre respectively. Patient characteristics, sexual behavior and demographics were collected using a questionnaire, completed on the day of the anal swab testing.

Results: We enrolled 150 MSM-PrEP and 152 MSM-HIV. Quality of anal swabs was sufficient in respectively 96.7% (n=145) and 96.1% (n=146). HR-HPV prevalence in MSM-PrEP was comparable with HR-HPV prevalence in MSM-HIV; respectively 74.5% (n=108) and 76.6% (n=111) tested positive for at least one HR-HPV (p=0.78). No significant difference in abnormal cytology was seen; 53.1% (n=77) of the MSM-PrEP and 57.2% (n=83) of MSM-HIV had either ASCUS, ASC-H, LSIL or HSIL (p=0.56).

Conclusion: The risk of HR-HPV infection and abnormal anal cytology in MSM-PrEP is comparable to that in MSM-HIV, both of which are higher than observed in HIV-negative MSM not using PrEP. This heightened prevalence of HPV in MSM-PrEP poses an increased risk for HSIL. Recent guidelines on anal screening from International Anal Neoplasia Society recommend screening for anal cancer in both MSM-HIV and HIV-negative MSM, reflecting respective anal cancer incidence rates of 70-100 per 100,000 person-years and 18-34 per 100,000 person-years. Our findings suggest that MSM-PrEP constitutes a distinct risk group for anal SCC positioned between MSM-HIV and HIV-negative MSM not using PrEP.

References: Gaisa M, Gypsyamber D et al. Epidemiology of anal human papillomavirus infection and high-grade squamous intraepithelial lesions in 29900 men according to HIV status, sexuality, and age: a collaborative pooled analysis of 64 studies. *Lancet HIV*. 2021;8(9):531-43.

Machalek D, Poynten M, Jin F et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. *Lancet Oncol*. 2012;13(5):487-500.

Stier E, Clarke M, Deshmukh A et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. *Int.J.Cancer*. 2024;154:1694-1702.

Disclosure: Nothing to disclose.

PP0823

PREVALENCE OF FUNCTIONAL CONSTIPATION AND ASSOCIATED FACTORS IN THAI INFANTS AND TODDLERS: A MULTI-CENTER CROSS-SECTIONAL STUDY

P. Sintusek¹, K. Chatpermporn¹

¹Chulalongkorn University, Pediatrics, Bangkok, Thailand

Contact E-Mail Address: Palittiya.s@chula.ac.th

Introduction: The global prevalence of pediatric functional constipation (FC) varies from 1 to 30% due to the heterogeneity of the studies in terms of target population sampling, method of data acquisition, diagnostic criteria, among others. Studies conducted by Osatakul *et al.* and Piriyanon *et al.* in Thai young children, utilizing Rome III criteria, indicated prevalence rates of 1.6% and 25%, respectively. However, there is currently no study on the prevalence of FC in Thai young children using the Rome IV criteria, mainly because no standardized questionnaire exists for this age group.

Aims & Methods: The Thai version of the Rome-IV Diagnostic Questionnaire for Pediatric Functional Gastrointestinal Disorder (R4PDQ)-Toddler was developed then authorized by the Rome foundation. Guardians of children aged 6-48 months from six hospitals in five regions of Thailand from August 2023 to February 2024 were surveyed with the questionnaire composed of demographic data, the R4PDQ-Toddler for defecation, and the associated factors of FC.

Results: With a 98.1% response rate, a total of 1,874 guardians participated. The prevalence of FC was 16.1% (95% CI 14.5%-17.8%). Most presenting symptoms were painful or hard bowel movements (81.5%), large diameter stools (77.5%) and excessive stool retention (72.2%). Independent associated factors were age >1 year [aOR=3.36 (95%CI 2.29-4.94)], first-degree relative history of constipation [aOR=2.48 (95%CI 1.85-3.35), fiber supplementation [aOR=7.85 (95%CI 3.56-17.30)], and stressful life events in family [aOR=1.41 (95%CI 1.03-1.92)].

Conclusion: The prevalence of FC in Thai young children has been increased. Older age, family history of constipation, stressful life events in the family and supplementary fibers were associated factors of FC, warranting further evaluation.

References: 1. Benninga MA, Nurko S, Faure C, Hyman PE, Roberts ISJ, Schechter NL. Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology*. 2016;150(6):1443-55. e2.

2. Koppen IJ, Vriesman MH, Saps M, Rajindrajith S, Shi X, van Etten-Jamaludin FS, et al. Prevalence of functional defecation disorders in children: a systematic review and meta-analysis. *The Journal of pediatrics*. 2018;198:121-30. e6.

3. Tran DL, Sintusek P. Functional constipation in children: What physicians should know. *World Journal of Gastroenterology*. 2023;29(8):1261.

Disclosure: All authors have COI.

PP0824

LIVING WITH FAECAL INCONTINENCE: A SYSTEMATIC REVIEW AND META-ETHNOGRAPHY

A. Ahmed¹, M. Khan², V. Williamson^{3,4}, E.V. Carrington⁵

¹Imperial College London, Translational Colorectal Research Laboratory, London, United Kingdom, ²The Royal College of Surgeons of Ireland, Dublin, Ireland, ³King's College London, IOPPN, London, United Kingdom, ⁴University of Exeter, Psychology Department, Exeter, United Kingdom, ⁵St Mary's Hospital, Imperial College NHS Trust, London, United Kingdom

Contact E-Mail Address: aa4919@ic.ac.uk

Introduction: Faecal incontinence (FI) affects up to 8.3% of the population and may have physical, psychological and social consequences (1). Sadly, patient experiences remain under-explored, and most symptom measures are based on clinical outcomes rather than key priorities or concerns of affected individuals (2).

Aims & Methods: This study aimed to describe the lived experience of FI through review of published qualitative studies. A systematic literature search of studies of patients with FI published between 2003-2023 was conducted across Medline, Embase, CINAHL and PsycINFO. Studies were included if they provided qualitative data on patient experiences of living with FI. Studies in children and those principally focused on experiences following stoma formation were excluded. Methodological quality was described using the Critical Appraisal Skills Programme (CASP) tool for qualitative studies. An inductive approach by 2 reviewers enabled identification of key concepts. Collaboration with a third reviewer then generated higher-order interpretations. Finally, a meta-ethnographic method was utilized to construct a comprehensive thematic framework of lived experiences of FI.

Results: Of the 3394 studies identified, 29 studies were included in this synthesis. All studies were judged to be of good quality. Six major themes were identified (figure 1): quality of life, adaptation, protection, wider environment, perception and healthcare experiences. The theme 'Quality of Life' reflected the impact of FI on mental health, physical health, social well-being and functional ability. 'Adaptation' encompassed behavioural changes, dietary modification, and adjustments to daily routine to manage FI. The theme 'Protection' comprised risk management strategies and symptom concealment. 'Wider Environment' described navigation of the professional and public environment. 'Perception' reflected the impact of FI on self-perception, as well as the perception of other people's attitudes towards FI. Finally, 'Healthcare Experiences' reflected patient experiences of accessing care and interactions with clinical care teams.

Conclusion: This qualitative synthesis offers a novel patient-centric framework of the lived experiences of FI and provides insight into the breadth of factors contributing to the burden of this condition. Many factors identified in this review are not represented in current outcome measures, highlighting the need for new ways of holistically assessing and measuring the impact of FI on patient wellbeing.

References: 1.Mack I, Hahn H, Gödel C, Enck P, Bharucha AE. Global prevalence of fecal incontinence in community-dwelling adults: a systematic review and meta-analysis. *Clinical Gastroenterology and Hepatology*. 2023 Sep 19.

2. Bedard K, Heymen S, Palsson OS, Bharucha AE, Whitehead WE. Relationship between symptoms and quality of life in fecal incontinence. *Neurogastroenterology & Motility*. 2018 Mar;30(3):e13241.

Disclosure: Nothing to disclose.

PP0825

EFFICACY OF PRANIC TREATMENT IN THE MANAGEMENT OF CHRONIC PAIN, ASSOCIATED MEDICAL CONDITIONS AND PSYCHOLOGICAL SYMPTOMS IN CHILDREN AND ADOLESCENTS

L. Flitcroft¹, A. Bhatia¹, H.M. Lee², C.H. Lo³

¹King's College Hospital, Pranic Psychotherapy and Pranic Healing Research and Development, London, United Kingdom, ²King's College Hospital, Paediatric Liver, GI and Nutrition Centre, 9RS, United Kingdom, ³University College London, Department of Statistical Science, London, United Kingdom

Contact E-Mail Address: anju.bhatia@nhs.net

Introduction: Chronic-pain and anxiety with increased school absences are common problems in children and adolescents. The majority of abdominal pain cases fulfil the Rome IV criteria for functional abdominal pain disorders (FAPDs).

Aims & Methods: We aim to evaluate the efficacy of Pranic treatment in the management of chronic-pain, non-pain-clinical-symptoms associated with medical diagnosis, psychological-symptoms and school attendance. A prospective, proof-of-concept single group study within Child Health, King's College Hospital, London, UK.

Eligibility criteria

- Chronic-pain
- Age range 5-21 years old
- Paediatric consultants' purposive selection of patients with difficult-to-manage chronic-pain
- Patients underwent 8-weekly treatment sessions and review Week-12,16,20
- Participant's psychological and medical diagnosis determined the corresponding Pranic Psychotherapy and Pranic Healing protocols.
- Pain-intensity score 0-10 (PVAS), Pain-frequency (PF), Non-pain-clinical-symptoms (NPCS) School attendance (SAA), variables measured with metric ordered questionnaires
- Psychological symptoms variables measured with binary categorical questionnaires.

Results:

- 100 participants underwent treatment, July 2022 – November 2023.
- M: F ratio 37:63. Median age 13.5 years.

At Baseline:

- 77% participant's medical diagnosis included Functional-abdominal – pain-disorders.
- 62% had experienced chronic-pain for 3 years or more.
- 98% non-zero PVAS score (median 8 = intense dreadful, horrible pain)
- 85% persistent non-pain-clinical-symptoms e. g chronic diarrhoea, chronic constipation, cyclical vomiting (median= 3= routine life disturbed)
- 78% reported school attendance had been regularly affected (median =2= school attendance regularly affected)
- 98% reported low mood and poor concentration, 83% sleep-difficulties, 79% fatigue
- 89% reported 'yes' to routine life being affected by symptoms.

Pranic Treatment Outcomes:

- 93/100 completed treatment 8-weekly treatment sessions
- 78/100 completed week-12, 16, 20 review.
- Pranic treatment proved beneficial to, Pain-Intensity and Pain-Frequency and School Attendance (PVAS (P-value<0.001)) (PF (P-value<0.001)) (SAA (P-value<0.001))
- Pranic Healing Protocols proved beneficial for Non-pain –clinical-symptoms (NPCS (P-value<0.001))
- Pranic Psychotherapy Protocols proved beneficial for psychological symptoms (Psychological symptoms (P-value<0.001)).

- The Kendall's coefficient for concordance for PVAS=0.904, PF=0.865, NPCS=0.703 and SAA=0.759 shows agreement in Patient's response to treatment.
- Benefits were sustained over 3 months follow-up period
- 78 participants' completing final review at the week -20 time point patient outcomes:
- 69/78 (88%) of symptomatic participants reported PVAS= 0= asymptomatic
- 66/68 (97%) of symptomatic patients NPCS = 0 = asymptomatic
- 63/77 (82%) of participants with school attendance affected reported SAA score =0 = school attendance no longer affected by symptoms
- 68/78 (87.2%) and 67/78 (85.9%) symptomatic participants reported resolution of low mood and poor concentration respectively.
- 71/78 (91%) and 72/78 (92.3%) symptomatic participants reported resolution of fatigue and sleep difficulties respectively.
- 68/78 (87.2%) of participants with routine life affected, regained the ability to participate in routine life activities.

Conclusion:

- Pranic treatment is capable of simultaneous improvements in psychological and physical symptoms.
- Resulting in clear improvements in chronic-pain and school attendance.
- Pranic treatment has an after-treatment effect with continuing improvements in behaviour and physical function.

References:

1. Cooper TE, Fisher E, Anderson B, Wilkinson NM, Williams DG, Eccleston C. Paracetamol (acetaminophen) for chronic non-cancer pain in children and adolescents. *Cochrane Database Syst Rev.* 2017 Aug 2;8(8): CD012539. doi: 10.1002/14651858.CD012539.pub2. PMID: 28770975; PMCID: PMC6484395.
2. Hylands-White N, Duarte RV, Raphael JH. An overview of treatment approaches for chronic pain management. *Rheumatol Int.* 2017 Jan;37(1):29-42. doi: 10.1007/s00296-016-3481-8. Epub 2016 Apr 23. PMID: 27107994.
3. Di Lorenzo C. Visceral hyperalgesia in children with functional abdominal pain. *J Pediatr.* 2001;139:838-43.
4. Master Choa Kok Sui: Miracles Through Pranic Healing- Practical Manual on Energy Healing, Fourth Edition, November 2017.
5. Master Choa Kok Sui: Advanced Pranic Healing – The Most Advanced Energy Healing System Using Color Pranas, October 2016.
6. Master Choa Kok Sui: Pranic Psychotherapy – Foremost Energy Healing System for Psychological Applications Second Edition, 2000.

Disclosure: Nothing to disclose.

PP0826

DOES BOTULINUM TOXIN STILL HAVE A ROLE TO PLAY IN THE TREATMENT OF CHRONIC ANAL FISSURE?

A. Guimarães¹, J. Pereira², J. Neves¹, A.C. Caetano³, T.F. Almeida Franco Leal³, D. Costa³, T. Carvalho¹, J. Damasceno⁴, Â. Rodrigues³, R. Gonçalves¹

¹Unidade Local de Saúde de Braga, Braga, Portugal, ²Unidade Local de Saúde de Matosinhos, Gastroenterologia, Águeda, Portugal, ³Unidade Local de Saúde de Braga, Gastroenterology, Braga, Portugal, ⁴Unidade Local de Saúde de Braga, Vila Nova de Gaia, Portugal

Contact E-Mail Address: andreaguimaraes32@gmail.com

Introduction: Chronic anal fissure is a frequent cause of referral to the proctology clinic and is associated with significant morbidity. In cases refractory to conservative measures, botulinum toxin (BT) is an alternative to a surgical approach, without the risk of permanent damage to the internal anal sphincter.

Aims & Methods: The aim of this study was to assess the efficacy of BT in anal fissure healing and to identify predictors of non-response. This was a retrospective, single-centre, observational study. Patients with chronic anal fissure who underwent TB between 2019 and 2023. Patients with a follow-up of less than 3 months or inflammatory bowel disease were excluded. On clinical reassessment, patients were categorised as complete, partial or refractory.

Results: Of the 118 patients selected, 80 were included. The average age was 49.1 ± 14.9 years, with 73.8% (n=59) of the patients female. The overall TB response rate was 62.0%. More than one TB session was carried out on 40.0% (n=32) of the patients, with an average of 1.5 ± 0.6 per patient, with an interval between sessions of 3.4 ± 5.8 months. On reassessment after the first application, 30.0% (n=24) showed a complete response, 56.3% (n=45) a partial response and 13.8% (n=11) were refractory. Of the partial or refractory responders, after completing the treatment cycle, 56.5% (n=13) showed a complete response, 26.1 (n=6) a partial response and 17.4% (n=4) were refractory. During a median follow-up of 10.0 [3-48] months, 7 patients became asymptomatic and 2 patients had a recurrence of the cleft. 21 patients (26.3%) were referred for surgery. The duration of symptoms was an independent predictor of TB treatment failure and the need for surgery (OR 4.895; p=0.049).

Conclusion: TB has a satisfactory response rate in the treatment of patients with chronic anal fissure, making it possible to avoid surgery in patients, specially with a short duration of symptoms.

Disclosure: Nothing to disclose.

PP0827

EFFICACY AND SAFETY OF OFFICE-BASED PROCEDURES FOR HEMORRHOIDAL DISEASE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

T. Carvalho¹, A.C. Caetano¹, B. Arroja¹, P. Mesquita², A.C. Gomes², I. Malta³, T. Gago³, A.R. Gonçalves⁴, R. Coelho⁴, S. Ponte⁵, P.S. Salgueiro⁵, F.M.D. Castro Poças⁵, A.C. Bravo⁶, C. Gouveia⁶, A.M. Oliveira⁷, M. Francisco⁷, A. Guimarães¹, J. Damasceno¹, J. Neves¹, R. Gonçalves¹, T. Leal¹

¹ULS de Braga, Gastroenterology, Braga, Portugal, ²ULS de Gaia e Espinho, Gastroenterology, Vila Nova de Gaia, Portugal, ³ULS do Algarve, Faro, Portugal, ⁴ULS de São João, Gastroenterology, Porto, Portugal, ⁵ULS de Santo António, Gastroenterology, Porto, Portugal, ⁶ULS de Loures-Odivelas, Gastroenterology, Loures, Portugal, ⁷ULS de Amadora/Sintra, Gastroenterology, Amadora, Portugal

Contact E-Mail Address: taniacarvalho1994@gmail.com

Introduction: Hemorrhoidal disease affects 2-7% of patients with inflammatory bowel disease (IBD) (1,2), but treatment recommendations are limited due to apparent higher morbidity in this subset of patients (3,4). Currently, there is limited data about hemorrhoidal disease treatment in IBD, there is even less information regarding non-surgical treatment.

Aims & Methods: The authors aim to evaluate the safety and efficacy of office-based procedures in hemorrhoidal disease in patients with IBD. This is a retrospective and Portuguese multicenter study (7 centers) that included patients with IBD who underwent office-based procedures for hemorrhoidal disease between July 2013 and July 2021. Data relating to IBD and hemorrhoidal disease were analyzed namely success, relapse, and complications.

Success was defined as a significant improvement in symptoms after office-based procedures, without the need for additional treatment. Relapse was defined as a worsening of symptoms, requiring new office-based procedures/surgery.

Results: 129 patients were included, 70% with ulcerative colitis; in Crohn's disease, 5.4% had a history of perianal disease. Only 62% of patients had endoscopic remission and 18% were on biologics. Regarding Goligher's classification, the majority had grade II (48%). 77 patients underwent rubber band ligation (RBL), 44 patients underwent polidocanol injection and 8 patients underwent both techniques, in a total of 304 procedures (median of 2(2) sessions/patient).

The treatment was effective in 88% of patients, of which 14% relapsed, with an average follow-up time of 55.3±34.5 months. Of 304 procedures, 17 (5.6%) procedures were complicated, in a total of 16 patients (12.4%), 2 (0.65%) required invasive treatment, without cases of pelvic sepsis. Success, relapse, and complications were not associated with IBD (type, medication, or remission at the time of treatment) (p>0.05). Success was greater in patients with Goligher grades I and II (p=0.037).

Complications were higher in patients undergoing RBL (p=0.030) and in patients with Goligher grade III (p=0.031).

Conclusion: This is the first study about office-based procedures for hemorrhoidal disease in IBD, showing similar efficacy to the general population, with a low rate of complications, and should therefore be recommended in these patients.

References:

1. Eglinton TW, Barclay ML, Gearry RB, Frizelle FA. The spectrum of perianal Crohn's disease in a population-based cohort. *Dis Colon Rectum*. 2012 Jul;55(7):773-7.
2. Choi YS, Kim DS, Lee DH, Lee JB, Lee EJ, Lee SD, et al. Clinical Characteristics and Incidence of Perianal Diseases in Patients With Ulcerative Colitis. *Ann Coloproctol*. 2018 Jun;34(3):138-143.

3. Jeffery PJ, Parks AG, Ritchie JK. Treatment of haemorrhoids in patients with inflammatory bowel disease. *Lancet*. 1977 May 21;1(8021):1084-5.
4. D'Ugo S, Franceschilli L, Cadeddu F, Leccesi L, Blanco Gdel V, Calabrese E, et al. Medical and surgical treatment of haemorrhoids and anal fissure in Crohn's disease: a critical appraisal. *BMC Gastroenterol*. 2013 Mar 11;13:47

Disclosure: Nothing to disclose.

PP0828

UNDERWATER ENDOSCOPIC MUCOSAL RESECTION OF RECTAL NEUROENDOCRINE TUMORS – A CASE SERIES OF AN INNOVATIVE ENDOSCOPIC APPROACH

F. Mendes¹, R. Morais¹, I. Gullo², G. Macedo¹

¹Centro Hospitalar Universitário São João, Department of Gastroenterology, Porto, Portugal, ²Centro Hospitalar Universitário São João, Department of Pathology, Porto, Portugal

Contact E-Mail Address: francisco.cnm@gmail.com

Introduction: Neuroendocrine neoplasms are a group of tumors originating from neuroendocrine cells and peptidergic neurons. Rectal neuroendocrine tumors (NETs) are the second most common location for gastrointestinal NETs, albeit representing only 2% of all rectal neoplasms. Most of these are nonfunctional and asymptomatic although pain, blood loss and perianal discomfort can occur in larger lesions.

Endoscopically, rectal NETs typically appear as small and well-delimited submucosal lesions, with a yellowish color. The risk of lymph node metastasis is related to the tumor size, therefore, the current guidelines consider endoscopic resection as an option for rectal NETs smaller than 2 centimeters.

The classical options for lesion removal include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). However, EMR has a higher risk of incomplete resection, whereas ESD is more invasive and has an increased risk of complications (namely bleeding and perforation).

In this setting, underwater endoscopic mucosal resection (UEMR) appeared as an alternative that facilitates the complete removal of a lesion through the filling of the intestinal cavity with water. Previous Eastern studies suggest a higher complete resection rate with this endoscopic technique when compared to conventional EMR.

Aims & Methods: The present study aimed to evaluate the outcomes of patients submitted to UEMR of rectal NETs in a reference center.

Results: A total of 5 patients underwent UEMR for rectal NETs (Table 1). 3 patients had a tumor from the proximal rectum and 2 patients from the distal rectum. The tumor size ranged between 4 and 8 millimeters.

After marking the lesion borders, the entire rectal cavity was filled with saline and UEMR was performed. The lesion scar was closed with endoscopic clips in all cases. In a single case, delayed rectal bleeding was observed 3 days after procedure, solved with application of an additional endoscopic clip, without the need of inpatient management. No other complications were reported.

A R0 resection was observed in 80% of the cases. In a single case a positive basolateral margin was observed. However, after performance of a second UEMR in the scar (where no endoscopic evidence of residual lesion was found), there was absence of lesion in the histopathological sample. All the tumors had a G1 grade in the WHO 2019 Classification for Neuroendocrine Tumors, with a Ki-67 index ranging between 1 and 3%.

In all the cases there was absence of residual lesion or recurrence in the follow up endoscopy.

Patient	Tumor size, millimeters	Resection margins (R)	Tumor grade (G)	Ki67 (%)	Recurrence
♂, 79	5	R0	G1	3	No
♀, 64	8	R0	G1	2	No
♂, 33	4	R0	G1	3	No
♀, 46	8	R0	G1	3	No
♂, 74	8	R1	G1	1	No

Conclusion: This case series showcases UEMR as an effective alternative to conventional EMR, achieving high satisfactory complete resection rates, while having a low rate of procedure related complications. Therefore, UEMR should be contemplated when considering an endoscopic removal for rectal neuroendocrine neoplasms.

References:

1. Rinke, Anja et al. "European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for colorectal neuroendocrine tumours." *Journal of neuroendocrinology* vol. 35,6 (2023)
2. Srirajaskanthan, Rajaventhana et al. "Optimising Outcomes and Surveillance Strategies of Rectal Neuroendocrine Neoplasms." *Cancers* vol. 15,10 2766. 15 May. 2023
3. Shi, Haitao et al. "Underwater endoscopic mucosal resection for rectal neuroendocrine tumors (with videos): a single center retrospective study." *BMC gastroenterology* vol. 22,1 276. 2 Jun. 2022
4. Okada, Masahiro et al. "Underwater Endoscopic Mucosal Resection of Small Rectal Neuroendocrine Tumors." *Frontiers in medicine* vol. 9 835013. 19 Apr. 2022

Disclosure: Nothing to disclose.

PP0829

BENIGN PROCTOLOGICAL PATHOLOGIES AND QUALITY OF LIFE: AN UNDERESTIMATED SOURCE OF DISABILITY

F. Faouzia¹, J. Imene¹, S. Leila¹

¹Monastir Medical Faculty, Gastro-enterology Departement, Monastir, Tunisia

Contact E-Mail Address: fofuaaa.fareees@gmail.com

Introduction: The aim of our study is to highlight the impact of these pathologies on quality of life using the BURDEN haemo/fiss score validated by the French Society of Colo-proctology (SNFCP).

Aims & Methods: This is a prospective cross-sectional study over a 3-month period (January, February and March 2024) including our patients with benign proctological pathology (hemorrhoidal pathology/anal fissure) examined in our proctology consultation.

Quality of life was assessed using the BURDEN haemo/fiss score, which comprises 23 questions covering four domains exploring physical and psychological problems, discomfort during defecation and impact on sexual life. Pain was rated using the VAS (Visual Analogue Scale) from 0 to 10.

Results: We enrolled 112 patients with a mean age of 48 ±15 years. Among our patients, 60.7% were women with a sex ratio of 0.64.

Hemorrhoidal pathology topped the list with a percentage of 68.8%, while patients with anal fissure presented 42.9%. Two conditions coexisted in 31.3% of cases (N=15).

The mean Hemo/Fiss score was 60.08±14.29 [extremes 28-93]. The mean score for each dimension of the score was 59.84±23.58 for physical disorders, 55.91±24.71 for psychological disorders, 76.86±21.37 for difficulty with defecation and 47.71±20.14 for sexual disorders.

All pathologies had a negative impact on quality of life, irrespective of sex and type of underlying proctological pathology (p>0.05), with significant concordance between the VAS and the BURDEN haemo/fiss score (p<0.001).

Forty-eight of our patients (42.9%) had unfavorable socioeconomic conditions, making it impossible to obtain the full prescribed treatment, which led to non-improvement and/or early recurrence of symptoms. Work stoppage was noted in 36.6% of our patients (N=41).

Conclusion: Our study clearly shows the deterioration in quality of life in patients with benign proctological pathologies, with work stoppage in a considerable number of our patients, often young, regardless of gender or the specific type of underlying pathology. This finding prompts us to pay particular attention to these conditions in all their dimensions.

References: Sailer M, Bussen D, Debus ES, Fuchs KH, Thiede A. Quality of life in patients with benign anorectal disorders. *Br J Surg.* 1998 Dec;85(12):1716-9.

Liu Y, Wang L, Liu J, Geng F, Li Y, Zheng L. The relationship between anal disease and quality of life: a bibliometric study. *Ann Transl Med.* 2022 Apr;10(8):484.

Disclosure: Nothing to disclose.

PP0830

ARTIFICIAL INTELLIGENCE AND HIGH-RESOLUTION ANOSCOPY: DEVELOPMENT OF AN INTEROPERABLE ARTIFICIAL INTELLIGENCE MODEL FOR THE DETECTION AND DIFFERENTIATION OF ANAL SQUAMOUS CELL CARCINOMA PRECURSORS – A MULTICENTRIC STUDY

M.J. Mascarenhas Saraiva¹, L. Spindler², T. Manzione³, M. Martins¹, N. Fathallah², T. Ribeiro¹, J. Afonso¹, F. Mendes¹, P. Cardoso¹, J. Fernandes⁴, J. Ferreira⁴, G. Macedo¹, S. Nadal³, V. de Parades²
¹Centro Hospitalar São João, Gastroenterology, Porto, Portugal,
²Hospital Paris Saint Joseph, Paris, France, ³Infectology Institute Emilio Ribas, Sao Paulo, Brazil, ⁴Faculty of Engineering of the University of Porto, Porto, Portugal

Contact E-Mail Address: miguelmascarenhassaraiva@gmail.com

Introduction: High-resolution anoscopy (HRA) plays a central role in the detection and treatment of precursors of anal squamous cell carcinoma (ASCC). The visual characterization of high-grade intraepithelial lesions (HSIL) is hampered by a limited interobserver agreement. Artificial intelligence (AI) algorithms have shown high levels of efficiency in detecting and differentiating HSIL from low-grade squamous intraepithelial lesions (LSIL) in HRA images. Nevertheless, these studies have been conducted using a digital videoproctoscope, whose use is not predicted in the standards of the International Anal Neoplasia Society (IANS). Our aim was to develop a deep learning system for automatic detection and differentiation of HSIL versus LSIL using HRA images from both conventional and digital proctoscopes.

Aims & Methods: A convolutional neural network (CNN) was developed based on 151 HRA exams from 137 patients undergoing HRA at two large volume centres (GH Paris Saint-Joseph, Paris, France and Emílio Ribas Infectiology Institute, São Paulo, Brazil), using conventional HRA (KLP 200 LED®, Kolplast) and digital HRA (THD Proctostation®, THD SpA). A total of 58,498 images were included, 29,212 images containing HSIL and 29,286 LSIL. Partial subanalyses were performed to evaluate the performance of the CNN in the subset of images with no staining (n=2,820), acetic acid (n=27,191), lugol (n=10,011), and after treatment of the anal canal (n=11,047). For these subanalyses, training, and testing datasets comprised 90% and 10% of each class's total number of images. The sensitivity, specificity, accuracy, positive and negative predictive values, and area under the curve (AUC) were calculated.

Results: The overall accuracy of the CNN in distinguishing HSIL from LSIL during the testing stage was 98.6%. The algorithm had an overall sensitivity and specificity of 97.3% and 99.1%, respectively. The overall AUC was 0.99. For staining with acetic acid, HSIL was differentiated from LSIL with

an overall accuracy of 96.4%, while for lugol and after therapeutic manipulation these values were 96.6% and 99.3%, respectively. The AUC ranged between 0.98 and 1.00 in these particular subgroups.

Conclusion: The introduction of AI algorithms to HRA may enhance the early diagnosis of ASCC precursors, and this system showed to perform adequately across conventional and digital HRA interfaces. Improving the detection of ASCC precursors may improve the treatment outcomes and prognosis. The developed AI model is the first model capable of performing adequately in different clinical sub settings and in different systems available on the market.

References:

1. Hillman, R.J.; Cuming, T.; Darragh, T. et al. 2016 IANS International Guidelines for Practice Standards in the Detection of Anal Cancer Precursors. *J Low Genit Tract Dis* 2016; 20: 283-291.
2. Mistrangelo, M.; Salzano, A. Progression of LSIL to HSIL or SCC: is anoscopy and biopsy good enough? *Tech Coloproctol* 2019; 23: 303-304.
3. Deshmukh, A.A.; Suk, R.; Shiels, M.S. et al. Recent Trends in Squamous Cell Carcinoma of the Anus Incidence and Mortality in the United States, 2001-2015. *J Natl Cancer Inst* 2020; 112: 829-838.
4. Palefsky, J.M.; Lee, J.Y.; Jay, N. et al. Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer. *New England Journal of Medicine* 2022; 386: 2273-2282.
5. Neukam, K.; Milanés Guisado, Y.; Fontillón, M. et al. High-resolution anoscopy in HIV-infected men: Assessment of the learning curve and factors that improve the performance. *Papillomavirus Res* 2019; 7: 62-66.
6. Saraiva, M.M.; Spindler, L.; Fathallah, N. et al. Artificial intelligence and high-resolution anoscopy: automatic identification of anal squamous cell carcinoma precursors using a convolutional neural network. *Tech Coloproctol* 2022; 26: 893-900.
7. Pathologists, C.o.A. Protocol for the Examination of Excision Specimens From Patients With Carcinoma of the Anus. 2021; 4.2.0.

Disclosure: Nothing to disclose.

PP0831

MILLIGAN AND MORGAN IN THE MANAGEMENT OF HEMORRHOIDAL DISEASE: PROCTOLOGY UNIT EXPERIENCE

S. Kaouissi¹, S. Mechhor¹, M. Cherkaoui Malki¹, H. El Bacha¹, N. Benzzoubair¹, I. Errabih¹

¹University Mohamed V, Department of Hepato-Gastroenterology and Proctology Medicine B, Rabat, Morocco

Contact E-Mail Address: S.kaoui@um5r.ac.ma

Introduction: Hemorrhoidal disease (HD) is the most common pathology in proctology, with an estimated prevalence of between 4.4% and 39%. It can be managed in a variety of ways: hygienic-dietary measures, medical, instrumental or surgical treatment. The latter is considered especially after failure of medical and instrumental treatment.

Aims & Methods: Aims : The aim of our study is to report our experience with Milligan and Morgan technique in the management of hemorrhoidal disease.

Materials and methods: This was a monocentric retrospective descriptive-analytical study conducted over a 12-year period: from January 2011 to January 2023. The data studied were age, sex, clinical manifestations, stage of HD on proctological examination and therapeutic data. All patients who underwent Milligan and Morgan hemorrhoidectomy (MMH) and presented with stage IV and III hemorrhoids (after failure of instrumental treatment) were included in our study. Excluded were asymptomatic patients, patients with surgical contraindications and other stages treated by non-surgical means. The statistical study was carried out using IBM-SPSS 20.0 software. The chi-2 test was used to compare categorical variables.

Results: 468 patients were enrolled during the study period. The mean age of this population was 41 years (22-71). The sex ratio M/F was 2,1. Clinical expression was dominated by rectal discharge in 246 patients (74%), proctalgia in 132 patients (28%), anal pruritus in 119 patients (25%) and anal oozing in 56 patients (12%). Proctological examination revealed stage IV haemorrhoids in 201 patients (43%) and stage III haemorrhoids in 267 patients (57%). 25 patients (5.3%) had an associated anal fissure. Anemia was present in 341 patients (72.8%), with a mean hemoglobin value of 7.8 g/dl. Transfusion was required in 65 patients (14%) who presented with severe anemia of less than 7g/dl. Colonoscopy was indicated in 87 patients (18.5%) over the age of 45 with rectal bleeding, and in 42 patients (9%) with a history of digestive cancer. Milligan and Morgan's indication was stage III hemorrhoids with severe anemia in 65 patients (14%), after failure of infrared photocoagulation in 194 patients (41.4%); after failure of HAL-RAR treatment n=8 (1.7%) and stage IV hemorrhoids in 201 patients (43%). The procedure performed was a hemorrhoidectomy. An open pedicle MMH type was performed. Patients with an associated anal fissure (5.3%) underwent the Bellan procedure in addition to hemorrhoidectomy. Immediate post-operative complications included post-operative pain in all our patients, urinary retention in 31 patients (6.6%), significant post-operative bleeding in 2 patients (0.5%) treated by electrocoagulation in the OR, and minimal post-operative bleeding in 117 patients (25%) treated by compression bandaging. The latter was reported in 43 patients (36.7%) with stage III hemorrhoids and 74 patients (63.2%) with stage IV hemorrhoids. This difference was statistically significant ($p < 0.001$). Late complications included delayed healing in 9 patients (1.9%), 4 of whom were diabetic, anal stenosis in 5 patients (1%), requiring sphincterotomy combined with anoplasty in 3 patients, and finger dilatation in 2 patients. Anal stenosis was reported in 4 patients who did not undergo postoperative digital rectal examination and 1 patient who did. This difference is statistically significant $p = 0.03$.

Conclusion:

MMH remains the gold standard for the treatment of hemorrhoidal disease. The results are satisfactory, especially in the long term. Post-hemorrhoidectomy anal stenosis remains the most serious complication.

Disclosure: Nothing to disclose.

PP0832

EXPERT'S PERCEPTION OF CHAT-GPT BASED ANSWERS TO COMMON PATIENT'S QUERIES IN GASTROINTESTINAL ENDOSCOPY: UNVEILING THE IMPACT OF AN AI CONVERSATIONAL TOOL

G. Calabrese^{1,2}, R. Maselli³, M.F. Maida⁴, F. Barbaro⁵, R. Morais⁶, O.M. Nardone⁷, E. Sinagra⁸, R. Di Mitri¹, S. Sferrazza¹

¹ARNAS Civico Hospital, Gastroenterology and Endoscopy Unit, Palermo, Italy, ²Federico II University Hospital, Clinical Medicine and Surgery, Naples, Italy, ³Humanitas Research Hospital, IRCCS, Endoscopy, Rozzano, Italy, ⁴University of Enna 'Kore', Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ⁵Gemelli Hospital, Digestive Endoscopy, Roma, Italy, ⁶Centro Hospitalar São João, Gastroenterology, Porto, Portugal, ⁷University of Naples Federico II, Public Health, Naples, Italy, ⁸HSR Giglio, Endoscopy and Gastroenterology Unit, Cefalù, Italy

Contact E-Mail Address: giulocalabrese94@gmail.com

Introduction: Chat Generative Pre-Trained Transformer (Chat-GPT) by OpenAI, released in November 2022, is an artificial intelligence (AI) language model that was designed to generate human-like text based on inputs provided. Given the high potential of a pre-trained technology, it has recently gained attention among healthcare professionals for its capabilities of communicating information. This technology has, indeed, proven to be effective in providing information to patients regarding specific queries and doubts in common gastrointestinal diseases, ensuring high-quality answers. Gastrointestinal (GI) endoscopy is perceived by patients as uncomfortable and worrying, despite the advancements regarding instrumentation and sedation.

Aims & Methods: We aimed to assess the effectiveness of Chat-GPT in answering common patients' queries on GI endoscopy in three domains (reliability, accuracy, and comprehensibility). Two healthcare providers selected the 18 most common patient queries regarding GI endoscopy. Questions, concerning pre-procedural, intraprocedural or post-procedural queries, were administered to Chat-GPT 4.0 with the following prelude "As a physician, how would you answer to a patient asking...". Afterwards, ten healthcare professionals, including eight physicians and two nurses, along with two non-healthcare professionals were asked to evaluate the AI-based answers. All 12 participants had expertise in GI endoscopy and were asked to rank all 18 answers according to a Likert scale for each of the following features: reliability (1 to 6 points), accuracy and comprehensibility (1 to 3 points). The one-way non-parametric ANOVA (Kruskal-Wallis test) was applied to test the distribution of respondents' ranks.

Results: The mean overall reliability was 5.2 ± 1.7 (Figure 1), with questions 3 and 8 receiving the highest score (5.7 ± 0.7 and 5.7 ± 0.7 , respectively), and questions 13 and 15 ranking the lowest (4.6 ± 0.9 and 4.8 ± 0.4 , respectively). The mean overall accuracy was 2.7 ± 0.4 , with most of the questions ranking more than 2.5, except for questions 1, 13 and 14, which all had 2.5 ± 0.5 scores. Finally, the mean overall comprehensibility was 2.9 ± 0.2 : regarding this specific feature, question 18 scored had the lower mean rank (2.5 ± 0.5). The mean ranks with standard deviations for each feature of all 18 answers are reported in Table 1.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Reliability	5.3 ± 0.5	5.3 ± 0.6	5.7 ± 0.7	5.5 ± 0.5	4.9 ± 0.9	4.8 ± 1.2	5.4 ± 0.7	5.7 ± 0.7	5.1 ± 0.7	5.3 ± 0.8	5.5 ± 0.5	5.4 ± 0.8	4.6 ± 0.9	4.9 ± 1.0	4.8 ± 0.4	5.4 ± 0.7	5.4 ± 0.7	5.0 ± 0.6
Accuracy	2.5 ± 0.5	2.6 ± 0.5	2.8 ± 0.5	3.0 ± 0.0	2.6 ± 0.5	2.7 ± 0.5	2.8 ± 0.4	2.9 ± 0.3	2.7 ± 0.5	2.9 ± 0.5	2.8 ± 0.5	2.8 ± 0.5	2.5 ± 0.5	2.5 ± 0.5	2.8 ± 0.4	2.8 ± 0.5	2.8 ± 0.4	2.8 ± 0.5
Comprehensibility	2.9 ± 0.3	2.9 ± 0.3	2.9 ± 0.3	3.0 ± 0.0	2.8 ± 0.5	2.8 ± 0.6	2.9 ± 0.3	2.9 ± 0.3	2.9 ± 0.3	2.9 ± 0.3	2.8 ± 0.4	2.9 ± 0.3	2.8 ± 0.4	2.8 ± 0.5	2.9 ± 0.3	2.8 ± 0.4	2.8 ± 0.3	2.5 ± 0.5

All participants have expressed a positive opinion regarding the potential use of the answers provided by the AI, except for answer number 13. The score distribution was not similar for all the 12 participants in each feature,

reliability ($p < 0.001$), accuracy ($p = 0.005$) and comprehensibility ($p = 0.006$).

Conclusion: The findings of our study show that Chat-GPT can deliver reliable, accurate and easy-to-understand responses to a broad range of common queries from patients undergoing GI endoscopy. The use of AI-based conversational programs, like Chat-GPT, holds promise as a valid option for physicians to support daily clinical practice, also within the setting of GI endoscopy.

Disclosure: Nothing to disclose.

PP0833

OPIOID ENTEROPATHY AND PANCREATOBILIOPATHY: FIRST DESCRIPTION OF A NEW ENTITY RESULTING FROM LONG-TERM OPIUM ADDICTION

K. Mathur¹, C.L. Birda¹, T. Yadav², B. Sureka², S.K. Singh¹, A. Agarwal¹

¹All India Institute of Medical Sciences, Jodhpur, Department of Gastroenterology, Jodhpur, India, ²All India Institute of Medical Sciences, Jodhpur, Department of Radiology, Jodhpur, India

Contact E-Mail Address: drashu123@gmail.com

Introduction: Opium addiction is common in north-western India. Opioid-induced bowel dysfunction (OIBD) and narcotic bowel syndrome are well-described gastrointestinal disorders in patients with opioid addiction. We describe patients with prolonged opium addiction presenting with ulcerocostrictive disease of the bowel and pancreatobiliary abnormalities.

Aims & Methods: We prospectively collected data on patients using opium for prolonged durations and presenting with gastrointestinal symptoms. Opioid enteropathy (OE) was diagnosed in patients with evidence of ulcerocostrictive disease of the bowel and opioid pancreatobiliary pathology (OPB) was diagnosed in patients with dilated common bile duct (CBD) and/or pancreatic duct (PD) (double-duct sign), with all other causes excluded by careful evaluation.

Results: Of 148 patients [mean age 57.3 ± 11.6 years; 145/148 (98%) males] with opioid addiction and gastrointestinal complaints, 59 (39.9%), 53 (35.8%), 18 (12.2%) & 18 (12.2%) patients were diagnosed with OIBD, isolated OE, isolated OPB, and combined OE+OPB, respectively. Mean duration of opioid consumption was 18.4 ± 10.9 years. Of 148 patients, 48 (32.4%) consumed raw opium (yields 9.5-14.2% morphine), 89 (60.1%) consumed opium husk (yields 0.1-0.3% of morphine), and 4 (2.7%) consumed tramadol tablets. Median duration of symptoms was 12 (3-60) months. Common presenting symptoms were pain abdomen ($n=116$, 78.4%), constipation ($n=93$, 62.8%), vomiting ($n=29$, 19.6%), anorexia ($n=79$, 53.4%), weight loss ($n=74$, 50%) and easy fatigability ($n=64$, 43.2%). Evaluation in patients with OE revealed anemia (69%) and hypoalbuminemia (74.6%) with a mean Hemoglobin of 9.5g/dL. Endoscopy revealed pyloric and duodenal strictures in 9.9% & 8.5% of the patients, respectively. Colonoscopy revealed multiple web-like focal circumferential partial strictures with superficial ulceration in terminal ileum in 8.5% of patients. CECT enterography showed multiple short-segment jejunal and ileal strictures in 73.2% of patients, while duodenal/pyloric strictures were seen in 8.5% & 9.9%, respectively. Histopathology from the stricture site (18 patients) showed only ischemic changes. Patients with OPB ($n=36$) revealed dilated CBD (mean diameter: 11.6 mm) (91.7%) and MPD (mean diameter: 5.7mm) (69.4%) up to papilla with normal LFTs and imaging, including endoscopic ultrasound. Conservative management with opioid deaddiction, iron supplements, rifaximin, and laxatives was done in all patients, with endoscopic balloon dilatation of pyloric stricture needed in six patients. Only 1/3 rd of the patients agreed and could undergo successful opioid de-addiction.

Conclusion: Long-term, high-dose opium addiction can lead to multifo-

cal ulceration and stricture formation in the GI tract, and pancreatobiliary dilatation. This entity should be recognized as an important differential of Crohn's disease in areas with a high prevalence of opium addiction. Further, these patients with double-duct sign are often subjected to evaluation and surgery, suspecting periampullary malignancies. Knowledge about this spectrum of disorders may prevent unnecessary diagnostic and surgical interventions.

Disclosure: Nothing to disclose.

PP0834

A SYSTEMATIC REVIEW AND META-ANALYSIS OF TEST PERFORMANCE IN RANDOMIZED CONTROLLED TRIALS FOR COLONOSCOPY SCREENING FOR COLORECTAL CANCER

C. Hamashima¹, T. Terasawa², K. Abe¹, S. Hosono³, S. Sasaki⁴, T. Katayama⁵, T. Tadano⁶, K. Hoshi⁷

¹Teikyo University, Tokyo, Japan, ²Fujita Health University, Toyoake, Japan, ³National Cancer Center, Tokyo, Japan, ⁴St. Luke's International Hospital Affiliated Clinic, Tokyo, Japan, ⁵Hyogo Prefecture University, Akashi, Japan, ⁶Miyagi Cancer Association, Sendai, Japan, ⁷National Health Institute, Wako, Japan

Contact E-Mail Address: chamashi@med.teikyo-u.ac.jp

Introduction: The modality for colorectal cancer (CRC) screening has transferred from guaiac fecal occult blood testing (gFOBT) to fecal immunochemical testing (FIT), but its sensitivity remains lower. While total colonoscopy (TCS) has been anticipated as a new modality for CRC screening, conclusive results based on randomized controlled trials (RCTs) are still pending. Test performance RCTs have been utilized to predict the effectiveness of new modalities for CRC screening. They were adopted for the evaluation of cancer screening using a stepwise approach in the World Endoscopic Evaluation (Young et al. Cancer 2016).

Aims & Methods: A systematic review of test performance RCTs for CRC screening was conducted. Candidate articles were searched from inception to October 14, 2023, using Ovid MEDLINE, Cochrane Central Registry, Embase, and Ichushi-web. We compared the test performance of TCS screening, referring to the following modalities: gFOBT, FIT, flexible sigmoidoscopy (FS), and CT colonography (CTC). Single and multiple rounds were searched. Test performance indicators included participation rates in CRC screening, advanced neoplasia (AN) detection rates, and CRC detection rates. The primary results were evaluated using an intention-to-screen (ITS) based network meta-analysis, and a per-protocol analysis was also performed.

Results: Seventeen RCTs (13 from Europe, two from the US, and one each from Israel and China), involving a total of 341,123 healthy screening invitees, were included. The median participation rates for the programs based on FIT, FS, and TCS were 50.4 % (28.6-94.0%), 32.3% (7.9-52.1%), and 21.5% (10.0-42.5%), respectively. In the network meta-analysis, participation rates for TCS screening were significantly lower than the programs based on FS (RR=0.58; CI: 0.37-0.89), FIT (RR=0.45; CI: 0.31-0.65), and gFOBT (RR=0.45; CI: 0.30-0.69). Detection rates for AN were consistently higher for TCS than for FIT (RR= 2.18, 95%CI:1.46-3.26) but not statistically significant for FS (RR=1.06, 95%CI: 0.65-1.73). Similarly, TCS had higher CRC detection rates compared to FIT (RR= 1.80, 95%CI:1.04-3.12) and FS (RR= 1.52, 95%CI:0.87-2.64). While AN and CRC detection rates for TCS were higher than those of CTC, the differences were not statistically significant (AN: RR= 1.02, 95%CI:0.65-1.73, CRC: RR= 0.73 95%CI: 0.32-1.64). The follow-up period of single-round RCTs was limited until diagnosis, but the screening frequency varied depending on the follow-up duration, which could affect effectiveness. Screening intervals were typically two years for FIT, five years for FS, and ten years for CS. One quasi-experimen-

tal study combined the following arms from different RCTs with extended follow-up: one-time CS, one-time FS, and four rounds of FIT (Grobbee et al. Clin Gastroenterol Hepatol 2020). The participation rate was higher for FIT (73%) compared to FS (31%) and CS (24%). Cumulative AN and CRC detection rates were higher for FIT (AN = 4.5%, 95%CI:4.2-4.9, CRC =0.5% 95%CI: 0.4-0.6), but nearly equivalent for CS (AN = 2.2%, 95%CI:1.8-2.6, CRC =0.2% 95%CI: 0.1-0.3) and FS (AN = 2.3%, 95%CI:2.0-2.7, CRC =0.2% 95%CI: 0.1-0.3).

Conclusion: The single-round test performance of colonoscopy screening might be superior to that of other modalities. To confirm the priority of TCS, it is insufficient to draw conclusions based on the results of a single-round performance, given variations in screening intervals and frequencies among other modalities. Cumulative effects among different modalities should be compared within the same follow-up period.

References: Young GP, Senore C, Mandel JS, et al. Recommendations for a step-wise comparative approach to the evaluation of new screening tests for colorectal cancer. Cancer. 2016;122(6):826-39.

Grobbee EJ, van der Lugt M, van Vuuren AJ, et al. Diagnostic yield of one-time colonoscopy vs one-time flexible sigmoidoscopy vs multiple rounds of mailed fecal immunohistochemical tests in colorectal cancer screening. Clin Gastroenterol Hepatol. 2020;18(3):667-75.

Disclosure: Nothing to disclose.

PP0835

A SINGLE-CENTRE ANALYSIS OF POST-COLONOSCOPY COLORECTAL CANCER

Y.J. Chew¹, S. Hebbbar², D. Olawuyi²

¹Royal Stoke University Hospital, Stoke-on-Trent, United Kingdom,

²Royal Stoke University Hospital, Stoke-on-Trent, Newcastle under Lyme, United Kingdom

Contact E-Mail Address: yunjie2k@doctors.net.uk

Introduction: Post colonoscopy colorectal cancer (PCCRC) is colorectal cancer diagnosed after a normal colonoscopy with no cancer found. In England, the rate of PCCRCs has been decreasing but remains around 6.5% for colonoscopies performed from 2011-2013¹. English study suggested that 80% of PCCRCs are avoidable². We aim to analyse PCCRC cases using the local data and determine the demographics, nature of cancer and the cause of PCCRC.

Aims & Methods: The PCCRCs are identified following the linkage of Hospital Episode Statistics, Bowel cancer screening programme (BCSP) and cancer registry datasets. As new colorectal cancers are registered with the National Cancer Registration and Analysis Service (NCRAS), PCCRC cases will be identified. Each colorectal cancer (ICD-10 code C18-20) provisionally registered within the Hospital Episode Statistics dataset will be identified and determined whether a colonoscopy was performed within 6- 48 months before the diagnosis which failed to identify the cancer.

This audit includes patients diagnosed with PCCRC 6-48 months after a colonoscopy was performed in a single medical centre in England.

Once the cases had been confirmed, we reviewed the clinical, pathology and radiological findings of each case. We also looked at interval cancer which the World Endoscopy Organisation (WEO) defines as one diagnosed before the next recommended interval. Important to note that all interval cancers are PCCRCs but not all PCCRCs are interval cancer.

Results: 39 cases were included and 29 were confirmed to be true PCCRC which fulfilled the above criteria. 7 did not meet the criteria. (2 index colonoscopies performed at other trusts, 3 missing data, 2 other types of cancers such as Neuroendocrine tumour and appendiceal tumour, 1 has <6 months to cancer diagnosis from index colonoscopy, 2 flexible sigmoidoscopy was performed as index colonoscopy to investigate per rectal bleed-

ing but subsequent cancer was found in ascending colons). 52% (n=15) of patients were male with a median age of cancer diagnosis at 74 years old (range 22-84). In terms of PCCRC, 24% (n=7) presented via the National Bowel Screening Programme (BCSP), 14% (n=4) presented with per rectal bleeding, 7% (n=2) presented with abnormal imaging and the same proportion of patients presented due to anaemia, non-specific change in bowel habit, weight loss, diarrhoea, abdominal pain and surveillance for family history of gene mutation. 3% (n=1) were diagnosed after presenting for polypectomy and 3% (n=1) presented with intestinal obstruction.

In terms of investigations that led to PCCRC, 45% (n=13) were via 2-weeks-wait colonoscopy, 24% (n=7) were via National Bowel Screening Programme, 17% (n=5) were diagnosed by Computed Tomography (CT) imaging, 7% (n=2) via flexible sigmoidoscopy and 7% (n=2) was via surgically resected sample. Upon diagnosis of PCCRC, 7% (n=2) tested positive for Lynch syndrome, 24% (n=7) was tested but no marker was found and 69% (n=20) was not tested. In terms of size of PCCRC, 66% (n=19) had tumour size >2cm. 66% (n=17) of tumour size was determined by histopathological sample, 21 (n=6) via endoscopy, 3% (n=1) via CT imaging and 17% (n=6) was not known.

In terms of PCCRC staging, 48% (n=14) was Dukes' A staging, 21% (n=6) was Dukes' B, 7% (n=2) was Dukes' C and 24% (n=7) was Dukes' D. 83% (n=24) was planned for curative treatment and 17% (n=5) was planned for palliative treatment. 52% (n=16) had surgical resection only, 17% (n=29) had surgical resection and chemotherapy, 3% (n=11) had surgical resection and radiotherapy, 3% (n=1) had surgical resection, chemotherapy and radiotherapy, 7% (n=2) had chemotherapy and radiotherapy, 3% (n=1) had chemotherapy only, 3% (n=1) had endoscopic resection only and 7% (n=2) had no treatment.

In terms of the type of interval cancer, 14% (n=4) was non-interval A, 7% (n=2) was non-interval B, 66% (n=19) was non-interval C and 21% (n=4) was interval cancer. Important to note was 66% (n=19) had no further follow-up or test arranged due to adequate examination on the index endoscopy. 90% of index endoscopies report no difficulties. 75% (n=22) was due to clinician factors, 10% (n=3) was due to administrative errors such as booking delay and 10% (n=3) was due to patient factors such as patient's decision and intercurrent illness.

Conclusion: The majority of the PCCRC had treatment with curative intent. Most PCCRC cases are due to clinician factors and measures needed to improve this. The high percentage of non-interval type C PCCRC would be explained by either a fast-growing cancer or a missed lesion since up to 90% of the index procedures reported no difficulty.

References:

1. Burr NE, Derbyshire E, Taylor J, *et al.* Variation in post-colonoscopy colorectal cancer across colonoscopy providers in English National Health Service: population-based cohort study. *BMJ* 2019;367:l6090. doi:10.1136/bmj.l6090
2. Anderson R, Burr NE, Valori R. Causes of Post-colonoscopy Colorectal Cancers Based on World Endoscopy Organization System of Analysis. *Gastroenterology* Published Online First: January 2020. doi:10.1053/j.gastro.2019.12.03

Disclosure: Nothing to disclose.

PP0836

IMPACT OF ELECTRONIC PATIENT RECORDS AND THE INTRODUCTION OF A CLINICAL NURSE SPECIALIST ENDOSCOPY ON ADENOMA DETECTION RATES

S. Corneillie¹, F. Dedeurwaerder², F. Marolleau³, P. Vandecandelaere², J. Dewyspelaere³, C. De Vloo², F. De Pauw², S. De Meulder², L. Harlet⁴, J. Decaestecker², L. Baert², F. Baert², J. Bossuyt⁵, L. Desomer⁴, D. De Wulf³

¹AZ DELTA, Clinical Nurse Specialist Endoscopy, Roeselare, Belgium, ²AZ DELTA, AZ Delta Rumbeke-Menen-Torhout, Department of Histopathology, Roeselare, Belgium, ³AZ DELTA, Gastroenterology and hepatology, Roeselare, Belgium, ⁴AZ DELTA, Gastroenterology and Hepatology, Roeselare, Belgium, ⁵AZ DELTA, Data-Analysis Oncology, Roeselare, Belgium

Contact E-Mail Address: sophie.corneillie@azdelta.be

Introduction: Colorectal cancer screening, particularly through colonoscopy, is a pivotal element of preventive healthcare. Understanding the multifaceted factors influencing Adenoma Detection Rates (ADR) is crucial for optimizing the effectiveness of screening programs. This study aims to provide a detailed analysis of the impact of electronic patient records, clinical interventions, and other variables on ADR trends in a gastroenterology unit.

Aims & Methods: Aim: This study aims to investigate the factors contributing to the increase in ADR over time through the implementation of a comprehensive colonoscopy Quality Indicator recording system.

Methods: This study investigates the trends in Adenoma Detection Rates (ADR) and associated factors in a gastroenterology unit over a four-year period. The primary outcome is the evolution of ADR, with secondary outcomes including the relationship between ADR and withdrawal time, endoscopists' experience, and the Boston Bowel Preparation Scale (BBPS). The introduction of electronic patient records in 2019 establishes the baseline for data analysis.

In 2022, a full-time clinical nurse specialist in endoscopy began actively monitoring key indicators, such as ADR, BBPS, and withdrawal time. These metrics were regularly communicated to endoscopists through a PowerBi dashboard. As part of clinical interventions, a patient preparation video was introduced to enhance communication and standardize information for patients undergoing colonoscopies.

Results: We included patients aged 50 or older, with a total of 3340 colonoscopies performed between January 2019 and September 2023. 8000 colonoscopies are performed per year, but we only include the adenoma screening indications.

The analysis revealed a significant increase in ADR in 2020, coinciding with the introduction of electronic patient records. This marked rise, at 13.5%, suggests a positive influence of improved record-keeping on diagnostic accuracy. However, subsequent years showed a more modest increase of 0.4%, indicating a potential plateau effect. In 2022, the introduction of a full-time clinical nurse specialist in endoscopy corresponded with changes in key indicators.

The BBPS showed a significant decrease in 2023 compared to 2022 (p=0.03), while a reverse trend was observed between 2020 and 2021 (p=0.03). Endoscopist's experience (p=0.2470), and BBPS scores (p=0.1652) were no significant predictors of the increased ADR. Adjusted for the other variables included in the model. These findings underscore the complex interplay of various factors influencing outcomes.

Conclusion: The dynamic nature of ADR observed in this study prompts a closer examination of the long-term effects of electronic patient records on diagnostic accuracy. The initial surge in ADR following their introduction suggests a positive and immediate impact on procedural outcomes. However, the subsequent stabilization of ADR raises questions about

the sustainability of this effect over time. The introduction of a full-time clinical nurse specialist in endoscopy in 2022 may have contributed to the observed changes in BBPS. This emphasizes the potential benefits of multidisciplinary collaboration in optimizing colonoscopy outcomes. The observed decrease in BBPS in 2023, coupled with the sustained ADR levels, suggests a need for ongoing assessment of clinical interventions. The patient preparation video, introduced as part of enhanced communication strategies, may have contributed to these changes. Future research should delve deeper into the nuanced impact of such interventions on procedural outcomes and patient experiences.

Disclosure: Nothing to disclose.

PP0837

ESTABLISHING A BRIDGE BETWEEN PATIENTS UNDERGOING GASTROSCOPY AND COLONOSCOPY: A RETROSPECTIVE CROSS-SECTIONAL STUDY

X. Chen¹, B. Wei¹, B. Xu¹, L. Ji¹, C. Yang¹, Q. Zhan¹

¹The Affiliated Wuxi People's Hospital of Nanjing Medical University, Department of Gastroenterology, Wuxi, China

Contact E-Mail Address: 3489654307@qq.com

Introduction: It remains unknown whether gastric histopathology is associated with the occurrence of colorectal diseases.

Aims & Methods: Aims : We aimed to clarify the association between gastric histopathology and colorectal diseases, especially colorectal polyps (CP). On this basis, we established risk prediction models for different colorectal diseases.

Methods: A retrospective cross-sectional study was conducted on 2540 patients who underwent gastroscopy and colonoscopy simultaneously in The Affiliated Wuxi People's Hospital of Nanjing Medical University from January 1, 2021 to August 31, 2023. Basic demographic data, previous medical history, clinical symptoms, important laboratory indicators, and gastric histopathology classification were collected for univariate and multivariate analysis. The nomogram model was constructed with R language while its calibration was tested by Hosmer-Lemeshow, its discrimination was evaluated by Area Under the ROC Curve (AUC), and its clinical efficacy was evaluated by Decision Curve Analysis (DCA).

Results: 1: According to the results of colonoscopy, patients were divided into Normal group (N=601); Non-adenomatous polyp group (N=576); Adenomatous polyp group (N=1116); Inflammatory bowel disease group (N=149) and Colorectal cancer group (N=98). The average age of the five groups was (55.04±13.95) years, (58.74±11.58) years, (61.83±10.19) years, (50.48±16.64) years, and (66.10±10.80) years, respectively. The CRC group had the largest proportion of males, accounting for 59.2% (n=58).

2: The results of gastroscopy were divided into: Normal; NAG (non-atrophic gastritis); AG or IM (atrophic gastritis/intestinal metaplasia); Gastric polyps; Esophageal cancer; and SC-patho (pathological gastric cancer). The association between indicators and colonoscopy results was analyzed to establish risk prediction models for different colorectal diseases. We found that gastric histopathology was significantly correlated with NAP and AP; for clinical symptoms, abdominal pain was significantly correlated with colorectal diseases, and the contribution ranking was: NAP>IBD>CRC>AP; hematochezia was significantly correlated with IBD; for clinical indicators, anemia was significantly correlated with AP, and CEA was significantly correlated with CRC; for previous medical history, previous colonoscopy examination was significantly correlated with colorectal diseases, and the contribution ranking was: NAP>CRC>AP>IBD; history of hypertension and rheumatism disease were significantly correlated with NAP; history of chronic kidney disease and rheumatism disease were significantly correlated with AP; history of chronic kidney disease

ease and gastrointestinal tumor were significantly correlated with CRC; history of hypertension and thyroid nodules were significantly correlated with IBD; for demographic indicators, age was significantly correlated with NAP, AP, and CRC; while BMI was significantly correlated with IBD.

3: Using R language to establish the nomogram prediction model, we could find that: all the prediction models had good discrimination, and the AUC of the CRC model reached 0.885. Through the calibration curve, we could find that all prediction models has strong consistency, among which the AP model has the highest consistency and the smallest absolute error value of 0.007.

Conclusion: The nomogram prediction model has good discrimination and calibration, and has good clinical value for predicting the occurrence probability of different colorectal diseases.

Disclosure: Nothing to disclose.

PP0838

DELINEATION OF RECURRENCE AMONG NON-EXPERT ENDOSCOPISTS IS LESS ACCURATE THAN EXPERTS BUT IS READILY TRAINABLE BY A SHORT LEARNING INTERVENTION

S. Smeets¹, M.E. Argenziano², L. Debels³, M. Montori², P.J. Poortmans¹, C. Schoonjans⁴, A. Sorge⁵, T. Tornai¹, L. Desomer⁶, D.J. Tate¹

¹University Hospital Ghent, Gastroenterology and Hepatology, Ghent, Belgium, ²Università politecnica delle Marche Ancona Italy, Gastroenterology and Hepatology, Ancona, Italy, ³University Hospital Brussels, Gastroenterology and Hepatology, Jette, Belgium, ⁴AZ Sint-Jan Brugge, Gastroenterology and Hepatology, Brugge, Belgium, ⁵Gent University Hospital, Gent, Belgium, ⁶Gastroenterologia ed Endoscopia digestiva, Milano, Italy, ⁶AZ Delta, Gastroenterology and Hepatology, Roeselare, Belgium

Contact E-Mail Address: sander.smeets@uzgent.be

Introduction: Endoscopic mucosal resection (EMR) is a safe and effective method to resect large (>20mm) non-pedunculated colorectal polyps (LNPCPs). Incorrect decision making regarding the endoscopic resection scar after EMR risks unrecognized residual or recurrent adenoma (RRA) propagating into post-colonoscopy colorectal cancer. Despite expert series suggesting that scar recognition and interrogation are well performed with a high negative predictive value(2), the performance of non-experts remains unknown.

Aims & Methods: We aimed to investigate the diagnostic performance of endoscopic imaging in detecting RRA at an endoscopic resection scar amongst non-experts and the impact of a learning intervention.

Methods: A survey containing 15 paired High-Definition White Light (HD-WL) and virtual chromoendoscopy (VC) images, a learning intervention on detection of RRA (LT), followed by 15 different HD-WL & VC images was circulated to the GIEQs foundation mailing list. Images were selected from a prospective database of surveillance after EMR. For each image the same questions were asked: Is this a resection scar? Is there evidence of RRA? What is your confidence? Demographic data collected included participant number of EMRs performed, current grade and years of experience. Comparisons were made to expert opinion derived at a consensus meeting of the senior authors regarding the appearances of the images using the approach set out in Desomer et al. 2017(2).

Results: 82 participants completed the survey (response rate: 4.1%) resulting in 2,460 observations. 15 (18.3%) participants were experienced (performed >100 EMRs).

The overall accuracy of RRA detection pre-LT was 75.3% (95%CI 73.5-77.2) vs post-LT: 79.5% (95%CI 77.2-82.0, p =.006). Specificity significantly im-

proved post-LT (50.0% [95%CI 44.1-55.4] pre vs 94.0% [95%CI 90.0-98.0] post, $p < .001$).

Both accuracy and specificity were significantly higher amongst experienced endoscopists (acc: 83.6% [95%CI 79.4-87.7], spec: 67.3% [95% CI 50.2-84.3]) versus inexperienced endoscopists (acc: 74.0% [95% CI 72.1-75.8], $P < .001$, spec: 46.7% [95% CI 41.1-52.3], $P < .003$) pre-LT. Specificity improved in both groups post-LT (experienced 67.3% [95%CI 50.2-84.3] vs 97.6% [95% 100-92.7], $P < .001$ and inexperienced 46.7% [95% CI 41.1-52.3] vs 93.5% [95% CI 88.3-98.7], $P < .001$). Furthermore the difference in specificity disappeared post-LT (spec experienced 97.6% [95% CI 100-92.7] vs inexperienced 93.5% (95% CI 88.3-98.7) $p = .440$).

	PRE learning intervention				POST learning intervention				P Overall PRE- vs POST-LT
	Experienced*	Inexperienced*	P*	Overall***	Experienced**	Inexperienced**	P**	Overall***	
Accuracy (95% CI)	83.6% (79.4-87.7)	74.0% (72.1-75.8)	<.001	75.3% (73.5-77.2)	82.6% (77.6-87.7)	78.7% (75.9-81.7)	0.220	79.5% (77.2-82.0)	.006
Sensitivity (95% CI)	73.3% (64.9-81.7)	71.7% (68.6-74.8)	.650	72.0% (69.1-74.8)	75.0% (67.2-82.2)	69.8% (65.6-74.1)	0.300	70.9% (67.5-74.5)	.649
Specificity (95% CI)	67.3% (50.2-84.3)	46.7% (41.1-52.3)	.003	50.0% (44.1-55.4)	97.6% (100-92.7)	93.5% (88.3-98.7)	0.440	94.0% (90.0-98.0)	<.001
PPV (95% CI)	85.4% (78.1-92.8)	68.3% (65.2-71.3)	<.001	70.9% (67.8-74.0)	99.3% (100.0-97.7)	97.8% (96.4-99.3)	0.338	98.0% (99.1-98.0)	<.001
NPV (95% CI)	85.4% (78.1-92.8)	68.3% (65.2-71.3)	<.001	81.3% (80.0-83.0)	99.3% (100.0-97.7)	97.8% (96.4-99.3)	0.338	65.1% (62.1-68.1)	<.001

RRA smaller than 10 mm was more likely to be missed (<10mm: 77.5%, <5mm: 58.9% of missed detections). RRA occupying $\leq 20\%$ of the scar accounted for two-thirds of missed detections (66.4%). RRA located on the edge of a scar (versus centrally) accounted for the vast majority of missed RRA (88.1%).

Conclusion: The accuracy of RRA detection in non-experts is low compared to previously published expert series, even amongst endoscopists performing EMR regularly. Low accuracy predominantly resulted from low specificity which was mitigated by the training intervention. These results suggest that the potential negative effects of missing RRA at an endoscopic resection scar (propagation between surveillance procedures and the potential for development of PCCRC) can be mitigated by training.

References: 1. Michielan A, Merola E, Vieceli F, Rogger TM, Crispino F, Sartori C, et al. Recurrence rates after piecemeal endoscopic mucosal resection of large colorectal laterally spreading tumors. *Ann Gastroenterol*. 2023;36(2):195-202.

2. Desomer L, Tuticci N, Tate DJ, Williams SJ, McLeod D, Bourke MJ. A standardized imaging protocol is accurate in detecting recurrence after EMR. *Gastrointestinal endoscopy*. Department of Gastroenterology and Hepatology, Westmead Hospital, Sydney, New South Wales, Australia.: Elsevier, Inc.; 2017. p. 518-26.

Disclosure: Nothing to disclose.

PP0839

CLINICAL OUTCOMES OF COLORECTAL NEOPLASM WITH INCOMPLETE ENDOSCOPIC SUBMUCOSAL DISSECTION

H.-H. Oh¹, C.-M. Im¹, K.-Y. Ma^{1,2}, D.-H. Kim¹, H.-S. Kim¹, Y.-E. Joo¹
¹Chonnam National University Medical School, Gwangju, South Korea, ²Mokpo Hankook Hospital, Mokpo, South Korea

Contact E-Mail Address: cksanr87@naver.com

Introduction: A positive resection margin after endoscopic submucosal dissection (ESD) of a colorectal neoplasm is associated with an increased risk of recurrence. However, it may be caused by cauterization or tangential specimen cutting. We aimed to identify the clinical significance of positive resection margins in colorectal neoplasms after ESD.

Aims & Methods: We reviewed 1010 patients who underwent colorectal ESD at two hospitals between 2015 and 2020. The inclusion criteria were that the patient 1) had an *en bloc* resection, 2) had at least one follow-up colonoscopy. The recurrence rates and presence of residual tumors in the surgical specimens were evaluated.

Results: A total of 632 patients were enrolled. Among them, 557 patients had complete resections, and 75 had incomplete resections with positive resection margins in vertical and/or horizontal margin. The rate of additional surgery after ESD and recurrence was significantly higher in patients with incomplete resection compared to patients with complete resection. However, in patients with non-invasive colorectal neoplasm, all 411 patients, including those with complete and incomplete resection, had no recurrence. Among 221 patients with invasive lesions, 39 underwent additional surgery due to non-curative resection. Positive vertical margin and lymphovascular invasion were associated with remnant tumors in the surgical specimen. Lymphovascular invasion was associated with lymph node metastasis. However, no remnant tumor nor lymph node metastases were found in patients with only one unfavorable histological factor, including 1) positive vertical margin, 2) a submucosal invasion depth > 1000 μ m, 3) lymphovascular invasion, 4) poorly differentiated cancer, and 5) high tumor-budding grade.

Conclusion: A positive resection margin after *en bloc* colorectal ESD for noninvasive lesions was not associated with recurrence. In T1 colorectal cancer with a positive vertical resection margin, salvage surgery can be considered in selected patients with additional risk factors.

Disclosure: Nothing to disclose.

PP0840

FACTORS ASSOCIATED WITH TECHNICAL DIFFICULTY IN COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: A HONAM ASSOCIATION FOR THE STUDY OF INTESTINAL DISEASE (HASID) MULTICENTER STUDY

H.-H. Oh¹, C.-M. Im¹, K.-Y. Ma¹, B.-C. Jin¹, H.-Y. Song², S.-J. Kim³, D.-H. Kim⁴, J. Lee³, S.-W. Kim¹, G.-S. Seo², Y.-E. Joo⁴, H.-S. Kim⁴
¹Chonnam National University Medical School, Gwangju, South Korea, ²Jeonbuk National University Medical School, Jeonju, South Korea, ³Wonkwang University School of Medicine, Iksan, South Korea, ⁴College of Medicine, Chosun University, Gwangju, South Korea

Contact E-Mail Address: yejoo@chonnam.ac.kr

Introduction: Colorectal endoscopic submucosal dissection (ESD) is promising but challenging procedure. It is not widely performed due to its technical difficulty. We aimed to find the predictive factors associated with technical difficulty in colorectal ESD before procedure.

Aims & Methods: Clinical data from patients who underwent ESD for colorectal tumor in five hospitals in Honam province of South Korea between 2015 to 2020 were reviewed retrospectively. Technically difficult colorectal ESD procedure was defined in three points. Long procedure time (longer than 60 minutes), occurrence of perforation and failure of *en bloc* resection. Factors associated with technically difficult ESD were included as main outcome measure.

Results: 1446 patients were identified and their data were analyzed. Median procedure time was 30.0 minutes and median long axis of the tumor was 20.1 mm. Technically difficult procedures including long procedure time were 231 cases (16.0%), perforation occurred in 34 cases (2.3%) and *en bloc* resection was done in 1292 cases (89.3%).

Tumor size larger than 35 mm (odd ratio [OR] 1.474, $p=0.047$), central depression or ulceration in the lesion (OR 1.474, $p=0.013$), previous endoscopic mucosal resection or polypectomy procedure (OR 2.428, $p=0.020$) were associated with technically difficult ESD. Descending colon located tumor (OR 5.355, $p<0.001$), use of IT knife (OR 4.157, $p=0.003$) were associated with perforation.

Conclusion: Recognizing factors associated with technically difficult ESD can help planning the ESD procedure beforehand.

Disclosure: Nothing to disclose.

PP0841

ANALYZING LEARNING CURVES OF EXPERT COLONOSCOPISTS IN SEDATION-FREE WATER EXCHANGE COLONOSCOPY

S. Li¹, Z. Wang¹, C. Yang¹

¹Tongji Hospital, School of Medicine, Tongji University, Department of Gastroenterology and Hepatology, Shanghai, China

Contact E-Mail Address: lishanshan327@alumni.tongji.edu.cn

Introduction: Water exchange, replacing air insufflation during colonoscopy's insertion phase, has become popular for its effectiveness in enhancing endoscopic quality. Its adoption by novices, who show improved performance, raises questions about its benefits for experienced colonoscopists.

This study examines the adaptation process of three seasoned colonoscopists to water exchange, evaluating if they achieve similar improvements, to understand its broader utility.

Aims & Methods: In this study, three expert colonoscopists, each with over 10,000 air insufflation colonoscopies, first conducted 100 standard procedures. They then switched to the water exchange technique for 100 more procedures across four groups. Key outcomes—cecal intubation rates, learning curves, pain scores, polyp detection, complications, abdominal compression, position changes, and bowel preparation quality—were compared between methods to evaluate the water exchange's effectiveness and patient experience.

Results: Cecal intubation success rates and median times for water exchange groups were over 90% and below 6 minutes, matching results from traditional air insufflation methods. No notable differences were found in intubation times between endoscopists A and B, but endoscopist C showed significant time variations, especially in the third quartile, indicating a performance shift ($P<0.001$).

A slight, non-significant decrease in abdominal compression was observed for endoscopist A, while endoscopist B's transition to water exchange significantly reduced compression needs (37% vs. 21%; $P<0.05$), showcasing its advantages. No changes were evident for endoscopist C. Position change demands differed significantly between methods for endoscopists B and C, hinting at endoscopist C's preference for air insufflation ($P=0.001$). In this study, the pain scores in the water exchange group were significantly lower than those in the air insufflation group ($P=0.008$)

for only one expert. For the other experts, although the number of patients with a pain score of 10 decreased and the number of patients with a pain score of 0 increased in the water exchange group, no significant difference was observed. This suggests that for seasoned professionals, the water method primarily played a significant role in reducing severe abdominal pain. For patients with mild pain, the effect was unclear.

An analysis of the learning curve, considering cecal intubation success and time, found no correlation with the number of water exchange procedures performed, indicating all endoscopists quickly adapted to the method without a marked learning curve, maintaining success rates above 90%.

Conclusion: The study found the water method effectively reduced severe abdominal pain, with its impact on mild pain less clear. Experts showed proficiency with this technique from the start, achieving 95% success rates in cecal intubation, indicating quick adaptation. Despite this, traditional colonoscopy's known drawbacks weren't significantly highlighted. However, experts familiar with conventional techniques found the water method more challenging and saw no major advantages for colorectal screening.

References: 1. Leung FW. Water Exchange to Facilitate Unsedated Colonoscopy-Reply. *Jama*, 2017,318:754-755.

2. de Groen PC. Water Exchange Insertion Colonoscopy-How You Can Do It Too. *Am J Gastroenterol*, 2019,114:703-704.

3. Cadoni S, Hassan C, Frazzoni L, et al. Impact of water exchange colonoscopy on endoscopy room efficiency: a systematic review and meta-analysis. *Gastrointest Endosc*, 2019,89:159-167.e113.

Disclosure: Nothing to disclose.

PP0842

PREVALENCE AND PREDICTIVE FACTORS OF COLORECTAL SESSILE SERRATED LESIONS IN YOUNGER INDIVIDUALS

J.-H. Yeh¹, C.-W. Lin², Y.-C. Lee³, J.-Y. Wang⁴

¹EDA Dachang hospital, I-shou University, Internal medicine, Kaohsiung City, Taiwan, ²EDA hospital, I-shou University, Internal medicine, Kaohsiung City, Taiwan, ³National Taiwan University Hospital, Taipei, Taiwan, ⁴Kaoshiung Medical University Hospital, Kaohsiung, Taiwan

Contact E-Mail Address: b9202078@gmail.com

Introduction: Sessile serrated lesions (SSLs) are obscured lesions predominantly at right sided colon and associated with interval colorectal cancer. However, the prevalence and risk factors among younger individuals remain unclear.

Aims & Methods: This retrospective study enrolled individuals who underwent index colonoscopy. The primary outcomes were SSL prevalence between younger (<50 years) and older (≥ 50 years) groups, whereas the secondary outcomes included clinically significant serrated polyps (CSSPs). Multivariable logistic regression was employed to identify predictors. The aim of this study is to investigate the prevalence of SSL of younger age people in the single center cohort. Individuals who visited outpatient services were mostly symptomatic, were eligible for screening colonoscopy, or had abnormal fecal/tumor marker test results.

Additionally, asymptomatic individuals who underwent health checkups at their own expense or who adhered to national labor law requirements were included. The exclusion criteria were as follows:

- (1) instances of duplicated cases due to prior colonoscopy examinations,
- (2) cases with inadequate bowel preparation,
- (3) history of hospitalization or colonoscopy as part of an emergency room visit,
- (4) cases of unsuccessful cecal intubation or flexible sigmoidoscopy, and;
- (5) suspicious or confirmed inflammatory bowel disease. Notably, indi-

viduals who had previously undergone colonoscopy at other hospitals, as confirmed by their electronic medical records or chart review, were also excluded.

Results: Of the 9854 eligible individuals, 4712 (47.8%) were categorized into the younger age group. Individuals in the younger age group exhibited a lower prevalence of adenomas (22.6% vs. 46.2%, $P < 0.001$) and right-sided adenomas (11.2% vs. 27.2%, $P < 0.001$) compared with their older counterparts. However, both groups exhibited a similar prevalence of SSLs (7.2% vs. 6.5%, $P = 0.157$) and CSSP (10.3% vs. 10.3%, $P = 0.956$). Multivariable analysis results revealed that age = 40–49 years (odds ratio [OR] = 1.81, 95% confidence interval [CI] = 1.01–3.23), longer withdrawal time (OR = 1.18, 95% CI = 1.15 – 1.21 per minute increment), and endoscopist performance (OR = 3.35, 95% CI = 2.44 – 4.58) were independent predictors of SSL detection in the younger age group. No significant correlation was observed between adenoma and SSL detection rates among endoscopists ($P = 0.083$).

	Younger age group (< 50 -years-old)	Elder age group (≥ 50 -years-old)	P value
Cases (%)	4712 (47.8)	5142 (52.1)	Not applicable
Symptomatic cases (%)	1985 (42.1)	2763 (53.7)	$< 0.001^*$
Sex (female, %)	2425 (51.5)	2649 (51.5)	$< 0.001^*$
Family history of CRC (%)	318 (6.7)	164 (3.2)	$< 0.001^*$
Adenoma (%)	1063 (22.6)	2375 (46.2)	$< 0.001^*$
Advanced adenoma (%)	188 (4.0)	728 (14.2)	$< 0.001^*$
SSL (%)	341 (7.2)	335 (6.5)	0.157
CSSP (%)	485 (10.3)	531 (10.3)	0.956
CRC (%)	19 (0.4)	72 (1.4)	$< 0.001^*$

Conclusion: SSLs are not uncommon among younger individuals. Moreover, diligent effort and expertise are of paramount importance in SSL detection. Future studies should explore the clinical significance of SSLs in younger age individuals.

References: 1. Murcia O, Juárez M, Hernández-Illán E et al. Serrated colorectal cancer: Molecular classification, prognosis, and response to chemotherapy. *World J Gastroenterol* 2016; 22: 3516-3530. doi:10.3748/wjg.v22.i13.3516

2. Meester RG, van Herk MM, Lansdorp-Vogelaar I et al. Prevalence and clinical features of sessile serrated polyps: a systematic review. *Gastroenterology* 2020; 159: 105-118. e125

3. Burnett-Hartman AN, Newcomb PA, Phipps AI et al. Colorectal endoscopy, advanced adenomas, and sessile serrated polyps: implications for proximal colon cancer. *The American journal of gastroenterology* 2012; 107: 1213-1219. doi:10.1038/ajg.2012.167

4. Zorzi M, Senore C, Da Re F et al. Detection rate and predictive factors of sessile serrated polyps in an organised colorectal cancer screening programme with immunochemical faecal occult blood test: the EQuiPE study (Evaluating Quality Indicators of the Performance of Endoscopy). *Gut* 2017; 66: 1233-1240

5. Lall V, Ismail AGM, Ayonrinde OT. Disparate age and sex distribution of sessile serrated lesions and conventional adenomas in an outpatient colonoscopy population—implications for colorectal cancer screening? *International Journal of Colorectal Disease* 2022; 37: 1569-1579

6. Kim HY, Kim SM, Seo J-H et al. Age-specific prevalence of serrated lesions and their subtypes by screening colonoscopy: a retrospective study. *BMC Gastroenterology* 2014; 14: 82. doi:10.1186/1471-230X-14-82

Disclosure: This study is recently accepted by Endoscopy (2024/02). We hope this research can be considered for the congress with its clinical importance and impact.

PP0843

CAN 5-MINUTE COLONOSCOPY WITHDRAWAL TIME BE THE BENCHMARK BASED ON EXPERIENCED ENDOSCOPISTS AND EXCELLENT BOWEL PREPARATION? A MULTICENTER, RANDOMIZED CONTROLLED, BACK-TO-BACK TRIAL IN CHINA

B. Wei¹, Y. Cheng², B. Xu¹, X. Chen¹, X. Zhu¹, Q. Zhan¹

¹The Affiliated Wuxi People's Hospital of Nanjing Medical University, Wuxi People's Hospital, Wuxi Medical Center, Wuxi, China, ²WUXI People's Hospital, Digestive Medicine, Wuxi, China

Contact E-Mail Address: weibingnicherish@163.com

Introduction: Although current quality indicators of colonoscopy recommend 6 minutes as the minimum standard for withdrawal time (WT), long-term implementation of the 6-minute WT results in low colonoscopy turnaround efficiency and it don't take into account the effects of endoscopists experience and the quality of bowel preparation of colonoscopy. Whether it is still necessary to adhere to the 6-minute WT standard under the condition of experienced endoscopists and excellent bowel preparation quality is worthy of further discussion. Therefore, this study based experienced endoscopists and excellent bowel preparation (Boston Bowel Preparation Scale score, BBPS ≥ 8) is aimed to compare the effects of 5-minute WT versus 6-minute WT on adenoma detection rate (ADR) and adenoma miss rate (AMR).

Aims & Methods: Aims : This study based experienced endoscopists and excellent bowel preparation (Boston Bowel Preparation Scale score, BBPS ≥ 8) is aimed to compare the effect of 5-minute WT versus 6-minute WT on adenoma detection rate (ADR) and adenoma miss rate (AMR).

Methods : This multicenter, randomized controlled trial involving 298 patients was conducted from June 2023 to February 2024 in 5 centers, including Wuxi People's Hospital, Jiangsu Province People's hospital, Xuzhou First People's Hospital, The Second Affiliated Hospital of Soochow University, Taizhou People's Hospital. Colonoscope was inserted and withdrew twice on each patient and all procedures for the same patient were done by the same endoscopist. Participants were randomly divided into the 5-minute WT group (the first WT-5-minute and the second WT-6-minute, n =161) and the 6-minute WT group (the first WT-6-minute and the second WT-6-minute, n=137), and a timer was used to adjust the withdrawal speed. The primary outcome was ADR and AMR.

Results: The baseline characteristics of the two groups were similar (Table 1) and colonoscopy characteristics of the patients in the two groups regarding quality of bowel preparation, cecal intubation rate, cecal intubation time, cecal intubation distance, number of abdominal compression, number of position change were comparable (Table 2). Overall ADR(44.5% vs 41.6%, $P = 0.613$), ADR in the first (37.2% vs 36.6%, $P = 0.918$) and second withdrawal (15.3% vs 14.3%, $P = 0.800$) were not significantly increased in the 6-minute WT group compared with the 5-minute WT group. Likewise, the overall advanced adenoma detection (AADR) (8.0% vs 6.8%, $P = 0.694$), AADR in the first (7.3% vs 6.8%, $P = 0.875$) and second withdrawal (1.5% vs 0.6%, $P = 0.888$) did not differ statistically. Further analysis showed that AMR (23.5% vs 24.6%, $P = 0.826$) and advanced adenoma miss rate (AAMR) (6.7% vs 13.3%, $P = 0.543$) were lower in the 5-minute WT group than in the 6-minute WT group, less adenomas and advanced adenomas were missed in the 5-minute WT group, although not statistically significant (Table 3).

Conclusion: Shortening WT from 6 to 5 minutes didn't reduce ADR based experienced endoscopists and excellent BBPS, a 5-minute WT benchmark was acceptable with experienced endoscopists and excellent bowel preparation quality of colonoscopy.

Disclosure: Nothing to disclose.

PP0844

MULTICENTER PROSPECTIVE FEASIBILITY STUDY OF COMPLIANCE, SAFETY, AND ACCEPTANCE OF COLON CAPSULE ENDOSCOPY (CCE) AND SMALL BOWEL CAPSULE ENDOSCOPY (SBCE) IN THE OUT-OF-CLINIC SETTING IN JAPAN (HOMECAM-J STUDY)

N. Ohmiya¹, A. Araki², K. Nakamura³, K. Ito⁴, N. Hotta⁵, A. Tsuboi⁶, Y. Kakugawa³, S. Oka⁶, Y. Saito³, T. Kato⁴, S. Tanaka⁷

¹Fujita Health University School of Medicine, Departments of Gastroenterology and Advanced Endoscopy, Toyoake, Japan,

²Toranomon Hospital, Health Management Center, Tokyo, Japan, ³National Cancer Center Hospital, Endoscopy Division, Tokyo, Japan, ⁴The Jikei University School of Medicine, Centre for Preventive Medicine, Tokyo, Japan, ⁵Masuko Memorial Hospital, Department of Internal Medicine, Nagoya, Japan, ⁶Hiroshima University Hospital, Department of Gastroenterology, Hiroshima, Japan, ⁷JA Onomichi General Hospital, Director, Onomichi, Japan

Contact E-Mail Address: nohmiya@med.nagoya-u.ac.jp

Introduction: The U.S. FDA has granted the PillCam™ SB3 @HOME program which allows patients to undergo SBCE at home. This program for SBCE remote use, however, is not cleared in the other countries, neither is a telehealth option of CCE worldwide.

Aims & Methods: We aimed to confirm compliance, safety, and acceptance of CCE and SBCE in the out-of-clinic setting in Japan. We enrolled 30 subjects who had not undergone CE (24 for CCE and 6 for SBCE) at 6 gastroenterological centers between June 2023 and February 2024. All examinees were provided with detailed instructions on how to interact with data-recorder automatic signaling, and for CCE examinees, low residue diet and a bowel preparation set including magnesium citrate, sodium picosulfate, PEG solution plus ascorbic acid, and castor oil. We prospectively collected data regarding baseline characteristics, compliance with procedures, CE results, acceptability with a subjectively categorized questionnaire survey, and adverse events using REDCap system (jRCTs042220163).

Results: Of 24 CCE examinees (male/female: 11/13, median age of 51 years, 23 for health check-up and 1 for positive fecal immunological test), 16 and 8 underwent CCE at home and at the workplace, respectively. Compliance rates of intake of low residue diet, recorder-capsule self-pairing, ingestion of CCE, intake of a bowel preparation set, return of equipment were all 100%. During the procedure, 12 examinees (50%) called the physician 18 times about when to finish (66.7%), how to take preparation (16.7%), and how to operate recorder (11.1%). Capsule excretion rate within examination time was 83% (20/24). In the 4 examinees who did not excrete the capsule, last images showed the rectum (n=1), transverse colon (n=1), ascending colon (n=1), and cecum (n=1). Median examination time between capsule ingestion and removal of sensor belt was 227 (80-1233) min; 208.5 (80-320) min and 697 (240-1233) min in examinees with or without capsule excretion, respectively ($P=0.0118$). The overall adequate endoscopic cleansing rate was 83%. Abnormalities were detected at 37.5% (9/24); colorectal polyps (25.0%), diverticula (8.3%), suspicious small bowel subepithelial tumor (4.2%). There was only one adverse event including intermittent abdominal pain. The proportions of examinees who reported "quite easy", "fairly easy", "moderate", "fairly hard", "quite hard", and wished for CCE as the next examination were 17%, 25%, 25%, 29%, 4%, and 67%, respectively.

Of 6 SBCE examinees (male/female: 4/2, median age of 39 years, 2 for obscure GI bleeding and 1 for chronic diarrhea, 1 for ileitis, 1 for abdominal pain, 1 for health check-up), 4 and 2 underwent SBCE at home and at the workplace, respectively. Compliance rates of recorder-capsule self-pairing, ingestion of SBCE, return of equipment were all 100%. During the procedure, 3 examinees (50%) called the physician 4 times about when to finish (75.0%) and how to operate recorder (25.0%). Total enteroscopy

rate within examination time was 100% (6/6). Median examination time between capsule ingestion and removal of sensor belt was 198 (158-372) min. The overall adequate endoscopic observation rate was 100%. Abnormalities were detected at 16.7% (1/6); duodenal polyp (n=1). There were no adverse events. The proportions of examinees who reported "quite easy", "fairly easy", and "moderate" were 33%, 33%, and 33%, respectively.

Conclusion: CCE and SBCE with all procedures in an out-of-clinic setting were feasible, safe, and comparable to those in a hospital setting, but remote consultations would be needed during the procedures.

Disclosure: Nothing to disclose.

PP0845

COMPUTER-AIDED DIAGNOSIS FOR THE RESECT AND DISCARD STRATEGY FOR COLORECTAL POLYPS: A SYSTEMATIC REVIEW AND META-ANALYSIS

T. Rizkala¹, C. Hassan¹, Y. Mori², M. Spadaccini¹, M. Misawa³, G. Antonelli⁴, E. Rondonotti⁵, E. Dekker⁶, B.B. Houwen⁷, O. Pech⁸, S. Baumer^{8,9}, D. von Renteln⁹, R. Maselli¹, A. Facciorusso¹⁰, M. Menini¹, A. Schilirò¹, K. Khalaf¹¹, H. Patel¹², D. Radadiya¹³, P. Bhandari¹⁴, S. Sultan¹⁵, P. Sharma¹³, D.K. Rex¹⁶, A. Repici¹, CADx analysis study group

¹Humanitas Clinical and Research Center –IRCCS–, Endoscopy Unit, Rozzano, Italy., Milano, Italy, ²University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway, ³Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ⁴Sapienza Università di Roma at Sant'Andrea University Hospital, Digestive and Liver diseases Unit, Roma, Italy, ⁵Ospedale Valduce, Gastroenterology Unit, Dept. of Gastroenterology, Como, Italy, ⁶AMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁷Amsterdam University Medical Centers, location AMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁸Krankenhaus Barmherzige Brüder Klinik für Gastroenterologie und Interventionelle Endoskopie - Klinik, Klinik für Gastroenterologie und, Regensburg, Germany, ⁹CHUM, Gastroenterology, Montreal, Canada, ¹⁰University of Foggia, Gastroenterology, Foggia, Italy, ¹¹University Of Toronto, Toronto, Canada, ¹²University Of Kansas Medical Center, Mission, United States of America, ¹³University of Kansas School of Medicine Dept. of Gastroenterology, Gastroenterology, Leawood, United States of America, ¹⁴Portsmouth University Hospital, Dept. of Gastroenterology, Portsmouth, United Kingdom, ¹⁵University of Minnesota, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Minneapolis, United States of America, ¹⁶IUPUI, Gastroenterology, Indiana, United States of America

Contact E-Mail Address: tommyrizkala@outlook.com

Introduction: The Resect and Discard strategy allows endoscopists to replace post-polypectomy pathology with real-time prediction of polyp histology during colonoscopy (optical diagnosis). The present systematic review and meta-analysis investigated how implementation of computer-aided diagnosis (CADx) for polyp pathology affected this optical diagnosis procedure.

Aims & Methods: We conducted a search of MEDLINE, EMBASE, and Scopus databases, covering studies published from inception to February 20, 2024. We included histologically verified accuracy diagnostic studies that evaluated the real-time optical diagnosis performance of CADx systems for polyps ≤5mm in the entire colon. The aim was to estimate the potential benefits and harms associated with integrating CADx assistance into the

endoscopist optical diagnosis, both before and after its implementation. The primary outcomes were the proportion of polyps that would have avoided pathological assessment (main benefit) and the proportion of polyps incorrectly predicted (main harm) due to false-positive or -negative optical diagnosis. Only diagnosis with a high-level of confidence were considered.

Results: A total of 11 studies with 7,400 polyps were eligible for analysis, providing stand-alone performance of CADx with sensitivity and specificity in identifying adenomatous histology of 87% (95% confidence interval [CI]: 0.82, 0.91) and 75% (95% CI: 0.68, 0.82), respectively. Three studies (4,086 polyps) were included to analyze the primary benefit/harm outcome measures. There was no significant difference between the CADx-unassisted and CADx-assisted strategies for the proportion of polyps that would have avoided pathological assessment (90% vs. 90%; risk ratio: 1.01; 95% CI: 0.99, 1.04; $I^2=53.49\%$; moderate certainty evidence). CADx-assisted strategy reduced the proportion of incorrectly predicted polyps as compared with CADx-unassisted (13% vs. 12%; risk ratio: 0.88; 95% CI: 0.79, 0.98; $I^2=0\%$; moderate certainty evidence) mainly due to a decrease in false-positive diagnosis.

Conclusion: CADx implementation did not result in clinically relevant benefits for the Resect-and-Discard strategy.

Disclosure: Cesare Hassan: Fujifilm Co. (consultancy); Medtronic Co. (consultancy), Yuichi Mori: Olympus Corp (consultancy, speaking honorarium, equipment loan); Cybernet System (ownership interest), Alessandro Repici: Fujifilm Co. (consultancy); Olympus Corp (consultancy); Medtronic Co. (consultancy).

PP0846

UNDERWATER ENDOSCOPIC MUCOSAL RESECTION AND HOT-SNARE POLYPECTOMY IN COLONOSCOPY

A. Steshenko¹, L. Marko¹, M. Gurin¹, R. Koreň¹, M. Štiastny¹, A. Slobodniková¹, T. Koňarčíková²

¹F. D. Roosevelt University Hospital in Banská Bystrica, II. Chirurgická klinika SZU, Banská Bystrica, Slovakia, ²Martinské biopické centrum, s.r.o., Banská Bystrica, Slovakia

Contact E-Mail Address: andriesteshenko@icloud.com

Introduction: Conventional endoscopic mucosal resection (CEMR) and underwater endoscopic mucosal resection (UEMR) are techniques for the removal of colorectal lesions.

Aims & Methods: The our study aim is to compare the efficacy and safety of UEMR versus CEMR in patients with lesions under 30mm in diameter. The study included 124 patients with colorectal lesions with a diameter < 20mm, 20-30mm, type 0-Ip (hot-snare polypectomy), 0-Is, 0-IIa or 0-IIa+Is according to the Paris Classification. Cases were divided into two groups: Group I 64/124(51,61%) CEMR cases (0-Is, 0-IIa, 0-IIa+Is - < 20mm 43,75%, 20-30mm 20,31%; type 0-Ip - 35,93%) and Group II 60/124(48,38%) UEMR patients (0-Is, 0-IIa, 0-IIa+Is - < 20mm 45%, 20-30mm 23,33%; type 0-Ip - 31,66%). Cases with deep submucosal invasion were not included. Optical evaluation with chromoscopy and NBI was performed by expert endoscopist, followed by endoscopic resection.

The outcomes were the lesion recurrence rate, en-bloc resection, R0 resection rates, adverse events. Data were analysed using Chi-sq, descriptive statistic by SPSS version 26.0.

Results: The recurrence rate was lower for II Group (UEMR) (1/14; 7,14%) in cases of 20-30mm lesions size (I Group (CEMR) - 2/13; 15,38%), and in 0-Ip (hot-snare polypectomy) cases (II Group (UEMR) - 1/19; 5,26%; I Group (CEMR) - 3/23; 13,04%); en-bloc resection rates was higher in II Group (UEMR) (13/14; 92,85%) in cases of 20-30mm lesions size. The R0 resection and adverse events showed the same tendency, only for polyps between

20 and 30 mm. There were no differences in the overall recurrence rate between groups. Underwater endoscopic mucosal resection was faster and easier to perform than CEMR.

Conclusion: Underwater endoscopic mucosal resection is safety method and could be considered for treatment of colorectal lesions with low adverse events rates.

References: Karl Kwok, Tri Tran, Daniel Lew. Polypectomy for large polyps with endoscopic mucosal resection. *Gastrointest Endoscopy Clin N Am* 32 (2022) 259–276.

<https://doi.org/10.1016/j.giec.2021.12.004>

Joaquín Rodríguez Sánchez, Marco A. Alvarez-Gonzalez, María Pellisé, et al. Underwater versus conventional EMR of large nonpedunculated colorectal lesions: a multicenter randomized controlled trial. *Gastrointest Endosc* 2023; Volume 97, No. 5: 941-51.e2.

Chandan S, Khan SR, Kumar A, et al. Efficacy and histologic accuracy of underwater versus conventional endoscopic mucosal resection for large (>20 mm) colorectal polyps: a comparative review and meta- analysis. *Gastrointest Endosc* 2021;94:471-82.e9.

Disclosure: Nothing to disclose.

PP0847

ENDOSCOPIC CHARACTERISTICS DIFFERENTIATING SESSILE SERRATED LESIONS AND MICROVESICULAR HYPERPLASTIC POLYPS FROM GOBLET CELL RICH HYPERPLASTIC POLYPS: A CROSS-SECTIONAL STUDY

O. Toyoshima¹, T. Nishizawa¹, S. Yoshida¹

¹Toyoshima Endoscopy Clinic, Gastroenterology, Setageya, Japan

Contact E-Mail Address: t@ichou.com

Introduction: Differentiating between colorectal serrated polyps (SPs) on endoscopy can be challenging since sessile serrated lesions (SSLs) and hyperplastic polyps (HPs) tend to have a similar appearance¹⁻⁴. Furthermore, the endoscopic differences between the two subtypes of HPs, namely microvesicular HP (MVHP) and goblet cell-rich HP (GCHP), are not well understood^{5,6}. Therefore, we compared the endoscopic features of SSL, MVHP, and GCHP.

Aims & Methods: This retrospective, cross-sectional study was conducted at the Toyoshima Endoscopy Clinic. We examined the polyp size, location, Paris classification type, mucus cap, indistinct border, expanded crypt opening, varicose microvascular vessels (VMV), and Japan NBI expert team (JNET) classification type. Multivariable analysis was performed to determine the endoscopic finding that predicted SP histology using a binomial logistic regression model. We constructed endoscopic microvesicular goblet (MG) score for differentiating SPs using the endoscopic findings associated with SP histology in the multivariable analysis, and calculated the area under the receiver operating characteristic curve (AUC) and diagnostic accuracy.

Results: A total of 1366 SPs were eligible for this study, including 321 SSLs, 718 MVHPs, and 327 GCHPs. The mean polyp size was 6.24 mm. SPs in the proximal colon accounted for 70.7%. In the comparison between MVHP and GCHP, a mucus cap (partial regression coefficient 1.44, 95% confidence interval [CI] 1.06-1.82), expanded crypt opening (1.92, 1.44-2.40), and VMV (1.04, 0.58-1.49) were more often found in MVHP in contrast to GCHP (Table). comparison of SSL and MVHP showed that SSLs were located in the proximal colon (0.70, 0.30-1.10), were larger (0.21, 0.16-0.25), and had mucus cap (0.54, 0.16-0.93) compared to MVHPs. On comparing the SSL plus MVHP group and GCHP group, larger size (0.12, 0.06-0.19), a mucus cap (1.76, 1.39-2.14), expanded crypt opening (2.04, 1.57-2.52), VMV (1.21, 0.75-1.68), and JNET type 2A (1.17, 0.73-1.61) were more often observed in SSL + MVHP group compared with GCHP. Mucus cap, expanded crypt opening, and VMV were each assigned 1 point and the sum of

the points was defined as the endoscopic MG score. In the examination of MVHPs and GCHPs, the AUC of the endoscopic MG score for predicting MVHP was 0.78 (95% CI 0.76-0.81) and the optimal cut-off value was 1; the sensitivity, specificity, and positive predictive value (PPV) were 74.7%, 75.5%, 87.0%, respectively. In the assessment of SSLs, MVHPs, and GCHPs, the AUC of the endoscopic MG score for predicting SSL plus MVHP group was 0.82 (0.79-0.84) and the optimal cut-off value was 1; the sensitivity, specificity, and PPV were 79.4%, 75.5%, and 91.2%, respectively.

	Partial regression coefficient	95% confidence interval	Degree of freedom	P value
Polyp size	0.04	-0.03, 0.11	1	0.23
Mucus cap	1.44	1.06, 1.82	1	<0.001
Indistinct border	0.07	-0.32, 0.46	1	0.73
Expanded crypt opening	1.92	1.44, 2.40	1	<0.001
VMV	1.04	0.58, 1.49	1	<0.001

Table. Multivariable analysis for comparison of endoscopic appearance between MVHP and GCHP.

Conclusion: MVHP and GCHP, while belonging to the same HP category, exhibited different endoscopic appearances such as mucus cap, expanded crypt opening, and VMV. Conversely, SSL and MVHP despite belonging to different histopathological categories, showed similar endoscopic appearances except for mucus cap. Moreover, SSL plus MVHP showed distinct endoscopic appearances compared to GCHP group. Considering MVHP and GCHP as separate entities can aid in the endoscopic diagnosis of SPs.

References: 1. Ijspeert JEG, de Wit K, van der Vlugt M, et al. Prevalence, distribution and risk of sessile serrated adenomas/polyps at a center with a high adenoma detection rate and experienced pathologists. *Endoscopy*. 2016;48(08):740-746.

2. Turner KO, Genta RM, Sonnenberg A. Lesions of All Types Exist in Colon Polyps of All Sizes. *Am J Gastroenterol*. 2018;113(2):303-306.

3. Zessner-Spitzenberg J, Waldmann E, Jiricka L, et al. Comparison of adenoma detection rate and proximal serrated polyp detection rate and their effect on post-colonoscopy colorectal cancer mortality in screening patients. *Endoscopy*. 2023;55(5):434-441.

4. Nishizawa T, Yoshida S, Toyoshima A, et al. Endoscopic diagnosis for colorectal sessile serrated lesions. *World J Gastroenterol*. 2021;27(13):1321-1329.

5. Qazi TM, O'Brien MJ, Farraye FA, et al, 3rd. Epidemiology of goblet cell and microvesicular hyperplastic polyps. *Am J Gastroenterol*. 2014;109(12):1922-1932.

6. Crockett SD, Barry EL, Mott LA, et al. Predictors of Incident Serrated Polyps: Results from a Large Multicenter Clinical Trial. *Cancer Epidemiol Biomarkers Prev*. 2022;31(5):1058-1067.

Disclosure: Nothing to disclose.

PP0848

AWITHDRAWN

PP0849

DIAGNOSTIC PERFORMANCE OF JAPAN NBI EXPERT TEAM (JNET) CLASSIFICATION AND CONECT CLASSIFICATION FOR LARGE COLORECTAL LATERALLY SPREADING LESIONS TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION: A LARGE WESTERN COHORT STUDY

C. Gabriel¹, J. Albouys¹, R. Legros¹, M. Dahan¹, H. Lepetit¹, C. Brule¹, S. Geyl¹, R. Collin¹, L. Alfaroni², P. Leclercq³, Z. Jean-Baptiste⁴, M. Pioche⁵, J. Jacques¹

¹CHU Limoges / University of Limoges, Department of gastroenterology, Limoges, France, ²IRCCS Humanitas Research Hospital, Milan, Italy, ³UZ Leuven, Gastroenterology, Liège, Belgium, ⁴CHU ST, Gastroentérologie, Verviers, Belgium, ⁵Hospices civils de Lyon, Gastroenterology and endoscopy, Lyon, France

Contact E-Mail Address: charlottegabriel@free.fr

Introduction: Endoscopic characterization aims to predict the histology of a lesion and thus the risk of cancer. This characterization step is essential, especially in the case of large superficial colorectal lesions, as the choice of resection technique directly depends on it. The JNET (Japan NBI Expert Team) classification is the classification proposed by European and Japanese guidelines to select the optimal therapeutic approach between EMR (endoscopic mucosal resection), ESD (endoscopic submucosal dissection), or surgery, but has not been evaluated in large laterally spreading lesions (LSTs) (>20 mm). We therefore evaluated the diagnostic performance of the JNET classification for predicting the risk of submucosal invasive cancer (SMIC) in LSTs >20 mm.

Aims & Methods: Single-center, prospective, observational study including all patients referred for endoscopic resection of lesions >20 mm, between 2017 and 2022. All LST samples with SMIC underwent a secondary pathological examination to establish the correlation between "covert" carcinoma (SMICs categorized as JNET 2A) and "buried" carcinoma (existence of SMICs more than 0.5 mm from the surface). The primary outcome was the diagnostic accuracy of the JNET classification for histological prediction of LSTs >20 mm. The secondary objective was to assess the combined performance of the JNET classification and pejorative macroscopic (macronodule >1 cm, Paris 0-IIC area, JNET 2B area, Non-Granular LST) criteria also called the CONECT classification. We also attempted to determine the characteristics and risk factors of LSTs with covert or buried carcinoma, and to identify potential associations between the two.

Results: 972 lesions were removed by en-bloc ESD, of which 110 (11.3%) of these lesions contained SMIC. The median lesion size was 57 mm. Of the 110 submucosal cancers, 33 had covert carcinoma and 35 were classified as buried carcinoma. The sensitivity and specificity for predicting high-grade dysplasia (HGD) to SMIC were 46% and 75% for JNET 2B and 87% and 38% for CONECT IIC, respectively; and for predicting superficial SMIC were 67% and 67% for JNET 2B and 94% and 27% for CONECT IIC, respectively. The false negative rates (FNR) (probability of missing SMIC) of JNET 2B and CONECT IIC were 31% (31/100) and 3% (3/100) for predicting SMIC, respectively; and 33% (16/48) and 6% (3/48) for predicting superficial SMIC, respectively. JNET 2B exhibited significantly higher specificity than CONECT IIC for predicting HGD to superficial SMIC (75% vs. 38%; p< 0.001) and for predicting isolated superficial cancer (67% vs. 27%; p< 0.0001). And CONECT IIC was significantly more sensitive than JNET 2B for predicting HGD to superficial SMIC (46% vs. 87%; p< 0.001) and for predicting isolated superficial cancer (67% vs. 97%; p< 0.0001). No association was found between covert carcinoma and buried carcinoma (p 0.889).

Conclusion: The JNET classification has low diagnostic accuracy for predicting the risk of submucosal cancer for large superficial colorectal lesions and for making decisions on *en bloc* endoscopic treatment using

ESD. If a selective ESD and piecemeal EMR strategy is used based on the submucosal cancer risk, the CONECT classification is preferred to prevent under-treatment of SMIC.

Disclosure: Nothing to disclose.

PP0850

PARIS-IS NODULES ≥ 10 MM COMMONLY OCCUR IN LARGE GRANULAR RECTAL LESIONS AND ARE A RISK FACTOR FOR COVERT SUPERFICIAL SUBMUCOSAL INVASIVE CANCER

P.J. Poortmans^{1,2,3}, L. Desomer^{4,3,5}, J. Gauci⁶, N. Burgess^{6,7}, M.J. Bourke^{6,7}, D.J. Tate^{2,3}

¹University Hospital Brussels (UZ Brussel), Gastroenterology and Hepatology, Jette, Belgium, ²University Hospital Ghent, Gastroenterology and Hepatology, Ghent, Belgium, ³University of Ghent, Faculty of Medicine, Ghent, Belgium, ⁴UZ Gent, Gastroenterology and Hepatology, Ghent, Belgium, ⁵AZ Delta, Gastroenterology, Roeselare, Belgium, ⁶Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia, ⁷University of Sydney, Western Clinical School, Sydney, Australia

Contact E-Mail Address: pjpoortmans@hotmail.com

Introduction: Cancer in large non pedunculated colorectal polyps (LNPCPs) may go unrecognised if it is not visible on the surface (hidden or COVERT cancer). Increasing size, non-granular morphology, rectosigmoid location and combined Paris classification have been identified as risk factors for COVERT cancer in LNPCPs.[1]

It is unknown whether the size of the dominant nodule (largest Is component) in LNPCPs is correlated with risk of COVERT cancer or depth of submucosal invasion (SMI).

Aims & Methods: The endoscopic appearance and histopathology of LNPCPs ≥ 20 mm was analysed from a prospectively collected multicenter database of polyps referred for endoscopic resection between November 2017 and November 2023. Visible (OVERT) cancers and all serrated polyps were removed. LNPCPs with large Is components (Paris 0-Is and 0-IIa+Is polyps with Is component ≥ 10 mm as defined by expert consensus and retrospective image review) were compared to LNPCPs without large Is component. The primary endpoint was the correlation between large Is component and presence and depth of SMI. Secondary end points were correlation between a large Is component and other risk factors for COVERT disease (location in the colon, size and morphology).

Results: 3470 LNPCPs without evidence of OVERT cancer were included, of which 265 (7.6%) contained a large Is component and 3205 (92.4%) did not.

LNPCPs with large Is component were more likely to contain SMI (4.9% [95% confidence interval (CI): 2.3% - 7.5%] vs. 2.1% [95% CI: 1.6% - 2.6%], $P < 0.01$). Subgroup analysis showed that LNPCPs with a large Is component were more likely to contain superficially invasive cancer (large Is: 2.3% [95% CI: 0.5% - 4.1%] vs. no large Is: 0.7% [95% CI: 0.4% - 1.0%], $P = 0.01$). There was no significant difference in presence of deep SMI between LNPCPs with a large nodular component vs. LNPCPs without large Is component (large Is: 2.6% [95% CI: 0.7% - 4.6%] vs. no large Is: 1.4% [95% CI: 1.0% - 1.8%], $P = 0.17$).

LNPCPs with large Is component were larger (≥ 40 mm; 57.0% [95% CI: 51.0% - 62.9%] vs. 37.8% [95% CI: 36.1% - 39.5%], $P < 0.01$), more often granular (86.8% [95% CI: 82.7% - 90.9%] vs. 58.0% [95% CI: 56.3% - 59.7%], $P < 0.01$) and found in the rectum (34.0% [95% CI: 28.3% - 39.7%] vs. 16.4% [95% CI: 15.1% - 17.7%], $P < 0.01$) vs. LNPCPs without large Is component (Table 1).

	No Large Is Component [95% CI]	Large Is Component [95% CI]	P-Value
Number of included LNPCPs	3205	265	-
Size ≥ 40 mm	37.8% [36.1% - 39.5%]	57.0% [51.0% - 62.9%]	< 0.01
Granular	58.0% [56.3% - 59.7%]	86.8% [82.7% - 90.9%]	< 0.01
Rectal location	16.4% [15.1% - 17.7%]	34.0% [28.3% - 39.7%]	< 0.01
SMI (all)	2.1% [1.6% - 2.6%]	4.9% [2.3% - 7.5%]	< 0.01
Superficially invasive	0.7% [0.4% - 1.0%]	2.3% [0.5% - 4.1%]	0.01
Deeply invasive	1.4% [1.0% - 1.8%]	2.6% [0.7% - 4.6%]	0.17

Table 1: Comparison of endoscopic features and histopathology between large colonic laterally spreading lesions without and with at least one large nodular (Is, size of the nodule ≥ 10 mm) component. LNPCPs, large non pedunculated colorectal polyps. SMI, submucosal invasion. CI, confidence interval.

Conclusion: LNPCPs with a Is component ≥ 10 mm are at higher risk of containing COVERT cancer which, if present, is commonly superficially invasive. These results have implications for choice of resection technique on detection of large rectal LNPCPs with nodules ≥ 10 mm and stratification of these patients to endoscopic en-bloc resection.

References: 1. Burgess, N.G., et al., *Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort*. Gastroenterology, 2017. 153: p. 732-742.e1.

Disclosure: Nothing to disclose.

PP0851

PROSPECTIVE EVALUATION OF THE USE OF ARTIFICIAL INTELLIGENCE-ASSISTED MONITORING OF EFFECTIVE WITHDRAWAL TIME VERSUS STANDARD WITHDRAWAL TIME ON ADENOMA DETECTION RATE

T.K.L. Lui¹, C.P.M. Lam¹, V.W.M. Tsui¹, E.W.P. To¹, L.L.Y. Mak¹, M.K.L. Ko¹, S.H.K. Liu¹, W.K. Leung¹

¹University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong

Contact E-Mail Address: tkllui@hku.hk

Introduction: Effective withdrawal time (EWT), as measured by Endo-Screener QC (Wision A.I.), is a novel artificial intelligence (AI)-derived colonoscopy quality metric, which measures the actual duration of clear images obtained during scope withdrawal from cecum to rectum. We have previously demonstrated the superiority of EWT to standard withdrawal time (SWT) on adenoma detection rate (ADR) in a retrospective study.(1) This prospective study determines the association between EWT and colonic lesion detection rates.

Aims & Methods: This was a prospective evaluation of the use of real-time determination of EWT, as measured by the EndoScreener QC, of endoscopists who were blinded to the output of the system. Patients were recruited in our hospital from Nov 2023 to Feb 2024. All examination was performed with high-definition endoscopes (EVIS-EXERA 290 video system, Olympus Optical, Tokyo, Japan) under white light. In all examination, colonoscope was first advanced to the cecum as confirmed by identification of the appendiceal orifice and ileocecal valve or by intubation of the ileum. After cecal intubation, the colonoscopy was slowly withdrawn. The AI derived (AI) real time effective mucosal examination monitor system (EndoScreen QC) was initiated during scope withdrawal, starting from cecum to anus. The SWT was defined as total withdrawal time from cecum to rectum after excluding polypectomy and biopsy time. All detected polyps were removed during scope withdrawal only. The size (measured with

biopsy forceps), location and morphology of each polyp was recorded by an independent observer. The bowel preparation quality was graded according to the Boston Bowel Preparation Scale. The primary outcome was the correlation between EWT and ADR, which was determined by the Pearson correlation coefficient (r); and compared with SWT. Other outcomes included correlation between EWT and polyp detection rate (PDR) or serrated lesion detection rate (SDR).

Results: In the prospective analysis, 185 colonoscopies performed by 9 endoscopists were analyzed. The mean age was 67.4 year (SD: 10.5) and 57.3% (n=106) were male. 83.9% (n=154) were diagnostic colonoscopy. The median Boston Bowel Preparation score (BBPS) was 7. The mean ADR was 49.2% (95% CI: 41.6-56.2, n=91), mean EWT was 4.4 (95% CI: 4.1-4.6) minutes and mean SWT was 7.1 (95% CI: 6.7-7.5) minutes. The correlation between EWT and ADR was significantly higher (r=0.98, 95%CI: 0.96-1.00) than between SWT and ADR (r=0.80, 95%CI: 0.53-0.98, p<0.01). For PDR, the correlation between EWT and PDR was also significantly higher than between SWT and PDR (r=0.97, 95%CI: 0.95-1.00 vs r=0.73, 95%CI: 0.30-0.98, p=0.02). However, there was no significant difference between EWT and SWT on SDR [r=0.92, 95%CI: 0.72-1.00 vs r=0.93, 95%CI: 0.86-0.98, p=0.89].

Number	185
Mean age in years (SD)	67.4 (10.5)
Male sex, % (n)	106 (57.3)
Indications:	
Screening, % (n)	31 (16.8)
Diagnostic, % (n)	154 (83.9)
Bowel preparation in BBPS, median (range)	7 (6-9)
Mean standard withdrawal time in mins (95%CI)	7.1 (6.7-7.5)
Mean EWT in mins (95%CI)	4.4 (4.1-4.6)
ADR %(n)	49.2 (91)
PDR %(n)	58.9 (109)
SDR % (n)	20.0 (37)
Mean number of adenoma (SD)	1.1 (0.1)
Mean number of polyp (SD)	1.6 (0.1)
Mean number of serrated lesion (SD)	0.4 (0.1)
r between SWT and ADR (95%CI)	0.80 (0.53-0.98)
r between EWT and ADR (95%CI)	0.98 (0.96-1.00)
r between SWT and PDR (95%CI)	0.73 (0.30-0.98)
r between EWT and PDR (95%CI)	0.97 (0.95-1.00)
r between SWT and SDR (95%CI)	0.93 (0.86-0.98)
r between EWT and SDR (95%CI)	0.92 (0.72-1.00)

Table 1: Baseline characteristics and outcomes of the study.

Conclusion: The novel AI-derived EWT demonstrated better correlation with ADR and PDR than SWT in this prospective study. Further studies should evaluate the role of applying real-time monitoring EWT on endoscopy training and quality improvement of endoscopists with low ADR.

References: 1. Lui TKL, Ko MKL, Liu JJ, Xiao X, Leung WK. Artificial intelligence-assisted real-time monitoring of effective withdrawal time during colonoscopy: a novel quality marker of colonoscopy. *Gastrointest Endosc.* 2024;99(3):419-27.e6.

Disclosure: The following companies had given donation to our team for research. Olympus, Fujifilm, Medronic, Wision AI, Insign Medical Co Ltd

PP0852
ENDOSCOPIC FREE-HAND SUTURING IS SAFE AND FEASIBLE FOR DEFECT CLOSURE IN THE UPPER GASTROINTESTINAL TRACT AND COLORECTUM: THE LARGEST RETROSPECTIVE ANALYSIS TO DATE

J.R. Wiessner¹, M. Heilmaier¹, J. Ulrich¹, M. Elnegouly¹, R.M. Schmid¹, M. Abdelhafez¹
¹Klinikum rechts der Isar, Technical University of Munich, Medical Clinic and Polyclinic II, Munich, Germany

Contact E-Mail Address: johannes.wiesner@gmx.de
Introduction: The management of post-interventional and iatrogenic defects in the gastrointestinal tract presents significant challenges in endoscopic practice, often carrying substantial risks for patients. Various closure techniques have been developed, yet consistently effective outcomes remain elusive in diverse scenarios. Endoscopic free-hand suturing (EFHS) using a needle holder is a new technique that has demonstrated potential for effectively addressing these defects. In this study, we present one of the largest cohorts to date, analyzing the safety and feasibility of endoscopic free-hand suturing across multiple scenarios and locations.

Aims & Methods: This study aimed to investigate the feasibility and safety of EFHS and the attainability of sustained closure following various procedures: endoscopic submucosal dissection (ESD), perforation, per-oral endoscopic myotomy (POEM), per-oral endoscopic myotomy for Zenker's diverticulum (Z-POEM), submucosal tunneling endoscopic resection (STER), and endoscopic submucosal excavation (ESE). ESD, or the respective above-mentioned interventions, were followed by EFHS, utilizing a gastroscope or colonoscope and a barbed absorbable wire (V-loc 180, Covidien, Dublin, Ireland). Needle steering involved a distal cap attachment and a needle holder (SutuArt; Olympus, Hamburg, Germany). Suturing was performed in a zigzag pattern at 5-10 mm intervals. For safety, the needle was concealed, and post-suturing, the remaining suture and needle were cut with a loop cutter (Olympus, Hamburg, Germany) for removal.

Results: In this retrospective single-center study, 30 post-interventional defects in 26 patients (female n = 10, male n = 16) and performed EFHS were retrospectively followed. Technical success, clinical success after the procedure, and severe EFHS-related adverse events were evaluated. EFHS was applied for defect closure after the following interventions and/or complications: colonic endoscopic submucosal dissection (n =10; cecum n =4, ascending n = 1, transverse n = 2, sigmoid n = 3), rectal endoscopic submucosal dissection (n = 9), gastric subepithelial lesion removal (n = 2; STER n = 1, ESE n = 1) duodenal perforation (n = 1), colonic perforation (n = 1), peroral endoscopic myotomy (POEM) (n = 1), peroral endoscopic myotomy for the treatment of Zenker's diverticulum (Z-POEM) (n = 2). The median of the resected area was 1450 mm² (range 500 – 3600 mm²). In none of the 26 patients were severe procedure-related events observed, specifically, there were no instances of bleeding or perforation. Endoscopic follow-up was conducted in 15 of 30 EFHS closures, demonstrating adequate closure in 13 cases, in 2 cases in the rectum, the mucosa was partially dehiscent, although showing re-epithelialization. The median time between the intervention and endoscopic follow-up was 15 days (range 1 - 69 days). The median duration of hospital stay after endoscopic intervention was 2 days (range 1 – 5 days).

Conclusion: Endoscopic free-hand suturing is safe and feasible within the gastrointestinal tract, including esophagus, stomach, duodenum, colon and rectum. Endoscopic free-hand suturing has the potential to enhance the safety of endoscopic interventions and reduce hospital stay duration.
Disclosure: Nothing to disclose.

A NOVEL TOOL PERFORMS SIMILARLY TO JNET AMONGST WESTERN EXPERTS IN THE DETECTION OF CANCER WITHIN LARGE NON-PEDUNCULATED COLORECTAL POLYPS: EXPERT VALIDATION OF CRIS

M.E. Argenziano^{1,2}, L. Debels^{3,1}, S. Smeets¹, M. Montori^{1,2}, P.J. Poortmans^{1,3}, T. Tornai¹, A. Sorge^{1,4}, M.F. Kaminski⁵, V.G. Lala⁶, R. Valori⁷, J. Anderson⁷, M.J. Bourke⁸, L. Desomer⁹, D.J. Tate¹
¹University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium, ²Università Politecnica delle Marche, Clinic of Gastroenterology, Hepatology, and Emergency Digestive Endoscopy, Ancona, Italy, ³Vrije Universiteit Brussel, Gastroenterology & Hepatology, Jette, Belgium, ⁴University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ⁵Maria Skłodowska-Curie Memorial Center and Institute of Oncology, Department of Gastroenterology, Warsaw, Poland, ⁶Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa, ⁷Gloucestershire NHS Foundation Trust - Medicine, Gloucestershire NHS Foundation Trust; Cheltenham/GB, Medicine, Cheltenham, United Kingdom, ⁸Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia, ⁹AZ Delta campus Rumbek, Gastroenterology and Hepatology, Roeselare, Belgium

Contact E-Mail Address: mariaeva.argenziano@gmail.com
Introduction: The JNET (Japan NBI Expert Team) classification can be used to predict large non-pedunculated colorectal polyp (LNPCP) histology and presence/depth of submucosal invasion (SMI). Japanese endoscopist accuracies >84% have not been replicated in the West; for example, in a recent study of European experts the accuracy of JNET was 55%. Furthermore, European guidelines suggest both low-grade dysplasia (LGD) and high-grade dysplasia (HGD) can be treated using endoscopic mucosal resection (EMR) thus there is no clinical consequence to interpreting HGD as JNET 2A (excluded in the original interpretation of JNET).
Aims & Methods: We aimed to validate a novel tool CRIS (Colorectal Regular-Irregular Score) by comparing it with JNET for LNPCP histology prediction amongst Western experts.
32 images of flat LNCPs under narrow-band imaging were consecutively obtained with matching histopathology data. Each image was rated (anonymous online survey) using JNET and then all the images were rated again (order randomised) using CRIS, a tool which simply asks whether the most disordered vascular pattern visible in the image is ‘regular(=CRIS-R), regularly-irregular(=CRIS-RI) or completely-irregular(=CRIS-I)’. No further explanation of JNET or CRIS was offered. Accuracy of JNET and CRIS vs. histopathology was analysed using the original JNET interpretation (where JNET 1/2A and CRIS-R = LGD) and a clinically relevant approach (where JNET1/2A and CRIS-R can also = HGD). JNET2B & CRIS-RI were matched to HGD & superficial SMI and JNET3 & CRIS-I to deep SMI. Correct treatment was defined as pEMR for LGD or HGD, en-bloc EMR/ESD for HGD or superficial SMI and surgery for deep SMI.

Results: 12 experts (median 150 colorectal EMRs and 13 ESDs/year) rated 32 images.
The overall accuracy of JNET vs. histopathology using the original JNET interpretation was 69.7% (95%CI 46.0-89.3%) and CRIS 69.6% (95%CI 45.3-88.7%). Expert agreement was similar between JNET (91.3% (95%CI) 82.8-98.3%) and CRIS (88.5% [95%CI 78.2-97.3%]) with K=0.64 (moderate) for JNET and K=0.57 (moderate) for CRIS.
The accuracy of JNET 2B was 51.7% (95%CI 45.9-57.4%) and JNET 3 85.8% (95%CI 81.2-89.3%). Comparably CRIS-RI and CRIS-I showed accuracies of 51% (95%CI 45.2-56.7%) and 85.1% (95%CI 80.4-88.7%) respectively. Correct treatment was determined in 144/288 (50.0%) observations using

JNET and 144 (50.0%) using CRIS. Using the clinically relevant approach the accuracy of JNET was 73.9% (95%CI 46.0-89.3%) vs. CRIS 72.3% (95%CI 45.3-88.7%).
The accuracy, sensitivity and specificity of JNET 1/2A changed by +13.2%, -8.0% and +38.0% and CRIS-R by 8.3%, -8.2% and 35.5%. Correct treatment determination increased by 29.5% to 79.5% for JNET and by 27.1% to 77.1% for CRIS.

	ORIGINAL JNET INTERPRETATION						CLINICALLY RELEVANT INTERPRETATION									
Imaging	JNET 1/2A	CRIS-R	JNET 2B	CRIS-RI	JNET 3	CRIS-I	JNET Overall	CRIS Overall	JNET 1/2A	CRIS-R	JNET 2B	CRIS-RI	JNET 3	CRIS-I	JNET Overall	CRIS Overall
Histology	LGD		HGD, superficial SMI		Deep SMI				LGD, HGD		HGD, superficial SMI		Deep SMI			
Accuracy % (95%CI)	62.5% (56.7 - 67.8%)	63.9% (58.0 - 69.0%)	51.7% (45.9 - 57.4%)	51.0% (45.2 - 56.7%)	85.8% (81.2 - 89.3%)	85.1% (80.4 - 88.7%)	69.7% (69.6%)	69.6% (45.3 - 88.7%)	75.7% (70.4 - 80.2%)	72.2% (66.7 - 77.0%)					73.9% (46.0 - 89.3%)	72.3% (45.3 - 88.7%)
Sensitivity % (95%CI)	77.4% (67.3 - 85.0%)	72.6% (62.0 - 81.0%)	27.6% (21.1 - 35.0%)	28.2% (21.7 - 35.7%)	75.0% (61.2 - 85.0%)	81.2% (66.0 - 89.8%)	53.8% (21.2 - 85.1%)	54.3% (21.7 - 89.8%)	69.4% (63.0 - 75.2%)	64.4% (57.7 - 70.4%)					58.4% (21.2 - 85.1%)	56.4% (21.7 - 89.8%)
Specificity % (95%CI)	56.4% (49.5 - 62.9%)	60.3% (53.0 - 67.0%)	80.3% (72.7 - 86.1%)	78.0% (70.2 - 84.2%)	87.9% (83.1 - 91.4%)	85.8% (80.8 - 89.6%)	76.6% (49.5 - 91.5%)	76.2% (53.4 - 89.7%)	94.4% (86.5 - 97.8%)	95.8% (88.4 - 98.5%)	no change				87.4% (72.7 - 97.8%)	85.8% (70.2 - 98.6%)
Correct treatment n (%) /288	42.2% (34.3 - 50.4)	43.0% (34.7 - 51.5)	62.3% (49.8 - 73.4)	60.3% (48.1 - 71.3)	84.2% (71.5 - 91.4%)	89.6% (81.4 - 95.5%)	50.0% (55.7)	50.0% (55.7)	97.4% (99.1)	97.9% (99.4)					79.5% (83.9)	77.1% (71.7 - 81.7%)

Conclusion: Both JNET and CRIS, a novel score named and described by 3 self-explanatory words, can be used by Western experts to accurately determine LNCP histology. This suggests JNET may be able to be simplified for non-experts. Importantly the accuracy of both JNET and CRIS can be increased by framing their interpretation versus histology in a clinically relevant fashion. This has significant implications for signposting patients to correct treatment after detection of LNCPs especially amongst non-experts.

References:

- Ferlitsch M, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Guideline (update 2024). In press.
- Kobayashi S, Yamada M, Takamaru H, et al. Diagnostic yield of the Japan NBI Expert Team (JNET) classification for endoscopic diagnosis of superficial colorectal neoplasms in a large-scale clinical practice database. United European Gastroenterol J. 2019;7(7):914-923. doi:10.1177/2050640619845987
- Sano Y, Tanaka S, Kudo SE, et al. Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. Dig Endosc 2016; 28: 526-533.
- Saito Y, Sakamoto T, Dekker E, Pioche M, Probst A, Ponchon T, Messmann H, Dinis-Ribeiro M, Matsuda T, Ikematsu H, Saito S, Wada Y, Oka S, Sano Y, Fujishiro M, Murakami Y, Ishikawa H, Inoue H, Tanaka S, Tajiri H; IEE-JNET Group. First report from the International Evaluation of Endoscopic classification Japan NBI Expert Team: International multicenter web trial. Dig Endosc. 2023 Sep 13. doi: 10.1111/den.14682. Epub ahead of print. PMID: 37702082.

Disclosure: DJT: Research support and consulting from Olympus, Pentax and Fujifilm.

PP0854

ENDOSCOPIC CALCIUM-ELECTROPORATION FOR PALLIATIVE THERAPY IN ADVANCED COLORECTAL CANCER: FIRST CASE SERIES FROM THE UNITED KINGDOM

A. Adeyeye¹, H. Ayubi², O. Olabintan², A. Eqbal², A. Emmanuel¹, A. Haji¹

¹King's College Hospital, Colorectal Surgery, London, United Kingdom, ²King's College Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: adeyeye_ademola@yahoo.com

Introduction: Colorectal cancer(CRC) is the commonest gastrointestinal cancer and the 2nd commonest cause of cancer-related mortality. Approximately 20% are metastatic and/or inoperable at diagnosis, usually requiring palliative treatment which may not be feasible in frail patients. Endoscopic Calcium-electroporation is a less aggressive alternative which uses controlled electric pulses to enhance cellular calcium influx and induce cell death via apoptosis/necrosis as well as pyroptosis.

Aims & Methods: The aim of this study is to determine efficacy and safety of Endoscopic electroporation using calcium in the palliative treatment of advanced CRC in a major UK hospital.

Consenting frail patients with locally symptomatic, inoperable sigmoid colon and rectal cancer were included. Diagnosis and staging were according to standard guidelines while frailty and/or risk was assessed using performance status(PFS), Charlson co-morbidity index(CCI) as well as American Society for Anesthesiology(ASA) score. Calcium Electroporation was administered via out-patient flexible endoscopy at intervals of two to three months with clinical and/or radiological reviews preceding each therapeutic session. Outcomes assessed include symptom relief, quality of life (QoL), survival rates and adverse events (AE).

Results: Fourteen sessions of Endoscopic Calcium-Electroporation were administered to 7 patients over 15months with an average age of 89.8years(85-93years). Luminal symptoms reported included rectal bleeding(N=5), constipation(N=3) and pain(N=2). Five out of seven patients had metastatic disease and none received chemotherapy or other oncologic treatment. The PFS and ASA for all subjects were >3 and 5 respectively while the average CCI was 15(0% estimated 10-year survival).

Symptomatic relief and improved QoL was reported in 71.4% of patients, usually after the 1st treatment session. The average survival rate was 85.7% with a mean life span of 8months (4-15months). No AE was recorded. One patient (who received a single session of treatment) in this cohort died after 11months from progression of the metastatic disease.

Conclusion: Endoscopic Calcium electroporation is a safe and effective palliative option in frail patients with advanced colorectal cancer. It should be considered in patients who are unfit for other conventional oncological therapies.

Disclosure: Nothing to disclose.

PP0855

SNARE TIP SOFT COAGULATION VS ARGON PLASMA COAGULATION AFTER LARGE NON-PEDUNCULATED COLORECTAL POLYP RESECTION: A META-ANALYSIS OF RANDOMIZED TRIALS

E.R. Smith¹, D. Ramai², Y. Wu¹, Y. Wang³, M.F. Maida^{4,5}, D.S. Dahiya⁶, S. Chandan⁷, A. Facciorusso⁸, M. Spadaccini^{9,10}, A. Shaukat¹¹

¹Baylor Scott & White Health, Department of Medicine, Round Rock, United States of America, ²University of Utah Health, Gastroenterology & Hepatology, Salt Lake City, United States of America, ³Perelman School of Medicine at the University of Pennsylvania, Division of Hospital Medicine, Philadelphia, United States of America, ⁴University of Enna 'Kore', Department of Medicine and Surgery, Enna, Italy, ⁵Umberto I Hospital, Gastroenterology Unit, Enna, Italy, ⁶The University of Kansas School of Medicine, Division of Gastroenterology, Hepatology & Motility, Kansas, United States of America, ⁷CHI Health Creighton University Medical Center, Division of Gastroenterology & Hepatology, Omaha, United States of America, ⁸University of Foggia, Gastroenterology Unit, Foggia, Italy, ⁹Humanitas University, Biomedical Science, Rozzano, Italy, ¹⁰Humanitas Clinical and Research Center -IRCCS, Endoscopy Unit, Rozzano, Italy, ¹¹New York University, Division of Gastroenterology & Hepatology, New York, United States of America

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: Thermal ablative methods (such as argon plasma coagulation (APC) and soft tip snare coagulation (STSC) are commonly used to treat polyp margins.

Aims & Methods: We aim to appraise the current literature and compare clinical outcomes between patients with treated (with APC vs STSC) and non-treated EMR margins.

We searched major databases from inception until November 2023 for RCTs comparing EMR of large non-pedunculated colorectal polyps with and without treated margins. Pooled data was analyzed for the primary outcome of recurrence at first screening colonoscopy, as well as adverse events. Analysis was performed using a random effects model and data was reported using 95% confidence intervals (CI).

Results: A total of five RCTs were found which included 1020 polyps (577 in treatment and 443 in control groups). Three studies included treatment with STSC and three studies used APC as the modality for margin ablation. Of included patients, 53% were female and average age was similar between treatment and control groups (65.9 vs 66.1 years). Overall, 71% of lesions were proximal to the splenic flexure. Mean follow up to first colonoscopy and average polyp size were comparable (6.3 vs 6.2 months; 28.2 mm vs 28.0 mm, respectively). Pooled analysis showed that margin ablation was associated with significantly lower rates of recurrence (OR = 0.267, 95% CI 0.18 - 0.4, P< 0.001) with low heterogeneity between studies (I²=0%, P = 0.47). Pooled analysis showed no significant difference between STSC and APC in terms of recurrence (OR = 0.6, 95% CI 0.27 - 1.7, I²=0%, P=0.3) or adverse events (OR = 0.67, 95% CI 0.3 - 1.6, I² 13%, P = 0.46).

Conclusion: Our study shows that ablation of EMR margins is very effective at preventing recurrence at first surveillance colonoscopy. We found no difference between STSC or APC in terms of polyp recurrence or adverse outcomes.

Disclosure: Nothing to disclose.

PP0856

COMPARATIVE EFFICACY OF DIFFERENT BOWEL PREPARATIONS FOR COLONOSCOPY: A NETWORK META-ANALYSIS

M.F. Maida^{1,2}, G. Marasco^{3,4}, L. Fuccio^{3,4}, A. Vitello⁵, F. Mocciaro⁶, M. Amata⁶, A. Fabbri^{3,4}, R. Di Mitri⁶, R. Vassallo⁷, D. Ramai⁸, C. Hassan^{9,10}, A. Repici^{9,10}, A. Facciorusso¹¹

¹University of Enna 'Kore', Department of Medicine and Surgery, Enna, Italy, ²Umberto I Hospital, Gastroenterology Unit, Enna, Italy, ³University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁴S. Orsola-Malpighi University Hospital, Bologna, Italy, ⁵S. Elia Hospital Caltanissetta, Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ⁶Arnas Civico-Di Cristina-Benfratelli Hospital, Gastroenterology and Endoscopy Unit, Palermo, Italy, ⁷Ospedale "Bucchieri la Ferla" Fatebenefratelli, Gastroenterology Unit, Palermo, Italy, ⁸University of Utah Health, Gastroenterology & Hepatology, Salt Lake City, United States of America, ⁹Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ¹⁰Humanitas Clinical and Research Center -IRCCS, Endoscopy Unit, Rozzano, Italy, ¹¹University of Foggia, Gastroenterology Unit, Foggia, Italy

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: The quality of a colonoscopy is heavily reliant on the effectiveness of bowel cleansing, which can impact the diagnostic accuracy and identification of adenomas. Various bowel cleansing products have been suggested, but their comparative effectiveness remains uncertain.

Aims & Methods: This systematic review and network meta-analysis aims to compare the performance of different bowel preparations for colonoscopy. MEDLINE, Embase, Scopus, and the Cochrane Library were systematically searched for randomized controlled trials (RCTs) comparing the efficacy of different bowel preparations administered as split or same-day regimen. The primary outcome was cleansing success (CS) defined as a total BBPS score of ≥ 6 . The secondary outcome was ADR.

Results: On network meta-analysis for CS (22 RCTs, 7179 patients, 14 bowel preparations assessed), 2L PEG+simethicone (RR=1.25 [95%CI=1.13-1.37]), 2L PEG+lactulose (RR=1.22 [95%CI=1.10-1.38]) and 1L PEG+ascorbate (ASC) (RR=1.03 [95%CI=1.01-1.06]) were significantly superior to 2L PEG+ASC. Overall, 2L PEG+lactulose resulted as the best product (SUCRA 0.94), followed by 2L PEG+simethicone (SUCRA 0.93), whereas 2L PEG+ASC showed the poorest performance. On network meta-analysis for ADR (17 RCTs, 6639 patients, 11 bowel preparations assessed), only 2L PEG+simethicone (RR=1.60 [95%CI=1.05-2.43]) resulted significantly superior to 2L PEG + ASC.

Conclusion: 2L PEG+simethicone, 2L PEG+lactulose, and 1L PEG+ASC seemed to provide high rates of cleansing success, albeit only 2L PEG+simethicone was associated with a significantly higher ADR. Consequently, these products should be preferred for bowel preparation of colonoscopy. Further randomized studies with adequate sample sizes are needed for a more accurate comparison of these products on ADR.

Disclosure: Nothing to disclose.

PP0857

TRENDS OF THE POLYP, ADENOMA, AND SESSILE SERRATED DETECTION RATE BY DIFFERENT AGE GROUPS IN INDIVIDUALS UNDERGOING COLONOSCOPY 2021–2023

L. Hornik¹, D. Janelidze¹, I. Lutsenko¹, S. Polishchuk¹

¹LLC "GASTROCENTER", Olymed, Endoscopy, Kyiv, Ukraine

Contact E-Mail Address: vanya.gornikk@gmail.com

Introduction: Colonoscopy plays a key role in colorectal cancer (CRC) screening. It is effective in reducing morbidity and mortality from CRC. To optimize quality of colonoscopy, performance measures (PM) have been identified and published by major international societies. While adenoma detection rate (ADR) is an imperative quality measure the sessile serrated lesion detection rate (SSLDR) is not currently a quality indicator for screening colonoscopy.

This study aimed to determine the trend of polyp detection rate (PDR), ADR, and SSLDR in participants in different age groups.

Aims & Methods: We performed a retrospective observational study of patients who underwent colonoscopy at Olymed, Kyiv, Ukraine from April 2021 through December 2023. All data were extracted and collected anonymously from the colonoscopy database and pathology reports and further analyzed. We divided patients by the different age groups and calculated PDR, ADR, and SSLDR for each group. PDR, ADR, and SSLDR were defined as the number of colonoscopies with at least one polyp, adenoma, and sessile serrated lesion detected respectively, divided by the total number of complete colonoscopies performed.

Results: This study was performed initially on 2676 patients who underwent colonoscopy from April 2021 through December 2023. Colonoscopies were mainly performed with colonoscopes with magnification and artificial intelligence assistance. After the exclusion of colonoscopies where examinations weren't extended to the cecum or Boston Bowel Preparation Scale < 6 the final study dataset consisted of 2402 colonoscopies. The patients were divided into 6 main groups and considering the discussion about lowering the screening age for CRC 2 additional groups were added. Results of PDR, ADR, and SSLDR for each group are shown in Table 1.

Age	Patients n	PDR	ADR	SSLDR
18-29	170	24.7%	7.7%	10.0%
30-39	422	43.6%	22.5%	18.0%
40-49	594	63.3%	40.0%	27.3%
50-59	605	75.9%	59.2%	27.9%
60-69	432	84.7%	70.6%	28.0%
≥ 70	179	86.0%	79.9%	18.4%
45-49	323	66.8%	44.9%	26.7%
≥ 50	1216	80.9%	66.3%	26.6%

Table 1.

Conclusion: This study reveals a notable trend of the PDR, ADR, and SSLDR in different age groups during colonoscopy. While ADR and PDR show an increase with patient age, a similar pattern is not observed with SSLDR. This finding underscores the importance of recognizing SSLs, particularly in younger adults, as they appear to be more common than previously assumed. Further investigation into the role of SSLs in the development of CRC, particularly among younger adults, is warranted. Additionally, there is a need to establish the ideal SSDR metric and define a target for endoscopists to meet.

By advancing our understanding of SSLs and their implications for CRC risk, we can improve screening and prevention strategies to reduce the burden of colorectal cancer in the population.

Disclosure: Nothing to disclose.

PP0858

DURATION-DEPENDENT RISK OF HYPOXEMIA IN COLONOSCOPY PROCEDURES

K. Sharif¹, E. Klang², O. Ukashi¹, Y. Sharif³, A. Lahat¹¹Chaim Sheba Medical Center Dept. of Gastroenterology, Dept. of Gastroenterology, Ramat Gan, Israel, ²Sheba Medical Center Hospital- Tel Hashomer, Ramat Gan, Israel, ³Hadassah Medical Centre, Department of Gastroenterology, Jerusalem, Israel

Contact E-Mail Address: kassemsharif@gmail.com

Introduction: Colonoscopy is a critical diagnostic and therapeutic procedure in gastroenterology. However, it carries risks, including hypoxemia, which can impact patient safety. Understanding the factors that contribute to the incidence of severe hypoxemia, specifically the role of procedure duration, is essential for improving patient outcomes.

Aims & Methods: This study aims to elucidate the relationship between the length of colonoscopy procedures and the occurrence of severe hypoxemia. We conducted a retrospective cohort study at Sheba Medical Center, Israel, including 21,524 adult patients who underwent colonoscopy from January 2020 to January 2024. The study focused on the incidence of severe hypoxemia, defined as a drop in oxygen saturation below 90%. Sedation protocols, involving a combination of Fentanyl, Midazolam, and Propofol, were personalized based on the endoscopist's discretion. Data were collected from electronic health records, covering patient demographics, clinical scores, sedation and procedure details, and outcomes. Statistical analyses, including logistic regression, were used to examine the association between procedure duration and hypoxemia, adjusting for various patient and procedural factors.

Results: The study found a significant correlation between colonoscopy duration and the risk of hypoxemia. Short procedures (under 20 minutes) had a 17.3% incidence of hypoxemia, which increased to 36.1% for procedures lasting over 60 minutes. Age and procedure duration were significant predictors of hypoxemia, with older patients and longer procedures associated with higher risks. The analysis highlighted the need for careful sedation management, especially in longer procedures.

	Duration <20 min	Duration 20-40 min	Duration 40-60 min	Duration ≥60 min	p-value
Age (years)	Median 56.0, IQR (42.4 - 68.1), Mean 54.1, SD ± 17.8	Median 62.7, IQR (50.9 - 71.9), Mean 59.8, SD ± 16.0	Median 68.6, IQR (59.4 - 74.8), Mean 66.1, SD ± 12.9	Median 67.0, IQR (56.5 - 74.9), Mean 64.4, SD ± 14.9	<0.001
Sex (n, %)	4814, (54.1%)	5446, (52.8%)	1001, (57.8%)	343, (59.2%)	<0.001
Inpatient (n, %)	797, (9.0%)	832, (8.1%)	177, (10.2%)	61, (10.5%)	<0.001
ASA Score	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.6	Median 2.0, IQR (2.0 - 2.0), Mean 2.0, SD ± 0.5	Median 2.0, IQR (2.0 - 2.0), Mean 2.1, SD ± 0.5	Median 2.0, IQR (2.0 - 2.0), Mean 2.1, SD ± 0.6	<0.001
Mallampati Score	Median 2.0, IQR (2.0 - 2.0), Mean 1.8, SD ± 0.4	Median 2.0, IQR (2.0 - 2.0), Mean 1.8, SD ± 0.4	Median 2.0, IQR (2.0 - 2.0), Mean 1.8, SD ± 0.4	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.4	<0.001
Midazolam (mg)	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.6	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.5	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.5	Median 2.0, IQR (2.0 - 2.0), Mean 1.9, SD ± 0.6	<0.001
Propofol (mg)	Median 200.0, IQR (100.0 - 200.0), Mean 185.9, SD ± 95.8	Median 200.0, IQR (160.0 - 300.0), Mean 229.9, SD ± 118.2	Median 300.0, IQR (200.0 - 400.0), Mean 300.6, SD ± 163.8	Median 300.0, IQR (200.0 - 500.0), Mean 380.3, SD ± 259.1	<0.001
Fentanyl (mcg)	Median 50.0, IQR (0.0 - 50.0), Mean 38.9, SD ± 28.2	Median 50.0, IQR (50.0 - 50.0), Mean 44.0, SD ± 26.4	Median 50.0, IQR (50.0 - 50.0), Mean 47.4, SD ± 30.0	Median 50.0, IQR (50.0 - 50.0), Mean 45.8, SD ± 30.2	<0.001
SatO2 < 90%	1540, (17.3%)	2494, (24.2%)	562, (32.4%)	209, (36.1%)	<0.001

Table 1- patient characteristics and outcomes based on the colonoscopy duration.

Conclusion: The duration of colonoscopy procedures significantly impacts the risk of severe hypoxemia, with longer durations associated with higher risks. This study underscores the importance of optimizing procedural efficiency and tailoring sedation protocols to individual patient risk profiles to enhance the safety of colonoscopy.

Further research is needed to develop strategies that minimize procedure duration without compromising the quality of care, thereby reducing the risk of hypoxemia and improving patient safety.

Disclosure: Nothing to disclose.

PP0859

ASSESSING THE IMPACT OF BOWEL PREPARATION QUALITY ON COLORECTAL CANCER SCREENING EFFECTIVENESS: A STUDY WITH UNEXPECTED RESULTS

M. Teixeira¹, S. Ramos Lopes¹, D. Tomás¹, A. Bastos¹, C. Teixeira¹, A.L. Alves¹¹Hospital de São Bernardo, Setúbal, Portugal

Contact E-Mail Address: madalenammteixeira@gmail.com

Introduction: The diagnostic accuracy of colorectal cancer (CRC) screening via colonoscopy is influenced by the quality of bowel preparation. The adenoma detection rate is another well-known quality measure for CRC screening colonoscopies. Counting the total number of adenomas identified during each colonoscopy can provide a more comprehensive assessment of the procedure's effectiveness. Adenomas that are 1 cm or larger, exhibit high-grade dysplasia, or have a villous architecture are considered advanced adenomas and carry a higher risk of progressing to adenocarcinoma.

Aims & Methods: The aims of our study were to assess whether there was an association between the adequacy of bowel preparation and both adenoma detection rate and the advanced adenoma detection rate, and to investigate whether there was a correlation between the quality of preparation and the number of adenomas detected per colonoscopy. We present a retrospective, single-center study of complete screening colonoscopies performed on patients with 50 years old or more, over 18 months (from April 2022 to September 2023), and their respective histological reports. Adequate preparation was considered if all colonic segments scored 2 or more points on the *Boston Bowel Preparation Scale* (BBPS). Statistical analysis was conducted using SPSS v29.0.

Results: 672 total colonoscopies were analyzed. The average age was 64.5 ± 8.0 years, and there was no predominance between genders. BBPS scores ranged from 0 to 9. The majority of patients had adequate bowel preparation (74%, n = 502), with BBPS scores of 6, 7, 8, and 9 in 37.7%, 7.0%, 22.9%, and 7% of cases, respectively. The adenoma detection rate was 41.2% and the detection rate of advanced adenomas was 16.4%. The number of adenomas detected per colonoscopy ranged from 0 to 11 adenomas. No association was found between having adequate preparation and having at least 1 adenoma (p>0.05) or having at least 1 advanced adenoma (p>0.05). There was no statistically significant difference in the average number of adenomas per colonoscopy between patients with and without adequate preparation (p>0.05). There was no correlation between the BBPS score and the number of adenomas per colonoscopy (p>0.05).

Conclusion: The detection rates of adenomas and advanced adenomas were not associated with the adequacy of bowel preparation. No correlation was found between the quality of preparation and the number of adenomas per colonoscopy. Despite the need to repeat another colonoscopy with adequate BBPS for optimal observation of the mucosa, concluding screening procedures in patients with inadequate bowel preparation has still proven to be useful. As long as it is considered safe, endoscopists should be encouraged to conclude all screening procedures.

Disclosure: Nothing to disclose.

PP0860

ENHANCING THE ADENOMA DETECTION RATE IN COLORECTAL CANCER SCREENING: ADENOMAS PER COLONOSCOPY AS A QUALITY METRIC

M. Teixeira¹, S. Ramos Lopes¹, D. Tomás¹, A. Bastos¹, C. Teixeira¹, A.L. Alves¹

¹Hospital de São Bernardo, Setúbal, Portugal

Contact E-Mail Address: madalenammteixeira@gmail.com

Introduction: Adenomas per Colonoscopy (APC) might serve as an adjunct quality metric to the Adenoma Detection Rate (ADR). This indicator is calculated by dividing the total number of detected adenomas by the number of colonoscopies performed. It motivates the operator to maximize adenoma identification and removal during screening procedures and allows a more comprehensive assessment of the colonoscopy's quality.

Aims & Methods: The aims of this study were to assess the association between the ADR and the APC metrics in colorectal cancer screening and to explore factors influencing each of these indicators. This retrospective, single-center study analyzed total screening colonoscopies conducted on 50 years old or more patients, over a period of 18 months (from April 2022 to September 2023) and their corresponding histological reports. Colonoscopies with at least one colonic segment with less than 2 points on the *Boston Bowel Preparation Scale* (BBPs) were excluded. Statistical analysis was performed using SPSS v29.0.

Results: 502 total colonoscopies were included. ADR was 41.7% and APC was 76.5%. The number of adenomas per colonoscopy ranged from 0 to 11 adenomas. There was a positive statistically significant association between the ADR and the APC ($\beta=0.6$, $p<0.001$). No statistically significant difference was found in the average age between patients with and without adenomas ($p>0.05$), nor a correlation between age and the number of APC ($p>0.05$). Men were 2.1 times more likely to have at least one adenoma ($p<0.05$) and the average number of adenomas per colonoscopy was statistically significant higher in men ($p<0.05$). The BBPS score was not associated with the detection of at least one adenoma or to the total number of adenomas per colonoscopy ($p>0.05$). The average withdrawal time was higher in patients with adenomas ($p<0.05$), and there was a positive, statistically significant, moderate correlation between withdrawal time and the number of APC ($r=0.5$; $p<0.001$). No association was found between the colonoscopy schedule, endoscopist fatigue or experience and the presence of at least one adenoma ($p>0.05$). The average number of adenomas per colonoscopy was also not statistically significantly different among the previously mentioned groups ($p>0.05$).

Conclusion: Our study confirmed a significant association between the ADR and the APC, encouraging the use of APC as a complementary metric in colorectal cancer screening. Influencing factors were similar between the two indicators. While gender and withdrawal time significantly influenced adenoma detection and the number of adenomas detected per colonoscopy, with men and longer procedures showing higher ADR and APC rates, other factors such as age, bowel preparation quality, and procedural variables showed no significant impact.

Disclosure: Nothing to disclose.

PP0861

CAN ARTIFICIAL INTELLIGENCE PREDICT HYPERPLASTIC POLYP HISTOLOGICAL SUBCLASSES BASED ON ENDOSCOPIC APPEARANCE?

A. Jans^{1,2}, B. Callaerts^{3,4}, P. Sinonquel^{1,2}, X. Sagaert⁵, I. Demedts^{1,2}, P. Roelandt^{1,2}, T. Eelbode^{3,4}, F. Maes^{3,4}, S. Tejpar^{1,6}, R. Bisschops^{1,2}

¹UZ Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ²KU Leuven, Departement Translational Research in Gastrointestinal Diseases (TARGID), Leuven, Belgium, ³KU Leuven, Department of Electrical Engineering (ESAT/PSI), Leuven, Belgium, ⁴UZ Leuven, Medical Imaging Research Center (MIRC), Leuven, Belgium, ⁵UZ Leuven, Department of Pathology, Leuven, Belgium, ⁶KU Leuven, Department of Oncology, Laboratory of Digestive Oncology, Leuven, Belgium

Contact E-Mail Address: alexander.jans@uzleuven.be

Introduction: Recent insights in polyp molecular biology have suggested that hyperplastic polyps (HP) are closely related to sessile serrated lesions (SSL). Their hallmark serrated crypts closely resemble those found in SSL. Furthermore, similar to SSL, specific subtypes of HP can harbor BRAFV600E-mutations. These findings, amongst others, have raised the hypothesis that some HP may have an intrinsic malignant potential through the serrated neoplasia pathway. However in everyday clinical practice, no routine HP subdifferentiation is performed.

Aims & Methods: In this single-center trial, we aimed to develop a deep learning algorithm capable of differentiating between the subclasses of hyperplastic polyps, namely microvesicular hyperplastic polyps (MVHP) and goblet cell-rich hyperplastic polyps (GCHP), based on their endoscopic appearance. We retrospectively selected 198 hyperplastic polyps in 127 patients. All polyps had high quality endoscopic video available in white light endoscopy and virtual chromoendoscopy (i-scan) using Pentax EC38-i20c and EC34-i10 endoscopes. We reviewed all histological slides with an expert pathologist and updated their pathology diagnosis using the MVHP/GCHP subdifferentiation. Of the total 198 HP, 144 were GCHP, 26 were MVHP and 28 were mixed GCHP/MVHP. We selected the polyps without mixed constitution for development of a deep learning algorithm. These 170 polyps were randomly split into 70% for training, 10% for validation and 20% for testing. Sequences of still images of the polyps were manually annotated and subsequently used to train a deep learning algorithm. The imbalance in the training dataset was adjusted by randomly oversampling the MVHP.

Results: We trained a deep learning algorithm using a convolutional neural network on 170 HP (144 GCHP and 26 MVHP). This model can differentiate between MVHP and GCHP based on still endoscopic images with an AUC of 0.743, corresponding to a sensitivity of 70% for MVHP. However due to the low prevalence of MVHP (14%) compared to GCHP (86%) the positive predictive value for MVHP is only 24.1%. The specificity (for GCHP) is 64.2%

	Predicted - MVHP (+)	Predicted - GCHP (-)
True - MVHP (+)	14	6
True - GCHP (-)	44	79

Conclusion: Our preliminary results show that a deep learning algorithm is capable of detecting MVHP with a good sensitivity (70%) based on their endoscopic appearance. However, due to the low prevalence of MVHP compared to GCHP, the positive predictive value for MVHP is only 24.1%. Moreover, the current algorithm has some difficulties correctly identifying the GCHP, as is shown by the rather low specificity of 64.2%. We plan to further expand the dataset to mitigate these issues, however this pilot study serves as a proof of concept that artificial intelligence is capable of predicting hyperplastic polyp subclasses based on endoscopic appearance.

Disclosure: AJ is supported by a grant of Research Foundation Flanders (1SHD924N).
PR is supported by a Clinical Mandate from Belgian Foundation against Cancer (Stichting tegen Kanker).
RB is supported by a grant of Research Foundation Flanders (G072621N) and an FKO grant of KU Leuven (BOF-FKO 2022). RB received speaker and consultancy fees and research support from Pentax Medical.
The authors of this manuscript have no other conflict of interest to declare.

PP0862
**FEW-SHOT LEARNING FOR CLASSIFICATION OF COLORECTAL
NEUROENDOCRINE TUMORS AND POLYPS ON ENDOSCOPIC IMAGES**

S. Zhu¹, J. Lin¹, L. Liu¹, C. Xu¹, J. Zhu¹
¹The First Affiliated Hospital of Soochow University, Department of Gastroenterology, Suzhou, China

Contact E-Mail Address: sqzhu2048@stu.suda.edu.cn
Introduction: Colorectal neuroendocrine tumors (NETs) and polyps have similar endoscopic manifestations and are easily misidentified. Due to the low incidence of NETs, it is difficult to obtain adequate images to fit deep-learning models. This study introduced a few-shot learning (FSL) model for the ternary classification of NETs and polyps on endoscopic images.
Aims & Methods: Three classes of endoscopic images (56 serrated lesions and polyps [SLPs], 86 traditional adenomas and 53 NETs) were collected from three datasets. First, three images from each class were randomly selected for Support Set (SS), while others for Query Set (QS). Second, ResNet50 V2 was pretrained based on ImageNet and then on esophageal endoscopic images Third, imaging eigenvectors were extracted based on a dual-pretrained model. Fourth, the Euclidean distances to the nine SS images were calculated for each QS image. Finally, a k-nearest neighbor classifier was used for classification based on Euclidean distances. The proposed FSL model was tested in three rounds.
Results: The performance of the FSL model (macro-area under the curve [AUC], 0.731; macro F1-score, 0.674; Matthews Correlation Coefficient [MCC], 0.526; Kappa, 0.523) was better than that of the traditional ResNet50 V2, junior endoscopist, and senior endoscopist. When identifying NETs, the proposed FSL model achieved the highest accuracy 0.823, sensitivity 0.653, precision 0.673 and F1-score 0.659, whereas the senior endoscopist achieved the highest specificity 0.904.
Conclusion: This study presented a FSL method based on transfer learning and metric learning to distinguish between SLPs, adenoma, and NETs on endoscopic images. This suggests that FSL might be an effective method for computer-aided diagnosis of rare diseases.
Disclosure: Nothing to disclose.

PP0863
**IS THERE AN IMPACT OF DEEP SEDATION WITH PROPOFOL ON
ADENOMA DETECTION RATE, POLYP DETECTION RATE, AND CECAL
INTUBATION RATE IN ELDERLY PATIENTS?**

I. Siranovic Pongrac¹, P. Cacic¹, A. Arefijev², S. Pelajic¹, N. Barsic^{1,3}, A. Biscanin^{1,3}, I. Lerotic^{1,4}, D. Hrabar^{1,3}, V. Tomasic¹
¹Sestre milosrdnice University Hospital Center, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ²Pula General Hospital, Pula, Croatia, ³University of Zagreb School of Medicine, Zagreb, Croatia, ⁴School of Medicine at the Catholic University of Croatia, Zagreb, Croatia

Contact E-Mail Address: irma.siranovic1995@gmail.com
Introduction: Early detection of colon adenomas and polyps lowers the risk of colorectal cancer development. Quality indicators for screening or diagnostic colonoscopy encompass the adenoma detection rate (ADR), polyp detection rate (PDR), and cecal intubation rate (CIR). Previous research on ADR, PDR, and CIR in groups of patients who were deeply sedated with propofol versus those who underwent colonoscopy without sedation is undetermined.
Aims & Methods: The objective of this study was to analyze the effects of deep sedation versus no sedation on ADR, PDR, and CIR in a population of elderly patients.
This was a retrospective cohort study that included adult patients over the age of 60, presenting for a first screening or diagnostic colonoscopy performed in the period from January 2017 to September 2023 at our clinical center. The exclusion criteria were emergency colonoscopies, inflammatory bowel diseases, intent therapeutic colonoscopies, and bowel preparation quality (based on the Boston Bowel Preparation Score, BBPS) of less than 6. Participants' characteristics were assessed using descriptive statistics. Normal distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were analyzed using Mann-Whitney test and categorical variables using Chi-square or Fisher exact test. Binary logistic regression was conducted to identify significant predictors of the outcomes. Two-tailed tests were conducted, and statistical significance was considered when p < 0.05.
Results: Among 2034 patients (46.4% female; mean age: 70 years) deep sedation was performed in 622 patients (30.6%). Total PDR was 51.65%, ADR was 33.3%, and CIR was 94.25%. Patients' characteristics are shown in table 1.
After adjusting for confounders (age, gender, BMI, BBPS for PDR/ADR and age, gender, BMI, BBPS, previous abdominal/pelvic operation, diverticulosis for CIR) no significant difference was shown in PDR, ADR and CIR between no-sedation and deep sedation groups. Higher BMI (B = .041, p < .01) and male gender (B = .36, p = .02) were independent predictors for ADR.

	No-sedation (N=1412)	Deep sedation with propofol (N=622)
Age*	70 (65-76)	68 (64-73)
Female gender *	655 (46.4%)	359 (57.7%)
BMI	27 (24.3 - 30.5)	27.1 (23.7 - 29.9)
BBPS	9 (6-9)	9 (6-9)
PDR	731 (51.8%)	320 (51.5%)
ADR	472 (33.5%)	202 (32.5%)
CIR	1316 (93.2%)	593 (95.3%)
Abdominal/pelvic operation	488 (34.6%)	186 (29.9)
Diverticulosis *	523 (37.1%)	272 (43.8%)

Table 1; Patient s' characteristics, BMI; Body mass index, BBPS; Boston bowel preparation scale, PDR; Polyp detection rate, ADR; Adenoma detection rate, CIR; Cecal intubation rate, *gender $\chi^2(3, N =2034)=27.37, p<0.01$, *diverticulosis $\chi^2(1, N =2031)=8.14, p<0.01$, *age $U=367989, z=-5.78; p<0,01$, PDR: $\chi^2(1, N =2033)=0,01, p=.92$, ADR: $\chi^2(1, N =2031)=0,17, p=.68$

Conclusion: In our mixed cohort of elderly patients undergoing screening and diagnostic colonoscopies, propofol-induced deep sedation did not enhance ADR, PDR, or CIR. Further research is needed to determine the impact of deep sedation on colonoscopy quality parameters in elderly patients.

Disclosure: Nothing to disclose.

PP0864

THE IMPORTANCE OF KNOWING WHAT IS INSIDE THE BOX: A CASE STUDY OF WHAT MIGHT GO WRONG IN ARTIFICIAL INTELLIGENCE TRAINING IN ENDOSCOPY

B. Callaerts^{1,2}, A. Jans^{3,4}, P. Sinouquel^{3,4}, X. Sagaert⁵,
I. Demedts^{3,4}, P. Roelandt^{3,4}, T. Eelbode^{1,2}, S. Tejpar^{2,6}, F. Maes^{1,2},
R. Bisschops^{3,4}

¹KU Leuven, Processing Speech & Images - Department of
Electrical Engineering (PSI/ESAT), Leuven, Belgium, ²UZ Leuven,
Medical Imaging Research Center (MIRC), Leuven, Belgium, ³KU
Leuven, Department of Translational Research in Gastrointestinal
Diseases (TARGID), Leuven, Belgium, ⁴UZ Leuven, Department
of Gastroenterology and Hepatology, Leuven, Belgium, ⁵UZ
Leuven, Department of Pathology, Leuven, Belgium, ⁶KU Leuven,
Laboratory of Digestive Oncology, Leuven, Belgium

Contact E-Mail Address: belian.callaerts@kuleuven.be

Introduction: The use of artificial intelligence (AI) in colonoscopy has already been shown enable a higher polyp detection and characterization. New applications are also being developed at an increasingly high pace, but there are potential pitfalls that might appear when developing new AI methods.

Aims & Methods: The aim of this case study is to show potential pitfalls that can arise during the training of new AI models, most importantly on smaller datasets. We aim to illustrate the hidden pitfalls that might arise during development, aside from known problems such as dataset imbalance and overfitting.

This case study is based on the development of an AI network for differentiating between hyperplastic polyp (HP) subclasses using colonoscopy imagery. The original primary outcome was to determine the feasibility of such a setup, while secondary outcome was to determine the effectiveness of such a model. Finally, the tertiary outcome was to use explainable AI techniques on the trained model to see which elements were picked up during training to correctly identify both HP subclasses. The specific technique used is the SHAP technique [1], which highlights the areas in an image used for the classification.

We retrospectively collected images of 198 polyps with histological assessment of hyperplastic polyps from different colonoscopy procedures. These polyps in these images were manually segmented and the histological slices were re-examined for further subclassification into goblet cell-rich hyperplastic polyps (GCHP) and microvesicular hyperplastic polyps (MVHP).

The dataset consists of 144 GCHP, 28 MVHP and 28 mixed MVHP/GCHP polyps, of which only the unmixed polyps were included in this study. The polyps were cropped out of the image with a margin of 50% to take the mucosa immediately surrounding the polyp into account. The total dataset was randomly split into training (70%), validation (10%) and test set (20%). Finally, the imbalanced training and validation datasets were balanced by randomly oversampling the images of MVHP.

Results: We obtained good results for this model, with sensitivity of 90% and 69,9% for MVHP and GCHP respectively and the area under the curve (AUC) was 86,6%. These results can be successfully presented and published, establishing our original primary and secondary objectives. The

problem is that when checking the model with explainable AI techniques to achieve our tertiary objective, we noticed a problem. For MVHP, the features in the image that were used, were usually either be the pit pattern or the existence of mucus. The images that were classified as GCHP seemed to be decided using the surrounding mucosa. The problem is that around 40% of the images classified as GCHP seemed to be selected using the black edges of the scope recording.

It seems that during training there were only black edges visible in training samples of GCHP, making the model assume that all samples with black edges are GCHP, which is obviously a wrong assumption. A simple solution such as randomly adding black edges in all samples solves this problem, correcting the result to a sensitivity of 70% and 64,2% for MVHP and GCHP respectively and with an AUC of 74,3%, which is slightly lower, but does not have the built-in problem.

Conclusion: In preliminary stages of AI development, it is always important to verify achieved results if possible. A model will try to capture features using all the available training data, but uncorrelated features might exist unintentionally. A good verification method is to open the black box-like AI model using explainable AI techniques.

References:

[1] Lundberg, Scott, and Su-In Lee. "A Unified Approach to Interpreting Model Predictions." *arXiv.Org*, 2017, <https://doi.org/10.48550/arxiv.1705.07874>.

Disclosure: Nothing to disclose.

PP0865

IMPACT OF A COMBINATION REGIMEN OF JIAWEI DACHENGQI DECOCTION AND SHUTAIQING ON INTESTINAL CLEANNES AND POLYP DETECTION RATE

X. Fan¹, J. Shen¹, H. Wang¹

¹Liping Hospital of Integrated Traditional Chinese and Western
Medicine, Hangzhou, China

Contact E-Mail Address: sjy_7159@163.com

Introduction: The objective of this study was to compare and analyze the effects of a combination of "Jiawei Dachengqi decoction and Shutaiqing" and "Shutaiqing" regimens on intestinal preparation, intestinal cleanness, and polyp detection rate in a randomized controlled study.

Aims & Methods: The study included 1,000 patients who came to the hospital for electronic colonoscopy and were randomly divided into two equal groups. Patients in the experimental group received a combination regimen of "Jiawei Dachengqi decoction and Shutaiqing" while patients in the control group received only "Shutaiqing". We compared the intestinal preparation and rates of polyp detection in the two groups.

Results: The quality of intestinal preparation ($U = 71254.000$, $P < 0.001$), pain assessment ($U = 53340.000$, $P < 0.001$), and adverse event assessment ($U = 56902.000$, $P < 0.001$) were significantly better than those of the control group. The rate of polyp detection in the experimental group (298/500 cases, 59.60%) was significantly higher than that in the control group (148/500 cases, 29.60%) ($\chi^2 = 91.062$, $P < 0.001$). Of those, the overall detection rates of inflammatory polyps, tubular adenomas, and tubular adenomas with low-grade intraepithelial neoplasia were significantly higher than those in the control group ($P < 0.05$). The polyp detection rate also significantly differed with different degrees of intestinal cleanness ($\chi^2 = 153.153$, $P < 0.001$). Compared with the control group, the rates of polyp detection in participants with intestinal cleanness of 8–9 points ($\chi^2 = 9.191$, $P = 0.002$) and 6–7 points ($\chi^2 = 15.723$, $P < 0.001$) were significantly higher.

Conclusion: The "Jiawei Dachengqi decoction combined with Shutaiqing" regimen was effective in reducing the dose of polyethylene glycol, improving the quality of intestinal preparation, effectively lowering the adverse

events and sensory evaluation of pain in participants, as well as enhancing the rate of polyp detection.

Disclosure: Nothing to disclose.

PP0866

CURRENT REALITIES OF SCREENING COLONOSCOPY IN UKRAINE: CHALLENGES AND OPPORTUNITIES

I. Hornik¹, A. Malovanna², M. Antoniv³, A. Dzhemiliev³, S. Polishchuk¹, I. Huivaniuk⁴, A. Prystaia⁵, S. Kopetskyi⁴, N. Melnitchouk³

¹LLC "GASTROCENTER", Olymed, Endoscopy, Kyiv, Ukraine,

²Top clinic Denis, Kyiv, Ukraine, ³Brigham and Women's Hospital, Boston, United States of America, ⁴Kyiv Regional Cancer Center, Department of Liver, Pancreatic Surgery and Peritoneal Malignancies, Kyiv, Ukraine, ⁵Feofaniya Clinical Hospital, Kyiv, Ukraine

Contact E-Mail Address: vanya.gornikk@gmail.com

Introduction: Colonoscopy plays a key role in colorectal cancer (CRC) screening. It is effective in reducing morbidity and mortality from CRC, which continues to be diagnosed at advanced stages in Ukraine. This research evaluates the challenges faced by endoscopists in Ukraine and suggests solutions to improve screening colonoscopy in Ukraine.

Aims & Methods: Semi-structured interviews were conducted with Ukrainian endoscopists regarding screening colonoscopy. Interview questions were first pilot-tested by a Ukrainian endoscopist and refined by a qualitative expert. Sampling continued until data saturation was achieved.

The interviews were recorded and transcribed. Rapid qualitative analysis was conducted. Two researchers independently coded the data and identified common themes. Interviews were conducted in Ukrainian and translated into English.

Results: Six endoscopists were interviewed. Six themes were developed: quality of endoscopy training; equipment and consumables; performance measures recording; cooperation with National Health Services of Ukraine (NHSU); collaboration with specialists in related fields and recommendations for improving quality of colonoscopy in Ukraine.

Most endoscopists cite poor quality of endoscopy training, insufficient provision of equipment and consumables, problems with collaboration between specialists. The top recommendations they cite for improvement of screening colonoscopy include equipment upgrade and consumables provision, the importance of structured training and coordination between related specialists. The most representative quotes for each theme are shown in Table 1.

Conclusion: These results summarize challenges and suggest solutions to improve screening colonoscopy in Ukraine, emphasizing the importance of structured training, equipment and consumables provision, co-operation with specialists in related fields, and the development of funding programs.

These results are important in establishing an effective country specific screening program.

Disclosure: Nothing to disclose.

Theme	Subtheme	Representative quote	Representative quote
Quality of endoscopy training		"The training methods have already changed: now they learn through videos, on mannequins with artificial intestines. Now, it's feasible to shift the approach of training young professionals. Establishing training centers with a modern curriculum: starting from diagnostics and progressing to advanced procedures." - Endoscopist 1.	"This is a very painful issue. I've done half one colonoscopy and zero gastroscopies. It's like I've gone through specialization, but I can't do anything." - Endoscopist 5.
			"It was a disappointment both in terms of the training provided and in terms of how the work was executed." - Endoscopist 6.
Equipment		"When it comes to equipment, I'd say I've been quite fortunate." - Endoscopist 6.	"The major challenge lies in having just one colonoscope. Everything is done through our own efforts, aiming for the department not to resemble the Soviet times." - Endoscopist 5.
		"We are waiting for new equipment to be provided." - Endoscopist 2.	"Something Happened With The Internet Connection: The Electricity Went Out." - Endoscopist 6.
Equipment and consumables		"We have all the necessary equipment for colon examinations." - Endoscopist 1.	"When it comes to consumables, compromises sometimes have to be made." - Endoscopist 6.
	Consumables	"I switched to disposable instrumentation a long time ago and always discuss this with the patient." - Endoscopist 4.	
Equipment processing		"There are no difficulties." - Endoscopist 4.	"We have manual processing. It takes a lot of time. We hope for an update on the processing equipment." - Endoscopist 2.
		"We have processing machines." - Endoscopist 1.	
Performance measures recording			"I do not document. We have such a large flow of patients that we lack the strength and motivation to handle it. The motivation to begin documentation would arise if it was mandatory for everyone." Endoscopist 4.
Relationship with National Health Services of Ukraine (NHSU)		"Yes, we are contracted. Everything is fine because there is a registrar who takes care of all this." - Endoscopist 5.	"Payments do not cover everything. Do more - pay less." And it should be: "Pay more and do the right thing." - Endoscopist 1.
			"If we had adequate funding, most of the problems would be solved. There is also a question about coding - we need to put the name in order" - Endoscopist 4.
Relationship with specialists in related fields		"Our doctors are pure love. There is understanding and feedback. Pathologists are wonderful. There is a team of anesthesiologists working with us." - Endoscopist 2.	"The main problem is primary health care physicians who do not understand the purpose of CRC screening." - Endoscopist 1.
		"As for the pathologists, until we started going to each other and seeing - there were problems. Working together - there are no questions." - Endoscopist 1.	"A complete disaster with histology." - Endoscopist 5.
Recommendations for improving colonoscopy quality in Ukraine.		"Surgeons have confidence in me, I have confidence in what they do." - Endoscopist 6.	"Until now, for surgeons, endoscopists have remained the ones who have to go in and see if there is something there or not." - Endoscopist 5
		"For development at the European level, coordinated actions of the state and associations, funding, and the development of funding programs are needed. If everyone acts separately, it won't be nationwide." - Endoscopist 1.	"For the development of any field of medicine, the doctor's motivation is important." - Endoscopist 6.
			"New equipment, training of doctors, promotion of endoscopy are needed." - Endoscopist 3.

Table 1.

PP0867

PREDICTING COLONIC PREPARATION: EVALUATING THE LAST BOWEL MOVEMENT APPEARANCE, BODY MASS INDEX, DIABETES, AND DIET DURATION

R. Saidani¹, D. Cherif², D. Habiba^{2,2}, H. Yaacoub^{2,2}, N. Maamouri²

¹La Rabta Hospital, Bizerte, Tunisia, ²La Rabta hospital, Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: raouia.saidani@etudiant-fmt.utm.tn

Introduction: Adequate colonic preparation is crucial for successful colonoscopy, ensuring optimal visualization of the colon and accurate diagnosis of potential abnormalities. Various factors have been implicated in influencing bowel preparation quality, including patient characteristics, dietary habits, and the chosen preparation regimen.

Aims & Methods: This study investigates factors influencing colonic preparation quality for colonoscopy, focusing on the last bowel movement appearance, body mass index (BMI), diabetes mellitus, diet duration, and age.

We prospectively analyzed data from 158 patients undergoing colonoscopy between August and September 2023. Bowel preparation quality was assessed using a pre-endoscopy visual aid based on the color of the patient's last bowel movement an hour before the procedure. Additionally, we compared the 1-day vs. 4-day bowel preparation regimens.

Results:

The pre-endoscopy visual aid effectively predicted adequate bowel cleansing. Patients with yellow and clear stools like urine (YCSU) or light orange and almost clear stools (LOAC) had significantly higher rates of successful bowel preparation (98.4%) compared to those with darker or murkier stools.

Increasing BMI values did not correlate with higher proportions of inadequate bowel preparation. Obese patients achieved successful bowel preparation at a similar rate (81.48%) to non-obese patients (76%).

Diabetic patients had significantly lower successful bowel preparation rates (55.5%) compared to non-diabetic patients (80.3%). However, cecal intubation rates were similar between both groups.

Diet duration significantly impacted colonic preparation. Patients on a 4-day regimen achieved a higher rate of successful preparation compared to those on a 1-day regimen ($p=0.042$).

Age was significantly associated with non-prepared colonoscopies ($p=0.033$). Patients with a BBPS score below 6 were more likely to be older than 70 years old.

Conclusion: This study highlights the effectiveness of the pre-endoscopy visual aid in predicting bowel preparation adequacy. While diabetes adversely affects bowel preparation success, BMI and age above 70 years old are also associated with higher rates of inadequate preparation. Extending diet duration from 1 to 4 days significantly improves colonic preparation quality.

Disclosure: Nothing to disclose.

PP0868

EFFICACY AND SAFETY OF A NOVEL FULLY SYNTHETIC AND SELF-ASSEMBLING PEPTIDE SOLUTION FOR SUBMUCOSAL INJECTION IN ENDOSCOPIC MUCOSAL RESECTION OF COLORECTAL TUMORS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

T. Fukuchi¹, K. Sato², Y. Nakano³, K. Kasuga⁴, H. Aoki⁵, K. Takizawa⁵, S. Kuribayashi², T. Uraoka²

¹Fujisawa City Hospital, Department of Gastroenterology, Fujisawa, Japan, ²Gunma University Graduate School of Medicine, Gastroenterology and Hepatology, Maebashi, Japan, ³Gunma Saiseikai Maebashi Hospital, Department of Gastroenterology, Maebashi, Japan, ⁴Isesaki Municipal Hospital, Department of Gastroenterology, Gunma, Japan, ⁵Koyukai Shin-Sapporo Hospital, Department of Gastroenterology and Endoscopy, Sapporo, Japan

Contact E-Mail Address: take3232@gmail.com

Introduction: Submucosal injection solutions create a mucosal cushion, which provides sufficient separation between the muscle layers and resection sites. It decreases the risk of perforation, without interfering with histological evaluation. In Japan, several submucosal injection solutions, including normal saline, hyaluronate solution, and sodium alginate, have been used during endoscopic resection procedures. A novel fully synthetic and self-assembling peptide solution, PuraLift (3-DMatrix, Tokyo, Japan), is a non-biologic preparation that self-assembles to form a gel composed of nanofibers upon contact with a neutral pH or the response to inorganic salts such Na⁺ and K⁺.

Aims & Methods: In the present study, we aimed to evaluate the efficacy and safety of PuraLift in endoscopic mucosal resections (EMRs) of colorectal neoplasms. This study included 70 patients with 110 neoplastic lesions, measuring 5–20 mm in the colorectal mucosa, from five referral hospitals in Japan, between January and May 2023, who underwent EMR with PuraLift. This study was conducted by board-certified fellows of the Japan Gastroenterological Endoscopy Society (48.2%) and the others. The primary outcome measures were included complete resection rate (en-bloc resection with a histopathologically negative resection margin) and maintenance of mucosal lesion lifting during endoscopic resection (calculated as the number of additional injections required due to the loss of mucosal lesion lifting). The secondary outcome was safety, evaluated by analyzing adverse events during the study period.

Results: The median age and sex ratio (male/female) of the patients were 67 (38–86) years and 43/27, respectively, and 14 patients (20%) were treated with antithrombotic agents. Among the lesions, 29 (26.4 %) were laterally spreading tumors, and the remaining were protruding lesions. The mean tumor size was 9.45 ± 3.26 mm (range: 5–20 mm).

Only two patients required an additional injection due to the loss of mucosal lesion lifting, and the mean injection volume was $2.01 (\pm 2.46)$ mL. En-bloc resection was performed for 109 lesions (99.1%). Eight lesions (7.3%) showed inconclusive horizontal margins on histopathological evaluation. No cases of bleeding, perforation, or other accidental intraoperative event was observed. Evaluation of the ease of EMR (injection and snaring) with PuraLift revealed easy or normal results for 99.1% (109/110) of the lesions.

Conclusion: This novel submucosal injection material enabled sufficient lifting of the colorectal intramucosal lesion during EMR, reducing the need for additional injections and total amount of local injections. Furthermore, this solution contains the same ingredients as the hemostatic material PuraStat (3-DMatrix); therefore, it may have a perioperative hemostatic effect and promote wound healing, contributing to the reduction of complications.

Disclosure: Nothing to disclose.

PP0869

EVALUATION OF CECAL WITHDRAWAL TIMER IN SCREENING COLONOSCOPY TESTS - A POTENTIAL TOOL FOR ENHANCING WITHDRAWAL TIME AND ADENOMA DETECTION RATE

A. Goldman¹, A. Lang¹, A. Levartovsky¹, I. Levy¹, I. Laish², S. Ben-Horin¹, U. Kopylov¹
¹Sheba Medical Center, Gastroenterology, Ramat Gan, Israel,
²Sheba Medical Center, Ramat Gan, Israel

Contact E-Mail Address: adamgoldm@gmail.com
Introduction: Effective colorectal cancer prevention relies on the quality of screening colonoscopy examinations. Cecal withdrawal time is significantly associated with adenoma detection rate (ADR), which is an established quality indicator for screening colonoscopy. Therefore, we introduced a real-time cecal withdrawal timer (CWT) that alerts the physician of the elapsed time since cecal intubation.
Aims & Methods: An observational, retrospective, single-center study to evaluate CWT in screening colonoscopy tests. The CWT is activated by a vocal command when the physician achieves cecal intubation. Following activation, the elapsed time is audio-announced every minute until the end of the procedure.
The ADR of colonoscopies with and without the CWT was evaluated following CWT implementation from January 2023 to February 2024. Moreover, the ADR of the entire department in this period was compared with the year before.
Results: Of 1,557 colonoscopies between January 2023 and February 2024, 908 (58.3%) were performed with the CWT with a median withdrawal time of 8.75 (IQR: 6.9-12.0) minutes.
During this period, the CWT usage was greater than 50% in 11 out of 14 months. Considering only months with CWT usage over 50%, the ADR of colonoscopies with CWT was 28.3% compared to 19.2% in those without (p<0.001).
Among physicians who performed at least 20 tests with and 20 tests without the CWT, 6 out of 8 demonstrated improved ADR with the cecal timer. Notably, the 2 physicians who did not improve ADR had baseline ADR exceeding 30%.
The overall ADR of the department between January 2023 and February 2024 was 25.5%, compared to 26.2% in 2022 (p=0.704).
Conclusion: Initial findings of the CWT program suggest its potential in enhancing screening colonoscopy quality indicators, although long-term prospective follow-up is warranted.
Disclosure: Nothing to declare.

PP0870

EFFICACY AND SAFETY OF CONSCIOUS SEDATION WITH MIDAZOLAM CONTINUOUS INFUSION FOR ESD PROCEDURES: A SINGLE CENTRE PROSPECTIVE STUDY

S. Gherzi¹, P. Apolito¹, S. Landi¹, M. Bassi¹, V. Cennamo¹
¹Maggiore Hospital, Gastroenterology and Interventional Endoscopy Unit, Bologna, Italy

Contact E-Mail Address: stefania.ghersi@ausl.bo.it
Introduction: To date sedation protocol for colorectal endoscopic submucosal dissection (ESD) has not been standardized. (1)
In a recent Italian survey 48,2% of responders perform colorectal ESD with anaesthesiologist assisted deep sedation. (2)
A randomized controlled trial showed an higher incidence (37.9%) of procedure discontinuation in upper GI ESD when performed with midazolam administration.(3)

The aim of this study was to analyse the efficacy and safety of colorectal ESD performed under endoscopist assisted conscious sedation with midazolam continuous infusion (MCI).
Aims & Methods: Consecutive patients who underwent standard and hybrid ESD for colorectal lesions in our institution from April 2017 to September 2023 were prospectively analysed.
In all procedures, a bolus of 0.05mg/kg followed by 0.07mg/kg/h continuous infusion of midazolam was administered with any further boluses and additional drugs (meperidine and scopolamine butyl bromide) according to the patient's level of sedation and pain control.
The main outcome was the incidence of discontinuation of the procedure due to a poor response to sedation.
The second outcome was the incidence and type of sedation side effects. Treatment outcomes, including adverse events were evaluated for each lesion.
Additional drugs administration and past medical history were collected.
Results: 101 ESDs were performed in the period of analysis.
In 5 out of 101 procedures (4.9%) was registered a discontinuation due to poor response to MCI sedation and was requested a conversion to anaesthesiologist assisted deep sedation to complete the procedure.
N. 96 cases were considered for safety analysis (M/F 49/47, median age 70yrs [IQR 14.25]; mean BMI 25.2 [SD: 2.92]).
Sedation drug doses are listed in Table 1.
Lesions had a mean size of 37.1mm [range 10-80], being mostly located in the rectum (96.9%).
En bloc rate was 85,4% , while R0 rate was 92,7%.
The incidence of sedation side effects was 13,5% (13/96): in 12 patients occurred bradycardia, while in 1 patient hypotension.
All those side effects were conservatively managed with medical therapy without occurrence of cerebrovascular or cardiac ischemic events.
In the univariate analysis, sedation side effect occurrence was associated with additional intraprocedural scopolamine butyl bromide administration and patient history of respiratory disease (p<0.05).
Among early adverse events, in 3 patients occurred superficial muscular damage, which was managed endoscopically, while in one patient occurred perforation, which required surgery.
Regarding late adverse events, in 5 patients was reported a late bleeding, which was treated endoscopically with success, whereas in 6 patients occurred post-polypectomy syndrome and in 4 patients occurred urinary retention, both resolved with medical therapy

Induction + Continuous infusion		Mg (mean)
Midazolam		19
Additional bolus	N(%)	Mg (mean)
Midazolam	91 (95)	2.5
Scopolamine	37 (38,5)	6.04
Meperidine	80 (83,3)	66.56

Table 1. Sedation drug doses

Conclusion: The use of MCI is a safe and effective sedation option for colorectal ESD procedures, with a low rate of procedure discontinuation.
References: (1) Kinugasa H, Higashi R, Miyahara K, et al. Dexmedetomidine for conscious sedation with colorectal endoscopic submucosal dissection: a prospective double-blind randomized controlled study. Clin Transl Gastroenterol. 2018;9(7):167
(2) Maselli R, Iacopini F, Azzolini F, et al. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes. Dig Liver Dis. 2020;52(1):64-71
(3) Ominami M, Nagami Y, Shiba M, et al. Comparison of propofol with midazolam in endoscopic submucosal dissection for esophageal squamous cell carcinoma: a randomized controlled trial. J Gastroenterol. 2018;53(3):397-406

Disclosure: V. Cennamo: Member of the scientific board of Olympus Italia; Consultant for Novità Medicali and Euromedical. All other authors disclosed no financial relationships.

PP0871

PREDICTIVE FACTORS OF INCOMPLETE SEDATION-FREE COLONOSCOPY

E. Chemkhi¹, M. Ayari¹, M. Ncir¹, N. Krifa¹, M.H. Douggui¹, T. Jomni¹

¹Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia

Contact E-Mail Address: ayari.myriam@hotmail.fr

Introduction: Colonoscopy is the gold standard of an optimal exploration of the colon. Complete colonoscopy stands as the cornerstone for detecting precancerous lesions and colorectal screening.

Aims & Methods: The aim of our study was to identify factors limiting the completeness of the colonoscopy. We retrospectively colonoscopy reports performed between August 2023 and April 2024. Colonoscopies performed under general anesthesia were excluded from our analysis. Demographics, clinical and endoscopic data were collected. We investigated predictive factors of incomplete examinations.

Results: In total, 400 performed colonoscopies were included. The mean age of the patients was 56.5 years $\pm$ 14.22 (ranging from 16 to 91 years) and a male-to-female ratio of 2. History of diabetes was present in 24% of patients, hypertension in 38% of patients, and 7.8% of patients had chronic inflammatory bowel disease. The predominant indications for colonoscopy were constipation in 29% of cases, digestive bleeding in 16.1% of cases, diarrhea in 11% of cases, anemia in 9% of cases, screening in 4.8% of cases, and anal fistula in 3.8% of cases. The cecum was intubated in 381 colonoscopies (79.8% of cases). Interruption of the endoscopic examination were attributed to various causes, including inadequate preparation (45.5%), poor tolerance (32.5%) and irreducible loops (13%). In univariate analysis, anemia ($p=0.033$), history of benign prostatic hyperplasia, tolerance ($p=0.05$), and poor preparation (assessed by the Boston Bowel Preparation Scale) ($p<0.0001$) were identified as associated factors to incomplete colonoscopy. Demographic characteristics, comorbidities, irritable bowel syndrome, body mass index, abdominal hernia, history of anterior abdominal surgery were not associated with incomplete examination. On multivariate analysis, poor tolerance ($p<0.0001$, OR= 2.45 95%IC: 1.667-3.672), colonic preparation ($p<0.0001$, OR= 4.04 95%IC: 2.384-6.845) were predictive factors of incomplete colonoscopies.

Conclusion: This study confirms the importance of addressing limiting factors of a complete colonoscopy to avoid rescheduling the procedure and to prevent its psychological impact and delay in management and economic burden. Adequate analgesia and improved preparation are necessary for successful cecal intubation.

Disclosure: Nothing to disclose.

PP0872

THE EFFECT OF SMARTPHONE APPLICATION ON THE QUALITY OF BOWEL PREPARATION FOR COLONOSCOPY

E. Ngamchokwathana¹, U. Kaosombatwattana¹,

O. Sattayalertyanyong¹, J. Limsrivilai², K. Maipang¹

¹Faculty of Medicine Siriraj Hospital, Mahidol University, Department of Medicine, Bangkok, Thailand, ²Siriraj Hospital, Department of Medicine, Bangkok, Thailand

Contact E-Mail Address: engicesi@gmail.com

Introduction:

Cancer is the second leading cause of death globally. Colon cancer is the fifth most prevalent type of cancer. Screening, particularly colonoscopy, reduces incidence by 40% and mortality by 50%. The process of bowel preparation before a colonoscopy is complex and requires the patient's compliance.

Enhanced education using a smartphone application has been shown to improve bowel preparation quality. However, heterogeneity was observed among the studies.

Aims & Methods: **AIMS:** To determine if providing instructions through an application enhances bowel preparation quality in Thai patients undergoing elective colonoscopy.

METHODS: From July 2022 to January 2024, a prospective, endoscopist-blinded, randomized, controlled trial was conducted. Consecutive patients aged > 18 years old who had convenient access to the Line application were randomly assigned in a 1:1 ratio to be educated via the smartphone application (APP group) or the standard education (control group). All patients received the same purgative regimen.

The primary outcome was the Boston Bowel Preparation Scales (BBPS). Secondary outcomes included adenoma detection and cecal intubation rates, cecal intubation time, withdrawal time, and patient satisfaction.

Results: The trial aims to recruit 488 patients. A total of 272 patients (APP group, $n = 131$; control group, $n = 141$) were preliminary analyzed. The mean age was 61.5 years old, and 29% were male.

The mean BBPS was comparable between the APP and control groups (8.30 ± 0.99 vs 8.51 ± 1.19 , $P = 0.173$). Both groups achieved adequate bowel preparation (BBPS ≥ 6) in 99.2% of cases.

All secondary outcomes corresponded with the primary outcome. In the subgroup analysis among the elderly, levels of education, income, and waiting times for colonoscopies, BBPS was not impacted by the providing methods. No adverse events related to education were observed.

Outcome	Control group		Intervention group		p-value
	(n = 141)		(n = 131)		
	n	(%)	n	(%)	
BBPS, mean ± SD	8.51	± 0.99	8.30	± 1.19	0.173
Adequate bowel preparation, BBPS ≥ 6	140	(99.2)	130	(99.2)	1.000
NPO time to colonoscopy (hour), mean ± SD	4.73	± 1.2	4.87	± 1.1	0.292
Withdrawal time (min), IQR	9	(6.3 – 12.0)	8	(6.4 – 10.4)	0.240
Polyp detection rate	75	(53.2)	64	(48.9)	0.475
Adenoma detection rate	54	(38.3)	43	(32.8)	0.346
Cancer	1	(0.7)	1	(0.8)	1.000
Satisfaction, IQR	4.2	(3.6 – 4.8)	4	(3.5 – 4.5)	0.084

Conclusion: Both standard and enhanced education using the smartphone application resulted in excellent bowel preparation. Eligible patients included in this study might influence this outcome. However, using the smartphone application was well-received and could potentially replace standard education for bowel preparation.

References:

1. Virani S, Bilheem S, Chansaard W, Chitapanarux I, Daoprasert K, Khuan-chana S, et al. National and Subnational Population-Based Incidence of Cancer in Thailand: Assessing Cancers with the Highest Burdens. *Cancers*. 2017;9(8):108.

2. May FP, Shaikat A. State of the Science on Quality Indicators for Colonoscopy and How to Achieve Them. *Official journal of the American College of Gastroenterology | ACG*. 2020;115(8):1183-90.

3. Desai M, Notalapati V, Bansal A, Buckles D, Bonino J, Olyae M, et al. Use of smartphone applications to improve quality of bowel preparation for colonoscopy: a systematic review and meta-analysis. *Endosc Int Open*. 2019;7(2):E216-E24.

Disclosure: Nothing to disclose.

PP0873

ASSESSING COLONOSCOPY ADHERENCE TO GUIDELINES: MITIGATING INAPPROPRIATE PROCEDURES AND MINIMIZING ENVIRONMENTAL IMPACT

S.Z. Rajani¹, C. Biswas¹, A. Salha¹, S. Mekala¹, A. Walker¹, R. Rameshshanker²

¹The Hillingdon Hospital NHS Foundation Trust, Gastroenterology, London, United Kingdom, ²The Hillingdon Hospital, Endoscopy, Bushey, United Kingdom

Contact E-Mail Address: sana.rajani@nhs.net

Introduction: In line with the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) position statement on reducing the environmental footprint of gastrointestinal (GI) endoscopy, reducing the current rate of unnecessary procedures is the most effective action to mitigate greenhouse gas (GHG) emission in GI endoscopy.¹ The study assesses colonoscopies for adherence to BSG guidelines and evaluates associated environmental burdens, considering that a standard colonoscopy produces 6.71 Kg of CO₂.²

Aims & Methods: It is a service evaluation of colonoscopy practice at our Endoscopy unit. The procedure requisitions were retrospectively analyzed for all colonoscopies done between January and June 2022 and their appropriateness was evaluated based on BSG/NICE guidelines. This activity included assessing non-invasive test reports, if any, recommended before colonoscopy. Repeat colonoscopies due to inadequate bowel preparation were included too.

Inappropriate indication for colonoscopy	Count	Percentage
Abdominal pain and bloating (no FIT/ FCP)	26	19%
Alternating bowel habits + Normal FCP/FIT	47	34%
Loose stools + Normal FCP/FIT	30	21%
Others	26	19%
Polyp surveillance at inappropriate intervals	3	2%
Unexplained weight loss+ Normal FCP/FIT	7	5%
Total	139	

Table 1.

Results: Out of 938 colonoscopies done in six months, 14.8% (n= 139) were inappropriate as per the clinical indication. Table 1 provides a summary of inappropriate indications for colonoscopy and their corresponding frequencies. Just over 7.9% (n= 75) of colonoscopies could have been avoided by performing less invasive tests like FIT or faecal calprotectin (FCP). About 4.2% (n=40) of the colonoscopies were repeated due to inadequate bowel preparation.

Conclusion: Just over 14.8% of colonoscopies were performed inappropriately. In 6 months, our unit contributed to an additional 933kg of CO₂ (estimated annual carbon print 3.74 tons). Every unit should implement robust vetting to reduce carbon costs secondary to inappropriate endoscopy.

References:

1. de Santiago ER, Dinis-Ribeiro M, Pohl H, Agrawal D, Arvanitakis M, Baddeley R, Bak E, Bhandari P, Bretthauer M, Burga P, Donnelly L. Reducing the environmental footprint of gastrointestinal endoscopy: European Society of gastrointestinal endoscopy (ESGE) and European Society of gastroenterology and endoscopy nurses and associates (ESGENA) position statement. *Endoscopy*. 2022 Aug;54(08):797-826.

2. Elli L, La Mura S, Rimondi A, Scaramella L, Tontini GE, Monica F, Soncini M, Topa M, Bortoluzzi F, Sorge A, Cavallaro F. The carbon cost of inappropriate endoscopy. *Gastrointestinal Endoscopy*. 2023 Sep 9.

Disclosure: Nothing to disclose.

PP0874

NEW ENDOSCOPIC PLATFORM TO FACILITATE ENDOSCOPIC SUBMUCOSAL DISSECTION

S. Kantsevov¹, J. White²

¹Mercy Medical Center, Institute for Digestive Health and Liver Disease, Baltimore, United States of America, ²Lumendi, Medical Affairs, Buckinghamshire, United Kingdom

Contact E-Mail Address: skan51@hotmail.com

Introduction: Endoscopic submucosal dissection (ESD) is gaining popularity around the world. However, ESD remains a technically difficult, labor-intensive and time-consuming procedure.

Aims & Methods: Study aim: To describe first clinical experience with recently developed new endoscopic platform to facilitate ESD. Methods: C¹ endoscopic platform (Lumendi LLC, Westport, CT, USA) is a flexible overtube with a balloon on its distal end and attached instrument channel. The C¹ was preloaded on top of any colonoscope and inserted into colon till pre-cancerous or early cancerous lesion is reached. After circumferential incision around the lesion was completed with a commercially available ESD knife, a specially designed flexible grasper (Lumendi LLC, Westport CT, USA) was advanced through the instrument channel.

The separated edge of the lesion was grasped with the grasper to facilitate ESD. After completion of the ESD, C¹ was used a conduit to deliver Overstitch endoscopic suturing device mounted on a double channel upper endoscope (GiF 2T180, Olympus, Center Valley, PA, USA) to the site of lesion removal to perform sutured closure of the post-ESD defect.

Results: C¹ platform was used in 7 patients (3 females, 4 males, age 62.1±10.1 years) with large (35.0±13.5 mm) sessile colonic polyps. Most lesions were located in anatomically difficult positions (splenic and hepatic flexure, appendix and ileocecal valve). On-demand inflation of the C¹ balloon facilitated advancement of the colonoscope through the colon and shortening and straightening of the colonic turns.

None of the patients required external pressure or a change of patient position and in all cases the colonoscope was successfully advanced to the cecum. When the lesion was reached, the balloon was distended providing stabilization of the colonoscope during ESD. Flexible grasper provided multidirectional dynamic retraction of the lesion making endoscopic dissection simple and fast (total ESD time 38.7±16.5 minutes with mean dissection speed 24.8 mm²/minute).

After completion of dissection, the lesion was retrieved through C¹ and then Overstitch suturing device was easily delivered to the ESD site. Suturing closure of post-ESD defects was successfully achieved in all patients. There were no device related adverse events during the study.

Conclusion: Newly developed C¹ endoscopic platform with a flexible grasper significantly facilitates colonic ESD.

Disclosure: Nothing to disclose.

PP0875

ENDOSCOPIC CLOSURE TECHNIQUE PERFORMANCE FOR IATROGENIC PERFORATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

J. Buttar¹, A. Jain¹, S. Jiang¹, H. Qian², E. Lam^{1,3}, M.J. Bourke^{4,5}, N. Shahidi^{1,3}

¹University of British Columbia, Department of Medicine, Vancouver, Canada, ²Centre of Advancing Health Outcomes, Vancouver, Canada, ³St. Paul's Hospital, Division of Gastroenterology, Vancouver, Canada, ⁴Westmead Clinical School, University of Sydney, Sydney, Australia, ⁵Westmead Hospital, Department of Gastroenterology and Hepatology, Sydney, Australia

Contact E-Mail Address: jubuttar@student.ubc.ca

Introduction: Perforation is the most feared endoscopy-related adverse event. Various closure techniques are now available including through-the-scope clips (TTSC), over-the-scope clips (OTSC) and over-the-scope suturing (OTSS).^{1,2} Given the lack of comparative performance estimates, we sought to systematically appraise TTSC, OTSC and OTSS performance for iatrogenic perforation.

Aims & Methods: MEDLINE and EMBASE were independently searched between 06 / 1947 – 01 / 2024 for citations evaluating TTSC, OTSC or OTSS performance. Technical success was defined as complete apposition of the borders of the defect with visual confirmation. Clinical success was defined as technical success with lack of further intervention. Pooled estimates using random-effects modelling were generated stratified by closure modality, location, perforation etiology, and time (year of publication).

Results: Thirty seven citations assessing 795 perforations were included. Pooled technical success and clinical success were 91.5% (95% confidence interval [CI] 87.9-94.1%; I² = 26%) and 86.3% (95% CI 81.9-89.8%; I² = 39%). Technical success of TTSC, OTSC and OTSS were 89.3% (95% CI 82.6-93.6%), 90.7% (95% CI 86.0-93.9%) and 94.9% (95% CI 83.8-98.5%; p=0.53). Clinical success of TTSC, OTSC and OTSS was 85.3% (95% CI 77.9-90.6%), 86.2% (95% CI 80.4-90.5%) and 94.9% (95% CI 83.8-98.5%) (p=0.24). Clinical success was significantly higher for tissue resection-related perforations (p = 0.02) and for perforations in the stomach (p < 0.04); no difference in clinical success was identified when stratifying by closure modality and time (all p > 0.05).

Conclusion: TTSC, OTSC and OTSS are effective for iatrogenic perforation management; specifically, tissue-resection related perforations and perforations in the stomach. No difference in performance was identified based on closure modality or time.

References: 1: Paspatis GA, Arvanitakis M, Dumonceau J-M, et al. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement – Update 2020. *Endoscopy* 2020;52:792-810.

2: Lee JH, Kedia P, Stavropoulos SN, et al. AGA Clinical Practice Update on Endoscopic Management of Perforations in Gastrointestinal Tract: Expert Review. *Clin Gastroenterol Hepatol* 2021;19:2252-2261.e2.

Disclosure: Eric Lam: Speaker Honorarium: Olympus, Pharmascience
Michael Bourke: Research Support: Olympus, Cook Medical, Boston Scientific.

Neal Shahidi: Speaker Honorarium: Boston Scientific, Pharmascience.

All other authors have no conflicts of interest to disclose.

PP0876

PREVALENCE OF ENDOSCOPICALLY CURABLE LOW-RISK CANCER AMONGST LARGE (≥20MM) NON-PEDUNCULATED POLYPS IN THE RIGHT COLON

J. Gauci¹, A. Whitfield^{1,2}, R. Medas³, C. Kerrison¹, F.V. Mandarino¹, D. Gibson⁴, T. O'Sullivan¹, O. Cronin¹, S. Gupta¹, B. Lam¹, V. Peranathan¹, L.F. Hourigan⁵, S. Zanati⁶, R. Singh⁷, S. Raftopoulos⁸, A.C Moss⁴, G. Brown⁴, A. Klein⁹, L. Desomer¹⁰, D.J. Tate¹¹, E. Lee^{1,2}, S. Williams¹, N. Burgess^{1,2}, M.J. Bourke^{2,12}

¹Westmead Hospital, Department of Gastroenterology and Hepatology, Sydney, Australia, ²University of Sydney, Medical School, Sydney, Australia, ³Centro Hospitalar São João, Gastroenterology, Pedrosa - Vila Nova de Gaia, Portugal, ⁴Alfred Hospital, Gastroenterology, Melbourne, Australia, ⁵Princess Alexandra, Brisbane, Australia, ⁶Royal Prince Alfred Hospital, Canterbury, Australia, ⁷Lyell McEwan Hospital, Adelaide, Australia, ⁸Sir Charles Gairdner Hospital, Perth, Australia, ⁹Ambam Heath Care Campus, Technion Institute of Technology, Haifa, Israel, ¹⁰AZ Delta Roeselare, University Hospital Ghent, Gastroenterology and Hepatology, Drongen, Belgium, ¹¹University Hospital Ghent, Gastroenterology and Hepatology, Gent, Belgium, ¹²Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: julia.gauci@yahoo.co.uk

Introduction: Endoscopic submucosal dissection (ESD) is increasingly promoted as the optimal treatment strategy for all large non-pedunculated colorectal polyps (LNPCP). The effect of a universal en bloc strategy on oncological outcomes for the treatment of LNCP in the right colon is unknown. We evaluated this in a large Western population.

Aims & Methods: We retrospectively analysed prospectively collected data from major tertiary centres where patients were referred for endoscopic resection (ER) of LNCP (N=5084). Patients found to have cancer after ER and those referred directly to surgery were included. The primary outcome was to determine the proportion of right colon LNCP with low-risk cancer.

Results: Over 180 months until June 2023, 3294 sporadic right colon LNCP in 2956 patients were referred for ER at 7 sites (median size 30mm [IQR 15]). 63 (2.1%) patients were referred directly to surgery and cancer was proven in 56 (88.9%). 2851/2956 (96.4%) LNCP underwent ER (median size 35mm [IQR 20]) of which 75 (2.6%) were cancers. The overall prevalence of cancer in the right colon was 4.4% (131/2956). Detailed histopathological analysis was possible in 115/131 (88%) cancers (71 after ER, 44 direct to surgery, Table 1). 23/2940 (0.78%) sporadic right colon LNCP were low-risk cancers.

	Direct to Surgery (n=44)	EMR Performed (n=71)	p
Depth of SM invasion (Kikuchi) N (%)			<0.001
SM1	4 (9.1)	22 (30.9)	
SM2/3	8 (18.2)	39 (54.9)	
Invasion beyond SM	32 (72.7)	10 (14.1)	
High tumour grade N (%)	5 (11.4)	9 (12.7)	1
LVI N (%)	8 (18.2)	12 (16.9)	1
High grade TB N (%)	5 (20.8)	10 (14.9)	0.68
Any high-risk histology (high tumour grade, LVI, high grade TB, deep SM invasion) N (%)	40 (90.9)	52 (73.2)	0.04

Table 1: Final Oncologic Outcomes; comparison between histopathologic variables of cases referred directly to surgery versus following endoscopic resection.

Conclusion: The proportion of right colon LNCP referred for ER containing low-risk cancer amenable to endoscopic cure was <1%, in a large, multicentre Western cohort. A universal ESD strategy for the management of right colon LNCP is unlikely to yield improved patient outcomes given the minimal impact on oncological outcomes, significant resource demands and increased adverse events.

Disclosure: Nothing to disclose.

PP0877

PROSPECTIVE VIDEO-BASED STUDY ASSESSING EFFECT OF COMPUTER-ASSISTED OPTICAL DIAGNOSIS ON DISTINGUISHING SESSILE SERRATED FROM HYPERPLASTIC AND ADENOMATOUS COLORECTAL POLYPS

D.H.(. Kim¹, S. Fournier², E. Medawar³, R. Djinbachian⁴, D.K. Rex⁵, H. Pohl⁶, A.N. Barkun⁷, Y. Saito⁷, A. Sethi⁸, P.W.Y. Chiu⁹, R. Maselli¹⁰, M. Pioche¹¹, J. Marks¹², M. Al Khaldi³, K. Pawlak¹³, H. Sebahang³, F. Benard¹⁴, R. Hajjar³, M. Zarandi-Nowroozi³, F. Schwenter³, M. Taghiakbari¹⁵, M. El Mehdi El Yamani³, D. von Renteln¹⁶

¹McGill University, Medicine, Montreal, Canada, ²McGill University, Montreal, Canada, ³Centre hospitalier de l'Université de Montréal, Montreal, Canada, ⁴Montreal University Hospital Research Center, Gastroenterology, Montréal, Canada, ⁵IUPUI, Gastroenterology, Indianapolis, United States of America, ⁶White River Junction VA Medical Center, New Hampshire, United States of America, ⁷National Cancer Center Hospital Endoscopy Division, Endoscopy Division, Tokyo, Japan, ⁸Columbia University Medical Center, New York, United States of America, ⁹Chinese University of Hong Kong, Department of Surgery, Hong Kong, Hong Kong, ¹⁰Humanitas University, Rozzano, Italy, ¹¹Hospices civils de Lyon, Gastroenterology and endoscopy, Lyon, France, ¹²University Hospitals Cleveland Medical Center, Cleveland, United States of America, ¹³Hospital of the Ministry of Interior and Administration, Department Gastroenterology, Endoscopy Unit, Szczecin, Poland, Szczecin, Poland, ¹⁴Centre Hospitalier Universitaire de Montreal, Montreal, Canada, ¹⁵University of Montreal, Longueuil, Canada, ¹⁶CHUM, Gastroenterology, Montreal, Canada

Contact E-Mail Address: dong.kim4@mail.mcgill.ca

Introduction: Computer-Aided Diagnosis (CADx) systems have become available to assist endoscopists with optical polyp diagnosis. However, current CADx systems have not been trained to recognize sessile serrated lesions (SSLs) and currently classify SSLs incorrectly either as hyperplastic or adenomatous. We aimed to assess the effect of current CADx systems on diagnostic accuracy of SSL recognition among a diverse group of endoscopists.

Aims & Methods: We conducted a prospective video-based study including 17 endoscopists (gastroenterologists and surgeons, experts, and trainees). Each endoscopist reviewed the same video and image series of 115 polyps (33% SL, 33% Hyperplastic Polyps (HP), 34% tubular adenoma (TA)). Histopathological diagnosis of the polyps was used as the gold standard for comparison. Presentation of polyps (SSL, TA, HP) was randomized so that 50% of the polyps seen were presented with displaying a CADx diagnosis for the polyp and 50% were presented without displaying a CADx diagnosis.

Results: A total of 1955 optical polyp diagnoses were performed. The optical diagnostic accuracy amongst various endoscopists to recognize SSLs was: expert gastroenterologists (52.3%, 95% Confidence Interval (CI) 46.3-58.3), trainee gastroenterologists (38.2%, CI 27.2-49.1), expert surgeons (22.1%, CI 16.2-28.0) and trainee surgeons (14.9%, CI 8.4-21.5). Further details are provided in Table 1. CADx identified 52.6% of SSL as HP and 47.4% as TA. CADx identified 60.5% of HP correctly and 82.1% of TA

correctly. The optical diagnostic accuracy for HP and TA improved among endoscopists when a correct CADx diagnosis was displayed to the endoscopists compared to when no CADx information was displayed (HP: 63.7% vs 38.4% / TA: 81.5% vs 70.5%; p=0.05). The optical diagnostic accuracy of the endoscopists worsened when the displayed CADx diagnosis was incorrect (HP: 24% / TA: 25%). The diagnostic accuracy of the endoscopists for SSL did not differ significantly when the CADx diagnosis, which is currently untrained to diagnose SSL and can only classify polyps as hyperplastic or adenomatous, was displayed (37.2% vs 33.1%, p=0.05).

	Sessile Serrated Lesion	Hyperplastic Polyp	Adenoma
CADx Alone	HP: 52.6 (36.8-68.5) TA: 47.4 (31.5-63.2)	Sn 60.5 (49.5-71.5) Sp 82.1 (70.0-94.1) PPV 86.8 (77.7-95.9) NPV 51.6 (39.2-64.1)	Sn 82.1 (70.0-94.1) Sp 60.5 (49.5-71.5) PPV 51.6 (39.2-64.1) NPV 86.8 (77.7-95.9)
CADx diagnosis NOT displayed All Endoscopists (n=17)	Sn 37.2 (31.9-42.4) Sp 78.6 (75.5-81.8) PPV 46.2 (40.1-52.2) NPV 71.7 (68.4-75.0)	Sn 38.4 (33.1-43.7) Sp 79.8 (76.8-82.9) PPV 48.4 (42.3-54.6) NPV 72.4 (69.2-75.7)	Sn 70.5 (65.6-75.4) Sp 64.7 (61.0-68.4) PPV 50.6 (46.1-55.2) NPV 81.0 (77.6-84.4)
CADx Displayed Correct Diagnosis All Endoscopists (n=17)	Sn 33.1 (28.0-38.3) Sp 79.4 (76.3-82.5) PPV 44.2 (38.0-50.5) NPV 70.6 (67.3-73.9)	Sn 63.7 (57.4-70.0) Sp 78.7 (74.9-82.5) PPV 60.2 (53.9-66.4) NPV 81.1 (77.4-84.8)	Sn 81.5 (76.9-86.2) Sp 86.5 (83.2-89.9) PPV 80.7 (76.0-85.3) NPV 87.2 (83.9-90.5)
CADx Displayed Incorrect Diagnosis All Endoscopists (n=17)		Sn 24.0 (15.6-32.4) Sp 77.4 (71.7-83.0) PPV 33.3 (22.4-44.2) NPV 68.3 (62.4-74.2)	Sn 25.0 (14.0-36.0) Sp 45.2 (39.1-51.4) PPV 9.8 (5.1-14.5) NPV 71.7 (64.7-78.7)
Breakdown of the performance by endoscopists category			
GE: Gastroenterologist Expert (n=7)			
GT: Gastroenterologist Trainee (n=2)			
SE: Surgery Expert (n=5)			
ST: Surgery Trainee (n=3)			
Overall	GE: 52.3 (46.3-58.3) GT: 38.2 (27.2-49.1) SE: 22.1 (16.2-28.0) ST: 14.9 (8.4-21.5)	GE: 35.0 (29.2-40.7) GT: 61.8 (50.9-72.8) SE: 53.7 (46.6-60.8) ST: 42.1 (33.0-51.2)	GE: 74.7 (69.6-79.9) GT: 64.1 (53.5-74.7) SE: 66.2 (59.5-72.8) ST: 74.4 (66.4-82.3)
CADx diagnosis NOT displayed	GE: 54.1 (45.7-62.6) GT: 39.5 (23.9-55.0) SE: 23.2 (14.7-31.6) ST: 19.3 (9.1-29.5)	GE: 27.8 (20.2-35.4) GT: 57.9 (42.2-73.6) SE: 53.7 (43.7-63.7) ST: 24.6 (13.4-35.7)	GE: 72.8 (65.3-80.3) GT: 66.7 (51.9-81.5) SE: 70.4 (61.4-79.4) ST: 69.5 (57.7-81.2)
CADx Displayed Correct Diagnosis	GE: 50.4 (41.9-58.9) GT: 36.8 (21.5-52.2) SE: 21.1 (12.9-29.3) ST: 10.5 (2.6-18.5)	GE: 50.6 (40.2-60.9) GT: 84.6 (70.7-98.5) SE: 67.2 (55.9-78.4) ST: 73.2 (59.6-86.7)	GE: 85.0 (78.4-91.5) GT: 75.0 (60.0-90.0) SE: 73.4 (63.7-83.2) ST: 91.5 (83.5-99.5)
CADx Displayed Incorrect Diagnosis		GE: 25.0 (12.2-37.8) GT: 25.0 (0.5-49.5) SE: 21.4 (6.2-36.6) ST: 25.0 (3.8-46.2)	GE: 37.5 (18.1-56.9) GT: 0.0 (0.0-0.0) SE: 16.7 (0.0-33.9) ST: 27.3 (1.0-53.6)

Table 1. CADx and endoscopists performance in optical diagnosis of SSL, HP and adenomas depending on the polyp histology in percentages of correct optical diagnoses with 95% confidence intervals. For SSL, CADx is not able to provide correct diagnosis; thus is presented as CADx shown as either HP or TA)

Sn: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value

Conclusion: Optical polyp diagnosis that includes SSL, TA, and HP recognition remains challenging. Current CADx systems when displaying correct diagnostic outputs improve diagnostic accuracy of the endoscopists. CADx systems not trained for SSL recognition do not significantly affect SSL recognition among endoscopists even if an incorrect diagnostic output (TA or HP) is displayed. Development of improved CADx systems with SSL recognition and higher diagnostic accuracy is warranted.

Disclosure: Dr Jeffrey Marks: Consultant for Boston Scientific and Steris Endoscopy.

PP0878

WITHDRAWN

PP0879

COMPARATIVE ANALYSIS OF PERFORMANCE SCORES ON A COLONOSCOPY SIMULATOR (MIKOTO): A NON-INFERIORITY STUDY WITH UK NATIONAL ENDOSCOPY DATABASE KEY PERFORMANCE INDICATORS

O. Olabintan¹, M. Tanne², A. Adeyeye¹, M. Anand¹, H. Ayubi¹, A. Eqbal¹, M. Patel³, S. Gulati³, A. Emmanuel⁴, A. Haji⁴, B. Hayee³
¹King's College Hospital NHS Foundation Trust, London, United Kingdom, ²King's College London, University of London, London, United Kingdom, ³King's Institute of Therapeutic Endoscopy, Gastroenterology, London, United Kingdom, ⁴King's College Hospital, Colorectal Surgery, London, United Kingdom

Contact E-Mail Address: mabel.tanne@kcl.ac.uk

Introduction: Gastrointestinal endoscopy training relies increasingly on simulation tools, especially in foundation years, to teach skills like scope handling and tip control. However, access to simulators offering accurate, real-time feedback is limited. Existing simulators also lack a performance score aligned with UK National Endoscopy Database (NED) Key Performance Indicators (KPIs) such as Caecal intubation rate (CIR), Polyp detection rate (PDR), and Colonoscopy comfort score (CCS).

The MIKOTO colonoscopy training simulator aims to replicate diagnostic colonoscopy conditions and provide real-time feedback based on a simulator score derived primarily from patient comfort during the procedure.

Aims & Methods: This study aimed to validate the comparability of real-time performance scores from the MIKOTO (colonoscopy training simulator) with endoscopists' NED KPIs. Conducted in a major UK Joint Advisory Group (JAG) accredited centre, the non-inferiority study involved 20 endoscopists of varying experience levels, categorized into Novice, Less Competent, Competent, and Expert groups based on their lifetime colonoscopy numbers. Endoscopists provided their NED KPIs before using the MIKOTO simulator. They then performed three full colonoscopies on the simulator, with caecal intubation time and MIKOTO scores collected after each attempt. Statistical analyses were performed to compare the results.

Results: The mean lifetime colonoscopies of the novices, less competent, competent and expert endoscopists were 31, 255, 593 and 2890 respectively. The median CIR for novices, less competent, competent and expert endoscopists were 31%, 92%, 97% and 99% respectively while the PDR across the groups were 7%, 20%, 30% and 45% respectively. In addition, the CCS for the various groups were 37.5%, 10%, 4% and 0.8%. The MIKOTO scores for novices, less competent, competent and expert endoscopists were 47, 69, 84 and 81 respectively. There is statistically significant correlations were observed between CCS, CIR, and MIKOTO scores across all groups (Table 1). No difference was found between Competent and Expert endoscopists in MIKOTO scores and CIR. Overall, higher MIKOTO scores were associated with better NED KPIs (Fig 1).

NED KPI	Novice (MSS=47)	Less competent (MSS=69)	Competent (MSS=84)	Expert (MSS=81)	P-value
PDR (%)	7	20	30	45	0.008
CIR (%)	31	92	97	99	0.566
*CCS (%)	37.5	10	4	0.8	0.003

Table 1: Comparison between NED-KPIs and MIKOTO simulator scores for different competency levels.

NED= National Endoscopy Database, KPI= Key performance Indicator, PDR= Polyp Detection rate, CIT= Caecal Intubation time, CIR= Caecal intubation rate, *CCS= Colonoscopy Comfort Score (% of patient where comfort level is recorded as moderate or severe discomfort), MSS= Mikoto Simulator Score

Conclusion: The MIKOTO simulator score closely aligns with NED KPIs for colonoscopy, potentially serving as a real-time indicator of endoscopic competence, and a valuable tool for early endoscopy training. Larger,

multi-institutional studies are needed to assess the integration of the MIKOTO simulator into UK endoscopy training for skill development and assessment.

Disclosure: No Conflict of interest

PP0880

NON GRANULAR AND GRANULAR MIXED LATERALLY SPREADING TUMOR, WHERE SUBMUCOSAL INVASION LIES BENEATH

G. Corrà¹, A. Gubbiotti², M. Bucci², F. Pelizzaro², L. Peraro³, D. Caroli³, E. Guido³, E. Rosa-Rizzotto³

¹University Hospital of Padua, Bassano del Grappa, Italy,

²University Hospital of Padua, Padova, Italy, ³Sant'Antonio Hospital, Padua, Padova, Italy

Contact E-Mail Address: alessandro.gubbiotti@aopd.veneto.it

Introduction: Endoscopic diagnosis and resection strategy of colorectal laterally spreading tumors (LSTs) is a relevant topic of debate. Current guidelines suggest that LSTs can be treated with endoscopic mucosal resection (EMR) provided that superficial submucosal invasion (SMI) stigmata are ruled out. By contrast, the treatment of choice for high risk SMI lesions should be en bloc resection with endoscopic submucosal dissection (ESD).

Aims & Methods: Since prediction of SMI risk is still challenging, in this study we evaluated which endoscopic features associated with presence of SMI in LSTs.

In this monocentric retrospective study, we included all patients with resected LSTs between January 2018 and November 2023. Lesions were classified according to morphology into granular (G), granular mixed (GM) and non granular (NG) phenotype. Paris Classification, Kudo pit Pattern, location and lesion diameter were evaluated as predictors of SMI. Univariate and multivariate logistic regression analysis was performed to assess predictors of SMI.

Results: Overall, 459 lesions were analyzed: n=172 NG-LST (37,5%), n=172 GM-LST (37,5%) and n=115 G-LST (25%). Superficial SMI was detected in 35 NG-LSTs (20,3%) , 21 GM-LSTs (12,2%) and 4 G-LSTs (3,5%). In the NG-LST group the prevalence of SMI was non-significantly higher in distal compared to proximal colon (24,5 % vs 17% , OR=1.59 [0.70-3.62] p=0.27). According to Paris classification, the risk of SMI was significantly higher in depressed NG-LSTs (Paris IIc- IIa + IIc) compared to non-depressed lesions (31 % vs. 12%, OR=3.62 [1.59-8.26]; p=0.002).

In GM-LSTs cohort, a not significantly higher SMI prevalence was reported comparing distal with proximal lesions (12,5% vs 5,9%, OR=2,26 [0.61-8.30] p=0.22), whereas rectal lesions showed significant higher risk than proximal lesions (22,9% vs 5,9 % , OR=5.87 [1.94-17.73]; p= 0.002). Kudo pit pattern Vi lesions in comparison to Kudo pit pattern IIIs/IIIL/IV lesions showed a significantly higher SMI prevalence both in NG-LSTs (32% vs. 2%, OR=36.57 [4.80-278.60]; p< 0.001) and in GM-LSTs (73% vs 5%, OR=40.36 [11.96-136.18]; p <0.001). Besides, in GM-LST group a lesion diameter ≥4 cm was associated with higher SMI prevalence only in rectal lesions (40% vs 5%, OR 11.33 [1.33-96.81]; p=0.03).

At the multivariate analysis, independent predictors of SMI presence were Kudo pit pattern Vi (OR 35.02 [4.31-284.85] p<0,001) in NG-LSTs, and Kudo pit pattern Vi (OR 74.15 [14.08-390.43], p<0.001) and rectal lesions (OR 13.45 [2.00- 90.25], p=0,007) in GM-LSTs.

Conclusion: Our study confirmed that NG-LST lesions deliver a higher overall risk of SMI than GM-LSTs and G-LSTs, independently on the location. GM-LSTs carried an intermediate risk of SMI and, considering only rectal lesions, size was an important risk factor for SMI. Furthermore, the Kudo pit pattern was an independent risk factor for SMI in both groups. As a consequence, our study stresses that a proper optical diagnosis is para-

mount in order to stratify SMI risk and choose the appropriate treatment for these lesions.

Disclosure: Nothing to disclose.

PP0881

ENDOSCOPIC RESECTION OF CIRCUMFERENTIAL AND NEAR-CIRCUMFERENTIAL LARGE NON-PEDUNCULATED COLORECTAL POLYPS – A WESTERN PARADIGM SHIFT

O. Olabintan¹, H. Ayubi¹, A. Egbal¹, M.-A. Noreillie², J. Bhoday³, M. Anand⁴, S. Thrumurthy¹, S. Gulati⁴, B. Hayee¹, A. Haji³, A. Emmanuel³

¹King's Institute of Therapeutic Endoscopy, Gastroenterology, London, United Kingdom, ²Leuven University Hospital, Gastroenterology, Leuven, Belgium, ³King's College Hospital, Colorectal Surgery, London, United Kingdom, ⁴King's College London, University of London, London, United Kingdom

Contact E-Mail Address: homira.ayubi@gmail.com

Introduction: Endoscopic resection (ER) of large non-pedunculated colorectal polyps (LNPCP) has advanced significantly, pushing boundaries to treat lesions of any size. However, a dearth of published data exists on the extremes of ER practice, particularly for large lesions creating circumferential or near-circumferential mucosal defects. While Japanese studies, focusing on ESD-resected LNCP, show conflicting outcomes, two prominent Western series lean towards EMR-resected lesions. The Western landscape is evolving, with a notable rise in ESD for LNCP.

Our study delivers fresh insights, presenting outcomes from ER with $\geq 75\%$ circumferential mucosal defects in a leading Western centre that predominantly favours ESD for such lesions. This signifies a transformative trend in ER methodology, underlining the efficacy of ESD in addressing intricate colorectal lesions, thereby shaping evolving standards.

Aims & Methods: 1477 ERs of LNCP $\geq 20\text{mm}$ were performed and grouped according to the extent of the mucosal defect and comparisons made between those with $< 75\%$ and $\geq 75\%$ defects. Independent predictors of stenosis were identified.

Results: 137 patients had ER leaving $\geq 75\%$ circumference defect, most located at or distal to the rectosigmoid, with $\geq 90\%$ defects in 29 and 100% in 14. 31 (22.6%) were resected using EMR and 106 (77.3%) using ESD. En bloc resection was achieved in 64%, increasing to 88% in the last 4 years of the study where ESD was increasingly employed routinely. Overall complications were more likely in these patients (11.7% versus 3.4%, $p < 0.001$), although there was no difference in the incidence of clinically significant perforation ($p = 0.41$) or post-procedure bleeding ($p = 0.45$).

101 patients had undergone surveillance. Stenosis developed in only 2 of 71 (2.8%) patients with defects $\geq 75\%$ circumference but 10 of 18 (55.6%) patients with defects $\geq 90\%$ and 10 of 12 patients (83.3%) with 100% circumferential defects. $\geq 90\%$ circumference defect was an independent risk factor for stenosis ($p < 0.001$).

All patients with stenosis were managed successfully with either expectant management if asymptomatic or balloon dilatation. None have required surgical intervention for stenosis. Recurrence was more likely in those with $\geq 75\%$ defect (OR 7.9, 95% CI 3.8-16.4, $p < 0.001$) but was acceptable at an incidence of 15% at SC1

Conclusion: This is the largest western series to date reporting on outcomes of ER of LNCP leaving near or fully circumferential defects, and the first to include significant numbers of ER performed by ESD. ER of LNCP resulting in defects $\geq 75\%$ of the luminal circumference is challenging but highly effective in avoiding surgery when performed in an expert centre. En bloc resection can be achieved in most cases, reducing recurrence. The only independent predictor of stenosis is $\geq 90\%$ circumference

defect but some patients improve with expectant management therefore pre-emptive intervention may not be warranted.

Disclosure: Nothing to disclose.

PP0882

THE YIELD OF COLONOSCOPY IN THE EVALUATION OF CONSTIPATION: AN AGE-BASED ANALYSIS OF OUTCOME

R. Taher Natour¹, A. Mari², D. Nicola¹, A.-R. Zeina³, A. Beshara¹, F. Younis¹, O. Gal¹, F. Abu Baker¹

¹Hillel Yaffe Medical Center, Gastroenterology and Hepatology, Hadera, Israel, ²Nazareth Hospital EMMS, Gastroenterology, Nazareth, Israel, ³Hillel Yaffe Medical Center, Radiology, Hadera, Israel

Contact E-Mail Address: randataher12@gmail.com

Introduction: Chronic constipation is a prevalent gastrointestinal complaint with increasing incidence among the aging population. Examining colonoscopy performance in chronic constipation across age groups, this study aims to comprehensively assess diagnostic yield and compare results with average-risk controls.

Aims & Methods: A retrospective analysis was conducted on 50,578 colonoscopy procedures performed over 12 years, including 5,478 constipated patients. An average-risk control group ($n = 4,100$) was included. Data extracted from electronic medical records covered demographics, operational aspects, and colonoscopy findings. The primary outcome measures included the diagnosis rate of colorectal cancer (CRC), polyp detection rate (PDR) and inflammatory bowel disease (IBD) diagnoses in constipated patients versus controls, with age-based and multivariate analyses.

Results: Constipated patients exhibited lower rates of adequate bowel preparation (92.7% vs. 85.3%; $p < 0.001$) and a lower cecal intubation rate. No significant variances between CRC and PDR were observed between constipated and controls, except for a potential of a slightly elevated CRC risk in constipated patients older than 80 (2.50% vs. 0% in controls; $p = 0.07$). However, multivariate analysis demonstrated that constipation did not confer an increased risk for CRC or polyp detection across all age groups.

Notably, younger constipated patients exhibited a higher rate of IBD diagnoses (1.7% vs. 0.1% in controls; $p < 0.001$).

Conclusion: Constipation did not confer an increased risk for CRC or polyps among all age groups, except for a potential signal of elevated CRC risk in patients older than 80, and was associated with higher rates of IBD in younger patients.

References:

1. Aziz I, Whitehead WE, Palsson OS, Törnblom H, Simrén M. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert Rev Gastroenterol Hepatol*. 2020 Jan;14(1):39-46.
2. Camilleri M, Brandler J. Refractory Constipation: How to Evaluate and Treat. *Gastroenterol Clin North Am*. 2020 Sep;49(3):623-642.
3. Shahini E, Sinagra E, Vitello A, Ranaldo R, Contaldo A, Facciorusso A, Maida M. Factors affecting the quality of bowel preparation for colonoscopy in hard-to-prepare patients: Evidence from the literature. *World J Gastroenterol*. 2023 Mar 21;29(11):1685-1707.
4. Mahmood S, Farooqui SM, Madhoun MF. Predictors of inadequate bowel preparation for colonoscopy: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol*. 2018;30:819-826.
5. Hassan C, East J, Radaelli F, Spada C, Benamouzig R, Bisschops R, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy*. 2019 Aug;51(8):775-794.

6. Włodarczyk J, Waśniewska A, Fichna J, Dzikowski A, Włodarczyk M. Current Overview on Clinical Management of Chronic Constipation. *J Clin Med*. 2021 Apr 16;10(8):1738.
7. James SL, van Langenberg DR, Taylor KM, Gibson PR. Characterization of ulcerative colitis-associated constipation syndrome (proximal constipation). *JGH Open*. 2018 Aug 5;2(5):217-222.

Disclosure: Nothing to disclose.

PP0883

COLON CAPSULE ENDOSCOPY: WHAT FACTORS PREDICT AN INCOMPLETE EXAMINATION?

M. Souto^{1,2,3}, A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, V. Macedo Silva^{1,2,3}, C. Arieira^{1,2,3}, B. Rosa^{1,2,3}, S. Leite^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga/Guimarães, Portugal, ³ICVS/3B's – PT Government Associated Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: mariana.souto9@gmail.com

Introduction: The most important factors for a successful colon capsule endoscopy (CCE) study are the quality of bowel preparation and the capsule excretion during battery life. Incomplete colonoscopy is one of the main indications for CCE.

Aims & Methods: The aim of this study was to analyze clinical and demographic factors for complete CCE after incomplete colonoscopy.

A retrospective single-center study was conducted, including patients consecutively submitted to CCE with previous incomplete colonoscopy. Complete examination was defined as visualization of hemorrhoidal plexuses during battery time. Demographic (gender and age) and clinical data (diabetes mellitus, hypertension, smoking, BMI, hypothyroidism, constipation, depression, opioid therapy, psychotropic medication and previous abdominal surgery) were collected.

Results: 197 patients were analyzed, with a mean age of 67 years, 71.6% were women. The main reasons for incomplete colonoscopy were impassable angulation (54.8%) and irreducible loop (40.1%).

CCE was incomplete in 32.5% (n=64) of cases. Bowel preparation was inadequate in 30.5% (n=60).

Constipation was a risk factor for incomplete CCE study (OR 2.962; p=0.021, 95% CI 1.178-7.264), as well as obesity (OR 4.407; p=0.020, 95% CI 1.263-15.373).

The clinical indication for the examination did not show a statistically significant relationship with the rate of incomplete examinations (p=0.603). There were no statistically significant differences between the percentage of incomplete CCE in patients with incomplete colonoscopy due to impassable angulation versus irreducible loop (33.3% vs 33.3%, p=1.000).

Conclusion: Constipation and obesity are factors associated with a higher risk of incomplete CCE study. In these patients, intensification or alteration of the bowel preparation protocols used may be considered.

Disclosure: Nothing to disclose.

PP0884

CLINICAL IMPLEMENTATION OF RESECT AND DISCARD USING COMPUTER-ASSISTED OPTICAL POLYP DIAGNOSIS (CADX): A PILOT STUDY

M. Taghiakbari¹, D.K. Rex², H. Pohl³, R. Djinbachian⁴, F. Huang⁵, D. von Renteln¹

¹Division of Gastroenterology, University of Montreal Hospital Center (CHUM), Montréal, Canada, ²Division of Gastroenterology/Hepatology Indiana University School of Medicine, Indianapolis, United States of America, ³Department of Veterans Affairs Medical Center, White River Junction, Vermont and The Geisel School of Medicine at Dartmouth, New Hampshire, United States of America, ⁴Division of Gastroenterology, University of Montreal Hospital Center (CHUM), Gastroenterology, Montréal, Canada, ⁵Faculty of Medicine, University of Montreal, Montréal, Canada

Contact E-Mail Address: mahtakbar@gmail.com

Introduction: Histopathological assessment remains the gold standard for evaluating diminutive colorectal polyps, despite the potential of optical diagnosis (OD) to reduce colonoscopy-associated costs (1). However, implementing OD strategies remains limited in clinical practice (2). This study aimed to evaluate patient acceptance of truly replacing pathology evaluation of diminutive polyps with resect and discard (RD) and diagnose and leave (DL) strategies using computer-aided polyp diagnosis (CADx).

Aims & Methods: In this prospective clinical pilot study at the Montreal University Hospital Center, 102 patients undergoing colonoscopy were invited to participate in the study. Patients received information on CADx, RD, DL and were informed that if they agree to participate in the study, we will diagnose all polyps using CADx during the colonoscopy, but polyps will be discarded or left in place and no pathology exams will be performed. For consenting patients, blue light imaging (BLI)-assisted CADx was used and endoscopists made the final histology determination and rated their confidence level (high vs. low) in the OD. Endoscopists also determined if high-risk features were present before using RD or DL strategies. Then all diminutive polyps optically diagnosed with high confidence as adenomas were resected and discarded and all diminutive rectosigmoid polyps optically diagnosed as hyperplastic with high confidence were left in situ. All polyps >5mm, with disagreement between endoscopists and CADx OD, low-confidence OD, or high-risk features (JNET 2b or higher) were sent for pathology evaluation. All cases were video recorded, and a quality review of the diagnoses performed with two expert endoscopists (DR and HP).

Results: Among the 102 patients approached, 97 (95%) accepted participating and utilization of CADx instead of pathology. Three stated that they did not want to participate in any research, and two patients stated that they did not trust OD or CADx as the reason for refusal. Overall, 164 diminutive polyps were removed in 97 patients (mean age=67.2 years), of which 36% were in the rectosigmoid and 64% in the proximal colon. CADx-assisted OD was performed on 97% of the polyps. The proportion of polyps with a low-confidence OD or disagreement between endoscopists' and CADx-based OD was 19/159 (11.9%). Overall, 98/159 (61.6%) polyps underwent the RD strategy, of which 4 polyps were discarded by the endoscopist's discretion despite disagreement between endoscopists and CADx OD. One of these 4 polyps had to undergo the DL strategy but was RD because of serrated features. One polyp in the proximal colon was resected and retrieved because of serrated features. 40 polyps were DL in the rectosigmoid, of which 1 polyp was neoplastic based on CADx and endoscopist's OD.

Conclusion: We observed a very high patient acceptance for truly replacing diminutive polyp histopathology with CADx-assisted OD. CADx-based OD was used to RD 98/159 (61.6%) or DL 40/159 (25.2%) diminutive polyps found in the cohort.

References:

- 1) Rex, Douglas K. It's not lack of evidence holding back resect and discard. *Gastrointestinal Endoscopy*, Volume 96, Issue 6, 1033 - 1035.
- 2) Willems P, Djinbachian R, Ditisheim S, Orkut S, Pohl H, Barkun A, Bouin M, Faulques B, von Renteln D. Uptake and barriers for implementation of the resect and discard strategy: an international survey. *Endosc Int Open*. 2020 May;8(5):E684-E692.

Disclosure: Dr Rex is a consultant for Olympus Corporation, Boston Scientific, Aries Pharmaceutical, Braintree Laboratories, Lumendi Ltd., Norgine, Endokey, GI Supply, Medtronic, and Acacia Pharmaceuticals; the recipient of research support from EndoAid, Olympus Corporation, Medivators, Erbe USA Inc, and Braintree Laboratories; and a shareholder in Satisfai Health. Dr Pohl has received research funding from Steris, Cosmo, and is an advisory board member of InterVenn. Dr von Renteln has received research funding from ERBE Elektromedizin GmbH, Ventage, Pendopharm, Fujifilm, and Pentax and has received consultant or speaker fees from Boston Scientific Inc, ERBE Elektromedizin GmbH, and Pendopharm. The remaining authors disclose no conflicts.

PP0885

INFLUENCE OF AGE ON COLORECTAL POLYP CHARACTERISTICS AND FACTORS ASSOCIATED WITH DYSPLASIA: A BI-CENTER RETROSPECTIVE-PROSPECTIVE STUDY

K. ElAmrani¹, H. Delsa¹, A. Nadi¹, F. Belabbes¹, O. Bahlaoui¹, A. Sair¹, Y. Bennani¹, N. Benjelloun¹, A. El Idrissi Lamghari¹, W. Khannoussi¹, I. Ben El Barhdadi¹

¹Faculty of Medicine, Mohammed VI University of Health Sciences (UM6SS), Gastroenterology and Hepatology, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco

Contact E-Mail Address: kenza2605@gmail.com

Introduction: Colorectal polyps are benign tumours detected by endoscopy, with a higher prevalence in older people. The adenoma-carcinoma sequence is well established. Therefore, systematic screening is important to remove them at an early stage.

Aims & Methods: This is a retrospective study including all polyps found during 1393 colonoscopies performed in 2 private university hospitals. According to age, 3 groups were defined: Group 1 (less than 45 years), Group 2 (between 45 and 65 years) and Group 3 (more than 65 years). Data were collected using an evaluation form and analyzed using Jamovi (version 2.4). The aim of our study is to investigate the effect of age on colorectal polyp characteristics and factors associated with the occurrence of dysplasia.

Results: Out of 1484 colonoscopies, we included 187 patients (12.6%) with 347 polyps. The mean age was 53.3 years [25 - 87 years], with a male predominance at 59% (male-to-female sex ratio: 1.4).

The 347 diagnosed polyps were distributed by age: 44 in Group 1 (12.8%), 171 in Group 2 (49.1%), and 132 (38%) in Group 3.

The mean number of polyps was higher in Groups 2 and 3 (respectively 2.16 and 2.06 polyps per patient). The mean number of adenomas was higher in Group 2 and 3 (72% and 74%) versus 54% in group 1.

The majority of polyps found were sessile (80%) with mean size of 6.7mm. all groups combined, the most common histological type was tubular adenomas (48%) followed by hyperplastic polyps (22%) with high rate of low-grade dysplasia (56-66%), and less than 10% of High-grade dysplasia. Statistical analysis revealed a statistically significant correlation between age and the number of polyps ($R=0.14$; $p < 0.01$) as well as their size ($R=0.13$; $p = 0.013$).

Low-grade dysplasia was statistically associated with polyp size ($p < 0.001$; $Z = 4.5$; OR 1.14 CI (1.08-1.2)), as well as certain histological types: tubular adenomas ($p < 0.001$ Z 4.8 OR 195) and tubulovillous adenomas ($p < 0.001$ Z 3.4 OR 45).

However, no statistically significant correlation was found between the occurrence of dysplasia and age, number, or macroscopic appearance of the polyps.

Conclusion: Polyps and age are risk factors for colorectal cancer. In our series, advanced age was statistically associated with an increase in the number and size of polyps.

Additionally, a correlation was found between the histological type of polyps and low-grade dysplasia. Our results support the recommendations to commence colorectal screening from age 45 to treat polyps at an early stage.

Disclosure: Nothing to disclose.

PP0886

COMPLEXITY OF ENDOSCOPIC RESECTION FOR APPENDICEAL ORIFICE LESIONS SUGGESTS CONSIDERATION OF BOTH SURGICAL AND ENDOSCOPIC OPTIONS

H. Ayubi¹, O. Olabintan¹, A. Egbal¹, M.-A. Noreillie¹, J. Bhoday², A. Adeyeye², M. Anand¹, B.H. Hayee¹, S. Gulati³, S. Thrumurthy⁴, A. Haji², A. Emmanuel²

¹King's College Hospital, Endoscopy and Gastroenterology, London, United Kingdom, ²King's College Hospital, Colorectal Surgery, London, United Kingdom, ³King's College Hospital, Gastroenterology, London, United Kingdom, ⁴King's College Hospital, Endoscopy and Upper GI surgery, London, United Kingdom

Contact E-Mail Address: homira.ayubi@gmail.com

Introduction: Large non-pedunculated colorectal polyps (LNPCP) and laterally spreading tumours (LST) >10mm involving the appendix orifice (AO) are notoriously challenging to treat with endoscopic resection (ER). Few studies report outcomes of conventional ER to treat these lesions. The optimal therapy and expected outcomes remain unclear.

Aims & Methods: We report the outcome after EMR and ESD of lesions involving the AO from a large series of ER performed at a tertiary referral centre. Patients undergoing ER at a tertiary referral centre between January 2011 and September 2023 were included. Involvement of the AO was defined as any LNCP or LST encroaching within 5mm of the orifice.

These were classified as encroaching the AO, involving part of the circumference of the AO and involving the full circumference of the AO. Techniques and outcomes of ER of lesions involving the AO were compared with other colorectal locations.

Results: ER was performed for 1596 LNCP and LSTs during the study period. 40 lesions involved the AO: 10 encroached within 5mm of the AO, 14 involved part of the circumference and 16 involved the full circumference. 25 (63%) were resected by EMR, 8 by ESD (20%) and 7 by Hybrid ESD (18%). Initial successful ER was similar for lesions involving the AO and other colonic LNCP (95.0% versus 97.6%, $p=0.27$).

Clinically significant perforation occurred in 3 patients with lesions involving the AO (2 with partial circumference involvement and 1 with complete circumference involvement) and was more frequent after ER of these lesions than others (7.5% versus 1.2%, $p<0.001$). 2 of these patients required surgery. The incidence of post procedure bleeding was similar ($p=0.44$).

One patient developed appendicitis, more than 12 months after resection. Recurrent/residual adenoma at first surveillance was significantly more likely after ER of AO lesions than others (22.2% versus 4.8%, $p<0.001$). Significantly more patients with lesions involving the AO ultimately required

surgery for any reason than patient with other colorectal lesions (12.5% versus 3.9%, $p=0.02$). This was significantly more likely for AO lesions involving the complete or partial circumference (18.8% versus 14.3% partial circumference involvement versus 0% encroaching AO versus 3.9% other locations, $p=0.004$).

Conclusion: These results demonstrate the challenging nature of ER for lesions involving the AO. Safe and effective ER without recurrence is achieved for many patients, including those with lesions involving the complete circumference, but significant complications, recurrence and surgery are more common with these lesions. Given there are relatively low risk minimal access surgical options to treat these lesions, these data will help inform detailed discussions with patients regarding the risks and benefits of ER (which differ from LNCP elsewhere in the colon).

Disclosure: Nothing to disclose.

PP0887

ASSOCIATION OF SUCCESSFUL COLONOSCOPY RATE AND QUALITY OF BOWEL PREPARATION BY TWO DIFFERENT BOWEL PREPARATION AGENTS

D. Narayanan M.J¹, D. Kesavelu², S. Sankaranarayanan²

¹Apollo Hospitals, Chennai, Pediatrics, Chennai, India, ²Apollo Hospitals, Chennai, Pediatric Gastroenterology, Chennai, India

Contact E-Mail Address: devnarayanan1995@gmail.com

Introduction: Intubation of the terminal ileum (TI) is the gold standard for completion of colonoscopy.

Our aim was to assess if this objective was achieved in our centre between endoscopists using various bowel preparations.

Poly ethylene glycol 4000 Vs Magnesium sulphate combined with potassium and sodium sulphates were the two commonly used bowel preparations. Magnesium containing preparations must be used with caution and avoided in patients with renal insufficiency, cardiac disease or pre-existing electrolyte abnormality and patients on diuretic therapy.

The Boston Bowel Preparation Scale was developed to limit inter-observer variability in the rating of bowel preparation quality, while preserving the ability to distinguish various degrees of bowel cleanliness and is mainly designed for adults. There is no dedicated bowel preparation score available for paediatric colonoscopies, BBPS is being used for critical comparison in our prospective cohort.

Aims & Methods: Objectives: To compare the intubation rate of TI between two endoscopists with quality of bowel preparation of colonoscopies in a tertiary health care centre and to assess the quality of bowel preparation of individual colonoscopies performed vis-a-vis, Boston bowel preparation scale as a prospective study over a period of 1 year.

Material and methods: A prospective study in a tertiary referral centre in children who underwent colonoscopies, aged 1 month to 17 years over a period of 1 year.

All children whose parents consented were included in the study. Results were collated using Microsoft Excel™. A total of 135 cases were enrolled during our study period.

Results:

1. TI intubation rate in PEG-4000 + bisacodyl based laxative formula is 87%
2. TI intubation rate in Magnesium/sodium/potassium based saline laxative formula is 79%
3. No side effects were encountered/ observed in either of the cohort.

Conclusion: In our study albeit the fact that our endoscopist chose different bowel preparations based on their anecdotal evidence based experience, we found that the bowel preparation was adequate.

There was no standardised paediatric bowel preparation globally and we

note that every hospital or department or clinician have devised their own bowel preparation based either on personal experience or current available scientific literature.

We also note that we do not have a BBPS for paediatrics which will of immense value for research evaluation and revalidation of bowel preps.

	BBPS (mean)	Sex (m:f)	Mean Age	Sensitivity	Specificity	P value	TI rate
Endoscopist # 1 PEG 4000+ Stimulant laxative	2.37	3:2	8.96	93%	82%	0.015	87%
Endoscopist # 2 Magnesium preparation	2.28	3:2	9.32	86%	77%	0.043	79%

© Ethical clearance was obtained from the institutional ethical committee.

References:

1. Hien PT, Thoi VH, Ha NT, Kalach N. Efficacy of Two Regimens for Colon Cleansing Using Polyethylene Glycol 4000: A Randomized Open Label Trial. *Indian Pediatr.* 2021 Dec 15;58(12):1119-1123. Epub 2021 May 28.
2. Goodman and Gilman's The pharmacological basis of therapeutics, 13th edition
3. Mamula, Petar, and Noor Nema. "Bowel Preparation for Pediatric Colonoscopy." *Frontiers in pediatrics* vol. 9 705624. 1 Sep. 2021
4. Barraclough H, Gillett P, Basude D, et al OC68 A multicentre assessment of adequacy of bowel preparation for paediatric ileocolonoscopy using the Boston bowel preparation scale (BBPS) *Frontline Gastroenterology* 2023;14:A42.

Disclosure: Nothing to disclose.

PP0888

PREVALENCE AND OUTCOMES OF SERRATED POLYPOSID SYNDROME IN GASTROENTEROLOGY PRACTICES: A PRELIMINARY ANALYSIS

S. Jiang¹, A. Zarrin¹, S. Bell¹, A. Wali^{1,2}, S. Selvanderan¹, R. Gilhotra¹, A. Dashti¹, C. Galorport^{1,2}, P. Tavakoli¹, W. Xiong³, R. Enns^{1,2}, J. Telford^{1,2}, N. Shahidi^{2,1}

¹University of British Columbia, Medicine, Vancouver, Canada, ²St. Paul's Hospital, Gastroenterology, Vancouver, Canada, ³University of British Columbia, Pathology and Laboratory Medicine, Vancouver, Canada

Contact E-Mail Address: sjiangx@gmail.com

Introduction: Serrated polyposis syndrome (SPS) is the most common polyposis syndrome found in approximately 1 in 125 screening colonoscopies and is associated with an increased risk of colorectal cancer (CRC).^{1,2} Diagnosing SPS can be challenging due to cumulative polyp tracking and physician awareness.³

Serrated polyposis syndrome prevalence and patient outcomes, outside of established SPS cohorts, remains unclear.

Aims & Methods: We sought to explore the prevalence of SPS within academic gastroenterology practices and patient outcomes. Between 2013-2018, using an established histopathology database, patients who underwent colonoscopy with 1 of 11 academic gastroenterologists and with at least 1 serrated lesion underwent complete chart review. All patients were screened for SPS based on 2019 WHO criteria.³

Demographic, procedural and patient outcome variables were reviewed for all patients meeting SPS diagnostic criteria. Interim analysis (2013-2018) was conducted on the available dataset (2013-2023).

Results: From 2013-2018, 1800 patients with at least 1 serrated polyp underwent complete chart review; of which 83 (4.6%) met criteria for SPS (58 WHO I, 10 WHO II, 15 WHO I/II). Median age at first colonoscopy was

58 years (IQR 50-68 years) and 58 (69.6%) were female. Eighteen patients (21.7%) were referred with fecal immunohistochemistry test (FIT) positivity. Only twenty-eight (33.7%) patients were diagnosed by the clinician. The median number of colonoscopies to diagnosis was 3 (IQR 2-4) over a median of 2 years (0-6 years). On index colonoscopy, patients with SPS had a median of 3 (IQR 2-5) serrated polyps with median largest size of 10mm (IQR 5-15), whereas patients without SPS had a median of 1 (IQR 1-2) serrated polyps with median largest size of 6mm (IQR 4-8) (both $p < 0.001$). CRC was found in 6 (7.2%) patients, either before or at diagnosis of SPS. Twelve (14.5%) patients underwent surgical resection; 5 (6%) for CRC and 7 (8%) for polyp burden. 71 (85.5%) patients with SPS were managed endoscopically.

Conclusion: In academic gastroenterology practices, the prevalence of SPS in patients with at least 1 serrated polyp was 4.6%; with only 33.7% receiving a formal diagnosis. This highlights the need for increased awareness and strategies for cumulative polyp burden tracking.

References:

1. IJspeert JEG, Bevan R, Senore C, et al. Detection rate of serrated polyps and serrated polyposis syndrome in colorectal cancer screening cohorts: a European overview. *Gut*. 2017;66(7):1225-1232. doi:10.1136/gutjnl-2015-310784
2. IJspeert JEG, Rana S a. Q, Atkinson NSS, et al. Clinical risk factors of colorectal cancer in patients with serrated polyposis syndrome: a multicentre cohort analysis. *Gut*. 2017;66(2):278-284. doi:10.1136/gutjnl-2015-310630
3. Hui VW, Steinhagen E, Levy RA, et al. Utilization of Colonoscopy and Pathology Reports for Identifying Patients Meeting the World Health Organization Criteria for Serrated Polyposis Syndrome. *Diseases of the Colon & Rectum*. 2014;57(7):846-850. doi:10.1097/DCR.0000000000000140

Disclosure: Nothing to disclose.

PP0889

ASSESSMENT AND REPORTING OF LARGE NON PEDUNCULATED COLORECTAL POLYPS OUTSIDE OF SPECIALIST CENTRES IS INCONSISTENT AND LEADS TO UNDERESTIMATION OF SIZE AND UNDER-DIAGNOSIS OF INVASIVE CANCER

M.-A. Noreillie¹, O. Olabintan¹, A. Egbal¹, H. Ayubi¹, J. Bhoday¹, H. Rashid¹, S. Thrumurthy¹, S. Gulati¹, B. Hayee¹, A. Emmanuel¹, A. Haji¹

¹King's College Hospital, London, United Kingdom

Contact E-Mail Address: ali.eqbal@nhs.net

Introduction: Endoscopic resection (ER) is the preferred treatment for large non-pedunculated colorectal polyps (LNPCP) in many centres. Despite standardized classification systems, discrepancies exist between the endoscopic assessment by experts in tertiary ER referral centres and endoscopists in peripheral settings. This significantly impacts planning for ER, leading to duplicated procedures and increased burdens on patients and healthcare.

Aims & Methods: Our aim was to compare the final morphology, surface characteristics, histological diagnosis, and lesion size of LNCPs referred to a tertiary center for consideration of ER with the exact descriptions provided during the initial referral.

We included patients with LNCP referred for ER at a tertiary referral centre between June 2022 and September 2023.

Clinical referrals were assessed for morphological classification (Paris/Japanese classifications), surface characteristics (pit pattern and/or vascular pattern), estimated lesion size, and preliminary endoscopic diagnosis.

We compared the endoscopic diagnosis and size with our unit's advanced endoscopic assessment. The final confirmed size of the lesion after ER was also recorded for comparison.

Results: A total of 328 LNCP were assessed and resected following referral during the study period. The location of LNCP was the most consistently reported feature by referring endoscopists (98.2%).

Standardised morphology according to Paris/Japanese classifications was reported in only 133 cases (40.7%). Pit pattern evaluation was reported in 109 cases (33.2%), while vascular pattern evaluation was reported in 66 cases (20.1%).

A size estimate was provided in 276 cases (84.2%). However, 51 cases (18.6%) underestimated the size by ≥ 20 mm compared to the final LNCP size after ER.

Regarding suspected diagnoses of invasive cancer, 50 cases (15.3%) were suspected, of which 15 had a final diagnosis of invasive cancer. In 277 cases (84.7%) with no suspicion of invasive cancer, 15 had a final diagnosis of invasive cancer, resulting in a sensitivity of 50% and specificity of 88% for a final diagnosis of invasive cancer.

After advanced endoscopic assessment, a diagnosis of likely invasive cancer was made for 41 LNCP, resulting in a sensitivity of 73% and specificity of 93% for a final diagnosis of invasive cancer. This sensitivity is however most likely an underestimation, due to the number of lesions that were previously manipulated (biopsies, attempted resection), complicating surface characterization.

Conclusion: Despite broad agreement on standardised reporting and classifications for endoscopic diagnosis, our study reveals significant deficiencies in the assessment of LNCP outside of specialist centres. The majority of referred LNCP lacked a morphological classification and detailed interrogation of surface characteristics.

These shortcomings, coupled with the limited sensitivity for diagnosing potential invasive cancer, hinder the ability to plan advanced resection without subjecting patients to a further procedure for lesion assessment, with its attendant patient and institutional burdens.

Moving forward, efforts should be made to improve the quality and consistency of LNCP assessment in non-specialist settings. This may involve enhanced training and education for endoscopists, as well as the development of standardized protocols for LNCP evaluation and referral. Further research is warranted to explore optimal strategies for improving diagnostic accuracy and streamlining patient management in this context.

Disclosure: Nothing to disclose.

PP0890

COLD VS HOT SNARE ENDOSCOPIC MUCOSAL RESECTION FOR LARGE (≥ 15 MM) FLAT NON-PEDUNCULATED COLORECTAL POLYPS: A RANDOMIZED CONTROLLED TRIAL

T. O'Sullivan^{1,2}, O. Cronin^{1,2}, A. van Hattem³, F.V. Mandarino¹, J. Gauci¹, C. Kerrison¹, A. Whitfield^{1,2}, S. Gupta^{1,2}, E. Lee¹, S. Williams¹, N. Burgess^{1,2}, M.J. Bourke^{1,2}

¹Westmead Hospital, Department of Gastroenterology and Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School, Sydney, Australia, ³Antoni van Leeuwenhoek ziekenhuis / Netherlands Cancer Institute, Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: Endoscopic mucosal resection (EMR) is standard of care for the management of large (≥ 20 mm) non-pedunculated colonic polyps (LNPCPs). Its efficacy and cost effectiveness were limited by recurrence. Margin thermal ablation (MTA) to the post-EMR defect, has greatly mitigated this problem. However, electrocautery-related complications of delayed bleeding and perforation incur significant morbidity.

Cold snare polypectomy is effective and safe for the resection of small polyps with negligible recurrence rates. Application of cold snare resection to LNPCPs, while an attractive alternative, lacks high-quality evidence. We conducted a randomized trial to compare the efficacy and safety of cold EMR (C-EMR) to conventional (H-EMR).

Aims & Methods: A prospective single-centre randomized controlled trial was conducted at an Australian tertiary referral centre for flat, 15-50mm adenomatous LNPCPs referred for endoscopic resection. Prior to resection, eligible LNPCPs were randomly assigned to EMR using a dedicated cold snare or conventional H-EMR with margin thermal ablation (control). First surveillance colonoscopy (SC1) was conducted 6 months following resection. Scars were evaluated with high-definition white-light, narrow-band imaging and biopsy. The primary outcome was endoscopically visible and/or histologically confirmed recurrence at SC1. Secondary outcomes were clinically significant post-EMR bleeding (CSPEB), delayed perforation and technical success.

Results: 931 LNPCPs were referred for endoscopic resection between November 2019-September 2023. 177 LNPCPs in 177 patients were randomized to either the C-EMR arm (n=87) or H-EMR arm (n=90). Treatment groups were equivalent with no significant difference in lesion size or technical success (86/87 (98.9%) vs 90/90 (100%); p=0.31). One C-EMR required conversion to H-EMR due to unexpected submucosal fibrosis. Following exclusions, 146 LNPCPs undertook SC1 (76 C-EMR, 70 H-EMR). 5 patients await surveillance. On intention to treat and per protocol analysis, recurrence was significantly greater in C-EMR (16/87, 18.4% vs 1/90, 1.1%; p<0.001 and 16/76, 21.1% vs 1/70, 1.4%; p<0.001 respectively). Significant deep mural injury (27/90 (30%) vs 0; p<0.001) and delayed perforation (1/90 (1.1%) vs 0; p=0.32) only occurred in the H-EMR group. CSPEB and intraprocedural bleeding were significantly greater in the H-EMR arm (7/90 (7.8%) vs 1/87 (1.1%); p = 0.034 and 12/90 (13.3%) vs C-EMR arm 1/87 (1.1%); p=0.002 respectively).

Conclusion: Compared to conventional H-EMR, C-EMR for flat, adenomatous LNPCPs, demonstrates superior safety with equivalent technical success. However, endoscopic recurrence is significantly greater for cold snare resection and is currently a limitation of the technique.

Disclosure: Michael Bourke: Research Support: Olympus Medical, Cook Medical, Boston Scientific

The remaining authors have no financial, professional, or personal conflicts of interest to disclose.

PP0891

IMPACT OF MARGIN THERMAL ABLATION ON RECURRENCE AFTER ENDOSCOPIC MUCOSAL RESECTION OF LARGE ($>/-40$ MM) COLORECTAL LESIONS

J. Gauci¹, C. Kerrison¹, A. Whitfield¹, T. O'Sullivan¹, F.V. Mandarino¹, B. Lam¹, O. Cronin¹, V. Perananthan¹, S. Gupta¹, R. Medas¹, E. Lee¹, N. Burgess¹, M.J. Bourke¹

¹Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: julia.gauci@yahoo.co.uk

Introduction: Endoscopic mucosal resection (EMR) of large ($>/-20$ mm) non-pedunculated colorectal polyps (LNPCP) $</-40$ mm is associated with an increased risk of recurrent or residual adenoma (RRA). Margin Thermal Ablation to the EMR defect margin using snare-tip soft coagulation (MTA) reduces the rate of RRA. We sought to analyse its effect in a large prospective cohort of LNPCP $>/-40$ mm.

Aims & Methods: We retrospectively analysed a prospectively collected cohort of consecutive patients who underwent EMR in an expert tissue resection centre. MTA technique was developed in 2012. Enrolment for the MTA randomised control occurred between July 2013-May 2016 and became standard practice from mid-2017. The cohort was divided into three phases: 'pre-MTA'; April 2008- June 2012, 'MTA adoption'; July 2012-June 2017 and 'standardised MTA'; July 2017-April 2023. The primary outcome was to compare the RRA rate between the three time periods.

Results: Over 15 years until April 2023, 973 LNPCP $>/-40$ mm in 973 patients underwent EMR (median lesion size 50mm, IQR 20mm) of which 893 (92%) were successful. 824 patients (median lesion size 50mm, IQR 20) underwent SC1 (median of 6 months [IQR 4]). The rates of RRA in the pre-MTA, MTA-adoption and standardised-MTA phases were 20.3% (n=45/221), 19.1% (n=59/309) and 4.4% (n=13/294) respectively (p<0.001). The rates of complete MTA in the pre-MTA, MTA adoption and standardised-MTA phases were 0, 38.2% (n=118/309) and 93.9% (n=276/294). 18 (6.1%) of cases within the standardised-MTA did not receive MTA due to difficult access (n=7), concern for stricture formation in fully circumferential LNPCP (n=9) or sedation-related issues (n=2). The rate of RRA in this group was 22.2% (n=4/18).

	Pre-MTA N=221	MTA-adoption N=309	Standardised-MTA N=294	p
Age, years median (IQR)	69 (16)	69 (15)	67 (15)	0.06
Lesion size, mm median (IQR)	50 (20)	50 (20)	50 (20)	0.17
Location n (%)				
• Right*	123 (55.7)	165 (53.4)	163 (55.4)	0.85
• Left	98	144	131	
RRA n (%)	45 (20.3)	59 (19.1)	13 (4.4)	<0.001
Complete MTA n (%)	0	118 (38.2)	276 (93.9)	<0.001
RRA in MTA Cohort n (%)	NA	3 (2.5)	9 (3.3)	<0.001
RRA in no MTA Cohort n (%)	45 (20.3)	56 (29.3)	4 (22.2)	0.11

*The right colon was defined as proximal to the splenic flexure

Conclusion: MTA post-EMR of LNPCP $>/-40$ mm (median size 50mm) significantly reduced the rate of RRA in a large, prospective cohort. When MTA was not applied, RRA was similar across the three time periods (p=0.1), indicating that the main impact on RRA reduction was the use of MTA with snare-tip soft coagulation, rather than a factor of EMR technique improvement over time.

Disclosure: Nothing to disclose.

PP0892

ROUTINE APPLICATION OF THE SYDNEY DEEP MURAL INJURY CLASSIFICATION SYSTEM ELIMINATES DELAYED PERFORATION

J. Gauci¹, F.V. Mandarino¹, C. Kerrison¹, A. Whitfield¹, B. Lam¹, L. Bracken¹, O. Cronin¹, S. Gupta¹, T. O'Sullivan¹, V. Peranathan¹, E. Lee¹, N. Burgess¹, M.J. Bourke¹

¹Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: julia.gauci@yahoo.co.uk

Introduction: Delayed perforation remains the most dreaded complication following endoscopic mucosal resection (EMR) of large (>/-20mm) non-pedunculated colorectal polyps (LNPCP) and is reported with a frequency of 1.1-3.6% (1,2). It is associated with prolonged hospitalisation and high rates of surgery and stoma formation. The Sydney Deep Mural Injury (DMI) Classification System (3) was first published in July 2016 and we sought to evaluate its subsequent impact on the frequency of delayed perforation

Aims & Methods: A prospective cohort of consecutive patients who underwent colonic EMR in an expert tissue resection centre was evaluated. Following EMR, the standard practice included methodical defect assessment, DMI classification and clip closure of DMI Type 2 or greater. DMI type 3 or greater was defined as significant DMI. Clip closure was performed using through-the-scope clips, targeting the area of DMI rather than complete defect closure.

Clinical follow-up by way of a structured telephone interview was conducted at two weeks to screen for adverse events. Routine endoscopic surveillance was performed 6 months post EMR. Data collected included patient and lesion characteristics, the rate of DMI by sub-type, rates of clip closure and the rate of delayed perforation.

Results: Between July 2016 and June 2023 (84 months), 1069 LNCP underwent EMR (median size 35mm, IQR 20). The rates of DMI, clip closure and perforation by DMI subtype are shown in Table 1. Two (2/1069 [0.19%]) delayed perforations were recorded.

Case 1 resulted after EMR of a 50mm LNCP involving the full circumference of the ileocaecal valve; the fat component within the defect created difficulty in accurately assessing the defect for DMI.

The patient was managed conservatively. Case 2 involved a 40mm LNCP in the ascending colon. No significant DMI was identified after EMR. Clip placement to prevent delayed bleeding was performed with the colon fully distended, creating a shearing effect on the muscularis propria.

The patient experienced post-procedural pain and cross-sectional imaging revealed gas and contrast leak. Right hemicolectomy with primary anastomosis was performed. One clip prong had penetrated beyond the muscularis propria.

Of the cases with significant DMI, 96% (n=47/49) were discharged on the same day. Successful endoscopic closure was achieved in 48 (98%). One case of DMI type III was not closed as the defect was located in the distal rectum, distal to the peritoneal reflection; there were no adverse events.

DMI Type	N (%)	Clip Closure n (%)	Delayed perforation n (%)
0	778 (72.8)	147 (18.9)	2 (0.25)
1	60 (5.6)	7 (11.6)	0
2	182 (17.0)	165 (90.7)	0
3	32 (3.0)	31 (96.9)	0
4	17 (1.6)	17(100)	0

Table 1: Rates of intra-procedural and delayed perforation by Sydney Deep Mural Injury (DMI) sub-type in 1069 LNCP which underwent conventional EMR between July 2016 and June 2023

Conclusion: Meticulous defect interrogation, accurate DMI classification and targeted clip closure of significant DMI resulted in a low rate (<0.2%) of delayed perforation in an expert tissue resection centre. Universal application of the Sydney DMI Classification system greatly attenuates the risk of delayed perforation.

References:

1. Heldwein W, Dollhopf M, Rosch T et al. The Munich Polypectomy Study (MUPS): prospective analysis of complications and risk factors in 4000 colonic snare polypectomies. *Endoscopy* 2005; 37: 1116-1122
2. Heresbach D, Kornhauser R, Seyrig JA et al. A national survey of endoscopic mucosal resection for superficial gastrointestinal neoplasia. *Endoscopy* 2010; 42: 806-813
3. Burgess NG, Bassan MS, McLeod D, Williams SJ, Byth K, Bourke MJ. Deep mural injury and perforation after colonic endoscopic mucosal resection: a new classification and analysis of risk factors. *Gut*. 2017 Oct;66(10):1779-1789

Disclosure: Nothing to disclose.

PP0893

RISK OF SUBMUCOSAL INVASIVE CANCER IN NON-GRANULAR LATERALLY SPREADING TUMORS (LST-NGS) IN A WESTERN TERTIARY REFERRAL CENTRE EXPERIENCE

S.L. Giannitti¹, L. Dottori¹, P.L. Marmo¹, S. Angeletti¹, E. Pilozzi², G. Esposito², B. Annibale¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea Hospital, Roma, Italy, ²Sant'Andrea Hospital, Sapienza University of Rome, Italy, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy

Contact E-Mail Address: loris.marmo@gmail.com

Introduction: Laterally spreading colorectal tumors (LSTs) are defined as ≥10 mm non polypoid lesions with lateral growth, representing between 1% and 6% of all colorectal lesions.

The clinical relevance of LSTs is strictly associated with the risk of covert (ie, without clear signs of invasion) submucosal invasive cancer (SMIC) due to its implications on both the endoscopic approach and the need of subsequent surgery.

Aims & Methods: According to European guidelines, Non-Granular Laterally Spreading Tumors (LSTNGs) require en-bloc resection due to the increased risk of covert submucosal Invasive cancer (SMIC). The overall reported SMIC of LST-NGs is 11.7 %, varying from near 5% for flat elevated (FE) to near 30% for pseudodepressed (PD) subtypes.

However, this risk stratification is mainly based on data from Asian cohorts, while Western data on LST-NGs management are heterogeneous and poor.

Thus, we aimed to evaluate risk stratification of SMIC in a Western cohort of LSTNGs according to endoscopical features.

All LST-NGs evaluated for resection in our academic tertiary referral centre from 2016 to 2022 and prospectively collected in a dedicated database (comprehending clinical, endoscopical and histological characteristics) were analysed. Univariate and multivariate analysis were conducted to assess predictors of covert SMIC.

Results: We included 197 LST-NGs, 149 (75.6%) FE and 48 (24.4%) PD. Mean age of patients (F: 39%) was 69.1±8.8 (yrs±SD). Mean lesions size was 22.4±8.6 (mm±SD).

The LSTs location was 149 (75.6%) in Right colon, 33 (16.8%) in Left colon and 15 (7.6%) in the Rectum. Vascular pattern was JNET 2A in 162 (82.2%), JNET 2B in 35 (17.8%), while pit pattern was invasive (Kudo Vi) in 30 (15.2%) and non-invasive (Kudo II-III) in 167 (84.8%).

SMIC was found in 22 (11.2%) of LST-NGs, 17 (77.3%) were PD and 5 (22.7%) were FE. Of these, 8 (36.4%) underwent surgery upfront and 14 (63.6%) were treated endoscopically, with an en-bloc resection in 85.7% of cases. Statistically significant predictive factors of SMIC were found to be: size >20 mm [OR (95%CI): 4.55 (1.62; 16.2)], Rectal location [OR (95%CI): 6.92 (2.09; 21.8)], PD subtype [OR (95%CI): 15.8 (5.77; 51.0)], Kudo Vi [OR (95%CI): 42.4 (14.4; 147)] and JNET 2B [OR (95%CI): 29.7 (10.4; 99.4)]. At multivariate analysis, Kudo Vi was the only independent predictor of SMIC.

Conclusion: Our data confirm that in LST-NGs size >20 mm, Rectal location, PD morphology, Kudo Vi and JNET2B are strongly associated with increased risk of SMIC, comparable to what shown in Eastern series. Furthermore, these data underline how an accurate optical diagnosis is crucial for establishing the best therapeutic approach.

References:

- Bogie RMM, Veldman MHJ, Snijders LARS, et al. Endoscopic subtypes of colorectal laterally spreading tumors (LSTs) and the risk of submucosal invasion: a meta-analysis [published correction appears in Endoscopy. 2018 Mar;50(3):C4]. Endoscopy. 2018;50(3):263-282
- Hao XW, Li P, Wang YJ, Ji M, Zhang ST, Shi HY. Predictors for malignant potential and deep submucosal invasion in colorectal laterally spreading tumors. World J Gastrointest Oncol. 2022;14(7):1337-1347.
- Ishigaki T, Kudo SE, Miyachi H, et al. Treatment policy for colonic laterally spreading tumors based on each clinicopathologic feature of 4 subtypes: actual status of pseudo-depressed type. Gastrointest Endosc. 2020;92(5):1083-1094.e6
- Pimentel-Nunes P, Libânio D, Bastiaansen BAJ, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. Endoscopy. 2022;54(6):591-622.
- D'amico F, Amato A, Iannone A, et al. Risk of Covert Submucosal Cancer in Patients With Granular Mixed Laterally Spreading Tumors. Clin. Gastroenterol. Hepatol. 2021;(19):1395-1401.

Disclosure: Nothing to disclose.

PP0894

ENDOSCOPIC FULL THICKNESS RESECTION IS A VIABLE ALTERNATIVE TO ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR HIGH-RISK COLONIC LESIONS

O. Cronin¹, K. Meys², S. Hacking², M. Alawad³, S. Yuen², J. Cohen², T.A Gonda³, M.J. Bourke⁴, G. Haber²

¹Northern Health, Gastroenterology, South Yarra, Australia, ²NYU Langone Health, New York, United States of America, ³Columbia University, Medicine, New York, United States of America, ⁴Westmead Hospital Sydney, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: olivergcrnoin@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is the primary resection modality recommended for high-risk colonic lesions to ensure an R0 resection. Endoscopic full-thickness resection (EFTR) is a viable alternative for complete resection of high-risk lesions. However there is little available data on endoscopic cure, size limitations and long-term outcomes following EFTR.

Aims & Methods: We aimed to evaluate long-term outcomes of patients with lesions containing high-grade dysplasia (HGD) and invasive cancer, resected by EFTR.

Consecutive non-lifting lesions referred to a single tertiary center with suspected localised advanced pathology for consideration of EFTR were prospectively studied. Multiple data points were recorded including tech-

nical success, EFTR histopathological data, complications, and follow-up surveillance data.

Results: Over a 4 year period to July 2023, 39 lesions were referred of which 33 (85%) underwent EFTR.

18/33 (55%) lesions contained cancer and 15/33 (45%) lesions contained HGD only. The median size of cancer was 7mm [Interquartile range (IQR) 4-10mm] contained within a median lesion size of 30mm (IQR 21-31mm). The median depth of invasion was 2550µm (IQR 1625-3075µm) and the deepest resected layer contained sub-serosal fat. Of the lesions containing cancer removed by FTR, 17/18 (94%) had an R0 resection. The case without an R0 resection had deep margin involvement, resected to the sub-serosa (depth 4000µm).

At 6 month [Interquartile range (IQR) 5-7 months] surveillance colonoscopy, there was 1/23 (4%) case with recurrence, successfully re-resected with FTR, with cure confirmed on second surveillance colonoscopy. Of the patients with cancer who were referred for surgical resection post-FTR, no (0/7, 0%) cases had residual cancer within the surgical specimen.

Conclusion: E-FTR is safe and effective for the resection of localised colorectal cancer. EFTR offers a viable alternative to ESD for lesions with advanced pathology. Compared to ESD, it has a shorter learning curve, is less resource intensive and has similar curative outcomes. Resection options need to be individualised and clearly outlined to the patient.

Disclosure: No conflicts.

PP0895

STRUCTURED ENDOSCOPIC TIP CONTROL TRAINING – AN EX-VIVO MODEL OF SNARE TIP SOFT COAGULATION IMPROVES PARTICIPANT TIP CONTROL (HAM-2 STUDY)

A. Sorge^{1,2}, M.E. Argenziano¹, P.J. Poortmans³, S. Smeets¹, T. Tornai¹, M. Montori¹, J.P. Pereira⁴, L. Debels¹, L. Desomer^{5,1}, D.J. Tate⁶

¹University Hospital of Ghent, Department of Gastroenterology and Hepatology, Ghent, Belgium,

²University of Milan, Department of pathophysiology and transplantation, Milan, Italy, ³Vrije Universiteit Brussel, Gastro-enterology & Hepatology, Jette, Belgium, ⁴Pedro Hispano Hospital, Advanced Endoscopy Center Carlos Moreira da Silva, Department of Gastroenterology, Matosinhos, Portugal, ⁵AZ Delta Hospital, Roeselare, Belgium, Gastroenterology and Hepatology, Roeselare, Belgium, ⁶University Hospital Ghent, Gastroenterology and Hepatology, Ghent, Belgium

Contact E-Mail Address: andreasorge6@gmail.com

Introduction: There are no objective performance metrics for basic endoscopic skills to guide training and career trajectory. The fidelity of endoscopic tip manipulation is a key skill akin to hand steadiness in surgery. Two recent studies using ex-vivo¹ and in-vivo² models of snare tip soft coagulation (STSC) applied to a polypectomy defect margin reliably stratified endoscopists by interventional profile, number, and complexity of polypectomies performed.

Aims & Methods: Tip-control of endoscopists with varied expertise was assessed using a STSC model containing 3D-printed figures constructed from 1-4 perfect intersecting circles (radius=17.2mm) (shape 1=1 circle, shape 4=4 circles) printed onto the centre of a single piece of cooked ham. The study consisted of two assessments (=all 4 shapes, maximum 5 minutes/shape), 1 initial, two sessions of training on the model, and a second final after the training. Videos of assessments were rated via a web application for accuracy and speed (=correct hits/second) by 6 blinded raters in a random order using a web application. Each video was rated three times by three different raters. Accuracy and speed were determined and

mutated into a composite-score (TIP-score) using Z-score normalization (score-mean/sd), added together with the addition of 5 to the result removing negative values.

Results: 13 endoscopists participated (1 expert, 7 endoscopy fellows, 5 trainees) performing 8 procedures each. 312 assessments of 104 STSC videos were performed. Overall median speed [pre 0.25 vs. post 0.34 correct hits/sec; $P<0.001$] and TIP-score [pre 4.6 vs. post 5.4; $P<0.001$] were significantly increased after training but accuracy was not [pre 93.8% vs. post 94.7; $P=0.1$].

Fellows had an overall accuracy of 94.2% (vs. 97.6% expert [$P<0.001$], vs. 94.1% trainees [$P<0.31$]), a speed of 0.29 correct hits/sec (vs. 0.55 expert [$P<0.001$], vs. 0.27 trainees [$P<0.001$]), and a TIP-score of 5.05 (vs. 7.1% expert [$P<0.001$], vs. 4.9% trainees [$P<0.02$]). The expert showed worse accuracy ($P=.006$), and no change in speed ($P=.1$) or TIP-score ($P=.9$) post-training.

Fellows and trainees showed no change in accuracy ($P=.06$, $.10$) but significantly increased speed (both $P<.001$) and TIP-score (both $P<.001$) post-training. Compared to trainees and fellows the expert was more accurate than fellows and trainees pre-training ($P<.001$) but not post- ($P=.40$).

Expert speed and TIP-scores were significantly superior to trainees (all $P<.001$) and fellows (all $P<.001$) in both pre- and post-training. Fellows were significantly superior to trainees in speed pre-post ($P=.03$ & $<.001$) and TIP-score only post-training ($P=.05$). The expert showed a significant decrease in accuracy pre- vs post- readings indicating that performance can vary in a single individual at different time points.

	PRE	POST		PRE	POST		PRE	post	
	ACCURACY	ACCURACY	P	SPEED	SPEED	P	TIP-score	TIP-score	P
	% (IQR)	% (IQR)		correct hits/s (IQR)	correct hits/s (IQR)		(IQR)	(IQR)	
Overall	93.8 (6.4)	94.7 (4.9)	.10	.25 (.10)	.34 (.16)	<.001	4.6 (1.7)	5.4 (1.7)	<.001
Expert	99.1 (1.9)	95.4 (3.1)	.006	.53 (.14)	.56 (.29)	.10	7.3 (1.3)	7.1 (1.6)	.90
Fellow	93.7 (6.5)	94.6 (5.8)	.06	.26 (.08)	.36 (.18)	<.001	4.7 (1.3)	5.4 (1.8)	<.001
Trainee	92.9 (5.1)	95.2 (5.5)	.10	.23 (.08)	.30 (.08)	<.001	4.3 (1.3)	5.2 (1.1)	<.001

Conclusion: An ex-vivo model to assess tip-control was found to stratify endoscopists by expertise. Furthermore, performing two structured training sessions using the model led to a significant increase in the tip-control of fellows, and trainees but not experts. These results have implications for standardising the assessment of endoscopic competency, benchmarking progress during training, and allowing expedited acquisition of complex endoscopic skills in an ex vivo setting.

References: ¹ L.K. Debels, S. Smeets, P. Poortmans, V. Lala, C. Jorissen, T. Lamiroy, L. Desomer, R. Valori, J. Anderson, D.J. Tate. ENDOSCOPIC TIP CONTROL - A SIMPLE, EX-VIVO MODEL WITH POTENTIAL FOR ENDOSCOPIST BENCHMARKING AND TRACKING OF PROGRESS OVER TIME. UEG Week 2023; United European Gastroenterology Journal 2023; 11 (Supplement 8)

² L. Debels, S. Smeets, P.J. Poortmans, C. Jorissen, V. Lala, T. Lamiroy, R.Valori, L.Desomer, J. Anderson, D.J.Tate. (2023). THE ACCURACY OF SNARE TIP SOFT COAGULATION APPLIED TO THE MARGIN OF POST ENDOSCOPIC MUCOSAL RESECTION DEFECTS CORRELATES WITH ENDOSCOPIST POLYPECTOMY EXPERIENCE AND PROCEDURAL DIFFICULTY. Gastrointestinal Endoscopy. 97. AB211-AB212. 10.1016/j.gie.2023.04.354.

Disclosure: DJT: Pentax medical, Fujifilm, and Olympus research support and consulting.

PP0896

USE OF HIGH-RESOLUTION COLONOSCOPY TO ACCURATELY MONITOR DISEASE PROGRESSION IN A MURINE MODEL OF COLITIS-ASSOCIATED COLORECTAL CANCER

S. Mashtoub^{1,2,3,4,5}, S. Mhlanga^{3,1}, S.G. Barreto^{4,6}, P. Hammond^{3,7}, G. Howarth^{3,1,8}

¹University of Adelaide, School of Biomedicine, Faculty of Health and Medical Sciences, Adelaide, Australia, ²The Queen Elizabeth Hospital, Discipline of Surgery, Woodville, Australia, ³Women's and Children's Hospital, Gastroenterology Department, North Adelaide, Australia, ⁴Flinders University, College of Medicine and Public Health, Bedford Park, Australia, ⁵University of Western Australia, School of Medicine, Perth, Australia, ⁶Flinders Medical Centre, Division of Surgery and Peri-operative Medicine, Bedford Park, Australia, ⁷University of Adelaide, Discipline of Paediatrics, Adelaide, Australia, ⁸University of Adelaide, School of Animal and Veterinary Sciences, Roseworthy, Australia

Contact E-Mail Address: suzanne.mashtoub@adelaide.edu.au

Introduction: Colonoscopy is a gold standard technique to survey and diagnose various diseases of the colon and rectum, including inflammatory bowel diseases (IBD) and colorectal cancer (CRC). Numerous mouse models of IBD and CRC have been developed to understand disease pathogenesis, monitor response to novel therapies and for pre-operative assessment, though often require euthanasia at various timepoints for monitoring. The azoxymethane (AOM)-dextran sulphate sodium (DSS) model of colitis-associated CRC accelerates the progression of tumour development, inducing colonic tumours that share the histopathological characteristics of human CRC.

Aims & Methods: Herein, we review techniques for monitoring colitis and tumour progression in AOM/DSS-induced colitis associated-CRC in mice. Female C57BL/6 mice were injected with AOM (7.4mg/kg; intraperitoneal) followed by *ad libitum* access to three DSS (7 days)/water (14 days) cycles. Colitis and tumour progression were monitored by colonoscopy on days 20, 41 and 62 using the Coloview miniendoscope system (Karl Storz, Tuttlingen, Germany), which includes a rigid straight forward colonoscope (1.9mm diameter) with operating sheath, air pump for insufflation, light source, camera and video monitor. The colonoscope was advanced to the splenic flexure at approximately 4cm and videos recorded upon withdrawal. Videos were assessed for colitis severity including colon thickening, vasculature pattern, fibrin, mucosal surface granularity and stool consistency, and colonic tumours counted. On the day of euthanasia (day 63), a total colectomy was performed and longitudinally opened to visualise and photograph tumours (Canon, Tokyo, Japan). Tumour number and size were determined using Olympus Soft Imaging Solutions software (Tokyo, Japan).

Results: In healthy control mice, there was an unobstructed circumferential view of the colonic mucosal surface which consistently appeared translucent (thin), shiny and smooth, without evidence of prominent vasculature or disrupted patterns; visualised stool was formed and mobile. In AOM/DSS mice, signs of mucosal inflammation were present from day 20, including less translucency hence mucosal thickening, loss of vasculature pattern, occasional bleeding, adherence of loose stool and evidence of small tumour development (approximately 10 per mouse). By day 40, mice demonstrated mucosal surface granularity with complete loss of translucency, fibrin development, bleeding and diarrhoea, often impairing circumferential view; this required intermittent and careful colonic clearance with saline. On day 62, visualisation was largely impaired in the setting of ongoing diarrhoea and near-impassable tumours, prompting careful navigation around tumours and colonic clearance using saline. On the day of euthanasia, direct visualisation of longitudinally opened colons

revealed tumours concentrated in the rectum and distal colon; tumour numbers directly correlated with colonoscopic assessment, highlighting that colonic tumours were confined to the anatomical location distal to the splenic flexure.

Conclusion: High-resolution colonoscopy represents an important, accurate and cost-effective technique for repeated monitoring of colitis activity and CRC development in mice. Advanced assessment can also be employed using temporal biopsies to analyse immunological and molecular parameters. Moreover, this technique lends itself to the evaluation of other colorectal diseases, including diverticular and fistulating disease, to promote the development of potential new therapies.

Disclosure: Nothing to disclose.

PP0897

EVALUATION OF A TRAINING PLATFORM USING AI-GENERATED IMAGES OF COLORECTAL POLYPS

R. Weber¹, P. Sodmann¹, Y. Chiang¹, V. Parayitam¹, I. Kafetzis¹, A. Hann¹

¹University Hospital Würzburg, Würzburg, Germany

Contact E-Mail Address: ronja.weber@stud-mail.uni-wuerzburg.de

Introduction: To prevent colorectal cancer, it is crucial to accurately identify and classify precancerous colonic lesions. Previous studies have shown that the classification of precancerous lesions still depends on the individual examiner. In this study, we attempted to create realistic AI-generated images for training physicians in the assessment of colorectal lesions. Artificially generated realistic images make it independent of patient data, allowing to specifically create various precancerous lesions and practice their classification.

Aims & Methods: We trained an AI using 25 million endoscopic images, that can generate images of different precancerous colorectal lesions. To show that the AI is capable of producing realistic-looking images, we designed a study in which we presented artificial polyps and real images of polyps to eleven physicians and asked them to discriminate between them. They were also asked about their level of confidence for the assignment. We used 20 real and 20 AI generated images. We included five experts and six beginners in this study. Beginners were defined as endoscopists who have performed less than 100 examinations or have been practicing for less than 2 years.

Results: Real images were identified as such with an accuracy of 79%, while only 66% of AI-generated images were recognized as artificially generated. The p-value is 0.0034. The physicians had a higher confidence when choosing an answer for real images (63%) and a lower for fake images (56%). Especially the AI-generated images that clearly showed mucosal vessels were classified as real images by many physicians.

Conclusion: In this study we were able to generate synthetic images with a high degree of authenticity. We have identified features that make images appear particularly realistic and we will continue to train the AI with these specific characteristics to achieve even higher quality. The images that were identified as most realistic will be used in further projects to classify precancerous lesions.

Disclosure: Nothing to disclose.

PP0898

WITHDRAWN

PP0899

ENDOSTYLE: ENDOSCOPIC IMAGE STYLE TRANSFER TO CUSTOMIZE DATA FOR ARTIFICIAL INTELLIGENCE MODELS

J. Troya^{1,2}, I. Kafetzis¹, R. Weber¹, D. Ziegler³, F. Puppe⁴, A. Nüchter³, A. Meining^{1,2}, A. Hann¹

¹University Hospital of Würzburg, Interventional and Experimental Endoscopy (InExEn), Internal Medicine II, Würzburg, Germany,

²Bavarian Cancer Research Center (BZKF), Würzburg, Germany,

³Julius-Maximilians-University, Department of informatics XVII: Robotics, Würzburg, Germany, ⁴Julius-Maximilians-University, Artificial intelligence and knowledgeable systems, Institute for Computer Science, Würzburg, Germany

Contact E-Mail Address: Hann_A@ukw.de

Introduction: The use of artificial intelligence (AI) systems in gastrointestinal endoscopy has become increasingly common. However, these systems are typically trained using data sourced exclusively from a single type of processor, limiting their use. In addition, the availability of expertly annotated images is limited in the medical field, which reduces the variability of the data and consequently the performance of AI systems.

Aims & Methods: The objective of this study is to develop and validate a novel AI-based system (EndoStyle) capable of generating multiple endoscopic images from a single source, simulating images captured by different processors from various manufacturers (Olympus EZ1500, Olympus CV-190, Olympus CV-170, Pentax EPK-i7000, and Storz-s1). Leveraging the StarGAN-v2 architecture, our AI model was fine-tuned using 239 875 images of 5 different endoscopic processors. Data was split into 90% for training and 10% for validation. The Fréchet Inception Distance (FID) was used as a metric to assess the quality of images created by the generative model. To further evaluate the performance of the developed AI model, 10 experienced endoscopists initially visualized 28 ten-second colonoscopy sequences in the testing phase. Subsequently, they were presented with three images and tasked with identifying those taken during the same colonoscopy procedure they viewed in the video. These images comprised images from another processor modified to resemble the processor of the video sequence (EndoStyle group), images from the same video sequence (positive control group), and images from distinct processors (negative control group).

Results: EndoStyle obtained an FID score of 38.5 during the validation phase (FID < 50 is considered excellent). In the testing phase, endoscopists selected in 60.1 % (220/366) that the EndoStyle group image belonged to the displayed video. The positive and negative control groups were selected in 86.8 % (243/280) and in 4.6 % (9/185), respectively. The proportion of selected images in the EndoStyle group was significantly different to the proportion of the positive and negative control group (both p<0.05).

Conclusion: This study demonstrates the potential of EndoStyle to mimic the visual characteristics of different endoscopic processors. The results suggest that EndoStyle successfully replicated the visual attributes of the targeted processor, as confirmed by endoscopists' selections. EndoStyle allows customizing the style of data to train AI models for a particular system. In addition, it could function as a data augmentation method to increase the variability, and hence the performance, of new AI models.

Disclosure: Nothing to disclose.

PP0900

AI-BASED PIPELINE FOR POLYP DETECTION AND IMAGE RETRIEVAL FROM COLONOSCOPY EXAMINATIONS

Y. Chiang¹, P. Sodmann¹, I. Kafetzis¹, T.J. Lux¹, Z. Saßmannshausen¹, J. Troya¹, M. Brand¹, W.G. Zoller², A. Meining¹, A. Hann¹

¹University Hospital Würzburg, Würzburg, Germany,

²Katharinenhospital, Department of Internal Medicine and Gastroenterology, Stuttgart, Germany

Contact E-Mail Address: Hann_A@ukw.de

Introduction: In colonoscopy reports, the total number of polyps discovered and the characteristics of the polyp images are essential data in determining follow-up timing and treatment. Using artificial intelligence (AI) to differentiate individual colorectal polyps may potentially provide the needed information and reduce workload during examinations, especially in cases with multiple polyps. However, there is currently no widely adopted solution to accomplish this goal.

Aims & Methods: In this study, we built an AI-based pipeline to discriminate frames with polyps from colonoscopy videos. The pipeline consists of a Neural Network to compute features of each image and a hierarchical density-based spatial clustering method to group the features. Through this pipeline, we intend to count the number of polyps appearing in colonoscopy videos. The AI model was trained on 398 full-length colonoscopy videos with frames containing polyps and was validated on 44 videos. These videos were recorded in 7 different endoscopy centers from November 2021 to November 2022. The pipeline was tested in 50 colonoscopies, which contained a total of 83 different polyps. Two evaluation metrics are used: the error in the number of polyps, to quantify the disparity between the actual and predicted numbers of polyps; and precision, to evaluate the accuracy of retrieving individual polyp images.

Results: Testing on frames with visible polyps obtained from 50 colonoscopy examinations demonstrated that the pipeline achieved an average error in the number of polyps of 1.3. And the average precision was 0.66, representing the probability of retrieving the corresponding individual polyp images. Among these examinations, there are 14 examinations with more than one polyp, which have an average error in the number of polyps of 1.1 and an average precision of 0.55.

Conclusion: We have developed a pipeline that utilizes artificial intelligence techniques to identify individual polyps and retrieve representative polyp images. Despite the pipeline encountering challenges in cases with only one polyp, it still holds potential. Overall, this approach provides a promising direction for retrieving individual polyp images.

Disclosure: Nothing to disclose.

PP0901

WITHDRAWN

PP0902

IMPACT OF BOWEL PREPARATION QUALITY ON COLONOSCOPY FINDINGS AND COLORECTAL CANCER DEATHS IN A NATION-WIDE COLORECTAL CANCER SCREENING PROGRAM

J. Zessner-Spitzenberg¹, E. Waldmann¹, L.-M. Rockenbauer¹, A. Klinger², E. Klenske¹, D. Penz³, A. Demschik¹, B. Majcher⁴, M. Trauner¹, M. Ferlitsch¹

¹Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Wien, Austria,

²Medical University of Vienna, Institute of Clinical Biometrics, Center for Medical Data Science, Wien, Austria, ³St. John of God Hospital, Department of Internal Medicine I, Vienna, Austria,

⁴Medical University of Vienna, St. Anna Children's Hospital, Division of Gastroenterology & Hepatology, Wien, Austria

Contact E-Mail Address: jasminzeszp@gmail.com

Introduction: Adequate bowel preparation is paramount for a high-quality screening colonoscopy. Despite the importance of adequate bowel preparation, there is a lack of large studies that associated the degree of bowel preparation with long-term colorectal cancer outcomes in screening patients.

Aims & Methods: In a large population-based screening program database in Austria, quality of bowel preparation was estimated according to the Aronchick scale by the endoscopist (excellent, good, fair, poor and inadequate bowel preparation). We used logistic regression to assess the influence of bowel preparation on the detection of different polyp types and the inter-physician variation in bowel preparation scoring. Time to event analyses were performed to investigate the association of bowel preparation with post-colonoscopy colorectal cancer (PCCRC) death.

Results: 335466 colonoscopies between 01/2012 and follow-up until 12/2022 were eligible for the analyses. As compared to excellent bowel preparation, adenoma detection was not significantly lower for good bowel preparation (OR 1.01, 95% CI 0.9971 - 1.0329, p = 0.1023), however, adenoma detection was significantly lower in fair bowel preparation (OR 0.97, 95% CI 0.9408 - 0.9939, p = 0.0166). Individuals who had fair or lower bowel preparation at screening colonoscopy had significantly higher hazards for PCCRC death (HR for fair bowel preparation 2.56, 95% CI 1.67 - 3.94, p < 0.001).

Conclusion: Fair bowel preparation on the Aronchick scale was not only associated with a lower adenoma detection probability, but also with increased risk for PCCRC death. Efforts should be made to increase bowel cleansing above fair scores.

Disclosure: MT had advised for Abbvie, Albireo, BiomX, Boehringer Ingelheim, Falk, Gilead, Genfit, Hightide, Intercept, Janssen, MSD, Novartis, Phenex, Pliant, Regulix, Siemens, Shire, has received grants / research support from Albireo, Alnylam, Cymabay, Falk Pharma, Gilead, Intercept, MSD, Takeda, UltraGenyx, had received speakersfees from BMS, Falk Foundation, Gilead, Intercept, Madrigal, MSD, Roche, has received travel grants from AbbVie, Falk Foundation, Gilead, Intercept, Janssen, Roche, the Medical Universities of Graz and Vienna have filed patents on medical use of norUDCA and is listed as co-inventor.

All other authors have no conflict of interest to declare.

PP0903

COMPARATIVE OPTICAL DIAGNOSIS PERFORMANCE OF AUTONOMOUS COMPUTER-AIDED DIAGNOSIS (CADX) VERSUS HUMAN-ASSISTED BY CADX. A SYSTEMATIC REVIEW AND META-ANALYSIS

T. Rizkala¹, C. Hassan², M. Spadaccini³, Y. Mori⁴, G. Antonelli⁵, P. Sharma⁶, A. Repici⁷

¹Humanitas Clinical and Research Center –IRCCS–, Endoscopy Unit, Rozzano, Italy., Milano, Italy, ²Humanitas University, Gastroenterology, Pieve Emanuele MI, Italy, ³Humanitas University, Biomedical Science, Rozzano, Italy, ⁴University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway, ⁵Sapienza Università di Roma at Sant'Andrea University Hospital, Digestive and Liver diseases Unit, Roma, Italy, ⁶University of Kansas School of Medicine Dept. of Gastroenterology, Gastroenterology, Leawood, United States of America, ⁷Ist. Clinico Humanitas Rozzano Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy

Contact E-Mail Address: tommyrizkala@outlook.com

Introduction: Computer-aided diagnosis (CADx) allows the real-time prediction of polyp histology during colonoscopy based on their appearance. This systematic review aims to compare the diagnostic performance of two future CADx utilization: the autonomous CADx strategy (CADx-alone) and the endoscopist with CADx assistance strategy (CADx-assisted).

Aims & Methods: We searched MEDLINE, EMBASE, and Scopus databases published before 20 March 2024. We screened for histologically-verified accuracy diagnostic studies that compared the real-time optical diagnosis performance of CADx-alone strategy versus CADx-assisted strategy for polyps ≤5mm. Only high confidence optical diagnosis were considered for the CADx-assisted optical diagnosis. A random effect model was used to calculate the pooled sensitivity, specificity, negative predictive value, positive predictive value and accuracy. Two separate analyses were performed: one on polyps in the whole colon and another restricted to rectosigmoid polyps.

Results: The analysis was based on seven studies. The entire colon, included 5,765 polyps for CADx-alone and 5,009 polyps for CADx-assisted; CADx-alone showed a significant reduction in sensitivity (88% vs. 93%; RR: 0.95; 95% CI: 0.92, 0.99; I²: 79.46%), negative predictive value (NPV) (85% vs. 90%; RR: 0.94; 95% CI: 0.91, 0.98; I²: 74.96%), PPV (81% vs. 83%; RR: 0.98; 95% CI: 0.96, 1.00; I²: 0%) and overall accuracy (84% vs. 86%; RR: 0.96; 95% CI: 0.95, 0.98; I²: 0%). However, there was no significant difference in specificity (74% vs. 75%; RR: 0.98; 95% CI: 0.94, 1.02; I²: 55.78%). When the analysis was restricted to rectosigmoid polyps, which included 2,515 polyps evaluated by CADx-alone and 2,153 by CADx-assisted, CADx-alone showed significantly lower specificity (83% vs. 85%; RR: 0.97; 95% CI: 0.95, 1.00; I²: 26.36%), PPV (73% vs. 79%; RR: 0.94; 95% CI: 0.89, 1.00; I²: 15.50%) and overall accuracy (86% vs. 88%; RR: 0.97; 95% CI: 0.95, 0.98; I²: 0%). No significant difference was observed in sensitivity (87% vs. 92%; RR: 0.96; 95% CI: 0.92, 1.01; I²: 33.60%) and NPV (94% vs. 95%; RR: 0.99; 95% CI: 0.97, 1.00; I²: 0%).

Conclusion: Our findings show that autonomous CADx failed to reach the CADx-assisted sensitivity, NPV, PPV and accuracy in the whole colon. When restricted to rectosigmoid polyps, autonomous CADx failed to reach specificity, PPV and accuracy. These findings underscore the necessity for further enhancements in the autonomous CADx diagnostic performance and the need for further studies that investigate the human-machine interaction.

Disclosure: Cesare Hassan: Fujifilm Co. (consultancy); Medtronic Co. (consultancy), Yuichi Mori: Olympus Corp (consultancy, speaking honorarium, equipment loan); Cybernet System (ownership interest), Alessandro Repici: Fujifilm Co. (consultancy); Olympus Corp (consultancy); Medtronic Co. (consultancy).

PP0904

REASONS FOR INCOMPLETE COLONOSCOPIES DURING SCREENING COLONOSCOPY

E. Fuchs¹, D. Penz¹, L.-M. Rockenbauer², J. Zessner-Spitzenberg², A. Demschik², A. Ferlitsch¹, M. Trauner², M. Ferlitsch², E. Waldmann²

¹St. John of God, Internal Medicine, Vienna, Austria, ²Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Wien, Austria

Contact E-Mail Address: Lisafuchs@me.com

Introduction: Screening colonoscopy is effective in preventing colorectal cancer by removing precancerous lesions. Incomplete examinations are associated with a higher risk of post-colonoscopy colorectal cancer. Therefore, the minimum standard for cecal intubation rate is >90%, and the target standard >95%. However, little is known about the distribution of reasons for incomplete colonoscopy in colorectal cancer screening programs.

Aims & Methods: Based on data from the Austrian quality assurance program for screening colonoscopy, we analyzed the reasons for incomplete colonoscopies. We further investigated whether the use of sedation and the adenoma detection rate (ADR) are associated with lower rates of complete examination.

Results: 489,800 screening colonoscopies were analyzed within the Austrian quality assurance program. Of these, 2.9% (n=14,325) were incomplete. 59.7% of those patients were female and 40.3% male. 85.4% of patients with an incomplete vs. 91.2% with a complete examination were sedated (p<0.001). The reasons for not reaching the cecum were insufficient bowel preparation in 23.3% (n=3335), pain in 23% (n=3291), stenosis in 11.7% (n=1674), complications in 1.6% (n=227), and other factors in 40.5% (n=5798). 69% of incomplete colonoscopies were performed by endoscopists with an ADR lower than 25% and 31% with an ADR over 25%. 54.6% of complete examinations were done by endoscopists with an ADR lower than 25% and 45.4% with an ADR over 25% (p<0.001).

Conclusion: The target standard of the cecal intubation rate has been achieved (97.1%). Incomplete colonoscopies were more often in female (84.4%) compared to male (40.3%), performed in unsedated patients and by endoscopists with an ADR <25%. The most common reason for not reaching the cecum was categorized as other factors (40.5%), this category is not well defined and requires further investigation.

Disclosure: Nothing to disclose.

PP0905

CORRELATION BETWEEN CONECT CLASSIFICATION AND HISTOLOGY OF COLONIC POLYPS: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

A. Benhamdane¹, S. Mrabti¹, T. Addajou¹, I. Mouslim¹, S. Hdiye¹, F. Aitiken¹, R. Chaibi¹, R. Berraida¹, E. Ilham¹, F. Rouibaa¹, H. Seddik¹
¹Mohammed V Military Hospital, Faculty of Medicine and Pharmacy of Rabat, Department of Gastroenterology II, Rabat, Morocco

Contact E-Mail Address: Ahlame.benhamdane@gmail.com

Introduction: The CONECT classification groups together all the predictive criteria from various classifications, enabling us both to predict the histology of polyps and to propose an appropriate therapeutic strategy. The use of this classification requires specific training for endoscopists.

Aims & Methods: This is a prospective descriptive and analytical study, spanning a period of 1 year between April 2023 and March 2024, on 68 colonic polyps identified in 50 colonoscopies performed for various indications. The CONECT classification includes: CONECT IH: hyperplastic

polyp, CONECCT IS: sessile scalloped lesion with or without dysplasia, CONECCT IIA: adenoma with low or high grade dysplasia, CONECCT IIC: low- or high-grade dysplastic adenoma or intramucosal or submucosal adenocarcinoma < 1000 microns, CONECCT IIC+ : intramucosal or submucosal adenocarcinoma of any depth, CONECCT III : deep invasive adenocarcinoma > 1000 microns in the submucosa.

The aim of our study is to evaluate the concordance between endoscopic prediction using the CONECCT classification and the definitive histology of lesions.

Results: 50 patients with 68 consecutive lesions were included in our study, the mean age of our patients was 59.29 with extremes ranging from 30 to 70 years. Our series was characterized by a male predominance of 73.5%, i.e. a sex ratio (M/F) of 0.73. The mean polyp size was 6.4 mm (3 - 20 mm), with the left colon being the most frequent site (29.4% of cases). All polyps were classified according to CONECCT, including 50 IIA, 10 IH, 4 IIC, and 4 IS. Concordance between CONECCT and definitive histology was 70.5%. Correct classification was achieved for 80% of hyperplastic polyps, 75% of scalloped polyps, 68% of low-grade adenomatous polyps and 75% of high-grade adenomatous polyps.

Conclusion: The correlation between histology and CONECCT classification remains insufficient, and further technical and training resources will be required to improve polyp characterization.

Disclosure: Nothing to disclose.

PP0906

DOUBLE BALLOON ENDOSCOPIC PLATFORM FACILITATES PERFORMANCE AND ENABLES COMPLETION OF DIFFICULT COLONOSCOPY

S. Kantsevov¹, A. Pokharel¹, K. Eckert¹, J. White²

¹Mercy Medical Center, Institute for Digestive Health and Liver Disease, Baltimore, United States of America, ²Lumendi, Medical Affairs, Buckinghamsire, United Kingdom

Contact E-Mail Address: skan51@hotmail.com

Introduction: Screening colonoscopy has become the gold standard in discovery and removal of colonic polyps and prevention of colon cancer. However, in 13.1-25.8% of patients colonoscopy was not completed and cecal intubation was not achieved.^{1,3} DiLumen® (Lumendi LLC, Westport CT, USA) double balloon endoscopic platform was developed to facilitate endoscopic interventions in gastrointestinal tract.

Aims & Methods: Aim: To evaluate use of DiLumen® to facilitate difficult colonoscopy.

Methods: DiLumen® is a flexible overtube with 2 balloons on its distal end. One (Aft) balloon is rigidly attached to the overtube and a second (For) balloon can be advanced forward or pulled back using 2 push rods moved by a slider located on the handle of DiLumen®. The assembled platform is pre-loaded on top of any colonoscope and introduced into the rectum. The colonoscope-DiLumen® assembly is advanced through sigmoid into descending colon where Aft-balloon is distended to fix the overtube inside the colonic segment. Then DiLumen® is pulled back to straighten and to shorten the colon. The colonoscope is advanced forward till transverse colon is reached. The Aft balloon is collapsed and DiLumen® is advanced into transverse colon over the colonoscope. The Aft balloon is distended inside the transverse colon and DiLumen® is pulled back now shortening and straightening the left colon. This process is repeated till the cecum is reached.

Results: We reviewed use of DiLumen® to facilitate colonoscopy in 53 patients (25 males, 28 females, mean age 68.0±10.1 years). Prior to referral for DiLumen®-assisted procedure, one colonoscopy attempt was unsuccessful in 31 patients, 19 patients had 2 unsuccessful colonoscopies, 2 patients had 3 unsuccessful colonoscopies and 1 patient had 4 unsuccessful

colonoscopy attempts. The most common reasons for failure were long, redundant, tortuous colons. DiLumen® effectively straightened and shortened the colon markedly facilitating advancement of the colonoscope and allowing successful examination of the entire colon with cecal intubation in all 53 patients (technical success 100%). Mean time to reach cecum was 13.1±6.8 minutes and total procedure time was 30.6±15.2 minutes. Normal colonic mucosa was seen in 13 patients (24.5%). Majority (75.5%) of patients had significant pathology found: only 1 polyp was found in 14 patients (26.4%), 2 polyps were found in 10 patients (18.9%), 3 and more (up to 9) polyps were found in 16 patients (30.2%). The polyps ranged in size from 3 to 80 mm and were found in all colonic segments from rectum to ileocecal valve.

Conclusion: Endoscopic double balloon interventional platform markedly facilitated colonic straightening and shortening and allowed successful completion of colonoscopy with removal of previously undetected colonic polyps in patients with difficult (long, redundant and tortuous) colon and unsuccessful previous colonoscopies.

References:

1. Witte TN, Enns R. The difficult colonoscopy. 2007 Aug; 21(8): 487-490.
2. Baxter NN, Goldwasser MA, Paszat L, Saskin R, Urbach DR, Rabeneck L. A population-based case control study of the effectiveness of colonoscopy for prevention of death from CRC. *Gastroenterology*. 2007;132:A-88.
3. Shah H, Paszat LF, Saskin R, Stukel TA, Rabeneck L. Factors associated with incomplete colonoscopy: A population-based study. *Gastroenterology*. 2007;132:2297-303.

Disclosure: Nothing to disclose.

PP0907

ACCURACY OF WHITE LIGHT ENDOSCOPY VERSUS NARROW BAND IMAGING IN SCAR ASSESSMENT AFTER COLORECTAL MUCOSAL RESECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.V. Fernandes¹, V. Antunes¹, O. Martins², T. Correa³, A.A. Prata⁴, A.C. Coan⁴, A.M. Reis⁵, E. Bulhões⁶, P. Romeiro⁷, N.J. Milioli⁸

¹Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ²Federal University of Juiz de Fora, Juiz de Fora, Brazil, ³Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁴Federal University of Espirito Santo, Vitória, Brazil, ⁵State University of Campinas, Campinas, Brazil, ⁶College of Higher Education of the United Amazon, Redenção, Brazil, ⁷Department of Medicine, University Center of Maceió, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction:

Endoscopic mucosal resection has been associated with lesion recurrence in 16%-27% of cases. Guidelines recommend endoscopic follow-up but it is unclear if endoscopic assessment has to include biopsies.

Aims & Methods: This study aims to evaluate the recurrence prediction of white light endoscopy (WLE) and narrow band imaging (NBI) in the assessment of colorectal mucosal resection scar. We performed a systematic review in PubMed, Embase, Cochrane and Web of Science databases, searching for studies comparing WLE and NBI. Statistical analysis included data pooling and heterogeneity testing. Quality of the included studies was assessed by Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2).

Results: The meta-analysis included 5 studies and 798 mucosal resections. The pooled sensitivity and specificity and AUC for WLE were 80.9% (95% CI 71.8% to 87.5%), 95.6% (95% CI 92.0% to 97.6%) and 0.917 (95%

CI 0.885 to 0.972), respectively. The pooled sensitivity and specificity and AUC for NBI were 92.1% (95% CI 87.3 to 95.2%), 94.1% (95% CI 91.9% to 95.7%) and 0.935 (95% CI 0.772 to 0.972), respectively. There was no difference in AUC of WLE and NBI ($p=0.633$).

Conclusion: Our study demonstrates a high sensitivity, specificity and accuracy for endoscopic diagnosis of recurrent lesions after colorectal mucosal resection, specially with NBI. In all cases of low confidence assessment, biopsy is required.

References:

- Desomer L, Tutticci N, Tate D, Williams S, McLeod D, Bourke M. A standardized imaging protocol is accurate in detecting recurrence after EMR. *Gastrointest Endosc.* 2017 Mar;85(3):518–26.
- Kandel P, Brand EC, Pelt J, Ball CT, Chen WC, Bouras EP, et al. Endoscopic scar assessment after colorectal endoscopic mucosal resection scars: when is biopsy necessary (EMR Scar Assessment Project for Endoscope (ESCAPE) trial). *Gut.* 2019 Sep;68(9):1633–41.
- Pu L, Chiam K, Yamamura T, Nakamura M, Berzin T, Mir F, et al. Narrow-band imaging for scar (NBI-SCAR) classification: From conception to multicenter validation. *J Gastroenterol Hepatol.* 2019 Sep;34:227–8.
- Riu Pons F, Andreu M, Gimeno Beltran J, Álvarez-Gonzalez MA, Seoane Urgorri A, Dedeu JM, et al. Narrow band imaging and white light endoscopy in the characterization of a polypectomy scar: A single-blind observational study. *World J Gastroenterol.* 2018 Dec 7;24(45):5179–88.

Disclosure: Nothing to disclose.

PP0908

ADENOMA DETECTION BY CHROMOENDOSCOPY WITH INDIGO CARMINE VERSUS ENDOCUFF: A RANDOMIZED CLINICAL TRIAL

M. Figueroa-Palafox¹, N.E. Aguilar-Olivos¹, R. Reyes-Avendaño¹, F. Rojas-Mendoza¹, J.A. Fernandez Rivero¹

¹Medica Sur Clinic and Foundation, Gastrointestinal Endoscopy Unit, Mexico City, Mexico

Contact E-Mail Address: dra.figueroa.gastro@gmail.com

Introduction: The adenoma detection rate (ADR) is the percentage of screening colonoscopies that detect at least one conventional adenoma verified by pathology. International guidelines recommend a minimum ADR of 25% (1,2), for every 1% increase in ADR reducing 3% and 5% the incidence of colorectal cancer and mortality, respectively (3). Increasing ADR under any context is highly desirable, so the primary outcome of our study is to compare the ADR using Endocuff versus indigo carmine staining.

Aims & Methods: A prospective, randomized, single-blind clinical trial was carried out on patients aged 45-85 years undergoing screening colonoscopy in a private tertiary hospital in Mexico City from December 2016 to September 2022. Patients were randomized 1:1 for Endocuff vision or indigo carmine group arms. The primary outcome was global ADR; secondary outcomes were ADR by segment, polyp detection rate (PDR) and serrated lesions detection rate (SDR).

Results: A total of 324 patients were analyzed, 163 in the Endocuff vision arm and 161 in the indigo carmine arm. The ADR was 46% (95% CI 54-38) in the Endocuff group and 52% (95% CI 60-44) in the indigo carmine group without significant difference ($p=0.27$), with a higher ADR in the right colon for the use of indigo carmine ($p=0.06$).

In the subgroup analysis, there was a higher PDR in the indigo carmine group (69 vs 79%, $p=0.03$) but no significant difference between groups in advanced adenomas or SDR ($p=0.23$)

	Endocuff vision (n=163)	Indigo carmine (n=161)	p-value
PPC, mean (SD)	2.1 (2.8)	3.4 (3.8)	0.0005
PDR, n (%)	112 (68.7)	127 (78.9)	0.03
APC, mean (SD)	0.8 (1.2)	1.4 (2.1)	0.002
ADR, n (%)	75 (46.0)	84 (52.2)	0.27
Right ADR, n (%)	40 (24.5)	55 (34.2)	0.06
Left ADR, n (%)	38 (23.3)	48 (29.8)	0.18
Advanced adenomas (10mm, villous features, high-grade dysplasia), n (%)	25 (15.3)	35 (21.7)	0.34
Carcinoma, n (%)	3 (1.8)	1 (0.6)	0.32
SDR, n (%)	4 (2.4)	8 (4.9)	0.23

Table 1. Outcomes results

APC, adenomas detected per colonoscopy; ADR, adenoma detection rate;

PPC, polyps detected per colonoscopy; PDR, polyp detection rate;

SDR, serrated lesions detection rate.

Conclusion: Any technique to improve ADR is useful and favorable over conventional colonoscopy, without a difference in the use of indigo carmine or Endocuff. In Mexico, ADR can be achieved as high as 46% to 52% with an added tool.

References:

- Rembacken B, Hassan C, Riemann JF, Chilton A, Rutter M, Dumonceau JM, et al. Quality in screening colonoscopy: Position statement of the European Society of Gastrointestinal Endoscopy (ESGE). *Endoscopy.* 2012;44(10):957–68.
- Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA - Journal of the American Medical Association.* 2021;325(19):1965–77.
- Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. *New England Journal of Medicine.* 2014;370(14):1298–306.

Disclosure: Nothing to disclose.

PP0909

A NOVEL COMPUTER-AIDED DIAGNOSTIC SYSTEM BASED ON THE YOLOV8 ALGORITHM FOR DETECTING CRUCIAL QUALITY INDICATORS IN COLONOSCOPY

W. Ahn¹, S. Hwang², S. Choi¹, J. Park¹, S.J. Park¹, J.H. Cheon¹, T.I. Kim¹, J.J. Park¹

¹Department of Internal Medicine, Institute of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea, ²Department of Precision Medicine, Wonju College of Medicine, Yonsei University Wonju College of Medicine, Wonju, South Korea

Contact E-Mail Address: woojin.ahn316@gmail.com

Introduction: To improve the effectiveness of screening colonoscopies, it is important to maintain a high level of colonoscopy quality. We aimed to develop an artificial intelligence (AI) system to monitor key quality indicators for colonoscopy.

Aims & Methods: We implemented and tested the YOLOv8 model in various configurations (ranging from nano to extra-large) across multiple datasets, including five public datasets: Kavasir-SEG, which consists of 5597 polyp images, and the Severance Hospital colonoscopy database, which comprises 6316 images including polyps, the ileocecal valve, appendix orifice, and fecal materials. The model focused on detecting polyps and key anatomical landmarks such as the ileocecal valve and appen-

dix orifice. Performance was evaluated based on the accuracy of detecting these features. Additionally, we investigated a novel path prediction method using a calibration plate and stereo matching.

Results: The integration of the YOLOv8 model into colonoscopy procedures has significantly improved the detection capabilities for colonic polyps, essential anatomical landmarks, and fecal materials indicative of bowel preparation quality. The precision and mAP50 for each metric were as follows: 0.90 and 0.85 for Polyp Detection, 0.99 and 0.94 for the Appendix Orifice, 0.90 and 0.82 for the Ileocecal Valve, 0.61 and 0.58 for Fecal Material, and 0.75 and 0.77 for Four-Class Detection, as detailed in Table 1. Additionally, a novel path prediction method has demonstrated potential for accurately measuring the colon path in short-term frames.

Category	Precision	Recall	mAP50	mAP50-95	Fitness
Polyp Detection	0.8993	0.8064	0.8531	0.6517	0.6719
Appendix orifice	0.9926	0.8292	0.9494	0.8559	0.8653
Ileocecal valve	0.9019	0.7716	0.8296	0.6242	0.6447
fecal material	0.6186	0.5408	0.5841	0.2996	0.3280
Four-Class Detection	0.7586	0.7618	0.7681	0.6435	0.6559

Table 1. Results of AI system for major quality indicators detection.

Conclusion: We developed a colonoscopy quality indicator monitoring system utilizing the YOLOv8 model. Further research is required to refine and validate the model's performance.

Disclosure: Nothing to disclose.

PP0910

ENDOSCOPIC INTERMUSCULAR DISSECTION (EID) AS FURTHER DEVELOPMENT OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) AND NEW PERSPECTIVE FOR THE ENDOSCOPIC RESECTION OF T1 RECTAL CANCERS AND HIGH-RISK LESIONS IN THE RECTUM - FIRST SINGLE-CENTER EXPERIENCE IN 8 CASES

J. Hochberger¹, M. Ho², S. Scharrer¹, M.L. Rocha³, H. Lenzen⁴, C. Rickert³

¹Vivantes Klinikum im Friedrichshain, Gastroenterology, Berlin, Germany, ²Vivantes Klinikum Friedrichshain, Dept. of Gastroenterology, Berlin, Germany, ³Vivantes Klinikum Friedrichshain, Pathology, Berlin, Germany, ⁴Hannover Medical School, Hepato-Gastroenterology, Hannover, Germany

Contact E-Mail Address: juehochber@mac.com

Introduction: In contrast to mucosal rectal T1 adeno-CA with an R0 rate of up to 92% at centers, the R0 RR in studies drops to 62-64% in case of deep sm infiltration.[1,2] Traditionally total mesorectal excision (TME) follows as completion surgery. Deep sm infiltration as isolated risk factor excluding L+, V+, G3 and Bd2-3 seems associated with a low risk of LN metastases of only 2.6%. [3] MRI and even EUS often lead to a significant T and N overstaging.[4] A min.-invasive diagn.-ther. resection procedure providing a clear histo-pathologic staging without potentially destroying parts of the meso-rectum as it has been reported for full thickness resection techniques would be desirable for potential later surgical resection (TME).[5] Endoscopic Intermuscular Dissection (EID), similar to PAEM uses a new flexible endoscopic dissection technique with separation of the circumferential and longitudinal muscular layer providing a specimen ideally including the entire mucosa, submucosa and the inner circumferential muscle layer.[6,7] The new technique achieved in a first prospective MC study including 67 patients a technical success rate of 96% and a histologic R0 resection rate of 85%.[5] In the following we report on our first experiences using EID as referral center for ESD.

Aims & Methods: To evaluate EID in lesions with biopsy proven ADC of the rectum without endoscopic, EUS or clinical signs of local infiltration. Rectal polyps with biopsy proven HGIEN and/or suspicious for local malignant infiltration. Additionally 2 patients were included who had undergone neo-adjuvant RT/Ch therapy 24 and 26 months before refusing definitive surgery (TME). Both presented with local flat polyps with histopathologically SSA (1) / hyperplastic polyp with focal LGIEN adenoma (2) for diagn.-therapeutic resection. After endoscopic, EUS, MRI, abd/th CT-staging and rectal digital examination without suspicion of local malignant infiltration pts were offered to prospectively undergo EID after extensive informed consent within a prospective protocol. All procedures were carried out under gen. anesthesia by an exp. interv. endoscopist with >1000 ESDs. Post-Op all pts. were hospitalized and closely monitored.

Results: From 11-2023 to 4-2024, 8 EIDs in 8 pts (3 f/ 5 m) were carried out (mean 63 y; 34-83y). 6/8 lesions lower rectum, 1/8 middle, 1/8 upper rectum. ‘En bloc’ resection was achieved in 100%. Histopathology showed 3x ADC G2, 3 x HGIEN and in both cases with neoadjuvant RT/Ch LGIEN adenoma. R0 resection was achieved in 2 of the 3 ADCs, with deep sm T1 infiltration in both but without any other risk factors. Tumor board recommendation was close clinical & imaging FU. In the 3rd ADC tumor infiltration reached the inner muscular layer (T2) and the pat. underwent uneventful TME 10 d after EID. All other cases were follow clinically. Mean length of hosp. stay was 7.1 days. Serious major complications did not occur. All pts. are closely followed with uneventful FU.

Conclusion: EID seems a new perspective for the endosc. resection of T1 ADC and high-risk polyps in the rectum. Two cases after potentially curative neo-adjuvant treatment for rectal cancer and refusal of TME show EID as potential diagnostic tool but have to be regard with caution due to a remaining risk of scattered tumor cells in the mesorectum with TME remaining the gold standard. More experience in multicenter prospective studies with matched pair analysis or a comparison to surgical local procedures (TAMIS etc.) is necessary for the final assessment of EID as new promising endoscopic technique.

References: 1. Watanabe D, Toyonaga T, Ooi M et al. Clinical outcomes of deep invasive submucosal colorectal cancer after ESD. Surg Endosc 2018; 32: 2123-30
2. Yamada M, Saito Y, Takamaru H et al. Long-term clinical outcomes of endoscopic submucosal dissection for colorectal neoplasms in 423 cases: a retrospective study. Endoscopy 2017;49: 233-42
3. Zwager LW, Bastiaansen BAJ, Montazeri NSM et al. Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis. Gastroenterology 2022;163:174-89
4. Detering R, van Oostendorp SE et al. MRI cT1-2 rectal cancer staging accuracy: a population-based study. Br J Surg 2020;107:1372-82
5. Eid Y, Alves A et al. Does previous transanal excision for early rectal cancer impair surgical outcomes and pathologic findings of completion total mesorectal excision? Results of a systematic review of the literature. J Visc Surg 2018; 155: 445–52
6. Moons LMG, Bastiaansen BAJ, Richir MC et al. Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum: a new endoscopic approach. Endoscopy 2022;54: 993-8
7. Toyonaga T, Ohara Y et al. Peranal endoscopic myectomy (PAEM) for rectal lesions with severe fibrosis and exhibiting the muscle-retracting sign. Endoscopy 2018; 50: 813–7

Disclosure: Nothing to disclose.

PP0911

INTERVENTIONAL CLOSURE FORM COMPLEX FISTULA AND ANASTOMOTIC INSUFFICIENCIES IN THE LOWER GI TRACT USING ENDOSCOPIC SUTURING

B. Walter^{1,2}, A. Fichtl^{1,2}, N. Sturm^{2,1}, M. Kornmann³, T. Seufferlein¹, M. Wagner¹

¹Universitätsklinikum Ulm, Klinik für Innere Medizin I, Ulm, Germany, ²University Hospital Ulm, Endoscopy Research Unit, Ulm, Germany, ³Universitätsklinikum Ulm, Klinik für Allgemeine- und Viszeralchirurgie, Ulm, Germany

Contact E-Mail Address: benjamin.walter@uniklinik-ulm.de

Introduction: Treatment of complex fistula and residual anastomotic insufficiencies remain a challenge even in an interdisciplinary setting. Endoscopic standard techniques for closure like clips, OTSC or SEMS are limited to special indications. Endoscopic suturing may offer an approach to close complex fistula orifices.

Aims & Methods: Endoscopic suturing was used for interventional closure of complex insufficiencies in the lower GI-tract. 5 consecutive patients were treated using standard Endosuturing (SutuArt, Olympus) or modified suture strategy using an additional working channel (ACEES). In three patients residual insufficiencies in the rectum were visible after complex vacuum therapy. In one patient a recto-vaginal fistula was clinical apparent. In one patient an iatrogenic perforation was occurred within dilation therapy for anastomotic stenosis. Due to size or location of the defects a standard closure technique was either not applicable or failed in a prior attempt.

Results: Technical success, defined as macroscopic defect closure, was achievable in 5 of 5 patients. Mean time for intervention was 57(±14)min. For 3 patients bimanual work using additional working channel enhanced endoscopic suturing (ACEES) was performed. In endoscopic surveillance permanent closure was achieved in 4 of 5 patients.

Conclusion: Endoscopic suturing is a newly available technique. Beyond its basic indication for defect closure after ESD this procedure, also in combination with bimanual suturing (ACEES), may offer an excellent opportunity for treatment of complex fistula.

Disclosure: Nothing to disclose.

PP0912

DIAGNOSTIC POTENTIAL OF FECAL IMMUNOCHEMICAL TESTING OUTSIDE THE NATIONAL COLORECTAL CANCER SCREENING PROGRAM IN DENMARK: A NATIONWIDE COHORT STUDY

J. Wheler¹, P. Jepsen², J. West³, C. Crooks⁴, D.J. Humes⁴, H. Toft Sørensen¹, M.K. Thomsen⁵

¹Aarhus University & Aarhus University Hospital, Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus, Denmark, ²Aarhus University Hospital, Department of Hepatology and Gastroenterology and Department of Clinical Epidemiology, Aarhus, Denmark, ³University of Nottingham and Aarhus University, Gastrointestinal and Liver Theme, National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC) and Lifespan and Population Health and Department of Clinical Medicine, Nottingham, United Kingdom, ⁴University of Nottingham, Gastrointestinal and Liver Theme, National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC) and Translational Medical Sciences, Nottingham, United Kingdom, ⁵Aarhus University, Aarhus University Hospital and Copenhagen University Hospital, Department of Clinical Epidemiology, Department of Clinical Medicine and Department of Oncology, Aarhus, Denmark

Contact E-Mail Address: janwhe@clin.au.dk

Introduction: Colorectal cancer (CRC) and other bowel diseases is a significant health concern globally. In several countries, the fecal immunochemical test (FIT) is a cornerstone in CRC screening for early detection of cancer in asymptomatic individuals. Moreover, the utility of FIT extends beyond this, as it is increasingly recommended for evaluating symptomatic patients as part of the clinical pathway to render possible or rule out serious bowel pathology. Therefore, we aimed to quantify the findings of serious bowel conditions following a non-screening FIT test in the Danish population.

Aims & Methods: This study investigated use of FIT beyond the national CRC screening program in Denmark. We aimed (1) to assess utilization patterns of FIT in contexts other than screening and (2) to examine ensuing diagnoses. Our goal was to quantify the findings of CRC and other bowel diseases in symptomatic patients, thereby assessing its broader potential. This cohort study was conducted within the Danish universal public healthcare system, delivered by five administrative regions. National CRC screening using FIT was initiated in 2014, but utilization of FIT for symptomatic patients varies between regions. The cut-off for a positive test is $\geq 10 \mu\text{g}$ haemoglobin/g faeces for symptomatic populations.

The study used data from the Danish Civil Registration System, the Danish National Patient Registry covering all Danish hospitals, and the Clinical Laboratory Information Register. The cohort included all patients who underwent FIT between 2014 and 2021 outside the Danish CRC screening program.

We employed descriptive statistics to examine FIT administration and demographic distributions across the Danish regions, as well as fecal haemoglobin levels among tested individuals. In addition, we estimated the cumulative incidence of CRC and inflammatory bowel disease (IBD) diagnoses following FIT, considering death as a competing risk and evaluated the proportion of diagnoses for CRC and IBD during the year following FIT.

Results: We identified 19,787 individuals who underwent FIT outside the national CRC screening program in 2014 to 2021. Of these, 4,283 (22%) individuals had a positive FIT result. Among tested individuals, 10,807 (55%) were female. Median age at testing was 64 years. Use of FIT varied across the regions, with 36% of the study cohort being from the Central Denmark Region, and 1.6% being from the Region of Southern Denmark.

Positive FIT cases had a shorter median time to CRC diagnosis (28 days)

and any diagnosis (36 days) compared to negative FIT cases (711 and 58 days, respectively). Within one year of the FIT, 370 (1.9%) individuals were diagnosed with CRC, with higher occurrence for FIT positive individuals (7.9%) than for FIT negative individuals (0.2%) (risk difference: 7.7 percentage points [95% CI: -3.2, 11.1]).

Among individuals with a positive FIT result, 83 (1.9%) were diagnosed with IBD within one year, compared to 51 (0.3%) individuals with a negative FIT (risk difference: 1.6 percentage points [95% CI: -5.8, 7.3]).

Conclusion: We found that FIT used outside the national CRC screening program had over 20% positivity. A positive test indicated higher risk of CRC and IBD. Differences in diagnoses are expected due to varied follow-up procedures after positive and negative FIT results. A negative test, while not definitive, suggests a potential to rule out disease and could reduce unnecessary investigations when assessing symptomatic patients.

Disclosure: Nothing to disclose.

PP0913

INVESTIGATION OF THE EFFICACY OF TEXTURE AND COLOR ENHANCEMENT IMAGING (TXI) ON IMPROVEMENT OF COLORECTAL POLYP DETECTION

Y. Biwata¹, E. Sakai², H. Sanada³, T. Shimizu², A. Iwasaki², K. Meguro³, Y. Takai², H. Fushimi¹, K. Shinagawa², Y. Honda², A. Nakajima⁴

¹Yokohama Rosai Hospital, Yokohama, Japan, ²Yokohama Sakae Kyosai Hospital, Yokohama, Japan, ³Shinyurigaoka General Hospital, Yokohama, Japan, ⁴Yokohama City University Hospital, Yokohama, Japan

Contact E-Mail Address: yusukeb0519@gmail.com

Introduction: Identification and subsequent removal of colorectal polyps has been demonstrated to deduce the mortality of colorectal cancer. However, approximately 25% of colorectal polyps can be missed under conventional endoscopic examination using white light imaging (WLI). Texture and color enhancement imaging (TXI) is a new modality developed to improve the detection of polyps, which enhancing the color tone and mucosal structure of lesions using an image color tone algorithm. We conducted a crossover prospective randomized observational study comparing the detection rate of colorectal polyps between WLI group and TXI group.

Aims & Methods: A total of 700 patients who underwent lower gastrointestinal endoscopy at Yokohama Sakae Kyosai Hospital between June 2022 and January 2023 were included in this study. After reaching the cecum, polyps were identified while the scope was withdrawn to the hepatic flexure in a randomly assigned observation mode. The scope was reinserted into the cecum and polyps were identified using the other observation mode. After evaluation of size and morphology of colorectal polyps, they were removed endoscopically and pathological evaluation was performed. Primary outcome was polyp detection rate. We also evaluated the characteristics of missed lesions. Additionally, multivariate logistic regression analysis was performed to reveal the factors affecting the polyp detection rate.

Results: There were no significant differences in age, sex, bowel cleanliness, or cecum intubation rate between TXI and WLI groups. Except in cases of inadequate bowel preparation and discontinuation, 336 and 338 patients were included in TXI and WLI groups, respectively. Although the total number of polyps were not differed between TXI and WLI groups (226 vs 210, p=0.48), the polyp detection rate was significantly higher in TXI group (37.5% vs 28.4%, p=0.01). The adenoma detection rate was also higher in TXI group (31.8% vs 24.9%, p=0.03). Additionally, the polyp miss rate was significantly lower in the TXI group (19.9% vs 32.4%, p=0.003).

No difference in polyp miss rate between the two groups for lesion sizes <5mm and 10mm>, but for lesions 5-9mm, the TXI group had a significantly lower polyp miss rate (12.3% vs 38.2%, p=0.001).

Multivariate logistic regression analysis revealed that TXI observation (OR 1.51, 95% CI 1.09-2.09, p=0.01) and older age (OR 1.71, 95% CI 1.18-2.48, p=0.004) were independent significant factors affection the colorectal polyp detection.

Prevalence and number of lesions according to study group	TXI (n = 336)	WLI (n = 338)	P value
Detected polyps, n	226	210	0.48
First inspection			
Patient with polyps, n (%)	126 (37.5%)	96 (28.4%)	0.014
Patient with adenomas, n (%)	107 (31.8%)	81 (24.9%)	0.026
The polyp miss rate	19.9%(45/226)	32.4%(68/210)	0.003
Subgroup analysis of missed lesions Polyp miss rate (PMR)			
Polyp size	TXI	WLI	P value
5-9mm	12.3% (8/65)	38.2% (29/76)	0.001

Conclusion: TXI may improve the identification of colorectal polyps, especially for small polyps.

References: Sakamoto T, Ikematsu H, Tamai N, Mizuguchi Y, Takamaru H, Murano T, Shinmura K, Sasabe M, Furuhashi H, Sumiyama K, Saito Y (2023) Detection of colorectal adenomas with Texture and Color Enhancement Imaging: multicenter observational study. Dig Endosc 35:529–537

Disclosure: Nothing to disclose.

PP0914

QUANTIFYING OBSERVATIONAL SKILLS FOR COLONOSCOPY USING ARTIFICIAL INTELLIGENCE

T. Shibuya¹, S. Kudo¹, M. Misawa¹, T. Okumura¹, K. Ichimasa¹, Y. Ide¹, K. Kondo¹, J. Kawashima¹, S. Semba¹, Y. Morita¹, Y. Minegishi¹, K. Mochizuki¹, M. Abe¹, Y. Kouyama¹, T. Sakurai¹, Y. Ogawa¹, N. Ogata¹, T. Hayashi¹, K. Wakamura¹, T. Baba¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan

Contact E-Mail Address: tswork0603@gmail.com

Introduction: Recently, artificial intelligence-based computer-aided detection (CAdE) for colonoscopy has garnered attention due to its effectiveness in increasing the adenoma detection rate (ADR). However, theoretically, CAdE systems cannot reduce exposure errors for polyps obscured by objects. In this regard, computer-aided quality improvement (CAQ) which expects to induce the meticulous mucosal inspection and leading to a reduction of blind spot area. In this study, we developed and evaluated CAQ for colonoscopy.

Aims & Methods: This was a single-center, retrospective study conducted from April 1, 2022 to October 31, 2023. We randomly extracted videos of the entire colonoscopies and created 18,922 training images. Quadrant images were made from one image and three endoscopists annotated the following scores; i) (overall) quality of image(not evaluable 0 or evaluable 1), ii) appropriate distance between the colon mucosa and the endoscope(Scored on a scale of 0 to 8), iii) the amount of residue in the colon,(Scored on a scale of 0 to 8) and iv) presence of blind area in the field of view (e.g., fold or flexure) (Scored on a scale of 0 to 4). We conducted supervised machine learning using annotated images. The CAQ deployed multi-head deep convolutional neural network model which can output multiclass prediction from one image. Consequently, the CAQ system outputs aforementioned score from colonoscopy video. To validate its performance, we randomly selected videos from the cecum to the hepatic flexure performed by 19 endoscopists and calculated CAQ model scores.

We compared CAQ scores between endoscopists with low and high ADR (ADR cutoff is 35%) and with and without the history of detecting early depressed-type colorectal cancer by endoscopists.

Results: 62 videos were included as validation samples. Among the 19 endoscopists, 11 had a low ADR and 8 had a high ADR. The results showed a significant difference in the rate of evaluable images between endoscopists with low and high ADR (median 70% vs. 77%, $p = 0.003$, t-test). There was also a significant difference in the evaluation score of the distance (median 3.8 vs. 4.2, $p = 0.003$, t-test). A significant difference was also obtained in the score for the amount of residue in the colon (median 5.3 vs. 5.7, $p = 0.01$, t-test). However, there was no significant difference in the scores evaluating the presence of blind areas (median 1.01 vs. 1.10, $p = 0.13$, t-test).

Among the 19 endoscopists, 5 endoscopists had a history of detecting early depressed-type colorectal cancer, while 14 did not. The results showed a significant difference was observed in the rate of evaluable images between endoscopists with and without a history of detecting early depressed-type colorectal cancer (median 80% vs. 71%, $p < 0.001$, t-test). Additionally, there was a difference in the evaluation scores for the distance (median 4.5 vs. 3.8, $p < 0.001$, t-test). There was also a difference in the scores assessing the presence or absence of blind spots (median 1.2 vs. 1.0, $p = 0.006$, t-test). Moreover, a significant difference was found in the evaluation scores for the amount of residue in the colon (median 5.9 vs. 5.3, $p < 0.001$, t-test).

Conclusion: The CAQ system developed in this study was able to quantify the skill of endoscopists. Such CAQ is expected to standardize the observation technique of colonoscopy and may lead to elucidation of detection techniques for significant lesions such as early depressed-type colorectal cancer.

Disclosure: Nothing to disclose.

PP0915

CLINICOPATHOLOGICAL FEATURE OF DEPRESSED-TYPE COLORECTAL NEOPLASM

S. Kudo¹, T. Shibuya¹, T. Okumura¹, K. Kondo¹, K. Sasabe¹, Y. Niimura¹, S. Semba¹, Y. Ide¹, Y. Minegishi¹, E. Tamura¹, Y. Kouyama¹, T. Sakurai¹, Y. Ogawa¹, K. Ichimasa¹, N. Ogata¹, M. Misawa¹, T. Hayashi¹, N. Sawada¹, K. Wakamura¹, T. Baba¹, F. Ishida¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan

Contact E-Mail Address: kudos@med.showa-u.ac.jp

Introduction: Several development concepts have been proposed for colorectal neoplasms in the carcinogenesis of colorectal cancer. One is “adenoma-carcinoma sequence”. In this concept, polypoid adenoma develops into early polypoid cancer and finally develops to advanced cancer. One is “serrated-pathway”. In this concept, serrated lesion develops into early cancer. The other is “de novo” pathway. In this concept, early cancers develop without preexisting adenoma. We investigated clinicopathological characteristics of depressed-type colorectal carcinomas considered as “de novo” pathway.

Aims & Methods: A total of 50119 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our center from April 2001 to December 2023 at Showa University Northern Yokohama Hospital. Of these, 1633 lesions were T1 cancers. According to the developmental morphology classification, they were divided into 3 types: 323 lesions (20.1%) were depressed-type, 602 lesions (36.9%) were flat-type and 703 lesions (43.0%) were protruded-type. We analyzed the pathological difference and recurrence of these types.

Results: The average tumor size were 15mm, 32mm, and 18mm in depressed-type, flat-type and protruded-type lesions, respectively. The rates of vessel invasion were 42%, 21% and 21%, that of poorly differentiated or mucinous adenocarcinoma were 14%, 10% and 15% in depressed-type, flat-type and protruded-type lesions, respectively. The rates of these pathological factors were significantly higher in depressed-type lesions than other types.

On the other hand, the rates of adenomatous component were 4%, 54% and 52%, and the rates of polypoid growth were 13%, 56% and 88%, respectively. These rates were significantly lower in depressed-type lesions than other types, suggesting that they emerge directly from normal epithelium without going through the adenomatous stage. The rate of distant metastasis or recurrence was observed in 0.8% (13/1633).

Conclusion: Depressed-type colorectal carcinomas had significantly lower adenomatous components and smaller size than flat-types or protruded-types, and they also contained worth pathological features than other types. So, depressed colorectal carcinoma can be the important lesions for clinical diagnosis. Therefore, during routine colonoscopy, we should give a greater attention to the morphological features of the depressed-type colorectal carcinomas.

Disclosure: Nothing to disclose.

PP0916

ENDOSONOGRAPHY-GUIDED COLOENTEROSTOMY: A SAFE AND EFFECTIVE ALTERNATIVE FOR PALLIATIVE MANAGEMENT OF MALIGNANT SMALL-BOWEL ILEUS – PRELIMINARY RESULTS

A. Weich¹, L. Retzbach¹, M. Brand¹, T. Kudlich¹, A. Wannhoff², K. Caca², A. Meining¹

¹University Hospital Wuerzburg, Medical Clinic II, Dept of Gastroenterology, Wuerzburg, Germany, ²Ludwigsburg Clinic, Medical Clinic, Department of Gastroenterology, Hemato-Onkology, Diabetology and Infectiology, Ludwigsburg, Germany

Contact E-Mail Address: weich_a@ukw.de

Introduction: Some malignant diseases such as ovarian carcinoma, neuroendocrine neoplasias or gastrointestinal cancers tend to manifest with peritoneal carcinomatosis. The accompanying small-bowel ileus (SBI) is often decisive for the prognosis even in an otherwise controlled oncologic setting while posing a significant burden on the patients quality of life (QoL). Conventional procedures of palliative care such as bypass surgery or gastric tube placement deliver unsatisfying results and are not well-tolerated by patients.

A new method for improving the quality of life and possibly survival may therefore be to restore the passage through the endosonographic (EUS) placement of lumen-apposing metal stents (LAMs) for creation of a colo-enterostomy (CE), without opening the abdominal cavity.

Aims & Methods: Aim of this ongoing multicenter intervention study is a comprehensive evaluation of feasibility and clinical value of CE in patients with malignant SBI. Biometric, technical and clinical data, symptoms, periinterventional management, QoL (EORTC QLQ-C30), adverse events as well as the ability to tolerate oncologic treatment and enteral nutrition are recorded longitudinally at predefined time points (d-1, d+2, d+10, d+34).

Results: We report on 10 patients that underwent EUS-guided CE so far. Eight of these patients (80%) were female and 4/10 (40%) had an intestinal neuroendocrine tumor, 4/10 (40%) an ovarian carcinoma and 2/10 (20%) colorectal cancer. The intervention was technically successful in 10/10 (100%) and clinically successful 9/10 (90%) patients. In one patient, only a second technically successful CE on day 3 could induce clinical symptom relief. Subsequently, all patients experienced considerable

improvement of ileus-related symptoms (e.g. vomiting, stool frequency, abdominal pain) and an increase in QoL to an extent, were 10/10 (100%) were able to tolerate enteral nutrition and 6/10 (60%) could be re-exposed to systemic oncologic treatment. All 4 patients (100%) depending on morphine based pain medication prior to SBI could be reintroduced to their previous regimen after the intervention.

Conclusion: EUS-guided CE for treatment of malignant SBI is feasible and safe. The intervention boasts a high technical and clinical success rate with immediate symptom relief and improved QoL. A relevant number of patients was enabled to be reintroduced to systemic oncologic treatment and morphine based pain medication. Larger cohorts and long-term data are needed to evaluate sustainability as well as possible impact on survival and to form the foundation for prospective trials.

Disclosure: Alexander Meining: Ovesco Consultant
Alexander Weich: Novartis Pharma GmbH Consultant.

PP0917

ENDOSCOPIC ULTRASOUND-GUIDED ENTERO-COLOSTOMY WITH LUMEN APPOSING METAL STENT AS A RESCUE TREATMENT FOR MALIGNANT INTESTINAL OCCLUSIONS: A MULTICENTRE STUDY

B. Neri^{1,2}, S. Stigliano², D. Biasutto², N. Citterio², A. Lisotti³, P. Fusaroli⁴, B.P. Mangiavillano⁵, G. Donatelli⁶, G. Tonini⁷, F.M. Di Matteo²

¹Università degli studi di Roma Tor Vergata, Medicina dei sistemi, Rome, Italy, ²Fondazione Policlinico Universitario Campus Bio-Medico, Therapeutic GI Endoscopy Unit, Roma, Italy, ³Hospital of Imola, University of Bologna, Gastroenterology Unit, Bologna, Italy, ⁴University of Bologna, Gastroenterology, Imola, Italy, ⁵Humanitas - Mater Domini, Gastrointestinal Endoscopy, Milano, Italy, ⁶Hôpital Privé des Peupliers, Ramsay Générale de Santé, Unité D' Endoscopie Interventionnelle, Paris, France, ⁷Fondazione Policlinico Universitario Campus Bio-Medico, Oncology Unit, Roma, Italy

Contact E-Mail Address: benedettoneri@gmail.com

Introduction: Surgery is the first-choice treatment for malignant intestinal obstruction (MIO), however many patients are deemed inoperable. Endoscopic ultrasound guided enterocolostomy (EUS-EC) with lumen apposing metal stents (LAMS) could represent a new treatment option.

Aims & Methods: The primary aim of the present multicentre retrospective study was to assess the technical success rate of EUS-EC in patients with malignant intestinal occlusion unfit for surgery. Secondary aims of the study included the clinical success rate, the safety of the procedure, the time of re-feeding, the duration of hospital stay and the clinical outcome.

All consecutive patients undergoing EUS-EC for MBO from November 2021 to September 2023 were retrospectively enrolled at four tertiary referral European centres. All cases were discussed in a multidisciplinary meeting. Inclusion criteria were:

- 1) malignant small bowel/colonic obstruction;
- 2) CT-scan showing ileal or colonic MIO with dilated intestinal loops <7 days from procedure;
- 3) multidisciplinary meeting discussion;
- 4) unfit for surgery;
- 5) unsafe colonic stent positioning.

Exclusion criteria were:

- 1) acute MIO requiring emergency treatment;
- 2) unavailability of CT scan <7 days;
- 3)rectal malignancy.

Demographic, clinical and procedural data including the clinical outcome and adverse events were recorded. Technical success was defined as ability to deploy the LAMS between the colon and the colonic or small bowel target, clinical success as resolution of MIO for at least 2 weeks from the procedure and adverse events defined and classified according to the AGREE classification. Data were expressed as median [range]. Comparisons were made by using the χ^2 test, Student t-test, or Mann-Whitney u-test.

Results: Twelve patients were enrolled (58.3% female, median age 72.5 [42-85] years). The most frequent cause of MIO was colonic adenocarcinoma in 9 (75%) patients. The majority (11 [91.7%]) of patients had a Stage IV disease and the median malignancy duration was 13 [1-108] years. Site of MIO was ileum and right colon in 3 (25%) patients and left colon in 6 (50%). In 83.3% of the procedures the LAMS used was the Hot AXIOS, in 16.7% the Hot SPAXUS. In 7 (58.3%) patients a EUS-guided ileo-colostomy was performed while in 5 (41.7%) a colo-colostomy. Technical success was achieved in all procedures (100%). No LAMS misdeployment or procedural adverse events were observed. Post-procedural complications were recorded in 3 (25%) patients, however direct correlation with the procedure could not be ascertained. Clinical success was achieved in 10 (83.3%) patients. The median time of oral diet resumption was 1 [1-2] day. The median post-procedure hospital stay was 9 [1-20] days and overall median survival was 47.5 [2-270] days.

When comparing EUS-guided ileo-colostomy vs colo-colostomy no difference were observed in terms of technical (7/7 [100%] vs 5/5 [100%], $p=1$) or clinical (5/7 [71.4%] vs 5/5 [100%], $p=0.6$) success or adverse events (3/7 [42.8%] vs 0/5 [0%], $p=0.31$). Time of re-feeding, duration of hospital stay and survival were also comparable between these 2 subgroups of patients ($p=0.06$, $p=0.78$, $p=0.2$, respectively).

Conclusion: EUS-EC is a feasible technique and could be considered as a valid alternative to standard approaches for MIO in highly selected patients.

References:

1. Jonica ER, Mahadev S, Gilman AJ, et al. EUS-guided enterocolostomy with lumen-apposing metal stent for palliation of malignant small-bowel obstruction (with video). *Gastrointest Endosc.* 2023; 97 (5): 927-933.

Disclosure: Nothing to disclose.

PP0918

EFFECTS OF OPIUM TINCTURE ON GASTROINTESTINAL FUNCTION AND MOTILITY IN HEALTHY VOLUNTEERS: A MAGNETIC RESONANCE IMAGING STUDY

E.B. Mark^{1,2}, T. Okdahl^{3,1}, D.G. Kahlke², L.E.M. Hansen², K. Krogh⁴, J.B. Frøkjær^{5,1}, A.M. Drewes^{1,2}

¹Aalborg University, Department of Clinical Medicine, Aalborg, Denmark, ²Aalborg University Hospital, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ³Aalborg University Hospital, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ⁴Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ⁵Aalborg University Hospital, Mech-Sense, Radiology Research Center, Department of Radiology, Aalborg, Denmark

Contact E-Mail Address: e.mark@rn.dk

Introduction: Opium tincture in oral solution has been used for antidiarrheal treatment for centuries, and it is often used to treat chronic idiopathic diarrhea as a secondary choice after loperamide and bulking agents. However, the underlying mechanisms of opium tincture on gastrointestinal function are not evident and have not been investigated in clinical trials. This study aimed to investigate the effects of opium tincture on gastrointestinal motility, intestinal volumes, and water content of different gut segments assessed by magnetic resonance imaging (MRI).

Aims & Methods: Twenty healthy volunteers were included in a randomized, placebo-controlled, cross-over study with 9-day treatment (30 drops per day of opium tincture corresponding to 15 mg of oral morphine or placebo). MRI was performed on day 1 (before treatment) and day 9 (during treatment) using a pan-alimentary scan protocol. Images were obtained during fasting and after a 285-kcal granola bar meal. MRI measurements included assessments of gastric volume, gastric emptying half-time, gastric motility, small bowel volume, small bowel water content, small bowel motility, colon volume, colon water content, and whole gut transit. Data was analyzed using repeated measure mixed models and adjusted using baseline data as a covariate and a Bonferroni post hoc correction.

Results: The median age of the included subjects was 24 years (range 20-72 years), and 10 subjects were female. Opium tincture delayed gastric half-emptying time as compared to placebo (mean [95% confidence intervals] values: 38.5 [35.3-41.6] min vs. 32.8 [29.9-35.8] min, $p=0.004$). Opium tincture increased gastric meal volumes 15 and 30 minutes after the meal as compared to placebo ($p<0.018$). Gastric contraction amplitude and frequency were not affected by treatment. Small bowel endpoints were not different between treatments (all $p>0.05$). Ascending-, transverse-, and descending colon volumes were increased after opium tincture as compared to placebo (ascending: 226 [197-253] ml vs 168 [140-195] ml, $p=0.003$; transverse: 208 [180-236] ml vs. 158 [131-185] ml, $p=0.017$; descending: 155 [125-184] ml vs. 110 [83-138] ml, $p=0.045$). T1-relaxation time (a proxy for water content) of the descending colon chyme was decreased during opium tincture as compared to placebo, indicating dryer feces (517 [425-609] ms vs. 690 [595-786] ms, $p=0.030$). Whole gut transit time was delayed during opium tincture as compared to placebo ($p=0.027$).

Conclusion: Opium tincture as compared to placebo induces changes in gastric and colonic motility and volumes as measured using a pan-alimentary MRI framework in a population of healthy volunteers. Based on the current results, opium tincture seems to affect the gastrointestinal tract in ways that are relevant for treating diarrhea. An improved understanding of how opioids affect gut functions may lead to a better understanding of and optimized management of diarrhea.

Disclosure: Nothing to disclose.

PP0919

DAY-TO-DAY PHYSIOLOGICAL VARIATION IN GASTROINTESTINAL MOTILITY AND VOLUMES USING A PAN-ALIMENTARY MAGNETIC RESONANCE IMAGING PROTOCOL

E.B. Mark^{1,2}, F.S. Magnuson^{3,4}, T. Okdahl^{2,1}, I.M. Larsen², K. Krogh^{3,4}, J.B. Frøkjær^{5,1}, A.M. Drewes^{1,2}

¹Aalborg University, Department of Clinical Medicine, Aalborg, Denmark, ²Aalborg University Hospital, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ³Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark, ⁴Aarhus University, Department of Clinical Medicine, Aarhus, Denmark, ⁵Aalborg University Hospital, Mech-Sense, Radiology Research Center, Department of Radiology, Aalborg, Denmark

Contact E-Mail Address: e.mark@rn.dk

Introduction: Gastrointestinal symptoms can originate from different segments of the gastrointestinal tract, however, symptoms seldom overlap with clinical findings. Magnetic resonance imaging (MRI) has lately shown promising results when investigating volume and motility disturbances in diseases like diabetes mellitus and Crohn's disease. MRI offers the possibility of examining the full gastrointestinal tract in one examination; however, to our knowledge, intrasubject physiological variability has not been investigated in detail.

The current study aimed to describe day-to-day intrasubject physiological variability in MRI-assessed segmental volumes and motility of the gastrointestinal tract in healthy volunteers.

Aims & Methods: Forty healthy volunteers were investigated with MRI at fasting and 0, 15, and 45 minutes after a 285-kcal meal. MRI measurements included gastric emptying half-time, small bowel motility, whole gut transit capsules, and volume assessments of the stomach, small bowel, and colon. The MRI protocol was repeated after a mean period of 10.5 weeks (a minimum of five weeks and a maximum of 24 weeks). Assessments of variability were performed using the intraclass correlation coefficient and [95% confidence intervals].

Results: Gastric emptying half-time was moderately reproducible with an ICC of 0.56 [0.28-0.75]. Gastric meal volumes showed overall poor reproducibility with the highest ICC at the fasting scan with an ICC of 0.35 [0.03-0.61], while gastric gas volumes showed poor to moderate reproducibility with the highest ICC of 0.56 [0.29-0.75] at the 0-minute scan. Small bowel motility showed the highest reproducibility at the fasting scan with an ICC of 0.60 [0.34-0.77] and the lowest reproducibility at the 45-minute scan with an ICC of 0.13 [-0.37-0.56]. Small bowel volumes at fasting were moderately reproducible with an ICC of 0.64 [0.40-0.79], while colon volume had an ICC of 0.45 [0.15-0.67]. Whole gut transit capsules showed poor reproducibility with an ICC of 0.30 [-0.15-0.66].

	N	Fasting scan (ICC)	0-minute scan (ICC)	15-minute scan (ICC)	45-minute scan (ICC)
Gastric half emptying time (t50)	36	0.56 [0.28-0.75]			
Gastric meal volume (meal ingested after fasting scan)	37	0.35 [0.03-0.61]	0.24 [-0.06-0.51]	0.31 [-0.1-0.57]	0.16 [0.45-0.62]
Gastric gas volume	37	0.43 [0.13-0.66]	0.56 [0.29-0.75]	0.51 [0.23-0.71]	0.45 [0.16-0.67]
Small bowel motility	37	0.60 [0.34-0.77]	0.25 [-0.08-0.53]	0.38 [0.07-0.63]	0.13 [-0.37-0.56]
Small bowel volume	37	0.64 [0.40-0.79]	0.77 [0.60-0.88]	0.65 [0.42-0.80]	0.68 [0.32-0.87]
Colon volume	37	0.45 [0.15-0.67]			
Whole gut transit	18	0.30 [-0.15-0.66]			

Table: Overview of day-to-day reliability on MRI-assessed endpoints in fasting and following a granola bar meal (285 kcal and 400 ml of water) using the intraclass correlation coefficient (ICC) and [95% confidence intervals].

Conclusion: Intrasubject physiological variation in MRI-assessed segmental volumes and motility of the gastrointestinal tract was high, and most comparisons resulted in indications of poor to moderate variability when interpreting the ICC values. When designing clinical studies or performing clinical patient examinations that include MRI-based assessments of the gastrointestinal tract, the normal physiological variation must be considered.

Disclosure: Nothing to disclose.

PP0920

SELF-SUPERVISED LEARNING FOR CLASSIFYING BOWEL OBSTRUCTION ON UPRIGHT ABDOMINAL RADIOGRAPHY: A RETROSPECTIVE COHORT STUDY

S. Zhu¹, R. Li², J. Lin¹, C. Xu¹, J. Zhu¹, R. Li¹
¹The First Affiliated Hospital of Soochow University, Department of Gastroenterology, Suzhou, China, ²The First Affiliated Hospital of Soochow University, Department of General Surgery, Suzhou, China

Contact E-Mail Address: sqzhu2048@stu.suda.edu.cn

Introduction: Accurate labeling of obstruction site on upright abdominal radiograph is a challenging task. The lack of ground truth leads to poor performance on supervised learning models. To address this issue, self-supervised learning (SSL) is proposed to classify normal, small bowel obstruction (SBO), and large bowel obstruction (LBO) radiographs using a few confirmed samples.

Aims & Methods: A total of 1500 confirmed and 1922 unlabeled radiographs were categorized based on the ground truth. The SSL model was firstly trained on the unlabeled radiographs, and then fine-tuned on the confirmed radiographs. ResNet50 and VGG16 were used for the embedded base encoders, whose weights and parameters were adjusted during training process. Furthermore, it was tested on an independent dataset, compared with supervised learning models and human interpreters. Finally, the t-SNE and Grad-CAM were used to visualize the model's interpretation.

Results: The proposed VGG16-backed SSL model showed superior classification performance (accuracy 0.847, F1-score 0.846, MCC 0.873, Kappa 0.770), followed by the ResNet50-backed model and senior radiologist. When recognizing SBO and LBO radiographs, the SSL model reached the best accuracy (0.907, 0.907) and F1-score (0.865, 0.860). Additionally, the SSL model exhibited better cluster performance through t-SNE and demonstrated outstanding lesion recognition ability through Grad-CAM.

Conclusion: The proposed SSL model exhibited outstanding performance in classifying bowel obstruction on upright abdominal radiograph, using unlabeled images and limited ground truth. Our study supports the feasibility of SSL model for computer-aided diagnosis of diseases that are difficult and time-consuming for labeling.

Disclosure: Nothing to disclose.

PP0921

STENTING AS BRIDGE TO SURGERY VERSUS EMERGENCY SURGERY FOR ACUTE LEFT COLONIC MALIGNANT OBSTRUCTION

C. Dai¹, K. He², Z. Fan², J. Ye¹
¹First Affiliated Hospital of Soochow University, Department of Gastroenterology, Suzhou, China, ²First Affiliated Hospital with Nanjing Medical University, Digestive Endoscopy Department, Nanjing, China

Contact E-Mail Address: daicg_soochow@163.com

Introduction: Emergency surgery (ES) is associated with higher morbidity and mortality for acute left colonic malignant obstruction. Since the first application of self-expandable metallic stent (SEMS), the technique has been popularly applied as "bridge to surgery (BTS)". The short-term clinical outcomes and long-term oncologic prognosis remain controversial.

Aims & Methods: This retrospective study aimed to compare the performance for managing acute left colonic malignant obstruction by ES or BTS. The medical records were collected from May 2015 to December 2019 in two tertiary hospitals in Eastern China. Patients were followed up after surgery every 6 months for 3 years and once a year afterwards. Clinical success was defined as resumption of intestinal function for 30 days without morbidity or mortality after surgical procedure. All demographics, intervention procedures and follow-up were analyzed for short-term and long-term outcomes. Risk factors for long-term survival were discussed as well.

Results: A total of 136 patients were eligible for the study, 67 in BTS group and 69 in ES group. No significant differences concerning demographics were found, including age, sex, body-mass index (BMI), symptoms, coexisting disorders, laboratory tests, preoperative radiotherapy or chemotherapy, previous history of abdominal surgery, cancer location, obstructive degree and TNM stage. Technical success of SEMS insertion was achieved in 64 patients (95.5%). The interval from SEMS placement to elective surgery was 16 days. Minor perforation was detected on 4 patients during the elective surgery, while no symptomatic complaint was recorded. BTS group showed better short-term performance, including less intraoperative decompressive intervention (85.1% vs. 69.6%, $p=0.045$), more complete decompression (64.2% vs. 27.5%, $p<0.001$), more primary anastomosis (65.7% vs. 17.4%, $p<0.001$), less temporary and permanent stoma (34.3% vs. 82.6%, 13.4% vs. 58.7%, both $p<0.001$), less intensive care unit requirement (10.4% vs. 27.5%, $p=0.011$), less intraoperative complications (3.0% vs. 13.0%, $p=0.031$) and reduced 30-day mortality (0 vs. 8.7%, $p=0.028$). Longer hospitalization was observed in the BTS group (21.7±13.3 days vs. 14.9±7.6 days, $p<0.001$). Postoperative hospitalization and total cost were comparable between the two groups. No significant difference was observed about clinical success (73.1% vs. 63.8%, $p=0.240$), overall mortality (53.7% vs. 64.4%, $p=0.247$) or long-term survival (52.0 months vs. 35.0 months, $p=0.121$). TNM stage IV, permanent stoma and postoperative complication were the independent risk factors for long-term survival.

	Patients under BTS n=67	Patients under ES n=69	T/x ²	p value
Intraoperative complication, no. (%)	2 (3.0%)	9 (13.0%)	4.626	0.031
ICU requirement, no. (%)	7 (10.4%)	19 (27.5%)	6.420	0.011
Temporary stoma, no. (%)	23(34.3%)	57(82.6%)	32.713	0.001
Permanent stoma, no. (%)	9(13.4%)	37/63(58.7%)	29.138	0.001
Postoperative hospitalization, day (mean±SD)	12.4±11.0	11.1±5.8	0.825	0.411
Total cost, ¥ (mean±SD)	63360.0±37302.9	56315.2±31224.4	1.180	0.240
Clinical success, no. (%)	49(73.1%)	44(63.8%)	1.379	0.240
30-day mortality, no. (%)	0	6 (8.7%)	/	0.028
Overall mortality, no. (%)	29/54 (53.7%)	38/59 (64.4%)	1.338	0.247

Table.1 Operation related characteristics.

Conclusion: SEMS served as a safe and effective bridge to elective surgery for acute left colonic malignant obstruction, without adverse effect on long-term survival. It significantly improved short-term outcomes by reducing perioperative complication, 30-day mortality and stoma. More prospective studies are necessary for further evaluating the clinical values of SEMS, and weighing its benefits against potential complications.

References:

1. Manfredi S, Sabbagh C, Vanbiervliet G, et al. Place of colorectal stents in therapeutic management of malignant large bowel obstructions. *Endoscopy*. 2014;46:546-552.
2. Frago R, Ramirez E, Millan M, et al. Current management of acute malignant large bowel obstruction: a systematic review. *Am J Surg*. 2014;207:127-138.
3. Arezzo A, Passera R, Lo Secco G, et al. Stent as bridge to surgery for left-sided malignant colonic obstruction reduces adverse events and stoma rate compared with emergency surgery: results of a systematic review and meta-analysis of randomized controlled trials. *Gastrointest Endosc*. 2017;86:416-426.
4. van Hooft JE, van Halsema EE, Vanbiervliet G, et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Gastrointest Endosc*. 2014;80:747-761 e741-775.
5. Pisano MA-O, Zorcolo L, Merli C, et al. 2017 WSES guidelines on colon and rectal cancer emergencies: obstruction and perforation. 2017.
6. Kawachi J, Kashiwagi H, Shimoyama R, et al. Comparison of efficacies of the self-expandable metallic stent versus transanal drainage tube and emergency surgery for malignant left-sided colon obstruction. *Asian J Surg*. 2018;41:498-505.

Disclosure: Nothing to disclose.

PP0922

ENDOSCOPIC RETROGRADE APPENDICITIS THERAPY FOR MANAGEMENT OF CHRONIC FECALITH APPENDICITIS

L. Ma¹, Z.-Q. Liu¹, Q.-L. Li¹, P.-H. Zhou¹

¹Zhongshan Hospital, Fudan University, Endoscopy Center and Endoscopy Research Institute, Shanghai, China

Contact E-Mail Address: maly14@fudan.edu.cn

Introduction: Chronic appendicitis is a condition with chronic abdominal pain or mild attacks of appendicitis, seriously affecting the patient's quality of life. Endoscopic retrograde appendicitis therapy (ERAT) has emerged as a promising, non-invasive treatment for acute uncomplicated appendicitis.

Aims & Methods: We aim to assess the safety and efficacy of ERAT for chronic fecalith appendicitis.

We retrospectively reviewed the medical records of consecutive patients who underwent ERAT for chronic fecalith appendicitis at Zhongshan Hospital, Fudan University, Shanghai, China between December 2017 and June 2023.

Clinicopathological characteristics, procedure-related parameters, AEs, and follow-up outcomes were analyzed.

Results: A total of 60 patients were included. ERAT intubation was successfully performed in all patients (100%). The median procedure time was 15 minutes (IQR, 12-25 minutes).

The postoperative abdominal pain scores were significantly reduced ($P < 0.0001$). Short-term adverse events included 5 cases of abdominal pain (8.3%) and 2 cases of fever (3.3%).

Long-term adverse events included recurrent abdominal pain in 3 cases (5.0%) and recurrent appendicitis in 2 cases (3.3%). The median time to recurrence was 5 months (IQR, 2-12 months).

Logistic regression analysis revealed appendiceal stenosis (OR=25.000, 95% CI, 1.114-561.281, $P=0.043$) and distorted appendix lumen (OR=12.500, 95% CI, 1.373-113.806, $P=0.025$) as significant risk factors for long-term adverse events.

Conclusion: ERAT may be a safe, effective and minimally invasive alternative approach for chronic fecalith appendicitis. Appendix lumen stenosis and distortion are risk factors of recurrence. Further large-scale prospective studies are necessary to assess the efficacy and safety of ERAT compared with antibiotic therapy and surgery.

Disclosure: Nothing to disclose.

PP0923

THE PREOPERATIVE AUTOLOGOUS BLOOD TATTOOING FOR LOCALIZATION IN LAPAROSCOPIC COLORECTAL SURGERY : A SAFETY AND EFFICACY COMPARISON STUDY

S. Roh¹, M. Kim²

¹Konyang University Hospital, Republic of Korea, Colorectal surgery, Daejeon, South Korea, ²Chungbuk National University Hospital, Colorectal surgery, Cheongju-si, Chungcheongbuk-do, South Korea

Contact E-Mail Address: rohsj2@naver.com

Introduction: There are several preoperative localization methods for laparoscopic colorectal surgery. ICG (indocyanine green) injection has recently been in the limelight for preoperative localization. However, although the incidence is low, ICG injections may cause complications due to allergic reactions. In this study, we tried to check the feasibility and safety of autologous blood tattooing as an alternative to ICG.

Aims & Methods: From august in 2017 to July 2023, a total of 42 patients were preoperative endoscopic localization. Through preoperative endoscopy, 33 patients underwent autologous blood tattooing and 9 patients underwent ICG tattooing. The surgeon checked visibility and other complication such as abscess or spillage at the start of surgery. The characteristics of patients, outcomes, and complications were collected retrospectively.

Results: Patients characteristics showed no significant difference between the two groups. As for the location of localization, sigmoid colon was the most common in both groups. The two groups each had one imprecise localization. In autologous blood tattooing patient, the omentum interfered with detection, and in ICG tattooing patient, blurring was severe. In addition, in patients with autologous blood tattooing, detection was not possible in 2 patients due to adhesion and technical failure. In the case of complications, there was only one spillage in the ICG group, which resulted in blurring.

Conclusion: Preoperative autologous blood tattooing is a simple and useful technique because it has high visibility, and no complication. This method has the advantage that it does not require additional agents or facilities and can be performed quickly and accurately through the patient's blood. However, unlike ICG tattooing, there is a disadvantage that it is difficult to secure a field of view when there is an obstruction structure such as an omentum. In the future, further study of large size will be needed.

Disclosure: Nothing to disclose.

PP0924

PREOPERATIVE PREDICTION OF POSTOPERATIVE COMPLICATIONS FOLLOWING MINIMALLY INVASIVE TOTAL MESORECTAL EXCISION UTILIZING ARTIFICIAL INTELLIGENCE

R. Geitenbeek¹, S. Baltus², M. Friebe², C. Tan³, I. Broeders², E. Consten¹, MIRECA

¹University Medical Center Groningen, Groningen, Netherlands,

²Meander Medical Center Amersfoort, Amersfoort, Netherlands,

³University of Twente, Faculty of Electrical Engineering, Mathematics and Computer Science, Twente, Netherlands

Contact E-Mail Address: maikiefriebe@gmail.com

Introduction: Recent investigations have highlighted specific dimensions within the bony pelvis as potential indicators of total mesorectal excision (TME) outcomes. However, manual pelvimetry is labor-intensive.

Aims & Methods: This study endeavors to develop an automated pelvimetry system employing artificial intelligence (AI) to facilitate the preoperative identification of high-risk patients. Specifically, our research aims to construct and validate an AI-based automated pelvimetry tool and assess the prognostic utility of pelvimetric measurements in predicting postoperative complications necessitating reintervention (Clavien Dindo classification ≥ 3) in patients undergoing minimally invasive TME. This study is a multicenter retrospective cohort investigation incorporating clinical and imaging data from 1,700 patients treated at eight experienced TME centers. Leveraging a Deep-Learning network, our algorithm locates multiple anatomical landmarks to quantify pelvic inlet, pelvic outlet, and depth distances accurately. The accuracy of the developed algorithm is compared against inter-observer variability observed in manually conducted pelvimetry. The prognostic significance of pelvimetry for (post-)operative outcomes is evaluated through multivariate regression analyses.

Results: The AI-driven landmark localization achieved a mean margin of error of 5 millimeters across various pelvic dimensions, while manual pelvimetry demonstrated an inter-observer variation of 2.5 millimeters. Analyses of pelvimetric measurements and postoperative complications identified pelvic depth as an independent predictor of such complications ($p < 0.001$).

Conclusion: An artificial intelligence algorithm could successfully be used for accurate automated pelvic dimension determination. These pelvimetric measurements hold promise as a valuable decision support tool for surgeons in preoperatively assessing the risk of postoperative complications following minimally invasive TME.

Disclosure: Nothing to disclose.

PP0925

COLD VERSUS HOT SNARE POLYPECTOMY AND COLD FORCEPS FOR SMALL COLORECTAL POLYPS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

N.M. Al-dardery¹, A. Mohammad Hussein², M. Tarek Hasan³, M. Mohamed El-sayed¹, A. Khaled Madeeh¹, M. El-Samahy⁴, A. Khaity⁵

¹Fayoum University, Faculty of Medicine, Fayoum,

Egypt, ²Al-Balqa' Applied University, Faculty of Medicine,

Salt, Jordan, ³Al-Azhar University, Intern Doctor, Faculty

of Medicine, Cairo, Egypt, ⁴Zagazig University, Faculty of

Medicine, Zagazig, Egypt, ⁵Elrazi University, Faculty of Medicine, Khartoum, Sudan

Contact E-Mail Address: ndardery449@gmail.com

Introduction: Endoscopic removal of colorectal polyps is a cornerstone of colorectal cancer prevention.¹

Optimal techniques for removing small polyps (≤ 10 mm) remain scarce,²⁻⁴ with cold snare polypectomy (CSP), hot snare polypectomy (HSP), and cold forceps (CF) being the main options.¹⁻⁴

Aims & Methods: This systematic review and network meta-analysis aims to compare the efficacy of these techniques for removing small colorectal polyps and determine the optimal approach.

We searched Web of Science, PubMed, Cochrane CENTRAL, and Scopus from inception until March 2024 for relevant randomized controlled trials and observational studies comparing CSP, HSP, and CF (including sub-techniques) for small polyp removal.

Records were screened for eligible studies, and all relevant outcomes were pooled as a risk ratio (RR) with the corresponding 95% confidence intervals (CI) in a network meta-analysis (NMA) model, using R software.

Results: Our findings from 13 studies (2767 patients) showed insignificant differences among HSP versus CSP in terms of complete resection rate (CRR) and incomplete resection rate (IRR) [RR 2.00, (95% CI, 0.53 to 7.51); $P = 0.74$] and [RR 1.24, (95% CI, 0.20 to 7.85); $P = 0.43$], respectively. In addition, no significant variance was detected between the CSP and CF in terms of complete histological polyp eradication (CHPE), incomplete histological polyp eradication (IHPE), and visual polyp eradication (VPE) [RR 0.97, (95% CI, 0.87 to 1.08); $P = 0.1$], [RR 1.36, (95% CI, 0.57 to 3.26); $P = 0.9$], and [RR 0.75, (95% CI, 0.62 to 0.91); $P = 0.07$], respectively.

Conclusion: In conclusion, our results revealed no significant difference between any of the techniques in terms of their success rate in completely removing the polyp. These findings suggest that all three methods might be equally effective for removing small polyps.

However, we recommend further studies with more participants, and longer follow-up periods might be needed to definitively determine the best approach for all situations. This could include considering factors like specific polyp characteristics or patient preferences.

References:

1. Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic Removal of Colorectal Lesions—Recommendations by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2020;158(4):1095-1129. doi:10.1053/j.gastro.2019.12.018
2. Abuelazm M, Mohamed I, Jaber FS, et al. Cold Versus Hot Snare Polypectomy for Colorectal Polyps: An Updated Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Clin Gastroenterol*. 2023;57(8). https://journals.lww.com/jcge/fulltext/2023/09000/cold_versus_hot_snare_polypectomy_for_colorectal.4.aspx.
3. Niu C, Bapaye J, Zhang J, et al. Systematic review and meta-analysis of cold snare polypectomy and hot snare polypectomy for colorectal polyps. *J Gastroenterol Hepatol*. 2023;38(9):1458-1467. doi:https://doi.org/10.1111/jgh.16312

4. CAVASSOLA PRP, MOURA DTH de, HIRSCH BS, LANDIM DL, BERNARDO WM, MOURA EGH de. HOT VERSUS COLD SNARE FOR COLORECTAL POLYPECTOMIES SIZED UP TO 10MM: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. *Arg Gastroenterol.* 2024;61. doi:10.1590/s0004-2803.246102023-143

Disclosure: Nothing to disclose.

PP0926

THE ROLE OF LASER FILAC™ IN THE MANAGEMENT OF ANAL FISTULAS: EXPERIENCE FROM MEDICINE SERVICE B

S. Mechhor¹, M. Cherkaoui Malki¹, H. El Bacha¹, N. Benzoubeir¹, I. Errabih¹

¹*Ibn Sina Hospital, Department of Gastroenterology, Hepatology and Proctology « Medicine B »; Ibn Sina University Hospital, Rabat, Morocco, Rabat, Morocco*

Contact E-Mail Address: salmamechhor@gmail.com

Introduction: “Complex” anal fistulas are characterized by a tract that cannot be laid open by fistulotomy without risking significant incontinence due to the depth of the tract and/or the patient's condition. Over the past 20 years, several techniques known as “sphincter-saving” have been proposed to address this surgical challenge. Among these techniques, FiLaC™ is one of the most recent. It involves closing the fistula tract by coagulation. The aim of our work is to evaluate the results of this technique in terms of healing of anal fistulas through a series of cases.

Aims & Methods: This is a descriptive prospective study conducted between May 2023 and March 2024 involving 14 patients who underwent treatment for anal fistula using the FiLaC™ technique. All patients underwent an initial surgical intervention to identify the fistula tract, place a loose seton, drain any abscess, and/or lay open any diverticula. The type of fistula tract was determined by the proctologist during this first operation. In cases of doubt about the quality of drainage, multi-operated fistula, and/or Crohn's disease, an MRI was performed. The procedure was performed under spinal anesthesia, and all patients received perioperative antibiotic prophylaxis. We used a 1.2 mm diameter radial fiber powered by the Leonardo Duel© diode laser platform. The primary outcome measure was fistula healing, clinically defined by closure of the internal and external openings and absence of pain and discharge.

Results: Fourteen patients were included, with a mean age of 45.1 +/- 2.1 years. Among our patients, 12 (85%) had cryptogenic fistulas, 1 case had a fistula as part of ano-perineal manifestations of Crohn's disease (CD), and one anal fistula was secondary to perianal tuberculosis. The fistula was classified as Parks 1 in 14.2% of cases, Parks 2 in 57.14% of cases, Parks 3 in 14.2% of cases, and Parks 4 in 14.2% of cases. The internal opening was tight in 64.28% of patients and gaping in 35.72%. The mean operative time before laser closure was 2.07. All patients had a seton drain placed. The mean time for drain removal was 124.90 seconds, and the mean delivered energy was 799.88 Joules. No cases of postoperative complications were reported. The mean follow-up was 2.21 months. Healing was achieved in 78.5% of cases, while in 21.5% of patients, closure of the internal and/or external opening was not achieved, and surgical revision was proposed. No cases of recurrence were reported.

Conclusion: The treatment of complex fistulas still presents a challenge: achieving fistula healing while preserving anal continence. Laser coagulation appears as a promising technique that can meet this challenge.

Disclosure: Nothing to disclose.

PP0927

IS FISSURECTOMY WITH ANOPLASTY BETTER THAN FISSURECTOMY ALONE?

S. Mechhor¹, M. Cherkaoui Malki¹, H. El Bacha¹, N. Benzoubeir¹, I. Errabih¹

¹*Ibn Sina Hospital, Department of Gastroenterology, Hepatology and Proctology « Medicine B »; Ibn Sina University Hospital, Rabat, Morocco, Rabat, Morocco*

Contact E-Mail Address: salmamechhor@gmail.com

Introduction: Anal fissure is a common reason for consultation in proctology. Surgery is proposed in cases of chronic, complicated, or recurrent anal fissure. Fissurectomy can be performed alone (FS) or combined with anoplasty (F+A). The benefit of the latter compared to fissurectomy alone has never been demonstrated. The objective of the study was to compare the effectiveness and tolerance of the two techniques.

Aims & Methods: This was a retrospective descriptive and analytical study conducted over a period of 18 years from January 2005 to August 2023, involving 2070 patients surgically treated for anal fissure. We included all patients without a proctological surgical history who were operated on for a single, non-infected idiopathic anal fissure. We evaluated postoperative pain, early postoperative complications (bleeding, dysuria, constipation, superinfection), and healing time. Statistical analysis was performed using SPSS 20.0 software. Qualitative variables were compared using the Chi-square test. Predictive factors for healing were identified using a binary logistic regression model in univariate and multivariate analysis.

Results: The overall prevalence of anal fissures compared to other reasons for proctology consultation was 55.9%. The median age of the patients was 40 [21-69], with a female-to-male ratio of 0.85. The anal fissure was posterior in 1493 (72.1%) patients and anterior in 577 (27.9%) patients. Other proctological pathologies (anal fistula, hemorrhoidal disease) were associated in 358 cases (17.3%). FS was performed in 1304 patients (62.9%) and F+A in 766 patients (37%). Sphincterotomy was associated in 357 patients (17.24%). The median postoperative follow-up was 2 [1-3.9] months. Continence was respected in all patients. The time to disappearance of postoperative pain was the same for both procedures: 1.1 +/- 0.5 months vs. 1.0 +/- 1.2 months, p=0.51, respectively for FS and F+A. The overall rate of early complications was 5.29%, with them being more frequent in cases of F+A: 7.1% vs. 2.3%, p=0.031. The healing rate was similar in both procedures: 92.9% vs. 97.7%, p=0.31. The median healing time was shorter in patients who underwent F+A: 1.5 +/- 0.2 months vs. 2.8 +/- 0.4 months, p = 0.0003. In multivariate analysis, independent risk factors associated with delayed healing were age ≥ 40 years [OR = 3.1; 95% CI [1.1 to 14.1] p = 0.004] and a history of diabetes [OR 6.5, 95% CI [1.7 to 43.2] p <0.001. The postoperative recurrence rate was similar in both procedures: 2.1% in the case of FS vs. 3.2% in the case of F+A, p=0.1.

Conclusion: Fissurectomy remains an effective procedure in the management of anal fissures. Our study showed that fissurectomy with anoplasty has the advantage of accelerating healing. However, at present, no technique is consensual, hence the importance of multicenter randomized studies evaluating both surgical techniques.

Disclosure: Nothing to disclose.

PP0928

PERIOPERATIVE MANAGEMENT FOR PATIENTS WITH HEMOPHILIA A UNDERGOING ENDOSCOPIC MUCOSAL RESECTION TO CONTROL POSTOPERATIVE DELAYED HEMORRHAGE

T. Xia¹, S. Feng¹, C. Dai¹, Y. Tang²

¹First Affiliated Hospital of Soochow University, Department of Gastroenterology, Suzhou, China, ²First Affiliated Hospital of Soochow University, Department of Hematology, Suzhou, China

Contact E-Mail Address: xiatingtingsuzhou@163.com

Introduction: Endoscopic mucosal resection (EMR) are popularly used to remove gastrointestinal polyps. Successful treatment will be hampered by postoperative delayed bleeding. Due to the deficiency of coagulation factors, the risk of hemorrhage increases for patients with hemophilia A. It is necessary to receive the infusion of clotting factor VIII (FVIII) during perioperative period. The infusion duration depends on operation trauma, while no accepted guidelines are reported for EMR.

Aims & Methods: We aim to describe perioperative management strategy for patients with hemophilia A undergoing EMR for controlling postoperative delayed hemorrhage. This study is designed as an observational study at First Affiliated Hospital of Soochow University and approved by the committee ethics (approval number: 2023-280). A total of six patients were included into analysis, including 2 gastric polyps and 4 colorectal polyps. The concentration of FVIII was monitored during perioperative period. The strategy of replace treatment was timely adjusted. Demographics and perioperative characteristics were recorded, including age, sex, body-mass index (BMI), the location and size of polyps, the testing results of FVIII, the infusion strategy and prognosis.

Results: The concentration of FVIII on admission ranged from 0.4%-26.2%. FVIII was infused preoperatively to increase the concentration to more than 20.0%, except for the patient whose initial FVIII concentration was 26.2%. No intraoperative hemorrhage was observed. The first three patients received the infusion of FVIII for just one day postoperatively, however, delayed bleeding attacked them. The longest interval from operation to hemorrhage was 15 days. The hemorrhage could be successfully controlled upon the infusion of FVIII. In contrast, the other three patients received appropriate infusion of FVIII during postoperative seven days (Table.1) to maintain the concentration over 20.0%. The total infusion dose of FVIII for each patient all exceeded 1500U. Eventually, no postoperative delayed bleeding was observed.

Patient No.	Age	Gender	BMI (kg/m ²)	Polyp location	FVIII concentration at admission	Preoperative FVIII infusion strategy	FVIII concentration on preoperative day	Postoperative FVIII infusion strategy	Postoperative delayed bleeding
1	29	Male	21.1	Stomach	0.4%	2000U qd*day1	28.6%	1000U qd*day1	Yes
2	43	Male	24.3	Stomach	12.6%	200U qd*day1-4	39.5%	1200U qd*day1	Yes
3	36	Male	24.6	Rectum	4.0%	1200U qd*day1	21.4%	1400U qd*day1	Yes
4	53	Male	17.4	Colon	19.5%	1000U qd*day1	43.0%	600U q12h*day1-2, 400U q12h*day3-4, 800U qod*day5-7	No
5	28	Female	21.8	Rectum	26.2%	No infusion	26.2%	400U qd*day3-6	No
6	58	Male	22.6	Colon	7.4%	1800U qd*day1	30.4%	800U qd*day1-3, 600U qd*day4-6	No

Table.1 Demographics and management strategy.

Conclusion: In spite of the super minimal invasiveness of endoscopic surgery, it is critical for patients with hemophilia A to receive enough FVIII infusion in peri-EMR management. The concentration of FVIII should be increased to more than 20% before EMR, no matter which infusion dose to be chosen. The duration of operation and the size of surgical wound are needed to be reduced. It is crucial to keep infusion of FVIII and maintain its concentration over 20% for at least 7 days postoperatively.

Furthermore, resumption of FVIII might be beneficial to the patients at high risk for delayed bleeding, including the aged (>60 years), larger lesions (>10mm) and rectal location. This is the first report about perioperative management when performing EMR on patients with haemophilia A. More researches are necessary for verifying the clinical benefits against potential complications.

References:

1. Fogarty PF, Kouides P. How we treat: patients with haemophilia undergoing screening colonoscopy. *Haemophilia* 2010; 16: 363-365. doi:10.1111/j.1365-2516.2009.02120.x
2. Hazendonk H, Heijdra JM, de Jager NCB et al. Analysis of current perioperative management with Haemate((R)) P/Humate P((R)) in von Willebrand disease: Identifying the need for personalized treatment. *Haemophilia* 2018; 24: 460-470. doi:10.1111/hae.13451
3. Kulkarni R. Comprehensive care of the patient with haemophilia and inhibitors undergoing surgery: practical aspects. *Haemophilia* 2013; 19: 2-10. doi:10.1111/j.1365-2516.2012.02922.x
4. Neufeld EJ, Solimeno L, Quon D et al. Perioperative management of haemophilia B: A critical appraisal of the evidence and current practices. *Haemophilia* 2017; 23: 821-831. doi:10.1111/hae.13279
5. Srivastava A, Brewer AK, Mauser-Bunschoten EP et al. Guidelines for the management of hemophilia. *Haemophilia* 2013; 19: e1-47. doi:10.1111/j.1365-2516.2012.02909.x

Disclosure: Nothing to disclose.

PP0929

EFFECT OF THE NUTRACEUTICAL “MICODIGEST 2.0” ON THE COMPLICATION RATE OF COLORECTAL CANCER SURGERY WITH CURATIVE INTENT: A RANDOMISED, DOUBLE-BLIND CLINICAL TRIAL (NCT04821258)

A.I. Díez-Martín¹, C. Regueiro Expósito¹, S. Zarraquiños Martínez², D. Remedios², C.A. Sánchez Gómez², S. Alonso Lorenzo³, R. Fernández Poceiro⁴, M.L. de Castro Parga³, V. Hernández Ramírez³, J. Cubiella^{1,2}

¹Fundación Pública Galega de Investigación Biomédica Galicia Sur, Research Group in Gastrointestinal Oncology, Ourense, Spain, ²Complexo Hospitalario Universitario de Ourense, Gastroenterology Department, Ourense, Spain, ³Complexo Hospitalario Universitario de Vigo, Gastroenterology Department, Vigo, Spain, ⁴Fundación Pública Galega de Investigación Biomédica Galicia Sur, Research Group in Gastrointestinal Diseases, Vigo, Spain

Contact E-Mail Address: astrid.diez@iisgaliciasur.es

Introduction: Fungal polysaccharides have the potential to reduce complications associated with surgery. This is due to their role in modulating the microbiota and their anti-inflammatory activity. Therefore, the nutraceutical MICODIGEST 2.0, composed of 9 fungal extracts, could be a valuable therapeutic resource to be considered in reducing the complications associated with colorectal surgery.

Aims & Methods: A randomised, double-blind clinical trial was conducted on patients with colorectal cancer (CRC) who were candidates for surgical treatment with curative intent¹. Patients were randomised to take the nutraceutical MICODIGEST 2.0 or a placebo, and were followed for 4-6 weeks until the time of surgery. At baseline and at the end of follow-up, analytical determinations were made for inflammatory parameters and assessments of nutritional status and quality of life. Adverse effects (AE) were also collected during the follow-up period. Post-surgical complications were collected at hospital discharge and assessed using the Clavien-Dindo (CD) classification.

Results: A total of 46 patients were included in the study, with a median age of 67 (62.3-72.8) years and a percentage of women of 50.0 %. A total of 26.1 % of patients had some type of postoperative complication. The majority of these complications were minor (84.4 %), classified as grade I (50 %) or grade II (50 %) according to the CD classification. The remaining complications were more severe (16.6 %), and were classified as grade III according to the CD classification. There were no significant differences between the two groups in terms of clinical characteristics, nutritional status, quality of life, or analytical determinations. The percentage of post-surgical complications was similar between patients treated with nutraceutical and those treated with placebo (25.9% vs. 26.3%, $p=0.9$). Adverse events were reported in a total of 14 patients (30.4%) during follow-up, of which only 7.1% were serious. However, the percentage of adverse events was not significantly different between the nutraceutical and placebo groups (33.3% vs. 41.1%, $p=0.5$). A comparison between patients with postoperative complications and those without revealed no significant difference. Similarly, no difference was found between data collected at baseline and at the end of the study.

Conclusion: The nutraceutical MICODIGEST 2.0 has not demonstrated a beneficial effect in reducing complications associated with surgery for CRC treated with curative intent. However, these results are limited to the sample size obtained and should be validated in larger cohorts of patients.

References: 1. Regueiro C et al. . JMIR Res Protoc. 2022 May 16;11(5):e34292.

Disclosure: Nothing to disclose.

PP0930

FIRST EXPERIENCES WITH THE USE OF VACSTENT FOR TREATMENT OF ANASTOMOTIC LEAKAGE IN THE LOWER GI TRACT

A. Herner¹, S. Baumeler², S. Nennstiel¹, M. Ramser³, P. Aepli², M. Turina³, C. Schlag¹

¹University Hospital Zurich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ²Luzerner Kantonsspital, Department of Gastroenterology and Hepatology, Lucerne, Switzerland, ³University Hospital Zurich, Department of Surgery and Transplantation, Zürich, Switzerland

Contact E-Mail Address: alexander.herner@usz.ch

Introduction: Anastomotic leakage is a serious complication following colorectal surgery and is associated with early and long-term morbidity and mortality. Various endoscopic and surgical approaches have been established for management. A new therapeutic option involves the placement of a fully covered VACstent for the lower GI tract (36x80 mm, MICRO-Tech, Düsseldorf, Germany), which offers advantages such as completely covering the defect, continuous drainage, and facilitating stool passage simultaneously. Here we report our initial experiences with the VACstent in the lower GI tract for treatment of anastomotic leakage.

Aims & Methods: The fully covered VACstent (36x80 mm) was placed endoscopically under direct visualization. A continuous negative pressure between -75 and -125 mmHg was applied. The VACstent was flushed daily with 20 ml of saline to prevent adhesions of the open-pored sponge of the stent. Six hours before the stent extraction/exchange, the negative pressure was discontinued. The integrity of the leak closure was confirmed visually and via fluoroscopy.

Results: Between February and April 2024, we treated four patients with anastomotic leakage (rectal leakage n=2, sigmoid leakage n=2) using the VACstent. The leakage was detected on the 7th ± 4 postoperative day. The leak was successfully sealed with the VACstent, and one to two exchanges were performed. The leak closure occurred after 17 ± 3 days. Inflammatory parameters such as CRP decreased by around 85 ± 13%. Three patients had a stoma before the VACstent was placed. The distance of the

leak from the anal canal averaged 10 ± 9 cm. Patients with leaks involving the anal canal required additional pain reliever. One patient experienced point-shaped erosion bleeding in the anal canal, which was effectively treated with APC.

Conclusion: The lower GI VACstent represents a novel promising and effective endoscopic treatment option for colonic anastomotic defects.

Disclosure: Nothing to disclose.

PP0931

WITHDRAWN

PP0932

LOW ANTERIOR RESECTION SYNDROME – A NEVERENDING CHALLENGE. WHAT IS THE ROLE OF THE ENTEROSORBENTS?

I. Froehner Junior^{1,2}, J.N. Buzato^{2,1}

¹Nossa Senhora das Graças Hospital, Gastrointestinal Motility and Continence, Curitiba, Brazil, ²PELVIA Gastrointestinal Motility and Continence, Curitiba, Brazil

Contact E-Mail Address: froehnerjr@yahoo.com.br

Introduction: Low anterior resection syndrome (LARS) occurs after trans-abdominal rectal surgical removal, most related to colorectal tumors. It has a significant impact on quality of life, so that some patients prefer a permanent stoma. Main symptoms are diarrhea, fecal incontinence, increased defecation frequency, disturbing fecal urgency and perception of incomplete evacuation.

Treatment is still challenging, and many protocols were developed so far. Enterosorbents are oral intestinal adsorbents, based on organic mineral with adsorption capacity towards some toxic and harmful substances in the gut, e.g., endotoxins and enterotoxins, physically binding them to its surface, reducing stool frequency and improving its consistency. Until the present day, little is known about their effect on LARS patients.

Aims & Methods: Fifteen consecutive adult patients were referred to treatment with the enterosorbent methylsilicic acid due to poor response to optimal clinical protocol to LARS.

Patients were asked to take one measuring spoon (5g) of 70% methylsilicic acid hydrogel added to 50 mL of water two times a day for a 30-day period.

Mean BSS, global improvement percentage, defecatory frequency, Constipation Scoring System (CSS) and Cleveland Clinic Incontinence Score (CCIS) were applied by the author to the patients during the first appointment and during the 30-day follow-up appointment.

All patients accepted to participate by signing the informed consent form, in compliance to the respective Ethical Committee authorization.

Results: Nine patients were female and average age was 32 years (+ 7 years). All patients informed no difficulty in complying with the enterosorbent protocol.

Initial mean defecatory frequency was 10 (+3). Mean CSS was 9 (+5) and CCIS was 15 (+5). Mean BSS was 5 (+ 2).

By the time of the 30-day follow-up appointment, mean defecatory frequency was 5 (+2). Mean CSS was 5 (+3), CCIS was 5 (+3), and mean BSS was 4 (+1), $p < 0,01$. Global improvement percentage was 52,3% (+ 10,2) with no side effects.

Conclusion: The enterosorbent methylsilicic acid hydrogel is a safe and valid tool in treating low anterior resection syndrome patients and may be suitable as a new therapeutic option.

References: 1 Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features, and Rome IV. Gastroenterology. 2016; 16: 223-7.

2 Benet LZ, Bowman CM, Koleske ML, Rinaldi CL, Sodhi JK. Understanding drug-drug interaction and pharmacogenomic changes in pharmacokinetics for metabolized drugs. *J Pharmacokinet Pharmacodyn*. 2019; 46: 155-63.

3 Froehner Junior I. Oral soluble fibers as a first approach to low anterior resection syndrome treatment. *Neurogastroenterol Motil*. 2023; 35: 77-8.

4 Froehner Junior I, Buzato JN. Fecal consistency as a marker of good response in the treatment of functional bowel movement disorders and the role of soluble fibers. [Presentation on 8^o Latin American Pelvic Floor International Congress - ALAPP; 2024 fev 21-24; Panamá City, Panamá, onsite]

5 Axelrod CH, Saps M. The role of fiber in the treatment of functional gastrointestinal disorders in children. *Nutrients*. 2018; 10: 1650-66.

6 Ingemansson A, Walter SA, Jones MP, Sjö Dahl J. Defecation symptoms in relation to stool consistency significantly reflect the dyssynergy pattern in high-resolution anorectal manometry in constipated patient. *J Clin Gastroenterol*. 2024; 58: 57-63.

7 Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FEM, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut*. 1992; 33: 818-24.

Disclosure: Nothing to disclose.

PP0933

EFFICACY AND SAFETY OF MULTI-LOOP TRACTION DEVICE-ASSISTED COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: A MULTICENTER RANDOMIZED CONTROLLED CLINICAL TRIAL

Y. Miura¹, Y. Tsuji¹, M. Ito², N. Tamai², H. Furuhashi³, H. Takamaru⁴, Y. Saito⁴, M. Fujishiro¹, K. Sumiyama²

¹Graduate School of Medicine, the University of Tokyo, Department of Gastroenterology, Tokyo, Japan, ²The Jikei University School of Medicine, Department of Endoscopy, Tokyo, Japan, ³Jikei University Kashiwa Hospital, Department of Endoscopy, Tokyo, Japan, ⁴National Cancer Center Hospital, Gastrointestinal Endoscopy Division, Tokyo, Japan

Contact E-Mail Address: yukomiu0317@gmail.com

Introduction: Colorectal endoscopic submucosal dissection (C-ESD) has been established as a standard treatment for colorectal neoplasms which need to be resected in an en bloc fashion. However, the dissection of thin submucosa under inadequate visualization is still technically demanding. A traction device is a key to this problem.

Aims & Methods: We recently developed a novel traction device (multi-loop traction device, MLTD; Boston Scientific Co. Ltd., Tokyo, Japan). The present study focuses on evaluating the effectiveness and safety of MLTD during C-ESD. A multicenter randomized controlled trial was conducted involving patients aged 20 years or older with colorectal lesions (≥ 20 mm) suspected of non-invasive carcinoma. Participants were randomly assigned in 1:1 ratio to undergo ESD with MLTD (MLTD-ESD group) or without any traction device (control group). In both groups, the operators were given the option to convert the treatment to the other group if endoscopist found it difficult to continue treatment under the conditions given in each group for more than 10 minutes. The primary endpoint was dissection speed, with key secondary endpoints being technical success rate and adverse events. The technical success rate was defined as the proportion of cases in which the protocol treatment was completed in each group.

Results: A total of 108 participants were randomized into the MLTD-ESD group (n = 53) and the control group (n = 55). Median dissection speeds were not significantly different between the MLTD-ESD group and the control group (14.8 [IQR: 8.9-23.9] vs. 13.3 [IQR: 8.9-18.8] mm²/min; P = 0.30).

However, the technical success rate was significantly higher in the MLTD-ESD group (96.2%) compared to the control group (71.0%).

There were two cases in which treatment was converted in the MLTD-ESD group, and 16 cases in which treatment was converted in the control group. There was no significant difference between the MLTD-ESD group and the control group in the en bloc resection rate (98.1% vs. 100%, P = 0.31), R0 resection rate (94.3% vs. 91.0%, P = 0.46) and the incidence of adverse events (7.5% vs. 9.1%, P = 0.77).

Two intraoperative perforations, one delayed bleeding, and one delayed perforation occurred in the MLTD-ESD group. All patients recovered with nonsurgical management.

The subgroup analysis among expert endoscopists with over 200 clinical ESD experiences showed a faster dissection speed in the MLTD-ESD group compared to the control group (21.6 [IQR: 15.5-28.8] vs. 14.4 [IQR: 9.9-21.2] mm²/min; P = 0.009).

Conclusion: The use of MLTD did not lead to a faster dissection speed during C-ESD in this multicenter randomized controlled trial. However, it was associated with a higher technical success rate, and faster ESD procedures among expert endoscopists.

To better define its role in C-ESD, further research with a more targeted approach is warranted.

Disclosure: Kazuki Sumiyama is named as an inventor in patent licensing of the "Multi-Loop Traction Device."

PP0934

OUTCOMES AND LEARNING CURVE OF ENDOSCOPIC SUBMUCOSAL DISSECTIONS OF COLON LESIONS IN A WESTERN COUNTRY

P.A. Lima¹, A. Mascarenhas¹, A.R. Franco¹, I. Simão¹, B.G. Rodrigues¹, R.R. Mendes¹, A. Gonçalves², D. Reis¹, C. Chagas¹, P. Barreiro^{1,3}

¹Unidade Local de Saúde Lisboa Ocidental, Gastroenterology, Lisbon, Portugal, ²Unidade Local de Saúde da Região de Leiria, Gastroenterology, Leiria, Portugal, ³Hospital dos Lusíadas de Lisboa, Advanced Endoscopy Center, Lisbon, Portugal

Contact E-Mail Address: pedro.lima97doc@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is used for en bloc resection of selected superficial lesions of the colon and rectum. ESD of colon lesions is particularly challenging, mostly limited to few reference centers in Western countries, with small series in the literature.

Aims & Methods: Assessment of outcomes of ESD of colon lesions and the relationship between endoscopist's experience.

Retrospective cohort study, from prospective collected data, including all consecutive patients submitted to ESD in the colon, in a tertiary Western center. The patients were divided into 3 groups, each made up of 63 patients, in chronological order of the procedure. The procedure was always performed by the same endoscopist.

Results: A total of 189 ESD in the colon were performed in 185 patients (60.8% male; median age 69), with an overall rate of en bloc, R0 and curative resections of 94.18%, 78.84% and 74.07%, respectively. There were 3 perforations (1,6%) all solved endoscopically, without any death or complications requiring surgical approach.

With increasing experience, a higher percentage of R0 and curative resections was found, with statistical significance (p-value = 0.0004 and 0.0006, respectively). In the first group, R0 was reached in 63.49%, whereas in the second group R0 was attained in 80.85% and in the third group in 92.06%. In terms of en bloc resection, there was no significant difference between the three groups (p-value = 0,067). Regarding perforations, there was no difference between the 3 groups (1 case in each).

Conclusion: In this real life study from a Western center, ESD for colonic lesions was very safe and with high rates of en bloc resections. However, a learning curve was observed with a significant increase in the rate of complete and curative resections over time.

Disclosure: Nothing to disclose.

PP0935

INNOVATIVE INTERVENTIONS: COMPARING ENDOSCOPIC DIRECT APPENDICITIS THERAPY WITH ENDOSCOPIC RETROGRADE APPENDICITIS THERAPY FOR UNCOMPLICATED APPENDICITIS

C. Jun¹, H. Silin¹, L. Ting², Z. Yu², L. Yang³, Z. Yingchun³, L. Yang-Bor⁴

¹South China Hospital of Shenzhen University, Department of Gastroenterology, Shenzhen, China, ²The First People's Hospital of Yunnan Province, Department of Gastroenterology, Kunming, China, ³Shenzhen Hospital of Southern Medical University, Department of Gastroenterology, Shenzhen, China, ⁴Xiamen Chang Gung Hospital, Endoscopy Center, Xiamen, China

Contact E-Mail Address: 66577177@qq.com

Introduction: Endoscopic retrograde appendicitis therapy (ERAT) offers an appendix-preserving approach, yet visual and specificity challenges persist. In contrast, endoscopic direct appendicitis therapy (EDAT) provides direct visual observation with diagnostic and therapeutic capabilities. This study aimed to assess the efficacy and feasibility of EDAT compared to ERAT in uncomplicated appendicitis.

Aims & Methods: We retrospectively reviewed of patients diagnosed with suspected uncomplicated appendicitis undergoing ERAT or EDAT from Jan 2021 to Mar 2024.

The primary outcome was to evaluate the intervention success of two groups.

The secondary outcomes included hospitalization, procedure time, stent placement, post-procedure hospitalization period, pain relief, recurrence, and endoscopic direct-view characteristics were compared.

Results: Sixty-nine patients were enrolled, among which 34 patients underwent ERAT and 35 patients underwent EDAT. EDAT showed significantly higher intervention success (100% and 85.3%, respectively, $p = 0.018$), and shorter hospitalization stay ($p = 0.003$), and post-procedure hospitalization stay ($p < 0.001$) compared to ERAT group. With comparable procedure time ($p = 0.915$) and recurrence ($p = 0.164$), significant fewer proportions of stent placements ($p < 0.001$), guidewire assists ($p < 0.001$), and post-procedure antibiotic administrations ($p = 0.036$) associated in EDAT group compared to ERAT group.

Conclusion: EDAT has demonstrated to be an effective and feasible approach, offering both diagnostic and therapeutic capabilities for uncomplicated appendicitis compared to ERAT.

References: 1 Sceats, L. A., Trickey, A. W., Morris, A. M., Kin, C. & Staudenmayer, K. L. Nonoperative Management of Uncomplicated Appendicitis Among Privately Insured Patients. *JAMA Surg* 154, 141-149 (2019). <https://doi.org/10.1001/jamasurg.2018.4282>

2 Wu, T., Yang, Y., Wu, Y., Lu, L. & Dong, S. Complications after appendectomy in patients with treated appendicitis: results from a retrospective study. *Ann Palliat Med* 10, 12546-12553 (2021). <https://doi.org/10.21037/apm-21-3295>

3 Song, M. Y. *et al.* Long-term effects of appendectomy in humans: is it the optimal management of appendicitis? *Expert Rev Gastroenterol Hepatol* 15, 657-664 (2021). <https://doi.org/10.1080/17474124.2021.1868298>

4 Masahata, K. *et al.* Generation of colonic IgA-secreting cells in the caecal patch. *Nature Communications* 5, 3704 (2014).

5 Ambe, P. C. Negative Appendectomy. It is Really Preventable? *Journal of Investigative Surgery* 32, 474-475 (2019). <https://doi.org/10.1080/08941939.2018.1453566>

6 Jeon, B. G. Predictive factors and outcomes of negative appendectomy. *Am J Surg* 213, 731-738 (2017). <https://doi.org/10.1016/j.amjsurg.2016.05.020>

7 A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis. *New England Journal of Medicine* 383, 1907-1919 (2020). <https://doi.org/doi:10.1056/NEJMoa2014320>

8 Salminen, P. *et al.* Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. *JAMA* 313, 2340-2348 (2015). <https://doi.org/10.1001/jama.2015.6154>

Disclosure: Nothing to disclose.

PP0936

ACCURACY OF PRE-RESECTION OPTICAL EVALUATION FOR SERRATED AND ADENOMATOUS LARGE NON-PEDUNCULATED COLORECTAL POLYPS

S. Jiang¹, A. Zarrin¹, A. Walia^{1,2}, C. Galorport^{1,2}, W. Xiong³, R. Trasolini^{1,4}, E. Lam^{1,2}, N. Shahidi^{2,1}

¹University of British Columbia, Medicine, Vancouver, Canada,

²St. Paul's Hospital, Gastroenterology, Vancouver, Canada,

³University of British Columbia, Pathology and Laboratory

Medicine, Vancouver, Canada, ⁴Vancouver General Hospital,

Gastroenterology, Vancouver, Canada

Contact E-Mail Address: sjiangx@gmail.com

Introduction: Optical evaluation differentiating between adenomatous and serrated histopathology is the first step in management of large non-pedunculated colorectal polyps (LNPCP) as it informs appropriate endoscopic resection technique selection. Performance of optical evaluation is modest for diminutive polyps but has not been reported for LNCP.¹

Aims & Methods: We sought to evaluate the performance of optical evaluation to differentiate between adenomatous and serrated histopathology for LNCP. Consecutive patients > 18 years of age who underwent endoscopic resection for a LNCP were enrolled in a prospective multi-center observation cohort study (ClinicalTrials.gov NCT05402696). Pre-resection optical evaluation was performed using high-definition white-light and narrow-band imaging (NBI) with or without near-focus. The Japanese NBI Expert Team (JNET) classification was used to differentiate between serrated (JNET I) vs. adenomatous (JNET IIA, IIB) LNCPs. Traditional serrated adenomas (TSA) and cancers were excluded from analysis. Sensitivity, specificity, and accuracy were used to evaluate optical evaluation performance.

Results: Between June 2022 to April 2024, 440 patients underwent 476 procedures for 558 LNCP. Median LNCP size was 30 mm (IQR 20-40) and 404 (72.4%) LNCP were proximal to the splenic flexure. Histopathology of all lesions included 365 (65.4%) adenomas, 137 (24.6%) serrated lesions, 34 (6.1%) cancers, and 22 (3.9%) other lesions, which included 6 (1.1%) TSA. Adenomatous histopathology was found predominantly in LNCP with Paris 0-IIA+IS (107/136, 78.7%) and Paris 0-IS (70/82, 85.4%) morphology. Paris 0-IIA lesions were both adenomatous (184/328, 56.1%) and serrated (125/328, 38.1%). Of 137 serrated LNCP, 133 (97.1%) were predicted as serrated, with sensitivity, specificity, and accuracy of 97.08% (95% CI 92.69-99.20), 99.45% (95% CI 98.03-99.93), and 98.80% (95% CI 97.42-99.56), respectively. Of 365 adenomatous LNCP, 350 (96.0%) were predicted as adenomatous, with sensitivity, specificity, and accuracy of 95.89% (95% CI 93.31- 97.68), 97.08% (95% CI 92.69- 99.20), and 96.22% (95% CI 94.15- 97.71), respectively.

	Serrated Histopathology, N (%)	Adenomatous Histopathology, N (%)
All lesions	137	365
Predicted Serrated	133 (97.1)	2 (0.5)
Predicted Adenomatous	4 (2.9)	350 (95.9)
Predicted Cancer	0 (0.0)	13 (3.6)
Sensitivity	97.08% (95% CI 92.69-99.20)	95.89% (95% CI 93.31- 97.68)
Specificity	99.45% (95% CI 98.03-99.93)	97.08% (95% CI 92.69- 99.20)
Accuracy	98.80% (95% CI 97.42-99.56)	96.22% (95% CI 94.15- 97.71)

Table 1: Optical Performance.

Conclusion: For LNPCP, optical evaluation had greater than 95% accuracy to differentiate between serrated and adenomatous lesions, forming the basis of a selective resection algorithm.

References: 1. Yamada M, Sakamoto T, Otake Y, Nakajima T, Kuchiba A, Taniguchi H, et al. Investigating endoscopic features of sessile serrated adenomas/polyps by using narrow-band imaging with optical magnification. *Gastrointestinal Endoscopy*. 2015 Jul 1;82(1):108–17.

Disclosure: Nothing to disclose.

PP0937

REAL WORLD EFFICACY OF A COLONIC SELECTIVE RESECTION ALGORITHM FOR LARGE NON-PEDUNCULATED COLON POLYPS

S. Jiang¹, A. Zarrin¹, A. Walia^{1,2}, C. Galorport^{1,2}, W. Xiong³, R. Trasolini^{1,4}, E. Lam^{1,2}, N. Shahidi^{1,2}

¹University of British Columbia, Medicine, Vancouver, Canada,

²St. Paul's Hospital, Gastroenterology, Vancouver, Canada,

³University of British Columbia, Pathology and Laboratory Medicine, Vancouver, Canada, ⁴Vancouver General Hospital, Gastroenterology, Vancouver, Canada

Contact E-Mail Address: sjiangx@gmail.com

Introduction: Endoscopic resection is the primary treatment strategy for most large (≥20 mm) non-pedunculated colonic polyps (LNPCP). A selective resection algorithm with endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) has been shown to be cost effective and optimizes oncologic outcomes in the rectum.^{1,2} However, an algorithm for the colon which incorporates cold snare resection (CSR) has not been described.

Aims & Methods: We sought to evaluate the performance of a colon-specific selective resection algorithm for LNPCP. Consecutive patients > 18 years of age who underwent endoscopic resection for a LNPCP were enrolled in a prospective multi-center observation cohort study (ClinicalTrials.gov NCT05402696). Modality selection was determined by optical evaluation using the Paris and the Japan NBI Expert Team classifications: 1) JNET I – CSR; 2) JNET IIA – EMR; 3) JNET IIB or Paris 0-IIC morphology – en bloc resection (EMR/ESD); 4) JNET III – referral to surgery/multi-disciplinary team review. Algorithm performance was evaluated by technical success (all neoplastic tissue removed at index procedure), procedure-related adverse events, referral to surgery, and recurrence at first surveillance colonoscopy (SC1).

Results: From June 2022 to April 2024, 382 patients underwent 402 procedures for 480 LNPCP. Median age was 67 years (IQR 62-74 years) and 174 (45.5%) were female. Median lesion size was 30 mm (IQR 20-40 mm) and 386 (80.4%) were located in the proximal colon. Cancer was present in 16 (3.3%) LNPCP. Based on optical evaluation, LNPCP were resected by CSR (25.8%), EMR (72.5%), and ESD (1.7%). Out of protocol deviations occurred in 23 (4.8%) LNPCP. Technical success was 97.0%, 100.0% and 100.0% for EMR, CSR, and ESD, respectively (p=0.172). Procedure duration was significantly shorter for CSR (median 10 min; IQR 5-15 min) compared to EMR (15 min; IQR 10-30 min) and ESD (55 min; IQR 38-90 min) (p<0.001).

Perforation was seen in 11 (3.3%), 1 (14.3%) and 0 (0%) patients undergoing EMR, ESD and CSR, respectively (p=0.030). There were no significant differences between resection modalities in their frequencies of clinically significant post-endoscopic resection bleeding (5.2%) or delayed perforation (0.0%). 26 (5.4%) LNPCP were referred to surgery. Of 194 lesions completing SC1, there were 4 recurrences (0.8%), comprised of 1 (0.8%) and 3 (0.9%) in the CSR and EMR group, respectively (p=1.000); all of which were treated endoscopically.

	N (%)	CSR, N (%)	EMR, N (%)	ESD, (N %)	P-value
Lesions attempted	480	124	348	8	
	Serrated	114 (91.9)	20 (5.7)[NS1]	0 (0.0)	<0.001
	Adenomatous	8 (6.5)	302 (86.8)	6 (75.0)	
	Cancer	0 (0.0)	14 (4.0)	2 (25.0)	
	Other	2 (1.6)	12 (3.4)[NS2]	0 (0.0)	
Duration in minutes (median, IQR)	10 (5-15)	15 (10-30)	55 (38-90)		<0.001
Technical success	124 (100.0)	338 (97.1)	8 (100.0)		0.172
Recurrence	1 (0.8)	3 (0.9)	0 (0.0)		1.000

Table 1: LNPCP Characteristics and Outcomes

Conclusion: A colon-specific selective resection algorithm for LNPCP using optical evaluation to select between CSR, EMR, and ESD has high efficacy, efficiency, and safety.

References:

1. Bahin, Farzan F., et al. Wide-field endoscopic mucosal resection versus endoscopic submucosal dissection for laterally spreading colorectal lesions: a cost-effectiveness analysis. *Gut* 67.11 (2018): 1965-1973.

2. Shahidi N, Vosko S, Gupta S, Whitfield A, Cronin O, O'Sullivan T, et al. A Rectum-Specific Selective Resection Algorithm Optimizes Oncologic Outcomes for Large Nonpedunculated Rectal Polyps. *Clin Gastroenterol Hepatol*. 2023 Jan;21(1):72-80.e2.

Disclosure: Nothing to disclose.

PP0938

LONG-TERM EFFICACY OF TRANSANAL DOPPLER-GUIDED HEMORRHOIDAL ARTERY LIGATION WITH MUCOPEXY (HAL-RAR) IN HEMORRHOIDAL DISEASE

C. Jioua¹, J. Benass², H. Laraqui³, M.t. Tajdine³

¹Mohamed V Military Instruction Hospital of Rabat, Gastroenterology unit 1, Rabat, Morocco, ²Mohamed V Military Instruction Hospital of Rabat, Gastroenterology unit 2, Rabat, Morocco, ³Mohamed V Military Instruction Hospital of Rabat, Proctology Surgery Department, Rabat, Morocco

Contact E-Mail Address: chaimaej.cj@gmail.com

Introduction: Doppler-guided artery ligation with Mucopexy, or HAL-RAR, is a minimally invasive surgical technique that allows for better postoperative comfort. An anoscope linked with a light source and a doppler probe allows the proctologist to locate the submucosal branches of the superior rectal artery and to ligate them via a transfixing parietal approach. Mucosal pexis is performed afterward: the mucosa of the prolapsed hemorrhoidal pedicles is vertically sutured, consequently leading to a plication of the prolapsed muco-hemorrhoidal tissue and its reposition inside the canal anal.

Nevertheless, long-term recurrence rate of internal hemorrhoidal disease after this procedure has been poorly studied. The aim of our study is to evaluate the long-term recurrence rate of hemorrhoidal disease post Doppler-guided artery ligation (HAL-RAR) with Mucopexy in our center

Aims & Methods: The aim of our study is to evaluate the long-term recurrence rate of hemorrhoidal disease post Doppler-guided artery ligation (HAL-RAR) with Mucopexy in our center.

Materials and Methods:

An ambispective observational and analytical study was conducted over a 5-year period, from January 2019 to January 2024. Surgical indications included grade II and III internal hemorrhoids that resisted to medical treatment and small localized non-circumferential grade IV hemorrhoids. Patients with external hemorrhoids, bulky grade IV hemorrhoids or pelvic floor disorders were excluded. All data were analyzed using Jamovi version 2.0.0.0 software. Patient characteristics were described as number and percentage for qualitative items and median (interquartile range [IQR]) or mean ($\pm$ standard deviation) for quantitative ones. A p value of ≤ 0.05 was deemed to be significant. Our primary objective was to evaluate the rate of recurrence more than 24 months after surgery. The secondary objectives were to determine the clinical features of relapsing patients.

Results: 114 patients were included in this study. The mean age was 46.5 ± 9.6 years. The sex ratio was 6 (16f, 98H). Preoperatively, 69% (n=79) of the patients reported proctalgia, 53% (n=60) post-defecation rectal pain and 58% (n=66) prolapse.

We staged the internal hemorrhoidal disease according to the Goligher classification, identifying 32 with grade II hemorrhoids, 61 with grade III hemorrhoids and 21 grade IV hemorrhoids. At the end of a median follow-up of 4 years (7-2), 9 patients (7.9%) presented a recurrence, made in 6 cases of a muco-hemorrhoidal prolapse and in 3 cases of post-defecation rectal bleeding. None of our patients presented with anal stenosis or incontinence during the follow-up period. In our study, there was no statistically significant relationship between the recurrence and the preoperative clinical symptomatology (p=0.21) nor with grade of hemorrhoids (p=0.17). Overall, 94% of the patients included were satisfied with this technique. 4 of the patients who relapsed benefited from Milligan-Morgan hemorrhoidectomy. However, they claimed that they were more satisfied following the HAL-RAR procedure

Conclusion: transanal doppler-guided hemorrhoidal artery ligation with mucopexy (HAL-RAR) is a safe, quick, easy to perform technique and can be considered an effective long-term treatment for internal hemorrhoidal disease.

Disclosure: Nothing to disclose.

PP0939

OUTCOMES OF ENDOSCOPIC INTERMUSCULAR DISSECTION FOR RECTAL NEUROENDOCRINE NEOPLASMS: A MULTI-CENTER RETROSPECTIVE STUDY

S. Liao¹, S. Huang¹, W. Gong², H. Lu³

¹South China Hospital of Shenzhen University, Gastroenterology, Shenzhen, China, ²Shenzhen Hospital of Southern Medical University, Gastroenterology, Shenzhen, China, ³Ningbo Medical Center Lihuli Hospital, Gastroenterology, NiBong, China

Contact E-Mail Address: 514718013@qq.com

Introduction: Endoscopic resection is the therapeutic standard for localized rectal neuroendocrine tumors (NETs), yet the innovative endoscopic intermuscular dissection (EID) technique remains under-examined. This study endeavors to assess the clinical outcomes and efficacy of EID in the management of rectal NETs.

Aims & Methods: This retrospective analysis compiled patient data from three esteemed institutions: South China Hospital of Shenzhen University, Shenzhen Hospital of Southern Medical University, and Ningbo Medical Center Lihuli Hospital. Subjects with rectal NETs treated via EID from November 2017 to November 2023 were evaluated. Primary endpoints

included technical and clinical success rates, while secondary endpoints involved procedural duration, postoperative hospital stay, adverse event occurrence, and longitudinal follow-up outcomes.

Results: A total of 18 patients (mean age 46.0; 72.2% male), with an average lesion size of 9.1 mm (SD 2.8), were enrolled, and 44.44% presented lesions over 10 mm in diameter. All patients (100%) reported technical and clinical success. Median operative time was 55 minutes (IQR: 43-67 minutes). Complete resection, validated by histopathological examination indicating G1 classification with clear margins, was accomplished universally. Median postoperative hospitalization was 5.6 ± 1.0 days, devoid of complications such as hemorrhage, perforation, infection, or pain. Over an average of 28.8 months of follow-up (SD 22.9 months), there was no evidence of residual or recurrent disease, nor distant metastasis.

Conclusion: EID is substantiated as a viable and effective technique for rectal NET management. The observed outcomes suggest that EID could be a significant addition to the therapeutic modalities for rectal NETs, meriting further scrutiny in future research.

References:

- [1] Liao Suhuan, Li Bo, Huang Longbin et al. Endoscopic intermuscular dissection in the management of a rectal neuroendocrine tumor. *Endoscopy* 2023; 55: E977-E979.
- [2] Kim J, Kim JH, Lee JY, et al. Clinical outcomes of endoscopic mucosal resection for rectal neuroendocrine tumor. *BMC Gastroenterol* 2018; 18: 77.
- [1] chaefer Marion, Albouys Jérémie, Geyl Sophie, et al. Endoscopic intermuscular dissection of a residual rectal neuroendocrine tumor with high-pressure injection and double-clip traction. *Endoscopy* 2023; 55: E1126-E1127.
- [2] Ichita Chikamasa, Sasaki Akiko, Kawachi Jun, et al. Endoscopic intermuscular dissection for a lower rectal gastrointestinal stromal tumor. *Endoscopy* 2023; 55: E258-E259.
- [3] De Cristofaro Elena, Rivory Jérôme, Jean Masgnaux Louis, et al. Repeat endoscopic intermuscular dissection of the visible scar after noncurative endoscopic intermuscular dissection of a rectal neuroendocrine tumor. *Endoscopy* 2024; 56: E205-E206.
- [4] Edward J Despott, Laura A Lucaciu, Alberto Murino et al. First report of gastric endoscopic intermuscular dissection. *Endoscopy*. 2024, 56: E132-E133.
- [5] Masgnaux Louis-Jean, Yzet Clara, Rivory Jérôme, et al. Endoscopic intermuscular dissection of rectal T1 cancer with adaptive traction: use of additional loops to improve traction directly on the circular muscular layer. *Endoscopy* 2023; 55: E410-E411.

Disclosure: There is no potential conflict of interest for all authors.

FUNCTIONAL OUTCOMES AND QUALITY OF LIFE FOLLOWING
OPEN VERSUS LAPAROSCOPIC VERSUS ROBOT-ASSISTED VERSUS
TRANSANAL TOTAL MESORECTAL EXCISION IN RECTAL CANCER
PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

R. Geitenbeek¹, T. Burghgraef², C. Moes¹, M. Friebe³, R. Hompes⁴,
A. Ranchor⁵, E. Consten¹, MIRECA

¹University Medical Center Groningen, Groningen, Netherlands,

²Meander Medical Center Amersfoort, Amersfoort, Netherlands,

³University Hospital Heidelberg, Heidelberg, Germany, ⁴Academic
Medical Centre, Department of Surgery, Amsterdam, Netherlands,

⁵University of Groningen, University Medical Center Groningen,
Department of Health Psychology, Groningen, Netherlands

Contact E-Mail Address: maikiefriebe@gmail.com

Introduction: The standard surgical treatment for rectal cancer is total mesorectal excision (TME), which may negatively affect patients' functional outcomes and quality of life (QoL). However, it is unclear how different TME techniques may impact patients' functional outcomes and QoL.

Aims & Methods: This systematic review and meta-analysis evaluated functional outcomes of urinary, sexual, and fecal functioning as well as QoL after open, laparoscopic (L-TME), robot-assisted (R-TME), and transanal total mesorectal excision (TaTME). A systematic review and meta-analysis, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statements, were conducted (PROSPERO: CRD42021240851). A literature review was performed (sources: PubMed, Medline, Embase, Scopus, Web of Science, and Cochrane Library databases; end-of-search date: September 1, 2023), and a quality assessment was performed using the Methodological index for non-randomized studies. A random-effects model was used to pool the data for the meta-analyses.

Results: Nineteen studies were included, reporting on 2495 patients (88 open TME, 1171 L-TME, 995 R-TME, and 241 TaTME). Quantitative analyses comparing L-TME vs. R-TME showed no significant differences regarding urinary and sexual functioning, except for urinary function at three months post-surgery, which favored R-TME (SMD [CI] -0.15 [-0.24 – -0.06], $p=0.02$; $n=401$). Qualitative analyses identified most studies did not find significant differences in urinary, sexual, and fecal functioning and QoL between different techniques.

Conclusion: This systematic review and meta-analysis suggests no significant differences in patients' urinary, sexual, and fecal functioning and their QoL between various TME techniques. However, further high-quality, randomized-controlled, and prospective cohort studies are needed to confirm these findings.

Disclosure: Nothing to disclose.

Poster
Liver

Liver

09:00-18:00 / Poster Exhibition

PP0941

COX-2 MEDIATES FERROPTOSIS THROUGH REGULATING NRF2 IN HEPATOCYTES

Z. Yang¹, H. Tong¹, C. Tang¹

¹West China Hospital, Sichuan University, Gastroenterology, Chengdu, China

Contact E-Mail Address: 1255046855@qq.com

Introduction: Ferroptosis is an iron-dependent form of regulated cell death (RCD) characterized by lipid peroxidation and excessive oxidation (1). Cyclooxygenase-2 (COX-2), as a pivotal inducible sensor of inflammation, has been regarded as a remarkable marker in ferroptosis. However, the regulation of COX-2 on hepatic ferroptosis is unknown.

Aims & Methods: The aim of this study is to investigate whether and how COX-2 modulate ferroptosis during liver fibrosis.

Thioacetamide (TAA)-induced liver fibrosis models were constructed, and mice were divided into *Cox-2*^{+/+} NS, *Cox-2*^{-/-} NS, *Cox-2*^{+/+} TAA and *Cox-2*^{-/-} TAA groups. Primary mice hepatocytes (PMHs) were isolated. Mitochondrial morphology, iron metabolism, lipid peroxidation, and major anti-oxidation element GPX4 and Nrf2 were examined.

Results: Our data showed that ferroptosis existed in liver fibrosis induced by TAA. COX-2 knockout markedly attenuated liver ferroptosis through recovery of mitochondrial morphology, reduction of hepatic iron (*Cox-2*^{+/+} TAA vs. *Cox-2*^{-/-} TAA: 0.48±0.12 mg/gram protein vs. 0.22±0.11 mg/gram protein, *p*=0.017), alleviation of lipid peroxidation mainly for polyunsaturated fatty acids (PUFAs) as well as remission of oxidation stress, the content of GSH dropped from 3.63±0.16 μmol/gprot to 2.24±0.24 μmol/gprot (*p*<0.001) with the decrease of GPX4 expression (*p*<0.05). Moreover, experiments in vitro also confirmed that inhibition of COX-2 significantly alleviated PMHs' ferroptosis through activating Nrf2.

Conclusion: Inhibition of COX-2 can effectively alleviate ferroptosis, representing the first demonstration of the functional role of COX-2 to regulate ferroptosis by Nrf2 in liver fibrosis.

References: (1) Li J, Cao F, Yin HL, Huang ZJ, Lin ZT, Mao N, Sun B, Wang G. Ferroptosis: past, present and future. *Cell Death Dis.* 2020 Feb 3;11(2):88. doi: 10.1038/s41419-020-2298-2.

Disclosure: Nothing to disclose.

PP0942

THE ROLE OF OSM/OSMRB SIGNALLING AXIS IN THE DEVELOPMENT OF MASLD-RELATED HEPATOCELLULAR CARCINOMA

J. Nurchis¹, S. Sutti², B. Foglia³, C. Rosso⁴, M. Maggiora¹, C. Bocca³, P. Carucci⁵, U. Chianese⁶, R. Benedetti⁶, S. Gaia⁷, E. Bugianesi⁸, L. Altucci⁶, E. Albano⁹, M. Parola¹⁰, S. Cannito¹

¹University of Turin, Department of Clinical And Biological Sciences, Turin, Italy, ²University Amedeo Avogadro of East Piedmont, Health Sciences and Interdisciplinary Research Center for Autoimmune Diseases, Novara, Italy, ³Università Degli Studi Di Torino, Clinical and Biological Sciences, Torino, Italy, ⁴University of Turin Dept. of Internal Medicine, Torino, Italy, ⁵Città della Salute e della Scienza di torino, Gastroenterologia, Turin, Italy, ⁶Università degli Studi della Campania Luigi Vanvitelli, Dipartimento di Medicina di Precisione, Napoli, Italy, ⁷San Giovanni Battista' Hospital, University of Turin. Italy, Turin, Italy, ⁸AOU Città della Salute e della Scienza University of Torino, Torino, Italy, Medical Sciences, Torino, Italy, ⁹Dept of Medical Sciences, University Amedeo Avogadro of East Piedmont, Novara, Italy, ¹⁰Università di Torino, Dept. of Clinical and Biological Sciences, Unit of Experimental Medicine, Torino, Italy

Contact E-Mail Address: jessica.nurchis@unito.it

Introduction: Oncostatin M (OSM) is a pleiotropic cytokine of the IL-6 family which can bind two different heterodimeric receptors: Glycoprotein 130 (GP130)/ Leukemia inhibitory factor receptor beta (LIFRβ) and GP130/ OSM receptor beta (OSMRβ) that is the receptor able to mediate the most relevant biological effects of OSM in mice. OSM was found to be involved in different aspects related to tumor development and progression in several cancers including hepatocellular carcinoma (HCC). High levels of OSM were found in cirrhotic patients with different etiology carrying HCC.

In particular, patients with HCC developed on a metabolic dysfunction-associated steatotic liver disease (MASLD) background showed increased OSM serum levels that correlate with clinical parameters and disease outcome.

Aims & Methods: The aim of the study is to explore the role of OSM as a cytokine able to modulate the tumor microenvironment and affect crucial events of MASLD-related HCC development and progression taking advantage of:

- a cohort of MASLD patients with HCC and related clinical data to correlate OSM levels with HCC incidence and severity;
- advanced molecular techniques to study gene expression changes on human THP1 macrophage cell lines and liver cancer cell lines (HepG2 cells);
- animal models to investigate the role of OSM/OSMRβ axis in the progression of MASLD-related HCC, in particular mice genetically manipulated to delete OSMRβ in hepatocytes (OSMRβ^{-/-} mice) as well as control WT littermates, submitted to the experimental DEN/CDAAs MASLD-related protocol of liver carcinogenesis.

Results: Data obtained indicate that liver tumor masses in OSMRβ^{-/-} mice differ significantly when compared to those observed in WT mice, including: I) a significant reduction in the angiogenic switch; II) an impaired proliferation indexes; III) a marked decreases in the recruitment/function of TAMs and Tregs lymphocytes. A similar immunosuppressive trend was observed in a small cohort of human patients with MASLD exhibiting fibrosis or HCC. Multiplex immunoassay analyses revealed a significant serum

increase of a subset of cytokines that may be related to the tumor immunosuppressive microenvironment (TIME) (like IL1 β , CCL2, IL8, CXCL13), and transcript levels of these cytokines correlate with OSM expression in MASLD patients. Of interest, higher serum levels of CCL15, a cytokine involved in favoring a TIME, were found to be associated with a worse prognosis in the cohort of MASLD-related HCC patients examined. CCL15 expression was increased in MASLD-related HCC compared to F3/F4 MASLD patients, and correlated with OSM expression.

Moreover, spatial transcriptomics analysis confirmed that CCL15 is mainly expressed by malignant hepatocytes in HCC patients of different etiologies. Furthermore, the transcript levels of CCL15 were increased in mice subjected to the DEN/CDAA carcinogenic protocol compared to mice fed a CSAA control diet or CDAA diet, and were drastic reduced in the DEN/CDAA OSMR $\beta^{-/-}$ mice.

Conclusion: These results suggest a possible crucial role of OSM in the progression of MASLD, contributing to the formation of an immunosuppressive tumor microenvironment that would facilitate tumor evasion mechanisms by the immune system.

Disclosure: Nothing to disclose.

PP0943

TARGETING OF INFLAMMATORY MONOCYTES VIA CCL2/CCR2 SIGNALING AS A THERAPEUTIC STRATEGY AGAINST AUTOIMMUNE HEPATITIS BY USING MACROPHAGE-DERIVED EXTRACELLULAR VESICLES

X. Fan¹, Y. Peng¹, J. Lin¹

¹Sichuan University, Chengdu, China

Contact E-Mail Address: 2021181620212@stu.scu.edu.cn

Introduction: Autoimmune hepatitis is a serious chronic liver disease with immune disorders, histological lesions and liver dysfunction, with a gradually increasing prevalence. Yet the cellular and molecular mechanisms of immune dysregulation in AIH are poorly understood.

Aims & Methods: Using proteomic analysis, we comprehensively profiled the differentially expressed proteins and signaling pathways of liver during human AIH. Then, monocytes and macrophage from blood and livers of AIH patients and controls were analyzed. The recruitment and polarization of monocyte-derived macrophages in AIH and the mechanism of CCL2/CCR2 axis activation were investigated by Concanavalin induced experimental AIH (EAH). The CCL2/CCR2 axis was blocked by CCL2 neutralizing antibody and CCR2 antagonist to determine its effect on AIH mice. Finally, M2 macrophage-derived extracellular vesicles (M2-EVs) were isolated and extracted as drug delivery tool of CCR2 antagonist, and its therapeutic effect on AIH mice was determined.

Results: Proteomic analysis took expression ratio (FC) > 1.5 times and P<0.05 as screening criteria, and a total of 1028 proteins were identified as increased or decreased. KEGG analysis suggested that differential expressed proteins were mainly associated with metabolic processes. The expression of mononuclear macrophage system marker proteins CD14, S100A9, CD163, CD68 and CD11b increased in the liver tissue of AIH patients as revealed by proteomic analysis and immunohistochemistry.

The proportion of classical monocytes in peripheral blood of AIH was increased, which was positively correlated with the levels of ALT and AST of AIH patients. The co-localization analysis of liver tissue suggested that CCL2 originated from Kupffer cells (KC), and the expression of CCR2 increased after circulating monocytes infiltrated liver. The expression of M1 marker in AIH liver tissue increased. AIH mouse models suggest mobilization of inflammatory monocytes on the bone marrow-liver axis and spleen-liver axis. Blocking-up of CCL2/CCR2 axis with CCL2 neutralizing antibody or CCR2 antagonist, respectively, alleviated liver injury in AIH mice, while recombinant CCL2 injection increased recruitment of inflam-

matory monocytes with bone marrow-liver axis and spleen-liver axis to liver, aggravating liver injury. CCR2 antagonist-M2-EV can target circulating mononuclear cells and activated mononuclear macrophages in the liver, respectively, to reduce liver injury in AIH mice.

Conclusion: AIH mediates the recruitment of inflammatory monocytes from bone marrow and spleen to liver through the CCL2/CCR2 axis, which can be inhibited by different methods to reduce liver inflammatory injury in AIH mice. M2-EVs delivers CCR2 antagonists targeting activated pro-inflammatory monocytes and hepato-splenic mononuclear macrophage system in the circulating pool, indicating that CCR2 antagonists-EVs could be a potential agent for liver and monocyte targeted therapy for AIH.

Disclosure: N/A

PP0944

PROTECTIVE EFFECT OF PUNICALAGIN ON ACUTE LIVER INJURY INDUCED BY CARBON TETRACHLORIDE IS ASSOCIATED WITH MACROPHAGE POLARIZATION

Y. Huang^{1,2}, Y. Huang¹, X. Wang¹

¹Fujian Medical University Union Hospital, Department of gastroenterology and Fujian Institute of Digestive disease, Fuzhou, China, ²Fujian Medical University Union Hospital, Fujian Clinical Research Center for Digestive System Tumor and Upper Gastrointestinal Diseases, Fuzhou, China

Contact E-Mail Address: 2003huangyh@sina.com

Introduction: Acute liver injury (ALI) is a common diseases and globally important public health issue. Without properly treatment, ALI rapidly progresses to acute liver failure, which seriously threaten the life of patients. Hepatic macrophages show extreme heterogeneity under both physiological and pathological conditions. The different polarization states of macrophages are closely related to the repair of ALI. Punicalagin (PUN), the most abundant ellagic tannin in pomegranate, is a polyphenolic active substance, exhibiting antioxidant and anti-inflammatory properties to facilitate tissue repair. However, the precise mechanism of PUN on ALI remains unclear.

Aims & Methods: The aim of present study was to explore the protective effect of PUN on ALI and underling mechanism and provide a new strategy and theoretical basement for ALI of PUN treatment. The ALI mouse model was induced by intraperitoneal injection of Carbon tetrachloride (CCl₄) and then treated with PUN. The liver function and pathological damage were detected by biochemical test and Hematoxylin-Eosin (H&E) staining. Enzyme-linked immunosorbent assay (ELISA) was used to detect the expression of pro-inflammatory and anti-inflammatory factors both in peripheral blood The liver non-parenchymal cells was isolated through collagenase perfusion in situ combined with density gradient centrifugation. The total number of macrophages and the proportion of M1/M2 macrophages in liver tissues were detected by multi-color flow cytometry and multiple immunofluorescence staining. The total and phosphorylated expression of nuclear factor-kappa B (NF- κ B), STAT1 and STAT3 in liver tissue were detected by Western blot (WB).

Results: PUN intervention had a protective effect on CCL4-induced ALI mice, as indicated by reducing liver index, attenuating the hydropic degeneration of hepatocytes and areas of liver injury and decreasing the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Meanwhile, PUN down-regulated the concentrations of pro-inflammatory factors IL-6 and TNF- α and up-regulated the expression of anti-inflammatory factor IL-10 in liver tissue and plasma of ALI mice by inhibiting activation of NF- κ B pathway. Multi-color flow cytometry and immunofluorescence staining showed that the total number of CD45⁺F4/80⁺ macrophages in CCL₄-induced ALI mice liver tissue was significantly increased compared

with those in the control group. Monocyte-derived macrophages (MDMs, CD45⁺F4/80⁺CD11b⁺) and M1 macrophages (CD45⁺CD86⁺) were significantly increased in the CCL₄-induced ALI mice liver tissue. Compared with ALI model mice, PUN treatment significantly reduced the total number of CD45⁺F4/80⁺ macrophages, the proportion of MDMs subsets and pro-inflammatory M1 macrophages, accompanied by increasing the proportion of anti-inflammatory M2 macrophages.

The results of multi-color immunofluorescence were consistent with those of flow cytometry. Western Blot showed that the levels of both phosphorylated STAT1 and STAT3 protein was remarked increased in the liver tissue of ALI mice, while PUN treatment inhibited the phosphorylation of STAT1 protein and promoted the phosphorylation of STAT3 protein.

Conclusion: The protective effect of PUN on acute liver injury induced by carbon tetrachloride is associated with microphage polarization.

Disclosure: Nothing to disclose.

PP0945

INFLAMMATORY T CELL RESPONSE INDUCED BY LSECTIN DOWNREGULATION IN CIRRHOSIS CONTRIBUTES TO ALTERATIONS OF THE LIVER-BRAIN AXIS IN AN AGED MODEL OF CIRRHOSIS

S. Martinez^{1,2}, O. Juanola^{2,1}, E. Angel^{2,1}, M.C Hadid¹, P. Boix¹, I. Gomez-hurtado^{1,3}, M.S. García Gutierrez⁴, F. Navarrete Rueda⁴, E. Caparrós^{1,2}, R. Frances^{1,2,3}

¹Universidad Miguel Hernández, Grupo de Inmunobiología Hepática e Intestinal, Dpto. Medicina Clínica, Alicante, Spain,

²IIS ISABIAL, Hospital General Universitario de Alicante,

Alicante, Spain, ³Instituto de Salud Carlos III, CIBERehd,

Madrid, Spain, ⁴Instituto de Neurociencias CSIC-UMH, Grupo de Neuropsicofarmacología Traslacional, Alicante, Spain

Contact E-Mail Address: eangel@umh.es

Introduction: During chronic liver disease (CLD) the loss of the innate receptor C-type lectin LSEctin, expressed mainly by liver sinusoidal endothelial cells (LSECs), is associated to the dysregulation of hepatic immune response and Th17 expansion in the liver. CLD is also accompanied by intestinal dysbiosis, both promoting systemic inflammation and metabolic alterations that affect neurocognitive function through the liver-brain axis. As aging may worsen neurological damage and CLD and its complications are more prevalent in the aging population, we assessed the relationship of LSEctin with liver and neurocognitive damage in an aged model of cirrhosis.

Aims & Methods: CLD was induced by oral administration of carbon tetrachloride (CCl₄) for 12 weeks (w) in young mice (6 w old) and aged mice (40 w old). Liver damage was assessed through histology and molecular biology. Levels of ammonia in different tissues were examined, and a panel of behavioural assays was conducted to assess neurological impairment. Leukocyte populations from brain and liver were studied by flow cytometry (FC).

Results: Hepatic damage was more severe following the induction of CLD in aged mice compared to young ones, exhibiting significantly elevated levels of ALT and AST as well as higher levels of histological markers of fibrosis and leukocyte recruitment. This damage was accompanied by both, a loss of endothelial cells (CD31⁺ in FC) and a decrease in LSEctin expression, especially in old cirrhotic livers.

Interestingly, we found a greater increase of Th17 (1.81 ± 0.58 vs 3.39 ± 0.63 % of CD4 cells, p = 0.003) and CD8 (12.90 ± 2.62 vs 19.22 ± 5.21 % of CD3 cells, p = 0.042) cells in the livers of aged cirrhotic mice as well. Additionally, ammonia concentrations were also higher in cirrhotic old mice than in young ones, in both serum (2.47 ± 0.74 vs 5.18 ± 2.36 nmol/uL, p = 0.015) and the brain (4.65 ± 0.41 vs 5.27 ± 0.86 nmol/uL, p = 0.114). Cirrhotic an-

imals showed motor impairment and a tendency towards anxiety compared to healthy controls. Aged cirrhotic animals exhibited a significantly higher severity index in motor function than the young ones (p = 0.023). Interestingly, only ammonia levels in the brain correlated with results in the open field test (r: -0.544, p = 0.003) and motor evaluation test (r: 0.444, p = 0.018), suggesting a direct relationship between brain ammonia and neurological impairment. Interestingly, we have found higher levels of CD8 cells (12.90 ± 2.62 vs 19.22 ± 5.21 % of CD3 cells, p = 0.042) in old cirrhotic mice' brains compared to young ones.

Conclusion: Aged animals exhibit lower hepatic levels of LSEctin along with more severe liver damage during the experimental cirrhosis model, with higher levels of ammonia and CD8 cells in the brain, correlating with worse neurological function. Immune imbalance in the liver favoured by LSEctin downregulation might modulate immune populations in the brain, contributing to neurocognitive damage. Young cirrhotic animals show similar neurocognitive impairment than healthy aged animals, appointing to a direct contribution of liver damage to neurological impairment during experimental cirrhosis.

Disclosure: Nothing to disclose.

PP0946

WITHDRAWN

PP0947

DIETARY SELENIUM INTAKE IN RELATION TO NON-ALCOHOLIC FATTY LIVER DISEASE ASSESSED BY FATTY LIVER INDEX AND HEPATIC STEATOSIS INDEX; A CROSS-SECTIONAL STUDY ON THE BASELINE DATA OF PROSPECTIVE PERSIAN KAVAR COHORT STUDY

S. Shojaei-Zarghani¹, A.R. Safarpour², M.R. Fattahi², M. Mehrabi¹

¹Shiraz University of Medical Sciences, Shiraz,

Iran, ²Gastroenterohepatology Research Center,

Gastroenterohepatology Research center, Shiraz, Iran

Contact E-Mail Address: shojaeisara@gmail.com

Introduction: Non-alcoholic fatty liver disease (NAFLD) encompasses a variety of hepatic disorders, including steatosis, steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma [1].

The global prevalence of NAFLD is 25.24%, with the highest rates related to the Middle East and South America [2].

This disorder is also becoming one of the most common causes of liver transplantation [3].

There is limited and conflicting evidence on the association between selenium and NAFLD.

Aims & Methods: Therefore, the present population-based cross-sectional study aimed to explore the relationship between dietary selenium intake and the risk of NAFLD.

A total of 3026 subjects from the PERSIAN (Prospective Epidemiological Research Studies in Iran) Kavar cohort study were included in the analysis. The daily selenium intake was evaluated using a semi-quantitative food frequency questionnaire, and energy-adjusted quintiles of selenium intake (µg/day) were calculated. NAFLD was defined as the fatty liver index (FLI) ≥ 60 or the hepatic steatosis index (HSI) > 36. The association between dietary selenium intake and NAFLD was evaluated using logistic regression analysis.

Results: The prevalence rates of NAFLD were 56.4% and 51.9%, based on the FLI and HSI markers, respectively. The odds ratios (ORs) for FLI-defined NAFLD were 1.31 (95% confidence interval (CI): 1.01–1.70) and 1.50 (95% CI: 1.13–1.99) for the fourth and fifth quintiles of selenium intake, respectively, after adjustment for sociodemographic variables, smok-

ing status, alcohol drinking, physical activity, and dietary factors (P trend=0.002). There was also a similar association between selenium intakes and HSI-defined NAFLD (OR=1.34 (95% CI: 1.03–1.75) for the fourth quintile and OR=1.50 (95% CI: 1.12–2.01) for the fifth quintile of selenium intake) (P trend=0.006).

Conclusion: In this large sample study, we observed a weak positive association between dietary selenium intake and NAFLD risk.

References: 1. Sayiner M, Koenig A, Henry L, Younossi ZM. Epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in the United States and the rest of the world. *Clin Liver Dis*. 2016. 10.1016/j.cld.2015.10.001.

2. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016. 10.1002/hep.28431.

3. Shaker M, Tabbaa A, Albeldawi M, Alkhouri N. Liver transplantation for nonalcoholic fatty liver disease: new challenges and new opportunities. *World J Gastroenterol*. 2014. 10.3748/wjg.v20.i18.5320.

Disclosure: None.

PP0948

EVALUATION OF INSULIN RESISTANCE AND LIPID-RELATED INDICES TO PREDICT THE PRESENCE OF NAFLD IN OBESE ADOLESCENTS

A. Yetim¹, M. Sahin², I. Kandemir¹, F. Bas¹

¹Istanbul University, Pediatrics, Istanbul, Turkey, ²Basaksehir Cam and Sakura City Hospital, Gastroenterology, Istanbul, Turkey

Contact E-Mail Address: memduh.sahin@sbu.edu.tr

Introduction: Non-alcoholic fatty liver disease (NAFLD) is an increasingly common health issue in obese children and adolescents. NAFLD does not occur in every obese patient and in some cases, ultrasonography is inadequate for diagnosis. In this study, BMI SDS, WC SDS, triponderal mass index (TPMI), HbA1c, HOMA-IR, TG/HDL, LAP index, triglyceride-glucose (TyG) index and aminotransferase index, used in the diagnosis of NAFLD in obese adolescents, were examined together and their diagnostic values for clinical use were compared.

Aims & Methods: Non-alcoholic fatty liver disease (NAFLD) is an increasingly common health issue in obese children and adolescents. NAFLD does not occur in every obese patient and in some cases, ultrasonography is inadequate for diagnosis. In this study, BMI SDS, WC SDS, triponderal mass index (TPMI), HbA1c, HOMA-IR, TG/HDL, LAP index, triglyceride-glucose (TyG) index and aminotransferase index, used in the diagnosis of NAFLD in obese adolescents, were examined together and their diagnostic values for clinical use were compared.

Results: In the comparison between NAFLD(+) and NAFLD(-) obese adolescent groups, HbA1c, HOMA-IR, aminotransferase index and TyG index were higher in the NAFLD (+) group ($p=0.012$; $p=0.001$; $p=0.012$; $p=0.002$, respectively). There was a positive correlation between liver fat percentage and HOMA-IR, TyG index, aminotransferase index and TG/HDL. According to regression analysis, male gender and HOMA-IR elevation were determined to be significant risk factors for NAFLD.

Conclusion: Even if no NAFLD is detected on USG imaging, evaluation of HOMA-IR and TyG index levels, especially in high-risk patients, will support the diagnosis of NAFLD. In obese adolescents with a HOMA-IR value of ≥ 4.55 and a TyG index value of ≥ 8.38 , evaluation should be made with liver MRI, even if no NAFLD is detected on ultrasound imaging. A basic chart with ALT, HOMA-IR, TyG, and gender with a diagnostic accuracy of 80%, positive predictive value of 82.5% and sensitivity of 80% may assist in diagnosis of NAFLD in obese adolescents.

Disclosure: None.

PP0949

MYELOID-MAS DEFICIENCY MODULATES THE GUT-LIVER AXIS IN MASLD MICE: AN UNFORESEEN PROTECTIVE MECHANISM

H. Jia¹, S. Zhang¹, S. Chen¹, L. Chen¹, J. Li¹, C. Yang¹

¹Tongji Hospital, School of Medicine, Tongji University, Department of Gastroenterology and Hepatology, Shanghai, China

Contact E-Mail Address: sian_jia@163.com

Introduction: The molecular mechanisms underlying lipid metabolism in metabolic dysfunction-associated steatotic liver disease (MASLD) regulated by the gut-liver axis remain poorly elucidated. Previous studies have shown that the important effector protein Mas in the RAS non-classical pathway ACE2/Ang(1-7)/Mas axis has multiple target effects such as regulating glucose metabolism and lipid metabolism, but the specific mechanism is unknown.¹⁻⁵

This study investigated the role of Mas by examining serum bile acid (BA) profile and fecal microbiota composition.

Aims & Methods: Serum and feces samples from MASLD patients and mouse models were analyzed using metabolomics and 16S rDNA. Mas was in vivo evaluated using mice with systemic (*Mas1^{-/-}*) and specific deletion of *Mas1* in myeloid cells (*LysM^{cre}Mas1^{fl/fl}*), intestinal epithelial cells (*Vil1^{cre}Mas1^{fl/fl}*), hepatocytes (*Alb^{cre}Mas1^{fl/fl}*), and endothelial cells (*Cdh5^{cre}Mas1^{fl/fl}*), after being fed with a methionine/choline-deficient (MCD) diet or high fat diet. Mouse bone marrow-derived macrophages and intestinal organoids were prepared for the in vitro experiments.

Results: The relative abundance of serum BA and fecal microbiota showed similar changes in both patients and mouse models with MASLD. In *Mas1^{-/-}*-MCD mice, the reduced chenodeoxycholic acid (CDCA) levels observed in patients with MASLD were effectively restored, along with a notable increase in beneficial gut microbiota like *Akkermansia* and *Bifidobacterium*. These changes were also associated with a significantly improved disease phenotype and enhanced intestinal barrier function. The enriched CDCA inhibits lipid accumulation by activating hepatic and intestinal farnesoid X receptor (FXR) signaling. At the same time, we determined that myeloid cells are the primary effector cells of Mas function through cell-specific knockout of *Mas1* in myeloid cells.

Considering the metabolic reprogramming of colonic epithelial cells facilitated by polyamines derived from macrophages,⁶ our findings highlight the crucial role of Mas in augmenting monocyte polyamine synthesis and promoting intestinal cell proliferation through the Mas-pS6-Arg1 pathway.

Conclusion: Myeloid-Mas deficiency improves the mouse MASLD phenotype by promoting polyamines synthesis, enhancing gut barrier function, increasing

beneficial gut microbiota, and enriching CDCA to activate hepatic and intestinal FXR signaling, thereby reducing lipid accumulation.

References:

1. Santos RAS, Sampaio WO, Alzamora AC, et al. The ACE2/Angiotensin-(1-7)/MAS Axis of the Renin-Angiotensin System: Focus on Angiotensin-(1-7). *Physiol Rev* 2018;98(1):505-53.
2. Hammer A, Yang G, Friedrich J, et al. Role of the receptor Mas in macrophage-mediated inflammation in vivo. *Proc Natl Acad Sci U S A* 2016;113(49):14109-14.
3. Feltenberger JD, Andrade JM, Paraiso A, et al. Oral formulation of angiotensin-(1-7) improves lipid metabolism and prevents high-fat diet-induced hepatic steatosis and inflammation in mice. *Hypertension* 2013;62(2):324-30.
4. Chen S, Lu Z, Jia H, et al. Hepatocyte-specific Mas activation enhances lipophagy and fatty acid oxidation to protect against acetaminophen-induced hepatotoxicity in mice. *J Hepatol* 2023;78(3):543-57.
5. Kong Y, Zhao X, Qiu M, et al. Tubular Mas receptor mediates lipid-induced kidney injury. *Cell Death Dis* 2021;12(1):110.

6. Fritsch SD, Sukhbaatar N, Gonzales K, et al. Metabolic support by macrophages sustains colonic epithelial homeostasis. *Cell Metabolism* 2023;35(11):1931-43.e8.
Disclosure: Nothing to disclose.

PP0950
ROLES OF MODIFIABLE RISK FACTORS IN MEDIATING THE CAUSAL EFFECT OF LIVER CIRRHOSIS ON COLORECTAL CANCER: A TWO-STEP MENDELIAN RANDOMIZATION STUDY

M. Yin¹, S. Xie¹, S. Zhang¹
¹Capital Medical University Affiliated Beijing Friendship Hospital, Beijing, China

Contact E-Mail Address: myyin4984@stu.suda.edu.cn
Introduction: This study aims to investigate the causal estimates of the correlation between liver cirrhosis and colorectal cancer (CRC) and assess the mediation effect of modifiable risk factors direct to clinical treatments.
Aims & Methods: We performed a two-step mendelian randomization (MR) analysis using publicly accessible summary-level data on liver cirrhosis and modifiable risk factors from databases except for the FinnGen, as well as CRC from the FinnGen. Single-nucleotide polymorphisms (SNPs) significantly related to exposures were selected as instrumental variables. A random-effects inverse variance weighted (IVW) method was used in the primary analysis and sensitivity analyses were complemented to ensure the reliability of causal associations. Gene set enrichment analysis (GSEA) was performed to explore the potential biological mechanisms of the causal associations.
Results: In the IVW analysis, liver cirrhosis was causally associated with CRC without adjusting for confounding factors (OR = 1.193, 95%CI = 1.008, 1.411, *p* =0.040). Multivariate MR analysis showed that body mass index, whole body fat mass, waist to hip ratio (WHR) and alcohol consumption were independent risk factors of CRC (*p* values < 0.05). The estimate of the mediator, WHR, is 0.013 and the standard error is 0.006. WHR explained 7.45% of the total effect of cirrhosis on CRC risk. GSEA analysis identified two intersection genes which worked both in liver cirrhosis and CRC tissues, namely SERPINE1 and ARKND1. The potential biological mechanisms might include epithelial-mesenchymal transition, coagulation, inflammatory response, and etc.

Exposure	Outcome	Method	nSNPs	Beta	Standard error	OR (95% CI)	p	Mediation effect (%)
Cirrhosis	Waist-to-hip ratio	IVW	3	0.044	0.009	1.045 (1.026, 1.064)	0.000*	
Cirrhosis	body mass index	Wald ratio	1	-0.041	0.010	0.960 (0.941, 0.980)	0.000*	
Cirrhosis	Alcoholic drinks per week	IVW	4	0.001	0.006	1.001 (0.988, 1.013)	0.914	
Cirrhosis	Whole body fat mass	IVW	4	0.007	0.022	1.007 (0.964, 1.052)	0.745	
Waist-to-hip ratio	Colorectal cancer	Multivariate IVW	228	0.302	0.107	1.352 (1.096, 1.667)	0.005*	0.013 (7.45%)
body mass index	Colorectal cancer	Multivariate IVW	462	0.006	0.090	1.006 (0.843, 1.200)	0.950	
Alcoholic drinks per week	Colorectal cancer	Multivariate IVW	33	-0.040	0.387	0.961 (0.450, 2.050)	0.918	
Whole body fat mass	Colorectal cancer	Multivariate IVW	396	0.045	0.090	1.046 (0.876, 1.250)	0.617	

Table 1. The mediator effect of modified risk factors on the causal association between liver cirrhosis and colorectal cancer.

Conclusion: Genetically predicted liver cirrhosis had potentially risk causal effect on CRC with the mediation by WHR. SERPINE1 and ARKND1 might be candidate targets for preventing CRC in patients with liver cirrhosis.
Disclosure: Nothing to disclose.

PP0951
WITHDRAWN

PP0952
WITHDRAWN

PP0953
PROGRESSION OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS AND NORMAL SERUM AMINOTRANSFERASE LEVELS: A 5-YEAR PROSPECTIVE COHORT

W. Euateerasarun¹, C. Bunchorntavaku¹
¹Rajavithi Hospital, Gastroenterology and Hepatology, Bangkok, Thailand

Contact E-Mail Address: Dr_chalermrat@yahoo.com
Introduction: The incidence and severity of metabolic dysfunction-associated steatotic liver disease (MASLD) are notably higher in individuals diagnosed with type 2 diabetes mellitus (T2DM). However, studies evaluating the progression of MASLD in patients with T2DM and normal serum aminotransferase (ALT) levels are limited.
Aims & Methods: This 5-year prospective cohort study aimed to evaluate the progression of MASLD in T2DM patients with normal ALT. People with type 2 diabetes who had MASLD (defined by controlled attenuation parameter (CAP) >250 dB/min) and ALT levels that stayed normal (defined by ALT ≤40 IU/L for at least two occasions spanning at least six months) at Rajavithi Hospital, Bangkok, from November 2016 to 2017 were included. We excluded patients with viral hepatitis and alcohol consumption exceeding moderate levels. Transient elastography (TE) and CAP measurements were performed at baseline and ≥5 years of follow-up. The cutoffs to define significant and advanced fibrosis were TE ≥8 kPa and TE ≥12 kPa, respectively. All patients were instructed to reduce their weight and abstain from herbal remedies; medications for comorbidities were prescribed without limitations, subject to the physician’s assessment. (most patients were under endocrinologist care.)
Results: The study included 84 patients, 57% of whom were female and had a mean age of 58.5 years. Of these, 62% were obese, with a mean BMI of 28.6 kg/m2. At baseline, the median TE was 6.92±3.35 kPa; 57 (68%) had no significant fibrosis, 22 (26%) had significant fibrosis, and 5 (6%) had advanced fibrosis, and after a 5-year follow-up, the median TE was 6.54±3.57 kPa; 69 (82%) had no significant fibrosis, 15 (18%) had significant fibrosis, and 2 (2%) had advanced fibrosis. During the follow-up, fibrosis decreased in 45 (54%), remained stable in 6 (7%), and increased in 33 (39%) patients, while a small proportion of patients experienced changes in the stages of fibrosis: 1.2% progressed from significant to advanced fibrosis; 17.4% regressed from advanced to significant fibrosis or transitioned from significant to no fibrosis; 12.8% remained stable with significant and advanced fibrosis; and the majority (66.3%) remained without significant fibrosis. A significant factor associated with fibrosis progression was alcohol consumption (*p*=0.013), while the use of angiotensin receptor blockers (*p*=0.042) was associated with fibrosis regression. Significant factors associated with steatosis progression included high baseline BMI (*p*=0.013), an increase in BMI ≥ 5% (*p*=0.04), high fasting plasma glucose, and LDL

cholesterol levels, while a decrease in BMI $\geq 5\%$ ($p=0.002$) the use of calcium channel blockers ($p=0.038$) and coffee consumption >3 cups per day ($p=0.031$) were associated with steatosis regression. ALT elevation during the follow-up occurred in a small proportion of patients, and it was not significantly associated with fibrosis or steatosis progression.

Conclusion: The majority of MASLD patients with T2DM and normal ALT maintained a relatively stable liver disease during 5 years of follow-up. Obesity, weight gain, alcohol consumption, and inadequate metabolic control were all associated with the progression of MASLD, whereas weight loss, coffee consumption, angiotensin receptor blockers, and calcium channel blockers were all associated with the improvement of MASLD.

Disclosure: I have Nothing to disclose.

PP0954

INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM IN POLYCYSTIC LIVER DISEASE: A RETROSPECTIVE STUDY

E. Carbone¹, F. Fianchi¹, I. Spinelli¹, E.C. Nista¹, A. Gasbarrini^{1,2}

¹Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Liver Diseases Unit, CEMAD Centro Malattie dell'Apparato Digerente, Roma, Italy, ²Università Cattolica del Sacro Cuore, Dipartimento di Medicina e Chirurgia Traslazionale, Roma, Italy

Contact E-Mail Address: carbone.eg@gmail.com

Introduction: Intraductal Papillary Mucinous Neoplasm (IPMN) is the most frequent type of pancreatic cystic neoplasm found in the general population. Due to the advances in imaging technologies, the rate of detection of pancreatic cystic neoplasms has been increasing in the past years. A large-scale single-center cohort study conducted in Seoul revealed a prevalence of 1.7% in asymptomatic healthy individuals [1].

Polycystic liver disease (PLD) is a rare disorder characterized by the presence of at least 10 parenchymal cysts in the liver. It may be inherited in an autosomal dominant fashion and, depending on the most prominent phenotype, PLD can be an isolated manifestation in autosomal dominant polycystic liver disease (ADPLD) or it can be an extrarenal manifestation in autosomal dominant polycystic kidney disease (ADPKD) [2,3].

In ADPKD, cysts can be detected also in the pancreas, seminal vesicles and arachnoid membrane [4]. In literature there are isolated reports of association between Intraductal Papillary Mucinous Neoplasm and Autosomal Dominant Polycystic Kidney Disease [5,6].

Aims & Methods: A retrospective observational study was conducted to include all PLD patients followed at CEMAD (Centro Malattie Apparato Digerente) Fondazione Policlinico Universitario A. Gemelli to determine the prevalence of IPMNs in PLD patients (isolated or associated to ADPKD) using abdominal resonance imaging (MRIs) and/or abdominal CT scan, in order to evaluate whether IPMN can be a not acknowledged manifestation of PLD.

Results: Abdominal MRIs and/or abdominal CT scans were examined for 92 PLD patients (56 ADPKD and 36 isolated PLD). IPMNs were detected in 8 patients (8.7% of total), 4 with isolated PLD (11.7% of total isolated PLD patients) and 4 with PLD in ADPKD (7% of total ADPKD patients). As for the IPMN site, body-tail localization of the IPMN was the most frequent detected (50% of total IPMNs).

Conclusion: A high prevalence of IPMN in PLD patients was found, which seems to be higher than prevalence found in the general population (8.7% vs 1.7%). Moreover, IPMN appeared to be more frequent in isolated PLD than in PLD associated with ADPKD (11.1% vs 7%). Our results suggest we should consider the possibility of IPMN being another extrahepatic manifestation of PLD. Of course, further studies in a larger population of patients are needed in order to confirm our findings.

	TOTAL	ISOLATED PLD	PLD IN ADPKD
N	92	36	56
Mean Age (years)	59.7	59.7	59.6
IPMN: N°	8 (8.7%)	4 (11.1%)	4 (7%)
IPMN site: head;	1 (12.5%);	0;	1 (25%);
body-tail;	4 (50%);	1 (25%);	3 (75%);
multifocal	3 (37.5%)	3 (75%)	0

References:

1. Chang YR, Park JK, Jang JY, Kwon W, Yoon JH, Kim SW. Incidental pancreatic cystic neoplasms in an asymptomatic healthy population of 21,745 individuals: Large-scale, single-center cohort study. *Medicine (Baltimore)*. 2016 Dec;95(51):e5535.
2. Lesioni benigne epatiche 2022: linea guida multisocietaria per la pratica clinica
3. EASL Clinical Practice Guidelines on the management of cystic liver diseases. *J Hepatol*. 2022 Oct;77(4):1083-1108. doi: 10.1016/j.jhep.2022.06.002. Epub 2022 Jun 18. Erratum in: *J Hepatol*. 2023 Nov;79(5):1338.
4. Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2024.
5. Sato Y, Mukai M, Sasaki M, Kitao A, Yoneda N, Kobayashi D, Imamura Y, Nakanuma Y. Intraductal papillary-mucinous neoplasm of the pancreas associated with polycystic liver and kidney disease. *Pathol Int*. 2009 Mar;59(3):201-4.
6. Naitoh H, Shoji H, Ishikawa I, Watanabe R, Furuta Y, Tomozawa S, Igashira H, Shinozaki S, Katsura H, Onozato R, Kudoh M. Intraductal papillary mucinous tumor of the pancreas associated with autosomal dominant polycystic kidney disease. *J Gastrointest Surg*. 2005 Jul-Aug;9(6):843-5.

Disclosure: Nothing to disclose.

PP0955

CARDIOVASCULAR DISEASE BURDEN IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS VERSUS MATCHED-CONTROL PATIENTS: DATA FROM THE UNCOVER-MASH LONGITUDINAL COHORT STUDY

E. Bugianesi¹, A. Mehta², K.K. Mangla³, A.S. Chandramouli⁴, K. Grau³, N. Krarup³, A.S. Patel³, K. Opuni³

¹Department of Medical Sciences, University of Turin, Turin, Italy,

²VCU Health Pauley Heart Center, Richmond, VA, United States

of America, ³Novo Nordisk A/S, Søborg, Denmark, ⁴Novo Nordisk

Service Center India Pvt Ltd, Bangalore, India

Contact E-Mail Address: keop@novonordisk.com

Introduction: Metabolic dysfunction-associated steatohepatitis (MASH) is linked to increased risk of cardiovascular (CV) disease (CVD), but many aspects of CVD burden in patients with MASH remain unknown. Particularly, data on the clinical burden of CVD and specific CV events in patients with non-cirrhotic MASH vs those without non-cirrhotic MASH are limited.

Aims & Methods: The aim of this real-world study was to assess CVD burden in patients with and without non-cirrhotic MASH. Patients with MASH were identified using the International Classification of Diseases code for non-alcoholic steatohepatitis (K75.81) from October 2015–June 2022, using data from a federated network (TriNetX). The index date was defined as the date of first MASH diagnosis. Exclusion criteria were viral hepatitis, alcohol use disorder, chronic liver diseases other than MASH or metabolic

dysfunction-associated steatotic liver disease, cirrhosis, decompensated MASH, hepatocellular carcinoma and human immunodeficiency virus. Patients with MASH were matched 1:1 to patients without MASH based on demographics (sex, age, year of start/end of insurance enrolment, and insurance scheme).

Outcomes were CVD prevalence (assessed up to 1 year prior to index) and risk of CV events(s) during follow-up (index date to end of enrolment, death or study end) amongst patients with no history of respective CV event(s) at baseline. For CV risk, cumulative incidence was plotted using Aalen-Johansen curves after adjusting for competing risk of non-CV death. Incidence rate (IR) was calculated per 100 person-years (PY) and hazard ratios (HR) were calculated using Cox proportional hazard models (crude and adjusted for CV risk factors [age, sex, type 2 diabetes (T2D), chronic kidney disease (CKD), obesity, hyperlipidaemia and hypertension]).

Results: In total, 9,642 patients (4,821 with MASH; 4,821 without MASH) were included. In both groups, mean (standard deviation) age was 50.8 (13.2) years and 58.5% were women. Compared with those without MASH, more patients with MASH had hypertension (58% vs 31%), hyperlipidaemia (57% vs 30%), obesity (45% vs 17%), T2D (41% vs 14%) and CKD (6% vs 3%) at baseline.

Prevalence of any CVD was higher in patients with MASH than without MASH (23% vs 12%), as was risk of any CV event (IR: 11.1 vs 4.5 per 100 PY; crude HR [95% confidence interval]: 2.72 [2.30, 3.22], $p < 0.0001$; adjusted HR: 2.27 [1.95, 2.66], $p < 0.0001$). Similar results were seen for individual CV events, namely ischaemic heart disease (IR: 5.3 vs 2.3), cerebrovascular disease (IR: 4.4 vs 2.1), atherosclerosis (IR: 3.9 vs 1.8), and heart failure (IR: 3.2 vs 1.5).

Conclusion: CVD prevalence at baseline and risk of CV events during follow-up were significantly higher in patients with non-cirrhotic MASH compared with matched controls without MASH in a real-world cohort. These data provide additional evidence of the association between MASH and CVD and complement a previous analysis of the unCoVer-MASH study.

Disclosure: EB has acted as a consultant for AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Gilead Sciences, Intercept Pharmaceuticals, Inventiva SA, Merck Sharp & Dohme (UK) limited, Novo Nordisk and Pfizer. AM has no conflicts of interest.

KKM, ASC, KG, NK and ASP are employees of Novo Nordisk A/S and own employee shares/stocks.

KEC has acted as a consultant for Theratechnologies and Novo Nordisk, and has received grants from Bristol Myers Squibb and Novartis.

PP0956

SARCOPENIA IN LIVER TRANSPLANT RECIPIENTS: AN EMERGING CHALLENGE OF LONG-TERM CARE.

A. Santonicola¹, M. Ruotolo¹, P. D'Addieco¹, M. Siniscalchi¹, C. Gizzi¹, C. Ciacci²

¹University of Salerno, Department of Medicine, Surgery and Dentistry, Scuola Medica Salernitana, Salerno, Italy, ²University of Salerno, Medicine Surgery Dentistry, Scuola Medica Salernitana, Salerno, Italy

Contact E-Mail Address: antonellasantonicola83@gmail.com

Introduction: Sarcopenia has been described in 10-70% of patients with cirrhosis and it negatively impacts the outcomes of liver transplant (LT). Less information is known about changes in body composition after LT, especially at long-term follow-up.

Aims & Methods: This study aims to assess the prevalence of sarcopenia and its possible associated factors in a cohort of LT recipients with a long-term follow-up. LT recipients were enrolled from the Liver Transplant Follow-up Center of the University Hospital of Salerno. Demographic characteristics, anthropometric data, data about LT, and prevalence of comorbidities were collected.

Patients underwent a physical examination, laboratory tests (including immunosuppressive drug levels), the Hand Grip Test for the evaluation of the manual grip force (FPM) using a calibrated hand-held dynamometer (DynX digital dynamometer - Akern), and a bioelectrical impedance analysis (BIVA), to assess body composition using the device "BIA 101" (Akern, Florence).

The considered cut-off FPM values were <27 kg for males and <16 kg for females. Appendicular lean mass (ASM) values lower than 20 kg in males and 15 kg in females and ASMM/ h² ratio lower than 7 kg/m² in males and 5.5 kg/m² in females were considered diagnostic for sarcopenia.

Parameter	B	S.E.	Wald	Sig.	Exp(B)	95.0% CI per	
						EXP(B)	EXP(B)
						Lower Limit	Upper Limit
Years of follow-up	.076	.075	1.019	.313	1.079	.931	1.250
BMI (Kg/m ²)	-1.066	.480	4.924	.026	.344	.134	.883
Age (years)	-.021	.058	.126	.723	.980	.874	1.098
Type of immunosuppression	-1.308	1.408	.863	.353	.270	.017	4.272
Etiology of LT	-.547	.462	1.403	.236	.579	.234	1.430
Constant	28.558	13.162	4.708	.030	3E+012		

Table 1. Linear regression model with the presence of sarcopenia at BIVA as dependent variable, and age, years of follow-up, BMI, type of immunosuppressive therapy (calcineurin inhibitors/mTOR inhibitors), and disease etiology at LT as covariates.

Legend: S.E.= Standard Error; BMI= body mass index; LT=liver transplant

Results: 81 LT recipients (57 males, 70.4%) were included. Mean age was 64.7±10.3 years, mean body mass index (BMI) was 27.8±4.3Kg/m²; 25/81 (30.9%) were obese. Seventeen patients (21%) underwent LT for Hepatitis B Virus Cirrhosis, 21 (25.9%) for Hepatitis C Virus Cirrhosis, 11 (13.6%) for alcoholic cirrhosis, 5 (6.1%) for NASH cirrhosis, the remaining for other causes (autoimmune diseases, cryptogenic). The mean follow-up after LT was 14.0 ±7.2 years. Thirty-five/81 (43.2%) LT recipients showed pathological FPM values and 18/81 (22.2%) showed BIVA values diagnostic for sarcopenia.

At logistic regression, the presence of sarcopenia at BIVA was significantly associated with low BMI whereas no significant associations were found with other covariates: age, years of follow-up, BMI, type of immunosuppressive therapy (calcineurin inhibitors/mTOR inhibitors), disease etiology

gy at LT. (Table 1).

Conclusion: Sarcopenia affects a significant percentage of LT patients, also at long-term follow-up. A low BMI seems to be associated with sarcopenia, whereas no correlation was found with the type of immunosuppression and the etiology of the disease at LT.

Disclosure: Nothing to disclose.

PP0957

HYPERHOMOCYSTEINEMIA IS ASSOCIATED TO MASLD INDEPENDENTLY FROM ATHEROSCLEROSIS

C. De Matteis¹, L. Crudele¹, E. Di Buduo¹, S. Cantatore¹, R. Gadaleta¹, M. Cariello¹, P. Suppressa¹, G. Antonica¹, E. Berardi¹, A. Moschetta¹

¹University of Bari "Aldo Moro", Department of Interdisciplinary Medicine, Bari, Italy

Contact E-Mail Address: antonio.moschetta@uniba.it

Introduction: Homocysteine (Hcy) levels are elevated in a variety of conditions, including cardiovascular diseases (CVD), diabetes, hyperinsulinemia, and metabolic-associated steatotic liver disease (MASLD). Although the relationship between MASLD and cardiovascular diseases (CVD) is epidemiologically well established (1), the pathogenetic process linking such conditions has not been completely clarified.

Aims & Methods: In this cross-sectional study, we analyzed Hcy levels in a population of 901 control and metabolic outpatients, considering the presence of MASLD and other dysmetabolic conditions, aiming to detect and deepen the putative role of Hcy in the relationship between liver steatosis and CVD. Hyperhomocysteinemia (HHcy) was defined for Hcy levels ≥ 15 $\mu\text{mol/L}$. Abdominal and carotid ultrasounds and comparison of Hcy levels were performed in all subjects.

Results: HHcy was identified in 140 subjects. Comparisons between subjects with Hcy <15 and Hcy >15 showed that the latter had significantly increased waist circumference (WC) ($p=0.00001$). HDL-c ($p=0.00071$) and 25-OH-Vitamin D ($p=0.00002$) levels were significantly lower, and triglycerides were significantly raised ($p=0.04979$) in subjects with HHcy compared to patients with Hcy <15 .

We evaluated Hcy levels in subjects with and without such conditions, finding that Hcy did not differ between patients with and without carotid plaques ($p=0.2182$), but was different in presence of liver steatosis ($p=0.00192$) (Table 1).

Subjects with HHcy had a strong association with liver steatosis (chi-square $p=0.00001$), whereas we did not find the same association in presence of atherosclerotic plaques (chi-square $p=0.08388$). ORs analysis showed that subjects with HHcy subjects displayed an increased risk of fatty liver, with an OR of 2.1 (95% CI 1.3-3.2, $p=0.00001$), whilst the risk of being diagnosed with atherosclerotic plaques, though slightly increased (OR 1.2, 95% CI 0.8-1.7), was not significant ($p=0.09938$).

We calculated chi-square and ORs for HHcy association with increased BMI and each criterion of the IDF definition of MetS. In the overall population, regardless of the liver steatosis diagnosis, the cardiometabolic risk conditions significantly associated with HHcy were impaired fasting glycemia (FPG) (OR 2.1, 95% CI 1.4-3.1, $p=0.00001$), hypertriglyceridemia (OR 1.8, 95% CI 1.2-2.6, $p=0.00028$) and arterial hypertension (AH) (OR 1.7, 95% CI 1.4-3.1, $p=0.00088$).

In subjects with MASLD, the same analysis highlighted higher ORs, with hypertriglyceridemia showing the highest OR (3.3, 95% CI 2.6-3.8, $p=0.00001$), followed by AH (OR 2.6, 95% CI 1.9-2.9, $p=0.00011$), FPG (OR 2.5, 95% CI 2.1-2.8, $p=0.00083$) and WC (OR 2.4, 95% CI 1.6-2.8, $p=0.00099$), whilst the BMI criterion was not associated with HHcy.

	NO Plaque N=313 (128M:185F)	Plaque N=343 (199M:144F)	p-value
Hcy	11.6 $\pm$ 6.3	12.1 $\pm$ 8.2	0.2182
	NO Steatosis N=321 (147M:174F)	Steatosis N=510 (282M:228F)	p-value
Hcy	12.6 $\pm$ 8.3	18.3 $\pm$ 9.2	0.00192**

Table 1. Comparison of homocysteine (Hcy) levels in patients with and without atherosclerotic plaque and liver steatosis.

Conclusion: Our data suggest an intriguing scenario where the reciprocal correlation between liver steatosis and HHcy may worsen underlying metabolic dysfunctions leading to CVD, and further exacerbate the key pathological features of MASLD. Addressing these interconnected risk factors could represent a crucial strategy for mitigating CVD burden in the increasingly prevalent population of patients with liver steatosis.

References:

(1). Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. Gut 2024;73:691-702.

Disclosure: Nothing to disclose.

PP0958

WITHDRAWN

PP0959

RECURRENT ACUTE LIVER FAILURE (RALF) IN CHILDREN – UNRAVELING THE MYSTERY

N. Dheivamani¹, D. Janakiraman¹, S. T A¹, S.K. R¹, W. Thomas¹

¹Institute Of Child Health, Madras Medical College, Tamil Nadu, Department Of Paediatric Gastroenterology, Chennai, India

Contact E-Mail Address: nirmalanatarajan89@gmail.com

Introduction: Pediatric Acute Liver Failure (PALF) presents a considerable threat to children with a high risk of mortality, despite its rarity. However, the exact cause remains unknown in about half of the cases, emphasizing the need for continued investigation and advancements in our understanding of the condition. Recurrent Acute Liver Failure (RALF) represents an even more uncommon phenomenon, defying diagnosis despite thorough examination. The advent of Whole Exome Sequencing offers hope in uncovering its elusive genetic origins, potentially shedding light on specific genetic disorders underlying this condition.

Aims & Methods: This study aimed to report spectrum of Recurrent Acute Liver Failure (RALF) cases and role of Whole Exome Sequencing (WES) in establishing a cause for RALF, during January 2023 – January 2024 in a tertiary care institute.

Results: We report 4 cases of Recurrent Acute Liver Failure (RALF). First case was a 5 year old 1st born female child of 3rd degree consanguineous marriage who presented with RALF during febrile episodes at 10 months, 18 months and 5 years. Child had low GGT (19 IU/L) cholestasis initially. Etiological workup for Wilson, infective, metabolic was normal. Provisionally, Fever Associated Infantile Liver Failure (ILFS) was thought. But, Upper GI endoscopy revealed esophageal varices confirming portal hypertension, and liver biopsy revealed- acute on chronic hepatitis with cirrhosis, confirming chronic liver disease, which was in contrast to complete liver function resolution seen in ILFS.

Change in gait and expressive language ability was lost from 3 years of age. The child had rigidity, increased deep tendon reflexes, tremor and ataxia on examination. Genetic analysis revealed homozygous (autosomal recessive) likely pathogenic variant of SCYL1 gene mutation leading to Spinocerebellar Ataxia 21.

The second child also presented with RALF at 8 months, 1 year and 1.5 years during febrile episodes, with low GGT Cholestasis. WES revealed pathogenic variant of SCYL1 gene mutation leading to Spinocerebellar Ataxia 21. Child died at 1.5 years of age.

Third child is a 10 year old girl presented with multiple fever-related RALF since 9 years of age and was asymptomatic in between episodes. As the cause was indeterminate after extensive evaluation, WES was done which revealed novel compound heterozygote mutation in RINT1 gene in exon 8 and 12.

The fourth child is a sibling of third case who succumbed with the first acute liver failure following a febrile episode at 12 years of age.

Conclusion: Understanding the genetic basis of PALF is crucial for accurate diagnosis and management. Genetic testing, including targeted gene sequencing or whole-exome sequencing, can help identify these mutations and provide insights into the underlying causes of PALF in affected individuals. This information is essential for personalized treatment approaches and genetic counseling for families. In addition to metabolic and mitochondrial diseases, mutations in genes related to both cytosolic and mitochondrial pathways—such as NBAS, TRMU, IRAS, MARS, RINT1, and SCYL1—have been implicated in pediatric acute liver failure (PALF).

References:

1. Lenz D, Schlieben LD, Shimura M, Bianzano A, Smirnov D, Kopajtich R, Berutti R, Adam R, Aldrian D, Baric I, Baumann U. Genetic landscape of pediatric acute liver failure of indeterminate origin. *Hepatology*. 2024 May 1;79(5):1075-87.
2. Çakır M, İssi F, Güven B, Yakici N, Karaguzel G, Selimoglu A. Rare Causes of Recurrent Acute Liver Failure In Children: Infantile Liver Failure Syndromes. *Klinische Pädiatrie*. 2023 Jul;235(04):245-9.
3. Youssef, Mariam et al. "CALFAN (Low γ -Glutamyl Transpeptidase (GGT) Cholestasis, Acute Liver Failure, and Neurodegeneration) Syndrome: A Case Report with 3-Year Follow-Up after Liver Transplantation in Early Adulthood." *Case reports in hepatology* vol. 2023 3010131. 31 Jul. 2023, doi:10.1155/2023/3010131

Disclosure: Nothing to disclose.

PP0960

FIBROSIS AND INFLAMMATION MARKERS IN PEDIATRIC METABOLIC-ASSOCIATED STEATOTIC LIVER DISEASE

N. Zavhorodnia¹, O. Tatarchuk², I. Klenina², O. Petishko²

¹SI "Institute Gastroenterology of NAMS of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine, ²SI "Institute Gastroenterology of NAMS of Ukraine", Research Department, Dnipro, Ukraine

Contact E-Mail Address: nzavgorodni75@gmail.com

Introduction: The non-invasive identification of liver fibrosis related to metabolic-associated steatotic liver disease is crucial for risk stratification in children [1]. Non-invasive tests, including serum collagen-derived and inflammatory markers, may represent a good surrogate for risk stratification [2].

Aims & Methods: The aim of our study was to investigate the differences in fibrosis and inflammation markers in children with metabolic-associated steatotic liver disease (MASLD) depending on the liver fibrosis presence. 94 patients aged 9 to 17 years (average age 12.15 $\pm$ 2.51 years) were included in the study. According to body mass index, transient elastography (Fibroscan®502 touch, Echosens, France) data patients were divided into 4 groups: 1 group consisted of 27 obese patients with MASLD and liver fibrosis $\geq$ F1 (METAVIR), 2 group - 35 obese patients with MASLD without fibrosis, 3 group - 18 obese patients without MASLD, 4 group (control) - 14 patients with normal weight without MASLD. Serum content of hydroxy-

proline free (HPf) and hydroxyproline protein-bound (HPp/b) according to Osadchuk and glycosaminoglycans (GAG) according to Rimington were evaluated. Serum IL-10 and IL-6 levels were evaluated by an ELISA kit (Wuhan Fine Biotech Co., Ltd, China).

Results: The levels of serum HPp/b were elevated in 100% of 1 group children compared to the control group as well as in 86.9% and 53.8% of 2 and 3 group children respectively ($p < 0.05$). HPp/b /HPf ratio was increased in children of 1 group by 1.4 times ($p < 0.05$), 2 group - by 1.4 times ($p < 0.05$), 3 group - by 1.3 times ($p < 0.05$) in comparison with the control group. Correlation of HPp/b /HPf ratio with CAP ($r = 0.307$; $p < 0.05$), liver stiffness ($r = 0.323$; $p < 0.05$) was found. Serum GAG content in 1 group of children was 1.3 times ($p < 0.05$) higher as well as IL-6 /IL-10 ratio was 5.4 times higher in comparison with the control group ($p < 0.05$).

Conclusion: Thus, an imbalance between the collagen synthesis and degradation in obese MASLD children was revealed combined with a shift towards pro-inflammatory cytokine production, which might promote fatty liver fibrosis development.

References:

1. Armandi A, Michel M, Gjini K, Emrich T, Bugianesi E, Schattenberg JM. Emerging concepts in the detection of liver fibrosis in non-alcoholic fatty liver disease. *Expert Rev Mol Diagn*. 2023;23(9):771-782. doi:10.1080/14737159.2023.2242779
2. Hammerich L, Tacke F. Hepatic inflammatory responses in liver fibrosis. *Nat Rev Gastroenterol Hepatol*. 2023;20(10):633-646. doi:10.1038/s41575-023-00807-x

Disclosure: Nothing to disclose.

PP0961

FROM HEPATIC STEATOSIS TO METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD): A HOSPITAL COHORT OF 450 PATIENTS

L. Elidrissi¹, H. Lahssini¹, M. Tahiri¹, F.Z. Elrhaoussi¹, F. Haddad¹, W. Hliwa¹, A. Bellabah¹, W. Badre¹

¹Ibn Rochd Hospital Center, Hepatology and gastro enterology, Casablanca, Morocco

Contact E-Mail Address: l.lailaelidrissi@gmail.com

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), is now recognized as the leading cause of chronic liver disease. Diagnosis can be made by simple tests available in primary care setting, particularly abdominal ultrasound and FIB4 index. More accurate assessment of fibrosis and specialized follow-up may be necessary to prevent progression to cirrhosis or hepatocellular carcinoma.

Aims & Methods: The aim of our study was to define the prevalence of hepatic steatosis and MASLD in a hospital cohort, to analyze the factors associated with MASLD in our population, and to select patients who need more accurate fibrosis assessment and closer follow up. A prospective descriptive and analytical study was conducted over a 7 months period. After consenting to participate to the study, patients consulting our department for gastroenterological or proctological complaints were included, excluding those followed up for known chronic liver disease.

Epidemiologic and clinical data were collected, followed by abdominal ultrasonography. We first divided our population into 2 groups according to the presence of steatosis on ultrasound. FIB4 index were then calculated for patients with steatosis. Statistical analysis was performed with IBM SPSS Statistics 20.0 software.

Results: Among the 450 patients included, the prevalence of hepatic steatosis was 24.88 %. The mean age was 50.6 (16 - 98 years). Older age ($p = 0.005$), obesity ($p = 0.02$) and diabetes ($p < 0.001$) were significantly asso-

ciated with the presence of steatosis. In the steatotic population, 37.5% were diabetic (88.09% of type 2 diabetes), and 20.5% hypertensive. All these patients were overweight or obese, with a mean BMI of 29.01 kg/m² and a mean waist circumference of 92.7 cm. Seven point fourteen percent were drinking alcohol, with an average intake of 25 g/week. Twenty-two patients (29.34%) were found to have a Fib4 > 1.3.

Comparing these two steatotic subgroups, we found a significant difference in diabetes and obesity, which were significantly more prevalent in the Fib4>1.3 group (p<0.001 and p=0.02, respectively).

Conclusion: Our study confirms the high prevalence of hepatic steatosis, especially MASLD, which becomes a major public health problem. Advanced age, diabetes and obesity were the main risk factors associated with MASLD in our study. These data highlight the importance of systematic screening for fibrosis in these populations, as well as specialized follow-up.

Disclosure: Nothing to disclose.

PP0962

THE GUT MICROBIOME IN OBESE CHILDREN WITH METABOLIC-ASSOCIATED STEATOTIC LIVER DISEASE DEPENDING ON THE GALLBLADDER FUNCTION

N. Zavhorodnia¹, O. Tatarchuk², I. Klenina², O. Petishko²

¹SI "Institute Gastroenterology of NAMS of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine, ²SI "Institute Gastroenterology of NAMS of Ukraine", Research Department, Dnipro, Ukraine

Contact E-Mail Address: nzavgorodni75@gmail.com

Introduction: Numerous studies suggested a pivotal role of gut microbiota and its metabolites in the development and progression of metabolic-associated steatotic liver disease (MASLD) [1]. So, modification of the gut microbiota and/or the metabolites could be beneficial in children with MASLD [2].

Aims & Methods: The aim of our study was to determine the gut microbiome composition in obese children with metabolic-associated steatotic liver disease (MASLD) depending on the contractile function of the gallbladder.

A survey included 73 children aged 10 to 17 years (mean age – 12.15 ± 2.51 years). According to body mass index, transient elastography (Fibroscan®502 touch, Echosens, France), and ultrasound data patients were divided into 3 groups: 1 group – 35 obese MASLD children with gallbladder hypokinesia, 2 group – 30 obese MASLD children with gallbladder normokinesia, 3 group (control) – 8 healthy children with normal weight and gallbladder normokinesia. Contractile gallbladder function was assessed by ultrasound examination after physiological nutritional load.

Qualitative and quantitative intestinal microbiome composition were investigated by bacterial culture method using ten-fold dilutions (10⁻¹ - 10⁻⁹) on a standard set of selective and differential diagnostic culture media for the aerobic and anaerobic microbes isolation. Fecal short-chain fatty acid (SCFA) content was evaluated with gas chromatography (Chromatec-Crystal-5000).

Results: An increase in the fecal butyric acid concentration in 2.0 times (p<0.05) was observed in MASLD children with gallbladder hypokinesia compared to the control group. Also, an increase in the fecal acetic acid concentration in 6.9 times (p<0.05) in 1 group children and in 6.8 times (p<0.01) in 2 group children was found compared to the control group. However, a significant decrease in the fecal propionic acid content in 2.4 times (p<0.001) in MASLD children with gallbladder hypokinesia and in 3.6 times (p<0.001) in MASLD children with gallbladder normokinesia was revealed compared to the control group.

Due to the increased content of fecal acetic and butyric acids, the total content of SCFA (Σ (C2-C4)) was increased in 2.3 times in 1 group children compared to the control group (p<0.05).

Patients with decompensated dysbiosis predominated in 1 group children (37.1% of patients). In 2 group children the subcompensated dysbiosis was more common (36.7% of patients). The concentration of *Lactobacillus* and *Enterococcus* in 1 group patients was significantly lower than in 2 group patients: in 1.9 times (p<0.05) and in 1.4 times (p<0.05), respectively.

Conclusion: Impaired contractile function of the gallbladder in MASLD children is associated with a sharp decrease in the number of major symbionts of the intestinal microbiota as well as increased production of fecal acetic and butyric SCFA.

References:

1. Effenberger M, Grander C, Grabherr F, Tilg H. Nonalcoholic Fatty Liver Disease and the Intestinal Microbiome: An Inseparable Link. *J Clin Transl Hepatol*. 2023;11(7):1498-1507. doi:10.14218/JCTH.2023.00069.
2. Bonsembiante L, Targher G, Maffei C. Non-alcoholic fatty liver disease in obese children and adolescents: a role for nutrition?. *Eur J Clin Nutr*. 2022;76(1):28-39. doi:10.1038/s41430-021-00928-z

Disclosure: Nothing to disclose.

PP0963

PREVALENCE OF MASLD AND ITS ASSOCIATION WITH THE CONSUMPTION OF SUGAR SWEETENED BEVERAGES AMONG A NON-COMMUNICABLE DISEASE COHORT IN RURAL TANZANIA

V. Calvez¹, F. Schiavello¹, J.R. Itambu², P. Belardi², E. Ndile², N. Bazzanini², B. Ndunguru³, A. Liguori¹, B. Mfaume², K. Mutalemwa², A. Gasbarrini⁴, G. Putoto⁵, L. Miele¹

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Catholic University of Rome, Department of Translational Medicine and Surgery, Rome, Italy, ²Tosamaganga Designated District Hospital, Iringa, Tanzania, ³Iringa District Council, Iringa, Tanzania, Iringa, Tanzania, ⁴Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁵CUAMM - Doctors with Africa, Padua, Italy

Contact E-Mail Address: valentino.calvez@gmail.com

Introduction: The global health community has increasingly shifted its focus toward non-communicable diseases (NCDs), recognizing them as a critical public health emergency, particularly pronounced in low and lower middle-income countries (LMICs)[1]. Metabolic dysfunction associated steatotic liver disease (MASLD) is the most common liver disease with a worldwide prevalence of 30%[2], and represent the leading cause of liver-related morbidity and mortality. The prevalence, associated factors, and consequences of MASLD in the African continent, particularly in SSA, remain poorly understood. Indeed, no SSA studies were included in the latest major literature review and meta-analysis on the global epidemiology of MASLD[2].

Tanzania, like many other SSA countries, is undergoing a demographic and epidemiological transition, leading to a marked increase in the burden of NCDs [3].

Aims & Methods: The primary aim of this study was to estimate the prevalence of MASLD among an NCDs population in rural Tanzania. Additionally, secondary objective was to investigate whether the consumption of sugary drinks is associated with MASLD.

This study entailed a retrospective analysis of a prospectively collected cohort of consecutive patients attending the NCDs outpatient clinic of Tosamaganga Hospital, from August 2022 to March 2023. Detailed socio-

demographic, clinical, laboratory, and abdominal ultrasound data were collected for all participants. Additionally, the Beverage Intake Questionnaire (BEVQ-15) was administered to evaluate their everyday drinking behaviors; and for each item, the average daily intake in fluid ounces (fl-oz), and calories (kcal) were calculated.

Results: Of 183 patients enrolled in the cohort, 128/183 (70%) were female. The mean age was 58±13.7 years and mean BMI was 28±6.67 Kg/m². Hypertension affected 141 individuals (77.0%), diabetes affected 77 (42.1%), and both conditions co-occurred in 35 patients (19.1%). Steatotic liver disease was found in 88/183 (48%) patients; with 39/88 (44.3%) of moderate or severe steatosis. MASLD was identified in all steatotic patients. Overall, on average the participants drank a mean of 12.6 fl-oz of SSB (throught sodas). MASLD patients drank an average of 22.4 fl-oz of SSB per day. Multivariable analysis revealed that BMI and daily SSB consumption (fl-oz) exhibited significant associations with MASLD, with respective OR of 1.16 (95% CI: 1.06 – 1.28, p = 0.002) and 1.19 (95% CI: 1.12 – 1.27, p < 0.001).

	Univariable model OR (CI 95%)	P-value	Multivariable model OR (CI 95%)	P-value
Gender male	0.50 (0.26 – 0.96)	0.039	1.28 (0.42 – 3.84)	0.663
Age (years)	1.02 (0.99 – 1.04)	0.087	0.92 (0.94 – 1.03)	0.422
BMI (Kg/m ²)	1.24 (1.16 – 1.33)	<0.001	1.16 (1.06 – 1.28)	0.002
Hypertension (%)	2.53 (1.22 – 5.27)	0.013	1.01 (0.24 – 4.14)	0.994
Hemoglobin (g/dL)	1.40 (1.13 – 1.72)	0.002	1.51 (1.07 – 2.15)	0.020
Sartans	3.58 (1.81 – 7.10)	<0.001	1.63 (0.52 – 5.09)	0.404
Insulin	0.27 (0.08 – 0.63)	0.005	1.63 (0.28 – 9.39)	0.585
Water, daily (fl-oz)	0.99 (0.98 – 1.00)	0.018	0.99 (0.98 – 1.00)	0.150
Sugar-sweetened beverages, daily (fl-oz)	1.19 (1.13 – 1.26)	<0.001	1.19 (1.12 – 1.27)	< 0.001

Conclusion: This study unveils a considerable prevalence of MASLD among the rural Tanzanian NCDs population, affecting nearly half (48%) of all patients studied. Timely identification of MASLD, facilitated by straightforward diagnostic means, holds pivotal importance for patient management and the dissemination of vital lifestyle modification guidance. Furthermore, our study, one of the pioneering efforts to demonstrate a significant association between SSB consumption and MASLD in an African context, underscores the imperative to heighten awareness regarding the risks posed by SSB consumption among NCDs patients and potentially the wider population.

References: [1] Boutayeb A. The Burden of Communicable and Non-Communicable Diseases in Developing Countries. Handbook of Disease Burdens and Quality of Life Measures 2010:531–46. https://doi.org/10.1007/978-0-387-78665-0_32.

[2] Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology* 2023;77:1335–47. <https://doi.org/10.1097/HEP.0000000000000004>.

[3] Gouda HN, Charlson F, Sorsdahl K, Ahmadzade S, Ferrari AJ, Erskine H, et al. Burden of non-communicable diseases in sub-Saharan Africa, 1990–2017: results from the Global Burden of Disease Study 2017. *Lancet Glob Health* 2019;7:e1375–87. [https://doi.org/10.1016/S2214-109X\(19\)30374-2](https://doi.org/10.1016/S2214-109X(19)30374-2).

Disclosure: Nothing to disclose.

PP0964

CLINICAL AND BIOLOGIC DIFFERENCE BETWEEN THE LEAN PHENOTYPE AND THE NON LEAN PHENOTYPE IN NAFLD

A. Nefzi¹, K. Ben Abdallah¹, N. Hemdani¹, A. Nakhli¹, Z. Benzarti¹, B. Bouchabou¹, R. Ennaifer¹

¹Mongi Slim Hopsital, Gastro-enterology and hepatology departement, Tunis, Tunisia

Contact E-Mail Address: khouloud.benabdallah@etudiant-fmt.utm.tn

Introduction: NAFLD has been linked to metabolic syndrome and obesity. Nowadays more lean patients, who do not necessarily have a metabolic syndrome are diagnosed with NAFLD.

Aims & Methods: We aim to determine the clinical and biological characteristics of patients diagnosed with NAFLD, and to compare patients with a lean phenotype to those overweight and obese. A retrospective and descriptive study was conducted in Mongi Slim hospital. Clinical and biological data were retrieved after consulting patient records, in addition to results of transient elastography. Lean phenotype was defined by having a body mass index of less than 25 kg/m².

Results: A total of 78 patients were included in this study, with a mean age of 55 ±10.3 years [26–77 years] and a gender ratio F/M of 1.5. Lean NAFLD was found in 23.1%. Type 2 diabetes, dyslipidemia and hypertension were found in 38.5%, 33.3% and 41% of patients respectively. Significant fibrosis was found in 16.7% of patients. Comparatively to overweight and obese patients, prevalence and diabetes was significantly lower in lean patients (45% vs. 16.7%; p=0.03). These patients also had significantly less abdominal fat than the fore mentioned groupe (waist circonference: 102.8 ±11.3 cm [83–140cm] vs. 83.16 ±6.5 cm [75–95cm]; p<0.001). Although hypertension and dyslipidemia were more prevalent in obese and overweight patients, difference between the two groups was not statistically significant (hypertension: 46.7% vs. 22.2%; p=0.06; Dyslipidemia: 38.3% vs. 16.7% ; p=0.08). Advanced fibrosis was present in comparable amount in the two groups of patients (p=0.1). In terms of prediction of fibrosis, the performance of the fib-4 and NFS score seem to be superior in the lean NAFLD group (p<0,001 respectively).

Conclusion: In this study, the prevalence of metabolic syndrome was greater in overweight and obese patients compared to lean patient all diagnosed with NAFLD. there seems to be no difference in the two groups in terms of prevalence of advanced fibrosis.

Disclosure: Nothing to disclose.

PP0965

WITHDRAWN

PP0966

LONG-TERM ADMINISTRATION OF PEMAFIBRATE PLUS SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITOR IN PATIENTS WITH DYSLIPIDEMIA AND TYPE 2 DIABETES COMPLICATED BY METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE

N. Furusyo¹, H. Ikezaki², A. Miyake¹, A. Hiroshima¹, H. Kitagawa¹, Y. Miyoshi¹, H. Tamura¹, M. Katayama¹, J. Maeda¹, T. Fuchida¹

¹Taihaku Avenue Clinic, Internal Medicine, Fukuoka, Japan,

²Kyushu University Hospital, Department of General Internal Medicine, Fukuoka, Japan

Contact E-Mail Address: nori820furu@icloud.com

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) has become the most common chronic liver disease in recent years. However, medications to improve MAFLD has no standard. Several potential agents have been widely investigated for the treatment of MAFLD. Pemafibrate, a selective peroxisome proliferator-activated receptor- α modulator, has been reported to improve dyslipidemia. Sodium-glucose cotransporter-2 inhibitor (SGLT2i) is an oral antidiabetes drug that promotes glucose excretion into the urine. These medications have potential therapeutic effects on MAFLD.

Aims & Methods: This retrospective study aimed to evaluate the effects of long-term administration of pemafibrate plus SGLT2i in patients with dyslipidemia and type 2 diabetes complicated by MAFLD. Transient elastography (FibroScan; Echosens, Paris, France) was used for liver stiffness measurement (LSM) and assessment of the controlled attenuation parameter (CAP). In total, 594 patients with dyslipidemia and type 2 diabetes complicated by MAFLD started pemafibrate plus SGLT2i treatment between 2019 and 2020 at our hospital. Pre- and post-treatment transient elastography data were compared.

Results: Following 3 years of pemafibrate plus SGLT2i treatment, the median LSM significantly decreased from 10.1 kPa to 6.4 kPa ($P < 0.001$) and the median CAP significantly decreased from 321 dB/m to 219 dB/m ($P < 0.001$), in spite of no significant reductions of the studied patients' weight. Moreover, serum parameters, including hemoglobin A1c, alanine aminotransferase, and gamma-glutamyl transferase, significantly decreased over the study period.

Conclusion: The findings of our study confirm that long-term administration of pemafibrate plus SGLT2i can improve hepatic fibrosis by ameliorating hepatic steatosis and inflammation in patients with dyslipidemia and type 2 diabetes complicated by MAFLD.

References: Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. *J Hepatol.* 2008; 48(5): 835-847.

Yamashita S, Masuda D, Matsuzawa Y. Clinical Applications of a Novel Selective PPAR α Modulator, Pemafibrate, in Dyslipidemia and Metabolic Diseases. *J Atheroscler Thromb.* 2019; 26(5): 389-402.

Mantovani A, Petracca G, Csermely A, et al. Sodium-Glucose Cotransporter-2 Inhibitors for Treatment of Nonalcoholic Fatty Liver Disease: A Meta-Analysis of Randomized Controlled Trials. *Metabolites.* 2020; 11(1): 22.

Murakami K, Sasaki Y, Asahiyama M, et al. Selective PPAR α Modulator Pemafibrate and Sodium-Glucose Cotransporter 2 Inhibitor Tofogliflozin Combination Treatment Improved Histopathology in Experimental Mice Model of Non-Alcoholic Steatohepatitis. *Cells.* 2022;11(4):720.

Disclosure: Nothing to disclose.

PP0967

DRUG-INDUCED LIVER INJURY CAUSED BY METAMIZOLE: IDENTIFICATION OF A PATHOGNOMONIC INJURY PATTERN

S. Weber¹, F. Erhardt¹, J. Allgeier¹, D. Saka¹, N. Donga¹, C. Lange¹, A.L. Gerbes¹

¹LMU Klinikum, Department of Medicine II, Munich, Germany

Contact E-Mail Address: sabine.weber@med.uni-muenchen.de

Introduction: Drug-induced liver injury (DILI) caused by metamizole has gained increasing attention in recent years^{1,2}. However, causality assessment remains a challenge, in particular in patients with multiple drug intake.

Aims & Methods: We further characterized metamizole DILI cases with the goal to identify typical patterns that can help adjudication. To this end, the data of 88 patients with metamizole intake from our prospective study on acute liver injury with potential drug-related cause were analysed. DILI diagnosis and causality assessment was based on clinical, laboratory and histological features as well as expert adjudication³. Alternative causes of liver injury were identified or ruled out by a thorough hepatological work-up.

Results: DILI was associated with metamizole in 63 of 324 DILI patients from our cohort (prevalence 19.4%). Out of the remaining 25 patients with metamizole intake, nine patients suffered from non-metamizole DILI and 16 patients from an alternative cause for liver injury (mainly autoimmune hepatitis [n=10] and biliary obstruction [n=4]). A distinctive phenotype was observed in 45 of the 63 metamizole DILI cases, which was characterized by a relatively long latency from the start of drug intake until recognition of liver injury (median: 51 days), high transaminases at onset (aspartate aminotransferase [AST] 36.9xULN, alanine aminotransferase [ALT] 42.5xULN) and a delayed peak of bilirubin with a median of 7 days after DILI recognition. Patients with this phenotype had higher rates of jaundice (100.0% vs. 62.8%, $p < 0.001$), coagulopathy (73.7% vs. 20.9%, $p < 0.001$) and acute liver failure (40.0% vs. 7.0%, $p < 0.001$) when compared to metamizole DILI cases without this clinical picture, non-metamizole DILI and non-DILI controls, however remission rates did not differ significantly when compared to the controls (71.1% vs. 76.7%, $p = 0.481$) or to the recovery rates described in larger registry studies on DILI in general⁴. Overall, adverse outcome as defined by death or liver transplantation was observed in nine patients with metamizole DILI (14.3%). On multivariate analysis, AST and INR at DILI recognition were the only parameters independently associated with this endpoint. Regarding prediction of an adverse outcome INR had the highest discrimination (c-statistic 0.89, 95% confidence interval [CI]: 0.74-0.99) and with this performed better than Hy's law, transaminases, bilirubin or the model for end-stage liver disease (MELD) score at baseline in terms of prognosis. INR at a cut-off of ≥ 1.95 showed a sensitivity and specificity as high as 77.8% and 93.5% for an adverse outcome.

	Metamizole signature pattern (n=40)	Control patients [†] (n=43)	p
AST at onset (xULN)	36.9 (2.5-115.3)	12.7 (1.2-213.8)	<0.001*
ALT at onset (xULN)	42.5 (3.9-138.5)	15.1 (0.8-223.0)	<0.001*
TBIL at onset (xULN)	9.8 (0.2-24.3)	1.4 (0.2-22.3)	<0.001*
Time to peak ALT (days)	1 (0-18)	1 (0-50)	0.467
Time to peak TBIL (days)	7 (0-22)	3 (0-82)	0.029*
Coagulopathy	33 (73.7 %)	9 (20.9 %)	<0.001*
Acute liver failure	18 (40.0 %)	3 (7.0 %)	<0.001*
Remission	32 (71.1 %)	33 (76.7 %)	0.481
Time to remission (weeks)	10 (3-168)	14 (1-87)	0.209

[†]Control cases are comprised of other metamizole DILI (n=18), non-metamizole DILI (n=9) and non-DILI cases with metamizole intake (n=16).

Conclusion: Patients with DILI due to metamizole can present with a specific pattern which can help to identify metamizole as the causative agent and avoid erroneous association of liver injury with innocent bystander medication. Outcome, however, is not associated with this clinical picture and should rather be predicted by AST and especially INR at onset.

References: 1 Sebode M, Reike-Kunze M, Weidemann S, et al. Metamizole: An underrated agent causing severe idiosyncratic drug-induced liver injury. *Br J Clin Pharmacol.* 2020;86(7):1406-15.

2 Weber S, Benesic A, Neumann J, et al. Liver injury associated with metamizole exposure: features of an underestimated adverse event. *Drug Saf.* 2021;44(6):669-80.

3 Bjornsson ES, Stephens C, Atallah E, et al. A new framework for advancing in drug-induced liver injury research. *The Prospective European DILI Registry.* *Liver Int.* 2023;43(1):115-26.

4 Chalasani N, Bonkovsky HL, Fontana R, et al. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN prospective study. *Gastroenterology.* 2015;148(7):1340-52 e7.

Disclosure: Sabine Weber and Alexander L. Gerbes received funding from TransBioLine (Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease; Grant Agreement ID: 821283). The TransBioLine project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 821283. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

PP0968

THROMBOXANE A₂ RECEPTOR SIGNALING IN MACROPHAGES PROMOTES LIVER REPAIR AFTER ACETAMINOPHEN-INDUCED LIVER INJURY BY INCREASING ACCUMULATION OF REPARATIVE MACROPHAGES AND PRODUCTION OF HGF

M. Tanabe^{1,2,3}, Y. Ito^{1,2}, K. Hosono^{1,2}, C. Kusano³, H. Amano^{1,2}

¹Kitasato University School of Medicine, Pharmacology, Sagamihara city, Japan, ²Kitasato University School of Medicine, Molecular pharmacology, Sagamihara city, Japan, ³Kitasato University School of Medicine, Gastroenterology, Sagamihara city, Japan

Contact E-Mail Address: mina.t@kitasato-u.ac.jp

Introduction: Acetaminophen (APAP) overdose causes severe acute liver failure. Impaired liver repair and regeneration after APAP hepatotoxicity leads to failed recovery and mortality. Accumulating evidence indicates that macrophages play an important role in liver repair after APAP-induced liver injury; however, underlying mechanisms of involvement of macrophages remain unknown.

Aims & Methods: We examined the role of endogenous thromboxane A₂ (TXA₂) in macrophages in liver repair after APAP-induced liver injury. APAP (300 mg/kg, ip) was administered to macrophage-specific thromboxane prostanoid receptor (TP) deficient mice (TP^{Δmac}) and control mice (Cont).

Results: Compared with Cont, TP^{Δmac} exhibited severe liver injury as indicated by increased levels of ALT, necrotic area, and pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) and decreased expression of hepatocyte growth factor (HGF) and PCNA, a marker of hepatocyte proliferation at 48 h after APAP treatment. CD68-positive macrophages less accumulated in the livers from TP^{Δmac}, accompanied by reduced expressions of chemokines such as CCL2, CCL7 and CCL9. Flow cytometry analysis revealed that the numbers of pro-inflammatory macrophages (M1) in TP^{Δmac} were higher than Cont, while the numbers of reparative macrophages (M2) in TP^{Δmac} were lower than Cont. In cultured bone marrow-derived macrophages

from TP^{Δmac}, M1-related gene expressions were increased and M2-related gene expressions were decreased. HGF treatment in TP^{Δmac} attenuated liver injury and promoted liver repair after APAP-induced liver injury.

Conclusion: TP receptor signaling in macrophages promoted liver repair after APAP-induced liver injury by accumulation of reparative macrophages and production of HGF in the livers.

Disclosure: Nothing to disclose.

PP0969

GLUCAGON-LIKE PEPTIDE RECEPTOR 1 ANALOGUE COULD REDUCE ALCOHOL INTAKE IN PEOPLE WITH ALCOHOL USE DISORDER: A SYSTEMATIC REVIEW

M. Subhani¹, A. Dhanda², J. King³, F.C Warren⁴, S. Creanor⁴, M.J Davies⁵, S. Bawden⁶, P. Gowland⁶, R. Bataller⁷, G.P. Aithal⁸
¹University Hospitals Nottingham and University of Nottingham, Gastroenterology, Nottingham, United Kingdom, ²University of Plymouth, Faculty of Health, Plymouth, United Kingdom, ³Loughborough University, National Centre for Sport and Exercise Medicine, School of Sport, Exercise and Health Sciences, Loughborough, United Kingdom, ⁴University of Exeter, Faculty of Health and Life Sciences, Exeter, United Kingdom, ⁵University of Leicester and the National Institute for Health Research Leicester, Diabetes Research Centre, Leicester, United Kingdom, ⁶University of Nottingham, Sir Peter Mansfield Imaging Centre School of Physics and Astronomy, Nottingham, United Kingdom, ⁷Hospital Clínic, Liver Unit, Barcelona, Spain, ⁸NIHR Nottingham Digestive Diseases Biomedical Research Unit, Nottingham University Hospitals, Nottingham, United Kingdom

Contact E-Mail Address: mohsan.subhani@nottingham.ac.uk

Introduction: Alcohol use disorder (AUD) remains a significant global health concern. Despite the availability of various pharmacological and behavioural interventions, alcohol-related mortality is rising.

Aims & Methods: This systematic review aimed to critically evaluate the existing literature on the role of glucagon-like peptide receptor 1 analogues (GLP-1 RAs) in people with AUD.

Electronic search was conducted on Ovid Medline, EMBASE, Cochrane Central and PsycINFO from inception to March 2024. Grey literature was searched. The primary outcome of the review was to explore the impact of GLP-1 RAs on self-reported alcohol intake in people with AUD. The extracted data were organized and synthesized to identify key findings and trends evaluating the potential impact of GLP-1 RAs on alcohol consumption in AUD. Narrative synthesis was done to provide a coherent and detailed narrative of the evidence, highlighting significant findings, relationships, and implications. PROSPERO (CRD42024531982).

Results: Seven studies comprising 88,163 participants were included; of these, 38,746 (43.9%) were treated with GLP-1 RAs. Pooled mean age was 49.6 years (SD=10.5), 56.9% (n=50,151/88157) were male, and if the study provided ethnicity 87.5 % (n=426/487) were white. An RCT comparing exenatide with placebo found no significant difference in self-reported alcohol measures at 26 weeks (percentage point reduction: heavy drink days: 6.0, 95% CI -7.4 to 19.4, p=0.37; total alcohol consumption: -42.0 g/30 days, 95% CI -507.7 to 423.7, p=0.86; days without alcohol use: -10.5, 95% CI -2.6 to 23.4, p=0.11). But in participants (n=30) with BMI > 30 kg/m², exenatide compared with placebo was associated with a significant reduction in heavy drinking days (percentage point reduction 23.6, 95% CI, -44.4 to -2.7, P=0.034) and in total alcohol consumed (-1,205 g, 95% CI, -2,206 to -204, P= 0.026). Another RCT showed dulaglutide users compared to placebo were 29% more likely to reduce weekly alcohol consumption (relative effect size: 0.71, p=0.04). In an observational study, authors reported with

liraglutide (n=42) 21.4% stopped and 78.6% reduced drinking ($p<0.05$). A prospective cohort control study showed people on semaglutide or tirzepatide (n=153) compared to no medication significantly reduced number of alcoholic drinks consumed and binge drinking ($p<0.05$). In a case series (n=6) semaglutide use was associated with a 9.5-point reduction in alcohol use disorder identification test score. A population-based study from Denmark (n=87,676) reported that at 90 days people on GLP-1 RAs compared to one on dipeptidyl peptidase-4 inhibitors (DPP-4) were less likely to experience alcohol-related events (HR 0.46, 95% CI 0.24 to 0.86) and effect remained positive long term (356-4619 days: HR 0.72, 95% CI 0.60–0.86). Two qualitative studies examining Reddit social media posts from people on GLP-1 RAs noted over two-thirds addressed a reduction in alcohol consumption. Functional brain imaging suggested significant reductions in cue reactivity were observed in the ventral striatum [$F(1,31) = 4.744$, $P = 0.037$, partial $\eta^2 = 0.133$], dorsal striatum [$F(1,31) = 6.124$, $P = 0.019$, partial $\eta^2 = 0.165$], and putamen [$F(1,31) = 4.730$, $P = 0.037$, partial $\eta^2 = 0.132$] after 26 weeks of exenatide treatment compared with placebo (Table 1). Two studies were of high quality, two medium, and three low.

Conclusion: GLP-1 RAs show promise in reducing alcohol consumption and improving outcomes in individuals with AUD, although heterogeneous study findings warrant further research to establish true effectiveness and safety of GLP-1 RAs in AUD.

References: 1. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* (London, England). 2018;392(10152):1015-35.

2. Klausen MK, et al. The role of glucagon-like peptide 1 (GLP-1) in addictive disorders. *British Journal of Pharmacology*. 2022;179(4):625-41.

3. Klausen MK, et al. Exenatide once weekly for alcohol use disorder investigated in a randomized, placebo-controlled clinical trial. *JCI Insight*. 2022;7(19).

4. Probst L, et al. Effects of dulaglutide on alcohol consumption during smoking cessation. *JCI Insight*. 2023;8(22).

5. SANJAY KALRA BK, AMIT SHARMA. Change in Alcohol Consumption Following Liraglutide Initiation: A Real Life Experience. *Clinical Diabetes* 2024.

6. Quddos F, et al. Semaglutide and Tirzepatide reduce alcohol consumption in individuals with obesity. *Scientific Reports*. 2023;13(1):20998.

7. Bremmer MP, Hendershot CS. Social Media as Pharmacovigilance: The Potential for Patient Reports to Inform Clinical Research on Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists for Substance Use Disorders. *Journal of Studies on Alcohol and Drugs*. 2023;85(1):5-10.

8. Wium-Andersen IK, et al Osler M. Use of GLP-1 receptor agonists and subsequent risk of alcohol-related events. A nationwide register-based cohort and self-controlled case series study. *Basic & Clinical Pharmacology & Toxicology*. 2022;131(5):372-9.

Disclosure: Nothing to disclose.

PP0970

ETIOLOGY, PROGNOSIS AND CLINICAL COURSE OF TOXIC HEPATITIS: A SINGLE CENTER EXPERIENCE

M.S. Saylam¹, D. Turan Gökçe², D. Ari², M.F. Acehan¹, İ. Ateş¹, M. Akdoğan Kayhan²

¹Ankara Bilkent City Hospital, Internal Medicine, Ankara, Turkey,

²Ankara Bilkent City Hospital, Gastroenterology, Ankara, Turkey

Contact E-Mail Address: dilaraturan89@yahoo.com

Introduction: Toxic hepatitis is a significant hepatic condition that can occur due to drugs, fungi, herbal agents and supplements, sometimes progressing fulminantly and resulting in transplantation or mortality. As it is a diagnosis of exclusion, it can be challenging to establish and the etiological factors vary societally. In our study, we investigated the etiology, epidemiology, factors related to prognosis, and clinical outcomes of patients diagnosed and treated for toxic hepatitis.

Aims & Methods: The demographic characteristics, etiological factors, laboratory and imaging results, biopsy findings, and information about the drugs used in the treatment of 254 patients hospitalized and treated for toxic hepatitis between February 2019 and June 2022 at Ankara Bilkent City Hospital were retrospectively examined. After evaluating the results according to the RUCAM scale, patients interpreted as possible and highly probable were included in the study, and they were classified based on severity as mild, moderate, severe or fatal.

Results: Of the patients included in the study, 60.6% were female, and 30.3% of these patients presented to the hospital with jaundice symptoms. The mean age of the patients was 43.9 years. Hepatocellular damage was observed in 68.5% of the developed liver toxicities. The most common etiological factors were antibiotics and NSAIDs in sequence. When antibiotic drugs were evaluated separately, amoxicillin-clavulanate (9.8%) was considered the most common antibiotic causing toxic hepatitis, and dextroketoprofen (9.1%) was identified as the most common NSAID. A total of 45 patients (18.1%) were associated with herbal and dietary supplements, while 18 patients (7.1%) were related to mushroom consumption in the etiology. Of the patients included in the study, 56% had a moderate or severe hepatitis course, 3 (1.18%) patients progressed to liver transplantation, and 6 (2.5%) patients died, including one post-transplant. The severity of toxic hepatitis was mild in 109 participants (42.9%), moderate in 89 patients (35.0%), severe in 48 patients (18.9%), and fatal in 8 patients (3.1%). In 5.9%, there was worsening of the disease (transition from mild or moderate severity to severe or fatal groups) after admission. In our study, 14.3% of patients in the severe-fatal group died due to acute liver failure or underwent liver transplantation. Both groups exhibited a dominant pattern of hepatocellular-type damage, and there was no difference in the evaluation of etiological factors between the groups. When biochemical parameters were evaluated, elevation in ALT, AST, LDH, initial and peak total bilirubin, direct bilirubin, initial and peak INR, prolonged prothrombin time, and low albumin were significant in both the severe patient group and the group admitted to intensive care. Liver biopsy was performed on 60 of the 254 patients included in the study.

Conclusion: In our study, the median age, gender distribution, dominant injury type, and the most commonly detected agents in etiology (NSAIDs and antibiotics) and dominant were consistent with the literature. Factors such as the consumption of Toxic hepatitis is a disease that can be challenging to diagnose and treat. Given that our center receives a high number of patient admissions, accepts patients from surrounding areas, and serves as a transplant center, we believe that the data we have obtained can closely approximate current and real data. We also believe that our study on these 254 patients will contribute to the literature in terms of etiological, epidemiological, and prognostic insights.

Disclosure: Nothing to disclose.

PP0971

DRUG-INDUCED HEPATITIS: ETIOLOGICAL PROFILE AND THERAPEUTIC MANAGEMENT

H. El Hiouy¹, H. El Bacha², S. Mechhor³, M. Cherkaoui Malki⁴, N. Benzzoubeir¹, I. Errabih⁵

¹Mohammed V university - faculty of medicine and pharmacy, hepato-gastro-enterology and proctology (clinic B) - Ibn Sina university hospital center, Rabat, Morocco, ²Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ³Ibn Sina Hospital, Medecine B, Rabat, Morocco, ⁴University Hospital Ibn Sina, Gastroenteroly B, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: houdaelhiouy@gmail.com

Introduction: Drug-induced hepatotoxicity is one of the main forms of iatrogenic pathology, which is often under-diagnosed. Numerous drugs are implicated and can cause hepatic damage reproducing the whole spectrum of non-iatrogenic liver pathology, ranging from a simple transient disturbance of the liver balance to fulminant, life-threatening hepatitis.

Aims & Methods: The aim of our work is to study the etiological profile and therapeutic management of drug-induced hepatitis.

This is a retrospective descriptive monocentric study from January 2010 to August 2023 of patients with drug-induced hepatitis in the Hepato-Gastro-Enterology and Proctology Department "Medicine B".

Diagnosis was based on the elimination of infectious, immunological and toxic causes of hepatitis. For all patients, viral serologies for hepatotropic viruses and a pharmacovigilance investigation were carried out before concluding that the cause was drug-induced.

Results: 194 patients were included in our study, with a mean age of 44.2 years, ranging from 23 to 84 years. Female predominance was observed, with 110 women (56.7%) versus 84 men (43.2%), so, a F/H sex ratio of 1.3. In 59 cases (30.4%), liver damage was discovered by chance during a biological check-up. In the other cases, clinical manifestations were dominated by jaundice in 112 patients (57.7%), followed by asthenia in 42 patients (21.6%), pruritus in 35 cases (18%) and fever in 17 cases (8.7%). Liver function tests showed cytolysis in 97 cases (50%), mixed disease in 74 patients (38.1%), and cholestasis in 23 patients (11.8%). The time to onset of clinical or biological signs of hepatotoxicity ranged from 03 days to 09 months. Severe acute hepatitis occurred in 70 cases (36%), including 48 cases (24.7%) of fulminant hepatitis. Viral serologies were negative in all cases. Liver biopsy was consistent with drug-induced hepatitis in 35 cases (18%). The main drugs implicated were anti-tuberculosis drugs in 110 cases (56.7%), followed by immunosuppressants, particularly azathioprine in 44 cases (22.6%), then paracetamol in 23 cases (11.8%), antidepressants in 6 cases (3%), and non-steroidal anti-inflammatory drugs (NSAIDs) in 3 cases (1.5%). Other drugs were less frequently associated with liver dysfunction, such as: allopurinol, fluconazole (1 case: 0.5%), synthetic antithyroid drugs (1 case: 0.5%), antiepileptics (Carbamazepine) (1 case: 0.5%), hypolipidemics (1 case: 0.5%), ciprofloxacin (1 case: 0.5%), anti TNF (Adalimumab) (1 case: 0.5%), and anti-angoretics (1 case: 0.5%).

Discontinuation of the treatment in question was considered in all patients. Patients with fulminant acute hepatitis were managed in intensive care, and N-acetylcysteine was introduced in patients admitted for paracetamol-induced hepatitis. The outcome was favorable in 160 patients (82.4%), while 34 patients (17.5%) died.

Conclusion: Drug-induced hepatitis is a delicate condition, given its polymorphic presentation and the diversity of potentially hepatotoxic drugs prescribed. Diagnosis is based on the elimination of other possible causes of liver dysfunction, a suggestive or compatible chronology between the administration of the drug and the onset of hepatitis, and a favorable evolution

after discontinuation of the drug. Prevention requires compliance with prescribing rules, early detection of signs of therapeutic intolerance and rigorous monitoring of progress under treatment.

Disclosure: Nothing to disclose.

PP0972

ELEVATED SERUM FERRITIN LEVELS AS A PREDICTIVE FACTOR OF SEVERITY AND COMPLICATIONS IN CIRRHOTIC PATIENTS

M. Rahaoui^{1,2}, F. Amri^{1,2}, H. Aissaoui³, K. Chahi^{1,2}, O. Elmqaddem^{1,2}, H. Koulali^{1,2}, Z. Abdelkrim^{1,2}, Z. Ismaili^{1,2}, G. Kharrasse^{1,2}

¹Mohammed VI University hospital center, Department of Hepato-gastroenterology, Oujda, Morocco, ²Digestive Disease Research Laboratory, Medical School, Mohammed first University, Oujda, Morocco, ³Laboratory of Epidemiology, Clinical Research, and Public Health, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco

Contact E-Mail Address: rahaouimaissae@gmail.com

Introduction: Cirrhosis is a chronic liver disorder characterized by fibrosis, leading to liver dysfunction and portal hypertension. Ferritin has emerged as a simple biomarker associated with prognosis in cirrhotic patients. Our study aimed to determine the presence of a significant relationship between serum ferritin levels and the incidence of complications.

Aims & Methods: In this retrospective descriptive and analytic study, serum ferritin levels were assessed in adult cirrhotic patients upon admission to our Hepato-Gastroenterology department at a University Hospital between March 2017 and March 2023. Subsequently, patients were evaluated for the occurrence of complications within the following year. Serum ferritin levels normal range were of 22 to 275 ng/ml for men and 4.63 to 204 ng/ml for women.

Results: Our study comprised 140 cirrhotic patients with varied etiologies, including 72 females and 68 males, with an average age of 58 ± 14.88 years (range: 21 to 90). These patients presented with varying disease stages and diverse etiologies.

Among patients with elevated ferritin levels, 86.4% experienced complication within the year following the measurement, compared to only 43.8% of patients with normal ferritin levels. The most commonly observed complication was hepatic encephalopathy, followed by variceal bleeding, and ascites. Our findings suggest a significant association between serum ferritin levels and the occurrence of complications within the subsequent year ($p < 0.001$).

These patients were distributed across different disease stages: 50 had Child-Pugh score A, 66 had Child-Pugh score B, and 24 had Child-Pugh score C. We used the Anova test to compare the average ferritin levels among the three groups. we found a significant difference between ferritin values in the 3 groups: A (88.27 ± 152), B (528 ± 1209), C (105 ± 128) ($p = 0.027$). And by using post Hoc tests, we found that this difference was significant between group A and B ($p = 0.04$), but non significant difference between A and C, and B and C.

Conclusion: In conclusion, our study reveals a significant association between elevated serum ferritin levels and increased incidence of complications in cirrhotic patients, highlighting ferritin as a potential prognostic marker for disease progression.

References: <https://www.sciencedirect.com/science/article/abs/pii/S1521691811000357?via%3Dihub>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6687222/>

Disclosure: Nothing to disclose.

PP0973

DIFFERENTIAL EXPRESSION OF P53 PROTEIN ISOFORMS AND THEIR ROLE IN THE PATHOGENESIS OF SPONTANEOUS BACTERIAL PERITONITIS

C. Macek¹, D. Tümen¹, C. Kunst¹, K. Gülow¹, M. Müller-Schilling¹

¹University Hospital Regensburg, Department for Internal Medicine 1, Regensburg, Germany

Contact E-Mail Address: celina.macek@stud.uni-regensburg.de

Introduction: Translocation of intestinal bacteria into the mesenteric lymph nodes and ascites plays a central role in the development of spontaneous bacterial peritonitis (SBP), a severe complication of liver cirrhosis. Immunosuppression, bacterial dysbiosis and increased intestinal permeability favor bacterial translocation. We have shown that the mucus layer in the intestine of patients with liver cirrhosis is thinner, supporting direct contact of bacteria with epithelial cells. This leads to degradation of cell-junctions (Haderer et al., Gut 2022), tissue damage and cellular stress. p53 is an important regulator of cellular stress responses. Depending on its specific isoforms, p53 can perform different functions. We investigate the association between bacterially induced cellular stress and the expression of different p53 isoforms using a novel luciferase-based reporter system (Truong et al. Nat Cell Biol 2021).

Aims & Methods: To quantify p53 isoform expression, we integrated exon-specific reporter systems (EXSISERS) into TP53 exons 2, 4, and 7. This allows distinction among three primary isoform groups (full-length p53, $\Delta 40p53$, and oncogenic $\Delta 133p53$ and $\Delta 160p53$) in HCT116 colon carcinoma cells. Using split proteins facilitates the removal of luciferase from the resultant p53 polypeptide, thereby maintaining the integrity of the p53 protein isoforms. This method enables the determination of the cellular ratio of p53 protein isoforms. HCT116 EXSISERS cells were co-cultured with a reference strain of *Escherichia coli* (*E. coli*) O6:Hnt, as well as clinical isolates of *E. coli* Ont:H7, Ont:H41, *Proteus mirabilis*, and *Klebsiella pneumonia* obtained from ascites of patients with SBP, for up to 2 hours. Isoform expression was quantified by measuring luciferase activities at intervals of 15 minutes to 2 hours using specific substrates. In addition, qPCR analyses were performed. Further, p53 isoform expression was evaluated after co-incubation with the cytokine IL-8 (mimicking inflammatory conditions) or bacterial components (LPS, MDP, CpG).

Results: Co-incubation with bacteria at MOI 5 resulted in upregulation of the cell-death inducing $\Delta 40p53$ isoform expression within 15 minutes. Simultaneously, we observed a gradual reduction of $\Delta 133p53$ and $\Delta 160p53$, known for their anti-apoptotic and pro-oncogenic properties, over a period of 2 hours.

Thus, after bacterial co-culture isoforms inducing cell death or cell cycle arrest were expressed at a constant level, while oncogenic isoforms were downregulated. Interestingly, stimulation with CpG motifs of bacterial DNA interacting with TLR9, resulted in an upregulation of $\Delta 40p53$ and a reduced expression of $\Delta 133p53$ and $\Delta 160p53$ similar to that observed after bacterial co-incubation. In contrast, bacterial co-culture of EXSISERS cells with IL-8, LPS or MDP resulted in a downregulation of $\Delta 40p53$ isoform expression after 15 minutes.

Conclusion: p53 plays a central role in SBP pathogenesis. Direct contact with bacteria induces the pro-apoptotic isoform $\Delta 40p53$ to eliminate damaged cells, while constant translation of full-length p53 triggers a cell cycle arrest allowing epithelial cells to adapt to bacterial stress. Thus, in SBP, there is a delicate balance between cell survival and cell death in the intestinal epithelium. While $\Delta 40p53$ remained unaffected by IL-8, CpG motifs of bacterial DNA induced $\Delta 40p53$ upregulation.

Further studies will decipher the signaling pathways and interactions leading to $\Delta 40p53$ activation in order to develop targeted therapeutic approaches to protect the epithelial barrier.

References: Haderer M, Neubert P, Rinner E, et al. Gut 2022;71:580–592.

Truong, DJ.J., Phlairaharn, T., Eßwein, B. et al. Nat Cell Biol 2021;23:652–663.

Disclosure: Nothing to disclose.

PP0974

TRANSITION FROM 2D TO 3D – INVESTIGATING BACTERIAL EFFECTS ON INTESTINAL BARRIER INTEGRITY IN SPONTANEOUS BACTERIAL PERITONITIS (SBP) USING SPHEROID AND ORGANOID MODELS

N. Hahn¹, M. Peisl-Gunckel¹, C. Kunst¹, K. Gülow¹,

M. Müller-Schilling¹

¹University Hospital Regensburg, Department of Internal Medicine I - Gastroenterology, Hepatology, Endocrinology, Rheumatology, Immunology and Infectious Diseases, Regensburg, Germany

Contact E-Mail Address: nele.hahn@stud.uni-regensburg.de

Introduction: The use of 3D cell culture models, including spheroids and organoids, has proven to be a valuable method to approximate *in vivo* conditions in basic research. Our recent work on the pathogenesis of spontaneous bacterial peritonitis (SBP) – a life-threatening complication of liver cirrhosis with a 1-year-mortality of 66% – shows that bacteria induce the degradation of important cell-cell contact proteins upon direct contact via various processes.

The resulting destabilization of the epithelial barrier enables bacterial translocation and thus represents a mechanism in the development of SBP (Haderer et al., Gut 2022).

To evaluate these processes under more physiological conditions, we investigate bacterial-induced effects on cell-cell contact proteins in a 3D spheroid model and subsequently in a patient-based organoid model.

Aims & Methods: To establish the method and create a reference, spheroids were generated from colon carcinoma cell line HCT116 with a concentration of 70,000 cells/ml. Spheroid development and formation of cell-cell contacts were assessed by fluorescence microscopy. Subsequently, bacterial-induced effects on the tight junction proteins Occludin, Claudin4 and Zonulin1 as well as on the adherens junction protein E-Cadherin were investigated after up to 12 hours of bacterial co-culture using qPCR, fluorescence microscopy and Western blot analysis. Bacterial co-culture was performed with the reference strain *Escherichia coli* (*E.coli*) O6:Hnt and the *E. coli* strain Ont:H41, which was isolated from the ascites of a patient with SBP.

In addition, organoids were generated from intestinal biopsies of patients with liver cirrhosis and co-cultured with both bacterial strains. Bacterial-induced effects on cell-cell-contact proteins were investigated using Western blot analysis.

Results: HCT116 cells formed spheroids composed of viable cells with well-defined cell-cell contacts. Co-culture with *E. coli* for up to 12 hours led to a significant degradation of Occludin (up to 60% reduction), E-Cadherin (up to 85% reduction) and Zonulin1 (up to 95% reduction), whereas Claudin4 levels remained mostly constant. Co-culture with heat-inactivated bacteria did not affect cell-cell contacts. The intensity of these effects was dependent on the respective protein, the bacterial strain used, as well as the multiplicity of infection (MOI) and the duration of the co-culture. Degradation of Occludin could also be visualized by fluorescence microscopy.

We were then able to transfer this experimental approach to an organoid setting. Bacterial-induced degradation of the epithelial barrier was confirmed in organoids, showing a clearly visible reduction of E-Cadherin, Occludin and Zonulin1 after 8 hours of bacterial co-culture. The intensity of the effects varied depending on the bacterial strain, with the patient strain showing a slightly higher level of aggressiveness.

Conclusion: Understanding the pathophysiological changes of the intestinal epithelial barrier in patients with liver cirrhosis is essential for advancing therapeutic strategies for SBP. In this context, a representative *ex vivo* model is crucial to draw reliable conclusions.

Our work shows that relevant mechanisms of SBP, such as bacterial-induced degradation of cell-cell contacts, can be successfully modeled in spheroids and organoids. Thus, our study provides an approach for further approximation to *in vivo* conditions – bridging the gap between basic research and clinical utility.

References:

Haderer M, Neubert P, Rinner E, Scholtis A, Broncy L, Gschwendtner H, Kandulski A, Pavel V, Mehrl A, Brochhausen C, Schlosser S, Gülow K, Kunst C, Müller M. Novel pathomechanism for spontaneous bacterial peritonitis: disruption of cell junctions by cellular and bacterial proteases. *Gut*. 2022 Mar;71(3):580-592. doi: 10.1136/gutjnl-2020-321663 . Epub 2021 Mar 11. PMID: 33707230; PMCID: PMC8862089.

Disclosure: Nothing to disclose.

PP0975

FRAILITY CORRELATES WITH GREATER ODDS OF ENCEPHALOPATHY, ASCITES, & SPONTANEOUS BACTERIAL PERITONITIS, A STUDY FROM PAKISTAN

F. Kayani¹, J. Khan¹

¹Bolan University of Medical and Health Sciences, Gastroenterology, Quetta, Pakistan

Contact E-Mail Address: farhana_kayani@hotmail.com

Introduction: Frailty is associated with morbidity and mortality in advanced cirrhosis. However, the information on the correlation between frailty and complications in decompensated cirrhosis is scarce. We aim to evaluate the impact of Frailty on risk of Hepatic encephalopathy (HE), Ascites, Spontaneous bacterial peritonitis (SBP) & impact of multidomain implementation on these outcomes.

Aims & Methods: We prospectively evaluated the impact of Frailty on the prevalence of ascites, HE, and SBP among cirrhotic adults. Frailty was defined by the Liver Frailty Index (LFI) and a level of > 4.4 was defined as frail. Development of complications (worsening ascites, HE or SBP) & unplanned hospitalization were recorded.

In this study one arm of frail continued with their normal diet and was taken as control and the other arm (intervention) was given training of taking 5 meals/day, containing appropriate protein and fat contents. Additional branched-chain amino acids were also given to these patients. Physical exercise (both cardiac and resistance) was advised. They were evaluated for a period of 6 months for the complication rates. Between-group comparisons used chi-squared methods and adjusted multivariate logistic regression.

Results: 179 patients were included (MELD 13.2±3.4, Child-Pugh A/B/C 34.9%/35.1%/30%), and 74.3% were frail. Compared to the robust group, pre-frail and frail patients had significantly higher cumulative 1-year probabilities of worsening ascites (0% vs. 8.5% vs. 18.4%, $p=.009$), and spontaneous bacterial peritonitis (0% vs. 13.5% vs. 34.2%, $p<.001$), encephalopathy (0% vs 28.9% vs 71.1%, $p=.02$ and unplanned hospitalizations (100% vs. 90.8% vs. 80.4%, $p=.014$).

Two models of multivariable Cox regression analysis were done and adjusted with MELD-Na and Child-Pugh C, frailty was associated with developing decompensation (HR 3.01, $p=.04$; and 2.98, $p=.04$, respectively) and unplanned hospitalization (HR 2.46, $p=.02$; and 2.39, $p=.03$, respectively). Control arm with frailty were significantly more likely to have ascites, HE, and SBP. (Control arm vs. interventional arm: ascites, 66% vs. 93%; HE, 81% vs. 49%; SBP, 4% vs. 16%, $p < 0.001$ for all).

Conclusion: Frailty is associated with higher odds of cirrhosis complications including ascites, HE, and SBP, which was observed across all liver disease etiologies.

With the implementation and mitigating the knowledge regarding PROPER DIET AND EXERCISE, WE CAN improve the condition of patients and can avoid complications.

Disclosure: Nothing to disclose.

PP0976

ENDOSCOPIC ULTRASOUND ASSESSMENT OF PORTAL HYPERTENSION VERSUS TRANSJUGULAR MEASUREMENTS

I. Dragomir¹, A. Seicean², B.D. Procopet³, C. Pojoga⁴, H. Stefanescu⁵

¹University of Medicine and Pharmacy Iuliu Hatieganu, Gastroenterology, Cluj-Napoca, Romania, ²University of Medicine and Pharmacy Iuliu Hatieganu, Regional Institute of Gastroenterology and Hepatology, Cluj Napoca, Romania, ³University of Medicine and Pharmacy "Iuliu Hatieganu", Gastroenterology 3rd Medical Clinic, Cluj-Napoca, Romania, ⁴IRGH, Gastroenterology, Cluj Napoca, Romania, ⁵Cluj-Napoca University of Medicine and Pharmacy 3rd Medical Clinic, Hepatology and Medical Imaging D, Hepatology, Cluj-Napoca, Romania

Contact E-Mail Address: dragomir.iirina@gmail.com

Introduction: Endoscopic ultrasound (EUS) has emerged as a new tool in assessing portal hypertension (PH). EUS portal pressure measurement (EUS-PPG) was described in few studies using a compact manometer, but the use of a pressure transducer connected to a pressure measurement monitor was previously described in a very small number of patients. The comparative assessment of portal pressure measured by EUS and transjugular route has not been done before. Our study aimed to compare the value of EUS-PPG and transjugular measurements (HVP, PPG) in patients with portal hypertension.

Aims & Methods: Patients with signs of PH on transabdominal imaging and need for haemodynamic and/or endoscopic assessment were included. Patients with platelet count <50000/ μ L and INR>2.5 were excluded. EUS was performed using a 22 G fine needle aspiration attached to a central venous pressure measurement monitor, and it evaluated the presence of gastrointestinal varices, portal vein (PV) diameter and pressure, median hepatic vein/inferior vena cava pressure. All patients had HVPG measurements through the transjugular approach under fluoroscopic guidance, and portal pressure was assessed in patients scheduled for portosystemic shunt (TIPS). The results obtained by the two methods were statistically analysed.

Results: We prospectively enrolled (January to December 2023) 19 patients of 50±14 years old, male to female ratio=2,1:1). The aetiology of PH was porto-sinusoidal vascular disease (n=3, 15%), alcohol cirrhosis (n=15, 75%), viral cirrhosis (n=1, 5%) and metabolic cirrhosis (n=1, 5%). The patients with cirrhosis had Child-Pugh class B or C in 50% of cases. The mean INR was 1.41 and the mean platelet level was 122.000/ μ L.

EUS-PPG was technically successful in 18 patients (94%), with one failure attributed to obesity and important perihepatic ascites which limited the needle deep advancement. The mean EUS-PPG was 13.15 ± 5.48 mmHg. 73% of patients had oesophageal and/or gastric varices present. The mean PV diameter was 12.8 ± 2.7 mm.

HVPG measurements were technically performed in 18 cases (94%), the one exception was related to anatomical factors impeding hepatic vein catheterisation. Mean HVPG was 14.7 ± 5.26 mmHg and it was similar to EUS-PPG ($p = 0.09$), with strong Pearson correlation coefficient ($r = 0.88$).

In patients scheduled for TIPS (n=10), mean PPG was 16±4,15 mmHg and it correlated with EUS-PPG ($r = 0,81$).

No difference was observed between the patients performing measurements during TIPS under general anaesthesia and the group assessed under mild sedation with midazolam. No adverse effects were noted.

Conclusion: The measurements of PH by transjugular route or EUS are comparable. EUS-PPG measurement with 22G needle proved to be an accurate and safe technique. Further investigation is required to determine its indications in patients requiring endoscopic assessment of portal hypertension

Disclosure: Nothing to disclose.

PP0977

THE MEAN PLATELET VOLUME (MPV) AS A PREDICTOR FACTOR OF SEVERITY IN CIRRHOTIC PATIENTS

M. Rahaoui^{1,2}, K. Chahi^{1,2}, H. Aissaoui³, F. Amri^{2,1}, O. Elmqaddem^{1,2}, H. Koulali^{1,2}, Z. Abdelkrim^{1,2}, Z. Ismaili^{2,1}, G. Kharrasse^{1,2}

¹Mohammed VI University Hospital Center, Department of Hepato-Gastroenterology, Oujda, Morocco, ²Digestive Disease Research Laboratory, Medical School, Mohammed First University, Oujda, Morocco, ³Laboratory of Epidemiology, Clinical Research, and Public Health, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco

Contact E-Mail Address: rahaouimaissae@gmail.com

Introduction: Mean platelet volume (MPV) is a routinely measured, non-invasive, and inexpensive parameter of complete blood count. Recent research suggests that MPV has the potential to serve as a valuable prognostic indicator in clinical practice. The aim of our study is to assess the relationship between MPV and the severity of cirrhosis.

Aims & Methods: we included in a cross-sectional study, 140 cirrhotic patients of various grades of severity and various etiologies, followed in our university Hepato-Gastroenterology department. MPV was assessed in all patients, with a normal range set between 7 and 9 fl. Our aim was to evaluate the relationship between MPV values and cirrhosis severity, as determined by Child-Pugh scores and the Model for End-Stage Liver Disease (MELD).

Results: Our study involved 140 cirrhotic patients with diverse etiologies and stages, including 72 females and 68 males, with an average age of 58 ± 14.88 years (range: 21 to 90). Among patients classified as Child A, only 52% had a high MPV, while in groups B and C, higher rates of MPV were noted, reaching 100% and 95.8% respectively. A significant relationship between MPV levels and Child stage was noted ($P < 0.001$).

These patients were distributed across different disease stages: 50 had Child-Pugh score A, 66 had Child-Pugh score B, and 24 had Child-Pugh score C. We used the ANOVAs test to compare the average MPV levels among the three groups. We found a significant difference between MPV values in the 3 groups: A (9.94 ± 1.2), B (11.56 ± 1.19), C (15.27 ± 3.51) ($p < 0.001$). And by using post Hoc tests, we found that this difference was significant between group A and B ($p < 0.001$), A and C ($p < 0.001$), and B and C ($p < 0.001$). Additionally, a significant positive correlation was observed between MPV and MELD score ($r: 0.7$; $p < 0.001$) using Pearson's correlation coefficient.

Conclusion: MPV can serve as a valuable and inexpensive biomarker in cirrhotic patients for assessing the severity and prognosis of the disease. However, further researches are needed to explore the full potential and utility of MPV in clinical practice.

Disclosure: Nothing to disclose.

PP0978

OUTCOMES AND PROGNOSTIC FACTORS OF CIRRHOTIC PATIENTS WITH ACUTE VARICEAL BLEEDING AND CONCURRENT HEPATOCELLULAR CARCINOMA: A CASE-CONTROL STUDY

G. Liu¹, T. Xiang¹, X. Wang², X. Luo³

¹West China Hospital Sichuan University, Chengdu, China,

²Sichuan University West China Hospital, Department of Gastroenterology and Hepatology, Chengdu, China,

³Westchina Hospital, Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: liuguofeng543@163.com

Introduction: The treatment outcomes and risk factors for the prognosis of acute variceal bleeding (AVB) in hepatocellular carcinoma (HCC) patients remain unclear. Hence, we assessed the clinical outcomes and prognostic factors of these patients.

Aims & Methods: To evaluate the treatment outcomes and risk factors of cirrhotic patients with hepatocellular carcinoma (HCC) and acute variceal bleeding (AVB).

This is a retrospective case-control study. Consecutive patients with HCC and AVB admitted between 2016 and 2022 were included. For each patient with HCC, a patient without HCC was matched by age, sex, and Child-Pugh class. Follow-up was continued until death and transplantation.

Results: A total of 620 patients were included. The five-day treatment failure and 6-week mortality rates of the whole cohort were 18.7% and 16.6%, respectively. Patients with HCC had higher 6-week mortality, respectively (24.2% vs. 9.0%, $P < 0.001$).

Among AVB patients with HCC, the Barcelona Clinic Liver Cancer (BCLC) stage (C-D vs. 0-B) (HR, 14.409; 95% CI, 5.758-36.055; $P < 0.001$), and Child-Pugh score (HR, 1.239, 95% CI, 1.121-1.370; $P < 0.001$) were independent risk factors of 6-week mortality in multivariate analysis.

Furthermore, the risk of 6-week mortality was 60.2% among patients with a Child-Pugh score ≥ 9 and BCLC stage C-D, much higher than patients with low Child-Pugh score (< 9) and earlier BCLC stage (0-B) ($P < 0.0001$).

Conclusion: Among patients with cirrhosis and AVB, patients with HCC had a worse outcome than patients without. The severity of liver disease and the stage of HCC are the main determinants of mortality in HCC patients.

Disclosure: Nothing to disclose.

PP0979

THE SEVERITY OF PORTAL VEIN THROMBOSIS IS ASSOCIATED WITH THE PROGNOSIS OF CIRRHOTIC PATIENTS WITH ACUTE VARICEAL BLEEDING

X. Wang¹, J. Huang¹, X. Luo², L. Yang¹

¹Sichuan University West China Hospital, Department of

Gastroenterology and Hepatology, Chengdu, China, ²Sichuan University West China Hospital, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: xiaozhe.wang@foxmail.com

Introduction: The clinical implications of portal vein thrombosis (PVT) on the prognosis of acute variceal bleeding (AVB) in cirrhosis remain under debate. Most studies have not been specifically designed to assess the severity of PVT.

Aims & Methods: This study aimed to evaluate the severity of PVT and its impact on outcomes in patients with cirrhosis and AVB. From January 2016 to December 2016, a total of 1541 consecutive cirrhotic patients admitted for AVB, with (n=432; 28.1%) or without PVT (n=1109; 71.9%), were

included retrospectively. The degree of luminal obstruction was used to classify the grades of PVT according to Baveno VII criteria. The primary endpoint was 6-week mortality.

Results: During the follow-up period, 179 patients (11.6%) died within 6 weeks. Patients with PVT had a higher risk of 6-week mortality compared to those without PVT (18.3% vs 8.9%; HR 2.12, 95% CI 1.52–2.94, $p < 0.001$). Among them, those with malignant main PVT had a significantly elevated risk (39.3% vs 9.2%; HR 4.86, 95% CI 2.74–8.62, $p < 0.001$). In the non-malignant PVT cohort, only completely occlusive main PVT was associated with increased 6-week mortality (completely occlusive 26.1% vs cavernous transformation 9.7% vs partially occlusive 6.5% vs minimally occlusive 5.9% vs without PVT 9.2%, $p = 0.023$). These results were consistent across various relevant subgroups.

Conclusion: Our study demonstrates that PVT is linked to a poorer outcome in cirrhotic patients with AVB, particularly in cases of malignant main PVT and completely occlusive main PVT.

Disclosure: None of the authors have any conflict of interest.

PP0980

EFFECT OF VOLUME OVERLOAD MEASURED BY VEXUS SYSTEM ON THE PROGRESSION TO HEPATORENAL SYNDROME AND VARIATION IN MELD NA SCALE IN PATIENTS WITH HEPATIC CIRRHOSIS DEVELOPING ACUTE KIDNEY INJURY

C. Jaramillo Buendía¹, J.R. Velazquez López¹, A.S. Villalvazo López¹, E. Rojas Campos², L.A. Evangelista Carrillo³

¹Instituto Mexicano del Seguro Social, Centro Médico Nacional de Occidente, Gastroenterología, Guadalajara, Mexico, ²Instituto Mexicano del Seguro Social, Unidad de investigación médica, Guadalajara, Mexico, ³Instituto Mexicano del Seguro Social, Centro Médico Nacional de Occidente, Nefrología, Guadalajara, Mexico

Contact E-Mail Address: rs_jaramillo@hotmail.com

Introduction: Acute kidney injury is a complication in patients with decompensated cirrhosis (26%). Hepatorenal syndrome has high morbidity and mortality (90%), characterized by renal functional circulatory changes. Abdominal ultrasound, as a medical tool, in the VexUS protocol assessing intravascular congestion (Inferior vena cava, suprahepatic vein, portal vein, and renal vein), could be routinely used in cirrhotic patients with acute kidney injury to objectify the degree of venous congestion and improve decision-making, changing the treatment paradigm with albumin.

Aims & Methods: Prospective, observational, and analytical cohort study in hospitalized hepatic cirrhosis patients with acute kidney injury due to acute decompensation, receiving intravenous albumin at a dose of 1 g/kg/day for 48 hours with subsequent assessment of response. Before albumin administration, abdominal ultrasound (VExUS) was performed to determine the venous congestion status (Period: July 2022 to December 2023). No sample calculation was performed, as all patients meeting selection criteria were included. Sociodemographic, clinical, and biochemical variables were recorded.

Results: Out of 36 patients, 16 (44.4%) responded to albumin therapy, while 20 (55.6%) did not respond. Analyzing according to the VExUS score, 12 patients with VExUS 0 had a response rate of 54.5%, and 10 did not respond (45.5%). When classifying patients based on the presence or absence of venous congestion (VExUS = 0 vs. VExUS 1 or 2), it was observed that in patients with venous congestion, 4 responded (28.6%) and 10 did not respond (71.4%), with a decrease in the p-value without reaching statistical significance.

A logistic regression analysis revealed that both the VExUS score and serum creatinine at admission are predictors of non-response to albumin. The presence of congestion (VExUS I or II) and a 1 mg/dL increase in creat-

inine were associated with a 5 and 10 times higher risk of non-response, respectively. Regarding the MELD Na score, the 14 deceased patients had a median of 32.5, while the 22 survivors had a median of 23.77.

Conclusion: Non-invasive diagnostic tools like ultrasound (VexUs), widely used due to availability, prove useful in determining the volume status of cirrhotic patients with acute kidney injury and hepatorenal syndrome. This helps establish the prognosis of response to a volume expander like albumin or the utility of other targeted therapeutic measures in patients with evidence of volume overload and/or abdominal hypertension data.

References:

1. Bhardwaj V, Vikneswaran G, Rola P, Raju S, Bhat RS, Jayakumar A, et al. Combination of Inferior Vena Cava Diameter, Hepatic Venous Flow, and Portal Vein Pulsatility Index: Venous Excess Ultrasound Score (VEX-US Score) in Predicting Acute Kidney Injury in Patients with Cardiorenal Syndrome: A Prospective Cohort Study. *Indian J Crit Care Med* 2020;24(9): 783–789.
2. David Jury and Andrew D. Shaw. Utility of bedside ultrasound derived hepatic and renal parenchymal flow patterns to guide management of acute kidney injury. *Curr Opin Crit Care* 2021; 27:587 – 592
3. Scott W. Biggins, Paulo Angeli, Guadalupe Garcia-Tsao, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver. *Diseases Hepatology*, VOL 74, NO. 2, 2021.
4. Douglas A Simonetto, Pere Gines, Patrick S Kamath. Hepatorenal syndrome: pathophysiology, diagnosis, and management. *BMJ* 2020;370: m2687.

Disclosure: Nothing to disclose.

PP0981

GASTROINTESTINAL BLEEDING DUE TO PORTAL HYPERTENSION IN CIRRHOSIS: PROGNOSTIC VALUE OF THE CAGIB SCORE

A. Menif¹, A. Ben Mohamed¹, M. Yakoubi¹, M. Moufida¹, G. Gharbi², A. Khsiba¹, M. Medhioub¹, M.L. Hamzaoui¹

¹Mohamed Taher Maamouri, Gastroenterology, Nabeul, Tunisia,

²Hbib Thameur Hospital, Gastroenterology Department, Tunis, Tunisia

Contact E-Mail Address: Alaaeddinemnif@gmail.com

Introduction: Gastrointestinal variceal bleeding is a serious complication of cirrhosis. Currently, no score has been validated to assess the prognosis of a bleeding episode in cirrhotic patients. The aim of our study was to evaluate the performance of the CAGIB score for recurrence and mortality following upper gastrointestinal bleeding in cirrhotic patients.

Aims & Methods: We conducted a retrospective study of cirrhotic patients hospitalized for upper gastrointestinal bleeding due to portal hypertension [2012–2022]. We calculated the scores CHILD-PUGH, MELD, MELD-Na, MELD 3.0, ALBI, ROCKALL, GBS, NLR and CAGIB, and compared their performance in terms of early recurrence (5-days), short-term recurrence (6-weeks) and early mortality (6-weeks) through the study of ROC curves (SPSS software, P significant if < 0.05).

Results: We included 105 patients with a mean age of 63 years and a sex ratio F/M=1.05. The origin of the bleeding was oesophageal varices rupture in 94.28% of cases and gastric varices rupture in 17.14%. Endoscopic treatment was performed in 96 patients, 90 of whom underwent band ligation of esophageal varices. Short-term recurrence was noted in 20% of patients. Early recurrence was noted in 3.8% of patients. Fourteen cases of early death were recorded. The CAGIB score was the best predictor of early recurrence (AUC=0.995, Sensibility=83.3%, Spécificity=99.6%, Odds Ratio=47, $p < 0.001$) but it has a poor prognostic value for short-term re-

currence ($p=0.08$). For early mortality, the CAGIB score performed better than the other scores ($AUC=0.891$) with a Sensibility=85.7% and Specificity=83.5% for predicting mortality from a cut-off ≥ 4.648 with an $OR=18$.

Conclusion: The CAGIB score had the best predictive value for early recurrence and mortality following an episode of upper gastrointestinal bleeding due to portal hypertension in cirrhosis. We therefore propose it as an easy-to-calculate and reproducible tool, for a cut-off >4.648 .

Disclosure: Nothing to disclose.

PP0982

ACUTE KIDNEY INJURY IN CIRRHOTIC PATIENTS EXPOSED TO IODINATED CONTRAST: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Vanzin Fernandes¹, V. Antunes¹, T. Correa², O. Martins³, A.A. Prata⁴, A.M. Reis⁵, A.C. Coan⁴, E. Bulhões⁶, P. Romeiro⁷, N.J. Milioli⁸

¹Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ²Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ³Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁴Federal University of Espírito Santo, Vitória, Brazil, ⁵State University of Campinas, Campinas, Brazil, ⁶College of Higher Education of the United Amazon, Redenção, Brazil, ⁷Department of Medicine, University Center of Maceió, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Iodinated contrast (IC) is one of the leading causes of acute kidney injury (AKI). Nephrotoxicity of IC in cirrhosis is a debated issue due to low-quality evidence.

Aims & Methods: This study aims to evaluate the association between exposition to IC in cirrhotic patients and the development of AKI. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies conducted in cirrhotic patients exposed to IC. The primary outcomes were: 1) AKI development in cirrhotic patients exposed or not to IC; and 2) AKI development in cirrhotic and health patients exposed to IC. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I^2 statistics.

Results: The meta-analyses included 4 studies and 1,055 patients. Three studies (911 patients) evaluated cirrhotic patients exposed or not exposed to IC. There was a significant increase in AKI in cirrhotic patients exposed to IC ($OR\ 3.10$; 95% $CI\ 1.45\ to\ 6.61$, $p=0.003$; $I^2=0\%$). Three studies (654 patients) evaluated cirrhotic and health patients exposed to IC. There was no difference in AKI comparing both groups ($OR\ 1.61$; 95% $CI\ 0.63\ to\ 4.16$, $p=0.322$; $I^2=0\%$).

Conclusion: Patients with cirrhosis exposed to IC showed higher incidence of AKI compared with those not exposed, but when compared with health individuals also exposed to IC the incidence of AKI seems to be the same.

References:

1. Campion D, Rizzo M, Ponzo P, Risso A, Giovo I, Rizzi F, et al. Risk of contrast-induced acute kidney injury in cirrhotic patients undergoing computed tomography: myth or reality? *J Hepatol.* 2020;73:S702.
2. Campion D, Ponzo P, Risso A, Caropreso P, Caviglia GP, Sanavia T, et al. A prospective, multicenter, three-cohort study evaluating contrast-induced acute kidney injury (CI-AKI) in patients with cirrhosis. *J Hepatol.* 2024;80(1):62–72.
3. Filomia R, Maimone S, Caccamo G, Saïtta C, Visconti L, Alibrandi A, et al. Acute kidney injury in cirrhotic patients undergoing contrast-enhanced computed tomography. *Medicine (Baltimore).* 2016 Sep;95(38):e4836.

4. Safi W, Rauscher I, Umgelter A. Contrast-induced acute kidney injury in cirrhotic patients. A retrospective analysis. *Ann Hepatol.* 2015 Nov;14(6):895–901.

5. Visconti L, Filomia R, Maimone S, Montuori F, Ricciardi CA, Di Mauro E, et al. SP211ACUTE KIDNEY INJURY IN CIRRHOTIC PATIENTS UNDERGOING CONTRAST-ENHANCED COMPUTED TOMOGRAPHY. *Nephrol Dial Transplant.* 2015 May;30(suppl_3):iii448–iii448.

Disclosure: Nothing to disclose.

PP0983

PARA-VESSELS AROUND CARDIA SIGNIFICANTLY AFFECT THE EFFICACY OF ENDOSCOPIC MANAGEMENT OF GASTROESOPHAGEAL VARICES

X. Huang¹, L. Wu¹, S. Chen¹

¹Zhongshan Hospital, Fudan University, Department of Gastroenterology and Hepatology, Shanghai, China

Contact E-Mail Address: huangxiaoquan1010@aliyun.com

Introduction: Acute variceal bleeding is a life-threatening complication of portal hypertension, and it has a high mortality rate, responsible for almost one-third of cirrhosis-related deaths¹. Collaterals develop between the portal vein tributaries and systemic veins under the sustained portal high pressure². Gastroesophageal varices are varices in direct continuity from the esophagus to the stomach, draining into the systemic circulation via the gastroesophageal venous system and/or the gastrophrenic venous system³. Para-gastric and para-esophageal varices are also important collaterals for reducing portal pressure and may influence the choice and effectiveness of treatment. Endoscopic gastric variceal tissue adhesive treatment followed by the endoscopic esophageal variceal ligation is the preferred treatment for the gastroesophageal varices⁴. However, some patients still experience re-bleeding after endoscopic treatment, even after the combination of drug and surgical therapy⁵. Clinical risk factors affecting the prognosis of gastroesophageal varices still remain to be analyzed.

Aims & Methods: The aim of this study was to investigate the effect of esophageal and gastric extraluminal vessels on the efficacy of endoscopic prevention of esophageal and gastric variceal bleeding. The clinical data of patients with cirrhosis-related esophageal and gastric varices who underwent endoscopic ligation and/or tissue adhesive treatment and hepatic venous-portal gradient (HVPG) measurement to prevent rebleeding between January 2020 and December 2020 were analyzed. According to the esophageal and gastric extraluminal blood vessels on portal vascular CT, patients were divided into no combined para-vessels group and with combined para-vessels group. The patients were followed up for re-bleeding and survival after endoscopic treatment for hematiostasis.

Results: A total of 69 patients were analyzed, 27 patients were combined with para-gastric or para-esophageal varices and 42 were not. Baseline characters including age, sex, hepatitis B, diabetes, hypertension and portal thrombosis were comparable between the two groups. Hemoglobin, prothrombin time and albumin levels were also comparable after the hospital admission, so was the HVPG (Median 14 (9-20) mmHg, $p=0.9951$). All patients received similar endoscopic treatment for the secondary prophylaxis of gastroesophageal variceal rebleeding. The median follow-up was 745 days. A total of 27 patients experienced rebleeding and 1 patient underwent liver transplantation. Kaplan-Meier analysis showed that the 3-year rebleeding after endoscopic treatment was significantly higher in patients with para-vessels than in patients without (74.33% vs 32.79%, $p=0.005$).

After further multivariate analysis including hepatitis B and albumin levels, the combination of para-vessels was found to be an independent predictor of rebleeding after endoscopic treatment in patients with gastroesophageal variceal bleeding ($HR\ 2.56$, 95% $CI\ 1.149-5.705$, $p=0.042$).

Conclusion: The presence of para-gastric and para-esophageal varices is an independent predictor of rebleeding after endoscopic treatment for gastroesophageal variceal bleeding. As a result, portal vascular CT is required to assess para-gastric and para-esophageal varices for patients with gastroesophageal variceal bleeding undergoing endoscopic treatment to prevent rebleeding. For patients with large para-varices, other treatment options, such as interventional transjugular portosystemic shunt are highly recommended for a better prognosis.

References:

1. de Franchis R, Primignani M. Natural history of portal hypertension in patients with cirrhosis. *Clinics in liver disease*. 2001;5(3):645-63.
2. Pillai AK, Andring B, Patel A, Trimmer C, Kalva SP. Portal hypertension: a review of portosystemic collateral pathways and endovascular interventions. *Clin Radiol*. 2015;70(10):1047-59.
3. Alqahtani SA, Jang S. Pathophysiology and Management of Variceal Bleeding. *Drugs*. 2021;81(6):647-67.
4. Jobe K, Henry Z. Endoscopic Treatment of Acute Esophageal and Gastric Variceal Bleeding. *Gastrointestinal endoscopy clinics of North America*. 2024;34(2):249-61.
5. Balcar L, Mandorfer M, Hernandez-Gea V, Procopet B, Meyer EL, Giraldez A, et al. Predicting survival in patients with 'non-high-risk' acute variceal bleeding receiving beta-blockers+ligation to prevent re-bleeding. *J Hepatol*. 2024;80(1):73-81.

Disclosure: Nothing to disclose.

PP0984

ACUTE VARICEAL BLEEDING DURING THE SARS-COV-2 PANDEMIC

G. Allo¹, S. Quickert², K. Große³, S. Baysal⁴, D. Nierhoff¹, C. Schramm⁴, T. Bruns³, P.A. Reuken², M. Bürger¹

¹University Hospital of Cologne, Faculty of Medicine, University of Cologne, Department for Gastroenterology and Hepatology, Cologne, Germany, ²University Hospital Jena, Department of Internal Medicine IV (Gastroenterology, Hepatology and Infectious Diseases), Jena, Germany, ³University Hospital RWTH Aachen, Department of Internal Medicine III, Aachen, Germany, ⁴Medical Faculty, University of Duisburg-Essen, Department of Gastroenterology, Hepatology and Transplant Medicine, Essen, Germany

Contact E-Mail Address: Gabriel.Allo@uk-koeln.de

Introduction: Acute variceal hemorrhage (AVH) is a dreaded complication of liver cirrhosis and continues to be associated with high mortality despite significant medical knowledge and advances in recent years. In addition, the severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) pandemic has led to a temporary reduction in the diagnosis, surveillance and treatment of chronic liver diseases and their complications due to the necessary protective measures.

Aims & Methods: This study aimed to analyze the impact of the SARS-COV-2 pandemic on the course of disease in patients with AVH. In this retrospective multi-center study of patients with AVH due to cirrhosis disease courses during to two different time periods (01.03.2016-28.02.2020, and 01.03.2020-28.02.2022, termed COVID period) were compared regarding patients baseline characteristics, management, post-bleeding infections, rebleeding and mortality.

Results: For the COVID and pre-COVID period 96 and 151 patients were analyzed, respectively. During the COVID period the amount of alcohol-associated liver disease or active alcohol consumption did not differ between cohorts (58.2% vs. 47.9%; p=0.147 and 44.2% vs 39.1%; p= 0.496). There was a trend towards a higher median Model for End-Stage Liver Disease (MELD) (16 vs. 19; p=0.06) while the Child-Pugh Score was comparable

(10 vs. 10; p=0.304). Intubation rates during endoscopy (16.1% vs. 16.0%; p= 1.000) as well as active bleeding rates (59.6% vs. 50.0%; p=0.150) did not differ but transjugular intrahepatic portosystemic shunt placement (11.3% vs. 23.2%; p=0.019) was performed more frequently during the pandemic.

Additionally, during the pandemic there was a trend to a higher incidence of post-bleeding infections in patients without present infection at the time of AVH, who received antibiotic prophylaxis (21.6% vs. 35.4%; p=0.068). A Coronavirus-infection was present in only one patient. The 6-week recurrent bleeding and mortality rates did not differ between groups (22.3% vs. 22.8%; p=1.000 and 30.1% vs. 32.2%; p=0.767).

Conclusion: Despite an observed trend to a higher incidence of post-bleeding infections and a lower MELD score mortality in patients with AVH was not increased during the SARS-COV-2 pandemic.

Disclosure: Nothing to disclose.

PP0985

THERAPEUTIC PLASMA EXCHANGE IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE

V. Matovic Zaric¹, I. Pantic², N. Bakovic², B. Korica², M. Vojnovic², T. Glisic², M. Dinic³, S. Milutinovic³, A. Milic³, I. Lolic¹, J. El Mezeni², M. Kartal¹, A. Tomovic², T. Milovanovic⁴

¹University Clinical Center of Serbia, Emergency center, Gastroenterology and Hepatology Department, Belgrade, Serbia, ²Clinic of Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, Serbia, ³University Clinical Center of Serbia, Emergency Center, Department of Therapeutic Apheresis Procedures, Belgrade, Serbia, ⁴University Clinical Center of Serbia, School of Medicine University of Belgrade, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia

Contact E-Mail Address: sloncemajmunce@gmail.com

Introduction: Acute-on-chronic liver failure (ACLF) is a severe form of acute decompensation of chronic liver disease with a high short-term mortality rate. It is characterized by excessive systemic inflammatory response and extrahepatic multiorgan failures (1).

Previously published data have shown that therapeutic plasma exchange (TPE) decreases mortality rate in patients with ACLF reducing cytokine levels, serum bilirubin, and coagulopathy (2,3).

Aims & Methods: This retrospective study was conducted at the University Clinical Center of Serbia. All patients diagnosed with ACLF according to the EASL criteria and treated with TPE from January 2021 to January 2024 were included. (1)

The main indication for providing TPE was serum bilirubin level >12 mg/dl with no improvement to standard medical treatment (SMT). The following scores were calculated at the hospital admission: Model for end-stage liver disease (MELD), Model for end-stage liver disease-Sodium (MELD-Na), Chronic Liver Failure Consortium- acute-on-chronic liver failure (CLIF-C ACLF). All patients were followed for 90 days. MELD and MELD-Na scores were calculated as well on the day 28.

The aims of this study were: assessment of 28-day and 90-day survival in patients with ACLF, the impact of TPE on MELD, and MELD-Na score.

Results: The study included 40 patients in whom SMT did not lead to improvement, of which 32 (80%) were male and 8 (20%) were female with a median age of 45.5 (39.75-58.5) years. The most frequent cause of liver cirrhosis was alcohol (n=28; 70%), followed by Wilson disease (n=4; 10%), metabolic dysfunction-associated fatty liver disease (MAFLD) (n=3; 7,5%), autoimmune hepatitis (n=2; 5%), primary biliary cholangitis (n=2; %%), AIH/ PSC syndrome overlap (n=1; 2.5%). Eighteen patients (45%) were previously diagnosed with acute decompensation (Table 1).

The average number of performed TPEs was 6 ± 12.73 . In alcohol-related liver disease (ALD) cirrhosis, alcoholic hepatitis was the main cause of ACLF in 22 (78.5%) patients. Twenty-two patients (55%) were diagnosed with Community-acquired infections. At admission, the average MELD and MELD-Na scores were 28.5 ± 6.43 and 31 ± 6.21 . The mean MELD and MELD-Na scores in surviving patients after 28 days were 24.3 ± 7.78 and 25.52 ± 7.58 , respectively. The average CLIF C-ACLF score at admission was 47 ± 8.07 . ACLF grade 1 was observed in 20 patients (50%), ACLF grade 2 in 18, (45%), and ACLF grade 3 in 2 (5%). The 28-day mortality in this study group was 37.5% (n=15), with 25% (n=5) in ACLF grade 1, 44.4% (n=8) in ACLF grade 2, and 100% (n=2) in ACLF grade 3. Ninety-day mortality was 62.5% (n=25). Regarding the ACLF grade, the following 90-day mortality was observed: grade 1-45% (n=9), grade 2-77.8% (n=14), and grade 3-100 (n=2). With the use of TPE in addition to SMT, a statistically significant decrease in MELD and MELD-Na as well was observed after 28 days ($p < 0.01$).

Variables	Total number (n=40)
Gender m/f	32(80%)/8(20%)
Age ^a	45.5 (39.75-58.5)
Etiology of liver cirrhosis:	
Alcohol	28 (70%)
Wilson disease	4 (10%)
MAFLD	3 (7.5%)
Autoimmune hepatitis	2(5%)
PBC	2 (5%)
PSC/AIH	1 (2.5%)
Previous acute decompensation	18 (45%)
ACLF grade I/II/III	20(50%)/18 (45%)/2 (5%)
28-day/90 day mortality	15(37.5%)/25 (62.5%)

Table 1. Baseline demographic and clinical characteristics.

Conclusion: TPE may be a beneficial treatment option for patients who do not respond to SMT, but in our study, short-term mortality is still high. New prospective randomized studies with a larger number of subjects are needed to examine this therapeutic modality accurately.

References: 1. European Association for the Study of the Liver (2023). EASL Clinical Practice Guidelines on acute-on-chronic liver failure. *Journal of Hepatology*, 79(2), 461–491.

2. Mao WL, Chen Y, Chen YM, Li LJ. Changes of serum cytokine levels in patients with acute on chronic liver failure treated by plasma exchange. *J Clin Gastroenterol*. 2011;45:551–555.

3. Chris-Olajia A, Kapoor A, Ricci KS, Lindenmeyer CC. Therapeutic plasma exchange in liver failure. *World J Hepatol*. 2021;13(8):904-915.

Disclosure: There is no conflict of interest.

PP0986

EFFECTS OF PROBIOTICS USE IN PATIENTS WITH LIVER CIRRHOSIS AND HEPATIC ENCEPHALOPATHY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

V. Antunes¹, E. Bulhoes², P. Romeiro³, A. Milani⁴, A.c. Covre Coan⁵, A. Prata⁵, O. Martins⁶, T. Correa⁷, N.J. Milioli⁸, M.V. Fernandes¹

¹Federal University of Health Sciences of Porto Alegre, Medicine

Department, Porto Alegre, Brazil, ²College of Higher Education

of the United Amazon, Medicine Department, Redenção, Brazil,

³University Center of Maceió, Department of Medicine, Maceió,

Brazil, ⁴State University of Campinas, Medicine Department,

Campinas, Brazil, ⁵Federal University of Espírito Santo, Medicine

Department, Vitoria, Brazil, ⁶Federal University of Juiz de Fora,

Medicine Department, Juiz de Fora, Brazil, ⁷Beth Israel Deaconess

Medical Center/Harvard Medical School, Medicine Department,

Boston, United States of America, ⁸Pontifical Catholic University of

Rio Grande do Sul, Medicine Department, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Bacterial translocation exacerbates circulatory dysfunction present in patients with liver cirrhosis. Probiotics can reduce bacterial translocation and consequently improve the outcomes in this population.

Aims & Methods: This study aims to evaluate the efficacy of probiotics in the cirrhotic patients. We performed a systematic review in PubMed, Embase and Cochrane Central database, searching for studies analyzing the effects of probiotics use in overt hepatic encephalopathy incidence in cirrhotic patients. A Bayesian network meta-analysis was conducted to estimate the relative effects between treatments using risk ratios (RR) and to rank each one according to the Surface Under the Cumulative Ranking Curve (SUCRA).

Results: We included eight studies, comprising 975 patients. The assessment of SUCRA values indicated that lactulose plus probiotics (0.95) emerged as the most effective prevention for overt hepatic encephalopathy. Moreover, lactulose plus probiotics demonstrated superior efficacy compared to lactulose (0.54), probiotics only (0.51), LOLA (0.48), placebo (0.24), and no therapy (0.21). The risk of overt hepatic encephalopathy was low for lactulose plus probiotics (0.000025; credible interval [CrI] 1.3x10¹⁶, 1.5), lactulose only (RR 0.64; CrI 0.09, 4.0), probiotics (RR 0.69; CrI 0.17, 2.9), LOLA (RR 0.64; CrI 0.04, 8.9) and no therapy (RR 1.1; CrI 0.22, 7.0).

Conclusion: In our network meta-analysis, the best results in the treatment of the patients with cirrhosis and hepatic encephalopathy was seen with the association of lactulose plus probiotics. Both drugs have good tolerability and are widely disponible, so we suggest considering this association.

Disclosure: Nothing to disclose.

PP0987

VALIDATION OF BAVENO VII CRITERIA: RECOMPENSATION OF DECOMPENSATED VIRAL CIRRHOSIS

S. Emna¹, A. Khsiba¹, H. Hassen¹, M. Medhioub², M. Moufida², H. Jaziri³, M.L. Hamzaoui²

¹Mohamed Taher Maamouri Hospital, Gastroenterology and Hepatology Department, Nabeul, Tunisia, ²Mohamed Taher Maamouri Hospital, Gastroenterology Department, Nabeul, Tunisia, ³Sahloul University Hospital, Gastroenterology Department, Sousse, Tunisia

Contact E-Mail Address: souilemamna1@gmail.com

Introduction: Managing decompensated cirrhosis is a significant challenge due to high morbidity and mortality rates. The recently proposed Baveno VII criteria provide a standardized definition to assess recompensation. In this study, we validated the Baveno VII definition of recompensation and aimed to evaluate recompensation factors in patients with decompensated viral cirrhosis.

Aims & Methods: This is a retrospective descriptive study over a 10-year period between 2012 and 2022, enrolling 99 patients from the hepato-gastroenterology department of Mohamed Taher Maamouri Hospital in Nabeul who had been treated for decompensated viral cirrhosis B or C and achieved sustained virological response with a follow-up of at least 12 months.

Results: A total of 99 patients with decompensated viral cirrhosis (B or C), who had received treatment and achieved sustained virological response, were included in the study. The mean age was 62 ± 11 years, and 56 patients were female. The most common mode of decompensation was ascites, observed in 81.8% of the patients. The mean MELD score was 15 ± 4 , and the majority (59.7%) were classified as Child-Pugh class B. Overall, 45.5% of the decompensated patients achieved recompensation during the study period. The recompensation rate was higher in patients with hepatitis B-related cirrhosis (51.1%) compared to those with hepatitis C-related cirrhosis (40.4%).

According to the results of logistic regression, four independent factors associated with recompensation were found: albumin (OR = 2.033, IC95% [1,461-2,827], $p < 0.001$), diabetes (OR = 0.003, IC95% [0.000-0.045], $p < 0.001$), Child Pugh score (OR = 0.162, IC95% [0.057-0.459], $p = 0.001$), INR (OR = 0.017, IC95% [0.000-0.939]).

Conclusion: This study identified key factors associated with recompensation in patients with viral decompensated cirrhosis, including serum albumin levels, INR values, history of diabetes, and severity of liver disease. The knowledge of recompensated indicators may help support the development of different prevention strategies to reduce the incidence of acute decompensation.

Disclosure: Nothing to disclose.

PP0988

ACCURACY OF NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN TO DIAGNOSIS ACUTE TUBULAR NECROSIS IN CIRRHOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.V. Fernandes¹, V. Antunes¹, T. Correa², O. Martins³, A.A. Prata⁴, A.c. Covre Coan⁴, A.M. Reis⁵, E. Bulhões⁶, P. Romeiro⁷, N.J. Milioli⁸

¹Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ²Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ³Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁴Federal University of Espírito Santo, Vitória, Brazil, ⁵State University of Campinas, Campinas, Brazil, ⁶College of Higher Education of the United Amazon, Redenção, Brazil, ⁷Department of Medicine, University Center of Maceió, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction:

Renal impairment is a common complication in cirrhosis. Urinary neutrophil gelatinase-associated lipocalin (NGAL) has shown promise in diagnosis of the different types of acute kidney injury (AKI) in cirrhosis.

Aims & Methods:

This study aims to evaluate the accuracy of NGAL in the differential diagnosis of acute tubular necrosis (ATN) in cirrhosis. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies analyzing NGAL as a biomarker of ATN. Statistical analysis included data pooling and heterogeneity testing. Quality of the included studies was assessed by Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2).

Results: The meta-analyses included 3 studies and 317 patients. The NGAL cut-off evaluated were similar between the three studies (delta 143 to 244 µg/g). The pooled sensitivity and specificity of NGAL in predicting ATN in cirrhosis were 78.7% (95% CI 68.4% to 86.4%) and 80.8% (95% CI 55.5% to 93.4%). The AUC was 0.866 (95% CI 0.646 to 0.955).

Conclusion: In patients with cirrhosis, urinary NGAL is a good predictor of ATN and can be used as an additional tool to the differential diagnosis of acute kidney injury.

Disclosure: Nothing to disclose.

PP0989

A 5-YEAR LONGITUDINAL STUDY ON REPEATED VARICEAL LIGATION IN ACUTE ESOPHAGEAL VARICEAL BLEEDING

P. Rattanachaisit^{1,2}, P. Prueksapanich³, R. Chaiteerakij³, P. Komolmit³, S. Treeprasertsuk³

¹Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Division of Gastroenterology, Department of Medicine, Bangkok, Thailand, ²Faculty of Medicine, Chulalongkorn University, Department of Physiology, Bangkok, Thailand, ³Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Division of Gastroenterology, Department of Medicine, Bangkok, Thailand

Contact E-Mail Address: pakkapon.r@gmail.com

Introduction: Acute esophageal variceal bleeding (EVB) typically requires initial treatment involving pharmacotherapy and endoscopy, particularly endoscopic variceal ligation (EVL). In cases of rebleeding, transjugular intrahepatic portosystemic shunt (TIPS) is recommended, but in regions with limited TIPS access, repeated endoscopic therapy is common. This study evaluates the outcomes of EVL in managing rebleeding and mortality in resource-constrained settings.

Aims & Methods: Patients experiencing acute EVB and undergoing EVL were followed for up to five years or until death. Treatment involved vasoactive drugs and EVL until variceal eradication was achieved. Primary endpoints included bleeding control effectiveness and the need for a second EVL session to manage rebleeding. Rebleeding and mortality rates at 6 weeks and 5 years were analyzed. Logistic regression analysis identified risk factors associated with rebleeding and mortality.

Results: Among 118 patients with acute EVB undergoing EVL, no treatment failures occurred within five days. Eighty-three percent were successfully controlled with one EVL session, while 17% required at least two sessions for recurrent bleeding. In the rebleeding group, no patients rebled within five days after the first EVL, but 75% rebled within 6 weeks. Second EVL was performed for these patients, with a failure rate of 25%. Recurrent EVBs were ultimately controlled by other endoscopic therapy. There was no significant difference in 6-week mortality between rebleeding (15%) and non-rebleeding (18%) groups ($p=0.72$). Factors associated with 6-week mortality included age, hepatocellular carcinoma, post-bleeding beta-blocker use, creatinine, bilirubin, albumin, Child-Pugh class, and MELD score (Table). Beta-blocker use was associated with preventing recurrent EVB within six months (OR 0.053, 95% CI: 0.004-0.687, $p=0.025$). Over five years, the rebleeding group showed a higher mortality trend (90%) compared to the non-rebleeding group (68.8%), though not statistically significant ($p=0.06$).

	OR (95%CI)	p
Age	1.04 (1.00-1.08)	0.04
HCC	4.05 (1.45-11.37)	0.01
Beta-blockers used after EVB	0.09 (0.03-0.29)	<0.001
Total bilirubin	1.1 (1.02-1.19)	0.02
Creatinine	1.83 (1.11-3.01)	0.02
Albumin	0.27 (0.10-0.75)	0.01
Child-Pugh class	2.50 (1.14-5.50)	0.02
MELD score	1.12 (1.04-1.20)	0.001

Conclusion: In resource-limited settings, multiple attempts of EVL demonstrate success in controlling rebleeding. Long-term trends indicate higher mortality in rebleeding cases, although not statistically significant.

Disclosure: The authors declare that they have no conflict of interest.

PP0990

IDENTIFICATION OF POTENTIAL EPIGENETIC MECHANISMS REGULATING LSECTIN EXPRESSION IN HEPATIC ANTIGEN PRESENTING CELLS

E. Angel Gomis^{1,2}, S. Martinez^{1,2}, I. Gomez-Hurtado^{3,4}, P. Boix^{1,2}, O. Juanola Juarez¹, E. Caparros^{2,5}, R. Frances Guarinos^{4,2,5}

¹Universidad Miguel Hernandez, Clinical Medicine, Alicante, Spain, ²IIS ISABIAL, Alicante, Spain, ³Hospital General Universitario de Alicante, Hospital General Alicante, Alicante, Spain, ⁴Instituto de Salud Carlos III, CIBERehd, Madrid, Spain, ⁵Clinical Medicine Department (Miguel Hernández University), San Juan De Alicante, Spain

Contact E-Mail Address: enrique.angel@goumh.umh.es

Introduction: LSEctin/*Clec4g* is a C-type lectin that recognizes pathogen patterns, and a T-cell ligand expressed by Kupffer Cells (KCs) and Liver Sinusoidal Endothelial Cells (LSECs). Its expression decreases during chronic liver disease progression, however, the mechanisms that regulate this process have not been fully characterised.

Aims & Methods: Given the relevance of epigenetic control in gene expression regulation during liver disease progression, our main aim was to characterise the epigenetic regulation of LSEctin regarding DNA methylation and Histone Posttranslational Modifications (HPTMs), main mechanisms of epigenetic gene regulation. For this purpose, immortalised KCs and LSECs lines were cultured and stimulated with selected epigenetic drugs: OTS186935 (Suv39h2 inhibitor), UNC0642 (G9a/Glp inhibitor), UNC1999 (EZH2/1 inhibitor), 5-Aza-2'-deoxycytidine (DNMT inhibitor) with or without IL-4, an LSEctin inducer. Simultaneously, probe-based methylation array and ChIP-Seq experiments were conducted in primary KCs and LSECs isolated from both control and an experimental chronic liver disease mice model, generated by a 12-week protocol of CCl₄ oral gavage.

Results: Different significant changes were observed in specific genomic loci, both in LSECs and Kupffer cells, these last particularly susceptible to methylation changes after CCl₄ treatment. We didn't observe significant changes at general methylation levels in KCs and LSECs methylome from untreated vs CCl₄-treated mice. Beta-values of specific probes for *Clec4g* gene body and promoter region resulted to be statistically significantly different, especially in Kupffer cells. ChIP-Seq of KCs and LSECs from both untreated and CCl₄-treated mice allowed the study of peak profile after immunoprecipitation with H3K9me3 and H3K27me3 antibodies. Both populations showed a differential peak profile at genomic level, but no differences at *Clec4g* gene body or proximal promoter. Pharmacological inhibition of histone-lysine N-methyltransferase enzymes for 48 h of treatment showed a downregulation in LSEctin expression. Consequently, LSEctin expression could be retrieved by IL-4+drug treatment, highlighting results obtained in KCs. Nevertheless, Ezh2/1 inhibition did not follow this trend, moderately increasing LSEctin expression after the treatment. In addition, LSEctin expression was upregulated by DNA passive demethylation due to DNMT inhibition, with a higher increase in Aza+IL-4 treated cells, thus supporting the potential role of DNA methylation in *Clec4g* regulation.

Conclusion: LSEctin expression upregulation by DNA passive demethylation together with methylation array analysis strongly points out DNA methylation as a regulatory mechanism of LSEctin expression. On the other hand, LSEctin expression modulation by epigenetic drugs, altogether with the absence of a specific peak profile at *Clec4g* suggests a more complex, indirect effect of HPTMs in the protein regulation.

Disclosure: Nothing to disclose.

PP0991

SCREENING FOR VIRAL HEPATITIS IN ALL INPATIENTS OF A UNIVERSITY INTERNAL MEDICINE DEPARTMENT

A. Protopapas¹, N. Protopapa¹, V. Kyritsi¹, A. Filippidis¹, C. Savopoulos¹, A. Protopapas¹

¹Aristotle University of Thessaloniki, AHEPA University Hospital, First Propedeutic Department of Internal Medicine, Thessaloniki, Greece

Contact E-Mail Address: adoprot@hotmail.com

Introduction: The use of effective vaccines and drugs has led the global community to set a goal of shrinking the prevalence of viral hepatitis by 2030. Most efforts are focused on screening large segments of the population that are unaware that they have these diseases.

Aims & Methods: The aim of our study was to screen a large number of hospitalised patients for viral hepatitis. Patients hospitalised between 1/2021 and 9/2023 at the First Propaedeutic Department of Internal Medicine of the Aristotle University of Thessaloniki were prospectively analysed. Patients with known pre-admission viral hepatitis or patients investigated for liver disease were omitted. Patients underwent testing for viral hepatitis B and C markers.

Results: A total of 3914 patients were screened. The mean age was 69.8 ± 16.9 years. 112 (2.9%) patients had positive surface antigen, and 1281 (32.8%) patients had evidence of prior HBV infection (Anti-Hbc+), of which most (952, 74.3%) had concurrent positive Anti-Hbs antibodies. The presence of positive surface antigen was more common in patients 41-65 years old (4.1%) compared to patients > 65 years old (2.4%) and patients ≤ 40 years old (2.7%). Patients born in a foreign country constituted 21.2% of patients with positive surface antigen, with the vast majority being in the 41-65 age group (58.3%). Also, the presence of prior infection had a significant correlation with patient age ($p < 0.001$), with patients >65 years of age having a much higher prevalence (39.9%) compared to patients 41-65 years (20.9%) and patients ≤ 40 years (9.5%). HBV DNA testing was performed in 65 patients (58% of positives), with 60 patients showing positive HBV DNA (92.3%). Of these, 13 had chronic HBV infection, and 47 had chronic HBV hepatitis. Finally, 28 patients (59.6%) received treatment. Regarding screening for hepatitis C, 102 patients (2.7%) showed anti-HCV (+), with 53 patients (52%) undergoing HCV RNA testing. The presence of positive anti-HCV antibodies was more common in patients ≤ 40 years (9.1%), compared to patients 41-64 years (3.5%) and patients > 65 years (1.6%); 29 patients showed positive HCV RNA (54.7%), with 13 patients eventually receiving treatment (44.8%).

Conclusion: The study confirms the high prevalence of viral hepatitis in our country. Additionally, a significant proportion of patients with previous hepatitis B infection is recorded, a fact that is of considerable importance in the era of widespread use of immunosuppressive therapies. The increased prevalence of HBV infection in patients aged 41-65 years is probably explained by the presence of many patients of foreign origin. Finally, an important factor regarding the low treatment initiation rates is probably the performance status of patients hospitalised in internal medicine departments in our country, with high rates of morbidity and both inpatient and outpatient mortality. To conclude, hospitalised patients are a population in which screening for viral hepatitis can be easily and effectively performed.

Disclosure: Nothing to disclose.

PP0992

WITHDRAWN

PP0993

EXTENDING HCV ELIMINATION EFFORTS TO UNDERSERVED POPULATIONS - A VIENNESE APPROACH FOR HCV CARE AMONG HOMELESS PEOPLE WITHOUT HEALTH INSURANCE

C. Schwarz^{1,2}, B. Becsi¹, S. Leick¹, S. Gremmel¹, L. Wien², E. Gutic³, T. Reiberger⁴, H. Haltmayer⁵, M. Gschwantler^{3,2}

¹Medical University of Vienna, Vienna, Austria, ²Klinik Ottakring, Vienna, Austria, ³neunerhaus Health Care Center, Vienna, Austria, ⁴Sigmund Freud University, Vienna, Austria, ⁵Suchthilfe Wien gGmbH, Vienna, Austria

Contact E-Mail Address: schwarz.caroline1990@gmail.com

Introduction: Despite the increased risk for hepatitis C virus (HCV) infection among people experiencing homelessness (PEH), tailored HCV elimination efforts are currently lacking as this population is often not covered by health insurance.

We present the first Austrian HCV elimination project for PEH and people without health insurance (PHI).

Aims & Methods: "neunerhaus", a low-threshold facility providing health care, support by social workers, and housing for >5.000 PEH and PHI per year in Vienna, served as a platform for this project. From March 2020, all PEH and PHI using one of the services offered by neunerhaus had the opportunity to receive serological antiHCV screening directly on-site. AntiHCV(+) blood samples were automatically tested for HCV-RNA via PCR (reflex testing). Through the establishment of an on-site hepatology service at neunerhaus, HCV-viremic individuals received treatment with direct-acting antiviral agents (DAA).

For the duration of DAA therapy, housing (PEH) was provided by neunerhaus while DAA treatment (PHI) was kindly provided by Abbvie and Gilead. Through social workers as well as at the neunerhaus housing facilities, PEH and PHI received support in DAA adherence.

Results: Serologic antiHCV screening was performed in 601 persons between March 2020 and July 2023, among whom 116 (19.3%) showed antiHCV(+). Negative HCV-RNA PCR results indicated HCV clearance in 24/116 (20.7%), while 92 (79.3%) individuals remained HCV viremic (HCV-RNA+). Among the 92 viremic patients, 36 (39.1%) already started DAA and 21/36 (58.3%) finished treatment. Sustained virologic response (SVR) was documented in 17/21 (81.0%) patients and in 4 (19.0%) post-treatment follow-up remains pending. No treatment interruptions were recorded among the study population.

Conclusion: Despite COVID19-related restrictions affecting most of the study period, a relevant number of underprivileged PEH and PHI underwent HCV screening through this project. HCV viremia was found in 15.3% of the overall cohort, underlining the need for specific HCV elimination strategies for PEH and PHI as an underserved population.

Furthermore, our data demonstrate the effectiveness of streamlined DAA therapy for PEH and PHI, provided that safe housing for the duration of therapy, support through social workers, and low-barrier health care are available.

Future HCV elimination strategies should include underserved populations such as PEH and PHI in whom HCV prevalence remains alarmingly high despite the availability of DAA treatment.

Disclosure: C.S. received travel support from Gilead, Abbvie, and Gebro; speaking honoraria from Abbvie and Gilead; and payments for consulting from Gilead.

E.G. received travel support from Gilead, Abbvie.

T.R. received grant support from Abbvie, Boehringer- Ingelheim, Gilead, MSD, Philips Healthcare, Gore; speaking honoraria from Abbvie, Gilead, Gore, Intercept, Roche, MSD; consulting/advisory board fee from Abbvie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from Boehringer-Ingelheim, Gilead, and Roche.

M.G. received grant support from Abbvie, Gilead and MSD; speaking honoraria from Abbvie, Gilead, Intercept, Janssen, BMS, Roche, Norgine, AstraZeneca, Falk, Shionogi, and MSD; consulting/advisory board fees from Abbvie, Gilead, Intercept, Janssen, BMS, Roche, Alnylam, Norgine, AstraZeneca, Falk, Shionogi and MSD; and travel support from Abbvie and Gilead.

PP0994

HCV MICROELIMINATION THROUGH INDIVIDUALIZED INTERVALS FOR DIRECTLY OBSERVED THERAPY - A STREAMLINED APPROACH TO HCV CARE FOR PWID

C. Schwarz^{2,1}, A. Schütz⁵, D.J.M. Bauer^{2,1}, E. Gutic², T. Reiberger¹, H. Haltmayer⁵, M. Gschwantler^{2,4}

¹Klinik Ottakring, Vienna, Austria, ²Medical University of Vienna, Vienna, Austria, ³Suchthilfe Wien gGmbH, Vienna, Austria,

⁴Sigmund Freud University, Vienna, Austria

Contact E-Mail Address: schwarz.caroline1990@gmail.com

Introduction: Treating hepatitis C virus (HCV) infection among people who inject drugs (PWID) on opioid agonist therapy (OAT) according to the concept of directly observed therapy (DOT) with direct-acting antiviral agents (DAA) is a highly effective approach to HCV microelimination. The principle behind DOT is DAA prescription via a low-threshold facility (LTF) and supervised OAT/DAA ingestion at a pharmacy or the LTI. In individuals with good adherence to OAT, the intervals for OAT/DAA dispensation may be extended from daily to once weekly.

However, the effect of these alterations in OAT/DAA dispensation schedules on sustained virologic response (SVR) rates remains unclear. We present an individualized approach to DAA DOT for PWID that was used throughout the COVID19 pandemic and thereby represents one of only few HCV elimination programs that were successfully continued during the pandemic.

Aims & Methods: Two groups of Viennese PWID were compared regarding DOT distribution intervals, SVR rates, and socioeconomic characteristics: The "COVID period" was defined as 15.3.2020-2.5.2023 and comprised 239 PWID starting DAA treatment within that time frame. The "pre-COVID period" was defined as 26.9.2014-14.3.2020 and consisted of 441 PWID who began DAA therapy during that period.

Results: Daily DOT was the most frequent OAT/DAA distribution schedule pre-COVID (348 PWID, 78.9%) while 19 (4.3%) were on 2-3 times weekly and 74 (16.8%) on once weekly distribution. By comparison, during COVID, only 75 (31.4%) PWID were on daily DOT, 60 (25.1%) underwent 2-3 times weekly and 104 (43.5%) once weekly dispensation regimens ($p<0.001$). SVR rates, however, were comparably high between the two treatment periods (167/168 [99.4%] COVID vs. 402/405 [99.3%] pre-COVID according to modified intention-to-treat analysis; $p=0.849$) and no significant difference concerning missed visits (59 [0.8%] COVID vs. 84 [0.4%] pre-COVID; $p=0.239$) was recorded.

During COVID, socioeconomic status among the study population was equal or worse as compared to pre-COVID (unemployment: 83.7% vs. 67.3%, $p=0.967$; homelessness: 38.5% vs. 35.1%, $p=0.227$; harmful alcohol use: 29.3% vs. 10.7%, $p<0.001$; ongoing intravenous drug use: 64.0% vs. 57.8%, $p=0.616$). No treatment interruptions or COVID19-related deaths were observed among the study population.

Conclusion: Individualized DOT featuring extended OAT/DAA distribution intervals resulted in similarly high SVR rates as traditional daily DOT. Hence, the effectiveness of DOT seems to primarily result from the streamlined approach to HCV care comprising low-barrier access to healthcare and DAA treatment via an LTI and is not mainly linked to strict supervision.

Disclosure: C.S. received travel support from Gilead, Abbvie, and Gebro; speaking honoraria from Abbvie and Gilead; and payments for consulting from Gilead.

D.B. received travel support from Gilead and AbbVie; speaking honoraria from AbbVie and Siemens and grant support from Gilead and AbbVie.

E.G. received travel support from Gilead, Abbvie.

T.R. received grant support from Abbvie, Boehringer-Ingelheim, Gilead, MSD, Philips Healthcare, Gore; speaking honoraria from Abbvie, Gilead, Gore, Intercept, Roche, MSD; consulting/advisory board fee from Abbvie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Siemens; and travel support from Boehringer-Ingelheim, Gilead, and Roche.

M.G. received grant support from Abbvie, Gilead and MSD; speaking honoraria from Abbvie, Gilead, Intercept, Janssen, BMS, Roche, Norgine, AstraZeneca, Falk, Shionogi, and MSD; consulting/advisory board fees from Abbvie, Gilead, Intercept, Janssen, BMS, Roche, Alnylam, Norgine, AstraZeneca, Falk, Shionogi and MSD; and travel support from Abbvie and Gilead.

PP0995

EMERGING TRENDS: RISING INCIDENCE OF ACUTE HEPATITIS A AMONG ADULTS AND CLINICAL CHARACTERISTICS

Y. Shahid¹, A. Subhan²

¹Aga Khan University Hospital, Gastroenterology, Karachi, Pakistan, ²Aga Khan University Hospital Karachi, Karachi, Pakistan

Contact E-Mail Address: yumnashahid664@gmail.com

Introduction: For decades, Hepatitis A virus (HAV) had been a leading cause of acute hepatitis among children and was less prevalent among adults. However, recently a paradigm shift has been observed in the epidemiology of HAV evident by cases of acute hepatitis due to HAV among adults. There has been a global surge in the incidence of acute hepatitis A among adults as shown in Korean and Brazilian studies.^{1,2} The objective of our study is to estimate the frequency of HAV among adult patients presented with acute viral hepatitis at Aga Khan University Hospital (AKUH), Karachi. To compare the clinical and laboratory characteristics of acute viral hepatitis due to HAV and Hepatitis E virus (HEV) infection among adults.

Aims & Methods: This was a retrospective cross sectional study conducted at AKUH from 2019 till 2023. All patients above 18 years age, diagnosed with acute viral hepatitis secondary to hepatotropic viruses were included. Non hepatotropic virus related acute hepatitis, autoimmune, alcoholic and other metabolic causes were excluded. Data regarding clinical and laboratory parameters was collected by reviewing patient medical records. Yearly trend of occurrence was noted, frequencies of HAV, HEV, HBV (Hepatitis B virus) and HCV (Hepatitis C virus) were recorded, comparative analysis was done between HAV and HEV using spss.

Results: A total of 396 patients were found to have acute hepatitis during our study duration. 234 patients were diagnosed with acute HAV infection, 157 patients were found to have acute HEV infection. Additionally, HBV infection was identified as the cause in three patients, whereas HCV infection was found in only two cases of acute hepatitis. The mean age of patients with HAV was 28 ± 8 while those with HEV was 30 ± 8 with a p value of 0.017 showing that older adults were affected with HEV infection. Higher levels of total bilirubin were seen in HEV infection while higher levels Alanine transaminase (ALT) were seen in HAV infection. (p value <0.005). Increased frequency of acute liver failure (ALF), coagulopathy and mortality was observed in HEV. 10 patients with HEV required ICU while only 4 patients with HAV required ICU (p value=0.038). 13 patients with HEV were found to have underlying chronic liver disease (CLD) while only one patient with HAV was found to have CLD (p value=0.000). Yearly

trends showed increasing occurrence of HAV infection among adults. (Table) Prolonged hospital stay was observed among HEV patients with a p value <0.005.

Year	HAV	HEV
2019	30	33
2020	27	28
2021	31	40
2022	61	19
2023	85	37
Total bilirubin (mean)	6.2 mg/dL	13.3 mg/dL (p 0.000)
ALT (mean)	3274 IU	1760 IU (p 0.000)
ALF	8	24 (p 0.000)
Mortality	2	11 (p 0.001)

Conclusion: HAV seems to be the rising cause of acute hepatitis among adults. This signifies the need of improved sanitation, hygiene and a robust vaccination programme against HAV among adult population. Although it is less severe than acute HEV infection which causes more morbidity and mortality. More epidemiological studies are needed to establish this increase in HAV among adults.

References: 1. Kim YJ, Lee HS. Increasing incidence of hepatitis A in Korean adults. *Intervirology*. 2010;53(1):10-4. doi: 10.1159/000252778. Epub 2010 Jan 5. PMID: 20068335.
2. Grandi G, Lopez LF, Burattini MN. Temporal Trends of Acute Hepatitis A in Brazil and Its Regions. *Viruses*. 2022 Dec 8;14(12):2737. doi: 10.3390/v14122737. PMID: 36560740; PMCID: PMC9784953.

Disclosure: Nothing to disclose.

PP0996

WITHDRAWN

PP0997

NEONATAL SCLEROSING CHOLANGITIS- PHENOTYPE GENOTYPE OBSERVATIONS OF NOVEL BIALLELIC VARIANTS AND SINGLE EXON DELETIONS IN DCDC2 GENE IN INDIAN CHILDREN – EXPANDING HORIZON

D. Janakiraman¹, N. Deivamani¹, S. T A¹, S.K. Child Health, Madras Medical College,R¹, W. Thomas¹
¹Institute Of Child Health/Madras Medical College, Paediatric Gastroenterology, Chennai, India

Contact E-Mail Address: rdherdhe9@gmail.com
Introduction: Neonatal Sclerosing Cholangitis (NSC) is associated with progressive biliary fibrosis that often requires liver transplantation in childhood. Children present early in life with jaundice, hepatosplenomegaly, hyperbilirubinemia and high serum gamma glutamyl transferase activity (GGT) or intracranial bleed. DCDC2 pathogenic variants have been reported to be associated with renal-hepatic ciliopathy with nephronophthisis, deafness, dyslexia and central nervous system impairment.
Aims & Methods: The aim of our study was to present the phenotypic genotypic observations in five Indian children with novel biallelic variants and single exon deletions in DCDC2 gene. Prospective data of children diagnosed with NSC between March 2023 to February 2024 in a tertiary care institute in India were analyzed.
Results: We report five cases of NSC with mutation in DCDC2 gene of which patient four and five were siblings. Mean age at first presentation was 51 days. All children had cholestatic jaundice with high Gamma-Glutamyl Transferase (GGT). Two children presented with seizures due to intracranial bleed at their second month of life, and other three with jaundice and

hepatosplenomegaly. Three children had variceal bleed within 3 years and endotherapy had been done. None of them had renal disease or deafness. Liver biopsy in two children showed portal fibrosis and cholestasis. Magnetic Resonance Imaging of one child showed focal narrowing and dilatations of bile duct while others had minimal intrahepatic biliary radical dilatation. On Next Generation Sequencing, four different novel variants were identified. Two novel variants with frame shift variant in exon7, c.840_841delinsT p.Lys280AsnfsTer4 (depth -181X), and splice site variant c.759+1_759+2dup in Intron6 were classified as likely pathogenic, as these variants were predicted to cause loss of function. Child with splice site variant had motor developmental delay, which improved with age. Homozygous single exon deletions in DCDC2 in exon2 [chr6:(?_24357674-24358132_?)del] and exon5 [chr6:(?_24291148-24291316_?)del], which were reported previously in patients with reading disability, language impairment were identified in three children. As these two children were 3years and 9months respectively at last follow up, reading and language impairment could not be definitely established.

Sl.no	Gender	Age at Presentation	Parental Consanguinity	Symptoms at onset	Pruritis	Variceal Bleed	Highest Bilirubin (mg/dl)	Highest GGT (IU/L)	Variant Nomenclature	Zygosity	Location	Change	Extrahepatic manifestations	Growth Retardation	Follow up
1	Female	1 month	No	Neonatal cholestasis	Yes	Yes, 3 years	8.4	1179	c.840_841delinsT p.Lys280AsnfsTer4 (depth -181X)	Homozygous	Exon 7	Frameshift variant	No	No	Alive till 13yrs Good synthetic function
2	Female	55 days	Yes	Cholestatic jaundice, subdural haematoma	Occasional pruritis	Yes, 3 years	9.9	130	c.759+1_759+2dup [Depth -92X]	Homozygous	Intron 6	Splice site variant	Motor developmental delay -improved after 2 yrs of age	No	Alive till 11 years Good synthetic function
3	Male	2 months	Yes	Intracranial bleed, neonatal cholestasis	No	Yes, 2.5 years	6.3	1997	chr6: (?_24357674_24358132_?)del	Homozygous	Exon 2	Deletion	No	No	Alive till 3.5 years Good synthetic function
4	Male	50days	Yes	Neonatal cholestasis	No	No	4.6	600	[chr6: (?_24291148-24291316_?)del]	Homozygous	Exon 5	Deletion	Growth retardation Developmental delay	Yes	Died at 2.5years (not of liver failure)
5	Female	2 months	Yes	Neonatal cholestasis	No	No	7.6	1287	[chr6: (?_24291148-24291316_?)del]	Homozygous	Exon 5	Deletion	Severe growth retardation	Yes	Alive till 1 year 4 months Good synthetic function

Conclusion: Till date only thirty-eight cases have been reported. Novel homozygous spice site, frameshift variants and homozygous single exon deletions of DCDC2 reported here widens the spectrum of DCDC2 in NSC.
References: 1. Wei, Xia, et al. “Neonatal sclerosing cholangitis with novel mutations in DCDC2 (doublecortin domain-containing protein 2) in Chinese children.” *Frontiers in pediatrics* 11 (2023): 1094895.
2. Lin, Yuxiang, et al. “Biallelic mutations in DCDC2 cause neonatal sclerosing cholangitis in a Chinese family.” *Clinics and Research in Hepatology and Gastroenterology* 44.5 (2020): e103-e108.
3. Grammatikopoulos, Tassos, et al. “Mutations in DCDC2 (doublecortin domain containing protein 2) in neonatal sclerosing cholangitis.” *Journal of hepatology* 65.6 (2016): 1179-1187.
4. Girard, Muriel, et al. “DCDC2 mutations cause neonatal sclerosing cholangitis.” *Human mutation* 37.10 (2016): 1025-1029.
Disclosure: Nothing to disclose.

PP0998

DIAGNOSIS AND SCREENING OF LOW PHOSPHOLIPID-ASSOCIATED CHOLELITHIASIS SYNDROME (LPAC): CHALLENGES AND PERSPECTIVES IN A MOROCCAN POPULATION

M. Aymane¹, H. Koulali², Y. Dendane¹, H. Bouamar¹, O. Elmqaddem¹, Z. Abdelkrim³, Z. Ismaili⁴, G. Kharrasse⁵

¹Université Mohammed Premier, Oujda, Morocco, ²Mohammed VI University Hospital, Hepatogastroenterology, Oujda, Morocco,

³Mohammed VI University Hospital, Mohammed the First University, CHU Med VI Oujda, Oujda, Morocco, ⁴Medical School, Hepato Gastroenterology, Oujda, Morocco, ⁵Faculty of medicine Oujda, Avicenne, Oujda, Morocco

Contact E-Mail Address: Aymanemouloudi@gmail.com

Introduction: Low Phospholipid-Associated Cholelithiasis (LPAC) syndrome is a rare disorder caused by mutations in the ABCB4 phospholipid transporter, found in biliary canaliculi. These mutations lead to a deficiency in phospholipids and the subsequent precipitation of cholesterol crystals within the small intrahepatic bile ducts. LPAC syndrome can be diagnosed following the emergence of biliary symptoms or through familial screening. The objective of our study is to characterize the epidemiological, clinical, and paraclinical data of patients monitored for LPAC syndrome in our institution and to assess therapeutic responses and outcomes.

Aims & Methods: We collected data from all patients diagnosed with LPAC syndrome at our institution. Diagnosis was established based on the presence of at least two of the following criteria: (1) age at onset of biliary symptoms ≤40 years; (2) presence of hyperechoic intrahepatic foci ("comet tails" or micro-spots); (3) recurrence of biliary symptoms post-cholecystectomy.

Results: 10 patients were included. The Average age at diagnosis was 33,6 years, with symptoms typically beginning around age 30. The sex ratio was 2/8 (M/F). A family history of biliary lithiasis and cholecystectomy before the age of 40 were found in 70% of cases. None of the female patients had a history of pregnancy-related cholestasis. 70% of the patients had undergone cholecystectomy prior to their LPAC diagnosis, with recurrence of biliary symptoms before age 40 in all these patients. Clinical presentations upon admission included symptomatic gallstone disease in 5 cases, acute cholangitis due to main bile duct stones in 4 cases, and acute lithiasic pancreatitis in 1 case. Hepatobiliary ultrasound was performed in all patients, revealing comet tail signs in 50% of cases, hyperechoic intrahepatic spots in 20% of cases, and intrahepatic stones in 50% of cases. Biochemical tests showed hyperbilirubinemia in 30% of cases, elevated Gamma-GT and alkaline phosphatase in 80% of cases, and hepatocellular damage in 40% of cases. A mutation in the ABCB4 gene was found in 2-patients. 8 patients benefit from An Ursodeoxycholic Acid (UDCA) dosage averaging 11mg/kg, experiencing significant clinical and biological improvements.

Conclusion: LPAC syndrome is a rare pathology in our series, predominantly affecting young, non-overweight women with personal and family history of early biliary stones occurrence. Treatment with Ursodeoxycholic Acid (UDCA) controlled symptoms in the majority of cases.

Disclosure: Nothing to disclose.

PP0999

SELADELPAR IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

E. Barbosa¹, P. Santo², S. Baraldo³, A. Nau⁴, M. Meine⁵, G. Meine⁶
¹Evangelical University of Goiás - UniEVANGÉLICA, Anápolis, Brazil,
²Federal University of São Carlos, São Carlos, Brazil, ³Barretos Cancer Hospital, Barretos, Brazil, ⁴Jaraguá Hospital, Jaraguá do Sul, Brazil, ⁵Pontifical Catholic University of Parana, Curitiba, Brazil, ⁶Feevale University, Novo Hamburgo, Brazil

Contact E-Mail Address: mcmeine@gmail.com

Introduction: Peroxisome proliferator-activated receptor delta (PPARδ) agonists, such as seladelpar, emerged as potential therapies for PBC and other cholestatic diseases. PPARδs are nuclear receptors widely expressed in hepatocytes, cholangiocytes, Kupffer cells, and hepatic stellate cells. Activation of this receptor may modify the progression of PBC, particularly through its bile acid retention mechanism and antifibrotic and anti-inflammatory effects, inducing biochemical and clinical improvement in PBC patients.

Aims & Methods: We aimed to compare the efficacy and safety of seladelpar vs placebo for treating patients with primary biliary cholangitis (PBC) and inadequate response or intolerance to ursodeoxycholic acid (UDCA). We systematically searched MEDLINE, Embase, and Cochrane databases from inception to March 12, 2024. Risk ratios (RRs) and mean differences (MDs) with 95% confidence intervals (CIs) were employed for dichotomous and continuous outcomes, respectively, using a random-effects model. We used Review Manager 5.4.1 for statistical analyses.

Results: We included 3 randomized clinical trials (395 patients). The results of the pooled analyses are shown in Table 1.

Outcome	Pooled effect estimate (95%CI)	P-value	I ² , %	Certainty of evidence
Composite biochemical response (week 4)	RR 6.67 (4.00 to 11.13)	<0.001	0	⊕⊕⊕⊕
Composite biochemical response (week 12)	RR 6.07 (3.71 to 9.9)	<0.001	0	⊕⊕⊕⊕
Least-squares percent change of ALP (week 4)	MD -34.28 (-39.56 to -29.00)	<0.001	29	⊕⊕⊕
Least-squares percent change of ALP (week 12)	MD -40.76 (-47.95 to -33.58)	<0.001	67	⊕⊕⊕
Alkaline phosphatase normalization (week 12)	RR 18.57 (3.81 to 90.42)	<0.001	0	⊕⊕⊕
Least-squares mean change of pruritus in overall population (week 12)	MD -0.64 (-1.06 to -0.22)	0.003	0	⊕⊕⊕⊕
Least-squares mean change of pruritus in patients with baseline NRS pruritus score ≥4 (week 12)	MD -1.24 (-2.03 to -0.45)	0.002	0	⊕⊕⊕
Any adverse event	RR 0.99 (0.90 to 1.10)	0.87	1	⊕⊕⊕⊕
Any serious adverse event	RR 0.88 (0.32 to 2.44)	0.81	0	⊕⊕⊕⊕

Table 1. Results from the pooled analyses.

⊕⊕⊕⊕, high-quality evidence; ⊕⊕⊕, moderate-quality evidence; 95%CI, 95% confidence interval; MD, mean difference; NRS, numerical rating scale; RR, risk ratio.

Compared with placebo, seladelpar increased the probability of achieving composite biochemical response both at week 4 (RR 6.7; 95% CI 4.0 to 11.1) and at week 12 (RR 6.1; 95% CI 3.7 to 9.9), decreased alkaline phosphatase levels both at week 4 (MD -34.3%; 95% CI -39.6 to -29.0%) and at week 12 (MD -40.8%; 95% CI -47.9 to -33.6), increased the probability of achieving alkaline phosphatase normalization at week 12 (RR 18.6; 95% CI 3.8 to 90.4), and decreased pruritus scores at week 12 in both the overall population (MD -0.6; 95% CI -1.1 to -0.2) and the population with baseline

pruritus score ≥ 4 (MD -1.2; 95% CI -2.0 to -0.4). Additionally, there was a non-significant difference between seladelpar and placebo in the risk of any adverse event (RR 1.0; 95% CI 0.9 to 1.1), any serious adverse event (RR 0.9; 95% CI 0.3 to 2.4), or any adverse event leading to treatment discontinuation (RR 0.7; 95% CI 0.2 to 2.0).

Conclusion: Seladelpar may be an effective and safe treatment option for patients with PBC and inadequate response or intolerance to UDCA. However, new large RCTs assessing long-term efficacy and safety outcomes are necessary to better evaluate its place in PBC management.

References:

1. Hirschfield GM, Shiffman ML, Gulamhusein A, et al. Seladelpar efficacy and safety at 3 months in patients with primary biliary cholangitis: ENHANCE, a phase 3, randomized, placebo-controlled study. *Hepatology* 2023;78:397–415.
2. Hirschfield GM, Bowlus CL, Mayo MJ, et al. A Phase 3 Trial of Seladelpar in Primary Biliary Cholangitis. *N Engl J Med* 2024;390:783–794.
3. Jones D, Boudes PF, Swain MG, et al. Seladelpar (MBX-8025), a selective PPAR- δ agonist, in patients with primary biliary cholangitis with an inadequate response to ursodeoxycholic acid: a double-blind, randomised, placebo-controlled, phase 2, proof-of-concept study. *The Lancet Gastroenterology & Hepatology* 2017;2:716–726.

Disclosure: The authors have no conflict of interest.

PP1000

CAROLI DISEASE AND SYNDROME: ABOUT 8 CASES

A. Khsiba¹, W. Sellami², M. Moufida³, I. Keskes⁴, A. Ben Mohamed⁵, M. Yakoubi⁶, G. Gharbi⁷, M. Medhioub⁸, M.L. Hamzaoui⁹

¹Faculté de médecine de Tunis, Tunisia Mohamed taher Maamouri hospital Nabeul Tunisia, Gastroenterology and Hepatology departement , Nabeul, Tunisia, Nabeul, Tunisia, ²Taher Maamouri Hospital, Nabeul, Tunisia, ³Mohamed Taheer Maamouri, Gastroenterology, Nabeul, Tunisia, ⁴Faculté de médecine de Sfax, Gastroenterology, Sfax, Tunisia, ⁵Department of Gastroenterology Mohamed Taheer Maamouri Hospital, Gastroenterology, Tunis, Tunisia, ⁶FMT, Gastro enterology, Tunis, Tunisia, ⁷Hbib Thameur hospital in tunis (Tunisia), Gastroenterology Department, Tunis, Tunisia, ⁸Mohamed taheer Maamouri hospital, Gastroenterology Department, Nabeul, Tunisia, ⁹Faculté de médecine de Tunis, Gastroenterology and Hepatology, Nabeul, Tunisia

Contact E-Mail Address: wamid8sellami@gmail.com

Introduction: Caroli disease (CD) is a rare congenital disease defined by the presence of segmental dilations in the intrahepatic bile ducts. It is called Caroli syndrome (CS) when it is associated with liver fibrosis or cirrhosis. It is often diffuse, rarely localized to a single lobe of the liver.

The aim of this study was to describe the epidemiological, clinical and therapeutic aspects as well as the observed complications associated with this pathology

Aims & Methods: We collected patients followed for CD or CS in the gastroenterology department of the Tahar Maamouri University Hospital in Nabeul from January 2008 to December 2018. We retrospectively collected epidemiological, clinical, radiological, therapeutic and evolutionary data.

Results: We collected 8 patients: 4 men and 4 women whose average age was 64 years (38–79 years). The circumstances of discovery were an acute cholangitis in two patients and biliary colic in six. The average time between the onset of symptoms and definitive diagnosis was 10 months with extremes ranging from 1 month to 10 years. A morphological assessment (abdominal ultrasound, abdominal CT or Biliary MRI) was carried

out in all patients. It showed dilation of the intrahepatic bile ducts (IHBD) in all cases. It was diffuse in four cases and localized to the left in 4 cases. It was associated with intrahepatic stones in 50% of patients (N=4). Gallstone lithiasis was associated in 38% of cases (N=3). Polycystic kidney disease was observed in 25% of patients (N=2). All patients had normal renal function.

Two patients had signs of portal hypertension consistent with a Caroli syndrome. In our series, complications were observed in 50% of cases such as: iterative attacks of acute cholangitis in two patients, acute pancreatitis due to a biliary lithiasis in one patient and a case of liver abscess in one patient.

Episodes of cholangitis were controlled by appropriate antibiotic therapy and ursodeoxycholic acid was prescribed in 3 patients at a dose of 15 mg/kg/day for intrahepatic lithiasis. Surgical treatment was carried out in 4 patients, consisting of a left hepatectomy in 3 patients with localized disease and a choledocotomy with hepaticojejunal anastomosis in one patient for lithiasis of the main bile duct. Endoscopic sphincterotomy was performed in 2 patients: one for residual lithiasis of the common bile duct in and one as sequential treatment. The median follow-up was 84 months, two deaths were observed: one secondary to hepatocellular failure and the other secondary to uncontrolled septic shock. In our series there was no case of cholangiocarcinoma.

Conclusion: The diagnosis of CD is often late. It should be considered in the presence of abscesses or recurrent cholangitis associated with the dilatation of the bile ducts. Hepatectomy of localized forms protects against septic complications and degeneration. Liver transplantation remains to be developed to treat patients with a diffuse form.

Disclosure: Nothing to disclose.

PP1247

CHALLENGES IN MANAGEMENT OF PRIMARY BILIARY CIRRHOSIS IN UNIVERSITY HOSPITAL LEWISHAM, A 2 -YEAR AUDIT

I. Mohamed¹, W. Hong¹, T. Al-Chalabi¹, S. Mohamed²

¹University Hospital Lewisham, Gastroenterology, London, United Kingdom, ²Assiut University Hospital, Gastroenterology and Tropical Medicine, Assiut, Egypt

Contact E-Mail Address: islam.mohamed2@nhs.net

Introduction: Primary Biliary cholangitis (PBC) is a cholestatic condition caused by autoimmune damage of the biliary channels and potentially Precipitating biliary liver cirrhosis and ESLD. The National PBC audit highlighted the nationwide variability in diagnosing and managing PBC (1). The BSG guideline-recommended standard dosing of UDCA (13–15 mg/kg/day) and prompt liver transplant assessment when indicated (2). Additionally, it endorsed early detection of cirrhosis with related screening to establish and treat hepatocellular carcinoma and oesophageal varices early and it supports adequate control of symptoms such as fatigue or itching which can be challenging (1,2).

Aims & Methods: We obtained medical records from our Electronic Prescription and Medication Administration (EPMA) team for all PBC patients on UDCA between May 2021 and May 2023. A total of 141 patients were identified; 45 and 12 patients were excluded as duplicate and incomplete records, respectively. Only 84 patients were included in this retrospective analysis all with confirmed PBC as defined by the BSG and BASL. Mostly Females (84%) with a mean age of 56.5 years old (35:78). Data were collected from clinic letters and medical records regarding UDCA dose per body weight, symptoms control, refer to liver transplantation, FibroScan and Variceal/HCC screening when liver cirrhosis is a concern.

Results: Our audit revealed that only 78% of the patients were on ideal dosing of UDCA as per documented body weight, additionally, no clear symptoms scoring (fatigue, itching, joint pain, etc) was used. However,

in the 19 patients with established biliary cirrhosis on fibroScan, there was good compliance with HCC screening (84%) and oesophageal varices screening (78.9%).

Additionally, only 7 patients were referred for liver transplant assessment or discussed with the tertiary center (see Table 1 for details).

Parameter	result
UDCA dose (13–15 mg/kg/ day)	66/84 (78%)
Associated conditions at diagnosis like Ulcerative colitis	4.7%
Symptoms Burden (fatigue and itching score)	Poor documentation and inconsistency throughout records.
FibroScan for liver cirrhosis (>13 Kpa)	19/84 established LC (22.6%)
Refer for liver transplantation assessment or discussions	7/84 (8.3%)
HCC screening (AFP & US)	17/19 (84%)
Variceal screening (Gastroscopy)	15/19 (78.9%)

Study Results (Table 1): - (UDCA, ursodeoxycholic acid - LC, liver cirrhosis - HCC, Hepatocellular carcinoma, AFP, alpha-fetoprotein- US, ultrasound)

Conclusion: More compliance with the recommended dose of UDCA in our patient is needed to achieve clinical outcomes and normalization of liver functions. there was great compliance with variceal and HCC screens in cirrhotic patients However we also advised prompt early referrals for liver transplant assessment. Furthermore, documentation and scoring of extrahepatic symptoms should be improved.

References: 1) Burke, Laura et al. “The National Audit of Primary Biliary Cholangitis (PBC) in the United Kingdom: Defining the Audit Dataset and Data Collection System.” *Cureus* vol. 14,6 e25609. 2 Jun. 2022, doi:10.7759/cureus.25609.

2) Hirschfield, Gideon M et al. “The British Society of Gastroenterology/ UK-PBC primary biliary cholangitis treatment and management guidelines.” *Gut* vol. 67,9 (2018): 1568-1594. doi:10.1136/gutjnl-2017-315259.

Disclosure: Nothing to disclose.

PP1001

IS MYCOPHENOLATE MOFETIL EFFECTIVE FOR PATIENTS WITH AUTOIMMUNE HEPATITIS WHO FAILED STANDARD THERAPY?: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS

O. Martins¹, V. Antunes², M.V. Fernandes², N.J. Milioli³, T. Correa⁴, A. Milani⁵, P. Romeiro⁶, A.C. Covre Coan⁷, A. Prata⁷, E. Bulhões⁸

¹Federal University of Juiz de Fora, Juiz de Fora, Brazil, ²Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ³Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ⁴Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁵State University of Campinas, Campinas, Brazil, ⁶University Center of Maceió, Maceió, Brazil, ⁷Federal University of Espirito Santo, Vitoria, Brazil, ⁸College of Higher Education of the United Amazon, Redenção, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction: Standard treatment of autoimmune hepatitis (AIH) typically includes a combination of azathioprine and corticosteroids. However, approximately 20% of patients do not respond well to this conventional therapy. In this scenario, mycophenolate mofetil (MMF) may be used as an alternative treatment for patients with intolerance or non-response to first-line options.

Aims & Methods: This study aims to evaluate the performance of MMF in intolerant or non-responders patients with AIH previously treated with conventional therapy. We performed a systematic review in PubMed, Embase, and Cochrane databases. We analyzed overall remission, remission at AZA intolerance, and remission at AZA non-response. We also

compared the outcome of overall remission in patients with AZA intolerance vs. AZA non-response. Statistical analyses were performed using R language 4.3.1.

Results: 21 studies and 646 patients were included. The pooled overall remission rate was 62.21 (95% CI 54.31, 70.10). We found an overall remission rate of 66.74 (95% CI 57.48, 76.00) in patients intolerant to AZA, and 27.80 (95% CI 11.56, 44.04) in AZA non-responders. The comparison of overall remission in both groups favored the intolerance group (OR 4.98; 95% CI 1.69, 14.72; p = 0.004).

Conclusion: MMF is effective in inducing remission in patients with AIH who failed the first-line treatment. The overall effect is more prominent in patients who failed conventional therapy due to intolerance. Non-response to AZA may be correlated to suboptimal response to MMF as well.

Disclosure: Nothing to disclose.

PP1002

MYCOPHENOLATE MOFETIL IS MORE EFFECTIVE THAN AZATHIOPRINE AS A FIRST-LINE AGENT TO INDUCE COMPLETE BIOCHEMICAL REMISSION IN PATIENTS WITH AUTOIMMUNE HEPATITIS: RESULTS FROM A SYSTEMATIC REVIEW AND META-ANALYSIS

O. Martins¹, E. Bulhões², M.V. Fernandes³, V. Antunes³, N.J. Milioli⁴, T. Correa⁵, A. Prata⁶, A.C. Covre Coan⁶, P. Romeiro⁷, A. Milani⁸
¹Federal University of Juiz de Fora, Juiz de Fora, Brazil, ²College of Higher Education of the United Amazon, Redenção, Brazil, ³Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ⁴Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ⁵Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁶Federal University of Espirito Santo, Vitoria, Brazil, ⁷University Center of Maceió, Maceió, Brazil, ⁸State University of Campinas, Campinas, Brazil

Contact E-Mail Address: nataliamilioli@gmail.com

Introduction: Mycophenolate mofetil (MMF) is considered an alternative treatment for patients with autoimmune hepatitis (AIH) who have insufficient response to azathioprine (AZA). However, it is hypothesized that MMF may be more effective than AZA to induce remission in treatment-naïve patients as well.

Aims & Methods: This study aims to compare the effectiveness of MMF and AZA in inducing remission in patients with treatment-naïve AIH. PubMed, Embase, and Cochrane were systematically searched for randomized controlled trials and observational studies. The primary outcome was complete biochemical remission (CBR) at the end of the follow-up period. The secondary outcome was non-response rate. Heterogeneity was examined using I² statistics, and a random-effects model was employed. Review manager 5.4 was used for statistical analyses.

Results: The meta-analysis included 3 studies (1 RCT and 2 observational) and 265 patients (180 in the MMF group vs. 85 in the AZA group). CBR was significantly higher in the MMF group (OR 3.81; 95% CI 1.98 to 7.36; p < 0.0001; I² = 0%). There was no significant difference between groups regarding the non-response rate (OR 0.46; 95% CI 0.14 to 1.52; p = 0.20; I² = 53%).

Conclusion: In patients with treatment-naïve AIH, MMF is more effective in inducing CBR compared to conventional treatment with AZA. Larger RCTs are needed to consolidate the evidence of MMF's impact on AIH treatment as a first-line agent and to provide concise insights for guiding clinical decisions.

Disclosure: Nothing to disclose.

PP1003

PORTAL HYPERTENSION AFTER LIVER TRANSPLANT: AN ITALIAN-SINGLE CENTER EXPERIENCE

M. Spigaroli¹, G. Cusi¹, M. Merli², L. Lapenna³, S. Di Cola¹, G. Mennini¹, S. Fonte¹

¹Policlinico Umberto I, La Sapienza Roma, Roma, Italy,

²Sapienza University of Rome, Department of Clinical Medicine, Gastroenterology, Rome, Italy, ³Università Sapienza Roma, Firenze, Italy

Contact E-Mail Address: margherita.spigaroli@uniroma1.it

Introduction: Post liver transplantation portal hypertension (post LT-PH) is an emerging late complication after LT and a challenging disorder.

Aims & Methods: The aim of this study is to describe the prevalence, risk factors, clinical consequences (oesophageal varices, ascites, portal vein thrombosis, hydrothorax, hepatic encephalopathy) and the mortality rate of post LT-PH. We retrospectively enrolled 358 patients receiving a liver transplant at the University Hospital Policlinico Umberto I, between 2000 and 2018 to ensure a follow-up period of at least 5 years. For the statistical analysis Chi squared test, Fisher Test and T test were used.

Results: In our cohort 54 (15%) patients developed post LT-PH. The average time between LT and the occurrence of clinical evidence of PH was 6 ± 3.7 years: specifically 5.4 ± 3.4 years in patients with cirrhosis recurrence, and 3.4 ± 4.5 years for all non-cirrhotic portal hypertension causes. Patients with post LT-PH showed significant differences from the other LT patients regarding the immunosuppression regimen, with a more frequent use of cyclosporine (27.7 vs 1.3% $p > 0.0001$). Etiology of portal hypertension was cirrhotic in 41 (76%) patients and non-cirrhotic in 12 (24%) patients. The most frequent etiologies of cirrhosis recurrence were HCV or HBV, biliary complications, chronic rejection, de novo autoimmune hepatitis. Among the non-cirrhotic portal hypertension, we identified 3 cases of Porto Sinusoidal Vascular Disorder (PSVD), 1 case of Budd-Chiari Syndrome de novo and several cases of pre or post-hepatic anastomotic stenosis. The most frequent complications of post LT-PH were gastroesophageal varices, ascites, and portal vein thrombosis. Four patients underwent TIPS placement for the management of gastrointestinal bleeding. Moreover, as expected, more patients with cirrhotic post LT-PH died for liver failure (61%) while in the non cirrhotic group only in 3 (25%) cases death was liver related (p value 0.0471).

Conclusion: PH may develop during the follow up of liver transplant patients. This event has been mainly reported due to cirrhosis recurrence, especially for viral etiology, and numbers will decrease following the introduction of efficacious antiviral therapies. Despite this, it is important to consider other causes of post LT-PH. In our cohort 3 cases of PSVD have been highlighted, which is a rare and sparsely described event in the literature among transplant patients. Gastroesophageal varices and ascites were the most frequent complications of portal hypertension. Close clinical and instrumental follow-up is suggested for early diagnosis and management.

Disclosure: Nothing to disclose.

PP1004

ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSY IN A PORCINE LIVER MODEL: A COMPARATIVE STUDY BETWEEN FRANSEEN AND NOVEL TRICORE NEEDLES

Y. Park^{1,2}, S.H. Kim^{3,4}, S.-S. Lee⁴, J.-H. Park^{3,2}

¹Asan Medical Center, Biomedical Engineering Research Center, Asan Institute for Life Sciences, Seoul, South Korea, ²University of Ulsan College of Medicine, Department of Convergence Medicine, Asan Medical Center, Seoul, South Korea, ³Asan Medical Center, Biomedical Engineering Research Center, Asan Institute for Life Sciences, Seoul, South Korea, ⁴University of Ulsan College of Medicine, Department of Gastroenterology, Asan Medical Center, Seoul, South Korea

Contact E-Mail Address: ybeen9733@amc.seoul.kr

Introduction: Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) is a reliable and minimally invasive method for obtaining tissue samples from organs like the pancreas, adrenal glands, and liver [1]. However, challenges in obtaining sufficient tissue samples persist due to limitations of needles, including design and materials [2]. To overcome these limitations, various FNB needles with different tip design and materials, such as Franseen and fork-tip needles, have been developed [3]. Nevertheless, ongoing enhancement of FNB needles remains crucial for increasing the diagnostic yield and efficacy of EUS-FNB.

Aims & Methods: This study aimed to compare the efficacy of newly designed Tricore needles with Franseen needles in a porcine liver model under EUS guidance. A total of four male Yorkshire pigs were randomly divided into two groups: the Franseen group and the Tricore group. Nine EUS-FNB procedures were performed on each pig using three FNB needles. All pigs were euthanized immediately after the final procedure. The maximum resistance force during the puncture and the angle of the FNB needle tip was measured to compare puncture performance of two FNB needles. Visibility under ultrasound, blood contamination, and tissue acquisition time were also evaluated immediately after the EUS-FNB procedure. The sufficiency of the specimen for diagnosis was assessed by measuring the total specimen area, number of fragments, fragment areas, and number of complete portal tracts (CPTs).

Results: Procedural outcomes were successful with no complications observed, yielding specimens with a 100% (36/36) success rate. The Franseen needle (5.97 ± 0.53 N) exhibited significantly higher resistance compared to the Tricore needle (3.83 ± 0.84 N, $P < 0.001$). The both needle tips were observed considerable bending pre- and post-procedure ($P < 0.01$); however, the Franseen needle ($84.58 \pm 39.69^\circ$) became more significantly bent than the Tricore needle ($32.82 \pm 14.17^\circ$, $P < 0.001$). The visibility under ultrasound of the Tricore needle was significantly higher than that of the Franseen group ($P < 0.01$). While blood contamination was similar between groups ($P = 0.926$), the Franseen group (59.90 ± 19.15 s) required significantly longer acquisition time than the Tricore group (48.94 ± 9.26 s, $P < 0.05$). Histological findings revealed significantly larger total specimen area ($P < 0.05$) and fragment area ($P < 0.001$) in the Tricore group compared to the Franseen group. Additionally, the Tricore group exhibited significantly higher number of CPTs ($P < 0.05$).

Conclusion: In conclusion, our study demonstrated that the newly designed Tricore EUS-FNB needle exhibits superior puncture ability and ultrasound visibility, while acquiring liver tissue specimens of greater quantity and quality compared to the commercially available Franseen needle. These findings suggest that the Tricore needle may offer a promising alternative for EUS-FNB procedures. Although further clinical validation is needed to confirm these findings, this novel needle design holds potential for improving the diagnostic yield and efficacy of EUS-FNB in clinical practice.

References: 1. Tanisaka, Y. *et al.* Comparison of Endoscopic Ultrasound-Guided Fine-Needle Aspiration and Biopsy Device for Lymphadenopathy. *Gastroenterol Res Pract* 2021, 6640862, doi:10.1155/2021/6640862 (2021).

2. Song, T. J. *et al.* The prospective randomized, controlled trial of endoscopic ultrasound-guided fine-needle aspiration using 22G and 19G aspiration needles for solid pancreatic or peripancreatic masses. *Am J Gastroenterol* 105, 1739–1745, doi:10.1038/ajg.2010.108 (2010).

3. Mohan, B. P. *et al.* Comparison of Franseen and fork-tip needles for EUS-guided fine-needle biopsy of solid mass lesions: A systematic review and meta-analysis. *Endosc Ultrasound* 8, 382–391, doi:10.4103/eus.eus_27_19 (2019).

Disclosure: Nothing to disclose.

PP1005

CONCORDANCE OF NON-INVASIVE TESTS FOR THE ASSESSMENT OF LIVER FIBROSIS

C. Pachón Martínez¹, L. Andrés Pascual¹, J. Hernández Bernad¹, M.L. Molina Fernández¹, P. Ladrón Abia¹, J.C. Pérez Álvarez¹, V. Gozalo Marín¹, C. Salas Martínez¹, E. Badia Aranda¹
¹Burgos University Hospital, Burgos, Spain

Contact E-Mail Address: carlospachon20@gmail.com

Introduction: Liver fibrosis consists in the abnormal accumulation of extracellular matrix proteins due to chronic inflammation. Liver biopsy has been considered the gold-standard for diagnosing and staging fibrosis, which is vital to establish the prognosis and guide therapeutic management. Nevertheless, it is an invasive technique with certain drawbacks which must not be neglected. Given this scenario, new radiologic and serum-based non invasive diagnostic tools have arisen to accurately predict liver stiffness.

Aims & Methods: The aim of the study is to evaluate the concordance between different non-invasive tests to assess liver fibrosis including transient elastography (TE), point shear wave speed measurement (SWM) and serum biomarkers (APRI and FIB-4). Moreover, a validation analysis for SWM was performed. It is a single-center, descriptive, observational and retrospective study. Eligible patients had a known history of chronic liver disease, with a maximum time interval between TE and SWM of 6 months. Subsequently, APRI and FIB-4 were calculated. A concordance and validation analysis was conducted in patients with alcoholic liver disease (ALD), metabolic dysfunction associated steatotic liver disease (MASLD) and combined (MetALD).

Results: A total of 267 patients (68 % male, mean age: 59 years) with chronic liver disease regarding multiple aetiologies were included; MASLD (28.5%) was the most prevalent subgroup. The global concordance for fibrosis staging between ET and SWM was adequate with an intraclass correlation coefficient (ICC) of 0.684. Stratified analysis demonstrated a solid concordance for ALD with an ICC 0.7; and moderate for MASLD and MetALD with an ICC 0.53 and 0.48 respectively. However, the overall concordance between ET/SWM and serum biomarkers (APRI, FIB-4) was poor with an ICC < 0.4. To evaluate the diagnostic performance of SWM receiver operating characteristic (ROC) curves were obtained. The global validation analysis was favourable with an area under the curve (AUC) of 0.92.

Conclusion: TE and SWM demonstrated an adequate overall concordance when assessing liver fibrosis, especially in ALD. SWM global validation analysis was favourable making it a reliable non-invasive technique for the evaluation of liver stiffness as a surrogate quantitative biomarker.

Disclosure: Nothing to disclose.

PP1006

ADHERENCE TO BAVENO VII RECOMMENDATIONS IN PORTAL HYPERTENSION SCREENING: WHERE DO WE STAND?

E. Cherif¹, A. Ben Mohamed¹, G. Gharbi¹, M. Yakoubi¹, M. Mahmoudi¹, A. Khsiba¹, M. Medhioub¹, M.L. Hamzaoui¹

¹Mohamed Taher Maamouri Hospital, Gastroenterology, Nabeul, Tunisia

Contact E-Mail Address: cherifemna93@gmail.com

Introduction: Since the advent of the BAVENO VII consensus, Transient elastography (Fibroscan) has taken on a key role in the assessment of clinically significant portal hypertension (CSPH) and the prediction of decompensation and death. A liver stiffness measurement (LSM) ≤ 15 kPa associated with platelets ≥ 150 G/L excludes CSPH (NPV > 90%), while a LSM > 25 kPa is very much in favor of CSPH (PPV > 90%). CSPH remains possible in non-obese patients with LSM between 20 and 25 kPa with platelets < 150 G/L or LSM between 15 and 20 kPa with platelets < 110 G/L but with a 40% risk of error.

Aims & Methods: We conducted this study to evaluate the reliability of transient elastography (TE) and platelet count in the diagnosis of CSPH, and to determine the extent of adherence to the consensus recommendations in our center.

This is a monocentric and retrospective study made in the gastroenterology and hepatology department of Mohamed Taher Maamouri Hospital in Nabeul, Tunisia, in which we collated reports of Fibroscans performed from March 2023 to March 2024.

We excluded patients with etiologies other than viral, alcoholic, or non-obese non-alcoholic steatohepatitis (NASH).

Platelet count and upper gastrointestinal endoscopy (EGD) data (if performed) were collected.

Data were entered and analyzed using SPSS version 27 software, with a significance level of 0.05.

Results: One hundred and fifty-nine Fibroscans were performed, of which 127 were included.

Women accounted for 64.6%, with a M/F sex ratio of 0.55. Mean age was 55.13 years [20-83].

The indications for Fibroscan were distributed as follows: 53.5% (68 patients) for non-obese NASH, 33.1% (42 patients) for HBV, 11.8% (15 patients) for HCV and only 2 cases for chronic ethylism.

The mean LSM value was 6.45 kPa [2-41.5], with thresholds distributed as follows; LSM < 5 kPa in 70 patients (55.1%), LSM between 5 and 10 kPa in 44 patients (34.6%), LSM between 10 and 15 kPa in seven patients (5.5%), LSM between 15 and 20 kPa in two patients (1.6%), LSM between 20 and 25 kPa in a single patient, and LSM > 25 kPa in three patients (2.4%).

The mean platelet count was 220 G/L [20-440], with a count > 150 G/L in 111 patients (87.4%), a count between 110 and 150 G/L in 13 patients (10.2%) and a count < 110 G/L in 3 patients.

Of all patients, 24 FOGDs were performed. Signs of Portal hypertension (PH) were noted in only 5 cases, represented by grade I esophageal varices. In analytical study, hepatic elastography and platelet count were significantly correlated with the presence of endoscopic PH ($p=0.009$). Indeed, among patients with signs of endoscopic PH, 60% had a LSM > 25 kPa, 20% had a LSM between 15 and 20 kPa with a platelet count < 110 G/L and only 20% had a LSM < 10 kPa.

Furthermore, the consensus recommendations for the indication or not of EGD were not respected in our center ($p=0.004$); of all endoscopies performed 87.5% (21 EGD) were not indicated, and we noted one case where EGD was indicated but not performed.

Conclusion: Our study highlighted the recommendations of the latest BAVENO VII consensus regarding the reliability of transient elastography and platelet count in the evaluation of CSPH ($p=0.009$). This must be taken

into consideration by practitioners in order to implement adequate preventive measures and to rationalize the indication of EGD which remains an inconvenient procedure for our patients.

Disclosure: Nothing to disclose.

PP1007

A DEEP LEARNING-BASED LINEAR SYSTEM FOR LIVER STATION IN ENDOSCOPIC ULTRASOUND

B. Xiao¹, W. Tan¹, J. Wang¹, L. Yao¹, H. Wu¹, C. Zhang¹, X. Li¹, C. Luo¹, R. Jiang¹, S. Tan¹, H. Hu¹, M. Deng¹, J. Wang¹, W. Zhou¹, J. Liu¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Wuhan, China

Contact E-Mail Address: biscuitcity@qq.com

Introduction: Endoscopic ultrasound (EUS) has made significant strides in recent decades, whose current application in liver is mainly concentrated in liver parenchymal diseases, vascular diseases and portal hypertension. Incorporating EUS into the hepatic examination process is advantageous, which requires the endoscopist to have a good grasp of the anatomy of the liver. However, the learning curve for EUS-guided operations is well known to be steep. Thus, in the evaluation of EUS liver, it is necessary to have a system assisting the endoscopist to complete the scan at each station. Based on the anatomical markers in the liver, we construct a system which can perform a comprehensive inspection of the liver segments through the scanning imaging of 8 stations.

Aims & Methods: EUS of the liver can be done from the stations as follows: Station 1: Left hepatic vein (LHV); Station 2: Umbilical portion of portal vein (PV); Station 3: PV trunk and common bile duct (CBD); Station 4: Middle hepatic vein (MHV) and venous ligament; Station 5: Inferior vena cava (IVC) and right hepatic vein (RHV); Station 6: Gallbladder (GB) and left and right branches of PV; Station 7: Anterior and posterior branches of right portal vein; Station 8: Right kidney.

The system was internally validated in images, and subsequently compared with the performance of EUS endoscopists. We retrospectively collected 2743 images from Hospital A for internal validation, and an independent dataset containing 340 images for human-machine competitions. To filter out the white light images, we apply a DCNN1 model primarily. The output ultrasound images are then fed into DCNN2. In this model, they are classified into standard and non-standard categories. And the DCNN3 is then activated with standard images. DCNN3 identifies certain features in the image and groups them into eight stations. We use accuracy (defined as the number of correctly classified images divided by the total number of images) to evaluate the performance of the model. In addition, a T-test with a significance level of 0.05 was performed to assess significant differences between endoscopists and the model.

Results: The accuracy of DCNN1 in white light image and EUS image classification reached 100% [200/200, 95%CI]. The accuracy of DCNN2 in standard and non-standard image classification reached 81.24%. For the classification of standard station images, the overall accuracy of DCNN3 on the internal image verification set was 92.52% [2572/2743, 95%CI]. In the man-machine competition, the system correctly classified the liver standard stations with an accuracy of 88.53% [301/340, 95%CI]. The average accuracy of the two specialists and ten endoscopists was 84.56% [575/680, 95%CI] and 74.99% [2548/3398, 95%CI], respectively. The P-value for this analysis was less than 0.0001, indicating a statistically significant difference between endoscopists and the model.

Conclusion: In this study, we have constructed an intelligence-assisted linear EUS system based on deep learning algorithms. The system allows for real-time localization of liver standard sub-stations and provides valuable guidance to endoscopists during procedures. The system's effective-

ness has been extensively validated through internal validations using images and. Moreover, in a competition with experienced endoscopists, our system has demonstrated superior accuracy, comparable to that of EUS specialists. The result shows that the system is expected to overcome the difficulties of ultrasonographic interpretation among trainees in liver ultrasound endoscopy.

Disclosure: Nothing to disclose.

PP1008

WITHDRAWN

PP1009

EXPRESSION OF DEIODINASES-3 IN HCC AS NEGATIVE PROGNOSTIC FACTOR

V. Cossiga¹, C. Luongo², R. Montalti³, G. Pontillo¹, M. Guarino¹, G. Rompianesi⁴, M.A. De Stefano², M. Giglio⁴, M. Capasso¹, A. De Conte¹, L. Ranieri¹, R.I. Troisi⁴, D. Salvatore², F. Morisco¹

¹University of Naples Federico II, Department of Clinical Medicine and Surgery, Diseases of the Liver and Biliary System Unit, Naples, Italy, ²University of Naples Federico II, Department of Clinical Medicine and Surgery, Endocrinology Unit, Naples, Italy, ³University of Naples Federico II, Department of Public Health, Naples, Italy, ⁴University of Naples Federico II, Department of Clinical Medicine and Surgery, Division of Hepato-Bilio-Pancreatic, Minimally Invasive and Robotic Surgery, Naples, Italy

Contact E-Mail Address: annachiara.deconte@gmail.com

Introduction: The complex signalling pathways of thyroid hormones (TH) has been recently involved in the liver diseases pathogenesis. Particularly, it has been proven that the expression of deiodinases type-1 and 3 (D1-3) changes during liver injury, but their role is still poorly understood in hepatocarcinogenesis process.

Aims & Methods: We aimed to evaluate the role of TH signalling pathway in liver carcinogenesis. In this prospective study, 49 patients underwent liver surgery for HCC in cirrhosis (31 cases) or for other non-neoplastic indication in non-cirrhotic context (18 controls). We evaluated genes and protein expression of the main TH metabolism factors (D1, Monocarboxylate transporter-MCT8, Thyroid receptors-TR alpha and beta, Kruppel-like factor-KLF-9 and TH-responsive SPOT-14 gene), with RT-PCR and Western blot analysis in HCC, cirrhotic tissue and healthy liver samples.

Results: RT-PCR analysis showed a progressive statistically significant decrease of D1 ($p=0.003$), MCT-8 ($p=0.001$), and TR β ($p=0.04$) mRNA expression from healthy liver to HCC. The expression of KLF9, involved in cell differentiation and proliferation, decreased accordingly ($p=0.01$). Similarly, the expression of SPOT14 decreased in relation to reduced TH activation ($p=0.009$). Western Blot analysis showed a decreased expression of D1 protein in all cirrhotic samples ($p=0.01$), while D3 increased in 50% of HCC ($p=0.02$). Among HCC patients, D3 expression was associated with poor tumor differentiation compared to D3 negative HCC subjects ($p=0.007$). Furthermore, at Kaplan-Meier analysis, overall survival of D3 positive HCC was significantly lower than D3 negative HCC ($p=0.04$).

Conclusion: These preliminary data showed that D3 expression could define a more severe phenotype of HCC with poor tumor differentiation and reduced survival. Moreover, the signalling pathway of TH is dysregulated in HCC, with intrahepatic hypothyroidism. However, these results need to be confirmed in large cohorts.

Disclosure: Nothing to disclose.

PP1010

WITHDRAWN

PP1011

HEPATOCELLULAR CARCINOMA DETECTED IN HEPATOMA SURVEILLANCE CLINIC HAVE BETTER OUTCOME THAN THOSE DIAGNOSED SYMPTOMATICALLY: ABERDEEN ROYAL INFIRMARY EXPERIENCE

A.K.A Elmdaah^{1,1}, D. Solymosi¹, S. English¹, L. Mcleman¹, B. Vijayan¹, C. Chandrashekar¹, A. Mukhopadhy¹, T. Nguyen¹, S. Harikumar¹

¹Aberdeen Royal Infirmary, Gastroenterology, Aberdeen, United Kingdom

Contact E-Mail Address: ali.elmdaah@nhs.scot

Introduction: HCC is well known complication of liver cirrhosis. The current standard of care for patients with cirrhosis involves systematic 6 monthly screening with ultrasound and serum alpha-fetoprotein testing. (1) The Aberdeen Hepatoma surveillance clinic has been instituted since 2005 and currently 707 patients under screening program. It is a one-stop nurse led clinic wherein the ultrasound scan, blood testing and clinical review is done in a single visit, with sequential visits planned every 6 months.

Aims & Methods: In this study we aimed to identify outcome of HCC detected in hepatoma clinic compared to those identified symptomatically. Data collected retrospectively of patients referred to HCC MDT at Aberdeen Royal infirmary over period of 5 years. Diagnosis of HCC was made based on liver ultrasound and serum AFP as per guidelines

Results: 130 patients were identified with HCC through both pathways. 17 patients were detected as part of the surveillance programme and the rest were directly referred to the HPB MDT through the symptomatic pathway. The predominant subjects were males 102 (78.4%) and the cause of liver cirrhosis was as follows: MASLD 39%, ARLD 29%, Chronic HCV 11%, HBV 4%, Haemochromatosis 3%, PBC 2%, autoimmune hepatitis and PSC 1%. The mean age of patients detected in the surveillance group was 65 years $\pm$ 6.14 SD as opposed to those in the symptomatic group 71 years $\pm$ 9.99 SD. AFP was normal in 50% of surveillance group. The BCLC staging in the surveillance group was stage 0-A (20%), stage B 45%. In the symptomatic group patients were in stage 0-A 7%, Stage B 22%, and stage C, D 55% respectively.

Curative options including liver transplant and resection was possible in 20 % of surveillance patients as opposed to 7% in symptomatic patients. Palliative options like RFA, TACE and Sorafenib was offered in 60% of surveillance patients and 42% of symptomatic patients. In 20 % of surveillance patients no treatment could be offered as opposed to 55% symptomatic patients.

Conclusion: The mean age of the patients detected in the surveillance clinic was 5 years less than the symptomatic group suggesting that the programme was picking patients early. More curative and palliative procedures could be offered to this subgroup for this reason. The BCLC staging confirmed that most patients in the surveillance programme were in the early stages as opposed to the symptomatic group. Despite having an entrenched surveillance programme most patients were presenting symptomatically, suggesting that more efforts are needed to identify patients with cirrhosis who are at an added risk for developing HCC.

References: 1. European Association for the Study of the Liver. EASL Policy Statement on liver cancer screening. Accessed 31 May 2022. Available from: <https://easl.eu/publication/easl-policy-statement-on-liver-cancer-screening/>.

Disclosure: Nothing to disclose.

PP1012

LIVER FUNCTION IS A PREDICTOR OF SURVIVAL IN PATIENTS WITH HEPATOCELLULAR CARCINOMA IN BEST SUPPORTIVE CARE

C. Campani¹, T.V. Li Cavoli¹, L. Bucci², V. Adotti¹, M. Rosi¹, F. Trevisani², F. Marra¹, Ita.li.Ca. Group

¹University of Florence, Florence, Italy, ²University of Bologna, Bologna, Italy

Contact E-Mail Address: tancredilicavoli@gmail.com

Introduction: The prognosis of patients with hepatocellular carcinoma (HCC) is very variable, and the relative contribution of tumour burden and liver dysfunction to survival is uncertain. Median overall survival (OS) of patients managed with best supportive care is around 3-6 months, although longer values may be observed in clinical practice. Aim of this study was to identify the factors linked to tumour or liver dysfunction associated with survival in patients with HCC treated with BSC.

Aims & Methods: We retrospectively evaluated the clinical characteristics of 1414 patients who had an indication for BSC recorded in the Ita.Li.Ca database between 2000 and 2020. We analysed both patient and tumour characteristics to identify predictors of OS.

Results: Median age was 69y and 76% of patients were male. Aetiology included chronic viral infection (68.3%), alcohol use disorder (30.9%) and non-alcoholic steatohepatitis (8.3%). 67.4% of patients had a performance status 0-1 and 41.4% were in Child-Pugh B class. Median MELD was 13.60% of patients had a multifocal HCC with a median number of 3 lesions and a median size of 33mm. 533 patients had vascular invasion. Median alpha-fetoprotein was 49.25 ng/ml. 111 patients were classified as BCLC-A, 148 as BCLC-B, 791 as BCLC-C and 325 as BCLC-D (12 unknown). No differences in terms of OS were observed considering the aetiology of liver disease or the presence of cirrhosis. Obesity ($p<0.001$), hypercholesterolemia ($p=0.036$) and hypertriglyceridemia ($p=0.034$) were associated with lower OS. Absence of symptoms (6 vs 10 months, $p<0.001$), lack of vascular invasion (9.1 vs 5.03, $p<0.001$), and absence of metastasis (8.167 vs 4.733, $p<0.001$) were associated with a better OS. Survival in BCLC-A patients was longer than in stages B or C. Survival progressively declined according to severity of liver function using three different scores (CPS, ALBI, pALBI, $p<0.001$). Women tended to survive longer (23 vs 19 months, $p=0.053$). Comparing patients surviving more or less than 12 months (398 vs 1016), age, size of lesions, albumin, bilirubin, alpha-fetoprotein, and MELD were significantly different. At Cox univariate analysis presence of cirrhosis, number and size of lesions, vascular invasion, metastasis, ALBI and pALBI grades, MELD and CPS were significantly associated with OS. Using different models to avoid collinearity ALBI, pALBI and CPS maintained an independent prognostic role on OS.

Conclusion: In a large series of patients with HCC in BSC, parameters of liver function are strongly associated with survival.

Disclosure: Nothing to disclose.

PP1013

RELIABLE PERFORMANCE OF MALBI GRADE-BASED RISK MODELS FOR PREDICTING THE PROGNOSIS OF PATIENTS WITH HEPATOCELLULAR CARCINOMA RECEIVING ATEZOLIZUMAB PLUS BEVACIZUMAB: COMPARATIVE ANALYSIS OF 13 RISK MODELS

T. Hatanaka¹, S. Kakizaki^{2,3}, A. Hiraoka⁴, T. Tada⁵, K. Kariyama⁶, J. Tani⁷, H. Toyoda⁸, M. Kaibori⁹, A. Naganuma¹⁰, Y. Yata¹¹, H. Kuroda¹², K. Nouse⁶, T. Kumada¹³,

The Real-life Practice Experts for HCC (RELPEC) Study Group, and HCC 48 Group (hepatocellular carcinoma experts from 48 clinics in Japan)

¹Gunma Saiseikai Maebashi Hospital, Department of Gastroenterology, Maebashi, Japan, ²NHO Takasaki General Medical Center, Department of Clinical Research, Takasaki, Japan, ³Gunma University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Maebashi, Japan, ⁴Ehime Prefectural Central Hospital, Gastroenterology Center, Matsuyama, Japan, ⁵Japanese Red Cross Himeji Hospital, Department of Internal Medicine, Himeji, Japan, ⁶Okayama City Hospital, Department of Gastroenterology, Okayama, Japan, ⁷Kagawa University, Gastroenterology and Neurology, Kita-gun,, Japan, ⁸Ogaki Municipal Hospital, Department of Gastroenterology and Hepatology, Ogaki, Japan, ⁹Kansai Medical University, Department of Surgery, Hirakata, Japan, ¹⁰NHO Takasaki General Medical Center, Department of Gastroenterology, Maebashi, Japan, ¹¹Hanwa Memorial Hospital, Department of Gastroenterology, Osaka, Japan, ¹²Iwate Medical University, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Morioka, Japan, ¹³Gifu Kyoritsu University, Department of Nursing, Ogaki, Japan

Contact E-Mail Address: hatanaka@qk9.so-net.ne.jp

Introduction: This study aimed to compare the prognostic performance of the risk models for patients with hepatocellular carcinoma (HCC) receiving atezolizumab and bevacizumab (Atez/Bev) as first-line treatment.

Aims & Methods: A total of 449 patients were included in this retrospective multicenter study. We compared the prognostic performance of 13 risk models for the 12- and 18-month survival status using area under the curve (AUC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI) analysis. We also constructed a calibration plot to assess the fitness of each model.

Results: Regarding the analysis of the 12-month survival status, none of the risk models demonstrated AUC values higher than the modified albumin-bilirubin (mALBI) grade. In the NRI analysis, only the Immunotherapy with AFP, BCLC staging, mALBI, and DCP evaluation (IMABALI-De score) exhibited a statistically significant improvement compared with the mALBI grade ($p=0.009$).

While the modified albumin-bilirubin grade (mALF) score and prognostic nutritional index (PNI) did not exhibit significant differences compared to the mALBI grade ($p=0.3$ and 0.2 , respectively), the remaining risk models were inferior to the mALBI grade. In the IDI analysis, none of the risk models showed a significant improvement compared with the mALBI grade. The calibration plot of the PNI was unsatisfactory. The results for the 18-month survival status were consistent with those for the 12-month survival status.

Conclusion: The mALBI grade, as well as the IMABALI-De and mALF scores (both of which are risk models based on mALBI grade), exhibited reliable performance in predicting the prognosis of HCC patients.

Disclosure: Takeshi Hatanaka received lecture fees from Eisai. Atsushi Hiraoka received lecture fees from Eli Lilly, AstraZeneca, and Chugai. Toshifumi Tada received lecture fees from AbbVie, Eisai, and Chugai. Hideno-

ri Toyoda received lecture fees from Eisai, Chugai, Takeda, Terumo, AbbVie, Gilead, Fujifilm WAKO, and Abbott. Hidekatsu Kuroda received lecture fee from Eisai. The other authors declare no conflicts of interest associated with this study.

PP1014

HEPATOCELLULAR CARCINOMA AND IMMUNOTHERAPY – OUR THREE YEARS EXPERIENCE

L. Milanez¹, T. Košir Božič², M. Zaplotnik², S. Štupar², Z. Hlebanja², S. Finderle², G. Boltežar², A. Šmid²

¹Medical Faculty, University of Ljubljana, Ljubljana, Slovenia,

²University Medical Centre Ljubljana, Clinical Department of Gastroenterology, Ljubljana, Slovenia

Contact E-Mail Address: lzabelamilanez99@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is the most common primary malignant liver cancer globally and ranks as the third leading cause of cancer-related mortality. Treatment with immune checkpoint inhibitors (most commonly atezolizumab in combination with bevacizumab) is the most effective first-line systemic therapy for patients with advanced HCC. Since it is a new method of treatment, there is little clinical data on the use of this combination of drugs in practice (outside of prospective studies).

This study aims to present the clinical outcomes of patients with HCC who underwent immunotherapy at our center over the past three years.

Aims & Methods: In this retrospective observational study, we included patients treated with the atezolizumab and bevacizumab combination between March 2020 and September 2023. Demographic information, general physical assessments, disease etiology, disease staging, liver cirrhosis status, portal hypertension and laboratory values (aminotransferases and total bilirubin) were collected. Adverse events were analyzed according to the Common Terminology Criteria (CTCAE). Descriptive statistics and survival analysis were performed using Statistical Package for the Social Sciences (SPSS) version 22.

Results: 53 HCC patients received atezolizumab and bevacizumab in studied time period, 8 (15.1%) females and 45 (84.9%) males. The median age at the initiation of immunotherapy was 68 years (range 41 – 84 years). Thirteen patients (24.5%) had esophageal varices prior to immunotherapy, with three (5.6%) requiring ligation. The majority of patients had liver cirrhosis A 27 (50.9%) according to Child Pugh criteria, a minority B (9.4%), and 21 patients (39.6%) were without cirrhosis.

The primary causes of the disease were alcohol (51.6%), metabolic dysfunction-associated steatotic liver disease (MASLD) (16.1%), hepatitis C virus (12.9%), hepatitis B virus (6.5%), and hemochromatosis (3.2%). Stage C HCC, according to The Barcelona Clinic Liver Cancer, World Health Organization (WHO) performance status 0, and absence of macrovascular invasion and extrahepatic spread were predominant at treatment initiation. Grade I or II adverse events occurred in almost all patients (98.1%).

Severe adverse events were present in 36 patients (67.9%). Due to severe side effects, 8 (15.1%) patients discontinued treatment, 2 (3.8%) died due to treatment related complications (encephalitis and bleeding from esophageal varices). Treatment was modified in 21 (39.6%) patients due to adverse events. The estimated median survival was 15.7 months.

Conclusion: The majority of patients with unresectable HCC, treated with a combination of atezolizumab and bevacizumab immunotherapy, experienced adverse events, primarily grades I-II. The immunotherapy combination proved to be more effective in patients with viral etiology of liver cirrhosis. The estimated median survival was 15.7 months. This combination of immunotherapy has been demonstrated to be a safe and effective treatment method. Currently, there is limited data regarding the utiliza-

tion of this treatment in standard clinical practice and our data aligns reasonably well with the findings of the registration study.

References:

1. McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of Hepatocellular Carcinoma. *Hepatology*. 2021 Jan;73 Suppl 1(Suppl 1):4–13.
2. Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. *J Hepatol*. 2022 Mar;76(3):681–93.
3. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med*. 2020 May 14;382(20):1894–905.
4. Lee YC, Huang WT, Lee MY, Tsao CJ, Feng YH. Bevacizumab and Atezolizumab for Unresectable Hepatocellular Carcinoma: Real-world Data in Taiwan-Tainan Medical Oncology Group H01 Trial. *In Vivo*. 2023;37(1):454–60.
5. Himmelsbach V, Pinter M, Scheiner B, Venerito M, Sinner F, Zimpel C, et al. Efficacy and Safety of Atezolizumab and Bevacizumab in the Real-World Treatment of Advanced Hepatocellular Carcinoma: Experience from Four Tertiary Centers. *Cancers (Basel)*. 2022 Mar 28;14(7):1722.
6. de Castro T, Jochheim LS, Bathon M, Welland S, Scheiner B, Shmanko K, et al. Atezolizumab and bevacizumab in patients with advanced hepatocellular carcinoma with impaired liver function and prior systemic therapy: a real-world experience. *Ther Adv Med Oncol*. 2022;14:17588359221080298.

Disclosure: Nothing to disclose.

PP1015

EFFECT OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN TREATMENT WITH ATEZOLIZUMAB-BEVACIZUMAB IN CIRRHOTIC AND NON-CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA

S. Pantzios¹, S. Rellou¹, A. Syriha¹, I. Stathopoulou¹, G. Barla¹, I. Elefsiniotis¹

¹General Oncology Hospital of Kifisia “Agiol Anargyroi”, Academic Department of Internal Medicine-Hepatogastroenterology Unit, Athens, Greece

Contact E-Mail Address: s_r_1235@hotmail.com

Introduction: The majority of hepatocellular carcinoma (HCC) patients has cirrhosis. The increased incidence of HCC in non-alcoholic steatohepatitis (NASH) and on the other hand the decrease of incidence of viral hepatitis, have as a result increased incidence of HCC in non-cirrhotic patients.

There are limited data for response differentiation in cirrhotic and non-cirrhotic patients regarding treatment with atezolizumab-bevacizumab¹. Elevated neutrophil-to-lymphocyte ratio (NLR) seems to be in favor of worst prognostic for immunotherapy.

Aims & Methods: The aim of this study was to determinate NLR in HCC for cirrhotic and non-cirrhotic patients as a biomarker for effective treatment. 57 patients with Barcelona Clinic Liver Cancer (BCLC) B/C HCC that received treatment with combination atezolizumab-bevacizumab in our referral center through the last three years were included. 45/57 were men, mean age was 66.3 years old and mean body mass index (BMI) was 27.23, 33 viral related HCC, 19 with diabetes, 29 ALBI-I, 41 BCLC-C, 16 BCLC-B, 22 macrovascular infiltration (MVI), 23 extrahepatic disease, 31 had received prior therapy.

Patients with NLR>3 categorized as NLR-H patients and the rest of them as NLR-L. Patients divided into 4 groups, depending on the presence of cirrhosis or not and NLR value, as follows: Group A (non-cirrhotic, NLR-L/N=13), group B (non-cirrhotic, NLR-H/N=14), group C (cirrhotic, NLR-L/N=11), group D (cirrhotic, NLR-H/N=19). The 4 groups were compared for their baseline characteristics and survival (OS and PFS) and multivariate

analysis were performed. Next, cirrhotic and non-cirrhotic patients were examined separately and compared for baseline characteristics and survival based on baseline NLR values and receipt of prior therapy.

Results: The groups were comparable in baseline characteristics except for liver disease etiology ($p<0.001$), ALBI score ($p=0.014$), MVI ($p<0.001$), BCLC ($p=0.014$) and prior treatment ($p=0.009$). Median OS was 30 months (m), 10m, 12m, 5m and median PFS was 14m, 4m, 8m, 2m for groups A, B, C, D respectively ($p<0.001$). In multivariate analysis, a statistically significant difference regarding worst survival was found in group D patients compared to group A ($p=0.005$, HR=0.1), group C ($p=0.032$, HR=0.333) and marginally group B ($p=0.055$, HR=0.321). In analysis of cirrhotic patients alone based on NLR, patients were comparable for all baseline characteristics. Cirrhotic patients with NLR-L had better OS (12m vs. 5m, $p=0.002$) and PFS (8m vs. 2m, $p=0.028$) compared to cirrhotic patients with NLR-H. NLR was an independent determinant of OS ($p=0.015$, HR=3.480). In analysis of non-cirrhotic patients based on NLR, patients were comparable except for prior treatment. Patients with NLR-L had significantly longer OS (30m vs 10m, $p=0.006$) and PFS (15m vs 4m, $p=0.01$). In multivariate analysis, only the presence of prior treatment and not NLR influenced survival. Patients were re-divided according to the presence or absence of prior therapy into 2 groups. Previously treated non-cirrhotic patients had better OS (30m vs 8m, $p<0.001$) and PFS (24m vs 4m, $p<0.001$). In the multivariate analysis, the presence of prior treatment was an independent factor determining survival in the non-cirrhotic patients.

Conclusion: Cirrhotic patients with high baseline NLR values show the worst survival among the subgroups. Baseline NLR is an independent determinant of OS in cirrhotic patients, but not PFS, while in non-cirrhotic patients receiving prior therapy is the only factor that independently determines both OS and PFS. The results need to be verified in larger patient cohorts.

References:

1. Cheng AL, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Lim HY, Kudo M, Breder V, Merle P, Kaseb AO, Li D, Verret W, Ma N, Nicholas A, Wang Y, Li L, Zhu AX, Finn RS. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. *J Hepatol*. 2022 Apr;76(4):862–873. doi: 10.1016/j.jhep.2021.11.030. Epub 2021 Dec 11. PMID: 34902530.

Disclosure: Nothing to disclose.

PP1016

ENDOSCOPIC ULTRASOUND-GUIDED LIVER BIOPSY USING A 22-G FINE-NEEDLE BIOPSY NEEDLE

I. Zhecheva¹, P. Karagoyozov¹, D. Koemdzhiev¹, C. Mihaylova¹

¹Acibadem City Clinic University Hospital Tokuda, Clinic of Gastroenterology, Sofia, Bulgaria

Contact E-Mail Address: i.jecheva1994@abv.bg

Introduction: Liver biopsy is a crucial diagnostic procedure for assessing hepatic pathologies, providing valuable insights into the etiology, severity, and prognosis of liver diseases. In recent years, Endoscopic Ultrasound-Guided Liver Biopsy (EUS-LB) using 22G-fine needle biopsy (FNB) needle has emerged as a promising alternative, leveraging the superior imaging capabilities of endoscopic ultrasound (EUS) to guide biopsy with increased precision and safety. The 22G-FNB needle features a crown tip with three symmetrical cutting edges that enable swift core tissue procurement for histological analysis. The 22G-FNB needle provide greater than 95% tissue adequacy and an excellent diagnostic accuracy.

Aims & Methods: The aim of our study is to evaluate the diagnostic utility and safety of a 22G-FNB needle using the slow-pull technique for EUS-LB of parenchymal and focal liver lesions.

We performed a retrospective analysis of prospective data base from January 2021 to March 2024. Each patient underwent an endoscopic ultrasound by using linear scope (Fujifilm EG-580UT) and fine needle biopsy using 22G - tip needle with the slow-pull aspiration technique:

- For 33 patients we used a 22G Trident™ - tip FNB needle (Micro-Tech Endoscopy);
- For 26 patients we used a 22G Acquire- tip FNB needle (Boston Scientific Corp.);
- For 4 patients we used a 22G SonoTip Top Gain - tip FNB needle (MediGlobe);

The median number of needle passes was approximately 3 (between 2 and 5).

Results: We identified 63 patients who underwent EUS-LB of the liver during the study period (28 men and 35 women): 47 (74.6%) of them were with malignant and 16 (25.4%) with benign disease. The median age of the patients was 56.9 years. The specimen was considered adequate in all 63 patients.

We classified the EUS-FNB of liver diseases into EUS-FNB of parenchymal and focal liver lesions.

- EUS-FNB of parenchymal liver disease were performed to 13 (20.6%) of the patients: cirrhosis was found in 2 (3.17%), nonalcoholic fatty liver disease – in 5 (7.9%) and cholestasis in 6 (9.5%).

- We performed EUS-FNB of focal liver lesions in 50 (79.36%) of the patients.

Metastasis were found in 39 (61.9%): pancreatic ductal adenocarcinoma was detected in 27 (42.8%), pancreatic acinar cell carcinoma – in 1 (1.58%), pancreatic neuroendocrine carcinoma – in 5 (7.9%), lung adenocarcinoma – in 3 (4.7%), ductal adenocarcinoma of breast – in 2 (3.17%), colorectal adenocarcinoma – in 1 (1.58%) and Ewing sarcoma – in 1 (1.58%).

Primary liver cancer - hepatocellular cancer was diagnosed in 4 (6.34%) patients.

Cholangiocarcinoma was found in 3 (4.7%) patients.

There were 3 (4.7%) patients with negative histology for tumor cells in the specimen: in 2 (3.17%) cases liver abscess was proved and 1 (1.58%) hepatic cyst.

No adverse events were observed during the first 48h and after a 30 days follow-up.

There was no death during the study period.

Conclusion: Our study illustrates that EUS-guided liver biopsy using a 22G - FNB needle provides adequate specimen for histologic analysis, lesser postprocedural recovery time and it is a safe, highly effective alternative to other methods of liver biopsy. The use of real time imaging guidance with doppler also helps to reduce the adverse events.

Disclosure: Nothing to disclose.

PP1017

CLINICAL CHARACTERISTICS AND PROGNOSIS OF DE NOVO HEPATOCELLULAR CARCINOMA AFTER TIPS PLACEMENT: A RETROSPECTIVE COHORT STUDY

S. Xiao¹

¹*Sichuan university/West China hospital, Department of Gastroenterology and Hepatology, Chengdu City, China*

Contact E-Mail Address: neoxiao1994@qq.com

Introduction: Portal hypertension often accompanies hepatocellular carcinoma (HCC) in cirrhosis. Transjugular intrahepatic portosystemic shunt (TIPS) serves as an effective intervention for portal hypertension, while HCC can exacerbate it.

Aims & Methods: To investigate the prognosis of post-TIPS HCC patients and factors influencing it. Retrospective analysis of post-TIPS HCC patients, assessing overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) using Kaplan-Meier, logistic regression, and Cox model.

Results: A total of 68 patients were included (April 2015 to October 2023). Forty-seven percent died during follow-up, with liver decompensation as a major cause (27.9% vs 10.3%, $P=0.18$). Median OS was 33 months, median PFS was 24 months, and ORR was 80%. The 2-year OS rates for BCLC stage 0, A, B, and C were 85.6%, 54.6%, 25%, and 0%, respectively. Tumor number (HR 1.58, $P=0.01$) and moderate to severe ascites (HR 5.16, $P=0.003$; HR 5.52, $P=0.01$) were OS risk factors, while mild to moderate ascites affected PFS (HR 3.19, $P=0.021$; HR 6.20, $P=0.002$). Age (HR 0.91, $P=0.031$) and ascites severity (HR 0.06, $P=0.022$; HR 0.025, $P=0.022$) influenced ORR.

Conclusion: Liver decompensation is a primary mortality cause in post-TIPS HCC. Ascites presence affects outcomes, underscoring post-TIPS ascites management importance.

Disclosure: Nothing to disclose.

PP1018

TREATMENT OF HEPATOCELLULAR CARCINOMA ACCORDING TO MULTIPARAMETRIC THERAPEUTIC HIERARCHY APPROACH: A PROSPECTIVE MULTICENTER VALIDATION STUDY

L. Canova¹, M.A. Iavarone¹, E. Alimenti¹, B. Antonelli², A.M. Ierardi³, S. Crespi³, M. Viganò⁴, G. Cabibbo⁵, A. Vitale⁶, A. Sangiovanni¹, P. Lampertico^{1,7}

¹Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ²General and Liver Transplant Surgery Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ³Radiology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ⁴Gastroenterology Hepatology and Transplantation Unit, ASST Papa Giovanni XXIII, Bergamo, Italy, ⁵Gastroenterology and Hepatology Unit, Department of Health Promotion, Mother & Child Care, Internal Medicine & Medical Specialties, University of Palermo, Palermo, Italy, ⁶Hepatobiliary Surgery and Liver Transplantation Unit, Azienda Ospedale-Università di Padova, Padova, Italy, ⁷CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Contact E-Mail Address: lorenzo.canova27@gmail.com

Introduction: Treatment strategy of hepatocellular carcinoma (HCC) is a complex decision-making process that considers several variables in clinical practice. A "multiparametric therapeutic approach" has been proposed (*Lancet Oncol* 2023): the feasibility of all treatments is evaluated systematically in a hierarchical order, to match each patient with the optimal therapy.

Aims & Methods: The aim of the study is to validate the reliability of the new multiparametric decisional framework (MPDF) and the impact of the different variables included in the framework on the final treatment decision in clinical practice. This is a prospective ongoing study with a first monocentric phase (A) and a second multicentric validation phase. Primary endpoints are: 1) adherence to MPDF for treatment allocation, 2) identification of the relative weight of variables involved in this MPDF for treatment decision, while secondary endpoints are overall survival and radiological response after treatment. The study includes all consecutive patients with HCC managed in each center from September 1st, 2023. The disease is staged according to Barcelona Clinic Liver Cancer (BCLC) classification, while patient's characterization is conducted by Charlson Comorbidity Index (CCI), Liver Frailty Index (LFI), Child-Pugh (CPT) and ALBI, MELD and skeletal muscle mass index by CT. Each patient is allocated to treatment according to MPDF, BCLC 2022 was the benchmark.

Results: As of November 1st, 2023, 48 patients were recruited into phase A of the study [median age 70 (52-87) years, 81% male, 37% HCV, 27% first treatment for HCC]. Thirteen (27%) patients were classified BCLC 0, 17 (35%) A, 6 (12.5%) B, 6 (12.5%) C and 6 (12.5%) D. The median CCI was 8 (4-13), the median LFI was 4.15 (2.99-4.81). Thirty-nine (81%) patients were in CPT class A, 7 (15%) in B and 2 (4%) in C, while 32 (67%) were classified ALBI grade 1 and 16 (33%) ALBI grade 2, and the median MELD score was 8.5 (6-22). Forty-four (92%) patients received treatment through a multidisciplinary team (MDT). According to the MPDF, 9 (19%) patients were allocated to liver transplant, 5 (10%) to laparoscopic surgical resection, 10 (21%) to microwave thermal ablation (MwTA), 7 (15%) to transarterial treatments (4 TACE and 3 TARE), 3 (6%) to other locoregional therapies (2 MwTA+TACE and 1 electrochemotherapy), 6 (13%) to systemic treatment and 5 (10%) to palliative care only. In 4 cases, the MDT decided for reassessment at 3 months. The treatment allocation was coherent to the BCLC 2022 in 69% BCLC 0, 82% BCLC A, 83% BCLC B, 67% BCLC C and 100% BCLC D.

Conclusion: Preliminary data of our ongoing prospective study suggest that personalized approach for HCC treatment by MPDF is feasible in clinical practice and might help ensuring a customized approach in a standardized framework. Updated data will be presented at the meeting.

Disclosure: Nothing to disclose.

PP1019

THE IMPACT OF METFORMIN ON THE OVERALL SURVIVAL OF DIABETIC PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA ON IMMUNOTHERAPY: A META-ANALYSIS

M.R. Dimaculangan¹, J.A. Cordero², F.A. Co², I.H. Cua¹

¹Institute of Digestive and Liver Diseases, St. Luke's Medical Center - Global City, Taguig, Philippines, ²Department of Medicine, St. Luke's Medical Center - Global City, Taguig, Philippines

Contact E-Mail Address: regdimaculangan@gmail.com

Introduction: Non-alcoholic steatohepatitis (NASH) is a common known risk factor for developing hepatocellular carcinoma (HCC). Many patients with NASH are given metformin, a widely prescribed medication for type 2 diabetes and obesity. Its primary mode of action involves the activation of AMP-activated protein kinase (AMPK), a central regulator of cellular energy homeostasis. Beyond its anti-hyperglycemic effects, it also exhibits pleiotropic properties that extend to modulating various cellular processes, including inflammation, metabolism, and immune response. In this similar mechanism, growing evidence indicates that metformin also has anti-cancer properties. It has shown significant synergistic effects in combination with standard chemotherapy and immune check-point inhibitors (ICI). However, its effect on advanced HCC treated with ICI (e.g. atezolizumab + bevacizumab, pembrolizumab, durvalumab) is not well understood.

Aims & Methods: This meta-analysis aims to determine the effect of metformin in the overall survival of diabetic patients with advanced HCC treated with ICIs. Major electronic databases and grey literature sources were searched up to January 2023 for studies assessing the effect of metformin in the survival of diabetic HCC patients on immunotherapy.

Results: The hazard ratios for the overall survival of metformin (experimental) vs non-metformin (control) groups were compared from the studies done by Kang 2022, Lin 2022 and Ramini 2023. Resulting I² of 0% (p value = 0.54) implies that heterogeneity does not exist. Resulting pooled hazard ratio of 1.08, with a narrow 95% confidence interval 0.85 to 1.38, is not significant (Z = 0.65, p = 0.51), implying no significant difference between the two groups. The forest plot also shows that the diamond market intersects the 1 axis or the line of no effect, suggesting that the hazard ratio is not significant. However, eyeballing the said forest plot, all 3 studies tend toward the non-metformin or control group which signifies a worse prognosis with metformin on HCC patients on ICIs.

Conclusion: The use of metformin has no significant difference in the overall survival in diabetic HCC patients receiving immunotherapy, although trends are leading towards worse prognosis. Hence, physicians must take into consideration the diabetes status of HCC patients on immunotherapy due to its impact on their clinical outcomes and negative prognostic effect of metformin use.

References: Papadakos SP, et al. The Emerging Role of Metformin in the Treatment of Hepatocellular Carcinoma: Is There Any Value in Repurposing Metformin for HCC Immunotherapy? *Cancers* (Basel). 2023 Jun 13;15(12):3161. doi: 10.3390/cancers15123161

Hua, Y., Zheng, Y., Yao, Y. et al. Metformin and cancer hallmarks: shedding new lights on therapeutic repurposing. *J Transl Med* 21, 403 (2023). <https://doi.org/10.1186/s12967-023-04263-8>

Disclosure: No conflict of interest.

PP1020

A MODIFIED CHARLSON COMORBIDITY INDEX TO IMPROVE MANAGEMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA: A STEP TOWARDS PRECISION MEDICINE

A. Eleonora¹, M.A. Iavarone^{1,2}, L. Canova¹, L. Argiento¹, E. Fracas¹, B. Antonelli³, A.M. Ierardi⁴, S. Crespi⁴, A. Zefelippo³, A. Sangiovanni¹, P. Lampertico^{1,2}

¹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy,

²University of Milan, Milan, Italy, Department of Pathophysiology and Transplantation, CRC "A. M. and A. Migliavacca" Center for Liver Disease, Milan, Italy, ³Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, General and Liver Transplant Surgery Unit, Milan, Italy, ⁴Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Radiology Department, Milan, Italy

Contact E-Mail Address: lorenzo.argiento@unimi.it

Introduction: Patients with hepatocellular carcinoma (HCC) frequently have comorbidities that limit access to treatments and might increase mortality. The Charlson comorbidity index (CCI) assigns a numeric score to 17 diseases according to their effect on mortality. In patients with cirrhosis and HCC, these variables might be excluded from the CCI (modified CCI, mCCI).

Aims & Methods: Aim of the study was to evaluate the performance of CCI and mCCI for HCC patients' characterization.

We used data from our retrospective monocentric study of patients with first HCC diagnosis. We evaluated the performance of CCI and mCCI in dissecting our population and predicting overall survival (OS). As secondary end-point, the impact of mCCI on adherence to Barcelona Clinic Liver Cancer (BCLC) staging and treatment allocation was evaluated.

Results: The study included 385 patients (289 males, 68 years median age, 78% Child Pugh (CPT) A, 66% viral etiology) with HCC (271 BCLC 0/A, 64 B, 40 C and 10 D). According to CCI, 94% of our patients were "high-risk" (CCI $\geq$ 5), 5.7% "intermediate-risk" (CCI 3-4) and 0.3% "low-risk" (CCI 0-2). These cutoffs were applied to mCCI: 21% "high-risk", 48% "intermediate-risk", and 31% "low-risk". Patients' mCCI correlated with CCI (Kendall's $\tau=0.47$; p-value< 0.0001). Overall, patients belonging to a "high" or "intermediate-risk" mCCI classes had a shorter OS as compared to "low-risk" patients (median OS 37 vs 49 vs 67 months, p-value=0.007). This was confirmed in BCLC 0/A (p-value=0.002). Moreover, "high-risk" mCCI class, worse CPT class, presence of varices, BCLC stage and AFP>200 ng/mL were independently associated to mortality [HR1.36 (95%CI 1.09-1.70, p-value=0.006; HR1.62 (95%CI 1.14-2.30), p-value=0.007; HR1.58 (95%CI 1.11-2.24), p-value=0.01; HR1.96 (95%CI 1.66-2.31) p-value<0.001; HR1.80 (1.17-2.79) p-value=0.008]. mCCI was also an independent predictor of mortality in BCLC 0/A, with higher tumor burden and worse CPT. No differences were observed in adherence to BCLC2022 algorithm and access to treatment among the mCCI risk classes.

Conclusion: mCCI better stratified patients with HCC as compared to CCI and independently predicted mortality. Implementation of a multiparametric therapeutic approach to treatment allocation including evaluation of comorbidities and frailty is warranted

Disclosure: Nothing to disclose.

PP1021

EVALUATION OF RISK FACTORS AND PROGNOSIS OF HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

S. Andreola Borba^{1,2}, B. Teston Cini³, L. de Lima Cezimbra⁴, V. Dall Agnol Bouvier⁴, J.M. Wolf², C.T. Schmidt Cerski^{5,6}, A. De Araujo^{7,8,2}

¹Universidade Federal do Rio Grande do Sul, Gastroenterology Department Post-Graduation Course, Porto Alegre, Brazil,

²Hospital Moinhos de Vento, Porto Alegre, Brazil, ³Hospital de Clínicas de Porto Alegre, Gastroenterology Department, Porto Alegre, Brazil, ⁴Universidade Federal do Rio Grande do Sul, School of Medicine, Porto Alegre, Brazil, ⁵Universidade Federal do Rio Grande do Sul, Pathology Department, Porto Alegre, Brazil, ⁶Hospital de Clínicas de Porto Alegre, Pathology Department, Porto Alegre, Brazil, ⁷Hospital de Clínicas de Porto Alegre, Gastroenterology and Hepatology, Porto Alegre, Brazil, ⁸Universidade Federal do Rio Grande do Sul, Gastroenterology and Hepatology, Porto Alegre, Brazil

Contact E-Mail Address: gastrosophiaborba@gmail.com

Introduction:

Transplantation techniques and immunosuppression treatments have been increasing notably in the past years, particularly when considering liver transplant (LT). LT is the preferred treatment for early-stage hepatocellular carcinoma (HCC). Despite the use of the Milan criteria, recurrence remains a major concern, with an estimated incidence ranging from 5% to 20%. Therefore, our objective is to assess potential risk factors, including clinical, laboratory and pathological parameters, as well as prognosis of HCC recurrence in LT recipients.

Aims & Methods:

Retrospective evaluation of medical records from a Brazilian tertiary hospital, including adults who were submitted to LT due to HCC, during the period of 01/01/2002 up to 31/12/2021. Patients who had a LT for other causes, who presented a follow-up less than 1 year or with incidental detection of HCC in the liver explants were excluded. Data collection included demographic information, immunosuppressive treatments, clinical, radiological and histopathological findings related to the HCC, as well as characteristics associated with the post-transplant follow-up and tumoral recurrence, including death. Primary outcome was recurrence of HCC, whereas secondary outcomes were survival and adopted treatments after cancer recurrence, as well as time elapsed until HCC recrudescence.

Results: 150 patients were included (males 95 [63.3%], median age 60 years-old [IQR 56-66]), 130 (86.6%) were classified as Milan-in. The main cirrhosis etiologies were viral (88%) and metALD (10%). Half of patients presented an A CHILD score (50%) and a median MELDNa score of 12 (IQR 9-14). Main locoregional therapies included transarterial chemoembolization (TACE) and percutaneous ethanol injection (PEI), accounting for 48 (32%) and 45 (30%) respectively. 47 (31.33%) patients underwent two or more locoregional therapy modalities, and downstaging was achieved in 20 patients (13.3%). Explant analysis with microvascular invasion and Milan-out were detected in 18 (12%) and 30 (20.1%) individuals, respectively. HCC recurrence occurred in 21/150 patients (14%), while non-HCC neoplasias in 27/150 (18.1%) after LT. The median time to recurrence was 30 months (IQR 20-43), and systemic therapy to HCC with sorafenib was used in 12/21 patients (57.14%). Among those who presented recurrence, 19/21 died (90.4%), and prognosis after recurrence was dismal (median survival of 14.5 months, IQR 3.25-33.5). Evaluation of possible associations between HCC recurrence and clinical, laboratorial, imaging and histopathological parameters was performed, but none showed impact on HCC recurrence after LT. However, there was a trend to an association between recurrence and CHILD score (p = 0.06) and smoking (p = 0.08).

Also, when evaluating patients who presented early recurrence (less than 24 months after LT), a trend of an association with the number of involved liver segments was found ($p = 0.07$).

Conclusion: Identifying patients at risk of HCC recurrence after LT remains as a great challenge. There are some parameters previously suggested as possible predictors, but, in accordance to literature findings, our study didn't identify significant associations.

Nonetheless, the possible association between early recurrence and the number of affected liver segments hasn't been studied yet, and this is the first study that suggests an association.

Thus, evaluating the number of liver segments affected by HCC might help physicians to identify patients with higher risk of recurrence, as well as giving another possible parameter to investigate in further studies.

Disclosure: Nothing to disclose.

PP1022

HEPATOCTE NUCLEAR FACTOR 1 ALPHA AS RISK FACTOR FOR HEPATOCELLULAR CARCINOMA DEVELOPMENT AMONG EGYPTIAN PATIENTS WITH AND WITHOUT DIABETES MELLITUS

M. Abdel-Samiee¹, I.S. Bedira², E. Tantawy³, O.M. Hendy², A.M. Rashad⁴, A.B. Zaid⁵

¹National Liver Institute-Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt, ²National Liver Institute - Egypt, Clinical Pathology, Shebin Alkawm, Egypt, ³Menoufia University Faculty of Science, Chemistry Division, Chemistry Department, Shebin Alkawm, Egypt, ⁴Menoufia University Faculty of Science, Shebin Alkawm, Egypt, ⁵National Liver Institute Hospital - Egypt, Shebin Alkawm, Egypt

Contact E-Mail Address: drmohammed100@yahoo.com

Introduction: HNF1A gene variants have been reported to be involved in developing mature onset diabetes mellitus (DM). Many studies reported the role of DM as a risk factor for hepatocellular carcinoma (HCC) development. To date, it has not been reported whether HNF1A gene variants are associated with the risk of DM in cirrhotic patients and their subsequent HCC.

Aims & Methods: **Aim:** To evaluate the HNF1A (the hepatocyte nuclear factor 1 homeobox A) genetic variants as a cofactor with DM for HCC development in HCV-infected patients.

Methods: This study was conducted on 140 subjects; 30 had HCC without DM, 30 HCC with DM, and 40 patients had DM with no HCV infection or had HCC; in addition, 80 healthy volunteers with matched ages and genders were enrolled in the study as a control group. Liver function tests, hepatitis viral markers, alpha-fetoprotein (AFP), fasting sugar and HBA1c and HNF1A (rs2464196 and rs1169310) using real-time polymerase chain reaction (PCR) were done for all participants.

	DM (n = 40)		HCC (n = 30)		HCC+DM (n = 30)		Control (n = 40)		χ^2	P
	No.	%	No.	%	No.	%	No.	%		
HNF SNP2 (rs1169310)										
CC	10	25.0	10	33.3	6	20.0	7	17.5		
CT	13	32.5	10	33.3	13	43.3	17	42.5	3.389	0.759
TT	17	42.5	10	33.3	11	36.7	16	40.0		
$H_{W}\chi^2$ (p)		0.037		0.068		0.552		0.508		
Allele										
C	33	41.3	30	50.0	25	41.7	31	38.8	1.910	0.591
	47	58.8	30	50.0	35	58.3	49	61.3		

Table 1: Comparison between the studied groups according to HNF SNP2 (rs1169310) genotypes and allele frequencies.

Results: The frequency of HNF1A rs2464196 (AA) genotype in patient groups (DM, HCC, HCC+DM) was significantly higher compared to the control group ($P=0.006$, $P=0.018$, $P<0.001$ respectively). The combined dominant model (AA + GA) of rs 2464196 was significantly higher than the (GG) genotype in patient groups (DM, HCC, HCC+DM) than the control group. In addition, the frequency of the AA genotype is more prevalent in HCC+DM (73%) compared to the group of DM or HCC patients.

In contrast, the HNF1A rs 1169310 (TT, TC or CC genotypes) showed no significant difference among the four studied groups and their T or C allele distributions.

Conclusion: This finding suggested that the HNF1A rs2464196 (AA) genotype could be associated with DM and may raise the possibility of HCC development among HCV-infected patients who harbour this genotype more than (GG).

On the contrary, the HNF1A rs 1169310 polymorphism was of no significance as a risk factor in the current study. Large scale studies are recommended on other variants of HNF1A to clarify the role of this gene in HCC development.

Disclosure: Nothing to disclose.

PP1023

ACCURACY OF RADIOMICS IN PREDICTING MACROTRABECULAR HEPATOCELLULAR CARCINOMA: A SYSTEMATIC REVIEW AND DIAGNOSTIC META-ANALYSIS

V. Antunes¹, E. Bulhoes², O. Martins³, T. Correa⁴, A. Prata⁵, A.c. Covre Coan⁵, A. Milani⁶, P. Romeiro⁷, N.J. Milioli⁸, M.V. Fernandes¹

¹Federal University of Health Sciences of Porto Alegre, Medicine Department, Porto Alegre, Brazil, ²College of Higher Education of the United Amazon, Medicine Department, Redenção, Brazil, ³Federal University of Juiz de Fora, Medicine Department, Juiz de Fora, Brazil, ⁴Beth Israel Deaconess Medical Center/Harvard Medical School, Medicine Department, Boston, United States of America, ⁵Federal University of Espirito Santo, Medicine Department, Vitoria, Brazil, ⁶State University of Campinas, Medicine Department, Campinas, Brazil, ⁷University Center of Maceió, Department of Medicine, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Medicine Department, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is the second-most deadly cancer. Pathological examination is the gold standard for subtype differentiation. Patients with macrotrabecular HCC (MTHCC) have more aggressive lesions, higher recurrence rates and poorer survival. Radiomics can be seen as a digital biopsy that allows a characterization of tumor heterogeneity and phenotypes.

Aims & Methods: This study aims to evaluate the diagnostic accuracy of radiomics in predicting MTHCC subtype, considering that this could change the approach of the patient.

We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies evaluating the diagnostic accuracy of radiomics in predicting the MTHCC subtype. Statistical analysis included data pooling and heterogeneity testing.

Results: The meta-analysis included 6 studies and 529 patients. Data of the training cohort were not considered.

When internal and external validation cohorts were available, both were considered. The pooled sensitivity and specificity and AUC of radiomics for predicting MTHCC were 75.3% (95% CI 66.4% to 82.5%), 71.8% (95% CI 60.6% to 80.8%) and 0.792 (95% CI 0.697 to 0.833).

Conclusion: Our study shows that radiomics does not have enough diagnostic accuracy to predict MTHCC with a high degree of certainty. However, this could be an additional resource to improve radiological diagnosis. Improvements in this field are necessary once the diagnosis of this HCC subtype can change the management of the patient.

Disclosure: Nothing to disclose.

PP1024

ANNEXINA2 AS A MARKER OF HEPATOCELLULAR CARCINOMA DETECTION AMONG PATIENTS WITH HEPATITIS C VIRUS-RELATED LIVER CIRRHOSIS AFTER HCV TREATMENT USING DIRECTLY ACTING ANTIVIRALS

M. Shater¹, A. Abd Elmoety¹, Y. Rostom², E. Elkemary³, H. Helal¹, A. Kamal¹

¹Alexandria University, Faculty of Medicine, Internal medicine, Hepatology, Alexandria, Egypt, ²Alexandria University, Faculty of Medicine, Medical Oncology and Nuclear Medicine, Alexandria, Egypt, ³Alexandria University, Faculty of Medicine, Clinical and Chemical Pathology, Alexandria, Egypt

Contact E-Mail Address: ahmed.kamal.med.scientific@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is considered the sixth most prevalent malignant tumor in the world, and it ranks first in Egypt. Early detection of HCC is of great value, as early stages can be treated with curative modalities. Current surveillance programs depend on ultrasonography with or without alpha-fetoprotein (AFP) measurement, but the ultrasonography is operator-dependent and has many limitations, while AFP is neither adequately sensitive nor specific. Serum Annexin A2 has the potential to be a promising biomarker for the early detection of HCC.

Aims & Methods: The aim of the present study is to evaluate the potential contribution of serum annexin A2 in the detection of hepatocellular carcinoma. This case-control study included four groups:

Group A: Early hepatocellular carcinoma; BCLC stages 0 and A.

Group B: Advanced hepatocellular carcinoma; BCLC Stage C.

Group C: liver cirrhosis without HCC.

Group D: healthy subjects as a control group.

Chronic hepatitis C was the cause of cirrhosis in the three groups (A, B, and C). All of them attained sustained virological response (SVR) after receiving treatment with direct-acting antiviral medications (DAAs). Subjects with other liver cirrhosis causes, those with active hepatitis C viremia, those with combined hepatitis B virus infection, and those with any other malignancy were excluded.

Assuming a common standard deviation (14.6) using the F test (one-way ANOVA power analysis), at significance level.05, a sample size of 100 participants (25 per group) was needed to achieve 80% power to detect an overall difference of at least .35 ng/mL in the mean of serum annexin A2 between the studied 4 groups.

Both serum AFP and annexin A2 were measured in all included subjects.

Results: One hundred subjects were included in the study, 25 in each group. There were no statistically significant differences between groups regarding age and sex. The 3 diseased groups were not statistically significantly different regarding the modified Child-Pugh scores (median was 5), ALBI grading, MELD scores, platelet counts, INR, albumin, and total serum bilirubin levels.

By ROC curve analysis, at a cut-off point >12 (ng/ml), AFP was a statistically significant discriminator between HCC patients (group A+B) and patients with liver cirrhosis (group C), with an area under the ROC curve (AUC) = 0.670 (95% CI 0.550 to 0.789) ($p = .017$), sensitivity of 60.00%, specificity of 76.00%, positive predictive value (PPV) of 83.30%, and negative predictive value (NPV) of 48.70%, but at the same cut-off point, AFP is not

a statistically significant discriminator between patients with early HCC (group A) and patients with liver cirrhosis (group C) with an AUC of 0.619 (95% CI 0.450 to 0.783) ($p = .148$), with a sensitivity of 52.00%, a specificity of 76.00%, a PPV of 68.40%, and a NPV of 61.30%.

Serum annexin A2 levels showed a significant difference between the advanced HCC and the early HCC groups compared to the group of healthy individuals (group D) ($p < .001$). Annexin A2 levels were also significantly higher between the early HCC and advanced HCC groups when compared to the cirrhosis-only group ($p = .005$ and $p < .001$, respectively).

Moreover, annexinA2 levels were significantly higher in the advanced HCC group when compared to the early HCC group ($p = .003$). Annexin A2 was also higher in the cirrhosis-only group than in the healthy group ($p = .002$). By ROC curve analysis, at a cut-off point >7.7 (ng/ml), serum annexin A2 was a statistically excellent discriminator between HCC patients (group A+B) and patients with liver cirrhosis (group C) with an AUC of 0.962 (95% CI 0.910 to 1.000) ($p < .0001$), with a sensitivity of 98.00%, a specificity of 88.00%, a PPV of 94.2%, and a NPV of 95.7%.

At the same cut-off point, annexinA2 is a statistically significant discriminator between patients with early HCC (group A) and those with liver cirrhosis (group C), with an AUC of 0.934 (95% CI 0.851 to 1.000) ($p > .001$), a sensitivity of 96.00%, a specificity of 88.00%, a PPV of 88.90%, and a NPV of 95.7%.

Conclusion: Serum annexin A2 is a promising biomarker that can improve the sensitivity of HCC detection among patients with liver cirrhosis after HCV eradication using DAAs.

Disclosure: Nothing to disclose.

PP1025

PRESENTING COMPLAINTS IN 250 PATIENTS WITH CONGENITAL PORTOSYSTEMIC SHUNTS

V. McLin¹, V. Casotti^{2,3}, S. Korff⁴, J. Wacker⁵, K. Mostaguir⁶, R. Superina⁷, L. Savale⁸, A.-L. Rougemont⁹, D. Debray¹⁰, International Registry of Congenital Portosystemic Shunts

¹Swiss Pediatric Liver Center, University Hospitals Geneva, Pediatrics, Gynecology and Obstetrics, Geneva, Switzerland,

²Hospital Papa Giovanni XXIII, Pediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy, ³Hospital Papa Giovanni XXIII, Pediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy, ⁴University Hospitals Geneva, Swiss Pediatric Liver Center, Geneva, Switzerland,

⁵University Hospitals Geneva, Pediatric Cardiology Unit, Geneva, Switzerland, ⁶University Hospitals Geneva, Clinical Research Center, Geneva, Switzerland, ⁷Lurie Children's, Pediatric Surgery and Transplantation, Chicago, United States of America, ⁸Hopital Bicetre, Pulmonary Medicine, Paris, France, ⁹University Hospitals Geneva, Division of Clinical Pathology, Diagnostic Department, Geneva, Switzerland, ¹⁰Hopital Necker Enfants Malades, Liver Transplantation, Paris, France

¹⁰Hopital Necker Enfants Malades, Liver Transplantation, Paris, France

Contact E-Mail Address: valerie.mclin@hcuge.ch

Introduction: Congenital portosystemic shunts (CPSS) are associated with an array of clinical signs and symptoms of varying severity in both adults and children. Yet, symptoms are often missed and ascribed to other etiologies. Understanding presenting complaints will increase awareness of this rare disorder.

To this end the International Registry of Congenital Portosystemic shunts (IRCPSS) was created. Here we report an up-to-date description of the patients enrolled in the IRCPSS focusing on presenting complaints.

Aims & Methods: Descriptive analysis of the ESPGHAN sponsored IRCPSS described in (1)

Results: 256 patients were enrolled - 125 females (49%). Type of CPSS was available for 212: 88 (41.5%) presented with intrahepatic (IHS) and 124 (58.5%) with extrahepatic (EHS) shunts. Clinical data were available for 71 with IHS and 106 with EHS. 51 (72 %) of IHS were asymptomatic. Of the 20 (28%) symptomatic, median age at diagnosis was 0.59 years (14 days-19.9 years). Presenting complaint included liver in 14, cardiopulmonary in 6, neurological in 2, other in 7. Of 56 IHS closed, 21 (37.5%) closed spontaneously before age 1. 29 (52%) were closed using interventional radiology. Among 106 patients with EHS, 72 (68%) were asymptomatic. Among symptomatic patients, median age at diagnosis was 7.49 years (14 days-24.9 years). Presenting complaints included liver in 15, cardiopulmonary in 13, neurological in 13, and other in 17. 74 patients had closed shunts at last follow-up; they were closed at a median age of 2.7 years (18 days- 25.4 years). Spontaneous closure was reported in 2 patients, otherwise closure was performed by interventional radiology in 25 (34%), or surgery in 40 (54%) and 7 undergoing LT.

Conclusion: Most shunts were asymptomatic at diagnosis. Among symptomatic patients, the median age at diagnosis was higher in EHS than IHS. IHS and EHS were equally likely to be closed, with IHS more likely to close spontaneously within the first year of life.

References:

1. Korff S, Mostaguir K, Beghetti M, D'Antiga L, Debray D, Franchi-Abella S, Gonzales E, Guerin F, Hachulla AL, Lambert V, Makrythanasis P, Roduit N, Savale L, Senat MV, Spaltenstein J, van Steenbeek F, Wildhaber BE, Zwahlen M, McLin VA. International registry of congenital porto-systemic shunts: a multi-centre, retrospective and prospective registry of neonates, children and adults with congenital porto-systemic shunts. *Orphanet J Rare Dis.* 2022 Jul 19;17(1):284.

Disclosure: Nothing to disclose.

PP1026

SPLEEN ELASTOGRAPHY IN NON-CIRRHOTIC CHRONIC EXTRA-HEPATIC PORTAL VEIN THROMBOSIS PATIENTS ALLOWS FOR PERSONALIZED SCREENING FOR ESOPHAGEAL AND GASTRIC VARICES

F. Capinha¹, C.N. Ferreira^{1,2}, L. Correia^{2,1}, H. Cortez-Pinto^{2,1}

¹Serviço de Gastrenterologia e Hepatologia, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, ²Clínica Universitária de Gastrenterologia, Faculdade de Medicina de Lisboa, Universidade de Lisboa, Lisboa, Portugal

Contact E-Mail Address: francisco.capinha96@gmail.com

Introduction: In patients with cirrhosis, a transient elastography value of spleen stiffness (SS) <40 kPa can be used to identify those with low probability of high-risk varices and in whom endoscopy may be avoided. We aimed to evaluate if SS <40kPa may be useful to select patients with non-cirrhotic chronic extrahepatic portal vein thrombosis (CEPVT) in whom upper gastrointestinal endoscopy (UGE) to screen for high risk esophageal varices (EV) or gastric varices (GV) may be avoided.

Aims & Methods: We performed a retrospective study including consecutive patients with non-cirrhotic CEPVT, with data from SS and upper gastrointestinal endoscopy (UGE) within a 2 years interval. We evaluated 42 patients and finally excluded 20 (No SS measurement -10, previous splenectomy - 7 and no UGE in the previous 2 years). We compared two groups of patients: Group A - Those with high risk EV/GV or those who previously underwent variceal endoscopic band ligation (EBL) and group B - patients without EV/small EV or GV. The performance of SS <40kPa as indicator of probability of high risk EV was evaluated.

Qualitative data-analysis was performed with Chi-squared test. Quantitative data with non-normal distribution was analyzed with Mann-Whitney test. A p value < 0.05 was considered significant.

Results: We included 22 patients, with a median age 44(3-77) years with, 55% (12) being females. From these, 50% (11) were included in group A with 2 of them having had a previous EV bleeding episode. Comparing the 2 groups, the median SS value was 75kPa (IQR=0) in group A and 35 kPa (IQR=2.5) in group B (p=0.009).

All of the patients in group A had SS value >40kPa and thus would not have been excluded from UGE.

In group B, 45% (n=5) of patients had SS value >40kPa would have undergone UGE despite not having high risk EV/GV. In this cohort the cut-off showed a sensitivity of 100% and a negative predictive value of 100% despite a low specificity (55%).

Conclusion: In our cohort, a SS <40kPa in patients with non-cirrhotic CEPVT had a high negative predictive value and can be useful to select those patients in whom endoscopy can be avoided.

Disclosure: Nothing to disclose.

PP1027

SPLEEN STIFFNESS IS CORRELATED WITH HEPATIC VENOUS PRESSURE GRADIENT AND CAN PREDICT TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT DYSFUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

V. Antunes¹, A.C. Covre Coan², T. Correa³, E. Bulhoes⁴, O. Martins⁵, A. Milani⁶, A. Prata², P. Romeiro⁷, N.J. Milioli⁸, M.V. Fernandes¹

¹Federal University of Health Sciences of Porto Alegre, Medicine Department, Porto Alegre, Brazil, ²Federal University of Espirito Santo, Medicine Department, Vitoria, Brazil, ³Beth Israel Deaconess Medical Center/Harvard Medical School, Medicine Department, Boston, United States of America, ⁴College of Higher Education of the United Amazon, Medicine Department, Redenção, Brazil, ⁵Federal University of Juiz de Fora, Medicine Department, Juiz de Fora, Brazil, ⁶State University of Campinas, Medicine Department, Campinas, Brazil, ⁷University Center of Maceió, Department of Medicine, Maceió, Brazil, ⁸Pontifical Catholic University of Rio Grande do Sul, Medicine Department, Porto Alegre, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Hepatic venous pressure gradient (HVPG) measurement is invasive. Non-invasive methods for evaluating the severity of portal hypertension in patients with transjugular intrahepatic portosystemic shunt (TIPS) are warranted.

Aims & Methods: This study aims to evaluate the efficacy of spleen stiffness in predicting HVPG and TIPS dysfunction. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies comparing spleen stiffness measurements pre-TIPS and post-TIPS. The primary outcome was spleen stiffness. The secondary outcome was spleen stiffness in the context of TIPS dysfunction. The MD was used for continuous outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I² statistics.

Results: The meta-analyses included 13 studies and 521 patients. There was a significant difference in spleen stiffness reduction after TIPS compared to baseline, measured by SSW m/s (MD -0.49; 95% CI -0.55 to -0.43; p<0.01; I²=0%) and by SSM kPa (MD -11.19; 95% CI -13.32 to -9.07; p<0.01; I²=0%). TIPS dysfunction was associated with increased spleen stiffness values (MD 0.35; 95% CI 0.24 to 0.45; p<0.01; I²=0%) compared to normal tips function similarly to those found in pre-TIPS patients.

Conclusion: Our study showed that spleen stiffness is a non-invasive measure to evaluate HPVG reduction after TIPS placement. Spleen stiffness may also be useful in monitoring TIPS dysfunction.

Disclosure: Nothing to disclose.

PP1028

INTEREST OF ANTICOAGULANTS IN THE EVOLUTION OF CHRONIC PORTAL THROMBOSIS IN A NON-CIRRHOTIC PATIENT

A. Lemrabott¹, M. Kadiri², N. Lagdali¹, F.-Z. Chabib³, C. Berhili¹, M. Borahma⁴, F.Z. Ajana⁵

¹university Mohammed V, IBN SINA hospital, Rabat, Morocco,

²Ibn Sina Hospital, Rabat, Morocco, ³Ibn Sina university Hospital, Rabat, Morocco, Medical Unit C, Seclin, France,

⁴Mohammed the Vth University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ⁵CHU IBN SINA, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: aichanelemrabott@gmail.com

Introduction: Cruoric thrombus in the portal vein represents the most frequent cause of infrahepatic portal hypertension. It most often complicates cirrhosis, but when it occurs in the absence of cirrhosis, it is favored by a pro-thrombotic state in 2/3 of patients. It can be total or partial, localized or extended to the spleno-mesenteric trunk. The absence of repermeabilization leads to the development of a collateral venous network known as portal cavernoma (or chronic PVT). Management is essentially based on treatment of the cause, and in the absence of contraindication, anticoagulation is recommended to prevent recurrence or extension of thrombosis. The aim of this study is to report our department's experience of the benefits of anticoagulation in cases of chronic portal thrombosis in a non-cirrhotic patient.

Aims & Methods: This is a retrospective, descriptive study over a 6-year period from 2018 to 2024, involving all patients with chronic portal thrombosis without cirrhosis on anticoagulation for more than 6 months. Curative-dose anticoagulation with vitamin K antagonists and rivaroxaban 20mg/d was administered in patients with a major pro-thrombotic risk factor, and anticoagulation with rivaroxaban dosed at 15 mg/d in a low risk.

Results: Out of 58 patients followed for chronic portal vein thrombosis, 17 were put on anticoagulants: vitamin K antagonist (VKA) and direct oral anticoagulants (DOACs), with a prevalence of 29.31%. The mean age was 45.6 years (31-72), with a sex ratio of 0.4 M/F. Two patient's groups were identified: Patients with thrombosis at high risk of recurrence, requiring lifelong anticoagulation this group included 10 patients for 58.8% : the dominant etiology is myeloproliferative syndrome in 60% of patients (n=6), followed by anti-phospholipid antibody syndrome in 40% (n=4). Treatment in these patients was based on curative anticoagulation with 3 patients on rivaroxaban 20mg/d, and 7 patients on adapted VKA with an INR target of between (2-3). In the second group at low risk of recurrence, receiving rivaroxaban 15mg/d, involving 41.1% of our patients (n=7). The etiologies were as follows: isolated protein C or S deficiency in 42.8% (n=3), celiac disease in 28.5% (n=2), hydatid cyst surgery in 14.2% (n=1), no etiology found in 14.2% of patients (n=1). The evolution was marked by the absence of thrombosis extension assessed by imaging after a minimum of 6 months' anticoagulant treatment in 58.8% of cases (n=10), a partial repermeabilization in 29.4% (n=5), And complete repermeabilization was observed in 11.7% (n=2).

Conclusion: Anticoagulant treatment proved effective in preventing recurrence and thrombotic extension in all patients in our study, as assessed by imaging, which, although not systematically recommended in the follow-up of portal cavernoma, enabled us to confirm non-extension of the thrombosis in 58.8% of cases, and partial repermeabilization in 29.4% and complete repermeabilization in 11.7% of patients, Hence the importance of early anticoagulation with etiological management.

Disclosure: Nothing to disclose.

PP1029

FACTORS PREDICTING SURVIVAL IN PATIENTS DIAGNOSED WITH HEPATOCELLULAR CARCINOMA (HCC) IN FAR NORTH QUEENSLAND, AUSTRALIA

H. Elangovan¹, J. Hanson²

¹The Princess Alexandra Hospital, Gastroenterology & Hepatology, Queensland, Australia, ²UNSW, Sydney, Australia

Contact E-Mail Address: hari338@hotmail.com

Introduction: Far-North Queensland a region of 380,000 km² in tropical Australia has a population of approximately 290,000, of whom 17% identify as Aboriginal and/or Torres Straits Islander Australians. The region has 3 of the 7 most disadvantaged local government areas in Australia. Performing HCC surveillance in dispersed, disadvantaged populations across vast distances is challenging, as many other health conditions compete for finite health resources. Over 80% of Aboriginal Australians in this region have the less oncogenic HBV/D genotype infection.

Aims & Methods: A retrospective cohort study of individuals diagnosed with HCC in Far North Queensland between Jan 2014 and Sep 2021. The study's primary outcome was overall survival.

Results: There were 169 individuals diagnosed with HCC during the study period, their mean (95 % confidence interval (CI)) age was 65 (64 - 67). First Nations Australians were not over-represented (15 % of the cohort). The most common risk factors for liver disease were alcohol use disorder (66%), chronic hepatitis C virus (HCV) (47 %) and metabolic dysfunction (24 %). HBV-related HCC was less common (10 %) and there were no reported cases in Aboriginal Australians. The mean (95 % CI) survival in the cohort was 421 (304 - 570) days. In multivariate analysis, death was more common in individuals with Child-Pugh C cirrhosis (hazard ratio (HR) (95 % CI): 3.63 (2.20 - 5.99), p < 0.0001) and individuals with HBV infection (HR (95 % CI): 2.17 (1.25 - 3.77), p = 0.006). Individuals with chronic HCV infection were less likely to die (HR (95 % CI): 0.46 (0.31 - 0.69), p < 0.0001). Only 24 % of the cohort was participating in HCC surveillance at time of diagnosis despite most patients having guideline-recommended indications for screening; individuals participating in HCC surveillance were less likely to die (HR (95 % CI): 0.54 (0.33 - 0.90), p = 0.02).

Conclusion: HCC surveillance is associated with improved survival, but uptake in the region is suboptimal and contributes to the very poor outcomes. The absence of HBV-related HCC in Aboriginal individuals despite a high community prevalence of HBV infection suggests that HBV genotype might be employed to inform optimal HCC surveillance strategies in this remote region of Australia.

Disclosure: None.

PP1030

HEPATOCELLULAR CARCINOMA SCREENING IN CIRRHOSIS: EXPERIENCES OF A PERIPHERAL IRISH HOSPITAL

T. Matthews¹, N. Salzberg¹, T. Thayeswaran¹, M. Kharief¹, P. O'Regan¹

¹South Tipperary General Hospital, Department of Gastroenterology, Clonmel, Ireland

Contact E-Mail Address: matthetj@tcd.ie

Introduction: 2018 European Association for the Study of the Liver (EASL) guidelines suggest a six-month radiological surveillance interval for cirrhotic patients with either Child-Pugh stage A and B, or C awaiting liver transplantation, to reduce hepatocellular carcinoma (HCC) associated mortality.

Aims & Methods: We aimed to audit our compliance with HCC screening guidelines.

Our hepatology clinic, liver elastography and radiology databases were cross referenced to yield 91 patients attending with cirrhosis over the years 2013 to 2022.

Results: 69% (n=63) were male. Median age at diagnosis was 58 years (IQR: 50-64.75). 84% (n=76) and 12% (n=11) had alcohol and non-alcoholic steatohepatitis (NASH) as a documented aetiology. Median MELD3 was 13 (IQR: 9-17). 14% (n=13) had died at the time of writing. Median age at death was 62 (IQR 52-66).

34% (n=31) and 46% (n=42) had radiological features of splenomegaly and hepatic steatosis respectively. 56% (n=51) had evidence of varices with 67% (n=34) of those taking non-selective beta blockers (NSBBs). 20% (n=18) had prior hepatic encephalopathies and 67% (n=12) of those were taking rifaximin. 33% (n=30) had prior GI bleeding. 71% (n=65) had prior ascites with 75% (n=49) prescribed diuresis. 4% (n=4) had prior documented hepatorenal syndrome. 10% (n=9) had prior spontaneous bacterial peritonitis (SBP) with 44% (n=4) taking secondary prophylaxis. 2% (n=2) had prior trans-jugular intrahepatic portosystemic shunts (TIPSS). 3% (n=3) had prior portal vein thrombosis.

5% (n=5) were diagnosed with HCC. Median age at time of HCC diagnosis was 74 years (IQR: 66-74). Median alpha-fetoprotein (AFP) at time of diagnosis was 10.9 (IQR: 5.4-756).

Patients with Child Pugh C cirrhosis (N=24, 18%) were excluded from the analysis.

167 surveillance studies on those with no more than Child Pugh B cirrhosis were analysed over the ten-year period. The median number of months between surveillance imaging was 9.77 months (IQR: 5.9-17.8). 40% of surveillance studies were carried out at an interval of greater than 12 months. The average number of months between imaging pre- and post-COVID were 12.8 and 8.26 months respectively (95% CIs: 10.9-14.8, 6.4-10.1).

60% (n=3) of HCC diagnoses were made in the absence of a known history of cirrhosis. Two patients with Child-Pugh C cirrhosis had HCC diagnosed. One was a male in his 60s who had a diagnosis made on ultrasound 10.5 months after prior surveillance at another site. Another male in his late 70s had a HCC diagnosis made 35 months after a prior ultrasound identified cirrhosis, though his performance status made surveillance inappropriate.

Conclusion: Alcohol was the most prevalent cause of cirrhosis in our cohort. 5% of our cohort were diagnosed with HCC, with none as a result of failures to follow surveillance guidelines. Surveillance intervals post March 2020 fell significantly (p < 0.01). This may be attributable to an increase in radiology resources in the latter part of the decade.

References:

European Association for the Study of the Liver. Electronic address: easl-office@easloffice.eu; European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J

Hepatol. 2018 Jul;69(1):182-236. doi: 10.1016/j.jhep.2018.03.019. Epub 2018 Apr 5. Erratum in: J Hepatol. 2019 Apr;70(4):817. PMID: 29628281.

Disclosure: Nothing to disclose.

PP1031

POPULATION-BASED HEPATITIS C SCREENING IS FEASIBLE IN COUNTRY WITH MODERATE SEROPREVALENCE: 21-MONTH RESULTS OF THE PROGRAM IN LITHUANIA AND SCENARIOS FOR ACHIEVING WHO ELIMINATION TARGETS

L. Kupcinskas¹, E. Čiupkevičienė², A. Voeller³, L. Jancoriene⁴, E. Kazenaite⁵, D. Razavi-Shearer³, V. Basyte-Bacevičė¹, J. Ward⁶, J. Petkeviciene², G. Urbonas⁷, J. Kupcinskas¹

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Department of Preventive Medicine, Kaunas, Lithuania, ³Center for Disease Analysis Foundation, Lafayette, United States of America, ⁴Vilnius University, Clinic of Infectious Diseases and Dermatovenereology, Vilnius, Lithuania, ⁵Vilnius university, Clinic of Gastroenterology, Nephrourology and Surgery, Vilnius, Lithuania, ⁶Coalition for Global Hepatitis Elimination, Decatur, United States of America, ⁷Lithuanian University of Health Sciences, Department of Family Medicine, Kaunas, Lithuania

Contact E-Mail Address: l.kupcinskas@gmail.com

Introduction: Lithuanian HCV screening program started on May, 2022. State health authorities pay general practitioners (GPs) a special promoting fee for performing serological tests for HCV antibodies: 1. For the population born in 1945-1994 (once per life) and 2. For people who inject drugs (PWID) or are HIV-infected (annual HCV testing). Such an initiative is the first in Central and Eastern Europe.

Aims & Methods: This study aimed to evaluate the results of the first 21-month of the program and different scenarios to achieve WHO 2030 targets. GPs invited people to perform a serum blood test for HCV antibodies. Anti-HCV positive patients were referred to a gastroenterologist or infectologist for HCV RNA testing, and if result was positive, direct-acting antiviral (DAA) therapy was prescribed. Information about patients was obtained from the database of the National Health Insurance Fund. The Markov disease progression model elaborated by the CDA Foundation was used to assess HCV elimination progress. The data from the 2022-2023 screening were used as inputs. Three scenarios were developed: the 'Base' scenario - return to pre-screening program level in 2023 and 2 scenarios with different extents of treatment.

Results: At the beginning of 2022, about 1.8 million people born in 1945-1994 lived in Lithuania. Between May 5, 2022 and January 31, 2024 from this population 1145121 people (63,6%) were tested for HCV antibodies. Positive test results were found in 1.23% of cases. In the risk group, 9604 PWID and HIV+ people were screened, of whom 30,1% were seropositive. All seropositive patients were referred to specialists. Viremia was detected in 58 %. During 21-month period 4811 patients were treated with DAA. The number of treated patients during 21 months of program increased 2,8 times in comparison to previous 21 month before program (Aug 2020 - Apr 2022). Treatment delay for 48% of HCV patients was related to organizational problems (consultation waiting line, some treatment restrictions, delay in drugs supply).

Solving organizational challenges, by the end of 2024 we expect to perform HCV antibody testing in 80% of the target population and treatment up to 70% of RNA-positive individuals, further aiming to cure all of infected patients by 2030. The Markov disease progression model to assess HCV elimination progress showed the following scenarios: Scenario 1: if the

same number of patients are treated as before the screening, the WHO targets will not be reached. Scenario 2: treating 70% of infected patients will meet most but not all WHO targets. Scenario 3: by treating all infected patients by 2030, the WHO target will be met by saving 150 lives and preventing 90 new cases of decompensated cirrhosis and 120 cases of hepatocellular carcinoma.

Conclusion: Our data show that in European country with moderate HCV seroprevalence a population-based screening program can be feasible, screening near 64 % (more than 1,1 million) of the population born between 1945 and 1994 during the first 21 months of the program. We hope that WHO 2030 goals can be achievable in Lithuania.

Disclosure: Nothing to disclose.

PP1032

PREVALENCE OF SEXUAL DYSFUNCTION IN PATIENTS WITH LIVER DISEASE

A.A.T. Alraeeini¹, M. Cherkaoui Malki², S. Mechhor³,
N. Benzoubeir⁴, I. Errabih⁴, H. El Bacha⁵

¹Faculty Of Medicine And Pharmacy - Mohammed V University, Hepato-gastro-enterology and proctology department (medicine B) - Ibn Sina university hospital center, Rabat, Morocco, ²University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ³Ibn Sina Hospital, Medecine B, Rabat, Morocco, ⁴Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco, ⁵Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco

Contact E-Mail Address: arafat4h@gmail.com

Introduction: Chronic liver disease, particularly cirrhosis, leads to significant morphological and psychological endocrine changes, which can have an impact on patients' sexual health. Although sexual health is an important parameter of quality of life, it remains little studied in hepatology.

Aims & Methods: The aim of our work is to study the prevalence and degree of sexual dysfunction in male patients with chronic liver disease, and the associated risk factors.

This is a monocentric, comparative, descriptive and analytical study conducted during the year 2023. We included male patients followed for chronic hepatopathies (group 1 (G1)) as well as a control group of subjects followed in gastroenterology consultation presenting no hepatic pathology (group 2 (G2)). Exclusion criteria were the existence of overt hepatic encephalopathy, cognitive disorders or active alcohol abuse, limiting the reliability of the survey.

Sexual health was assessed using the IIEF (International Index of Erectile Function) questionnaire, which covers five domains: erection, orgasm, desire, satisfaction with intercourse and overall satisfaction. Two software packages were used for statistical analysis: Jamovi version 2.3.28 and Microsoft Excel.

Results: Our study included 120 patients, 60 followed for chronic liver disease, and 60 without liver pathology (control group).

Mean age was 44.6 years (21-73 years).

In the group of patients with hepatopathies, we found:

34 (65%) cirrhotics, 24 (40%) of whom had a history of decompensation. 18 (30%) HBV, 11 (18%) HCV, 5 (8%) NAFLD, 5 (8%) of undetermined cause, 5 (8%) portal hypertension, 4 (6.6%) portal thrombosis, 12 (19.8%) others. Patients in the liver disease group had more erectile dysfunction, orgasmic dysfunction, disorders of desire, disorders of sexual satisfaction and disorders of overall satisfaction compared with the control group, with respectively 40/60 (66.6%) vs 16/60 (26.6%) $p = 0.003$; 35/60 (58.3%) vs 14/60 (23.3%) $p = 0.012$; 41/60 (68.3%) vs 10/60 (16.6%) $p < 0.001$; 38/60 (63.3%) vs 18/60 (30%) $p < 0.001$; and 45/60 (75%) vs 17/60 (28.3%) $p < 0.001$.

After statistical analysis, cirrhosis was the only statistically significant risk factor for sexual dysfunction in our study (OR 7.9; $p = 0.012$).

Moreover, 100% of patients said they had never been asked about their sexual health during a consultation.

Conclusion: Sexual dysfunction is common in patients followed for liver disease, with cirrhosis as the main risk factor. Sexual dysfunction should be systematically screened, with a multidisciplinary approach to the management of these patients.

Disclosure: Nothing to disclose.

PP1033

FACTORS INFLUENCING THE QUALITY OF LIFE IN CIRRHOTIC PATIENTS

E. Mrabet¹, S. Meriam¹, H. Jlassi¹, S. Soua¹, N. Bibani¹, D. Gargouri¹
¹Habib Thameur Hospital, Hepatology and Gastroenterology, Tunis, Tunisia

Contact E-Mail Address: emna.mrabet.95@gmail.com

Introduction: Cirrhosis is a chronic liver disease that, due to its natural progression and complications, affects the quality of life (QOL). Tunisian data related to the QOL of cirrhotic patients are limited. Our objectives were to evaluate the QOL of cirrhotic patients and identify factors influencing it.

Aims & Methods: We conducted a cross-sectional study, including cirrhotic patients followed in our outpatient clinic. QOL was assessed using the following questionnaires: Chronic liver disease questionnaire (CLDQ) (QOL impairment threshold defined at five), 36-item short form (SF-36), The Hospital anxiety and depression scale, the Clinical frailty scale, the fatigue severity scale, the Insomnia severity index, and the Work productivity and activity impairment index.

Patient data regarding medical history, cirrhosis characteristics, and socio-economic conditions were collected.

Statistical analysis was performed using the SPSS software (significance threshold $p = 0.05$).

Results: One hundred (56 women and 44 men) were included, with an average age of 60.62 years. The cirrhosis was due to viral hepatitis in 55% of cases with a CHILD-PUGH score classified as B or C (49 cases). Thirty-four patients had a history of upper gastro-intestinal bleeding. Thirty patients presented with ascites.

The mean SF-36 was 54.06, and the mean CLDQ was 4.7. Twenty-five patients experienced anxiety, and 35 had depression, 22 suffered from clinically patent insomnia.

In multivariate analysis. The factors identified as influencing the SF-36 were the education level ($p = 0.014$), the CHILD-PUGH score ($p = 0.016$), the presence of esophageal varices ($p = 0.016$) or ascites ($p = 0.012$), anemia ($p = 0.016$), and low serum albumin levels ($p = 0.014$).

The factors influencing CLDQ were the CHILD-PUGH score ($p = 0.020$), the presence of ascites ($p = 0.012$), anemia ($p = 0.025$), and low serum albumin levels ($p = 0.018$).

A CLDQ below five was associated with a CHILD-PUGH score B or C ($p = 0.012$), the presence of ascites ($p = 0.011$), a portal vein thrombosis ($p = 0.048$), and low serum albumin levels ($p = 0.010$).

Conclusion: The results of our study highlight the importance of assessing QOL during cirrhosis and developing comprehensive care for our patients

Disclosure: Nothing to disclose.

Poster
Biliary

Biliary

09:00-18:00 / Poster Exhibition

PP1034

THE CONCENTRATIONS OF TNFRSF14 AND LIGHT IN THE SERA AND BILE OF THE PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

S. K^{1,2}, H. Fujiwara^{2,1}, S. Mizuno³, T. Kishikawa¹, T. Nakatsuka¹, N. Takahara¹, Y. Nakai^{4,5}, R. Tateishi¹, M. Fujishiro¹

¹The University of Tokyo, Gastroenterology, Tokyo, Japan,

²The Institute of Medical Science, Asahi Life Foundation, Gastroenterology, Tokyo, Japan, ³Saitama Medical University, Gastroenterology and Hepatology, Saitama, Japan, ⁴The University of Tokyo, Endoscopy and Endoscopic Surgery, Tokyo, Japan, ⁵Tokyo Women's Medical University, Gastroenterology, Tokyo, Japan

Contact E-Mail Address: sachiko.kanai.419@gmail.com

Introduction: Primary sclerosing cholangitis (PSC) is an idiopathic cholestatic disease. Recent genome-wide studies (GWAS) have identified about 30 disease susceptible genes to PSC.

We investigated the expression profiles of these genes in the liver biopsy samples of the patients with PSC, and revealed that the expression of TNFRSF14, which is a one of the risk genes for PSC, was upregulated in the biliary epithelial cell (BEC) of PSC compared to that in normal liver tissue and primary biliary cholangitis (PBC) liver tissue. TNFRSF14 is a member of the tumor necrosis factor receptor superfamily associated with inflammation and fibrosis. We also clarified that the expression of LIGHT, an active ligand for TNFRSF14, was elevated in the BEC of PSC¹.

These molecules are mainly expressed on lymphocytes, and in other inflammatory diseases, many reports have mentioned to the associations between these molecules in the sera and the disease progression.

Aims & Methods: Aims: In this study, we aimed to evaluate the concentrations of these molecules in the sera and bile of PSC.

Methods: The concentrations of soluble TNFRSF14 and LIGHT in the sera and bile were measured by enzyme-linked immunosorbent assay. The samples were collected from the following cases:

- Serum: 73 patients with PSC, 35 patients with PBC and 53 healthy controls.
- Bile: 15 patients with PSC, 12 patients with malignant biliary obstruction (MBO), 19 patients with biliary lithiasis (BL).

The bile samples were obtained during endoscopic retrograde cholangiopancreatography. The median values of the serum (s) and bile (b) concentrations of each group were evaluated by Mann-Whitney U test.

Results: sTNFRSF14 in the PSC group was significantly higher than those in the healthy controls (6.301 v.s. 4.247 pg/mL, $P < 0.001$) and the PBC group (4.987 pg/mL, $P < 0.001$).

sLIGHT in the PSC group was 87 pg/mL, which was higher than those in the healthy controls (61 pg/mL, $P = 0.012$), and was comparable to those in the PBC group (106 pg/mL, $P = 0.142$).

bTNFRSF14 in the PSC group was 2,005 pg/mL, showing no significant difference compared to those in the MBO (1,794 pg/mL, $P = 0.516$) and the BL group (1,987 pg/mL, $P = 0.504$).

bLIGHT in the PSC group was 523 pg/mL, remarkably higher than those in the MBO (82 pg/mL, $P < 0.001$) and the BL group (268 pg/mL, $P = 0.024$).

Conclusion: sTNFRSF14 in the PSC group was higher than those in the healthy control and the PBC group, and this result was equivalent to the previous report about the upregulated expression in the liver biopsy samples. While soluble LIGHT was secreted non-specifically in the sera of cholestatic liver disease, the elevated bile concentration of LIGHT can be involved in the unique biology of PSC. Further research is needed to elucidate the involvement of these two molecules in the pathogenesis of PSC.

References: 1. Digestive Liver Disease 2024 Feb;56(2):305-311.

Disclosure: Nothing to disclose.

PP1035

THE EFFECT OF URSODEOXYCHOLIC ACID (UDCA) ON SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH BILIARY SLUDGE AND EARLY STAGE OF CHOLELITHIASIS IN ROUTINE PRACTICE: MULTICENTER OBSERVATIONAL STUDY RESULTS

K. Raikhelson¹, E. Kondrashina¹, E. Pazenko¹, T. Kuznetsova²

¹Saint-Petersburg State University, Scientific and Educational Center of Gastroenterology and Hepatology, Saint-Petersburg, Russian Federation, ²Binnopharmgroup, Moscow, Russian Federation

Contact E-Mail Address: kaboi@rambler.ru

Introduction: As known, biliary sludge has mostly asymptomatic course, thus lack of data for biliary sludge diagnostics and treatment in Russia is observed.

Aims & Methods: Evaluation of the effectiveness and safety of therapy with UDCA in patients with the biliary sludge and early stage of cholelithiasis in routine practice.

Multicenter observational study (10 sites in total) has been conducted. Patients with the biliary sludge and/or early stage of cholelithiasis were enrolled. The main inclusion criteria were ultrasound (US) criteria (biliary sludge or low density stones less than 1 cm), history of uncomplicated cholelithiasis. Patients were given UDCA (10 mg/kg/day).

Other medication were also given to address their abdominal symptoms (include pain that does not meet the criteria for biliary colic) in accordance with approved standards. The duration of the observation was 180 days.

Primary outcome was to evaluate the effect of complex therapy with UDCA on the patients': quality of life, pain syndrome (include appearance biliary colic), changes in severity of other symptoms. The secondary outcomes were dynamics of US characteristics of the biliary system and the safety of UDCA.

Results: 1056 patients were included in the study: with biliary sludge – 948 (89.8%), stones – 270 (25.6%), of which sludge plus stones – 162 (15.3%). At baseline, 40.2% patients had mild or medium abdominal pain, 44% - abdominal discomfort, 35.5% - sensitivity to abdominal palpation. The most common complaint was bitter taste in mouth (529 patients, 50.1%). Statistically significant increase of the quality of life and decrease the frequency of abdominal pain on 60 days and 180 days of treatment was shown.

There was a statistically significant decrease in the frequency of several symptoms such as: nausea, bitter taste in mouth, heartburn, feeling of fullness after eating, bloating, flatulence at the end of treatment compared to the baseline ($p < 0.001$).

Parameter	Base	60 days	p(0-60 d)	Visit 7	p(0-180 d)
SF-36, physical, scores	49.9	53.5	<0.001	54.9	<0.001
SF-36, mental, scores	46.9	50.7	<0.001	52.5	<0.001
No pain, %	59.8	95.2	<0.001	99.3	<0.001

Results of repeated US showed the positive effect complex therapy with UDCA. The frequency of biliary sludge had decreased from 89.8% to 12%, the frequency of gallbladder stones - from 25.6% to 9.8%, simultaneous of biliary sludge and gallbladder stones - from 15.3% to 0.3%. There were no patients with enlargement of the gallbladder (against 8.5% at baseline). In the vast majority of patients these parameters returned to normal level (ALT in 94.9% of cases, AST in 95.5%, direct bilirubin in 94.8%, total bilirubin in 92.2%, alkaline phosphatase in 95.0%). Among patients with normal values during treatment were recorded increase ALT (5 cases), total bilirubin (6), GGT (4), alkaline phosphatase (2).

High safety of treatment with UDCA was recorded: 4 adverse events associated with taking UDCA, no serious adverse events. Compliance in the vast majority of patients (fluctuations 83.3-90.1% of patients during the study) was high.

Conclusion: The results of this practice study have shown the effectiveness of complex therapy with UDCA in patients with cholelithiasis and biliary sludge. Complex therapy with UDCA improved patients' quality of life, reduced the frequency of mild and moderate abdominal pain, prevents biliary colic. Results demonstrated that UDCA was highly safe. Thus, the UDCA may be extensively used in patients with biliary sludge & early stage of cholelithiasis and may prevent excessive surgery intervention.

Disclosure: Current study was conducted with the financial support of Binnopharm Group

PP1036

FACTORS ASSOCIATED WITH SPONTANEOUS MIGRATION OF STONES FOR COMMON BILE DUCT

R. Chaibi¹, I. Mouslim¹, F. Aitiken¹, S. Hdiye¹, A. Benhamdane¹, T. Addajou¹, S. Mrabti¹, R. Berraida¹, E. Ilham², F. Rouibaa³, H. Seddik⁴

¹Mohamed V Military Instruction Hospital, Gastroenterology II, Rabat, Morocco, ²Faculte De Medecine Et De Pharmacie De Rabat, Gastroenterology, Rabat, Morocco, ³Military hospital Mohamed V-Souissi University, Hay Ryad - 10100, Rabat, Morocco, ⁴Mohammed V Military Teaching Hospital, Mohammed V – Souissi University, Hepato-Gastro-Enterology II, Rabat, Morocco

Contact E-Mail Address: reemchaibi46@gmail.com

Introduction: Common bile duct (CBD) stones can spontaneously migrate through the duodenal papilla. In this case, ERCP may be unnecessary and a significant rate of complications may be avoided..

Aims & Methods: Aims: The aim of our study is to evaluate the factors associated with spontaneous migration of CBD stones.

Methods: This is a retrospective descriptive and analytical study including 547 patients who underwent ERCP for CBD stones between January 2019 and September 2023.

All patients underwent MRCP for the diagnosis of CBD stones.

MRCP was considered positive if stones were present in CBD.

A positive ERCP was defined as the presence of stones in the VBP on cholangiography.

Patients were classified into 2 groups:

- Group A (n=309): positive MRCP and positive ERCP.

- Group B (n=265): positive MRCP but negative ERCP.

Statistical analysis was performed using JAMOVI software.

Results: The mean age in group A was 59.1 +/- 13.8 years and in group B 56.9 +/- 13.2 years, with no statistically significant difference (p=0.056). The sex ratio (M/F) in group A was 0.7 and in group B 0.54, with a significant female predominance in both groups (p=0.03).

There was no statistically significant difference between the 2 groups in CBD diameter or presence of a perampullary diverticulum.

Comparing group A versus group B, patients with small stone diameter (P=0.001), a single stone (p=0.001) and distal stones (P=0.04) tended to pass their stones spontaneously.

Conclusion: In our study, the factors associated with spontaneous migration of CBD stones were a small stone diameter, a single stone and distal stones.

Disclosure: Nothing to disclose.

PP1037

EARLY PREDICTORS OF SUCCESSFUL KASAI PORTOENTEROSTOMY

A. Maria¹, N. Wadhwa¹, S. Badwal², A. Prasad³, S. Aggarwal³

¹Sir Ganga Ram Hospital, New Delhi, Pediatric Gastroenterology Hepatology and Liver Transplant, New Delhi, India, ²Sir Ganga Ram Hospital, New Delhi, Pathology, New Delhi, India, ³Sir Ganga Ram Hospital, New Delhi, Pediatric Surgery, New Delhi, India

Contact E-Mail Address: arjunmaria0@gmail.com

Introduction: This study was done to identify factors associated with successful Kasai Portoenterostomy (KPE)

Aims & Methods: Retrospective analysis of 49 infants who underwent KPE between January 2018 to October 2023. Successful KPE was defined as total bilirubin < 1 mg/dl by 6 months of age. None of the patients received post KPE steroids and none were tested for concomitant CMV.

Results: The median age at KPE was 71 (59-83) days, with 21 (42.9%) less than 65 days. Median follow up was of 11 (6-36) months with native liver survival in 27 (55.1%). Thirty six (73.5%) were type III biliary atresia and 2 (4%) were associated with other congenital anomalies. Successful KPE was in 22 (44.9%). Age less than 65 days at the time of KPE was significantly associated with successful KPE (42.9% vs 57.1%, OR 5, 95% CI 1.472 -16.988, p=0.009). Weight (p=0.932), total bilirubin (p=0.907), direct bilirubin (p=0.667), AST (p=0.837), ALT (p=0.937), Total protein (p=0.051), albumin (p=0.201) and INR (p=0.220) at the time of surgery did not affect outcome. Ishak fibrosis grade (p=0.267) and inflammation grade (p=0.743) were not associated with outcome. Post surgery, lower total bilirubin (7.95 mg/dl vs 10.1 mg/dl, MD 0.07 to 4.66, p=0.043) and direct bilirubin (4.92 mg/dl vs 6.5 mg/dl, MD 0.16 to 3.03, p=0.03) by post operative day 7 were associated with a successful outcome. Parameters like ascites for more than 7 days (p=0.071), albumin (p=0.431), AST (p=0.091), ALT (p=0.108) and INR (p=0.241) at 7 days post KPE did not affect the outcome. Seventeen patients suffered from complications post KPE with sepsis in 17, bowel perforation in 3 and biliary ascites in 2. Presence of complications post KPE did not affect the outcome (p=0.825). Twenty (40.8%) patients suffered from a median of 1 (1-3) cholangitis episodes. However, cholangitis was not associated with outcome (p=0.374). On logistic regression analysis age less than 65 days (OR 8.024, 95% CI 1.865 to 34.530, p=0.005) and lower total bilirubin at day 7 post KPE (OR 0.789, 95% CI 0.642 to 0.970, p=0.028) were found to be significantly associated with successful KPE increasing the correctness of classification of model from 55.1% to 73.5%

Conclusion: There is a 8 folds increase in successful outcome if KPE is done at less than 65 days of age. Bilirubin at post operative day 7 is an early predictor of successful KPE.

Disclosure: Nothing to disclose.

PP1038

COMPARISON OF SHORT-COURSE VERSUS LONG-COURSE ANTIMICROBIAL TREATMENT FOR ACUTE CHOLANGITIS WITH GRAM-POSITIVE BACTEREMIA AFTER ERCP

Y. Kim¹, K. Ishikawa², K. Nakamura³, Y. Murashima¹, H. Ikusaka¹,
R. Yokosuka¹, T. Yamazaki¹, Y. Suzuki¹, S. Okuyama¹, K. Takagi¹,
K. Fukuda¹

¹St. Luke's International Hospital, Gastroenterology, Tokyo,
Japan, ²St. Luke's International Hospital, Infectious Diseases,
Tokyo, Japan, ³Tokyo Dental College, Ichikawa General Hospital,
Gastroenterology, Chiba, Japan

Contact E-Mail Address: yunte.soccer.05@gmail.com

Introduction: There is no clear duration of antimicrobial treatment of acute cholangitis complicated by Gram-positive coccus (GPC) bacteremia. The American guideline¹ suggests 4-7 days of antimicrobial treatment after appropriate source control, irrespective of the organism or presence of bacteremia, while the Japanese guideline² suggests 14 days when GPC bacteremia is present.

However, data to support these recommendations are limited and deviation from real-world practice is proposed, therefore, studies for adequate treatment duration are warranted.

Aims & Methods: We conducted a single-center, retrospective study of adult patients with acute cholangitis with GPC bacteremia treated with ERCP (Endoscopic Retrograde Cholangiopancreatography) from July 2003 to December 2023. We analyzed two groups according to the duration of effective antimicrobial treatment: short-course (SCT, <14 days) and long-course (LCT, ≥14 days). We constructed logistic regression models for mortality and a composite outcome, including mortality, recurrence, and infection of the same organism related to cholangitis. Malignant biliary strictures were excluded.

Results: A total of 45 patients with acute cholangitis complicated by GPC bacteremia underwent ERCP in our hospital, 22 in the SCT group and 23 in the LCT group. The median duration of antimicrobial treatment was 9 days (IQR 5.5-12.5) in the SCT group and 16 days (IQR 14.5-19.5) in the LCT group, with a significant difference between the two groups ($p<0.05$).

There were no significant differences in age, gender, severity, cause of cholangitis, the complication rate of pancreatitis and cholecystitis, heart valve disease, community acquisition, number of positive blood cultures, rate of echocardiography during treatment, intravascular devices or time to biliary drainage between the two groups.

Common bile duct stones were the most common cause with 82.2% of all patients, followed by diverticulum and stent obstruction with 8.9% and 6.7%, respectively.

Regarding the causative organisms, mixed infections were found in 71.1%, and *Enterococcus spp.* was the most common strain with 66.7%, of which *E. faecalis* with 23.3%, *E. faecium* with 16.7%, and followed by *Streptococcus spp.* with 31.1% of all patients, with no significant differences between the two groups.

Regarding antibiotics, penicillins were most commonly used with 73.3%, followed by cephalosporins with 66.7%, and glycopeptides with 26.7% in all patients. Penicillins (91.3% vs. 54.5%, $p<0.05$) and glycopeptides (43.4% vs. 9.1%, $p<0.05$) were used more frequently in the LCT group.

The 30-day mortality and reinfection with the same organisms within 3 months were 0.0% in both groups, and the length of hospital stay was significantly shorter in the SCT group (median 14.0 vs 10.5 days, $p<0.05$). The rate of cholangitis recurrence within 3 months was 5% (1/20) in the SCT group and 9.5% (2/22) in the LCT group, with no significant difference.

	Shorter (<14 days) n=22 (%)	Longer (≥14 days) n=23 (%)	p-value
30-day mortality, n(%)	0 (0%)	0 (0%)	
Recurrence of cholangitis, n(%)			
Yes	1 (5.0%)	2 (9.1%)	0.715
No	19 (95.0%)	20 (90.9%)	
Reinfection due to the same organism within 3 months, n(%)			
Yes	0	0	0.968
No	20 (100%)	22 (100%)	
Length of hospital stay (median days, IQR)	10.5 (7-13)	14.0 (10-18.5)	0.032

Conclusion: For acute cholangitis complicated by GPC bacteremia, antimicrobial treatment for less than 14 days might be considered after appropriate biliary drainage.

References: 1. Solomkin JS et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:133-164.

2. Gomi H et al. Tokyo Guidelines 2018: antimicrobial therapy for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25:3-16.

Disclosure: Nothing to disclose.

PP1039

PREDICTING FACTORS OF ACUTE GANGRENOUS CHOLECYSTITIS IN PATIENTS TREATED WITH LAPAROSCOPIC CHOLECYSTECTOMY: A SINGLE CENTER RETROSPECTIVE STUDY

K. Hayoung¹, J.-y. Seo¹, H. Hong¹, S. Park¹

¹Bundang Jesaeng General Hospital, Department of
Gastroenterology, Gyeonggi-do, South Korea

Contact E-Mail Address: gkdud0921@naver.com

Introduction: Acute gangrenous cholecystitis, a severe complication of cholecystitis, carries a high risks of morbidity and mortality. Despite its severity, preoperative diagnosis is challenging, often only confirmed during surgery, highlighting the need for effective pre-operative predictors to facilitate timely surgical intervention. Therefore, we analyzed various factors that could predict acute gangrenous cholecystitis in patients undergoing laparoscopic cholecystectomy.

Aims & Methods: We conducted a retrospective review of patients who underwent laparoscopic cholecystectomy at Bundang Jesaeng General Hospital between January 2018 and December 2021. From this group, we included only those patients who proceeded directly to surgery without any radiologic interventional treatments. Prior to surgery, all patients underwent an ultrasonographic examination of the gallbladder.

Results: Our study investigated 314 patients diagnosed with acute cholecystitis, of which 37 (11.8%) were identified with acute gangrenous cholecystitis.

Analysis revealed that patients with gangrenous cholecystitis were significantly older, more likely to be male, and had a higher prevalence of chronic kidney disease compared to those with uncomplicated cholecystitis. Laboratory results indicated higher WBC, C-reactive protein, and delta neutrophil index (DNI) levels in gangrenous cases, with a DNI level of 0.5% or higher marking a notable increase in risk.

Ultrasound findings showed a higher incidence of sonographic Murphy's signs (9% vs. 21.6%, $p=0.039$), thickened gallbladder wall (3.1 ± 0.9 mm vs 5.2 ± 0.9 mm, $p<0.001$) and defects (0.4% vs. 5.6%, $p=0.035$) in gangrenous cholecystitis.

Univariate and multivariate analyses highlighted that a thickened gallbladder wall remained a significant predictor of gangrenous cholecystitis ($p<0.001$).

	Univariate analysis				Multivariable analysis			
	OR	95% CI		p value	OR	95% CI		p value
		Lower	Upper			Lower	Upper	
Thickened GB wall (≥ 4 mm)	85.64	24.95	538.84	< 0.001	79.37	20.39	579.91	< 0.001

Conclusion: Patients diagnosed with gangrenous cholecystitis were typically older, more frequently male, and had a higher prevalence of chronic kidney disease. The results of this study suggest that thickened GB wall (≥ 4 mm) is an effective predictor of gangrenous cholecystitis; therefore, urgent management is recommended for these patients due to the high morbidity and mortality associated with the condition.

Disclosure: Nothing to disclose.

PP1040

CHARACTERISTICS AND METABOLIC POTENTIAL OF BILIARY MICROBIOTA IN PATIENTS WITH GIANT COMMON BILE DUCT STONES

C. Dai¹, S. Feng¹, T. Xia¹, C. Xu¹, J. Ye¹

¹First Affiliated Hospital of Soochow University, Department of Gastroenterology, Suzhou, China

Contact E-Mail Address: daicg_soochow@163.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is an effective minimally invasive approach for the treatment of choledocholithiasis, while successful extraction is hampered by large diameter of stones. Emerging studies have revealed the close correlation between biliary microbiota and common bile duct stones (CBDS).

Aims & Methods: We aimed to investigate the community characteristics and metabolic functions of biliary microbiota in patients with giant CBDS. The present study was designed as a case-control study, which was approved by the ethics committee of First Affiliated Hospital of Soochow University (approval number: 2020-082). Consecutive patients were prospectively enrolled from February 2023 to October 2023. The inclusion criteria were as follows: (1) CBDS were confirmed by at least one imaging examination; (2) no antibiotics use within three months. The patients who had a history of surgery involved in upper gastrointestinal tract or hepatobiliary system were excluded. The CBDS would be recognized as a giant stone if its diameter was larger than 15mm and the diameter ratio of stone against CBD was larger than 1.0. Bile samples were collected through ERCP. The microbiota was analyzed using 16S rRNA sequencing. Metabolic functions were predicted by PICRUSTs 2.0 calculation based on MetaCyc database. Bile acids were tested and identified using ultra performance liquid chromatography-tandem mass spectrometry.

Results: A total of 26 patients were successfully included into final analysis, 8 in giant stone (GS) group and 18 in control group. No significant difference concerning demographics was found between the two groups (Table.1). Distinct biliary microbial composition was identified in patients with giant CBDS, with a significantly higher abundance of Firmicutes at phylum level. The unique composition at genus level mainly consisted of *Enterococcus*, *Citrobacter*, *Lactobacillus*, *Pyramidobacter*, *Bifidobacterium* and *Shewanella*. *Pyramidobacter* was exclusively found in GS group, along with the absence of *Robinsoniella* and *Coprococcus*. The contents of free bile acids were significantly higher in GS group, including cholic acid (98.39μmol/mL vs. 26.15μmol/mL, $p=0.035$), chenodesoxycholic acid (54.69μmol/mL vs. 5.86μmol/mL, $p=0.022$) and ursodeoxycholic acid (2.70μmol/mL vs. 0.17μmol/mL, $p=0.047$). Decreasing tendency of conjugated bile acids were also observed. Metabolic pathways concerning cholelithiasis were abundant in GS group, including geranylgeranyl diphosphate biosynthesis, gluconeogenesis, glycolysis and L-methionine biosynthesis.

	GS group n=8	Control group n=18	p value
Age, years (mean±SD)	83.50±6.28	66.67±14.48	0.001
Gender, male/female	6/2	13/5	1.000
BMI, kg/m ² (mean±SD)	20.43±3.06	22.54±2.11	0.052
Stone no., single/multiple	2/6	8/10	0.420
TBIL, μmol/L, (median)	24.55	20.10	0.429
DBIL, μmol/L, (median)	17.10	8.80	0.198
γ-GGT, U/L, (median)	444.80	255.00	0.574
ALP, U/L, (median)	276.20	123.65	0.110
CA199, U/mL, (median)	15.47	9.22	0.261

Table.1 Patient demographics and preoperative characteristics.

Conclusion: This study demonstrated the community structure and metabolic potential of biliary microbiota in patients with giant CBDS. The unique biliary microbial composition holds valuable predictive potential for clinical conditions. These findings provide new insights into the etiology of giant CBDS from the perspective of biliary microbiota.

References:

1. Committee ASOP, Buxbaum JL, Abbas Fehmi SM, Sultan S, Fishman DS, Qumseya BJ, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. *Gastrointest Endosc* 2019;89:1075-1105 e15.
2. Manes G, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, et al. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2019;51:472-491.
3. Nicoletti A, Ponziani FR, Nardella E, Ianaro G, Gasbarrini A, Zileri Dal Verme L. Biliary tract microbiota: a new kid on the block of liver diseases? *Eur Rev Med Pharmacol Sci* 2020;24:2750-2775.
4. Tan W, Chen R, Song J, He D, Wu J, Chen X, et al. Microbiota analysis with next-generation 16S rDNA gene sequencing in recurrent common bile duct stones. *Ann Transl Med* 2022;10:576.
5. Molinero N, Ruiz L, Milani C, Gutierrez-Diaz I, Sanchez B, Mangifesta M, et al. The human gallbladder microbiome is related to the physiological state and the biliary metabolic profile. *Microbiome* 2019;7:100.
6. Shen H, Zhu J, Ye F, Xu D, Fang L, Yang J, et al. Biliary Microbial Structure of Gallstone Patients With a History of Endoscopic Sphincterotomy Surgery. *Front Cell Infect Microbiol* 2020;10:594778.

Disclosure: Nothing to disclose.

PP1041

APPLICATION OF EUS OR MRCP PRIOR TO ERCP IN PATIENTS WITH SUSPECTED CHOLEDOCHOLITHIASIS IN CLINICAL PRACTICE

M.J. de Jong^{1,2}, M.M. Engels^{3,2}, C. Sperna Weiland^{4,2}, R. Krol⁵, T.M. Bisseling¹, E.-J.M. van Geenen¹, P.D. Siersema^{1,6}, F. van Delft¹, J. van Hooft³

¹Radboud university medical center, Gastroenterology & Hepatology, Nijmegen, Netherlands, ²St. Antonius Hospital, Research & Development, Nieuwegein, Netherlands, ³Leiden University Medical Center, Gastroenterology & Hepatology, Leiden, Netherlands, ⁴Jeroen Bosch Hospital, Gastroenterology and Hepatology, 's Hertogenbosch, Netherlands, ⁵Maas Hospital Pantein, Gastroenterology & Hepatology, Beugen, Netherlands, ⁶Erasmus University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: mike.dejong@radboudumc.nl

Introduction: Patients with symptomatic cholelithiasis can be stratified according to the 2019 European Society for Gastrointestinal Endoscopy (ESGE) guideline into low-, intermediate- and high-likelihood categories for the presence of choledocholithiasis. For the intermediate group, endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography (MRCP) is recommended to assess whether an endoscopic retrograde cholangiopancreatography (ERCP) is necessary prior to cholecystectomy. The aim of the study is to investigate adherence to the guideline for diagnostic and treatment strategy for cholelithiasis in daily clinical practice.

Aims & Methods: Multicenter, retrospective cross-sectional observational study of the diagnostic pathway of patients with suspicion of choledocholithiasis between 2019 and 2021. Patients were stratified according to the ESGE guideline.

Results: A total of 305 patients were included in the analysis and stratified into low (17%), intermediate (40%) and high (43%) likelihood of choledocholithiasis. In these three categories, 182 (60%) patients underwent ERCP. Adherence to the ESGE guideline recommendation to perform additional imaging was 59.7% overall and was the highest in the intermediate group (83.6%) ($p < 0.001$). In 195 patients who underwent additional imaging, 55 ERCPs (28.2%) could be avoided.

Conclusion: This study shows that stratification according to the ESGE guidelines is useful to reduce the number of unnecessary diagnostic imaging procedures and ERCPs in patients with a suspicion of choledocholithiasis. It can be worthwhile to perform EUS prior the ERCP in the same session.

Disclosure: Mike J.P. de Jong, Megan M.L. Engels, Christina J. Sperna Weiland, Tanya M. Bisseling, Robin Krol and Foke van Delft have no conflict of interest or financial ties to disclose. Jeanin E. van Hooft reports lecture fees from Cook Medical, dr. Falk Pharma, Boston Scientific, AbbVie, and consultancy fees from Olympus. Erwin M. van Geenen reports research grants from Olympus, Boston Scientific, and MTW Endoskopie. Peter D. Siersema reports research grants from Pentax and Fujifilm. All outside the submitted work.

PP1042

PERCUTANEOUS CHOLECYSTOSTOMY IN SEVERE ACUTE CHOLECYSTITIS, COULD BE USED AS A DEFINITIVE TREATMENT IN UNFIT PATIENT

K. Abdelsaid¹, B. Jayasankar², Y. Abdulaal³

¹East Kent University Hospital NHS Trust, General Surgery, Margate, United Kingdom, ²North West Anglia NHS Foundation Trust, Cambridge, United Kingdom, ³Maidstone and Tunbridge Wells NHS Trust, Tunbridge Wells, United Kingdom

Contact E-Mail Address: Kirolos.Abdelsaid@nhs.net

Introduction: Although percutaneous cholecystostomy (PC) is generally accepted as a bridge to definitive therapy for acute cholecystitis (AC), which remains cholecystectomy, some patients did not undergo cholecystectomy, mainly due to contraindications to surgery. Here, we aimed to investigate the predictors of recurrence and the outcome after PC.

Aims & Methods: This is a retrospective study from a single general hospital at Tunbridge Wells, United Kingdom. One hundred twenty-six patients who presented with AC grade 3 and were initially managed with PC were included. In addition, the proportion of patients who did not undergo subsequent laparoscopic cholecystectomy (LC) and their characteristics were analyzed.

Results: The mean age of the study cohort was 72 (36-98) years, and the median length of drain insertion was 39.5 days. The majority (52%) presented with severe AC grade 3 with failed medical treatment to control the disease, while 7% had an emphysematous gallbladder. Eighty percent of patients did not develop any further attacks of AC after PC removal. The most common comorbidity was hypertension (35%). The mean age-adjusted Charlson comorbidity score was 3.72. Thirty-six percent (45/126) of the study cohort underwent LC, while the remaining patients did not receive any surgical intervention. Nine percent were deemed unfit for surgery. Forty-one patients (33%) were managed conservatively as they did not have a further attack of cholecystitis after PC removal or had a mild attack managed with antibiotics. In addition, 22% experienced procedural complications, including a blocked stent, pain, and cellulitis around the tube. The 30-day mortality rate of patients who did not undergo LC was 5%. Predictors of interval cholecystectomy were younger age, calculus cholecystitis, low Charlson index score, and uncomplicated and shorter length of hospital stay with PC.

Conclusion: Most severe AC patients treated initially with PC did not undergo subsequent LC. Therefore, PC in high-surgical-risk patients with AC could be a definitive treatment.

References: 1. NICE: Cholelithiasis and cholecystitis scope. (2014). <https://www.nice.org.uk/guidance/cg188/documents/cholelithiasis-and-cholecystitis-final-scope2>.

2. Yokoe M, Hata J, Takada T, et al.: Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci. 2018, 25:41-54. 10.1002/jhbp.515

3. Okamoto K, Takada T, Strasberg SM, et al.: TG13 management bundles for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2013, 20:55-59. 10.1007/s00534-012-0562-2

4. Ansaloni L, Pisano M, Coccolini F, et al.: 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg. 2016, 11:25. 10.1186/s13017-016-0082-5

5. Riall TS, Zhang D, Townsend CM Jr, Kuo YF, Goodwin JS: Failure to perform cholecystectomy for acute cholecystitis in elderly patients is associated with increased morbidity, mortality, and cost. J Am Coll Surg. 2010, 210:668-677. 10.1016/j.jamcollsurg.2009.12.031

6. Winblad A, Gullstrand P, Svanvik J, Sandström P: Systematic review of cholecystostomy as a treatment option in acute cholecystitis. HPB (Oxford). 2009, 11:183-193. 10.1111/j.1477-2574.2009.00052.x

7. Johansson M, Thune A, Blomqvist A, Nelvin L, Lundell L: Management of acute cholecystitis in the laparoscopic era: results of a prospective, randomized clinical trial. *J Gastrointest Surg.* 2003, 5:642-645.10.1016/S1091-255X(03)00065-9

Disclosure: Nothing to disclose.

PP1043

URSODEOXYCHOLIC ACID IS NOT ASSOCIATED WITH REDUCED RECURRENCE OF PRIMARY COMMON BILE DUCT STONES

F. Mazzawi¹, Y. Gorelik¹, T. Arraf¹, S. Dibbiny², K. Yassin¹, I. Khamaysi², A. Klein¹

¹Rambam Health Care Campus, Gastroenterology, Haifa, Israel,

²Rabin Medical Center, Director, Division of Gastroenterology, Petah Tikva, Israel

Contact E-Mail Address: fares.maz262@gmail.com

Introduction: Recurrence of common bile duct (CBD) stones after initial treatment is estimated to occur in 5%-20% of cases¹, requiring additional interventions and is associated with adverse patient outcomes. Previous small scale studies evaluated the role of UDCA in the prevention of CBD stone^{2,3}. We aimed to investigate whether UDCA is effective in preventing de-novo CBD stone formation.

Aims & Methods: This was a cohort analysis. We analyzed the electronic records of patients diagnosed with cholangitis or choledocholithiasis who underwent endoscopic retrograde cholangiopancreatography (ERCP) with evidence of complete common bile duct (CBD) stone removal. Due to the lack of consistent evidence, recommendations for using ursodeoxycholic acid (UDCA) to prevent stone recurrence varied among endoscopists. All patients were contacted and interviewed after providing informed consent. The follow-up period was defined as the time from the index ERCP to either evidence of CBD stone recurrence or the date of the patient interview. The primary outcome was a documented case of CBD stone recurrence. We compared baseline variables and outcomes between patients who were recommended to receive UDCA following ERCP and those who did not receive a UDCA recommendation. We performed univariate survival analysis using the log rank score to compare survival distributions between groups.

Results: Ninety-eight patients were included in the analysis and contacted. Of these, 50 patients received a recommendation for UDCA treatment, and 30 patients took UDCA. Additionally, 48 patients did not receive any recommendation for UDCA, contributing to a total of 68 patients who did not take UDCA. Comparison of baseline characteristics, index ERCP findings and outcomes between groups is presented in *Table 1*. There were no significant differences in patient ages and rate of major comorbidities. Most patients undergone cholecystectomy more than 24 months prior to the index ERCP. Previous sphincterectomy was more common in the UDCA treatment group (70% vs 17.6%; $p < 0.01$). No marked differences were noted in regard to other index ERCP findings between the two groups including papillary anatomy, number, size, type of stones and technique of stone removal (*Table 1*). No significant difference in stone recurrence was between patients who took and did not take UDCA (recurrence in 8/30 patients [26.7%] and 22/68 [32.4%] respectively, $P = 0.75$). There was no significant difference in survival without recurrence between the two groups ($p = 0.84$).

Conclusion: Our findings do not suggest efficacy of UDCA in prevention of de-novo CBD stone recurrence after cholecystectomy and complete CBD clearance.

References:

1. Lammert F, Acalovschi M, Ercolani G, et al. EASL Clinical Practice Guidelines on the prevention, diagnosis and treatment of gallstones. *J Hepatol.* 2016;65(1):146-181. doi:10.1016/J.JHEP.2016.03.005

2. Yamamoto R, Tazuma S, Kanno K, et al. Ursodeoxycholic acid after bile duct stone removal and risk factors for recurrence: a randomized trial. *J Hepatobiliary Pancreat Sci.* 2016;23(2):132-136. doi:10.1002/jhbp.316

3. Swobodnik W, Janowitz P, Kratzer W, et al. [Preventing the recurrence of common bile duct calculi following endoscopic papillotomy with ursodeoxycholic acid]. *Z Gastroenterol.* 1990;28(11):621-625.

Disclosure: The authors report no conflict of interests

PP1044

MAGNOLOL INHIBITS THE PROLIFERATION OF CHOLANGIOCARCINOMA THROUGH THE JAK2/STAT3 SIGNALING PATHWAY IN VIVO AND IN VITRO

Y. Bian^{1,2,3,4}, J. Yang^{1,2,3,4,5}

¹Hangzhou First People's Hospital, Gastroenterology, Hangzhou, China, ²Department of Gastroenterology, Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, China, ³Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China, ⁴Hangzhou Institute of Digestive Diseases, Hangzhou, China, ⁵Key Laboratory of Clinical Cancer Pharmacology and Toxicology Research of Zhejiang Province, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: Cholangiocarcinoma (CCA), a highly aggressive solid tumor with a five-year survival rate of only 5-15%, presents a significant challenge in terms of treatment efficacy. Consequently, there is a pressing demand for the identification of a safe and efficacious therapeutic approach for CCA. Magnolol, a compound derived from the Chinese herbal medicine *Magnolia officinalis*, has garnered attention for its potential anti-cancer properties. Nonetheless, the precise mechanism underlying the interaction between magnolol and CCA remains ambiguous.

Aims & Methods: Aims: The aim of this research is to investigate the inhibitory effect of magnolol on the proliferation of cholangiocarcinoma and elucidate the underlying mechanism.

Methods: At the cellular level, a series of experiments were conducted utilizing CCA cell lines, including assessments such as cell viability assay, EdU assay, colony formation assay, Transwell assay, and wound-healing assay, to investigate the impact of magnolol on CCA. Furthermore, a zebrafish model of cholangiocarcinoma was developed to examine the effects of magnolol on proliferation, angiogenesis, metastasis, and apoptosis. Additionally, a subcutaneous xenograft tumor model was established in nude mice to explore the effects of magnolol *in vivo*. Lastly, bioinformatics analysis, molecular docking, and western blot were performed to investigate the anticancer mechanism of magnolol.

Results: This study, utilized cellular-level experiments to demonstrate the inhibitory effects of magnolol on the proliferation, migration, and invasion of CCA in a time- and dose-dependent manner. Additionally, a zebrafish model was established to confirm the efficacy of magnolol in suppressing tumor growth, angiogenesis, and metastasis, as well as inducing apoptosis in CCA cells. Moreover, magnolol demonstrates its anti-tumor efficacy at a lower concentration compared to gemcitabine. Furthermore, our study utilizing a subcutaneous xenograft tumor model illustrates that magnolol effectively inhibits the advancement of CCA with minimal toxicity. Mechanistically, magnolol was found to downregulate the JAK2/STAT3 signaling pathway.

Conclusion: Overall, our research verified that magnolol had promising anti-tumor effects by targeting the JAK2/STAT3 pathway, which laid a solid foundation for CCA management.

Disclosure: The authors declare that there are no conflicts of interest.

PP1045

STENT-DIRECTED IRREVERSIBLE ELECTROPORATION FOR NOVEL MINIMALLY INVASIVE ENDOBILIARY NON-THERMAL ABLATION

S.H. Kim^{1,2}, Y. Park^{1,3}, S.-S. Lee², J.-H. Park^{1,3}

¹Asan Medical Center, Biomedical Engineering Research Center, Asan Institute for Life Sciences, Seoul, South Korea, ²University of Ulsan College of Medicine, Department of Gastroenterology, Asan Medical Center, Seoul, South Korea, ³University of Ulsan College of Medicine, Department of Convergence Medicine, Asan Medical Center, Seoul, South Korea

Contact E-Mail Address: zxcuiop55@gmail.com

Introduction: Minimally invasive irreversible electroporation (IRE) has gained increasing attention for the treatment of endobiliary tumors.^[1-3] However, the clinical application of IRE in hollow organs has been limited due to the lack of suitable electrode designs that can ensure sufficient electrode-tissue contact.^[4] Recently, a novel stent-directed electrode (SDE) made of chemically polished nickel-titanium (Ni-Ti) alloy wires was developed for localized endobiliary IRE.

Aims & Methods: The aim of this study was to investigate feasibility and efficacy of localized IRE using a SDE in both *in vitro* and *in vivo* models. Ni-Ti wires were chemically polished to improve surface roughness and electrical conductivity. The SDE was fabricated using the polished wires, and its mechanical properties were characterized. The cytotoxicity and cell viability after IRE treatment were investigated using a colon cancer cell line. The optimal IRE parameter for the *in vivo* study was determined through triphenyl tetrazolium chloride-stained potato model (field strength: 500 V/cm, pulse width: 100 μ s, pulse interval: 2,000 μ s, number of pulses: 32). Subsequently, the safety and efficacy of endobiliary IRE using the SDE were evaluated in a porcine common bile duct model.

Results: The chemical polishing process significantly improved the surface roughness, current density, and electrical conductivity of the polished Ni-Ti wires while maintaining their mechanical properties compared with the control wire ($p < 0.001$). The polished Ni-Ti wire electrode effectively delivered electrical energy to cancer cells, cytotoxicity and cell viability were proportionally decreased according to the electric field strength increased ($p < 0.001$). IRE-treated potato tissue clearly revealed irreversibly and reversibly electroporated areas containing dead cells in electrical strength-dependent manner. *In vivo* studies showed that the SDE could be successfully delivered to the target site and achieve uniform and localized ablation of the ductal mucosa without causing severe complications. Histological analyses showed significantly increased apoptosis ($p < 0.001$), heat shock protein expression ($p < 0.01$), and inflammatory cell infiltration ($p < 0.05$) in the IRE-treated tissues compared to the sham control group.

Conclusion: The novel SDE made of chemically polished Ni-Ti wires demonstrated excellent performance for endobiliary IRE in terms of surface characteristics, electrical properties, and ablation efficacy. The *in vivo* experiments confirmed the safety and efficacy of the stent-directed IRE using the SE for the treatment of endobiliary tumors in a porcine model. These results suggest that this minimally invasive technique may provide a promising treatment option for endobiliary tumors of the gastrointestinal and urinary tracts. Additional preclinical and clinical studies are necessary to assess the long-term safety and efficacy of this technique for various clinical applications.

References: [1] Al-Sakere, B.; André, F.; Bernat, C.; Connault, E.; Opolon, P.; Davalos, R. V.; Rubinsky, B.; Mir, L. M. Tumor Ablation with Irreversible Electroporation. *PLoS One* 2007, 2, No. e1135.

[2] Silk, M.; Tahour, D.; Srimathveeravalli, G.; Solomon, S. B.; Thornton, R. H. The State of Irreversible Electroporation in Interventional Oncology. In *Seminars in interventional radiology*; Thieme Medical Publishers, 2014; pp. 111–117.

[3] Wagstaff, P. G. K.; Buijs, M.; van den Bos, W.; de Bruin, D. M.; Zondervan, P. J.; de la Rosette, J. J.; Pes, M. P. L. Irreversible Electroporation: State of the Art. *Oncotargets Ther.* 2016, 2437–2446.

[4] Sánchez-Velázquez, P.; Castellví, Q.; Villanueva, A.; Quesada, R.; Pañella, C.; Cáceres, M.; Dorcaratto, D.; Andaluz, A.; Moll, X.; Trujillo, M.; Burdío, J. M.; Berjano, E.; Grande, L.; Ivorra, A.; Burdío, F. Irreversible Electroporation of the Liver: Is There a Safe Limit to the Ablation Volume? *Sci. Rep.* 2016, 6, 23781.

Disclosure: Nothing to disclose.

PP1046

IMAGE-ENHANCED ENDOSCOPIC IMAGES FOR CATEGORIZING GALLBLADDER LESIONS IN RESECTED POST-CHOLECYSTECTOMY SPECIMENS: A PRELIMINARY STUDY

K. Kobayashi^{1,2}, M. Ayaki², T. Nomura², K. Nakatani³, H. Kamada³, M. Ono¹, H. Kobara³

¹Kagawa University, Division of Innovative Medicine for Hepatobiliary and Pancreatology, Kagawa, Japan, ²HITO Medical Center, Department of Gastroenterology and Hepatology, Ehime, Japan, ³Kagawa University, Department of Gastroenterology and Neurology, Kagawa, Japan

Contact E-Mail Address: kobayashi.kiyoyuki@kagawa-u.ac.jp

Introduction: The diagnosis of gallbladder (GB) lesions depends on imaging findings, and the definitive diagnosis is still challenging. Meanwhile, the advancement of cholangioscopy has enabled targeted biopsy under direct vision, leading to the improved diagnosis of bile duct lesions. We have reported cholangioscopy-guided targeted biopsy in the GB and characteristic endoscopic images of GB lesions by image-enhanced endoscopy (IEE)¹⁻³.

In the near future, biliary endoscopy with IEE may expectedly work for diagnosing GB lesions.

Aims & Methods: This study aimed to investigate the characteristics endoscopic IEE findings of each disease in the lumen of the GB in resected GB specimens. 50 patients who underwent cholecystectomy between November 2020 and July 2022 were included.

Immediately after cholecystectomy, resected GB specimens was incised contralaterally to the liver bed, and the GB lumen was observed with white light and Narrow Band Imaging (NBI) magnification under saline flooding whenever possible using a magnifying gastroscope (GIF-H290Z or XZ1200; Olympus). The obtained endoscopic images were contrasted with the pathological findings (Ethics Committee Approval No. R2-22, 20210507002).

Results: The preoperative diagnosis of 50 patients included 6 cases of GB cancer, 29 of cholelithiasis, 8 of GB polyps, 2 of adenomyosis of the GB, 1 of xanthogranulomatous cholecystitis, and 4 of gastric cancer. The lumen of the GB removed during gastric cancer surgery appeared to be normal, with a regular arrangement of cylindrical epithelium on endoscopic image and a uniform vascular pattern.

Cancerous areas in patients with early-stage cancer exhibited irregular papillary surface, multi-caliber and irregular distribution of vasculature, while cancerous areas in patients with advanced cancer showed non-structure and irregular dilated and tortuous vasculature. In other cases where chronic inflammation was suggested, the vessels were slightly dilated, but not irregularly dilated or tortuous.

Conclusion: Endoscopic IEE images in resected GB specimens were mainly characterized to distinguish the stage of GB cancers. This trial may contribute to the establishment of classification for GB lesions under direct vision. We also present a typical GB cancer diagnosed by cholangioscopic biopsy in clinical practice.

References: 1. Kobayashi K, Kobara H, Masaki T. Characteristic endoscopic images of gallbladder lesions in resected post-cholecystectomy specimens. *Dig Endosc.* 2021 Nov;33(7):1196.

2. Kobayashi K, Kobara H, Masaki T. Novel cholangioscopy-guided targeted biopsy for diagnosing gallbladder carcinoma. *Dig Endosc.* 2021 May;33(4):e51-e53.

3. Kamada H, Kobara H, Yamana H, et al. Endoscopic direct visualization of gallbladder polypoid lesion using peroral digital single-operator cholangioscopy. *Endoscopy.* 2021 Jul;53(7):E263-E264.

Disclosure: Kiyoyuki Kobayashi, Masafumi Ono: Division of Innovative Medicine for Hepatobiliary and Pancreatology is an endowment department, supported with an unrestricted grant from HITO Medical Center.

PP1047

THE IMPACT OF ENDOSCOPIC BILIARY DRAINAGE ON THE NUTRITIONAL STATUS OF PATIENTS WITH MALIGNANT PERIHILAR OR PERIAMPULLARY BILIARY STRICTURES

M. Acharki^{1,2}, Y. Essadni¹, I. Boussena², N. Kabbaj¹, A. Bour²
¹EFD-HGE Unit, Ibn Sina Hospital, Mohammed V University, Rabat, Morocco, ²Department of biology, Laboratory of biology and health, Team of nutrition, food and health science, Faculty of science, Ibn Tofail University, Kénitra, Morocco

Contact E-Mail Address: essadni.yasmine@gmail.com

Introduction: Malignant biliary obstruction is the cause of numerous complications affecting nutritional status. Biliary drainage with stenting is the recommended palliative treatment for these patients. This study assesses the impact of biliary drainage on nutritional status by comparing patients before and after the procedure.

Aims & Methods: The aim of this study was to evaluate, through a retrospective analysis, the variation in patients nutritional status before and after biliary drainage whether in perihilar or periampullary strictures. We studied 200 patients with malignant biliary stenosis who underwent endoscopic biliary drainage.

Demographic, anthropometric and clinical data were collected before and after drainage in two stages (1 month and 3 months). Statistical analysis was performed using SPSS26 software.

	BEFORE DRAINAGE	1 MONTH AFTER DRAINAGE		3 MONTHS AFTER DRAINAGE	
	Mean (SD) or %	Mean (SD) or %	P value	Mean (SD) or %	P value
WHO score					
- STAGE 0	4.1%	14.4%		25%	
- STAGE 1	43.2%	53.2%	0.000	53.6%	0.000
- STAGE 2	52.1%	24.3%		17.9%	
- STAGE 3	0.6%	3.6%		8.1%	
WEIGHT (Kg)	56.95 kg (±9.83)	57 kg (±10.11)	0.000	59.27 kg (±10.14)	0.000
BMI Kg/m ²	19.63 kg/ m ² (±3.42)	19.66kg/m ² (±3.40)	0.000	20.39 kg/m ² (±3.46)	0.000
NRI					
Normal nutrition	0 (0%)	12 (6.84%)		25 (17.24%)	
Moderate undernutrition	70 (35%)	86 (48.86%)	0.000	79 (54.48%)	0.000
Severe undernutrition	130 (65%)	78 (44.31%)		41 (35.17%)	
ALBUMIN (ALB)	29 g/l (±4.31)	32 g/l (±5.48)	0.000	34.52 g/l (±4.5)	0.000
TOTAL BILIRUBIN (TB)	200.72mg/l (±105.94)	32.82mg/l (±34.3)	0.000	15.03mg/l (±23.96)	0.000
C-REACTIVE PROTEIN (CRP)	61.73 mg/l	57.1mg/l	0.89	56mg/l	0.80

Table.

Results: The results showed a significant increase in mean weight, reaching 59.27kg after 3 months (p<0.05). Mean BMI also increased significantly, (20.39kg/m² after 3 months (p<0.05)). NRI (Nutritional risk index) decreased significantly after drainage. 35.17% still had severe undernutrition after 3 months (p<0.05). Mean ALB (Albumin) increased significantly, (34.52g/l after 3 months (p<0.05)). Mean TB (Total Bilirubin) also decreased significantly, (15.03mg/l after 3 months (p<0.05)).

However, the decrease in CRP was not statistically significant. The WHO performance score showed significant improvement, with 25% of patients presenting with Stage 0 after 3 months. Pruritus and jaundice were absent in 100% of patients after 3 months, and vomiting absent in 90% of patients after 3 months (p<0.05). When comparing the perihilar and periampullary stenosis groups, no significant differences were observed for any of the parameters studied.

Conclusion: The study suggest that endoscopic biliary drainage significantly improves the nutritional and clinical status of patients with malignant biliary strictures, independently of the location of the obstruction.

Disclosure: No conflict of interest.

PP1048

ACUTE UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH BILIARY TRACT CANCER

J.C. Schumacher¹, A. Martin¹, P. Kasper¹, S. Lang¹, M. Bürger¹, D. Nierhoff¹, T. Goesser¹, G. Allo¹

¹University of Cologne, Faculty of Medicine and University Hospital Cologne, Department of Gastroenterology and Hepatology, Cologne, Germany

Contact E-Mail Address: jan.schumacher@uk-koeln.de

Introduction: Upper gastrointestinal bleeding (UGIB) is associated with an unfavorable prognosis in cancer patients. In biliary tract cancers (BTCs), little is known about the occurrence of UGIB and its prognostic relevance for the course of the disease.

Aims & Methods: The aim of this study was to analyze the prevalence of UGIB in BTC patients, compare therapeutic approaches for efficacy, and identify parameters associated with survival and recurrence rates. This retrospective observational study included all patients with BTCs and UGIB, that were treated in our tertiary care hospital between 2010 and 2023.

Results: A total of 1033 patients with BTC were analyzed. 41 (4.0%) of these patients had a total of 60 bleeding events. At the time of the bleeding event, 30.8% of patients displayed symptoms of shock, and 67.5% received red blood cell transfusions.

The most common causes of bleeding were tumor infiltration (24.4%), variceal bleeding (19.5%), or ulcer bleeding (14.6%). At the time of presentation, 56.4% of patients had stage IV cancer. Most patients had perihilar (39.0%) or intrahepatic (34.1%) cholangiocarcinoma.

At index bleeding, endoscopic treatment was performed in 41,5% of cases, while conservative measures (53,7%) or interventional radiological procedures (4.9%) were used in the remaining cases. In cases of bleeding caused by tumor infiltration, endoscopic hemostasis was usually performed using hemostatic powder (18.8%) or clip application (12.5%).

Admission to an intermediate or intensive care unit (odds ratio 6.7; 95% CI 1.5 – 33.9) as well as symptoms of shock at the time of the bleeding event (odds ratio 2.6; 95% CI 0.5 – 15.6) were risk factors of rebleeding within 14 days.

In patients with UGIB due to tumor infiltration, bleeding recurred after endoscopic therapy in 33.3% of cases. With conservative therapy, the recurrence rate was 28.6%. Survival of Patients with UGIB due to tumor infiltration was significantly shorter compared with patients having non-tumor-associated UGIB (median survival 0.93 vs. 6.5 months, log-rank test p = 0.018).

Conclusion: UGIB is a rare but serious complication in patients with BTC. Patients with major bleeding episodes should be closely monitored for short-term rebleeding. The occurrence of UGIB due to tumor infiltration is associated with adverse outcomes and significantly shortened survival time.

Disclosure: Nothing to disclose.

PP1049

CONTRIBUTION OF BILIARY MRI IN THE DIAGNOSIS OF EXTRAHEPATIC CHOLANGIOCARCINOMA

H. El Hiouy¹, M. Cherkaoui Malki², H. El Bacha³, S. Mechhor⁴, N. Benzoubeir¹, I. Errabih⁵

¹Mohammed V university - faculty of medicine and pharmacy, hepato-gastro-enterology and proctology (clinic B) - Ibn Sina university hospital center, Rabat, Morocco, ²University Hospital Ibn Sina, Gastroenterology B, Rabat, Morocco, ³Hopital ibn sina / universite mohamed v / faculte de medecine, gastroenterologie et hepatologie, Rabat, Morocco, ⁴Ibn Sina Hospital, Medecine B, Rabat, Morocco, ⁵Ibn Sina University Hospital, Dept. de Médecine B, Rabat, Morocco

Contact E-Mail Address: houdaelhiouy@gmail.com

Introduction: Cholangiocarcinoma defines a group of tumors with a poor prognosis arising from the epithelial cells of the bile ducts. They can occur anywhere along the biliary tree. The diagnosis of cholangiocarcinoma represents a real challenge, given the difficulties of accessing a cytological diagnosis. Anatomopathological diagnosis remains the “gold standard”, but in certain situations, biliary-MRI may suffice to make a positive diagnosis.

Aims & Methods: The aim of our work is to study the contribution of biliary-MRI to the diagnosis of extrahepatic cholangiocarcinoma. This is a retrospective descriptive monocentric study extending over a 02-year period (January 2021-August 2023) collecting cases of extrahepatic cholangiocarcinoma hospitalized in the Hepato-Gastro-Enterology and Proctology Department “Medicine B”. We only included patients whose diagnosis was evoked by the radiological appearance of biliary MRI.

Results: 27 patients were included in our study, with a mean age of 65.5 ± 10 years. Male predominance was observed, with 16 men (59.2%) and 11 women (40.7%), so, a M/F sex ratio of 1.45.

The circumstances of discovery were dominated by altered general condition, which was reported in 18 patients (66.6%), jaundice in 16 (59.2%), and angiocholitis in 11 (40.7%). Biologically, median total bilirubin was 203 [129- 264], median CEA 6 [3- 120], and median CA 19-9 976 [60- 1933]. The tumor was distal in 6 patients (22.2%), and hilar in 21 (77.7%), including 13 cases (48.1%) classified as bismuth IV, 3 cases (11.1%) as bismuth III; bismuth II in 3 (11.1%), and bismuth I in one (3.7%). The process was infiltrative in 25 cases (92.5%), budding in 2 cases (7.4%), and stenosing in 19 cases (70.3%). In all our patients, the cholangiocarcinoma presented as an irregular process, enhanced late and progressively after contrast injection, with diffusion restriction, and with different signal intensities: Hypo-signal T1 in 19 cases (70.3%), iso signal T1 in 07 cases (25.9%), hyper signal T2 in 14 cases (51.8%), intermediate signal T2 in 11 patients (40.7%), and iso signal T2 in 2 patients (7.4%). Liver metastases were noted in 9 patients: bilobar in 8 (29.6%) and unilobar in one (3.7%).

The diagnosis of cholangiocarcinoma was confirmed histologically in 11 patients (40.7%). Only 3 patients (11.1%) underwent surgery, while treatment was palliative in 25 patients (92.5%).

Conclusion: The definitive diagnosis of cholangiocarcinoma remains histological, but Biliary-MRI plays an essential role. Our study showed that

late and progressive enhancement with T1 hyposignal and T2 hypersignal were the most frequent cholangiographic sequences in the diagnosis of extrahepatic cholangiocarcinoma.

Disclosure: Nothing to disclose.

PP1050

SHORT VERSUS LONG COURSE ANTIBIOTICS AFTER ERCP IN PATIENTS WITH ACUTE CHOLANGITIS IN A REFERRAL HOSPITAL

J.P. Garcia Marmolejo¹, C. Diaz Brochero², I.T. Ordoñez², A.M. Leguizamo³, R. Vargas-Rubio³

¹Javeriana University - Hospital San Ignacio, Bogota DC, Colombia, ²Javeriana University - Hospital San Ignacio, Infectology, Bogota DC, Colombia, ³Javeriana University-Hospital San Ignacio, Gastroenterology, Bogota DC, Colombia

Contact E-Mail Address: jpgarciamarmolejo@gmail.com

Introduction: Acute cholangitis is an important cause of mortality and morbidity, especially in elderly patients and those with multiple comorbidities. However, the appropriate duration of antibiotic therapy after biliary drainage remains controversial. The aim of this study is to evaluate the efficacy of a short versus a long course of antibiotics after biliary drainage in patients with acute cholangitis.

Aims & Methods: Retrospective analytical cohort study of patients with acute cholangitis treated at a fourth level hospital in Bogotá, Colombia, from 2014 to 2022. Short antibiotic therapy was defined as ≤ 4 days after successful post-ERCP drainage. The primary outcome was a composite of in-hospital mortality, ICU admission, and hospital readmission 30 days after discharge.

A univariate and multivariate logistic regression model was performed to assess the association between duration of antibiotic therapy and the primary composite outcome.

Variable	Univariate analysis		Multivariate analysis	
	OR (CI 95%)	p value	OR (CI 95%)	p value
SCT	1.73 (0.76-3.89)	0.18	-	-
Oncological pathology	1.51 (0.47-4.87)	0.48	1.77 (0.96-3.29)	0.06
Previous antibiotic use*	0.66 (0.15 -2.87)	0.57	-	-
Previous hospitalization*	0.86 (0.19-3.51)	0.84	-	-
Etiology				
Non-tumorous	Reference	Ref	-	-
Tumor	0.80 (0.25-2.6)	0.70	-	-
Severity (Tokyo score)				
I	Reference	Ref	2.70 (0.98-9.54)	0.07
II	2.72 (0.96-9.77)	0.08	32.07 (11.84 113.16)	<0.001
III	30.67 (10.57-113.97)	<0.001		
Bacteremia	1.34 (0.68-2.59)	0.38	-	-
Carbapenem resistance	5.21 (1.24-23.66)	0.02	4.07 (1.02-16.96)	0.04

Table. Univariate and multivariate analysis of clinical factors associated with mortality, ICU admission or hospital readmission at 30 days in patients with acute cholangitis undergoing ERCP

*In the three months prior to the index hospitalization. SCT: Short course therapy; OR: Odds Ratio, 95% CI: 95% Confidence Interval.

Results: 317 patients were included. E. coli was the most commonly isolated microorganism regardless of severity, and 54% proved 100% antimicrobial susceptibility. 59 patients received short therapy and 258 received long therapy. There were no statistically significant differences in the primary outcome (p=1), but a longer hospital stay was observed in the long-term treatment group (p<0.001). The presence of Tokyo III severity and carbapenem resistance were risk factors for the primary outcome (OR 32.07; 95% CI 11.84-113.16, p<0.001) and (OR 4.07; 95% CI 1.02-16.96, p=0.04) respectively.

Conclusion: Shorter courses of antibiotics after ERCP drainage can be considered a therapeutic option for patients with acute cholangitis. However, the methodological limitations of this study should be considered.

References:

- [1] M. Ahmed, "Acute cholangitis - an update," *World J Gastrointest Pathophysiol*, vol. 9, no. 1, pp. 1–7, Feb. 2018, doi: 10.4291/wjgp.v9.i1.1.
- [2] S. Kiriya et al., "Clinical application and verification of the TG13 diagnostic and severity grading criteria for acute cholangitis: an international multicenter observational study," *J Hepatobiliary Pancreat Sci*, vol. 24, no. 6, pp. 329–337, Jun. 2017, doi: 10.1002/jhbp.458.
- [3] R. Mohan et al., "Validation of Tokyo Guidelines 2007 and Tokyo Guidelines 2013/2018 Criteria for Acute Cholangitis and Predictors of In-Hospital Mortality," *Visceral Medicine*, vol. 37, no. 5. S. Karger AG, pp. 434–442, Oct. 01, 2021. doi: 10.1159/000516424.
- [4] R. Mohan, S. W. L. Goh, G. W. Tan, S. P. Junnarkar, C. W. Huey, and V. G. Shelat, "Validation of TG07 and TG13/TG18 criteria for acute cholangitis and predictors of in-hospital mortality in patients over 80 years old," *Clin Exp Hepatol*, vol. 7, no. 4, pp. 396–405, 2021, doi: 10.5114/ceh.2021.110996.
- [5] P. A. Lipsett and H. A. Pitt, "Acute Cholangitis."
- [6] Z. An, A. L. Braseth, and N. Sahar, "Acute Cholangitis: Causes, Diagnosis, and Management," *Gastroenterology Clinics of North America*, vol. 50, no. 2. W.B. Saunders, pp. 403–414, Jun. 01, 2021. doi: 10.1016/j.gtc.2021.02.005.

Disclosure: Nothing to disclose.

PP1051

SINGLE-SESSION ERCP WITH COLONOSCOPE AND DUODENOSCOPE IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: A FEASIBILITY STUDY

Z. Jin¹, H. Jin², X. Zhang²

¹Hangzhou geriatric hospital, Department of gastroenterology, Hangzhou, China, ²Hangzhou First People's Hospital, Gastroenterology, Hangzhou, China

Contact E-Mail Address: kingz1025@163.com

Introduction: ERCP in patients with surgically altered anatomy (SAA) is one of the most challenging endoscopic procedures. For patients in whom cannulation cannot be achieved with a colonoscope, we placed a tube with the tip near the papilla/anastomosis, and the end out of patient's mouth; a duodenoscope was then inserted following tube placement to finish ERCP in the same session.

Aims & Methods: The aim of the current study was the evaluation of feasibility and safety of two-step ERCP (Figure 1) for biliopancreatic interventions in patients with SAA. Patients with SAA receiving two-step ERCP at a single endoscopic reference center were retrospectively enrolled between January 2016 and June 2023.

Results: 58 patients (20 female, 38 male), median age 58 years (range 43–88) and biliary (n=45) and pancreatic (n=13) indications for two-step-ERCP were enrolled. Types of surgical reconstruction: Roux-enY n=47, Billroth II with Braun anastomosis n=11.

Technical success rates for intubation, cannulation and interventions were 94.8%, 85.5% and 100%, respectively. Overall two-step-ERCP-success rate was 77.6%. One major complication occurred (1.7%; intestinal perforation during intubation).

Conclusion: The current study showed for the first-time feasibility and safety of two-step-ERCP with colonoscope and duodenoscope in SAA patients at an expert center. This data justifies further evaluation of this new technique preferably in a prospective multicenter trial.

Disclosure: Nothing to disclose.

PP1052

UNFORTUNATE GENDER DISPARITIES IN PATIENTS WITH SPHINCTER OF ODDI DYSFUNCTION (SOD) UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP): A DECADE LONG STUDY

J. John¹, C.J. Foster², B. Blair³, L. Joo³, N. Dasu⁴, M. Bakhit⁴, Y. Khalid⁵

¹Jefferson Health NJ, Internal Medicine, Cherry Hill, United States of America, ²Jefferson Health NJ, Interventional Gastroenterology, Cherry Hill, United States of America, ³Jefferson Health NJ, Gastroenterology, Cherry Hill, United States of America, ⁴Beth Israel Lahey Hospital and Medical Center, Interventional Endoscopy/Gastroenterology, Burlington, United States of America, ⁵Geisinger Health System/ Wright Center for GME, Scranton, United States of America

Contact E-Mail Address: nrdsu4@gmail.com

Introduction: The sphincter of Oddi (SOD) is a valve composed of smooth muscle which helps regulate the flow of pancreaticobiliary secretions into the duodenum. SOD can involve the biliary sphincter, pancreatic sphincter, or both. Several studies have shown that patients with SOD have higher complications when undergoing endoscopic retrograde cholangiopancreatography (ERCP).

This study aimed to identify risk factors that contribute to worsened in-hospital outcomes in patients with SOD undergoing ERCP as well as to identify high-risk populations. We sought to identify gender differences between these two populations because gender disparities in health care can be linked to worse health outcomes.

Aims & Methods: The National Inpatient Sample (NIS) is an extensive, publicly available all-payer inpatient care database in the USA. We distinguished between adult patients (> 18 years old) undergoing ERCP with SOD and those without SOD from the years 2010–2020.

Multivariate logistic regression and linear regression analyses using the Kernel Method with propensity matching were employed to account for confounders. STATA 17 MP was used to compute the odds ratios of in-hospital mortality, average length of hospital stay (LOS), and hospital charges (TOTHC). Weights were used to generate nationally and regionally representative estimates.

Results: 3,100 of the 2,176,350 patients undergoing ERCP (2010–2020) had SOD, of which a total of 2,564 female patients (82.68%) were found. Female patients had a significantly higher mortality than males (15.55% Female vs. 3.11% Male, p<0.01) as well as a higher overall mortality rate (OR 2.5, CI 2.1–2.9, p<0.0001).

Additional gender disparities were found after adjusting for age, race, BMI, hospital region, hospital bed size, socioeconomic status, teaching status (teach vs. non-teach), and hospital location (urban vs. rural): female patients had higher LOS (+5.5 days, CI 4.5–6.5 days, p<0.0001) and TOTHC (+\$51,856, CI \$47,533–\$56,179, p<0.0001) compared to male patients. Analysis of post-procedural complications is noted in Table 1.

Conclusion: Significant disparities between male and female patients were observed in this retrospective nationwide cohort of over 2.1 million patients. Female patients with SOD undergoing ERCP had higher overall mortality, mortality rate, and increased LOS and TOTHC when compared to males.

Our study identified risk factors and post-procedural complications such as aspiration, perforation, sepsis, etc (outlined in Table 1) in patients with SOD undergoing ERCP that lead to worse overall outcomes. To help minimize risks and lessen the healthcare burden, the underlying causes of gender differences should be further investigated through randomized controlled trials.

Disclosure: Nothing to disclose.

PP1053

THE IMPACT OF COVID-19 PANDEMIC ON ERCP IN THE AOSTA VALLEY TERTIARY CARE MEDICAL CENTER

S. Okolicsanyi¹, L. Nicoletti¹, M. Diotallevi¹, C. Giacomazzi², R. Lolli¹

¹Azienda USL Valle d'Aosta, Gastroenterology and Digestive Endoscopy, Umberto Parini Hospital, Department of Medicine, Aosta, Italy, ²Azienda USL Valle d'Aosta, Microbiology, Umberto Parini Hospital, Department of Clinical Pathology, Aosta, Italy

Contact E-Mail Address: sokolicsanyi@ausl.vda.it

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is an essential technique for pancreato-biliary diseases. Pancreato-biliary infection occurs after 0.4–0.8% of endoscopic biliary procedures, with cholangitis and sepsis occurring in up to 3% of cases. These episodes must always be taken seriously because fatality has been reported in 8–20% of such cases.

During the pandemic from coronavirus disease 19, recommendations by the European Society of Gastrointestinal Endoscopy (ESGE) suggested postponing elective procedures, use of triage, use of personal protective equipment and creation of differentiated in-hospital pathways, in order to protect both patients and endoscopy unit personnel.

Currently, it is not known whether, as a result of the change in these procedures, the overall mortality and the infection's rate related to ERCP has been modified in the post-COVID era.

Aims & Methods: In this study, we retrospectively compared ERCP activity, post-ERCP infection rate and 30 days-mortality in our tertiary center before and after the adoption of new criteria for patient's selection and protective equipment implementation, specifically from October 2016 to December 2019 (before COVID) and from January 2020 to March 2023 (after COVID).

Results: During the 39 months before COVID, we performed 417 ERCP for 285 patients, while in the same amount of time after COVID, we executed 257 consecutive ERCP for 191 patients. The indications for performing ERCP were made for obstructive cholangitis caused by stones, by pancreatic or bile ducts neoplasms, by malignant lymph nodes or for post-surgical complications.

Positive blood cultures done within 1 week from ERCP were 13 among 417 exams before COVID and 9 among 257 ERCP after COVID, with septicemia related to ERCP only in 2 procedures (0.5%) before COVID and another 2 (0.8%) after COVID. Cultures resulted positive for *Klebsiella pneumoniae* and *Candida albicans* in the first group, while in the group after COVID, patient's blood cultures were positive for *Enterococcus faecium* and *Klebsiella oxytoca*.

Overall mortality at 30-days after ERCP accounted for 16 patients (5.6%) during 39 months considered before COVID and 9 patients (4.7%) after COVID. In the first group, the fatal complications were related to ERCP in 2 cases (0.7% of patients), due to the perforation of the digestive tract, while in the second group, 1 patient (0.5%) had a septic shock from *Klebsiella oxytoca* after ERCP.

Conclusion: In conclusion, our retrospective analysis of a real life cohort of consecutive patients undergoing ERCP in a single tertiary center, demonstrated that the shortages of medical resources caused a significant drop in the ERCP activity, notably about 38%.

Ultimately, the delay due to the COVID pandemic, the rational use of antibiotics and the intensification of personal protective equipment did not change significantly the rate of adverse events, like post-ERCP septicemia (0.5–0.8% before and after COVID respectively), or the 30-days mortality rate after ERCP (0.7%–0.5% before and after COVID respectively).

References:

- Khashab MA, Tariq A, Tariq U, et al. Delayed and unsuccessful endoscopic retrograde cholangiopancreatography are associated with worse outcomes in patients with acute cholangitis. *Clin Gastroenterol Hepatol* 2012;10:1157-61
 - Gralnek I M, Hassan C, Beilenhoff U et al. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. *Endoscopy*. 2020;52:483–490.
 - Dumonceau JM, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, Beyna T, Dinis-Ribeiro M, Hritz I, Mariani A, Paspatis G, Radaelli F, Lakhtakia S, Veitch AM, van Hooft JE. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2020 Feb;52(2):127-149.
 - Casini B, Pan A, Guarini A, Rivara C, Zullo A, Monica F, Cimbri M, Casarano S, Inglese A, Vaghi A, Schifano L, Capezzuto E, Da Massa Carrara P, Pasquale L; Working Team on Infections in Endoscopy. Multisocieties position paper: Microbiological surveillance on flexible endoscopes. *Dig Liver Dis*. 2021; 53(9):1105-1111.
- Disclosure:** Nothing to disclose.

PP1054

IN-HOSPITAL OUTCOMES OF PATIENTS WITH COVID-19 UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

J. John¹, C.J. Foster², B. Blair³, L. Joo³, N. Dasu², H. Suga³, Y. Khalid⁴

¹Jefferson Health NJ, Internal Medicine, Cherry Hill, United States of America, ²Beth Israel Lahey Hospital and Medical Center, Interventional Endoscopy/Gastroenterology, Burlington, United States of America, ³Jefferson Health NJ, Gastroenterology, Cherry Hill, United States of America, ⁴Geisinger Health System/ Wright Center for GME, Scranton, United States of America

Contact E-Mail Address: nrdsu4@gmail.com

Introduction: The novel coronavirus emerged in 2019 and led to a worldwide pandemic. COVID-19 had a catastrophic effect on the world's population, resulting in millions of deaths. Our study aimed to evaluate and determine the outcomes of patients who had an underlying diagnosis of COVID-19 and to assess overall mortality, length of stay (LOS), and total hospital charges (TOTHC) associated with patients undergoing ERCP who had a concomitant diagnosis of COVID-19.

Aims & Methods: We identified patients 18 years and older with COVID-19 undergoing ERCP versus those undergoing ERCP only from the National Inpatient Sample (NIS) from 2020. The NIS is a large publicly available all-payer inpatient care database in the USA. Using STATA 17 MP, multivariate regression analysis was used to calculate the odds ratios of in-hospital mortality, the average LOS, and TOTHC.

Results: We identified 1,685,745 patients with COVID-19, of which 161,985 underwent ERCP. The analysis revealed that mortality was increased (OR 1.41, p<0.001, CI: 1.24 - 1.69), LOS was increased (+2.59 days, p<0.0001, CI: 1.17 - 4.01), and TOTHC were increased (+ \$56,220.52, p<0.0001, CI: \$28,340.61- \$84,100.44) for patients undergoing ERCP with COVID 19 compared to patients undergoing ERCP without COVID-19.

The presence of acute kidney injury (AKI) (OR 6.49, p<0.0001, CI: 6.18- 6.81), Stroke (CVA) (OR 1.75, p<0.035, CI: 1.04- 2.94), Non-ST-elevation myocardial infarction (NSTEMI) (OR 2.58, p<0.0001, CI: 2.41- 2.76), coronary artery disease (CAD) (OR 1.47, p<0.001, CI: 1.182 -1.83), and hemodialysis (HD) (OR 4.37, p<0.0001, CI: 4.02- 4.75) worsened mortality in patients with COVID-19 undergoing ERCP.

The presence of AKI (+ 8.56 days, p<0.0001, CI: 8.20- 8.92), venous thrombo-embolism (+8.82 days, p<0.0001, CI: 6.83- 10.82), CVA (+3.92 days,

$p < 0.003$, CI: 1.35 - 6.48), and HD (+5.72 days, $p < 0.0001$, CI: 5.32 - 6.11) led to an increase in LOS in patients with COVID-19 undergoing ERCP. The presence of hypertension (\$1,577.52, $p < 0.021$, CI: \$241.04- \$2,914.00), AKI (\$187,274.00, $p < 0.0001$, CI: \$175,994.50 - \$198,553.50), VTE (\$103,434.30, $p < 0.0001$, CI: \$70,698.35 - \$136,170.30), cerebrovascular accident (CVA) (\$50,131.06, $p < 0.034$, CI: \$3,697.798- \$96,564.33), NSTEMI (\$38,293.22, $p < 0.0001$, CI: \$31,289.62 - \$45,296.81), obesity (\$11,439.68, $p < 0.0001$, CI: \$9,247.63 - \$13,631.74) and HD (\$135,782.10, $p < 0.0001$, CI: \$124,296.70- \$147,267.60) led to increased TOTHC in patients with COVID-19 undergoing ERCP.

Conclusion: Compared to patients without COVID-19, concomitant COVID-19 in patients undergoing ERCP led to an increased overall mortality, total hospital charges, and length of stay. We also identified positive predictors of mortality, as well as increased LOS and TOTHC in this patient population.

Disclosure: Nothing to disclose.

PP1055

SAFETY AND EFFICACY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN CIRRHOTIC PATIENTS WITH OBSTRUCTIVE JAUNDICE

M. Elbasiony¹, A. Farag¹, E. Khalil¹, R. Saad¹

¹Mansoura university, Gastroenterology, Dakahleya, Egypt

Contact E-Mail Address: elbasiony.m@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has become the main treatment modality for many pancreatobiliary disorders. There are limited prospective studies regarding safety of ERCP in cirrhotic patients. We evaluated the outcome of ERCP in a group of cirrhotic patients in comparison to non cirrhotic group.

Aims & Methods: the aim of the study was to investigate complications and success of ERCP in cirrhotic patients. In this prospective (cohort) comparative study, 54 cirrhotic patients undergoing therapeutic ERCP were compared to 65 non cirrhotics as control group. Basic patient pre endoscopic, interventional data and 30 days follow up data were collected and analysed.

Results: One hundred and nineteen consecutive patients were prospectively enrolled in this study. The most common indication for ERCP in both groups was choledocholithiasis. (70.4% in cirrhotics vs 53.8% in non cirrhotics). There was no significant difference in the frequency of overall complications between cirrhotics and noncirrhotics (11.1% vs 12.3 respectively, $P=0.84$). Incidence of individual complications in cirrhotics versus non cirrhotics were as follows :Post-ERCP pancreatitis (PEP) (0% vs 4.6%, $P=0.250$), bleeding (3.7 vs 3.1%, $p=0.375$), cholangitis (7.4% vs 3.1%, $p=0.4$), perforation (0% vs 1.5%). All were non significant. Regarding 30 days mortality among our patients, it was higher in the cirrhotic group but did not reach the level of statistical significance (11.5% in cirrhotics versus 4.6% in non cirrhotics; $P=0.18$). Clinical success was insignificantly higher in the non cirrhotic group (87.7% vs 79.6%, $p=0.478$). On multivariable analysis, the independent predictors of mortality among our patients were previous history of variceal bleeding, presence of splenomegaly and ascites and occurrence of post ERCP cholangitis. There was significant delay in improvement of serum bilirubin level in the cirrhotic group.

Conclusion: ERCP is considered safe and effective (as regard clinical success) in cirrhotic patients with results comparable to non cirrhotics, however advanced status of liver disease leads to delay in improvement of serum bilirubin in cirrhotic patients and this delay should not be considered as failure of ERCP procedure.

Disclosure: Nothing to disclose.

PP1056

MORPHOLOGY OF THE PAPILLA CAN PREDICT PROCEDURAL SAFETY AND EFFICACY OF ERCP - A RETROSPECTIVE COHORT STUDY

E. Tari^{1,2}, T. Tóth³, P. Hegyi^{1,2,4}, B. Eröss^{1,2,4}

¹Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Medical School, University of Pecs, First Department of Medicine, Pecs, Hungary, ⁴Medical School, University of Pecs, Centre for Translational Medicine, Pecs, Hungary

Contact E-Mail Address: edina.tari@gmail.com

Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) is the most commonly used therapeutic procedure for pancreatobiliary disorders. Despite the essential role of bile duct cannulation in procedural safety and success, research on this topic is still limited. Certain studies suggest that the anatomy of the papilla affects its efficacy and safety.

Aims & Methods: We aimed to assess the influence of papilla morphology on ERCP outcomes and adverse events.

Patients with a naive papilla scheduled for ERCP were reviewed in a single tertiary care center between September 2022 and January 2023. The papilla was classified into one of four types using the Haralddson classification system. Data on the presence of a periampullary diverticulum (PAD) was also assessed. The indications for ERCP, the rate of post-ERCP adverse events (pancreatitis, bleeding, and perforation), the rate of failed cannulation, and the need and type for rescue cannulations were collected. For the effect size measure, event rates or risk ratios were calculated. For categorical data, the χ^2 test, and for the test of subgroup (papilla type) differences, a "Cochrane Q" test was used.

Results: A total of 231 patients with naive papillae were included. We found a statistically significant difference in the event rate for cannulation failure between the different papilla types. The highest rate was observed in the case of type II ("small") papilla (14%), followed by type I ("regular") (13%) and type III ("protruding or bulging") (8%). The event rate was lowest in the case of type IV ("creased or ridged") papilla (6%). The presence of PAD was associated with a higher risk of cannulation failure (RR: 2.64; CI: 1.22 - 5.39).

Moreover, a statistically significant difference in the rate of post-ERCP pancreatitis was observed between the papilla types. The event rate was the highest in type III ("protruding or bulging") and IV ("creased or ridged") papilla (13%). The lowest rate was observed in type I ("regular") and II ("small") papillae, 6%. There was no significant difference between the post-ERCP bleeding and perforation rate in the different papilla types, likely due to the low event number. The need and the types of the various rescue cannulation techniques also significantly differed between the papilla types.

Conclusion: Certain papilla morphologies are associated with a higher rate of cannulation failure and PEP. The presence of PAD is also associated with an increased rate of cannulation failure. Moreover, we can conclude that the preferred rescue cannulation technique differs between the papilla types.

Disclosure: Nothing to disclose.

PP1057

NATIVE PAPILLA CANNULATION IS NOT ASSOCIATED WITH INCREASED ADVERSE EVENTS OR TECHNICAL FAILURE RATES AMONG TRAINEES

O. Osagiede¹, D. Fluxa¹, M. Mahfouz¹, P.T. Kröner¹, J.E. Corral¹, F. Lukens¹

¹Mayo Clinic, Division of Gastroenterology and Hepatology, Jacksonville, United States of America

Contact E-Mail Address: lukens.frank@mayo.edu

Introduction: The deep selective cannulation of the bile duct or pancreatic duct has been described as the cornerstone of a successful endoscopic retrograde cholangiopancreatography (ERCP), and perhaps the most challenging aspect of the procedure for trainees. A selective cannulation rate of >80–90% of native papilla cases is usually considered as a good surrogate marker of trainee competence. We aimed to assess whether the presence of a native papilla influences differences in ERCP outcomes and adverse events between trainees and attending endoscopists.

Aims & Methods: We conducted a retrospective study of 1384 patients who underwent ERCP in a single large tertiary insitution between January 2019 and July 2023. Clinical data were prospectively collected during routine ERCP procedures. Demographics, native papilla rates, ASGE-grading system of procedure complexity, cholangioscopy, procedure and fluoroscopy time, adverse events, and technical success rates were compared between ERCP with and without trainee involvement. Technical success was defined as successful cannulation and achievement of therapeutic goal. Categorical variables were compared using Pearson's chi-square test and continuous variables using a standard t-test. Multivariate regressions were performed to adjust for sex, age, clinical setting, and ASGE complexity.

Results: A total number of 903 (65.3%) procedures had a trainee involved and 481 (34.7%) did not have a trainee involved. The mean patient age was 62 years, 53% were male. The proportion of difficult cases (ASGE Grade ≥3) was in 17.3% with trainees involved vs. 15.4% without trainees involved (p = 0.504). The proportion of native papilla was 44.2% with trainee involvement vs. 42% without trainee involvement (p = 0.434). The native papilla was successfully cannulated in 94% with trainees vs. 93.6% without trainees involved (p = 0.839).

Cholangioscopy was used in 11.3% of cases with trainees involved vs. 9.2% without trainees involved (p = 0.218). Trainee participation added 4.8 mins to average procedure time (aOR: 1.04, p = 0.001) and 0.6 mins to fluoroscopy time (aOR: 0.93, p = 0.159). No significant difference was noted between trainees and attending endoscopist in the odds of ERCP adverse events (aOR: 1.9, p = 0.27) or native papilla cannulation/technical success (aOR: 3.11, p = 0.062) for native papilla cases, but procedure time remained longer among trainees (aOR 1.03, p = 0.008)

Conclusion: Native papilla cannulation success > 90% was achieved in this study with trainee participation. Native papilla cannulation performed by trainees was associated with increased procedure time but was not associated with a significant difference in ERCP technical success rates or adverse events.

Variable	aOR (95% CI)	P-value ^b
Procedure time ^a	1.031 (1.008-1.054)	0.0075
Fluoroscopy time ^a	0.944 (0.849-1.051)	0.2941
Cholangioscopy	0.681 (0.282-1.646)	0.3935
Native papilla cannulation/ ERCP technical success	3.107 (0.946-10.21)	0.0618
ERCP adverse events	1.895 (0.608-5.905)	0.2701

Table. Adjusted odds ratios for ERCP outcomes with and without trainee involvement for native papilla only

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography.

a. Based on increasing time intervals

b. Adjusting for sex, age, and clinical setting.

References:

Voiosu, T., Bălănescu, P., Voiosu, A., Benguş, A., Preda, C., Umans, D. S., Bogdan Mateescu, R., & van Hooft, J. E. (2019). Measuring trainee competence in performing endoscopic retrograde cholangiopancreatography: A systematic review of the literature. United European gastroenterology journal, 7(2), 239–249

Mohamed R, Lethebe BC, Gonzalez-Moreno E, Kayal A, Bass S, Cole M, Turbide C, Chau M, Koury HF, Brenner DR, Hilsden RJ, Elmunzer BJ, Keswani RN, Wani S, Heitman SJ, Forbes N. Morphology of the major papilla predicts ERCP procedural outcomes and adverse events. Surg Endosc. 2021 Dec;35(12):6455-6465.

Disclosure: Nothing to disclose.

PP1058

IMPACT OF THE ASGE GRADING SYSTEM OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) ON ERCP OUTCOMES IN A TERTIARY REFERRAL CENTER

O. Osagiede¹, D. Fluxa¹, M. Mahfouz¹, P.T. Kröner¹, J.E. Corral¹, F. Lukens¹

¹Mayo Clinic, Division of Gastroenterology and Hepatology, Jacksonville, United States of America

Contact E-Mail Address: lukens.frank@mayo.edu

Introduction: The American Society for Gastrointestinal Endoscopy (ASGE) grading system for endoscopic retrograde cholangiopancreatography (ERCP) has been shown to predict success and adverse events rates. We compared ERCP outcomes and adverse events between complex and non-complex procedures using the ASGE-grading system. Our study also sought to assess the impact of the ASGE-grading system on ERCP outcomes with and without trainee involvement.

Aims & Methods: We conducted a retrospective study of 1392 patients who underwent ERCP procedures in a single large tertiary insitution between January 2019 and July 2023. Clinical data were prospectively collected during routine ERCP procedures. Demographics, cholangioscopy, procedure and fluoroscopy time, adverse events, and technical success rates were compared between complex (ASGE Grade ≥3) and non-complex (ASGE Grade <3) ERCP procedures as well as with and without trainee involvement. Categorical variables were compared using Pearson's chi-square test and continuous variables using a standard t-test. Multivariate regressions were performed to adjust for sex, age, clinical setting, and native papilla.

Results: Approximately 83.3% of ERCPs were ASGE Grade <3 and 16.7% were ASGE Grade ≥3. The mean patient age was 62 years, 53% were male. The ampulla was native in 45.3% of ASGE Grade <3 vs. 34.1% of ASGE Grade ≥3 (P=0.002). Cholangioscopy was needed in 1% of ASGE Grade <3 vs. 58.6% of ASGE Grade ≥3 (aOR: 72.2, P <0.001). Procedure and flurosco- py time were longer by 25.4 mins (aOR: 1.04, P < 0.001) and 5 mins (aOR: 1.24, P < 0.001) respectively for ASGE Grade ≥3 . Adverse events (aOR: 0.44, P= 0.274) and technical success (aOR: 1.00, P= 0.983) were similar in both groups.

No significant difference was noted between trainees and attending en- doscopist in the odds of ERCP adverse events or technical success for ASGE Grade <3 or ASGE Grade ≥3 respectively.

Conclusion: ERCPs with ASGE Grade ≥3 is associated with increased pro- cedure and fluoroscopy time, and displayed increased odds of requiring cholangioscopy. ERCP technical success and adverse events did not sig- nificantly differ with trainee participation regardless of procedural com- plexity.

Variable	aOR (95% CI)	P-value ^b
Procedure time ^a	1.040 (1.021- 1.059)	< 0.001
Fluoroscopy time ^a	1.236 (1.137- 1.343)	< 0.001
Cholangioscopy	72.2 (34.3- 151.6)	< 0.001
ERCP technical success	1.00	0.983
ERCP adverse events	0.438 (0.1-1.9)	0.274

Table. ERCP outcomes for complex (ASGE Grade ≥ 3) vs. non-complex procedures (ASGE Grade <3). N=1392.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography.

a. Based on increasing time intervals

b. Adjusting for native papilla

References: References

1. Sahar, N., La Selva, D., Gluck, M., Gan, S. I., Irani, S., Larsen, M., Ross, A. S., & Kozarek, R. A. (2019). The ASGE grading system for ERCP can predict success and complication rates in a tertiary referral hospital. *Surgical endoscopy*, 33(2), 448–453
2. Zhou, F., Zhan, X., Song, C., Li, G., Hong, J., Chen, Y., & Zhou, X. (2022). The assessment of the ASGE-grading system of ERCP: a large-sample retrospective study. *Surgical endoscopy*, 36(9), 6480–6487

Disclosure: Nothing to disclose.

PP1059

EFFICACY OF DETACHABLE BILIARY PLASTIC STENTS WITHOUT FLANGES IN PREVENTING POST-ERCP CHOLANGITIS IN PATIENTS WITH COMMON BILE DUCT STONES: A COMPARATIVE STUDY

Z. Huang^{1,2,3,4}, J. Yang^{1,2,3,4,5}

¹Hangzhou First People's Hospital, Gastroenterology, Hangzhou, China, ²Department of Gastroenterology, Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, China, ³Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China, ⁴Hangzhou Institute of Digestive Diseases, Hangzhou, China, ⁵Key Laboratory of Clinical Cancer Pharmacology and Toxicology Research of Zhejiang Province, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: ERCP is effective for common bile duct stone treatment but carries post-op risks like pancreatitis and cholangitis. Biliary drainage post-surgery is vital, with methods like ENBD and ERBD being common. ENBD allows monitoring but has drawbacks like infection and inconvenience. ERBD mitigates these but can cause complications. A new solution, Detachable biliary plastic stents without flanges, uses soft materials for self-expulsion, reducing the need for further procedures and patient burden.

Aims & Methods: This study aimed to investigate the efficacy and safety of using detachable biliary plastic stents without flanges for the prevention of cholangitis following endoscopic retrograde cholangiopancreatography (ERCP) in patients with common bile duct stones.

The study cohort comprised patients diagnosed with common bile duct stones and treated at the First People's Hospital affiliated with West Lake University School of Medicine between January 2019 and January 2024. Participants were randomly assigned to either the group receiving detachable biliary plastic stents without flanges or the nasobiliary drainage group. In the former group, the stents were deployed for biliary drainage following the clearance of stones during ERCP. The latter group received nasobiliary drains for similar purposes. Comprehensive clinical data were gathered, encompassing preoperative and postoperative details, includ-

ing laboratory investigations, endoscopic procedures, complications, hospital stay, and comfort levels assessed using the Visual Analogue Scale (VAS). Additionally, the incidence of cholangitis, the rate of spontaneous drain removal, and stent detachment were compared between the two groups.

Results: 1. The study included 820 patients who underwent ERCP for common bile duct stones. After accounting for 10 patients lost to follow-up, a total of 810 patients were analyzed, with equal distribution across both study groups. The incidence of postoperative cholangitis was 2.0% in the stent group and 3.0% in the nasobiliary drainage group, showing no significant difference ($P=0.365$). Pancreatitis occurred in 2.7% of patients in the stent group and 4.2% in the drainage group, also not statistically significant ($P=0.248$). No instances of perforation or bleeding were reported in either group.

2. The median postoperative hospital stay was significantly shorter in the stent group at 2.0 days (range: 1.0 to 4.0d) compared to 3.0 days (range: 2.0 to 5.0d) in the nasobiliary drainage group ($P<0.001$).

3. The VAS scores for postoperative comfort were significantly lower in the stent group with a mean of 2.86 ± 1.08 versus 5.13 ± 2.19 in the nasobiliary drainage group ($P<0.001$).

4. All 405 patients in the stent group returned for follow-up one month postoperatively. Stent detachment was confirmed in 373 patients (92.1%). Among the 32 patients with retained stents, two developed cholangitis, and two reported recurrent abdominal pain, resulting in a complication rate of 1.0%. In the nasobiliary drainage group, 10 patients (2.5%) spontaneously removed their drains, with an average age of 72.2 ± 8.3 years.

Conclusion: The deployment of detachable biliary plastic stents without flanges following ERCP for common bile duct stones is as effective as traditional nasobiliary drainage in preventing postoperative cholangitis. This approach offers enhanced patient comfort, reduced hospital stay, and a high rate of spontaneous stent detachment, demonstrating its safety and efficacy in clinical practice.

Disclosure: The authors declare that there are no conflicts of interest.

PP1060

PREVALENCE, CLINICAL FEATURES AND ROLE OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN BILIARY ASCARIASIS MANAGEMENT

N. Ahmed¹

¹Sindh institute of advanced endoscopy and gastroenterology karachi, Gadtroenterology, Karachi, Pakistan

Contact E-Mail Address: nasierahmedkhan@gmail.com

Introduction: Hepatobiliary and pancreatic ascariasis (HPA) is caused by entry of the nematode, *Ascaris lumbricoides* (A. lumbricoides), from the duodenum in to the biliary and pancreatic ductal lumen[1]. Patient present with wide spectrum of symptoms of biliary and pancreatic disease.i.e 1.biliary colic

2. acute cholangitis.3.acalculous cholecystitis.4 hepatic abscess

5. acute pancreatitis 6. recurrent pyogenic cholangitis. Ascariasis is prevalent worldwide with an overall prevalence of 25%. An estimated 1.4 billion people are infected.

Aims & Methods: To evaluate the prevalence,clinical features, technical success, complications, and role of ERCP in management of biliary ascariasis.The results of all the procedures were evaluated retrospectively and the prevalence of biliary parasitosis was evaluated.Technical success of the procedure was defined as achieving the diagnostic information or succeeding with endoscopic therapy.

Results: A total of 6070 patients were treated with ERCP for different indications in our departments

All ERCPs were analyzed during a 6-year period from Jan 2018 to Dec 2023. 29 patients were identified with biliary ascariasis on the basis of ERCP results. There were 7 men and 22 women, with a mean age of 28.5 years ranging from 16 to 55 years. Most of the patients were from Karachi (25, 86.2%). Remaining patients were from Hyderabad (2, 6.89%) and Sukkur (2, 6.89%). Abdominal pain was the predominant symptom in all patients with duration ranging from 1 week up to 3 years. Bilirubin was raised in 16 out of 29 (55.17%) patients with mean bilirubin of 7.7 mg/dl and range of 2.16 to 26.7 mg/dl. ALP was raised in 27 out of 29 patients (93.1%) with range of 140 u/L to 2670 u/L (normal upper limit 120 u/L and mean of 448.36 u/L). Ultrasound abdomen showed worm in 12 out of 29 patients (41.3%) and Dilated CBD was seen in 25 out of 29 patients (86.21%) with mean of 1.1 cm. 4 patients had dilated IHD as well. On ERCP, worms were seen as linear filling defect in common bile duct (CBD) in 15 (51.72%) cases and CBD along with intrahepatic ducts in 3 cases (10.34%). 11 (37.93%) patients had worm coming out of ampullary orifice and was removed by a grasper. Out of 29 patients, 5 had stone in CBD and three had pus indicating cholangitis. Only 2 patients developed minor bleeding which was controlled without any intervention.

In all of the cases we successfully and safely removed all the worms endoscopically without having any surgical outcome. The worms were removed by balloon trawl. All the patients received mebendazole following the endoscopic therapy and were dewormed. There was no procedure-related mortality in our patients.

Conclusion: ERCP is a contemporary procedure; our results are the depiction of the fact that ERCP should be utilized for the treatment of biliary ascariasis as a prime procedure.

References: Biliary ascariasis. A common cause of biliary and pancreatic disease in an endemic area

M S Khuroo et al. *Gastroenterology*. 1985 Feb.

Clinical features and management of biliary ascariasis in a non-endemic area

S P Misra et al. *Postgrad Med J*. 2000 Jan.

Pancreatic-biliary ascariasis: experience of 300 cases

F Sandouk et al. *Am J Gastroenterol*. 1997 Dec.

Hepatobiliary and pancreatic ascariasis

Mohammad S Khuroo et al. *World J Gastroenterol*. 2016.

Hepatobiliary and pancreatic ascariasis in India

M S Khuroo et al. *Lancet*. 1990.

My 40-Year Encounter with ERCP: A Saga of Service, Syndromes, and Solutions

Mohammad S Khuroo. *J Clin Exp Hepatol*. 2023 Nov-Dec.

Disclosure: Nothing to disclose.

PP1061

PERIAMPULLARY DIVERTICULUM INTERFERES ERCP PROCEDURES AND PROMOTES THE RECURRENCE OF COMMON BILE DUCT STONES

X. Xie¹, Y. Li¹, Y. Guo¹, Y. Chen¹, X. Li¹, C. Wang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology and Hepatology, Chengdu, China

Contact E-Mail Address: 2090659140@qq.com

Introduction: Periapillary diverticulum (PAD) is ordinarily asymptomatic, which is inspected occasionally during gastroscopy and endoscopic retrograde cholangiopancreatography (ERCP). Previous studies demonstrated inconsistent effect of PAD on ERCP procedures and choledocholithiasis recurrence. Thus, this study was aimed to investigate the impact of different types of PAD on the technical success, post-ERCP complications and the safety of different stone extraction methods, as well as the association of PAD with the recurrence of common bile duct stones (CBDS).

Aims & Methods: The ERCP database (March 2019 to March 2021) in West China Hospital of Sichuan University was retrospectively reviewed. Inclusion criteria were: 1) presence of original duodenal papilla; 2) patients with CBDS. However, patients with the following characteristics were excluded: 1) ERCP for other reasons; 2) absence of original papilla; 3) duodenal ampullary mass; 4) anatomical abnormalities caused by surgery; 5) under 18 years old; 6) incomplete clinical data.

In this study, PAD is classified into three types based on the location of the duodenal papilla within the diverticulum (type I), the edge of the diverticulum (type II), and the outside of the diverticulum (type III). The successful cannulation, procedures of ERCP and post-ERCP complications were compared between the PAD group and the non-PAD group, as well as among the different types of PAD groups. The patients with successful stone removal were followed up every 6 months until December 2023 to determine whether PAD was associated with the recurrence of CBDS.

Results: A total of 830 CBDS cases with original duodenal papilla were eventually enrolled, including 239 cases with PAD and 591 cases without PAD. The successful cannulation rate in the PAD group was lower than that in the non-PAD group (96.7% vs. 99.2%, $P = 0.013$). According to the different types of PAD, the successful cannulation rate of type I PAD was lower compared with non-PAD group (76.9% vs. 99.2%, $P < 0.001$). Additionally, PAD was associated with a wider bile duct diameter (1.55 ± 0.58 vs. 1.37 ± 0.50 mm, $P < 0.001$), larger stone size (1.21 ± 0.68 vs. 0.97 ± 0.54 mm, $P < 0.001$) and a higher rate of endoscopic sphincterotomy (EST) combined with endoscopic papillary balloon dilation (EPBD) (29.0% vs. 15.7%, $P < 0.001$) and mechanical lithotripsy (41.6% vs. 26.5%, $P < 0.001$) during the ERCP procedure. But PAD did not affect the incidence of post-ERCP complications.

Of note, PAD group had a higher recurrence rate (18.8% vs. 7.3%, $P < 0.001$) and shorter recurrence-free time (39.9 ± 13.3 vs. 42.8 ± 9.8 months, $P = 0.005$) compared with non-PAD group during follow-up period. Based on multivariate analysis, the presence of PAD (OR = 3.265, 95%CI: 1.854-5.751) was an independent risk factor for the recurrence of CBDS, after adjusting for age, gender and other factors.

Conclusion: PAD, especially type I PAD, decreased successful cannulation rate and increased the complexity of stone extraction of ERCP in CBDS. However, PAD did not affect the incidence of post-ERCP complications in CBDS, nor did it affect the choice of stone removal methods. PAD was an independent risk factor for the recurrence of CBDS.

Disclosure: Nothing to disclose.

PP1062

IMPACT OF PERIAMPULLARY DIVERTICULUM ON THE OUTCOME OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

M.T.-A. Khalil¹, S. Shabeeb¹, A. Wazeery¹, H. Abdelbaqy², M. Alborai³

¹Faculty of Medicine, South Valley University, Egypt, Internal Medicine, Qena, Egypt, ²Luxor University, General Surgery, Luxor, Egypt, ³Al-Azhar University, Department of Internal Medicine, Cairo, Egypt

Contact E-Mail Address: alborai@earth-eg.org

Introduction: Periapillary diverticulum (PAD) is associated with a higher incidence of biliary stone formation and common bile duct (CBD) obstruction. Endoscopic retrograde cholangiopancreatography (ERCP) is an effective therapeutic procedure in case of biliary obstruction, however; the presence of PAD and its different types could affect ERCP outcome [1-3].

Aims & Methods: Aim: To study the impact of periampullary diverticulum on the outcome of ERCP regarding the cannulation technique, the procedure time, the success rate and the complications.

Method: A Retrospective study included all patients subjected to ERCP procedures at Qena university hospitals, South Valley University, Qena, Egypt from February 2019 to August 2023. ERCP Will be performed under general anaesthesia with endotracheal intubation according to our centre policy by an expert ERCP endoscopist using Pentax duodenoscopy (ED-3490TK, Pentax Incorporation, Tokyo, Japan). Papilla of vater will be examined endoscopically before starting cannulation trials to evaluate presence of diverticulum, type, size and its relation to the papilla. Data were analyzed using Statistics Package for Social Sciences (SPSS) version 26, p-value < 0.05 was considered significant.

Results: A Total of 686 patients subjected to ERCP procedure for different indications were included in this study, males were 273 patients (39.8%), the mean age was 53.7±17 years, the overall procedure success rate was 91% and the overall complications rate was 6%. Almost all cannulation techniques were used in our cases including wire-guided cannulation (WGC), transpapillary fistulotomy (TPF), double-guidewire technique (DGT), transpapillary papillotomy (TPP), and transpancreatic septotomy with pancreatic stent insertion (TPS). PAD was detected during ERCP procedure in 61 patients (9%). There was statistically significant higher age (65.3 vs 52.6, $p < 0.001$) and statistically insignificant higher frequency of males (41% versus 39.7%, $p = 0.8$) in patients with PAD compared to patients without PAD. During ERCP procedures, presence of PAD was associated with higher number of cannulation attempts (3.5 versus 2.5, $p < 0.005$), longer time required for cannulation (8 vs 5.1 minutes, $p < 0.01$), and amazingly; higher rate of cannulation success (100% vs 98%, $p = 0.2$), and longer total procedure time (50.4 ± 21.9 minutes vs 47.01 ± 24.04, $p = 0.2$). There was no significant predilection of certain cannulation technique in PAD patients; higher WGC: 68% vs 67%, higher TPS (1.8% vs 0.5%), equal chance for WGC: 24.6% vs 24.6% and less chance for TPP: 0.7 vs 0%. The overall procedure success rate was lower in PAD patients (85.2% vs 91.2%, $p = 0.1$). Post-ERCP pain was noticed more frequently in PAD patients (4.9% vs 3.4%, $p = 0.5$) while the overall complication rate with lower (1.6% vs 6.4%, $p = 0.1$).

Conclusion: We concluded that PAD is increasingly detected during ERCP procedure in elderly patients, and despite it requires higher number of cannulation attempts and longer time for cannulation, it has no negative impact on the overall success rate or complication rate of ERCP.

References:

1. Chen L, Xia L, Lu Y, Bie L, Gong B. Influence of periampullary diverticulum on the occurrence of pancreaticobiliary diseases and outcomes of endoscopic retrograde cholangiopancreatography. *Eur J Gastroenterol Hepatol.* 2017;29:105–11.
2. Banerjee AK, Celentano V, Khan J, Longcroft-Wheaton G, Quine A, Bhandari P. Practical gastrointestinal investigation of iron deficiency anaemia:ij Expert Rev Gastroenterol Hepatol. 2018;12(3):249-256.
3. Omar MA. Effect of periampullary diverticulum on technical success and complications of endoscopic retrograde cholangiopancreatography: Single center experience. *J Dig Endosc.* 2015;6:149–57

Disclosure: Nothing to disclose.

PP1063

ENTEROSCOPY-ASSISTED ERCP IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: RESULTS OF AN INTERNATIONAL, MULTICENTRE, PROSPECTIVE REGISTRY (SAMISEN) USING MOTORIZED SPIRAL ENTEROSCOPY

T. Moreels¹, L. Aabakken², M. Arvanitakis³, M. Knabe⁴, T. Beyna⁵

¹Cliniques universitaires Saint-Luc, Div. of Hepato-Gastroenterology, Brussels, Belgium, ²Rikshospitalet-Radiumhospitalet HF, Dept. Of Medical Gastroenterology, Oslo, Norway, ³ERASME University Hospital, Université Libre de Bruxelles, Gastroenterology Department, Brussels, Belgium, ⁴University of Frankfurt, Gastroenterology, Frankfurt, Germany, ⁵Evangel. Krankenhaus Düsseldorf, Department of Internal Medicine, Düsseldorf, Germany

Contact E-Mail Address: marianna.arvanitakis@gmail.com

Introduction: Motorized Spiral Enteroscopy (MSE) was introduced into clinical practice and initial trials at expert centres proved it to be safe and effective for deep enteroscopy even in patients with surgically altered anatomy.

Aims & Methods: Prospective study of efficacy and safety of MSE to perform biliary endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy at 5 European centers. Pancreatic indications were excluded. Primary objective: procedural success and serious adverse event (SAE) rate.

Secondary objectives: diagnostic and therapeutic yield, procedural time, and patient radiation exposure. The study was prematurely terminated because of MSE withdrawal from the market in July 2023 by the manufacturer (and sponsor of the study). Trial registration: NCT05129449 (clinicaltrials.gov)

Results: 89 patients were enrolled, 1 was excluded because of pancreatic indication: 51 (58%) males and 37 (42%) females with mean age of 58 years (range 24-92) and mean bodyweight of 74 kg (range 44-178). Surgically altered anatomy was based on Billroth II reconstruction (29.5%) or Roux-en-Y reconstruction (70.5%), either with naive papilla (39%) or hepaticojejunostomy (61%). Biliary ERCP indications were mainly anastomotic stricture treatment and/or biliary stone removal. 57% of the procedures were performed under general anesthesia with intubation, the remaining under deep sedation. Technical success was defined by the combination of successful enteroscopy followed by cannulation of the bile duct and endoscopic therapy. Enteroscopy was possible in 65/88 patients (74%) in a mean time of 29 min (range 4-104). Bile duct cannulation with cholangiography was possible in 54/88 (61%) and therapeutic ERCP was technically successful in 48/88 (54%). In Billroth II reconstructions technical success was achieved in 13/26 (50%) compared to 35/62 (57%, $p = 0.0574$ Chi square) in Roux-en-Y reconstructions. Technical success was achieved in 17/34 (50%) in patients with intact naive papilla compared to 31/54 (57%, $p = 0.4968$ Chi square) in hepaticojejunostomy. In 21 patients with bariatric Roux-en-Y gastric bypass surgery technical success was 12/21 (57%). In July 2023 the study was prematurely terminated because of MSE withdrawal from the market by the manufacturer because of safety issues. Overall, in 12/88 (14%) patients adverse events (AE) were recorded, of which 6 (7%) were considered serious. Only 1 was related to MSE enteroscopy, 4 to the ERCP procedure and 1 related to the use of a duodenoscope that replaced MSE after reaching the bile duct. MSE enteroscopy-related SAE was a perforation of the proximal oesophagus during MSE insertion. The patient underwent surgical repair and recovered. ERCP-related SAE were cholangitis in 2, sphincterotomy bleeding in 1 and suspicion of air embolism in 1. There was 1 intestinal perforation occurring during duodenoscope insertion that replaced MSE to facilitate ERCP. There was no procedure-related mortality.

Conclusion: This prospective multicentre study was prematurely discontinued due to MSE withdrawal from the market by the manufacturer because of safety issues. In total 88 patients underwent enteroscopy-assisted biliary ERCP in different types of surgically altered anatomy, resulting in an overall technical success rate of 54%. This result is lower as compared to literature data based on balloon-assisted enteroscopy. SAE rate was 7% with only 1 SAE attributable to the use of MSE (oesophageal perforation). MSE allows enteroscopy-assisted ERCP in patients with surgically altered anatomy, but other techniques may be preferred.

Disclosure: The study was sponsored by Olympus Europe (Hamburg).

PP1064
SINGLE OPERATOR CHOLANGIOSCOPY IN THE MANAGEMENT OF PROXIMALLY MIGRATED BILIARY STENTS – SINGLE CENTER EXPERIENCE

Y. Petkova¹, P. Karagoyozov¹
¹*Acibadem City Clinic University Hospital Tokuda, Clinic of Gastroenterology, Sofia, Bulgaria*

Contact E-Mail Address: petko.karagoyozov@gmail.com

Introduction: Endoscopic biliary stenting is a well-established therapy in the management of hepatobiliary diseases. However, migration is reported in 5%-10% of cases. Management of proximally migrated stents using standard techniques(guidewire cannulation, snare, forceps, Schohenra stent retriever) can be technically challenging sometimes. Cholangioscopy and retrieval under direct visualization could be a useful tool in such difficult cases.

Aims & Methods: To evaluate the application of single-operator cholangioscopy in the management of proximally migrated biliary stents in terms of efficacy and safety.

Methods:We performed a retrospective analysis of the data of a prospective group of patients. The cohort included consecutive 100 cases of proximally migrated stents from January 2018 through March 2024. We evaluated the retrieval technique, success rate, and adverse events.

Results: Patients were divided into two groups. In the first collective of patients- cholangioscopy was not performed n=62/62%. We found a technical success rate – defined as successful stent extraction in 69,35% of cases/n=43/. In 19 of the cases removal was not achieved, followed by placement of new plastic stent n=19/30.65%/.In the second group, n=38/38%/. cholangioscopy with single operator cholangioscope was the retrieval technique with a technical success rate of 100%.

There was a statistical difference between the two groups in terms of technical success in favor of the group with cholangioscopy - Pearson chi-square $\chi^2=21.534$, $p<0.001$.

Cholangioscopy was performed either after the failure of standard techniques or as the first-choice tool for stent removal. In five cases we performed pancreatoscopy for extraction of migrated pancreatic stents with only one case of postprocedure pancreatitis.

We experienced adverse events/AE/ in 17 cases as pancreatitis was the most common complication n=11/64,71% of all AE/, followed by cholangitis n=5/29,41% of all AE/ and one case of bleeding n=1/5,88%/. In the first group, the rate of adverse events was 17,74%/n=11/ against 13,95%/n=6/ for the second group.

There was no significant statistical difference in the rate of AE between the two groups. The mean procedure duration was 34,35 minutes for the first group and 42,24 minutes for the second with a statistically significant difference $p=0.029$ in favor of the first group.

However, it is important to note that in some cases cholangioscopy was performed after the failure of standard techniques which by itself prolonged the procedure time.

Type of AE	Group 1	Group 2
Pancreatitis	N=7/63,64% of AE for the group; 41,18% of all AE; 63,64% of all cases of pancreatitis/	N=4/66,67% of AE for the group;23,53% of all AE;33,36% of all cases of pancreatitis/
Cholangitis	N=3/27,27% of AE for the group; 17,65% of all AE;60% of all cases of cholangitis/	N=2/33,33% of AE for the group; 11,76% of all AE;40% of cases of cholangitis/
Bleeding	N=1/9,09% of AE of the group;5,88% of all AE;100% of cases of bleeding/	NA

Conclusion: Cholangioscopy is a safe and effective technique for the extraction of migrated biliary stents with a high rate of efficacy and an acceptable rate of adverse events. It could be proposed as a first choice in cases where failure of standard techniques is suspected/persistent stenosis, residual bile duct stones/.

Disclosure: Nothing to disclose.

PP1065
CHARACTERIZING LARGE COMMON BILE DUCT STONES: DEFINING SIZE AND CLINICAL IMPLICATIONS

O. Nacir¹, F. Lairani¹, A. Ait Errami¹, S. Oubaha^{1,2}, Z. Samlani¹, K. Krati¹
¹*Department of GastroEnterology and Hepatology, Mohammed VI University Hospital Centrer, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco,*
²*Department of Physiology, Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Marrakech, Morocco*

Contact E-Mail Address: o.nacir@uca.ac.ma

Introduction: The precise definition of a large stone is ambiguous, with sizes often ranging from 10 to 15 mm. Authors refer to a stone as “large” if its size exceeds the diameter of the CBD by more than 2mm (ratio of stone size to CBD diameter > 1).

Aims & Methods: Our study aimed to determine the threshold at which the diameter of the stone leads to endoscopic treatment failure.This research is a retrospective analysis that encompassed all patients who had endoscopic retrograde cholangiopancreatography (ERCP) for the treatment of common bile duct stones from January 2019 to December 2022. The examination of the ROC curve helped identify the threshold at which the diameter of the stone can predict the failure of the ERCP.

Results: We enrolled a total of 181 patients, with a mean age of 64 years (ranging from 22 to 103 years), and a male-to-female sex ratio of 0.41. The primary reasons for doing ERCP were the presence of remaining or recurring gallstones (69%, n = 129) or the need for sequential therapy (18%, n = 33). The efficacy of the first therapy was 61.5%. The mean stone size was 12.5mm, with a range of 3-40mm. Upon examining the ROC curve, it was determined that a diameter of 12 mm provided the highest accurate prediction of endoscopic treatment failure, with a sensitivity of 74% and a specificity of 73%. Univariate analysis revealed that the presence of a stone bigger than 12 mm was a significant predictor of failure of routine endoscopic therapy ($p = 0.001$). The average ratio of stone size to diameter of the CBD was 0.74 [0.27-1.67]. In our series, we found no significant association between this factor and ERCP failure ($p = 0.276$).

Conclusion: Within our dataset, we observed that stones larger than 12 mm were indicative of a higher likelihood of ERCP failure. There was no significant correlation between the ratio of stone size to the diameter of the common bile duct (CBD) and the failure of endoscopic therapy.

Disclosure: Nothing to disclose.

PP1066

CLINICAL PROFILE, MICROBIOLOGICAL SPECTRUM IN BILE AND PATIENT OUTCOMES IN CASES OF ACUTE BACTERIAL CHOLANGITIS

A.K. Singh¹, K. Mehta², A. Ahuja², S. Sachdeva¹, G. Padia¹, A. Dalal¹, A. Kumar¹, S. Srivastava¹, U. Sonika¹, B.C. Sharma¹

¹GB Pant Institute of Post Graduate Medical Education and Research, Department of Gastroenterology, New Delhi, India,

²Maulana Azad Medical College, New Delhi, India

Contact E-Mail Address: kartikmht0@gmail.com

Introduction: Acute bacterial cholangitis is a medical emergency, requiring prompt antibiotic administration and biliary decompression. Normally, bile is devoid of microbes. Obstruction

of the biliary system leads to bile stagnation, which predisposes to bacterial proliferation. Bacteria enter the bile duct from duodenum. Also, the increased bile duct pressure in the

obstructed biliary system leads to systemic dissemination of bacteria via cholangio-venous reflux leading to septicemia. Indiscriminate and widespread use of antibiotics over the years has altered the antibiotic sensitivity pattern of micro-organisms and the emergence of multidrug resistant bacteria pose a therapeutic challenge which needs further study.

Aims & Methods: We aimed to analyze the clinico-microbiological profile and outcomes of patients with acute bacterial cholangitis, who underwent endoscopic retrograde cholangiopancreatography (ERCP) at a tertiary care hospital. Data on consecutive patients (n=116) with acute cholangitis who underwent ERCP, from January 2019 to August 2020, was retrospectively extracted. The demographic, clinical, etiological and biochemical profile was recorded. Also, bile culture reports, and antibiotic sensitivity pattern of organisms was recorded.

Diagnosis of cholangitis was based on presence of fever and/or leukocytosis, in patients with biliary obstruction (cholestatic liver function tests, biliary dilatation on imaging). Organ failure was present if patients had altered sensorium, hypotension (systolic blood pressure <90 mm Hg), renal failure (serum creatinine >1.5 mg/dL), hypoxia (blood oxygen saturation <90%).

Results: The mean age of our study cohort was 47.56 +/- 13.58 years and 64.7% were females. Patients presented with abdominal pain (89.6%), jaundice (84.4%) and fever (56.8%) with 41.4% patients exhibiting Charcot's triad and 1 having Reynolds' pentad.

30 (25.8%) patients had organ failure with renal failure being the most common. 5 patients had multiple organ failure, all of which died during hospitalization. 60.3% patients had a benign cause of biliary obstruction; choledocholithiasis was the most common benign cause. Other benign causes included post cholecystectomy bile duct stricture, chronic pancreatitis, portal biliopathy. The most common malignant cause was carcinoma gall bladder (43.5%) followed by peri-ampullary carcinoma (30.4%), carcinoma head of pancreas (13%).

Positive bile culture was seen in 95 (81.9%) patients; of which 17 (17.9%) had polymicrobial growth in bile. 92.9% organisms were gram negative bacteria (GNB). *Escherichia coli* (45.13%) was the most common GNB followed by *Pseudomonas* (29.2%). 8 patients had gram positive organisms on culture (*Enterococcus*, 7.1%).

Most common Multi-drug resistant organisms isolated were carbapenem-resistant Enterobacteriaceae. *Escherichia coli* and *Klebsiella* were most sensitive to amikacin, netilmicin and tigecycline. *Pseudomonas* had greatest sensitivity to amikacin, netilmicin and colistin.

80 (69%) patients were naïve, whereas the remaining 36 patients had previously undergone ERCP. 10.3 % patients died during hospital stay. Median duration of hospital stay was 6 (3-60) days.

Old age, lower serum albumin, higher blood urea and serum creatinine, septic shock and malignant etiology of biliary obstruction were associ-

ated with mortality on univariate analysis. On multivariate analysis, low serum albumin and septic shock were associated with higher in-hospital mortality.

Conclusion: Indiscriminate antibiotic use has resulted in increasing prevalence of multi-drug resistant organisms, with emergence of carbapenem resistant organisms posing a major therapeutic challenge.

Disclosure: Nothing to disclose.

PP1067

POST-LIVER TRANSPLANT ANASTOMOTIC STRICTURES – PREDICTORS FOR SUCCESSFUL ENDOSCOPIC REMODELLING AND NEED FOR SURGICAL INTERVENTION

B. Ward¹, A. Hussienbux¹, A. On¹, S. Everett¹, B. Paranandi¹, M. Huggett¹

¹Leeds Teaching Hospitals Trust, Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: ben.ward13@nhs.net

Introduction: Biliary strictures are a recognised complication of liver transplant. The criteria for proceeding with Endoscopic Retrograde Cholangiography [ERC] remains a subject of contention.

This study seeks to explore management strategies of anastomotic strictures, compare rates of successful remodelling and complication rates.

Aims & Methods: All patients with a post-liver transplant stricture who underwent ERC in a tertiary centre between 2016 and 2023 were included. Categorical divisions were made between patients with a single anastomotic stricture and multi-focal or hilar strictures.

Time for stricture development, pre and post-ERC liver serum markers, frequency of procedures performed, percentage successfully remodelled by ERC, percentage referred for surgical intervention and associated adverse events were retrospectively recorded.

Results: During the specified period, 107 patients with prior liver transplant (70 male, 37 female, median age 55.5 (IQR 15)) with a biliary stricture were referred for ERC. 88/107 had a single anastomotic stricture whereas 19 had multi-focal or hilar strictures. Median time from transplant to radiological discovery of biliary stricture was 5 months with 71% occurring within 12 months.

Patients with a diagnosis of a single anastomotic stricture (n=88) underwent a total of 237 total ERCs (mean 2.6 per patient). There was a significant improvement in liver function profile and bilirubin after ERC (unpaired t-test - p<0.01).

The number of remodelled strictures was 64/88 (72.7%). There were 32 ERC associated complications (13.5%); 10 cholangitis, 9 pancreatitis, 13 other. Ten patients were referred for surgical intervention (11.4%).

Patients with multi-focal / hilar strictures (n=19) underwent a total of 45 ERCs (mean 2.4 per patient). There was a non-significant improvement in bilirubin (P=0.096) and ALP (P= 0.184) after ERC and a significant improvement in ALT (P<0.02). The number of remodelled strictures was 7/19 (36.8%). There were 8 ERC associated complications (17.8%), 7 cholangitis and 1 pancreatitis. Five patients were referred for surgical intervention (26.3%).

Single anastomotic strictures, when compared to multi-focal strictures, were associated with a higher re-modelling rate (χ^2 , p= 0.003) and reduced need for surgical intervention (χ^2 , p = 0.089).

Conclusion: ERC is efficacious in managing single anastomotic strictures but significantly less effective in multi-focal proximal strictures. A significant complication rate in this cohort needs to be taken into consideration when planning intervention.

However, the majority of these patients can be managed via ERC without the need for surgical intervention.

References: Jarlot-Gas C, Muscari F, Mokrane FZ, et al. Management of anastomotic biliary stricture after liver transplantation and impact on survival. *HPB (Oxford)*. 2021;23(8):1259-1268. doi:10.1016/j.hpb.2020.12.008

Disclosure: Nothing to disclose.

PP1068

SAFETY OF EARLY DISCHARGE POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP): A SINGLE CENTRE EXPERIENCE IN SINGAPORE

N.W.W. Cheong¹, W.K. Ng¹, P. Shen², L. Bin Senawi², J.Y.L. Lim², C.H. Neo², C.W. Ng²

¹Tan Tock Seng Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ²Tan Tock Seng Hospital, Medical Ambulatory Center, Singapore, Singapore

Contact E-Mail Address: nicholas.cheong@mohh.com.sg

Introduction: Early discharge post ERCP can potentially reduce strain on the tight bed occupancy status in tertiary hospitals.

Aims & Methods: The aim of this study is to evaluate the safety of early discharge (<24 hours) for patients who had undergone ERCP in a tertiary hospital in Singapore.

This is a retrospective observational study which reviewed patients who were admitted in the TTSH Medical Ambulatory Center (MAC) and discharged within 16 hours post ERCP. To assess safety of this service, electronic medical records of patients admitted between January 2022 and February 2024 were reviewed. Complications post ERCP, predisposing factors, patient demographics were reviewed.

Results: There were 400 patients admitted to MAC for early discharge after ERCP during this period. The overall complication rate was 5.8% (23 patients). Post-ERCP pancreatitis was diagnosed in 1.8% (7 patients) of the admissions, whereas those who developed post-ERCP cholangitis accounted for 3.5% (14 patients). 1 patient developed non-specific chills with no fever nor abdominal pain (not conclusive for either cholangitis or pancreatitis) 2 days post discharge from MAC. 1 patient had post ERCP cholangiopancreatitis (0.3%). No other patients presented with complications related to ERCP after discharge.

	Post ERCP Cholangitis	Post ERCP Pancreatitis	Post ERCP Cholangiopancreatitis	Others
Number	14	7	1	1
Age (years)	Median:72 Youngest: 32 Oldest: 80	Median:72 Youngest: 56 Oldest: 85	63	74
Gender distribution	Male: 7 Female: 7	Male: 1 Female: 6	Female: 1	Male: 1
Risk factors	Diabetes Mellitus, Concurrent cholangioscopy, Complex pancreato-biliary anatomy	Complex pancreato-biliary anatomy, Female gender, Difficult cannulation	Complex pancreato-biliary anatomy	Not Applicable
Onset post ERCP (hours)				
1-6	2	3	5 hours (1 patient)	unclear
7-11	5	3		
12-16	7	1		

Out of the 23 patients with post ERCP complications, 5 (21.7%) patients developed within 1-6 hours (3 pancreatitis, 2 cholangitis). 8 (34.8%) patients (3 pancreatitis, 5 cholangitis) developed within 7-11 hours, whereas 8 (34.8%) patients (1 pancreatitis, 7 cholangitis) developed within 12-16 hours post ERCP. 1 patient with cholangiopancreatitis presented within 6 hours.

Of the 14 patients with post ERCP cholangitis, 7 were females and 7 were males. The median age (years) for this group was 72, youngest being 32 and eldest 80. 6 patients in this group had undergone a concurrent spy-glass cholangioscopy during ERCP. All of them received prophylactic antibiotics prior to cholangioscopy. It was also noted that there were 6 patients in this group of post ERCP cholangitis with Diabetes Mellitus

Out of 7 patients with post ERCP pancreatitis, 6 were females and 1 was male. The median age (years) for this group was 72, youngest being 56 and eldest being 85. All but 1 patient in this group had sphincterotomy performed. All patients in this group received 100 milligrams of rectal diclofenac for prophylactically. Only 1 patient had documented difficult cannulation.

Conclusion: From this study, it could be concluded that it was safe to allow early discharge for patients who had undergone ERCP, if there is a clear monitoring protocol and discharge plans. The onset of post ERCP pancreatitis tend to be earlier compared to those who developed post ERCP cholangitis. There is female predominance in the post ERCP pancreatitis group. The patients who develop post ERCP pancreatitis tend to be older. Complex pancreato-biliary anatomy is a significant risk for post ERCP complications. As there were 94.2% of the patients who remained well after ERCP, they could be potentially discharged even earlier (<10 hours). Further research could focus on early identification of patients who are likely going to develop post ERCP complications to facilitate early discharge, thus relieving tight bed occupancy status.

References: Hui, C., Lai, K. C., Wong, W., Yuen, M., Ng, M., Chan, C., Hu, W., Cheung, W., Lai, C., amp; Wong, B. C. (2004). Outpatients undergoing therapeutic endoscopic retrograde cholangiopancreatography: Six-hour versus overnight observation. *Journal of Gastroenterology and Hepatology*, 19(10), 1163–1168

Jeurnink, S. M., Siersema, P. D., Steyerberg, E. W., Dees, J., Poley, J., Haringsma, J., amp; Kuipers, E. J. (2011). Predictors of complications after endoscopic retrograde cholangiopancreatography: a prognostic model for early discharge. *Surgical Endoscopy and Other Interventional Techniques*, 25(9), 2892–2900.

Disclosure: There is no conflict of interest to declare.

PP1069

OTHER WAYS OF TRANSITION – PANCREATICOBILIARY ENDOSCOPY IN THE PEDIATRIC POPULATION. SINGLE, TERTIARY-CARE CENTER EXPERIENCE

B. Gellért¹, M. Horváth¹, Z. Péter¹, S. Attila², I. Hritz¹

¹Semmelweis University, Budapest, Hungary, Department of Surgery, Transplantation and Gastroenterology, Division of Interventional Gastroenterology, Budapest, Hungary,

²Semmelweis University, Budapest, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary

Contact E-Mail Address: gellert.balint@icloud.com

Introduction: Endoscopic interventions in children require specialized training and expertise due to unique anatomy and physiology challenges. Pancreaticobiliary endoscopies represent highlighted procedures in this population due to the often-unusual indications and the inherent high risk of complications.

Aims & Methods: The current work demonstrates our experience in pancreaticobiliary endoscopy in the pediatric population. We retrospectively analyzed data on all patients <18 years old who underwent endoscopic retrograde cholangiopancreatography (ERCP) or endoscopic ultrasound (EUS) from 2021 to the present days at our department. We collected demographical data, indications, procedural findings, interventions, and complications.

Results: Overall, 19 ERCPs and 7 EUS procedures were performed on 24 children with regular endoscopes. 15 were males, and the mean age was 10.7 years (± 4.7). Indications for ERCP included bile duct stones, benign stricture, pancreatic divisum and disconnected duct syndrome. Successful intervention was carried out in 18 cases, while there was one case of unsuccessful deep pancreatic duct cannulation due to abnormality of the duct. There was one case of perforation (Stapfer II), which was effectively managed endoscopically by placing a fully covered self-expanding metallic stent. 1 case of mild post-ERCP acute pancreatitis occurred following ERCP. EUS was performed for chronic pancreatitis, pancreatic cystic neoplasia, acute necrotizing pancreatitis, biliary compression and polycystic pancreas. 3 tissue acquisitions were done and one EUS-guided transluminal drainage was established. There were no complications.

Conclusion: To our knowledge, this is the most comprehensive domestic dataset of pancreaticobiliary endoscopies in children. Our findings imply that ERCP and EUS are effective diagnostic and treatment modalities in pediatric patients with acceptable safety profiles.

Disclosure: Nothing to disclose.

PP1070

SAFETY AND EFFICACY OF SPYGLASS™ CHOLANGIOPANCREATOSCOPY IN ROUTINE CLINICAL PRACTICE AT A TERTIARY HOSPITAL IN RIO DE JANEIRO

D.E. Coelho Neto^{1,2}, C. Louise Costa de Faria^{3,4}, I. Garcia Teixeira^{3,4}, M.E. de Miranda Lins^{3,4}, S. Pinheiro Machado de Carvalho^{3,4}, T. Peres Piva^{3,4}, M. Ernesto Coelho^{3,4}, G. Ernesto Coelho^{3,4}, M. Rodriguez Camarinha Loureiro^{3,4}, J.F. Ernesto Coelho⁵

¹Estácio de Sá University, Surgery and Intervencional Endoscopy, Rio de Janeiro, Brazil, ²Head of Gastrointestinal and Endoscopy Service Hospital Vitória and Samaritano Barra and Pró-Cardiaco, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ³Souza Marques Medical School, Rio de Janeiro, Brazil, ⁴LAED - Digestive Endoscopy Academic League, Rio de Janeiro, Brazil, ⁵Federal University of Rio de Janeiro Medical School, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil

Contact E-Mail Address: coelhodjalma@yahoo.com

Introduction: This study examined the efficacy and safety of cholangiopancreatography using the SpyGlass™ system in routine clinical practice.

Aims & Methods: Clinical data from endoscopic retrograde cholangiopancreatography (ERCP) performed at a regional hospital from January 2021 to January 2024 were retrieved from an electronic database and reviewed. All patients undergoing SpyGlass™ Cholangiopancreatography were included. Patient demographics, procedure indications, technical success rates, clinical success rates, and complication rates were analyzed. A sub-analysis of clinical outcomes was performed comparing legacy SpyGlass (fiber optic) and other digital systems.

Results: Out of 2,550 ERCP procedures performed, 97 patients underwent 100 cholangiopancreatography procedures. Clinical indications were: difficult common bile duct (CBD) stones (39.2%, n = 38), indeterminate CBD stricture (50.5%, n = 49), indeterminate pancreatic duct stricture (8.2%, n = 8), and proximally migrated CBD stent (2.1%, n = 2). Complete stone extraction was achieved in 36 (94.7%) out of 38 patients. Among patients with strictures, the correct diagnosis of malignancy based on image visualization was achieved in all 11 cases. Sensitivity and specificity of SpyBite™ biopsies were 91.8% (95% confidence interval (CI) 48.2%-97.7%) and 100.0% (95% CI 15.8%-100.0%), respectively. Proximally migrated CBD stent was successfully extracted. Complications included pancreatitis (1.03%, n = 1), suspected sealed perforation after laser lithotripsy

treated with a biliary stent (1.03%, n = 1), and cholangitis (5.15%, n = 5).

Conclusion: SpyGlass™ cholangiopancreatography is a safe and effective tool in routine clinical practice.

Disclosure: Nothing to disclose.

PP1071

DIGITAL SINGLE-OPERATOR CHOLANGIOSCOPY IN THE DIAGNOSIS AND TREATMENT OF BILIO-PANCREATIC DISEASES: A SINGLE-CENTRE EXPERIENCE

E. Bronzini¹, M. Blois¹, C. Sterpi¹, G. Leonardi¹, F. Rettura¹, M.R. Falcone¹, B. Toro¹, R. Manta¹

¹U.O.C. Endoscopia digestiva Area Vasta Azienda USL Toscana Nord Ovest, Livorno, Italy

Contact E-Mail Address: bronzinifrancesco90@gmail.com

Introduction: Single-operator cholangioscopy with SpyGlass™ DS Direct Visualization System (Boston Scientific Corp.) allows easier and more effective management of bilio-pancreatic diseases, with a relatively low rate of adverse events. Its main applications are the treatment of difficult biliary lithiasis and the diagnosis of indeterminate biliary strictures, although data confirming its efficacy are still limited. In the present study, we evaluated efficacy and safety of single-operator digital cholangioscopy in a secondary digestive endoscopy centre.

Aims & Methods: We retrospectively evaluated 113 consecutive patients undergoing SpyGlass™ DS cholangioscopy between February 2016 and September 2022 at our centre. Demographic and procedural characteristics and post-procedural outcomes were collected for the purpose of statistical analysis.

Results: A total of 126 SpyGlass™ DS procedures were performed on 113 patients (females 69, 61.1% - males 44, 38.9%) with a mean age of 73.4 $\pm$ SD 17 years. 92% of the patients underwent only one procedure, while the remaining 8% required 2 to 4 consecutive procedures. Indications were treatment of difficult biliary stones (85/126, 67.5%), diagnosis of indeterminate biliary strictures (30/126, 23.8%) and others (11/126, 8.7%). Holmium laser lithotripsy was the most frequently used (76/85, 89.4%). Complete clearance was achieved in almost all cases (80/85, 94.1%) with an average number of sessions of 1.05. The complete clearance rate at the first session was 93.75%.

40 diagnostic procedures were performed to characterise indeterminate biliary strictures, since diagnostic cholangioscopy was required for incidental biliary stricture in 10 patients who initially underwent lithotripsy. In 36/40 patients (90%) a stricture was confirmed and among these 72.2% required targeted biopsies with SpyBite™ forceps (21/36, 58.3% malignant biliary strictures - 15/36, 41.7% benign biliary strictures). The sensitivity, specificity and accuracy values at follow-up were 90%, 93% and 92% for the visual impression at cholangioscopic imaging and 86%, 100% and 88% for the histological examination of the targeted biopsy. A total of two cases of cholangioscopy-related adverse events were reported (2/126, 1.59%): one mild pancreatitis and one mild cholangitis.

Conclusion: The data obtained from our experience confirm the therapeutic and diagnostic value of digital single-operator cholangioscopy in the management of bilio-pancreatic diseases. Cholangioscopy-guided lithotripsy has been shown to have a high rate of complete clearance already at the first session. Regarding the management of indeterminate biliary stenosis, sensitivity of visual impression was superior to that of targeted biopsy; conversely, specificity of histological examination by targeted biopsy appeared superior. Prospective and multicentre studies would be advisable to consolidate the role of cholangioscopy in the management of bilio-pancreatic pathology.

Disclosure: Nothing to disclose.

PP1072

RETRIEVAL OF PROXIMALLY MIGRATED PLASTIC STENTS IN
ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY:
INSIGHTS FROM A SINGLE-CENTER STUDY

L. Santos¹, M. José Temido¹, M. Cristiano¹, P. Rocha¹,
D. Perdigoto^{1,2}, M. Gravito-Soares^{1,2}, S. Mendes¹, N. Almeida^{1,2},
D. Gomes^{1,2}, P. Figueiredo^{1,2}

¹Gastroenterology Department, Centro Hospitalar e Universitário de Coimbra, Unidade Local de Saúde de Coimbra, Coimbra, Portugal, ²Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Contact E-Mail Address: luispedroasantos@gmail.com

Introduction: Plastic stent placement during endoscopic retrograde cholangiopancreatography (ERCP) is a well-established therapy for a wide variety of obstructive biliary and pancreatic disorders. While proximal or distal stent migration is uncommon, with migration rates ranging from 4.1% to 13.5%, it can result in serious complications. Endoscopic retrieval of proximally migrated stents is intricate and may present a technical challenge to the endoscopist.

Aims & Methods: Aims: This study aims to ascertain the proximal stent migration rate, complications associated, risk factors, success rate, and the endoscopic techniques applied for retrieval.

Materials and Methods: We conducted a retrospective cohort study including 546 consecutive ERCP procedures performed at a tertiary center between January 2022 and March 2023. Data regarding indications for stenting, presentation of migration, stent length and diameter, endoscopic retrieval techniques, and success rate were collected.

Results: Overall, a total of 429 plastic stents were inserted (372 biliary and 57 pancreatic) in 245 patients. Proximal migration occurred in 2.8% of cases (9 biliary and 3 pancreatic), all of which were asymptomatic. Stent length <10cm (p=0.08) was identified as a risk factor for proximal migration. The success rate of endoscopic retrieval was 100%. Stent extraction was accomplished on the first attempt in 9 cases (75%), with three cases (25%) requiring re-attempt. Retrieval techniques employed included the Soehendra stent retriever (n=5, 41.7%), forceps (n=3, 25%), snare (n=3, 25%), and balloon catheter (n=1, 8.3%). Cholangiopancreatography-assisted retrieval was necessary in two cases as a rescue therapy. Notably, there were no complications or procedure-related mortality.

Conclusion: ERCP is an effective and safe approach for the retrieval of proximally migrated plastic stents, however, it requires experience with different techniques and endoscopic accessories. In challenging scenarios, cholangiopancreatography-assisted stent retrieval may offer a viable solution when conventional methods are unsuccessful. Our cohort analysis revealed that stent length <10cm was potentially associated with an increased risk of proximal migration.

Disclosure: Nothing to disclose.

PP1073

THE INFLUENCE OF PERIAMPULLARY DIVERTICULUM ON THE ERCP
OUTCOMES: A TERTIARY CENTER EXPERIENCE

Y. Cagır¹, M.B. Durak², V. Kilic¹, O. Coskun¹, I. Tenlik¹, I. Yuksel^{1,3}
¹Ankara Bilkent City Hospital, Department of Gastroenterology, Ankara, Turkey, ²Hacettepe University, Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey, ³Ankara Yildirim Beyazit University, Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey

Contact E-Mail Address: yvzcgr@hotmail.com

Introduction: Patients with periampullary diverticulum (PAD) are often found accidentally and may increase the complication risk of endoscopic retrograde cholangiopancreatography (ERCP) or may decrease success cannulation rates.

Aims & Methods: We aimed to compare ERCP procedures and outcomes in naive patients with or without PAD. All ERCP procedure and outcomes data of 3072 patients between January 2021 and December 2023 referred to our tertiary center were retrospectively analyzed. ERCP procedures were divided into two groups based on the presence or absence of PAD.

Results: A total of 929 naive patients underwent ERCP, of whom 135 (14.5%) patients with PAD and 794 (85.5%) patients without PAD. Median age of the patients with PAD was significantly higher than the patients without PAD (73 years vs. 60 years, p<0.001), but the two groups had a similar regarding the genders.

The median ERCP procedure time (20 min vs. 18 min, P=0.410), cannulation time (8 min vs. 7 min, P=0.491) did not differ in patients with and without PAD respectively. Successful cannulation rate in the group with PAD was 134 (99.3%), and in the group without PAD was 791 (99.6%), there was no difference between the two groups (P=0.467). One of the indications of ERCP procedure, choledocholithiasis was a more common reason in patients with PAD than in those without PAD [116 (85.9%) vs. 551 (69.4%), p<0.001]. Indications of other ERCP procedures in patients without PAD, malignant biliary strictures [93 (11.7%) vs. 6 (4.4%), P=0.011] and biliary leak [94 (11.8%) vs. 6 (4.4%), P=0.010] were more frequent reasons than in the patients with PAD. There were no significant differences between the patients with PAD and without PAD in term of all ERCP-related complications [6 (4.5%) vs. 73 (9.2%) respectively, P=0.751].

Our results showed notable differences in cannulation techniques between the two groups. Rate of the selective cannulation technique in the patients with PAD was higher than the patients without PAD [102 (75.6%) vs. 506 (63.7%) respectively, P=0.008]. Needle knife fistulotomy in patients without PAD was a higher rate of using technique than in the patients with PAD [139 (17.5%) vs. 8 (5.9%) respectively, P=0.001]. In the Li-Tanaka classification, the distribution of the PAD types identified 9.6% type 1 diverticula, 20.7% type 2A diverticula, 35.6% type 2B diverticula, 18.5% type 3 diverticula, 9.6% type 4A diverticula and 5.9% type 4B diverticula. Li-Tanaka type 2B (35.6%) was the most common type of the diverticula. There was no significant difference seen in any parameter in the PAD subgroups.

Conclusion: Our study revealed that ages of the patients with PAD was significantly higher than the patients without PAD. In the presented study, the overall success rates and total durations of the ERCP procedures were unaffected by the presence of PAD. The overall cannulation rates and complications following the procedures were unaffected by the type of the diverticulum.

The periampullary diverticulum does not affect the success and duration of cannulation, while it may affect the type of cannulation.

Disclosure: Nothing to disclose.

PP1074

WITHDRAWN

PP1075

A COMPARISON OF ERCP OUTCOMES OF THE NONAGENARIAN PATIENTS AND YOUNGER ADULT PATIENTS

M.b. Durak¹, I. Yuksel², Y. Cagır³

¹Hacettepe University Medicine of Faculty, Gastroenterology, Ankara, Turkey, ²Yildirim Beyazıt University, School Of Medicine, Diskapi Yildirim Beyazıt Education And Research Hos, Gastroenterology, Ankara, Turkey, ³Ankara Bilkent City Hospital, Gastroenterology, Ankara, Turkey

Contact E-Mail Address: doctormbd@gmail.com

Introduction: There are few studies evaluating the safety of endoscopic retrograde cholangiopancreatography (ERCP) in patients aged 90 years and above (nonagenarian). This study's main goal was to compare the technical success and complications of ERCP in patients over 90 years or younger patient group.

Aims & Methods: 929 naive patients who underwent ERCP at the tertiary referral center between January 2021 and December 2023 were retrospectively analyzed. The patient's medical records were reviewed for comorbidities, periampullary diverticulum, cannulation time, cannulation method, technical success, procedure duration, and ERCP-related complications.

	Total (n= 929)	Age ≥90 (n=34, 3.7%)	Age <90 (n=895, 96.3%)	P-value
Gender, female, n (%)	539 (58)	25 (73.5)	514 (57.4)	0.062
Age, years	63 (47-74)	91 (90-93.25)	61 (47-73)	-
ERCP procedure time, min	18 (12-28)	18.5 (11.75-23.25)	18 (12-28)	0.660
Total cannulation time, min	7 (3-15)	8 (2.75-15.5)	7 (3-15)	0.824
Indications of ERCP procedure, n (%)				
Cholelithiasis	667 (71.8)	28 (82.4)	639 (71.4)	0.142
Malignant biliary strictures	99 (10.7)	3 (8.8)	96 (10.7)	
Benign biliary strictures	44 (4.7)	-	44 (4.9)	
Biliary leak	100 (10.8)	1 (2.9)	99 (11.1)	
Others	19 (2)	2 (5.9)	17 (1.9)	
Complications, n (%)				
Post ERCP Pancreatitis	42 (4.5)	1 (2.9)	41 (4.6)	0.970
Perforation	4 (0.4)	-	4 (0.4)	
Bleeding	27 (2.9)	2 (5.9)	25 (2.8)	
Cholangitis	3 (0.3)	-	3 (0.3)	
Others (Cardiopulmonary)	2 (0.2)	-	2 (0.2)	
Past surgery history, n (%)				
History of cholecystectomy	241 (25.9)	10 (29.4)	231 (25.8)	0.638
Operation Billroth I and II	4 (0.4)	1 (2.9)	3 (0.3)	0.139
Cannulation techniques, n (%)				
Selective	608 (65.4)	27 (79.4)	581 (64.9)	0.440
Precut	45 (4.8)	-	45 (5)	
Needle-knife fistulotomy	147 (15.8)	4 (11.8)	143 (16)	
Double guide wire (DGW)	63 (6.8)	3 (8.8)	60 (6.7)	
Trans-pancreatic biliary sphincterotomy	12 (1.3)	-	12 (1.3)	
Periampullary Diverticulum type, n (%)				
1	13 (1.4)	1 (2.9)	12 (1.3)	0.472
2A	28 (3)	1 (2.9)	27 (3)	
2B	48 (5.2)	4 (11.8)	44 (4.9)	
3	25 (2.7)	-	25 (2.8)	
4A	13 (1.4)	1 (2.9)	12 (1.3)	
4B	8 (0.9)	-	8 (0.9)	

Results: A total of 929 naive patients underwent ERCP; 895 (96.3%) patients were < 90 years old and 34 (3.7%) patients were ≥ 90 years old. The median ERCP procedure time (18.5 min vs. 18 min, P=0.660), and cannulation time (8 min vs. 7 min, P=0.824) did not differ in patients with two groups respectively.

The successful cannulation rate in the nonagenarian group was 34 (100%), and in the younger group was 891 (99.6%), there was no significant difference between the two groups (P=1).

The main indication of the ERCP procedure was choledocholithiasis in both groups. There was no significant difference in the ERCP-related complications between the two groups. The main cannulation technique was selective sphincterotomy in both groups.

There was no significant difference in cannulation techniques between the two groups. Patients belonging to the nonagenarian group had a higher frequency of periampullary diverticulum (20.6%) compared to the younger group (14.3%).

Type 2B diverticula was the most seen in both groups (11.8% vs. 4.9%). However, there was no significant difference in the presence of periampullary diverticulum between the two groups. The number of chronic concomitant diseases (cardiovascular diseases, chronic lung diseases, chronic renal diseases) was significantly higher in the nonagenarian group [13 (38.2%) vs. 114 (12.7%), P<0.001].

Conclusion: In this study, we showed that ERCP was a safe and successful procedure in patients with nonagenarians. Although comorbidities were substantially higher, ERCP was a successful procedure for nonagenarian patients because the rates of complications are similar to those of younger adult patients.

Disclosure: Nothing to disclose.

PP1076

WITHDRAWN

PP1077

WITHDRAWN

PP1078

THE RESULTS OF USING NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAID-S) PROPHYLAXIS IN POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) PANCREATITIS - A REAL-LIFE DATA FROM A SINGLE TERTIARY CENTRE

D. Bakula¹, S. Pelajic¹, I. Siranovic Pongrac¹, M. Nikolic¹, G. Mirosevic², N. Ljubicic¹

¹University Hospital Centre Sisters of Mercy, Division Of Gastroenterology, Department Of Internal Medicine, Zagreb, Croatia, ²University Hospital Centre Sisters of Mercy, Division Of Endocrinology, Department Of Internal Medicine, Zagreb, Croatia

Contact E-Mail Address: dejan.bakula@gmail.com

Introduction: ERCP is a commonly used endoscopic procedure for diagnosing and treating disorders of pancreaticobiliary system. NSAIDs have been proven to minimize the risk of post-ERCP pancreatitis, which occurs in approximately 8% of average-risk procedures (1,2).

This study aimed to analyze the occurrence of post-ERCP pancreatitis in patients in whom ERCP was performed for the first time, before and after the use of NSAIDs in routine clinical practice.

Aims & Methods: Between January 2012 and December 2014 and between January 2019 and December 2021, 621 and 664 patients, respectively, were consecutively evaluated. In all those patients therapeutic ERCP procedure with biliary sphincterotomy has been done for the first time and the post-procedure complications were consecutively evaluated. NSAIDs were administered in a form of rectal suppositories at least an hour before the procedure.

Post-ERCP pancreatitis was defined as an appearance of pain with elevated amylase concentrations at least 3x above the upper limit of normal for more than 24 hours after the procedure. Chi-Square test and Mann-Whit-

ney U tests were used to compare discrete and continuous variables where $p<0.05$ was considered statistically significant.

Results: A total of 1285 ERCP-naïve patients were analyzed. Patients were split into two groups, one receiving and the other not receiving NSAID prophylaxis (667 vs 618 patients, respectively). Patients who received NSAID prophylaxis showed a significantly lower incidence of post-ERCP pancreatitis (2.9% vs. 7.8%, $p<0.05$) and transient hyperamylasemia (9.3% vs. 28.2%, $p<0.05$), as well (Table 1).

Conclusion: Real-life experience from a single tertiary center demonstrated that including NSAID prophylaxis into standard clinical practice resulted in a considerable reduction in post-ERCP pancreatitis and hyperamylasemia.

Patients	667	618
Age (years mean $\pm$ SD)	68 $\pm$ 15	67 $\pm$ 15
Male/Female (n)	328/339	249/369
Cholelithiasis	399 (59.8%)	436(70.5%)
Cholangitis	145 (21.7%)	75(12%)
Malignant biliary obstruction	120 (17.8%)	101(16.4%)
Acute pancreatitis	55 (8.2%)	57 (9.2%)
Miscellaneous	58 (8.7%)	33 (5.3%)
Post ERCP pancreatitis n (%)	20 (3.1%)	48 (7.8%) *
Hyperamylasemia n (%)	46 (6.9%)	174 (28%)*

Table 1. NSAID non-NSAID
Chi-Square test and Mann-Whitney U tests, * $p<0.05$

References:

1. Buxbaum JL, Freeman M, Amateau SK, Chalhoub JM, Coelho-Prabhu N, Desai M, Elhanafi SE, Forbes N, Fujii-Lau LL, Kohli DR, Kwon RS, Machicado JD, Marya NB, Pawa S, Ruan WH, Sheth SG, Thiruvengadam NR, Thosani NC, Qumseya BJ; (ASGE Standards of Practice Committee Chair). American Society for Gastrointestinal Endoscopy guideline on post-ERCP pancreatitis prevention strategies: summary and recommendations. *Gastrointest Endosc.* 2023 Feb;97(2):153-162. doi: 10.1016/j.gie.2022.10.005. Epub 2022 Dec 12. PMID: 36517310.

2. Pekgöz M. Post-endoscopic retrograde cholangiopancreatography pancreatitis: A systematic review for prevention and treatment. *World J Gastroenterol* 2019;25:4019-4042.

Disclosure: no conflict of interest

PP1079

MULTIDRUG RESISTANCE PATTERNS IN ACUTE CHOLANGITIS: A PROSPECTIVE MULTICENTER STUDY ON ANTIMICROBIAL RESISTANCE (ARISE)

B. Miutescu¹, D. Vuletic¹, F. Bratosin², D. Gunsahin³, S. Zenovia⁴, G. Balan⁴, V. Sandru⁵
¹“Victor Babes” University of Medicine and Pharmacy, Timisoara, Romania, ²“Victor Babes” University of Medicine and Pharmacy Timisoara, Timisoara, Romania, ³Emergency University Hospital, Bucharest, Romania, ⁴“Grigore T. Popa” University of Medicine and Pharmacy, Iasi, Romania, ⁵“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

Contact E-Mail Address: bmiutescu@yahoo.com
Introduction: The “Antimicrobial Resistance in Acute Cholangitis” (ARISE) study is a prospective investigation focused on the antimicrobial resistance patterns in patients with acute cholangitis undergoing ERCP. Conducted across multiple tertiary gastroenterology centers in Romania, this study aims to identify, analyze, and mitigate the challenges posed by multidrug-resistant (MDR) organisms in managing acute cholangitis.

Aims & Methods: Data collected included microbial cultures from bile samples, patient demographics, clinical outcomes, and antibiotic resistance profiles. From the study’s onset in January 2024, 138 eligible patients were identified as having positive bile cultures. Among these patients, the predominant symptoms included abdominal pain (82.6%), jaundice (71%), and fever or shaking chills (36.2%). The diagnosis of acute cholangitis was established using TG18 criteria.

Results: Bile cultures were positive in 71.0% of cases. The most frequently isolated bacteria were *Escherichia coli*, found in 23.2% of positive cultures, followed closely by *Enterococcus* spp., present in 22.5% of cases. *Klebsiella pneumoniae* was also notably prevalent, identified in 7.2% of the bile samples. Ciprofloxacin showed the highest resistance rate among the tested antibiotics, with a resistance rate of 23.9%. Ampicillin and gentamicin displayed significant resistance rates at 10.9% and 18.8%, respectively. Piperacillin/tazobactam and trimethoprim/sulfamethoxazole each showed a resistance rate of 15.2%.

The study’s data on tigecycline and linezolid showed lower resistance rates, with tigecycline maintaining a sensitivity rate of 20.3% and linezolid at 19.6% in cultures where testing was applicable. In comparison, their resistance rates were only 0.7% for each.

Multidrug resistance was identified in a significant fraction of isolates, with 15.2% of samples. A concerning finding was the presence of MDR strains of *Escherichia coli*, which exhibited resistance rates to ampicillin (21.0% sensitivity, 10.9% resistance) and amoxicillin/clavulanic acid (17.4% sensitivity, 14.5% resistance).

Conclusion: We observed a concerning prevalence of MDR organisms in acute cholangitis cases, particularly against antibiotics such as ampicillin, gentamicin, and ciprofloxacin, with a high incidence of MDR *Escherichia coli* strains.

Disclosure: Nothing to disclose.

PP1080

STUBBORN STRICTURES! A RETROSPECTIVE ANALYSIS OF SOEHENDRA STENT RETRIEVER IN MANAGEMENT OF BILIARY AND PANCREATIC STRICTURES

M. Asim¹, N. Zakaria², A. Altaf³
¹Sindh Institute of Advanced Endoscopy and Gastroenterology (SIAG), Karachi, Pakistan, ²Sindh Institute of Advanced Endoscopy and Gastroenterology, Karachi, Pakistan, ³Sindh Institute of Advanced Endoscopy and Gastroenterology (SIAG), Gastroenterology, Karachi, Pakistan

Contact E-Mail Address: asimsharif22@gmail.com
Introduction: Biliary strictures are defined as narrowing in the intrahepatic or extra hepatic biliary system, resulting in upstream dilatation, stagnant bile flow, ultimately causing biliary obstruction. Patients may present with a variety of symptoms including jaundice, pruritis, weight loss, along with development of recurrent cholangitis, stone formation and liver abscesses. This results in immediate and long term morbidity and mortality. It therefore warrants immediate investigation and treatment. In ERCP, endoscopic techniques exist that allow strictures to be traversed. These include wire guided catheter techniques, balloon dilators and stent placement. When traditional techniques fail, Soehendra stent retriever can be used.
Aims & Methods: Patients with evidence of benign/malignant biliary or pancreatic stricture were retrospectively analyzed. The pancreatic or biliary strictures allowed passage of 0.035 inch guidewire, without allowing passage of >5.5fr cannulotomes, 5.8fr balloon dilators, or soehendra stricture dilator. After successful biliary cannulation and guide wire access, a SSR would be passed through the wire to the distal end of the stricture.

The SSR handle would be rotated clockwise, allowing the SSR to cross the stricture. Once the stricture is dilated, a stent would then be placed.

Results: A total of 72 patients were analyzed. Of these, 38 (52%) were female and 35 (48%) were male. The average age was 44.8 years. Predominant symptoms included jaundice in 36 (50%) patients, and abdominal pain in 35 (48.6%). A total of 59 (81.9) ERCPs were for biliary strictures, and 13 (18%) were for pancreatic strictures.

The predominant findings prior to biliary ERCP included evidence of CBD stricture in 31(52%) cases, unspecified obstructive jaundice in 30 (50.8%) cases, peri-ampullary growth in 13 (22%) patients, and cbd stones in 11 (18%) patients. The main indication for pancreatic ERCP was Chronic Pancreatitis in 100% cases. Out of the 72 patients, 2 (2.7%) developed brief hemobilia during ERCP controlled spontaneously. No patient was demonstrated to have major bleed. No evidence of duct injury, evident by dye extravastion, or perforation was observed. A stent could not be passed in 7 cases (9.7%) despite SSR traversing stricture.

Conclusion: SSR is a useful device for crossing biliary and pancreatic stricture that otherwise could not be negotiated with established techniques. It is safe, and tolerable for strictures defying conventional wire guided techniques

Disclosure: Nothing to disclose.

PP1081

FEASIBILITY OF THREE DIMENSIONAL CHOLANGIOGRAM RECONSTRUCTION FOR COMPLEX BILIARY STRICTURES UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY (ERC). -A PILOT STUDY

G. Kakked¹, A. Maniak¹, K. Garg¹, C. Chapman¹, A. Singh¹, I. Waxman¹, N.A. Mehta¹

¹Rush university medical center, Gastroenterology, Chicago, United States of America

Contact E-Mail Address: drkakked1@gmail.com

Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) is pivotal in managing complex biliary strictures due to various causes like Cholangiocarcinoma (CCA), Primary Sclerosing Cholangitis (PSC), and mass-related intrahepatic strictures. Traditional ERCP relies on two-dimensional (2D) X-ray imaging, which often presents challenges in accurately localizing and selectively cannulating specific intrahepatic ducts. This study aims to assess the feasibility and effectiveness of three-dimensional (3D) fluoroscopic ERCP in diagnosing and treating complex biliary strictures.

Aims & Methods: We conducted a prospective pilot study, approved by the Institutional Review Board. Adult patients scheduled for ERCP for complex biliary strictures were enrolled. Exclusions included inability or unwillingness to consent, existing percutaneous biliary drainage, or unfeasible selective trans-papillary biliary cannulation.

Performance of 3D ERCP Patients were positioned on a 3D fluoroscopic table. ERCP followed standard protocols, with high-volume contrast injections opacifying bile ducts. After achieving full biliary tree opacification, a balloon was inflated in the distal bile duct in preparation for 3D imaging. To minimize radiation exposure to staff, the endoscope was fixed in a holder, and the room was evacuated before 3D image acquisition. These images were reconstructed to produce detailed 3D visuals of the target area, aiding real-time therapeutic maneuvers like selective intrahepatic duct cannulation.

Data Collection and Analysis Data included continuous variables (mean $\pm$ standard deviation) and categorical variables (percentages). Radiation exposure was quantified separately for ERCP and 3D reconstruction, using thermoluminescent dosimeters. Results were reported as Effective Surface Dose (ESD) in mGy and Dose Area Product in mGy.cm².

Results: Eighteen patients (median age 66.6) underwent 3D ERCP. 40% had a malignant biliary structure etiology, with 50% showing both intrahepatic and extrahepatic bile duct involvement. 3D reconstruction facilitated successful selective wire cannulation in 80% of cases, previously unachievable with conventional ERCP. One case provided crucial imaging for liver resection planning. The additional radiation dose was 16.44 mGy.cm².

Conclusion: This pilot study proves the feasibility of 3D ERCP in managing complex biliary strictures. This first-of-its-kind study highlights the utility of 3D reconstruction in ERCP. While significantly aiding selective intrahepatic duct cannulation and surgical planning for cholangiocarcinoma resections, it doubles the procedure's radiation exposure, potentially raising cancer risk to 1 in 1000. However the dose needed is significantly lower the IR guided biliary interventions. Further larger studies are required to evaluate the clinical efficacy of 3D ERCP.

Disclosure: Nothing to disclose.

PP1082

OPTIMAL TIMING FOR A SECOND ERCP AFTER FAILURE OF INITIAL BILIARY CANNULATION FOLLOWING PRECUT SPHINCTEROTOMY IN DIFFICULT BILIARY CANNULATION: A RANDOMIZED CLINICAL TRIAL

K. Amalou¹, N. Benboudiaf¹, H. Chetroub¹, K. Saidani¹

¹HCA, Gastroenterology, Algiers, Algeria

Contact E-Mail Address: amalou_kh@yahoo.fr

Introduction: Precut sphincterotomy is a technique usually employed for difficult biliary cannulation during endoscopic retrograde cholangiopancreatography (ERCP), it increases the success of deep biliary cannulation, but the method fails at the initial ERCP in 5-12% of cases. Although other invasive strategies are often used to access the bile duct, a second ERCP may be effective and safe.

Aims & Methods: We evaluated the efficacy, safety, and factors related to a second ERCP after failed cannulation using a precut sphincterotomy.

Method: In this prospective, monocenter, randomized, clinical trial, patients who were referred for therapeutic biliary ERCP and difficult biliary cannulation with failed cannulation after precut, a second ERCP was performed. They were randomized to early repeat ERCP within 4 days (Group A) or after 7 days after precut (Group B). Efficacy was based on the cannulation rate of the second ERCP, and safety was assessed in terms of adverse events.

Results: We identified 238 patients with failed cannulation after precut, and a second ERCP was performed in 154(64.7%). Pancreatitis post ERCP developed in 5 of the 77 patients (6.4%) in Group A and 11 of the 77 (14.8%) in Group B (odds ratio [OR] 0.55; 95% confidence interval [CI] 0.16–0.78). The incidence of PEP was significantly lower in the early precut group (5/77, 6.4%) than in the delayed precut subgroup (11/77 [14.8%]; OR 0.42, 95%CI 0.17–1.07). There were no differences in biliary cannulation success rates, bleeding, perforation, and cholangitis.

Conclusion:

A second ERCP after failure of initial biliary cannulation following precut appears to be safe and effective. early precut can significantly reduce the incidence of PEP. Repeated biliary cannulation attempts are a real risk factor for this complication.

Disclosure: Nothing to disclose.

PP1083

EFFICACY AND SAFETY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN PEDIATRIC POPULATION

E. Batıbay¹, C. Efe¹, O. Yüksekayla¹, M. Polat², S. Barutçu³

¹Harran, Urfa, Turkey, ²Mehmet Akif Inan, Urfatut, Turkey,

³Gaziantep, Gaziatep, Turkey

Contact E-Mail Address: ersin0824@gmail.com

Introduction: Data regarding diagnostic and/or therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in pediatric population is limited. ERCP is very rarely necessary in this population and most of ERCP procedures are usually performed by adult endoscopists. We evaluated the efficacy and safety of ERCP in pediatric patients.

Aims & Methods: We retrospectively evaluated data of pediatric patients who underwent ERCP during the period of 2013 and 2024 from two adult gastroenterology centers (Harran University and Gaziantep University Gastroenterology)

Results: We included 80 patients (40%, male) with median age of 13 years (range: 3-17) at the time of ERCP procedure. ERCP was performed in 73 patients (91 %) due to biliary disorders while in 7 patients (9%), pancreatic diseases were the indication. ERCP was performed under sedation (propofol ± midazolam ± ketamine). The most common reason was choledocholithiasis (n=35, 44%) followed by hydatid cyst complications (n=22, 27%), and post-liver transplant complications (n=6, 7%).

Overall, the procedure was successful in 79 (99%) patients while in only one patient common bile duct could not be cannulated due to tumor invasion. Post ERCP pancreatitis developed in 5 (6.2%) patients and was mild in all. No major adverse event was observed.

Conclusion: Our data suggest that ERCP is a safe and effective method in the management of pancreatobiliary diseases in pediatric patients.

References: none

Disclosure: Nothing to disclose.

PP1084

FREEHAND PRECUT- A SAVIOR FOR DIFFICULT ERCP- RETROSPECTIVE ANALYSIS OF 3000 ERCPS AT TERTIARY CARE CENTER IN INDIA

P. Desai¹, C. Patel¹, M.V Kabrawala¹, R. Prajapati¹, R. Kakadiya¹, N. Patel¹, M. Sethia¹

¹SIDS Hospital & Research Centre, Endoscopy, Surat, India

Contact E-Mail Address: riteshpriajapati87@gmail.com

Introduction: With the advent of EUS guided biliary interventions, there is a lot of hype created that ERCP will cease to be performed. The most important and limiting factor for ERCP is successful bile duct cannulation. We have studied a large series of our cases and tried to study the impact of properly performed precut on success of bile duct cannulation.

Aims & Methods: Aim: To analyze the efficacy of freehand precut for selective cannulation in difficult ERCP and its role in improving technical success rate, obviating need for EUS guided / other rendezvous techniques.

Methods: Retrospective analysis of 3000 patients undergoing ERCP from 2017 till date for varied etiologies. No. of patients required precut accessotomy were noted and technical success rate was measured.

Results: No. of patients analyzed- 3000. Selective biliary cannulation- 2452 (81.74%). Difficult cannulations requiring freehand precut accessotomy- 548 (18.26%). Technical success after precut achieving biliary access- 539 (98.36%). Failure of biliary cannulation even after precut- 09 (1.64%). Most common etiology in precut cases stone disease 360 (65.70%) followed by malignant lesions 118 (21.53%), benign strictures 28 (5.11%),

post cholecystectomy biliary leak 28 (5.11%), post traumatic biliary leak 10 (1.82%), post hydatid surgery biliary leak 02 (0.36%), post central hepatectomy biliary leak 02 (0.36%).

Most common cause for failure in precut cases was extensive edema and deformed anatomy. Of all failed cases 3 were large stones who were subjected to surgery and 6 were malignant lesions who were subjected to EUS guided biliary drainage.

Conclusion: Free hand precut technique, done correctly, is a savior in difficult cannulation cases and it increases the success rate of selective biliary cannulation significantly avoiding the need for other costlier techniques such as EUS guided / Rendezvous techniques.

References: Mariani A, Di Leo M, Giardullo N, Giussani A, Marini M, Buffoli F, Cipolletta L, Radaelli F, Ravelli P, Lombardi G, D'Onofrio V, Macchiarelli R, Iiritano E, Le Grazie M, Pantaleo G, Testoni PA. Early precut sphincterotomy for difficult biliary access to reduce post-ERCP pancreatitis: a randomized trial. *Endoscopy*. 2016 Jun;48(6):530-5. doi: 10.1055/s-0042-102250. Epub 2016 Mar 18. PMID: 26990509.

Davee T, Garcia JA, Baron TH. Precut sphincterotomy for selective biliary duct cannulation during endoscopic retrograde cholangiopancreatography. *Ann Gastroenterol*. 2012;25(4):291-302. PMID: 24714256; PMCID: PMC3959408.

Disclosure: Nothing to disclose.

PP1085

WIRE GUIDED CANNULATION

N. Ahmed¹

¹Sindh Institute of Advanced Endoscopy and Gastroenterology, Gastroenterology, Karachi, Pakistan

Contact E-Mail Address: nasierahmedkhan@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has evolved from a diagnostic to a therapeutic procedure for pancreatobiliary pathologies. Successful cannulation of pancreatobiliary ducts especially deep biliary cannulation (DBC) through the ampulla is of prime importance and involves a spectrum of different techniques (1). Safe technique of DBC cannulation is a necessary prerequisite to most biliary interventionists and is still under constant evolution, with an aim to decrease the incidence of complications related to it (2). Initial technique of DBC was a conventional contrast-assisted cannulation (CC), it has been replaced by a less traumatic and preferred wire-guided cannulation technique (WGC) (4). Previous technique of CC had an approximate success rate of 65% (5). Repeated unsuccessful attempts to cannulate with CC, may result in trauma to the papilla; intramural injection and inadvertent pancreatic duct injections, increasing the risk of post-ERCP pancreatitis (PEP) (6). WGC technique was first introduced by Siegel (7) in 1987, aiming to increase the success rate of biliary cannulation and a possible decrease in the rate of PEP.

Pancreatitis is the commonest complication of ERCP, with rates ranging from 1% to 40%, but figures of 2% to 6% are typical in most large prospective studies (8). Multivariate analysis in most studies have revealed following factors involved in PEP; suspected sphincter of Oddi dysfunction, young age, history of PEP, difficult or failed cannulation, pancreatic duct injection, pancreatic sphincterotomy (especially minor papilla), balloon dilatation of intact biliary sphincter and precut sphincterotomy (9); widespread prophylactic administration of these agents may significantly reduce the incidence of PEP, resulting in major clinical and economic benefit (8). Mechanical approaches are pancreatic duct (PD) stent placement and WGC; PD stent has a definite role in prevention but the utility of WGC is still debatable (10). Hypothesis behind the preventive use of WGC is to reduce the mechanical trauma to the papilla or pancreatic sphincter,

thus avoiding an increase in hydrostatic pressure associated with contrast injection (8) ERCP in this part of the world is under evolutionary phase with few tertiary care centers and this is the first study of its type from our center. Our aim was to analyze the success and complications with the wire-guide technique.

Aims & Methods: To evaluate the clinical features, laboratory values, success of cannulation with the wire-guided and complications related to wire-guided cannulation (WGC) technique, in patients who underwent endoscopic retrograde cholangiopancreatography (ERCP).

Results: This analysis was performed on patients records registered in our wards, between January 2016 to may 2023. A total of 5400 patients underwent 7000 ERCP procedures for a diagnostic or therapeutic purpose; 1527 patients were included. 1480 ERCPs (96.9%) were performed for therapeutic purpose and 47 (3.1%) for diagnostic purpose. There were 631 (41.3%) men and 896 (58.7%) women with a mean age of 47.3 ± 0.3 . Technical success was achieved in all the cases (100%); our first procedure successful cannulation rate was 92.3% in 1410 patients, with a repeat procedure and success in all the remaining 117 (7.7%) patients. There was no procedure-related mortality in our patients. ERCP affected management in 97.3% (1486/1527 procedures).

Conclusion: WGC technique is helpful and efficacious technique and may increase the success rate of biliary or pancreatic duct cannulation.

References: 1. Navaneethan U, Konjeti R, Venkatesh PG, Sanaka MR, Parsi MA. Early precut sphincterotomy and the risk of ERCP related complications: An updated meta-analysis. *World J Gastrointest Endosc.* 2014 May 16; 6(5):200-8. doi: 10.4253/wjge.v6.i5.200.

2. Lee TH, Hwang SO, Choi HJ, Jung Y, Cha SW, Chung IK et al. Sequential algorithm analysis to facilitate selective biliary access for difficult biliary cannulation in ERCP: a prospective clinical study. *BMC Gastroenterol.* 2014 Feb 17; 14:30.

3. Song BJ, Kang DH. Prevention of post ERCP pancreatitis: the endoscopic technique. *Clin Endosc.* 2014 May; 47(3):217-21.

4. Li QY, Pan L, Ling Q, He JD, Zhang LX, Zheng SS. Single-operator wire-guided cannulation technique enables easier cannulation of ERCP. *Dig Dis Sci.* 2012 Dec; 57(12):3293-8.

5. Karamanolis G, Katsikani A, Viazis N, Stefanidis G, Manolakopoulos S, Sgouros S, et al. A prospective cross-over study using a sphincterotome and a guidewire to increase the success rate of common bile duct cannulation. *World J Gastroenterol.* 2005 Mar 21; 11(11):1649-52.

6. Choudhary A, Winn J, Siddique S, Arif M, Arif Z, Hammoud GM, et al. Effect of precut sphincterotomy on post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and meta-analysis. *World J Gastroenterol.* 2014 Apr 14; 20(14):4093-101.

Disclosure: Nothing to disclose.

PP1086

WITHDRAWN

PP1087

PREDICTORS OF RECURRENT BILE DUCT STONE AFTER CLEARANCE BY ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

L. Mouslim¹, A. Benhamdane¹, R. Chaibi², S. Hdiye¹, F. Ait iken¹, T. Addajou¹, S. Mrabti¹, R. Berraida¹, E. Ilham¹, F. Rouibaa¹, H. Seddik¹

¹Mohamed V Military training hospital, Rabat, Morocco, ²Mohamed V Military training hospital, Rabat, Morocco, Rabat, Morocco

Contact E-Mail Address: imane.mouslim@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is now the gold standard for the treatment of bile duct stones. However, recurrence stones is frequent after their complete removal by endoscopic treatment.

Aims & Methods: The present study is retrospective, descriptive and analytic, including all patients who underwent ERCP for common bile duct (CBD) stones between January 2008 and January 2024.

Recurrent CBD stone was defined as the finding of a stone at least 6 months after the initial ERCP in which complete stone extraction was performed.

Factors associated with recurrent CBD stones were studied by logistic regression analysis.

Statistical analysis was performed using Jamovi software.

The aim of our study is to identify predictors of recurrent CBD stones after ERCP.

Results: Among 1151 patients who underwent ERCP for lithiasis pathology, 88 patients or 7.7% had recurrent CBD stone.

Mean age of the patients was 64.5 ± 13.4 years, with extremes ranging from 22 to 94 years. Sex ratio (M/F) was 0.69, with a female predominance of 59.1%.

20.5% of patients presented with acute angiocholitis and 6.8% with acute pancreatitis.

A periampullary diverticulum was found in 5.7% of patients (n=5).

In univariate analysis, the risk factors for recurrent CBD stone were: older age (OR :37; IC95% : [10,7- 127,2] ; p<0,001), female gender (OR :9,9 ;IC95% : [4,49-22,04] ; p<0,001), CBD diameter > 15 mm (OR : 7,36 ;IC95% : [5,51-9,8] ; p<0,001), presence of angiocholitis (OR : 2.06 ;IC95% : [1,12-3,8] ; p=0,02), number of CBD stones (OR :8,61; IC95% : [6,51-11,39] ; p=0,018), size of CBD stones (OR :2,51 ;IC95% : [1,43-4,39] ; p=0,001), while enlargement EST (OR :0,18; IC95% : [0,08-0,44] ; p<0,001) was a protective factor. After multivariate analysis, and adjusting for the factors studied, only older age (OR:1.96; CI95%: [1.94-2.93]; p=0.001), number of CBD stones (OR: 1.99; CI95%: [1,2-3,4] ; p=0,037) and size of CBD stones (OR :4,06; IC95% : [3,51-6,72] ; p=0,003) were risk factors, and enlargement EST (OR :0,31; IC95% : [0,11-0,85] ; p=0,024) was protective factor.

Conclusion: In our study, the predictive factors for recurrent CBD stones were advanced age, the presence of impaction and a large stone.

Disclosure: Nothing to disclose.

PP1088

DIAGNOSTIC PERFORMANCE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY IN MALIGNANT LESIONS OF THE HEPATIC HILUM: A RETROSPECTIVE ANALYSIS FROM A TERTIARY REFERRAL CENTRE.

F. Borrelli de Andreis^{1,2}, N. Alberghina³, G. Rizzatti², A. Tringali², F. Attili², T. Schepis², G. Costamagna¹, C. Spada²

¹Ospedale Gemelli Isola – Isola Tiberina, Centre of Excellence in Gastrointestinal and Metabolic Disorders, Digestive Endoscopy Unit, Rome, Italy, ²Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Medical and Surgical Sciences, Rome, Italy, ³Azienda Ospedaliera per l’Emergenza “Cannizzaro”, Digestive Endoscopy Unit, Catania, Italy

Contact E-Mail Address: federica.bda@gmail.com

Introduction: Diagnosing hepatic hilar malignancies is challenging due to the complex anatomical location and intricate nature of these lesions, necessitating advanced imaging modalities and specialised diagnostic approaches. To date, limited and dated studies with small sample sizes have focused on the diagnostic utility of endoscopic ultrasound fine-needle aspiration (EUS-FNA) in suspected malignancy of the hepatic hilum. However, only a few case series have reported similar findings for EUS fine-needle biopsy (EUS-FNB).

Aims & Methods: To address this gap, our study aims at assessing the diagnostic performance and safety profile of EUS-FNB as a first-line tool in the diagnostic approach for suspected hepatic hilum malignancies. A single-centre, retrospective analysis of all the patients with biliary strictures and lesions involving the hepatic hilum who underwent EUS-FNB from October 2014 to April 2023 was conducted. All included patients were monitored after EUS-FNB via clinical follow-up for a minimum of 6 months or until death (follow-up <6 months). A descriptive statistical analysis for all the variables was performed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were finally calculated.

Variables	Patients (n=83)
Prior upper GI surgery, n (%)	5 (6.0)
Pancreaticoduodenectomy	1 (1.2)
Roux-en-Y gastric bypass	2 (2.4)
Distal gastrectomy (Billroth I reconstruction)	1 (1.2)
Ivor Lewis esophagectomy	1 (1.2)
Lesion size, mean ± SD	29.10 ± 13.66
Biopsy needle diameter, n (%)	
19G	2 (2.4)
20G	1 (1.2)
22G	76 (91.6)
25G	4 (4.8)
Passes, n (%)	
2	13 (15.7)
3	53 (63.9)
4	17 (20.4)
Presence of biliary stent, n (%)	19 (22.9)
Sample adequacy, n (%)	77 (92.8)
Repeated EUS-FNB, n (%)	9 (10.8)
Final histological results, n (%)	
CCA	63 (75.9)
HCC	3 (3.6)
Metastasis	5 (6.0)
NEN	2 (2.4)
Multiple myeloma	1 (1.2)
Undefined dysplasia	1 (1.2)
Non-malignant	8 (9.7)

Table 1. Characteristics of the study population and EUS-FNB procedures.

Legend: CCA: cholangiocarcinoma; EUS-FNB: endoscopic ultrasound-guided fine needle biopsy, GI: gastrointestinal; HCC: hepatocellular carcinoma; NEN: neuroendocrine neoplasm; SD: standard deviation.

Results: A total of 83 consecutive subjects (M:F 51:32, mean age 69.01±10.10) with a radiological suspicion of malignant lesion of the hepatic hilum were included in the analysis (details in Table 1). Sensitivity, specificity, PPV, and NPV were 88.00% (95%CI: 78.44-94.36), 100.00% (95%CI: 63.06-100.00), 100.00% (95%CI: 94.56-100.00), and 47.06% (95%CI: 32.50-62.13), respectively. Overall accuracy was 89.16% (95%CI: 80.41-94.92).

The repetition of EUS-FNB after the first non-diagnostic one demonstrated increased sensitivity (92.00%, 95%CI: 83.40-97.01%) and overall accuracy (92.77%, 95%CI: 84.93-97.30%). Importantly, histological results were not affected by prior surgery of the upper gastrointestinal tract (n=5, p=0.083), or the presence of a biliary stent in place (n=19, p=0.728). The reported post-procedural adverse events were cholangitis (n=3, 3.6%) and mild pancreatitis (n=1, 1.2%).

Conclusion: This study emphasises the efficacy and safety of EUS-FNB as a first-line diagnostic tool for lesions of the hepatic hilum. Further prospective studies are warranted to determine the diagnostic performance of EUS-FNB for hilar lesions in comparison with ERCP-guided biopsies or brushing.

References:

1. Navaneethan U, Njei B, Venkatesh PG et al. Endoscopic ultrasound in the diagnosis of cholangiocarcinoma as the etiology of biliary strictures: a systematic review and meta-analysis. *Gastroenterol Rep (Oxf)*. 2015 Aug;3(3):209-15.

Disclosure: Nothing to disclose.

PP1089

OPTIMIZING EUS-GUIDED CHOLEDOCHODUODENOSTOMY WITH LUMEN-APPPOSING METAL STENTS FOR PRIMARY DRAINAGE OF MALIGNANT DISTAL BILIARY OBSTRUCTION (SCORPION-IIP): A PROSPECTIVE PILOT STUDY

J.A. Fritzsche^{1,2,3}, P. Fockens^{1,2,3,4}, M.G. Besselink^{2,3,5}, O.R. Busch^{2,3,5}, F. Daams^{2,3,6}, M.C.B. Wielenga^{1,2,3}, J.W. Wilmink^{3,7}, R.P. Voermans^{1,2,3}, R.L. van Wanrooij^{2,3,4}

¹Amsterdam UMC, location University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³Cancer Center Amsterdam, Amsterdam, Netherlands, ⁴Amsterdam UMC, location Vrije Universiteit, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁵Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands, ⁶Amsterdam UMC, location Vrije Universiteit, Department of Surgery, Amsterdam, Netherlands, ⁷Amsterdam UMC, location University of Amsterdam, Department of Medical Oncology, Amsterdam, Netherlands

Contact E-Mail Address: j.a.fritzsche@amsterdamumc.nl

Introduction: EUS-guided choledochoduodenostomy (EUS-CDS) with a lumen-apposing metal stent (LAMS) is an alternative for ERCP in patients with a malignant distal biliary obstruction (MBO).(1,2) The main drawback of EUS-CDS using LAMS is the high rate of stent dysfunction which leads to cholangitis and reinterventions.(3,4)

Presumably, the short length and perpendicular angle of the LAMS to the bile duct contribute to the risk of stent dysfunction.(5) Therefore, the aim was to investigate whether placement of a fully covered self-expandable metal stent (FCSEMS) through the LAMS, thereby changing the axis of biliary drainage towards the descending duodenum, will decrease the risk of stent dysfunction while maintaining high technical success and low adverse event rates.

Aims & Methods: We performed a prospective pilot study in patients with proven MBO and a bile duct diameter of at least 12mm, requiring biliary drainage, excluding patients with gastric outlet obstruction. Patients underwent biliary drainage with (as first procedure) EUS-CDS using a 6 or 8 mm LAMS with a 6 cm by 8 or 10 mm FCSEMS placed through the LAMS. Primary outcome was stent dysfunction, defined as recurrent jaundice after initial clinical success, ongoing jaundice in combination with persistent dilatation of the bile ducts, or cholangitis. Secondary outcomes were technical success, clinical success, and adverse events (AEs).

Results: Overall, 27 consecutive patients eligible for EUS-CDS were enrolled. The placement of a LAMS was successful in 24/27 patients (89%), and placement of FCSEMS through the LAMS was successful in 20/24 patients (83%), in the remaining 4 patients a coaxial double pigtail stent was placed. In 2 patients there was persistent cholestasis requiring stent revision (10%), leading to a clinical success rate of 90%. No patients developed stent dysfunction after initial clinical success.

Periprocedural AEs occurred in 3 patients (11%) due to LAMS maldeployment which was solved intraprocedurally in all patients. In 1 patient this led to biliary peritonitis and fluid collections requiring percutaneous drainage, the other 2 patients recovered uneventfully.

Two patients experienced cholecystitis within 30 days after the procedure (10%), one patient who also had concomitant renal failure subsequently deceased.

The other patient recovered after antibiotics and percutaneous drainage. Two other patients deceased within 30 days which was unrelated to the procedure.

Median age, y (IQR)	69 (62.5-77.5)
Male sex, n (%)	14 (51.9)
Type of tumor, n (%)	
· Pancreatic ductal adenocarcinoma	27 (100)
Tumor stage, n (%)	
· Resectable	16 (59.3)
· Locally advanced	5 (18.5)
· Metastatic	6 (22.2)
Median serum total bilirubin, $\mu\text{mol/L}$ (IQR)	224 (182-336.5)
Median diameter common bile duct, mm (IQR)	16 (16-20)

Table. Baseline characteristics in 27 patients undergoing EUS-CDS.

Conclusion: This study showed a stent dysfunction rate of 10% following technically successful EUS-CDS with placement of a FCSEMS through the LAMS. Improving the LAMS design may reduce the rate of stent dysfunction by improving the direction of bile flow through the stent towards the descending duodenum.

References: 1. Teoh AYB, Napoleon B, Kunda R et al. EUS - guided choledochoduodenostomy using lumen apposing stent versus ERCP with covered metallic stents in patients with unresectable malignant distal biliary obstruction. A multi-center randomized controlled trial. (DRA-MBO trial). *Gastroenterology*. 2023.

2. Chen YI, Sahai A, Donatelli G et al. Endoscopic Ultrasound-Guided Biliary Drainage of First Intent With a Lumen-Apposing Metal Stent vs Endoscopic Retrograde Cholangiopancreatography in Malignant Distal Biliary Obstruction: A Multicenter Randomized Controlled Study (ELEMENT Trial). *Gastroenterology*. 2023.

3. Vanella G, Bronswijk M, Dell'Anna G et al. Classification, risk factors, and management of lumen apposing metal stent dysfunction during follow-up of endoscopic ultrasound-guided choledochoduodenostomy: Multicenter evaluation from the Leuven-Amsterdam-Milan Study Group. *Dig Endosc*. 2023.

4. Fritzsche JA, Fockens P, Besselink MG et al. Endoscopic ultrasound-guided choledochoduodenostomy using single-step lumen-apposing metal stents for primary drainage of malignant distal biliary obstruction (SCOR-PION-p): a prospective pilot study. *Endoscopy*. 2023.

5. El Chafic AH, Shah JN, Hamerski C et al. EUS-Guided Choledochoduodenostomy for Distal Malignant Biliary Obstruction Using Electrocautery-Enhanced Lumen-Apposing Metal Stents: First US, Multicenter Experience. *Dig Dis Sci*. 2019.

Disclosure: Jeska A. Fritzsche, Marc G. Besselink, Olivier R. Busch and Mattheus C.B. Wielenga have no conflicts of interest or financial ties to disclose. Paul Fockens performed as a consultant for Olympus and Cook Endoscopy. Freek Daams reports research grants from Medtronic, and received speaker's fees from Medtronic, and proctoring fees from Intuitive. Johanna W. Wilmink reports research grants from Servier, Merck, Nordic and Astra Zeneca. Rogier P. Voermans reports research grants from Boston Scientific and Prion Medical, performed as a consultant for Boston Scientific, and received speaker's fees from Mylan and Zambon. Roy L.J. van Wanrooij performed as a consultant for Boston Scientific. All outside the submitted work.

PP1090

ENDOSCOPIC ULTRASOUND-GUIDED TECHNIQUES FOR BILIARY DRAINAGE - COMPARATIVE ANALYSIS OF SINGLE CENTER DATA

Y. Petkova¹, P. Karagoyzov¹

¹Acibadem City Clinic University Hospital Tokuda, Clinic of Gastroenterology, Sofia, Bulgaria

Contact E-Mail Address: petko.karagoyzov@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography /ERCP/ is the standard technique in the treatment of unresectable malignant biliary obstruction/MBO/, unfortunately, a failure rate of 3% up to 12 % and a rate of complications up to 6,85% have been reported in the literature. Endoscopic ultrasound-guided biliary drainage/EUS – BD/ is a feasible alternative for biliary drainage, applicable especially with surgically altered anatomy. With several techniques available, hepaticogastrostomy /EUS - HGS/ and choledochoduodenostomy/EUS - CDS/ are most commonly performed amongst them.

Aims & Methods: To compare the most commonly used techniques for endoscopic ultrasound-guided biliary drainage in terms of efficacy and safety.

Methods: Retrospective analysis of a prospective database of patients undergoing EUS -BD in a single tertiary referral center. EUS-BD was performed after the failure of ERCP or as a first choice of drainage procedure in patients with altered anatomy. 102 patients were included in the EUS-HGS group 94,12%(n=96) with malignant biliary obstruction and 5.12%(n=6) with benign underlying disease. Of 24 patients included in the EUS-CDS group 95,83% (n=23) had underlying malignancy against one patient with benign disease.

Results: Considering the application of EUS – BD as a first choice of drainage procedure for patients with surgically altered anatomy we had 46 patients in the HGS group (45.1%) against 16.67%(n=4) for the CDS group. In 56/44,44%/ cases EUS BD was performed during the same session after unsuccessful cannulation. Evaluating results in terms of technical success rate, defined as successful stent placement – we found a 98,04 % success rate for the EUS-HGS group and 95,83% in the EUS-CDS group. We defined clinical success as a drop in the bilirubin levels by one-half in the first week following the procedure. The results between the two groups were not significantly different - 80.46% for the HGS against 80,95% for the CBS group. Concerning adverse events during the procedure, we found a ratio of 7.84% for the patients undergone HGS and 4,76% for EUS – CDS with no significant difference. The most common AE found was proximal stent misdeployment/n=3/. All of the events were managed either conservatively or during the same session with the placement of fully covered SEMS. Concerning early AE /during the first 7 days / we experienced 14,71% early

adverse events in the HGS group/ $n=15/$ and 16,67%/ $n=4/$ in the CDS group with most common event postprocedure infection with no significant difference.

Conclusion: The two most common transluminal techniques for EUS biliary drainage - HGS and CDS are a promising tool with comparable technical and clinical success rates, adverse events, and overall survival. Both procedures are valid alternatives after failed ERCP or as a first step especially in patients with surgically altered anatomy.

Disclosure: Nothing to disclose.

PP1091

WITHDRAWN

PP1092

TRANS-DUODENAL GALLBLADDER EUS-GUIDED DRAINAGE: A SINGLE CENTER EXPERIENCE

M. Marasco¹, S. Godat², B. Annibale³, F. Panzuto³, D. Galasso⁴

¹Digestive Disease Unit, Sant'Andrea University Hospital, Department of Medical-Surgical Sciences and Translational Medicine, Sapienza University, Rome, Italy, ²Service de gastroentérologie et d'hépatologie, CHUV, Université de Lausanne, Lausanne, Switzerland, ³Digestive Disease Unit, Sant'Andrea University Hospital, Department of Medical Surgical Sciences and Translational Medicine, Sapienza University, Rome, Italy, ⁴Gastroenterology Unit, Hopital Riviera Chablais Gastroenterologie, Rennaz (Vaud), Switzerland

Contact E-Mail Address: matteomarasco93@gmail.com

Introduction: Endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) is becoming an important and effective alternative to percutaneous drainage (PTD) for patients not suitable for surgery. It is also an acceptable option for biliary drainage in oncologic patient, if retrograde drainage failed. Placing of a lumen apposing metal stent (LAMS) for EUS-GBD allows the removal of gallbladder stones too, so becoming a possible alternative to surgery in very selected cases.

Aims & Methods: The study aims to describe our endoscopic experience and management in patients unfit for surgery and in those oncologically advanced. Retrospectively analyzed cases with EUS-GBD, from December 2019 to September 2023, in a single peripheral hospital (Hopital Riviera-Chablais), using 3 types of LAMS (10x10mm, 15x10mm, 16x20mm), delivered with an electrocautery-enhanced catheter.

Results: EUS-GBD was performed in 23 patients (15:8=M:F) with median age of 83 years old (52-89). 13 patients (56.2%) had advanced cancer (6 pancreatic metastatic cancer, 5 cholangiocarcinoma, 1 breast metastatic cancer, 1 metastatic pulmonary NET) and 10 patients were affected by symptomatic lithiasic cholecystitis and they were not considered fit for surgery (whose 2 already received a PTD). EUS-GBD was attempted through the duodenum in all cases but one, previously treated with PTD and that was drained through the stomach.

In one case, the stent was mis-deployed through the duodenum (without entering the gallbladder lumen), so requiring the placement of an over-the-scope-clip and a different biliary drainage for biliary obstruction in an oncological patient. A 15x10 mm LAMS was used in 14 cases, 10x10 mm LAMS was used in 6 cases (including the failed one), and 16x20 mm in 2 cases. A double pigtail 5 Fr 7cm was placed through all 22 successfully placed LAMS. 3 patients underwent electrohydraulic-lithotripsy (EHL) through the LAMS after 4-8 weeks. In 5 patients LAMS was then removed.

Generally, except one complication, it was not described short term or long-term adverse events. 6/23 (26%) patients died for oncological disease progression and for other causes not procedure related.

Conclusion: EUS-GBD represents a promising therapeutic approach in patients with high risk of mortality. Considering the high rate of clinical and technical success as well as the possibility of managing endoscopically potential complications, this approach could be also proposed in peripheral centers and not only in advanced endoscopic ones.

References:

1. Anthony Yuen Bun Teoh et al. EUS-guided gallbladder drainage versus laparoscopic cholecystectomy for acute cholecystitis: a propensity score analysis with 1-year follow-up data, *Gastrointestinal Endoscopy*, Volume 93, Issue 3, 2021.
2. van der Merwe SW et al. Therapeutic endoscopic ultrasound: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2022 Feb;54(2):185-205.
3. McDonagh, P et al. Endoscopic Ultrasound-Guided Gallbladder Drainage for Malignant Biliary Obstruction: A Systematic Review. *Cancers* 2023, 15, 2988.

Disclosure: Nothing to disclose.

PP1093

WITHDRAWN

PP1094

SAFETY OF ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHO-DUODENOSTOMY IN PATIENTS WITH MALIGNANT OBSTRUCTION AND ASCITES

A. Kulkarni¹, S. Mukewar¹, A. Daphale¹, B. Bhaware¹, S.V. Mukewar¹, A. Patel¹

¹Midas Multispeciality Hospital, Midas Heights, Gastroenterology, Nagpur, India

Contact E-Mail Address: akshaykulkarni262@gmail.com

Introduction: Ascites of any etiology presents a major problem in patients with malignant biliary obstruction (MBO) and failed ERCP, where trans-mural drainage is indicated, but presumed to be unsafe due to the risk of bile leak. We planned to evaluate the safety of Endoscopic Ultrasound-guided choledochoduodenostomy (EUS-CDS) in our patients with ascites.

Aims & Methods: We planned to evaluate the safety of endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) in malignant biliary obstruction (MBO) and ascites in a retrospective study. Prospectively maintained records of consecutive patients with MBO, with or without ascites, and undergoing EUS-CDS for biliary drainage, were retrospectively analysed. Technical success was defined as successful stent deployment, while clinical success was defined as biliary decompression (biochemical and radiological), and relief in cholangitis. Complications such as bile leak, fever and abdominal pain were recorded, and the data were compared between patients with and without ascites.

Results: Between November 2019 and March 2024, 60 patients underwent EUS-CDS for MBO. Of these, 38 (65%) were males and the mean age was 61.49 years. At the time of the procedure, 18 patients had ascites (30%) had ascites, of which 11 had Grade II and 7 had Grade III ascites. The most common malignancies were pancreatic cancer (28), peri-ampullary carcinoma (12) and distal cholangiocarcinoma (9).

Other lesions seen were duodenal cancer (5), malignant lymph node metastases causing MBO (4) and gall bladder cancer (2). Technical success was achieved in 100% procedures, and clinical success was also achieved in all

the patients. In the group with ascites, 3 patients had bile leak, which was managed conservatively with percutaneous trans-hepatic biliary drainage (PTBD). One patient had fever responsive to antibiotics; the other two had mild abdominal pain responding to analgesics. In the group without ascites, two patients had bile leak, one had mild pain, and the other two had self-limited fever.

Conclusion: EUS-guided drainage is generally presumed to be contraindicated in the presence of ascites [1].

EUS-hepatico-gastrostomy has been shown to be safe in the presence of ascites [2].

Our study shows that EUS-CDS is safe & effective in MBO with ascites. Further, larger studies are needed to evaluate its long-term safety and the effect on the survival and quality of life of the patients.

References:

1. Sundaram S, Dhir V. EUS-guided biliary drainage for malignant hilar biliary obstruction: A concise review. *Endosc Ultrasound*. 2021 May-Jun;10(3):154-160. doi: 10.4103/EUS-D-21-00004.
2. I.Yasuda T, Hara K, Mizuno N et al. Safety of endoscopic ultrasound-guided hepatico-gastrostomy in patients with malignant biliary obstruction and ascites. *Clin Endosc*. 2023 Sep 7. doi: 10.5946/ce.2023.075

Disclosure: Nothing to disclose.

PP1095

ENHANCING MRCP PRECISION: A COMPREHENSIVE ANALYSIS OF THE IMPACT OF INTRAMUSCULAR GLUCAGON ADMINISTRATION ON BILIARY VISUALIZATION

F. Abu Baker¹, O. Shibolet², R. Taher Natour¹, D. Nicola¹, A. Beshara¹, O. Gal¹, A.-R. Zeina³

¹Hillel Yaffe medical center, Gastroenterology and hepatology, Hadera, Israel, ²Tel-Aviv Medical Center, Gastroenterology, Tel-Aviv, Israel, ³Hillel Yaffe medical center, Radiology, Hadera, Israel

Contact E-Mail Address: randataher12@gmail.com

Introduction: Magnetic resonance cholangiopancreatography (MRCP) has continuously evolved to enhance visualization capabilities. However, diagnosing biliary ductal system pathology, particularly early Primary sclerosing cholangitis (PSC), remains challenging.

Aims & Methods: This study investigates the influence of intramuscular glucagon (IMG) administration on final image quality and pancreato-biliary ductal system diameter in MRCP.

Forty patients (57.5% female; average age 34.45 ± 8.2) referred for Magnetic Resonance Enterography (MRE) underwent MRCP before and 8-12 minutes after IMG administration. Coronal T2-weighted fast spin-echo high-resolution 3D MRCP images were analyzed quantitatively and qualitatively by two independent MRI specialists. Quantitative assessments included transverse diameter measurements of 5 predefined biliary ductal (CBD, LHD, RHD...) and 3 pancreatic duct segments (head, body, tail). Qualitative evaluation used a five-point Likert-type scale (1=perfect visualization; 5=not visible) for the respective predefined segments. Interobserver variation was assessed using the Intraclass Correlation Coefficient (ICC).

Results: Following IMG administration, the diameters of all corresponding biliary and pancreatic segments significantly increased, with consistently strong interobserver agreement demonstrated pre and post IMG administration. Moreover, in qualitative analysis, post-IMG administration scores indicated a significant decrease ($P < 0.01$) in visualization scores, signifying improved visualization at all corresponding points for both radiologists compared to the pre-glucagon administration scores. The ICC scores pre and post IMG administration demonstrated moderate to strong agreement.

Conclusion: IMG administration improves MRCP imaging parameters by increasing ductal diameters and enhancing biliary tree visualization, underscoring its potential to aid in the detection of subtle or early pathological changes.

Disclosure: Nothing to disclose.

PP1096

WITHDRAWN

PP1097

EFFICACY AND SAFETY OF SEQUENTIAL CUTTING OF NASOBILIARY TUBES AS AN ALTERNATIVE TO STENT PLACEMENT AFTER NASOBILIARY DRAINAGE FOR THE TREATMENT OF HILAR MALIGNANT BILIARY STRICTURE

W. Chen^{1,2,3,4}, J. Yang^{2,3,4,5}

¹Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou, China, ²Department of Gastroenterology, Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, China, ³Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China, ⁴Hangzhou Institute of Digestive Diseases, Hangzhou, China, ⁵Key Laboratory of Clinical Cancer Pharmacology and Toxicology Research of Zhejiang Province, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: Hilar malignant biliary stricture, caused by malignant tumors, often leads to late diagnosis due to subtle initial symptoms, resulting in poor outcomes. Effective endoscopic interventions significantly improve quality of life and survival, yet often lead to post-operative complications like cholangitis.

Aims & Methods: This study aims to assess the effectiveness and safety of utilizing sequential nasobiliary tube cutting as an alternative to stent placement post-nasobiliary drainage in patients, specifically in mitigating post-operative cholangitis. Additionally, to identify risk factors associated with the development of post-operative cholangitis.

Patients diagnosed at Hangzhou First People's Hospital from January 2015 to January 2023 were divided into nasobiliary tube cutting group and conventional stent group. The former underwent nasobiliary drainage followed by tube cutting when stable, transitioning from external to internal drainage, while the latter received standard stent placement. Statistical analyses compared postoperative cholangitis incidence, drainage success, interventions, complications, and hospital stay, further examining risk factors for postoperative cholangitis.

Results: 1. This study encompassed a total of 208 patients, with 103 in the nasobiliary tube cutting group and 105 in the conventional stent group. Postoperative cholangitis occurred in 40 patients, with 12 cases (11.7%) in the nasobiliary tube cutting group and 28 cases (26.7%) in the conventional stent group, showing a statistically significant difference between the two groups ($P=0.006$). The number of patients whose total bilirubin levels decreased by more than 50% within 7 days postoperatively was 50 (48.5%) in the nasobiliary tube cutting group and 29 (27.6%) in the conventional stent group, a statistically significant difference favoring the nasobiliary tube cutting group ($P=0.002$). There was no statistically significant difference in the overall drainage success rate between the two groups ($P=0.207$). Besides postoperative cholangitis, there were no statistically significant differences in other postoperative complications between the two groups ($P>0.05$). The postoperative hospital stay was

longer for patients in the nasobiliary tube cutting group than those in the conventional stent group, with median durations of 10.0 (7.0, 14.0) days versus 7.0 (5.5, 12.5) days, respectively, a difference that was statistically significant ($P=0.024$).

2. Based on whether postoperative cholangitis occurred, the patients were further categorized into a postoperative cholangitis group ($n=40$) and a non-postoperative cholangitis group ($n=168$). Univariate analysis revealed significant differences between the postoperative cholangitis group and the non-postoperative cholangitis group in terms of gender (male), Bismuth-Corlette classification (Type IV), number of ERCP procedures (≥ 2 times), and re-intervention ($P<0.05$). Multivariate logistic regression analysis identified Bismuth-Corlette classification (Type IV) ($OR=3.207$, 95%CI: 1.253-8.210, $P=0.015$) as an independent risk factor for developing postoperative cholangitis.

Conclusion: For patients with hilar malignant biliary stricture, sequential cutting of nasobiliary tubes as an alternative to stent placement after nasobiliary drainage can reduce the incidence of postoperative cholangitis and achieve early successful drainage, but it results in a prolonged postoperative hospital stay. Bismuth-Corlette classification (Type IV) is an independent risk factor for the development of postoperative cholangitis.

References:

- [1] VALLE J W, KELLEY R K, NERVI B, et al. Biliary tract cancer [J]. *Lancet* (London, England), 2021, 397(10272): 428-444.
- [2] KHALAF N, EL-SERAG H B, ABRAMS H R, et al. Burden of Pancreatic Cancer: From Epidemiology to Practice [J]. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, 2021, 19(5): 876-884.
- [3] ELMUNZER B J, MARANKI J L, GÓMEZ V, et al. ACG Clinical Guideline: Diagnosis and Management of Biliary Strictures [J]. *Am J Gastroenterol*, 2023, 118(3): 405-426.
- [4] PIMPINELLI M, MAKAR M, KAHALEH M. Endoscopic management of benign and malignant hilar stricture [J]. *Digestive endoscopy: official journal of the Japan Gastroenterological Endoscopy Society*, 2023, 35(4): 443-452.
- [5] BANG J Y, HAWES R, VARADARAJULU S. Endoscopic biliary drainage for malignant distal biliary obstruction: Which is better - endoscopic retrograde cholangiopancreatography or endoscopic ultrasound? [J]. *Digestive endoscopy: official journal of the Japan Gastroenterological Endoscopy Society*, 2022, 34(2): 317-324.
- [6] IRISAWA A, MIYOSHI H, ITOI T, et al. Recent innovations in therapeutic endoscopy for pancreatobiliary diseases [J]. *Digestive endoscopy: official journal of the Japan Gastroenterological Endoscopy Society*, 2020, 32(3): 309-315.

Disclosure: The authors declare that there are no conflicts of interest.

PP1098

LONG-TERM RESULTS ON TREATMENT OF HEPATICOJEJUNOSTOMY ANASTOMOTIC STRICTURE WITH FCSEMS BY SINGLE BALLOON ENTEROSTOMY & EUS

M. Kida¹, K. Okuwaki¹, T. Hanaoka¹, A. Tamaki¹, K. Adachi¹, J. Ishizaki¹, M. Watanabe¹, T. Iwai¹, C. Kusano¹

¹Kitasato University, Endoscopy Center, Sagami-hara, Japan

Contact E-Mail Address: m-kida@kitasato-u.ac.jp

Introduction: Hepaticojejunostomy anastomotic stricture (HJAS) is one of the common adverse events after bile duct reconstruction surgery, which is reported to occur in 3–13%. Endoscopic approach using BE-ERCP has become the first choice due to less invasiveness, and long-term resolution rate is reported 50-90%.

Aims & Methods: In order to treat symptomatic hepatico-jejunostomy anastomosis stenosis (HJAS), we firstly perform balloon dilation or plastic

stent or fully covered self-expandable metallic stent (FCSEMS) by single balloon ERCP (SBE-ERCP) and secondary insert FCSEMS by EUS-BD, in cases of severe stenosis or non-canalulation.

Then we have investigated the efficacy of FCSEMS for HJAS. From January 2015 to December 2022, we have performed 698 procedures of SBE-ERCP in 348 cases and inserted FCSEMS in 37 cases with symptomatic HJAS (only benign cases, excluded malignancy). We have planned to deploy FCSEMS for 6 months and removed it after that. Then we investigated resolution rate of HJAS at removing FCSEMS, complication, and long-term resolution rate of HJAS after FCSEMS.

Results: Subjects were Male 26: Female 11 and Median age was 70 y/o. Surgical operation were 33 cases in B-II+PPPD/ 4 cases in R-Y. Reason of deploying FCSEMS by SBE-ERCP were unresolved stenosis by balloon dilation or plastic stent (PS) in 29 cases. And FCSEMS for severe stenosis in 6 cases were inserted by direct EUS-Choledocho-jejunostomy (EUS-CJS) and undetectable HJA in 2 cases by Rendezvous EUS-HGS. Additionally, side by side PS were inserted in 32 cases.

Finally total subjects were 36, except for 1 case not reached to 6 months. Although 1 FCSEMS migrated into intrahepatic bile duct, 21 FCSEMS were removed endoscopically and remaining 15 FCSEMS were spontaneously dislocated after resolving HJAS. Resolution rate of HJAS at removing FCSEMS were 92% (33/36). Remained 3 cases were treated by additional deploying FCSEMS for 141 days in average.

In median 19.0 (0.4-69.1) months followed up period, complications were non-obstructive cholangitis in 8 cases which were treated conservatively and intrahepatic stone in 2 cases which were treated by SBE.

Resolution rate of HJAS at 1, 2, 3 years was 100%, 100%, and 100%. Recurrent HJAS occurred in 1 case at 46 months and treated by re-FCSEMS for 189 days.

Conclusion: Treatment of HJAS by FCSEMS were effective in long term period. SBE, EUS-CJS, and EUS-HGS were complimentary each other.

Disclosure: Nothing to disclose.

PP1099

SAFETY AND EFFICACY OF KAFFES INTRADUCTAL SELF-EXPANDING METAL STENTS IN THE MANAGEMENT OF POST-LIVER TRANSPLANT ANASTOMOTIC STRICTURES

C. Lim¹, J. Ng¹, B. Sarraf¹, R. Vaughan², M. Efthymiou¹, L.Z.C.T. Pu¹, S. Chandran¹

¹Austin Health, Gastroenterology and Hepatology, Heidelberg, Australia, ²Austin Hospital, Ivanhoe, Australia

Contact E-Mail Address: raselith@gmail.com

Introduction: Endoscopic management is the first-line therapy for post-liver-transplant anastomotic strictures. Although the optimal duration of treatment with plastic stents has been reported to be 8-12 months, data on safety and duration for metal stents in this setting is scarce. Due to limited access to endoscopic retrograde cholangiopancreatography (ERCP) during the COVID-19 pandemic in our centre, there was a change in practice towards increased usage and length-of-stay of the Kaffes biliary intraductal self-expanding stent in patients with suitable anatomy. This was mainly due to the theoretical benefit of Kaffes stents allowing for longer indwelling periods compared to the traditional plastic stents.

Aims & Methods: To compare the safety and efficacy profile of different stenting durations using Kaffes stents.

Adult liver transplant recipients aged 18 years and above who underwent ERCP were retrospectively identified during a 10-year period through a database query. Unplanned admissions post-Kaffes stent insertion were identified manually through electronic and scanned medical records. The main outcome was the incidence of complications when stents were left

indwelling for 3 months vs 6 months. Stent efficacy was calculated via rates of stricture recurrence between patients that had stenting courses for ≤ 120 d or > 120 d.

Results: During the study period, a total of 66 ERCPs with Kaffes insertion were performed in 54 patients throughout their stenting course. In 33 ERCPs, the stent was removed or exchanged on a 3-month interval. No pancreatitis, perforations or deaths occurred. Minor post-ERCP complications were similar between the 3-month (abdominal pain and intraductal migration) and 6-month (abdominal pain, septic shower and embedded stent) groups - 6.1% vs 9.1% respectively, $P = 0.40$. All strictures resolved at the end of the stenting course, but the stenting course was variable from 3 to 22 months. The recurrence rate for stenting courses lasting for up to 120 d was 71.4% and 21.4% for stenting courses of 121 d or over ($P = 0.03$). There were 28 patients that were treated with a single ERCP with Kaffes, 21 with removal after 120 d and 7 within 120 d. There was a significant improvement in stricture recurrence when the Kaffes was removed after 120 d when a single ERCP was used for the entire stenting course (71.0% vs 10.0%, $P = 0.01$).

Conclusion: Utilising a single Kaffes intraductal fully-covered metal stent for at least 4 months is safe and efficacious for the management of post-transplant anastomotic strictures.

Disclosure: Nothing to disclose.

PP1100

WHAT IS THE BEST ULTRASOUND-GUIDED BILIARY DRAINAGE STRATEGY IN CASE OF GASTRIC OUTLET OBSTRUCTION? A MULTICENTER RETROSPECTIVE STUDY

T. Beuchard¹, J.P. Ratone², M. Schaefer³, R. Legros¹, J. Albouys¹, H. Lepetit¹, M. Dahan¹, F. Caillol², M. Giovannini², J.-B. Chevaux³, M. Barthet⁴, I. Boutellier⁴, L. Poincloux⁵, T. Guilmoteau⁵, T. Wallenhorst⁶, T. Grainville⁶, Y.-I. Chen⁷, Y. Charif⁷, F. Farimah⁸, M.A. Khashab⁸, E. Perez-Cuadrado-Robles⁹, A. Debourdeau¹⁰, Y. Dahel², J.-M. Gonzalez⁴, J. Jacques¹

¹CHU Limoges, Limoges, France, ²Institut Paoli-Calmettes, Department of Endoscopy, Marseille, France, ³CHU Nancy, Nancy, France, ⁴Hopital Nord, Gastroenterology, Marseille, France, ⁵CHU Clermont-Ferrand, Service de Médecine Digestive et Hépatobiliaire, Clermont-Ferrand, France,

⁶CHU Rennes-Pontchaillou, Endoscopy Unit, Rennes, France, ⁷McGill University Health Center, Montreal, Canada,

⁸The Johns Hopkins Hospital, Baltimore, United States of America, ⁹Georges-Pompidou European Hospital, Department of Gastroenterology, Paris, France, ¹⁰CHU de Montpellier, Gastroentérologie et Transplantation Hépatique, Montpellier, France

Contact E-Mail Address: thomas.beuchard@gmail.com

Introduction: Pancreatic cancers are dramatically increasing. At an advanced stage, pancreatic cancers can cause biliary obstruction (BO) and gastric outlet obstruction (GOO). The coexistence of BO and GOO is not uncommon and can lead to the inability to access the papilla resulting in ERCP failure or impossibility. The development of therapeutic endoscopic ultrasonography (EUS) has created new treatment options for double stenosis management. Optimising nutritional status by appropriate GOO management and an efficient biliary drainage are an important part of the oncological treatment of these patients.

This study aimed to compare the EUS-biliary drainage efficiencies in case of GOO in order to find the best therapeutic strategy.

Aims & Methods: We conducted an international multicenter retrospective study in 10 centers. All patients who underwent EUS-guided cho-

ledochoduodenostomy (EUS-CDS) or hepaticogastrostomy (EUS-HGS) between 2017 and 2023 for biliary obstruction that occurred simultaneously or after the management of duodenal obstruction were eligible for inclusion.

Patients with previous biliary drainage or a post-procedural follow-up shorter than 30 days (unless death occurs before) were excluded. Patients were followed until death or if they underwent pancreaticoduodenectomy.

Primary outcome was the rate of biliary stent obstruction requiring a new intervention. Secondary outcomes included technical and clinical success (defined as a reduction of bilirubin levels by at least 50 % at day 15 or normalization at day 30) and procedure-related adverse events.

Results: 204 patients from 10 centers have been included. The mean age was 70 years [62-78]. The mean bilirubinemia was 162.8 $\mu\text{mol/L}$ (+/- 124.61). 65 % suffered from pancreatic cancer and more than half had a metastatic disease. 12.3 % had ascite. 79.9 % of patients underwent management for simultaneous biliary and gastric outlet obstruction.

The biliary drainage technical success was 96 % and the clinical success was 88 %. 33.3 % were treated by EUS-CDS + enteral stenting (ES) combination (A), 4.4 % by EUS-CDS + EUS-guided gastroenterostomy (EUS-GE) (B), 42.6 % by EUS-HGS + ES (C) and 19.6 % by EUS-HGS + EUS-GE (D).

The median follow-up was 95 days but 84.8 % of the patients died at the end of the follow-up. No difference was observed between the groups in term of technical success and clinical success (respectively $p=0.359$ and $p=0.899$).

The post procedural severe adverse events (AGREE ≥ 3) rate was 9.3 % with a significative difference between combinations (A = 4.3 % ; B = 0 % ; C = 15.1 % ; D = 7.5 % ; $p = 0.022$), occurring more frequently in patients treated with EUS-HGS.

The biliary stent obstruction rate during follow-up was 16.2% with a significative difference between groups (A = 16.4 % ; B = 44.4 % ; C = 21.5 % ; D = 5.1 % ; $p = 0.023$ %), in favour of EUS-HGS + EUS-GE combination.

Conclusion: Patients suffering from combined BO and GOO have a poor prognostic. The combination of EUS-HGS + EUS-GE appears to be the most effective in reducing the rate of biliary stent dysfunction. However, this efficacy comes at the cost of severe adverse events, suggesting that these fragile patients should be managed in a centre of adequate expertise.

Disclosure: Nothing to disclose.

PP1101

EUS-CDS IS ASSOCIATED WITH LESS COMPLICATIONS COMPARED TO PTBD AFTER A FAILED ERCP IN PATIENTS WITH A DISTAL MALIGNANT COMMON BILE DUCT OBSTRUCTION: PROSPECTIVE OUTCOMES OF A DUTCH REGISTRY

M.J. de Jong¹, F. van Delft¹, E.-J.M. Van Geenen¹, A. Bogte², R.C. Verdonk³, N.G. Venneman⁴, J.M. Vrolijk⁵, J.W.A. Straathof⁶, R. Bijlsma⁷, S. Kuiken⁸, R. Quispel⁹, M. Hadithi¹⁰, K.V. Basiliya¹¹, F.P. Vleggaar², T.M. Bisseling¹, T. de Wijkerslooth¹², M.J. Bruno¹³, R.L. Van Wanrooij¹⁴, P.D. Siersema^{13,1}

¹Radboud University Medical Center, Gastroenterology & Hepatology, Nijmegen, Netherlands, ²University Medical Center Utrecht, Gastroenterology & Hepatology, Utrecht, Netherlands, ³St. Antonius Ziekenhuis, Gastroenterology & Hepatology, Nieuwegein, Netherlands, ⁴Medisch Spectrum Twente, Gastroenterology & Hepatology, Enschede, Netherlands, ⁵Rijnstate Hospital, Gastroenterology & Hepatology, Arnhem, Netherlands, ⁶Máxima Medical Center, Gastroenterology & Hepatology, Veldhoven, Netherlands, ⁷Martini Hospital, Gastroenterology & Hepatology, Groningen, Netherlands, ⁸Onze Lieve Vrouwe Gasthuis, Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁹Reinier de Graaf Gasthuis, Gastroenterology & Hepatology, Delft, Netherlands, ¹⁰Maasstad Hospital, Gastroenterology & Hepatology, Rotterdam, Netherlands, ¹¹Leiden University Medical Center, Gastroenterology & Hepatology, Leiden, Netherlands, ¹²Antoni van Leeuwenhoek Hospital, Gastroenterology & Hepatology, Amsterdam, Netherlands, ¹³Erasmus University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands, ¹⁴Amsterdam University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: mike.dejong@radboudumc.nl

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) with placement of a self-expanding metal stent (SEMS) is the gold standard for drainage in case of malignant obstruction of the distal common bile duct (CBD). Nevertheless, 12.5% of these procedures fail. Percutaneous transhepatic biliary drainage (PTBD) is the most frequently used alternative, despite a reported 30-day mortality of 15-20% and morbidity of up to 60%. EUS-guided choledochoduodenostomy (EUS-CDS) with a lumen apposing metal stent (LAMS) is an emerging alternative drainage modality. Data on the long-term outcomes of these alternative techniques are limited.

Therefore, this Dutch registry aimed to provide insight in the chosen drainage modality after a failed ERCP-procedure and evaluated the outcomes prospectively.

Aims & Methods: This multicenter investigator-initiated registry included consecutive patients with malignant obstruction of the distal CBD after an unsuccessful ERCP over an inclusion period of 18 months. Patients were treated by either EUS-CDS or PTBD based by discretion of the endoscopist. Follow-up duration was 180 days. Primary endpoints were procedure-related morbidity and mortality within 90 days post-procedure.

Results: In total, 55 patients were included in the registry. EUS-CDS was performed in 44 patients (technical success 98%) and PTBD in 11 patients (technical success 100%). Median post-procedural hospital stay was four days shorter in the EUS-CDS group compared to the PTBD group (1 day (IQR 1-2 days) vs. 5 days (IQR 2-6 days), respectively; $p=0.003$). Median bilirubin reduction after 30 days was 117.5 $\mu\text{mol/L}$ (IQR 50.3-210.0 $\mu\text{mol/L}$) in the EUS-CDS group and 102 $\mu\text{mol/L}$ (IQR 83-191 $\mu\text{mol/L}$) in the PTBD group ($p=1.00$). Furthermore, LAMS was in place for a median of 85.5 days (IQR 28.5-180 days), while the PTBD needed revision after 21 days (IQR 7-32 days; $p=0.001$). Procedure-related morbidity after 90 days was 54.5%

in the EUS-CDS group and 100% in the PTBD group ($p=0.004$). In the EUS-CDS group, 37.5% of the patients developed infectious complications and 48.5% non-infectious complications compared to 77.8%, and 72.7%, respectively in the PTBD-group.

Additionally, mortality rates within 90 days were higher in the PTBD group (63.6% vs 22.7%; $p=0.024$).

Conclusion: EUS-CDS is associated with less complications compared to PTBD after a failed ERCP in patients with malignant distal CBD obstruction, as it results in a shorter post-procedural hospital admission and lower morbidity and mortality rates. Although, a randomized controlled trial is needed to confirm this superiority.

Disclosure: Frank P. Vleggaar acts as a consultant for Boston Scientific. Marco J. Bruno received research support from Boston Scientific, Cook Medical, Pentax Medical, Mylan, ChiRoStim and acts as a consultant/lecturer for Boston Scientific, Cook Medical, Pentax Medical and AMBU. Roy L. J. van Wanrooij has a consultancy agreement with Boston Scientific. Peter D. Siersema reports research grants from Pentax and Fujifilm. All outside the submitted work. The other authors have nothing to disclose.

PP1102

WITHDRAWN

PP1103

SUPRA-PAPILLARY VERSUS TRANS-PAPILLARY STENTING FOR MALIGNANT BILIARY OBSTRUCTION: AN UPDATED META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

O. Martins¹, V. Antunes², C. Florêncio de Mesquita³, T. Correa⁴, M. Fernandes², N. Milioli⁵, A. Prata⁶, A. Milani⁷, A.C. Coan⁶, E. Bulhões⁸, P. Romeiro⁹, S. Baraldo¹⁰

¹Federal University of Juiz de Fora, Juiz de Fora, Brazil,

²Federal University of Health Sciences of Porto Alegre, Porto

Alegre, Brazil, ³Federal University of Pernambuco, Recife, Brazil,

⁴Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America, ⁵Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ⁶Federal University of Espirito Santo, Vitoria, Brazil, ⁷State University of Campinas, Campinas, Brazil, ⁸College of Higher Education of the United Amazon, Redenção, Brazil, ⁹University Center of Maceió, Maceió, Brazil, ¹⁰Department of Endoscopy, Barretos Cancer Hospital, Barretos, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Malignant biliary obstruction (MBO) encompasses a variety of malignancies arising from the pancreaticobiliary system. The relatively common occurrence of duodenobiliary reflux (DBR) in patients with transpapillary stent placement for palliative management raises the importance of the development of alternative methods to prevent adverse outcomes.

Aims & Methods: We aimed to compare supra-papillary to trans-papillary stenting in patients with MBO for stent dysfunction and adverse events. PubMed, Embase, and Cochrane were systematically searched for randomized controlled trials (RCTs). The primary outcome was stent occlusion. Secondary outcomes included stent migration, occurrence of cholangitis or pancreatitis, cumulative duration of stent patency in days, and patient survival in days. Statistical analyses were conducted using R (version 4.3.1) and a random-effects model was employed.

Results: We found 3 RCTs with 161 patients (80 in the supra-papilla stent group vs. 81 in the trans-papilla group). Supra-papillary stent placement was associated with significantly lower rates of stent occlusion (OR 0.42;

95% CI 0.20 to 0.87; $p = 0.019$), and longer cumulative duration of stent patency (MD 77.59; 95% CI 23.84 to 131.34; $p < 0.01$). The Trial Sequential Analysis for this outcome showed that this study has surpassed the required information size ($n = 158$) to ascertain the statistical difference for this outcome.

The analyses of stent migration ($p = 0.471$) occurrence of cholangitis ($p = 0.525$), and patient survival ($p = 0.05$) revealed no significant difference between both groups.

Conclusion: We found a significant improvement in stent occlusion rates and cumulative duration of stent patency favoring the supra-papilla group, with no difference for stent migration, occurrence of cholangitis, and patient survival for this comparison.

Disclosure: Nothing to disclose.

PP1104

LONG-TERM OUTCOMES OF BILIARY STENTING IN PATIENTS WITH UNRESECTABLE BILIOPANCREATIC MALIGNANCIES

J. Benass¹, C. Jioua¹, I. Mouslim¹, T. Addajou¹, R. Berraida¹, F. Rouibaa¹, H. Seddik¹

¹Mohammed V military teaching hospital, Gastroenterology II, Rabat, Morocco

Contact E-Mail Address: jihane.benass@gmail.com

Introduction: The prevalence of biliopancreatic malignancies is steadily increasing. Most patients are inoperable due to the typically advanced stage of the disease at the time of diagnosis and require biliary drainage. Despite numerous large-scale studies, the identification of predictive factors for survival in these cancers to improve their prognosis remains a challenge.

The aim of our study was to evaluate the survival of patients who underwent biliary stenting as part of the management of unresectable biliopancreatic malignancies and to assess the factors influencing the survival rate.

Aims & Methods: We conducted an observational cohort study between January 1, 2021, and March 28, 2024. All patients who underwent biliary drainage for obstructive jaundice due to biliopancreatic cancer (pancreatic head adenocarcinoma, peri-hilar cholangiocarcinoma, gallbladder cancer, ampulloma) were included. Contraindications to palliative chemotherapy were poor general condition (ECOG/WHO performance status 3 or more) and hyperbilirubinemia due to inadequate biliary drainage.

Results: 82 patients were included in our study. The mean age in our series was 63.4 $\pm$ 12 years. The sex ratio was 1. The median survival was 350 days (95% CI 268 – 514). 49.4% had pancreatic head adenocarcinoma, 30.6% had cholangiocarcinomas, 10% had ampullomas, and 10% had gallbladder cancer.

The median survival for pancreatic head adenocarcinoma was 450 days vs. 562 days for ampullomas, 356 days for cholangiocarcinomas, and 301 days for gallbladder cancer.

The type of cancer did not have a statistically significant difference on median survival ($p = 0.95$).

15% of patients had failed ERCP and underwent percutaneous biliary drainage. They had a 2.5 times higher risk of death (RR = 2.57, 95% CI 1.26-5.25, $p = 0.01$). Indeed, the median survival without death in cases of percutaneous drainage was 39 days vs. 375 in cases of successful ERCP ($p = 0.007$).

65% of patients were able to undergo palliative chemotherapy after stenting. The median survival with chemotherapy was 562 days vs. 30 days for patients who could not initiate it ($p < 0.001$). The latter had a 10 times higher risk of death in the month following stent placement (RR = 10.7, 95% CI 5.23-21.9, $p < 0.001$).

In our series, the presence of pancreatic head adenocarcinoma was associated with a higher probability of receiving chemotherapy ($p = 0.04$). However, it did not have a significant impact on median survival.

In multivariate analysis, only palliative chemotherapy seemed to improve the survival median ($p < 0.001$), while recurrence of jaundice and stent occlusion were associated with death ($p = 0.03$).

Conclusion: According to the results of our study, the prognosis of unresectable biliopancreatic cancers is poor but appears to be improved by a successful biliary stenting. Patients in whom biliary stent placement was a bridging procedure that allows chemotherapy seem to have higher survival rates. The generalization of endoscopic ultrasound-guided biliary drainage as an alternative to biliary percutaneous drainage could improve the survival rate in patients with failed ERCP.

Disclosure: Nothing to disclose.

PP1105

BRAIDED-TYPE STENT VERSUS LASER-CUT-TYPE STENT FOR PATIENTS WITH DISTAL MALIGNANT BILIARY OBSTRUCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Prata¹, V. Antunes², A.C. Covre Coan¹, O. Martins³, M.V. Fernandes², N.J. Milioli⁴, T. Correa⁵, E. Bulhões⁶, P. Romeiro⁷, A. Reis⁸

¹Federal University of Espírito Santo, Vitória, Brazil,

²Federal University of Health Sciences of Porto Alegre, Porto

Alegre, Brazil, ³Federal University of Juiz de Fora, Juiz de Fora,

Brazil, ⁴Pontifical Catholic University of Rio Grande do Sul, Porto

Alegre, Brazil, ⁵Beth Israel Deaconess Medical Center/Harvard

Medical School, Boston, United States of America, ⁶College

of Higher Education of the United Amazon, Manaus, Brazil,

⁷Department of Medicine, University Center of Maceió, Maceió,

Brazil, ⁸State University of Campinas, Faculdade de Medicina,

Campinas, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: There are two types of covered self-expandable metallic stents (CSEMS): laser-cut (L) and braided (B). The B-type has a strong axial force and can cause problems such as recurrent obstructive jaundice and cholangitis. The L-type is less stressful for the bile duct.

Aims & Methods: This study aims to compare CSEMS B-type versus L-type in patients with unresectable distal malignant biliary obstruction. We performed a systematic review in PubMed, Embase and Cochrane databases, searching for studies comparing both types of CSEMS in this population. The primary outcome was stent occlusion.

The secondary outcomes were tumor ingrowth, tumor overgrowth, stent migration, pancreatitis and cholecystitis. The odds ratio (OR) was used for binary outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I^2 statistics.

Results: The meta-analyses included 4 studies and 430 patients. There was no significant difference for any outcome: stent occlusion (OR 1.28; 95% CI 0.73 to 2.23; $p=0.388$; $I^2=0\%$), tumor ingrowth (OR 1.12; 95% CI 0.46 to 2.76; $p=0.800$; $I^2=0\%$), tumor overgrowth (OR 1.23; 95% CI 0.36 to 4.25; $p=0.740$; $I^2=0\%$), stent migration (OR 1.60; 95% CI 0.28 to 9.20; $p=0.600$; $I^2=73\%$), pancreatitis (OR 1.28; 95% CI 0.53 to 2.90; $p=0.559$; $I^2=0\%$) and cholecystitis (OR 0.73; 95% CI 0.26 to 2.06; $p=0.553$; $I^2=0\%$).

Conclusion: In patients with distal malignant biliary obstruction, no significant difference was observed between CSEMS B-type and L-type.

References: 1. HASEGAWA, S. et al. Braided-type stent versus laser-cut-type stent for patients with unresectable distal malignant biliary obstruction: a randomized controlled trial. *Gastrointestinal Endoscopy*, v. 99, n. 5, p. 739-746.e1, 1 maio 2024.

2. OKUNO, M. et al. The evaluation of bilateral stenting using braided or laser-cut self-expandable metallic stent for malignant hilar biliary obstruction. *Surgical Endoscopy*, v. 37, n. 11, p. 8489–8497, 1 nov. 2023.
3. KITAGAWA, K. et al. Laser-cut-type versus braided-type covered self-expandable metallic stents for distal biliary obstruction caused by pancreatic carcinoma: a retrospective comparative cohort study. *Clinical Endoscopy*, v. 55, n. 3, p. 434–442, 1 maio 2022.
4. TANISAKA, Y. et al. Can the laser-cut covered self-expandable metallic stent be the first choice for patients with unresectable distal malignant biliary obstruction? (with video). *Journal of Hepato-Biliary-Pancreatic Sciences*, v. 29, n. 5, p. 585–593, 1 maio 2022.

Disclosure: Nothing to disclose.

PP1106

12-MM VERSUS 10-MM METALLIC STENTS FOR DISTAL BILIARY OBSTRUCTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Prata¹, A.C. Covre Coan¹, V. Antunes², N.J. Milioli³, E.S. Bulhões Júnior⁴, A. Reis⁵, P. Romeiro⁶, O. Martins⁷, T. Correa⁸, M.V. Fernandes²

¹Federal University of Espírito Santo, Vitória, Brazil, ²Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, ³Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, ⁴College of Higher Education of the United Amazon, Manaus, Brazil, ⁵State University of Campinas, Campinas, Brazil, ⁶Department of Medicine, University Center of Maceió, Maceió, Brazil, ⁷Federal University of Juiz de Fora, Juiz de Fora, Brazil, ⁸Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, Brazil

Contact E-Mail Address: mvfmed@gmail.com

Introduction: Endoscopic drainage of malignant biliary obstruction using metal stents is widely used to treat obstructive jaundice. However, the occurrence of stent occlusion or migration raises the hypothesis using stents with larger diameters may be associated with better outcomes.

Aims & Methods: PubMed, Embase, and Cochrane were systematically searched for randomized controlled trials (RCTs) and observational studies comparing 10-mm vs. 12-mm metallic stents for recurrent unresectable biliary obstruction. The primary outcome was stent obstruction. Secondary outcomes included overall adverse events and stent migration. Statistical analyses were performed using R software version 4.3.1.

The odds ratio (OR) was used for binary outcomes, and the mean difference (MD) for continuous outcomes with their respective 95% confidence interval (CI). Heterogeneity was assessed using the Cochran Q test and I² statistics.

Results: We included six studies comprising 592 patients who underwent stent placement. Of those, 328 patients received a 10mm and 264 patients a 12mm stent. 12mm stent is associated with a lower incidence of stent obstruction (OR 0.48; 95% CI 0.27 to 0.88; p=0.02; I²=53%). However, no statistically significant differences between groups were found for stent migration (OR 0.68; 95% CI 0.39 to 1.19; p=0.18; I²=0%) and incidence of adverse events (OR 0.84; 95% CI 0.39 to 1.82; p=0.66; I²=46%).

Conclusion: 12-mm metallic stents significantly reduce the incidence of stent obstruction compared to 10-mm stents in managing recurrent unresectable biliary obstruction. However, our analysis did not demonstrate statistically significant differences between the two stent sizes regarding stent migration and overall adverse events.

References: 1. CHIKUGO, K. et al. Re-intervention with 10-mm vs 12-mm covered self-expandable metallic stent for recurrent unresectable distal biliary obstruction in patients with previous stent implantation. *Journal of Hepato-Biliary-Pancreatic Sciences*.

2. NAKAOKA, K. et al. Evaluation of a 12-mm diameter covered self-expandable end bare metal stent for malignant biliary obstruction. *Endoscopy International Open*.
3. LEE, H. W. et al. Usefulness of newly modified fully covered metallic stent of 12 mm in diameter and anti-migration feature for periampullary malignant biliary strictures: Comparison with conventional standard metal stent. *Journal of Gastroenterology and Hepatology*.
4. MUKAI, T. et al. Comparison of covered self-expandable metallic stents with 12-mm and 10-mm diameters for unresectable malignant distal biliary obstructions: a prospective randomized trial. *Gastrointestinal Endoscopy*.
5. DO, M. Y. et al. Safety and Efficacy of a Large-Bore Biliary Metallic Stent for Malignant Biliary Obstruction. *Journal of Clinical Medicine*.
6. CAILLOL, F. et al. Evaluation of a new metal biliary stent of 12-mm diameter: A case control study. *Journal of Gastrointestinal and Digestive System*.

Disclosure: Nothing to disclose.

PP1107

ENDOSCOPIC BILIARY DRAINAGE IN THE PALLIATIVE TREATMENT OF KLATSKIN TUMORS: OUTCOMES AND FACTORS ASSOCIATED WITH SUCCESS OR FAILURE

S. Hdiye¹, F. Aitiken¹, R. Chaibi¹, I. Mouslim¹, A. Benhamdane¹, T. Addajou¹, S. Mrabti¹, R. Berraida¹, E. Ilham¹, F. Rouibaa¹, H. Seddik¹

¹Mohammed V Military Hospital, Faculty of Medicine and Pharmacy of Rabat, Department of Gastroenterology II, Rabat, Morocco

Contact E-Mail Address: shdiye@gmail.com

Introduction: Klatskin's tumor is a cholangiocarcinoma that develops from the right or left bile ducts and the upper part of the main bile duct. They are usually diagnosed at an advanced, inoperable stage, and have an extremely poor prognosis.

Biliary drainage is proposed in palliative situation and carries a high risk of infectious complications.

The aim of our work is to report the results of endoscopic biliary drainage as well as the factors associated with its success or failure.

Aims & Methods: This is a retrospective and analytical study of 75 patients, conducted between 2012 and 2024, including all patients admitted with Klatskin's tumor and for whom endoscopic drainage was indicated. Factors associated with the success or failure of endoscopic treatment were studied by logistic regression analysis.

Statistical analysis was performed using SPSS version 22.0 software.

Results: The average age of our patients was 62.67 +/-12 years with extremes ranging from 31 years to 93 years. Our series was characterized by a male predominance of 68% or a sex ratio of 2.12.

Cholangiocarcinoma was classified as bismuth IV in 50.6% of patients, bismuth IIIa in 30% of patients, bismuth IIIb in 13% of patients and bismuth II in 6% of patients.

Sixteen percent of patients had liver metastases.

Endoscopic drainage was successfully performed in 81.3% of patients by plastic prosthesis in 32% of cases (n=24), by a metal prosthesis in 45.2% (n=34) and by nasobiliary drain in 4.1% (n=3).

Forty-seven percent of patients (n=35) had dilatation of the stenosis prior to prosthesis placement.

Causes of stenting failure were primarily related to failure of papilla catheterization, failure to pass the guidewire through the stenosis, or duodenal invasion by the tumor.

In multivariate analysis and adjusting for age, gender, Bismuth tumor type, presence of metastases and endoscopic dilatation of the stenosis,

only the presence of metastases, endoscopic dilatation of the stenosis and Bismuth tumor type modified the outcome.

The Bismuth classification affect the success rate.

Indeed, endoscopic dilatation of the stenosis prior to stenting increases the success rate fourfold. Prosthesis increases the success rate by a factor of 4 [OR=4; p=0.01], whereas the presence of metastases decreases this rate by 65% [OR=0.35; p<0.001].

However, tumors classified as Bismuth IV [OR=8; p<0.001] or Bismuth IIIa [OR=5; p=0.004] were associated with a risk of endoscopic treatment failure.

Conclusion: Our study suggests that the presence of metastatic hilar cholangiocarcinoma classified as Bismuth IV or Bismuth IIIa appear to be associated with failure of endoscopic biliary drainage of Klatskin's tumors, whereas endoscopic dilatation prior to prosthesis placement appears to be associated with success.

Disclosure: Nothing to disclose.

PP1108

STUDY OF OUTCOME AND SUCCESS RATE IN PERCUTANEOUS TRANSHEPATIC BILIARY STENT FOR MALIGNANT BILIARY OBSTRUCTION IN SRINAGARIND HOSPITAL, KHON KAEN UNIVERSITY

C. Rattananukrom¹, P. Eysawat², T. Sutthichaimongkol¹, W. Manasiriruk¹, J. Chindaprasit³, A. Ahooja²

¹Division of Gastroenterology and Hepatology, Department of Medicine, Srinagarind hospital, Khon Kaen University, Khon Kaen, Thailand, ²Department of Radiology, Srinagarind hospital, Khon Kaen University, Khon Kaen, Thailand, ³Division of Oncology, Department of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand

Contact E-Mail Address: chitra@kku.ac.th

Introduction: Malignant biliary obstruction (MBO) is likely to be inoperative at first presentation. Palliative biliary drainage is essential to increase overall survival. Percutaneous transhepatic biliary stent (PTBS) is one of the most effective and safe procedure of biliary drainage in malignant biliary obstruction.

However, there is no previous study in outcome, success rate and complications of PTBS insertion for biliary drainage of MBO in Thai population.

Aims & Methods: Aims: to determine outcome, success rate and complications of PTBS insertion in MBO in tertiary care medical center in Thailand. Methods: A retrospective cohort study was performed on 41 patients with MBO underwent PTBS insertion from 2015 to 2021. Technical data, success rate, and outcome data including survival analysis, occlusion rate and complications were analysed.

Results: Of 41 patients, PTBS insertion had technical success 82.93% and functional success 70.59%. Median survival time of patients was 95 days (IQR 50-147 days). Occlusion rate occurred in only 22.6% of patients and all of them underwent percutaneous transhepatic biliary drainage (PTBD) as alternative palliative biliary drainage. Mean occlusion free survival time was 77.14 days (SD 51.68 days).

Majority of patients (79.4%) did not have PTBS-related complications. The most common complication was acute cholangitis that found only in 6 patients (17.6%). Median complication free survival was 91 days (IQR 60-155 days).

For the group of patients with functional success after PTBS insertion, the cumulative survival rates in 30-day, 120-day, and 390-day and cumulative occlusion-free survival rates were statistically significantly better than those with functional failure (p=0.030 and p=0.007).

Demographic data	Patients
Age(year), mean (SD)	64.02 (9.21)
Male (%)	20 (48.78)
Etiologies of MBO	
Cholangiocarcinoma (%)	33 (80.49)
-Hilar type (%)	32 (96.97)
-Distal type (%)	1 (3.03)
Pancreatic cancer (%)	3 (7.32)
Ampullary cancer (%)	3 (7.32)
Survival data after PTBS insertion	Days
Overall survival, median (IQR)	95 (50-147)
Occlusion free survival, mean (SD)	77.14 (51.58)
Complication free survival, median (IQR)	91 (60-155)

Conclusion: Outcomes and success rate of PTBS insertion in Srinagarind hospital were 82.93% in technical success and 70.59% in functional success. Functional success of PTBS insertion was the most important issue that related with better cumulative survival and occlusion-free survival.

References: 1. Shim DJ et al. Percutaneous Metallic Stent Placement for Palliative Management of Malignant Biliary Hilar Obstruction. Korean J Radiol. 2018;19(4):597-605.

2. Zu QQ, Zhang JX, Wang B, Ye W, Liu S, Shi HB. Percutaneous transpapillary biliary stent placement for distal malignant biliary obstruction: Outcomes and survival analysis. Turk J Gastroenterol. 2019;30(8):714-21.

3. Fucilli F, Licinio R, Lorusso D, Giorgio P, Caruso ML. One stage percutaneous transhepatic biliary stenting for malignant jaundice: a safe, quick and economical option of treatment. Eur Rev Med Pharmacol Sci. 2019;23(17):7684-93.

4. Jeong YW, Shin KD, Kim SH, Kim IH, Kim SW, Lee KA, et al. [The safety assessment of percutaneous transhepatic transpapillary stent insertion in malignant obstructive jaundice: regarding the risk of pancreatitis and the effect of preliminary endoscopic sphincterotomy]. Korean J Gastroenterol. 2009;54(6):390-4.

5. Kozlov AV, Tarazov PG, Polikarpov AA, Popov VV. [Complications of trans- and suprapapillary percutaneous and transhepatic stenting of bile ducts in patients with mechanical jaundice of tumorous etiology]. Vestn Khir Im I I Grek. 2011;170(4):79-83.

6. Sun XR, Tang CW, Lu WM, Xu YQ, Feng WM, Bao Y, et al. Endoscopic Biliary Stenting Versus Percutaneous Transhepatic Biliary Stenting in Advanced Malignant Biliary Obstruction: Cost-effectiveness Analysis. Hepatogastroenterology. 2014;61(131):563-6.

Disclosure: Nothing to disclose.

PP1109

WITHDRAWN

PP1110

INNOVATIVE APPLICATION OF TIP-SPLIT DRAINAGE TUBE IN LAPAROSCOPIC HEPATOBILIARY SURGERY: A PARADIGM SHIFT FOR BILIARY FISTULA PREVENTION

Y. Hu¹, X. Yao¹, M. Yang¹

¹The First Affiliated Hospital, Fujian Medical University, Fuzhou, China

Contact E-Mail Address: huyuhai118@gmail.com

Introduction: Cholecystectomy is a common procedure in hepatobiliary surgery, with iatrogenic injury often leading to biliary fistula. Laparoscopic subtotal cholecystectomy (LSC) is employed when achieving a critical view of safety is challenging, but it comes with a high complication rate, including bile leaks. Laparoscopic common bile duct exploration (LCBDE) with laparoscopic cholecystectomy (LC) is utilized for cholecystolithiasis complicated with common bile duct (CBD) stones. Handling the CBD incision during LCBDE involves two approaches: indwelling T-tube drainage and primary suture.

Aims & Methods: Our research explores routine extra-drainage with tip-split drainage tubes (TSDT) for LCBDE+LC and LSC to reduce postoperative biliary fistulas. Early inspection of the cystohepatic triangle determines the feasibility of achieving a critical view of safety. If unattainable, LSC is considered, with attempts at standard laparoscopic cholecystectomy. TSDT drainage is decided based on the identification of bile flow from the cystic duct orifice. For cases without bile flow, TSDT drainage alone is used. If bile flow is identified, a purse-string suture of the cystic duct is performed, followed by TSDT placement. The LCBDE approach involves a longitudinal incision matching the stone's diameter. Choledochoscope exploration is completed with absorbable sutures or T-tube placement based on inflammation or the likelihood of residual stones. The TSDT is then placed.

Results: Our study, spanning 350 cases over five years, showed a high TSDT success rate, with no postoperative ERCP or PTCD interventions required. A learning curve of 1 to 2 cases was observed. Out of 350 patients, 30 underwent LSC and 320 LCBDE, resulting in 17 postoperative biliary fistula cases. Twelve were Grade A with no change in clinical management, and five were Grade B requiring minimal adjustments. All Grade A cases resolved within a week, while Grade B cases lasted over a week. Follow-up continued until bile leakage disappeared before catheter removal, with no progression to Grade C or relaparotomy requirements.

Conclusion: Our innovative TSDT technique effectively reduces postoperative bile leaks after LSC and LCBDE. Although not previously reported, TSDT appears superior to routine extra-drainage, being less technically demanding and less risky. General surgeons can likely adopt TSDT widely for improved hepatobiliary surgery outcomes.

Disclosure: Nothing to disclose.

PP1111

POST-CHOLECYSTECTOMY GUT MICROBIOME CHANGES AND CLINICAL IMPACT: A SYSTEMATIC REVIEW WITH NARRATIVE SYNTHESIS

T.L. Ang¹, S.H. Koo², D. Ang¹, C.K. Tan¹, L.M. Wang³

¹Changi General Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ²Changi General Hospital, Research Laboratory, Clinical Trials and Research Unit, Singapore, Singapore, ³Changi General Hospital, SingHealth, Laboratory Medicine, Pathology Section, Singapore, Singapore

Contact E-Mail Address: ang.tiing.leong@singhealth.com.sg

Introduction: Cholecystectomy (CCE) is commonly performed for treatment of gallstone disease. However, CCE may result in post-CCE syndrome (PCS) and diarrhea (PCD) in a subgroup of patients. In addition, epidemiological association of CCE with colorectal cancer (CRC) and metabolic-associated fatty liver disease (MAFLD) has raised concerns. CCE is expected to affect the enterohepatic circulation and result in gut microbiome changes. Such changes may account for clinical symptoms and risk for CRC and MAFLD. However, the spectrum and type of gut microbiome changes post-CCE has not been fully quantified and results have been inconsistent.

Aims & Methods: This systematic review aimed to clarify the effect of CCE on gut microbiome composition and the clinical impact. A systematic search was conducted on PubMed, Web of Science and Scopus in March 2024, combining keywords such as "cholecystectomy" or "post-cholecystectomy" with "gut microbiome" or "gut dysbiosis". Reference and citation searches were conducted on included articles. Original articles irrespective of study design that described gut microbiome changes post-CCE were included. Articles were independently reviewed by two authors and data were extracted and synthesized using narrative review. The quality of studies was assessed using the Newcastle-Ottawa scale.

Results: A total of 1373 articles (after excluding duplicates) were initially selected, and after review of the titles and abstracts, 14 eligible studies were identified and the full text reviewed. There were 3 prospective cohort and 11 cross-sectional/ case control cohort studies, of which 13 examined the bacteria microbiome using 16S rRNA gene sequencing, and 1 cross-sectional study examined the fungal microbiome using ITS1 rDNA gene sequencing. Changes in microbiome diversity indices and relative abundances were inconsistent. Among 3 prospective cohort studies, an increase in phylum Bacteroidetes was observed in a study with post-CCE interval more than 3 months, but not in the study with 3-month post-CCE interval. One study reported no change at the phylum level, but an effect for the class Clostridia and the orders Clostridiales and Coriobacteriales within 3 days of CCE. An increase in phylum Bacteroidetes post-CCE was also seen in 3 other cross-sectional studies. Five studies attempted to correlate post-CCE microbiome changes with symptoms. A decreased Firmicutes/ Bacteroidetes (F/B) ratio was observed in patients with PCS/ PCD in 3 out of 5 studies. Although changes in relative abundances of taxa correlated with symptoms, these were inconsistent, with an increase in genus *Prevotella* being the only common finding in 2 out of these 5 studies. Other significant observations post-CCE included a decrease of the potentially beneficial genus *Faecalibacterium* and an increase in the opportunistic pathogen *Escherichia/Shigella*, as well as an attenuated aging-associated intestinal microbiota. The single cross-sectional study that examined post-CCE fungal microbiome changes found that the relative abundance of *Candida glabrata* and *Aspergillus* were enriched, and *Candida albicans* was depleted.

Conclusion: CCE is associated with significant changes in gut microbiome diversity and relative abundances of taxa. Such changes have been correlated with clinical symptoms. These microbiome changes may potentially explain the risk of CRC and MAFLD noted in epidemiological studies.

Discordant results between studies may relate to differences in patient populations and study methodologies.

Disclosure: Nothing to disclose.

PP1112

ANTIBIOTIC PROPHYLAXIS IN EMERGENCY CHOLECYSTECTOMY FOR MILD TO MODERATE ACUTE CHOLECYSTITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

M.H. Elkasaby^{1,2}, H. Elsayed^{3,2}, D.C. Charo^{4,2}, M.A. Rashed^{1,2}, O. Elkoumi^{5,2}, I.M. ElHaddad^{6,2}, A. Gadallah^{7,2}, A. Ramadan^{8,2}

¹Faculty of Medicine, Al-Azhar University, Cairo, Egypt, ²Negida Academy, Medical Research Group of Egypt (MRGE), Cairo, Egypt, ³Faculty of Medicine, Tanta University, Tanta, Egypt, ⁴Ministry of Health, General Surgery, Latakia, Syria, ⁵Faculty of Medicine, Suez University, Suez, Egypt, ⁶Faculty of Medicine, Al-Azhar University, Damietta, Egypt, ⁷Ain Shams University, Faculty of Medicine, Cairo, Egypt, ⁸South Valley University, Faculty of Medicine, Qena, Egypt

Contact E-Mail Address: mohamedhamouda2182000@gmail.com

Introduction: Emergency cholecystectomy is the mainstay in treating acute cholecystitis (AC). In actual practice, perioperative prophylactic antibiotics are used to prevent postoperative infectious complications (PIC), but their effectiveness lacks evidence. We aim to investigate the efficacy of prophylactic antibiotics in emergency cholecystectomy.

Aims & Methods: We searched PubMed, Embase, Cochrane CENTRAL, Web of Science (WOS), and Scopus up to June 14, 2023. We included randomized controlled trials (RCTs) that involved patients diagnosed with mild to moderate AC according to Tokyo guidelines who were undergoing emergency cholecystectomy and were administered preoperative and/or postoperative antibiotics as an intervention group and compared to a placebo group. For dichotomous data, we applied the risk ratio (RR) and the 95% confidence interval (CI), while for continuous data, we used the mean difference (MD) and 95% CI.

Results: We included seven RCTs encompassing a collective sample size of 1747 patients. Our analysis showed no significant differences regarding total PIC (RR= 0.84 with 95% CI (0.63, 1.12), P=0.23), surgical site infection (RR= 0.79 with 95% CI (0.56, 1.12), P=0.19), distant infections (RR= 1.01 with 95% CI (0.55, 1.88), P=0.97), non-infectious complications (RR= 0.84 with 95% CI (0.64, 1.11), P=0.22), mortality (RR= 0.34 with 95% CI (0.04, 3.23), P=0.35), and readmission (RR= 0.69 with 95% CI (0.43, 1.11), P=0.13).

Conclusion: Perioperative antibiotics in patients with mild to moderate acute cholecystitis did not show a significant reduction of postoperative infectious complications after emergency cholecystectomy. (PROSPERO registration number: CRD42023438755).

References: 1. van Braak WG, Ponten JEH, Loozen CS, Schots JPM, van Geloven AAW, Donkervoort SC, et al. Antibiotic prophylaxis for acute cholecystectomy: PEANUTS II multicentre randomized non-inferiority clinical trial. *Br J Surg.* 2022 Feb;109(3):267–73.

2. Park SE, Choi HJ, You YK, Hong TH. Clinical significance of preoperative antibiotic use in mild to moderate acute inflammatory gallbladder disease: A randomized controlled trial. *J Hepato-Biliary-Pancreat Sci.* 2023 Apr;30(4):482–92.

3. Kim EY, Yoon YC, Choi HJ, Kim KH, Park JH, Hong TH. Is there a real role of postoperative antibiotic administration for mild/moderate acute cholecystitis? A prospective randomized controlled trial. *J Hepato-Biliary-Pancreat Sci.* 2017 Oct;24(10):550–8.

Disclosure: Nothing to disclose.

PP1113

SINGLE-DIGITAL CHOLANGIOSCOPY-ASSOCIATED ADVERSE EVENTS IN SLOVAKIA – RETROSPECTIVE ANALYSIS

P. Vojtek¹, J. Strachan², J. Usak¹, J. Rajec¹, D. Polák³, M. Bruncak², L. Skladany², K. Kadlecikova¹, K. Kucerova¹, R. Hustak¹, J. Martinek⁴

¹University Hospital Trnava, Department of gastroenterology and internal medicine, Trnava, Slovakia, ²F.D. Roosevelt University Hospital, Department of Internal Medicine, Banska Bystrica, Slovakia, Banska Bystrica, Slovakia, ³Faculty hospital Zilina, Gastrocentre, Zilina, Slovakia, ⁴Institute for Clinical and Experimental Medicine Gastroenterology & Hepatology, Department of Hepatogastroenterology, Praha 4, Czech Republic

Contact E-Mail Address: 2vojto22@gmail.com

Introduction: Single-operator cholangioscopy (SOC) has become an important diagnostic utility principally indicated for the diagnosis of indeterminate strictures of the biliary system and for the treatment of difficult biliary or pancreatic stone(s). However, SOC carries additional risks compared to standard endoscopic retrograde cholangiopancreatography.

Aims & Methods: We performed a retrospective analysis of all SOC between 2015-2023 in three tertiary centres in Slovakia. The primary outcome was the frequency and severity of adverse events (AEs) after SOC according to the AGREE classification. The operating characteristics of the SOC to detect malignant lesions and treat lithiasis with electrohydraulic (EHL) or laser lithotripsy (LL) were also analysed.

Results: A total of 182 SOC (180 peroral, 2 percutaneous) were performed in 149 patients (pts) [48,9 % female; mean age 59,8 years (range: 20 – 91)]. The main indications for SOC were determination of biliary strictures [92 (51%)] and removal of stones from the common bile duct or the intrahepatic duct stones [82 (45%)] and pancreatic stone(s) [8 (4%)], whereas in 54% procedures EHL was used for the treatment of stones. Overall, AEs occurred in 14% (25/182); cholangitis 7% (Grade II), pancreatitis 6% (Grade I) and bleeding 1% (Grade II) according to AGREE. AEs occurred more frequently after diagnostic (14/25) compared to therapeutic procedures (11/25). There was no difference in overall AEs between EHL and LL, however, LL was associated with a higher single session disruption and shorter procedure time compared to EHL. Indeterminate stricture was evaluated in 56 non- PCS pts, while PSC stenosis was evaluated in 18 pts. A woman underwent simultaneously peroral and percutaneous SOC to disrupt 60 mm of stone in the same session. Tissue sampling was performed in 74 procedures, diagnostic accuracy for visual and histological assessment achieved 97.8% vs 83.2% respectively.

Conclusion: (1) SOC provides a high diagnostic yield in patients with undetermined biliary stenosis;

(2) SOC guided stone lithotripsy was effective in most patients and (3) The most frequent complication was cholangitis in 7% of patients.

Additionally, this is the first Slovak analysis of the efficacy and safety of SOC in clinical practice.

Disclosure:

Nothing to disclose.

PP1114

PREDICTORS OF FAILURE OF ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY IN CLEARING BILE DUCT STONE ON THE INITIAL PROCEDURE.

F. Aitiken¹, S. Hdiye², I. Mouslim¹, R. Chaibi¹, A. Benhamdane¹, T. Addajou¹, R. Berraida¹, E. Ilham¹, F. Rouibaa¹, H. Seddik³

¹Military hospital Mohamed V-Souissi University, Hay Ryad - 10100, Rabat, Morocco, ²Military Hospital Of Instruction Mohamed V, Sale, Morocco, ³Mohammed V Military Teaching Hospital, Mohammed V – Souissi University, Hepato-Gastro-Enterology II, Rabat, Morocco

Contact E-Mail Address: Firdaouss.aitiken@gmail.com

Introduction: Evaluate the predictive factors of failure rate of clearing the biliary system from stones at the initial ERCP.

Aims & Methods: This is a retrospective descriptive and analytical study from September 2004 to September 2023.

All patients with bile duct stones, who underwent ERCP with endoscopic sphincterotomy and stone extraction by standard techniques (extraction balloon or Dormia basket) were included in this study.

Results: A total of 1080 ERCPs were performed to extract biliary duct stones.

The mean age was 58.9 +/- 14.4 years and 59.5% were females.

The mean diameter of the Bile duct was 13.4 +/- 4.31 mm. The presence of a biliary stricture in 6.3%.

The primary vacuity rate was 75.1%. Supplementary techniques were used in 22.7% of cases.

On univariate analysis, the predictive factors for failure after use of standard techniques were: age(OR: 0.9;CI95%:-0.03- -0.01;p<0.001); gender(OR:0.7;CI95%:-0.5--0.02;p=0.036); previous cholecystectomy (OR: 1.3,CI95%:0.02-0.6;p=0.035);presence of angiocholitis(OR: 0.4; CI95%:-1.1- -0.4;p<0.001); dilatation of the CBD >15mm (OR:0.8,CI95%:-0.2-0.1;p<0.001), biliary stricture (OR:0.3;CI95%:-1.7--0.7;p<0.001) and the presence of impacted and/or large stone (OR:0.1;CI95%:-2--1;p<0.001).

On multivariate analysis, only the presence of angiocholitis (OR:1.9;CI95%: 0.2-1;p=0.001), impacted and/or large stone (OR:2.5;CI95%:0.5-1.3;p<0.001), dilatation of the CBD >15mm (OR:0.88;CI95%:-0.17--0.07;p<0.001), and biliary stricture (OR:2.9;CI95%:0.4-1.7;p=0.002) were significantly associated with failure of the primary CBD vacuity rate.

The overall vacuity rate after using the supplementary techniques was 92.4%.

Conclusion: In our study, predictive factors for failure of the primary CBD vacuity rate were the presence of angiocholitis, impacted and/or large stone, dilatation of the CBD (>15mm) and biliary stricture.

Disclosure: Nothing to disclose.

PP1115

ENDOBILIARY RADIOFREQUENCY ABLATION USING A NOVEL BIPOLAR STENT-BASED ELECTRODE FOR MALIGNANT BILIARY OBSTRUCTION: PRECLINICAL STUDY IN PORCINE MODEL

Y. Park^{1,2}, D.-S. Won¹, S.H. Kim^{1,3}, S.-S. Lee³, J.-H. Park^{1,2}

¹Asan Medical Center, Biomedical Engineering Research Center, Asan Institute for Life Sciences, Seoul, South Korea, ²University of Ulsan College of Medicine, Department of Convergence Medicine, Asan Medical Center, Seoul, South Korea, ³University of Ulsan College of Medicine, Department of Gastroenterology, Asan Medical Center, Seoul, South Korea

Contact E-Mail Address: ybeen9733@amc.seoul.kr

Introduction: Malignant biliary obstruction (MBO) poses significant therapeutic challenges, particularly in patients ineligible for surgery [1]. Endobiliary radiofrequency ablation (RFA) has emerged as a promising palliative therapy, aiming to enhance stent patency and patient survival [2]. However, conventional catheter-based electrodes may encounter limitations, such as incomplete tumor ablation due to insufficient contact with the inner wall of the bile duct [3].

Aims & Methods: This study aimed to validate the feasibility of the stent-based electrode (SBE)-RFA system with polarity-switching and evaluate its efficacy in achieving circumferential ablation lesions in the porcine bile duct. A bipolar SBE consisting of two electrodes fabricated by braiding nitinol wires was designed and characterized along with a custom RFA generator capable of a polarity-switching system. *Ex vivo* studies using porcine livers were performed to evaluate the ablation ranges under various ablation protocols combining output power and ablation times.

Subsequently, an animal study involving nine male Yorkshire pigs was performed, employing selected protocols based on *ex vivo* findings. The RFA procedure was conducted in the porcine common bile duct (CBD) under fluoroscopic guidance, with pre- and post-procedural assessments including cholangiography, endoscopic examination, and histological analysis.

Results: The SBE with custom RFA generator was demonstrated that temperature feedback and power output were accurate and showed high reproducibility. The SBE was successfully positioned at the correct location during the procedure through fluoroscopy and ultrasound guidance, and complete contact with the bile duct wall was confirmed. The ablation ranges of the porcine liver increased with output power and time, showing proportional growth and an even ablation area between electrodes. Endobiliary RFA in the porcine CBD was technically successful without ductal perforation, resulting in luminal narrowing proportional to output power and ablation time. Mucosal damage, including hemorrhagic erosion and erythema, was observed, intensifying with higher RFA-related parameters. Histological examination revealed increased inflammatory cell infiltration, hemorrhage, and cellular necrosis in correlation with output power and time. Additionally, the ablation area in the porcine CBD was formed in an even circumferential shape, and this also proportionally increased as output power and time increased.

Conclusion: In conclusion, this study demonstrates the technical feasibility and efficacy of endobiliary RFA utilizing a novel bipolar SBE-RFA system with polarity-switching system. This system exhibited controlled and predictable ablation ranges in the porcine CBD, offering potential as a palliative therapeutic option for unresectable MBO. Although further studies in obstructive animal models and long-term efficacy assessments are necessary, these findings suggest that promising prospects form the clinical application of the bipolar SBE-RFA system in managing MBO.

References: [1] Sumiyoshi T, Shima Y, Okabayashi T, Negoro Y, Shimada Y, Iwata J, et al. Chemoradiotherapy for Initially Unresectable Locally Advanced Cholangiocarcinoma. *World J Surg.* 2018;42(9):2910-8.

[2] Oh D, Chong J, Song TJ, Park DH, Lee SS, Seo DW, et al. The usefulness of endobiliary radiofrequency ablation before metal stent placement in unresectable malignant hilar obstruction. *J Gastroenterol Hepatol*. 2022;37(11):2083-90.

[3] Inoue T, Yoneda M. Updated evidence on the clinical impact of endoscopic radiofrequency ablation in the treatment of malignant biliary obstruction. *Dig Endosc*. 2022;34(2):345-58.

Disclosure: Nothing to disclose.

PP1116

FORGING NEW PATHS: GROUNDBREAKING INSIGHTS FROM MEXICO'S FIRST COMPARATIVE STUDY ON ENDOSCOPIC ULTRASOUND-GUIDED BILIODIGESTIVE DERIVATIONS

R. Sosa¹, L.A. Waller-Gonzalez¹, R. Soto-Solis¹, A.R. Guzman-Carcamo¹, M.S. Gallardo-Luna¹, D. Bringas-Vasquez¹, E.P. Alonso-Lopez¹, A.K. Rojas Hernandez¹, H.F. Narvaez-Gonzalez¹, L.O. Rodriguez-Muñoz¹, Unidad de Endoscopia Gastrointestinal, Centro Medico Nacional "20 de Noviembre"

¹Centro Medico Nacional "20 de Noviembre", *GI Endoscopy, Cdmx, Mexico*

Contact E-Mail Address: raulsomasx@gmail.com

Introduction: Biliodigestive diversions are surgical procedures aimed at bypassing obstructions or restoring the flow of bile from the liver to the digestive tract. These procedures are commonly performed in patients with biliary tract obstructions caused by conditions such as tumors, strictures, or stones. By creating an alternate pathway for bile drainage, biliodigestive diversions help alleviate symptoms and prevent complications associated with biliary obstruction, improving the patient's quality of life and overall prognosis.

There are various techniques for biliodigestive diversions, including hepaticojejunostomy, hepaticogastrostomy, and choledochoduodenostomy, each tailored to the specific needs and anatomical considerations of the patient.

Aims & Methods: Aims: Compare the efficacy and safety of biliodigestive diversion procedures, hepaticogastrostomy and choledochoduodenostomy, in patients with biliary tract obstructions.

Methods: Restrospective comparative study in patients with biliary tract obstructions undergoing either hepaticogastrostomy or choledochoduodenostomy at Centro Medico Nacional 20 de Noviembre will be included in the study from 2018- 2024.

Results: We evaluated 65 patients in total, median age 65 years, 44% were female, we had 3 biliodigestive procedures: Coledocoduthdenostomy 50%, Hepaticogastrostomy 28.1% and Rendez-vous 12.5%, the type of prothesis were 10x8 30%, 8x8 10%, Hot Axius in 5%, 10x6 16%, technical success reported was 87.5% and clinical success was 89.1. Five patients experienced complications, with peritonitis being the most frequent, followed by bleeding.

These findings underscore the importance of vigilant post-procedural monitoring and prompt management of complications to ensure optimal patient outcomes.

Conclusion: These results are encouraging and suggest that both choledochoduodenostomy and hepaticogastrostomy are effective procedures for addressing biliary obstructions in this patient cohort.

Additional Considerations that we want to mention, It's important to note that both technical and clinical success are important indicators of procedure efficacy and safety and that further analysis would be helpful to explore any association between the type of procedure performed and long-term outcomes, such as patency duration and patient quality of life. Over-

all, these results provide valuable insights into the practice of endoscopic ultrasound-guided biliodigestive diversion in Mexico and may serve as a basis for future research and clinical practice in this field.

References:

Arvanitakis, M., Gkolfakis, P., Despott, E. J., Ballarin, A., Beyna, T., Boeykens, K., Elbe, P., Gisbertz, I., Hoyois, A., Mosteanu, O., Sanders, D. S., Schmidt, P. T., Schneider, S. M., & van Hooft, J. E. (2021). Endoscopic management of enteral tubes in adult patients - Part 1: Definitions and indications European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*, 53(1), 81–92. <https://doi.org/10.1055/a-1303-7449>

Oh, D., Han, S. Y., Lee, S. H., Kim, S. H., Paik, W. H., Chon, H. K., Song, T. J., Park, S. W., & Cho, J. H. (2024). Comparison of long-term outcomes of endoscopic ultrasound-guided hepaticogastrostomy and choledochoduodenostomy for distal malignant biliary obstruction: a multicenter retrospective study. *Therapeutic Advances in Gastroenterology*, 17. <https://doi.org/10.1177/17562848241239551>

Gkolfakis, P., Arvanitakis, M., Despott, E. J., Ballarin, A., Beyna, T., Boeykens, K., Elbe, P., Gisbertz, I., Hoyois, A., Mosteanu, O., Sanders, D. S., Schmidt, P. T., Schneider, S. M., & van Hooft, J. E. (2021). Endoscopic management of enteral tubes in adult patients - Part 2: Peri- And post-procedural management European Society of Gastrointestinal Endoscopy (ESGE) Guideline. In *Endoscopy* (Vol. 53, Issue 2, pp. 178–195). Georg Thieme Verlag. <https://doi.org/10.1055/a-1331-8080>

Disclosure: Nothing to disclose.

PP1117

ADVERSE EVENTS ASSOCIATED WITH ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE

K. Todovichin¹, I. Zhecheva¹, P. Karagyozov¹

¹Acibadem City Clinic Tokuda Hospital, Interventional Department, Clinic of Gastroenterology, Sofia, Bulgaria

Contact E-Mail Address: petko.karagyozov@gmail.com

Introduction: Endoscopic ultrasound-guided biliary drainage (EUS – BD) has become widely accepted over the past several years for complicated biliary drainage when conventional endoscopic retrograde cholangiopancreatography is not successful or feasible due to variety of constrains. The success rate of the procedure is between 90% an 97% and the complication rate is less than 10%.

Aims & Methods: The aim of the study is to evaluate the safety and efficacy of EUS-BD performed in our unit while assessing the risk factors associated with the procedure.

We performed retrospective analysis of a prospective data base from March 2020 to October 2023. The patients underwent EUS – BD using linear scope (Fujifilm EG – 580UT). Several procedures are possible. The procedure was tailored to individual patient's anatomy.

Results: We identified 140 patients who underwent EUS-BD during the study period (men- 75, women- 65) – 130 (92.8%) with malignant and 10 (7.1%) with benign disease. Gender distribution shows higher rate of post-procedural complications in men (29,7% vs 21,5%), nevertheless there is no statistically significant correlation between gender and complication rate. The medium age of the patients was 66.3 years (38 years – 92 years). No statistically significant correlation was found between age, presence of arterial hypertension, diabetes mellitus and adverse events.

We analyzed the different therapeutic modalities including EUS - CDS (n = 20), EUS - HGS (n = 88), antegrade stenting (n = 12) and rendezvous (n = 13), hepaticojejunostomy (n = 5), cholecystogastrostomy and -duodenostomy (n = 2). We found no statistically significant correlation between the type of technical modality and the incidence of peri- and post-procedural complications.

The technical success was 96.6% (n = 137). Mean duration of the procedure was 42.15 min. (10 min. – 170min.). Mean hospital stay was 5 days (2 days – 10 days). Adverse events were detected in 38 patients (27.1%). The various complications that have been reported were classified into periprocedural and postprocedural:

- Periprocedural adverse events were detected in 7 (5%) patients: 2 (1.4%) with bleeding, 2 (1.4%) with stent migration, 3 (2.1%) with loss of access.
- Postprocedural complications are detected in 29 (20.7%) and we divided into:
 1. Early (up to 7 days after procedure) – n = 21 (15%) of them 13 (9.3%) with cholangitis, 3 (2.1%) with abdominal pain, 1 (0.7%) with bleeding, 2 (1.4%) with pancreatitis, 1 (0.7%) with pneumoperitoneum and 1 (0.7%) patient with biloma.
 2. Late (a week after the procedure) – n = 8 (5.7%) with cholangitis.
- There were 2 deaths related to the procedure (1.4%) in patients with advanced oncologic disease.

All cases were managed conservatively and did not require surgery, intensive care or interventional radiology. Three (2.1%) of the periprocedural complications were solved by performing PTBD immediately after EUS-BD by the same team.

Conclusion: EUS-BD is effective tool for biliary drainage both in naïve patients and those with altered biliary anatomy. Along with the possibility of emergency PTBD, it has favourable technical and clinical success rate and safety profile and therefore the potential to shift the current paradigms that define management of complicated biliary obstruction.

References: 1. Hatamaru K, Kitano M. EUS-guided biliary drainage for difficult cannulation. *Endosc Ultrasound* 2019;8(Suppl 1):S67–S71

2. Baars JE, Kaffes AJ, Saxena P. EUS-guided biliary drainage: a comprehensive review of the literature. *Endosc Ultrasound* 2018;7(01):4–9

3. Kakked G, Salameh H, Cheesman AR, Kumta NA, Nagula S, DiMaio CJ. Primary EUS-guided biliary drainage versus ERCP drainage for the management of malignant biliary obstruction: a systematic review and meta-analysis. *Endosc Ultrasound* 2020;9(05): 298–307

4. Khan MA, Akbar A, Baron TH, et al. Endoscopic ultrasound-guided biliary drainage: a systematic review and meta-analysis. *Dig Dis Sci* 2016;61(03):684–703

5. Giri S, Mohan BP, Jearth V, Kale A, Angadi S, Afzalpurkar S, Harindranath S, Sundaram S. Adverse events with EUS-guided biliary drainage: a systematic review and meta-analysis. *Gastrointest Endosc.* 2023 Oct;98(4):515–523

6. van der Merwe SW, van Wanrooij RLJ, Bronswijk M, et al. Therapeutic endoscopic ultrasound: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2022;54:185–205

7. Ogura T, Higuchi K. Endoscopic ultrasound-guided hepaticogastrotomy: technical review and tips to prevent adverse events. *Gut Liver* 2021;15(02):196–205

8. Ogura T, Higuchi K. Technical review of developments in endoscopic ultrasound-guided hepaticogastrotomy. *Clin Endosc* 2021;54(05):651–659

Disclosure: Also presented on ESGE DAYS 2024.

PP1118

THE IMPACT OF CHOLANGIOSCOPE DIAMETER VARIATION ON CHOLANGIOSCOPY OUTCOMES: A RETROSPECTIVE COMPARATIVE STUDY

C. Robles-Medrandá¹, J. Baquerizo-Burgos¹, M. Puga-Tejada¹, J. Alcivar-Vasquez², R. Del Valle¹, H. Alvarado-Escobar¹, M. Egas-Izquierdo¹, D. Cunto¹, M. Arevalo-Mora^{1,2}, H. Pitanga-Lukashok¹

¹Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Guayaquil, Ecuador, ²Larkin Community Hospital, South Miami, United States of America

Contact E-Mail Address: miguel.puga01@hotmail.com

Introduction: Digital single-operator cholangioscopy (DSOC) stands as an invaluable diagnostic and therapeutic instrument, offering direct visualization of the biliary ducts. The use of cholangioscopes with higher diameter may raise concerns regarding patient discomfort and safety.

Smaller diameter cholangioscopes could offer enhanced maneuverability and decreased risk of adverse events, improving procedural success rates.

Aims & Methods: The aim of this study is to compare the impact of cholangioscope diameter variation on cholangioscopy outcomes, with a focus on procedure success rates. A retrospective, comparative study performed in patients who underwent either diagnostic or therapeutic DSOC from January 2021 to August 2023 were retrospectively collected. A p < 0.05 was considered statistically significant.

Results: A total of 128 procedures were performed in 119 patients. Median age was 62.5 (44 – 71) and 46.1% were female. 52.3% of procedures were performed with the 9.3F cholangioscope, 53 (41.4%) were performed with the 11.1F, and 6.2% procedures were performed with the 7F cholangioscope. The 9.3F cholangioscope was used mainly for diagnostic procedures (61.2%) when compared to the 11.1F (39.6%) (P= .01). The most common diagnostic indication was indeterminate biliary stricture (9.3F: 31.3% vs 11.1F: 13.2%) (P= .01).

Most lesions were in the common bile duct (CBD). Two procedures performed with the 9.3F scope switched to a lower caliber scope (7F) to surpass the lesions, while 4 procedures performed with 11.1F required the application of a 9.3F to surpass the lesions and finish the procedures (P=.176). The 9.3F allowed the evaluation of the intrahepatic ducts in 6 procedures. More therapeutic procedures were performed with the 11.1F cholangioscope (60.4%), while 38.8% with the 9.3F. The main indication was lithotripsy.

Most procedures with a stone size >20mm were performed with the 11.1F (61%) (P=.01), with a total removal of stones of 64.5%. Technical success was higher in the 9.3F (97.0% vs 90.6%), clinical success was higher in the 11.1F (96.2% vs 94.0%).

All cases performed with the 7F cholangioscope were diagnostic, 7/8 procedures with 7F allow a complete evaluation of the intrahepatic ducts, 1/8 had a complete post-surgical CBD stenosis, and achieved a 100% technical and clinical success rate.

Conclusion: Cholangioscope diameter should be tailored to the specific diagnostic or therapeutic needs. While the 9.3F cholangioscope is more suitable for diagnostic procedures and has a higher technical success rate, the 11.1F is preferable for therapeutic interventions, particularly for larger biliary stones where higher caliber lithotripter is required. The 7F cholangioscope presents an effective alternative for complete intrahepatic duct evaluations.

References: 1. Gerges C, Beyna T, Tang RSY, et al. Digital single-operator peroral cholangioscopy-guided biopsy sampling versus ERCP-guided brushing for indeterminate biliary strictures: a prospective, randomized, multicenter trial (with video). *Gastrointestinal Endoscopy.* 2020;91(5):1105–13.

2. Kahaleh M, Gaidhane M, Shahid HM, et al. Digital single-operator cholangioscopy interobserver study using a new classification: the Mendoza Classification (with video). *Gastrointestinal Endoscopy*. 2022;95(2):319–26.

Disclosure: Carlos Robles-Medranda is a key opinion leader and consultant for Pentax Medical, Steris, Medtronic, Motus, Micro-tech, G-Tech Medical Supply, CREO Medical, EndoSound, and mdconsgroup. All other authors have nothing to declare.

Poster
Pancreas

Pancreas

09:00-18:00 / Poster Exhibition

PP1119

ISLET AUTOANTIBODY POSITIVITY ACCORDING TO GLUCOSE TOLERANCE AND AGE IN CYSTIC FIBROSIS: SYSTEMATIC REVIEW AND META-ANALYSIS

R. Molnár^{1,2}, B. Bódy^{1,2}, B. Varga³, R. Tóth¹, T. Kói¹, K. Ocskay², A. Párnitzky^{2,4}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Heim Pál National Pediatric Institute, Budapest, Hungary, ³University of Pécs, Medical School, Pécs, Hungary, ⁴University of Pécs, Institute for Translational Medicine, Pécs, Hungary

Contact E-Mail Address: reginamolnar23@gmail.com

Introduction: With chronic inflammation, recurrent infections, and dysbiosis, people with CF (pwCF) are predisposed to autoimmunity. However, the role of autoimmune-mediated pancreatic beta-cell damage is yet unclear in the development of cystic fibrosis-related abnormal glucose tolerance (CF-AGT).

Aims & Methods: We aimed to assess the prevalence of various islet autoantibodies (AABs) according to glucose tolerance and age and the risk associated with islet AAB positivity for developing CF-AGT. A systematic search across four databases (CENTRAL, Embase, PubMed, Web of Science) identified studies reporting on AABs against glutamic acid decarboxylase (GADA), insulin (IAA), islet cell (ICA), insulinoma-associated protein 2 (IA-2A), and zinc transporter 8 (ZnT8A) in pwCF (CRD42020155846). Prevalence and odds ratios (OR) were calculated with 95% confidence intervals (CI) using a random effects model with subgroup analysis by glucose tolerance and age.

Results: Analysis of 20 eligible studies (2229 pwCF) revealed an overall prevalence of islet AAB positivity at 4% (CI: 2-9%) and multiple positivity at 1% (CI: 0-11%). IAA exhibited the highest prevalence at 6% (CI: 3-14%), followed by GADA at 5% (CI: 2-11%). IA-2A and ICA had prevalence rates of 2% (CI: 1-7%) and 1% (CI: 0-9%), respectively. Islet AAB prevalence trended higher in children than adults and in CFRD vs. non-CFRD. Notably, CFRD showed significantly higher odds for multiple (OR 2.71, CI: 1.49-4.93) and any AAB positivity (OR 2.82, CI: 1.22-6.51) compared to the non-CFRD group. Among the AABs, GADA exhibited the strongest CFRD association (OR 4.63, CI: 3.42-6.28), with also significant associations for ICA and IA-2A (OR 3.57, CI: 1.05-12.18 and OR 2.36, CI: 1.29-4.34).

Conclusion: While islet AAB prevalence remains low in pwCF overall, higher AAB prevalence was detected in childhood, and islet AAB positivity was associated with CFRD, emphasizing the need for early screening. Timely intervention in these high-risk groups is essential to manage early-onset CF-AGT and prevent potential complications.

Disclosure: Nothing to disclose.

PP1120

EXPLORING LONG-TERM VIABILITY AND GENE EXPRESSION DYNAMICS IN MOUSE PANCREATIC DUCTAL ORGANOID

V. Szabó^{1,2,3}, G. Groma^{4,5}, P. Pallagi^{1,2,3}, J. Maléth^{1,2,3}

¹University Of Szeged, Department of Medicine, Szeged, Hungary,

²University of Szeged, ELKH-USZ Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary,

³University of Szeged, HCEMM-USZ Molecular Gastroenterology Research Group, Szeged, Hungary, ⁴University of Szeged, HUN-

REN-USZ, Dermatological Research Group, Szeged, Hungary,

⁵University of Szeged, Department of Dermatology and Allergology, Szeged, Hungary

Contact E-Mail Address: szaboviktoria1104@gmail.com

Introduction: Organoid models simulate organ function and structure, offering a physiologically relevant platform for studying organ development, disease mechanisms, and drug responses. Mouse pancreatic ductal organoids serve as valuable models for pancreatic research, yet their long-term viability remains uncertain. Simultaneously, pancreatic cancer, predominantly pancreatic ductal adenocarcinoma (PDAC), poses significant clinical challenges globally. Despite its prevalence and lethality, the genetic alterations driving PDAC progression remain largely elusive. Thus, understanding the gene expression changes in PDAC is crucial for therapeutic advancements.

Aims & Methods: Our study aimed to sustain mouse pancreatic ductal organoids long-term and explore associated gene expression changes, focusing on cancer-related markers. Ductal organoid cultures from wild-type FVB/N mice (N=3) were propagated for 40 passages (p40). RNA was isolated at various time points (p3/5/10/20/30/40) for transcriptomic analysis, with p3 serving as the starting time point. Passaging frequency and organoid morphology were monitored. Transcriptomic data underwent Ingenuity Pathway Analysis (IPA) to elucidate changes over passages in the organoids.

Results: The passaging frequency subsequently declined with time. The morphology of the organoids underwent noticeable changes starting from p20, characterized by the emergence of outgrowths surrounding the domes and the presence of adhesions in the organoids. The preliminary findings from the transcriptome data indicate that the markers associated with ductal cell fate and brush border development exhibit the greatest transcripts per million (TPM) values at p10. The expression of *Cftr*, *Ano1*, and *Adcy8*, which play a crucial role in maintaining the balance of ions in ductal cells, exhibited a notable decline starting at p20. Similarly, starting from p20, the TPM values of cancer-related markers exhibited an unregulated escalation, and there was a notable alteration in the expression of genes that govern the G1/S checkpoint regulation in the cell cycle.

Conclusion: Our research shows that mouse organoid cultures are sustainable for studying ductal cell functionality up to p10. Additionally, we observed potential signs of spontaneous carcinogenesis making suggesting that this model could be utilized for *in vitro* tumorigenesis studies. These findings have the potential to enhance comprehension of the mechanisms involved in the progression of PDAC.

Disclosure: Nothing to disclose.

PP1121

THE EFFECTS OF CFTR MODULATOR THERAPY ON ENDOCRINE PANCREATIC FUNCTION IN PATIENTS WITH CYSTIC FIBROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

S. Kiss¹, M.F. Juhász¹, K. Ocskay¹, T. Kóti², A. Párnicsky^{1,2,3}

¹Heim Pál National Pediatric Institute, Budapest, Hungary, ²Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ³Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary

Contact E-Mail Address: kisszabolcs1995@gmail.com

Introduction: CFTR modulators represent a groundbreaking therapeutic approach in cystic fibrosis (CF) management, targeting the underlying cause of the disease. These therapies have the potential to directly influence pancreatic beta-cell function and pathways involved in insulin secretion, thereby improving the glycemic status of people with CF (pwCF).

Aims & Methods: We aimed to evaluate the effect of CFTR modulator therapy on endocrine pancreatic function in patients with CF. A systematic search of three databases (PubMed, Embase, and CENTRAL) was conducted up to March 6, 2024, to identify studies examining the impact of CFTR modulators on glucose metabolism in pwCF comparing variables before and after CFTR modulator therapy.

Outcomes of interest included measures from oral glucose tolerance tests (OGTT), continuous glucose monitoring (CGM), and glycated hemoglobin (HbA1c). Meta-analysis was initiated using random-effects models to estimate pooled mean differences (MD) and 95% confidence intervals (CIs). Subgroup analyses were created based on CFTR modulators and length of therapy.

Covariate regression analyses were made to assess the relationship between therapy length and pooled MD. A p-value less than 0.05 was considered to be statistically significant. The study protocol was registered in PROSPERO with registration number CRD42024516198.

Results: A total of 1081 records were identified, 73 of which proved to be eligible for inclusion. Pooled analysis of CFTR modulators did not demonstrate a significant effect on 60-minute and 120-minute plasma glucose levels (Table 1). However, elexacaftor/tezacaftor/ivacaftor therapy resulted in significantly reduced plasma glucose levels at 120 minutes (MD: -1.80 mmol/L; 95% CI -2.60, -1.00). Average glucose, glycemic variability, and % of time below 3.9 mmol/L interstitial glucose level were comparable before and after therapy. Meta-regression revealed no significant effect of length of therapy on 60- and 120-minute plasma glucose levels (p=0.512 and p=0.631 respectively).

Outcome	N° of included studies (N° of patients)	Result of the meta-analysis (mean difference with 95% CI)	Statistical heterogeneity
OGTT 60' plasma glucose	11 (253)	0.34 mmol/L (95% CI -0.54, 1.21)	I ² = 79% (95% CI 62, 88), p<0.001
OGTT 60' plasma glucose (lumacaftor/ivacaftor subgroup)	4 (72)	1.41 mmol/L (95% CI -0.60, 3.42)	I ² = 80% (95% CI 46, 92), p=0.002
OGTT 60' plasma glucose (elexacaftor/tezacaftor/ivacaftor subgroup)	6 (133)	-0.05 mmol/L (95% CI -1.28, 1.18)	I ² = 81% (95% CI 58, 91), p<0.001
OGTT 120' plasma glucose	15 (338)	-0.62 mmol/L (95% CI -1.29, 0.04)	I ² = 80% (95% CI 67, 87), p<0.001
OGTT 120' plasma glucose (lumacaftor/ivacaftor subgroup)	5 (116)	-0.73 mmol/L (95% CI -1.90, 0.44)	I ² = 68% (95% CI 18, 88), p=0.013
OGTT 120' plasma glucose (elexacaftor/tezacaftor/ivacaftor subgroup)	3 (86)	-1.80 mmol/L (95% CI -2.60, -1.00)	I ² = 0% (95% CI 0, 90), p=0.750
Average glucose	5 (65)	-0.16 mmol/L (95% CI -0.49, 0.17)	I ² = 0% (95% CI 0, 79), p=0.428
Glycemic variability (standard deviation of glucose level)	3 (30)	-0.12 mmol/L (95% CI -0.30, 0.06)	I ² = 0% (95% CI 0, 90), p=0.859
% of time below 3.9 mmol/L glucose level	4 (41)	-0.12 % (95% CI -0.60, 0.37)	I ² = 0% (95% CI 0, 85), p=0.460

Conclusion: Our results revealed an improvement in the 120-minute OGTT plasma glucose level in the elexacaftor/tezacaftor/ivacaftor subgroup. The absence of significant changes in other analyses may indicate that these medications could potentially slow or halt the deterioration of glucose metabolism. Further prospective studies are required to overcome the limitation of a relatively small patient number and to validate our findings.

Disclosure: Nothing to disclose.

PP1122

CLINICAL PERFORMANCE OF AN AUTOMATED TURBIDIMETRIC IMMUNOASSAY TO QUANTIFY FECAL PANCREATIC ELASTASE

L. Anchling¹, D. Trapani-Vondran¹, U. Aldinger¹, H. Ilgü¹, J. Afonso¹, M. Schneider¹, T. Schuster¹, S. Neu¹, L. Voigtländer², H. Laumen², J. Rosendahl², C.-B. Gerhold¹

¹BÜHLMANN Laboratories AG, Schönenbuch, Switzerland, ²Klinik und Poliklinik für Innere Medizin I, Department für Innere Medizin, Halle, Germany

Contact E-Mail Address: lea@buhlmannlabs.ch

Introduction: Pancreatic exocrine insufficiency (PEI) is defined as a reduction of pancreatic exocrine activity in the intestine at a level that prevents normal digestion(1). PEI leads to malnutrition-related complications and a reduced quality of life. Faecal pancreatic elastase is an ideal biomarker to assess pancreatic function in patients experiencing PEI. Due to its high stability, faecal pancreatic elastase is concentrated during intestinal passage, thus reflecting the total overall pancreatic secretion.

Aims & Methods: The aim of this work was to evaluate the clinical performance of a particle-enhanced turbidimetric immunoassay (PETIA) that allows automated quantification of pancreatic elastase in faecal extracts on clinical chemistry analyzers. Hundred and eighty-nine samples from 76 controls and 113 diagnosed patients were used to compare the turbidimetric immunoassay and a reference ELISA assay performance. For both assays, sensitivity and specificity were determined using a cutoff of 200 µg/g. Moreover, for samples within the measuring range for both assays, a kappa value and the overall agreement were assessed.

Results: A better clinical performance was obtained by the turbidimetric immunoassay compared to the reference ELISA assay. The turbidimetric immunoassay revealed a sensitivity and specificity of 78% and 74%, respectively, while the reference ELISA assay revealed a sensitivity and specificity of 74% and 68%, respectively. The hundred and twelve samples used to perform a method comparison showed a relative bias at the cutoff (200 µg/g) of -5.72% and an overall analytical agreement between the turbidimetric immunoassay and the reference ELISA assay of 85.7%. Cohen's kappa agreement showed a substantial agreement of 0.70.

Conclusion: The turbidimetric immunoassay showed good diagnostic performance and a strong agreement with the reference ELISA assay. The particle-enhanced turbidimetric immunoassay is an accurate, non-invasive, automated test and an ideal assay for large-scale determination of pancreatic elastase levels in fecal extracts.

References: (1) Philips ME, et al. BMJ Open Gastro 2021; 8: e000643

Disclosure: "All authors are employees of BÜHLMANN Laboratories AG"

PP1123

DIABETES-ASSOCIATED REGULATORY SEQUENCES REVEAL NOVEL PATHWAYS IN PANCREATIC DEVELOPMENT AND DISEASE

S. Merz¹, S. Heller¹, C. Julier², A. Kleger¹¹University Hospital Ulm, Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, ²Institut Cochin, Inserm U1016, Groupe "Génétique des diabètes", Paris, France**Contact E-Mail Address:** sandra.heller@uni-ulm.de

Introduction: Rare early onset cases of diabetes stem from single gene mutations, whereas frequent gene variants can also contribute to multifactorial diabetes, indicating shared disease mechanisms. Our recent study has identified *ONECUT1* as a gene implicated in both monogenic and multifactorial diabetes, establishing it as crucial target for investigating fundamental signaling pathways in diabetes pathology [1,2]. However, numerous diabetic characteristics remain unexplained by typical genetic alterations, highlighting the underestimated significance of the non-coding genome. We have identified a neonatal diabetes patient carrying a heterozygous *ONECUT1* truncating variant. Remarkably, the patient exhibited a phenotype akin to individuals with homozygous *ONECUT1* truncating mutations. Upon further examination, we detected an additional heterozygous deletion in the non-coding genome, leading us to hypothesize that it could impact the regulation of the remaining *ONECUT1* allele. Consequently, the dysregulation of the *ONECUT1*-dependent transcriptional machinery crucial for proper beta-cell development occurs, ultimately leading to the severe diabetic phenotype observed in the patient.

Aims & Methods: Following deletion of specific genomic regions in human embryonic stem cells, we initiated their differentiation into the pancreatic endocrine lineage and meticulously characterized the developmental stages.

Results: Importantly, we successfully replicated the patient's diabetic phenotype, elucidating deficiencies in both pancreatic development and beta-cell functionality. The differentiation of pancreatic progenitors was notably hindered by the loss of the regulatory region associated with nearly complete ablation of *ONECUT1*. Moreover, the stem cell-derived islets exhibited a reduced number of beta-cells as well as impaired insulin secretion, even in heterozygous knockouts.

Conclusion: Altogether, our ongoing comprehensive mechanistic characterization provides insights into the precise role of the identified regulatory element in pancreatic beta-cell development and diabetes pathophysiology, emphasizing the significance of the non-coding genome. By unveiling unknown molecular pathomechanisms linked to alterations in regulatory sequences, we contribute to a deeper understanding of the pancreatic transcriptional network and establish the foundation for personalized diabetes treatment.

References: [1] Philippi, A., Heller, S., Costa, I.G. *et al.* Mutations and variants of *ONECUT1* in diabetes. *Nat Med* 27, 1928–1940 (2021). <https://doi.org/10.1038/s41591-021-01502-7>

[2] Heller, S., Li, Z., Lin, Q. *et al.* Transcriptional changes and the role of *ONECUT1* in hPSC pancreatic differentiation. *Commun Biol* 4, 1298 (2021). <https://doi.org/10.1038/s42003-021-02818-3>

Disclosure: Nothing to disclose.

PP1124

SAFETY AND EFFECTIVENESS OF CHOLECYSTECTOMY IN PREGNANT WOMEN WITH MILD BILIARY PANCREATITIS. PRELIMINARY RESULTS OF THE BORN STUDY

D. Tarján^{1,2}, E.Á. Szalai^{3,2}, B. Eross⁴, V. Liviu², S. Chooklin⁵, M. Hirth⁶, G. Sandblom⁷, V. Sandblom⁸, A. Edergren⁸, A. Tlili⁹, S. Sirtl¹⁰, D. de la Iglesia Gracia¹¹, F. Kurti¹², D. Wu¹³, A. Gherbon¹⁴, L. Nawacki¹⁵, A. Constantinescu¹⁶, N. Shirinskaya¹⁷, S. Pandanaboyana¹⁸, T. Ikeura¹⁹, T. Cúrdia Gonçalves²⁰, A. Bouzid²¹, L. Rasmussen²², B. Andersson²³, N. Ács²⁴, N. Farkas²⁵, A. Mikó²⁶, P. Hegyi²⁷

¹Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Semmelweis University, Department of Restorative Dentistry and Endodontics, Budapest, Hungary, ⁴Semmelweis University, Institute for Translational Medicine, Budapest, Hungary, ⁵Lviv Regional Clinical Hospital, Department of Surgery, Lviv, Ukraine, ⁶University of Heidelberg, Department of Medicine II, Medical Faculty Mannheim, Heidelberg, Germany, ⁷Karolinska Institutet, Clintec, Stockholm, Sweden, ⁸Karolinska Institutet, Stockholm, Sweden, ⁹University Hospital of Gabes, Faculty of medicine of Sfax, Department of General Surgery, Sfax, Tunisia, ¹⁰LMU University Hospital, Department of Medicine II, Munich, Germany, ¹¹University Hospital of Santiago de Compostela, Gastroenterology Department, Santiago de Compostela, Spain, ¹²University Hospital Center "Mother Theresa", Department of Gastroenterology and Hepatology, Tirana, Albania, ¹³Peking Union Medical College Hospital, State Key Laboratory of Complex Severe and Rare Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, ¹⁴"Victor Babes" University of Medicine and Pharmacy, Department VII Internal Medicine - Diabetes, Nutrition, Metabolic Diseases and Systemic Rheumatology, Timisoara, Romania, ¹⁵The Jan Kochanowski University in Kielce, Kielce, Poland, ¹⁶Floreasca Emergency Clinic Hospital Bucharest, Gastroenterology, Bucharest, Romania, ¹⁷Omsk State Medical University, Omsk, Russian Federation, ¹⁸Freeman hospital, Newcastle upon tyne, United Kingdom, ¹⁹Kansai Medical University Hospital, Division of Gastroenterology and Hepatology, Osaka, Japan, ²⁰Hospital da Senhora da Oliveira - Guimarães, Gastroenterology Department, Guimarães, Portugal, ²¹Mahmoud Matri Hospital, Ariana, Tunisia, ²²Hvidovre Hospital, Department of Surgical Gastroenterology, Hvidovre, Denmark, ²³Skane University Hospital and Institution for Clinical Sciences Lund, Department of Surgery, Lund, Sweden, ²⁴Semmelweis University, Department of Obstetrics and Gynecology, Budapest, Hungary, ²⁵University of Pécs, Institute for Translational Medicine, Pécs, Hungary, ²⁶University of Pécs, Medical School, Institute For Translational Medicine, Pécs, Hungary, ²⁷University of Pecs, Centre for Translational Medicine, Pecs, Hungary

Contact E-Mail Address: dori.tarjan@gmail.com

Introduction: Acute biliary pancreatitis in pregnant patients poses a rare yet significant challenge for clinicians. While early cholecystectomy is a recommended approach after mild biliary pancreatitis in the general population to prevent recurrence and mitigate gallstone-related complications, specific guidelines for managing acute pancreatitis (AP) in pregnant patients are lacking.

Aims & Methods: This study aimed to investigate the safety and effectiveness of cholecystectomy during pregnancy following an episode of mild acute biliary pancreatitis. An international survey was conducted across seventeen centers worldwide in 2023, using both Excel and Redcap plat-

forms. The survey encompassed questions related to demographic information, clinical presentation, management strategies, timing of cholecystectomy, approaches to the procedure, complications, and outcomes (including recurrence of AP, other gallstone-related complications, and maternal and fetal outcomes). Descriptive statistics were calculated for continuous variables, while categorical values were represented as case numbers and percentages. Statistical significance was determined using a t-test and the Mann–Whitney U and Mood's test.

Results: The study included pregnant women who underwent cholecystectomy during or after pregnancy. According to our international survey, 22% (11/50) of patients had cholecystectomy during pregnancy. Patients who underwent cholecystectomy had a lower rate of readmission due to recurrent AP episodes or other gallstone-related complications (0% and 28%; 0/11 and 11/39). There were no significant differences in cholecystectomy-related complications (9.1% and 12%; 1/11 and 3/26). The incidence of preterm birth was 11% and 8.1% (1/9 and 3/37), while fetal loss rates were 18% (2/11) both fetal losses occurred when surgery was performed in the first trimester and 0% (0/39).

Conclusion: Cholecystectomy effectively prevents the recurrence of AP and other biliary complications, with no observed differences in intra- and postoperative complications during and after pregnancy. Thus, cholecystectomy should be performed in mild biliary pancreatitis in the second and third trimesters of pregnancy. Further studies are needed to evaluate the safety of cholecystectomy in the first trimester.

Disclosure: Nothing to disclose.

PP1125

RISK FACTORS FOR POST-ACUTE PANCREATITIS DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

O.J. Zahariev^{1,2}, S. Bunduc^{2,3}, A. Kovacs^{2,4}, D. Demeter^{2,5}, L. Havelda^{1,2}, B.C. Budai^{1,2}, D.S. Veres^{2,6}, N. Hosszúfalusi^{2,4}, B.M. Eröss^{1,2,7}, B. Teutsch^{2,7}, M.F. Juhász^{8,7}, P. Hegyi^{1,2,7,9}

¹Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁴Semmelweis University, Department of Internal Medicine and Hematology, Budapest, Hungary, ⁵Central Hospital of Northern Pest - Military Hospital, Dietetic Services, Budapest, Hungary, ⁶Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁷University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ⁸Heim Pál National Pediatric Institute, Budapest, Hungary, ⁹University of Szeged, Interdisciplinary Centre of Excellence for Research Development and Innovation, Translational Pancreatology Research Group, Szeged, Hungary

Contact E-Mail Address: olga.zahariev@gmail.com

Introduction: Approximately 40% of patients develop diabetes mellitus (DM) after acute pancreatitis (AP). Even a single episode of mild AP confers a two-fold increase in DM risk compared to the general population. Nonetheless, information on risk factors is limited.

Aims & Methods: We aimed to identify risk factors for developing PD or DM following AP.

We conducted a systematic search of three databases up until September 4, 2023, to get direct, within-study comparisons of risk factors on the incidence of PD and DM in patients with AP. If it was not possible to distinguish the PD and DM incidence rates, we presented it as a composite outcome: PD/DM. The random-effects model was used in the meta-analysis to compute pooled odds ratios (OR) with 95% confidence intervals (CI).

Results: The 61 eligible studies reported on 79 risk factors. The meta-analysis included 50 studies, 76,797 participants and 34 risk factor and outcome pairs. We found that the odds of developing DM was significantly higher if the AP was severe or moderately severe (OR: 2.11; CI: 1.30–3.41), the etiology was alcoholic (OR: 1.82; CI: 1.09–3.04), organ failure occurred (OR: 3.19; CI: 0.55–18.64), the patient had recurrent AP (OR: 1.89; CI: 0.95–3.77), liver cirrhosis (OR: 2.48; CI: 0.18–34.25), chronic kidney disease (OR: 2.10; CI: 1.85–2.38), dyslipidemia (OR: 1.82; CI: 0.68–4.84) or was obese (OR: 1.85; CI: 1.43–2.38). A higher probability of developing PD/DM was linked to severe and moderately severe AP (OR: 4.32; CI: 1.76–10.60), pancreatic necrosis (OR: 5.53; CI: 1.59–19.21) and hypertriglyceridemic AP etiology (OR: 3.27; CI: 0.17–63.91).

Conclusion: A number of factors increase the risk of developing PD or DM following AP, including severe and moderately severe AP, alcoholic and hypertriglyceridemic etiologies, pancreatic necrosis, organ failure, recurrent acute pancreatitis and comorbidities of obesity, chronic kidney disease, liver disease, and dyslipidemia.

Disclosure: Nothing to disclose.

PP1126

NUTRITIONAL STATUS OF ACUTE PANCREATITIS PATIENTS

O.J. Zahariev^{1,2}, K.L. Vámosy¹, B.C. Budai^{1,2}, L. Havelda^{1,2}, B.M. Eröss^{1,2,3}, J.P. Hegyi^{1,2}, F.H. Petlickij¹, P. Hegyi^{1,2,3,4}
¹Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ⁴University of Szeged, Interdisciplinary Centre of Excellence for Research Development and Innovation, Translational Pancreatology Research Group, Szeged, Hungary

Contact E-Mail Address: olga.zahariev@gmail.com

Introduction: Malnutrition has been shown to worsen the course and outcome of many diseases. However, the Malnutrition Universal Screening Tool (MUST), an internationally accepted nutritional score, has not been widely studied in acute pancreatitis, despite the known fact that the dietary habits of patients with pancreatitis of different etiologies vary.

Aims & Methods: Our objective was to examine the MUST score in pancreatitis.

All patients were assessed for MUST on admission at Semmelweis University Institute of Pancreatic Diseases between 04.10.2021 and 21.02.2024. The MUST score was compared with the etiology and outcome of the disease.

Results: Of the 1148 patients admitted to the unit 994 patients had complete data on MUST score and severity and 992 patients had data on etiology.

Most patients were at low risk of malnutrition (MUST 0) 76,3% (n=760), 10,7% (n=107) had a moderate risk (MUST 1) and 12,9% (n=129) had a high risk (MUST score greater than 1). In patients with a MUST score over two alcoholic etiology was the most common (44,4%), while in patients at low risk of malnutrition biliary etiology was predominant (51,3%). Overweight and obese patients (BMI 25+) typically had biliary AP (47,9%, 61,3%), while normal and underweight patients most often had alcoholic AP (46,4%, 41,3%).

The largest proportion of obese patients (BMI 30+) were seen in hypertriglyceridemic AP (72,2%) compared to other etiologies. The proportion of non-mild AP severity was similar in patients with MUST scores of 0, 1, and 2 (32,7%, 35,5%, and 30,1%, respectively), rising to 50% in patients with MUST scores over two. The largest proportion of severe cases (19,4%) was seen in patients with MUST scores over two.

Conclusion: Patients with higher BMI and lower malnutrition risk tend to have more often biliary etiology, while higher MUST score and lower BMI is characteristic of alcoholic AP. Malnutrition is a risk factor for severe AP.

Disclosure: Nothing to disclose.

PP1127

IDENTIFYING PREDICTORS FOR THE EVOLUTION OF ACUTE PANCREATITIS INTO RECURRENT AND CHRONIC FORMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

E.-B. Gagy^{1,2}, M. Obeidat¹, E. Tari³, S. Váncsa^{3,1}, Á. Zolcsák¹, P. Banovcin⁴, P.J. Hegyi^{1,3}, P. Hegyi^{3,1}, B. Eross^{3,1}

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Selye János Doctoral College for Advanced Studies, Semmelweis University, Budapest, Hungary, ³Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ⁴JESSENIUS FACULTY OF MEDICINE, COMENIUS UNIVERSITY, Department of Gastroenterology, Martin, Slovakia

Contact E-Mail Address: endre.gg@gmail.com

Introduction: The transition from acute pancreatitis (AP) to recurrent (RAP) and chronic (CP) pancreatitis poses significant clinical challenges.

Aims & Methods: This systematic review and meta-analysis aimed to identify risk factors associated with this progression. Following the protocol registration on PROSPERO (CRD42022368931), we searched Medline, Embase, and Cochrane databases up to December 19th, 2023, for studies examining risk factors for the evolution of AP into RAP or CP. Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using the random effects model. Heterogeneity was evaluated using the I^2 statistic. The risk of bias assessment was performed using the Quality in Prognostic Studies (QUIPS) tool.

Results: A total of 124 articles were included in the meta-analysis, and several risk factors were identified for the progression of AP into RAP and CP. We found the following risk factors of AP recurrence: male gender, smoking, alcoholic etiology, hypertriglyceridemia, diabetes mellitus, pseudocyst, etc. The pooled OR for the male gender was 1.49 (95% CI: 1.31-1.62, $I^2=25\%$), for smoking was 1.47 (95% CI: 1.22-1.71, $I^2=57\%$), for alcoholic etiology was 1.78 (95% CI: 1.45-2.14, $I^2=78\%$), for hypertriglyceridemia was 2.48 (95% CI: 2.16-2.83, $I^2=9\%$), for diabetes mellitus was 1.51 (95% CI: 1.21-1.75, $I^2=0\%$), for pseudocyst was 2.23 (95% CI: 1.61-3.12, $I^2=0\%$). We also found risk factors of RAP progression into CP. The risk of bias was moderate in the majority of the included studies.

Conclusion: These findings suggest that addressing modifiable risk factors might be key in preventing the progression of pancreatitis

Disclosure: Nothing to disclose.

PP1128

PREDICTING ACUTE PANCREATITIS SEVERITY WITH CT-DERIVED BODY COMPOSITION: A RETROSPECTIVE STUDY

R.Z. Borbély^{1,2}, V. Vass^{1,3}, K. Márta^{1,3}, B. Teutsch^{1,4}, B. Eross^{1,3}, P.J. Hegyi^{1,3}, Á. Vincze⁵, E.Á. Szalai^{1,6}, A. Szentesi⁷, N. Faluhelyi^{1,8}, P. Hegyi^{1,3,7,9}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Bajcsy-Zsilinszky Hospital and Clinic, Department of Medical Imaging, Budapest, Hungary, ³Semmelweis University, Institute for Pancreatic Diseases, Budapest, Hungary, ⁴Semmelweis University, Department of Radiology, Medical Imaging Center, Budapest, Hungary, ⁵University of Pécs, Division of Gastroenterology, Medical School, Pécs, Hungary, ⁶Semmelweis University, Department of Restorative Dentistry and Endodontics, Budapest, Hungary, ⁷University of Pécs, Institute for Translational Medicine, Pécs, Hungary, ⁸University of Pécs, Department of Medical Imaging, Medical School, Pécs, Hungary, ⁹University of Szeged, Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, Szeged, Hungary

Contact E-Mail Address: borbely.ruben@stud.semmelweis.hu

Introduction: Accurately predicting the severity of acute pancreatitis (AP) is a challenge in clinical practice. Recent advancements in artificial intelligence and neural network computing enable the use of CT scans for body composition analysis in addition to their diagnostic role. However, the prognostic application of various CT metrics has been inconsistent, resulting in conflicting data regarding the most reliable indicators of disease severity.

Aims & Methods: Our study aimed to evaluate the key CT body composition metrics for predicting severity in patients with acute pancreatitis (AP). We conducted a retrospective analysis of 279 AP patients from the University of Pécs, Hungary, all of whom underwent a CT scan within the first 24 hours of admission to the Department of Gastroenterology. Using the TotalSegmentator tool¹ of the 3D Slicer software, we measured the areas of visceral and subcutaneous adipose tissues (VAT and SAT) and skeletal muscle (SMA) at the level of the third lumbar vertebra (L3), with the results in square centimeters.

These area measurements were then normalized for patient height by dividing them by the square of the patient's height to produce indices similar to the Body Mass Index (BMI), namely the VATI (Visceral Adipose Tissue Index), SATI (Subcutaneous Adipose Tissue Index), and SMI (Skeletal Muscle Index).

We also quantified the average muscle radio-density in Hounsfield Units (HU), indicative of fatty muscle infiltration - associated with lower density values. We explored these metrics as potential predictors of severe AP, as defined by the Revised Atlanta Criteria².

To assess predictive accuracy, we created receiver operating characteristic (ROC) curves and computed the area under the curve (AUC) for both genders separately due to inherent differences in normal values. The actual clinical progression of AP in these patients provided the reference standard. All statistical analyses were done using IBM SPSS Statistics software; preliminary results are available below.

Results: The data encompassed 174 male and 105 female patients, with an AP severity distribution of 139 mild, 116 moderately severe, and 24 severe cases. The AUC values for various CT metrics, differentiated by gender, are displayed in the subsequent table.

CT metric	Metric type	Value associated with severe AP	AUC for Females	AUC for Males
SMA	area	Low	0.57	0.59
SMI	index	Inconsistent	0.58	0.54
SAT	area	High	0.55	0.68
SATI	index	High	0.57	0.69
VAT	area	High	0.66	0.63
VATI	index	High	0.72	0.65
Muscle radio-density	average CT density	Low	0.64	0.72
Visceral / Subcutaneous fat area	ratio	Inconsistent	0.6	0.57
Fat / Muscle area	ratio	High	0.66	0.74

Conclusion: CT-derived body composition metrics demonstrate substantial prognostic value in identifying severe AP. Index-based metrics demonstrated slightly improved accuracy over simple area measurements. Elevated levels of subcutaneous and visceral fat emerged as predictors of severe AP, as evidenced by the SAT, SATI, VAT, and VATI metrics. Furthermore, a decreased muscle radio-density was a better predictor of severity than the skeletal muscle area (SMA) or skeletal muscle index (SMI) alone. The combination of significant fat accumulation and skeletal muscle loss - often referred to as sarcopenic obesity - was also predictive of more severe AP. Determining the precise cutoff values for these metrics to optimize predictive accuracy continues to be a key objective of our ongoing research.

References:

- 1 - Wasserthal J, Breit HC, Meyer MT, Pradella M, Hinck D, Sauter AW, Heye T, Boll DT, Cyriac J, Yang S, Bach M, Segeroth M. TotalSegmentator: Robust Segmentation of 104 Anatomic Structures in CT Images. *Radiol Artif Intell.* 2023 Jul 5;5(5):e230024. doi: 10.1148/ryai.230024. PMID: 37795137; PMCID: PMC10546353.
- 2 - Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut.* 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779. Epub 2012 Oct 25. PMID: 23100216.

Disclosure: Nothing to disclose.

PP1129

INVESTIGATING THE PREVALENCE OF ANXIETY AND DEPRESSION IN PATIENTS WITH PANCREATITIS

T. Feher^{1,2}, M. Obeidat¹, Á. Zolcsák^{1,3}, R. Papp^{1,4}, B. Teutsch^{1,5,6}, M.A. Engh¹, R. Csaba¹, L. Réthy¹, P. Hegyi^{1,2,6}, R. Nagy^{1,6,7}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Semmelweis University, Institute for Pancreatic Diseases, Budapest, Hungary, ³Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁴Semmelweis University, Centre of Science and Innovations, Budapest, Hungary, ⁵Semmelweis University, Department of Radiology, Medical Imaging Centre, Budapest, Hungary, ⁶Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁷Heim Pál National Pediatric Institute, Budapest, Hungary

Contact E-Mail Address: fehertibordaniel@gmail.com

Introduction: The bidirectional interplay of the brain-gut axis alongside manifestations of anxiety and depression has already been demonstrated. Despite this fact, routine mental health assessments and interventions are not well-established in the treatment of acute (AP) and chronic pancreatitis (CP), potentially worsening clinical outcomes.

Our objective is to achieve a comprehensive understanding of the mind-body connection within the context of pancreatitis by assessing the prevalence of depression and anxiety in patients with AP and CP.

Aims & Methods: Our protocol was registered on PROSPERO (CRD42023481739). We conducted a systematic search on 10 November 2023 in three databases (MEDLINE, Embase, and CENTRAL) to identify studies reporting the occurrence of depressive and anxiety-related symptoms in pancreatitis. The pooled proportion rate with 95% confidence intervals (CI) was calculated using a random-effects model.

Results: The prevalence of depressive symptoms was 16% in AP (CI 0.06; 0.39), while it was 34% in CP (CI 0.27; 0.43). The prevalence of anxiety symptoms in AP and CP was 15% (CI 0.07; 0.32) and 35% (CI 0.26; 0.45), respectively.

Conclusion: Anxiety and depression are significantly more frequently observed among individuals with pancreatitis compared to the general population. These conditions occur twice as often in CP compared to AP. Thus, we underscore the significance of psychological interventions in this patient population.

Disclosure: Nothing to disclose.

PP1130

HYPERCALCEMIA CAUSES MORE SEVERE PANCREATITIS

G. Gieszinger¹, B. Kui¹, P. Hegyi², P.J. Hegyi², Á. Vincze³, B. Erőss⁴, A. Szentesi⁵, V. Vass², Z. Abonyi-Tóth², F. Izbéki⁶, L. Czakó¹

¹Albert Szent-Györgyi Medical School, University of Szeged, Department of Internal Medicine, Center for Gastroenterology, Szeged, Hungary, ²Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ³University of Pécs, Division of Gastroenterology, First Department of Medicine, Pécs, Hungary, ⁴Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary, ⁵Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁶Szent György Teaching Hospital of County Fejér, Székesfehérvár, Hungary

Contact E-Mail Address: gieszinger.gabor@gmail.com

Introduction: Acute pancreatitis (AP) is one of the most common gastroenterological diseases requiring admission to the hospital. The main etiological factors of AP are gallstones and excessive alcohol consumption, but rarer causes, such as hypercalcemia, should keep on mind. Only few cases are reported in the literature, and the severity of hypercalcaemia-induced acute pancreatitis is not known.

Aims & Methods: We aim to assess the occurrence and severity of hypercalcaemia-induced AP and compare it with the clinical characteristics of AP caused by other etiological factors. We collected patients from the Hungarian Acute Pancreatitis Registry, Hungarian GOULASH study and the Europe-wide EASY study, who had AP and had a serum calcium level above 2.6 mmol/l. Patients were divided into three groups: hypercalcaemia-induced AP, where no other etiology than hypercalcemia were present, mixed etiology group, where both hypercalcemia and other etiologies were revealed and the control group with normal serum calcium level. Propensity score matching adjusted by age, sex, diabetes, lipid disorder, previous pancreatic disease was made and several outcome parameters were analyzed during the statistical analysis. Hypercalcemic cases were divided into 3 subgroups based on the level of serum calcium: mild (2.6 < >3.0 mmol/l), moderate (3.0 < >3.5 mmol/l) or severe hypercalcemia (>3.5 mmol/l).

Results: 1.02% of our AP patients (19/1867) had clear hypercalcemic etiology and 3.75 % (70/1867) of the patients had mixed etiology, 1778 patients were in the control group. There was no difference in the mean ages of the patients in the three groups (57.3± 16.3 and 56.1 ± 20.1 vs. 55.1 ±

14.6 years). Severe AP was significantly more frequent in patients with hypercalcemia-induced AP compared to the control group [21.05% (4/19) vs 6.13% (109/1778); odds ratio: 4.08 (95% CI, 1.08-15.38)]. Renal failure was more frequent in hypercalcemic etiology compared to AP patients with normal serum calcium level [27.27% (3/11) vs 5.35% (95/1776); odds ratio: 6.63, (95% CI, 1.36-32.35)].

There was no significant difference in CRP, amylase, lipase, WBC, creatinine, length of hospital stay, mortality, intensive care admission, the presence of pancreatic necrosis, pseudocysts, and other organ failure between the hypercalcemic or mixed etiology and the control groups.

There was no significant difference in the severity of AP between the mixed etiology and normal serum calcium groups. The outcome of acute pancreatitis was not influenced by the severity of hypercalcemia within the hypercalcemic group.

Conclusion: Hypercalcemia-induced AP has a higher risk for developing into severe AP and renal failure compared to other etiology.

Disclosure: Nothing to disclose.

PP1131

CLINICAL AND LABORATORY FACTORS ASSOCIATED TO ANTIBIOTIC USE IN ACUTE PANCREATITIS

R. Mendoza-Rodriguez¹, F. Valverde-López², T. Tripana-Iglesias¹, A. Lancho-Muñoz¹, E. Lopez-Gonzalez¹, J.G. Martínez-Cara³, E. Redondo-Cerezo⁴

¹Virgen de las Nieves University Hospital, Granada, Spain, ²Virgen de las Nieves University Hospital, Gastroenterology and Hepatology, Granada, Spain, ³Virgen de las Nieves University Hospital, Endoscopy Unit, Granada, Spain, ⁴Virgen de las Nieves University Hospital, Gastroenterology, Granada, Spain

Contact E-Mail Address: fcovalverde89@gmail.com

Introduction: Infectious complications are a significant concern in Acute Pancreatitis (AP), contributing to increased morbidity and mortality. Antibiotics are crucial in their management and should be initiated when infection is suspected. However, their overuse can lead to complications and antimicrobial resistance.

Aims & Methods: The aim of this retrospective study is to evaluate antibiotic utilization in real-world practice within a Spanish cohort and identify clinical and laboratory factors associated with their use. Patients admitted to our tertiary center for acute pancreatitis were included. Clinical and laboratory parameters routinely used in acute pancreatitis were collected upon admission and after 48 hours. Any infections (mainly infected necrosis, acute cholangitis following Tokyo 2018 criteria, pneumonia, and urinary tract infections) were documented, and patients were followed until discharge or death.

Poor outcomes, such as severe acute pancreatitis based on the Atlanta 2012 classification and death, were assessed in patients who received antibiotics and those who did not.

Results: 211 patients were recruited from July 2017 to December 2017. 111 (52.6%) were women, and in 170 (61.8%) the etiology was biliary. Antibiotic therapy was used in 77 (36.5%) patients, 21 had severe acute pancreatitis (9.95%) and 11 died (5.21%).

Comparison between patients to whom antibiotics were prescribed and those who did not are shown on Table 1. Variables included in the logistic regression were SIRS on admission, PCR > 150mg/dL after 48h, PCT > 1 ng/ml on admission and BT > 3mg/dL on admission with the presence of SIRS and BT > 3 mg/dL at admission proving to be significant in the end.

N (%)	No antibiotics 134 (63,5%)	Need of antibiotics 77 (36,5%)	P value
Leucocytes, mean (sd)	12.642 (5.317)	14.390 (5.536)	< 0,005
Procalcitonin > 1 ng/ml, n (%)	13 (11,6)	18 (26,5)	< 0.01
Total Bilirubin , mean (sd)	1.68 (1.84)	2.74 (2.57)	0,001
C reactive protein after 48h, mean (sd)	128 (112)	173 (129)	0,022
Temperature (Celsius), mean (sd)	36,2 (0,5)	36,3 (0,607)	n.s
SIRS, n (%)	13 (9,7)	29 (37,6)	<0.001
Extrapneumonic infection, n (%)	4 (1,9)	25 (32,4)	<0.001
Severe Acute Pancreatitis, n (%)	6 (4,4)	15 (19)	0.001
Death, n (%)	2 (1,4)	9 (11,6)	0.001

Table 1. Patient Characteristics: Comparison between patients with Indicated antibiotic therapy and those without antibiotic therapy.

Conclusion: Antibiotic therapy is routinely used in AP due to infected necrosis, acute cholangitis, or extrapancreatic infections. However, the early inflammatory response typical in AP makes it troublesome to distinguish whether sepsis is occurring due to an extrapancreatic infection, leading to potential overuse of antibiotics. In our sample, antibiotics were used in 36.5% of patients, and those developed SAP and death more often. Among clinical and laboratory factors related to antibiotic use, only total bilirubin > 3mg/dL and the presence of SIRS on admission were independently related to the need for antibiotics. However, it is possible that some patients with SIRS and high bilirubin on admission do not truly require antibiotics, as these changes can also be due to AP. Although procalcitonin has been positioned as a potential marker of infection and can guide the need for antibiotics, future research could explore other factors to better select patients without overt infection for empiric antibiotic therapy.

Disclosure: Nothing to disclose.

PP1132

A LARGE COHORT STUDY REGARDING THE HYPERTRIGLYCERIDEMIA INDUCED ACUTE PANCREATITIS

M.-R. Pahomeanu¹, A.I. Ghiță¹, D.I. Constantinescu¹, D.G. Grigore¹, A.D. Bota¹, C. Tieranu², L. Negreanu³, Bucharest Acute Pancreatitis Index Study Group

¹Carol Davila University of Medicine and Pharmacy Bucharest, Faculty of Medicine, Bucharest, Romania, ²Elias Emergency University Hospital, Gastroenterology, Bucharest, Romania, ³Spitalul Universitar de Urgenta Bucuresti, Internal Medicine Gastroenterology, Bucharest, Romania

Contact E-Mail Address: mihai.pahomeanu@drd.umfcd.ro

Introduction: This study aims to examine the extent of notable variations in recurrence rates, admissions to the intensive care unit (ICU), length of hospital stay (LoS), morphological characteristics, disease severity, and patient age between hypertriglyceridemia-induced acute pancreatitis (HTG-AP) and other causes of acute pancreatitis (OAP).

Aims & Methods: A retrospective, single-center cohort study was conducted using data from the BUC-API registry, which includes 1,855 consecutive cases of acute pancreatitis. We aim to seek if there are differences between cases with HTG-AP and OAP regarding demographical and clinical data.

Results: Our analysis reveals a modest association between HTG-AP and increased recurrence rates ($\chi^2(1)=6.9$, $p<0.01$, Cramer's $V=0.07$). Patients with HTG-AP had a median age of 44.5 years and experienced longer ICU stays (median=7.0 days) compared to those with OAP (median=3.0 days). Furthermore, patients with HTG-AP were more likely to develop acute peripancreatic fluid collections, require ICU admission, experience severe disease, and be treated in a gastroenterology ward ($p=0.02$, $p<0.01$, respectively).

		HTG-AP (n=58)	OAP (n=1514)	p-value
Severity	Mild	19 (32.8%)	796 (52.6%)	p<0.01
ICU	Yes	10 (17.2%)	125 (8.3%)	p=0.02
Ward of care	Gastroenterology	42 (72.4%)	744 (49.1%)	p<0.01
Recurrence or first attack	Recurrence	18 (31.0%)	265 (17.5%)	p<0.01
Morphology	APFC	9 (15.5%)	110 (7.3%)	p=0.02
	Normal pancreas	1 (1.7%)	241 (15.9%)	
Age (years)	Median	44.5 (IQR=9)	57.0 (IQR=25)	p<0.01
Length of stay (days)	Median	8.3 (IQR=9.3)	7.0 (IQR=5.0)	p=0.01
Length of stay ICU (days)	Median	7.0 (IQR=22.5)	3.0 (IQR=4.0)	p<0.01

Table 1 – Comparative analysis. Only findings with p-value <=0.01 presented.

Conclusion: HTG-AP is frequently linked with intensive care needs. The association between HTG-AP and recurrence may be linked to suboptimal adherence to lipid-lowering therapy. The typical profile of an HTG-AP patient is a middle-aged, mainly male individual with a history of acute pancreatitis, necessitating gastroenterology ward care, facing longer ICU and hospital stays, at a higher risk for severe acute pancreatitis (SAP), and with an increased likelihood of developing acute peripancreatic fluid collection (APFC).

References:

1. A. L. Yang și J. McNabb-Baltar, “Hypertriglyceridemia and acute pancreatitis”, *PANCREATOLOGY*, vol. 20, nr. 5, pp. 795–800, iul. 2020, doi: 10.1016/j.pan.2020.06.005.
2. D. Mosztbacher *et al.*, “Hypertriglyceridemia-induced acute pancreatitis: A prospective, multicenter, international cohort analysis of 716 acute pancreatitis cases”, *PANCREATOLOGY*, vol. 20, nr. 4, pp. 608–616, iun. 2020, doi: 10.1016/j.pan.2020.03.018.
3. V. P. Pulipati, E. A. Brinton, și B. Hatipoglu, “Management of Mild-to-Moderate Hypertriglyceridemia”, *Endocr. Pract.*, vol. 28, nr. 11, pp. 1187–1195, nov. 2022, doi: 10.1016/j.eprac.2022.07.003.
4. R. A. Carr, B. J. Rejowski, G. A. Cote, H. A. Pitt, și N. J. Zyromski, “Systematic review of hypertriglyceridemia-induced acute pancreatitis: A more virulent etiology?”, *PANCREATOLOGY*, vol. 16, nr. 4, pp. 469–476, aug. 2016, doi: 10.1016/j.pan.2016.02.011.

Disclosure: Nothing to disclose.

PP1133

RISK FACTORS OF PANCREATIC EXOCRINE INSUFFICIENCY ASSOCIATED AFTER ACUTE PANCREATITIS – A SYSTEMATIC REVIEW AND META-ANALYSIS

O. Eperjesi^{1,2}, M. Bucur¹, A. Rancz¹, Á. Zolcsák^{1,3}, M.A. Engh¹, M. Obeidat¹, B. Erőss^{1,4,5}, P. Ferdinándy^{1,6}, A. Szentesi^{1,5}, P. Hegyi^{1,4}, S. Bunduc^{1,7,8}

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Department of Internal Medicine, Toldy Ferenc Hospital, Cegléd, Hungary, ³Department of Biophysics and Radiation Biology, Semmelweis University, Budapest, Hungary, ⁴Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary, ⁵Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁶Department of Pharmacology and Pharmacotherapy, Medical Faculty, Semmelweis University, Budapest, Hungary, ⁷Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁸Digestive Disease and Liver Transplant Center, Fundeni Clinical Institute, Bucharest, Romania

Contact E-Mail Address: eperjesiorsi1348@gmail.com

Introduction: 96–98% of patients survive acute pancreatitis (AP), but in the post-AP phase, patients are at high risk of morbidity and mortality. It has been shown that pancreatic exocrine insufficiency can occur after AP.

Aims & Methods: We aimed to investigate the rate, risk factors, and the effect of pancreatic enzyme replacement therapy (PERT) for PEI in patients with AP. The study protocol was registered on PROSPERO (CRD42024516403). We conducted a systematic search on 5 February 2024 in three databases (PubMed, EMBASE, and CENTRAL). We included in the analysis studies reporting on risk factors and PERT efficacy in PEI associated with AP. Pooled proportion and odds ratios (OR) with a 95% confidence interval (CI) were calculated using a random effect model.

Results: Fifty-six articles were included in our meta-analysis. Among 17896 patients with AP, the pooled proportion of PEI was 20 % ([CI]: 15–26). The odds of PEI development were two-fold higher in severe acute pancreatitis (OR=2.44, [CI]: 0.98–6.11) compared with mild or moderate AP and three times higher after necrosectomy compared to patients without necrosectomy (OR=3.26, [CI]: 1.6–6.64). There was no significant difference between the odds of PEI among AP patients with necrosis (OR=1.43, [CI]: 0.32–6.45) and those without necrosis. However, the odds of PEI were twice as high in patients with infected necrosis (OR=2.13, [CI]: 0.93–4.87) than in patients with sterile necrosis. Pancreatic enzyme replacement therapy was prescribed for 22% ([CI]: 16–30) of patients after AP.

Conclusion: One in five patients with AP develops PEI. The rate is higher in patients with severe AP, infected necrosis, or who need necrosectomy. Patients with AP should be screened for PEI to allow timely PERT administration.

Disclosure: Nothing to disclose.

PP1134

UTILITY OF DYNAMIC ASSESSMENT OF FACTORS RELATED TO SEVERE ACUTE PANCREATITIS

F. Valverde-López¹, M. Libroero-Jimenez², E. Lopez-Gonzalez², M. Lecuona-Muñoz², J.G. Martínez-Cara³, E. Redondo-Cerezo⁴
¹Virgen de las Nieves University Hospital, Gastroenterology and Hepatology, Granada, Spain, ²Virgen de las Nieves University Hospital, Granada, Spain, ³Virgen de las Nieves University Hospital, Endoscopy Unit, Granada, Spain, ⁴Virgen de las Nieves University Hospital, Gastroenterology, Granada, Spain

Contact E-Mail Address: fcovalverde89@gmail.com

Introduction: Acute pancreatitis (AP) carries an overall mortality rate of 4.2%, but in cases of severe acute pancreatitis (SAP), mortality dramatically increases to over 50%. Despite the use of several scoring systems to predict SAP in the early stages of the disease, their clinical value is limited as their performance does not significantly influence decision-making due to their low post-test probability. Although early prediction upon admission would be ideal, the development of a marker that accurately predicts severity at this stage seems unlikely. Therefore, a dynamic assessment based on early identification of changes in clinical and laboratory parameters within the first 48 hours could prove valuable in detecting unfavorable outcomes.

Aims & Methods: The aim of our study was to evaluate the clinical utility of changes in routine clinical and laboratory parameters within the first 48 hours of admission in a Spanish cohort, based on likelihood ratios and post-test probability of severe acute pancreatitis (SAP). Patients admitted to our tertiary hospital with a diagnosis of acute pancreatitis were included. Demographic information, comorbidities, and the Bedside Index for Severity in Acute Pancreatitis (BISAP) score were collected upon admission, while vital signs, routine laboratory parameters typically used in acute pancreatitis, and the Systemic Inflammatory Response Syndrome (SIRS) criteria were collected upon admission and after 48 hours. Patients were followed until death or discharge and categorized into mild to moderately severe and severe acute pancreatitis groups.

Results: 227 patients were included in the study. The mean age was 65.3 years (standard deviation 18.9), and 115 patients were women (50.7%). Among them, 22 (10.7%) developed severe acute pancreatitis, and 13 (5.7%) died. BISAP $\geq$ 2, rising BUN, increasing heart rate over 20 beats per minute, and persistent SIRS were identified as independent risk factors for severe acute pancreatitis. The positive likelihood ratio and post-test probability of SAP are shown in Table 1. When combining the parameters independently related to SAP, we found that BISAP $\geq$ 2 combined with persistent SIRS after 48 hours and any rise in BUN combined with persistent SIRS showed the highest post-test probabilities (82% and 80%, respectively).

Predictor	+ LR (CI 95%)	+ Post-test probability of SAP
Rise in heart rate > 20 bpm	3.27 (1.44-7.43)	26% (13-44%)
Rising BUN	3.57 (2.52- 5.04)	28% (21-35%)
Rising Hematocrit	1.59 (0.75-3.36)	15% (8-28%)
BISAP $\geq$ 2	2.81 (2.16-3.66)	23% (19-28%)
SIRS on admission	2.80 (1.74-4.48)	23% (16-32%)
SIRS after 48h	12 (5.11-26)	56% (36-74%)
BISAP $\geq$ 2 and rising BUN	8.22 (4.80-14)	47% (34-60%)
BISAP $\geq$ 2 and SIRS after 48h	42 (9.62-181)	82% (51-95%)

Table 1. Positive likelihood ratio of clinical and laboratory parameters related to SAP with a pre-test probability of 10.7%.

Conclusion: Monitoring the evolution of the disease in the first hours is crucial, especially in patients who develop organ failure. For those who do not, dynamic assessment of known risk factors for SAP can be valuable

in clinical practice. In our sample, the combination of BISAP and dynamic assessment of BUN, heart rate, and SIRS raised the probability of SAP up to 80%.

Ideally, assessing the specific incidence of SAP in multicenter cohorts within a specific area and the impact of these and other factors that aid in monitoring patient evolution would provide valuable insights.

Disclosure: Nothing to disclose.

PP1135

ALTERED ENDOCRINE FUNCTION IN A MOUSE MODEL OF CHRONIC PANCREATITIS

A. Ébert¹, T. Gajdos², M. Erdélyi², R. Ormos², G. Koszta¹, P. Hegyi³, V. Venglovecz¹

¹University of Szeged, Department of Pharmacology and Pharmacotherapy, Szeged, Hungary, ²University of Szeged, Department of Optics and Quantum Electronics, Szeged, Hungary, ³University of Pecs, Centre for Translational Medicine, Pecs, Hungary

Contact E-Mail Address: venglovecz.viktoria@med.u-szeged.hu

Introduction: It is well known that chronic pancreatitis increases the risk of diabetes development, however, the underlying mechanism is not completely clear. Therefore, our aim in this study was to investigate the function of the endocrine pancreas in a mouse model of CP, with particular regard to the expression of the cystic fibrosis conductance regulator (CFTR) chloride channel, which presumably plays role in beta cell insulin secretion.

Aims & Methods: CP was induced in FVB/N mice by i.p. administration of cerulein. Following completion of disease development, we performed i.p. glucose tolerance tests (GTT) and ELISA. Freshly dissected pancreatic tissues were either fixed in paraformaldehyde for pathology or digested enzymatically for isolation of islets. Islets were dispersed and the cells were stained for CFTR, insulin and glucagon and imaged with direct stochastic optical reconstruction microscopy.

Results: GTT after four weeks of disease development shows decreased glucose tolerance and decreased, elongated insulin response to glucose load. The expression of CFTR in beta-cells is decreased after two weeks of disease development, but exceeds the control in the third week, proceeding the increased glucose intolerance. Inflammation alters islet cell composition by increasing α -cell mass and decreasing β -cell mass.

Conclusion: Regeneration processes in CP resulted in increased expression of CFTR in β -cells that seems to correlate with increased basal insulin secretion and decreased glucose tolerance. This study was supported by the CFRD-SRC Grant (SRC007) and the National Research, Development and Innovation Office (SNN134497).

Disclosure: Nothing to disclose.

PP1136

CLINICAL, RADIOLOGICAL AND ENDOSCOPIC ULTRASOUND FINDINGS IN GROOVE PANCREATITIS: A SINGLE-CENTER RETROSPECTIVE STUDY

D.E. Coelho Neto^{1,2}, S. Pinheiro Machado de Carvalho^{3,4}, T. Peres Piva^{3,4}, F. Tarcsay Marques Neto^{3,4}, T. Xavier de Andrade^{3,4}, V. Miranda Albo Cardoso^{3,4}, L. Jabor Veiga^{3,4}, C. Peres da Costa Duarte^{3,4}, G. Issa Ernesto Coelho^{3,4}, M. Issa Ernesto Coelho^{3,4}, J.F. Ernesto Coelho⁵, J.C. Ardengh⁶

¹Head of Gastrointestinal and Endoscopy Service Hospital Vitória and Samaritano Barra and Pró-Cardíaco, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ²Estácio de Sá University, Surgery and Intervencional Endoscopy, Rio de Janeiro, Brazil, ³Souza Marques Medical School, Rio de Janeiro, Brazil, ⁴LAED - Digestive Endoscopy Academic League, Rio de Janeiro, Brazil, ⁵Federal University of Rio de Janeiro Medical School, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ⁶Ribeirão Preto Medical School, (University of São Paulo), Surgery and Anatomy, Ribeirão Preto, Brazil

Contact E-Mail Address: issamari05@yahoo.com.br

Introduction: Groove pancreatitis is a rare form of focal disease that affects the groove area. As this form of pancreatitis can be mistaken for malignancy, it should be considered in patients with mass lesions in the head of the pancreas or duodenal stenosis to avoid unnecessary surgical procedures. The aim of the study was to document the clinical, radiological and endoscopic characteristics and treatment outcomes of patients with this disease.

Aims & Methods: This retrospective multicenter observational study included all patients diagnosed with one or more imaging criteria suggestive of groove pancreatitis at the participating centers. Patients with confirmed malignant findings on fine-needle aspiration/biopsy were excluded. All patients were followed up in their own centers and evaluated retrospectively.

Results: Of the 30 patients initially included with imaging criteria suggestive of groove pancreatitis, 9 patients (30%) were excluded due to malignant fine-needle aspiration results by endoscopic ultrasound or biopsy. The average age of the 21 patients included was 49 ± 10.6 years, with a male predominance of 71%. There was a history of smoking in 66.7% and alcohol consumption in 76.2% of the patients. The main endoscopic finding was gastric outlet obstruction in 16 patients (76.2%). There was thickening of the duodenal wall in 9 (42.8%), 5 (23.8%) and 16 (76.2%) patients on computed tomography, magnetic resonance imaging and endoscopic ultrasound, respectively. In addition, pancreatic head enlargement/mass was observed in 10 (47.6%), 8 (38.1%) and 12 (57.1%) patients, and duodenal wall cysts in 5 (23.8%), 1 (4.8%) and 11 (52.4%) patients, respectively. Conservative and endoscopic treatment achieved favorable results in more than 90% of patients.

Conclusion: Groove pancreatitis should be considered in any case with duodenal stenosis, duodenal wall cysts or thickening of the groove area. Various imaging modalities, including computed tomography, endoscopic ultrasound and magnetic resonance imaging, play a valuable role in characterizing groove pancreatitis. However, endoscopic fine-needle aspiration or biopsy should be considered in all cases to diagnose groove pancreatitis and exclude malignancy, which can have similar results.

Disclosure: Nothing to disclose.

PP1137

ENHANCING PANCREATIC CARE - EXPERIENCES OF A SPECIALIZED UNIT FOR BENIGN PANCREATIC DISORDERS

K. Kilani¹, M. Keller¹, T. Seufferlein¹, M. Kornmann², N. Rahbari², L. Perkhofer¹, A. Kleger¹

¹Ulm University, Internal Medicine I, Ulm, Germany, ²Ulm University, Department of Surgery, Ulm, Germany

Contact E-Mail Address: alexander.kleger@uni-ulm.de

Introduction: Benign pancreatic disorders pose significant challenges in diagnosis, treatment, and management due to their complex nature and diverse etiology. As the prevalence of pancreatic diseases continues to rise, the demand for specialized care and expertise becomes imperative. Thus the Section of Interdisciplinary Pancreatology (SIP) has been launched in 2023 at Ulm University Hospital to manage a broad spectrum of pancreatic disorders, encompassing cystic pancreatic lesions, autoimmune pancreatitis and IgG4-related disease (IgG4-RD), and all types of chronic pancreatitis.

Here, we will present insights from two years of experience within this unit, focusing on the disease spectrum, the impact of a multidisciplinary board structure, and the direct advantages of Patient-Reported Outcome Measures (PROMs) in enhancing patient care.

Aims & Methods: To basically show the structure of an interdisciplinary section of pancreatology and emphasise resulting advantages and chances in pancreas care. Moreover, descriptive analyses from PROMs, impact on decision making and paths will be shown.

Results: The structured implementation of the SIP created a level of interdisciplinarity that has not been achieved before. Thus collaborative efforts resulted in relevant changes of daily-patient care and patient paths. This is assessed and further shown by the integration of PROMs that are continuously recorded. By systematically collecting patient-reported data on symptoms, functional status, and treatment outcomes, the division gains valuable insights into the patient experience and treatment efficacy and allows patient centered therapy management. Specifically by the integration of a dedicated multidisciplinary board to review cases of benign pancreatic disorders, consensus-driven decision-making optimized diagnostic accuracy and therapeutic planning, fostering individualized approaches. One of these successful approaches that has been established are high numbers of hybrid procedures in robotic enucleation of pancreatic cysts.

Conclusion: In conclusion, our two-years experience in a division of interdisciplinary pancreatology underscores its efficacy in addressing the diverse array of pancreatic disorders. Through collaborative decision-making, regular case reviews, and the integration of PROMs, the SIP exemplifies a patient-centric approach to pancreatic care that prioritizes clinical excellence, interdisciplinary collaboration, and continuous quality improvement.

Disclosure: Nothing to disclose.

PP1138

QUALITY OF MANAGEMENT AND ADHERENCE TO UNITED EUROPEAN GASTROENTEROLOGY GUIDELINE ON IMMUNOGLOBULIN-G4-RELATED DIGESTIVE DISEASE

M. Vujasinovic^{1,2}, M. Lanzillotta^{3,4}, E. Culver^{5,6}, V. Rebours⁷, J.P. Drenth⁸, M. Stojkovic Lalosevic⁹, J. Vikse¹⁰, N. Gubergits¹¹, M. Hirth^{12,13}, V. Cardinale¹⁴, R. Motta^{6,5}, E. della Torre^{3,4}, N. Sciberras¹⁵, M.F. Maida¹⁶, A. Trikola¹⁷, F. Lammert^{18,19}, C. Descourvieres⁷, C.Y. Ponsioen⁸, J.B. Frøkjær²⁰, A. Schneider^{13,12}, D. Alvaro¹⁴, G. Capurso^{4,21}, M. Löhr^{22,2}

¹Karolinska Institutet, Department of Medicine Huddinge, Stockholm, Sweden, ²Karolinska University Hospital, Department of Upper Abdominal Diseases, Stockholm, Sweden, ³IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (Unirar), Milan, Italy, ⁴Università Vita-Salute San Raffaele, IRCCS San Raffaele Scientific Institute, Milan, Italy, ⁵University of Oxford, Oxford, United Kingdom, ⁶John Radcliffe Hospital and Nuffield Department of Medicine, Translational Gastroenterology Unit, Oxford, United Kingdom, ⁷Hospital Beaujon, Pancreatology and Digestive Oncology Department, Clichy, France, ⁸Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁹Clinical Center of Serbia, Department of Gastroenterology and Hepatology, Belgrade, Serbia, ¹⁰Stavanger University Hospital, Department of Rheumatology, Stavanger, Norway, ¹¹Multidisciplinary Clinic Into Sana, Odesa, Ukraine, ¹²University of Heidelberg, Medical Faculty at Mannheim, Mannheim, Germany, ¹³University Medical Center Mannheim, Department of Medicine II, Mannheim, Germany, ¹⁴Sapienza University of Rome, Department of Translational and Precision Medicine, Division of Gastroenterology, Rome, Italy, ¹⁵Mater Dei Hospital, Department of Gastroenterology, Msida, Malta, ¹⁶Department of Medicine and Surgery, University of Enna 'Kore', Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ¹⁷Naval Hospital of Athens, Gastrointestinal Department, Athens, Greece, ¹⁸Hannover Medical School, Health Sciences, Hannover, Germany, ¹⁹Saarland University Medical Center, Department of Medicine II, Homburg, Germany, ²⁰Aalborg University Hospital, Department of Radiology, Aalborg, Denmark, ²¹IRCCS San Raffaele Scientific Institute, Division of Pancreatic Surgery and Endosonography Division, Pancreas Translational and Clinical Research Center, Milan, Italy, ²²Karolinska Institutet, CLINTEC, Stockholm, Sweden

Contact E-Mail Address: mvujas@gmail.com

Introduction: United European Gastroenterology (UEG) Guideline on IgG4-related digestive disease provides evidence-based recommendations for the diagnosis and management of immunoglobulin G4 (IgG4)-related digestive disease in adults and children. IgG4-related digestive disease can be diagnosed only with a comprehensive work-up that includes histology, organ morphology at imaging, serology, search for other organ involvement, and response to glucocorticoid treatment. Indications for treatment are symptomatic patients with obstructive jaundice, abdominal pain, posterior pancreatic pain, and involvement of extra-pancreatic digestive organs. Treatment with glucocorticoids should be weight-based and initiated at a dose of 0.6–0.8 mg/kg body weight/day orally for 1 month to induce remission and then be tapered within two additional months. Response to initial treatment should be assessed at week 2–4 with clinical, biochemical, and morphological markers.

Aims & Methods: The aim of this study is to evaluate the adherence to diagnostic, therapeutic and management recommendations of the IgG4 guideline across Europe. The invitation to participate in the study was

published at My Connect UEG platform. Questions in the survey were related to the organ involvement, diagnosis, treatment and follow up of newly diagnosed patients with IgG4-related digestive diseases in the three-year period (January 2021 - December 2023) after the publication of the guideline in 2020. We have received data from 14 European centers (12 countries).

Results: One hundred ninety-nine patients (76% males) were included in this multicentric study.

IgG4-related digestive disease was diagnosed in 54, 75, and 70 patients during 2021, 2022 and 2023 respectively.

Most of the patients had concomitant pancreatic and biliary tree involvement (46%), followed by pancreatic (34%), biliary tree (19%), esophageal (1.5%) or bowel (0.5%) involvement. Among autoimmune pancreatitis (AIP) patients, 76% received a definite diagnosis.

The combination of CT and MRI was employed in 63% of the patients, whereas 13% received only either CT or MRI.

Endoscopic ultrasound was performed in 56% of the patients.

Pancreatic exocrine and endocrine function at baseline were controlled in 78% and 76% of the patients, respectively.

Most of the patients (72%) received induction treatment with glucocorticoids (GC) according to UEG guidelines, whereas 8%, 7%, and 13% received a different GC scheme, a different drug, or no treatment, respectively.

Eleven patients underwent surgery due to suspected cancer.

Follow up assessment was performed according to guidelines (between 2-4 weeks from treatment start) in 48% of the patients and after 4 weeks in 38% of the patients, but 7% did not receive any follow-up imaging.

Among the 37 patients with biliary tract and liver involvement, 51% underwent MRI and CT, while EUS was used in 43% of the patients.

Treatment and imaging follow up mirrored UEG guidelines in 78% and 57% of the patients, respectively.

Five patients underwent surgery due to suspected cancer.

Three cases of IgG4-RD of the esophagus and one case of IgG4-related bowel disease were detected.

Conclusion: IgG4-related digestive disease was diagnosed in pancreas and the bile duct (concomitant or isolated) in most of the patients. IgG4-related disease in other digestive organs is very rare. Adherence to the European guidelines is high in the context of diagnosis and the first line treatment. Surgery was performed in 8% of all cases due to the suspected cancer. There are still differences across Europe regarding the follow up of patients.

Disclosure: Dr Vujasinovic and Dr Löhr have received lecture fees from Abbott and Viatrix.

Dr Ponsioen received research grants from Gilead and Perspectum and consultancy fees from Chemomab and NGM.

PP1139

PRESENCE OF TYPE 2 DIABETES MELLITUS IS ASSOCIATED WITH INCREASED SHEAR-WAVE VELOCITY IN PANCREATIC PARENCHYMA OF BRANCH-DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM: A PROPENSITY SCORE MATCHED ANALYSIS

T. Mori¹, S. Shintani², A. Itoh¹, O. Inatomi²

¹National Hospital Organization Higashi-ohmi General Medical Center, Division of Gastroenterology, Higashi-ohmi, Japan, ²Shiga University of Medical Science, Division of Gastroenterology, Otsu, Japan

Contact E-Mail Address: moritai@belle.shiga-med.ac.jp

Introduction: In branch-duct intraductal papillary mucinous neoplasm (BD-IPMN), pancreatic ductal adenocarcinoma (PDAC) develops in the parenchyma of the pancreas. However, it is unclear why PDAC occurs from sites beyond the cysts. Endoscopic ultrasound guided shear-wave elastography (EUS-SWE) is a new imaging modality for the quantification of tissue fibrosis as hardness. In this study, we investigated the clinical features of pancreatic parenchyma in BD-IPMN patients.

Aims & Methods: We selected 138 patients in the BD-IPMN group and 47 patients in the normal group who underwent EUS-SWE from April 2020 to March 2022. We used propensity score matching with age in a 2:1 ratio (76 patients in the BD-IPMN group and 38 in the normal group). Elastic velocity measured by EUS-SWE (Vs, m/s) in the pancreatic body at least 5 measurements were examined. Each Vs had a reliability measurement (VsN, %) and >50% was considered reliable. ALOKA ARIETTA 850 (FUJIFILM, Tokyo, Japan) and GF-UCT260 (Olympus, Tokyo, Japan) were used.

Results: The patients were 43.3% males with a mean age of 65.8 years in the BD-IPMN groups and 50.0% with 65.5 in the normal group with no significant difference in clinical background. Type 2 diabetes mellitus (T2DM) was observed in 25.0% of the BD-IPMN group and 21.1% of the normal group, and a history of alcohol consumption (>60g/day) was 3.0% in the BD-IPMN group. The Vs values were 1.95 ± 0.71 m/s in the BD-IPMN group and 1.64 ± 0.46 m/s in the normal group, which were significantly higher in the BD-IPMN group ($p=0.02$). EUS findings (Hyperechoic foci and strands: 42.1%, Hyperechoic duct wall: 22.4%, Lobularity: 5.3%, Dilated side branch: 18.4%) were observed in the BD-IPMN group. In multivariate analysis, the presence of T2DM and EUS findings (more than one) was an independent factor to increase the Vs value ($p=0.04$, <0.001). Secondly, the normal group and the BD-IPMN group were divided into 4 groups according to the presence or absence of T2DM. The Vs value was 2.47 m/s in the BD-IPMN with T2DM group which was higher compared to the absence of T2DM (1.77 m/s, $p<0.001$), and there was no significant difference in the normal group regardless of T2DM (1.63 and 1.67 m/s). There was no correlation between age and Vs value.

Conclusion: In the BD-IPMN patients, the stiffness of pancreatic parenchyma was significantly higher than the normal pancreas. Furthermore, the coexistence of T2DM was a risk factor that increased pancreatic stiffness. The results suggest the presence of inflammation and fibrosis, and long-term surveillance may find a relationship with carcinogenesis.

Disclosure: Nothing to disclose.

PP1140

CYSTIC TUMOURS OF THE PANCREAS: THE VALUE OF ENDOSCOPIC ULTRASOUND

Z. Tammouch¹, M. Salioun¹, F. Bouhamou¹, A. Mohamed¹, S. Ilham¹, N. Kabbaj²

¹Ibn Sina Hospital, EFD-hepatogastroenterology, Rabat, Morocco,

²Ibn Sina Hospital, mohamed 5 s EFD-Hepatogastroenterology unit, Rue Mfadel Cherkaoui, quartier Souissi, Rabat, Morocco

Contact E-Mail Address: zoulikhatammouch@gmail.com

Introduction: Cystic pancreatic tumors are rare tumours that are increasingly being discovered incidentally due in part to the improved performance of pancreatic imaging modalities (ultrasound, multidetector CT scan, MRI) and advancements in knowledge regarding the characteristics of these lesions. They are represented by serous cystadenomas (SC), mucinous cystadenomas (MC), intraductal papillary mucinous neoplasms (IPMN), and solid pseudopapillary tumors of the pancreas (SPTP). The aim is to study the epidemiological, clinical, biological, and etiological aspects of these pancreatic tumors.

Aims & Methods: This single-centre study was carried out from September 2015 to August 2023 and included all patients with cystic tumours of the pancreas. False pancreatic cysts were excluded from the study. Epidemiological, clinical, biological and echo-endoscopic data were collected from endoscopic-ultrasounds registers. All endoscopic-ultrasounds were performed under Propofol sedation using a Pentax-type radial and/or linear video echo-endoscope, and cytoponctions were performed using 19 G echotip needles for biochemical analysis of the cystic fluid and/or anatomopathological study.

Results: Out of a total of 649 biliopancreatic endoscopic ultrasounds performed, 53 patients were included, representing a prevalence of 8.16%. The mean age was 62.3 years (29-82 years) with a clear female predominance (Sex Ratio = 0.65). Discovery circumstances were incidental findings in 21 cases (39%), epigastric pain in 17 cases (32%), acute pancreatitis in 6 cases (11.3%), jaundice in 6 cases (11.3%), and abdominal pain in 3 cases (5.6%). Biochemically, cholestasis was found in 12 cases (22.6%), cytology in 5 cases (9.4%), and elevated Ca19-9 in 6 cases (11.3%). Endoscopic ultrasound revealed the location, number, and size of the tumor: 21 cases (39.6%) were located in the pancreatic head, 13 cases (24.5%) in the body, 9 cases (17%) in the tail, and 10 cases (18.9%) were multifocal, with an average tumor size of 28.5 mm (1.9-76 mm). Communication with pancreatic ducts was observed in 35 cases (66%), and Wirsung duct dilation in 16 cases (30.1%). Cytology was performed in 27 cases (51%). The endoscopic ultrasound appearance combined with cystic fluid analysis favored IPMN in 42 cases (79.2%), mucinous cystadenoma in 5 cases (9.4%), serous cystadenoma in 3 cases (5.7%), and SPTP in 3 cases (5.7%).

Conclusion: Cystic pancreatic tumors are rare neoplasms predominantly affecting women in their sixties, often discovered incidentally. They predominantly occur in the pancreatic head and are mainly comprised of IPMN followed by mucinous cystadenomas, with serous cystadenomas and SPTPs being less common.

Disclosure: no links of interest.

PP1141

APPLICATION OF A DIGITAL TOOL (ICYST) IN THE MANAGEMENT OF PATIENTS WITH PANCREATIC CYSTIC LESIONS: USEFUL OR FUTILE?

A. Trigo¹, M. Ruão², M. Gravito-Soares^{2,1}, N.P. Almeida^{1,2}, P. Narra Figueiredo^{2,1}

¹Unidade local de saúde de Coimbra, Gastroenterology, Coimbra, Portugal, ²Faculdade de Medicina de Coimbra, Coimbra, Portugal

Contact E-Mail Address: andre-497@hotmail.com

Introduction: Pancreatic cystic lesions (PCLs) have an increasing incidence and their management should be guided by recent guidelines. Currently, there is an electronic tool available, called iCyst, which can assist physicians in determining patient follow-up. The aim of this study was to retrospectively determine, using the iCyst application, whether guidelines were correctly followed at the time of diagnosis and, if not, whether this had a negative impact on patients.

Aims & Methods: Patients with PCLs followed in the outpatient clinic of the Gastroenterology Department of a large tertiary center between January 2022 and December 2023 were included.

Results: One hundred patients were evaluated (female sex - 60%; mean age - 64.2 ± 12.5 years; mean follow-up time - 4.3 ± 2.8 years). Comparing the suggestions of iCyst with what was implemented, it was found that the guidelines were respected to the following extents: European - 73%; AGA - 71%; IAP - 58%. In 9% of cases, none of the guidelines were applied. Regarding follow-up, a significant increase (>5 mm) in lesion size was observed in 11% of cases. Of the 9 patients in whom no guideline was followed, only 1 had dimensional growth, which was an IPMN with high-risk features and surgical indication; however, this patient refused any intervention and subsequently died from a non-pancreatic cause. In the remaining patients with lesion growth, in 6 cases, the plan followed was similar to that proposed by all three guidelines simultaneously, in 3 to that proposed by the EU and AGA guidelines, and in one case, the IAP guideline was followed. There was no statistically significant association between evolution and the implemented guideline.

Conclusion: The results show that, in the vast majority of evaluated patients, the plan proposed by at least one of the three international recommendations was respected, especially the European. It is noteworthy that there seems to be no correlation between strict adherence to these guidelines and the final outcome for the patient.

References: 1. Klibansky DA, Reid-Lombardo KM, Gordon SR, Gardner TB. The clinical relevance of the increasing incidence of intraductal papillary mucinous neoplasm. *Clin Gastroenterol Hepatol*. 2012 May;10(5):555–8. 2. Bassi C, Sarr MG, Lillemoe KD, Reber HA. Natural History of Intraductal Papillary Mucinous Neoplasms (IPMN): Current Evidence and Implications for Management. *Journal of Gastrointestinal Surgery*. 2008 Apr 1;12(4):645–50. 3. Mella JM, Gómez EJ, Omodeo M, Manzotti M, Roel M, Pereyra L, et al. Prevalence of incidental clinically relevant pancreatic cysts at diagnosis based on current guidelines. *Gastroenterología y Hepatología*. 2018 May 1;41(5):293–301. 4. Chang YR, Park JK, Jang JY, Kwon W, Yoon JH, Kim SW. Incidental pancreatic cystic neoplasms in an asymptomatic healthy population of 21,745 individuals: Large-scale, single-center cohort study. *Medicine*. 2016 Dec;95(51):e5535. 5. Farrell JJ. Pancreatic Cysts and Guidelines. *Dig Dis Sci*. 2017 Jul 1;62(7):1827–39.

Disclosure: Nothing to disclose.

PP1142

SURGICAL TACTICS FOR THE TREATMENT OF IPMN, WHAT'S NEW

L. Pererva¹, V. Kopchak¹, I. Khomiak¹, V. Shkarban¹, Y. Khilko¹, V. Khanenko¹, P. Azadov¹, Z. Holobor²

¹Shalimov National Scientific Center of Surgery and

Transplantology, Pancreatic and bile ducts surgery, Kyiv, Ukraine,

²Bogomolets National Medical University, Kyiv, Ukraine

Contact E-Mail Address: Liudmylapererva@gmail.com

Introduction: Until recently, all cystic tumours were treated surgically, including intraductal papillary mucinous neoplasms of the branch type (BD-IPMN). Currently, most patients with BD-IPMN are being followed up.

Aims & Methods: The aims of this study was to estimate the results of treatment of patients with IPMN.

A total of 228 patients with cystic pancreatic tumours who were treated at our department between 2012 and 2023 were included in the analysis. IPMN was diagnosed in 78 (34.2%) patients. All patients with IPMN were divided into two groups. The primary group included 56 patients who underwent surgery between 2018 and 2023 in accordance with the proposed algorithms.

The comparison group comprised 22 patients who underwent surgery between 2012 and 2017. The two groups demonstrated comparable demographic characteristics, including age, gender distribution, and pathological structure.

In the diagnostic algorithm, we always perform MRI with the DWI and with magnetic resonance cholangiopancreatography. We also perform endoscopic ultrasound with fine-needle aspiration if required.

Until 2018, all types of IPMN were operated. Since 2018, we have revised our tactics. Indications for surgery were considered to be the presence of central and mixed type of IPMN or branch duct of IPMN with the presence of HRS and WF.

Of the 22 patients in the control group, central type IPMN was diagnosed in 10 patients (adenocarcinoma was diagnosed in 9, 1 patient was unresectable at the time of diagnosis), mixed type in 4 (2 patients had malignant tumours, 1 patient was unresectable at the time of diagnosis, 1 patient did not undergo surgery), and branch type in 8 (4 patients had malignant tumours, 2 patients - benign and in 2 patients we did not perform surgery). 17 patients with IPMN underwent surgery. Pancreatoduodenectomy (PDE) was performed in 9 patients, total pancreatectomy (TPE) in 1, distal pancreatectomy (DPE) in 7. Five patients were not operated: 2 patients had unresectable tumours diagnosed preoperatively, 2 patients with BD-IPMN were offered observation, 1 patient with mixed type IPMN refused surgery.

IPMN was diagnosed in 56 (40.6%) patients in the main group. Adenocarcinoma on the background of IPMN was diagnosed in 21 (37.5%) patients, all patients with central or mixed type of IPMN, of which PDE was performed in 12 patients, DPE with splenectomy in 8 patients, TPE - in 1 patient. IPMN with mild or severe dysplasia was diagnosed in 20 (35.7%) patients. Of these, PDE was performed in 13 patients, TPE in 1 patient and DPE in 6 patients. In 15 (26.8%) patients BD-IPMN without HGD and WF was diagnosed.

Results: In the comparison group, 17 (77.3%) patients underwent resection. Complications occurred in 6 (35.3%) patients, 3 of which were pancreatogenic complications (17.6%). In the main group, 41 (73.2%) patients underwent surgery. Complications occurred in 11 patients (26.8%). There was no mortality among these patients in either group. Of the 2 patients in the comparison group who were followed up, 1 patient had no progression of the disease, 1 patient was lost to follow-up, the outcome is unknown. Of the 15 patients in the main group with BD IPMN who were followed, none had disease progression.

Conclusion: The treatment of IPMN of the pancreas requires an individualized approach. In select patients, surveillance of presumed BD-IPMN can be safely discontinued. When choosing a wait-and-see approach in patients with BD-IPMN, it is imperative that the diagnosis not raise doubts.

Disclosure: Nothing to disclose.

PP1143

HYPERTHERMIA IMPROVES GEMCITABINE SENSITIVITY OF PANCREATIC CANCER CELLS BY SUPPRESSING THE EPHRIN A4/ β -CATENIN AXIS AND ACTIVATING DEOXYCYTIDINE KINASE

H. Jin¹, W. Gu¹, L. Lu¹, H. Shen¹, Q. He¹, J. Yang¹, X. Zhang¹

¹Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Gastroenterology, Hangzhou, China

Contact E-Mail Address: lbjhb2013@163.com

Introduction: Previously, our investigations have underscored the potential of hyperthermia to improve the therapeutic efficacy of gemcitabine (GEM) in pancreatic cancer (PC). Nonetheless, the precise underlying mechanisms remain elusive.

Aims & Methods: We aimed to explore the underlying mechanisms of how hyperthermia enhances GEM sensitivity of PC cells. We engineered two GEM-resistant PC cell lines (BxPC-3/GEM and PANC-1/GEM) and treated them with GEM alongside hyperthermia. The impact of hyperthermia on the therapeutic potency of GEM was ascertained through 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay, assessment of the concentration of its active metabolite difluorodeoxycytidine triphosphate (dFdCTP), and evaluation of deoxycytidine kinase (dCK) activity. Lentivirus-mediated dCK silencing was further employed to validate its involvement in mediating the GEM-sensitizing effect of hyperthermia. The mechanism underlying hyperthermia-mediated dCK activation was explored using bioinformatics analyses. The interplay between hyperthermia and the ephrin A4 (EFNA4)/ β -catenin/dCK axis was investigated, and their roles in GEM resistance was further explored via the establishment of xenograft tumor models in nude mice.

Results: Hyperthermia restored dCK expression in GEM-resistant cell lines, concurrently enhancing GEM sensitivity and fostering DNA damage and cell death. These observed effects were negated by dCK silencing. Regarding the mechanism, hyperthermia activated dCK by downregulating EFNA4 expression and mitigating β -catenin activation. Overexpression of EFNA4 activated the β -catenin while suppressing dCK, thus diminishing cellular GEM sensitivity—a phenomenon remediated by the β -catenin antagonist MSAB. Consistently, *in vivo*, hyperthermia augmented the therapeutic efficacy of GEM on xenograft tumors through modulation of the ephrin A4/ β -catenin/dCK axis.

Conclusion: This study delineates the role of hyperthermia in enhancing GEM sensitivity of PC cells, primarily mediated through the suppression of the EFNA4/ β -catenin axis and activation of dCK.

Disclosure: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

PP1144

FORMONONETIN COMBINED WITH SALVIANOLIC ACID B INHIBITS THE PROGRESSION OF PANCREATIC CANCER THROUGH DOWN-REGULATING MBOAT2

Y. Xu¹, Y. Wang², X. Zhang³, J. Yang³, H. Jin³

¹Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Hangzhou, China, ²Key Laboratory of Integrated Traditional Chinese and Western Medicine for Biliary and Pancreatic Diseases of Zhejiang Province, Affiliated Hangzhou First People's Hospital, Hangzhou, China, ³School of Medicine, Westlake University, Hangzhou, China

Contact E-Mail Address: wangyu@zcmu.edu.cn

Introduction: Pancreatic cancer (PC) presents as a highly aggressive malignancy characterized by limited treatment modalities and a poor prognosis. Its prevalence is steadily increasing, with projections indicating that it will rank as the second most common cause of cancer-related mortality by the year 2030, reflecting a substantial escalation in the global burden [1].

Due to the early metastasis of PC and the limited efficacy of current treatment for advanced stages, the overall five-year survival rate remains below 9% [2-3]. Therefore, the development of novel therapeutic approaches is crucial.

In recent years, there has been a surge of interest in natural products due to their perceived potential as anti-cancer agents. Our initial findings suggest that the co-administration of Formononetin (FMN, a compound derived from *Astragalus mongholicus*) combined with Salvianolic Acid B (SalB, one of the major water-soluble components of *Salvia miltiorrhiza*), referred to as "FcS" in subsequent sections of this study, effectively suppresses the proliferation, metastasis, and promotes apoptosis of Panc-1 cells in a zebrafish embryo xenograft model. While FMN and SalB individually inhibited the PC cell viability, their combined treatment exhibited a stronger and significant suppressive effect. However, the mechanism of this combined treatment suppressing the malignant progression of PC remains unclear.

Aims & Methods: This study aims to assess the potential therapeutic effectiveness of FcS therapy for PC, with a focus on investigating the impact of this treatment strategy on PC cell survival, proliferation, and migration capabilities through a series of experiments conducted *in vitro* and *in vivo*. Additionally, our study investigated the expression of MBOAT2 in PC and its correlation with prognosis and tumor invasion.

The proliferation of PC cells was evaluated through the utilization of CCK-8 and EdU assay *in vitro* experiments to investigate the effects of FcS. Wound healing assay and transwell assay were conducted to assess the impact of FcS on the migration and invasion of PC cells. Through molecular docking and analysis of the Cancer Genome Atlas (TCGA) database, the potential regulatory factor MBOAT2 was identified. A Mboat2 knockdown cell line was established and treated with FcS to investigate the interaction between MBOAT2 and FcS. *In vivo* experiments were conducted using the LSL-Kras (G12D/+), LSL-Trp53 (R172H/+), and Pdx-1-Cre (KPC) transgenic mouse model, with tumor weight serving as a measure of the effects of FcS. Immunohistochemistry was utilized to assess protein expression levels from mice tumor tissues.

Results: Experiments conducted on three PC cell lines revealed that treatment with FcS resulted in reduced cell viability, inhibited proliferation, and decreased cell migration and invasion.

Furthermore, analysis of TCGA data was utilized to investigate the impact of FcS on MBOAT2 expression in pancreatic cancer cells, demonstrating a down-regulation of MBOAT2 and subsequent reductions in viability, proliferation, and invasion.

Additionally, the study identified the JAK/STAT signaling pathway as a potential regulatory mechanism. *In vivo* administration of FcS also exhibited tumor growth suppression in a KPC transgenic mouse model.

Conclusion: FcS treatment may be effective in suppressing the growth and invasion of PC cells through the downregulation of MBOAT2. The unique contribution of this research lies in the therapeutic impact of combining natural compounds and identifying MBOAT2 as a potential target, along with the involvement of the JAK/STAT signaling pathway.

References:

1. Wungki, Park,Akhil, Chawla,Eileen M, O'Reilly,Pancreatic Cancer: A Review [J]. JAMA, 2021, 851-862. <https://doi.org/10.1001/jama.2021.13027>
2. Rebecca L, Siegel,Kimberly D, Miller,Ahmedin, Jemal,Cancer statistics [J]. CA Cancer J Clin. 2020, 7-30. <https://doi.org/10.3322/caac.21590>
3. Ahmedin, Jemal,Rebecca, Siegel,Elizabeth, Ward et al. Cancer statistics [J]. CA Cancer J Clin, 2006,106-130. <https://doi.org/10.3322/canj-clin.56.2.106>

Disclosure: Nothing to disclose.

PP1145

ANALYSIS OF PERIPHERAL BLOOD STEM AND PROGENITOR MARKERS mRNA EXPRESSION IN PANCREATIC NEOPLASTIC AND INFLAMMATORY DISEASES

K. Dabkowski¹, M. Tarnowski², K. Safranow³, M. Dąbkowska⁴, A. Kosiorowska⁴, K. Pukacka⁴, T. Starzynska⁵

¹Pomeranian Medical University, Dept. of Gastroenterology, Szczecin, Poland, ², Pomeranian Medical University, Department of Physiology in Health Sciences, Szczecin, Poland, ³Pomeranian Medical University, Department of Biochemistry and Medical Chemistry, Szczecin, Poland, ⁴Pomeranian Medical University, Independent Laboratory of Pharmacokinetic and Clinical Pharmacy, Szczecin, Poland, ⁵Pomeranian Medical University Dept. of Gastroenterology, Department of Gastroenterology, Szczecin, Poland

Contact E-Mail Address: dabkowskikrzysztof@wp.pl

Introduction: The development of pancreatic malignancies is related to metabolic and genetic alterations. Genetic alterations of both progenitor genes and stem cells genes and markers were described in pancreatic neoplastic and inflammatory disorders.

In our study we comprehensively assess the expression of mRNA of both stem cells and progenitor pancreatic genes in peripheral blood of patients with pancreatic malignancy in different clinical stages, neuroendocrine tumors, and pancreatic inflammatory disorders (acute (AP) and chronic pancreatitis (CP)), to identify the tumor markers and underlying mechanisms of tumor progression.

Aims & Methods: Our aim was to assess the peripheral blood mononuclear cells (PBMNCs) messenger RNA (mRNA) expression profile of stem cell genes (*OCT4*, *NANOG*) and pancreatic progenitor genes (*CK19*, *HES1*, *INS*, *PDX1*) in selected pancreatic diseases: neoplastic (cancer, neuroendocrine tumors) and inflammatory (acute and chronic pancreatitis).

The 49 patients with pancreatic neoplastic diseases (37 with cancer, 12 with neuroendocrine tumors) and 48 patients with pancreatitis (28 with acute, 23 with chronic) and 34 patients from gender and age-matched control group hospitalized in tertiary center were enrolled into the study. Venous blood was collected and RNA was isolated from PBMNCs. The mRNA expression of 6 stem cell and pancreatic progenitor genes: *OCT4* (POU class 5 homeobox 1), *NANOG*, *CK19* (keratin 19), *HES1* (hes family bHLH transcription factor 1), *INS* (insulin), *PDX1* (pancreatic and duodenal homeobox 1) was assessed by real-time quantitative PCR. The results were analyzed statistically and their associations with available clinical,

biochemical and morphological data (WBC, ERY, PLT, CRP, Ca 19.9, weight, height and BMI) were studied with Kruskal Wallis test, Mann-Whitney U test and Spearman rank correlation coefficient.

Results: We found that the expression of gene characteristic for early stem cells *NANOG* (p=0.03) and the expression of genes encoding insulin and cytokeratin 19 (*INS* p=0.02, *CK19* p=0.005) was increased in pancreatic cancer patients. However, it was not significantly different in other neoplastic (neuroendocrine) and inflammatory conditions.

Moreover, we found that *OCT4*, *HES1*, *PDX1* expression is significantly decreased in PBMNCs of patients with pancreatitis (both acute and chronic). There were no significant differences in genetic expression between the patients with different stages of pancreatic cancer and patients with acute pancreatitis with different severity (mild vs moderate/severe). What is more, *CK19* overexpression correlated with inflammatory markers (both CRP and WBC) in patients with pancreatic cancer.

Conclusion: PBMNCs mRNA expression of selected stem and progenitor genes (*NANOG*, *INS*, *CK19*) may serve as a marker of pancreatic cancer and correlates with coexisting inflammation.

Disclosure: Nothing to disclose.

PP1146

MULTIPLE SEQUENCING AND MULTI-MARKER STAINING REVEALS THE MOLECULAR SUBTYPES AND MICROENVIRONMENT FEATURES OF PANCREATIC DUCTAL ADENOCARCINOMA IN THE CHINESE POPULATION

S. Shen¹, H. Li¹, Z. Shi¹, S. Zhou¹, S. Nie¹, Y. Yu¹, Q. Zhou¹, K. Liu¹, Y. Lv¹, X. Zou¹, L. Wang¹

¹Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Gastroenterology, Nanjing, China

Contact E-Mail Address: shanshanshen33@hotmail.com

Introduction: The prognosis of Pancreatic ductal adenocarcinoma (PDAC) remains poor with a 5-year overall survival of around 10%. In previous whole-genome studies of PDAC in the West, four common mutations have been identified, including KRAS, TP53, SMAD4, and CDKN2A. Due to limited research on Asian populations, we utilized multi-omics sequencing and immune microenvironment evaluation using multiple biomarkers to present the tumor and microenvironment characteristics of PDAC in the Chinese population.

Aims & Methods: The current study obtained 95 primary treatment-naïve PDAC samples from Chinese patients who underwent curative surgery. RNA-sequencing was carried out on all 95 samples, with paired normal sample sequencing for 27 cases, and WES-sequencing for 73 patients. Additionally, to assess the microenvironment features, various markers including immune cell markers, immune checkpoint markers, stroma markers, and markers related to tumor proliferation and subtype were examined using immunohistochemistry (IHC).

Furthermore, Olink sequencing was performed on serum samples from a subset of the cohort (25.26%).

Results: KRAS mutations were found in about 76.7% (56/73) of the samples, with most mutations occurring on codon 12 of exon 2, including G12D (30%), G12V (22%), Q61H (12%), and G12R (7%).

Additionally, oncogenic fusions such as MET and BRAF, as well as EGFR gain, were identified in KRAS wild-type PDAC samples. Tumors with KRAS wild-type displayed higher levels of CD3, CD4, and CD8 T cells, and lower levels of CD68 and CD206 macrophages. Additionally, the KRAS wild-type group exhibited a greater number of PD1-positive samples.

Pathological staining can yield results consistent with RNA sequencing to categorize PDAC into tumor subtypes (basal-like, classical, and double positive) and stromal subtypes (deserted, active, and hybrid) with prognostic significance. It is noteworthy that PDAC tissues with both basal-like

and classical subtype components (double positive) contain more tertiary lymphoid structures (TLS) and B cells, suggesting potential responsiveness to immunotherapy.

Conclusion: Chinese individuals have a higher proportion of KRAS wild-type PDAC patients, which represents a potentially actionable and immunologically active tumor subtype. Simplified tumor and stromal subtypes based on pathological staining methods are more clinically practical and provide prognostic and therapeutic implications.

Disclosure: Nothing to disclose.

PP1147

PSYCHOLOGICAL BURDEN IN A PANCREATIC CANCER SURVEILLANCE PROGRAM BASED ON “INDIVIDUALS AT RISK”

A. Vesterberg¹, E. Asplund^{2,1}, M. Vujasinovic^{2,3},
C. Haddad-Ringborg⁴, Y. Wengström⁴, J.-M. Löhr^{2,1}

¹Karolinska Institutet, CLINTEC, Stockholm, Sweden, ²Karolinska University Hospital, Department of Upper Abdominal Diseases, Stockholm, Sweden, ³Karolinska Institutet, Department of Medicine Huddinge, Stockholm, Sweden, ⁴Karolinska Institutet, Division of Nursing, Department of Neurobiology Care Science and Society, Stockholm, Sweden

Contact E-Mail Address: mvujas@gmail.com

Introduction: The prognosis for pancreatic cancer is poor, it is an aggressive cancer and comes with few or unspecific symptoms. Diagnosis at an early stage is vital for survival and chance for curative treatment. Surveillance programs for high-risk individuals, so called, “individuals at risk” are therefore of utter importance. However, there is limited data on the psychological burden within participants of these programs.

Aims & Methods: The aim was to investigate the psychological burden for participants in a pancreatic cancer surveillance program. Additionally, this study aimed to explore whether psychological burden was related to the individual's risk-level for pancreatic cancer.

Results: In total, 278 patients answered the questionnaire. Results indicated high cancer worry among respondents with high scores on CWS (mean=16.45). A majority of 69.3% had scores indicating high cancer worry (cut-off ≥ 14). Anxiety was not equally high among respondents (mean STAI-T = 35.13; STAI-S=35.9). Female gender and younger age were significantly correlated with higher cancer worry and anxiety (Chi2-tests and linear regression analysis). Outcomes in coping and perceived health were similar to normative populations.

Conclusion: Cancer worry is particularly high within participants, among these women and younger individuals have more cancer worry and anxiety. No correlation was found between risk-level and psychological burden.

Disclosure: None.

PP1148

PREDICTIVE FACTORS OF ACTUAL FIVE-YEAR RECURRENCE-FREE SURVIVAL AFTER UPFRONT SURGERY FOR RESECTABLE PANCREATIC CANCER. -EXPLORATION OF PATIENTS WHO DID NOT REQUIRE NEOADJUVANT TREATMENT-

T. Sugiura¹

¹Shizuoka Cancer Center, Division of Hepato-Biliary-Pancreatic Surgery, Sunto-Nagaizumi, Japan

Contact E-Mail Address: t.sugiura@scchr.jp

Introduction: Neoadjuvant treatment for resectable pancreatic cancer (R-PC) is expected to decrease the postoperative recurrence and prolong the survival. However, It remains unclear whether NAC is necessary for all patients.

Aims & Methods: The present study investigated the prognostic factors associated with actual five-year recurrence-free survival (RFS) after upfront surgery for R-PC in patients who were deemed not to require neoadjuvant treatment. Between 2007 and 2016, 316 patients who underwent pancreatectomy for radiologically R-PC were retrospectively reviewed to evaluate the predictors of actual 5-year RFS. Predictors were identified using logistic regression analysis of preoperative evaluable factors. The cutoff values for continuous variables were determined based on a minimum P-value approach (model 1) or the value that maximized the rate of five-year RFS survivors (model 2).

Results: Fifty-one patients (16.1%) achieved a 5-year RFS. A tumor size ≤ 23 mm, absence of serosal invasion on computed tomography (CT), and neutrophil-to-lymphocyte ratio (NLR) < 1.0 , were significantly associated with the 5-year RFS in model 1. A prognostic nutritional index (PNI) ≥ 58 and the absence of serosal invasion and extrapancreatic nerve plexus invasion on CT were significantly associated with 5-year RFS in model 2. Only six (11.8%, model 1) and four (7.8%, model 2) patients had all three prognostic factors, and their 5-year RFS rates were 83.3% and 100%, respectively.

Conclusion: A modest number of patients who underwent upfront surgery achieved 5-year RFS, but only approximately 10% of them could be identified preoperatively. Based on these results, almost all R-PC patients are forced to undergo NAT in daily practice.

Disclosure: Nothing to disclose.

PP1149

PREDICTING PANCREATIC CANCER FROM ARTIFICIAL INTELLIGENCE-BASED PANCREATIC VOLUME CHANGES ON CT IMAGING OVER TIME

J. Nakahodo¹, W. Ujita¹, M. Suzuki², M. Kikuyama³, S.-i. Horiguchi⁴, M. Toi⁵, M. Kurata⁶, K. Chiba¹, H. Tabata¹, T. Kamisawa¹, T. Iizuka¹

¹Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Gastroenterology, Tokyo, Japan, ²Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Radiology, Tokyo, Japan, ³Tokyo Women's Medical University, Gastroenterology, Tokyo, Japan, ⁴Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Pathology, Tokyo, Japan, ⁵Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Breast Surgery, Tokyo, Japan, ⁶University of Tsukuba Mito Clinical Education and Training center, Surgery, Mito, Japan

Contact E-Mail Address: nakajun58@yahoo.co.jp

Introduction: A previous study, which found that focal parenchymal atrophy of the pancreas is an indirect sign of small pancreatic cancer (PC), documented the changes in the pancreas until cancer onset. [1-3] However, the pancreas atrophies and changes with age, so issues remain regarding the criteria for determining pancreatic atrophy as a sign of PC. The application of artificial intelligence (AI) technology to quantify changes in the pancreas over time and predict the onset of PC and high-risk groups for PC from objective indicators has the potential to facilitate early detection of PC.

Aims & Methods: Based on the rate of change in the pancreatic volume on computed tomography (CT) using AI technology, the present study predicted PC onset. Forty patients in whom PC was histopathologically diagnosed at Komagome Hospital between 2015 and 2023 and who had a history of three or more follow-up CT examinations over five years before PC onset (the PC group) were analyzed. Forty patients who underwent CT periodically for malignant skin disease but had no pancreatic disease were enrolled into a non-PC group. Patients with pancreatic carcinoma in situ (pancreatic intraepithelial neoplasm), an intraductal papillary mucinous neoplasm or chronic pancreatitis with multiple calcifications were excluded. Changes in the pancreatic volume in the groups over time were then compared using CT images taken one year or earlier before PC onset. The pancreatic volume was calculated using SYNAPSE VINCENT cloud (Fuji Film, Japan), an AI image application program. Age and pancreas volume were combined to create a scatter diagram, and the rate of pancreatic volume change (the temporal pancreatic volume change coefficient) was calculated from the regression line and compared.

Results: The lesion site in PC group included the head (n=17), body (n=7), and tail (n=16). The median maximum tumor diameter was 31 mm (interquartile range: 27-37). A comparison of the two groups found a cStage classification of IB, IIA, IIB, III, and IV in eight, ten, three, eight, and 11 patients, respectively. The median age was 72.5 and 72.5 years in the respective group (P=0.182). The male: female ratio was 23:17 and 24:16 (P=0.820), the median observation period was 83.5 and 107 months (P<0.05); the mean number of examinations was 10.7 and 18; the total number of CT examinations was 430 and 745; the mean total pancreatic volume was 74.4 and 78.15 ml (P<0.01); and the mean pancreatic volume change coefficient was -0.141 and -0.036 (P=0.01), respectively. The rate of decrease in the pancreatic volume was faster in the PC group with increasing age, the average being 8.46 ml over five years in the PC group compared to 2.16 ml in the non-PC group. The cutoff value for the coefficient of pancreatic volume change over time was set at -0.125. The sensitivity was 50%, the specificity was 90%, the positive predictive value was 83%, and the AUC value was 0.67.

Conclusion: In comparison with the age-related changes in the pancreas, the rate of decrease in the pancreatic volume was faster in the PC group, suggesting that PC onset may be predicted using images obtained one year or earlier before PC onset. These findings further suggested that identifying patients with a high risk of PC may be possible by creating a pancreatic volume histogram using AI technology based on age at the time of CT, intervals between past examinations, and the rate of decrease in the pancreatic volume.

References: [1] Nakahodo J, Kikuyama M, Nojiri S, et al. Pancreatology. 2020 Dec;20(8):1689-1697.

[2] Nakahodo J, Kikuyama M, Fukumura Y, et al. Pancreatology. 2022 Dec;22(8):1148-1158

[3] Kikuyama M, Nakahodo J, Honda G, et al. Pancreatology. 2023 Jun;23(4):420-428.

Disclosure: Nothing to disclose.

PP1150

THE EFFECTIVENESS OF CHECK SCORE SHEET FOR THE EARLY DETECTION OF PANCREATIC CANCER IN GASTROENTEROLOGY CLINIC

Y. Kawaguchi¹, Y. Kawashima¹

¹Kawaguchi Gastroenterology Clinic, Yokohama, Japan

Contact E-Mail Address: y711kawa@gmail.com

Introduction: The early-stage pancreatic cancer (e-PC; stage I/II) detection rate is very low at approximately 25%. The role of general physician is very important for e-PC detection.

Aims & Methods: The aim of this study was to evaluate the effectiveness of the check score sheet used clinical findings to detect e-PC in gastroenterology clinic.

Patients of clinic with a score of ≥ 2 points on clinical findings were enrolled: symptoms of abdominal pain/back pain and/or body weight loss (1 point), high amylase, lipase and/or trypsin (1 point), high carbohydrate antigen 19-9 (CA19-9) (1 point), new-onset or worsened diabetes (2 point), family history of pancreatic cancer (2 points) and ultrasonography (US) findings including direct (e.g., a solid pancreatic tumor) and/or indirect findings (e.g., dilatation of a pancreatic diameter of ≥ 2 mm and/or cystic lesions) (2 points). Abdominal CT and/or EUS (Endoscopic ultrasonography) were performed for all these enrolled patients, and we evaluated about pancreatic disease and pancreatic cancer detection rates of this check score sheet.

Results: Between July 2017 and March 2024, 621 patients (mean age 67.6 years, female 391 [63%]), were enrolled in clinic. The 458 pancreatic cystic disease (IPMN and SCN) cases (73.7%), the 28 chronic pancreatitis disease cases (4.5%), the 18 PC patients (2.9%) and the 10 pancreatic solid disease (SPN and NEM) (1.6%) were detected by abdominal CT and/or EUS. The 6 patients with e-PC were detected. The mean clinical finding score of the PC group (3.2 ± 1.4) was significantly higher than that of the overall non-PC group (2.2 ± 0.6) ($p < 0.05$). US findings were significantly more frequent in the PC group than in the non-PC group ($p < 0.05$). Although the sensitivity of direct findings by US was 42.3%, that of indirect-findings was 91.7% in the PC group.

Conclusion: Many pancreatic diseases, which may have potential of pancreatic cancer in future, were detected by this simple check score of ≥ 2 points on clinical findings. And in clinic pancreatic cancers were detected efficiently. Indirect findings by US may play an important role in improving the e-PC detection rate.

Disclosure: Nothing to disclose.

PP1151

IMPACT OF TISSUE HETEROGENEITY OF PANCREATIC CANCER ON
ENDOSCOPIC ULTRASOUND GUIDED SHEAR-WAVE MEASUREMENTST. Yasuda¹, S. Shintani², T. Fujimoto¹, O. Inatomi²¹Nagahama Red Cross Hospital, Nagahama, Japan, ²Shiga University of Medical Science, Division of Gastroenterology, Otsu, Japan**Contact E-Mail Address:** tomyamukun0415@gmail.com**Introduction:** Endoscopic ultrasound guided Shear wave elastography (EUS-SWE) is a noninvasive technique to evaluate organ fibrosis as hardness. Velocity of SWE (Vs, m/s) enables to quantify, and the measured value isalso evaluated with confidence index: VsN (Percentage of the net amount of effective of Vs, %). EUS-SWE has been reported as a useful diagnostic modality for chronic pancreatitis (S Shintani et al *JMU* 2023). As for pancreatic cancer, previous reports using transabdominal ultrasound have reported only that Vs of pancreatic cancer is elevated, but there are no reports of VsN or using EUS devices. In this study, we examined the characteristics of pancreatic cancer using EUS-SWE.**Aims & Methods:** The subjects were patients who underwent EUS-SWE at Shiga University Hospital from April 2019 to December 2022. The retrospective study was conducted with 121 patients (pancreatic cancer, chronic pancreatitis, normal pancreas). EUS-SWE was performed at least 5 times, and the median value was measured. Vs and VsN were measured at central site of tumor cases, and pancreatic body with chronic pancreatitis and normal cases. Histogram analysis (Complexity) at the SWE measurement site was also performed to evaluate tissue heterogeneity. ALOKA ARIETTA 850 (FIJIFILM, Tokyo, Japan) and GF-UCT260 (Olympus Co., Tokyo, Japan) was used.**Results:** The subjects were 69 cases of pancreatic cancer (39 males, age: 68.9±10.6 years), 10 cases of chronic pancreatitis (6 males, age: 74.3±5.5 years), and 42 normal cases (22 males, age: 57.5±11.1 years) The EUS-SWE results (pancreatic cancer / chronic pancreatitis / normal) were Success rate (%): 87.2 / 93.5 / 98.1, Vs (m/s): 2.27±0.61 / 2.6±0.67 / 1.68±0.49, VsN (%): 22.6±15.9 / 76.2±21.2 / 79.6±20.6. Complexity: 30.1±12.3 / 23.9±4.8 / 13.5±10.6 indicate that heterogeneity within the tissue is higher in the order of pancreatic cancer > chronic pancreatitis > normal group. VsN and Complexity were inversely correlated, and the higher the tissue heterogeneity, the lower the VsN ($r=-0.45$, $p<0.001$, Spearman correlation test).**Conclusion:** Vs was increased in pancreatic cancer compared to normal pancreas. However, VsN was more likely to be decreased in pancreatic cancer, which associated with higher tissue heterogeneity. EUS-SWE for pancreatic cancer should consider tissue heterogeneity.**References:** none**Disclosure:** Nothing to disclose.

PP1152

EXOCRINE PANCREATIC INSUFFICIENCY AND ADVANCED PANCREATIC
CANCER - A NATIONAL REGISTRY ANALYSISJ. Schütz¹, A. Kleger², T.J. Ettrich¹, T. Seufferlein¹, L. Perkhofer¹¹Ulm University, Internal Medicine I, Ulm, Germany, ²Institute of Molecular Oncology and Stem Cell Biology, Ulm University Hospital, Ulm, Germany**Contact E-Mail Address:** lukas.perkhofer@gmail.com**Introduction:** Diagnostic algorithms and treatment of exocrine pancreatic insufficiency (PEI) in patients after pancreatic surgery have been sufficiently established. Comparable systematically collected data in patients with advanced pancreatic cancer (PDAC) is largely missing. In line, national European guideline recommendations for diagnosis and therapy remain controversial.**Aims & Methods:** A registry based analysis of prospectively collected data with regard to PEI was done in patients with advanced PDAC. Data collection was based on EORTC questionnaires (QLQ-c30 and Pan26) and supplemented with fecal Elastase-1 measurements and specific treatment information.**Results:** In a period over 5 years more than 100 patients could be included in the analysis at several specialised centres. Compared to other GI cancers (e.g. colon) potential PEI associated symptoms were stated more frequently. In this real-world setting fecal Elastase-1 measurement was not done routinely by centers and surprisingly carried out only in few cases. Frequency of pancreatic enzyme replacement therapy in PDAC patients was below the reported incidence in the literature of PEI in this cohort.**Conclusion:** Awareness of PEI in advanced pancreatic cancer seems underrepresented. This survey illustrates the need for further prospective in-depth evaluation.**Disclosure:** Nothing to disclose.

PP1153

PREOPERATIVE LYMPH NODE METASTASIS AS A PROGNOSTIC
FACTOR IN PATIENTS WITH OPERABLE PANCREATIC CANCERS. Ito¹, T. Okuzono¹¹Sendai Kousei Hospital, Gastroenterological Medicine, Sendai, Japan**Contact E-Mail Address:** tabletennis2775@yahoo.co.jp**Introduction:** Pancreatic cancer is a fatal disease with a poor prognosis. Even after curative surgery, the overall survival (OS) is low, owing to the high frequency of relapses or surgical complications. Neoadjuvant chemotherapy (NAC) has recently been reported to improve OS; however, early postoperative death has been reported in some cases. Conversely, chemotherapy for unresectable pancreatic cancer is progressing; the median OS has been extended to approximately 15 months. Therefore, it is necessary that we carefully consider the possibility of surgery including NAC. There are many reports based on postoperative staging; however, there are few reports about preoperative prognostic factors in pancreatic cancer. This study aimed to evaluate these factors in patients with operable pancreatic cancer.**Aims & Methods:** Between April 2010 and March 2023, 284 patients were diagnosed with resectable (R) or borderline resectable (BR) pancreatic cancer at the Sendai Kousei Hospital. Sixteen patients who were diagnosed with unresectable cancer after NAC were excluded. The preoperative clinical factors and OS were retrospectively evaluated. Survival data were compared using the log-rank test. P-value <0.05 was considered statistically significant. Clinical factors included in the univariate analysis

ses were as follows: age (<75 years vs. ≥ 75 years), sex, region (head vs. body and tail), resectability (R vs. BR), CA19-9 (<37.0 U/ml vs. ≥ 37.0 U/ml), preoperative chemotherapy (upfront surgery vs. NAC), and staging (evaluated using computed tomography). Clinical staging was determined using preoperative TNM classification based on the General Rules for the Study of Pancreatic Cancer in Japan (8th Edition). Multivariate analysis was performed using a Cox proportional hazards regression model.

Results: The median follow-up period for OS analysis was 30.6 months. Among the clinical parameters, lymph node metastasis (clinical N1; cN1), tumor extent (cT3 or T4), and CA19-9 (≥ 37.0 U/ml) were significant predictors for OS in the univariate analysis. The median OS of the upfront surgery group (n=214) and the NAC group (n=54) were 28.7 and 39.7 month, respectively, showing an increase of approximately 11 months, which was not significant (p=0.33). Multivariate analysis revealed that only lymph node metastasis (cN1) remained an independent OS predictor (Hazard Ratio, 2.004; 95%CI 1.453-2.875; p<0.001). Median OS was 39.7 and 12.9 months in the cN0 (n=204) and cN1 groups (n=64) (p<0.001), respectively. The survival rate at three years were 51.8% and 21.3% in the cN0 and cN1 groups, respectively.

Conclusion: Preoperative lymph node metastasis was the strongest prognostic factor in patients with resectable or borderline resectable pancreatic cancer.

Disclosure: Nothing to disclose.

PP1154

FEASIBILITY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY FOR GENERATING PATIENT-DERIVED ORGANOID OF PANCREATIC DUCTAL ADENOCARCINOMA: PRELIMINARY RESULTS FROM A SINGLE-CENTRE PROSPECTIVE DATABASE

F. Borrelli de Andreis^{1,2}, V. Panzeri³, V. Ruta³, E. Cesari³, F. Attili², C. Spada², C. Sette³

¹Gemelli Isola - Isola Tiberina Hospital, Centre of Excellence of Gastrointestinal and Metabolic Disorders, Rome, Italy, ²Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Medical and Surgical Sciences, Rome, Italy, ³Università Cattolica del Sacro Cuore, Organoids Unit, Department of Neuroscience, Section of Human Anatomy, Rome, Italy

Contact E-Mail Address: federica.bda@gmail.com

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is notorious for its aggressive nature and grim prognosis, underscoring the urgent need for personalized pre-clinical models to develop targeted therapies. Patient-derived organoids (PDOs) are three-dimensional models of human tumours that have emerged as promising research tools.

Aims & Methods: Our study aimed to assess the feasibility of endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) for the generation of PDAC-PDOs. A single-centre prospective database was established to collect data from suspected PDAC patients undergoing EUS-FNB for histological confirmation between May and October 2023. All biopsies were performed using a 22G-needle. Two to three biopsies were taken for histological examination before performing a single-pass FNB to establish PDO cultures. The primary outcome was the successful propagation of PDAC-PDOs for at least three passages (P3). Secondary outcomes included sample adequacy, diagnostic rate, and safety.

Results: A total of 22 patients (M:F 13:9, median age 66.5 years, range 55-86) were enrolled. One case was subsequently diagnosed as pancreatic lymphoma and excluded. PDAC-PDOs were successfully established in 9 out of 21 PDAC cases, resulting in a success rate of 43% (please see Table 1 for further details on singular included patients). Sample adequacy and diagnostic rates were both achieved in 100% of subjects. The presence of

a biliary stent during EUS-FNB did not impact the success rate of PDAC-PDO generation (n=1 in the generated PDAC-PDOs group vs n=3 in the non-generated PDAC-PDOs group; p>0.05). No adverse events related to the procedure occurred.

Patient	Gender	Age	Lesion Size (cm)	Pancreatic Location	Sample Adequacy	Adverse Events
1	Male	62	3.5	Head	Yes	No
2	Female	85	3.0	Head	Yes	No
3	Male	61	1.2	Head	Yes	No
4	Male	68	3.5	Tail	Yes	No
5	Female	59	4.0	Head	Yes	No
6	Male	56	4.0	Body	Yes	No
7	Female	64	4.5	Tail	Yes	No
8	Female	60	5.0	Head	Yes	No
9	Female	58	4.0	Neck	Yes	No

Conclusion: This study demonstrates that PDAC-PDOs can be successfully generated through EUS-FNB sampling with a single-pass fine needle biopsy, without compromising the safety profile of the procedure.

References: Tiriach H, Bucobo JC, Tzimas D, Grewel S, Lacombe JF, Rowehl LM, Nagula S, Wu M, Kim J, Sasson A, Vignesh S, Martello L, Munoz-Sagastibelza M, Somma J, Tuveson DA, Li E, Buscaglia JM. Successful creation of pancreatic cancer organoids by means of EUS-guided fine-needle biopsy sampling for personalized cancer treatment. *Gastrointest Endosc.* 2018 Jun;87(6):1474-1480. doi: 10.1016/j.gie.2017.12.032.

Disclosure: Nothing to disclose.

PP1155

ATTITUDES TOWARD GENETIC TESTING, FAMILY PLANNING AND PREIMPLANTATION GENETIC TESTING IN FAMILIES WITH A GERMLINE CDKN2A PATHOGENIC VARIANT

A. Onnekink¹, D. Klatte^{1,2}, J. van Hooft¹, S. van den Berg¹, S. van der Zwaan¹, R. van Doorn³, C. Hinnen^{4,5}, T. Potjer⁶, E. Bleiker^{7,6,8}, M. van leerdam^{1,9}

¹Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ²Mayo Clinic, Gastroenterology and Hepatology, Jacksonville, Florida, Netherlands, ³Leiden University Medical Center, Dermatology, Leiden, Netherlands, ⁴Leiden University Medical Center, Psycho-Oncology, Leiden, Netherlands, ⁵Spaarne Gasthuis, Medical Psychology, Haarlem, Netherlands, ⁶Leiden University Medical Center, Clinical Genetics, Leiden, Netherlands, ⁷Netherlands Cancer Institute, Division of Psychosocial Research and Epidemiology, Amsterdam, Netherlands, ⁸Netherlands Cancer Institute, Clinical Genetics, Amsterdam, Netherlands, ⁹Netherlands Cancer Institute, Gastrointestinal Oncology, Amsterdam, Netherlands

Contact E-Mail Address: a.m.onnekink@lumc.nl

Introduction: Individuals with a germline *CDKN2A* pathogenic variant (PV) have an increased lifetime risk of up to 70% for melanoma and up to 20% for pancreatic cancer, and are recommended to undergo skin and pancreatic cancer surveillance. Little is known about the psychosocial issues associated with this hereditary cancer syndrome.

Aims & Methods: This cross-sectional study included confirmed *CDKN2A* PV carriers and those with a 50% risk of the PV (at-risk carriers) under cancer surveillance. Individuals ≥ 18 years were identified from the skin and pancreatic cancer surveillance programs at the Leiden University Medical Center and invited for a one-time questionnaire with study-specific questions concerning genetic testing, family planning, and preimplantation genetic testing (PGT).

Results: A total of 537 individuals were screened for eligibility, of whom 208 of 366 (57%) confirmed carriers (56% female, median age 54 years [IQR 46-63]) and 39 of 171 (23%) at-risk carriers (59% female, median age of 26 years [IQR 22-32]) participated in the study. Primary motivations for genetic testing were to gain control over their personal and children's cancer risk, as well as increasing cancer surveillance practices. In contrast, concerns about obtaining a mortgage and life insurance were frequently cited as reasons for postponing genetic testing.

Family planning decisions remained largely unaffected in both confirmed and at-risk carriers; however, the majority of confirmed carriers were still unaware of their familial or personal cancer risk when starting a family. More than 60% of the participants were unfamiliar with PGT and only a minority (19% of confirmed carriers and 10% of at-risk carriers) would be open to considering PGT as a reproductive option (Table 1).

	Confirmed carriers (n = 208)	At-risk carriers (n = 39)
Have you heard of PGT before? ^a		
No	134 (66%)	24 (62%)
Yes	68 (34%)	15 (39%)
Would you have preferred to receive counseling about PGT? ^a		
Yes	43 (21%)	4 (10%)
I don't know	64 (32%)	15 (36%)
No	95 (47%)	21 (54%)
Would you (have) consider(ed) using PGT for family planning? ^b		
Yes	38 (19%)	4 (10%)
Maybe	66 (33%)	25 (64%)
No	95 (47%)	10 (26%)

Table 1. Attitudes toward PGT

PGT, preimplantation genetic testing; PV, pathogenic variant. ^a 6 confirmed carriers missing. ^b 9 confirmed carriers missing.

Conclusion: This study found different attitudes toward genetic testing, family planning, and PGT among individuals affected by the *CDKN2A* PV. Understanding these different attitudes can help clinicians to address the complexities surrounding these issues, especially for younger individuals facing difficult decisions about the timing of genetic testing, family planning, and the potential use of reproductive assisted options.

Disclosure: Nothing to disclose.

PP1156

INSIGHTS INTO EARLY ONSET PANCREATIC CANCER: CLINICAL AND EPIDEMIOLOGICAL ANALYSIS

F. Amri¹, O. Elmqaddem¹, H. Koulali¹, A. Zazour¹, Z. Ismaili¹, G. Kharrasse¹

¹Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Hepato-Gastroenterology, Oujda, Morocco

Contact E-Mail Address: fakh.amr@gmail.com

Introduction: The reported prevalence of early onset pancreatic cancer (EOPC), defined in this context as pancreatic cancer diagnosed in individuals under the age of 50, ranges from 4% to 18%. Its incidence has shown a significant increase compared to later onset pancreatic cancer (LOEP). However, there remains limited understanding regarding the extent of this escalation and which subgroups are predominantly affected. This study aims to characterize the clinical and epidemiological characteristics of EOPC in comparison to LOPC.

Aims & Methods: We conducted a retrospective analysis of consecutive pancreatic cancer (PC) patients with definitive histopathological diagnoses, treated at our institution between January 2018 and December 2023. This study aims to characterize the clinical and epidemiological characteristics of EOPC in comparison to LOPC.

Results: Among 223 patients with pancreatic cancer (PC), 37 (16.6%) had EOPC. The mean age of these patients was 37 ± 7 years (range: 18-50). No significant difference in terms of sex was found, with a male predominance in both groups (54.1% in EOPC vs. 55.9% in LOPC). Regarding risk factors, no significant difference was observed between the two groups for smoking, alcohol consumption, obesity, and diabetes. However, a significant increase in family history of pancreatic cancer was noted in the EOPC group (10.8% vs. 1.6%, OR: 3.7 [95% CI: 1.8 – 7.6], p=0.003). No significant difference was found between the two groups regarding tumor stage; cancer was resectable in 27% of cases in the EOPC group compared to 16.1% in the LOPC group (p=0.240). Regarding nutritional status, according to the Nutritional Risk Index (NRI), younger patients had a lower risk of severe malnutrition (18.9% vs. 39.8%, OR: 0.4 [95% confidence interval: 0.2 -0.9], p=0.01), and the mean albumin level was significantly higher in the EOPC group (36 ± 4 vs. 33 ± 5 g/L, p=0.016).

Conclusion: Our study not only highlights the substantial prevalence of EOPC, but also underscores the presence of distinct clinical and epidemiological differences compared to LOPC. Notable findings include a heightened familial predisposition, disparities in nutritional status. These insights emphasize the imperative for tailored screening and management strategies to effectively address the nuances of EOPC.

Disclosure: Nothing to disclose.

PP1157

CANNABINOIDS IN PANCREATIC CANCER PALLIATIVE CARE: A SYSTEMATIC REVIEW AND META-ANALYSIS

I. Creanga-Murariu^{1,2,3}, I.-I. Rezus^{1,2}, R. Karami¹, A. Rancz¹, D.S. Veres¹, M.A. Engh¹, M. Obeidat¹, S. Bunduc^{4,5}, B.-I. Tamba², P. Hegyi^{1,6,7}

¹Centre For Translational Medicine, Semmelweis University, Budapest, Hungary, ²“Grigore T. Popa” Medicine and Pharmacy University/Advanced Center for Research and Development in Experimental Medicine (CEMEX), Iasi, Romania, ³Regional Institute of Oncology, Iasi, Romania, ⁴Fundeni Clinical Institute, Gastroenterology and Hepatology, Bucharest, Romania, ⁵Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁶University of Pécs/Institute for Translational Medicine, Pécs, Hungary, ⁷Semmelweis University/Institute of Pancreatic Diseases, Budapest, Hungary

Contact E-Mail Address: ioana.creanga@d.umfiasi.ro

Introduction: Pancreas adenocarcinoma is the 6th leading cause of cancer-related death worldwide. Most patients are diagnosed with advanced disease, which is associated with distressing symptoms such as pain, fatigue, or anorexia. Cannabinoids are a new class of drugs for the palliation of cancer-associated symptoms; however, they lack clear indication.

Aims & Methods: Our aim is to investigate the safety and efficacy of cannabinoids for symptom control in advanced cancer patients. The study protocol was registered on PROSPERO (CRD42023479375), and a systematic search was conducted using three main databases (PubMed, Embase, and CENTRAL).

Interventional and observational articles, where cancer patients were administered any type of cannabinoid for symptom control, including pain, constipation, nausea and insomnia, were eligible for analysis. The change from baseline in symptom intensity was assessed, for which weighted means and pooled proportions were calculated with a 95% confidence interval (CI) and a random-effects model.

Results: After title-abstract and full-text selection, 96 articles were found to be eligible. Pain, constipation, nausea, and insomnia improvement were assessed using different types of symptom rating scales (0-absence

of symptom, highest score-worst symptom intensity). The preliminary results show that cannabinoids do not improve pain compared to placebo, the mean change from baseline was 0.17 (-0.53; 0.87 95% CI); nor constipation, mean change from baseline of 0.05 (-0.65; 0.75 95% CI). Cannabinoids modestly improve sleep quality, with a mean change from baseline of -0.14 (-0.85; 0.58 95% CI), and nausea, the mean difference from baseline -0.06 (-0.42; 0.29 95%CI), however not clinically significant.

Conclusion: Cannabinoids could be beneficial for advanced pancreatic cancer patients. However, the effects may vary significantly depending on the type of cannabinoid, dosage, and form of administration. These preliminary results need to be followed by further analysis based on subgroups, so proper indication/contraindication of the drugs can be suggested.

Disclosure: Nothing to disclose.

PP1158

PREVENTION OF POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH PANCREATIC CANCER FOLLOWING PANCREATODUODENECTOMY

L. Pererva¹, V. Kopchak¹, V. Shkarban¹, V. Khanenko¹, P. Azadov¹, V. Trachuk¹, Z. Holobor²

¹Shalimov National Scientific Center of Surgery and Transplantology, Pancreatic and bile ducts surgery, Kyiv, Ukraine, ²Bogomolets National Medical University, Kyiv, Ukraine

Contact E-Mail Address: Liudmylapererva@gmail.com

Introduction: Despite improvements in the perioperative care of patients with pancreatic cancer the incidence of postoperative complications following pancreatic resections remains high.

Aims & Methods: The objective of this study was to develop surgical techniques to prevent postoperative complications following pancreatoduodenectomy. A retrospective analysis was conducted on the surgical outcomes of 456 patients with resectable pancreatic and periampullary cancer who underwent pancreatoduodenectomy between 2015 and October 2023. Since November 2018, new surgical tactics have been implemented to prevent the occurrence of postoperative pancreatic fistula (POPF) and other postoperative complications. Preliminary data indicates that the development of postoperative complications after pancreatoduodenectomy correlates with postoperative pancreatic fistula, the presence of sarcopenia has been demonstrated to significantly affect the number of clinically relevant postoperative pancreatic fistula and other postoperative complications.

Since that time, we have used new approaches: our modification of the pancreatic fistula risk score, which assesses pancreatic density according to the degree of pancreatic fibrosis. Depending on the risk, we used our surgical tactics. In cases with a high risk of postoperative pancreatic fistula, during pancreaticojejunostomy we used external pancreatic stent. In patients with intermediate risk we performed invaginated duct to mucosa pancreaticojejunostomy. In low-risk patients, the technique of pancreaticojejunostomous anastomosis was considered by the operating surgeon. We performed early removal of abdominal drains in patients with low risk of pancreatic fistula. Prior to surgery, the presence of sarcopenia was assessed, and nutritional support was provided to patients with sarcopenia. During the period from November 2018 to October 2023, proposed mitigation strategies were applied to 227 patients in the main group. The comparison group consisted of 229 patients who underwent surgery without the use of the developed surgical strategies between January 2015 and October 2018.

Results: The groups were comparable in terms of sex, age, laboratory results, disease stage, American Society of Anesthesiologists score, and comorbidities. In the main group, 26 patients (11.4%) experienced POPF

grade B or C. In the comparison group, 64 out of 229 patients (27.9%) experienced a postoperative pancreatic fistula of grade B or C, which is significantly higher than the main group ($\chi^2=19.5$, $p=0.0001$). Furthermore, the main group had a significantly lower level of postoperative complications compared to the comparison group. A total of 69 patients (30.1%) in the main group experienced complications, while 94 patients (41.0%) in the comparison group did so ($\chi^2=5.6$, $p=0.02$). The mortality rate in the main group was reduced from 2.2% to 1.3% due to the developed tactics ($\chi^2=0.49$, $p=0.5$).

Conclusion: The surgical tactics developed to prevent postoperative pancreatic fistula after pancreatoduodenectomy were found to significantly reduce its occurrence from 27.9% to 11.4%, postoperative complications from 41.0% to 30.1%, and mortality from 2.2% to 1.3% ($\chi^2=0.49$, $p=0.5$).

Disclosure: Nothing to disclose.

PP1159

THE ROLE OF CHEMOTHERAPY IN THE MANAGEMENT OF PANCREATIC MUCINOUS ADENOCARCINOMA: A RETROSPECTIVE COHORT

M.A. Ali¹, A. Ellaithy²

¹South Valley University, Qena Faculty of Medicine, Qena, Egypt,

²Suez Canal University, Gastroenterology, Ismailia, Egypt

Contact E-Mail Address: mohammedahmedalihassan2003@gmail.com

Introduction: Mucinous adenocarcinoma (MAC) is a mucin-producing tumor. In MAC, about >50% of the tumor is composed of extracellular mucin with clear malignant epithelial cells in clumps and layers. Pancreatic MAC represents only 3.5% of all pancreatic tumors and 5.1% of all MAC cases [1]. Few studies with Poor evidence investigated the survival of pancreatic MAC, especially for patients treated with chemotherapy.

Aims & Methods: In this study, we aimed to assess the impact of chemotherapy on the survival outcome in pancreatic MAC. We conducted a retrospective cohort study Using the Surveillance Epidemiology and End Results (SEER) database. We extracted the data of 4837 patients diagnosed with pancreatic MAC from 2000 to 2020. patients were sub-stratified according to the treatment modality into Surgical and Non-surgical groups. We conducted a survival analysis by Kaplan–Meier and Log-rank test using Jamovi v2.3.26 software. Cox regression analysis was conducted to investigate the association between other risk factors and survival.

Results: The median age for pancreatic MAC was 68 years (IQR: 59-76) [2] [3] with a 5-year Relative survival of 8.3%. The 5-year Relative survival in the group treated Surgically was significantly improved compared to the Non-surgical group (35% and 1.7%; $P<0.001$). In the Group that had surgical intervention, systemic Chemotherapy showed no significant survival benefit compared to who had no chemotherapy (33.1% and 37.3%; $P=0.15$). In the group treated medically, Chemotherapy showed a significant survival benefit compared to the group who received no chemotherapy with a 2-year relative survival of 11.6% and 4.2% while the 5-year relative survival was 1.4% and 2.1% ($P<0.001$) [4] [5]. COX-regression model showed males had better survival outcomes compared to females (HR=0.88, 95%CI: 0.83-0.93, $P<0.001$) while African Americans had worse survival compared to Caucasians (HR=1.15, 95%CI: 1.05-1.27, $P=0.003$) [6] [7][8][9].

Conclusion: Pancreatic MAC is an extremely aggressive tumor with poor survival outcome. Surgery had a significant survival benefit of 33% compared to medical treatment only which highlights surgery as the modality of choice for pancreatic MAC. Chemotherapy improved the survival of patients who were not treated surgically. Further evaluation of each patient is needed to confirm if the patient is qualified for the surgical intervention and chemotherapy. Males and Caucasians seem to have better survival compared to females and African Americans.

References:

1. Benesch MGK, Mathieson A. Epidemiology of Mucinous Adenocarcinomas. *Cancers (Basel)*. 2020 Oct 30;12(11):3193. doi: 10.3390/cancers12113193. PMID: 33143115; PMCID: PMC7692300.
2. The jamovi project (2022). jamovi. (Version 2.3) [Computer Software]. Retrieved from <https://www.jamovi.org>.
3. R Core Team (2021). R: A Language and environment for statistical computing. (Version 4.1) [Computer software]. Retrieved from <https://cran.r-project.org>. (R packages retrieved from MRAN snapshot 2022-01-01).
4. Terry M Therneau (2020). A Package for Survival Analysis in R. [R package]. Retrieved from <https://cran.r-project.org/package=survival>.
5. Terry M. Therneau and Patricia M. Grambsch (2000). Modeling Survival Data: Extending the Cox Model. Springer.
6. Ewen Harrison and Tom Drake and Riinu Ots (2019). finalfit: Quickly Create Elegant Regression Results Tables and Plots when Modelling. [R package]. Retrieved from <https://CRAN.R-project.org/package=finalfit>.
7. Hidalgo B, Goodman M. (2013). Multivariate or Multivariable Regression?. *Am J Public Health*.. link, 103, 39-40.
8. Emily C. Zabor (2022). Survival analysis in R: A detailed tutorial on conducting survival analyses in R, including an introduction to the basics of survival analysis, landmark analyses and time-dependent covariates, competing risks, and a selection of advanced topics.. [GitHub Repository]. Retrieved from <https://github.com/zabore/tutorials>. link.
9. Serdar Balci (2022). ClinicoPath jamovi Module doi:10.5281/zenodo.3997188. [R package]. Retrieved from <https://github.com/sbalci/ClinicoPathJamoviModule>. link.

Disclosure: Nothing to disclose.

PP1160

THE RISK OF MULTIPLE PRIMARY GASTROINTESTINAL TUMORS FOLLOWING PRIMARY PANCREATIC CANCER

A. Abdelhamed¹, A. Ellaithy²

¹Zagazig University, Gastroenterology, Al Sharqia, Egypt, ²Suez Canal University, Gastroenterology, Ismailia, Egypt

Contact E-Mail Address: athartahoon24@gmail.com

Introduction: Pancreatic cancer is the seventh leading cause of deaths worldwide representing 4.7% of all cancers. Cancer head of pancreas is the most common (45.95%) while 13.2% arise in the tail and 11.35% in the body.

The association between the three parts of pancreas(head, body and tail) and the risk of multiple primary gastrointestinal (GI) malignancies were poorly discussed in the literature.

The aim of this study is to assess the risk of multiple primary GI malignancies following primary pancreatic cancer with further stratification by the primary site as head, body and tail.

Aims & Methods: We used Surveillance, Epidemiology, End result (SEER) database to extract data of pancreatic cancer patients diagnosed from 2000 to 2020 .we further stratified them by site (head, body, tail). We used MP- SIR session to assess the Excess Absolute Risk (EAR) per 10,000. We calculated SIR as observed/expected (O/E) with 95% confidence interval and P-value was considered significant if P<0.05.

Results: Out of 221800 patients with pancreatic cancer ,1284 patients had GI second primary malignancy (SPM) with O/E of 2.28 (P<0.05, 95% CI: 2.15-2.41, EAR=35.96). In cancer head of pancreas, we observed 578 had GI SPM with O/E of 2.03 (P<0.05, 95% CI: 1.87-2.21, EAR=29.43) with significant increased risk of small intestine SPM in the first year after diagnosis (O/E 23.44, P<0.05,95% CI: 18.64-29.10, EAR=17.11). In cancer body of pancreas, 125 had GI SPM with O/E of 2.12 (P<0.05,EAR=29.54) with increased

risk of stomach SPM in the 0-11 months interval. In cancer tail of pancreas, 187 patients had GI SPM (O/E of 2.31 P<0.05, EAR=31.93) with increased risk of other sites of pancreas and the stomach SPM.

Conclusion: Pancreatic cancer has very poor prognosis and significantly increased risk to develop second primary GI malignancies by two folds especially in small intestine, stomach, colon and liver. Cancer head of pancreas has the highest risk of multiple primary GI tumors compared to the other sites especially for small intestine in the first year after diagnosis. These results would take part in understanding the potential risk of GI SPM for better management plan and outcome and encourage to pay more attention for early GI malignancies screening after the diagnosis of pancreatic cancer.

Disclosure: Nothing to disclose.

PP1161

PANCREATIC CANCER BIOMARKERS SUCH AS INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3, MACROPHAGE MIGRATION INHIBITORY FACTOR AND ADRENOMEDULLIN IN THE DIFFERENTIATION OF CHRONIC PANCREATITIS FROM PANCREATIC DUCTAL ADENOCARCINOMA

B. Włodarczyk¹, L. Durko¹, P. Włodarczyk², R. Talar-Wojnarowska¹, E. Malecka-Wojcieszko¹

¹Medical University of Lodz, Department of Digestive Tract Diseases, Lodz, Poland, ²University of Lodz, Faculty of Economics and Sociology, Lodz, Poland

Contact E-Mail Address: barrbara.wlodarczyk@gmail.com

Introduction: Insulin-like growth factor binding protein-3 (IGFBP-3), macrophage migration inhibitory factor (MIF) and adrenomedullin (ADM) are connected with pancreatic ductal adenocarcinoma (PDAC) development. **Aims & Methods:** Evaluation of serum levels of IGFBP-3, MIF and ADM in patients with chronic pancreatitis (CP), PDAC and control group and their potential role for differentiation of CP and PDAC. The study included 70 CP, 73 PDAC, and 23 healthy subjects as a control group. Serum concentrations of IGFBP-3, MIF, and ADM were measured with ELISA (Corgenix UK Ltd, R&D Systems). Diagnostic efficiency of the biomarkers was assessed by means of AUROC calculation. The Cambridge and TNM scales were used.

Results: Mean IGFBP-3 serum level was significantly higher in CP patients vs. controls (3.98 ± 2.44 ng/ml vs. 1.40 ± 1.45 ng/ml, p<0.05). Mean IGFBP-3 level was also higher in CP than in PDAC group (3.98 ± 2.44 ng/ml vs. 2.02 ± 1.69 ng/ml, p<0.05). Mean MIF serum level was also significantly higher in CP patients vs. control group (8589.50 ± 3607.78 pg/ml vs. 7365.76 ± 5009.52 pg/ml, p<0.05). Mean MIF level was also higher in CP vs. PDAC patients (8589.50 ± 3607.78 pg/ml vs. 8160.2 ± 4840.32 pg/ml, p>0.05), but the difference was not statistically significant. Mean ADM serum level was significantly lower in CP vs. controls (76.72 ± 135.02 ng/ml vs. 177.12 ± 348.99 ng/ml, p<0.05), but it did not differ between CP and PDAC patients (76.72 ± 135.02 ng/ml vs. 152.72 ± 285.43 ng/ml, p>0.05). Mean CA19-9 serum concentration was 50.98 +/- 153.44 U/ml in CP vs. 439.33 +/- 441.24 U/ml in PDAC; p<0.0000). Mean MIF and ADM levels did not show significant differences between CP and PDAC groups. AUROCs for MIF, IGFBP-3 and ADM ranged below 0.75, which is lower than the AUROC for CA19-9 (0.8703; 0.8120 within 95% CI). CA19-9 & IGFBP-3 taken together showed AUROC equal to 0.8676 (0.8094 within 95% CI). When additional variable IGFBP-2 was added AUROC raised to 0.8912 (0.8378 within 95% CI). When data on CA19-9, IGFBP-2 and IGFBP-3 were considered together with patients' age and sex – AUROC was 0.9535 (0.9227 within 95% CI). Male sex and advanced age raised the probability of PDAC. When examining markers' differentiation according to the degree of advancement of CP and PDAC, it was found that CA19-9 better differentiates groups at an

early stage of disease development (1 & 2 Cambridge in CP vs. I & II TNM in PDAC), AUROC 0.9259 vs. 0.8755. The combination of CA 19-9, IGFBP-2, IGFBP-3, age and sex gave better results in the advanced group, AUROC 0.9591 vs. 0.9708.

Conclusion: Panel of IGFBP-3, MIF, ADM and CA19-9 may be useful in PDAC and CP differentiation. Further studies are necessary to confirm those findings.

Disclosure: Nothing to disclose.

PP1162

WITHDRAWN

PP1163

MACHINE LEARNING PREDICTION METHODS FOR PANCREATIC DUCTAL ADENOCARCINOMA PROGNOSIS ASSESSMENT

B. Ungureanu¹, D.-I. Gheonea¹, C.V. Georgescu², A. Turcu-Stiolica³, I. Rogoveanu¹, A. Saftoiu⁴

¹University of Medicine and Pharmacy of Craiova, Gastroenterology, Craiova, Romania, ²University of Medicine and Pharmacy of Craiova, Pathology, Craiova, Romania, ³University of Medicine and Pharmacy of Craiova, Pharmacoeconomics, Craiova, Romania, ⁴Carol Davila University of Medicine and Pharmacy, Gastroenterology, Bucharest, Romania

Contact E-Mail Address: boboungureanu@gmail.com

Introduction: Pancreatic Ductal Adenocarcinoma (PDAC) is a lethal cancer accounting for over 90% of pancreatic cancer cases and it aggressively develops metastases. It is currently the 4th leading cause of all cancer deaths in both males and females, with expectations to become the 2nd most by 2030. PDAC prognosis is grim with most being unresectable at the time of diagnosis.

Aims & Methods: Our objective was to develop machine learning algorithms based on clinicopathologic characteristics and biomarker levels to determine a prognostication model for PDAC assessment. A total of 76 patients diagnosed by EUS-FNB sampling with PDAC were included in the study. Clinical, paraclinical, and specific biomarker expressions were collected. We considered the following: alcohol consumption, smoking, diabetes type II, CRP, albumin, neutrophil/lymphocyte, thrombocyte/lymphocyte, CRP/albumin, CEA, CA 19.9, CA125, plasma levels of mir107 and CD63 immunohistochemistry expression. The endpoint was to compare T1-T2 with T3-T4 stages by using various algorithms.

We calculated error rates for Latent Dirichlet Allocation (LDA), Quadratic Discriminant Analysis (QDA), and Logistic Regression (LR). To evaluate the model and check how well it performs on unseen data, we took a validation set and checked the model's performance on it. Then modeled K-Nearest Neighbors (K-NN), where we demonstrated the validation set performance check.

Results: The 4 models had high accuracy ranging from 0.77 to 1, the best model was QDA and the worst was K-NN. LDA obtained an accuracy of 85% showing that the Neutrophil/Lymphocyte ratio will most influence a T1+T2 stage, and the PRC/Albumin and Thrombocyte/Lymphocyte ratio will lead to a T3+T4 stage. LR obtained an accuracy of 83%. Platelet/Lymphocyte ratio, PRC/Albumin, and CD63 indicators can be used for high prediction of T3+T4 stage, and Neutrophil/Lymphocyte ratio, PRC, and mir107 are suitable indicators for T1+T2 stage prediction.

Conclusion: Machine-learning methods based on clinicopathologic and biomarkers may serve as an auxiliary method to diagnose and predict PDAC prognosis.

Disclosure: Nothing to disclose.

PP1164

THE IMPACT OF EUS ON THE DIAGNOSIS, STAGING, HISTOLOGICAL PROOF, AND TREATMENT OF COMPLICATIONS OF SOLID PANCREATIC TUMORS: A SINGLE-CENTER SERIES

I. Qarch¹, M. Borahma², N. Lagdali², M. Kadiri², C. Berhili², F.-Z. Chabib², F.Z. Ajana³

¹Mohammed V university, Medicine C-Hépatogastroenterology, Rabat, Morocco, ²Mohammed the Vth University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ³CHU IBN SINA, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: ismail.qarch@gmail.com

Introduction: The sensitivity of endoscopic ultrasound (EUS) in detecting pancreatic tumors exceeds 90% and can detect tumors with a diameter of less than 2 cm. EUS plays an important role in the management of patients with pancreatic cancer, providing precise diagnosis, determining local-regional extension and resectability assessment, conducting biopsies, and managing complications.

The objective of our study was to specify the impact of EUS on the diagnosis, staging, histological proof, and treatment of complications of solid pancreatic tumors.

Aims & Methods: A retrospective study was conducted over 5 years (2019-2024), including all patients admitted with clinical suspicion of solid pancreatic tumors and who experienced EUS.

Results: Out of the 115 patients admitted with clinical suspicion of pancreatic tumor, 86 (74.8%) had undergone EUS. The mean age was 68.2 years, ranging from 30 to 90 years, with a clear male predominance (sex ratio 1.1). Biological assessment showed cholangitis grade I and grade II in 35.6% (n=31) of cases, and grade III in 4 patients (4.6%).

EUS revealed a pancreatic mass in 98.9% (n=85) of cases, with 75.5% (n=64) in the head, 14% (n=12) in the uncinate process, 7% (n=6) in the body, and 3.5% (n=3) in the neck. The size was over 3 cm in 59 cases (69.4%), between 2-3 cm in 23 cases (27.1%), and less than 2 cm in 3 cases (3.5%). double duct dilation was shown in 57 cases (66.3%), isolated bile duct dilation in 31 cases (36%), and isolated Wirsung duct dilation in 4 cases (4.6%). Pancreatic atrophy was observed in 31.4% (n=27) of cases.

EUS allowed the determination of vascular invasion in 78 cases (90.7%), invasion of the portal trunk (TP) and superior mesenteric vein (SMV) was present in 43 cases (55.1%), with invasion over >180 in 28 cases (35.9%) and <180 in 15 cases (19.2%), thrombosis in 3 cases (3.5%), and absence of invasion in 15 cases (19.2%).

Invasion of the celiac trunk (CT) and superior mesenteric artery (SMA) was present in 31 cases (39.9%), with invasion over >180 in 22 cases (28.2%) and <180 in 9 cases (11.6%), thrombosis in 2 cases (2.3%), and absence of invasion in 24 cases (30.7%). Invasion of the common hepatic artery (CHA) was present in 6 cases (7.7%), with invasion over >180 in 5 cases (83.3%) and <180 in one case (16.7%), and absence of invasion in 6 cases (7.7%). Locoregional lymph node extension was observed in 12 cases (15.4%), invasion of the common bile duct (CBD) in one case (1.3%), duodenal invasion in 3 cases (3.9%), secondary hepatic localization in 7 cases (9%), and peritoneal in 2 cases (2.6%).

Cytopuncture under EUS was performed in 70 cases (89.7%), the results of which were conclusive in 65.4% (n=51) of cases and inconclusive in 24.6% (n=19). The histological type was adenocarcinoma in 48 cases (94.1%), clear cell carcinoma, squamous cell carcinoma, and neuroendocrine tumor in one case (1.9%).

Therapeutically, EUS allowed the treatment of pancreatic abdominal pain resistant to medical treatment by celiac plexus block in 2 cases, neurolysis in one case, and also performing antegrade hepatic gastric biliary drainage after the failure of retrograde drainage due to duodenal strictures in 5 cases.

Conclusion: EUS reveals pancreatic tumors in 98.9% of cases, with its main importance lying in locoregional staging, where vascular invasion was correctly determined in 90.7% of cases, and lymph node extension in 15.4%. The value of EUS lies in determining histological type (65.4%), as well as therapeutic aspects such as pain management and biliary drainage.

Disclosure: Nothing to disclose.

PP1165

METABOLIC IMPLICATIONS OF PANCREATIC STEATOSIS: INSIGHTS AND CORRELATION ANALYSIS WITH MRI FINDINGS

S.S. De Lucia¹, E.C. Nista¹, L. Soldovieri², E. Genco³, M.G. Brizi³, F.M. Sessa³, E. Gori³, G. Di Giuseppe², G. Palumbo¹, A. Gasbarrini¹, T. Mezza²

¹IRCCS Policlinico Universitario A. Gemelli - Università Cattolica del Sacro Cuore, Pancreas Unit, CEMAD Centro Malattie dell'Apparato Digerente, Medicina Interna e Gastroenterologia, Rome, Italy, ²IRCCS Policlinico Universitario A. Gemelli - Università Cattolica del Sacro Cuore, Dipartimento di Scienze Mediche e Chirurgiche, Centro Malattie Endocrine e Metaboliche, Rome, Italy, ³IRCCS Policlinico Universitario A. Gemelli - Università Cattolica del Sacro Cuore, Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Radiologia addomino-pelvica, Rome, Italy

Contact E-Mail Address: saras.delucia@gmail.com

Introduction: Pancreatic steatosis (PS) frequently coexists with metabolic dysregulation, including insulin resistance, type 2 diabetes, and obesity. Magnetic resonance imaging (MRI) can be useful in quantifying intrapancreatic fat through the three-dimensional volumetric multi-echo gradient echo sequence (IDEAL-Q) to obtain pancreatic proton density fat fraction (P-PDFF).

Aims & Methods: Our study aims to establish a correlation between P-PDFF and metabolic indices. We enrolled 26 patients with increased parenchymal echogenicity in the pancreatic body on ultrasound evaluation and subsequently subjected them to MRI for quantification of intrapancreatic fat. The mean age of the patients was 56.26 years, including 16 women and 10 men, with an average BMI of 29.33±8.38 kg/m². Patients underwent standard oral glucose tolerance test (OGTT) with 75g glucose load. We calculated the area under the curve of glucose (AUC-Glu) and insulin (AUC-Ins) responses during OGTT.

Further, we evaluated beta-cell function through Disposition Index and Insulinogenic Index and insulin sensitivity through Matsuda Index and Homeostasis Model Assessment Index (HOMA-IR). MRI was performed in order to calculate PDFF within three pancreatic body regions of interest (ROIs). Linear correlations were conducted between mean PDFF and metabolic parameters, including the Matsuda Index, HOMA-IR, Insulinogenic Index, Disposition Index, and BMI.

Results: In the cohort of patients, 73.1% presented normal glucose tolerance (NGT), while the remaining 26.9% displayed impaired glucose tolerance (IGT).

Diabetic patients were excluded from the analysis. Stratification of patients was conducted according to the median of P-PDFF. Comparative analysis between these stratified groups revealed no statistically significant differences in Matsuda Index, HOMA-IR, Insulinogenic Index, or Disposition Index. Linear correlations between the mean PDFF and the analyzed metabolic parameters revealed no statistically significant associations, except for BMI ($p < 0.05$).

Conclusion: Our findings suggest there is no significant correlation between PDFF measured pancreatic steatosis, with glucose levels, insulin secretion and beta cell function. However, PDFF was significantly related

to BMI suggesting that overweight and obesity is significantly related to pancreatic fat accumulation. Our study seem to suggest that pancreatic fat accumulation does not impact on endocrine pancreatic function.

Disclosure: Nothing to disclose.

PP1166

MORPHOLOGY OF THE PAPILLA CAN PREDICT PROCEDURAL SAFETY AND EFFICACY OF ERCP - A SYSTEMATIC REVIEW AND META-ANALYSIS

E. Tari^{1,2}, E.B. Gagy^{2,1}, A. Rancz², D.S. Veres^{2,2}, S. Váncsa^{3,4,5}, P.J. Hegyi^{3,4,5}, K. Hagymási^{4,6}, P. Hegyi^{3,4,5}, B. Eröss^{3,4,5}

¹Semmelweis University, Institute of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Semmelweis University, Selye János Doctoral College for Advanced Studies, Budapest, Hungary, ⁴Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁵Medical School, University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ⁶Semmelweis University, Department of Surgery, Transplantation, and Gastroenterology, Budapest, Hungary

Contact E-Mail Address: edina.tari@gmail.com

Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) is the most commonly used therapeutic procedure for pancreaticobiliary disorders. However, how to best achieve safe and effective bile duct cannulation is still debated. Endoscopists doing ERCP routinely recognize the differences in the macroscopic appearance of the major papilla. This has led to a conception that certain appearances of the papilla are more difficult to cannulate and, therefore, more prone to adverse events.

Aims & Methods: We aimed to quantify the influence of papilla morphology on ERCP outcomes.

PROSPERO registration number: CRD42022360894. We systematically searched three medical databases from inception in September 2022. Studies detailing the cannulation or the rate of adverse events in the context of papilla morphology were included. For the primary classification of the major papilla, the Haraldsson system was used, differentiating four morphological types. Data on studies using other classification systems were also collected. A pooled event rate with a 95% confidence interval (CI) was used for the effect size measure. For the test of subgroup differences, a "Cochrane Q" test was used. The risk of bias assessment was performed using the Joanna Briggs Institute Critical Appraisal tool for studies reporting prevalence.

Results: A total of 17 studies were eligible, and 14 were included in the quantitative synthesis. In studies using the Haraldsson classification, the rate of difficult cannulation was the lowest in type I ("regular") papilla (26%; CI: 18–37), followed by type III ("protruding or bulging") (35%; CI: 25–48) and type II ("small") papilla (39%; CI: 28–52). The highest rate was observed in the case of type IV ("creased or ridged") papilla (41%; CI: 28–55). For post-ERCP pancreatitis, the event rate was the highest in type II ("small") papilla (11%; CI: 8–15) and the lowest in type I ("regular") (6%; CI: 5–8) and III ("protruding or bulging") papilla (6%; CI: 4–8). There was no statistically significant difference in the cannulation failure and post-ERCP bleeding event rates between the different papilla types. Similar trends were observed in the analyses including other classification systems comparable to the Haraldsson's. Most studies carried a low risk of bias.

Conclusion: In conclusion, other types are associated with a higher rate of difficult cannulation compared to the regular papilla type. The small papilla is associated with a higher rate of post-ERCP pancreatitis.

Disclosure: Nothing to disclose.

PP1167

EXPLORING THE ROLE OF ECHO-ENDOSCOPY IN UNRAVELING ACUTE PANCREATITIS ETIOLOGY: A RETROSPECTIVE STUDY

F. Amri¹, C. Belkhatat¹, O. Elmqaddem¹, H. Koulali¹, A. Zazour¹, G. Kharrasse¹, Z. Ismaili¹

¹Mohammed VI university hospital, Faculty of Medicine and Pharmacy, Mohammed First University,, Department of Hepato-Gastroenterology, Oujda, Morocco

Contact E-Mail Address: fakh.amr@gmail.com

Introduction: Acute pancreatitis (AP) can pose challenges in diagnosing its underlying cause, with 10-30% of cases remaining elusive despite thorough clinical, biological, and morphological assessments. Echo-endoscopy (EUS) is particularly effective in exploring the bilio-pancreatic region. Our study aims to assess the role of EUS in elucidating the etiology of unexplained AP.

Aims & Methods: We performed a retrospective descriptive study at a university hospital's gastroenterology department between January 2018 and December 2023. It involved 118 patients diagnosed with AP, whose etiology was either suspected or remained undetermined after an initial radiobiological assessment (US, CT scan and MRI). These patients underwent EUS as part of their diagnostic evaluation.

Results: The average age of our patients was 55 ± 16 years, with a predominance of females (73.7%) and a male-to-female sex ratio of 0.35. 32.2% of patients had undergone cholecystectomy. 94.1% were admitted for their first episode of AP, while 5.9% had experienced at least one previous episode. Jaundice was observed in 29.7% of cases, and liver tests abnormalities were noted in 38.5%. Following initial radiological evaluation (ultrasonography, CT scan, MRCP), 53.4% of patients had biliary duct dilatation without visible obstruction, 33.9% had no dilatation, and 12.7% had diagnostic uncertainty. The diagnostic yield of EUS was 83%: micro lithiasis of the main bile duct accounted for 75.4% of cases, tumor-related causes for 4.2%, IPMN in 2 cases, biliopancreatic junction anomaly in 1 case, and Pancreas Divisum in 1 case. EUS findings were normal in 17% of cases.

Conclusion: EUS shows promise in elucidating the etiology of unexplained AP, boasting a high diagnostic yield in exploring the bilio-pancreatic region. Integrating EUS into diagnostic protocols could enhance the management of patients with AP, particularly in cases where initial investigations are inconclusive.

Disclosure: Nothing to disclose.

PP1168

ENDOSCOPIC PAPILLECTOMY FOR LATERALLY SPREADING AMPULLARY LESIONS

K. Vu Trung¹, E. Abou-Ali², F. Auriemma³, A. Gulla⁴, S. Regnér⁵, S. Gaujoux⁶, M. Hollenbach⁷, ESAP study group

¹University of Leipzig Medical Center, Leipzig, Germany, ²Paris Descartes University and COCHIN Hospital, APHP, Paris, France, Paris, France, ³Humanitas Mater Domini, Gastroenterology and Digestive Endoscopy, Castellanza, Italy, ⁴Institute of Clinical Medicine, Faculty of Medicine, Vilnius University/Vilnius University Hospital, Department of Surgery, Vilnius, Lithuania, ⁵Lund University Dept of Surgery, Surgery Research Unit, Malmö, Sweden, ⁶Pitié-Salpêtrière Hospital, Médecine Sorbonne Université, APHP, Paris, France, ⁷Marburg University UKGM, Department of Gastroenterology, Hepatology, Infectious Diseases, Endocrinology, Marburg, Germany

Contact E-Mail Address: marcus.hollenbach@web.de

Introduction: Endoscopic papillectomy (EP) is a standard endoscopic treatment for ampullary lesions (AL), most of which are small and limited to the papillary mound. Laterally spreading lesions (LSL) of the papilla Vateri represent a rare subtype of AL, characterized by extension beyond the ampullary mound and extensive involvement of the surrounding duodenum. In this study, we analyzed the outcomes of EP in matched cohorts, comparing cases of LSL with non-LSL of the ampulla.

Aims & Methods: The ESAP study encompassed 1422 endoscopic papillectomies (EPs). We employed propensity-score matching using the nearest-neighbor method using age, gender, comorbidities and histologic subtype as cofactors. The main outcomes assessed were complete resection (R0), technical success, complications, and recurrence.

Results: Propensity-score-based matching identified 232 patients (116 non-LSL and 116 LSL) with comparable baseline characteristics. LSL sizes were significantly larger compared to non-LSL (median 27.0mm vs. 16.5mm, p<0.001). Therefore, en bloc resection rates were significantly higher in the non-LSL group (71.6% vs. 34.5%, p<0.001). After first intervention, the R0-rate was significantly lower in the LSL group (54.3% vs. 69.0%, p=0.002). Following repeated interventions (such as EP, RFA, APC), the technical success was comparable in both groups at 82.8% (p=1.00). There were significantly more recurrences in the LSL group (23.8% vs. 8.6%, p=0.013). Complication rate exhibited no significant variance between the two groups.

Conclusion: LSL can be safely managed endoscopically, though repeated interventions are necessary for outcomes comparable to non-LSL. The higher risk of recurrence in LSL necessitates a vigilant surveillance strategy.

Disclosure: Honoraria from FUJIFILM

PP1169

POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS WAS AN INDEPENDENT RISK FACTOR OF PANCREATIC CANCER DEVELOPMENT IN PATIENTS WITH TYPE 2 DIABETES

K.S. Cheung^{1,2}, J.T. Tan¹, X. Mao^{2,1}, W.-K. Seto^{2,1}

¹The University of Hong Kong, Department of Medicine, School of Clinical Medicine, Hong Kong, Hong Kong, ²The University of Hong Kong-Shenzhen Hospital, Department of Medicine, Shenzhen, China

Contact E-Mail Address: mongolhorse2002@gmail.com

Introduction: Both acute pancreatitis and diabetes mellitus (DM) are known risk factors for pancreatic cancer (PC) development. However, whether post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is an independent risk factor for PC is under-investigated.

Aims & Methods: We aimed to investigate whether PEP was associated with a higher risk of PC after adjusting for known risk factors of PC among type 2 diabetes (T2D) patients.

All newly diagnosed T2D patients aged ≥18 years between January 1993 and December 2020 from Hong Kong's electronic healthcare database were studied. DM was identified by (i) two abnormal HbA1c ≥6.5% or fasting glucose ≥7 mmol/L test results, (ii) anti-DM medications use, or (iii) International Classification of Diseases Ninth Revision (ICD-9) code 250. Exclusion criteria included history of PC, pancreatic neuroendocrine tumor, serous cystadenoma, and chronic pancreatitis. Index date was defined as three years after T2D diagnosis in order to avoid reverse causality, as new onset diabetes (NOD) may signify underlying pre-existing PC. Primary outcome was PC development. Primary exposure of interest was PEP, which was identified by an amylase or lipase level at least three times the upper limit of normal more than 24 hours and within 7 days after ERCP.

We divided the cohort into three groups:

- (i) those who had never underwent ERCP before index date [ERCP(-)],
- (ii) history of ERCP without PEP [ERCP(+)/PEP(-)], and;
- (iii) history of PEP [ERCP(+)/PEP(+)].

The comparison of ERCP(+)/PEP(+) group with ERCP(+)/PEP(-) group serves to address indication bias (and hence higher PC risk) necessitating performance of ERCP. Covariates were age, sex, lifestyle factors, metabolic disorders, time-weighted mean HbA1c, cardiovascular diseases, other anti-DM medications, non-aspirin non-steroidal anti-inflammatory drugs, statins, and episode of history of acute pancreatitis. Multivariable Cox regression models were used to calculate adjusted hazard ratios (aHRs) of PC with exposure of interest.

	No. of patients	No. of events	Person-years*	Crude incidence rate	HR (95% CI) [†]	p-value
Whole cohort						
ERCP(-)	751,184	1,491	6,776,558	0.22	Ref	-
ERCP(+)/PEP(-)	20,990	1,024	228,958	4.47	16.8 (15.5 – 18.3)	<0.001
ERCP(+)/PEP(+)	375	12	2,521	4.76	28.0 (15.7 – 50.2)	<0.001
ERCP-cohort						
ERCP(+)/PEP(-)	20,990	1,024	228,958	4.47	Ref	-
ERCP(+)/PEP(+)	375	12	2,521	4.76	1.94 (1.08 – 3.48)	0.025

* Person 1,0000 person-years

† Adjusted for covariates mentioned above

Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; PEP, post-ERCP pancreatitis; HR, hazard ratio; Ref, reference; 95% CI, 95% confidence interval

Table 1. Association between risk of pancreatic cancer and post-ERCP pancreatitis.

Results: We identified 772,549 T2D patients (mean [SD] age:60.6 [12.4] years;50.3% male), of whom 751,184 (97.2%) was ERCP(-) group, 20,990 (2.7%) ERCP(+)/PEP(-) group, and 375 (0.05%) ERCP(+)/PEP(+) group. The mean (SD) duration of follow-up was 9.1 (+/-5.9) years, and 2,128 (0.3%) incident PC cases were recorded with an incidence rate of 3.0 per 10000 person-years. The PC crude incidence rate was 0.22, 4.47 and 4.76 per 10,000 person-years among ERCP(-), ERCP(+)/PEP(-) and ERCP(+)/PEP(+) groups, respectively. Compared with ERCP(-), ERCP(+)/PEP(-) and ERCP(+)/PEP(+) were associated with a higher risk of PC (aHR:16.8, 95%CI:15.5-18.3; aHR:28.0, 95%CI:15.7-50.2) (Table 1). Compared with ERCP(+)/PEP(-), the aHR of PC was 1.94 (95%CI:1.08-3.48) with ERCP(+)/PEP(+).

Conclusion: In a large population of T2D patients, PEP was an independent risk factor of PC development. Our study findings further consolidate the necessity of minimizing the occurrence of PEP to not just prevent short-term complications of acute pancreatitis but also PC development.

Disclosure: Nothing to disclose.

PP1170

DELAY RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN PATIENTS WITH MILD BILIARY ETIOLOGY ACUTE PANCREATITIS AND EVIDENCE OF COMMON BILE DUCT STONE NEGATIVELY INFLUENCE REFEEDING TIME, TOTAL LENGTH OF HOSPITALIZATION AND RELATED COMPLICATIONS

R. Di Pangrazio^{1,2}, M. Signoretti², M. Marasco³, G. Esposito⁴, M. Rinzivillo⁵, F. Panzuto⁵, B. Annibale²

¹Sapienza University, Sant'Andrea University Hospital, Department of Medical-Surgical Sciences and Translational Medicine, Sapienza University of Rome. Digestive Disease Unit, Sant'Andrea University Hospital, Rome (Lazio) - Italy, Rome, Italy, ²Sant'Andrea Hospital, Digestive and Liver disease, Rome, Italy, ³Sapienza, Department of Digestive Disease, Rome, Italy, ⁴Sant'Andrea Hospital, Sapienza University of Rome, Italy, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy, ⁵Sant'Andrea University Hospital, Digestive Disease Unit, Rome, Italy

Contact E-Mail Address: dipangrazioriccardo@gmail.com

Introduction: Acute pancreatitis (AP) is one of the most common gastrointestinal disorders with biliary etiology (BE) being the most common cause in Italy. Recent guidelines suggest medical therapy over an early retrograde cholangiopancreatography (ERCP) in patients with AP and evidence of biliary obstruction (BO) unless acute cholangitis (AC). Although in AP the refeeding shall be offered as soon as clinically tolerated, in clinical practice in patients with BO, it is usually postponed after ERCP. This study aims to evaluate whether delayed ERCP influences early refeeding, total length of hospital stay and hospitalization-related complications in patients with BE-AP and BO.

Aims & Methods: Single center retrospective study including patients with AP admitted to our unit from January 2020 to March 2024. Refeeding was evaluated as oral refeeding in mild AP and oral or enteral refeeding via enteral-feeding tube in moderate to severe AP.

Results: Overall, 109 patients were included: with a median age of 68 (19-98), 57% men. Biliary etiology in 57%, 12% alcoholic, 3% idiopathic and 28% other causes. Regarding the severity of AP, 60% of patients had mild, 28% moderate, and 12% severe pancreatitis. Mild AP had a median length of stay of 5 days (1-22), moderate/severe AP, 14 days (3-32). Patients with BE AP had a similar median length of hospital stay compared to those with non-biliary etiology (NBE), 7 days (BE 2-27) vs 6 days (NBE 1-32). Overall, 21% of patients with BE-AP without cholangitis had BO on radiological examinations and were scheduled for a not urgent ERCP. BE patients with mild AP and BO had a statistically significant difference in terms of median

length of hospital stay (10 days, 3-22), and median fasting days (7 days, 4-18) compared to those without BO [5 days (2-15) and 3 days (1-14), respectively] ($p<0.05$). The median time from admission to ERCP was 7 days (4-17). Furthermore, the percentage of hospitalization-related complications (vascular, renal, pulmonary, and infective) was, as expected, directly proportional to the length of hospital stay.

Conclusion: In a real-world setting, delayed refeeding was observed in patients with mild BE-AP and evidence of BO with no indication to an early ERCP. This probably reflect the concerns of clinicians regarding clinical and biochemical worsening after refeeding in presence of BO. ERCP and refeeding delay also negatively influence the length of hospitalization and related complications.

References:

Marianna Arvanitakis, Johann Ockenga, Mihailo Bezmarevic, Luca Gianotti, Željko Krznarić, Dileep N. Lobo, Christian Löser, Christian Madl, Remy Meier, Mary Phillips, Henrik Højgaard Rasmussen, Jeanin E. Van Hooft, Stephan C. Bischoff. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. *Clinical Nutrition* 2020 Mar;39(3):612-631

Scott Tenner, MD, MPH, JD, FACP, Santhi Swaroop Vege, MD, MACG, Sunil G. Sheth, MD, Bryan Sauer, MD, MSc, FACP, Allison Yang, MD, MPH, Darwin L. Conwell, MD, MSc, FACP, Rena H. Yadlapati, MD, MHS, FACP and Timothy B. Gardner, MD, FACP. American College of Gastroenterology Guidelines: Management of Acute Pancreatitis. *Am J Gastroenterol* 2024;119:419-437

Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology* 2013 Jul-Aug;13(4 Suppl 2):e1-15

Disclosure: Nothing to disclose.

PP1171

COMPARATIVE DIAGNOSTIC PERFORMANCE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) VERSUS ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY (EUS-FNB) FOR TISSUE SAMPLING OF SOLID PANCREATIC AND NON-PANCREATIC LESIONS WITHOUT ROSE: A PROSPECTIVE MULTICENTER STUDY

A. Alzamzamy¹, H. Okasha², A. El-Habashi³, A. Abdel-Latif²

¹Military Medical Academy, Department of Gastroenterology and Hepatology, Cairo, Egypt, ²Kasr Al-Aini School of Medicine, Cairo University, Internal Medicine Department, Division of Gastroenterology and Hepatology, Cairo, Egypt, ³National Cancer Institute, Cairo University, Department of Pathology, Cairo, Egypt

Contact E-Mail Address: dr_zamzamy@hotmail.com

Introduction: Endoscopic ultrasound-guided tissue acquisition, including both fine needle aspiration (EUS-FNA) and fine needle biopsy (EUS-FNB), has been widely performed to obtain samples from pancreatic and non-pancreatic lesions.^{1,2} The impact of the diagnostic yield between FNA and FNB remains unclear.

Aims & Methods: We conducted this study to compare the diagnostic performance and accuracy of the 22-gauge FNA needles with the 22-gauge FNB needles in sampling solid pancreatic and non-pancreatic lesions. This is a prospective multicenter study conducted on 465 cases presented with solid pancreatic or non-pancreatic lesions.

Results: Patients were 275 male and 190 females with a mean age of 59 years. Three hundred twenty-seven patients had solid pancreatic lesions, while 138 had non-pancreatic lesions; 245 cases underwent EUS-FNA, and the remaining 211 cases underwent EUS-FNB. The presence of intact tissue core and sample adequacy were significantly higher in the FNB cases in solid pancreatic and non-pancreatic lesions. Blood contamination was significantly more in cell blocks and smears of EUS-FNA compared to that of EUS-FNB in solid pancreatic and non-pancreatic lesions. Based

on histologic assessment of cell block only, EUS-FNB had more diagnostic accuracy (99%) than FNA (61%) (P -value <0.005). However, cytological diagnosis by smears only showed no significant difference. The combined cytological and histological evaluation had 100% sensitivity, specificity, and accuracy.

Conclusion: EUS-FNA and EUS-FNB have comparable accuracy in diagnosing solid pancreatic and non-pancreatic lesions without ROSE. EUS-FNB is superior to EUS-FNA in acquiring intact tissue core and adequate samples with little blood contamination. Based on histological assessment (cell block/tissue core) only, EUS-FNA has less accuracy than EUS-FNB in diagnosing solid pancreatic lesions.

References:

1. Wani S, Muthusamy VR, McGrath CM, et al. AGA white paper: optimizing endoscopic ultrasound-guided tissue acquisition and future directions. *Clin Gastroenterol Hepatol* 2018; 16: 318-27.
2. Wong T, Pattarapuntakul T, Netinatsunton N, et al. Diagnostic performance of endoscopic ultrasound-guided tissue acquisition by EUS-FNA versus EUS-FNB for solid pancreatic mass without ROSE: a retrospective study. *World J Surg Oncol*. 2022; 20(1): 215. doi:10.1186/s12957-022-02682-3.

Disclosure: Nothing to disclose.

PP1172

DIAGNOSIS OF PANCREATIC SOLID LESIONS BY ULTRASOUND ENDOSCOPY (EUS) FINE-NEEDLE BIOPSY WITH FRANSEEN NEEDLES: MACROSCOPIC ON-SITE (MOSE) VERSUS RAPID ON-SITE (ROSE) EVALUATION. IS THE PATHOLOGIST NECESSARY IN THE ENDOSCOPY SUITE?

E. Pijoan Comas¹, D. Vázquez Gómez², N. Zaragoza Velasco³, A.L. Vargas García¹, M.A. Albuquerque Miranda⁴, N. Torres Monclús², M. Figa⁵, R. Ballester Clau², M. Planella de Rubinat², F. González-Huix Lladó⁶

¹Clínica Girona - Hospital de Palamós, Gastroenterology, Girona - Palamós, Spain, ²Hospital Universitari Arnau de Vilanova, Gastroenterology, Lleida, Spain, ³Hospital Universitari Arnau de Vilanova, Gastroenterology and Hepatology, Lleida, Spain, ⁴Hospital de Palamós - Clínica Girona, Gastroenterology, Girona - Palamós, Spain, ⁵Clínica Girona, Gastroenterology, Girona, Spain, ⁶Clínica Girona - Hospital Universitari Arnau de Vilanova, Girona - Lleida, Spain

Contact E-Mail Address: evapijoancomas@gmail.com

Introduction: Biopsy samples obtained with fine-needle biopsy (FNB-EUS) using Franseen needles by EUS with endoscopist evaluation (Macroscopic OnSite Evaluation: MOSE) improves the diagnostic accuracy of pancreatic solid lesions. The achievement of macroscopic visible core (MVC) >4mm has a high diagnostic accuracy with MOSE.

Aims & Methods: Aim: To compare diagnostic accuracy of Rapid On-Site Evaluation (ROSE) and MOSE by endoscopist in pancreatic solid lesions. Methods: Prospective bicentric study, consecutive recruitment of patients with pancreatic solid lesions in 2 general hospitals (MOSE was performed in hospital A and ROSE in hospital B). Franseen needles were used (Adquire, Boston Scientific). We evaluated: 1) diagnostic achievement and accuracy (including sensitivity, specificity, positive predictive value and negative predictive value) in solid pancreatic lesions; 2) MVC >4mm acquisition; and 3) number of needle passes needed with MOSE vs ROSE.

Results: A total of 132 patients were included (33 women, 68 men, median age 68,2±1,025). MOSE was performed in 90 (68.2%) and ROSE in 42 (31.8%); in 110 (83.3%) malign and 22 (16.7%) benign pancreatic solid lesions. Correct diagnosis by EUS-FNB was achieved in 89.4% patients (with

MOSE 88.8%; and ROSE 92.9%; $p=0.54$). Sensitivity was 100%, specificity 89%, PPV 81.3% and NPV 100% (with MOSE: sensitivity 100%, specificity 87.5%, PPV 88.8% and NPV 100%; with ROSE: sensitivity 100%, specificity 92.1%, PPV 92.6% and NPV 100%). MVC >4mm was obtained in 72.7% (71.1% in MOSE, 76.2% in ROSE, $p=0.67$). There were no statistically significant differences in diagnosis achievement between MVC >4mm and <4mm (88.6% in MOSE and 90.6% in ROSE, $p=0.74$). No differences in number of passes necessary to achieve diagnosis was found between MOSE and ROSE.

Conclusion: Evaluation of biopsy samples of pancreatic solid lesions obtained by FNB-EUS with Franseen needles by endoscopist (MOSE) has a diagnostic accuracy similar to ROSE, making unnecessary the presence of a pathologist in the endoscopy suite.

Disclosure: Nothing to disclose.

PP1173

EUS-GUIDED PANCREATIC DUCT DRAINAGE: ENDOSCOPIC AND CLINICAL PRACTICE EXPERIENCE

M. Marasco¹, S. Godat², B. Annibale¹, F. Panzuto¹, D. Galasso³

¹Digestive Disease Unit, Sant'Andrea University Hospital, Department of Medical Surgical Sciences and Translational Medicine, Sapienza University, Rome, Italy, ²Service de gastroentérologie et d'hépatologie, CHUV, Université de Lausanne, Lausanne, Switzerland, ³Gastroenterology Unit, Hopital Riviera Chablais Gastroenterologie, Rennaz (Vaud), Switzerland

Contact E-Mail Address: matteomarasco93@gmail.com

Introduction: EUS-guided pancreatic duct drainage (EUS-PDD) is an endoscopic procedure which is indicated in symptomatic patients with evidence of pancreatic duct obstruction after failure or impossibility to perform transpapillary drainage or EWSL in the context of chronic pancreatitis or altered anatomy causes (e.g. Whipple or Roux-en-Y surgery). Nowadays, it is a challenging procedure performed by few endoscopist. Clinical and technical success rate is still lacking and heterogenous, therefore acquisition of new data and experience is necessary.

Aims & Methods: This study aims to describe our initial endoscopic experience evaluating also some clinical aspects. This is a retrospective observational single-center study including patients (pts) undergone EUS-PDD from March 2018 to July 2023 using plastic stent (7Fr 10cm), delivered with an electrocautery-enhanced catheter, after failure or impossibility to transpapillary drainage. It was evaluated exocrine pancreatic function by fecal elastase (FE-1) and nutritional markers (prealbumin and magnesium).

Results: Total of 15 pts with median age of 72 years old. 13 pts (86.6%) had a chronic pancreatitis diagnosis with radiological evidence duct pancreatic alterations (5 stenosis, 3 lithiasis, 4 both, 1 duct rupture); 2 pts had a post-surgical stenosis. All pts were symptomatic: 6 pts (40%) shows multiple episodes of acute pancreatitis and 9 (60%) had abdominal pain non responder to medical therapy. Pancreatic duct had median dilatation of 7 mm (4-15.6 mm). Every transmural access was performed through gastric wall with single plastic stent (7Fr 10cm) placement. Technical success was obtained in 11 pts (73%) of which 2 pts had early stent migration; in 4 pts (26.6%) EUS-PDD failed. No other adverse events. 13 (86.6%) had a condition of pancreatic exocrine insufficiency: FE-1 between 200 µg/g and 100 µg/g in 8 pts and FE-1 < 100 µg/g in 5 pts under pancreatic enzyme replacement therapy. Magnesium median value was 0.74 mmol/L (0.5-0.8 mmol/L) and prealbumin median value was 0.22 g/L (0.11-0.26 g/L), both at the low normal serum level. After 4 weeks, it was placed a second plastic stent in 8 pts and during clinical follow-up (3 and 6 months), pts had no pain and described improvement of general quality of life and nutritional markers.

Conclusion: EUS-guided pancreatic duct drainage remains a challenging endoscopic procedure indicated only for selected cases and performed by expert endoscopists. However, it seems to have a reasonable clinical success rate but we need further data to improve endoscopic experience and clinical awareness.

References: 1. Chandan S et al. Efficacy and safety of endoscopic ultrasound-guided pancreatic duct drainage (EUS-PDD): A systematic review and meta-analysis of 714 patients. *Endosc Int Open*. 2020 Nov;8(11):E1664-E1672.

2. Teh JL et al. Techniques and Outcomes of Endoscopic Ultrasound Guided-Pancreatic Duct Drainage (EUS-PDD). *J Clin Med*. 2023 Feb 17;12(4):1626.

Disclosure: Nothing to disclose.

PP1174

ABSOLUTE BETTER THAN PERCENTAGE

R. Yarlagadda¹

¹Citizens Hospitals(AOI), Department Of Digestive Disease Sciences, Hyderabad, India

Contact E-Mail Address: raghuyar@gmail.com

Introduction: For symptomatic walled off necrosis(WON) drainage, initial assessment of WON is done by percentage of debris and accordingly LAMS, irrigation and necrosectomy(DEN) are performed. This percentage assessment may go wrong once the fluid is drained off. Percentage of debris may not adequately represent the necrosectomy sessions or time. More necrosectomy procedures, require longer endoscopy time, multiple accessories, intravenous sedation and higher costs.

Aims & Methods: This study is aimed at finding the relation between debris amount and necrosectomy sessions. Consecutive symptomatic WON patients who underwent drainage and necrosectomy are enrolled for this study. Collections without definite wall or irregular shaped collections, trans duodenal drainages are excluded. Percentage of debris in WON is assessed. Solid component of collection is measured directly (length, width, sector, segment). Volume of debris is calculated using mathematical calculations for ellipsoid segment calculations. Every patient underwent CT abdomen 24-48hrs after drainage to assess stent position, any complications and amount of resolution of collection. In difficult to define cases by EUS, CT done after WON drainage is used for calculating the amount of debris.

Results: Five patients of symptomatic WON who underwent drainage and necrosectomy are included in this study. Three male and two female. Average debris percent is 28 % highest being 50 %. Necrosectomy is done in all cases following the step up approach. Mean volume of debris is 182.2 cm³. Mean number of necrosectomy sessions are 2.5. On an average, 50-80cc of debris is removed per hour. More amount of debris requires more number of hours of necrosectomy or more sessions of necrosectomy as depicted in the table 1.

Serial no	Etiology	Debris %	Size of collection (cm)	Necrosectomy sessions	Volume of debris
1	Biliary	30%	15.2 x 8 x 4.6	3	232
2	Biliary	30%	8 x 6.2 x 5.1	2	183
3	Alcoholic	20%	6.3 x 4.2 x 3.7	2	178
4	Idiopathic	50%	10.5 x 7.3 x 4	3	220
5	Hypertriglyceridemia	10%	12 x 7 x 3.5	1	98

Conclusion: In the presence of fluid, debris in WON may be under or over-estimated if assessed by percentage. Absolute volume of debris is a better measure to quantify than percentage for deciding and planning on necrosectomy. More volume of debris requires more duration or number of necrosectomy sessions.

References:

1. Kumar N, Conwell DL, Thompson CC. Direct Endoscopic Necrosectomy Versus Step-Up Approach for Walled-Off Pancreatic Necrosis: Comparison of Clinical Outcome and Health Care Utilization. *Pancreas*. 2014 Aug 11
 2. Seicean A, Pojoga C, Mostean O, Bolboaca S, Ilie M, Rimbas M, Gheorghiu M, Lucaciu L, Bartos A, Al Hajjar N, Sandru V, Constantinescu G, Seicean R. What is the Impact of the Proportion of Solid Necrotic Content on the Number of Necrosectomies during EUS-Guided Drainage using Lumen-Apposing Metallic Stents of Pancreatic Walled-off Necrosis ?. *JGLD [Internet]*. 12Dec.2020
 3. Rana S, Bhasin D, Kathiresan J et al. Do the morphological features of walled off pancreatic necrosis on endoscopic ultrasound determine the outcome of endoscopic transmural drainage? *Endosc Ultrasound* 2014; 3: 118
 4. Pal P, Lakhtakia S, Jagtap N et al. Interobserver Agreement on "assessment of debris" during endoscopic ultrasound-guided drainage of walled-off pancreatic necrosis. *Tech Innov Gastrointest Endosc* 2023; 25: 213–220
- Disclosure:** Nothing to disclose.

PP1175

DIAGNOSTIC VALUE OF EE-FNB IN PATIENTS AT RISK OF PANCREATIC CANCER WITHOUT OBSTRUCTIVE JAUNDICE IN FAMILIES WITH BREAST CANCER AND WITH FOCAL LESION ON COMPUTERIZED TOMOGRAPHY/MAGNETIC RESONANCE

D.E. Coelho Neto^{1,2}, G. Issa Ernesto Coelho^{3,4},
M. Issa Ernesto Coelho^{3,4}, M. Vilhena Alves dos Santos^{3,4},
 J. Campos Machado^{3,4}, S. Pinheiro Machado de Carvalho^{3,4},
 T. Peres Piva^{3,4}, J.F. Ernesto Coelho⁵, J.C. Ardengh⁶
¹Head of Gastrointestinal and Endoscopy Service Hospital Vitória and Samaritano Barra and Pró-Cardiaco o, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ²Estácio de Sá University, Surgery and Intervencional Endoscopy, Rio de Janeiro, Brazil, ³Souza Marques Medical School, Rio de Janeiro, Brazil, ⁴LAED - Digestive Endoscopy Academic League, Rio de Janeiro, Brazil, ⁵Federal University of Rio de Janeiro Medical School, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ⁶Ribeirão Preto Medical School. (University of São Paulo), Surgery and Anatomy, Ribeirão Preto, Brazil

Contact E-Mail Address: marianaissa0501@gmail.com

Introduction: An increased risk of pancreatic cancer has been reported in families with breast cancer history carrying BRCA1 and BRCA2 mutations. Pancreatic cancer is associated with familial and hereditary cancer syndromes. Multigene panel testing for pancreatic cancer detected germline variants BRCA1/2, PALB2, ATM, TP53, MLH1, STK11/LKB1, APC, CDKN2A, and SPINK1/PRSS1 as high-risk genes. Active pancreatic surveillance using computed tomography (CT), magnetic resonance imaging (MRI), and echoendoscopic (EE) are recommended for high-risk individuals who have a family history of pancreatic cancer or harbor these pathogenic germline variants to improve the detection rate and the prognosis of pancreatic cancer. We evaluated the performance characteristics of echoendoscopically guided fine needle biopsy (EE-FNB) in this subset of patients.

Aims & Methods: This is a retrospective analysis of a prospective database total of 99 families with ≥1 case of breast cancer tested for mutations in BRCA1 and/or BRCA2. The eligible patients were the ones that underwent EE-FNB at a tertiary hospital with an Oncology center due a focal pancreatic lesion observed on CT/MRI, from January 2022 to January 2024. Patients were excluded if (1) they had obstructive jaundice or (2) the lesion appeared cystic on CT/MRI. The main outcome measures were (1) prevalence of the association between BRCA 2 positive and pancreatic cancer (2) performance characteristics of EE-FNB for identification of malignancy.

Results: In the 99 patients in the study, a focal pancreatic lesion was identified with pancreatic adenocarcinoma by EE-FNB. The final diagnosis included 20 patients with breast cancer and BRCA2 positive undergoing oncological treatment or follow-up, with a mean age of 32.8 +/- 2.2 years. EE was performed in an average of 19 +/- 11.3 days. EE-FNB showed an accuracy of 100% for the diagnosis of malignant neoplasia, with a sensitivity of 100%, specificity of 100%.

Conclusion: EE-FNB diagnostic yield was substantial in established high-risk mutation carriers, is highly accurate in patients with focal pancreatic lesion on CT/MRI, without obstructive jaundice. EE-FNB can potentially be used as a definitive diagnostic test in the management of these patients.

Disclosure: Nothing to disclose.

PP1176

EUS-GUIDED LUMEN APPOSING METAL STENTS (LAMS) WITH AND WITHOUT ELECTRO-CAUTERY FOR DRAINAGE OF WALLED-OFF PANCREATIC NECROSIS

N.L-H. Bekkali¹, E. Selvaraj¹, C.F Dietrich², B. Braden^{1,3}

¹Oxford University Hospitals NHS Foundation Trust, Translational Gastroenterology Unit, Oxford, United Kingdom, ²Hirslanden Beau Site, Allgemeine Innere Medizin der Kliniken, Bern, Switzerland, ³University of Münster, Medical Department, Münster, Germany

Contact E-Mail Address: braden@em.uni-frankfurt.de

Introduction: EUS-guided drainage using lumen-apposing metal stents (LAMS) has become standard treatment of symptomatic walled-off necrosis (WON). The development of these fully covered self-expanding metal stents with special design of the flanges and large diameter, improved the drainage of debris and facilitated further direct endoscopic necrosectomy. Delivery systems with integrated electro-cautery (EC) enable direct access and stent deployment whilst the conventional stent insertion technique requires several steps including access using a needle or cystotome, wire insertion and enlargement of the created tract before the stent placement.

Aims & Methods: In this single center study, we aimed to compare the practicality of EUS-guided procedures and their outcome between conventional LAMS (cLAMS) and those with integrated EC (LAMS-EC).

From our prospectively maintained database, we included consecutive patients undergoing EUS-guided LAMS insertion with or without integrated electro-cautery for drainage of walled-off necrosis. Infection of the walled-off pancreatic necrosis, biliary compression with cholestasis or gastric outlet obstruction were accepted indications for intervention. Data on procedure time, sedation, hospital stay, technical and clinical success as well as adverse events were analysed.

Results: We analysed 107 consecutive procedures of transmural EUS-stenting for drainage of walled-off necrosis. 39 cLAMS and 68 LAMS-EC were placed successfully. Mean size of the walled-off necrosis was 12.9 ± 4.2 cm with mean 30% ± 15% solid necrosis.

Procedure times were shorter with LAMS-EC (18.0 ± 6.6 min vs. 39.7 ± 8.3 min; p<0.05). All EUS-guided procedures with cLAMS drainage were performed under propofol sedation administered by an anaesthetic team. In the LAMS-EC group, 36 patients tolerated the procedure under iv sedation (fentanyl/midazolam) in left lateral position and 17 interventions were performed as daycase procedures. None of the patients developed sedation related adverse events such as aspiration.

Adverse events, technical success and clinical outcome did not differ between both groups.

Conclusion: The findings of this study suggest that cLAMS and EC-LAMS achieve similar rates of technical and clinical success without difference in the rate of adverse events. Compared to cLAMS, deployment of EC-LAMS

is faster and technically less demanding. This might allow to perform the procedure under conventional intravenous sedation and as daycase procedure in carefully selected patients.

Disclosure: Nothing to disclose.

PP1177

FACTORS AFFECTING THE DIAGNOSTIC ACCURACY OF EUS-FNA/B FOR PANCREATIC AND PERIPANCREATIC LESIONS: A TWO-CENTER EXPERIENCE

M. Fragaki¹, A. Stamou², D.-E. Arna¹, E. Koukouliti², T. Voulgaris³, A. Anagnostou³, K. Triantafyllou², A. Vezakis³, G.A. Paspatis¹, I.S Papanikolaou²

¹Venizeleion General Hospital, Department of Gastroenterology, Heraklion, Greece, ²Attikon University Hospital, Hepatogastroenterology Unit, Athens, Greece, ³Aretaieion Hospital, Department of Surgery, Athens, Greece

Contact E-Mail Address: ispapn@hotmail.com

Introduction: EUS-FNA and EUS-FNB have become the standard of care for the diagnosis of pancreatic and peripancreatic tumors, and several factors are associated with its diagnostic accuracy. The aim of this study is to evaluate factors that are associated with the diagnostic accuracy of EUS-FNA/B in two referral centers

Aims & Methods: Data from patients with pancreatic and peripancreatic lesions who underwent EUS-FNA/B from 2017 to 2023 were collected retrospectively. The associations between mass location, mass size, needle type, number of needle passes, the presence of a biliary stent and the cytology result were analyzed.

Results: A total of 438 patients underwent 440 EUS-FNA/B procedures. The overall accuracy of EUS-FNA/B was 90,6% (398/440). Mass location on the head of the pancreas was associated with a higher diagnostic accuracy ($p<0.05$). Two or more needle passes were statistically significantly correlated with higher diagnostic accuracy ($p<0.05$) compared to single-pass EUS-FNA/B. Mass size, needle type and presence of a biliary stent did not reach statistical significance for the diagnostic yield of the cytology. A subgroup of 109 patients (24,7%) had lesions in the corpus or the tail of the pancreas. In this subgroup, tumor size greater than 3 cm was statistically significant correlated with a diagnostic cytology result ($p<0.05$).

Conclusion: The results of this study suggest that 2 or more needle passes and lesions in the head of the pancreas are associated with higher diagnostic accuracy of EUS-FNA/B in two referral centers.

References: Johnson G et al. Curriculum for ERCP and endoscopic ultrasound training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy 2021; 53: 1071–1087

Disclosure: Nothing to disclose.

PP1178

COMPARISON OF DIAGNOSTIC PERFORMANCE OF EUS-FNA GUIDED TISSUE ACQUISITION VERSUS EUS-FNB FOR SOLID PANCREATIC MASS WITHOUT ROSE: RETROSPECTIVE STUDY

D.E. Coelho Neto^{1,2}, A.C. de Oliveira Campos^{3,4}, B. Carvalho do Vale^{3,4}, F. Villas Bôas Legentil^{3,4}, G. Campos Machado^{3,4}, G. Lyons^{3,4}, S.P.M.d.C. Sofia Pinheiro Machado de Carvalho^{3,4}, I. Peres Piva^{3,4}, J.F. Ernesto Coelho⁵, J.C. Ardengh⁶, G. Issa Ernesto Coelho^{3,4}, M. Issa Ernesto Coelho^{3,4}

¹Estácio de Sá University, Surgery and Intervencional Endoscopy, Rio de Janeiro, Brazil, ²Head of Gastrointestinal and Endoscopy Service Hospital Vitória and Samaritano Barra and Pró-Cardiaco o, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ³Souza Marques Medical School, Rio de Janeiro, Brazil, ⁴LAED - Digestive Endoscopy Academic League, Rio de Janeiro, Brazil, ⁵Federal University of Rio de Janeiro Medical School, Gastrointestinal and Endoscopy, Rio de Janeiro, Brazil, ⁶Ribeirão Preto Medical School. (University of São Paulo), Surgery and Anatomy., Ribeirão Preto, Brazil

Contact E-Mail Address: thais.pivasm@gmail.com

Introduction: Endoscopic ultrasound-guided (EUS) tissue acquisition is an established diagnostic procedure for solid pancreatic mass. However, the diagnostic yield between fine needle aspiration (FNA) and fine needle biopsy (FNB) remains unclear. The aim of the study was to evaluate and compare the diagnostic yields between FNA and FNB using puncture by conventional needle aspiration (PAA) and Franseen-tip needles of the same size, 22G, in patients retrospectively. All procedures were performed without a cytologist on site. The diagnostic yield and average number of needle passes between FNB and FNA were then compared.

Aims & Methods: All cases of EUS-PAA by FNA or FNB for solid pancreatic mass between January 2017 and October 2020 in a tertiary care hospital were retrospectively reviewed. All procedures were performed without a cytologist on site. The diagnostic yield and the average number of needle passes between FNB and FNA were then compared.

Results: 91 patients (FNA n = 45; BNF, n = 46) with solid pancreatic mass detected by cross-sectional imaging underwent EUS-PAA. The average age was 62.3 ± 12.8 years, 55 (60.4%) were female. Age, sex, mass location, tumor size, and disease stage on imaging studies were not significantly different between the two groups. Diagnostic yield was higher in EUS-FNB (96%) than in EUS-FNA (91%). The average number of needle passes was clearly lower in FNB than in FNA (2.8 vs. 3.8, $p<0.001$). The total procedure time was shorter in BNF (24 min) than in FNAC (31 min). The rate of adverse events between FNB and FNA was not significantly different.

Conclusion: The diagnostic yield of solid pancreatic mass was higher in FNB with a Franseen-tip needle than in FNA with a conventional needle in a center where ROSE is not available, without serious adverse events. Additionally, FNB had fewer needle passes and a shorter total procedure time.

Disclosure: Nothing to disclose.

PP1179

THE FINAL RESULTS OF PANCREATIC FIBROSIS NON-INVASIVE ASSESSMENT BY MULTIDETECTOR COMPUTED TOMOGRAPHY

I. Khatkov^{1,2}, K. Lesko¹, D. Bordin^{1,2,3}, E. Dubtsova¹, N. Karnaukhov¹, N. Makarenko¹, I. Savina¹, M. Kiriukova¹, D. Salimgereeva¹, L. Vinokurova¹

¹The AS Loginov Moscow Clinical Scientific Center of the Moscow Health Department, Moscow, Russian Federation,

²A.I. Yevdokimov Moscow State University of Medicine and Dentistry of the Ministry of Healthcare of the Russian Federation, Moscow, Russian Federation, ³Tver State Medical University, Tver, Russian Federation

Contact E-Mail Address: k_lesko@mail.ru

Introduction: Pancreatic fibrosis is a part of the pathogenesis in most pancreatic disorders and plays a crucial role in chronic pancreatitis development. Therefore, pancreatic fibrosis early diagnosis gives an invaluable opportunity to be a part of the strategy for preventing disease progression. Thus, it makes non-invasive pancreatic fibrosis evaluation techniques research perspective.

Aims & Methods: Aim was to clarify relationships between pancreatic fibrosis grade and results of multidetector computed tomography (MDCT) post-processing parameters. Methods. Results of contrast-enhanced 128-row MDCT from 148 patients (mean age 57.4±13.8) who underwent surgery from April 2022 to October 2023 due to pancreatic tumors and advanced chronic pancreatitis were analyzed.

We calculated contrast enhancement ratio (CER) between venous phase and non-contrast MDCT, and normalized CER (NCER) during the pancreatic phase and venous phase, also we measured pancreas density during MDCT examination. Pancreatic fibrosis morphological grade was assessed according to Klöppel & Maillet's scoring system [1] and scaled into three grades: mild, moderate and severe pancreatic fibrosis.

Results: We received a significant ($p=0.007$) growth of CER in patients with severe pancreatic fibrosis (mean CER=1.12±0.6) compared with CER in patients with mild pancreatic fibrosis (mean CER=0.79±0.3). Unenhanced pancreas density (UPD) value was significantly ($p=0.001$) lower in patients with severe pancreatic fibrosis (31.5±11.8 HU) than in patients with mild pancreatic fibrosis (39.8±8.5 HU). Mean CER and UPD value were significantly ($p=0.001$) different in patients with morphological signs of inflammation (1.13±0.7 and 33.5±11.4, respectively), than in patients without these signs (0.79±0.3 and 39.1±8.7, respectively). CER and UPD value showed a statistically significant correlation with morphologically inflammation signs presence (Spearman's rho 0.28 and -0.28, $p=0.001$, respectively) and pancreatic fibrosis grade (Spearman's rho 0.26, $p=0.001$ and -0.32, $p=0.0001$).

There were no significant influences of pancreatic fibrosis on NCER values in pancreatic phase and venous phase, which we had shown in publications of our preliminary results [2]. We suppose the main reason of this fact is study groups enlargement as well as measurement technique improvement, led to results clarification.

Conclusion: MDCT pancreatic tissue enhancement indicator, as CER, significantly increased in patients with severe pancreatic fibrosis as well as in those who had morphological signs of inflammation. UPD value can also provide additional information due to its decrease as pancreatic fibrosis progresses. Consequently, it could be useful for noninvasive pancreatic fibrosis diagnosis and prognosis.

References:

1. Esposito I, Hruban RH, Verbeke C, et al. Guidelines on the histopathology of chronic pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the

American Pancreatic Association, the Japan Pancreas Society, and the European Pancreatic Club. *Pancreatology*. 2020;20(4):586-593. doi:10.1016/j.pan.2020.04.009

2. Khatkov IE, Bordin DS, Lesko KA, et al. Contrast-Enhanced Computed Tomography and Laboratory Parameters as Non-Invasive Diagnostic Markers of Pancreatic Fibrosis. *Diagnostics*. 2023; 13(14):2435. https://doi.org/10.3390/diagnostics13142435

Disclosure: This study was conducted within the healthcare research project "Assessment of pancreatic fibrosis as a prognostic factor for its diseases course" funded by Autonomous non-profit organization "Moscow Center for Innovative Technologies in Healthcare" administered by the Moscow Healthcare Department.

PP1180

MINIMAL-INVASIVE METHODS CONTROL PAIN WITH FEWER SIDE EFFECTS COMPARED TO OPIOID TREATMENT IN PATIENTS WITH UNRESECTABLE PANCREATIC CANCER – SYSTEMATIC REVIEW AND META-ANALYSIS

L.I. Rezus^{1,2,3,4}, I. Creanga-Murariu^{1,5,4,6}, A. Rancz¹, O.C. Ibude^{1,7}, M. Obeidat¹, R. Papp^{1,8,9}, D.S. Veres¹, B.-I. Tamba^{1,5,4}, P. Hegyi^{1,10,11,12}, B. Teutsch^{1,13,14}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Radiology, Iasi, Romania, ³"Sf. Spiridon" Emergency County Hospital, Radiology, Iasi, Romania, ⁴Advanced Research and Development Center for Experimental Medicine, Iasi, Romania, ⁵"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Pharmacology, Iasi, Romania, ⁶Regional Oncological Institute Iasi, Medical oncology, Iasi, Romania, ⁷Semmelweis University, Faculty of Medicine, Budapest, Hungary, ⁸Semmelweis University, Department of Pharmacology and Pharmacotherapy Medical Faculty, Semmelweis University, Budapest, Hungary, Budapest, Hungary, ⁹Semmelweis University, Department of Aviation and Space Medicine, Budapest, Hungary, ¹⁰Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary, ¹¹University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ¹²Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research Development and Innovation, University of Szeged, Szeged, Hungary, ¹³Medical Imaging Centre, Semmelweis University, Budapest, Hungary, ¹⁴Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, Pécs, Hungary

Contact E-Mail Address: rezusioanairina@gmail.com

Introduction: Pancreatic cancer (PC) is the fourth-leading cause of cancer-related death, with over 80% of patients having unresectable disease upon diagnosis. Despite opioid treatment, more than 70% of this population is experiencing chronic pain during the disease, along with a plethora of side effects. In the past decades, interventional radiological procedures have gained a significant role in pain management.

Aims & Methods: Our study aims to identify the most effective approach for managing pain in individuals with unresectable pancreatic cancer. We registered the study on PROSPERO (CRD42023477094) and systematically searched five major scientific databases on the 29th of October, 2023. Only randomised controlled trials (RCTs) reporting on adult patients diagnosed with unresectable PC and cancer-related pain undergoing medical or interventional treatment were considered eligible. The main intervention groups were endoscopic ultrasound-guided celiac plexus neurolysis (EUS-CPN), percutaneous celiac plexus neurolysis (P-CPN), high-intensity focused ultrasound (HIFU), and pharmacological therapy (opioids). Our

outcomes of interest were pain, survival, and adverse events. Pooled means and proportions were calculated with 95% confidence intervals (CIs), and a random-effects model was applied.

Results: After title-abstract and full-text article selection, 1644 patients of 21 RCTs were found eligible. The pain was assessed using the 11-point Visual Analogue Scale from randomisation at 4, 8 and 12 weeks to determine its dynamic over time. Pain values at baseline were 6.09 (CI: 4.24-7.94) for EUS-CPN, 6.67 (CI: 5.20-8.14) for P-CPN, 6.57 (CI: 4.98-8.15) for HIFU, and 6.47 (CI: 5.02-7.93) for opioids. At one month, the overall pain score was 1.53 (CI: 0.23- 2.82) for EUS-CPN, 2.21 (CI: 1.43-2.91) for P-CPN and 2.68 (CI: 1.94-3.42) for opioids. At two and three months after randomisation, there was a slow but continuous increase in pain scores for all treatment groups. The median survival time in days was 126.22 (CI: 87.21-165.31) for pharmacological treatment and 86.71 (CI: 62.45-136.88) for P-CPN. Patients receiving only opioids developed more adverse events compared to P-CPN, the most common being nausea, vomiting, and constipation. EUS-CPN had the lowest rate of adverse events.

Conclusion: Our study shows that minimal-invasive pain treatments provide pain control with fewer adverse events associated, with EUS-CPN having the most promising results. However, further RCTs with higher sample sizes are needed to confirm our findings.

References:

1. Wong et al., Effect of Neurolytic Celiac Plexus Block on Pain Relief, Quality of Life, and Survival in Patients with Unresectable Pancreatic Cancer - A Randomized Controlled Trial JAMA. 2004; 291:1092-1099
2. Dong et al., Neurolytic Splanchnic Nerve Block and Pain Relief, Survival, and Quality of Life in Unresectable Pancreatic Cancer: A Randomized Controlled Trial, Anesthesiology 2021; 135:686-98
3. Gao et al., A randomized clinical trial of nerve block to manage end-stage pancreatic cancerous pain, Tumor Biol. (2014) 35:2297-2301
4. Kanno et al., Efficacy of EUS-guided celiac plexus neurolysis compared with medication alone for unresectable pancreatic cancer in the oxycodone/fentanyl era: a prospective randomized control study, Gastrointest Endosc 2020;92:120-30
5. Zhang et al., Effect of Neurolytic Celiac Plexus Block Guided by Computerized Tomography on Pancreatic Cancer Pain, Dig Dis Sci (2008) 53:856-860
6. Lv et al., High-intensity focused ultrasound therapy in combination with gemcitabine for unresectable pancreatic carcinoma, Therapeutics and Clinical Risk Management 2016;12 687-691
7. Li et al., Retrospective analysis of high intensity focused ultrasound combined with S-1 in the treatment of metastatic pancreatic cancer after failure of gemcitabine, Am J Cancer Res 2016;6(1):84-90

Disclosure: Nothing to disclose.

PP1181

EFFICACY AND SAFETY OF EUS-GUIDED DRAINAGE IN POST-PANCREATCTOMY VS. POST-PANCREATITIS FLUID COLLECTIONS WITHOUT NECROSIS

M. Razpotnik¹, A. Wree¹, M. Sigal¹, C. Makris¹, F.J. Körner¹, Ö. Celebi¹, T.M. Holtmann¹, D. Aretakis¹, A. Adler¹, F. Tacke¹, C. Jürgensen¹

¹Charité - Universitätsmedizin Berlin, Department of Hepatology and Gastroenterology, Campus Virchow-Klinikum (CVK) and Campus Charité Mitte (CCM), Berlin, Germany

Contact E-Mail Address: marcel.razpotnik@gmail.com

Introduction: The etiology and natural history of fluid collections complicating pancreatic resection differ from those associated with pancreatitis. Understanding whether one group benefits more from EUS-guided drainage could facilitate the development of condition-specific treatment protocols.

Aims & Methods: We aimed to compare the efficacy and safety of EUS-guided drainage of fluid collections following pancreatic resection and post-pancreatitis pseudocysts.

This study evaluates the outcomes of patients who underwent EUS-guided drainage for pancreatic fluid collection without necrosis complicating pancreatic resection (PR) at a high-volume tertiary university center from 2018 to 2022. These patients were compared to a matched cohort with post-pancreatitis (PP) fluid collections without solid components, using a 1:1 ratio for confounding factors.

In both conditions, treatment was standardized to involve the implantation of 10 French double-pigtail stents as the therapeutic modality. Primary outcomes included the duration of hospital stay and the total number of interventions required for treatment success. This encompassed the initial intervention, stent removals and replacements, and any additional procedures, such as managing complications during a 12-month follow-up.

Early clinical success of EUS-guided drainage was defined as:

1. a reduction of the collection to <50% within 3 months, as confirmed by follow-up imaging, and;
2. clinical improvement.

Late clinical success was determined by the complete resolution of the lesion within 12 months.

Secondary endpoints were the duration of ICU stay, mortality, and adverse events, defined according to the lexicon of the American Society of Gastrointestinal Endoscopy¹.

Results: In the final analysis, 54 patients (70.4% male, mean age 57.7 ± 13.9) were included, 27 in each group. The most common cause within the PP group was alcohol-induced pancreatitis (40.7%), followed by biliary (18.5%) and idiopathic (14.8%) etiology. In the PR- group most patients have had a pancreatic tail resection (55.6%), followed by pylorus-preserving pancreaticoduodenectomy (22.2%) and total or subtotal pancreatic resection (22.2%).

No significant differences were observed between the cohorts in relation to potential confounding variables, including age, gender, comorbidities, presence of fluid infection, number and type of stents utilized, time interval to initial intervention, and pre-drainage size of fluid collections. The number of reinterventions and clinical success after EUS-guided drainage were similar in both groups.

While the overall hospital stay was not significantly different between the groups, the PP patients showed a significantly longer need for ICU services compared to the post-surgery group (11.9 vs. 1.7 days, p=0.03). The complications rate tends to be higher in the post-pancreatitis group but did not reach significance due to the low number of events that occurred (29.6 vs. 7.4%, p=0.08).

Fluid collection			
Factors	Post- pancreatectomy	Post- pancreatitis	p-value
Age (years)	57.9 (52.8-63.2)	52.6 (48.1-57.1)	0.11
Male	20 (74.1%)	18 (66.7%)	0.77
BMI (kg/m ²)	25.1 (22.5-27.7)	24.4 (21.9-26.9)	0.67
Comorbidities	16 (59%)	20 (74.1%)	0.37
Cardiac	3 (11%)	7 (25.9%)	0.29
Pulmonary	2 (7%)	7 (25.9%)	0.13
Size (mm)	73.7 (60.4- 86.9)	66.5 (54.5-78.6)	0.41
Infection	11 (40.7%)	11 (40.7%)	0.78
Number of Stents	1 (1-5)	1 (1-5)	0.98
Time to intervention (days)	30 (7-100)	24 (2-90)	0.47
Outcomes			
Re-Interventions	3.0 (2.3-3.7)	3.5 (2.5-4.4)	0.44
Hospital stay	24.1 (18.2-29.9)	30.6 (11.6-49.7)	0.47
ICU stay	1.7 (0.5-2.9)	11.9 (1.5-22.3)	0.03
Early outcome	22 (81.5%)	21 (77.8%)	0.99
Late outcome	27 (100%)	27 (100%)	
Complications	2 (7.4%)	8 (29.6%)	0.08
Mortality	1 (3.7%)	3 (11.1%)	0.60

Table.

Conclusion: Despite comparable clinical outcomes after EUS-guided drainage in both groups, patients with post-pancreatitis fluid collection were associated with greater ICU utilization and tended to experience higher complication rates at initial intervention.

References: 1. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc.* 2010 Mar;71(3):446-54.

Disclosure: Nothing to disclose.

PP1182

OPTIMIZING PANCREATIC WON MANAGEMENT: THE QNI CLASSIFICATION APPROACH FOR ENDOSCOPIC DRAINAGE

R.-I. Orzan^{1,2}, C. Pojoga^{2,3}, C. Hagi^{1,2}, V. Rednic^{1,2}, G. Molnar², A. Seicean^{1,2}

¹Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, ²Regional Institute of Gastroenterology and Hepatology Cluj-Napoca, Cluj-Napoca, Romania, ³Băbes-Bolyai University Clinical Psychology and Psychotherapy Department, Cluj-Napoca, Romania

Contact E-Mail Address: andradaseicean@GMAIL.COM

Introduction: Pancreatic walled-off necrosis (WON) presents a significant challenge in acute pancreatitis management, often necessitating endoscopic intervention for drainage and necrosectomy. However, the optimal selection of stent type for endoscopic drainage remains debatable. This study aimed to evaluate the utility of the QNI classification in guiding stent selection for WON drainage.

Aims & Methods: We conducted a retrospective analysis of patients who underwent endoscopic drainage and necrosectomy for symptomatic pancreatic WON at a tertiary referral center between January 2022 and September 2023.

Patients were divided into two groups based on the QNI classification: Group 1 consisted of patients who had WON affecting 1 quadrant or 2 quadrants with a necrosis of less than 30%.

Group 2 consisted of patients whose WON had affected 3 quadrants, 2 quadrants with 30% necrosis, or 1 quadrant with more than 60% necrosis at the time of the index procedure.

A WON-based decision was made by the endoscopist regarding the use of LAMS or plastic stents. Necrosectomy was performed in cases of infection following WON drainage. Resolution was considered in clinically asymptomatic patients with WON < 30 mm at the 3-month imaging follow-up.

Results: Forty-eight patients were included in the study, with a mean age of 55.7 (±12.28) and a male-to-female ratio of 2.4:1, 20 patients in Group 1 and 28 patients in Group 2. Except for infection, which occurred more frequently in Group 2, the indications for drainage (pain, weight loss) were similar between the two groups (28% vs 5%, $p=0.03$). LAMS were used more frequently in group 2 than in group 1 (64% vs 40%, $p=0.001$). The mean number of endoscopic procedures in Group 1 was 1.7 and in Group 2 it was 3. The interval between endoscopic procedures in Group 1 and Group 2 was 20.3 days and 12.4 days, respectively ($p=0.05$). Clinical resolution at 3 months showed no significant difference between groups, with rates of 90% vs 85% ($p=0.87$), and the complication rates was 10% vs 14.2% ($p=NS$). Percutaneous drainage was done in 0% vs 7.14% cases, and surgery was required in 0% vs 7.1% of cases.

Conclusion: As a result of the newly proposed QNI classification system, patients can be guided in the selection of LAMS placement as well as for multidisciplinary management. Severe QNI scores may need more aggressive interventions, yet outcomes are comparable to those with milder disease.

References: Baroud, S., Chandrasekhara, V., Storm, A. C., Law, R. J., Vargas, E. J., Levy, M. J., Mahmoud, T., Bazerbachi, F., Bofill-Garcia, A., Ghazi, R., Maselli, D. B., Martin, J. A., Vege, S. S., Takahashi, N., Petersen, B. T., Topazian, M. D., & Abu Dayyeh, B. K. (2023). Novel classification system for walled-off necrosis: a step toward standardized nomenclature and risk-stratification framework. *Gastrointestinal endoscopy*, 97(2), 300–308.

Disclosure: Nothing to disclose.

PP1183

EFFICACY AND SAFETY OF ENDOSCOPIC ULTRASOUND-GUIDED RADIOFREQUENCY ABLATION OF PANCREATIC TUMORS - INITIAL EXPERIENCE OF SINGLE CENTER

Y. Petkova¹, P. Karagyzov¹, A. Petreska²

¹Acibadem City Clinic University Hospital Tokuda, Clinic of Gastroenterology, Sofia, Bulgaria, ²Acibadem University Hospital Tokuda, Clinic of Liver, Biliary, Pancreatic and interventional surgery, Sofia, Bulgaria

Contact E-Mail Address: petko.karagyzov@gmail.com

Introduction: Surgery is the mainstay therapeutic strategy for pancreatic tumors. Although effective, the rates of peri-operative morbidity and mortality remain a concerning issue. This poses the need for developing less invasive, safe but effective techniques. Endoscopic ultrasound-guided radiofrequency ablation/EUS RFA/ is a novel tool for targeted local destruction, applicable for pancreatic neuroendocrine tumors /PanNEN/, locally advanced adenocarcinoma, and cystic pancreatic neoplasms.

Aims & Methods: To evaluate EUS RFA of pancreatic tumors in terms of efficacy and safety. Primary endpoint was clinical success rate defined as a complete response after the procedure and during follow-up. The secondary endpoint was the assessment of adverse events/AE/ associated with the procedure.

Methods: Retrospective analysis of a prospective database including all consecutive patients who were treated with EUS RFA for the period August 2022 – December 2023 in a single tertiary center. We evaluated electronic patient records and gathered data on patients' baseline characteristics, procedure characteristics, and outcomes. The follow-up of the group included imaging studies - computed tomography and/or contrast-enhanced EUS, done on the third and the sixth month post-procedure.

Results: Ten sessions of RFA in seven patients were performed. Male to female ratio was 4:3, with a mean age of 65.42 years. The procedures were performed with EUS-guided RFA 19 G Needle. The group included five patients with neuroendocrine tumors - two with non-functional pNEN –

G1 grade of differentiation and three with insulinoma; one patient with metastasis from renal cell carcinoma, and one patient with pancreatic ductal adenocarcinoma. The mean size of the lesions was 23.5714 ± 4.755 ($\pm 20.17\%$)mm. Technical success defined as successful puncture of the lesion and application of alternating current was achieved in all cases. Clinical success defined as the disappearance of lesions on imaging studies at the 3rd and 6th month was achieved in 85,71 % of the patients. In three of the patients, we performed a second session on the third month during follow-up due to signs of vital tissue. In the 6th month during follow-up in two of them, we found a complete response. There was no correlation between response rate and functional status of neuroendocrine tumors as well as no association of procedure outcome and location of lesions. In terms of efficacy, we found a negative correlation between lesion size and response rate. We observed the resolution of symptoms due to hormonal hypersecretion in the cases of insulinoma in the first 24 postprocedural hours with no events of hypoglycemia. No early or late adverse events were reported in the observed group.

Patient	Histology	Size of lesion	Number of sessions	Number of passes during the session	Response	Adverse events
1	NF PanNET ki-67-2% G1	43/27mm	2	4	Partial response after 2 sessions	None
2	NF PanNET ki-67-2% G1	22/15mm	1	3	Complete response after one session	None
3	FNET - insulinoma G1	20mm	2	4	Clinical response after one session; complete response after second session	None
4	Metastasis from renal cell carcinoma	18/15mm	2	3	complete response after two sessions	None
5	Locally advanced adenocarcinoma	38mm	1	3	Complete response after one session	None
6	NET Insulinoma G1	17/13mm	1	3	complete response after one session	None
7	NET Insulinoma G1	7mm	1	2	Complete response after one session	None

Conclusion: EUS RFA is a highly effective and safe mini-invasive technique for treating pancreatic tumors, especially PanNENs. It could be offered to selected patients as an alternative to surgical treatment, providing targeted selective local tissue destruction. The procedure can be applied as an adjunctive tool in the palliative treatment of locally advanced ductal adenocarcinoma but more data are needed.

Disclosure: Nothing to disclose.

PP1184

ADVANCEMENTS IN ENDOSCOPIC PANCREATIC NECROSECTOMY: INSIGHTS FROM THE LAMS ERA

N.S. Malhi¹, R. Grover¹, J.S. Dhingra¹

¹Advanced Gastroenterology Institute (A.G.I.), The GASTROCITI, Ludhiana, India

Contact E-Mail Address: doctorjasmeet@gmail.com

Introduction: Walled-off pancreatic necrosis (WOPN) stands as a grave complication of acute pancreatitis, posing a substantial risk of sepsis-induced multiple organ failure when infected. Traditional surgical debridement, though effective, often entails elevated rates of adverse events and mortality. However, the emergence of endoscopic ultrasound (EUS)-guided cysto-gastrostomy employing LAMS presents a promising alternative for WOPN treatment, offering advantages in managing necrotic

collections via endoscopic necrosectomy. This study aims to evaluate the technical and clinical success as primary objectives, alongside assessing adverse events and recurrence rates as secondary objectives.

Aims & Methods: We conducted a retrospective analysis of consecutive patients diagnosed with infected walled-off pancreatic necrosis (WOPN) and treated over a 48-month period from March 2020 to February 2024. The treatment protocol involved the placement of a novel LAMS – HOT AXIOS stent, utilizing an electrocautery-enhanced delivery system. This was followed by direct endoscopic necrosectomy (DEN), performed immediately post-stent deployment and repeated at intervals of 3 to 7 days until complete resolution was attained. All procedures were performed by expert clinicians under anesthesia with meticulous management of the necrotic cavity.

Results: 31 patients diagnosed with infected WOPN underwent EUS assessment for LAMS placement. 5 patients were excluded: 3 due to cavity distance from gastric wall and 2 due to large amount of solid necrotic tissue (>30%). 26 patients underwent LAMS placement with average age 34.5 years. Drainage indications included sepsis with infected collection (53.8%), pain (23%), gastric outlet obstruction (11.5%), and a combination of these (11.5%). For primary LAMS insertion, 100% technical success rate was achieved. Technical success rates for complete endoscopic necrosectomy were 30.8% & 69.2% at the end of 7 days & 14 days respectively. In cases of failed endoscopic necrosectomy, persistently infected necrosis, clinical deterioration, or complications, a step-up approach was pursued, leading to ultimately a surgical intervention in 23% (6 patients). Complications during endoscopic necrosectomy included transient self-limiting bleeding in 6 patients (23%), aspiration pneumonitis in 3 patients (11.5%), and spurting bleed from necrotic bed necessitating intra-procedural clip placement in one patient. Average procedure duration was 55 minutes with an average of 3 sessions required per patient. Clinical success, defined as pure endoscopic management without the need for surgical or radiological intervention, was achieved in 11 patients (42.3%). 6 patients (23%) required angioembolization, 6 patients (23%) required surgical intervention for incomplete drainage/sepsis and 3 patients (11.5%) required percutaneous catheter drain placement. Average hospital stay was 19 days. Patients who underwent successful endoscopic necrosectomy with LAMS were subjected to MRCP to identify disconnected ducts before LAMS removal, which occurred after an average duration of 18 days. Following stent removal, 11 patients (42.3%) required double pigtail plastic stent (5 Fr x 3 cm) placement due to disconnected ducts. Patients were followed up for an average of 60 days with no recurrences observed during this period.

Conclusion: Adoption of specialized LAMS and subsequent direct endoscopic necrosectomy produced commendable results in managing infected WOPNs. This approach showcased remarkable technical success and favorable clinical outcomes when executed according to established protocols in expert hands.

Disclosure: Nothing to disclose.

Poster
Other

Other

09:00-18:00 / Poster Exhibition

PP1185

THE ECONOMIC IMPACT OF USTEKINUMAB IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASE: A TARGETED LITERATURE REVIEW

K. Shastri¹, K. Clarke², M. Ainslie-Garcia², N. Ferko²

¹Fresenius Kabi SwissBioSim GmbH, Eysins, Switzerland,

²EVERSANA, Burlington, Canada

Contact E-Mail Address: kunal.shastri@fresenius-kabi.com

Introduction: Ustekinumab, an interleukin (IL) 12/23 inhibitor is a biologic used to treat inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). Clinical and real-world evidence has demonstrated its ability to provide a clinically meaningful response and remission among patients; however, the economic impact of its use may not be favourable from the payer perspective. The objective of this targeted literature review was to understand the economic impact of ustekinumab reference product in the treatment of patients with IBD.

Aims & Methods: A literature search was conducted in MEDLINE for economic publications that evaluate the economic impact of ustekinumab or include ustekinumab within their analyses. Search terms included "budget impact model", "budget impact analysis", "cost-utility", "cost-effect", "ulcerative colitis", "Crohn's disease" and "ustekinumab" from database inception until Feb 8th, 2024. Only studies published in English were eligible for inclusion.

Results: A total of 30 hits were screened for inclusion, yielding 12 relevant studies that discussed economic implications of ustekinumab. Five articles were conducted from the US payer perspective, two from the Japanese payer perspective, and one each from the Canadian, Swedish, Polish, French, and German perspectives. The economic models included budget impact models (n = 2), cost-effectiveness models (n = 8), and cost per responder/remitter analyses (n = 2). Five studies used a CD patient population, six studies focused on UC, and one study included a mixed population of CD and UC. In CD studies, two found ustekinumab was cost-effective: these studies were conducted from the perspective of Polish and Swedish payers in CD patients who failed anti-TNF therapy. Both studies used a Markov based model to assess cost-effectiveness of treatments. In the remaining CD studies, ustekinumab was associated with the highest cost per responder/remitter (Japanese payer perspective) and was dominated by other treatments in cost-effectiveness analyses (US payer perspective). The studies conducted in the UC patient population also found that, although clinically effective, ustekinumab was dominated (based on the incremental cost effectiveness ratio [ICER]) by other biologics included in the analyses (eg, vedolizumab and infliximab). Similar to the CD patient population, the cost per responder/remitter was highest for ustekinumab compared to five other therapies including tofacitinib and golimumab (US payer perspective). However, in two UC studies, ustekinumab was observed to be more effective than the most cost-effective treatment option (from the Japanese and US payer perspectives), highlighting that its price negatively affected its ICER. Moreover, cost-effectiveness analyses conducted by the German and Canadian perspectives, demonstrated that ustekinumab was not a cost-effective therapy at the current willingness to pay threshold (0% probability). Note, that no studies tested the possible cost-effectiveness of an ustekinumab biosimilar which would positively influence the cost associated with ustekinumab treatment.

Conclusion: This literature review demonstrated that, despite its high efficacy, ustekinumab is among the highest costing biologics available for the treatment of IBD with low probabilities of cost-effectiveness across several studies.

As the economic burden for IBD is increasing globally, cost-saving therapeutic options such as biosimilars may help to provide savings that can be redistributed in a healthcare system or provide funds to expand patient access.

Disclosure: Kunal Shastri is an employee of Fresenius Kabi a manufacturer of biosimilars. Kerise Clarke, Margaret Ainslie-Garcia, Nicole Ferko are employees of EVERSANA a company who receives consulting fees from Fresenius Kabi.

PP1186

WHY DO MANY PEOPLE WITH DISORDERS OF GUT-BRAIN INTERACTION (DGBI) NOT SEEK MEDICAL CARE? ANSWERS FROM A NEW ASSESSMENT INSTRUMENT

T. Taft¹, O.S. Palsson², D. Drossman³, M. Simrén⁴, J. Tack⁵, A. Mikocka-Walus⁶, S. Hoffman⁷, A.D. Sperber⁸

¹The Rome Foundation Research Institute, Chapel Hill, United States of America, ²University of North Carolina, Chapel Hill, Dept. of Medicine, Chapel Hill, NC, United States of America, ³Drossman Gastroenterology - Drossman Gastroenterology, Drossman Gastroenterology; Chapel Hill/US, Drossman Gastroenterology, Chapel Hill, United States of America, ⁴Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Dept of Internal Medicine, Gothenburg, Sweden, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium, ⁶Deakin University, Burwood, Australia, ⁷Northwestern University, Feinberg School of Medicine, Chicago, United States of America, ⁸Ben-Gurion University of the Negev, Faculty of Health Sciences, Farod, Israel

Contact E-Mail Address: ttaft@theromefoundation.org

Introduction: A large proportion of people with DGBI in the general population, including irritable bowel syndrome (IBS) and functional dyspepsia (FD), do not seek healthcare (HC) for their condition, but their reasons are poorly understood. We aimed to develop a questionnaire to assess different reasons an individual may not consult a doctor for current gastrointestinal (GI) symptoms.

Aims & Methods: The Reasons for Not Seeking Healthcare (RNSH) questionnaire was created from content derived from 8 focus groups with 23 DGBI patients in the United States and Australia and guided by author experience. Participants rated how important each of 21 items is in causing them not to see a doctor for current (within the last 3 months) GI symptoms on a 4-point Likert scale (Not at all, A Little, Moderately, Very). Adults in 9 countries (Canada, China, Germany, Japan, Mexico, Poland, Romania, Spain, United States) completed an online survey including the RNSH, the Rome IV Diagnostic questions for IBS and FD, and questions about medical history, HC utilization, and demographics.

Respondents who experienced gastroduodenal or bowel symptoms in the past 3 months but had not sought care for those symptoms were included in Exploratory Principal Component Factor Analysis (PCFA) with Promax

rotation evaluating the structure and potential sub-scales of RNSH. Items for each factor were summed and transformed into equal 0-100 subscales. Reliability of the RNSH was also assessed.

Results: A total of 17,663 adults completed the online survey and 12,666 (80%) of those had GI symptoms in the last 3 months but had not sought care for them: 51% female; mean age 45.5 years (SD=16.3); 5.7% had Rome IV IBS and 10.7% had FD. Of these, 73.7% had never sought care for digestive problems. The RNSH questionnaire demonstrated very good internal consistency (Cronbach α = 0.88) and split-half reliability (Guttman λ^2 = 0.89). PCFA yielded 3 factors; 4 items were removed due to poor loading. Reasons for not seeking care include: “negative HC expectations”, “prefer non-medical alternatives”, and “prefer a wait-and-see approach”. The 3 factors collectively accounted for 48% of the variance (Adjusted R^2) in RNSH score. The strongest factor keeping people from seeking HC for GI symptoms (highest standardized mean subscale score) was adopting a “wait and see” approach (Table).

People meeting Rome IV criteria for IBS or FD were markedly more likely to avoid seeking care due to negative HC expectations than those who did not meet Rome criteria ($p<.001$) with a medium effect size ($d=0.48$) and to prefer using non-medical alternatives ($p<.001$) with a small effect size ($d=0.29$). No differences existed between the two groups for preferring a wait-and-see approach ($p=.087$).

Subscale	Items	Eigenvalue	Variance	Mean Adjusted Score [95% CI]		
				All (N=12,666)	No IBS or FD (N=11,038)	IBS or FD (N=1,628)
Negative HC Expectations	8	6.46	19.6%	29.97 [29.6-30.4]	28.61 [28.2-29.0]	39.21 [38.1-40.3]
Prefer Non-medical Alternatives	5	2.21	14.7%	27.84 [27.4-28.2]	27.00 [26.6-27.4]	33.51 [32.4-34.6]
Wait and See Approach	4	1.41	13.6%	51.26 [50.7-51.6]	50.99 [50.5-51.5]	52.26 [51.1-53.4]

Table. Factor Structure with Mean Adjusted Scores for the Three Sub-Scales of the RNSH.

Conclusion: This study identified, and showed the relative importance of, three distinct factors that keep people from seeing a doctor for their current digestive symptoms. Specifically, people with IBS or FD may avoid seeking HC based on negative expectations for such care or prefer to use alternative methods such as diet modification or stress reduction techniques. The RNSH may be useful for identifying and helping to overcome specific barriers to timely DGBI treatment that may lead to poorer outcomes.

Disclosure: Nothing to disclose.

PP1187

HEALTHCARE RESOURCE UTILIZATION AND COSTS IN CROHN'S DISEASE AND ULCERATIVE COLITIS PATIENTS INITIATING USTEKINUMAB TREATMENT VIA JANSSEN'S BIOADVANCE® PROGRAM

L.E Targownik¹, M. Latour², E. Pone³, K. Boyerahmadi², H. Yang⁴, J. Ling⁴, A. Tehrani⁴, S. Golden⁴, J.K. Marshall⁵

¹Mount Sinai Hospital, Gastroenterology and Hepatology, Toronto, Canada, ²Janssen Canada, Medical Affairs, Toronto, Canada, ³Janssen Canada, Government Affairs and Market Access, Toronto, Canada, ⁴IQVIA, Mississauga, Canada, ⁵McMaster University, Division of Gastroenterology, Hamilton, Canada

Contact E-Mail Address: Laura.Targownik@sinahealth.ca

Introduction: There is limited research on HealthCare Resource Utilization (HCRU) and costs among patients receiving ustekinumab (UST) treatment. This study aims to evaluate HCRU and costs in patients with Crohn's Disease (CD) and Ulcerative Colitis (UC) who received UST treatment through Janssen's BIOADVANCE® patient support program (PSP) in Ontario, Canada.

Aims & Methods: The primary objective of this study is to compare annual HCRU and costs (excluding medication expenses) during a period of one year before initiating UST treatment and up to four years post-initiation. This retrospective observational study analyzed data from a consecutive cohort of Ontario CD and UC patients who initiated UST treatment through Janssen's BIOADVANCE® PSP.

Patients were indexed based on their first recorded UST prescription fill, spanning from January 1, 2017, to July 31, 2021, for CD patients, and from February 1, 2020, to July 31, 2021, for UC patients.

Quasi-identifiers (date of birth, gender, postal code, indication) were used for probabilistic linkage of patients in BIOADVANCE® PSP to those in Ontario Crohn's and Colitis Cohort (OCCC) from the Institute for Clinical Evaluative Sciences (ICES). A follow-up period for up to four years post-index date was used to assess all-cause and IBD-specific HCRU and costs. A 12-month lookback period was utilized to establish baseline demographic and clinical profiles and baseline HCRU and costs.

A mixed gamma regression model was employed to compare costs before and after UST initiation. IBD-specific HCRU and costs included general practitioner visits, specialist visits, emergency department visits, inpatient hospitalization, and same-day surgeries. IBD-specific HCRU and costs were identified based on the IBD-specific diagnosis code as the most responsible diagnosis.

Results: A probabilistic linkage of 88.1% for CD cases and UC cases was achieved. A total of 2,279 patients with CD and 626 patients with UC were included. UST was the initial biologic therapy for 35.72% and 22.68% of patients with CD and UC, respectively. The average time since diagnosis was 10.72 years for CD and 8.07 years for UC. The mean age was 45.6 $\pm$ 17.2 years for UC patients and 45.7 $\pm$ 16.2 years for CD patients. UC showed a male-female ratio of 56% to 44%, whereas for CD, it was 46% to 54%. IBD-specific HCRU and costs significantly decreased post-UST initiation in Years 1, 2, and 3 for both CD patients and UC patients, compared to baseline (Table).

IBD Specific Costs (\$ CAD)		Year 1	p-value	Year 2	p-value	Year 3	p-value
Mean +/- (SD)							
Crohn's Disease	(n)	n=2,279		n=1,659		n=1,057	
	Baseline (BL)	2,754 ± 6,025	0.0057	2,851 ± 6,361	<0.0001	2,861 ± 6,428	<0.0001
	Follow-up (FU)	2,206 ± 7,550		1,644 ± 5,300		1,417 ± 5,194	
Ulcerative Colitis	(n)	n=626		n=317		n=49	
	Baseline (BL)	3,373 ± 6,745	0.0203	3,910 ± 8,051	<0.0001	6,277 ± 11,499	0.0037
	Follow-up (FU)	2,535 ± 7,865		1,491 ± 4,808		1,335 ± 4,121	

Table.

Specifically in Year 2, inpatient hospitalization cost was reduced by 43.7% for CD (BL \$1,642 vs. FU \$925, p= 0.0001) and 67.3% for UC (BL \$2,315 vs. FU \$756, p= 0.0011). Total physician visit cost was reduced by 33.6% for CD (BL \$728 vs. FL \$483, p<0.0001) and 45.8% for UC (BL \$858 vs. FL \$465, p= <0.0001).

Conclusion: Initiation of UST through the BIOADVANCE® PSP was related to substantial reductions in IBD-specific HCRU and costs among patients with CD and UC in Ontario, Canada.

These findings underscore the potential benefits of UST as an advanced therapy in IBD treatment, in managing CD and UC, and support its role in optimizing patient outcomes while reducing the burden on healthcare resources.

References: Data source:

1. Janssen BIOADVANCE® Database (January 1, 2016 – March 31, 2023) and Ontario Crohn’s and Colitis Cohort (OCCC) data in Institute for Clinical Evaluative Sciences (ICES).

Disclosure: Laura Targownik has received grants from AbbVie Canada, Janssen Canada and Pfizer Canada; consulting fees from AbbVie, Takeda, Janssen, Pfizer, Amgen, Viartis, Fresenius Kabi, Bristol Myers Squibb, Sanofi, Lilly; honoraria from AbbVie, Takeda, Janssen, Pfizer, Amgen, Viartis, Fresenius Kabi, Bristol Myers Squibb, Sanofi; has participated on a data safety monitoring board of advisory board for GoodCap Pharmaceuticals, Pfizer, Takeda, Janssen, Bristol Myers Squibb, and is a member of the Crohn’s and Colitis Canada Scientific and Medical Advisory Board; Eneida Pone, Martin G. Latour, and Kasra Boyerahmadi are Janssen employee, and Huijuan Yang, Juejing Ling, Ali Tehrani, and Shane Golden are employee of IQVIA, and John K Marhsall is a consultant for AbbVie, Amgen, Bausch Health, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, Lilly, Organon, Paladin, Pfizer, Pharmascience, Roche, Sandoz, Takeda, Viartis and a speaker for AbbVie, Amgen, Bausch Health, Ferring, Fresenius Kabi, Janssen, Lupin, Organon, Pfizer, Pharmascience, Roche, Takeda.

PP1188

TELEREGULATION IN GASTROENTEROLOGY AND THE BOTTLENECK OF SPECIALIZED HEALTH CARE

L. Rosevics¹, A. Dotti¹, E.C. dos Santos Cerutti¹, F. Bianchi¹, K.C. Kampa¹, M. Rocha¹
¹Complexo Hospital de Clínicas - Universidade Federal do Paraná, Curitiba, Brazil

Contact E-Mail Address: le.rosevics@yahoo.com.br

Introduction: The increase in population and the presence of bottlenecks in specialized health care access demonstrate the importance of developing measures for better management. Telemedicine was widely established during the COVID-19 pandemic, and in this context the implementation of teleregulation aims to bring greater resoluteness to health systems.

Aims & Methods: The main objective of the present study is to evaluate the results of teleregulation in gastroenterology in the referrals in a large Brazilian city.

The secondary objectives were to evaluate agreement between the primary care physician in requesting exams or specialist referral and evaluate the number of incorrect referrals and patients who should have been prioritized, to suggest points for continuing medical education.

Methodology: This is a retrospective cross-sectional study of primary health care teleregulations requests for gastroenterology carried out in the city of Curitiba-PR-Brazil by the Gastroenterology team at the Clinical Hospital Complex of the Federal University of Paraná. Teleregulation data were collected between the months of October 2022 and June 2023 in pa-

tients over 18 years old. Patient demographic data was collected, as well as the reason for requesting and its outcome. Requests for reassessment were excluded.

Results: Of the 3000 teleregulations screened in the period, 71.1% were included, of which 68.17% were from female patients, with an average age of 54.32 +/- 16.19 years. The reasons for referral and the outcome are shown in table 1.

Incorrect requests were 6.61%, and the main reasons were acute conditions, exams already requested and patient awaiting appointment, asymptomatic patients, out of criteria for screening colonoscopy, incomplete information and without sufficient basic tests for specialized clinical reasoning. Among all patients, 14.95% of cases were prioritized.

Reasons for referral	n 2133 (%)	Outcome	n (%)
Requesting exams	1368 (64,13)	Gastroenterologists agreed	1212 (88,6)
		Gastroenterologists did not agree	156 (11,40)
Discuss conduct	568 (26,63)	Patients maintained in primary health care	130 (22,89)
		Additional information requested	47 (8,27)
		Additional exams requested	304 (53,52)
		Referred to specialist	87 (15,32)
Request a referral to a specialist	197 (9,24)	Referred to specialist	129 (65,48)
		Patients maintained in primary health care	68 (34,52)

Table 1. Reasons for referrals and outcomes.

Conclusion: The present study highlights that tereregulation represents an important tool in health management, being able to bring resolution in 89.9% of cases.

Disclosure: Nothing to disclose.

PP1189

WITHDRAWN

PP1190

A COST ANALYSIS OF PROPOFOL SEDATION FOR OUTPATIENT ENDOSCOPY IN THE ITALIAN HEALTHCARE SYSTEM

F.V. Mandarinò¹, G. Gribaudo², L. Fanti¹, N. Salmeri³, A. Barchi¹, E. Fasulo¹, G. Dell’Anna¹, E. Viale¹, D. Esposito¹, M. Napolitano¹, L. Massimino¹, F. Azzolini¹, L. Quario⁴, M. Agostoni⁴, L.G. Mantovani², P.A. Cortesi², S. Danese¹
¹San Raffaele Hospital, Gastroenterology and Gastrointestinal Endoscopy, Milan, Italy, ²University of Milan-Bicocca, Research Centre on Public Health (CESP), Monza, Italy, ³San Raffaele Hospital, Gynecology/Obstetrics Unit, Milan, Italy, ⁴San Raffaele Hospital, Department of Anesthesiology, Milan, Italy

Contact E-Mail Address: mandarino.francesco@hsr.it

Introduction: In recent years, propofol has become the sedative of choice for gastrointestinal endoscopy. Despite large cohort studies demonstrating its safety and effectiveness, the adoption of Non-Anesthesiologist Administration of Propofol (NAAP) in clinical practice still faces numerous challenges, both in Europe and globally. Consequently, propofol-based sedation remains largely in the hands of anesthesia professionals.

Aims & Methods: This study was conducted in two phases. Initially, a preliminary analysis was carried out to compare adverse event (AE) rates between NAAP and Anesthesiologist Administration of Propofol (AAP) at a tertiary academic center (San Raffaele Hospital, Milan, Italy). In the second phase, potential cost savings from implementing NAAP over AAP at the hospital, local, and national levels were examined.

Propensity score matching (PSM), based on age, sex, body mass index (BMI), and ASA Physical Status Classification System score, was used to compare the two cohorts. A 3-year budget impact model (BIM) was implemented based on the annual volume of outpatient endoscopy procedures performed at San Raffaele Hospital and estimates of the Italian adult population by Italian National Institute of Statistics (ISTAT).

Results: From May 2019 to October 2021, 2,721 patients who underwent esophagogastroduodenoscopy (EGD) (2,439 NAAP and 282 AAP) and 2,748 who underwent colonoscopy (2,491 NAAP and 257 AAP) in outpatient setting were enrolled.

Only diagnostic procedures were included. After PSM, the EGD cohort included 282 patients under NAAP and 188 under AAP, while the colonoscopy cohort consisted of 256 patients under NAAP and 174 under AAP.

No significant differences in AE rates were observed between the groups in both the EGD (overall: NAAP 1.1% vs AAP 0.8%, $p=0.815$; after PSM: NAAP 0.4% vs. AAP 1.0%, $p=0.452$) and colonoscopy cohorts (overall: NAAP 1.7% vs AAP 3.5%, $p=0.202$; after PSM: NAAP 3.5% vs. AAP 0.6%, $p=0.249$). All AEs were managed without leading to major or long-term sequelae.

According to the BIM, a complete implementation of NAAP instead of AAP for patients classified as ASA 1 and 2 would lead to financial savings of €851,649 at our hospital, €8.3 million for the Local Health Authority of Milan, €19.8 million for the Lombardy region, and €124.7 million for the Italian National Health System over the triennium 2023-2025.

Conclusion: NAAP is a safe sedation modality for outpatient gastrointestinal endoscopy, with AE rates comparable to those of AAP. Its widespread implementation, at the expense of AAP, could result in savings exceeding €120 million for the Italian National Health System over the triennium 2023-2025.

References: NAAP is a safe sedation modality with AE rates comparable to AAP. The widespread implementation of NAAP, rather than reliance on anesthesiologist-led propofol sedation, could result in savings exceeding €120 million for the Italian National Health System over the triennium 2023-2025.

Disclosure: Nothing to disclose.

PP1191

PRE- AND DURING COVID-19 ANALYSIS OF EARLY AND LATE-ONSET COLORECTAL CANCER CASES AMONG AFRICAN AMERICANS: DOES RACE MATTER?

H. Brim¹, L. Gayathri Chirumamilla¹, F. Aduli², K. Angsom², A. Laiyemo¹, C. Suryanarayana Reddy², R. Oskrochi³, H. Ashktorab²

¹Howard University, Medicine, Washington Dc, United States of America, ²Howard University GI division, Medicine, Washington, United States of America, ³Middle East American University, Kuwait, Kuwait

Contact E-Mail Address: hashktorab1@gmail.com

Introduction: The incidence of early-onset colorectal cancer (EOCRC, <45 years) is on the rise among adults, including African Americans (AA).

Aims & Methods: Aim: To investigate differences between EOCRC and late-onset colorectal cancer (LOCRC, >45 years) in AA patients and understand the trend patterns in the last decade, particularly during the COVID era. Methods: We conducted a retrospective review of patient records at Howard University Hospital from 2011 to 2022. Our analysis included demographics, clinical presentations, pathology reports, and colonoscopy records. A three-year interval analyses were performed, with a specific focus on the COVID-19 period (2020-2022) and compared it with preceding years to discern temporal trends. Our cohort consisted of 23 EOCRC individuals, and 192 LOCRC.

Results: The majority (80%) of our cohort consisted of AA. A high proportion of males were diagnosed with colorectal cancer (CRC) during the COVID-19 period (2020-2022), with rates of 87.5% in EOCRC versus 75% in LOCRC, in contrast to a nearly equal gender distribution in preceding years. The incidence of CRC fluctuated over the study period, with a higher observed incidence between 2011-2013 that gradually declined until 2019, followed by a notable spike during the COVID era (2020-2022), particularly in EOCRC patients probably due to an increase in smoking, alcohol consumption, and obesity in both LOCRC and EOCRC groups.

The predominant initial symptom for EOCRC patients persisted as abdominal pain. However, our temporal analysis uncovered a noteworthy rise in the incidence of altered bowel habits (75% vs. 50%) and hematochezia (75% vs. 52%), especially in the recent COVID era in EOCRC patients compared to LOCRC patients. Importantly, these shifts were noted to be the primary indications for colonoscopy among EOCRC patients ($p=0.044$). In the COVID era, EOCRC patients exhibited a predominant left-side occurrence ($p=0.040$), unlike the balanced distribution in 2017-2019. Overall, LOCRC patients mostly had cancers on their right side. Analysis of cancer stage revealed a significant shift in EOCRC patients presenting in stage 4 during 2011-2016 to stage 2 in the COVID era ($p=0.042$), suggesting increased awareness or a more symptomatic presentation that led to early diagnostic evaluation. There was no statistically significant difference in cancer type between the groups, with adenocarcinoma being the most common. due to decreased screening.

Conclusion: In our study, we found a notable increase in CRC during the COVID-19 era, especially among young AA males. Shifts in lifestyle and clinical presentations highlight the necessity for addressing the health-care strategies in this group. EOCRC patients showed left-sided cancer predominance and a shift from stage 4 to stage 2, suggesting potential improvements in awareness and early detection.

Disclosure: None.

PP1192

UNVEILING COLON CLEANSING QUALITY: A FACE-OFF BETWEEN ARTIFICIAL INTELLIGENCE AND CONVENTIONAL METHODS USING BOWL IMAGE FEATURES

L. Amer¹, N. Kaouk², T. Yaacoub², R. Slim¹, J. Amara¹, K. Honein¹, E. Mikhael¹, S. El Helou¹, E. Mahfouz¹, C. Yaghi¹

¹Hotel Dieu de France - Saint Joseph University, Gastroenterology and hepatology department, Beirut, Lebanon, ²Saint Joseph University, Department of telecommunications engineering, Beirut, Lebanon

Contact E-Mail Address: santaelhelou@gmail.com

Introduction: The quality of colonic preparation remains a critical benchmark in ensuring the efficacy of colonoscopy procedures (1). Despite concerted efforts and elaborate protocols, inadequate preparation persists in up to 20% of colonoscopies (2).

To address this challenge, there is a need for innovative solutions to assess bowel preparation providing more reliable and standardized results before the procedure.

Aims & Methods: The aim of this study is to assess and compare the predictive accuracy of models predicated on artificial neural network frameworks with those established via traditional logistic regression analysis, to predict the efficacy of the bowel preparation using bowl images characteristics. This prospective study included 512 bowl images from 100 patients taken after the second dose of a split-dose preparation (using high volume while adhering to a three day low fiber diet), between April 2023 and October 2023 in Hotel Dieu de France, a tertiary hospital center in Beirut. The Boston bowel preparation scale (BBPS) was divided into two cat-

egories: Adequate (≥ 8) and Inadequate (< 8). Manual cropping techniques were employed to refine accuracy and extract images' features using snipping tool. Then, we specified the corresponding mean scores of the image in RGB (Red, Green, Blue) and HSV (Hue, Saturation, Value). Two statistical analysis strategies were considered: the artificial neural network analysis, and the logistic regression analysis.

Results: The artificial neural network for predicting the BBPS from the bowl image characteristics showed an AUROC = 0.797, and an accuracy of 90.4% for the training group (forming 68.2% of the sample), and 92.8% for the testing group (representing 31.8% of the sample). For the traditional statistical analysis, a threshold was defined for each image feature using the area under the ROC curve (AUC). Each feature was categorized into four quartiles. The binary logistic regression showed a significant correlation between blue (threshold= 67) and green colors (threshold= 98), the saturation (threshold= 0.63064), the first quartile of the hue (threshold ≤ 0.073), and the last quartile of the value (threshold ≥ 0.527). Then, a binary logistic regression formula was established: $-1.23 \times \text{First quartile of the hue (threshold} \leq 0.073) - 1.7 \times \text{Last quartile of the Value (threshold} \geq 0.527) - 1.321 \times \text{Saturation (threshold= 0.63064) + 0.688} \times \text{Blue (threshold= 67) + 1.08} \times \text{Green (threshold=98) + 2.932}$. The AUROC of the new formula was equal to 0.787 and revealed a threshold= 1.55. The classification based on the new formula (BBPS as dependent factor) showed an accuracy of 88.1%.

Conclusion: The characteristics of the bowl images serve as predictive indicators of colonic preparation quality. A model utilizing artificial neural network architecture yields higher accuracy in prediction than one derived from conventional statistical methods. This method may allow the adjustment of the preparation strategy before undergoing colonoscopy to improve the outcome of the procedure.

References:

1. Rex DK. Key quality indicators in colonoscopy. *Gastroenterol Rep (Oxf)*. 2023 Mar 10;11:goad009. doi: 10.1093/gastro/goad009. PMID: 36911141; PMCID: PMC10005623.

2. van Riswijk MLM, van Keulen KE, Neumann H, Siersema PD. An intraprocedural bowel cleansing system for difficult-to-prepare patients-A multicenter prospective feasibility study. *United European Gastroenterol J*. 2024 Feb;12(1):56-65. doi: 10.1002/ueg2.12501. Epub 2024 Jan 11. PMID: 38213079; PMCID: PMC10859716.

Disclosure: Nothing to disclose.

PP1193
ENDOSCOPISTS' KNOWLEDGE, PERCEPTIONS, AND ATTITUDE
TOWARDS THE USE OF ARTIFICIAL INTELLIGENCE IN ENDOSCOPY - A
SYSTEMATIC REVIEW

N. Wan^{1,2}, C. Chan¹, J.L. Tan^{1,2},
M.A.A. Chinnaratha Mohamedashrafali^{1,2}, R. Singh^{1,2}
¹Lyell McEwin Hospital, Gastroenterology, Adelaide, Australia,
²University of Adelaide, Faculty of Health and Medical Sciences,
Adelaide, Australia

Contact E-Mail Address: nicholas.wan@sa.gov.au

Introduction: Artificial Intelligence (AI) is rapidly evolving in the field of gastrointestinal (GI) endoscopy. However, the prevailing perceptions and attitudes of endoscopists towards AI remain poorly understood.

Aims & Methods: This review aims to provide a summary on the current views and perspectives covering the incorporation of AI into GI endoscopy, as well as to identify any obstacles hindering its adoption. Electronic databases including MEDLINE, PubMed, and Scopus were searched from inception to 25th March 2024 to identify qualitative studies, such as questionnaires or surveys, conducted on endoscopists regarding the use of AI

in GI endoscopy. The Joanna Briggs Institute (JBI) critical appraisal checklist was used to assess study quality. Qualitative synthesis of included studies was conducted by employing thematic analysis classified into the following five domains:

- 1) Knowledge and attitudes towards AI,
- 2) Perception on the ability of AI to improve accuracy and quality of endoscopy,
- 3) Impact of AI on endoscopists,
- 4) Impact of AI on patients and;
- 5) Barriers towards the implementation of AI.

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (Registration ID: INPALS202430064).

Results: Ten studies were included in this systematic review comprising of 1587 endoscopists across Europe (32.6%), North America (42.8%), and Asia (24.6%). Domain 1: Most endoscopists (69–100%) reported having basic knowledge of AI. Furthermore, the majority (79.5–87.5%) expressed interest and optimism regarding the use of AI in endoscopy. Domain 2: Most respondents (62.5–97%) supported the notion that AI would positively impact endoscopic performance and quality. Domain 3: There were mixed perceptions regarding the extent of operator dependence on AI (6.2–62.8% agreement), and whether AI would prolong procedural time (21–81.3% in agreement).

Most endoscopists (71–100%) disagreed that AI would replace them at work. Domain 4: A substantial proportion of respondents (81.3%) felt that AI would lead to an increase in the quality of patient care. Only a minority of endoscopists (6.2–24%) felt that AI could improve the patient-physician relationship and provide empathetic care. Domain 5: A significant proportion of endoscopists (75.2–91%) identified costs as a potential barrier to the implementation of AI in endoscopy. Opinions on ethical concerns and the lack of regulation varied (12.5–100% and 35–88%, respectively), with many endoscopists feeling that there was need for clear guidelines and regulations when integrating AI into clinical practice.

Included Studies	Country	Sample size	Domains covered:	1) Awareness and knowledge	2) Improving endoscopic performance	3) Impacts on Endoscopists	4) Impacts on patients	5) Barriers to implementation
Wadhwa et al. (2020)	USA	n = 124		X	X	X	-	X
Kochhar et al. (2021)	USA	n = 165		X	X	-	X	X
Leenhardt et al. (2021)	UK	n = 333		X	X	X	X	X
Van der Zander et al. (2022)	Netherlands	n = 80		X	X	X	X	X
Tian et al. (2022)	China	n = 210		X	X	X	X	X
Tham et al. (2022)	Singapore	n = 16		X	X	X	X	X
Kader et al. (2022)	UK	n = 104		X	X	-	-	X
Nehme et al. (2023)	USA	n = 16		X	X	X	-	X
Goh et al. (2023)	Singapore	n = 165		X	X	X	X	X
Leggett et al. (2024)	USA	n = 374		X	X	X	X	X

Table 1. Study characteristics of included studies

Conclusion: Overall, there is a positive attitude towards the use of AI in endoscopy. However, concerns regarding impact on clinical practice, costs and medicolegal considerations remain. The establishment of robust regulatory frameworks is imperative to ensure successful integration of AI into clinical practice.

Disclosure: Nothing to disclose.

PP1194

A PRE-TRAINING MODEL FOR INTESTINAL METAPLASIA RECOGNITION IN THE GASTRIC CORPUS: PRELIMINARY DATA ANALYSIS

I. Ligato¹, G. De Magistris², E. Dilaghi¹, G. Cozza¹, A. Ciardiello³, E. Lahner¹, B. Annibale¹, S. Giagu³, C. Napoli², G. Esposito¹
¹Sant'Andrea Hospital, Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy, ²Sapienza University of Rome, Department of Computer, Control and Management Engineering, Rome, Italy, ³Sapienza University of Rome, Physics Department, Rome, Italy

Contact E-Mail Address: giulio.cozza@uniroma1.it

Introduction: Gastric cancer (GC) is a significant healthcare concern and the recognition of high-risk patients is crucial. The common mechanism for the progression of GC is the Correa cascade, which outlines a multi-step progression from chronic gastritis through atrophic gastritis, intestinal metaplasia (IM), dysplasia and finally GC. The detection of IM in the stomach is not always easy, especially when it is focal. While electronic chromoendoscopy has demonstrated high diagnostic accuracy for IM, its limited availability and the variable expertise of endoscopists pose challenges. Additionally, the potential of artificial intelligence (AI) to aid endoscopists has obtained significant attention.

Aims & Methods: This study aims to develop a deep-learning system to assist in IM diagnosis based on endoscopic image patches. A retrospective dataset of endoscopic images from gastroscopies conducted at Sant'Andrea Hospital, La Sapienza University of Rome between January 2020 and December 2023 was collected. All the gastroscopies were performed using both White Light Imaging (WLI) and Blue Light Imaging (BLI) assessment and targeted biopsies or biopsies according to the updated Sydney system protocol were conducted. Only BLI-assessed gastric corpus images were analyzed for the preliminary machine learning model development data. We tested the most common CNN architecture for image classification (VGG, ResNet, Inception). We used a dataset of coarsely segmented images to extract patches and we cast the problem to a classification task over patches. From each segmented image we extracted 20 patches (with possible overlap). We trained the model to classify patches (positive vs negative). Then we used a voting scheme over patches to classify an entire image.

Results: Best results obtained with ResNet50 architecture without Pre-training. The dataset included 1384 high-resolution corpus BLI images from 300 patients with 721 images classified as GIM-negative and 663 as GIM-positive. Then we obtained a dataset of 10 569 patches that we split into training-set (8264 patches), validation-set (1202 patches), and test-set (1103 patches). On the patches test-set we obtained a specificity of 76%, and a sensitivity of 72%. The classification of the entire image was obtained through a learnable voting scheme, in which each patch expressed its vote (positive or negative). We used the validation set to optimize the following hyperparameters: the decision threshold and the number of positive patches that made the entire image classified as positive. With the best configuration we obtained a specificity of 70% and a sensitivity of 100%, but of course we could use a different voting scheme to trade specificity with sensitivity at need.

Conclusion: The study addresses common challenges in medical scenarios, such as limited data availability and the need to work with a specific dataset, without access to pre-trained models, the difficulty of storing images and the poor quality of routine endoscopic images. Despite constraints, the proposed approach delivers promising results suitable for preliminary data screening, showing a high specificity and sensitivity. Furthermore, using the voting scheme, the best configuration showed a sensitivity of 100% that could permit to aid the endoscopist in the diagnosis of gastric intestinal metaplasia with a zero percentage of false negatives.

Disclosure: Nothing to disclose.

PP1195

USABILITY OF A SMARTPHONE APPLICATION TO SUPPORT PERIOPERATIVE MANAGEMENT OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC NEOPLASM

A. Inaba¹, M. Kunio², A. Kobayashi², T. Hanadate², H. Yamashita¹, H. Sunakawa^{1,3}, K. Nakajo^{1,3}, T. Kadota¹, K. Shinmura¹, T. Yano^{1,3}
¹National Cancer Center Hospital East, Gastroenterology and Endoscopy, Kashiwa, Japan, ²MICIN, Inc., Chiyodaku, Japan, ³National Cancer Center Hospital East, Medical Device Innovation Center, Kashiwa, Japan

Contact E-Mail Address: ainaba@east.ncc.go.jp

Introduction: Endoscopic submucosal dissection (ESD) for early gastric neoplasm in Japan is generally performed in the hospitalization to deal with perioperative complications. Although early detection of patients' symptoms is possible during hospitalization, it is difficult to perceive the symptoms during the period of home care after discharge from the hospital.

To solve this problem, we developed a smartphone application (app) to support perioperative management of ESD for early gastric neoplasm that collects data on the patient's own condition and shares this data with medical institutions.

Aims & Methods: The aim of this study was to evaluate the usability of the app during the perioperative period of ESD for early gastric neoplasm. This study was a single center prospective observational study. Patients who own their smartphone and underwent ESD for early gastric neoplasm at our hospital from August 2023 to February 2024 were included.

Exclusion criteria were as follows;

- i) patients with severe dementia,
- ii) patients who use implantable medical electrical devices such as pacemakers.

Patient downloaded the app to their smartphones prior to ESD and entered their vital signs and symptoms according to the medical questionnaire (including the daily defecation state and the contents of the meals consumed, and these images were also uploaded as needed by the patients) via the app in the morning and at night each day from the day before ESD to the day one month after ESD.

One week after discharge, patients had an online medical examination with a physician using the app. The app included an informational website with ESD procedures, preparation for hospitalization, and precautions for life after discharge, and the patient could check this website at any time.

The primary endpoint was the usage the app that was calculated by: the number of times the patient answered the medical questionnaire / total number of times the questionnaire was delivered. The secondary endpoint was the patients' usability of the app based on a questionnaire survey.

Results: Fifteen patients were enrolled during the period. The median age was 65 years (range; 46-75 years), male / female = 9 / 6. The tumor location was upper / middle / lower = 7 / 6 / 2, and the median tumor size was 14mm (range; 4-75 mm). The median hospital stay was 7 days (range; 6-9 days).

For the primary endpoint, the usage rate of the app was 88.8% (90.9% in the morning and 86.7% at night). All patients had no severe adverse events after discharge. For the usability through the questionnaire survey, all patients found it easy to input their dairy data, and 13 patients (86.7%) answered that daily input into the app has improved their own health awareness. Regarding the online medical examination, 14 patients (93.3%) reported that they had no problem conducting the online connection, and 12 patients (80.0%) reported that they felt more relieved by

talking to a physician. Fourteen patients (93.3%) indicated that the informational website helped them to be more attentive to their daily life.

Conclusion: Using the app during the perioperative period of ESD for early gastric neoplasm, it was possible to collect data of patients simply. It was expected that the app for perioperative management will improve patients' health awareness and be useful to understanding the status of ESD perioperative patients after discharge from the hospital.

Disclosure: Nothing to disclose.

PP1196

EFFICACY OF A STOOL STATE CHECK APPLICATION USING ARTIFICIAL INTELLIGENCE DURING BOWEL PREPARATION BEFORE COLONOSCOPY: A MULTICENTER PROSPECTIVE STUDY (SCAN STUDY)

N. Sugimura¹, D. Hirata¹, Y. Sano¹, T. Yamada², S. Oosera², M. Kanazawa³, H. Kon³, H. Hosaka⁴, H. Tanaka⁴, T. Uraoka⁴, D. Sato⁵, Y. Yoda⁵, H. Takamaru⁶, Y. Saito⁶, T. Gocho⁷, K. Konda⁷, A. Katagiri⁷, K. Yamaguchi⁸, T. Matsuda⁸, A. Imai⁹, H. Fujimoto⁹, H. Matsuzaki¹⁰, N. Takeshita¹⁰, M. Wakabayashi¹¹, A. Inaba¹², H. Ikematsu^{13,12}, K. Shinmura¹²

¹Sano Hospital, Gastrointestinal center, Kobe, Japan, ²Saku Central Hospital Advanced Care Center, Saku, Japan, ³Kon naika clinic, Chiba, Japan, ⁴Gunma University Graduate School of Medicine, Gastroenterology and Hepatology, Maebashi, Japan, ⁵Saitama Prefectural Cancer Center, Ina-machi, Japan, ⁶National Cancer Center Hospital, Endoscopy Division, Tokyo, Japan, ⁷Showa University School of Medicine, Department of Medicine, Division of Gastroenterology, Gastroenterology, Tokyo, Japan, ⁸Omori Medical Center Toho University, Tokyo, Japan, ⁹Aizawa Hospital, Matsumoto, Japan, ¹⁰Jmees, Inc., Kashiwa, Japan, ¹¹National Cancer Center, Tokyo, Japan, ¹²National Cancer Center Hospital East, Kashiwa, Japan, ¹³The University of Tokyo, IMSUT Hospital, Tokyo, Japan

Contact E-Mail Address: naokisfreedom@gmail.com

Introduction: In Japan, the stool state during bowel preparation (BP) is one of indicators for starting a total colonoscopy (TCS). For one reason, we have the concept that the clearer the stool state during BP for TCS is, the less residue there is in the colon. During BP, the patients or medical staffs assess patients' stool state using a visual scale. However, the visual scale lacks objectivity and is judged differently by those who assess it. In addition, checking the stool may increase their stress and workload. To address these issues, we developed a smartphone application (app) allows an artificial intelligence (AI)-based evaluation of the patient's stool state during BP and the viewer to enable the real-time sharing of patients' stool images and the app's evaluation with medical staffs.

Aims & Methods: The aim of this study was to assess the feasibility of performing TCS with appropriate quality using the app and the viewer. This study was a prospective observational study conducted from November 2022 to December 2023 involving patients scheduled for TCS at 10 domestic facilities in Japan. Inclusion criteria were as follows; i) patient age between 20 and 70 years old, ii) patient who own their smartphone. Exclusion criteria were as follows; i) patient with known entire or sub-entire circumferential colorectal cancer, ii) patient after colorectal resection, iii) patient with inflammatory bowel disease, and iv) patient with severe dementia. The procedures of BP followed the usual practice of each facility. The patients downloaded the app to their smartphone and captured their stool during BP, while medical staffs reviewed the app's evaluation either through the app or the viewer. The app displayed the evaluation results as follows; 1 star: solid to muddy stools, 2 stars: cloudy watery stools, 3 stars: clear watery stools. TCS was performed when the app displayed 3 stars.

The primary endpoint was the proportion of patients with Boston Bowel Preparation Score (BBPS) ≥ 6 . BBPS was evaluated by the endoscopist who performed the TCS. Secondary endpoint included adenoma detection rate (ADR), cecal intubation rate (CIR), withdrawal time for negative TCS, and average BBPS. Additionally, we evaluated patient's satisfaction with the app and medical staff's workload burden with the app and the viewer usage via questionnaire surveys. We set the threshold primary endpoint of 90% and the expected value of 95% based on European guidelines. The required sample size was 316, using the binomial distribution with a one-sided alpha of 2.5% and power of 90%. To account for ineligible patients, the target number of patients was set at 340.

Results: A total of 343 patients enrolled in the study. Finally, 326 patients were included in the analysis, comprising 188 males and 138 females, with a median age of 57 years. The primary endpoint was 99.1% (95%CI: 97.3-99.8%). ADR and CIR were 46.9% and 99.7%, respectively. The median withdrawal time for negative TCS was 9 minutes and 45 seconds. The average BBPS was 8.5. In the questionnaire survey, 295 patients (90.5%) indicated they would like to use the app next TCS. Moreover, 67 medical staffs answered the questionnaire and 60 out of 67 (89.6%) reported a reduction in workload burden.

Conclusion: The proportion of patients with a BBPS ≥ 6 in the TCS using the app exceeded the set expected value in addition to the threshold value. The app and the viewer are expected to provide TCS with enough quality and also allow real-time monitoring of BP progress, leading to a reduction in burden on both patients and medical staffs.

Disclosure: Nothing to disclose.

PP1197

REDUCING OUTPATIENT VISITS IN FIT-BASED CRC SCREENING PROGRAMS - FEASIBILITY OF A DIGITAL INTAKE TOOL

F.E. Marijnissen¹, E.E.C. Rijnders¹, M.M. Tieleman², D. Leemreis- van Noord³, L.M.M. Wolters⁴, J.M. Jansen⁵, I. Schot⁶, F.C. Bekkering⁷, A.N. Reijm¹, S.M. van Baalen¹, S.Y. Ismail⁸, I. Lansdorp-Vogelaar⁹, P.J.F. de Jonge¹, M.C.W. Spaander¹
¹Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Bravis Hospital, Gastroenterology and Hepatology, Roosendaal, Netherlands, ³Franciscus Gasthuis & Vlietland, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁴Albert Schweitzer Hospital, Gastroenterology and Hepatology, Dordrecht, Netherlands, ⁵PoliDirect Klinieken, Gastroenterology and Hepatology, Breda, Netherlands, ⁶IJsselland Hospital, Gastroenterology and Hepatology, Capelle a/d IJssel, Netherlands, ⁷DC Klinieken, Almere, Netherlands, ⁸Erasmus University Medical Center, Section Medical Psychology and Psychotherapy, Department of Psychiatry, Rotterdam, Netherlands, ⁹Erasmus University Medical Center, Public Health, Rotterdam, Netherlands

Contact E-Mail Address: f.marijnissen@erasmusmc.nl

Introduction: Currently, all screenees of the Dutch colorectal cancer (CRC) screening program with a positive faecal immunochemical test (FIT) undergo face-to-face counselling at an outpatient clinic. In order to reduce the burden for screenees and healthcare systems, we have developed a Digital Intake Tool (DIT) for the Dutch CRC screening population. A web-application that facilitates the entire pre-colonoscopy counselling process digitally, eliminating the need for a physician. In this study we evaluated whether the DIT could replace in-person counselling.

Aims & Methods: A prospective non-inferiority trial was conducted in seven centres, including academic and regional hospitals, and endoscopy centres. All participants received DIT-counselling. The DIT guided partic-

ipants through the counselling process, which included spoken animated videos for patient education, a medical questionnaire for health assessment, and the collection of pre-procedural informed consent. For screeners in who no additional information was required, colonoscopy was scheduled without an in-person visit.

The primary outcome was the proportion of participants achieving adequate bowel preparation, defined as a Boston Bowel preparation Scale (BBPS) score of ≥ 6 . BBPS scores were compared to patients that received in-person counselling. To assess whether the DIT could replace the 'human touch' of in-person counselling, we evaluated patient-reported outcomes related to anxiety, psychological distress and satisfaction as secondary outcomes.

Results: Between October 2021 and September 2023, 1000 (58.8%) out of 1690 approached patients were included. Median age was 64.0 years with 45% being female. DIT-counselling achieved a BBPS of ≥ 6 in 96.5% of the participants, compared to 97.6% after in-person counselling, demonstrating non-inferiority (-1.1% , 95% CI $-2.64 - 0.444$, non-inferiority margin -8%). A significant reduction in outpatient visits was established, with only 3.4% requiring face-to-face consultations, and 40.9% of the participants could be scheduled for colonoscopy solely via DIT-counselling. After digital counselling, a significant decrease in distress was reported on a 11-point Likert scale ($Z = -6.136$ $p < 0.001$). Also anxiety levels, measured by the STAI-6, decreased ($Z = -3.210$ $p = 0.001$). Nearly all participants (98.9%), were satisfied with the information provided, mean score of 8.5 (SD 1.0) and 88.9% would choose the DIT again, while 5.3% preferred face-to-face counselling.

Conclusion: This study showed that digital counselling can replace in-person counselling for FIT-positive screeners of the CRC screening program. An adequate bowel preparation was achieved in $>96\%$ of the participants, meeting the 90% requirement of the CRC screening program. A substantial reduction in in-person outpatient visits was established, and patients reported highly positive experiences after digital counselling. Implementing this home-based approach will decrease the burden for patients and healthcare systems. Patients can receive care at the comfort of their own home at their own time, reducing travel and carbon emissions, while healthcare systems increase their outpatient capacity.

Disclosure: This study received a PPP-allowance provided by Health-Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships.

PP1198

DOMAIN-SPECIFIC DATA AUGMENTATION IMPROVES ROBUSTNESS OF DEEP LEARNING SYSTEMS IN ENDOSCOPY

M.R. Jong¹, C. Kusters², Q.N. van Bokhorst¹, J. Jukema¹, K. Fockens¹, R. van Eijck van Heslinga¹, B.B. Houwen¹, T. Jaspers², T. Boers², M. van der Vlugt¹, E. Dekker¹, F. van der Sommen², P. de With², J. de Groof¹, J.J. Bergman¹, BONSAI Consortium
¹Amsterdam UMC, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²Technische Universiteit Eindhoven, Electrical Engineering, Eindhoven, Netherlands

Contact E-Mail Address: r.a.h.vaneijckvanheslinga@amsterdamumc.nl

Introduction: Artificial intelligence (AI) systems in endoscopy are predominantly developed in expert centers using standardized, high-quality imaging. However, performance of these systems may decline due to heterogeneous imaging conditions found in daily clinical practice. A primary source of this variability is the diversity in post-processing enhancement settings used across different endoscopy units. These enhancement settings may improve image quality parameters such as color, contrast and sharpness. While often subtle to the human eye, these alterations can significantly im-

pact the accuracy of AI predictions. A potential solution is to simulate the heterogeneity of these enhancement settings during the AI systems training phase using domain-specific data augmentation methods.

Aims & Methods: We aimed to evaluate the negative impact of post-processing enhancement settings on AI performance and explore domain-specific data augmentation as a method to mitigate performance loss.

We investigated two commonly used AI systems in endoscopy: a computer-aided detection (CADE) system for Barrett's neoplasia¹ and a computer-aided diagnosis (CADx) system for the optical diagnosis of colorectal polyps². First, both systems were trained using their original datasets, which comprised limited variability of enhancement settings. These CAD systems were then tested across a wide range of test sets. Each test set comprised the same images but were displayed with a different enhancement setting. This represented the image heterogeneity of daily clinical practice. Finally, both CAD systems were retrained using domain-specific data augmentation. This involved the use of a proprietary software tool to precisely simulate the variability of the complete spectrum of available enhancement settings during training. The array of test sets was then re-evaluated by these updated CAD systems.

Results: The CADE and CADx system trained using their original training set, displayed substantial performance variability across the different test sets. Depending on the test sets enhancement setting, the CADE system displayed sensitivity scores between 83% and 92%, a 9% difference. Specificity scores ranged between 84% and 91%, a 7% difference. Similarly, the CADx system reached differences of up to 7% (78-85%) for sensitivity and 18% (45-63%) for specificity. After retraining both CAD systems using domain-specific data augmentation, sensitivity and specificity variability was reduced to 2% (89-91%) and 1% (90-91%) for CADE and 2% (78-80%) and 8% (55-63%) for CADx.

Conclusion: The performance of current endoscopic AI systems can vary substantially depending on the post-processing enhancement setting of its input data. Domain-specific data augmentation can effectively reduce this variability to ensure consistent performance across different endoscopy units.

References: 1. Fockens N, Jong MR, Jukema JB, Pouw RE, Duits LC, Van Munster SN, et al. A deep learning system for detection of early Barrett's neoplasia: a model development and validation study. *The Lancet Digit Health*. 2023;5:905-21.

2. Houwen BB, Hazewinkel Y, Giotis I, Vleugels JL, Mostafavi NS, van Putten P, et al. Real-time computer-aided diagnosis system for optical diagnosis of diminutive colorectal polyps including sessile serrated lesions: a prospective, multicenter study with benchmarking against screening endoscopists. *Endoscopy*. 2022;54(S 01):eP133.

Disclosure: Nothing to disclose.

PP1199

INTRODUCING INNOVATIVE LOW-CODE/NO-CODE APPLICATIONS IN ENDOSCOPY: AN ERCP AND EUS APP FOR STREAMLINING TRIAGE, ENHANCING SAFETY, AND BUILDING REGIONAL CONNECTIVITY FOR A HIGH VOLUME, LARGE TERTIARY REFERRAL HOSPITAL

C. Kerrison¹, B. Lam¹, A. Whitfield¹, J. Gauci¹, F.V. Mandarin¹, V. Perananthan¹, E. Lee¹, S.J. Williams¹, N.G Burgess¹, M.J. Bourke¹

¹Westmead Hospital, Gastroenterology and Hepatology, Westmead, NSW, Australia

Contact E-Mail Address: brian.lam@health.nsw.gov.au

Introduction: Low-code/no-code (LCNC) application development remains underutilised as a clinician-driven solution for daily hospital tasks. Existing paper-based systems used for triage and booking of endoscopy referrals are inefficient, prone to documentation errors, and contribute to paper wastage.

Aims & Methods: Our objective was to create an online referral pathway and real-time tracking board for Endoscopic Retrograde Cholangiopancreatography (ERCP) and Endoscopic Ultrasound (EUS) to replace the current paper-based system at a large tertiary referral hospital.

Using Microsoft's Power Platform™, PowerApps™, and Power Automate™, gastroenterology clinicians developed an online referral system, bookings and management board, and automated notifications centre for inpatient and outpatient ERCP and EUS referrals. After 2 months of usability testing, the system went live in May 2023, results were monitored to April 2024.

Results: 1,392 requests for ERCP and EUS were monitored using the online clinician-built board, 762 (55%) originating from the new online referral pathway, 405 (29%) were manually uploaded from existing paper requests and 225 (16%) re-bookings facilitated by a re-request feature in the app. Of the total requests, 1030 (74%) were tracked to completion of the procedure, with 219 pending procedures and 103 awaiting future surveillance, while 32 were declined and 8 on hold. Of the online referrals, 170 triggered high suspicion of cancer notifications, with 90% prioritised to first procedure dates within 2 weeks or less. Online referrals additionally had 100% documentation of patient co-morbidities, and anti-platelet / anti-coagulant history through compulsory user input for safer triage, this compared to 44% of the original paper-based requests. On average 187 automated email and push notifications per month informed referrers of confirmed booking dates and delayed or completed procedures, as patients moved through the board. 21 of 165 referring doctors responded to a survey representing six referring hospitals, 100% found the online referral system very or somewhat easy to fill out, 95% found the automated messages helpful, and one third booked a follow up clinic after receiving a completed notification. 100% of responders recommending continuing with the system.

Conclusion: Clinician-built LCNC applications are underutilised as solutions to common tasks in healthcare. Our ERCP and EUS referral pathway and patient tracking board has enhanced clinical decision making and efficiency of triage in a high-volume large referral hospital, while providing co-ordinated input and feedback to referrers and other endoscopy staff. The boards real-time interface provides a full patient journey overview and has additional layers of safety checks, essential for these interventional procedures. The online referral pathway board and app were created using standard business Microsoft 365™ licencing and is available on Microsoft Teams mobile or desktop for accessible and secure use and can be integrated into other hospital systems.

Disclosure: Nil

PP1200

THE USE-AI STUDY: A MULTICENTER, SINGLE BLIND PROOF-OF-CONCEPT STUDY ON THE USE OF AI IN GASTROINTESTINAL ENDOSCOPY

G.E. Tontini¹, T. Pessarelli¹, L. Elli², E. Rondonotti³, A. Murino⁴, U. Kopylov⁵, C. Calabrese⁶, F. Barbaro⁷, E. Toth⁸, F. Caprioli¹, M. Bertolotti⁹, C. Natali⁹, F. Cabitza⁹

¹University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ²Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, ³Ospedale Valduce, Gastroenterology Unit, Dept. of Gastroenterology, Como, Italy, ⁴Royal Free Unit for Endoscopy, Royal Free Unit for Endoscopy, Department of Gastroenterology, London, United Kingdom, ⁵Chaim Sheba Medical Center Ramat Gan Israel, Gastroenterology, Ramat Gan, Israel, ⁶University of Bologna, Bologna, Italy, ⁷Gemelli Hospital, Digestive Endoscopy, Roma, Italy, ⁸Lund University, Malmö, Sweden, ⁹Università degli Studi di Milano-Bicocca, Dipartimento Di Informatica, Sistemistica E Comunicazione, Milano, Italy

Contact E-Mail Address: tommaso.pes@gmail.com

Introduction: The use of artificial intelligence (AI) systems for decision support has recently gained great popularity in the medicine.¹ However, recent studies have shown possible limitations emerging from the interaction between humans and AI. Among these, the term "automation bias (AB)" refers to human errors deriving from over-relying on AI's false alarms such that the human changes a correct initial interpretation.² AB is poorly investigated in the medical field and was never tested in the gastroenterological setting.

Aims & Methods: The aim of the study was to investigate the impact of AI on human diagnostic performance in gastrointestinal endoscopy, including AB.

Ninety high-quality endoscopic videoclips (16 seconds) extracted from small bowel (SB) capsule endoscopy (N=60) and proctosigmoidoscopy (N=30) were edited with the addition of a mock AI system designed with diagnostic accuracy, sensitivity and specificity of 80%, 86% and 75%. The ground truth was settled on the agreement of 9 established experts about the presence of SB lesions with significant hemorrhagic potential according to the Saurin classification (30 videoclips), inflammatory lesions relevant for the diagnosis of SB Crohn's disease according to the Lewis score (30 videoclips) and assessing the Ulcerative Colitis (UC) Endoscopic Index of Severity (30 videos). The videoclips were randomly divided into three sessions and submitted around Europe to fully trained endoscopist, trainees and endoscopic technicians. Participants were instructed to the accuracy measures of AI annotations and scored each videoclip first without, then with AI support. Participants' performances with and without AI were calculated. Subgroup analyses were made after stratification by participants' experience level in each endoscopic setting and test performances.

Results: A total of 12.660 videoclips (both with and without AI) were visualized in 422 sessions (182, 118 and 122 participants completed the first, second and third session, respectively). A strong and significant difference between the respondents' performance (N=281) when they were unaided by AI (average accuracy (M)=0.78, [0.77, 0.79] and when they were supported by the AI (M=0.81, [0.80, 0.82], paired t-test, t(276)=11.2, p<0.001) was found. Size effect and the evidence in favour of a significant positive effect of AI were large, 0.67 (Cohen's D) and very large (Bayes Factor>100), respectively. Interestingly, no significant difference between trainees and specialists both in regard to their performance, either unaided, M=0.77 [0.74, 0.79] vs M=0.78, [0.77, 0.79] or aided M=0.80 [0.78, 0.82] vs M=0.81 [0.80, 0.82] and their accuracy improvement (M=0.03, [0.02, 0.05] vs M=0.03, [0.02, 0.04] (unaided t-value=-0.89, p=0.37; aided t-value=-0.69,

$p=0.49$, difference t -value=0.54, $p=0.59$) were found. A strong leveller effect emerged, with low-performers improving their accuracy much more than top-performers (average improvement 5%, [0.04, 0.06] vs 1%, [0.00, 0.02], paired T test, $t=6.53$, $p<0.001$). Nine percent of the final decisions involved disregarding correct AI advice in favour of incorrect human judgment, while AB occurred in 2% of cases.

Conclusion: In this study, the application of AI to assess SB bleeding, SB inflammatory lesions, and UC activity brings significant improvement in diagnostic accuracy, with the benefit appearing to be greater in the low-performers. However, in rare cases, AI may induce diagnostic errors due to AB. Future studies directly evaluating the impact of AI in real-life clinical settings are needed to confirm these data.

References:

1. Cabitza F, Campagner A, Angius R, Natali C, Reverberi C. 2023. AI Shall Have No Dominion: on How to Measure Technology Dominance in AI-supported Human decision-making. In Proceedings of the 2023 CHI Conference on Human Factors in Computing Systems (CHI '23). Association for Computing Machinery, New York, NY, USA, Article 354, 1–20. <https://doi.org/10.1145/3544548.3581095>
2. Reverberi, C., Rigon, T., Solari, A. et al. Experimental evidence of effective human-AI collaboration in medical decision-making. *Sci Rep* 12, 14952 (2022). <https://doi.org/10.1038/s41598-022-18751-2>

Disclosure: Nothing to disclose.

PP1201

A NEXT STEP FOR AI DRIVEN PANENDOSCOPY - DEVELOPMENT OF CONVOLUTIONAL NEURAL NETWORK FOR EVALUATION OF SMALL BOWEL AND COLON CLEANSING DURING DEVICE ASSISTED ENTEROSCOPY

M. Martins¹, M.J. Mascarenhas Saraiva¹, J. Afonso¹, P. Cardoso¹, M.J. Almeida¹, T. Ribeiro¹, F. Mendes¹, J. Mota¹, A.P. Andrade¹, H. Cardoso¹, J. Ferreira², G. Macedo¹

¹São João University Hospital, Gastroenterology, Porto, Portugal,

²Faculty of Engineering of University Porto, Department of Mechanical Engineering, Porto, Portugal

Contact E-Mail Address: miguel.pedro96@gmail.com

Introduction: Device-assisted enteroscopy (DAE) offers comprehensive examination of the gastrointestinal tract, but its efficacy is dependent on adequate bowel preparation. While prior research explored AI models for colonoscopy cleansing, there is a lack of studies evaluating both small bowel and colon cleansing during DAE.

Aims & Methods: The aim of this study was to develop and validate a convolutional neural network (CNN) capable of automatically classifying bowel cleansing levels during DAE, encompassing both small bowel and colon regions. We retrospectively analyzed 28 procedures (single balloon, double-balloon and motorized spiral enteroscopy) from a high-volume center. Bowel preparation was graded as excellent ($\geq 90\%$ visible mucosa), satisfactory (50-90%), or unsatisfactory ($<50\%$). A dataset of 88,623 images (training: 90%, testing: 10%) was used, covering both small bowel and colon areas. The CNN's performance was evaluated against expert consensus using sensitivity, specificity, accuracy, and AUC-ROC.

Results: We included 51948 frames that were considered excellent, 28820 frames that were considered satisfactory and 7855 frames that were considered unsatisfactory. The CNN demonstrated the following performance metrics: excellent cleansing (sensitivity: 97.8%, specificity: 80.3%, accuracy: 90.6%, AUC-ROC: 0.95), satisfactory cleansing (sensitivity: 81.8%, specificity: 97.9%, accuracy: 92.7%, AUC-ROC: 0.95), and unsatisfactory cleansing (sensitivity: 68.7%, specificity: 99.5%, accuracy: 96.8%, AUC-ROC: 0.96).

Conclusion: This study presents the first globally developed CNN for accurate classification of bowel cleansing throughout DAE, encompassing both small bowel and colon. This advancement represents a necessary step for optimizing diagnostic accuracy and therapeutic efficacy in gastrointestinal procedures, namely DAE, underscoring the pivotal role of innovative technologies in advancing medical practice

Disclosure: Nothing to disclose.

PP1202

PERFORMANCE OF LARGE LANGUAGE MODELS IN INTERPRETATION AND SUMMARIZATION OF ENDOSCOPY REPORTS: A COMPARATIVE ANALYSIS

K. Ju¹, Q. Kong¹, F. Chen¹, H. Liu¹, Y. Li¹, Y. Li¹

¹Qilu Hospital of Shandong University, Jinan, China

Contact E-Mail Address: 15621052001@163.com

Introduction: Large language models (LLMs) offer new opportunities for the transformation of healthcare. One potential application of these models is to serve as consulting tools for patients.

Aims & Methods: The study aimed to assess the performance of different LLMs for the interpretation and summarization of endoscopy reports. This study was conducted in March 2024, and involved three mainstream LLMs (Claude 3 opus, Gemini pro, and GPT-4) which were tasked with interpreting and summarizing six fictitious endoscopy reports based on common clinical scenarios. Three gastroenterologists used Likert scales to blindly score the content generated by the LLMs, evaluating their accuracy, completeness, comprehensibility, or conciseness. Inter-rater reliability analysis and correlation analysis were performed on the scoring dimensions. The interpretation of the reports was also evaluated for readability and safety.

Results: The acceptable proportions for the interpretations in terms of accuracy, completeness, and comprehensibility were 100%, 94.4%, and 100%. For the impressions, the acceptable proportions for accuracy, completeness, and conciseness were 94.4%, 72.2%, and 100%, respectively. Interpretations from Claude 3 opus ($p<0.001$) and GPT-4 ($p<0.0001$) were significantly more legible than fictitious reports, while interpretations from Gemini pro showed no differences. For score based on Likert scales, the overall mean interpretation score for Claude 3 opus ($p=0.025$) and GPT-4 ($p=0.027$) was significantly higher than that from Gemini pro. Regarding impressions, Claude 3 opus ($p=0.011$) and GPT-4 ($p=0.009$) also achieved significantly higher overall mean score than Gemini pro.

Conclusion: LLMs excel in interpreting and summarizing endoscopy reports, but inter-model differences exist. Further optimization and development of specialized LLMs for endoscopic text processing applications may be warranted.

Disclosure: Nothing to disclose.

PP1203

FAST-TRACKING ERCP LEARNING WITH THE BOŠKOSKI-COSTAMAGNA TRAINER: RESULTS OF A MULTICENTER RANDOMIZED CLINICAL TRIAL

S. Campos¹, I. Boskoski², T.A. Voiosu³, M. Salmon⁴, G. Costamagna⁵, J. Deviere⁶, M. Arvanitakis⁷, ERCP Training Group
¹Centre Hospitalier de Luxembourg, Gastro-Entérologie / Endoscopie Digestive, Luxembourg, Luxembourg, ²Catholic University of Rome Digestive Endoscopy Unit, Digestive Endoscopy Unit, Rome, Italy, ³Colentina Hospital, Gastroenterology, Bucharest, Romania, ⁴Université Libre de Bruxelles, Brussels, Belgium, ⁵Università Cattolica del Sacro Cuore, Digestive Endoscopy Unit, Roma, Italy, ⁶Erasme University Hospital, Dept. of Gastroenterology, Bruxelles, Belgium, ⁷ERASME University Hospital, Université Libre de Bruxelles, Gastroenterology Department, Brussels, Belgium

Contact E-Mail Address: saratcampos@gmail.com

Introduction: Increased interest in ERCP simulator-based education is driven by the need for efficient and safe endoscopy training in a dedicated environment.

This study assessed whether a structured training program including initial training with the Boškoski-Costamagna ERCP Trainer (BCT) offers benefits to conventional training.

Aims & Methods: This was a one-year prospective, multicenter, parallel-arm, randomized controlled trial involving 16 novice ERCP trainees randomly assigned to study (SG) and control (CG) groups. Both underwent hands-on ERCP training. Additionally, SG had simulator-based training during the first three months. Performance was evaluated with TEESAT score in all ERCPs with any degree of trainee involvement until each trainee completed a minimum of 60 ERCPs. The primary outcome was overall trainee competence rate; secondary outcomes included successful biliary cannulation and adverse event (AE) rates. Learning curves were generated cumulatively over the training period. Both outcomes and the analysis of specific ERCP steps predictive of overall competence were assessed using mixed-effect logistic regression models (MELR). The most effective predictive model of overall competence was identified using a stepwise backward procedure. MELR was employed to investigate potential confounding factors.

Results: 1,106 ERCPs were included (SG=562, CG=544). SG trainees demonstrated higher success in native biliary cannulation (SG=52%, CG=42%, $p<0.001$), achieved faster biliary cannulation [SG=3(6)min, CG=5(8)min, $p<0.001$], and showed a faster evolution on overall performance, native biliary cannulation, and sphincterotomy. Successful biliary cannulation [OR=10.10, 95% CI (5.15-19.83)] and sphincterotomy [OR=7.71, 95% CI (3.77-15.76)] were the most important predictors for overall competence. The multivariate random-effects model demonstrated an almost significant association between simulator-based training [OR=3.24, 95% CI (1.01-10.39), $p=0.049$] and overall competence, accounting for biliary cannulation, sphincterotomy, and stone removal. No confounding factors were identified.

Conclusion: This study suggests that early simulator training with BCT accelerates the learning curve of trainees in performing key steps of the ERCP procedure and improves overall competence as assessed by dedicated tools during ERCP training.

Disclosure: Nothing to disclose.

PP1204

AN EFFECTIVE STRATEGY FOR THE IMPLEMENTATION OF SCREENING FOR HEREDITARY COLORECTAL CANCER IN CLINICAL PRACTICE. THE ROMANIAN EXPERIENCE

G.-E. Gilca-Blanariu^{1,2}, S. Morarasu^{1,3}, B. Cotruta⁴, L.S. Diaconu^{5,6}, F.A. Tomescu^{5,6}, A.G. Bocioaga⁷, S. Chiriac^{1,2}, A. Constantinescu^{5,6}, E. Gafton³, E.M. Ionescu⁸, D.-M. Maftai⁸, B. Miutescu⁹, A.-M. Musina³, O. Oniciuc¹⁰, M. Palaga⁸, A. Pieptu³, H. Pitutiu¹¹, O.M. Plotogea¹², I.V. Popa¹, E. Rinja¹³, V. Rednic¹⁴, A. Andone¹⁵, A. Saizu⁴, A. Trandafir¹⁶, E.D. Dobru^{15,17}, A. Popescu⁹, H.M. Chiu¹⁸, G. Dimofte^{1,3}, S. Sanduleanu-Dascalescu¹⁹, Heritage.Ro
¹Grigore T Popa University of Medicine and Pharmacy Iasi Romania, Iasi, Romania, ²Sf Spiridon County Clinical Emergency Hospital, Iasi, Iasi, Romania, ³Regional Oncology Institute, Iasi, Romania, ⁴Fundeni Clinical Hospital Dept. of Gastroenterology, Gastroenterology and Hepatology, Bucharest, Romania, ⁵Bucharest Emergency University Hospital, Gastroenterology, Bucharest, Romania, ⁶Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁷University Of Medicine And Pharmacy Of Craiova, Craiova, Romania, ⁸Elias Emergency Hospital Gastroenterology and Hepatology, Gastroenterology, Bucharest, Romania, ⁹Victor Babes University Of Medicine And Pharmacy, Gastroenterology, Timisoara, Romania, ¹⁰Al.I.Cuza University Iasi, Computer Science, Iasi, Romania, ¹¹Gastromed Clinic, Cluj Napoca, Romania, ¹²Floreasca Clinical Emergency Hospital Bucharest, Department of Gastroenterology, Bucharest, Romania, ¹³Bucharest Clinical Emergency Hospital, Gastroenterology and Interventional Endoscopy, Bucharest, Romania, ¹⁴Regional Institute of Gastroenterology-Hepatology "Prof.Dr. Octavian Fodor", Gastroenterology, Cluj-Napoca, Romania, ¹⁵University of Medicine, Pharmacy, Sciences and Technology "George Emil Palade" Targu Mures, Targu Mures, Romania, ¹⁶Clinical Emergency Hospital, Gastroenterology, Constanta, Romania, ¹⁷County Hospital Mures - Gastroenterology, County Hospital Mures; Targu Mures/RO, Gastroenterology, Targu Mures, Romania, ¹⁸National Taiwan University, Taipei, Taiwan, ¹⁹GROW School of Oncology and Developmental Biology, Maastricht University, Maastricht, Netherlands

Contact E-Mail Address: georgiana.gilca@gmail.com

Introduction: Early recognition and risk-targeted surveillance of patients with hereditary colorectal cancer (HCRC) and familial CRC (FCRC) reduce CRC incidence, improving in turn the effectiveness of population-based organised screening programmes. However, HCRC/FCRC often remain under-recognized and suboptimally managed and opportunities for CRC prevention are often missed. In 2020, pilot screening programmes for CRC have been started in Romania. In this context, a screening initiative for high-risk groups was started at national level, as an adjunct to population-based screening.

Here, we present our experience in setting up an interdisciplinary team as a first step in implementing a screening programme for HCRC/ FCRC with coverage across the country.

Aims & Methods: We used a stepwise approach: first, an evidence-based educational intervention was provided in order to create a national network of clinical specialists; next, implementation of this knowledge in clinical practice and setting-up of a HCRC registry. Between Nov 2022-Jan 2023, we trained clinicians from university hospitals and cancer centers covering the main administrative regions of the country, using an evidence-based online curriculum (weekly, 12 weeks, in total +/-22 hours) for achieving mastery standards (excellence for all) on the recognition and management of HCRC/FCRC. The curriculum was created by an interna-

tional panel of GI experts and education experts. The training consisted of pre-class preparation (online study of clinical guidelines, instructional videos), virtual classroom (live active learning session with case-based quizzes and targeted feedback) and post-class tutoring sessions (case-based quizzes with instructor/ peer feedback). Pretest and posttest(s) scores were measured. The main outcomes were the proportion of participants reaching the minimum passing standard (MPS) and the learning effect size. Wilcoxon signed-rank test was used to compare the differences between test scores and Cohen's d coefficients for effect size. Secondary outcome was the course satisfaction.

Results: We enrolled 20 gastroenterologists and 3 non-gastroenterologists (median 37.8 (28-58) years, 61% female, from academic (82.6%) and cancer (17.4%) centers. None received previous training in HCRC/FCRC. At baseline, none of the participants reached the MPS. At the final post-test, all participants reached/ exceeded the MPS. Median test scores significantly increased from pretest to initial posttest and final posttest: 55 (45-62)% vs 84 (82-86)% vs 91 (87-97)%, ($P < 0.0001$). The educational sessions produced a very large learning effect size compared to pretest scores (Cohen's $d = 3.91$, 95%CI=2.33-5.50). All participants expressed very high satisfaction about course participation. Immediately after the course, they implemented the acquired knowledge into practice, set up local interdisciplinary teams and continued training of their peers/ students. A 2-step approach to genetic testing was adopted in clinical practice: (universal) IHC/ MSI and in case of a dMMR tumor, targeted germline testing.

Conclusion: We launched a national screening initiative for HCRC/ FCRC as an adjunct to population-based CRC screening. Evidence-based education to achieve mastery standards on HCRC recognition was the first critical step in creating an expert working group to coordinate the performance of clinicogenetic diagnosis and targeted risk-reducing interventions. Efforts are currently underway for achieving full rollout of the training program across the country and ultimately set-up a hereditary cancer registry.

Disclosure: Nothing to disclose.

PP1205

A COMPREHENSIVE STUDY ON GASTROENTEROLOGISTS' BELIEFS, ATTITUDES, AND KNOWLEDGE OF PHYSICAL ACTIVITY AND EXERCISE

F.B. Kumbaroğlu¹, T. Düger¹, P. Özdemir², Y.H. Balaban³

¹Hacettepe University, Department of Physical Therapy and Rehabilitation, Ankara, Turkey, ²Hacettepe University, Department of Biostatistics, Ankara, Turkey, ³Hacettepe University, Department of Gastroenterology, Ankara, Turkey

Contact E-Mail Address: birguloflaz@gmail.com

Introduction: Physical inactivity is currently recognized as a global epidemic that necessitates collective action, and affects approximately 33% of the global population (1,2).

Physical inactivity is known to be a significant risk factor for several gastrointestinal diseases such as colon cancer, metabolic dysfunction-associated steatotic liver disease, and inflammatory bowel diseases (3-5).

Aims & Methods: The aim of this study was to determine the beliefs, attitudes, and knowledge levels of gastroenterologists on Physical Activity (PA), and exercise. A survey was created by researchers to assess the beliefs, attitudes, and knowledge levels of gastroenterologists regarding PA, exercise, and healthy nutrition. Exploratory Factor Analysis (EFA) was conducted to simplify the survey interpretation by reducing the number of items into sub-dimensions and assessing construct validity. The internal consistency of each factor was assessed using Cronbach's alpha. Latent class analysis was conducted to categorize gastroenterologists' responses to items, identify positive and negative attitudes classes towards each factor.

Results: The study involved 143 gastroenterologists who were residents (30%), clinicians (29%), or academicians (41%). A majority of the gastroenterologists (78%) thought they had knowledge about physical activity and exercise. Following the provided brief information, this rate increased to 93%. Based on the participants' responses, EFA identified five factors in the questionnaire: i. effectiveness of PA and exercise; ii. necessity or harm of PA and exercise; iii. barriers to recommend exercise; iv. success in behavior change in patients; v. tendency to consult a physiotherapist or dietitian. The responses to the five factors determined by EFA were categorized into two classes as positive and negative attitudes by latent class analysis (Table 1). The items showed high or satisfactory levels of internal consistency overall and for specific factors, ranging between 0.559 and 0.842. Although, 46% of the participants believed in the effectiveness of PA and exercise, 24% of them believed that PA was unnecessary or harmful. Three out of four gastroenterologists reported difficulty in prescribing exercise for patients with comorbidities. Additionally, they reported a rate of 81% for consulting their patients with a physiotherapist or a dietitian and a rate of 88% for achieving successful modification of patients' diet or exercise program. However, the reported rates for regularly or consistently seeking advice from a dietitian and physiotherapist were significantly different (respectively 36% and 76%; $p < 0.001$).

Factors	Positive attitudes N (%)	Negative attitudes N (%)
Factor 1 Effectiveness of PA and exercise	66 (46)	77 (54)
Factor 2 Necessity or harm of PA and exercise	34 (24)	109 (76)
Factor 3 Barriers to recommend exercise	109 (76)	34 (24)
Factor 4 Success in behavior change in patients	126 (88)	17 (12)
Factor 5 Tendency to consult a physiotherapist or dietitian	116 (81)	27 (19)

Conclusion: The gastroenterologists have an awareness on their lack of knowledge about lifestyle modifications, and also are willing to consult with physiotherapists, especially for the patients with comorbidities. Participation of gastroenterologists in training seminars on PA counseling and strengthening multidisciplinary collaboration may contribute to the improvement of health services.

References: 1. Kohl 3rd HW, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: global action for public health. *The Lancet*. 2012;380(9838):294-305.

2. Pratt M, Varela AR, Salvo D, Kohl III HW, Ding D. Attacking the pandemic of physical inactivity: what is holding us back? : BMJ Publishing Group Ltd and British Association of Sport and Exercise Medicine; 2020. p. 760-2.

3. Izquierdo-Gomez R, Martínez-Gómez D, Shields N, Del Rosario Ortolá-Vidal M, Rodríguez-Artalejo F, Cabanas-Sánchez V. The role of physical activity in the association between disability and mortality among US older adults: a nationwide prospective cohort study. *Geroscience*. 2024.

4. Rector RS, Thyfault JP. Does physical inactivity cause nonalcoholic fatty liver disease? *Journal of applied physiology*. 2011;111(6):1828-35.

5. Gravina AG, Pellegrino R, Durante T, Palladino G, D'Onofrio R, Mammone S, et al. Inflammatory bowel diseases patients suffer from significant low levels and barriers to physical activity: The "BE-FIT-IBD" study. *World Journal of Gastroenterology*. 2023;29(41):5668.

Disclosure: Nothing to disclose.

PP1206

EXPLORING CONTRIBUTORY FACTORS IN ENDOSCOPY-RELATED PATIENT SAFETY INCIDENTS INVOLVING DEATH AND SEVERE HARM OUTCOMES: A CONTENT ANALYSIS OF PATIENT SAFETY INCIDENT REPORTS FROM ENGLAND AND WALES USING A HUMAN FACTORS FRAMEWORK

J. Tawn¹, A. Saghir¹, D. Das², A. Chilton³, S. Kadri⁴, M.F. Peerally²
¹University of Leicester, Leicester, United Kingdom, ²University Of Leicester, Leicester, United Kingdom, ³Kettering General Hospital FT, Gastroenterology, Kettering, United Kingdom, ⁴University Hospitals of Leicester, Gastroenterology, Leicester, United Kingdom

Contact E-Mail Address: jamestawn123@outlook.com

Introduction: Patient safety incidents (PSIs) occur across healthcare and evaluating these events presents an opportunity to learn, improve work systems and prevent future harm. Patient harm related to the care of patients due to undergo endoscopy, during endoscopy or during post-endoscopy care are devastating events calling for careful systems-based analyses to explore contributory factors to improve safety. The Systems Engineering Initiative for Patient Safety (SEIPS) model provides a framework for analysing PSIs to identify contributory factors (C.Fs) across the wider healthcare system, and has been used to analyse incidents and improve patient safety across a range of settings, although it has not been used previously for incidents related to endoscopy care (1,2). A large cohort of endoscopy PSIs across England and Wales were analysed using SEIPS, focussing on cases with patient fatality or severe harm outcomes.

Aims & Methods: This study aims to identify C.Fs to endoscopy-related PSIs involving death and severe harm outcomes, reported to a national incident database across England and Wales.

PSI reports involving endoscopy-related care between January 2017 and January 2022 were obtained from the National Reporting and Learning System (NRLS) and analysed using content analysis, enriched by the SEIPS framework. Descriptive data was also reported.

Results: Of 6,971 reported endoscopy PSIs, 125 involved death and 305 involved severe harm. After exclusion of unrelated PSIs, 368 (5.3%) were analysed, spanning pre-procedure (126;34%), peri-procedure (104;28%) and post-procedure (138;38%) care. Follow-up Issues (115;31%) and known complications (109;30%) were the most frequent incident types. Content analysis was performed on 176 PSIs (48% of included PSIs with severe harm and death outcomes) with sufficient narrative data. Using SEIPS, C.Fs related to "People and Teams" were the most common (see table 1), identified 106 times (36%) across 77 (44%) incidents, with the most common subtype being 'Communication', identified 70 times across 57 incidents (32%). Organisational factors were identified 88 times (29%) across 78 (44%) incidents, with the most common being 'Resource Availability'. Task factors were identified 61 times (20%) across 52 (30%) incidents, with the most common being 'Documentation'. Technology and Tools factors were identified 23 times (8%) across 23 (13%) incidents, with the most common being 'Referral System Failures'. External environment factors were identified 13 times across 13 (4%) incidents, with the most common being 'Pandemic Disruption'. Physical Environment factors were identified 8 times (3%) across 7 (4%) incidents, with the most common being 'Out-of-hours Environment'.

SEIPS Contributory factors	References across all incidents, n (%)	Incidents, n (%)
People and Teams	106 (36%)	77 (44%)
Organisation	88 (29%)	78 (44%)
Task factors	61 (20%)	52 (30%)
Technology and tools	23 (8%)	23 (13%)
External environment	13 (4%)	13 (4%)
Physical environment	8 (2%)	7 (4%)

Conclusion: This study highlights the importance of applying a systems approach to understand the complex interplay of C.Fs in endoscopy-related PSIs resulting in severe harm or death. The SEIPS framework revealed that factors related to people and teams, organization, and tasks were the most common contributors to these incidents. Addressing these factors through targeted interventions could potentially mitigate future incidents and improve patient safety in endoscopy services.

References:

1. Carayon P, Schoofs Hundt A, Karsh B, Gurses AP, Alvarado CJ, Smith M, et al. Work system design for patient safety: the SEIPS model. *Quality & safety in health care* 2006 Dec;15(suppl 1):i50-i58.
2. Frith KH. Medication errors in the intensive care unit: literature review using the SEIPS model. *AACN advanced critical care* 2013 Oct 1;24(4):389-404.

Disclosure: This project is funded by grants from the Medical Protection Society Foundation and the Midlands Gastroenterology Society.

PP1207

THE EFFICACY OF AN E-LEARNING SYSTEM TO IMPROVE PATHOLOGICAL DIAGNOSIS OF GASTRIC CANCER: GLOBAL RANDOMIZED CONTROLLED TRIAL

T. Yao¹, K. Yao², S. Nimura³, Y. Takahashi⁴, N. Uedo⁵, T. Moriyama⁶, H. Ishikawa⁷

¹Juntendo University Graduate School of Medicine, Department of Human Pathology, Tokyo, Japan, ²Fukuoka University Chikushi Hospital, Department of Clinical Medicine Research Center, Fukuoka, Japan, ³Fukuoka University Chikushi Hospital, Department of Pathology, Fukuoka, Japan, ⁴FAST Inc, Department of Development, Tokyo, Japan, ⁵Osaka International Cancer Institute, Department of Gastrointestinal Oncology, Osaka, Japan, ⁶Kyushu University Hospital, International Medical Department, Fukuoka, Japan, ⁷Graduate School of Medical Science Kyoto Prefectural University of Medicine, Department of Molecular-Targeting Prevention, Kyoto, Japan

Contact E-Mail Address: tyao@juntendo.ac.jp

Introduction: Even if early gastric cancer is detected endoscopically, if a pathological diagnosis of cancer is not made based on biopsy tissue, there is a risk that curative endoscopic resection will not be performed, and the cancer will be left untreated until it becomes an advanced cancer.

The intramucosal component of early gastric cancer collected by biopsy often shows no signs of invasion and has low atypia, making it often difficult to determine whether it is a neoplasia or a non-neoplasia.

To solve these problems, we developed an e-learning system that improves the pathological diagnosis of gastric biopsies and evaluated its effectiveness using an Internet connection.

Aims & Methods: The design of this study was a randomized controlled trial. All tests and e-learning were conducted using the Internet. After receiving the pre-test (60 questions on biopsy tissue photos), participants were randomly assigned to either an e-learning group (E-group) or a non-e-learning group (NE-group), and only members of the E-group had access to the e-learning system.

Two months later after the pre-test, both two groups received the post-test (the same 60 questions as the pre-test). The primary endpoint was the difference in the rate of improvement in test results between the two groups.

Results: 215 pathologists from 36 countries who were assessed for eligibility were included in this study, with 106 assigned to the E-group and 109 to the NE-group. Using the test score (88.3 points) of the top 30% (34/109) of the NE-group as the cutoff value, high-ranking participants (more than

88.3 points) were 57 among 106 participants in the E-group. There were significantly more high-ranking participants in the E-group than in the NE-group ($p=0.00048$).

Conclusion: This global research demonstrated the efficacy of the developed e-learning system in improving the histopathological diagnosis of gastric cancer.

Disclosure: Nothing to disclose.

PP1208

SOCIAL MEDIA SENTIMENTS AMONG MEDICAL PROFESSIONALS: MELD 3.0 COMPARED TO MELD-NA ON TWITTER

R. Rammohan¹, S.G. Magam¹, M. Joy¹, D. Natt¹, W. Lau¹, A. Tadikonda¹, S.R. Magam¹, L. Pannikodu¹, J. Desai¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rrammoha@numc.edu

Introduction: Our study investigates healthcare professionals' sentiments, particularly among physicians, regarding the adoption of MELD 3.0 for assessing short-term survival in end-stage liver disease patients. The Model for End-Stage Liver Disease (MELD) has been a reliable measure for short-term survival. Its current version, MELDNa, includes crucial parameters such as international normalized ratio, serum bilirubin, creatinine, and sodium, vital for organ allocation in liver transplants. MELD 3.0, introduced in June 2023, enhances predictive accuracy by incorporating additional variables, including sex and serum albumin, and addresses gender disparities on the transplant waitlist.

Aims & Methods: We used the Twitter application programming interface (API), Hypertext preprocessor (PAP), and Response capture interface (RAI) to collect the response across Twitter. we conducted a Chi-Square Test for Independence to assess whether there was a significant association between the sentiment labels across the datasets. This test helped determine if the sentiments in one dataset were dependent on those in the other. Additionally, we calculated Cohen's Kappa, a measure of inter-rater agreement, to quantify the level of agreement between the datasets, considering the probability of random agreement. Lastly, we used trend analysis, visualizing sentiment distributions over time, to observe sentiment changes and patterns across different years.

Results: Between December 2019 and November 2023, we collected a total of 74,684 responses. Out of these, there were 220,980 positive, 11,710 negative, and 11,154 neutral responses for MELD 3.0. For MELD-NA, we observed 11,724 positive, 10,832 negative, and 7,164 neutral responses. Comparing MELD 3.0 to MELD-NA, we found that MELD 3.0 exhibited significantly more positive sentiments (Chi-Square: 29.68, $p < 0.01$). Additionally, there was a 15.85% sentiment agreement for MELD 3.0, with a Cohen Kappa coefficient of 0.249.

These results indicate that there is a statistically significant association between the sentiment labels in the two datasets, and there is relatively high agreement in sentiment for MELD 3.0.

Conclusion: In this study, we explored healthcare professionals' views on adopting MELD 3.0 for evaluating end-stage liver disease patients' short-term survival. MELD has been a reliable measure, with MELDNa incorporating essential parameters for organ allocation in liver transplants. MELD 3.0, introduced in June 2023, enhances accuracy and addresses gender disparities.

Using Twitter data, we found that MELD 3.0 garnered significantly more positive sentiments compared to MELD-NA. There was also a notable level of sentiment agreement, highlighting the potential acceptance and value of MELD 3.0 among healthcare professionals.

References: O'Dell HW, McMichael BJ, Lee S, Karp JL, VanHorn RL, Karp SJ. Public attitudes toward contemporary issues in liver allocation. *Am J Transplant*. 2019 Apr;19(4):1212-1217. doi: 10.1111/ajt.15227. Epub 2019 Jan 22. PMID: 30582275.

Disclosure: Nothing to disclose.

PP1209

A GLIMPSE INTO TRAINING IN BASIC DIGESTIVE ENDOSCOPY: A NATIONAL CROSS-SECTIONAL E-SURVEY FROM THE ITALIAN ASSOCIATION OF YOUNG GASTROENTEROLOGISTS AND ENDOSCOPISTS

F. Borrelli de Andreis^{1,2}, M. La Marca³, P. Apolito⁴, L. Frazzoni⁵, D. Paduano⁶, L.R. Lopetuso⁷, C. Petruzzellis⁸, AGGEI Endoscopy Study Group

¹Gemelli Isola - Isola Tiberina Hospital, Centre of Excellence of Gastrointestinal and Metabolic Disorders, Rome, Italy, ²Università Cattolica del Sacro Cuore, Rome, Italy, ³AUSL Romagna Infermi Hospital Rimini, Rimini, Italy, ⁴Gastroenterology and Interventional Endoscopy Unit, AUSL Bologna, Surgical Department, Bologna, Italy, ⁵S.Orsola-Malpighi Hospital, Department of Medical and Surgical Sciences, Bologna, Italy, ⁶Gastrointestinal Endoscopy Unit, Humanitas Mater Domini, Castellanza, Italy, ⁷Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Medical and Surgical Sciences, Rome, Italy, ⁸Arnas Garibaldi Nesima Hospital, Internal Medicine, Gastroenterology, Digestive Endoscopy, Catania, Italy

Contact E-Mail Address: federica.bda@gmail.com

Introduction: Gastrointestinal (GI) endoscopy demands complex cognitive and practical skills. Yet, the landscape of training in this field remains heterogeneous and often lacks standardisation, with an absence of data specific to training practices within Italy.

Aims & Methods: This study aims at elucidating the current practices and perceptions of basic GI endoscopy training among Italian trainees. A national cross-sectional e-survey was conducted between November 2023 and April 2024. Participants were recruited from the Italian Association of Young Gastroenterologists and Endoscopists (AGGEI). The e-survey included questions regarding demographics, training experiences, perceived proficiency levels, and opinions on current training programs and resources. Descriptive and inferential statistical analysis was finally performed to identify trends and disparities based on gender.

Results: A total of 108 (M:F 63:45, 0 non-binary) GI endoscopy trainees out of 788 (13.7%) AGGEI members responded to the e-survey. Among them, 63 (58.3%) were under 30 years old with a majority (73,67.6%) working in university hospitals, being all gastroenterology residents. 49(45.4%) and 41(38%) started endoscopy during their second or third year of residency, respectively. 44(40.7%) spent 30-40 hours per week in the endoscopy room. A significant portion (61,56.6%) lacked a designated endoscopy mentor, while those who had one reported daily meetings (29,55.8%). Regarding the consistency of teaching among different instructors or mentors, 50(46.3%) perceived variability, 39(36.1%) moderate consistency, and only 11(10.2%) very high consistency, though most respondents (44,40.7%) preferred a standardised approach. 96(88.9%) responders attended a GI endoscopy observership before performing procedures, with 48(44.4%) finding this beneficial. Colonoscopy practice typically began concurrently with esophagogastroduodenoscopies (EGDs), with over half starting at least 20 procedures per week for both EGDs and colonoscopies. Only 16(14.8%) completed a core curriculum in more than 75% of the procedures. On a 5-point scale, confidence in cognitive skills was rated 4 by 42(48.9%) and 5 by 15(13.9%), while confidence in motor skills was rated 4 by 37(34.3%) and 5 by 21(19.4%). Most programs did not include

simulators (85,78.7%), though 27(39.7%) participants considered the simulation-based training helpful, particularly for beginners. Competence in endoscopy was primarily assessed based on trainers' subjective opinion (47,43.5%) or a minimum number of completed procedures (35,32.4%), with only 8(7.4%) using skill assessment tools. 45(41.7%) responders received training in performing urgent endoscopy procedures, while 26(24.1%) reported that advanced procedures were not included in their training.

Overall, the endoscopy training programs were rated as excellent by 19(17.6%), very good by 37(34.3%), and good by 46(42.6%), with only 6(5.6%) rating them as fair. Additionally, no statistically significant differences between males and females were observed for any of the variables considered.

Conclusion: This national e-survey highlights the heterogeneous scenario of basic GI endoscopy training among young gastroenterologists and endoscopists in Italy. The findings underscore the need for enhanced standardisation and structured training pathways to ensure consistent competency levels across trainees. Investment in simulation-based training and the development of standardised curricula may serve to address existing gaps and optimise the quality of endoscopic training programs.

References:

1. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res*. 2004 Sep 29;6(3):e34. doi: 10.2196/jmir.6.3.e34.
2. Antonelli G, Voiosu AM, Pawlak KM et al. Training in basic gastrointestinal endoscopic procedures: a European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) Position Statement. *Endoscopy*. 2024 Feb;56(2):131-150. doi: 10.1055/a-2205-2613. Epub 2023 Dec 1.

Disclosure: Nothing to disclose.

PP1210

EQUITY IN HEALTHCARE: EXPLORING RACIAL AND ECONOMIC DISPARITIES IN COLONOSCOPY PREPARATION

R. Rammohan¹, S.G. Magam¹, M. Joy¹, D. Natt¹, W. Lau¹, A. Tadikonda¹, S.R. Magam¹, L. Pannikodu¹, J. Desai¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: dnatt@numc.edu

Introduction: The impact of race, socio-economic status, and insurance on colonoscopy preparation is a critical aspect of understanding healthcare disparities. Colonoscopy, essential for colorectal cancer detection and prevention, demonstrates varied effectiveness across different demographics.

This study aims to explore how these factors influence the quality of colon prep, a vital step in the procedure. By examining the interplay between race, socioeconomic background, and insurance coverage, we can uncover potential disparities in patient outcomes. Such insights are crucial for healthcare providers and policymakers to ensure equitable access to effective screenings, thereby enhancing the success rates of colonoscopies in diverse populations.

Aims & Methods: Colonoscopy records from 2010-2023 were retrospectively collected. Data included colonoscopy report, Gender, Race, Poor Colon Prep quality, socioeconomic status, and Insurance status. Chi-squared tests were conducted to identify statistically significant associations between poor colon prep outcomes and categorical variables: race, socioeconomic status, and insurance status. A Logistic Regression analysis was carried out to assess the combined impact of multiple fac-

tors on poor colon prep. The results were interpreted based on p-values, coefficients, and confidence intervals obtained from statistical tests. The significance level was set at 0.05 for all tests.

Results: A total of 3330 who underwent colonoscopy between 2010-2023 were included in the study group, of which 2135 (64%) were female. The racial distributions were 807 (24.2%) Hispanics, 1665 (48%) white, 501 (15%) Blacks, 232 (6%) Asians, 129 (3%) Others. Race significantly impacts poor colon prep outcomes (Chi-sq. 40.78, p-value <0.01). Low Socioeconomic status is also significantly linked to poor prep (Chi-sq. ≈ 20.86, p-value ≈ 0.00011). Patients with no Insurance were statistically associated with poor colon prep (Chi-sq. ≈ 15.48, p-value ≈ 0.000083). Logistic regression, suggested insurance status as potentially influential (coefficient ≈ -0.2140, p-value ≈ 0.068). The model's pseudo-R-squared value was 0.003725.

These findings stress the importance of considering demographic and socio-economic factors in colonoscopy patient management, acknowledging study limitations like dataset scope and model explanatory power.

Conclusion: Our study on race and colonoscopy preparation reveals significant disparities in colon prep quality among racial groups influenced by socio-economic status and insurance coverage. The study finds race, low socio-economic status, and lack of insurance significantly affect colon prep outcomes. While acknowledging its limitations, this study emphasizes the need for healthcare professionals and policymakers to consider these demographic factors, aiming for equitable colorectal cancer screening and prevention.

References: 1. Millien VO, Mansour NM. Bowel Preparation for Colonoscopy in 2020: A Look at the Past, Present, and Future. *Curr Gastroenterol Rep*. 2020 May 6;22(6):28. doi: 10.1007/s11894-020-00764-4. PMID: 32377915.

Disclosure: Nothing to disclose.

PP1211

EXAMINING THE INTERPLAY BETWEEN RACE, GENDER, AND GASTRIC INTESTINAL METAPLASIA IN CANCER DEVELOPMENT

R. Rammohan¹, S.G. Magam¹, M. Joy¹, D. Natt¹, S.R. Magam¹, L. Pannikodu¹, A. Tadikonda¹, J. Desai¹, P. Mustacchia¹

¹Nassau University Medical center, Department of Gastroenterology, East Meadow, United States of America

Contact E-Mail Address: rrammoha@numc.edu

Introduction: The impact of race and gender on the development of gastric cancer among patients with gastric intestinal metaplasia is a complex and multifaceted issue. While gastric intestinal metaplasia is a precursor to gastric cancer, studies suggest that race and gender may play significant roles in influencing the progression of this condition to malignancy. Understanding the interplay between these factors is essential for developing targeted prevention and intervention strategies to reduce the burden of gastric cancer within diverse populations.

Aims & Methods: Our retrospective study, spanning 2009-2023, included all Gastric intestinal metaplasia patients. We collected data on comorbidities, Gastric cancer incidence, Gender, race insurance, and socioeconomic factors CPT and ICD codes. we employed logistic regression and Chi-square testing to analyze the impact of race and gender on the incidence of gastric cancer. Logistic regression was used to ascertain the statistical significance and effect size of race and gender on the likelihood of gastric cancer.

The logistic regression model's findings were further explored through a Chi-square test of independence, which evaluated the association between race and gastric cancer across different racial groups. The results were visually represented through a bar graph, illustrating the predicted probabilities of gastric cancer by race, enhanced with the model's overall p-value for the race variable.

Results: A total of 378 patients diagnosed with gastric intestinal metaplasia were included in the study, of which 72 patients developed gastric cancer in 14 years. 38 (51.3%) patients were female. Among the races 24(33%) Asians, 16(21.6%) Hispanics, 14(19%) Whites, 20 (27.7%) African American. Logistic regression revealed that race has a statistically significant association with the incidence of gastric cancer ($p < 0.001$), with the odds of gastric cancer increased in Asians (Coefficient: 0.68, $p < 0.05$). In contrast, gender did not show a significant impact ($p = 0.847$). Further examination using a Chi-square test confirmed a significant association between race and gastric cancer (Chi-square = 37.83, $p < 0.001$).

Conclusion: In conclusion, our study underscores the intricate relationship between race and the development of gastric cancer in patients with gastric intestinal metaplasia. The findings reveal a significant association between race, particularly among Asians, and an increased likelihood of gastric cancer. However, gender did not demonstrate a significant impact in our study cohort. These results emphasize the importance of tailored interventions and screenings for at-risk populations, considering the role of race in gastric cancer progression. Further research is needed to delve deeper into the underlying mechanisms of these disparities and to develop more targeted prevention strategies.

References: Rubio CA, Befrits R. Gastric intestinal metaplasia. *J Clin Pathol*. 2004 Aug;57(8):894-5. doi: 10.1136/jcp.2003.015370. PMID: 15280418; PMCID: PMC1770388.

Disclosure: Nothing to disclose.

PP1212

WHAT DO PATIENTS WITH INFLAMMATORY BOWEL DISEASE KNOW ABOUT THEIR PATHOLOGY?

C. Garcia¹, M.A. Rafael¹, F. Bordalo Ferreira¹, L. Martins Figueiredo¹, J. Carvalho e Branco¹, L.C.C. Lourenço¹, A.M. Oliveira¹, A. Martins¹, L. Brazao Almeida Santos¹

¹Hospital Prof. Doutor Fernando Fonseca, Gastroenterology, Lisbon, Portugal

Contact E-Mail Address: catealmeidag@hotmail.com

Introduction: Shared decision-making is defended as an ideal model in the management of patients with chronic pathology, namely inflammatory bowel disease (IBD).

The objective of this study was to identify knowledge gaps in IBD population, as well as correlate with patient demographic and sociocultural factors, to implement strategies aimed at improving care provision and patient empowerment.

Aims & Methods: Application of a survey to patients with IBD under biological therapy in a Day Hospital, from March 4th to 22nd 2024, and subsequent descriptive analysis.

Results: Out of the 102 patients with IBD (65% Crohn's Disease, 31% Ulcerative Colitis), 53% were men and 47% women, the majority of whom are Portuguese up to 50 years of age, with at least secondary education. The majority obtains information through health professionals and the Internet. The self-assessment of knowledge was higher than the demonstrated knowledge (90% consider themselves to be informed). The majority prefers to obtain oral information from health professionals or information leaflets (although only 50% had received information leaflets prior to starting biologics).

The population over 50 years old, with a lower level of education and diagnosed more than 2 years ago, tends to have important knowledge gaps. 46% are unaware what medication can worsen the disease and 24% are unaware of the impact of tobacco. 56% of patients believe that a restrictive diet should be preferred, with 59% never being evaluated by a nutritionist, although 63% have already discussed this topic with their

doctor. 85% of women are unaware of the implications of IBD on fertility, pregnancy and breastfeeding, particularly the population under 30 years of age and with a lower level of education.

Conclusion: The application of a survey across IBD population under biological therapy allowed to detect important gaps in the transmission of information adapted to each patient and identify key points to be optimized during the medical appointment or in dedicated Nursing and Nutrition appointments.

References: 1. Xu D, Zhang H, Chen Y. Patients' views of shared decision making in inflammatory bowel disease: a survey in China. *BMC Med Inform Decis Mak*. 2021 Dec 6;21(1):340. doi: 10.1186/s12911-021-01702-8. PMID: 34872536; PMCID: PMC8650369.

2. Al Khoury, A., Balram, B., Bessissow, T. *et al*. Patient Perspectives and Expectations in Inflammatory Bowel Disease: A Systematic Review. *Dig Dis Sci*, 1956–1974 (2022). <https://doi.org/10.1007/s10620-021-07025-y>

3. A.F.A. Neto, P.M.N. Figueiredo, C. Correia. Patient Empowerment in Inflammatory Bowel Disease– Regarding Shared Decision-Making in the Treatment of IBD. *Revista Portuguesa de Coloproctologia*. Maio/Agosto 2022.

4. Song K, Wu D. Shared decision-making in the management of patients with inflammatory bowel disease. *World J Gastroenterol*. 2022 Jul 14;28(26):3092-3100. doi: 10.3748/wjg.v28.i26.3092. PMID: 36051346; PMCID: PMC9331519.

Disclosure: Nothing to disclose.

PP1213

IMPACT OF AN ONLINE MICROBIOTA EDUCATION PROGRAM ON HEALTHCARE PROFESSIONALS' KNOWLEDGE

A. Gimenez¹, B. de Alarcón-Gómez¹, I. Sibuet¹, D. Clape¹
¹Xpeer MedEd SL, Barcelona, Spain

Contact E-Mail Address: alicia@xpeer.app

Introduction: While there is increasing awareness of the importance of microbiota education for healthcare professionals (HCPs), there is variability in the extent of coverage and accessibility of educational resources across different settings and regions.

Aims & Methods: We aimed to evaluate the effectiveness of an online educational program with the learning objectives to understand the critical role of gut microbiota (GM) in health and disease, recognize its significance across the lifespan, and apply evidence-based approaches to clinical practice.

We implemented an enduring on-demand continuing medical education (CME) program consisting of 6 independent 1-hour courses. It is accessible on an EACCME®-accredited CME platform and is delivered by expert faculty in a video micro-learning format, available in 7 languages.

After each course, learners completed an evaluation survey and a 10-question multiple-choice test. AI-based analysis was conducted on survey responses to identify learners' intention to change. A pre- vs post-assessment model, using 3 multiple-choice questions per course, was employed to evaluate educational effectiveness, with statistical analysis conducted using a paired samples t-test and Cohen's d with correction to estimate effect size. Data collection spanned from the program launch in July 2021 through April 2024.

Results: 5,216 learners from 118 countries enrolled in the program, primarily physicians (led by gastroenterologists, and followed by family medicine and general practice), with nurses also represented.

Evaluation survey ratings (n=1195) indicated high levels of satisfaction, with scores of 4.5/5 for 'Fulfillment of expected learning outcomes,' 4.6/5 for 'Usefulness for professional activity,' and 4.6/5 for 'Scientifically based and balanced information.'

91% of participants agreed to implement the learnt information in their practice. We identified the following common themes reflecting intentions to change after completing the courses:

Patient education (use of probiotics, treatment expectations, importance of GM for health)

Enhanced management of gastrointestinal conditions such as irritable bowel syndrome

More cautious use of antibiotics

Greater emphasis on maternal and child health (breastfeeding, use of probiotics)

More active probiotics incorporation in daily clinical practice

More careful probiotic selection (strain specificity, individual patient needs)

Across the program, participants achieved an average of 77% correct responses in the multiple-choice test, with 70.41% correctly answering at least 80% of questions. Analysis of pre- and post-course assessments (n=224; collected Feb-April 2024), showed that the average percentage of correct answers increased from 54.8% at the baseline (pre-course tests) to 73.0% in the post-course tests ($p < 0.001$), and revealed a moderate educational impact, with a Cohen's d of 0.59. The percentage of learners who correctly answered all three questions in a course increased from an average of 19.9% at the baseline to 42.1% in the final assessment.

Conclusion: The comprehensive online microlearning-based program saw significant participation from a global audience, attracting not only gastroenterologists but also a diverse range of HCPs. Our data revealed significant improvements in clinicians' knowledge, and intentions to change patient care practices. These findings support the need to update and extend such CME activities to ensure that HCPs are well-equipped to understand and address the role of microbiota in patient care.

Disclosure: Nothing to disclose.

PP1214

WHAT MOTIVATES MEDICAL INTERNS TO PURSUE IN GASTROENTEROLOGY? A MULTICENTRIC CROSS-SECTIONAL STUDY

A. Achemlal¹, S. Berrag¹, C. Haddad Hachimi¹, S. Azammam¹, M. Amine¹, S. Oualaalou¹, S. Ouahid¹, R. Laroussi¹, N. Fouad¹, T. Adioui¹, M. Tamzaourte¹

¹Mohamed V Military Training Hospital, Gastro Enterology 1, Rabat, Morocco

Contact E-Mail Address: achemlal.amine@gmail.com

Introduction: Gastroenterology (GE) is a medical discipline that studies all diseases of the digestive system. It comprises several areas of study and offers a large variety of sub-specializations: proctology, interventional endoscopy or even digestive oncology. The decisive elements in the choice of this specialty vary among interns. The aim of our study is to determine the various factors influencing the choice of gastroenterology as a specialty among medical interns.

Aims & Methods: This is a cross-sectional, multicentric, survey-type study, conducted from September 1 to 30, 2023, involving 7 national medical faculties. All medical interns, regardless of sex or age, participated in our study.

An electronic survey with 29 items was created using Google Forms®. It was divided into two parts: the first part contained 13 questions on socio-demographic characteristics and exposure to GE during the academic curriculum, while the second part concerned the factors motivating the choice or not of GE as a specialty.

A statistical analysis using the Fisher's exact test was performed. P values of < 0.05 were considered statistically significant. Data were analyzed using Jamovi (Version 2.3).

Results: A total of 329 responses were collected: the majority were women 208 (63.2) with a F/M sex ratio of 1.7 and a median age of 27 [25; 28] years. The majority had already completed a GE rotation during their training course n=205 (62.3), of which 90 (44.1) had found it "satisfactory". More than half of the participants n= 178 (54.1) had already considered GE as a future specialty, and this choice was mostly made during GE lectures given in medical school n= 66 (36.9). Among those who had never considered GE, the main reasons were lack of interest in the specialty, the fact that it is a medical specialty, lack of information about GE, potential remuneration, and dissatisfaction with GE rotation during the training course (59.2%, 28.9%, 13.9%, 10.4% and 10% respectively).

Among those who finally opted for GE, the majority were women (70.2% vs. 29.8%, $p=0.004$). Satisfaction with the GE rotation during the training course had an impact on the final choice: "satisfactory" vs. "mediocre" (43.8% vs. 6.3% $p=0.009$).

Multivariate analysis showed that early interest in fields such as endoscopy (OR= 4.46, CI95%: 1.44-13.78, $p=0.009$) or proctology (OR= 4.26, CI95%: 1.01-18.01, $p=0.05$) increased the chance of choosing GE.

Conclusion: This study showed that there is a gender disparity in the choice of GE as a specialty. The fact that it is a medical discipline may lead men to choose another path. Our study also highlighted the importance of GE training courses during the medical curriculum to motivate interns to join our specialty, as well as the need to spotlight certain areas such as endoscopy or proctology.

Disclosure: Nothing to disclose.

PP1215

ASSESSING ENDOSCOPIC TRAINING IN GASTROENTEROLOGY FELLOWSHIPS: A MULTICENTRIC CROSS SECTIONAL PILOT STUDY

A. Achemlal¹, N. Fouad¹, S. Ouahid¹, S. Azammam¹, M. Amine¹, S. Oualaalou¹, C. Jioua¹, B. Yannick¹, R. Laroussi¹, A. Touibi¹, T. Adioui¹, M. Tamzaourte¹

¹Mohamed V Military Training Hospital, Gastro Enterology 1, Rabat, Morocco

Contact E-Mail Address: achemlal.amine@gmail.com

Introduction: Gastroenterology is a medical specialty that includes several areas of study. Endoscopy occupies a central role in professional practice, whether in hospitals or in the private sector. The quality of initial training and the different needs of trainees are key to the quality of care delivered to the population. This study aims to assess endoscopic training experience during fellowship.

Aims & Methods: This is a cross-sectional, multicenter study conducted on gastroenterology residents practicing endoscopy and in the final phase of their curriculum (6th, 7th and 8th semesters). Postgraduated doctors have been excluded from the study. An electronic survey made by Google Forms and was sent nationwide on January 9, 2024. The survey consisted of 42 questions divided into 3 parts:

The first part focused on the participants' socio-demographic data and their endoscopic experience, the second part focused on the quality of training of core endoscopic skills (cognitive and motor skills) during fellowship where a 5-point Likert scale was used to express residents' satisfaction with their skills, ranging from 1="very dissatisfied", 2="dissatisfied", 3="neither satisfied nor dissatisfied", 4="satisfied" and 5="very satisfied".

The third part included questions in which participants expressed their needs and expectations for improving their training in endoscopy.

A statistical analysis using the Student-t test and the Fisher's exact test were performed. P values of < 0.05 were considered statistically significant. Data were analyzed using Jamovi (Version 2.3).

Results: We were able to collect data from 56 respondents. Most were female residents $n=40$ (71.4) with a mean age of 29.2 ± 2.5 years. The majority of fellows started practicing EGD in their 4th semester (91.1%), and colonoscopy in their 6th semester (57%). On average, the fellows are supervised by 5 senior doctors, including 2 who practice interventional endoscopy.

Furthermore, 37.5% of participants report performing approximately more than 100 EGDs, 14.2% more than 100 colonoscopies, 80.4% report that they have performed less than 20 endoscopic variceal ligation and 14.3% have performed more than 10 polypectomies. An average rating score of 3.34 (1= very dissatisfied; 5= very satisfied) concerning the quality of training and feedback on cognitive aspects of endoscopy was found and we reported greatest emphasis for Procedure indication/contraindication and least on Capsule endoscopy interpretation.

The quality of training in technical aspects of endoscopy was rated higher (average rating score of 3.5). We reported greatest emphasis for Withdrawal/mucosal inspection and least on Esophageal dilation.

A significant association between motor skills and cognitive skills was found with a $p<0.001$.

Finally, to improve their training, 87.5% of respondents considered simulation to be important/very important, 98.2% of respondents intend to complete their endoscopy training at the end of their curriculum, and 87.5% are prepared to finance such a project (median: 1000 USD [1000;3000]).

Conclusion: Despite a significant improvement in training sites and technical facilities, training in endoscopy in healthcare institutions does not yet provide all the cognitive and technical skills required to enable fellows to be fully autonomous.

With the development of endoscopic procedures, it seems essential for fellows to be able to perform more standard endoscopic procedures such as polypectomy and mucosectomy by the end of their curriculum. This may involve introducing regular endoscopy conferences and simulation training as a part of the curriculum.

Disclosure: Nothing to disclose.

PP1216

ASSESSING THE IMPACT OF A STRUCTURED CAPSULE ENDOSCOPY TRAINING PROGRAM USING A NEW VALIDATED ASSESSMENT TOOL

T. Lima Capela^{1,2,3}, J. Carlos Goncalves^{1,2,3}, A.I. Ferreira^{1,2,3}, V. Macedo Silva^{1,2,3}, C. Macedo^{1,2,3}, C. Arieira^{1,2,3}, S. Xavier^{1,2,3}, T. Cúrdia Gonçalves^{1,2,3}, P.B. Carvalho^{1,2,3}, F. Dias de Castro^{1,2,3}, J.L.T.M. Magalhães^{1,2,3}, B. Rosa^{1,2,3}, M.J. Moreira Basto^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Gastroenterology Department, Hospital da Senhora da Oliveira, Unidade Local de Saúde do Alto Ave, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: There is scarce evidence regarding the impact of capsule endoscopy (CE) training programs.

Aims & Methods: We aimed to develop and validate a simple capsule endoscopy (CE) training assessment tool, the Capsule Endoscopy Training Assessment (CETA), and prospectively use it to analyze the learning progression achieved by participants in our CE training program.

Over a 3-year period, all participants in our CE training program completed pretraining and posttraining CETA, ranging between 0-100%, and encompassing theoretical questions and interpretation of segmented CE videos. We compared the mean differences in overall, theoretical, and practical pretraining-posttraining CETA and assessed the influence of pre-

vious endoscopic experience (upper gastrointestinal endoscopy [UGE], colonoscopy, device-assisted enteroscopy [DAE] and CE) using generalized linear models.

Results: Fifty-seven participants were included. After training, there was a significant increase in participants' overall (mean difference, 26.3; 95% confidence interval [CI], 20.70 to 31.83), theoretical (mean difference, 27.2; 95% CI, 19.81 to 34.57), and practical (mean difference, 25.9; 95% CI, 20.09 to 31.63) CETA components.

Compared to those without experience, participants with previous experience with these techniques had higher overall pretraining CETA (UGE, mean difference, 15.8; 95% CI, 5.79 to 25.75; colonoscopy, mean difference, 12.5; 95% CI, 2.35 to 22.65; DAE, mean difference, 14.2; 95% CI, 3.92 to 24.54, CE, mean difference, 16.3; 95% CI, 8.72 to 23.93), lower mean difference between overall pretraining and posttraining CETA (UGE, rate ratio, 0.76; 95% CI, 0.63 to 0.91; colonoscopy, (rate ratio, 0.80; 95% CI, 0.67 to 0.9; DAE, (rate ratio, 0.84; 95% CI, 0.73 to 0.97; CE, rate ratio, 0.81; 95% CI, 0.72 to 0.92, respectively) but not significantly different overall post-training CETA.

Conclusion: CETA is a valid and useful tool in assessing the learning progression achieved by participants after CE training program. We demonstrated a significant improvement in participants' CETA after training, being the least experienced participants in endoscopic procedures who benefited the most from CE training.

Disclosure: Nothing to disclose.

PP1217

UNVEILING CHATGPT'S LIMITATIONS IN EUROPEAN BOARD OF GASTROENTEROLOGY AND HEPATOLOGY EXAM: INCONSISTENCIES AND CHALLENGES IN COMPLEX MEDICAL REASONING

C. Simsek¹, P. Vanek², I.N. Sendur¹, C. Hassan³, H. Heinrich⁴
¹Hacettepe University, Division of Gastroenterology, Hepatology and Endoscopy, Ankara, Turkey, ²Palacký University Olomouc, 2nd Department of Medicine - Gastroenterology and Geriatrics, Olomouc, Czech Republic, ³Humanitas University, Gastroenterology, Rome, Italy, ⁴Clarunis Universitäres Bauchzentrum, Gastroenterology, Basel, Switzerland

Contact E-Mail Address: cemgsimsek@gmail.com

Introduction: The integration of artificial intelligence (AI) in medicine has the potential to revolutionize healthcare. Exams, such as the European Board of Gastroenterology and Hepatology (EBEGH) exam, are currently the gold standard for assessing medical competency and provide credentialing across several EU countries. This study evaluates the performance of ChatGPT in the high-stakes EBEGH exam by assessing its strengths and limitations in managing complex medical content, focusing on its ability to handle various question types, cognitive task demands, and subspecialty domains.

Aims & Methods: Utilizing a dataset of 200 EBEGH study questions, we analyzed ChatGPT4's performance across question complexity, cognitive task demands, subspecialty domains, and patient-centeredness. The dataset ensured the same number of questions and a balanced representation of subspecialties and focused on textual questions, excluding visual questions. Each question was asked to the model 5 times, with the most frequent answer selected as the final response.

A suitable prompt for the task was used for all questions. Logistic regression, ANOVA, and chi-square tests investigated the impact of these factors on the AI's likelihood of correct responses, performance variance, and categorical data associations. Krippendorff's Alpha evaluated ChatGPT4's precision in replicating responses across multiple iterations. The study questions were categorized based on cognitive task complexity using

Bloom's taxonomy, and the evidence base supporting each question was copied from the question bank reference. The model's performance was further analyzed in relation to the interdisciplinary nature of the questions and procedural knowledge requirements.

Results: ChatGPT correctly answered a mean of 67.5% (n=135, range 121-142) of the questions, with performance significantly influenced by question complexity. Low complexity cases significantly increased the odds of correct responses by 3.87 times, (p=0.001), while medium complexity cases showed a similar trend by 2.82 times (p=0.013). Non-patient-centered questions significantly decreased the odds of correct answers (OR=0.30, p=0.030). The model demonstrated inconsistency in replicating responses (Krippendorff's Alpha=0.00219).

Questions requiring higher cognitive tasks, such as analysis and evaluation, posed significant challenges for the model (p<0.01). The AI's performance was not significantly influenced by the interdisciplinary nature of the questions or the requirement for procedural knowledge.

Conclusion: While ChatGPT effectively handles simpler queries, its performance in complex, specialized medical testing scenarios, such as EBEGH exams, is currently limited. The AI's performance varies across specialties, question types, and cognitive task demands, and it demonstrates inconsistency in replicating responses.

These findings underscore the need for a cautious and nuanced approach to integrating AI in high-stakes medical examinations, particularly in domains requiring deep understanding and patient-centered considerations. The EBEGH exam's ability to effectively challenge ChatGPT demonstrates its value as a robust tool for evaluating medical knowledge and expertise.

Disclosure: Nothing to disclose.

PP1218

AN INNOVATIVE INTERPROFESSIONAL APPROACH TO THERAPEUTIC DRUG MONITORING OF CARBAPENEMS IMPROVES QUALITY OF CARE IN THE TREATMENT OF PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE ON THE INTENSIVE CARE UNIT

S. Schmid¹, K. Zimmermann¹, C. Koch¹, A. Mehrl¹, V. Pavel¹, S. Schlosser-Hupf¹, M. Müller-Schilling¹, A. Kratzer²

¹University Hospital Regensburg, Department of Internal Medicine I, Regensburg, Germany, ²University Hospital Regensburg, Hospital Pharmacy, Regensburg, Germany

Contact E-Mail Address: Stephan.Schmid@ukr.de

Introduction: Acute-on-chronic liver failure (ACLF) is a severe complication in patients with liver cirrhosis, often escalating rapidly and requiring urgent interventions. Meropenem, an important antibiotic for treating severe infections, necessitates accurate dosing to be effective and safe.

Aims & Methods: In this study aims the impact of implementing therapeutic drug monitoring (TDM) for meropenem in ACLF patients in an intensive care unit (ICU) with an innovative interprofessional approach was assessed.

An interprofessional team of physicians, hospital pharmacists, and staff nurses collaborated to optimize meropenem therapy through TDM. Meropenem was administered via continuous infusion following an initial loading dose, with serum levels monitored twice weekly using high-performance liquid chromatography (HPLC). The evaluation metrics included serum meropenem concentrations, compliance with the interprofessional team's recommendations, and total consumption of the antibiotic.

Results: The initial TDM results showed a mean meropenem serum concentration of 20.9 ± 9.6 mg/L. Of note, only 16.0% of the patients had serum concentrations within the designated target range, while 84.0% exceeded it. Follow-up measurements in Week 2 and Week 3 showed improved targeting, with average concentrations of 15.2 ± 5.7 mg/L and

11.9 ± 2.3 mg/L, respectively. By Week 2, 41.7% of patients were within the target range, and by Week 3, this increased to 50%. The advice of the interprofessional team was fully implemented.

Furthermore, there was a notable reduction in meropenem usage: from 42.1 RDD/100 patient days in the preceding period to 37.9 RDD/100 patient days during the study, marking a 10.0% decrease in application density.

Conclusion: The introduction of an interprofessional TDM approach for meropenem in patients with ACLF significantly improved dosing of carbapenems. Our innovative interprofessional approach brought serum levels within desired ranges more effectively and managed to reduce overall meropenem consumption.

The study underscores the value of innovative collaborative, interprofessional efforts in optimizing drug therapy, particularly in complex ICU settings, enhancing patient safety and treatment efficacy.

Disclosure: Nothing to disclose.

PP1219

THE IMPACT OF GASTROINTESTINAL ENDOSCOPIES ON MUSCULOSKELETAL DISORDERS

L. Bugeja¹, P. Ellul², M. Thoufeeq³, A. Muruganathan⁴, S. Chetcuti Zammit⁵

¹Mater Dei Hospital, Malta, Gastroenterology, Attard, Malta, ²Mater Dei Hospital, Mater Dei Hospital, Msida, Malta, ³Sheffield Teaching Hospitals, Endoscopy, Sheffield, United Kingdom, ⁴Royal Wolverhampton NHS Trust, New Cross Hospital Site, Wolverhampton, United Kingdom, ⁵Mater Dei Hospital Malta, Gastroenterology, Msida, Malta

Contact E-Mail Address: luke.bugeja.1@gmail.com

Introduction: Musculoskeletal (MSK) injuries are frequent occupational hazards amongst endoscopists, partly attributed to the physically demanding nature and prolonged durations of endoscopic procedures. Understanding the prevalence and patterns of these injuries is crucial to improve the endoscopist's occupational health by implementing appropriate preventive strategies.

Aims & Methods: Aim: The primary aim of this study was to determine the prevalence and distribution of MSK injuries among endoscopists. Endoscopists from across the world were surveyed regarding the types and frequencies of procedures they perform to evaluate the prevalence of MSK injuries among endoscopists with varying procedural type and frequency. The secondary aim was to investigate whether additional factors, such as exercise habits during adulthood and adolescence and the endoscopy environment, influence the frequency of reported MSK injuries.

Method: An international questionnaire-based study was conducted among endoscopists practising in numerous healthcare centres. Data gathered included the frequency and localisation of injuries, type of endoscopic procedures carried out, access to occupational health (OH) and ergonomics of the endoscopy theatre.

Additionally, the study explored the potential impact of past and present exercise practice during adulthood and adolescence on the prevalence of MSK injuries.

Results: 174 endoscopists participated in this study, from 25 countries. The most commonly reported MSK complaints were back, neck, shoulder and hand pain (Table 1).

Endoscopists' experience was as follows; 32.2% -0-5 years, 46% -5-20 years and 21.8% -20 years of experience. Only 35.1% of participants had formal training on scope handling at the start of training.

Percentage of endoscopists reporting pain	
Back Pain	23.6%
Neck Pain	19.5%
Shoulder Pain	16.0%
Hand Pain	14.9%
Thumb Pain	13.2%
Hip Pain	7.4%
Elbow Pain	6.7%
Finger Pain	5.1%

Table 1: Pain in endoscopists.

Participants reported to use 1, 2, 3 and 4 monitors respectively during endoscopy sessions: 37.9%, 56.0%, 4.6% and 0.6%. 75.9 % of participants ensure that their screen is at eye level during endoscopies, whilst 75.3% ensure that the monitor is the right distance away.

23% of participants stated that they have had a formal diagnosis of an occupation related injury or have been reviewed by a physiotherapist / orthopaedic surgeon because of an endoscopy related injury. In contrast, only 13.2% of patients have reported their occupational injury to OH services.

51.1% of participants have had MSK injuries that they think are attributable to current endoscopy practices. However, only 13.2% have sought help from the OH team. 74% of these felt they were supported by the OH team.

10.9% of participants have been diagnosed with osteoarthritis or an inflammatory arthropathy, unrelated to work.

Conclusion: This study provides a valuable insight into the relationship between endoscopic procedures and the occurrence of MSK injuries among endoscopists, offering opportunities for prevention to safeguard the health of endoscopists and to encourage them to seek help for such injuries.

Disclosure: The authors declare they have no conflict of interest.

PP1220

TOWARDS GREENER ENDOSCOPY: IMPACT OF A SUSTAINABILITY INTERVENTION ON ENDOSCOPIC WASTE CARBON FOOTPRINT

M. Dias Blanco¹, S. Lopes², S. Costa³, J.A. Cunha Neves⁴
¹NOVA National School of Public Health, NOVA University Lisbon, Lisboa, Portugal, ²NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisboa, Portugal, ³Unidade Local de Saúde Santa Maria, Gastroenterology, Lisboa, Portugal, ⁴Unidade Local de Saúde do Algarve, Gastroenterology, Portimão, Portugal

Contact E-Mail Address: joaoacunhaneves@gmail.com

Introduction: Climate change is responsible for increasing global health consequences and healthcare-related expenses. Despite efforts to address these issues, the healthcare sector remains a significant contributor to the world's carbon footprint due to increasing greenhouse gas emissions, compromising its own sustainability. Particularly, endoscopy stands out as the second highest waste generator per clinical procedure, largely attributed to its resource-intensive processes and extensive use of single-use devices.

This study aimed to assess the waste carbon footprint generated at a high-volume tertiary endoscopy center both before and after implementing a targeted sustainability intervention. Additionally, we assessed the intervention's impact on the daily workflow of the endoscopy staff.

Aims & Methods: A 3-stage prospective interventional study was conducted from December 2023 until March 2024. Pre-intervention: four-week observational audit, during which daily endoscopic waste (landfill, regu-

lated medical waste (RMW), and recycled paper and plastic) was weighed in both endoscopy rooms and recovery areas. Intervention: following data collection, a dedicated training session was conducted for the endoscopy staff.

The session included a presentation of the collected data and outlined key sustainability strategies aimed at enhancing waste segregation.

Additionally, recycling streams were established with placement of dedicated bins in assessment areas. Post-intervention: four-week period during which daily endoscopic waste was weighed in both endoscopy rooms and recovery areas.

Weighing was conducted using an engineer-calibrated scale. For the purpose of this study, waste carbon footprint calculations were based on the equivalence of 1kg of landfill waste to 1kgCO_{2e} and 1kg of RMW to 3kgCO_{2e}. Upon conclusion of the study, an anonymous survey was distributed to all staff members to assess the impact of the study on the daily work routine.

Results: Total waste carbon footprint was reduced by 28.2%. In endoscopy rooms, waste carbon footprint decreased 20.4% (pre- vs. post-intervention: 1472.8kgCO_{2e} vs. 1173.7kgCO_{2e}, p=0.552). RMW was reduced by 24.4% (pre- vs. post-intervention: 462.8kg vs. 336.3kg, p=0.020), whereas landfill waste (pre- vs. post-intervention: 72.2 vs. 151.1, p<0.001) and recycling waste increased (paper – pre- vs. post-intervention: 0 vs. 21, p<0.001; plastic – pre- vs. post-intervention: 0 vs. 33.6, p<0.001). Mean endoscopy load was similar (pre- vs. post-intervention: 517 vs. 541, p=0.48).

In recovery areas, waste carbon footprint decreased 58.3% (pre- vs. post-intervention: 386.7kgCO_{2e} vs. 161.1kgCO_{2e}, p=0.002). RMW was reduced by 42.1% (pre- vs. post-intervention: 109.4kg vs. 28kg, p<0.001), whereas landfill waste (pre- vs. post-intervention: 58.4 vs. 77.2, p=0.040) and recycling waste increased (paper – pre- vs. post-intervention: 0 vs. 6, p<0.001; plastic – pre- vs. post-intervention: 0 vs. 9.9, p<0.001).

All staff members agreed the project did not disrupt their daily work routine, emerging as a valuable asset for promoting further sustainable practices.

Conclusion: Our study demonstrated that reducing RMW and implementing daily recycling in endoscopy rooms and recovery areas are attainable objectives that do not hinder endoscopy productivity. As a result, a yearly reduction of 2104kgCO_{2e} could be achieved in our endoscopy unit.

Additionally, this study highlighted the effectiveness of educational initiatives in raising awareness towards more sustainable endoscopy practices.

Disclosure: Nothing to disclose.

PP1221

A SCALABLE, REPRODUCIBLE APPROACH TO CASE-BASED TRAINING FOR PRE-ENDOSCOPIC MANAGEMENT OF ANTICOAGULANTS

T.J. Lux¹, A. Meining¹

¹University Hospital Würzburg, Internal Medicine II, Gastroenterology, Würzburg, Germany

Contact E-Mail Address: Lux_T1@ukw.de

Introduction: Guidelines reflect the latest, evidence based consensus for our clinical routine. The existing recommendations are numerous and subject to frequent change. Current learning methods are predominantly non-interactive. Although case-based learning is recognized as an cost effective educational tool [1, 2], it is often constrained by the limited number of available up-to-date case examples. To our knowledge, there is no reproducible and easily maintainable source for case-based training on guideline content.

Aims & Methods: We aimed to develop a versatile framework for the procedural generation of cases that represent a set of guideline recommendations in a structured format.

For this prototype, we evaluated recommendations for the pre-endoscopic assessment of risks for major bleeding or thromboembolic events based on the German guideline for quality in gastrointestinal endoscopy [3] (Chapters 3.2.2 to 3.2.5) to identify necessary information for database population (e.g., interventions with high or low bleeding risks). A list of case templates was then created, each consisting of a selected guideline excerpt along with a set of predefined properties inherited by the resulting cases. Undefined parameters were generated using random values reflecting unremarkable findings to introduce diversity.

The platform, including the database definition, was developed as a Python web application using the Django framework. Pre-defined database content such as entries for diseases, classifications, interventions, and guideline excerpts are stored in easily extendable or modifiable ".yaml" files.

Results: We established a structured database which stores the data required to determine risk of thromboembolic event. This includes pre-existing diseases (e.g., chronic kidney disease (CKD), atrial fibrillation) with corresponding classifications (e.g., CKD Stage 1 - 5), laboratory values (e.g., hemoglobin, eGFR), and relevant previous events (e.g., stroke, coronary in-stent stenosis).

Furthermore, the database contains data to determine bleeding risk including different interventions (e.g., polypectomy, EMR, ESD, eFTRD, ultrasound guided biopsies as well as patient factors like liver cirrhosis) and lesions. Lesions like polyps may also be specified using morphology (Paris or lateral spreading type classification), location (organ and organ part), and size.

The resulting Python-based Django web application can repeatedly generate lists of different cases representing the same set of predefined guideline recommendations. Moreover, future changes can be easily adapted by modifying the implemented rules or guideline texts.

Based on the desired focus - for example apixaban intake and different stages of CKD - the user may define a list of case templates which represent those aspects. Additionally, the user adds the desired questions for the trainee including corresponding guideline citations. Those cases may then be presented to trainees. In our prototype, the trainee was instructed to assess the risk of bleeding and thromboembolic events. The trainee was also asked to determine the pausing of each drug before the procedure if it is necessary. After completing a case, we present the relevant guideline excerpts, including exact citations, to the trainee.

Conclusion: Our platform can be adapted to other domains and future guideline updates can be incorporated with minimal effort, making this tool suitable for diverse case-based learning or for evaluating knowledge in a consistent, benchmark-like manner.

References: [1] Thistlethwaite, J. E., et al. (2012). The effectiveness of case-based learning in health professional education. A BEME systematic review: BEME Guide No. 23. *_Medical Teacher_,* 34(6), e421-e444. <https://doi.org/10.3109/0142159X.2012.680939>

[2] McLean, S. F. (2016). Case-Based Learning and its Application in Medical and Health-Care Fields: A Review of Worldwide Literature. *Journal of Medical Education and Curricular Development*, 3. <https://doi.org/10.4137/JMECD.S20377>

[3] Denzer, E. et al. (2015) S2k guideline: quality requirements for gastrointestinal endoscopy, AWMF registry no. 021-022, <http://dx.doi.org/10.1055/s-0041-109520>

Disclosure: Nothing to disclose.

PP1222

ENHANCING HEALTHCARE OUTCOMES THROUGH INTERPROFESSIONAL TRAINING WARDS: A COMPREHENSIVE STUDY OF PATIENT CARE, COST EFFICIENCY, AND EDUCATIONAL BENEFITS AT THE A-STAR REGENSBURG

J. Dörr¹, E. Aichner¹, M. Meier¹, S. Abaladejo-Fuertes¹, K. Ruttman^{1,2}, J. Heine¹, P. Dobsch¹, B. Michels¹, S. Schmid¹, M. Müller-Schilling³, S. Schlosser¹

¹University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany, ²University Hospital Regensburg, Nursing Development Department of the Care Management Head Office, Regensburg, Germany, ³University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany

Contact E-Mail Address: jonas-lennart.doerr@stud.uni-regensburg.de

Introduction: Interprofessional teamwork is essential in modern healthcare, with interprofessional training wards established since 1996 to enhance professional collaboration and communication. Despite their importance in optimizing patient care and training, research into patient outcomes in these wards is limited and often restricted to patient satisfaction. This study expands existing research by comparing patient outcomes in the interprofessional training ward Regensburg (A-STAR) and conventional wards, hypothesizing that interprofessional training wards offer no disadvantage to patient outcomes.

Aims & Methods: This comprehensive study, which delved into various aspects of interprofessional training wards, was conducted at the University Hospital Regensburg from October 2019 to December 2023. To ensure a robust analysis, we assessed patient outcomes, cost efficiency, patient and family satisfaction, and gainage of interprofessional competence in the interprofessional training ward A-STAR. Our data collection methods were diverse, including digital and paper-based anonymous standardized questionnaires (Collaboration and Satisfaction About Care Decisions (CSACD), Family Satisfaction in the Intensive Care Unit—(FS-ICU)), and information from the clinical data system.

Results: The study analyzed outcomes from 1,482 A-STAR and 5,752 conventional ward patients, revealing that the clinical outcomes of A-STAR patients, such as discharges against medical advice, complication-driven readmissions, ICU transfers, and mortality rates were similar to those in conventional wards. A-STAR was also more cost-effective, generating higher profits per case due to increased revenues and reduced material costs. A-STAR received high satisfaction ratings from patients and family members regarding treatment and decision-making. Moreover, medical students and nursing apprentices reported significant improvements in their ability to make interprofessional medical decisions after their training periods (medical students: mean difference -8.23, p=0.004; nursing apprentices: mean difference -9.5, p=0.003).

Conclusion: Interprofessional training wards like A-STAR ensure comparable patient care to conventional wards and enhance the educational experience for healthcare students. Our findings demonstrate that these wards are cost-effective and beneficial for patient and family satisfaction. This underscores the importance of integrating interprofessional training wards into medical curricula, as they significantly improve interprofessional collaboration and decision-making skills, which are crucial for patient safety and fostering a positive team atmosphere. In light of these compelling results, the study strongly advocates for the expansion of such training models in healthcare settings to better equip future professionals for the complexities of modern medical practice.

Disclosure: Nothing to disclose.

PP1223

TESTOSTERONE AND ESTRADIOL'S PROTECTIVE INFLUENCE ON PRIMARY LIVER CANCER

Y. Hu¹, W. Ou¹, M. Yang¹, T. Chen²

¹The First Affiliated Hospital, Fujian Medical University, Department of Hepatopancreatobiliary Surgery, Fuzhou, China, ²The First Affiliated Hospital, Fujian Medical University, Department of Laboratory Medicine, Fuzhou, China

Contact E-Mail Address: huyuhai118@gmail.com

Introduction: Primary liver cancer (PLC) poses a significant global health threat, with sex hormones implicated in its pathogenesis. Testosterone and estradiol's influence on PLC risk remains debated. Mendelian randomization (MR) offers a robust method to assess causal relationships.

Aims & Methods: Aims: Investigate the causal relationship between testosterone and estradiol levels and the risk of primary liver cancer (PLC) using Mendelian randomization (MR) analysis, while assessing potential mediators such as tumor necrosis factor receptor superfamily member 9 (TNFRS9) and urokinase-type plasminogen activator (uPA).

Methods: We conducted MR analyses using genome-wide association study (GWAS) data to investigate the causal impact of testosterone and estradiol on PLC risk. Tumor necrosis factor receptor superfamily member 9 (TNFRS9) and urokinase-type plasminogen activator (uPA) were explored as potential mediators.

Results: Our MR analysis revealed a protective effect of testosterone and estradiol against PLC. Testosterone was negatively associated with PLC risk (OR = 0.9987, P = 0.0316), with TNFRS9 mediating 9.1% of this effect. Estradiol exhibited a negative correlation with PLC risk (OR = 0.9985, P = 0.0125), with uPA mediating 8% of this effect.

Conclusion: Contrary to traditional beliefs, both testosterone and estradiol demonstrate protective effects against PLC. TNFRS9 and uPA pathways mediate a significant portion of these effects, providing novel insights into the sex hormone-PLC relationship and potential therapeutic targets. Further research should validate these findings across diverse populations.

Disclosure: Nothing to disclose.

PP1224

OCCUPATIONAL STRAIN AND REPRODUCTIVE HEALTH: A COMPARATIVE STUDY OF PREGNANCY OUTCOMES IN FEMALE VISCERAL MEDICINE DOCTORS

S. Schlosser¹, F. Hüttl², V. Tripke², Y. Huber³, M. Hollenbach⁴, N. Sommer⁵, M. Roth-Hochreutener⁶, J.J. Staudacher^{7,8}, JUGA (DGVS) and CAJC (DGAV) Study Group

¹University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany, ²University Medical Center Mainz, Department of General, Visceral, and Transplantation Surgery, Mainz, Germany, ³Mainz University Medical Center, Department of Internal Medicine, Mainz, Germany, ⁴Marburg University UKGM, Department of Gastroenterology, Hepatology, Infectious Diseases, Endocrinology, Marburg, Germany, ⁵University Hospital Bonn, Department of General, Visceral, Thoracic and Vascular Surgery, Bonn, Germany, ⁶University Hospital of Zurich, Department of Reproductive Endocrinology, Zurich, Switzerland, ⁷Charité - University Medicine Berlin Campus Benjamin Franklin, Medical Department, Division of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany, ⁸Berlin Institute of Health at Charité University Medicine Berlin, Berlin, Germany

Contact E-Mail Address: Sophie.Schlosser@gmx.de

Introduction: Recent research has highlighted significant health risks associated with pregnancy among female surgeons in USA. They reported increased risks of infertility and pregnancy complications among female surgeons, attributed to work schedules and delayed childbearing due to professional demands (1).

Aims & Methods: This joint study by the Young Gastroenterology (JUGA) and Surgical Working Group of Young Surgeons (CAJC) of the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS) and the German Society for General and Visceral Surgery (DGAV) focuses on the prevalence and factors of major pregnancy complications among female visceral medicine doctors in Germany and compares their experiences with a non-doctor control group from lawyers and teachers.

Utilizing an anonymous online survey, responses from 352 doctors detailing 757 pregnancies and 92 non-doctors with 172 pregnancies were collected and analyzed.

Generalized Linear Mixed Models (GLMM) were employed to assess risk factors linked with pregnancy complications, with particular attention to work conditions and use of assisted reproductive technologies.

Results: The study revealed no differences in maternal age at first live birth, number of births as well as the overall frequency and number of pregnancy complications between female visceral medicine doctors and non-doctors. However, visceral medicine doctors experienced higher rates of pregnancy loss (23.1% vs. 13.7%, p = 0.008) and intrauterine growth restriction (3.0% vs. 0.0%; p = 0.025). Work hours, especially close to end of pregnancy and during nights and weekends, were significantly longer for doctors (p ≤ 0.001) and associated with pregnancy complications.

Additionally, a higher proportion of doctors expected pregnancy to have more impact on their career compared to non-doctors (90.3% vs. 70.1%; p = 0.001), with both groups commonly aligning family planning with career goals.

Conclusion: These results reveal significant differences in pregnancy-related complications, with a higher prevalence among medical professionals, likely influenced by working hours and times.

Further analysis is warranted to better understand the underlying factors contributing to these disparities and to inform targeted interventions.

References:

1. Rangel EL, Castillo-Angeles M, Easter SR, et al. Incidence of Infertility and Pregnancy Complications in US Female Surgeons. *JAMA Surg.* 2021;156(10):905–915. doi:10.1001/jamasurg.2021.3301

Disclosure: Nothing to disclose.

PP1225

THE NATIONAL BOWEL CANCER SCREENING PROGRAM AND ACCESSIBILITY FOR PEOPLE WITH DISABILITY: A QUALITATIVE INVESTIGATION OF LIVED EXPERIENCE WITHIN THE AUSTRALIAN CONTEXT

N. Marinucci¹, K. Baker¹, S. Pager², B. Hutchison², E. Miller³, C. Mendoza⁴, L. Cramb⁵, G.J. Holtmann¹

¹Queensland Health, Department of Gastroenterology, Woolloongabba, Australia, ²Queensland Health, Health Equity and Access Team, Eight Mile Plains, Australia, ³Queensland University of Technology, Faculty of Creative Industries, Education & Social Justice, School of Design, Kelvin Grove, Australia, ⁴Queenslanders with Disability Network, Spring Hill, Australia, ⁵Gold Coast University Hospital, Department of Gastroenterology, Southport, Australia

Contact E-Mail Address: g.holtmann@uq.edu.au

Introduction: The societal benefits of population-based bowel cancer screening are well documented in both an Australian and global context. Australia's National Bowel Cancer Screening Program (NBCSP) has helped reduce rates of bowel cancer morbidity and mortality since its inception in 2006.⁽¹⁾

Despite the reported successes of the NBCSP, there are limitations in participation data for sub-populations, making it difficult to demonstrate equitable program impacts across the diverse Australian population. One of these groups is people with disability.

While available data is limited, that which is available shows that people with severe or profound activity limitations participating in the NBCSP show higher screening positivity rates (13% vs 7%), a lower diagnostics assessment follow-up rate (43% vs 64%) and experience a longer median time between positive screen and diagnostic assessment (63 days vs 49 days), demonstrating further disparities and accessibility issues. ⁽²⁾

Aims & Methods: This study aimed to create knowledge gains on barriers and enablers to accessing the NBCSP for people with disability. To our knowledge this is the first Australian study to collect data on support needs for people with disability (and their carers) when accessing the NBCSP. Multiple qualitative data collection methods were adopted, including arts-based methods such as visual experience, storytelling and photo-elicitation to provide rich and empathic insight into the experience of completing an iFOBT for people with disability. This process was facilitated throughout online in-depth interviews. Participants were recruited through Queenslanders with a Disability Network.

Results: 15 participants with diverse communication, mobility and self-care abilities participated in the online in-depth interviews. Preliminary analysis of data findings indicates several key system level barriers preventing equal access to participating in the NBCSP. Kit packaging, instruction format and complexity level, size of collection tubes for faecal sample and the need for additional carer support to complete the kit was listed as key barriers across the participant cohort.

While barriers differed significantly between disability sub-populations, several synergies remained around the need for simplification of instructions, improved kit packaging and design and the need for prompts or helpline information to facilitate engagement with a carer to support ease of iFOBT completion. Photos submitted by participants about their experience

accessing the kit highlighted that although everyone in Australia receives the kit the same way (in the mail) not everyone completes the kit in the same way, with many people needing supports and assistance to navigate kit completion successfully.

Conclusion: This study provided novel, critically needed information and empathetic insights into the lived experience for people with a disability. Results highlighted the need for priority population consideration and consumer consultation to improve the design of the iFOBT, with particular focus on the packaging/kit instructions, with a call for easy read formats, inclusive video guides and references to support carer engagement. Many additional barriers exist that impact the ability for diverse population groups to participate in the program and without reasonable adjustments and navigation inclusions in Program design, disparities between and across population groups will continue to exist. Findings will be shared and used to shape policy and practice impacting system level barriers to equal program access for diverse populations across Australia.

References: 1. Analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program 2018. Australian Institute of Health and Welfare; 2018.

2. Health Alo, Welfare. National Bowel Cancer Screening Program monitoring report 2022. Canberra: AIHW; 2022.

Disclosure: Nothing to disclose.

PP1226

EXPLORING THE AGE SPECTRUM OF REAL-WORLD PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MACHINE LEARNING APPROACH

H. Knight¹, S. Barlow¹, G. O'Neill¹, W. Jones¹, A. Faye², J. Adler³, S. Dave⁴

¹Adelphi Real World, Bollington, United Kingdom, ²NYU Langone Inflammatory Bowel Disease Center, New York, United States of America, ³University of Michigan, Ann Arbor, United States of America, ⁴Generation Patient, Indianapolis, United States of America

Contact E-Mail Address: hannah.knight@adelphigroup.com

Introduction: Ulcerative colitis (UC) is a chronic, gastroenterological disease, heterogenic in presentation¹. Little is known regarding where specific clinical characteristic heterogeneity lies in the context of age groups.

Aims & Methods: We aimed to investigate whether naturally occurring age groups existed among adult patients with UC based on symptomatology and health-related quality of life (HRQoL) and to assess differences in the symptomatology and flaring status of these age groups. Data were drawn from the Adelphi Disease Specific Programme™ for UC, a cross-sectional survey of gastroenterologists (GIs) and UC patients in France, Germany, Italy, Spain, the United Kingdom (UK), the United States (US) and Japan from Jan 2020–Mar 2021. GIs reported data for their next seven consulting patients, including demographics, clinical characteristics, and components of the Mayo score, allowing full Mayo scores to be calculated for all patients. Patients voluntarily reported on HRQoL via the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). 10-fold cross-validation was used to identify age groupings by adjusting knot placement in linear splines of age in regression models with outcomes of patients' Mayo scores and SIBDQ scores. Patients' clinical characteristics across the age groups were compared using bivariate analysis.

Results: Overall, 3052 patients with UC were included (55.8% male, mean [standard deviation; SD] BMI 24.1 [3.9], mean [SD] disease duration 5.1 [5.9] yrs), of which 960 had known SIBDQ scores (52.1% male, mean [SD] BMI 23.5 [3.5], mean [SD] disease duration 3.1 [6.2] yrs).

Age groupings based on Mayo scores were 18–28 yrs (n=651), 29–60 yrs (n=2114), 61+ yrs (n=287). Current flaring status was significantly differ-

ent across groups with 19.2% of patients in the 18-28 yrs group flaring ($p<0.01$). Of symptoms with the greatest difference in prevalence between age groups, prevalence of rectal bleeding, abdominal pain, bloody diarrhoea, bowel movement urgency, and anaemia differed, although the results were not always significant.

Age groupings based on SIBDQ scores were 18-37 yrs ($n=506$), 38-40 yrs ($n=83$), 41-50 yrs ($n=173$), and 50+ yrs ($n=198$). Flaring differed significantly across age groups. Among symptoms with the greatest difference in prevalence between age groups, prevalence of flatulence, fatigue/tiredness, abdominal pain, abdominal distension, and anaemia differed, although not always significantly.

Mayo Deri-ved Age Cate-gories	18-28 Yrs (n=651)	29-60 Yrs (n=2114)	61+ Yrs (n=287)	P value	SIB- DQ	18-37 (n=506)	38-40 (n=83)	41-50 (n=173)	50+ (n=198)	P value
Sex, male, n (%)	345 (53.0)	1189 (56.2)	169 (58.9)	0.19	Deri-ved	260 (51.4)	43 (51.8)	84 (48.6)	113 (57.1)	0.40
BMI, mean (SD)	22.67 (3.1)	24.26 (3.9)	26.00 (5.1)	<0.01	Age	22.85 (3.1)	23.48 (4.1)	23.48 (3.3)	24.94 (4.0)	<0.01
Time since diagnosis (yrs)	n=609	n=1874	n=249		Cate-gories	n=470	n=75	n=154	n=172	
Mean (SD)	2.53 (2.7)	5.36 (5.7)	9.13 (9.5)	<0.01		3.15 (3.3)	6.13 (5.6)	6.94 (6.1)	9.01 (9.6)	<0.01
UC Disease Location, n (%)	n=592	n=1888	n=251			n=450	n=70	n=152	n=179	
Ulcerative proctitis	93 (15.7)	311 (16.5)	38 (15.1)			71 (15.8)	12 (17.1)	25 (16.5)	26 (14.5)	
Proctosigmoiditis	119 (20.1)	383 (20.3)	47 (18.7)	0.74		97 (21.6)	14 (20.0)	30 (19.7)	42 (23.5)	0.58
Left-sided colitis	171 (28.9)	594 (31.5)	82 (32.7)			146 (32.4)	30 (42.9)	61 (40.1)	62 (34.6)	
Pan-ulcerative (total) colitis	209 (35.3)	600 (31.8)	84 (33.5)			136 (30.2)	14 (20.0)	36 (23.7)	49 (27.4)	
Symptoms with greatest difference in prevalence (top five), n (%)	n=640	n=2100	n=285							
Rectal bleeding	91 (14.2)	222 (10.6)	22 (7.7)	<0.01						
Abdominal pain	167 (26.1)	545 (26.0)	57 (20.0)	0.08						
Diarrhoea (bloody)	118 (18.4)	321 (15.3)	36 (12.6)	0.05						
Bowel movement urgency	148 (23.1)	435 (20.7)	52 (18.3)	0.21						
Anaemia	146 (22.8)	442 (21.1)	77 (27.0)	0.06						
Symptoms with greatest difference in prevalence (top five), n (%)						n=506	n=83	n=173	n=198	
Flatulence						48 (9.5)	17 (20.5)	23 (13.3)	26 (13.3)	0.03
Fatigue/ tiredness						117 (23.2)	12 (14.5)	36 (20.8)	37 (18.9)	0.26
Abdominal pain						132 (26.1)	29 (34.9)	56 (32.4)	51 (26.0)	0.18
Abdominal distension						78 (15.5)	7 (8.4)	26 (15.0)	22 (11.2)	0.22
Anemia						105 (20.8)	16 (19.3)	37 (21.4)	51 (26.0)	0.46
Current flaring status, n (%)	n=610	n=1950	n=250			n=478	n=73	n=157	n=170	
Currently flaring	117 (19.2)	267 (13.7)	37 (14.8)	<0.01		66 (13.8)	6 (8.2)	24 (15.3)	29 (17.0)	0.32

BMI – body mass index; SD – standard deviation; UC – ulcerative colitis; Yrs – Years

Missing data not imputed; n numbers given where sample size varies (patients with known data)

Table 1. Patient demographics and clinical characteristics.

Conclusion: Naturally occurring age groups were identified by exploring disease activity measures and HRQoL outcomes. Further analyses found differences in flaring status and symptomatology across age groups. This highlights that age should be considered when treating patients with UC as patients of different ages are likely to present and respond differently. While further research is warranted, aspects of treatments in clinical trials, such as safety and efficacy, should be tested within different age cohorts, and publicising individual age data would aid in enabling the analysis of drug disposition and safety in patients with UC.

References: 1. Guan Q. A Comprehensive Review and Update on the Pathogenesis of Inflammatory Bowel Disease. *Journal of Immunology Research*. 2019;2019:7247238.

Disclosure: Nothing to disclose.

PP1227

WITHDRAWN

PP1228

ENDOSCOPY-RELATED HAND INJURIES AND USABILITY OF ENDOSCOPES IN JAPANESE FEMALE ENDOSCOPISTS

S. Nakajima^{1,2}, S. Ono^{3,2}, S. Owada^{4,2}, A. Sakatani^{5,2}, N. Tomita^{6,2}, M. Tsuda^{7,2}, M. Yamada^{8,2}, S. Katsuki⁹, N. Sakamoto¹⁰

¹Hokkaido University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ²Hokkaido Chapter of the Women Endoscopists Career Support Committee, Japan Gastroenterological Endoscopy Society, Otaru, Japan, ³Hokkaido University Hospital, Division of Endoscopy, Sapporo, Japan, ⁴Muroran City General Hospital, Department of Gastroenterology, Muroran, Japan, ⁵Asahikawa Medical University, Department of Gastroenterology, Asahikawa, Japan, ⁶Otaru Ekisaikai Hospital, Department of Gastroenterology, Otaru, Japan, ⁷Sapporo Cancer Screening Center, Public Interest Foundation Hokkaido Cancer Society, Department of Gastroenterology, Sapporo, Japan, ⁸Steel Memorial Muroran Hospital, Department of Gastroenterology, Muroran, Japan, ⁹Otaru Ekisaikai Hospital Center of Gastroenterology, Center of Gastroenterology, Otaru, Japan, ¹⁰Steel Memorial Muroran Hospital, Department of Gastroenterology, Sapporo, Japan

Contact E-Mail Address: onosho@med.hokudai.ac.jp

Introduction: Recently, much attention has been given to the well-being of health care workers, but endoscopists are no exception. Endoscopy examinations require complex and repetitive maneuvers that can put a strain on the musculoskeletal system. Female endoscopists are greatly disadvantaged in muscle strength and hand size compared to male endoscopists when operating a one-size-fits-all endoscope. Although there have been some reports, especially from Western countries, on endoscopy-related injuries (ERI), there have been a few reports on ERI from Japan.¹⁻³ A survey was conducted to examine ERI with a focus on hand disorders and operability of endoscope handles for Japanese female endoscopists.

Aims & Methods: Our aim was to examine ERI with a focus on hand disorders and operability of endoscope handles for Japanese female endoscopists from a survey.

A survey was designed in the Hokkaido chapter of the Women Endoscopists Career Support Committee in the Japan Gastroenterological Endoscopy Society (JGES). An anonymous electronic questionnaire was distributed to endoscopists who have been performing endoscopy in Japan. Participants accessed the Google form web site during the period from July to December in 2023.

A 25-item survey with multiple choice answers was created. Twelve items were dedicated to obtaining non-identifiable demographic data and practice-related information such as the number of endoscopies performed per week performed by each participant. Six-items focused on ERI including current and past injuries and the duration and severity of injuries. The other 7-items were about the usability of the current endoscope handle and practice of ergonomic endoscopy. ERI were defined as past or present endoscopy-related muscle and joint disorders including pain, discomfort, movement restriction and numbness.

Results: Data for 352 endoscopists were analyzed. The incidences of ERI were 55.6% (150/270) in men and 61.0% (50/82) in women and the most common site of ERI was the hands including fingers, thumbs and wrists followed by the lower back and then the neck (incidence of 28.1% in hands, 26.4% in lower back and 24.1% in neck). ERI in hands occurred in 35.4% of the women and increased with age. There were significant differences in age and endoscopy career between female endoscopists with and those without ERI in the hands, and there were no relations to glove size, number of endoscopy procedures and usability of the endoscopy handle. Regardless of the presence or absence of hand injuries, many fe-

male endoscopists were not satisfied with the shape and usability of endoscopes (75.6%). Especially for female with small hands (gloves size 6 or smaller), the current endoscope handle is so large and they cannot reach the left and right angle knobs with their fingers.

Conclusion: In conclusion, ERI in hands were related to long endoscopy career and aging in female endoscopists. Improved usability of endoscopes and ergonomic endoscopy are important for female endoscopists to continue clinical practice.

References: 1. Diana Y, Tommaso B, Gastone C *et al.* Musculoskeletal injuries in gastrointestinal endoscopists: a systematic review. *Expert Rev Gastroenterol Hepatol* 2017; 11: 939–947.

2. Pawa S, Kwon RS, Fishman DS *et al.* American Society for Gastrointestinal Endoscopy guideline on the role of ergonomics for prevention of endoscopy-related injury: summary and recommendations. *Gastrointest Endosc* 2023; 98: 482–491.

3. Matsuzaki I, Ebara T, Tsunemi M *et al.* Effects of endoscopy-related procedure time on musculoskeletal disorders in Japanese endoscopists: a cross-sectional study. *Endosc Int Open* 2021; 9: E674–E683.

Disclosure: Nothing to disclose.

PP1229

GENDER DISPARITIES IN GASTROENTEROLOGY: PARENTHOOD'S IMPACT ON CAREER AND TRAINING

S. Schlosser¹, Y. Huber², K. Hamesch³, O. Cahyadi⁴, E. Geissler⁵, J.J. Staudacher^{6,7}, JUGA (DGVS) study group

¹University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany, ²Mainz University Medical Center, Department of Internal Medicine, Mainz, Germany, ³University Hospital Aachen, Gastroenterology, Metabolic disorders and Intensive care, Aachen, Germany, ⁴Ruhr-University-Bochum, St. Josef-Hospital, Department of Gastroenterology, Bochum, Germany, ⁵Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, Department of Visceral, Thoracic and Vascular Surgery, Dresden, Germany, ⁶Charité - University Medicine Berlin Campus Benjamin Franklin, Medical Department, Division of gastroenterology, infectiology and rheumatology, Berlin, Germany, ⁷Berlin Institute of Health at Charité University Medicine Berlin, Berlin, Germany

Contact E-Mail Address: Sophie.Schlosser@gmx.de

Introduction: Career trajectories in gastroenterology can be influenced by parenthood, with potential disparities between genders in academic progression and workload management. This abstract presents findings from a survey by the Young Gastroenterology section of the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS), exploring the impact of parenthood on academic achievements and training within the field.

Aims & Methods: This study was conducted through an anonymous online survey distributed via email to DGVS members. The survey was accessible from April 4, 2023, to June 19, 2023, and was conducted exclusively in German. It employed a combination of single and multiple-choice questions, with all questions being skippable to ensure participant comfort and engagement.

Depending on respondents' answers, query logic branched to gather comprehensive data on various aspects of parenthood and career progression in gastroenterology. The survey aimed to identify differences between male and female gastroenterologists with children in terms of academic positions, training delays, and work hours.

Results: The survey garnered 811 responses, distributed among 173 women without children, 206 mothers, 179 men without children, and 251 fathers. Significant gender disparities were found: Most notably, female physicians reported that childbearing often postponed their specialist training ($p < 0.001$), whereas men indicated that their training was seldom delayed. Employment data revealed that women with children typically worked fewer hours, whereas the majority of men, regardless of parental status, worked over 50 hours per week. Fatherhood predominantly led to full-time employment of at least 40 hours per week, suggesting that parenthood induces part-time work mainly among women. No childless men reported work hour reduction as a cause for delayed specialist status, in stark contrast to over half of the mothers citing this as a significant reason for their postponed completion of training. Post-childbirth work adaptations were markedly different: while men's work hours generally remained unchanged across all specialties, women were particularly less active in endoscopy after the birth of their first child (58%). Women with children held professorships less frequently than their childless or male counterparts ($p < 0.001$). Men with children were less likely to lack an academic degree.

Conclusion: The survey indicates that parenthood has a differential impact on the professional development of male and female gastroenterologists. Mothers are more likely to experience delays in training and are less represented in high academic positions. In contrast, fatherhood correlates with sustained or increased work hours, reflecting a gendered divide in work-life balance within gastroenterology. These findings highlight the need for structural changes in the medical profession to support equitable career progression for gastroenterologists, regardless of gender and parental status.

Disclosure: Nothing to disclose.

PP1230

COVID-19 INFECTION AND ILLNESS HISTORY IS LINKED TO HIGHER RATES OF IRRITABLE BOWEL SYNDROME (IBS) AND FUNCTIONAL DYSPEPSIA (FD) WORLDWIDE

O.S. Palsson¹, I. Aziz², T.H. Taft³, M. Simrén⁴, J. Tack⁵, D.A. Drossman³, M. Grover⁶, A.D. Sperber⁷

¹University of North Carolina, Chapel Hill, Dept. of Medicine, Chapel Hill, NC, United States of America, ²University of Sheffield, Academic Department of Gastroenterology, Sheffield, United Kingdom, ³Rome Foundation Research Institute, Raleigh, United States of America, ⁴Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Dept of Internal Medicine, Gothenburg, Sweden, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium, ⁶Mayo Clinic, Division of Gastroenterology and Hepatology, Rochester, MN, United States of America, ⁷Ben-Gurion University of the Negev, Faculty of Health Sciences, Farad, Israel

Contact E-Mail Address: Olafur_Palsson@med.unc.edu

Introduction: Multiple recent studies suggest that COVID-19 (COVID) infection may increase risk of developing Disorders of Gut-Brain Interaction (DGBI). However, the extent of this effect on a population level, and how directly it is related to COVID illness, remains poorly understood.

Aims & Methods: We aimed to test in a multi-national sample the a priori hypotheses that IBS and FD prevalence rates (1) have increased after the COVID-19 pandemic, and are higher in individuals (2) who were more ill with their COVID infection, (3) who have long COVID, and (4) who were not vaccinated for COVID. A population-based Internet survey with pre-defined demographic quotas to obtain equivalent sex and age distribution

across countries was conducted nationwide in 9 countries (Canada, China, Germany, Japan, Mexico, Poland, Romania, Spain, United States) in late 2023, and included demographic questions, Rome IV IBS and FD diagnostic questions, and questions about history of COVID infection and illness. Group prevalence was compared with Chi-Square tests to test the 4 hypotheses. For hypothesis 1, the total sample was compared to a pre-pandemic Rome Foundation Global Epidemiology Study (RFGES; Sperber et al. *Gastroenterology* 2021;160(1):99-114) sample from the same 9 countries, surveyed with comparable methodology in 2017-2018, using weighting to equalize country sample sizes.

Results: The survey was completed by 17,663 participants (50.2% females; mean age 46.3 years, range 18-96). People in the current sample had higher prevalence of both Rome IV IBS [% and 95% CI: 7.9% (7.5, 8.3) vs. 3.8% (3.5, 4.1); $p < 0.0001$] and FD [12.7% (12.2, 13.2) vs. 7.0% (6.6, 7.4); $p < 0.0001$] compared to the pre-COVID RFGES sample (N=19,669, 50.2% females, mean age 45.4 years, range 18-95) for the same countries. The post-vs. pre-pandemic prevalence of FD and IBS was numerically higher in all countries, and in all age and sex subgroups. In the current survey, people who reported having had test-confirmed COVID (41.3%) had higher IBS [9.4% (8.8, 10.1) vs. 6.8% (6.3, 7.2); $p < 0.0001$] and FD [14.6% (13.8, 15.4) vs. 11.3% (10.7, 11.9); $p < 0.0001$] prevalence than those without a COVID test-positive history. Those who were moderately or very ill during COVID infection had higher prevalence of IBS [12.0% (10.9, 13.0) vs. 6.8% (6.0, 7.7); $p < 0.0001$] and FD [17.6% (16.4, 18.9) vs. 11.4% (10.4, 12.4); $p < 0.0001$] compared to those with mild or no symptoms, and even higher if they had new-onset GI symptoms during their COVID illness (15.1% IBS, 21.3% FD). People with current lingering symptoms from past COVID infection ("long COVID") had higher IBS [16.3% (14.4, 18.3) vs. 7.8% (7.1, 8.5); $p < 0.0001$] and FD [22.9% (20.7, 25.1) vs. 12.6% (11.8, 13.5); $p < 0.0001$] prevalence than fully recovered individuals. People who had not been vaccinated for COVID (19.4% of the sample) had higher prevalence of FD [14.3% (13.1, 15.4) vs. 12.3% (11.7, 12.8); $p < 0.0001$] but not IBS [8.4% (7.4, 9.4) vs. 7.7% (7.3, 8.2); $p = 0.18$] compared to the vaccinated.

Conclusion: Our findings indicate that both IBS and FD prevalence rates are significantly higher now among adults worldwide than before the COVID-19 pandemic. Greater illness severity during COVID infection and current long COVID status show striking associations with elevated prevalence of these DGBI. Although retrospective infection/illness self-report cannot prove causation, this pattern of findings strongly implicates COVID-related illness as a potent driver of subsequent vulnerability to having IBS and FD, leading to an increased population prevalence of these disorders.

Disclosure: Nothing to disclose.

PP1231

WITHDRAWN

PP1232

TREATMENT OF LIVER INJURY WITH URSODEOXYCHOLIC ACID IN PATIENTS WITH COVID-19

K. Safonova¹, N. Dekhnich¹, A. Punin², N. Oliferuk³, T. Kuznetsova³
¹Smolensky State Medical University, University hospital №1, Smolensk, Russian Federation, ²Smolensky State Medical University, Therapy department, Smolensk, Russian Federation, ³Binnopharmgroup, Moscow, Russian Federation

Contact E-Mail Address: n.dekhnich@mail.ru

Introduction: Liver damage is often observed in COVID-19 patients, especially in severe cases. It may be caused by a systemic inflammatory response, cytokine storm, immune dysregulation, hypoxemia, multiorgan dysfunction syndrome, and the use of COVID-19 drugs (1). Abnormal liver function tests were observed in up to 52% of COVID-19 patients (2).

Ursodeoxycholic acid (UDCA) inhibits the production of pro-inflammatory cytokines involved in the cytokine storm development. Thus, it may be beneficial in restoring liver function in patients with COVID-19 and hepatic injury

Aims & Methods: This non-interventional prospective study aimed to evaluate efficacy and safety of UDCA in adult patients with signs of liver damage and COVID-19 infection.

140 patients (mean age 67.43 ± 14.40 ; 67 males) with laboratory-confirmed COVID-19 and hepatic injury were enrolled, 93% of them had moderate COVID-19. Hepatic injury referred to elevated level of at least one of the following parameters: alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) or total bilirubin. UDCA was prescribed to 70 patients for up to 2 months. The control group comprised of 70 patients with COVID-19 and hepatic injury who were not prescribed UDCA

Results: At baseline, both ALT and AST levels were elevated above the upper limit of normal (ULN) dualfold in 25% of patients of the total population, by three-fold in 20%. Isolated elevation of ALT by more than 2-3 times above the ULN was observed in 31% of patients, isolated elevation of AST – in 8%. Hepatocellular liver injury was diagnosed in 62.85% of patients in the UDCA group and 57.14% in the control. Mean $\pm$ standard deviation (SD) ALT levels at baseline were 79.44 ± 81.43 and 66.98 ± 32.34 IU/L in the UDCA and control groups, respectively (not significant, NS). On day 10, the ALT levels were 45.75 ± 39.17 and 69.72 ± 64.99 IU/L ($p = 0.002$ between the groups), on day 60 – 17.39 ± 7.61 and 21.59 ± 9.14 IU/L ($p = 0.011$). Mean AST levels at baseline were 82.57 ± 97.12 and 62.24 ± 50.77 IU/L in the UDCA and control groups, respectively (NS), a significant difference between the groups was noted on day 60: 17.39 ± 7.42 and 22.68 ± 7.62 IU/L respectively ($p < 0.001$).

A significantly lower ALP and total bilirubin levels were observed in the UDCA group compared to control on day 60 (ALP: 57.49 ± 27.91 vs. 74.09 ± 21.85 IU/L, $p < 0.001$; total bilirubin: 10.32 ± 3.60 vs. 15.03 ± 10.34 μ mol/L, $p < 0.001$). GGT levels were similar in both groups on all visits.

At baseline, hepatomegaly was observed on sonography in 48,57% and 51,43% (NS) of patients in the UDCA and control groups, respectively. By day 60 hepatomegaly remained in only 21,43% patients in the UDCA group but in 48,57% in the control group ($p < 0.001$ between the group). Biliary dyskinesia was initially observed in 24,29% and 27,14% of patients in the UDCA and control groups respectively, by day 60 it persisted in 1,43% and 15,71% of patients, respectively ($p = 0.007$).

Positive dynamics on ultrasound and normalization of liver size during treatment were observed in 60.0% of patients in the UDCA group and 7.1% in the control group, while negative dynamics were observed in 0% and 25.7% of patients, respectively.

No changes were seen in 27.1% and 50.0% of patients, respectively.

Conclusion: Oral administration of UDCA to patients with COVID-19 and liver damage demonstrated a faster normalization of liver function, as evidenced by the reduction in elevated levels of ALT, AST, ALP, and total bilirubin, as well as the restoration of liver size.

References:

1. Luxemburger H, Thimme R. SARS-CoV-2 and the liver: clinical and immunological features in chronic liver disease. *Gut*. 2023 Sep 1;72(9):1783–94.
2. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020 Mar 17;323(11):1061–9.
3. Ko WK, Lee SH, Kim SJ, Jo MJ, Kumar H, Han IB, et al. Anti-inflammatory effects of ursodeoxycholic acid by lipopolysaccharide-stimulated inflammatory responses in RAW 264.7 macrophages. *PLOS ONE*. 2017;12(6):e0180673.
4. Talebian R, Panahipour L, Gruber R. Ursodeoxycholic acid attenuates the expression of proinflammatory cytokines in periodontal cells. *J Periodontol*. 2020 Aug;91(8):1098–104.

Disclosure: Current study was conducted with the financial support of Binnopharm Group

PP1233

PREVALENCE AND RISK FACTORS OF LIVER INJURY AMONG HOSPITALIZED PATIENTS WITH SEVERE OR CRITICAL COURSE OF COVID-19 INFECTION

D. Knutová¹, P. Vrbová¹, S. Nachtmann¹, J. Smaha¹, K. Tarabová², J. Payer¹, T. Koller¹

¹Comenius University Faculty of Medicine and University Hospital Bratislava, 5. Department of Internal Medicine, Bratislava, Slovakia, ²Comenius University Faculty of Medicine and University Hospital Bratislava, 1st Department of Anaesthesiology and Intensive Care Medicine, Bratislava, Slovakia

Contact E-Mail Address: knutovadana@gmail.com

Introduction: Several studies have found that the course of infection by COVID-19 virus is often associated with varying degrees of hepatic damage, but the occurrence and its risk factors is yet to be mapped. The aim of the study was first, to determine the prevalence of liver injury in patients hospitalized for COVID19 infection.

Second, to compare the groups with severe and critical course of COVID19. Third, to identify independent risk factors of several types of liver injury in the group of critically ill patients.

Aims & Methods: During several waves of the pandemic, we collected data about cases hospitalized for COVID-19 pneumonia in two groups: severe course, group 1 and critical course with mechanical ventilation, group 2. We recorded basic demographic parameters, comorbidities and their chronic treatment, clinical status and laboratory findings at admission, administered treatment and evolution of hepatic tests during hospitalization, maximum levels of ALT, ALP, and bilirubin.

We defined liver injury according to the Common terminology criteria for adverse events v.5.0: ALT > 5 times the upper limit of normal (ULN, cytolytic damage 2nd degree), ALT > 3 times and bilirubin > 2 times ULN (Hy's law), ALP > 5 times ULN (cholestatic damage 2nd degree). In the group 2, we also identified independent risk factors for individual adverse events.

Results: 345 patients had available data, 58.3 % were men, with a median age of 66 years, a the Charlson comorbidity index of 4.0, BMI of 28.4, with an initial CRP of 97 mg/l, an oxygen saturation of 91.5 %, and leukocytes 7.7 x10.9/l. There were 201 patients in group 1 and 144 patients in group 2. Group 2 differed significantly (p < 0.001) from group 1 in median age (61.5 vs. 71 years), proportion of men (70 vs. 49.8%), comorbidity index (2 vs. 6),

initial CRP (117 vs. 86.8 mg/l), by entry ALT (0.75 vs. 0.49) and AST (1.0 vs. 0.77ukat/l), but not by a history of liver disease or cirrhosis (11.1 vs. 15.5 % and 2.1 vs. 3.0 %). In group 2, all defined events of liver injury were significantly more frequent (P<0.001): elevation of ALT > 5xULN (39.4 vs. 5%), Hy's law (30.3 vs. 3%), ALP > 5xULN (26.5 vs. 2%).

In group 2, the independent risk factors for ALT elevation > 5xULN were: entry AST (OR 1.75), aminoglycoside antibiotics (OR=4.28), methylprednisolone (OR=2.7), tigacycline (OR=3.06) and mean erythrocyte volume (OR=0.92). Hy's law risk factors were: history of hepatopathy (OR=3.3), aminoglycoside antibiotics (OR=4.04), caspofungin (OR=3.43) and linezolid (OR=3.07). Risk factors for ALP > 5xULN were: methylprednisolone (OR=4.1), level of fibrinogen on admission (OR=1.45), number of types of antibiotics administered (OR=1.41) and albumin on admission (OR=0.86).

Conclusion: Adverse events of liver injury among critically ill patients with COVID-19 were 8 to 12 times more frequent compared to patients with a severe course. The risk factors were mainly the initial state of the liver (history of hepatopathy, AST, albumin), methylprednisolone and selected antimicrobial drugs.

Disclosure: Nothing to disclose.

PP1234

LIVER FIBROSIS INDEX FIB4 AND COVID-19: A SERIES OF 330 PATIENTS IN AN INTENSIVE CARE UNIT

L. Elidrissi¹, A. Darif¹, M. Tahiri¹, F.z. Elrhaoussi¹, F. Haddad¹, W. Hliwa¹, A. Bellabah¹, W. Badre¹, B. Charra²

¹Ibn Rochd Hospital Center, Hepatology and gastro enterology, Casablanca, Morocco, ²Ibn Rochd Hospital Center, Medical Intensive Care Unit, Casablanca, Morocco

Contact E-Mail Address: l.lailaelidrissi@gmail.com

Introduction: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is recognized as the cause of a severe multisystem disease that may require intensive care unit (ICU) treatment. Because of its known hepatic tropism, this virus may be responsible for fatal liver damage. The aim of our study was to evaluate the association between elevated fib4 and the incidence of death in patients hospitalized for SARS-CoV-2 infection in an ICU.

Aims & Methods: We conducted a retrospective descriptive and analytical study including patients hospitalized for COVID19 between 2020 and 2021 in an intensive care unit. A description of the collected clinical and biological variables was first performed with calculation of the FIB4 index. We then performed an analytical study using SPSS software to determine the association between high FIB4 score and infection severity, estimated by mortality and length of hospital stay.

Results: A total of 330 patients were enrolled, with a clear male predominance of 64.2% and a sex ratio of 1.7. The mean age was 62.5 years. Diabetes and hypertension, at 45.5% and 38.2%, respectively, were the most common comorbidities. Sixteen point one percent of patients were smokers and 9.4% were overweight or obese. Overall, 68.2% of patients had cytolysis on admission and 13.3% had thrombocytopenia. Twenty seven point three percent of patients had a fib4>3.25. Median hospital stay was 7.5 days (1-100). Fib4 > 3.25 was significantly associated with death (p=0.006), as were age over 60 years (p=0.025), the presence of pre-existing lung disease (p=0.054), AST levels (p=0.001) and ALT levels (p=0.008). In contrast, fib4 > 3.25 was not significantly associated with longer hospital stay. On multivariate analysis, fib4 > 3.25 was significantly associated with the occurrence of death (odds ratio, 2.109; 95% CI, 1.0054 to 4.43), whereas age (p=0.09), platelet count (p=0.075), ASAT level (p=0.8) and ALAT level (p=0.503) showed no significant difference between the 2 groups.

Conclusion: According to our results, fib4>3.25 was significantly associated with a higher mortality in IUC patients with COVID19.

Disclosure: Nothing to disclose.

PP1235

HOSPITALIZATION OUTCOMES AND LONG-TERM GASTROINTESTINAL SYMPTOMS FLUCTUATION OF IRRITABLE BOWEL SYNDROME OR FUNCTIONAL DYSPESIA PATIENTS POSITIVE AFTER COVID-19

G. Marasco¹, K. Hod², C. Cremon³, M.R. Barbaro¹, A. Kagramanova⁴, D.S. Bordin⁵, V.L. Drug⁶, P. Fusaroli⁷, S.Y. Mohamed⁸, C. Ricci⁹, M. Bellini¹⁰, M.M. Rahman¹¹, L. Melcarne¹², J. Santos¹³, B. Lobo Alvarez¹⁴, S. Bor¹⁵, S. Yapali¹⁶, S. Lukic¹⁷, M. Trajkovska¹⁸, D.L. Dumitrascu¹⁹, A. Pietrangelo²⁰, M. Simrén²¹, J. Sjölund²², N. Tornkvist²³, U.C. Ghoshal²⁴, O. Kolokolnikova²⁵, A. Colecchia²⁶, J. Serra²⁷, G. Maconi²⁸, R. De Giorgio²⁹, S. Danese³⁰, P. Portincasa³¹, A. Di Sabatino³², M. Maggio³³, E. Philippou³⁴, Y.Y. Lee³⁵, V. Stanghellini¹, G. Barbaro¹, GI-COVID19 study group

¹University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ²Assuta Medical Center, Tel Aviv, Israel,

³IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ⁴The Loginov Moscow Clinical Scientific Centre, Department of inflammatory bowel diseases, Moscow, Balaschiha, Russian Federation, ⁵A.S. Loginov Moscow Clinical Scientific Center, Department of pancreatic, biliary and upper GI diseases, Moscow, Russian Federation, ⁶University of Medicine and Pharmacy "Grigore T Popa", Iasi, Romania, Gastroenterology, Iasi, Romania, ⁷University of Bologna, Gastroenterology, Imola, Italy, ⁸Zagazig University, Internal Medicine, Zagazig, Egypt, ⁹Università Degli Studi Di Brescia, Dept. of Exp and Clin Sciences, Brescia, Italy, ¹⁰Dept. Of Translational Medicine, Dept. of Translational Research and New Technologies in Medicine and Surgery -University of Pisa, Pisa, Italy, ¹¹Sheikh Russel Gastroenterology Institute and Hospital, Department of Gastroenterology, Dhaka, Bangladesh, ¹²Hospital Universitario Parc Taulí, Gastroenterology, Sabadell, Spain, ¹³Institut de Recerca Vall d'Hebron, Department of Gastroenterology, Barcelona, Spain, ¹⁴Hospital General Vall d'Hebrón, Research Unit Gastroenterology Department Funda, Barcelona, Spain, ¹⁵Ege University Dept of Gastroenterology Ege Reflux Study Group, School of Medicine, Section Gastroenterology, Izmir, Turkey, ¹⁶Acibadem Mehmet Ali Aydinlar University, Gastroenterology, Istanbul, Turkey, ¹⁷Clinic for Gastroenterology, Belgrade, Serbia, ¹⁸Clinic of Gastroenterohepatology, Ultrasound department, Skopje, North Macedonia, ¹⁹Juliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, 2nd Medical Dept., Cluj-Napoca, Romania, ²⁰University of Modena and Reggio Emilia, Medicine and Medical Specialties, Modena, Italy, ²¹Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Dept of Internal Medicine, Gothenburg, Sweden, ²²Institute of medicine, Departement of internal medicine and clinical nutrition, Gothenburg, Sweden, ²³Sahlgrenska Universitetssjukhuset, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden, ²⁴Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ²⁵Meds, Gastroenterology, Krasnogorsk, Russian Federation, ²⁶Modena Hospital, Gastroenterology and Digestive Endoscopy Unit, Modena, Italy, ²⁷University Hospital Vall d'Hebron, Digestive System Research Unit, Barcelona, Spain, ²⁸Luigi Sacco University Hospital Gastroenterology Unit Biomed and Clinical Sciences, Department Of Biomedical And Clinical Sciences – L.Sacco

University Hospital - Milan Italy, Milan, Italy, ²⁹University of Ferrara, Dept. Endocrinology and Internal Medicine, Ferrara, Italy, ³⁰Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal immunopathology, Milan, Italy, ³¹University of Bari Medical School, Division Internal Medicine Clinica Medica "Augusto Murri", Bari, Italy, ³²IRCCS Policlinico S. Matteo, Prima Clinica Medica, Pavia, Italy, ³³University of Parma, Parma, Italy, ³⁴University of Cyprus, Nicosia, Cyprus, ³⁵Universiti Sains Malaysia, Kota Bharu, Malaysia

Contact E-Mail Address: giovannimarasco89@gmail.com

Introduction: Exposure to COVID-19 has been shown previously associated with a higher risk for long-term gastrointestinal symptoms and disorders of gut-brain interaction (DGBI) occurrence, including irritable bowel syndrome (IBS) (1). However, it is still unclear whether SARS-CoV-2's effects on the gastrointestinal tract are more severe in patients already diagnosed with a DGBI and symptoms fluctuations in these patients over time after COVID-19 exposure.

Aims & Methods: To explore hospitalization outcomes and gastrointestinal (GI) symptoms fluctuation over a 1-year follow-up of COVID-19 patients with IBS or functional dyspepsia (FD) at enrollment compared to COVID-19 patients without any previous GI symptoms/disorders/diseases/surgeries.

In this retrospective multicenter cohort study, patient charts were reviewed for demographic data, medical history including GI chronic diseases, and hospitalization outcomes. All participants completed the Gastrointestinal Symptom Rating Scale (GSRS) over 4 time points: at COVID-19 onset, at 1, 6, and 12 months, and the Hospital Anxiety and Depression Scale (HADS) over 2 time points: at 6 and 12 months. The cohort was divided into two groups: (1) IBS/FD group (2) control group.

Results: A total of 599 patients were eligible for the study (n=61 IBS/FD group, n=538 control group). There were no differences between the groups regarding hospitalization outcomes. There was a significant decrease in both IBS/FD and control groups in depression [6.17±4.45 at 6 months and 3.17±4.14 at 12 months for IBS/FD group (p=0.007) and 3.55±4.02 at 6 months and 3.05±3.74 at 12 months for the control groups (p=0.019), respectively] and anxiety levels over time [5.94±4.32 at 6 months and 4.10±4.58 at 12 months for IBS/FD group (p=0.019) and 3.58±3.71 at 6 months and 3.26±3.65 at 12 months for the control groups (p<0.001), respectively]. The pooled Odds Ratios (OR) of the effect of IBS/FD over 4 time points ranged from 1.93 for diarrhea to 5.10 for increased distention, and were statistically significant for all GI symptoms, even after adjustments for gender, depression, and anxiety. While there was a significant improvement over time in the severity of abdominal pain (p=0.008), hunger pains (p=0.011), nausea (p=0.001), diarrhea (p=0.005) and loose stool (p=0.007), there was also a significant deterioration in constipation (p=0.002), hard stool (p<0.001) and feeling of incomplete evacuation (p=0.007) among the IBS/FD group.

Conclusion: Gastrointestinal symptoms within and between the control group and the IBS/FD group changed over time after COVID-19 onset. Patients with IBS or FD at enrollment showed increased complaints of constipation, hard stool, and incomplete evacuation after COVID-19 exposure.

References: 1. Marasco G, Cremon C, Barbaro MR the GI-COVID19 study group, et al Post COVID-19 irritable bowel syndrome. Gut 2023;72:484-492.

Disclosure: Nothing to disclose.

PP1236

SEROLOGICAL RESPONSE TO VACCINATION AGAINST SARS-COV2 IN PATIENTS WITH CROHN'S DISEASE

R. Bourguiba¹, M. Ayari², S. Bellakhel¹, K. Dridi³, W. Helali¹, M.H. Dougui², T. Jomni²

¹Internal Security Forces Hospital La Marsa, Internal Medicine, Tunis, Tunisia, ²Internal Security Forces Hospital La Marsa, Gastroenterology, Tunis, Tunisia, ³Internal Security Forces Hospital La Marsa, Laboratories, Tunis, Tunisia

Contact E-Mail Address: ayari.myriam@hotmail.fr

Introduction: Inflammatory bowel disease physiopathology involves various factors including the host immune system and management often requires immunosuppressive therapy posing, consequently, challenges in the context of vaccination. The advent of vaccines against SARS-CoV-2 a major role in the global fight against the pandemic, however questions regarding efficacy in specific patient populations particularly those with underlying immune-mediated conditions such as Crohn's disease are raised.

Aims & Methods: The aim of our study was to assess the humoral response in patients with CD under conventional immunosuppressive or biotherapies and to compare with healthy controls. We conducted a single-center descriptive study involving CD patients who had received at least one dose of the SARS-CoV-2 vaccine between January and June 2022. Additionally, healthy volunteers (HV) who had received at least one vaccine dose were included. To evaluate the humoral response, we assessed quantitative Anti-SARS-CoV-2 antibodies (using IgM and IgG assays) with the VIDAS® method for all participants.

Results: In total, we collected a total of 58 blood samples (28 patients with CD and 30 HV), the median age was 48.39 years $\pm$ 12.14. Regarding medical treatment of CD, 12 patients were on biotherapies: Infliximab (n=9), Adalimumab (n=2) and Ustekinumab (n=1). Twenty-one patients had conventional immunosuppressive: azathioprine (n=19), methotrexate (n=1), corticosteroids > 10 mg/d (n=2). The majority of the patients had received at least 2 doses of the vaccine with a median number of doses in both groups was 2 IC95% [1-4]. There was no statistically significant difference regarding the number or the type of the vaccine between the 2 groups. CD patients had a lower mean level of Ig G against SARS-Cov2 antibodies (20.34 IU +/- 15.57) comparing to healthy controls (32.97 +/- 10.18) with statically significant difference (p= 0.001). Regarding the type of treatment, there was no significant difference of the level of antibodies between conventional immunosuppressive drugs and biotherapies In CD patients.

Conclusion: This study highlights an altered immune response in patients with Crohn's disease, reflected in a reduced humoral response compared to healthy controls. Assessing the serological response to SARS-CoV2 vaccination in this vulnerable population is of paramount importance for optimizing vaccination strategies and protecting the public.

Disclosure: Nothing to disclose.

PP1237

MANAGEMENT OF CODE STATUS IN PATIENTS UNDERGOING ENDOSCOPIC PROCEDURES - SURVEY ON THE CURRENT CLINICAL PRACTICES AND BELIEFS OF PORTUGUESE GASTROENTEROLOGISTS

A.R. Franco¹, P.A. Lima¹, I. Simao¹, R.R. Mendes¹, A. Mascarenhas¹, R. Barosa¹, C. Chagas¹

¹Unidade Local de Saúde Lisboa Ocidental, Gastroenterology, Lisboa, Portugal

Contact E-Mail Address: ana.rita.franco@campus.ul.pt

Introduction: Cardiorespiratory arrest is a recognized complication of endoscopic procedures, particularly when sedation is administered. Hospitalized patients, especially those with a prescribed Do Not Resuscitate (DNR) order, are more likely to have severe underlying illness, and consequently a higher risk of cardiorespiratory complications. Additionally, the request for endoscopic exams, especially urgent ones, in this group of patients is becoming increasingly common.

Aims & Methods: The aim of this study was to assess the current clinical practices, as well as the beliefs of gastroenterologists in Portugal regarding the management of the code status in hospitalized patients with prescribed DNR undergoing endoscopic procedures.

Self-reported data was obtained through a voluntary and anonymous survey of gastroenterologists and gastroenterology trainees in Portugal.

Results: One hundred and forty five gastroenterologists, of which 26 (17.9%) were trainees, responded to the survey, with an average age of 42 years (27-83 years), and 59.3% female. The majority are aware of the patient's code status prior to the endoscopic procedure (73.1%, n=106). However, DNR is rarely discussed (<25% of cases) with the patient/legal representative (66.9%, n=97) or attending physician (58.6%, n=85). In patients with prescribed DNR, the rate of reversal prior to the procedure is rarely performed (reversal in all or almost all in 8.3%, n=12). Most respondents are unaware of the procedures necessary for DNR prescription (81.3%, n=118), as well as existing national/international recommendations on DNR reversal (96.5%, n=140). Regarding personal beliefs, the majority consider that in these patients DNR should be reversed to an intermediate option that includes limited resuscitation maneuvers according to the patient's preference (62.1%, n=90). They also believe that the urgency of a procedure should not influence the decision to reverse DNR (n=89, 61.4%), and that if DNR is reversed, it should be done by the attending physician who initially prescribed it (91.7%, n=133). Finally, respondents are divided when asked if they would perform an endoscopic procedure on a patient with prescribed DNR that has not been previously reversed: 49.7% answered yes (n=72), 22.1% no (n=32), and 28.3% have no formed opinion (n=41). There is a consensus on the need for recommendations on this topic for gastroenterologists (97.9%, n=142).

Conclusion: The majority of Gastroenterologists rarely reverse DNR before endoscopic procedures, however, it is mostly advocated that limited resuscitation maneuvers should be offered according to patient preference. Most are unaware of the existence of institutional, national, or international policies regarding DNR. These findings suggest considerable variation in knowledge and approach to hospitalized patients with DNR, highlighting the need for specific recommendations for Gastroenterology in this area.

References: H. Carneiro A, Carneiro R. DNR A Decisão de Não Reanimar. Revista Portuguesa de Medicina Interna [Internet]. 5 de Dezembro de 2021 Braga I, Dutschmann L, Fiuza T, Almeida H, Gil V, Brandão T. Implementação da Ordem de Não Reanimar. Revista Ordem Médicos. 2012;133:20-23.

Wada K, Szego MJ. Revisiting code status in patients undergoing GI endoscopy with a "do not resuscitate" order. Gastrointest Endosc. 2019 Feb;89(2):380-382.

Feld LD, Mergener K, Rubin DT, Rao VL. Management of code status in the periendoscopic period: a national survey of current practices and beliefs of U.S. gastroenterologists. *Gastrointest Endosc.* 2021 Jul;94(1):172-177.e2.

Disclosure: Nothing to disclose.

PP1238

WORK-LIFE CONFLICT AND ITS HEALTH EFFECTS ON MOROCCAN GASTROENTEROLOGISTS

B. Aourarh¹, S. Berrag¹, S. Ouahid¹, R. Laaroussi¹, A. Touibi¹, I. Radouane¹, N. Fouad¹, T. Adioui¹, M. Tamzaourte¹

¹Military Teaching Hospital Mohamed V, Rabat, Morocco

Contact E-Mail Address: benayad.aourarh@gmail.com

Introduction: Gastroenterologists are exposed to various health-related risks in their professional roles,

Because they have various roles including endoscopists, clinicians, and in some cases, academic professionals. Our study aims to assess the work-life balance model and the prevalence of work-related physical and mental symptoms, as well as the effects of work-life balance on the health of Moroccan gastroenterologists.

Aims & Methods: A total of 152 gastroenterologists from various cities in the country participated in an anonymous electronic questionnaire regarding their daily activities and symptoms. A work-life balance ratio was calculated by dividing the number of working hours (per week) by the number of hours spent outside of work (including activities and sleep). Musculoskeletal, gastrointestinal, and mental symptoms were recorded. The Maslach Burnout Inventory (MBI) was used to measure the burnout score.

Data was entered and analyzed using the JAMOVI 2.2 software for Mac.

Results: 152 Moroccan gastroenterologists were included in the study, with 72.4% being female and 27.6% male, resulting in a sex ratio of 0.38. The median age of the respondents was 31 years (range: 26 to 64 years), with 61.8% being married, of which 70.2% were married to physicians. The mean number of working hours per week was 50.2 ± 12.7 , with a median number of endoscopies per week of 6.5 (range: 2 to 12). 86.8% reported musculoskeletal disorders, and 71.1% reported digestive disorders. Regarding mental symptoms, 23.7% reported anxiety, and 46.1% reported depression, with 21.1% experiencing both simultaneously.

The median work-life balance ratio was 0.42 (range: 0.32-0.55).

In univariate analysis, this ratio was not correlated with sex or musculoskeletal and digestive symptoms but was correlated with age ($p < 0.001$) and mental symptoms ($p < 0.001$ for depression and $p = 0.007$ for anxiety). However, in multivariate analysis by adjusting the parameters studied, namely age, sex, presence of confirmed depression, and confirmed anxiety, only age emerged as an associated factor (Beta = $-0.24 + (-0.46; 0.013)$). Using the MBI scale, 72.4% of the respondents were found to be experiencing burnout. Burnout was not correlated with sex but was associated with the work-life balance ratio ($p = 0.04$). It is noteworthy that two of the three categories of this scale, namely depersonalization and personal accomplishment, were associated with the age of the respondents ($p = 0.002$ and $p = 0.003$). Indeed, a moderate negative correlation was found between age and depersonalization ($r = -0.32$), and a moderate positive correlation was found between age and personal accomplishment ($r = 0.31$).

Conclusion: Moroccan gastroenterologists suffer from musculoskeletal, digestive, and mental symptoms, and are prone to burnout likely due to long and laboring work. Our study found that younger individuals worked more and were more likely to experience burnout, particularly with decreased empathy towards patients and diminished personal accomplishment.

Disclosure: No conflict of interest was noted.

PP1239

THE USE OF GRIP STRENGTH MEASUREMENT IN HIGH-VOLUME ENDOSCOPISTS AND NON-INTERVENTIONAL GASTROENTEROLOGISTS - A NEW APPROACH FOR THE ASSESSMENT AND PREVENTION OF MUSCULOSKELETAL HEALTH DISORDER IN GASTROINTESTINAL ENDOSCOPY?

N. Sturm¹, A. Fichtl¹, M. Wagner^{1,2}, F. Baumann³, B. Walter^{1,2},

Endoscopic Research Unit, University Hospital Ulm

¹University Hospital Ulm, Department of Internal Medicine

I, Ulm, Germany, ²University Hospital Ulm, Department of

Interdisciplinary Endoscopy, Ulm, Germany, ³University Hospital

Cologne, Department of Internal Medicine I / Center for

Integrated Oncology, Cologne, Germany

Contact E-Mail Address: benjamin.walter@uniklinik-ulm.de

Introduction: Up to 80% of practicing GI endoscopists are affected by musculoskeletal health disorder with significant influence on personal health, absence from work and reduction of endoscopic workload (1). It is estimated that overuse injury is a main mechanism of health impairment, but methods to prevent musculoskeletal disorder in GI endoscopists are elusive. Since hand grip strength measurement has been identified as an important indicator of musculoskeletal health and physical fitness (2), the further evaluation of hand grip strength in working endoscopists in comparison to non-endoscopists might bring further evidence to prevent musculoskeletal health disorder in GI endoscopists.

Aims & Methods: In this prospective single-center pilot study, measurement of hand grip strength was conducted on 20 workdays by a high-volume GI endoscopist and a gastroenterologist who did not perform endoscopic procedures before and after work at University Hospital Ulm. For hand grip strength measurement, JAMAR® Plus Hand Dynamometer was used according to the Southampton protocol (3). Three serial measurements were performed with each hand to obtain an average grip strength at each measurement point. Statistical analysis was performed using SPSS Statistics 29 (IBM, USA). Mann-Whitney U test, students t-test, univariate analysis of variation (ANOVA) and Kruskal-Wallis test were performed whenever applicable.

Results: Average hand grip strength of the high-volume endoscopist was not significantly higher than the hand grip strength of the non-endoscopic working gastroenterologist (left hand: 102.2 lbs vs. 93.3 lbs, $p=0.26$; right hand: 114.0 lbs vs. 108.2 lbs, $p=0.44$). In comparison, hand grip strength was significantly higher after work in non-endoscopist subject for both hands (left: 89.2 lbs vs. 95.4 lbs, $p=0.025$; right: 95.9 lbs vs. 101.4 lbs, $p=0.035$) while the participating endoscopist had a significant lower grip strength after work (left: 107.4 lbs vs. 95.2 lbs, $p<0.001$; right: 106.8 lbs vs. 95.6 lbs, $p<0.001$). In both subjects, the day of the week (beginning vs. end of the week) had no effect on hand grip strength.

Conclusion: As hand grip strength is associated with health performance status, significant difference can be observed between endoscopists and non-endoscopists in the impairment of hand grip strength within a workday. To prevent musculoskeletal health issues in endoscopists, timing and effect of health interventions could be implemented by evidence from hand grip strength measurement. Therefore, further observation studies are mandatory to develop methods to prevent musculoskeletal health disorder especially for high-volume endoscopists.

References: 1. Sturm, N., Leukert, J., Perkhof, L. et al. The impact of endoscopic activity on musculoskeletal disorders of high-volume endoscopists in Germany. *Sci Rep* 12, 8538 (2022). <https://doi.org/10.1038/s41598-022-12400-4>

2. Kim, S.H., Kim, T., Park, J.C. et al. Usefulness of hand grip strength to estimate other physical fitness parameters in older adults. *Sci Rep* 12, 17496 (2022). <https://doi.org/10.1038/s41598-022-22477-6>

3.Helen C. Roberts, Hayley J. Denison, Helen J. Martin, Harnish P. Patel, Holly Syddall, Cyrus Cooper, Avan Aihie Sayer, A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach, *Age and Ageing*, Volume 40, Issue 4, July 2011, Pages 423–429, <https://doi.org/10.1093/ageing/afr051>

Disclosure: Nothing to disclose.

PP1240

A QUESTIONNAIRE SURVEY-BASED ANALYSIS FOR LYNCH SYNDROME SCREENING AND SURVEILLANCE TRENDS AMONG GASTROENTEROLOGISTS IN JAPAN

Y. Urabe¹, S. Oka², H. Ishikawa³, T. Nakajima⁴, K. Tanakaya⁵, H. Ishida⁶, S. Tanaka⁷

¹Hiroshima University, Hiroshima, Japan, ²Hiroshima University Hospital, Gastroenterology and Metabolism, Hiroshima, Japan,

³Kyoto Prefectural University of Medicine, Molecular-Targeting Cancer Prevention, Kyoto, Japan, ⁴School of Public Health, Kyoto University, Medical Ethics and Medical Genetics, Kyoto, Japan, ⁵National Hospital Organization Iwakuni Clinical Center, Department of Surgery, Yamaguchi, Japan, ⁶Saitama Medical Center, Department of Digestive Tract and General Surgery,, Saitama, Japan, ⁷JA Onomichi General Hospital, Endoscopy and Medicine, Onomichi, Japan

Contact E-Mail Address: beyan13@hiroshima-u.ac.jp

Introduction: Recently, in Japan, insurance coverage for microsatellite instability (MSI) testing as a companion diagnostic agent for immune-checkpoint inhibitors and comprehensive cancer genome profiling has highlighted the growing importance of Lynch syndrome (LS) awareness among gastroenterologists.

Aims & Methods: Our aim was to assess the shifts in knowledge regarding LS and practice trends among Japanese gastroenterologists. We conducted a questionnaire survey on physicians' knowledge and practice trends regarding LS in their facilities, collaborating with the councilors of the Japanese Society of Gastroenterology in 2020 and 2022. The knowledge survey on LS encompassed an understanding of the genetic background of LS, primary and secondary screening methods for LS, and spillover effects of comprehensive cancer genome profiling tests on LS practice. Meanwhile, the practice trends survey on LS examined information on the LS screening methods utilized, the number of patients screened for LS, and LS surveillance methods. Each questionnaire item was compared between the first and second surveys to determine the proportion of physicians who chose each option based on the total number of physicians who completed the questionnaire. The responses of physicians who participated in both surveys were analyzed to assess changes in their responses to each question.

Results: The knowledge survey was completed by 146 in the first survey and 228 doctors in the second survey. Besides, the practice trend survey was completed by 362 in the first survey and 195 doctors, respectively, in the second survey. The second survey revealed a significant increase in several key indicators compared to the first survey. These included the number of physicians opting for universal tumor screening as the primary screening method for LS (26/195 vs. 20/354), the proportion of physicians conducting the BRAF V600E test for chemotherapy selection (100/195 vs. 137/354), the number of newly diagnosed patients with LS in the last 3 years per physician (1.64±4.15 vs. 0.96±3.27), and the number of patients with LS currently under surveillance per physician (2.00±5.09 vs. 1.15±4.03). Among physicians who participated in both surveys, the knowledge about primary and secondary screening methods, the proportion offering BRAF V600E testing in colorectal cancer tissue and perform-

ing screening tests for endometrial cancer, and the number of patients with LS currently under surveillance per physician were significantly higher in the second survey than in the first survey. Physicians who initiating or strengthening the inspection of primary and secondary screening for LS between the first and second surveys had a significantly higher proportions of increasing currently surviving patients with LS compared with those who continued or discontinued screening tests. (13/33 vs. 13/100, 11/33 vs. 13/100)

Conclusion: In conclusion, there has been a notable increase in both the number of patients diagnosed with LS and the number of patients screened for LS in Japan in recent years. This increase can be attributed to an increase in the number of physicians performing primary screening, such as universal tumor screening, and secondary screening utilizing MSI and immunohistochemistry for mismatch repair protein tests.

Disclosure: This study was supported by a research grant from The Japanese Society of Gastroenterology.

PP1241

RESULTS AND LEARNING CURVE AFTER IMPLEMENTATION OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN STOMACH AND RECTUM – PROSPECTIVE ANALYSIS FROM TWO WESTERN ENDOSCOPISTS

H. Coelho¹, F. Correia¹, F. Ferreira¹, M. Cardoso¹, A. Martins¹, D. Horta¹, J. Canena^{1,2}, L. Lourenço^{1,2}

¹Hospital Professor Doutor Fernando Fonseca, Gastroenterology, Amadora, Portugal, ²Hospital CUF Tejo, Gastroenterology, Lisboa, Portugal

Contact E-Mail Address: henriquecoelho.1996@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) enables the *en bloc* resection of superficial lesions of the gastrointestinal tract. Initially developed in the East, the implementation of the technique has been more difficult in the West, mainly due to the lower incidence of gastric neoplasia.

Aims & Methods: In our study, we aimed to evaluate the clinical outcomes since the introduction of the ESD technique in two distinct centers and describe the learning curve of 2 endoscopists that performed the procedures. This is a prospective analysis composed of patients that underwent rectal and gastric ESD between 2019 and 2024. We evaluated *en bloc* and R0 resection rates and recurrence rates. Complications were defined as adverse events related to the procedure that required reintervention or prolongation of the hospital stay. The area of the resected lesion was calculated in cm² (assuming an elliptical shape) and the speed of dissection in cm²/hour.

Using cumulative sum analysis, we identified the procedure in which a significant increase in the speed of dissection was observed and compared outcomes in the two time periods defined by this cut-off.

Results: We included a total sample of 100 patients (59% male, age 69.9±5.4 years).

Gastric ESD was conducted in 56 patients (57% male, age 59.3±2.9 years). *En bloc* resection rate was 98.2% (n=55) and R0 resection was 91.1% (n=51). 10.7% of the procedures had complications (1 perforation, 2 lesions of the muscular layer and 3 post-procedural bleedings). The mean area of the resected specimens was 7.8 ± 5.0 cm². The mean dissection speed was 8.2 ± 5.2 cm²/hour. The mean hospital stay was 1.3 ± 0.3 days.

There was a significant increase in proficiency by the procedure number 27. When comparing the two groups, there was a tendency for an increase in R0 resection (88.9% vs 93.0%, p=0.294) and a decrease in the recurrence rate (12% vs 5%, p=0.194) in the later time period. There was a significant reduction in the complication rate (18.5% vs 3.4%, p<0.001).

Rectal ESD was performed in 44 patients (61.4% male, age 71.5 ± 3.1 years). *En bloc* resection was 97.7% (n=43) and R0 resection was 86.4% (n=38). The complication rate was 38.6% (9 post-procedural bleedings; 8 post-coagulation syndromes), none of which required surgical treatment. The mean area of the resected specimens was 13.4 ± 4.6 cm² and mean dissection speed was 6.5 ± 4.1 cm²/hour. The mean hospital stay was 2.2 ± 0.7 days.

There was a significant increase in proficiency by the procedure number 33. The R0 resection rate was similar between groups (85%vs82%, $p=0.34$), with a tendency to a decrease in complication rate (36%vs27%, $p=0.29$). A total of 9 adenocarcinomas were resected, with endoscopic cure in 88.9% cases (n=8).

Conclusion: We believe that the evaluation of the results of this intervention allows not only to assure that the quality criteria are being met but also to aid in the creation of learning programs for trainees. The learning curve associated with gastric ESD was steeper than that of rectal ESD. It appears that rectal ESD requires a larger number of procedures until the quality criteria proposed by the European Society of Gastrointestinal Endoscopy are met.

Disclosure: No conflict of interest.

PP1242

ENDOSCOPIC MANAGEMENT OF GASTROINTESTINAL SUBEPITHELIAL LESIONS IN A SPANISH TERTIARY HOSPITAL

C. Amor Costa¹, M. Tavecchia Castro¹, P. De Maria Pallares¹, E. Martín-Arranz^{1,2}, G. Ruiz Fernandez¹, E. Marin Serrano¹, C. Amiama Roig¹, I. González Díaz¹, C. Froilan Torres¹, A. Burgos García¹

¹Hospital La Paz, Gastroenterology and Hepatology, Madrid, Spain, ²Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain

Contact E-Mail Address: carmenamorcc@gmail.com

Introduction: Subepithelial lesions (SELs) are a common incidental finding in the gastrointestinal tract during endoscopy. Endoscopic ultrasonography (EUS) is the best tool to characterize SELs features and in several cases it allows anatomopathological diagnosis after fine-needle biopsy (FNB) or aspiration (FNA) (1).

The indication and technique for endoscopic resection of SELs depend on the type, size, depth of invasion and location (1).

Superficial SELs can be resected using endoscopic submucosal dissection (ESD)(2) and others can even be removed by endoscopic mucosal resection (EMR), such as neuroendocrine tumors (NETs) ≤ 10 mm (3).

Aims & Methods: The aim of this study is to assess the endoscopic management of SEL. A unicentric retrospective study was performed. There were collected the LSE endoscopically removed in an advanced endoscopy center between 2017 and 2024. The resection technique was at the discretion of the endoscopist. Those LSE that required surgical treatment were excluded.

Results: 50 lesions were included, the main characteristics are described in table 1.

In bloc resection (R0) was achieved in 45 SELs (90%). There were 5 cases (10%) of fragmentated resection (R1), 2 (40%) resected by ESD, 1 hybrid (20%) and 2 (40%) with hot snare. The mean size of R1 lesions was 17.2 mm (SD +/- 14.0). The histology and location were: 3 rectal NETs (60%) and 2 gastric fibroid polyps (40%).

The histopathological result of 13 SELs (26%) revealed focal contact with the deep margin. 12 (92.3%) were NETs located: 8 (66.7%) in rectum, 3 (25%) in duodenum and 1 (8.3%) gastric.

USE was performed in 21 cases (42%). In 8 LSE (38.1%) FNA was performed,

and only in 3 (37.5%) was the histopathological sample representative: 1 GIST (33.3%) and 2 NETs (66.7%). 18 (85.7%) of them were located in the muscularis mucosa or submucosa. 2 LSE (9.5%) involved the muscular layer: 1 GIST (50%) and 1 fibroid polyp (50%). Both cases were resected using ESD and a perforation was documented during the procedure in each. There were 10 (18%) complications registered: 7 bleeding (70%), 2 perforations (20%) and 1 gastrostomy (10%) to retrieve the lesion. 7 of them (70%) required endoscopic treatment, 2 (20%) surgical treatment, and in 1 case (10%) no treatment was needed. ESD presented a higher tendency of complication rates compared to the other techniques.

In 20 patients (40%) a revision endoscopy was performed, only 1 (5%) recurrence of a gastric NET was registered one year after the resection.

Variable	N 50
Men (%)	27 (54)
Age (mean, SD)	64 (14)
Gastrointestinal localization (%):	
Gastric	- 20 (40)
Duodenum	- 6 (12)
Colon	- 3 (6)
Rectum	- 21 (42)
Size (mm) (mean, SD)	14.16 (13.1)
Type of LSE (%):	
NET	33 (66)
GIST	1 (2)
Leiomioma	3 (6)
Lipoma	6 (12)
Fibroid polyp	7 (14)
Resection technique (%):	
ESD	13 (26)
RME	4 (8)
L-RME	18 (36)
Endoloop	3 (6)
Hybrid	4 (8)
Hot snare polypectomy	7 (14)
Cold snare polypectomy	1 (2)
In bloc resection (R0) (%)	45 (90)
USE performed (%)	21 (42%)
Gastric	13 (61.2)
Duodenum	4 (19.1)
Rectum	4 (19.1)
Complications (%)	10 (20)
Hemorrhage	7 (70)
Perforation	2 (20)
Other	1 (10)

Conclusion: In our experience the most frequent SELs are gastric NETs and the main resection technique is L-EMR which achieves high rates of R0 with low complications. ESD is the second most used technique with a higher tendency for complication rates. The risk of recurrence after resection appears to be low.

References:

1. Deprez, Pierre H et al. "Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE) Guideline." *Endoscopy* vol. 54,4 (2022): 412-429. doi:10.1055/a-1751-5742
2. Ma, Xiao-Xin et al. "Endoscopic treatment and management of rectal neuroendocrine tumors less than 10 mm in diameter." *World journal of gastrointestinal endoscopy* vol. 15,2 (2023): 19-31. doi:10.4253/wjge.v15.i2.19
3. Santos-Antunes, João et al. "Retrospective analysis of the outcomes of endoscopic submucosal dissection for the diagnosis and treatment of subepithelial lesions in a center with high expertise." *Annals of gastroenterology* vol. 35,1 (2022): 68-73. doi:10.20524/aog.2021.0675

Disclosure: Nothing to disclose.

PP1243

SINGLE-CENTER EXPERIENCE OF MANAGMENT OF PERFORATION AFTER ENDOSCOPICAL SUBMUCOSAL DISSECTION (ESD) USING OVER-THE-SCOPE CLIP (OTSC)

G. Leonardi¹, B. Toro¹, F. Bronzini¹, F. Rettura¹, M. Blois¹, M.R. Falcone¹, C. Sterpi¹, R. Manta¹

¹Ospedale di Livorno, Livorno, Italy

Contact E-Mail Address: francesco.bronzini@uslnordovest.toscana.it

Introduction: The Endoscopic Submucosal Dissection (ESD) is an advanced resection technique for removing “en bloc” gastrointestinal (GI) lesions, bigger than 20 mm and with macroscopic features of no deep infiltration (limited to the submucosal). It is a complex procedure and, therefore, with risk of complications (early and/or delayed), first of all bleeding, then perforation.

Aims & Methods: Our aim is to confirm the pivotal role of Over-The-Scope Clip (OTSC) for management of perforation occurred during the ESD. Our Centre started the ESD technique from March 2023 by an expert endoscopist, with a colleague in training, and we have included in a database the information of all procedures carried out from that period to September 2023.

Results: Were included 34 adult patient (M/F: 19/15) with an age mean of 69 years. The mean lesions size was of 31 mm ± 20 for the upper-GI, 25 mm ± 15 for the lower-GI. Histological findings were reported in the tab. 1. All procedures were performed under general anesthetic care. Lesions were successfully resected “en bloc” in all patients (100%) by ESD procedure using minimal CO2 insufflation. The overall intraprocedure perforation occurred in 3 out of 34 (8,8%): 1 out of 18 was located in the upper-GI tract (fundus); 2 out of 16 lesions were located in the lower-GI tract (1 in the ascending colon and 1 in the descending colon, respectively).

According to clinical and medical stability of the patients, all the parietal defect were treated successfully, at the end of the complete ESD, by positioning OTSC, allowing a full-thickness closure of the GI tract defect, avoiding emergency surgery. The R0 rate was of 94.1%, with two cases that underwent to surgery because of “pT2” at the final histological report.

Conclusion: OTSC is a known safe and efficacy device for closing perforation occurred during ESD, in the course of the same endoscopic procedure. More and larger studies are needed to further validate these findings.

Disclosure: Nothing to disclose.

PP1244

USE OF A DYNAMIC SELF-ADJUSTING PROSTHESES (P.A.D.) IN INGUINAL HERNIA REPAIR: OUR EXPERIENCE IN 200 PATIENTS

A. Alvigi¹

¹University of Naples “Federico II”, Naples, Italy

Contact E-Mail Address: dr.antonioalvigi@outlook.it

Introduction: P.A.D. is a therapeutic solution for inguinal hernias, featuring a double polypropylene mesh anchored to the inguinal canal. Its adaptable design accommodates morphological variations during positional changes. A trapezoidal area, determined through patient studies, guides the shape and placement of the prostheses. The lower prosthesis fits this area and is anchored to the internal oblique muscle, while the upper prosthesis is secured to the pubic tubercle and inguinal ligament. Dynamic adjustments between the prostheses ensure continuous support and prevent weak areas. The procedure aims for well-stretched, tension-free prostheses parallel to the inguinal floor, minimizing risks associated with traditional techniques.

Aims & Methods: Between September 01, 2022, and September 30, 2023, our General Surgery department at the Santa Maria della Pietà dei Religiosi Camilliani Hospital in Casoria (Naples) conducted 300 inguinal hernioplasties on male patients. Prior to surgery, all patients underwent laboratory and radiological examinations. A standardized inguinal hernioplasty procedure using P.A.D. was performed for all patients. The procedure involved a 5-6 cm incision between the iliac spine and the pubic tubercle, followed by dissection of skin, subcutis, and Scarpa’s fascia. The aponeurosis of the external oblique muscle was identified and opened, allowing access to the external inguinal ring. The ilioinguinal and iliohypogastric nerves were identified, and the cremaster muscle was dissected to access the hernial sac and spermatic cord. The type of inguinal hernia was determined, and appropriate steps were taken to address it, including reduction of the hernia sac and plication of the transversalis fascia if necessary. Pre-hernial lipomas were resected, and additional exploration was conducted to reduce the risk of recurrence. The P.A.D. was affixed using a standardized procedure, followed by closure of the external oblique muscle, subcutis, and skin. Patients were able to walk within 3-4 hours post-surgery and were discharged within 6-8 hours or the following day for afternoon surgeries. Follow-up evaluations were conducted up to 6 months post-surgery to monitor for complications such as hematomas, seromas, pain, inflammation, infection, and recurrence.

Results: Out of 200 recruited, a total of 120 patients underwent open groin right hernia repair with a right:left ratio of 1.3:1. Their age ranged from 0 to 88 years with a mean age of 33.94 ± 23.40 years. Among the patients, 60.2% of the hernias occurred in ages below 50 years; 3.6% had bilateral hernias. Post-operative complication rate was 2.3%, hematoma resulted as the most common one (0.65%). Relapses in 6 months were 0.5%.

Relapses	0.5%
Seromas	0.4%
Hematomas	0.65%
Wound infections	0.5%
Pain over 4 days	2.5%
Persistent neuralgia beyond 7 days	0.15%

Conclusion: The inguinal hernioplasty technique with P.A.D. is currently standardized. We have found the technique to be easy to replicate and easy to perform, even in cases of large hernias. Under no circumstances did we have to cut out and modify the size and shape of the pre-shaped P.A.D. which therefore adapted well to the anatomy of the IC. Postoperative complications, both short and long term, were limited, similar to the results found in scientific literature. This suggests that the P.A.D. inguinal hernioplasty technique is a valid alternative as an open onlay inguinal hernioplasty technique.

Disclosure: Nothing to disclose.

PP1245

CORRELATION BETWEEN BOWEL SOUNDS VERSUS CLINICAL AND ENDOSCOPIC DATA : AI-POWERED ANALYSIS

K. Bouslama¹, N.G. Abassi², A. Nakhli¹, D. Pohl³, D. Gillet⁴, C. Frei⁵, N. Hemdani¹, B. Bouchabou¹, Z. Benzarti¹, R. Ennaifer¹

¹University of Tunis Manar (Faculty of Medicine of Tunis) / Mongi Slim Hospital, Gastroenterology Department, Tunis, Tunisia, ²EPFL (Ecole Polytechnique Fédérale de Lausanne) / DigeHealth, Zurich, Switzerland, ³University Hospital Zurich, Gastroenterology and Hepatology, Zürich, Switzerland, ⁴EPFL - Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, ⁵DigeHealth, Zurich, Switzerland

Contact E-Mail Address: kais.bouslama@gmail.com

Introduction: Bowel sound analysis holds promise as a non-invasive, cost-effective alternative to conventional diagnostic methods. However, standardized recording and interpretation methods are lacking. Our study aims to address this gap by investigating the correlations between bowel sounds and clinical/endoscopic data in patients.

Aims & Methods: We conducted a single-center, observational, cross-sectional study at the Mongi Slim Hospital's Gastroenterology Department. The study included patients scheduled for colonoscopy who had followed a residue-free diet for at least three days and ingested a bowel prep the day before the examination. We collected the patients' medical and surgical history, their digestive complaints, and performed a bariatric assessment. Bowel sounds were then recorded for 5 minutes using a modified version of the Littman® CORE Digital stethoscope and were then analyzed using AI programs to extract acoustic features. Afterwards, these features were compared with clinical and endoscopic data to establish correlations.

Results: We included 95 patients in our study (mean age = 56.32 years, sex ratio M/F = 1.02). Colonoscopy was performed in 83 patients (87.37%) and was total in 62 patients (74.70%). At least one endoscopic anomaly was present in 47 patients (54.63%). The most common finding was polyps in 27 patients, representing 57.45% of patients with an endoscopic anomaly. We labeled 33,837 bowel sounds from the 95 recordings of the included patients, with an average of 356.18 bowel sound labels per recording. The mean ratio of bowel sound duration to recording duration was 22.75%, corresponding to 68 seconds of bowel sounds out of the 5 minutes recorded.

In the analytical study, we found that gender was correlated with the RMS and Envelope features, with p-values of 0.021 and 0.032, respectively, suggesting that men tend to have an increased overall amplitude of the signal, while women exhibit a greater variability of amplitude over time. Difficulty passing gas was also correlated with RMS and Envelope with p-values of 0.039 and 0.032, respectively, implying that patients having trouble passing gas produce sounds with lower average amplitude and increased variability over the course of the signal.

Difficulty passing gas was also correlated with Spectral Contrast with a p-value of 0.036. This means that in these patients, the spectral energy is evenly distributed across frequencies and there are no major frequency variations over the course of the signal.

The presence of an endoscopic anomaly was also correlated with RMS and Envelope with p-values of 0.027 and 0.024, respectively, suggesting that in the presence of an endoscopic anomaly, the average amplitude of the signal would be lower, and the amplitude of the sounds would be more variable over the course of the signal.

We also found that the presence of polyp(s) was correlated with RMS and Envelope with p-values of 0.041 and 0.042, respectively, indicating that in the presence of polyp(s), the average signal amplitude is lower, and the amplitude of the sounds is more variable over the course of the signal.

Conclusion: Although conducted under experimental conditions, since we used a controlled diet and bowel prep, this study demonstrated promising correlation between bowel sounds and both clinical data and endoscopic findings in patients, particularly the amplitude of bowel sounds and its variations over time. Further studies are needed to verify these correlations under more real-life conditions.

References:

- Wang N, Testa A, Marshall BJ. Development of a bowel sound detector adapted to demonstrate the effect of food intake. Biomed Eng OnLine. 4 janv 2022;21(1):1.
 - Inderjeeth AJ, Webberley KM, Muir J, Marshall BJ. The potential of computerised analysis of bowel sounds for diagnosis of gastrointestinal conditions: a systematic review. Syst Rev. déc 2018;7(1):124.
 - Nowak JK, Nowak R, Radzikowski K, Grulkowski I, Walkowiak J. Automated Bowel Sound Analysis: An Overview. Sensors. janv 2021;21(16):5294.
 - Redij R, Kaur A, Muddaloor P, Sethi AK, Aedma K, Rajagopal A, et al. Practicing Digital Gastroenterology through Phonoenterography Leveraging Artificial Intelligence: Future Perspectives Using Microwave Systems. Sensors. janv 2023;23(4):2302.
 - Yoshino H, Abe Y, Yoshino T, Ohsato K. Clinical application of spectral analysis of bowel sounds in intestinal obstruction. Dis Colon Rectum. sept 1990;33(9):753.
 - Craine BL, Silpa M, O'Toole CJ. Computerized Auscultation Applied to Irritable Bowel Syndrome. Dig Dis Sci. 1 sept 1999;44(9):1887-92.
- Disclosure:** This study was conducted along with DigeHealth, a swiss start-up working on developing a non invasive monitoring system for bowel disorders.

PP1246

THE IMPACT OF CFTR MODULATOR THERAPY ON LOWER AIRWAY MICROBIOTA IN PEOPLE WITH CYSTIC FIBROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.F. Juhász¹, K. Ocskay¹, A. Párniczky^{1,2}

¹Heim Pál National Pediatric Institute, Budapest, Hungary,

²Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary

Contact E-Mail Address: flixjuhsz@gmail.com

Introduction: In people with cystic fibrosis (CF), CFTR modulator therapy has resulted in marked improvements in pulmonary exacerbations, lung function, body weight, and quality of life. However, it remains unclear how restoring CFTR function modifies existing airway infection and inflammation. Understanding the dynamics of airway microbiome changes in response to modulator therapy plays an essential role in developing strategies for managing airway infections.

Aims & Methods: Our aim was to conduct a systematic review and meta-analysis of all available studies.

We conducted a systematic search on the 26th January, 2024 in MEDLINE, Embase, Web of Science, Scopus and CENTRAL. We performed a random-effects meta-analysis of any provided data pertaining to lower airway microbiota composition before versus after the initiation of CFTR modulator therapy. We calculated mean difference (MD) and standardized MD (SMD) with 95% confidence intervals (CI) and visualized the results on forest plots. Chi-squared tests were performed and I² values calculated to assess statistical heterogeneity.

Results: 30 studies were eligible for inclusion, with most prospectively examining people with CF before and 4-12 months after the initiation of CFTR modulator therapy. The initiation of CFTR modulator therapy was associated with an increase in lower airway alpha-diversity (Shannon index; SMD: +0.39 (95% CI: +0.20 - +0.59), p<0.0001), evenness (Pielou index;

SMD: +0.84 (95% CI: +0.55 - +1.12), $p < 0.00001$) as well as a reduction in the relative abundance of classical CF lung pathogen species *Pseudomonas* (MD: -7.1% (95% CI: -1.2% - -13.1%), $p = 0.02$) and *Staphylococcus* (MD: -4.3% (95% CI: -2.0% - -6.6%), $p = 0.0003$).

Conclusion: Our results demonstrate a clear and statistically significant association between the initiation of CFTR modulator therapy and the stabilization of lower airway microbiota in terms of increased biodiversity, more balanced distribution of microbial species and reduction in the abundance of potentially pathogenic species, all of which contribute to a lower risk of respiratory tract infections.

Disclosure: Nothing to disclose.

Index of Authors and Co-Authors

Presenting authors are identified by abstract numbers in boldface type.

United European Gastroenterology Journal

2024, Vol 12 (S8) | © Author(s) 2024

Reprints and permissions: [wiley.com/en-gb/permissions](https://www.wiley.com/en-gb/permissions)

DOI: 10.1002/ueg2.12616 | onlinelibrary.wiley.com/journal/20506414

UNITED EUROPEAN
GASTROENTEROLOGY
ueg journal
WILEY

A

- Aabakken, L. MP044, PP1063
Aabrek, T.B. OP021, **MP341**, PP0417
Aamodt, G. MP341
Aamr, M. MP121
Aarvik, A. MP085
Abadía Barno, M. OP184
Abad-Santos, F. MP664
Abaladejo-Fuertes, S. PP1222
Abassi, N.G. PP1245
Abasszade, J. MP074
Abbas, R. MP229, MP516
Abbasi Montazeri, E. PP0256
Abbatemarco, A.M. PP0547
Abbatiello, C. MP364
Abbott-Tate, S. **PP0203**
AbdAllah, O. PP0201
Abdallah Elsheimy, H. MP531
Abdawn, Z. PP0482
Abdelaal, U.M. PP0287
Abdelaali, I. PP0453, PP0551
Abdelbadiee, S. MP556
Abdelbaqy, H. PP1062
Abdelghani, M. PP0201
Abdelhafez, M. MP280, MP377, PP0206, PP0852
Abdelhamed, A. **PP1160**
Abdelhameed, A. MP471
Abdelkrim, Z. MP405, PP0261, PP0677, PP0972, PP0977, PP0998
Abdel-Latif, A. PP1171
Abdelmassi, S. PP0238
Abd Elmoety, A. PP1024
Abdelraheem, M. PP0341
Abdelrahim, H. MP485
Abdelsaid, K. **PP1042**
Abdel-Salam, S. MP121
Abd-El salam, S. PP0287
Abdelsameea, E. MP409
Abdel-Samiee, M. **MP409**, **PP0175**, **PP1022**
Abdelwahab, N. PP0456
Abdulaal, Y. PP1042
Abdulai, R. MP660
Abdulai, R.M. OP210
Abdulkhakov, R. MP547, PP0271
Abdulkhakov, R.A. MP427, MP578
Abdulkhakov, R.A. PP0280
Abdulkhakov, S. MP427, **MP578**
Abdulkhakov, S.R. PP0280
Abdullaey, A. PP0117
Abdullah, M. PP0771
Abdulrehman, M. PP0747
Abe, K. PP0834
Abe, M. PP0914
Abe, S. OP028
Abell, T. PP0220
Abergel, A. MP634
Abid, R. MP072
Abildtrup, M. MP037
Abitbol, V. MP156, PP0377
Abonyi-Tóth, Z. OP012, MP379, MP648, PP1130
Abou-Ali, E. PP1168
AbouGabal, A.K. MP409
Abraham, B.P. OP085
Abrantes, D. **VC03**, PP0532
Abreu, B. **PP0226**, PP0468, PP0532, PP0751
Abreu, M.T. OP193, MP342, MP617, PP0354, PP0355
Abril, C. OP043
Abu Baker, F. OP221, PP0723, PP0882, PP1095
Abu-Elfath, A. MP121
Abu Farsakh, N. OP042
Abuoelhassan, A. PP0287
Acar, Ş. MP416
Acedo, P. MP131
Acehan, M.F. PP0970
Aceituno, M. MP508, MP510
Acharki, M. PP1047
Achemlal, A. **MP375**, **PP1214**, **PP1215**
Achondo, J. PP0084
Acosta, D. MP674
Adachi, K. PP1098
Adam Hassan, F. PP0349
Adami, H.O. OP123
Adami Chaim, E. PP0263
Adamo, G. MP092, MP263, MP662, MP663
Adamou, F. **PP0261**
Adams, A. MP629
Adams, D. MP050, MP252, PP0307
Addajou, T. MP559, PP0742, PP0905, PP1036, PP1087, PP1104, PP1107, PP1114
Adeyeye, A. OP143, MP221, MP277, MP282, **PP0854**, PP0879, PP0886
Adi, B. MP387
Adiou, T. MP375, PP1214, PP1215, PP1238
Adler, A. OP167, MP021, PP1181
Adler, J. PP1226
Adly, N. MP531
Admiraal - van den Berg, I. MP573
Adolph, T. OP018
Adotti, V. PP1012
Adriana, S. MP694
Adris, N. PP0352
Adsul, S. PP0556
Aduli, F. PP1191
Aepli, P. PP0930
Aepli, P.R. OP122, PP0074
af Björkesten, C.-G. MP506
Afif, W. **PP0564**, PP0584
Afifi, A. PP0538
Afonso, J. PP1122
Afonso, J. OP205, PP0207, PP0329, PP0830, PP1201
Afshar, M. PP0651
Afzali, A. MP671, MP672, PP0611
Agarwal, A. **PP0833**
Agazzi, S. MP013
Agboton, C. **PP0611**
Aggarwal, S. PP1037
Aggelogiannopoulou, P. MP134
Aggelopoulos, G. MP134
Aghdassi, A.A. MP642
Agibalova, T. PP0388
Agnes, S. MP539
Agostinho, C. PP0236, PP0819
Agostinho, C. MP189
Agostoni, M. PP1190
Agrawal, M. PP0422
Agrawal, S. OP051
Aguanno, D. MP453
Aguas, M. OP043, OP213, MP510, PP0362, PP0382, PP0404
Agudo Castillo, B. OP099, OP228
Aguerrí, A. PP0404
Aguila, E. MP432
Aguila, E.J. OP039
Aguilar, A. MP054, **MP159**
Aguilar-Olivos, N.E. PP0908
Aguilera Sancho-Tello, V. MP128
Ahadova, A. MP463
Aharbil, F. PP0662
Ahmad, M. MP644
Ahmad, O.F. MP0227
Ahmed, A. MP315
Ahmed, A. **PP0824**
Ahmed, B. PP0190, PP0213
Ahmed, B. PP0515
Ahmed, H.A. PP0425
Ahmed, H.S. **MP699**
Ahmed, M. MP034
Ahmed, N. **PP0246**, **PP1060**, **PP1085**
Ahmed, R. MP315
Ahmed, S. MP484
Ahmed, Y. MP608
Ahmed Kamel Ahmed, N. PP0032
Ahmed Medhat, M. MP121
Ahn, S. MP603
Ahn, W. **PP0909**
Aho, I. MP308
Ahoja, A. PP1108
Ahuja, A. MP724, PP1066
Ahumarán, G. MP429, MP430
Ai, Y. OP120
Aichholzer, M. OP117, PP0805
Aichner, E. PP1222
Aidibi, A. MP440
Aighobahi, E. **PP0509**
Aigner, E. OP183, MP173
Aikins, A. MP631
Ailloud, F. OP137
Ainora, M.E. MP645, PP0958
Ainslie-Garcia, M. PP0667, PP1185
Ainsworth, M.A. OP024, PP0509
Aira, A. PP0693
Aissaoui, H. PP0972, PP0977
Ait errami, A. PP0202
Ait Errami, A. PP0682, PP1065
Aithal, G.P. PP0969
Aitken, F. MP559, PP0742, PP0905, PP1036, PP1107, **PP1114**
Ait iken, F. PP1087
Ajana, F.Z. MP129, PP0109, PP1028, PP1164
Ajioka, Y. PP0432
Ajmi, S. PP0619
Akagi, Y. PP0432
Akban, U. **MP296**
Akdoğan Kayhan, M. PP0970
Akimoto, N. MP036, MP038, MP040, **MP404**, PP0150, PP0151, PP0160, PP0168, PP0582
Akimoto, T. MP458, PP0683
Akir, S. MP375
Akpınar, H. MP421
Aktas, B.C. MP220
Alaerts, K. PP0691
Alahmad, M. PP0425, PP0443
Alajmi, A. **PP0573**
Alakberi, A. PP0443
Ali, A. PP0425
Alam, M. MP118, PP0643
Alamri, T. PP0201
Al-Ani, Z. PP0229
Alañon, P. PP0439
Alavinejad, P. **PP0256**
Alawad, M. PP0894
Alba, C. PP0684
Albæk Jacobsen, H. OP017
Al Bakir, I. PP0680
Albano, E. PP0942
Albano, S. MP410
Albarelo, L. MP260, PP0135
Albeniz, E. MP068
Albéniz, E. MP428, MP549
Albéniz-Arbizu, E. MP031
Albergati, I. PP0132
Albergati, I.V. OP054, MP395, MP398, **MP604**
Alberghina, N. PP1088
Albers, S.C. **OP223**, OP224, **OP225**
Albert Palomares, S. **PP0451**
Alboraie, M. **MP121**, **PP1062**
Albouys, J. MP285, PP0849, PP1100
Albouys, J. MP068
Albshesh, A. PP0054, **PP0506**
Albuquerque Miranda, M.A. PP1172
Alcaide, N. OP009, MP428
Alcala Gonzalez, L.G. **MP054**, MP159
Alcala-Gonzalez, L. MP057
Al-Chalabi, T. MP601
Alcivar-Vasquez, J. MP109, MP137, MP191, MP359, MP407, MP554, PP0204, PP1118
Al-dardery, N.M. **PP0925**
Aldegue, X. MP522
Aldinger, U. PP1122
Aldinio, G. MP256, PP0078
Aldrighetti, L. MP027, MP536
Aleknavicene, I. OP022, **PP0446**
Aleksandrova, R. **MP127**
Alekseenko, S. MP427, MP547, PP0273
Alekseenko, S.A. PP0280
Alemanni, L.V. MP364
Alexandre, L. OP038, MP711
Alexandrino, G. MP408
Alexopoulos, T. PP0048, PP0073, PP0089, **PP0245**
Alfambra, E. OP213
Alfaro, E. OP009, MP427, MP549
Alfarone, L. MP068, MP285, PP0244, PP0849
Alfego, D. MP631, PP0467
Alfieri, N. PP0613, PP0637
Alfredo, D.L. PP0285
Algaba, A. MP508
Algara San Nicolas, M. OP043
Algara Soriano, V. PP0403
Algera, J. MP574, PP0802
Al Hajjar, N. MP424
Alhalabi, L. PP0154
Ali, M.A. **PP1159**
Alicante, S. MP063
Alimenti, E. MP466, PP1018
Aljaberi, R. MP298
Aljahl, E. PP0201
Alkandari, A.A. OP203, PP0165, PP0768
Alkhalaf, A. OP112, MP717
Al Khaldi, M. PP0877
Alkhattabi, M. PP0531
Alkhouri, N. OP057, **OP061**
Allard, J.P. MP141
Allard, S. PP0822
Allawadhi, P. MP644
Allegretti, J. OP045, OP082, OP084, OP193, MP670
Allegretti, J.R. OP079
Al-Lehibi, A. MP137, PP0201
Allen, B. MP478
Allez, M. MP453, **MP630**, PP0386, PP0395
Allgeier, J. **OP182**, PP0967
Allgöwer, C. **MP086**
Allin, K. OP017, MP507
Allo, G. **PP0984**, PP1048
Allocca, M. OP081, MP149, MP152, **MP388**, MP389, MP511, PP0431, PP0476, PP0488, PP0517, PP0626
Allsworth, M. MP287, MP608
Almarzoqi, N.A. PP0443

Almazán, R. MP014
Almeida, E. PP0164
Almeida, J.C. PP0138
Almeida, M.J. OP205, MP060, PP0329, PP1201
Almeida, N. PP1072
Almeida, N.P. MP301, MP557, PP0291, PP0429, PP1141
Almeida, V. MP555
Almeida Franco Leal, T.F. PP0826
Almholt, K. OP058
Aloi, M. MP344, PP0392, PP0433, PP0491
Alonso, L. OP132
Alonso, M. PP0585
Alonso, S. MP064
Alonso-Abreu, I. OP043, MP510, PP0557
Alonso Cotoner, C. PP0805
Alonso-Cotoner, C. OP117, MP051
Alonso-Galán, H. MP510, MP674
Alonso-Gomez, M. PP0676
Alonso-Lopez, E.P. PP1116
Alonso Lorenzo, S. PP0929
Alonso Salgueiro, I. OP110
Alphonsus, L. PP0627
Al-Quraishi, B. MP225
Alraeeini, A.A.T. **PP0028, PP1032**
Al Saidi, R. **PP0154**
Alshair, M. PP0201
Alsharqi, D. **PP0222**
Altadill, A. MP673
Altaf, A. PP1080
Altamimi, E. **PP0341**
Altay, C. MP421
Altenaiji, K. **PP0425**
Althuis, N.M. PP0454
Altıntaş, E. MP416
Altomare, A. MP313, MP607
Altonbary, A. MP121, PP0201
Altstädt, A. **MP312**
Altstaedt, A. OP048
Altucci, L. PP0942
Altuzarra Ranedo, Y. PP0079
Altwegg, R. MP156, PP0374, PP0676
Aluko, P. MP262
Alunni-Fabbronio, M. MP468
Alvarado, D.M. MP452
Alvarado-Escobar, H. MP359, MP407, PP1118
Alvarez Herrero, L. OP115
Alvaro, D. OP064, PP1138
Alves, A.L. MP555
Alves, A.L. PP0485, PP0859, PP0860
Alves, B. PP0747
Alves, S. PP0195, PP0196, PP0197
Alvigi, A. **PP1244**
Alvisi, P. PP0433
Alyavi, B. PP0117
Alzaabi, M.N. PP0425
Alzamzamy, A. MP121, PP0201, **PP1171**
Al-Zarrad, D. **PP0642**
Amal, J. **PP0456**
Amalou, K. **OP097, MP176, MP533, PP1082**
Amamou, A. MP114
Amano, H. PP0968
Amanzada, A. OP229
Amara, J. MP106, MP229, MP516, PP0297, PP1192
Amaro, P. MP189, MP555, PP0236
Amata, M. MP137, PP0856
Amato, A. MP193
Amatucci, V. PP0393
Ambrosio, C. PP0473
Ambrozova, M. MP517
Amer, L. MP229, MP516, PP0297, PP1192
Amiama Roig, C. OP184, PP0469, PP1242
Amici, G. MP728
Amil-Dias, J. OP208
Amin, H.M. PP0019
Amin, I. MP718
Amin, M.A. **MP531**
Amine, M. MP375, PP1214, PP1215
Amiot, A. OP095, MP002, MP156, MP339, PP0377
Amkhaou, F. PP0213
Ammar, N. **PP0660**
Ammattatelli, F. MP344
Ammer-Herrmenau, C. OP229, MP298
Amodio, A. MP237
Amodio, D. MP625
Amolins, R. PP0096
Amooee, S. PP0303
Amor Costa, C. **PP0469, PP1242**
Amorena Muro, E. PP0076
Amores, Z.R. PP0030
Amorim Lopes, M. **PP0340**, PP0343
Amorós García., C. PP0403
Amoroso, C. OP129
Amouri, A. PP0660
Amouyal, S. OP027, OP110
Amri, F. **MP418**, PP0677, PP0972, PP0977, **PP1156, PP1167**
Amrutkar, M.P. MP085
An, P. **PP0534**
Anagnostou, A. PP1177
Ananchuensook, P. MP231
Anand, M. OP143, MP221, MP277, PP0879, PP0881, PP0886
Anarak, C. MP483
Anbar, R. PP0671
Anchling, L. **PP1122**
Anderloni, A. OP171, MP013, MP132, MP193, MP540
Andersen, G.T. MP035
Andersen, I.L. OP003, MP657, MP658
Andersen, K.K. MP007
Anderson, J.K. OP078, OP194
Anderson, J. PP0853
Anderson, K. OP077
Anderson, P. MP074
Anderson, S.H. MP628
Andersson, B. PP1124
Andersson, K. OP011
Andersson-Engels, S. PP0499
Ando, R. PP0234
Ando, Y. MP460
Andone, A. PP1204
Andrade, A. **MP394**
Andrade, A.P. OP205, PP0207, PP0329, PP1201
Andrade, L. MP286
Andraos, J. MP078
Andreadou, A. PP0599
Andreassen, H. MP044
Andreev, D.N. PP0280
Andreola Borba, S. **PP1021**
Andreozzi, M. **MP193, MP584**, PP0166
Andresen, V. MP164
Andrés Pascual, L. PP1005
Andreu-Sánchez, S. OP001, OP020
Andreuzzi, E. MP395, MP398
Andrews, C.N. OP153
Andrin, B. PP0576
Andrisani, G. MP281, MP502, MP714, PP0707
Andronic, D. PP0749
Ang, D. PP1111
Ang, T.L. MP218, **PP1111**
Ang, Y. OP038, OP114, PP0106
Angel, D. **PP0217**
Angel, E. **PP0945**
Angeles, T. **MP447, PP0604**
Angeletti, S. PP0893
Angel Gomis, E. **PP0990**
Angesom, K. PP1191
Anggiansah, A. OP076
Angioli, R. MP313
Angiuoni, M. PP0492
Angriman, I. MP223
Angueira, T. MP428
Angueira, T. MP508
Angyal, D. PP0420
Anjie, S. MP387
Annese, V. MP722
Anne Verlo, K. OP190
Annibale, B. OP140, MP203, MP205, MP241, MP261, MP491, MP728, PP0007, PP0129, PP0130, PP0325, PP0893, PP1092, PP1170, PP1173, PP1194
Ann Van Koughnnett, J. PP0598
Anschutz, T. MP622, MP677, PP0588, PP0589
Anschütz, M. PP0593
Anselmi, D. MP271
Ansorge, N. MP479
Anstee, Q.M. OP058
Anstee, Q. OP057
Antal-Szalmás, P. MP354
Anton, C. **PP0749**
Anton, S. PP0585
Antón Ausejo, R. PP0008
Antonelli, B. MP469, PP1018, PP1020
Antonelli, G. OP126, MP011, PP0845, PP0903
Antonica, G. PP0957
Antoniozzi, A. PP0023
Antonitsch, L. MP638
Antoniv, M. PP0866
Anttila, V.-J. MP506
Antunes, H. **OP208**
Antunes, V. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0986, PP0988, PP1001, PP1002, PP1023, PP1027, PP1103, PP1105, PP1106
Antunović, T. PP0449
Anwar, U. PP0060
Anyanwu, S. MP333
Anzelon, T. MP568
Ao, X. MP349
Aoki, H. PP0868
Aoun, K. PP0402
Aourarh, B. **MP1238**
Apadula, L. MP024, MP244, MP583
Aparicio Cabezudo, M. MP052
Apolito, P. PP0870, PP1209
Apollonio, M. PP0652
Aponte, F. MP333, PP0589
Apostolopoulos, P. PP0330
Appiahene, P. MP485, PP0101
Appleyard, M. MP065
Apyratina, V. PP0292
Arab, N. OP189
Aragona, G. MP193
Arai, R. PP0149
Arakaki, J. PP0432
Araki, A. PP0844
Arango, A. PP0693
Aransay, A.M. OP023, PP0364, PP0381
Arataki, K. PP0574
Araújo, R. PP0770
Araujo-Gil, W. MP429, MP430
Arauzo-Bravo, M.J. MP624
Arcaniolo, D. PP0452
Archer, M. PP0627, PP0706
Archer, S. MP386
Archer, T. MP322
Archibugi, L. **OP136, MP024**, MP244, MP542, MP583
Arcidiacono, P.G. MP024, MP027, MP137, MP188, MP244, MP536, MP540, MP542, MP583
Ardengh, J.C. PP1136, PP1175, PP1178
Ardila, O. **PP0268**
Ardizzone, S. MP275, PP0015
Ardizzone, S.G. MP271
Arobi, N. MP149, PP0642
Arefijev, A. PP0863
Areia, M. OP009, MP433, MP547, PP0195, PP0196, PP0197, PP0271, PP0273
Arena, M. PP0707
Arenas, A. MP429, MP430
Arenillas, J. OP219
Arese, D. MP441
Aretakis, D. PP1181
Arevalo Mora, M.G. MP137
Arevalo-Mora, M. MP109, MP191, MP359, MP407, MP554, PP0204, PP1118
Argenziano, M.E. VC02, **VC08**, MP019, PP0730, PP0838, **PP0853**, PP0895
Argiento, L. **PP1020**
Argiolas, G. PP0442
Argmann, C. MP150
Argüelles-Arias, F. OP196, MP620
Argüello, R.J. OP110
Argumánez Tello, V. PP0404
Argyriou, K. OP169
Argyriou, O. PP0680
Argyropoulos, T. PP0330
Ari, D. PP0970
Arias García, L. OP151, OP213, MP268, MP343, MP510
Arias-García, L. OP187, MP508
Arias-González, L. OP211, MP664
Arias Vasquez, A. PP0805
Arias-Vasquez, A. OP117
Arieira, C. PP0486, PP0789, PP0883, PP1216
Arif, A. **PP0753**
Arihiro, K. PP0444
Arimoto, J. OP145, PP0171
Arisaka, Y. MP693
Ariyoshi, M. **MP457**
Arizi, X. OP206
Arkkila, P. MP308, MP506
Arlt, A. OP229
Armandi, A. MP233
Armanini, F. MP659, PP0347
Armer, R. OP077
Armesto Gonzalez, E. MP343
Armesto González, E.M. OP213
Armstrong, M. MP524
Armuzzi, A. OP084, OP106, OP150, **MP003**, MP330, MP333, MP390, MP571, PP0431, PP0542, PP0555, PP0588, PP0639
Arna, D.-E. PP1177
Arnauts, K. **MP112**, MP445, MP564
Arndtz, S. MP284
Arnelo, U. PP0186
Arnold, A. PP0249
Arnott, I. PP0579, PP0674
Arola, J. MP593
Aronen, A. MP182
Arora, V. OP192, MP617
Arosa-Garcia, L. PP0373
Arpa, G. MP656
Arraf, T. MP283, PP1043
Arranz Hernández, L. OP151, MP268
Arrigo, S. PP0433
Arroja, B. PP0526, PP0552, PP0827
Arroyo, M. MP674
Arroyo, M.T. MP510
Arroyo-Villarino, M.T. MP343, MP508
Arslanow, A. MP071
Artifon, E.L.A. VC07
Arts, J. MP434
Artuso, G. PP0348
Aruanno, A. PP0082
Aruljothy, A. PP0531
Arvanitakis, M. MP298, **PP1063**, PP1203
Arvizu, M. MP042, MP043, MP050, **MP252**, PP0307, PP0308
Arya, N. PP0556
Asahara, H. MP368
Asahara, M. MP368
Asahara, Y. MP368
Asaji, N. PP0686

Asak, Ø. MP341
Asak, Ø. PP0417
Asendorf, T. OP229
Asenjo-Lobos, C. MP287
Ashida, R. MP239, MP360
Ashina, S. MP083
Ashizuka, S. PP0419
Ashktorab, H. **PP1191**
Ashok, D. OP210, MP492
Asim, M. **PP1080**
Aslam, F. PP0642
Aslam, N. MP033, PP0098, **PP0106**, PP0227, PP0240
Aslam, P. OP203
Asmaa, A. **PP0034**, **PP0401**
Asmar, A. MP106
Asmarinah, - PP0771
Asnicar, F. MP659, PP0347
Asokkumar, R. PP0161
Asonuma, K. PP0465
Asplund, E. PP1147
Asrani, S. MP600
Asscher, V.E.R. PP0641
Assem, M. PP0287
Asser Karsdal, M. OP024
Assi, Z. PP0228
Assmann, S. **PP0791**
Assmann, S.L. **PP0792**
Asti, E. OP075, PP0094, PP0095
Atalla, H. PP0201
Atanasiu, C. MP156, PP0377
Atanasova, V. PP0338
Atay, A. PP0527
Ateş, İ. PP0970
Athanasiadou, E. **PP0205**, **PP0528**
Atkinson, C. OP212, PP0594
Atreya, R. OP193, MP620, PP0529
Atrott, K. PP0369
Attaluri, A. PP0220
Attanasio, M. PP0586
Attauabi, M. **OP174**, **MP336**, MP391, **PP0411**, **PP0498**
Attila, S. PP1069
Attili, F. MP028, PP1088, PP1154
Auer, J. PP0810
Augoustaki, A. MP062
Auletta, D. PP0433
Auletta, S. MP632
Aurangzeb, I. **PP0434**, PP0435
Auricchio, R. **PP0320**
Auriemma, F. **MP137**, **PP0707**, PP1168
Auth, M.K.-H. OP208
Autran Nebel, J. MP554
Avci, B. MP480
Avedano, L. PP0422
Avery, K. MP568
Avitabile, E. MP071
Avni-Biron, I. OP093
Avolio, A.W. MP539
Awadie, H. PP0184
Awwad, N. MP225
Ayaki, M. PP1046
Ayari, M. MP131, **MP473**, PP0453, PP0456, PP0551, **PP0727**, PP0772, **PP0471**, **PP1236**
Aydemir, C. PP0154
Aydemir, N. OP190
Aykut, B.M. PP0625
Aymane, M. **PP0998**
Ayodele, O. PP0632, PP0646
Ayubi, H. **OP143**, MP221, MP277, MP282, **PP0055**, PP0854, PP0879, **PP0881**, **PP0886**, PP0889
Ayude Galego, M. PP0666
Azad, N.S. OP133
Azadov, P. PP1142, PP1158
Azammam, S. MP375, PP1214, PP1215
Azevedo Rodrigues, J. PP0050, PP0051, PP0062
Aziz, I. PP1230
Aziz, Q. MP307, PP0434, PP0435
Aziz-Kalbhenn, H. MP579, PP0009
Azkargorta, M. OP023, PP0364, PP0381, PP0382
Azzam, Z.S. MP184
Azzolini, F. MP281, MP441, MP722, PP0183, PP1190
Azzouzi, D. **MP129**
Åberg, F. MP593
Ábrahám, S. PP0675
Ács, N. PP1124
Álvarez-García, M. PP0076
Balaban, M. PP0312
Balaban, Y.H. PP1205
Balafas, S. PP0135
Balaguer, F. MP522, PP0693
Balan, G. MP175, PP1079
Balata, A. PP0112
Balboa, J.C. PP0755
Balcar, L. OP186, MP077, MP173, MP465, MP638
Balcazar, K. MP568
Baldassano, H. PP0255
Baldan Martin, M. **OP023**, **PP0364**, **PP0381**, **PP0382**
Baldán-Martin, M. MP503, PP0362
Baldassano, R. OP172
Baldeo, M. **MP432**
Balderramo, D. OP045
Baldi, C. MP271
Baldo, L. MP522
Baldock, D. **PP0569**
Balint, A. MP158, MP627, PP0584, PP0675, PP0710, PP0713, PP0731, PP0732, PP0746
Bálint, A. PP0614
Ballaban, A.Y. MP488
Ballester Clau, R. PP1172
Ballet, N. PP0778
Ballew, O. PP0635
Balogh, F. PP0420
Balser, S. **PP0593**
Balsiger, L. **MP056**, MP160, PP0039, PP0066, **PP0806**
Baltus, S. PP0924
Balyan, R. MP447
Balzoni, L.M. PP0612
Bamias, G. OP148, MP676, PP0568
Bañales, J.M. MP530
Bananis, E. MP686
Banda, I. MP608
Bando, E. **PP0134**
Banerjee, R. MP387, **PP0437**
Bang, J.Y. **OP227**
Bang, S. OP135, MP482
Bangdiwala, S.I. OP119, MP164
Bangma, A. OP071
Banjoya, S. PP0133
Banks, J. PP0305
Banks, M. OP037, OP038, MP033, MP325, PP0165, PP0227, PP0768
Banna, S. MP283
Banno, S. MP316
Banovcin, P. MP053, MP435, PP0056, PP0065, PP0097, PP1127
Bao, P. OP193
Bapaye, A. PP0766
Bapaye, H. PP0766
Baquerizo-Burgos, J. MP109, MP191, MP359, MP407, MP554, PP0204, PP1118
Bar, N. PP0796
Bara, R. MP090
Barà, R. MP441, PP0517
Barada, K. OP220
Baraldo, S. PP0816, PP0999, PP1103
Baran, N. MP390
Barauskas, G. MP591
Barba, E. MP428
Barbara, G. OP117, MP051, MP059, MP659, PP0347, PP0779, PP0797, PP0805, PP0813, PP1235
Barbara, J. PP0317
Barbaro, F. MP281, MP502, MP514, PP0832, PP1200
Barbaro, M.R. OP121, MP059, **PP0779**, PP0797, PP0813, PP1235
Barbera, C. MP137, MP193
Barber Caselles, C. MP054, MP159
Barberio, B. MP149, PP0481, PP0587, PP0633
Barbosa, E. PP0999
Barbosa, E.C. PP0816
Barbosa, W. PP0343
Barchi, A. MP090, **MP260**, MP441, MP491, MP722, PP0183, PP1190
Bard, A. MP253
Bargas Bárbara, A. **MP005**, **PP0468**, PP0532, **PP0751**
Bar-Gil Shitrit, A. MP339
Barjas, E. VC03, PP0751
Barkan, R. MP273
Barker, F. **PP0524**
Barker, S. PP0630
Barkun, A.N. OP124, PP0706, PP0877
Barla, G. PP1015
Barlow, N. MP568
Barlow, S. PP1226
Barmashenko, G. MP479
Barnes, A. PP0577
Barnich, N. MP402, PP0363, PP0395
Bar-on, T. **PP0233**
Barone, M. MP057
Barosa, R. PP1237
Barragan, C. PP0638
Barrau, M. OP189, **PP0608**
Barrault, C. MP634
Barreiro, P. PP0934
Barreiro Alonso, E. MP031, MP428
Barreiro de Acosta, M. OP150, OP151, OP187, **OP196**, MP268, MP334, **PP0373**
Barreiro-de Acosta, M. MP674
Barreiro-de Acosta, M. **OP043**, **PP0424**, PP0557, **PP0615**
Barret, M. MP068, MP318, MP440, PP0185
Barreto, F. MP365, PP0093, PP0255
Barreto, S.G. PP0896
Barrias, S.M. PP0050, PP0051, PP0062
Barrientos, V. MP287
Barrio, J. OP009, OP151, MP268, MP428, MP433, MP503, MP510, MP547, MP549, PP0076, PP0271, PP0273, PP0557
Barrio Andrés, J. OP191, PP0364
Barros, S. PP0708, PP0774
Barsic, N. MP417, PP0863
Barta, B. MP446
Barth, I. PP0345
Bärthel, S. MP453
Barthet, M. PP1100
Bartholomeusz, D. MP478, MP589
Bartolucci, C. MP313
Bartolucci, P. PP0483
Bartram, A. **OP063**, MP712
Barugola, G. PP0570, PP0664, PP0673
Barutçu, S. MP416, PP0625, PP1083
Bar-Yoseph, H. MP512
Baryshnikova, N.V. PP0280
Baryshnikova, N.V. MP552, PP0276, **PP0292**
Bas, F. PP0948
Bascur, F. MP287
Bas-Cutrina, F. OP187
Basdeo, S. PP0083
Basiliya, K. MP132
Basiliya, K.V. PP1101
Basnayake, C. PP0602
Basra, R. PP0227
Bassett, P. OP088
Bassi, M. PP0870
Bassotti, G. MP261
Bassu, I. MP606
Bastiaansen, B.A. OP223, OP224, OP225
Bastida, G. MP334, PP0404
Bastide, L. PP0608
Bastón-Rey, I. OP023, OP043, MP503, PP0362, PP0364, PP0373, PP0381, PP0382, PP0424, PP0615, PP0666
Bastos, A. PP0859, PP0860
Bastos, R.P. MP365, PP0093, PP0255
Bastovaya, O. MP566
Basyte-Bacevičė, V. PP1031

- Bataller, R. MP071, PP0969
 Batibay, E. **PP1083**
 Batocoy, K. PP0351
 Batra, S.K. OP134, MP085
 Battaglia, S. MP722
 Battan, M.S. MP237
 Baudot, A. PP0692
 Bauer, D. OP186
 Bauer, D.J.M. OP183, MP638, PP0994
 Bauer, D.J.M. MP077
 Bauer, R. MP579
 Bauer, Y. PP0447
 Baumann, F. PP1239
 Baumeler, S. PP0930
 Baumer, S. PP0845
 Baunwall, S.M.D. OP154, MP140
 Bawa, D. OP039
 Bawden, S. PP0969
 Baweja, G. MP532
 Baygani, S. MP616
 Baygani, S.K. OP044, OP046
 Bay Hansen, S. PP0411
 Bay-Jensen, A.-C. OP024, OP172, MP565, PP0502, PP0509
 Baysal, S. PP0984
 Baz López, A.M. PP0666
 Bazoze, M. MP217
 Bazzanini, N. PP0963
 Bazzu, P. MP310, MP606
 Beales, I. OP038, OP105, MP711
 Beany, A. **OP039**
 Beaton, M. PP0531, PP0556, PP0627
 Beattie, W. PP0389
 Beaufort, I.N. **OP115**
 Beaufrand, C. PP0778
 Beaugerie, L. MP267, PP0386
 Beaumont, H. PP0332
 Becerra Hoebel, P. OP050
 Becherucci, G. MP223
 Becker, C. MP462
 Becsi, B. PP0993
 Bedal, K. PP0009, PP0692
 Bedini, O.A. MP429, MP430
 Bedira, I.S. PP1022
 Bednarik, D. MP194
 Bednarz, J. MP478
 Beek, K. MP117, PP0523
 Beelen, E.M. OP188
 Beer-Gabel, M. PP0796
 Beglinger, C. OP048, MP312
 Begun, J. OP082
 Behn, C.-O. MP195
 Behrenbruch, C.C. PP0602
 Beij, A. **MP022**
 Bejarano Rengifo, J. PP0268
 Beka, E. MP254, MP676, PP0568
 Bekiari, E. MP692, MP695
 Bekkali, N.L.-H. PP1176
 Bekkering, F. OP225
 Bekkering, F.C. PP1197
 Belabbes, F. PP0885
 Belardi, P. PP0963
 Belfield, A. OP077
 Belkhatay, C. PP1167
 Bell, S. MP074
 Bell, S. PP0888
 Bellabah, A. PP0961, PP1234
 Bellakhel, S. PP1236
 Belle, A. MP068, PP0185
 Bellini, G. PP0782
 Bellini, M. MP263, MP663, PP0285, PP0782, PP0793, PP0794, PP1235
 Bello, F. PP0085
 Belloni, L. OP140, MP203, MP205
 Belluardo, N. PP0645
 Belostotsky, N. PP0322
 Belouski, S. MP568
 Belousova, E. PP0513
 Belousova, L. MP552, PP0276
 Belousova, O. MP230
 Bemelman, W.A. PP0540
 Ben Abdallah, K. **PP0964**
 Ben Abdelwahed, M. PP0669
 Ben Abid, M. PP0402
 Benallaoua, M. PP0804
 Benamouzig, R. PP0804
 Benard, F. PP0877
 Bénard, M.V. **PP0815**
 Benass, J. PP0742, PP0938, **PP1104**
 Benboudiaf, N. OP097, MP533, PP1082
 Ben Brahim, E. PP0361
 Bencardino, S. PP0517
 Ben Chaaben, N. PP0669
 Bendia, E. MP491
 Bendtsen, F. OP174, OP204, MP007, MP336, MP391, PP0411, PP0498, PP0535
 Bendtsen, K.M. OP058
 Benedetti, R. PP0942
 Ben El Barhdadi, I. PP0885
 Beneria, A. MP159
 Benezech, A. PP0377
 Bengi, G. MP421
 Bengi, G. MP416
 Bengtson, M.B. OP021, MP341
 Bengtson, M.-B. PP0417
 Bengus, A. MP538
 Ben Haj Ali, R. **MP422**
 Benhamdane, A. MP559, PP0742, **PP0905**, PP1036, PP1087, PP1107, PP1114
 Ben Hamida, S. PP0760
 Benhayoun Sadafiyne, Y. PP0651
 Ben-Horin, S. MP592, PP0506, PP0589, PP0869
 Benítez, J.M. PP0403, PP0436
 Benítez, J.M. MP510, PP0382, PP0557
 Benítez, O. MP508
 Benitez Cantero, J.M. PP0362, PP0439
 Benjelloun, N. PP0885
 Benmellouka, H. MP176
 Ben Mohamed, A. MP422, PP0259, PP0294, PP0981, PP1000, PP1006
 Ben Mustapha, N. PP0543, PP0590
 Bennani, Y. PP0885
 Benninga, M. PP0815
 Bennink, R. MP039
 Benny, S. **PP0795**
 Ben Romdhane, N.I. PP0727
 Ben Safta, N. PP0543, PP0590
 Ben Slama, A. MP215, PP0430, PP0495, PP0619
 Bento-Miranda, M. MP365, PP0093, PP0255
 Ben Tov, A. MP512
 Benvenuti, L. PP0782
 Benzarti, Z. PP0456, PP0964, PP1245
 Benzoni, I. PP0139
 Benzzebair, N. PP0026, PP0028, PP0034, PP0400, PP0401, PP0657, PP0658, PP0681, PP0831, PP0926, PP0927, PP0971, PP1032, PP1049
 Ber, Y. PP0362
 Berardi, E. PP0957
 Bercik, P. OP005
 Berenguer Haym, M. MP128
 Berezina, O. PP0004, PP0242
 Berg, D. MP720
 Bergamo, F. MP223
 Bergemalm, D. OP021
 Berger, A.E. PP0608
 Berger, A.-E. OP189
 Berger, A. MP068, MP318, MP440
 Bergez, G. **MP318**
 Bergholz, R. VC01
 Bergman, D. OP214, OP216, MP047, MP174, **MP214**, **MP505**
 Bergman, J.J. OP049, OP112, OP113, OP116, MP039, MP367, MP715, MP717, PP0162, PP0167, PP1198
 Bergsten, E. OP095
 Berhili, K. MP129, PP0109, PP1028, PP1164
 Berkeley Cotter, J. MP171, MP637, PP0477, PP0486, PP0750, PP0757, PP0761, PP0789, PP0883, PP1216
 Berman, G. PP0465, PP0671
 Bermejo, F. OP009, OP023, OP043, OP151, OP187, MP268, MP428, MP433, MP503, MP674, PP0271, PP0362, PP0364, PP0381, PP0382
 Bernabè, G. MP569
 Bernal, L. OP187
 Bernard, E.-J. MP154
 Bernardes, C. MP365, PP0093, PP0255
 Bernardi, D. OP075, PP0094, PP0095
 Bernardini, N. PP0782
 Bernardo, S. PP0592, PP0628
 Bernardoni, L. MP130
 Bernardos Martín, E. OP213, MP343
 Bernatsky, S. PP0564
 Berner-Hansen, M. OP161, OP168
 Bernhofer, S. PP0020
 Ber Nieto, Y. OP023, OP196, MP503, PP0364, PP0381, PP0382
 Bernklev, T. PP0417
 Bernstein, C.N. MP444
 Bernuzzi, M. PP0570
 Berrag, S. MP375, PP1214, PP1238
 Berraida, R. MP559, PP0742, PP0905, PP1036, PP1087, PP1104, PP1107, PP1114
 Berretti, D. MP540
 Bertani, H. MP540
 Bertin, L. PP0481, **PP0633**
 Bertocchi, E. PP0673
 Bertoli, D. PP0046
 Bertolotti, M. PP1200
 Bertrand, C. MP527
 Bertrand, V. PP0410
 Bertrand, V. MP345
 Berzin, T. MP554
 Beshara, A. OP221, PP0723, PP0882, PP1095
 Besó Delgado, M. MP014
 Besselink, M.G. MP022, MP030, MP702, PP1089
 Bessissow, T. PP0546, PP0584
 Bestetti, A. MP061
 Beswick, E.J. MP400
 Betoré, E. PP0076
 Betoré Glaria, E. OP187
 Bettaieb, H. PP0551
 Bettenworth, D. OP085
 Bettolo, J. OP157
 Beuchard, T. **PP1100**
 Beuers, U. MP702
 Beutel, A.K. **OP200**, **MP483**
 Beuvon, F. PP0185
 Beyer, G. OP229, MP298, MP644
 Beyna, T. OP112, MP280, MP317, MP324, PP1063
 Bezault, M. MP630, PP0395
 Bezirard, V. PP0778
 Bezmarevic, M. MP298
 Bezzio, C. OP106, OP150, MP013, MP389, MP390, MP571, PP0431, PP0488
 Bhandari, M. PP0232
 Bhandari, P. MP136
 Bhandari, P. OP122, OP203, MP553, PP0165, PP0768, PP0845
 Bharath, P. PP0437
 Bhatia, A. **PP0825**
 Bhatia, P. PP0603
 Bhattacharai, S. **MP420**
 Bhatti, T. PP0314
 Bhaware, B. PP1094
 Bhoday, J. OP143, MP221, MP277, MP282, PP0881, PP0886, PP0889
 Bhowmick, M. **MP004**, MP420
 Bhujade, H. PP0394
 Bi, Y. MP245, MP697
 Biagi, F. MP013, MP045, MP653, MP656, PP0315
 Biagini, M.R. OP175
 Bian, Y. PP1044
 Bianchi, F. PP1188
 Bianchi, P.I. MP656
 Bianco, F. **PP0813**
 Biancone, L. PP0426, PP0427, PP0621
 Biasutto, D. MP607, PP0917
 Bibani, N. PP0402, PP1033
 Bideau, K. MP634
 Biedermann, L. **OP207**, **MP258**, MP264, MP489, **MP493**, PP0074, PP0080
 Biedermann, P. PP0542, PP0555
 Bielski, A. **PP0610**
 Bigaeva, E. OP071, MP147
 Bigot, N.B. MP149
 Bijlsma, R. OP065, PP1101
 Bilgili, A. PP0072, PP0270
 Billiauw, L. OP157, PP0349
 Billin, A. PP0600
 Billings, S. PP0045
 Bills, M. MP478, MP589
 Bina, N. MP063
 Binda, C. **MP084**, MP137, MP193, **MP364**, MP540
 Binder, M.V. MP429
 Bingxin, X. MP015
 Bin Senawi, L. PP1068
 Biolato, M. PP0958
 Biral, R. PP0074
 Birch, E. MP332
 Birchall, M. MP553
 Birck, M. PP0564
 Birda, C.L. PP0833
 Birka, I. **PP0096**
 Birkel, M. PP0020
 Birligea, M. **MP538**, MP539
 Birznies, G. PP0042, PP0057, PP0058
 Biscanin, A. PP0541, PP0863
 Bisogno, R. MP390
 Bisschops, R. OP112, OP126, MP016, MP317, MP392, MP553, PP0861, PP0864
 Bisseling, T.M. MP023, PP1041, PP1101
 Bisso Zein, J.K. PP0076
 Biswas, C. PP0873
 Bittel, M. MP165
 Bitter, I. OP117, PP0805
 Biwata, Y. **PP0913**
 Bizarro Ponte, S. MP414
 Bizouard, G. PP0407
 B. Jensen, A. OP174
 Björk, J.R. OP071
 Black, C. MP166
 Blackwell, S. MP151
 Blair, B. MP534, MP704, PP1052, PP1054
 Blaker, P. MP326
 Blanco, D. PP0547
 Blasi, V. PP0613
 Blas-Jhon, L. PP0076
 Blaydon, D. OP053, MP384
 Blazevic, N. **MP417**
 Bleiker, E. MP082, PP1155
 Blesl, A. OP169, MP339
 Blijleven, M.J.H. MP211
 Bloem, S. MP211
 Bloemen, J.G. PP0484
 Bloemendaal, A.L. PP0484
 Blois, M. PP1071, PP1243
 Blokzijl, H. MP127, MP600
 Blom, J. OP123
 Blomgren, P. PP0369
 Blomsten, A. PP0806
 Bluiminc, S. **MP362**, **MP705**
 Blumenstein, I. MP327, MP619, MP677, PP0624
 Bo, Y. **PP0342**
 Boarino, V. MP059
 Bocca, C. PP0942

Bocioaga, A.G. PP1204
 Boczkowski, J. PP0321
 Bodelier, A. PP0567
 Bódi, N. PP0811
 Bodini, G. PP0652
 Bodó, E. MP303
 Bodunova, N. PP0004
 Bódy, B. **MP576**, PP1119
 Boers, T. MP715, MP717, PP0167, PP1198
 Boets, B. PP0691
 Bogdanova, I. PP0238
 Bogdanski, A. **MP245**, MP697
 Bognár, A.S. PP0563
 Bognár, Z. MP104
 Bogomolov, P. MP433, MP547, PP0271, PP0273
 Bogomolov, P.O. PP0280
 Bøgsted, M. OP017, MP507
 Bogte, A. PP1101
 Bohbot, J.-M. PP0690
 Boisseau, N. PP0363
 Boitel, A. PP0398
 Boitos, I. PP0337
 Boix, P. PP0945, PP0990
 Bojarski, C. MP650
 Bojic, D. OP079
 Bokemeyer, B. **MP329**
 Bolado Concejo, F. OP016, OP171
 Boland, A. PP0597
 Boland, B.S. MP684
 Bolca, S. OP081, OP156, **MP582**
 Bolívar-Prados, M. PP0049
 Bollen, T.L. MP022
 Bolognani, F. OP158, OP159, MP146, MP148
 Bolstad, N. OP003
 Boltežar, G. PP1014
 Boltin, D. MP433, PP0271, **PP0272**
 Bonanomi, A.G. OP175
 Bonaterra, G. PP0009
 Bongiovanni, B. MP653
 Boni, L. MP010
 Bonifacio, C. MP584
 Bonne-Annee, S. PP0600
 Bonnet-Dodel, M. MP149
 Bonnet Yderstraede, K. OP154
 Bonomi, A.M. MP702
 Bonsing, B. MP030
 Boonekamp, K.E. OP066
 Boonstra, J.J. OP225
 Booth, S. MP556
 Bor, R. MP627, PP0584, PP0614, PP0675, PP0710, PP0713, PP0731, PP0732, PP0746
 Bor, S. PP1235
 Borahma, M. MP129, PP0109, PP0201, PP1028, PP1164
 Borbély, R.Z. **PP1128**
 Bordalo Ferreira, F. PP1212
 Bordet, M. MP285
 Bordier, V. MP312
 Bordignon, G. MP223
 Bordin, D.S. **PP0280**
 Bordin, D. PP1179
 Bordin, D.S. MP427, MP433, MP547, MP552, **PP0004**, **PP0242**, PP0271, PP0273, PP0276, PP1235
 Borges Chaves, C. MP079, MP499, **MP555**, **MP557**, PP0365, **PP0819**
 Borghi, C. PP0285
 Boris Nygård, S. OP060
 Börk, J.R. MP127
 Borkovskiy, T. **PP0218**
 Bornschein, J. PP0012
 Boros, E. **MP379**, PP0021
 Borraccino, A.V. PP0463, PP0480
 Borrelli de Andreis, F. MP028, **PP1088**, **PP1154**, **PP1209**
 Borrow, D.-M. MP091
 Bortlík, M. PP0575
 Bortoli, P. PP0431
 Borup, C. PP0607
 Bos, S. OP077
 Bos, V. **OP112**
 Bosca-Watt, M.M. MP674
 Boscá Watts, M.M. OP191, OP213
 Bosch, O. MP510
 Boschetti, E. PP0347
 Boschetti, G. PP0676
 Bosco, N. PP0778
 Boskoski, I. MP311, MP539, MP605, PP0247, PP1203
 Bosman, M. OP117, **OP121**, PP0805
 Bosques Padilla, F.J. MP429, MP430
 Bossa, F. OP106
 Bosso, S. **MP028**
 Bossuyt, J. MP521, PP0836
 Bossuyt, P. **OP128**, OP147, MP328, MP339, MP614, PP0556, **PP0562**
 Boston, I. MP554
 Bostrom, S. MP657
 Bosze, Z. PP0584, PP0675, **PP0710**, **PP0713**, PP0731, PP0732, PP0746
 Bósze, Z. PP0614
 Bota, A.D. PP1132
 Botta, B. OP064
 Bottari, A. MP663, PP0794
 Bouamar, H. MP418, PP0998
 Bouaouina, F. OP097
 Bouattour, M. OP034
 Bouazza, N. MP070
 Boubonaris, A. MP676
 Bouchabou, B. PP0456, PP0964, PP1245
 Bouchard, S. OP124, OP142
 Boudabous, M. PP0660
 Boudokhane, M. PP0551
 Boudreau, F. PP0387
 Bouguen, G. OP189, MP156
 Bouhamou, F. PP1140
 Bouhlei, W. PP0669
 Bouhmidi-Assakali, A. PP0557
 Bouhnik, Y. MP002, PP0595, **PP0651**
 Bouhout, K. MP345
 Bouillon, V. **PP0622**
 Boulahfa, J. PP0651
 Bour, A. PP1047
 Bouratbine, A. PP0402
 Bourdillel, J. PP0349
 Bourgonje, A.R. **OP001**, OP020, **OP111**, **MP150**, MP210, PP0397, PP0511
 Bourguiba, R. PP1236
 Bourke, M.J. OP112, MP069, MP284, MP317, MP371, MP381, PP0179, PP0184, PP0769, PP0850, PP0853, PP0875, PP0876, PP0890, PP0891, PP0892, PP0894, PP0898, PP1199
 Bourke, R. PP0597
 Bourreille, A. MP630
 Bourrier, A. MP267, PP0377
 Bouslama, K. **PP1245**
 Boussena, I. PP1047
 Bousvaros, A. OP192, MP613
 Boutellier, I. PP1100
 Boutros, M. OP066
 Bouvet, J. PP0395
 Bouvy, N.D. MP362
 Bouwense, S.A. MP022
 Bouwknegt, D.G. **MP337**, PP0397, PP0440
 Bouzid, A. PP1124
 Bove, V. MP311, MP539, MP605, PP0247
 Boveri, S. OP075
 Bowker-Howell, F.J. PP0305
 Boxhoorn, L. MP022
 Boyar, R. MP341
 Boyar, R. PP0417
 Boye, T.L. OP024, PP0509
 Boyerahmadi, K. PP1187
 Boyko, N. **PP0010**
 Boyle, B. MP287, MP608
 Boysen, T. MP391, PP0535
 Bozhychko, M. MP480
 Bozorg, S.R. **OP216**
 Bozsó, B. **MP354**
 Bozzarelli, S. MP584
 Braad, M. MP387
 Bracken, L. PP0179, PP0892
 Braden, B. **PP1176**
 Braga, M.C. MP261
 Bragança, S. **MP067**, PP0532
 Bragg, R. **PP0019**, **PP0726**
 Braham Ep Krifa, A. MP215, PP0430, PP0495, PP0619
 Brambilla, P. PP0471
 Bramuzzo, M. PP0433
 Branchi, F. OP167, MP021, MP650
 Brand, M. PP0178, PP0221, PP0900, PP0916
 Brand, S. MP630
 Brand, S. PP0074
 Brandao, A. MP373
 Brandt, M.W. OP204
 Branigan, P. OP102, MP563
 Branquinho, D. MP003, PP0544
 Braquet, T. MP274
 Brar, G. PP0571
 Bratosin, F. PP1079
 Brav, E. MP249
 Bravo, A.C. MP005, **MP690**, **MP698**, PP0033, **PP0138**, **PP0422**, PP0468, **PP0532**, PP0751, PP0827
 Bravo-Lopez, S. MP643
 Brazao Almeida Santos, L. PP1212
 Brazier, F. MP185, PP0518
 Brecciaroli, M. PP0433
 Bredenoord, A.J. OP207, MP490, MP493
 Bredenoord, A. OP209, PP0077
 Bredenoord, A.J. MP484
 Bredon, M. OP110
 Brenes, Y. MP343
 Bressler, B. OP045, OP082, OP084, MP154, MP670
 Bretthauer, M. OP123, OP178, MP278
 Breukink, S.O. PP0484, PP0791, PP0792
 Breunig, M. OP013, OP069, MP086
 Brew, C. MP556
 Brezina, J. MP708
 Brglez Jurecic, N. MP547, PP0273
 Bricca, L. **OP056**
 Brickner, L. PP0272
 Briau, B. MP068
 Brignola, S. MP223
 Brillo, A. OP016
 Brim, H. PP1191
 Brinch, D. MP013
 Bringas-Vasquez, D. PP1116
 Bringeland, E.A. PP0119
 Brito, D. PP0195, PP0196, PP0197
 Brito, N. OP095
 Britton, J. OP114, PP0106
 Brizi, M.G. MP645, PP1165
 Brochhausen, C. MP413
 Brock, B. PP0046
 Brock, C. PP0046
 Brodsky, P. MP448
 Brodyuk, N. PP0759
 Broeders, B. MP723, **PP0063**, PP0066
 Broeders, I. PP0924
 Broekman, M. MP219
 Broër, C. MP387
 Brohet, R.M. OP222, OP226, MP222
 Brombin, C. PP0135
 Brøndum, R.F. OP017, MP507
 Bronsky, J. PP0580
 Bronswijk, M. MP137
 Bronzini, F. **PP1071**, **PP1243**
 Brookes, M.J. MP151
 Brosel Martínez, M. PP0008
 Brosens, L. MP039
 Brosens, L.A.A. OP115
 Brosnan-Cashman, J. PP0375
 Brown, E. PP0019
 Brown, G. MP284, PP0876
 Brown, S. MP037, **PP0545**, **PP0616**
 Brown, S. PP0680
 Brown Hajdukova, E. PP0438
 Bruccoleri, M. MP469
 Bruehlmann, S. OP153
 Bruguera, P. MP071
 Bruland, T. OP109, PP0367, PP0445
 Brule, C. PP0849
 Brun, P. MP569
 Bruncak, M. PP1113
 Bruneel, W. MP521
 Brunet, E. OP043, OP191
 Brunet, J. MP522
 Brunet Mas, E. MP673
 Brunetta, J. PP0822
 Brunk, T. PP0221
 Brunner, M. MP298
 Bruno, A. MP152
 Bruno, M.J. MP022, MP023, MP132, MP535, PP1101
 Bruns, T. PP0984
 Bryant, R.V. PP0576
 Bubeck, M. PP0372
 Bucci, C. MP560
 Bucci, L. PP1012
 Bucci, M. MP406, PP0752, PP0880
 Buchkremer, J. OP167, MP021
 Buchstab, O. MP644
 Buckley, M. MP213
 Bucur, M. PP0335, PP1133
 Buda, A. MP063, MP259, MP392
 Budai, B.C. MP304, PP1125, PP1126
 Budczies, J. MP479
 Buderus, S. OP208
 Budjanto, S. PP0771
 Budree, S. MP250
 Budzinskaya, A. **PP0496**
 Budzyn, K. **OP123**
 Buendia, M. OP026
 Buendía Fuentes, F. MP128
 Bugajski, M. OP123
 Bugeja, L. **PP1219**
 Bugianesi, E. **OP058**
 Bugianesi, E. MP236, PP0942, PP0955
 Buisson, A. MP149, **MP155**, MP156, MP217, MP266, MP630, PP0377, PP0395, PP0422, PP0548, **PP0659**
 Bujanda, L. OP151, OP213, MP428, MP433, MP503, MP547, PP0271, PP0273
 Bujanda**, L. PP0257
 Bujanda Fernández de Piérola, L. OP023, OP043, OP187, MP268, MP343, MP427, PP0364, PP0381
 Bulajic, M. MP310, **MP606**
 Bulhoes, E. PP0986, PP1023, PP1027, PP1105
 Bulhões, E. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0988
 Bulhões, E. PP1001, PP1002, PP1103
 Bulhões Júnior, E.S. PP1106
 Bulmer, D. PP0434
 Bulmer, D.C. PP0435
 Bulthuis, M.L.C. PP0397, PP0511
 Bumane, R. MP427, MP547, PP0271, PP0273
 Bunchornstavakul, C. **PP0953**
 Bundalovic-Torma, C. OP153
 Bunde, T. MP280
 Bunduc, S. MP297, **MP586**, PP1125, PP1133, PP1157
 Buño Soto, A. OP184
 Burcul, I. PP0541
 Bures, J. **MP587**, **PP0225**, PP0759
 Burgell, R.E. PP0071
 Bürger, M. PP0984, PP1048
 Burgess, N. MP284
 Burgess, N. PP0179, PP0769, PP0850, PP0876, PP0890, PP0891, PP0892

Burgess, N.G. MP317, MP381, PP0184, PP1199
 Burgess, N.G. MP069, MP371
 Burghart, L. MP347, MP638
 Burghgraef, T. MP070, PP0940
 Burghgraef, T.A. MP219
 Burgos García, A. PP1242
 Burgos-Santamaría, D. MP549
 Burhan, S. MP513
 Burisch, J. OP174, OP190, OP204, MP007, **MP149**, MP336, MP391, PP0411, PP0498, PP0502, PP0535
 Burkart, C. MP479
 Burke, L. MP383, PP0457, PP0482, PP0499
 Burkhart, R. OP133
 Burkov, S.G. PP0280
 Burmei, S. PP0010
 Burns, R. PP0521
 Burr, N.E. OP037, MP325
 Burra, P. MP406
 Burrack, S. OP208
 Burrelli Scotti, G. PP0023
 Burri, E. PP0074
 Busana, A. OP229
 Busato, L. PP0491
 Busatto, A. OP199, MP476
 Buscarini, E. MP063
 Busch, C.B.E. **OP049**
 Busch, O.R. MP030, MP702, PP1089
 Busche, P. PP0810
 Businello, G. MP223
 Buskens, C.J. OP188, MP117, MP151, PP0484, PP0523, PP0540
 Busquets, D. PP0557
 Busquets-Barenys, J. MP138
 Busquets Casals, D. OP043, OP187, OP191, OP213, MP334, MP343, MP508
 Busslinger, G. **PP0390**
 Bustamante, M. MP430
 Buszkiewicz, M. OP123
 Butler, K. MP326
 Butler, T. MP431, PP0266, PP0289
 Butler, T.J. MP427
 Butt, J. MP203, MP205
 Butt, M. MP725
 Butt, M.F. PP0809
 Butt, M. PP0019
 Butt, N. PP0571, PP0705, PP0740
 Buttar, J. **PP0875**
 Butwicka, A. MP214
 Buxbaum, J.L. OP171
 Buzás, G.M. MP433, MP552, PP0276
 Buzato, J.N. PP0790, PP0932
 Buzunova, Y. PP0496
 Bychkov, M. PP0720
 Bychkova, S. **PP0720**
 Byeon, J.-S. PP0441
 Byrne, M. MP380
 Byrnes, V. MP651
 Bzdrya, M. PP0697

C
 Caballero, N. PP0755
 Caballero-Mateos, A.M. MP157, PP0606
 Caballol, B. OP026
 Cabello Tapia, M.J. MP157, PP0606
 Cabello Tapia, M.J. MP674
 Cabibbo, G. MP170, PP1018
 Cabitza, F. PP1200
 Caboni, P. PP0378
 Cabrera Hinojosa, D. MP429, MP430
 Cabriada Nuño, J.L. MP116
 Caca, K. PP0916
 Cacho Soblechero, I. PP0079
 Cacic, P. **PP0541**, PP0863
 Cade, R. MP139
 Cadime, A.T. PP0195, PP0196, PP0197
 Cadoni, M. PP0418

Cadranel, J.-F.D. MP634
 Caetano, A.C. MP286, PP0526, PP0826, PP0827
 Caetano, C. MP386
 Cafarelli, A. MP390
 Cagir, Y. PP0527, **PP1073**, PP1075
 Cahova, M. MP708
 Cahyadi, O. MP131, MP280, MP610, PP1229
 Cai, T. PP0137
 Cai, X. MP142
 Cai, X. PP0636
 Cailleaux, P.-E. PP0299
 Caillio, L. MP440, PP0377
 Caillol, F. PP1100
 Caio, G. MP659, PP0309, PP0310, PP0347
 Calabrese, C. PP1200
 Calabrese, E. **MP389**, **PP0488**, PP0621
 Calabrese, F. MP137, PP0707
 Calabrese, F. PP0652
 Calabrese, G. MP152, MP276, **MP281**, PP0476, PP0481, **PP0670**, **PP0832**
 Calabrò, A. MP659, PP0347
 Calafat Sard, M. OP151, MP268, PP0035
 Calavrezos, L. MP298
 Caldart, F. MP130, **MP237**
 Caldeira, P. PP0774
 Calder, S. PP0059
 Calderon, S. OP200, MP483
 Calderone, S. PP0452, PP0629, PP0645, PP0670
 Caldwell, J.M. MP488
 Calia, M. PP0470
 Callaerts, B. PP0861, **PP0864**
 Calm, A. PP0755
 Calmejane, L. **MP156**
 Cało, N. MP298
 Caloro, A. PP0069
 Calvet, X. OP023, MP503, MP510, MP674, PP0364
 Calvet Calvo, X. OP151, MP268, MP508, MP673, PP0381
 Calvez, V. **MP006**, **PP0963**
 Calvez, V. PP0613
 Calviño Suarez, C. OP213, MP343, PP0424
 Calviño-Suarez, C. PP0373
 Calvo, M. **OP187**
 Calvo Moya, M.I. OP043, OP213, MP343
 Camacho, K.D. PP0368
 Camacho-Montaño, L.M. OP171
 Camarca, A. MP652, PP0302
 Camardese, G. MP340, PP0612
 Camargo Camero, R. OP151, OP213, MP268, MP343
 Camba-Gomez, M. PP0373
 Camenforte, N. PP0688
 Camera, S. PP0492
 Camicia, L. MP395, **MP398**
 Caminati, M. MP491
 Camma, C. MP084
 Cammarata, G. MP059
 Cammarota, G. OP096, MP269, MP340, MP577, PP0393, PP0637, PP0654, PP0656
 Cammarota, S. PP0324
 Campagnola, P. MP237
 Campani, C. OP034, PP1012
 Campelo, P. **PP0789**
 Campigotto, M. OP169, MP604, PP0629
 Campioli, E. OP075
 Campmans-Kuijpers, M.J. PP0345
 Campos, S. **PP1203**
 Campos Machado, G. PP1178
 Campos Machado, J. PP1175
 Campos Nuñez, C. MP429, MP430
 Campos Ribeiro, M. OP027
 Camprubí-Font, C. PP0688

Camps, B. OP043
 Camus, M. MP104
 Cananzi, M. PP0433
 Canbay, A. **OP219**
 Cancelli, L. PP0794
 Cancro do Cólon, Reto e Canal Anal, G.M. PP0748
 Candia, F. MP059
 Candia, R. MP429, MP430
 Canena, J. PP1241
 Canesi, S. OP054
 Canhoto, M. MP005, PP0468
 Cannito, S. PP0942
 Cannizzaro, R. OP054, MP395, MP398, PP0132
 Cano-Catala, A. MP552, PP0276, PP0277, PP0285
 Cano-Catalá, A. PP0289
 Cano Català, A. PP0284
 Cano-Català, A. OP009, MP427, MP428, MP429, MP430, MP433, MP547, MP549, PP0271, PP0272, PP0273, PP0275, PP0280
 Cano-Contreras, A. PP0288
 Canova, L. **MP466**, MP469, **PP1018**, PP1020
 Cantatore, S. PP0957
 Cantisani, N.M. PP0139
 Cantone, E. MP729, PP0086, PP0087
 Cantù, P. MP540, PP0129, PP0130
 Canu, T. MP390
 Cao, J. PP0638
 Cao, Q. MP687
 Cao, X. PP0181, **PP0241**
 Caparros, E. PP0990
 Caparrós, E. PP0945
 Capasso, M. MP410, PP1009
 Capellà, G. MP522
 Capinha, F. PP0193, **PP1026**
 Capobianco, I. MP006, PP0393, **PP0613**
 Capogreco, A. MP281, MP714, PP0244
 Capozzi, F. MP410
 Cappelleri, J.C. PP0548
 Cappellini, A. OP013, **MP656**
 Cappello, M. OP106, PP0645
 Cappendijk, V. MP022
 Caprioli, F. OP106, OP129, MP010, MP389, MP622, PP0414, PP0476, PP0488, PP0629, PP1200
 Caprioli, S. OP199, MP476
 Capuano, A. **OP054**
 Capurso, G. OP016, OP136, MP024, MP027, MP186, MP188, MP244, MP480, MP536, MP542, MP583, PP1138
 Caputo, F. PP0310
 Carabotti, M. MP728
 Carbone, E. **PP0954**
 Carbone, F. MP160, MP723, PP0039, PP0063, PP0066, PP0070
 Carbone, L. MP006
 Carbonell, N. MP634
 Carbonnel, F. MP630, PP0608
 Card, T. MP272
 Cárdenas-Jaén, K. PP0403
 Cardinale, V. OP064, PP1138
 Cardinali, S. PP0958
 Cardoso, H. OP205, PP0207, PP0329, PP1201
 Cardoso, M. MP067, MP408, PP1241
 Cardoso, M. MP346
 Cardoso, P. OP099, OP205, MP060, **PP0329**, PP0830, PP1201
 Cardoso, R.A. PP0770
 Cardozo-Ojeda, E.F. MP568
 Cariello, M. PP0957
 Carini, A. PP0431, PP0626
 Cariola, L. MP275
 Carlessi, R. MP115, MP177
 Carlier, H. PP0550
 Carlin, J.L. PP0042, **PP0057**, **PP0058**

Carlino, G. MP311, MP361, **MP502**, **MP605**, PP0247
 Carlomagno, D. MP415, **PP0818**
 Carlos Goncalves, J. **MP171**, **PP0477**, **PP0486**, **PP0750**, PP0757, PP0761, PP1216
 Carlotta, C. MP223
 Carlson, M. OP021
 Carlsson, S. OP214
 Carmichael, C. PP0438
 Carmona Campos, A. PP0666
 Carneiro, F. PP0138
 Carneiro de Moura, M. MP346
 Carnevale, L. PP0491
 Carbolante, G. MP395, MP398
 Carol, M. MP071
 Caroli, D. PP0752, PP0880
 Caroline, L. MP634
 Caron, B. MP156, PP0377, PP0553
 Carparelli, S. OP106
 Carpentier-Pourquier, M. PP0185
 Carpinelli, M. PP0320
 Carpio, G. OP064
 Carpio, A. PP0493
 Carpio, D. OP151
 Carpo, D. MP268
 Carrara, S. OP136, MP130, MP584, PP0754
 Carriles Linares, A. **MP571**
 Carriles Lineares, A.A. MP390
 Carrilho-Ribeiro, L. PP0193
 Carrillo, B. PP0439
 Carrington, E.V. MP055, PP0788, PP0824
 Carrion, S. PP0049
 Carrión Bolorino, S. PP0076
 Carroccio, A. MP045, MP659, PP0347
 Carrozza, L. MP170, MP639
 Carswell, S. OP229
 Carter, D. PP0054, PP0501, PP0506, **PP0796**
 Carucci, P. PP0942
 Carugno, M. PP0414
 Caruso, C. PP0613
 Carvalhana, S. MP346
 Carvalhas Gabrielli, A.M. PP0629
 Carvalho, A.T. PP0193
 Carvalho, P.B. PP0750, PP0757, PP0761, PP1216
 Carvalho, R. MP408
 Carvalho, T. MP286, **PP0526**, PP0826, **PP0827**
 Carvalho, T. PP0552
 Carvalho do Vale, B. PP1178
 Carvalho e Branco, J. MP408, PP1212
 Carvello, M. MP571
 Casà, A. PP0645
 Casabona-Francés, S. MP664, PP0076
 Casals, C. PP0693
 Casals Seoane, F. PP0364
 Casals-Seoane, F. OP171
 Casanova, G. **PP0693**
 Casanova, M.J. OP023, OP213, **MP339**, MP503, MP510, PP0362, PP0364, PP0381, PP0382, **PP0557**
 Casari, I. MP177
 Casas-Deza, D. OP171
 Cascant Ortolano, L. PP0810
 Cascella, F. PP0473
 Casciani, F. OP136
 Casella, M. MP241
 Casillas, L. OP185
 Casorla Perez, L. MP452
 Casotti, V. PP1025
 Cassinotti, A. **PP0508**
 Castagliuolo, I. MP569
 Castán, S. MP014
 Castaño-Milla, C. MP343
 Castaño Rodríguez, N. OP141
 Castelhana, N. **PP0343**
 Castellet, S. PP0585
 Castelli, F. OP157

Castells, A. MP522
Castéra, L. OP060
Castiglione, F. MP152, MP389, PP0476, PP0481, PP0488, PP0670
Castillo, J. MP522
Castillo Grau, P. OP184
Castri, F. PP0082
Castro, F. PP0084
Castro, M.F. **MP355**
Castro, R. MP346, MP530
Castro-Fernández, C. OP196
Castro-Fernández, M. OP009, MP428, MP433, MP547, MP549, PP0271, PP0273
Castro-Palomino, J.C. OP196
Castro Poças, F.M.D. PP0827
Castro Poceiro, J. OP043
Castro-Poceiro, J. OP187
Catalan-Serra, I. **OP109**, MP339
Cataldi, F. OP207, MP449, MP493
Cataldo, I. MP223
Catapano, V. PP0087
Cattani Mottes, M. OP169
Cavadas, D. PP0747
Cavagna, C. PP0587
Cavalcoli, F. PP0129, PP0130
Cavalieri, D. MP659, PP0347
Caveney, S. PP0075
Cavestro, G.M. **PP0135**, **PP0348**
Cavicchi, M. MP156
Cazimirovitz, A. MP694
Cazzetta, S. MP043
Cazzo, E. PP0263
Ceballos, D. OP043, OP213, MP674, PP0557
Ceballos Santos, D.S. OP151, MP268, PP0362, PP0382
Ceccarelli, L. PP0508, PP0629
Ceccarelli, M. MP625
Cecinato, P. MP281
Cedron, H. MP429, MP430
Cefaliello, A. MP716, **MP729**, PP0086, PP0087
Cefalo, F. MP725
Celebi, Ö. OP167, MP021, PP1181
Celiberto, F. PP0269
Celis, J. OP077
Celotti, A. PP0139
Celsa, C. MP170
Cemîrtan, A. PP0749
Cennamo, V. MP132, PP0870
Centritto, A. PP0553
Cepero, C. OP187
Ceravolo, R. PP0782
Cercato, C. MP527
Cerkauskaite, D. PP0821
Cerrillo Bataller, E. OP191, PP0404
Cerrito, L. OP034
Cervera, M. MP071
Cesari, E. PP1154
Cesarini, A. MP438, PP0324
Ceulemans, M. **OP008**, MP160
Ceyhan, G.O. OP132
Cha, B. MP581, PP0744
Chaaban, L. PP0521
Chaalal, S. PP0407
Chabib, F.Z. MP129
Chabib, F.-Z. PP0109, PP1028, PP1164
Chabrun, E. MP068
Chadli, A. PP0361
Chae, J.H. MP096
Chafai, N. MP267, MP274
Chagas, C. PP0934, PP1237
Chahi, K. **PP0677**, PP0972, PP0977
Chahuán Abde, J. MP429, MP430
Chaibi, R. **MP559**, PP0742, PP0905, **PP1036**, PP1087, PP1107, PP1114
Chaiteerakij, R. PP0989
Chalakatevaki, K. MP676, PP0568
Chalita, M. OP092
Challine, A. MP274
Challoukh, F. PP0024
Chamaillard, M. OP095
Chamalidou, E.-P. PP0743
Chan, C. PP0623
Chan, C. PP1193
Chan, E.W.Y. PP0695
Chan, M.W. OP112
Chan, S. OP098
Chan, W. MP093
Chana, A. PP0642
Chand, M. OP088
Chandan, S. MP136, PP0855
Chan-Diehl, F. MP623
Chandramouli, A.S. PP0955
Chandran, S. PP1099
Chandrashekar, C. PP1011
Chang, C. PP0600
Chang, C.-Y. MP713
Chang, J.H. PP0694
Chang, J. PP0623
Chang, J.W. MP258
Chang, K. OP050
Chang, S. MP680
Chang, Y.-C. MP363
Chanyshev, M. PP0004
Chaparro, M. OP150, OP169, **OP213**, MP334, MP342, MP343, MP508, **MP510**, **MP674**, **PP0542**, PP0550, PP0555, PP0565
Chaparro*, M. OP023, OP187, MP339, MP503, PP0362, PP0364, PP0381, PP0382, PP0557
Chapelle, N. MP318
Chapman, C. PP1081
Chapman, J.C. MP614
Chapman, P. PP0352
Chapman, T. MP629
Chapon, J. PP0659
Charabaty, A. OP044
Charernboon, T. PP0786
Charif, Y. PP1100
Charkaoui, M. MP156
Charkaoui, M. MP002
Charlois, A.-L. PP0676
Charo, D.C. PP1112
Charpy, C. OP095
Charra, B. PP1234
Charriez, C. MP486
Chartier, L. PP0630, PP0631
Chateau, T. PP0553
Chatonidis, V. MP134
Chatpermorn, K. PP0823
Chatterjee, A. **PP0603**
Chatterjee, A. PP0203
Chatzikosma, C. MP290
Chatzinikolaou, M.L. MP676
Chatzinikolaou, M.-L. PP0568
Chaudhari, U. MP383, MP392, PP0479
Chaussade, S. MP068
Chavan, R. MP541
Chavatte, P. MP306
Chaves, C. MP189
Chaves, J. PP0164
Chegodar, A. PP0004
Chehade, M. **OP210**, **MP490**, **MP660**
Chehaidar, A. MP473, PP0453, PP0551, PP0727, PP0772
Cheikh, I. PP0760
Cheinquer, N. MP042, **MP043**, MP250, MP252, PP0307, PP0308
Chemkhi, E. PP0871
Chen, B. OP052, **MP207**
Chen, D. OP134, **MP035**, MP085
Chen, F. PP1202
Chen, H. PP0358
Chen, H. OP007
Chen, H. MP401
Chen, H. OP120, MP675
Chen, K. MP567
Chen, L.Y.E. **MP218**
Chen, L. PP0533
Chen, L. PP0949
Chen, L. PP0358
Chen, M. MP012
Chen, M. MP618, MP671, MP675, PP0100, PP0550, PP0565
Chen, Q. PP0296, PP0342, PP0687, PP0787
Chen, S. OP070, MP076, MP126, MP411, PP0983
Chen, S. **MP596**, PP0949
Chen, S. MP111
Chen, S. MP620
Chen, T. PP1223
Chen, W. PP1097
Chen, W. PP0358
Chen, W. MP012
Chen, X. OP120
Chen, X. OP007, **MP687**
Chen, X. MP015, **PP0837**, PP0843
Chen, Y. MP474
Chen, Y.J. PP0053
Chen, Y.-I. PP1100
Chen, Y. PP0083
Chen, Y. PP1061
Chen, Y. MP500, PP0396, **PP0636**, PP0644
Chen, Y. MP161
Chendey, T. PP0010
Cheng, E. MP327, MP385
Cheng, H.-H. MP363
Cheng, J. OP025
Cheng, J. MP397
Cheng, L. MP620
Cheng, Y. MP015, PP0843
Cheon, J.H. PP0558, PP0733, PP0909
Cheong, N.W.W. **PP1068**
Cherif, D. MP046, PP0318, PP0346, PP0350, PP0516, PP0525, PP0867
Cherif, E. **PP1006**
Cherkaoui Malki, M. **PP0026**, PP0028, PP0034, PP0400, PP0401, PP0657, PP0658, PP0681, PP0831, PP0926, PP0927, PP0971, PP1032, PP1049
Chetcuti Zammit, S. PP1219
Chetroub, H. OP097, PP1082
Cheung, D.Y. **PP0278**
Cheung, K.-S. MP246
Cheung, P.F.-Y. MP479
Cheung, S. OP088
Chevaux, J.-B. MP068, PP1100
Chevreux, G. OP027, OP110
Chew, Y.J. PP0088, **PP0835**
Chey, W. PP0220
Chi, X. PP0455
Chia, D.K.A. PP0192
Chianese, U. PP0942
Chiang, Y. PP0897, PP0900
Chiappetta, M.F. MP281
Chiara Matteucci, M. PP0805
Chiarioni, G. PP0793
Chiba, H. OP145, VC04, PP0171
Chiba, K. PP1149
Chibambo, L. OP038
Chieffo, D.P.R. MP340
Chilan-Puley, A. MP554
Child Health, Madras Medical College, R, S.K. PP0997
Chilton, A. PP1206
Chiminazzo, V. MP223
Chindaprasirt, J. PP1108
Chinen, K. OP231
Chini, A. MP716
Chinnaratha Mohamedashrafali, M.A.A. PP1193
Chinnery, G. PP0293
Chinthala, H. PP0700
Chiriach, M.T. **MP462**
Chiriach, S. MP080, PP1204
Chitnis, M. PP0680
Chitteti, B.R. PP0600
Chiu, C.-T. MP687
Chiu, H.M. PP1204
Chiu, P.W.Y. MP377, PP0877
Chkolnaia, Z. **MP002**
Chlorakis, G. **MP062**
Chloupkova, R. MP517
Chmiela, M. MP543, PP0252
Cho, I.R. MP599
Cho, T. PP0331
Cho, Y.S. MP066, PP0143
Choi, A. MP304
Choi, D. MP621
Choi, H.-S. MP196, PP0848
Choi, I.J. PP0215
Choi, J.H. MP599
Choi, J.J. MP232
Choi, J.W. MP066, PP0143
Choi, N. MP621
Choi, S. PP0909
Choi, S.I. PP0295
Choi, Y. **MP144**, MP548, MP551, MP603, **PP0126**, PP0127, PP0131, PP0336
Choi, Y.J. MP232, PP0215
Choi, Y. **MP066**, **PP0143**
Chollet, C. OP157
Chollet, L. OP027
Chooklin, S. MP298, PP1124
Choon, X.Y. MP326, **MP628**
Chou, C.-K. PP0187
Chou, J.-W. MP687
Chow, V. **PP0638**
Chowdhury, R. PP0521
Chowdhury, S.D. PP0027, PP0700
Chrisaugis, L. MP254
Christensen, B. PP0389, PP0533, PP0648
Christensen, H.S. OP017, MP507
Christensen, S.G. PP0422
Christiansen, D. OP190
Christodoulou, D.K. MP676, PP0330, PP0568, **PP0583**
Chromy, D. MP638
Chrostek, M. PP0209
Chtourou, L. PP0660
Chu, J. PP0146
Chu, M. **PP0161**
Chu, S. MP568
Chua, L. PP0559, PP0655
Chuah, Y.Y. **PP0187**
Chuang, S.-C. MP363
Chuenprapai, P. PP0786
Chun, H. OP072
Chun, H.J. MP196, PP0848
Chun, J. MP546
Chun, J. OP092
Chun, K.Y. **OP173**, MP631, PP0467
Chung, C.-S. MP713
Chung, C.H. MP385
Chung, H. MP502, PP0189, PP0192
Chung, J.-W. MP456
Chung, M.-J. MP482
Church, P. OP172
Ciacci, C. MP045, MP261, PP0956
Ciafardini, C. OP129
Ciardiello, A. PP1194
Cicala, M. MP261, MP313, MP607
Cicalini, C. MP013
Ciccocioppo, R. OP169, PP0347, PP0570
Cid, L. MP064
Gigarrán Vicente, B. MP649
Ciglar, L. MP390
Cihoric, M. MP300
Cijevschi Prelipcean, C. PP0536
Cillo, U. MP406
Cimbora, D. MP350
Cindoruk, M. MP416, PP0625
Cingolani, S. OP140, MP203, **MP205**
Cini, L. **PP0078**
Cinque, S. PP0473
Cinti, F. MP455
Cintoni, M. MP645
Ciorba, M. **MP452**, **PP0399**
Cipriano, M.A. MP555

- Cipullo, M. MP073, MP632
 Ciriza de Los Rios, C. MP052
 Ciriza de los Rios, C. PP0079
 Citarella, A. PP0324
 Citterio, N. **MP607**, PP0707, PP0917
 Ciupkeviciene, E. MP545
 Civera Peris, M.I. MP014
 Clairet, V. PP0398
 Claparols, M. PP0693
 Clape, D. PP1213
 Clark, D. PP0678
 Clark, K. PP0031
 Clarke, A. PP0369
 Clarke, K. PP0667, PP1185
 Clarke, M. **PP0214**
 Clasquin, E. OP147
 Clavé, P. PP0049
 Clavo, N. MP287
 Clax, P. OP207
 Cleirigh Buttner, F. MP208
 Clement, D. MP037
 Clemow, D. MP617
 Clevy, L. PP0407
 Clift, K. MP245
 Cline, M. PP0220
 Clucas, C. PP0458, PP0459, PP0460
 Cluzeau, V. PP0489
 Co, F.A. PP1019
 Coan, A.C. PP1103
 Coan, A.C. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982
 Cobián, J. PP0076
 Cocaïgn-Bousquet1, M. PP0778
 Coe, C. MP213
 Coelho, H. **PP1241**
 Coelho, R. PP0827
 Coelho Neto, D.E. **PP1070**, PP1136, PP1175, PP1178
 Coelho-Rocha, M. MP365
 Coffin, B. MP156
 Cogliandro, R.F. MP057
 Coguric, V. **PP0591**
 Cohen, A. OP219
 Cohen, B.L. MP681, PP0588
 Cohen, J. PP0894
 Cohen, R.D. MP621
 Cohen, Y. MP184
 Coilly, A. MP634
 Coimbra, M. PP0164
 Cojocariu, E.C. MP294
 Colaci, N. PP0570, PP0664
 Colantuono, S. PP0613
 Cole, F. PP0217
 Colecchia, A. MP059, PP1235
 Colecchia, L. MP059
 Colella, F. MP390
 Coleman, C.I. OP219
 Coletta, M. MP256, MP491, PP0076, PP0078, PP0094, PP0095
 Colhoun, H. MP527
 Coli, F. MP265
 Collard, M. MP274
 Collazo Moreno, A.J.R. OP171
 Colleypriest, B. OP037, MP325
 Colli, M. MP564
 Collij, V. PP0379
 Collin, R. PP0849
 Collins, M.H. OP207, MP493
 Collins, P. PP0701
 Collins, S. PP0779
 Colombel, J.-F. OP104, OP149, MP149, MP150, MP615, MP622, PP0422, PP0556, **PP0588**, PP0589
 Colombo, F. **MP271**, MP275
 Colombo, M. MP193, MP584, PP0166
 Colomier, E. MP723
 Coluccio, C. MP084, MP364
 Colwill, M. MP326
 Coman, L. PP0312
 Combaret, L. PP0363
 Comerford, M. MP431, PP0266
 Comes, D.J. MP362, MP705
 Cominelli, F. MP008
 Compare, D. OP009, PP0452, PP0473
 Complido, E. PP0041
 Conceição, D. MP061, MP494
 Conchillo, J.M. PP0052
 Conde Amiel, I. MP128
 Conde-Andrade, J. PP0373
 Condori Mamani, C.A. MP298
 Conforti, F. OP129, PP0414, PP0629
 Congia, M. PP0442
 Connaughton, R. MP319, PP0214
 Connell, W.R. PP0602
 Connor, S. MP387
 Connor, S.J. PP0602
 Conrad, C.C. **MP195**, MP324
 Conrad, C.C. VC01
 Conrad, J. PP0685
 Conradi, L.-C. PP0230
 Conrath, K. MP582
 Consonni, D. MP709
 Constantine-Cooke, N. PP0579, PP0674
 Constantinescu, A. PP1124, PP1204
 Constantinescu, D.I. PP1132
 Consten, E. MP070, PP0924, PP0940
 Consten, E.C.J. MP220
 Consten, E.C. OP223, OP226, MP219, MP222
 Conti Bellocchi, M.C. **OP169**, **MP130**, MP237
 Contreras, J. MP287
 Cook, M.E. OP168
 Cook, M.E. OP230
 Cooney, J. **MP485**, **PP0101**
 Copaci, I. PP0300
 Copova, I. PP0580
 Coppieters, W. OP019
 Coppola, A. MP073
 Coppola, F. MP441, MP714
 Coppola, G. MP269, PP0393, PP0613, **PP0637**, PP0654, PP0656
 Corazziari, E.S. **MP261**
 Corbett, G. MP132
 Corbi, Á. OP026
 Corcos, O. OP157
 Cordeiro, J. MP060
 Cordero, J.A. PP1019
 Coriat, R. MP318, PP0185
 Corina, M. PP0647
 Cormio, S. PP0463, PP0480
 Cormeille, S. **MP521**, **PP0836**
 Coron, E. MP440
 Corovic, I. PP0763
 Corpino, M. PP0442
 Corra', G. PP0013
 Corrà, G. PP0752, PP0880
 Corral, J.E. PP1057, PP1058
 Corraliza, A.M. OP026
 Corre, F. PP0185
 Correa, T. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0986, PP0988, PP1001, PP1002, PP1023, PP1027, PP1103, PP1105, PP1106
 Corrêa, P.A.F.P. PP0725
 Correia, C. PP0819
 Correia, F. PP1241
 Correia, L. PP0193, PP0592, PP0628, PP1026
 Correia Gomes, L. **MP061**, **PP0747**
 Corridoni, D. MP008
 Corrigall, D. PP0217
 Corsetti, M. MP725, PP0068, PP0794, PP0809
 Côte-Real, F. PP0033
 Cortés, H. PP0755
 Cortesi, P.A. PP1190
 Cortez Pinto, J. VC03
 Cortez-Pinto, H. MP346, PP0592, PP0628, PP1026
 Cortez-Pinto, J. MP061
 Coskun, O. PP1073
 Coss Adame, E. MP430
 Coss-Adame, E. MP429, PP0288
 Cossais, F. MP720
 Cosseddu, V. MP310, MP606
 Cossiga, V. MP410, PP1009
 Costa, B. MP690, MP698
 Costa, C. MP169, MP520, PP0620, PP0661
 Costa, D. MP286, PP0552, PP0826
 Costa, I. MP086
 Costa, J. MP373
 Costa, L. PP0255
 Costa, M. MP189, MP555, PP0050, PP0051, PP0062, PP0236
 Costa, M.N. MP067, MP408
 Costa, R.S. MP286
 Costa, S. PP1220
 Costa Cardoso, C. PP0429
 Costamagna, G. MP310, MP539, MP606, PP1088, PP1203
 Costantini, C. MP057
 Costantino, A. MP653, PP0327
 Costanzini, A. MP057, MP659, PP0310, **PP0347**
 Costa-Santos, M.P. MP690, MP698
 Costigan, C. **MP431**, PP0223, **PP0266**, PP0514
 Costigan, O. MP431, PP0266
 Cotruta, B. PP1204
 Cotte, E. MP070, PP0676
 Couch, J. MP272
 Coughlin, E. PP0222
 Cougnaud, L. PP0447
 Coulter, J. PP0548
 Coupé, V.M.H. OP180
 Courtoux, Z. PP0019
 Couturier, F. MP328
 Couvert, A. PP0363
 Covino, M. PP0613
 Covotta, F. MP415
 Covre Coan, A.c. PP0986, PP0988, PP1001, PP1002, PP1023, PP1027, PP1105, PP1106
 Coyle, C. MP262
 Cozza, G. **OP140**, MP203, MP205, PP0007, **PP1194**
 Craciun, A. PP0184
 Cramb, L. PP1225
 Crandall, W. OP192, MP613
 Craveiro, F. MP414
 Cravo, M. MP690, MP698
 Creanga-Murariu, I. **PP1157**, PP1180
 Creanor, S. PP0969
 Creed, E. **PP0031**
 Cremer, A. OP169, **MP009**, MP328, PP0622
 Cremer, J. OP008
 Cremon, C. MP059, PP0779, PP0797, PP0813, PP1235
 Crepalidi, M. PP0587
 Crespi, S. PP1018, PP1020
 Crestani, S. MP059
 Creusot, L. OP027, OP110
 Cricca, M. MP084
 Cricri, M. PP0670
 Crinò, S.F. MP130, MP136, MP137, MP193, MP237
 Cristiano, M. MP499, MP555, MP557, PP0812, PP0819, PP1072
 Cristofaro, L. MP364
 Croce', S.L. MP395
 Crocé, S.L. PP0132
 Crocé, L.S. OP054, MP398
 Crocetto, F. PP0452
 Croft, N.M. OP127
 Croitouru, K. PP0422
 Crone, E. **MP287**, **MP608**
 Cronin, O. MP069, MP284, MP371, MP381, PP0179, PP0184, PP0769, PP0876, PP0890, PP0891, PP0892, **PP0894**, **PP0898**
 Crooks, C. MP172, MP519, PP0912
 Crosby, C.M. PP0547
 Crosby, C.M. PP0354, PP0355
 Cross, A.J. OP179
 Cross, R. PP0547
 Cross, R.K. MP680, MP684
 Cross, S.S. PP0309
 Crotty, R. MP383, PP0457, PP0482, PP0499
 Crouch, B. MP478, MP589
 Crowley, E. PP0627
 Crucillà, S. MP237
 Crudele, L. PP0957
 Cruz Aguilar, R. PP0685
 Cruz Costa, M. PP0255
 Csaba, R. PP1129
 Csajbók, D. MP304
 Csákány-Papp, N. OP015, MP446
 Csefko, K. MP627
 Cua, D. MP563
 Cua, I.H. PP1019
 Cuadrado, A. OP009, MP428
 Cuatrecasas, M. MP031
 Cubiella, J. **MP014**, MP064, PP0929
 Cuccagna, E. MP389, PP0488
 Cuccia, G. OP106, MP006, MP269, PP0654, PP0656
 Cuerda, C. PP0298
 Cuesta Cortijo, R. MP014
 Cuffe, M. **MP166**
 Cui, J. OP120
 Culetto, A. MP285
 Cullen, G. MP213
 Culver, E. MP351, PP1138
 Culver, E.L. **MP350**
 Cunha, A. PP0164
 Cunha Neves, J.A. **PP1220**
 Cunneen, C. PP0588
 Cunningham, D. OP133
 Cunto, D. MP109, MP191, MP359, MP407, MP554, PP0204, PP1118
 Cúrdia Gonçalves, T. OP169, MP298, PP1124, PP1216
 Curiel, D.T. PP0399
 Curin, K. MP078
 Currie, K.S. PP0369
 Curvers, W.L. MP022
 Cusi, G. PP1003
 Cusi, K. OP058
 Cusmai, L. OP075, PP0094
 Custovic, N. MP588
 Cuzzucreea, A. **PP0653**
 Cyran, J. **PP0116**
 Czako, L. PP1130
 Czika, D. PP0311, PP0312
 Čelková, P. PP0097
 Čiupkeviciene, E. PP1031
D
 Daams, F. MP030, MP702, PP1089
 Dabbebi, H. MP046, PP0346, PP0350, PP0516, PP0525
 Dąbkowska, M. PP1145
 Dąbkowski, K. **PP1145**
 D'Addieco, P. PP0956
 Dahan, M. MP068, MP285, PP0849, PP1100
 Dahel, Y. PP1100
 Dahiya, D.S. PP0855
 Dahiya, P. MP610
 Dahiyat, B. MP568
 Dahl, E.E. OP204
 Dahl, M. **MP448**
 Dahmani, W. PP0353, PP0430, PP0495, PP0619
 Dai, C. **PP0921**, PP0928, **PP1040**
 Dai, N. PP0181, PP0241
 Dai, N. OP120
 Dainese Plichon, R. PP0076
 Daito, K. PP0432
 Dajti, E. MP059, MP364
 Dakó, E. MP251, PP0306
 Dakó, S. MP251, PP0306
 Dalal, A. MP724, PP1066
 d'Alba, L. MP261

Dal Buono, A. MP390, MP571, MP584, PP0431
D´Alessio, S. **PP0371**
Dalgic, B. OP208
Da Lio, C. MP223
Dall Agnol Bouvier, V. PP1021
Dallerba, E. MP177
Dallio, M. **MP073**, MP632
Dall'Oglio, S. PP0035
Dalloyaux, D. MP023
Dalmasso, G. MP402, PP0363
Dal Santo, L. MP223
Damasceno, J. PP0526, PP0826, PP0827
Damasceno e Costa, J. **MP286**, **PP0552**
D'Amato, M. PP0807, PP0808
D'Ambrosio, F. PP0958
D'Ambrosio, R. MP466
D'Amico, F. **OP148**, **MP152**, MP388, **MP511**, PP0431, **PP0517**, PP0626
Dan, W. PP0455
Danelli, P. MP271
Danelli, P.G. MP275
Danese, S. OP042, OP078, **OP079**, OP083, OP104, OP105, OP149, OP156, OP195, MP090, MP152, MP260, MP327, MP388, MP441, MP449, MP511, MP618, **MP672**, MP684, MP688, MP689, MP722, PP0129, PP0130, PP0183, PP0354, PP0355, PP0371, PP0431, PP0471, PP0517, **PP0544**, PP0556, PP0605, PP0620, PP0626, PP1190, PP1235
Dang, T.T. PP0265
D'Angelo, A. **MP440**
Daniel, F. OP220
Danielak, A. **OP055**
Daniels, N. PP0691
Daniluk, J. PP0610
Danis, N. MP421
Danjo, M. MP242
Danne, C. OP027, OP110
Danset, J.-B. MP442
D'Antonio, E. PP0645
D'Antonio, L. PP0320
Dao, T. MP634
Dao, V.L. PP0265
Dao, V.H. **PP0265**
Daperno, M. PP0450
Daphale, A. PP0766, PP1094
D'Aprano, A. MP714
Daravigas, D. MP692
D'Arcangelo, F. **MP406**
D'Arcangelo, G. **MP344**, **PP0392**, **PP0433**, **PP0491**
Dardanov, D. PP0821
Darif, A. PP1234
Darre-Ness, O. MP044
Dart, R. MP628
Das, D. PP1206
Das, S. OP185
Das, T. MP718
Dashti, A. PP0888
Da Silva, A. MP402
Da Silva Lima, F. OP027
da Silva Mendes, S. PP0526
da Silva Mesquita, P.F. **MP169**, **MP520**, PP0620, **PP0661**
Dass, S. PP0700
Dasu, K. MP704
Dasu, N. **MP534**, **MP704**, **PP1052**, **PP1054**
D'Auria, G. MP652, PP0302
Dauvarte, H. MP131
Dave, K. MP258
Dave, S. PP1226
Daveran-Mingot, M.-L. PP0778
Davey, S. PP0680
David, C.J. MP635
David, G. PP0420
David, R. MP377
Dávid, A. PP0584
Dávida, L. MP179
Davids, M. MP573
Davidsen, L. **OP230**, **MP168**
Davies, J. PP0680
Davies, M.J. PP0969
Davila-Piñón, P. **MP064**
Davis, E. MP326
Davra, V. MP568
de Alarcón-Gómez, B. PP1213
Dean, L. MP326
Dean, M. PP0435
Deane, C. **MP319**
De Angelis, C.G. OP199, MP476
De Araujo, A. PP1021
De Barba, C. PP0629, PP0633
Debbabi, H. PP0318
Debels, L. VC02, VC08, **MP019**, PP0730, PP0838, PP0853, PP0895
De Biasio, F. PP0613
de Boer, K.(. PP0554
de Boer, N.H. MP573
de Boer, N.K.H. PP0490
de Boer, N.K. OP188, PP0484
de Boer, S. OP162
De Bona, M. MP259
de Bortoli, N. **MP092**, MP256, MP263, MP491, MP662, MP663, MP727, PP0794
De Bortoli, N. OP075, MP259, PP0095
De Bortoli, N. PP0094
Debourdeau, A. PP1100
Debove, C. MP267, MP274
Debray, D. PP1025
de Bruijn, C.M. PP0815
Decaestecker, J. PP0836
De Carlo, G. MP607
De Carolis, L. MP244, MP583
de Castro, L. OP151
de Castro Parga, M.L. PP0929
De Castro Parga, L. MP064, MP268, **PP0474**
De Castro Parga, M.L. OP043, OP187, MP508
Decker, A. MP661
Decker, T. MP479
De Conte, A. **PP1009**
De Cristofaro, E. **MP068**, MP389, PP0488
De Deo, D. PP0707
Dedeurwaerder, F. PP0836
Dedeurwaerdere, F. MP521
Defraigne-Paigneur, E. PP0530
De Francesco, C. PP0621, PP0629
de Francisco, R. OP043
De Francisco, R. MP503, PP0364
de Francisco García, R.M. OP023, MP508, PP0362, PP0381, PP0382
de Franco, G.M. MP562
Degand, T. MP068, MP440
Degasper, E. MP466
De Giacomo, C. PP0433
De Giorgio, R. PP057, MP659, PP0310, PP0347, PP1235
de Graaf, M. PP0780
De Gregorio, M. **PP0602**
De Grey-Warter, F. MP262
de Groof, J. MP715, MP717, PP0167, PP1198
De Groot, J.W.B. OP226
Degryse, S. PP0375
De Hertogh, G. OP112, OP131, PP0560
Dei Tos, A.P. MP223
Deivamani, N. MP309, PP0997
de Jong, D.M. **MP132**, **MP535**
de Jong, G.M. PP0484
de Jong, M.J. **MP023**, MP030, **PP1041**, **PP1101**
de Jong, S. OP071, MP147
De Jong, D. PP0553
de Jonge, C.S. PP0801
de Jonge, L. **PP0711**
de Jonge, P.J. MP132
de Jonge, P.J.F. PP1197
de Jonge, V. PP0561
de Jonge, W.J. MP209, MP314, MP573, MP629
De Jorge Turrión, M.Á. OP213, MP343
Dejour, V. PP0518
de Keizer, B. MP039
Dekhnich, N. **PP1232**
Dekhnich, N.N. PP0280
Dekker, E. OP162, OP180, OP181, OP223, OP224, OP225, PP0845, PP1198
de Kleer, J.W.M. **MP314**
de Kruif, A. MP387
De la Iglesia-García, D. MP649
De la Iglesia-García, D. MP480
de la Iglesia Gracia, D. PP1124
Del Amor, R. MP383, MP392, PP0479
de la Riva, S. PP0076
Delatolas, V. MP134
Del Chierico, F. MP313, PP0393
Del Corso, G. MP263, MP662, MP663
De Ledinghen, V. MP634
Deleenheer, B. **PP0298**
de Leeuw, M. MP582
De Leo, L. PP0069
Delgado-Guillena, P. MP674
Delgado-Guillena, P.G. **MP031**
Del Gaudio, A. MP006, **MP269**, **PP0654**, **PP0656**
de Lima Cezimbra, L. PP1021
Dell'Anna, G. MP027, MP260, **MP441**, MP536, **MP722**, PP0183, PP1190
Dell'Aquila, P. PP0463, PP0480
della Torre, E. PP1138
Della-Torre, E. MP350
Dell'Era, A. MP275, PP0015
Delliponti, M. MP540
Dellon, E.S. OP207, OP209, MP484, MP486, MP488, MP490, MP493, PP0077
Dell'Oro, C. **MP055**, **PP0788**
Delmas, J. MP402, PP0363
Delmotte, V. PP0530
Delrio, P. PP0670
Delsa, H. PP0885
De Luca, L. MP137, PP0707
De Luca, T. OP064
De Lucia, S.S. **MP539**, **PP1165**
del Valle, R. PP0204
Del Valle, R. MP191, MP359, PP1118
Del Valle Zavala, R. MP109, MP407, MP554
Del Vecchio, G. PP0471
Del Vecchio, L.E. **MP011**, **MP514**
Del Zanna, E. **MP041**
de-Madaria, E. OP171, MP186, MP480
De Magistris, G. PP1194
De Marchi, G. OP016
De Marco, A. PP0166
Demaré, N. PP0804
De Maria Pallares, P. PP1242
De Matteis, C. PP0957
De Matthaeis, N. PP0958
Demedts, I. OP126, PP0861, PP0864
de Meij, T.G. PP0490
de Meij, T.G.J. MP573
de Meijer, V.E. MP127, MP600
de Menezes, R. OP113
Demeter, D. PP1125
Demeter, M. PP0056
Demetter, P. MP009
De Meulder, S. PP0836
De Meyere, L. OP157
Demignot, S. PP0395
Demir, I.E. OP132, PP0388
Demir, M. OP067
de Miranda Lins, M.E. PP1070
Demirbaş, O.B. PP0625
Demirbaş Yücel, S. **PP0072**, **PP0270**
Demirci, S. MP558
Demschik, A. PP0741, PP0902, PP0904
Demurtas, M. MP625, PP0418
Dendane, Y. PP0998
De Nes, L. MP362
Deng, H. MP397
Deng, H. MP161
Deng, K. MP288, MP372, PP0001
Deng, M. PP1007
Deng, Q. MP349
Deng, Z. OP010
Deniz, E. PP0527
Denkovski, M. MP427, MP433, MP547, PP0271, PP0273
Denost, Q. MP070
Denzer, U.W. OP229
De Oliveira, C. MP486, PP0083
de Oliveira Campos, A.C. PP1178
de Oliveira Formiga, R. OP027
De Oliveira Formiga, R. **OP110**
De Palma, G. PP0670
De Palma, G.D. MP716
de Parades, V. PP0830
De Pauw, F. PP0836
de Pinho Morais, L.J. PP0340
De Prado, Á. PP0381
de Pretis, N. MP130, MP237
Deprez, P.H. MP137, MP318
de Reuver, P. MP705
De Reuver, P.R. MP362
de Ridder, L. OP127
de Ridder, R. MP022
Derikx, J.P.M. MP573
Derksen, W.J. MP030
Dermine, S. OP157, **PP0349**
de Roberto, G. MP281
De Rossi, G. PP0129, PP0130
Derrien, M. MP145, PP0691
Derval, E. PP0518
Desai, A. **PP0014**
Desai, J. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211
Desai, M. OP085, MP684
Desai, P. OP217, PP1084
De Salvo, C. MP008
De Santis, S. MP008
Desch, A.N. PP0632, PP0646
Descourvières, C. PP1138
Desideri, F. MP540
De Siena, M. MP311, MP605, PP0247
De Silva, T.A. PP0627
De Simoni, O. MP223
De Sio, M. PP0452
de Sire, R. MP281, **PP0244**
De Sire, R. MP714
Desjarlais, J. MP568
Deslandres, É. OP124, OP142
Desmarest, M. PP0398
Desomer, L. VC02, VC08, MP019, MP521, PP0730, PP0836, PP0838, PP0850, PP0853, PP0876, PP0895
Desprez, C. PP0299, PP0799
Desreumaux, P. MP306
Desseux, C. **MP402**
De Stefano, M.A. PP1009
Determann, M. PP0369
De Terwangne, C. PP0622
Detlie, T.E. OP021, MP341, PP0417
Detoraki, A. MP729, PP0086, PP0087
Deutsch (Mlynarsky), L. PP0218, PP0671
Devanarayana, N.M. PP0102
Devani, M. MP013
Deviere, J. PP1203
de Vlam, K. PP0494
De Vloo, C. PP0836
Devonshire, G. MP376
de Voogd, F. PP0464, PP0500, PP0504, PP0540
De Vos, M. MP009
De Vos, S. MP112, MP564
de Vos Tot Nederveen Cappel, W.H. OP226, MP222

De Vos Tot Nederveen Cappel, W. OP222

de Vries, A.C. OP086, OP188, PP0484, PP0561, PP0567

de Waard, T. MP629

Dewar, D.H. **PP0756**

de Wijkerslooth, T. OP225, PP1101

de Wilde, R.F. MP030

Dewint, P. OP081, OP112, OP126

Dewit, O. MP328

de With, P. MP715, MP717, PP0167, PP1198

De Wulf, D. OP112, OP126, MP521, PP0836

Dewyspelaere, J. PP0836

Deyaert, S. PP0692

De Zen, F. MP143

D Georgopoulos, S. MP433

D'Haens, G. OP031, **MP683**, **PP0549**

D'Haens, G.R. OP083, **OP147**, MP117, MP387, MP614, MP617, MP618, MP622, MP629, PP0464, PP0500, PP0503, PP0504, PP0523, PP0540, PP0550, PP0554, PP0556, **PP0565**, PP0588

D'Haens, G. OP042, OP079, OP131, MP390, **MP671**, MP681, PP0560

D'Haens, G.R. MP209

Dhanda, A. PP0969

Dhaoui, A. PP0727

Dhar, A. OP037, MP325, MP485

Dhar, J. OP098, MP137

Dhar Chowdhury, S. PP0795

Dheivamani, N. MP633, **PP0959**

Dhesi, E. MP616

Dhingra, J.S. **PP0025**, **PP0141**, **PP0820**, **PP1184**

Diaconu, C. MP538

Diaconu, L.S. PP1204

Diamond, M.S. MP452

Dias Blanco, M. PP1220

Dias de Castro, F. PP1216

Diaz, J. MP568

Díaz, A. MP071

Díaz-Argüeso, L. MP537

Díaz Brochero, C. PP1050

Díaz Tartera, H.O. PP0219

Dibbiny, S. PP1043

Di Biase, A. MP059

Dibitetto, S. OP199, MP476

Di Buduo, E. PP0957

Dickens, A. OP004

Dickman, R. PP0796

Di Cola, S. MP295, PP1003

Didden, P. OP224

Didkowska, J. PP0112

Di Domenico, A. PP0492

Diebold, J. PP0074

Diéguez, A. MP383

Diehl, R. MP661

Dienethal, A. MP0624

Dieninyte - Misiune, E. MP131, PP0169

Dietrich, C.F. PP1176

Dietsche, I. OP132

Díez-Martin, A.I. **PP0929**

Díez-Martin, A.I. MP064

Diez-Sanchez, A. OP134

Di Filippo, I. PP0086

Dighe, S. PP0544

Di Girolamo, E. PP0670

Di Girolamo, G. MP729

Di Giuseppe, G. MP455, PP1165

Dignass, A. OP045, **OP082**, OP083, OP102, OP148, MP617, **MP670**

Dijkgraaf, M.G.W. PP0554

Dijkstra, G. OP020, OP188, MP147, MP210, MP337, PP0397, PP0440, PP0448, PP0511

Dijkstra-Muncan, V. MP314

Dilaghi, E. MP203, MP491, **MP728**, PP0007, PP0325, PP1194

Di Leo, A. MP552, PP0017, PP0269, PP0276, PP0301, PP0463, PP0480

Dilillo, D. PP0433

Di Lorenzo, A. PP0463, PP0480

Di Luna, I. PP0139

Dimache, M. PP0749

Dimaculangan, M.R. **PP1019**

Di Maio, F. MP310, MP606

Di Marco, V. MP170

Di Marcotullio, L. OP064

Di Matteo, F. MP137, MP193, MP281, MP607, PP0707

Di Matteo, F.M. MP714, PP0917

Di Mauro, D. MP298

Dimcewski, G.G. MP646

Di Meo, C. OP064

Di Mitri, R. MP137, MP276, MP281, MP540, PP0645, PP0832, PP0856

Dimitriadis, S. MP131, **MP610**

Dimofte, G. PP1204

Dimopoulou, K. PP0330

Din, M.u. PP0219

Di Nardo, F. MP073, MP632

Dinelli, M.E. PP0470

Ding, N.S. PP0602

Ding, S. OP139, MP370, MP459

Ding, S. MP452

Ding, X. OP120

Ding, Y. MP687

Dinic, M. PP0985

Dinis-Ribeiro, M. MP317, MP373, **PP0164**, PP0739

Diotallevi, M. PP1053

Diouf, M. PP0518

Dipace, V. MP256

Di Pangrazio, R. MP241, **PP1170**

Di Paolo, D. MP063

Di Paolo, M.C. PP0508

Di Petrillo, A. MP625, **PP0378**

Di Pierro, P. MP729

di Pietro, M. OP063, OP065, MP374, MP376, MP494, MP712, MP718

Di Pietro, M. OP038

Di Rosa, C. MP607

Di Sabatino, A. OP096, MP013, MP261, MP656, MP0129, PP0130, PP0779, PP1235

Di Salvo, C. PP0782

Di Sario, A. PP0629

Di Sario, G. MP188

Di Serio, C. PP0135

Di Siena, E. MP395, MP398

Distante, M. MP344, PP0392

Distler, F. MP016

Ditunno, I. MP383, PP0269, PP0479, PP0482, PP0499, PP0505

Di Vincenzo, F. **MP340**, **MP624**, **PP0612**, PP0613

Diz-Lois Palomares, M.T. OP213, MP510, MP674

Diz-Lois Palomares, M.T. OP043, OP187

Djinbachian, R. OP124, OP142, PP0877, PP0884

Djuranovic, S. PP0578

Dmitriev, I. PP0399

Do, A. PP0043

Dobashi, A. **MP323**, MP439

Dobek, C. PP0077

Dobrosavljević, A. MP523

Dobru, E.D. PP1204

Dobsch, P. PP1222

Dobszai, D. **MP304**, PP0335

Docsa, T. MP721

Dogliani, C. MP024, MP188

Doherty, G.A. MP213, MP330

Dohos, D. PP0563

Doi, S. OP231

Doki, Y. MP197

Dolina, J. PP0105

Doller, J. MP642

Dolu, S. **MP421**

Dolwani, S. **OP177**, PP0539

Domek-Łopacińska, K. PP0075

Domenech, E. OP043

Domenech Morral, E. OP151, OP187, MP216, MP268, MP334, MP508, PP0035, PP0755

Domingues, Â. **PP0770**

Dominguez Cajal, M. MP433

Dominguez-Carbajales, R. MP064

Dominguez Gómez, R. MP666

Dominguez Muñoz, J.E. **OP016**, OP198, MP537, MP640, **MP643**, **MP647**, **MP649**, PP0024, PP0373, PP0424, PP0615

Dominguez-Novoa, Y. OP016, OP198, MP537, **MP640**, MP649, **PP0024**

Dominguez-Ortega, G. OP208

Dominik, N. **OP186**, MP072, MP077

Domislovic, V. OP024, MP131

Donaldson, K. PP0753

Donapati, V.R. MP541

Donatelli, G. PP0917

Donate Ortega, J. OP171

Donato, M.M. PP0291

Donato, P. OP036, MP079

Dong, B. OP078, OP194

Dong, C. PP0726

Dong, L. MP350

Dong, X. MP012

Donga, N. OP182, PP0967

Döngelli, H. MP421

Donkervoort, S.C. MP705

D'Onofrio, A.M. MP340, PP0612

Dore, J. **PP0690**

Dore, M.P. PP0285

Doré Hansen, M. PP0367, PP0445

Dorn, L. OP183, MP638

Dorofeyev, A. PP0010

Dorosulic, Z. PP0541

Dörr, J. **PP1222**

Dorrington, A. **PP0678**

Dosedelova, V. PP0105

dos Santos Cerutti, E.C. PP1188

Dot, M. MP013, **PP0315**

Dotan, I. OP093, MP273, MP512, **MP614**, MP684, PP0354, PP0355, PP0553

Dotan, O. MP447

Dotsenko, V. OP002, **OP004**, MP248

Dotti, A. PP1188

Dottori, L. OP140, MP203, MP205, PP0007, PP0129, PP0130, PP0325, PP0893

Douds, A. OP032, MP100, MP105, MP108, MP123

Dougui, M.H. MP473, PP0453, PP0456, PP0551, PP0727, PP0772, PP0871, PP1236

Doukas, M. OP188

Doulberis, M. OP009, MP549, MP552, PP0276, **PP0284**

Doumbe-Mandengue, P. PP0185

Dourado, R. MP690, MP698

Dover, D.C. OP219

D'ovidio, V. MP261

Doyle, A. PP0604

Doyle, M. PP0597

Doyle-Scharff, M. **PP0421**

Doynova, M. MP582

Dr, L. PP0506

Dragasevic, S. PP0578

Drago, A. PP0139

Dragomir, I. **PP0976**

Dragoni, G. OP175

Dranga, M. **PP0536**

Drapkina, O. PP0952

Drastich, P. MP708, PP0575

Draxinger, W. MP513

Dray, X. PP0332, PP0386

Dreesen, E. MP217

Drenth, J.P. MP023, MP705, PP0332, PP1138

Drewe, J. MP312

Drewes, A.M. OP154, OP168, OP230, MP168, MP186, PP0046, PP0801, PP0918, PP0919

Drews, J. MP280

Dreymann, J. MP447

Dridi, K. PP1236

Drobne, D. MP335

Drossman, D. MP164, PP1186

Drossman, D.A. PP1230

Drozdo, V. PP0800

Drug, V. MP104

Drug, V.L. MP099, PP1235

D'Souza, B. PP0602

Du, Y. PP0124

Du, Y. MP397

Duan, L. OP118, PP0091

Duan, M. MP190

Duarte, M.A. PP0033

Dubenco, E. MP333

Dubinsky, M. MP614, **PP0458**

Dubinsky, M.C. **OP192**, OP212, MP003, MP150, MP333, MP449, **MP613**, MP617, MP686, PP0471, PP0550, PP0565, PP0594

Dubois, A. MP070

Dubroff, J. MP136

Dubrule, S. MP167

Dubtsova, E. PP1179

Dubuquoy, C. MP306

Dubussy, C. OP019

Ducloux, D. PP0398

Dudley-Brown, S. PP0521

Due Lorentsen, R. PP0607

Dueñas, N. MP522

Dueñas Sadornil, C. OP191

Duffey, J. PP0099

Düger, T. PP1205

Dugic, A. MP131

Duhoky, R. MP070

Duijvestein, M. OP086, OP188, PP0484, PP0554, PP0567

Duits, L. OP113, MP367, MP717, PP0167

Dukes, E. MP430

Duku, M. MP553, PP0098, PP0104, PP0106, PP0227

Dulai, P.S. OP046, MP385, MP619

Dulai, P.S. OP195, MP623, MP688, MP689

Dulcine, M. OP207, MP342, MP493

Dulskas, A. **PP0821**

Dumea, E. MP538

Dumitrascu, D.L. PP0337

Dumitrascu, D.L. OP117, OP121, MP051, MP164, PP0038, PP0805, PP1235

Dumoulin, A. MP145

Duncanson, K. **MP609**, PP0043

Dunn, J.M. OP076, MP091, MP727

Dupont, M. MP414

Dupont-Lucas, C. MP345, PP0410

DuPrie, M. OP193

Duque, J.M. MP510

Durak, M.b. **PP1075**

Durak, M.B. PP0527, PP1073

Durand, F. MP634

Durand, F. MP618, PP0458, PP0459, PP0460, PP0559

Duricova, D. MP149, MP339, PP0575

Durilova, M. PP0580

Durko, L. PP1161

Dürr, A. OP229

Durrani, S. MP492

Duru, G. PP0608

Dusek, L. MP587

Dušek, L. MP517

Dusetti, I. OP129

Dussias, N. **PP0640**

Dussias, N.K. PP0668

Dutt, S. OP208

Dutta, A.K. PP0027, PP0700, PP0795

Dutta, U. PP0394, PP0603

Duun-Henriksen, A.K. MP527

Duval, A. PP0363
 DuVall, G. OP042
 Duvvur, N.R. OP051
 Dvir, R. MP592
 Dyall, L. PP0642
 Dyrli, O.T. OP003
 Dzhemiliev, A. PP0866
 Dzhogova, M. **PP0338**
 Đuriček, M. MP053, MP131, MP435,
 PP0056, PP0097

E
 East, J.E. PP0165, PP0539, PP0768
 Eastman, W.J. MP383, PP0479
 Ebbo, M. MP350
 Ebela, I. PP0279
 Ebert, A. OP215
 Ebigbo, A. OP206, MP377, MP380
 Ebisawa, Y. **OP145**, PP0171
 Ebrahimi, F. OP214, MP047, **MP174**,
 MP214, MP505, MP594
 Eccleston, J. OP104
 Echarri, A. MP510
 Eckenberger, J. PP0479
 Eckersley, K. OP077
 Eckert, K. PP0906
 Eder, P. OP169, PP0610
 Edergren, A. PP1124
 Edmonds, M. PP0706
 Eelbode, T. OP126, PP0861, PP0864
 Efe, C. PP1083
 Efimov, B. PP0513
 Efken, P. MP329, MP682
 Efsthathiou, S. PP0466, PP0728
 Efthymiou, M. PP1099
 Eftimie Spitz, R. **MP124**
 Egami, H. PP0216
 Egan, C. PP0214
 Egas Izquierdo, M. PP0204
 Egas-Izquierdo, M. MP109, MP191,
 MP359, MP407, MP554, PP1118
 Eguchi, H. MP197
 Eguchi, Y. MP425
 Ehehalt, R. MP329
 Eid, A. MP121
 Eida, H. PP0133
 Eiras, M. PP0739
 Eisele, L. MP153
 Eiseler, T. MP479
 Ekbohm, A. OP164
 Ekizce, M. **OP062**, OP200, **MP088**
 Ekmen, N. MP416
 El Amrani, K. **PP0885**
 Elangovan, H. **PP1029**
 El Asmar, N. OP220
 El-Azab, G. PP0287
 El Bacha, H. PP0026, PP0028,
 PP0034, PP0201, PP0400, PP0401,
 PP0657, PP0658, PP0681, PP0831,
 PP0926, PP0927, PP0971, PP1032,
 PP1049
 Elbasiony, M. PP0201
 Elbasiony, M. MP121, **PP1055**
 El-Domiaty, N. **PP0185**
 Elefsiniotis, I. PP1015
 Eleonora, A. **MP469**, PP1020
 Elford, A. MP326, PP0579, **PP0648**,
PP0674
 ElGehiny, A. MP471
 Elguzouli, K. MP471
 El-Habashi, A. PP1171
 ElHaddad, I.M. PP1112
 El Helou, S. **PP1192**
 El Hiouy, H. **PP0971**, **PP1049**
 El-Hussuna, A. PP0821
 Elias, A. MP184
 Elias, S.G. OP115
 Elidrissi, L. **PP0961**, **PP1234**
 El Idrissi Lamghari, A. PP0885
 Elisei, W. PP0442
 Eliwa, A. MP121
 Elizalde, M. MP162

Elkasaby, M.H. **PP1112**
 Elkemary, E. PP1024
 El Khoury, B. MP442
 Elkoumi, O. PP1112
 Ellaithy, A. **MP034**, **MP472**, PP0722,
 PP1159, PP1160
 Ellaithy, I. MP034, MP472
 Ellakany, A. PP0287
 Ellegaard, A.-M.G. PP0717
 Ellenrieder, V. OP229, PP0230
 Elleuch, N. MP215, PP0353, MP0430,
 PP0495, PP0619
 Elli, L. MP041, MP540, MP653,
 PP0327, PP1200
 Ellina, M. MP254
 Elloumi Ep Kharrat, H. OP0760
 Ellrichmann, I.D. VC01
 Ellrichmann, M. **VC01**, MP132,
 MP195, MP324, MP513, MP720
 Ellul, P. OP169, MP149, PP0316,
 PP0317, PP1219
 Elmahdi, R. **OP215**, PP0416
 Elmdaah, A.K.A. **PP1011**
 El Mehdi El Yamani, M. PP0877
 El Mezeni, J. PP0985
 Elmore, U. MP722, PP0135
 Elmquaddem, O. MP405, MP418,
 PP0261, PP0677, PP0972, PP0977,
 PP0998, PP1156, PP1167
 Elnegouly, M. PP0206, PP0852
 Elomaa, K. **PP0415**
 Elortza, F. OP023, PP0364, PP0381,
 PP0382
 Elorza, A. OP043, OP187
 Elosua González, A. PP0493
 El Oumami, O. PP0377
 Elphick, M. **MP322**
 El-Raey, F. MP121
 Elrhaoussi, F.Z. PP1234
 Elrhaoussi, F.Z. PP0190, PP0213,
 PP0515, PP0961
 Elsabaawy, M. PP0287
 El-Sakka, A.A. MP034
 El-Samahy, M. PP0032, PP0925
 Elsayed, A. **PP0722**
 Elsayed, H. PP1112
 Elsayed, K. MP098
 Elshaarawy, O. MP121, MP131
 Elshafei, M. **MP097**
 El-Shawaf, M. MP225
 ElSheikh, W. OP220
 Elsiddig, M.M. PP0214
 Elsing, L. OP229
 Elvas, L. PP0195, PP0196, PP0197
 Elvo, B. PP0139
 Elwenspoek, M. PP0305
 Emanuel, G. MP682
 Emerenziani, S. MP313
 Eminler, A.T. PP0072, PP0270
 Emma, E.P. **PP0672**
 Emmanuelidou, G. MP254
 Emmanuel, A. OP143, MP221,
 MP277, MP282, PP0854, PP0879,
 PP0881, PP0886, PP0889
 Emna, S. PP0353, **PP0987**
 Emond, P. OP110
 Enache, I. **PP0311**, PP0312
 Engebretsen, K.A. MP236
 Engels, M.M. PP1041
 Eng, M.A. PP1129, PP1133, PP1157
 Engjom, T. MP646
 English, S. PP1011
 Ennaifer, R. PP0456, PP0964, PP1245
 Enns, R. PP0888
 Enticott, J. MP358
 Eperjesi, O. OP016, **PP1133**
 Eqbal, A. OP143, **MP221**, **MP277**,
 MP282, PP0854, PP0879, PP0881,
 PP0886, **PP0889**
 Era, B. PP0378
 Erchinger, F.G. MP646
 Erdelyi, Z. PP0420
 Erdélyi, M. PP1135

Erdmann, J.I. MP030, MP702
 Erdozain Sosa, J.C. OP184
 Ergul, M. PP0527
 Erhardt, F. OP182, PP0967
 Eriksson, C. OP021
 Eriksson, J. OP164
 Erikstrup, C. OP154
 Ermina, S. MP080
 Ermolova, A. PP0388
 Ernesto Coelho, G. PP1070
 Ernesto Coelho, J.F. PP1070, PP1136,
 PP1175, PP1178
 Ernesto Coelho, M. PP1070
 Ernst, J. **MP568**
 Ernst, M. **MP413**
 Eross, B. MP099, MP194, MP297,
 MP379, PP0021, PP0563, PP1124,
 PP1127, PP1128
 Erőss, B. OP012, MP104, MP298,
 MP612, MP648, PP1056, PP1130,
 PP1133, PP1166
 Erőss, B.M. PP1125, PP1126
 Errabih, I. PP0026, PP0028, PP0034,
 PP0400, PP0401, PP0657, PP0658,
 PP0681, PP0831, PP0926, PP0927,
 PP0971, PP1032, PP1049
 Esaki, M. PP0419
 Escher, J.C. OP208
 Escobar, R. OP044, OP131, PP0560
 Escudero-Hernández, C. **PP0391**
 Escuer Turu, J. MP138
 Eshuis, W.J. PP0162
 Eskandar, K. MP678
 Espadaler Mazo, J. PP0813
 España, D. PP0049
 Espina, S. PP0076
 Espinet, M.L. PP0321
 Espinheira, M.d.C. OP208
 Esposito, A. MP390
 Esposito, D. MP441, MP722, PP1190
 Esposito, G. MP728, PP0893, PP1170,
 PP1194
 Esposito, K. PP0452
 Esquerda, G. PP0255
 Esquerre, N. PP0374
 Essadni, Y. **PP1047**
 Essers, B. PP0814
 Estcourt, L. OP032, MP105, MP123
 Esteller, M. OP026
 Esteve, M. PP0557
 Esteve Comas, M. OP191, MP508,
 PP0362, PP0382
 Estevinho, M.M. MP169, MP520,
 PP0573, **PP0620**, PP0661
 Estudillo, L. OP132
 Ettorre, G.M. MP539
 Ettrich, T. MP479
 Ettrich, T.J. OP062, PP1152
 Euatereasarun, W. PP0953
 Eussen, M.M. MP362
 Eutamene, H. **PP0778**
 Evangelista Carrillo, L.A. PP0980
 Evenepoel, M. **PP0691**
 Everett, S. MP296, PP1067
 Everhov, Å.H. OP216
 Exacoustos, C. PP0426
 Exposito, L. PP0422
 Eyosawat, P. PP1108
 Ezaki, T. MP693
 Ezratty, N. PP0804
 Ezz-Eldin, M. PP0287
 Ébert, A. MP299, PP1135

F
 Fabbri, A. PP0856
 Fabbri, C. OP171, MP011, MP084,
 MP137, MP193, MP364, MP540
 Fabbri, S. MP084, MP364
 Faber, K.N. OP071, PP0368, PP0511
 Faber, M. MP568
 Fabian, A. MP627, PP0584, PP0675,
 PP0710, PP0713, PP0731, **PP0732**,
PP0746
 Fabian, O. MP708
 Fábíán, A. PP0614
 Fabrellas, N. MP071
 Facanali, M. VC07
 Facchetti, F. MP466
 Facchin, S. PP0013
 Facchini, C. OP075, PP0094, PP0095
 Facci, L. MP223
 Facciorusso, A. MP136, MP137,
 MP193, MP276, MP542, PP0244,
 PP0707, PP0845, PP0855, PP0856
 Facciotti, F. OP129, **MP010**
 Fadieienko, G. MP427, MP547,
 PP0273
 Faes, M. OP105, PP0605
 Faggiani, I. MP152
 Fahr, L. MP644
 Fairlie, T. PP0043
 Fais, A. PP0378
 Faiz, O. PP0680
 Falasca, M. MP115, MP177
 Falcão, S. MP005
 Falco, M. PP0087
 Falcone, A. MP607
 Falcone, M.R. PP1071, PP1243
 Falconi, M. OP136, MP024, MP027,
 MP188, MP244, MP536, MP583
 Faleschini, G. MP310, MP606
 Fallentin, E. OP174
 Falt, P. OP229
 Faluhelyi, N. MP048, MP194, PP1128
 Familiari, P. MP539
 Fan, H. MP401
 Fan, X. MP125, MP349, MP353,
 PP0943
 Fan, X. PP0865
 Fan, Z. PP0921
 Fang, X. OP120, MP161
 Fang, X. MP164
 Fang, Y. PP0194, PP0224
 Fanizza, J. MP090, MP722
 Fantasia, S. MP476
 Fanti, L. MP722, PP1190
 Fantini, M.C. OP106, OP150, OP169,
MP625, PP0378, PP0418, PP0476,
 PP0629
 Fantognon, G. MP634
 Faouzia, F. **PP0829**
 Farag, A. PP1055
 Farahmand, S. OP025
 Farcas, R. **PP0038**
 Farimah, F. PP1100
 Fariña Sarasqueta, A. OP224, OP225
 Farinati, F. PP0285
 Farkas, B. MP158, MP627, PP0584,
PP0614, PP0675, PP0710, PP0746
 Farkas, K. MP158, MP446, MP627,
 PP0520, PP0584, PP0614, PP0675,
 PP0710, PP0713, PP0731, PP0732,
 PP0746
 Farkas, N. MP251, PP1124
 Färkkilä, M.A. MP593, MP709
 Faro, T. MP453
 Farouk, M. PP0201
 Farrag, K. PP0624
 Farré, R. MP051, MP056, PP0039
 Farrell, R.J. PP0214, PP0737
 FarrellBinns, G. PP0031
 Faserl, K. OP018
 Fasoulas, K. MP676, PP0568
 Fasulo, E. MP090, MP260, MP441,
 MP722, PP0183, PP1190
 Fathallah, N. PP0830

Fattahi, M.R. PP0947
 Faty, L. **MP405**
 Faustino, F. PP0193
 Favale, A. MP625, PP0378, **PP0418**
 Favia, A.D. OP212, PP0594
 Favia, N. **PP0017**
 Fawzi, M. MP531
 Fayad, L. **PP0521**
 Faye, A. PP1226
 Fazal, Y. PP0210
 Fdez-Riverola, F. MP064
 Feagan, B. OP079, OP131
 Feagan, B.G. **OP078**, OP102, **OP105**, OP194, MP484, MP563, MP670, PP0447, PP0556, PP0560, PP0605
 Fear, E. MP621
 Fedai, A.B. PP0527
 Fedatto Beraldo, R. PP0343
 Federica, D.V. MP269, PP0637, PP0654, PP0656
 Federico, A. MP073, MP632
 Fedrizzi, L. PP0414
 Feher, K.E. **MP179**
 Feher, T. **PP1129**
 Fehringer, M. OP111
 Feijó, D. **OP036**, **MP079**, **MP189**, MP555, MP557, **PP0236**, **PP0365**, PP0819
 Fekih, M. PP0543, PP0590
 Feldbacher, N. PP0339
 Felice, F. **MP285**
 Felici, C. MP188
 Felipez Varela, N. MP031
 Felsenreich, D.M. OP186
 Feng, R. OP007
 Feng, S. PP0928, PP1040
 Feng, Y. MP029
 Fennell, E. PP0482
 Fennessy, A. MP131, **PP0597**
 Feo Ortega, S. MP664, PP0076
 Feo-Ortega, S. OP208
 Ferber-Reyes, F. MP109, MP407
 Ferdinande, L. VC08
 Ferdinandy, P. MP303
 Ferdinándy, P. PP1133
 Ferdosi, H. PP0053, PP0066
 Ferencova, N. MP435, PP0065
 Fərid Vidadi Oğlu, Q. MP547, PP0273
 Ferko, N. PP0667, PP1185
 Ferlitsch, A. PP0904
 Ferlitsch, M. PP0741, PP0902, PP0904
 Fernanda Soares Ruppert Reis, G. PP0263
 Fernandes, D. PP0526
 Fernandes, D.A. MP346, **MP530**
 Fernandes, J. PP0830
 Fernandes, M. **PP1103**
 Fernandes, M.V. MP331, **MP464**, MP679, PP0649, PP0650, **PP0907**, **PP0986**, **PP0988**, PP1001, PP1002, **PP1023**, **PP1027**, **PP1105**, **PP1106**
 Fernandes, N. PP0642
 Fernandes, S.R. MP620, PP0592, PP0628
 Fernandes, V. PP0059
 Fernandez, R. PP0016, PP0018
 Fernández, H. MP510
 Fernández, N. MP064
 Fernández Aceñero, M.J. PP0079
 Fernandez-Bermejo, M. OP009, MP428
 Fernández Cabrera, I. OP171
 Fernández-Clotet, A. OP026, OP213, MP343, MP674
 Fernández-Esparrach, M.G. MP031
 Fernandez-Fernandez, S. PP0076
 Fernandez García, R. MP291
 Fernandez-García, R. MP103, MP107
 Fernández-Pacheco, J. MP664
 Fernández-Pato, A. OP108
 Fernández Poceiro, R. PP0929
 Fernandez Rivero, J.A. PP0908
 Fernández Salazar, L. OP023, PP0364
 Fernández-Salazar, L. OP009, MP428
 Fernández-Salazar, L. MP503, MP510, PP0362, PP0381, PP0382, PP0557
 Fernández-Salgado, E. MP510
 Fernández-Urién Sainz, I. MP132
 Fernandez Y Viesca, M. MP298
 Fernando-Mehta, G. MP665
 Fericola, G.C. MP562
 Ferracane, C. OP106, PP0645
 Ferrajoli, G.F. PP0612
 Ferrandino, G. MP287, MP608
 Ferrante, M. OP083, MP145, MP445, MP622, PP0494, PP0550, PP0565
 Ferranti, P. MP652, PP0302
 Ferrara, F. MP259
 Ferrara, P. MP313
 Ferrarese, A. MP406
 Ferrarese, D. MP340
 Ferrari, D. PP0095
 Ferravante, F. MP313
 Ferreira, A.O. PP0751
 Ferreira, A.I. MP171, MP637, PP0477, PP0486, PP0750, PP0757, PP0761, PP0789, PP0883, PP1216
 Ferreira, A.T. MP386, **MP414**
 Ferreira, C.N. PP0193, PP1026
 Ferreira, D.G. MP386
 Ferreira, F. PP1241
 Ferreira, J. OP099
 Ferreira, J. OP205, MP060, PP0329, PP0830, PP1201
 Ferreira, J.M. MP414
 Ferreira, M. MP189, MP555, PP0236, PP0365
 Ferreira, M. PP0365
 Ferreira Pereira, L. PP0340
 Ferreiro-Iglesias, R. OP043, MP508, MP510, PP0373, PP0424, PP0615
 Ferrer, J.A. OP043
 Ferretti, V. MP540
 Ferruccio, C. MP466
 Ferry, M. PP0222
 Festa, S. OP106, OP169, PP0621, PP0629
 Festen, E.A.M. OP020, PP0379
 Festen, E.A.M. MP210
 Festen, E.A.M. OP071, MP127, PP0368
 Festen, E.A. MP147, MP600, PP0448
 Festen, E.A.M. PP0440
 Festen, S. MP030
 Fettiplace, J. OP185
 Fetz, A. PP0147
 Fiacca, M. MP137, PP0707
 Fiadeiro, R. OP037, MP325
 Fianchi, F. MP455, PP0082, PP0954
 Ficari, F. PP0672
 Fichera, A. PP0670
 Fichna, J. MP400
 Fichtl, A. OP0911, PP1239
 Fidaleo, M. PP0393
 Fidalgo, C. MP690, MP698
 Fidalgo, C.A. PP0422
 Figa, M. PP1172
 Figueira, M. OP213
 Figueiredo, P. OP036, MP499, PP0365, PP1072
 Figueroa-Palafox, M. **PP0908**
 Fikree, A. PP0037
 Filice, M.E. MP662
 Filip, R. MP339
 Filipovic, M. MP719
 Filipovic, M.R. MP199
 Filippidis, A. PP0743, PP0991
 Filtenborg Brandt, C. OP190
 Finderle, S. PP1014
 Fine, Z. MP621
 Finta, A. **MP020**, MP255
 Fiorani, M. OP096, MP577
 Fioravanti, G. PP0427
 Fiore, M. PP0392
 Fiori, E. PP0023
 Fiorillo, M. **PP0426**, PP0427, PP0621
 Fiorini, G. MP427, MP549, MP552, PP0276, PP0285
 Fiorino, G. MP151, MP152, MP339, MP388, MP511, PP0422, PP0517
 Fischer, A. PP0249
 Fischer, I. OP130
 Fischer, M. OP128, MP618, PP0562
 Fischer, S. **PP0529**
 Fischman, M. **MP184**, **MP273**, PP0553
 Fischmann, D. PP0529
 Fisher, M. PP0057, PP0058
 Fishman, S. OP084, PP0232, PP0233
 Fitzgerald, R. MP374, MP376, MP712
 Fitzgerald, R.C. OP063
 FitzGerald, R. PP0289
 Fitzpatrick, C. MP287
 Fitzpatrick, C. PP0484
 Flad, E. **OP048**, MP312
 Flaminio, M. PP0087
 Flanagan, E. MP074
 Flanagan, E. MP339
 Fleming, C. MP070
 Fležar, M. OP011
 Flitcroft, L. PP0825
 Florêncio de Mesquita, C. PP1103
 Flores, V. MP428, MP549
 Flores Rendon, A.R. MP429, MP430
 Florholmen, J. **PP0475**
 Floria, D.-E. **MP099**, MP104, MP612, **PP0563**
 Fluxa, D. PP1057, PP1058
 Flynn, E.J. OP212, PP0594
 Focht, G. OP172
 Fockens, K. MP715, PP0167, PP1198
 Fockens, P. OP181, OP225, MP022, MP030, PP1089
 Fogarasi, B. PP0563
 Foglia, B. PP0942
 Földesi, I. PP0520
 Földvári-Nagy, L. MP099
 F. O'Mahony, J. PP0128
 Fominykh, Y. PP0292
 Fong, S. MP326
 Fons, A.B. **PP0641**
 Fonseca, D. MP287, MP608
 Fonseca, J. PP0033
 Fonseca, R. PP0747
 Fonte, S. PP1003
 Fonticelli, M. PP0452
 Foong, D. PP0059
 Forastiere, D. PP0463, PP0480
 Ford, A.C. MP166, PP0481
 Ford, S.M. MP614
 Formichetti, J. MP310, MP606
 Formisano, E. PP0652
 Fornai, M. PP0782
 Forsberg, A. **OP164**
 Forti, E. MP137, MP540
 Fortunato, C. MP137, MP244
 Fortunato, C. MP024, MP583
 Foruny, J.R. OP191
 Fossnacht, K.G. MP199
 Foss, N.B. MP300
 Fossmark, R. PP0115, **PP0119**
 Foster, C.J. MP534, MP704, PP1052, PP1054
 Foteinogiannopoulou, K. MP676, PP0568
 Fotoulaki, M. OP208
 Fouad, N. MP375, PP1214, PP1215, PP1238
 Fouquier, J. OP060
 Fourie, A. OP193
 Fournier, S. PP0877
 Fournier-Poizat, C. OP060
 Fousekis, F. PP0330
 Fox, A. MP139
 Fox, M. OP076, PP0037, PP0810
 Fiquih Chetouani, M. PP0451
 Fracas, E. PP0414, PP1020
 Fradejas, P. OP043
 Fragaki, M. OP169, PP1177
 Frahm, C. MP280
 Fraile, M. PP0755
 Frances, R. PP0945
 Franceschi, F. PP0285
 Frances Guarinos, R. PP0990
 Franchellucci, G. PP0166, PP0244, PP0707
 Franchimont, D. OP019, MP009, MP328, PP0622
 Franchin, M. PP0426
 Franchitti, M. MP203
 Franchitto, M. OP064
 Francis, I.E. **PP0293**
 Francisco, C.P. PP0161
 Francisco, M. **MP408**, PP0827
 Franco, A.R. PP0934, **PP1237**
 Franco, J. PP0526
 Franculescu-Berteau, A. **PP0300**
 Frank, R. MP448
 Franke, A. MP572
 Franke, A. PP0074
 Frankenbach, P. OP005
 Franklin, J. PP0638
 Franz, R. OP155
 Franzato, B. MP223
 Fraquelli, M. MP389, PP0488
 Frasca, P. MP577
 Frasson, L. PP0633
 Frasson, M. MP151
 Frattaroli, F. **PP0023**
 Frattaroli, S. PP0023
 Fratto, M.C. MP090
 Frazzoni, L. MP011, PP1209
 Frederiks, C.N. OP116, **MP039**
 Freeman, T. OP193
 Freeman, T.C. MP563
 Freeney, T. PP0632, PP0646
 Frei, C. PP1245
 Frei, N. MP367
 Frei, N. OP113
 Freidenberg, A. OP093
 Freiha, P. **PP0483**
 Freire, M. MP393, PP0556
 Freitas, T. MP169, MP520, PP0661
 Freitz, B. MP592
 Fremberg Ilvemark, J. MP391, PP0535
 Frias-Gomes, C. MP005, PP0468, PP0532
 Frick, A. **MP465**, MP691
 Friebe, M. **MP070**, **MP219**, **PP0924**, **PP0940**
 Friedenberga, A. MP273
 Friedman, J. MP118, **MP450**, PP0635, PP0643
 Friedrich, J.E. OP132
 Friedrich, N. PP0230
 Friedrich, S. PP0559
 Fries, W. PP0621, PP0629, PP0645
 Friess, H. OP132
 Frigerio, S. **OP031**
 Frigo, F. MP027, MP188, MP441, MP536
 Frigstad, S.O. MP341, PP0417
 Frim, L. MP379, PP0021
 Frisancho Morales, L.E. MP673
 Friss, C. MP512
 Fritz, L. OP186, MP173
 Fritzsche, J.A. **MP030**, MP702, **PP1089**
 Froehner Junior, I. **PP0790**, **PP0932**
 Froilan Torres, C. PP1242
 Frøkjær, J.B. OP168, PP0918, PP0919, PP1138
 Frost, F. OP229
 Frulloni, L. OP169, MP130, MP237
 Fruman, D. MP483
 Frustaci, M.E. MP671
 Frutos, C. PP0436
 Fu, J. OP001
 Fu, P. MP012

- Fu, W. OP139, MP370
- Fuccio, L. MP011, MP441, MP722, PP0856
- Fuchida, T. PP0966
- Fuchs, E. PP0741, **PP0904**
- Fuchs, K.H. PP0178
- Fudim, E. MP592
- Fugazza, A. MP137, MP193, MP540, MP584, PP0166
- Fuglsang, K. OP190
- Fujie, M. PP0735
- Fujigaki, S. MP693
- Fujii, T. OP083, MP620
- Fujimori, S. MP040
- Fujimori, S. MP038
- Fujimoto, A. OP091
- Fujimoto, H. PP1196
- Fujimoto, T. PP1151
- Fujioka, S. PP0419
- Fujisaki, J. PP0111
- Fujisawa, T. OP101, OP231, MP302, MP423
- Fujishiro, M. PP0933, PP1034
- Fujita, K. MP693
- Fujiwara, H. PP1034
- Fujiwara, H. MP460
- Fujiwara, S. PP0331
- Fujiya, K. PP0134
- Fukai, Y. PP0767
- Fukaura, K. PP0114
- Fukuchi, T. **PP0868**
- Fukuda, K. PP1038
- Fukuda, M. MP323
- Fukudo, S. MP164
- Fukunaga, T. OP014
- Fukuya, H. **PP0172**
- Fullard, M. OP037, MP325
- Fülöp, P. PP0306
- Fumery, M. OP189, MP149, MP156, MP185, MP217, MP345, MP630, **PP0374**, PP0395, **PP0410**, PP0518, PP0608
- Furfaro, F. MP152, MP388, MP389, MP511, PP0431, PP0488, PP0517, PP0626
- Fürst, E.R. MP297
- Furuhashi, H. PP0933
- Furukawa, K.-i. PP0134
- Furukawa, S. PP0334
- Furumatsu, K. MP693
- Furusyo, N. **PP0966**
- Furuta, K. PP0133
- Furuta, Y. PP0419
- Furuya, K. PP0767
- Furuya, M. PP0462, PP0702
- Fusaroli, P. MP137, MP193, PP0917, PP1235
- Fusco, W. **OP096**, MP577
- Fushimi, H. PP0913
- Fushimi, S. **PP0159**
- Fuss, A. **PP0634**
- Füssel, K. MP707
- Füstös, D.D. PP0306
- Futakuchi, T. MP323
- Futami, K. PP0432
- Fytili, P. PP0073, PP0089, PP0245
- Gabbiadini, R. MP132, MP390, MP571, PP0431
- Gabbrielli, A. MP237
- Gabriel, A. MP141
- Gabriel, C. **PP0849**
- Gabrielli, V. MP287
- Gabriëls, R.Y. PP0107
- Gabrielyan, A. MP580
- Gacesa, R. OP001, OP108, MP127, **MP575**, MP600, PP0368, PP0379, PP0490
- Gach, T. OP125
- Gadaleta, R. PP0957
- Gadallah, A. PP1112
- Gadour, E. **PP0201**
- Gadsby, I. PP0616
- Gafton, E. PP1204
- Gagliostro, G. PP0433
- Gago, T. PP0774, PP0827
- Gagyi, E.B. PP1166
- Gagyi, E.-B. MP379, **PP1127**
- Gahlon, G. PP0548
- Gaia, S. PP0942
- Gaiani, F. OP199
- Gaidhane, M. PP0766
- Gajdán, L. OP012, MP648
- Gajdos, T. PP1135
- Gal, O. PP0723, PP0882, PP1095
- Galang, R.L. PP0030
- Galardo, G. PP0818
- Galasso, D. MP137, PP1092, PP1173
- Galateanu, B. MP538
- Galavazi, M.C. PP0182
- Galbusera, A. PP0621
- Galeano, G. PP0269
- Galego-Fernández, M. MP537
- Galla, Z. MP299
- Gallardo-Luna, M.S. PP1116
- Galle, P.R. MP233
- Galletti, S. PP0958
- Galli, A. OP175
- Galli, R. PP0015
- Gallo, C. PP0129, PP0130
- Gallo, G. MP151, PP0821
- Galon, M. MP485
- Galorport, C. PP0888, PP0936, PP0937
- Galsgaard, E.D. OP058
- Galtieri, P.A. MP714
- Galvao Neto, M. PP0232
- Gálvez Castillo, C. PP0008
- Gambato, M. MP406
- Gambini, G. MP540
- Gamelas, V. PP0255
- Gamito, E. PP0485
- Gammell, Y. PP0597
- Gandelman, O. MP287, MP608
- Gandhi, V. MP042, PP0308
- Gandolfi, F. MP571
- Ganesh, G. MP387
- Ganeshan, M. PP0539
- Ganuza, M. OP171
- Gao, F. MP247
- Gao, J. OP118
- Gao, L. MP486
- Gao, X. MP687
- Gao, X. MP401
- Garasi, C. OP080
- Garattini, S. PP0139
- Garborg, K. MP044
- García, C. **PP1212**
- García, M.J. OP023, MP503, PP0364, PP0381
- García-Alonso, F.J. OP023, MP334
- García Ballester, T. PP0008
- García-Bosch, O. MP508
- García-Brenes, M. PP0403
- García-Brenes, M.A. PP0684
- García Carrizo, F. OP030
- García de la Filia, I. MP674
- García Donday, M. PP213
- García Eliz, M. MP128
- García García de Paredes, A. OP171
- García-Gil, L.J. MP522
- García Gutierrez, M.S. PP0945
- García-Lopez, S. OP043
- García-López, S. OP151, OP196, MP268
- García Marmolejo, J.P. **PP1050**
- García Montes, C. PP0263
- García Morales, N. OP191, PP0076
- García-Morales, N. MP064, PP0557
- García-Planella, E. MP334
- García Ramirez, L. PP0469
- Garcias, M. MP394
- García Sague, B. MP673
- García- Salido, A. MP343
- García-Samaniego Rey, J. OP184
- García Sánchez, A. OP184
- García Sepulcre, M.F. OP043, OP187
- García Sepulcre, M. MP674
- García-Sepulcre, M.F. OP151, MP268
- García-Sumalla, A. MP138
- García Teixeira, I. PP1070
- Garcillán, B. MP216
- Garcovich, M. PP0958
- Garg, K. PP1081
- Gargallo-Puyuelo, C.J. OP151, MP268
- Gargallo-Puyuelo, C.J. OP043, OP187
- Gargaritano, J.L. **PP0351**
- Gargouri, D. PP0402, PP1033
- Garmaeva, S. OP108
- Garre, A. MP428, MP433, MP510, MP547, MP549, PP0271, PP0273, PP0557
- Garrido, A. PP0404
- Garrido-Trigo, A. OP026
- Garrison, A. MP622, PP0588, PP0589
- Gasbarrini, A. OP009, OP034, OP096, MP006, MP008, MP028, MP261, MP269, MP340, MP427, MP433, MP455, MP547, MP549, MP552, MP624, MP645, PP0082, PP0271, PP0273, PP0276, PP0285, PP0393, PP0612, PP0613, PP0637, PP0656, PP0954, PP0958, PP0963, PP1165
- Gasché, C. MP465
- Gatt, K. MP149
- Gatta, L. PP0285
- Gatti, M. OP175
- Gauci, D. PP0317
- Gauci, J. MP069, MP284, MP317, MP371, MP381, **PP0179**, **PP0184**, PP0769, PP0850, **PP0876**, PP0890, **PP0891**, **PP0892**, PP1199
- Gaudenzio, N. PP0435
- Gaudio, E. OP064
- Gaujoux, S. PP1168
- Gaulton, K.J. MP481
- Gaup, S.B. PP0475
- Gautam, R. PP0499
- Gautam, S. MP710
- Gauthier, A. MP153
- Gauthier, L. PP0407
- Gavin, P.G. PP0075
- Gavrilescu, O. PP0536
- Gay, C. PP0676
- Gayathri Chirumamilla, L. PP1191
- Gayoso Gayo, R. OP184
- Gdoura, H. PP0660
- Geccherle, A. PP0570, PP0664, PP0673
- Gecioniene, A. OP152
- Gecse, K.B. MP339, PP0464, PP0504, PP0540
- Gecse, K.B. MP117, MP151, **MP342**, MP387, MP628, PP0484, PP0500, PP0523, PP0553
- Gedgaudas, R. OP107, **MP289**, **MP468**
- Gedgaudas*, R. PP0012
- Geer, T. MP479
- Geeratragool, T. **PP0786**
- Geerlings, C.V. OP181
- Geertsema, S. **PP0511**
- Geisel, D. PP0249
- Geissler, E. PP1229
- Geissler, M.E. MP131
- Geisz, A. MP642
- Geitenbeek, R. OP223, MP070, PP0924, PP0940
- Geitenbeek, R.T. MP219
- Geithus, S. MP035
- Geldof, J. **PP0494**
- Geller, M. PP0307
- Geller, M.G. MP050, MP252
- Gellért, B. **PP1069**
- Gemignani, L. OP148
- Gemilyan, M. MP580
- Gemmell*, M.R. PP0012
- Genco, E. MP645, PP1165
- Genda, T. MP101, PP0152
- Genin, M. MP306
- Genne, P. PP119
- Gensluckner, S. MP173
- Gensthaler, L. OP186
- Gentile, C. MP137, PP0707
- Gentile, E. MP057
- Gentry, T. OP037, MP325
- Georges, M. OP019
- Georgescu, C.V. PP1163
- Georgiadou, G. PP0205, PP0528
- Geppert, C. PP0529
- Geramizadeh, B. PP0303
- Gerbes, A.L. OP182, PP0967
- Gerges, C. MP324
- Gerhardt, A. MP479
- Gerhold, C.-B. PP1122
- Germani, G. MP406
- Germanidis, G. MP676, PP0568
- Germinaro, M. OP045, OP082, OP084, OP102, MP670
- Gerstner, O. PP0596
- Gerstorfer, M. PP0390
- Gertner, J. **MP033**, PP0106, PP0227
- Gervoska, D. MP624
- Gessler, N. MP280
- Geybels, M. OP058
- Geyl, S. MP156, PP0849
- G. Gravina, A. OP009, MP549
- Ghadimi, M. PP0230
- Ghanem, H.S. MP409
- Gharbi, G. MP422, **PP0259**, **PP0294**, PP0981, PP1000, PP1006
- Ghauri, D.M. PP0499
- Ghelfi, L. PP0132
- Gheonea, D.-I. PP1163
- Gheorghe, C. MP586
- Gheorghe, E. OP227
- Gherbon, A. PP1124
- Gherşi, S. **PP0870**
- Ghersin, I. MP184
- Ghestem, V. PP0374
- Ghia, J.-E. **MP444**
- Ghiboub, M. **MP209**
- Ghilardi, L. MP185
- Ghisa, M. MP256, MP259, MP491, MP662, PP0076, PP0285
- Ghisletti, S.M.L. MP571
- Ghiță, A.I. PP1132
- Ghoneem, E. PP0201
- Ghoris, Y. PP0425
- Ghoris, Y.A. PP0443
- Ghosh, S. MP114, MP383, MP392, PP0457, PP0479, PP0482, PP0499, PP0505, PP0550, PP0565
- Ghoshal, U.C. PP1235
- Ghura, S. MP042, **MP050**, MP252, PP0307, PP0308
- Giaccari, A. MP455
- Giacomazzi, C. PP1053
- Giagu, S. PP1194
- Giakoumis, M. MP676, PP0568
- Giampalma, E. MP084
- Gianfrancesco, I.M. **MP718**
- Giangaspero, A. PP0301
- Giannagrecu, E. PP0645
- Giannakopoulos, A. MP134

Giannakouloupoulou, E. MP676, PP0568
Giannelis, P. MP676, PP0568
Giannini, E.G. OP034, OP199, MP476, PP0652
Giannitti, S.L. PP0893
Giardullo, A. MP652
Giaslakitiotis, K. PP0428
Gibble, T.H. PP0566
Gibbons, E. PP0222, **PP0737**
Gibiino, G. MP084, MP364
Gibson, D. PP0876
Gielisse, E. OP225
Giesbrecht, K. **PP0685**
Gieswinkel, A. MP233
Gieszinger, G. **PP1130**
Gigi, E. MP692, MP695
Giglio, M. PP1009
Gilca-Blanariu, G.-E. MP175, **PP1204**
Gilhotra, R. PP0888
Gilissen, L. PP0484
Gill, J. PP0604
Gillard, R. PP0530
Gillesberg, F. MP565
Gillet, D. PP1245
Gilletta De Saint Joseph, C. MP330
Gilman, E. MP329
Gil-Redondo, R. OP023, MP503, PP0364, PP0381
Gil Rojas, S. MP549
Gimenez, A. **PP1213**
Gimeno Pitarch, L. PP0403
Gimeno-Pitarch, L. MP674
Ginard, D. MP510, PP0403, PP0422
Giner, Á. OP026
Ginès, P. MP071
Ginesta Frings, C.A. MP287
Ginghina, O. MP538
Gionchetti, P. PP0640, PP0668
Giordano, A. OP151, MP268
Giorgini, G. MP491
Giorio, L. MP112, **MP445**, **MP564**
Giouleme, O. MP692
Giovannini, M. OP098, PP1100
Giovannini, R. MP057
Girardi, B. PP0269
Giri, S. **MP541**
Girleanu, I. MP080
Girod, P. **MP213**
Girotra, M. PP0210
Gisbert, J. OP151, MP268, MP427, MP508, PP0272, PP0284, PP0285
Gisbert, J.P. MP510, PP0289
Gisbert, J.P. OP043, OP213, MP674, PP0275, PP0280
Gisbert*, J.P. OP023, PP0364, PP0381, PP0382
Gisbert*, J.P. PP0286, PP0557
Gisbert**, J.P. PP0257
Gisbertz, S.S. MP039
Gischke, M. MP642
Giuffrè, M. MP604
Giuffrida, P. MP084
Giugliano, F.P. MP662
Giustacchini, P. MP310
Giustiniani, M.C. PP0958
Gizzi, C. PP0956
Gjerstad, N. PP0313
Gkamaloutsos, C. MP676, PP0568
Gkolafakis, P. MP134, PP0104
Glasbey, J. PP0821
Glavaš, S. MP588
Glez-Peña, D. MP064
Glisic, T. PP0985
Gloria, M.L. MP005, PP0468, PP0751
Glória, L. VC03, PP0532
Glover, S. OP104
Glover, S.C. MP681
Głowacka, U. OP055, **MP199**
Glushchenko, A. PP0004
Gluud, L.L. MP300
Gluud, L.L. OP058
Glykeria, T. MP692
Gobbato, A. MP059
Gocho, T. PP1196
Godat, S. PP1092, PP1173
Godbole, S. PP0437
Goddard, A. PP0600
Godfrey, G. OP219
Godfrey, J. PP0545, PP0616
Godina, M. MP223
Godny, L. OP093, MP273
Goederle, L. MP235
Goel, S. OP037, MP325
Goesser, T. PP1048
Goetgebuer, R. PP0504
Goetsch, M. MP003, MP686, PP0354, PP0355, PP0547
Goetz, M. MP298
Gogenur, I. OP190
Goggins, M. OP133
Gogou, C. MP290
Goh, V. PP0632
Gökbulut, V. MP416
Gökce, E. **MP135**, **PP0243**
Gökden, Y. MP416
Golan, T. MP592
Golden, S. PP1187
Gölder, S. MP377
Goldis, E.-A. MP149
Goldman, A. **PP0869**
Gologan, A.N. **MP175**
Gologan, D.S. MP175
Gologan, E. MP175, PP0749
Golovics, P.A. PP0420
Goltstein, L. **PP0332**
Golubeva, J. PP0952
Gomes, A.C. PP0827
Gomes, D. MP499, PP1072
Gomes, P. PP0778
Gomes, P. PP0033
Gómez, M.J. PP0362
Gómez-Amorin, Á. MP014
Gomez-Camarero, J. MP428, MP433
Gómez Delgado, E. OP213, MP674
Gomez-Escudero, O. MP429, MP430
Gomez-hurtado, I. PP0945
Gomez-Hurtado, I. PP0990
Gómez Moreno, A.Z. OP187
Gómez Rioja, R. OP184
Gómez Rodríguez, B.J. OP009, MP428, MP433, MP547, MP549, MP552, PP0271, PP0273, PP0276
Gómez-Varela, D. MP453
Gomollón, F. OP148, MP508
Gonçalves, A.R. PP0827
Gonçalves, A.R. PP0592, PP0628
Gonçalves, A. PP0033, PP0934
Gonçalves, J. MP298, MP346
Gonçalves, N. MP005, MP414
Gonçalves, R. MP286, PP0526, PP0552, PP0826, PP0827
Gonçalves Da Cunha, P. MP031
Gonciarz, W. **MP543**, **PP0252**
Gonczi, L. **PP0420**
Gonda, M. **MP693**
Gonda, T. OP228
Gonda, T.A. PP0894, PP0898
Gondolesi, G.E. MP141
Gong, W. PP0939
Gonsalkorala, E. MP065
Gonsalves, N. MP487
Gonzalez, J.-M. MP440, PP1100
González, Y. MP674
González-Cervera, J. OP211
González De La Higuera Carnicer, B. MP298
González Díaz, I. PP0469, PP1242
Gonzalez Gonzalez, L. PP0035
Gonzalez Haba, M. **OP099**
González-Haba Ruiz, M. OP228
Gonzalez Huezio, M.S. MP429, MP430
González-Huix Lladó, F. PP1172
González Lama, Y. OP151, MP268
Gonzalez-Lopez, J. PP0615
González-Muñoz, C. OP043
González Padilla, S. OP187
González-Suárez, B. OP191, PP0693
Goodman, A. PP0210
Goodman, A.J. PP0898
Goodoory, V. MP166, MP322
Goossens, M. PP0822
Gopal, S. **PP0522**
Gopalakrishnan, S. PP0367
Gophna, U. OP093
Gorcheva, Z. MP131
Gordijn, S.J. PP0397
Gordillo, C.H. PP0382
Gordillo, J. MP508
Gordon, H. MP339
Gordon, M. PP0539
Gorelik, Y. **MP283**, **MP512**, PP1043
Gori, E. PP1165
Gornals, J.B. OP191, **MP138**
Gorney, V. PP0369
Gorpas, D. PP0107
Goto, C. PP0328, PP0702, PP0703
Goto, O. MP404, PP0150, PP0151, PP0160, PP0168
Gotoda, T. PP0144, PP0173
Gottlieb, K.T. PP0479
Gottschalk, I.B. OP204
Gouiaa, D. PP0543, PP0590
Goulis, I. MP676, PP0568
Gourcerol, G. PP0299, PP0799
Gourgiotis, S. PP0229
Gout, J. OP062, OP200, MP088, MP481
Gouveia, C. PP0812
Gouveia, C. MP005, PP0226, PP0468, PP0827
Gouya-Lechner, G. OP209
Gower-Rousseau, C. MP345, PP0410
Gowland, P. PP0969
Gozalo Marín, V. PP1005
Grabauskyte, I. MP591
Grabherr, F. OP018
Grad, S. PP0038
Grafakou, M.E. **MP579**
Gräfe, S.K. PP0685
Graham, D. MP033
Graham, D.G. PP0227
Grainger, R. PP0223, PP0514
Grainville, T. MP285, PP1100
G. Rajendra, S. PP0646
Gralneq, I. MP104
Granata, L. PP0285
Granja, A. PP0076
Grant-Casey, J. OP032, MP100, MP105, MP108, MP123
Granziera, M. **PP0132**
Grassalkovich, A. MP299
Grassia, R. MP540, PP0139
Grasskemper, L. MP329
Grasso, M. MP406
Gratacós-Ginés, J. MP071
Grau, K. PP0955
Graupera, I. MP071
Gravina, A. PP0392
Gravina, A.G. OP106, OP169, MP552, PP0276, PP0285, **PP0452**, PP0629
Gravito-Soares, E. MP189, MP301, MP499, MP555, PP0236, **PP0291**
Gravito-Soares, M. MP189, **MP301**, MP499, MP555, PP0236, PP0291, PP1072, PP1141
Graziano, F. PP0433
Greco, L. PP0320
Grecu, E. PP0378
Green, D. PP0556
Green, P.H. MP047
Greene, G. OP177
Greenlees, N. PP0674
Grega, T. MP517, **PP0759**
Gregor, J. PP0531, PP0627
Gregori, D. MP223
Greinwald, R. OP208
Grellier, N. **MP267**, PP0647
Gremmel, S. PP0993
Greuter, T. OP130, MP264, PP0074
Gribaudo, G. PP1190
Gridnyev, O. MP427, MP547, PP0273
Grieco, A. PP0958
Griesbaum, M. **MP210**
Griffin, J.H. PP0371
Griffith, J. MP677
Griffiths, A. OP127, OP172
Griffiths, G. PP0099
Grigore, D.G. PP1132
Grigoryan, M. MP580
Grigoryan, S. **MP580**
Grigoryeva, T.V. MP578
Grimaldi, M. PP057
Grimpen, F. MP065
Grisan, E. MP383, MP392, PP0479
Grixti, M.D. PP0316, PP0317
Gröchenig, H.P. PP0080
Grochowska, A. MP110
Groen, S. **MP162**
Groh, M.-L. MP165
Groh, G. OP197, PP1120
Gromov, A.A. PP0537
Gränbech, J.E. MP035
Gronnier, C. MP440
Grootjans, J. OP031
Groot Koerkamp, B. MP030
Gros, B. **PP0436**, **PP0439**, **PP0579**, PP0674
Gross, G. MP573
Große, K. PP0984
Grossi, L. PP0629
Grossmann, L. MP324
Grosso, A. PP0794
Grova, M. OP106, PP0645
Grover, M. PP1230
Grover, R. PP0025, PP0141, PP0820, PP1184
Grueso-Navarro, E. OP211, MP664
Gruionu, G. OP227
Gruionu, L. OP227
Grumeza, M.K. MP175
Gründemann, C. PP0810
Grune, T. OP094
Gryzto, B. OP055
Gschwantler, M. OP183, MP638, PP0993, PP0994
Gu, A. OP047
Gu, W. PP1143
Gu, Y. MP161
Guadenzio, N. PP0434
Guagnozzi, D. MP664, PP0076
Gualtieri, L. MP311, MP605, **PP0247**
Guardiola, J. OP151, OP187, OP191, MP216, MP268, MP508, MP522, PP0557, **PP0585**
Guardiola Arévalo, A. PP0076
Guarino, A.D. OP169, PP0670
Guarino, M. MP410, PP1009
Guarino, M.P.L. MP313, MP607
Guay, H. PP0375
Guazzarotti, G. MP027
Gubbiotti, A. MP281, **PP0752**, **PP0880**
Gubergits, N. PP1138
Gudiño, V. OP026
Guedens, T. MP434
Guedes, A. MP005, MP149, PP0468, PP0532
Guedes, T. MP414, PP0050, PP0051, PP0062
Guediche, A. PP0669
Guérin, A. MP183
Guerra, G.R. PP0602
Guerra, I. OP213, MP343, PP0557
Guerra del Río, E. MP510
Guerriero, S. MP223
Guglielmetti, S. PP0779
Guglielmo, N. MP539
Guido, E. PP0752, PP0880
Guilbert, L. **OP171**, OP229, MP182
Guillen-del-Castillo, A. MP054

Guillo, L. MP156, **PP0377**
Guillon, N. MP345, PP0410
Guilmoteau, T. PP1100
Guimarães, A. MP286, PP0526, PP0552, **PP0826**, PP0827
Guizzetti, L. PP0546, PP0627, PP0706
Gujrathi, S. MP568
Gulati, S. OP143, MP221, MP277, **MP282**, PP0879, PP0881, PP0886, PP0889
Gulay, K. MP483
Gulbinas, A. MP591
Guliyev, F. PP0275
Gulla, A. PP1168
Gullo, I. PP0138, PP0828
Gülow, K. MP413, PP0973, PP0974
Gunsahin, D. PP1079
Günther, C. PP0372
Guo, H. OP118
Guo, J. MP026
Guo, X. PP0354, PP0355, PP0548
Guo, Y. PP1061
Guo, Y. MP012
Guo, Y. MP161
Gupta, P. MP004, MP420
Gupta, S. MP069, MP284, MP317, MP371, MP381, PP0179, PP0184, PP0769, PP0876, PP0890, PP0891, PP0892
Gupta, V. MP655
Gurin, M. PP0846
Gurjar, K. MP153
Gurung, S. PP0031
Gutermuth, J. PP0822
Güther, C. MP280
Gutic, E. PP0993, PP0994
Gutiérrez, A. OP151, MP268, MP334
Gutiérrez, C. PP0755
Gutiérrez-Casbas, A. PP0403
Gutiérrez-Casbas, A. OP023, OP150, OP213, MP343, MP503, MP510, PP0362, PP0364, PP0381, PP0382, PP0557
Gutiérrez-Junquera, C. OP208, PP0076
Gutiérrez-Rios, L. **PP0755**
Guzman, K. **MP544**, **PP0290**
Guzman-Carcamo, A.R. PP1116
Guzzardo, V. MP223
Gweon, T.-G. PP0694
Gyawali, C. OP075, MP093, PP0094, PP0095
Gyimesi, J. MP654
Gyökeres, T.Z. PP0021

H
Ha, C. MP333, MP620, PP0589
Ha, S. **PP0295**
Haans, J.J.L. PP0641
Haazen, L. OP081, OP156, MP582
Haber, G. MP317, PP0894, PP0898
Haberkamp, S. PP0529
Habiba, D. PP0867
Haboubi, H.N. MP485
Habu, T. MP404, PP0150, **PP0151**, PP0160, PP0168
Hachisu, Y. PP0767
Häcker, D. MP143
Hacking, S. PP0894
Hackney, E. PP0726
Haddad, F. PP0190, PP0213, PP0515, PP0961, PP1234
Haddad Hachimi, C. PP1214
Haddad-Ringborg, C. PP1147
Hadi, A. MP131, MP182, MP298
Hadid, M.C. PP0945
Hadiithi, M. MP022, MP023, PP1101
Hadjinicolaou, A.V. **OP038**, MP494
Hadjinicolaou, A.V. MP718
Haering, M. MP262
Hageman, I. MP629
Hagen, L. OP134, MP085

Hägendorn, R. MP379
Hagiu, C. MP424, PP1182
Hagiwara, A. PP0736
Hagström, H. MP047
Hagymási, K. MP048, PP1166
Hahn, N. **PP0974**
Haidar Ahmad, A. OP027
Haidry, R. OP050
Haidry, R.J. PP0227
Haidry, R.J. OP112, MP553, PP0098, PP0104, PP0240
Haig, A. PP0678
Haines, C. MP448
Haj, S. PP0506
Hajdune Dr. Varga, M.M. MP627
Haji, A. OP143, MP221, MP277, MP282, PP0055, PP0165, PP0768, PP0854, PP0879, PP0881, PP0886, PP0889
Hajjar, R. PP0877
Hakim, S. MP185
Hakvoort, T.B.M. MP573
Halbrook, C.J. OP200, MP483
Hale, M.F. MP326
Halfvarson, J. OP021, PP0447
Halfvarsson, J. OP214
Halilbasic, E. MP347
Halim, M.A. PP0219
Hall, B. PP0214, PP0222, PP0737
Haller, D. OP094, MP143, MP453
Halliday, A. MP602
Halling, M.L. **PP0360**
Halm, U.P. MP280
Halper, A. MP250
Haltmayer, H. PP0993, PP0994
Halvorsen, N. OP123
Hamada, K. MP321
Hamada, S. PP0172
Hamada, T. OP231, MP181, MP302, MP423
Hamakubo, R. MP040
Hamashima, C. **PP0834**
Hamborg, T. MP208
Hamdy, S. OP114
Hammersak, E. MP335
Hamesch, K. OP229, **MP131**, MP610, PP1229
Hamkubo, R. MP038
Hamm, J. **OP229**, MP298
Hammami, A. MP215, PP0353, PP0430, PP0495, PP0619
Hammarqvist, E.P. PP0367
Hammer, H.F. PP0776
Hammer, J. **MP691**, **PP0060**, **PP0776**
Hammer, K. PP0060
Hammer, L. OP130
Hammond, P. PP0896
Hammoudi, N. MP630
Hamza, V. MP131
Hamzaoui, M.L. MP422, PP0259, PP0294, PP0981, PP0987, PP1000, PP1006
Han, K. MP232
Han, M.-L. **PP0113**
Han, S. MP456
Han, S.W. PP0576
Han, S. OP010
Han, T. MP012
Han, W. PP0128
Han, X. MP370
Han, Y.H. MP456
Hanabata, N. OP089
Hanada, K. **MP242**
Hanadate, T. PP1195
Hanai, T. PP0432
Hanaoka, T. PP1098
Hanauer, S. OP149
Handa, O. PP0011, PP0158
Handberg, A. PP0775
Hanevelt, J. **OP222**, **OP226**, **MP222**
Hanigan, K. MP065
Hank, T. MP590
Hänle, M. OP062

Hanly, M. MP213
Hann, A. **PP0178**, **PP0221**, PP0897, **PP0899**, **PP0900**
Hann, M. PP0701
Hanna, M. PP0524
Hanna-Jairala, I. MP429, MP430
Hannink, G. MP705
Hansen, L.E.M. PP0918
Hanson, J. PP1029
Hanzel, J. **MP335**
Hanzel, J. PP0556
Hanzii, O. MP230
Hao, S. MP568
Hao, X. MP370, MP459
Haq, E. PP0435
Haque, M. PP0571
Hara, E. OP028
Harada, N. PP0172
Harb, M. **MP442**
Harder, L.M. OP058
Hardwick, R. PP0229
Harikumar, S. PP1011
Harki, J. **MP065**
Harlan III, W. PP0556
Härle, A. MP088, MP481
Harlet, L. PP0836
Haroön, S. PP0497
Harpaz, N. OP131, PP0560
Harper, A.M. PP0305
Harper, S. OP215
Harpur, L. MP213
Harput, Z.n. **MP416**
Harris, S. **MP486**, **MP488**, MP665, MP683, PP0549
Harrison, S.A. OP059, OP061, MP526, MP528
Harrow, P. OP176, MP326
Hart, A. **MP616**, **MP681**
Hart, A.L. **MP208**, PP0435
Hart, A. PP0434
Hart, A. OP193
Hartl, L. OP186, MP072, MP077, MP173, MP638
Hartley, I. PP0602
Hartmann, B. PP0717
Hartono, J.L. MP142
Harvey, N. PP0497
Harvey, P. PP0497
Harvey, P. MP326
Hasani, F. **MP240**
Hasanov, R. MP0275
Hasegawa, Y. MP323
Hashimoto, S. OP231
Hasler, C. PP0074
Hasler, W. PP0220
Hassan, C. OP090, OP123, OP126, MP011, MP063, MP137, MP276, MP278, MP542, MP714, PP0166, PP0244, PP0707, PP0754, PP0845, PP0856, PP0903, PP1217
Hassany, S. PP0287
Hassen, H. **PP0619**, PP0987
Hassine, H. MP046, PP0318, PP0346, PP0516, PP0525
Hasukic, I. MP131, MP552, PP0276
Hatakeyama, T. OP087
Hatanaka, T. OP035, MP467, **PP1013**
Hatem, Y. PP0806
Hattersley, G. **MP494**
Hattori, T. PP0134
Hauber, B. PP0548
Hauptmann, L. OP186
Havelda, L. MP304, **PP0335**, PP1125, PP1126
Haveman, J.W. MP147
Hawes, R. OP227
Haworth, J. OP075, PP0094, PP0095
Hayakawa, Y. MP035
Hayasaka, S. **PP0216**
Hayashi, A. OP145, PP0171
Hayashi, M. PP0153
Hayashi, N. OP101, OP231, **MP302**, MP423

Hayashi, T. OP202, PP0734, PP0738, PP0914, PP0915
Hayashi, Y. PP0125
Hayat, A. MP651
Hayat, J. MP485, PP0101
Hayee, B. OP122, MP221, MP277, MP282, PP0165, PP0768, PP0879, PP0881, PP0889
Hayee, B.H. OP143, PP0055, PP0886
Hayes, B. MP383, PP0457, PP0482, PP0499
Hayoung, K. **PP1039**
Hazen, S.-M. OP223
Hazen, W.L. MP022
Hazoyan, A. MP580
Hdiye, S. MP559, PP0742, PP0905, PP1036, PP1087, **PP1107**, PP1114
He, J. OP133
He, K. PP0921
He, Q. PP1143
He, T. **OP007**
He, Z. MP401
Healey, C. OP037, MP325
Hearnshaw, S. OP032, MP100, MP105, MP108, MP123
Heatta-Speicher, T. OP148
Hebbard, S. PP0835
Hebbard, G. PP0071
Hebuterne, X. OP189, MP630, PP0489, PP0608, PP0653
Hecht, P.M. MP620
Hecht, P.M. MP619
Hecker, J. MP572
Hector, H.S. MP565
Hedhli, R. PP0361
Hedin, C.R.H. OP021
Heetmeyer, J. MP143
Hegge, S. PP0475
Hegyi, J.P. PP1126
Hegyi, P. OP016, OP229, MP099, MP194, MP297, MP298, MP299, MP304, MP379, PP0021, PP0563, PP1124, PP1125, PP1127, PP1128, PP1129, PP1135, PP1157, PP1180
Hegyi, P. OP012, MP104, MP303, MP612, MP648, PP0335, PP1056, PP1126, PP1130, PP1133, PP1166
Hegyi, P.J. OP229, MP297, PP1127, PP1128
Hegyi, P.J. OP012, PP1130, PP1166
Heidarpour, H. MP240
Heidenreich, S. MP602
Heilmair, M. **PP0206**, PP0852
Heimes, H. MP143
Heimke, M. MP513
Heindl, F. PP0388
Heine, J. PP1222
Heinrich, H. MP131, PP1217
Heinze, T. MP513
Heisterkamp, J. MP705
Hejzmanova, K. MP517, MP587
Hejmadi, R. PP0482
Helal, H. PP1024
Helal, I. PP0361
Helali, W. PP1236
Heldt, R. PP0648
Heller, S. **MP081**, **PP1123**
Helliwell, J. PP0077
Hellms, T. MP329, MP682
Hellström, P.M. PP0219
Helou, S. MP106, MP229, MP516, **PP0297**
Heltovics, G. MP446
Heluwaert, F. MP634
Helwig, U. OP130, MP682
Helyes, Z. MP162
Hemdani, N. PP0456, PP0964, PP1245
Hempel, A. PP0388
Hemrike, T. **PP0438**
Henderson, A. PP0101

Hendriks, D. OP208
Hendrikx, T. OP067, MP235
Hendy, O.M. PP1022
Hennan, J. OP057
Henneman, P. MP629
Hennlich, B. MP638
Henriksen, M. PP0417
Henrique, M. MP530
Henrique, M. MP346
Hens, B. PP0503
Hensel, A. PP0692
Henson, C. **PP0701**
Hentschel, V. MP305
Hepkema, B.G. MP600
Her, Y. PP0006
Heredia, A. OP196
Herghelegiu, B.-E. PP0178
Hering, N. PP0372
Herlihy, L. **MP611**
Hermida, S. MP674
Hermida Pérez, B. MP428
Hermoso, M. MP147, MP0368
Hermoso, M.A. OP071
Herms, Q. **MP071**
Hernandez, G. MP511
Hernandez, V. MP149
Hernández, L. OP009, OP187, MP428, MP433, MP547, MP549, PP0271, PP0273
Hernández, V. MP343, MP510
Hernández Bernad, J. PP1005
Hernandez Camba, A. OP043
Hernández-Camoiras, J. MP014, MP064
Hernández Martínez, A. MP157, MP674, PP0606
Hernández-Martínez, Á. MP510
Hernández Ramírez, V. PP0474, PP0929
Hernández Rodríguez, R.T. **MP293**
Hernández Villalba, L. MP031, MP343, MP427, MP552, PP0276
Herner, A. **PP0930**
Herrera, K. PP0084
Herrera, S. PP0688
Herrerías, G. PP0343
Herrero, J. MP064
Herrero-Fresneda, I. **MP058**
Herreros, B. MP674
Herreros Martínez, B. PP0008
Herrmann, J.-S. MP195
Hervías Cruz, D. OP213, MP343
Hesampour, F. MP444
Hesser, H. PP0182
Hessmann, E. MP088
Heuer, T. MP324
Hiasa, Y. MP475, PP0111, PP0153, PP0334
Hibi, T. OP212, PP0465, PP0594
Hicks, L. MP055, PP0788
Hida, K. PP0432
Hidalgo, A. MP544, PP0290
Hidding, I.J. **OP020**, OP108, PP0379, PP0490
Hien Le, H. **MP248**
Hifumi Hara, N. MP102, PP0263
Higashino, M. PP0216
Higgins, C. MP326
Higgins, P.D. OP104
Higuchi, K. MP404, PP0150, PP0151, PP0160, PP0168
Higuera de la Tijera, F. MP429, MP430
Hihara, D. PP0736
Hiji, C. MP375
Hilbe, R. OP018
Hill, B. OP061
Hill, T. MP172
Hillary, T. PP0494
Hillen, K. MP250
Hils, M. OP002
Himoff, J. MP393
Hind, J. MP638
Hindmarsh, A. PP0229
Hindryckx, P. VC06, MP132, MP135, MP680, PP0243
Hinnen, C. MP082, PP1155
Hino, K. PP0248
Hinokuchi, M. OP231
Hintersteiner, M. **MP077**
Hipler, N. OP152, PP0136
Hiraaki, E. MP242
Hirahara, K. MP667
Hirai, R. **MP461**
Hirano, D. PP0574
Hirano, I. OP207, MP493, MP660
Hirano, K. OP101
Hiraoka, A. OP035, MP467, PP1013
Hirasawa, T. MP561, PP0125
Hirata, D. PP1196
Hirata, S. **MP321**
Hirata, Y. MP693
Hirayama, A. PP0103
Hirooka, Y. OP101
Hirose, S. PP0331
Hiroshima, A. PP0966
Hirth, M. PP1124, PP1138
Hisamatsu, T. OP042, **OP045**, OP082, OP102, OP128, OP131, MP178, MP617, MP618, MP670, PP0560, PP0562
Hiyama, Y. MP457, PP0444
Hjort, R. MP657, **MP658**
Hlavatý, M. **MP708**
Hlebanja, Z. PP1014
Hliwa, W. PP0190, PP0213, PP0515, PP0961, PP1234
Ho, L.K.Y. PP0192
Ho, M. PP0910
Ho, V. PP0059, PP0220
Hoang, H.T.M. **PP0363**
Hoang, L. MP085
Hoang, T. **PP0147**
Hobson, A. PP0094, PP0095
Hobson, A.R. OP075
Hochberger, J. **PP0910**
Hod, K. PP1235
Hodžić, S. MP552, PP0276
Hoebinger, C. OP067, **MP235**
Hoedt, E. MP609
Hoefling, S. MP479
Hoeks, M.P. PP0332
Hoekx, S. MP145
Hoentjen, F. OP147
Hoey, P. **PP0352**
Hofer, B. OP186, MP072, MP173, **MP347**
Hofer, B.S. MP077
Hoferica, J. MP053, MP435
Hoffert, Y. **MP217**
Hoffman, S. PP1186
Hoffmeister, A. OP229
Hoflack, J. MP119
Høgsberg, I.M. OP168
Hohwieler, L.M. OP069, MP086
Høime Hansen, S. PP0607
Høivik, M.L. OP021, MP330, MP341, PP0417
Hold, G. PP0012
Holden, E. MP711
Hollande, C. OP034
Holleman, F. OP049
Hollenbach, M. OP229, MP131, **PP1168**, PP1224
Hollenberg, M. PP0503
Holmberg, L. OP164
Holme, O. OP123
Holmes, G.H. MP045
Holm Hansen, E. OP190
Holobor, Z. PP1142, PP1158
Holst, J.J. PP0717
Holstein, H. PP0511
Holstein, H.J. **PP0397**
Holten, K.I.A. MP341, PP0417
Holtmann, G.J. PP0043, PP0059, **PP1225**
Holtmann, T.M. OP167, MP021, PP1181
Holton, J. PP0285
Holvoet, T. MP328
Holweg, C.T.J. OP103, MP327
Hölz, H. MP143
Hompes, R. OP223, OP224, MP070, MP219, PP0940
Hon, E. OP131, MP618, PP0560, PP0566
Honap, S. MP326, **PP0553**
Honda, Y. PP0913
Honein, K. MP106, MP229, MP516, PP0297, PP1192
Hone-Lopez, S. OP065
Hong, F. PP0600
Hong, H.S. PP0441
Hong, H. **PP0090**, PP1039
Hong, J. MP581, PP0744
Hong, S.W. PP0441
Hong, W. MP601
Hong, Z. PP0678
Honing, J. OP038
Honkoop, P. MP022
Honrubia-López, R. PP0076
Hoogenboom, F.J. PP0484
Hoogenboom, S. MP590
Hoogwater, F.J. MP030
Hoorens, A. VC08
Hoque, S. OP194, MP618, **PP0428**
Horavova, B. PP0209
Horiguchi, S.-i. PP1149
Horikawa, Y. PP0159
Horio, R. PP0328, PP0462, PP0702, PP0703
Horiuchi, Y. PP0111
Horjus Talabur Horje, C. OP188
Horne, M. OP114
Hornik, I. **PP0857, PP0866**
Horrigán, J. MP387
Horst, L.J. MP707
Hörstke, N. OP111
Horta, D. MP067, PP1241
Horvath, A. **PP0339**
Horvath, E. MP262
Horváth, M. PP1069
Horynski, M. PP0556
Hosaka, H. PP1196
Hoshi, K. PP0834
Hoshimoto, A. MP036, MP038, MP040, MP404
Hosono, K. PP0968
Hosono, S. PP0834
Hosotani, K. OP089
Hossain, E. **OP122**
Hosseini, S. MP240
Hosszúfalusi, N. PP1125
Hotta, K. OP089, OP091
Hotta, N. PP0844
Hou, R. OP025
Hou, X. OP120, MP161
Houben, E. OP219
Houben, M. OP112, OP225, MP717
Houdeville, C. PP0332
Houghton, L.A. PP0068
Hougui, O.E. **PP0228**
Houmani, Z. PP0201
Hourigan, L.F. PP0876
Horneaux de Moura, D.T. MP061
Horneaux de Moura, E.G. MP061
Houslay, K. OP077
Houwen, B.B. PP0845, PP1198
Hovde, Ø. PP0417
Howaldt, S. PP0595
Howard, G. MP249
Howarth, G. PP0630, PP0631, PP0896
Hoyer, K. **OP154**
Høyer, K.L. MP168
Hoyois, A. MP328
Hrabar, D. MP417, PP0541, PP0863
Hrasko, Z. MP462
Hradsky, O. **PP0575**, PP0580
Hreinsson, J. OP119, PP0806
Hritz, I. PP1069
Hrunka, M. PP0580
Hrvat, F. MP390, MP571
Hsieh, M.-T. MP713
Hsieh, T.-L. MP363
Hsieh, W. MP478, MP589
Hsu, M. MP448
Htet, H. OP203, **PP0165, PP0768**
Hu, C. MP198
Hu, H. MP026
Hu, H. PP1007
Hu, N. PP0091
Hu, S. OP020, MP600
Hu, S. PP0146
Hu, X. PP0376
Hu, Y. MP012
Hu, Y. MP683, PP0549
Hu, Y. **PP1110, PP1223**
Hu, Y. OP027
Huang, A. OP047
Huang, C. MP353
Huang, F. PP0884
Huang, G. PP0600
Huang, H. OP068, MP641
Huang, I.-H. PP0066
Huang, J. PP0979
Huang, K.-H. OP045, OP082, OP084, OP102, MP670
Huang, K. OP120
Huang, L. **MP378**
Huang, P.-C. MP363
Huang, S. PP0939
Huang, W.-H. **MP363**
Huang, X. OP070, MP076, **MP126**, MP411, **PP0983**
Huang, Y. MP026
Huang, Y.W. MP141
Huang, Y. PP0944
Huang, Y. **PP0944**
Huang, Y. MP500
Huang, Y. MP136
Huang, Z. OP027
Huang, Z. PP1059
Huang, Z. PP0053
Huang, Z. MP453
Huber, R. MP513
Huber, Y. PP1224, PP1229
Hübl, W. MP638
Hübner, E. PP0391
Hucl, T. MP192
Huerta Madrigal, A. MP031
Huggett, M. PP1067
Huggett, M.T. MP296
Hugova, K. PP0191, PP0225
Huguet, J.M. OP009, MP428, MP433, MP547, MP549, PP0271, PP0273
Huguet, J.M. OP151, OP187, MP268, MP343, MP427, MP674
Huguet, J.M. OP213, MP510
Huh, S. OP159
Hui, W. MP247
Hui, J. MP162
Huivaniuk, I. PP0866
Hujova, A. **MP192**
Huledal, G. OP011
Hulshoff, M. OP147
Hultqvist, M. MP451
Humes, D. **MP272**
Humes, D.J. MP519, PP0912
Hunfeld, K.-P. PP0685
Hung, K. MP568
Hung, K.E. OP079
Hungin, A.P. PP0099
Hunter, J. MP074
Hunter Gible, T. OP212, MP613, MP617, PP0594
Hupé, M. **MP266**
Huppertz-Hauss, G. OP021, MP341, PP0417
Hur, E.M. MP565
Hur, P. PP0548
Hurley, M. PP0499

Huseynov, H. PP0275
Hussain, S. **PP0386**
Hussaini, B. MP393
Hussein, B. PP0287
Hussein, H. PP0201
Hussenbux, A. MP296, PP1067
Hustak, R. PP1113
Hutchings, A. PP0019
Hutchison, B. PP1225
Hutinet, C. OP157
Hüttl, F. PP1224
Hutton, M. PP0598
Huyghe, P. OP008
Hvas, C.L. OP154, MP140, MP168
Hveem, K. MP658
Hvistendahl, M.K. OP158, MP140, MP146, MP148
Hwang, H.W. PP0441
Hwang, S. PP0909
Hwang, S.W. PP0441
Hyams, J. OP192, MP613
Hyöty, H. MP248
Hyötyläinen, T. OP004
Hyvärinen, K. MP593

Iaccarino, J. PP0613
Iacobini, F. PP0426
Iacopini, F. OP126, MP011
Iacopino, L. PP0135
Iacucci, M. **MP383**, MP392, PP0457, **PP0479**, **PP0482**, PP0499, PP0505, PP0539
Iadanza, G. MP073
Iade-Vergara, B.M. MP339
Iakovlev, A. **MP566**
Ianevski, A. OP134, MP035
Ianiro, G. OP096, MP276, MP455, MP577, PP0082
Iannone, A. PP0017, PP0269
Iavarone, M.A. MP466, MP469, PP1018, PP1020
Ibba, I. MP625, PP0418
Ibing, S. MP150
Ibishev, R. PP0275
Iborra, I. PP0755
Iborra, M. MP508, PP0404, PP0557
Iboshi, Y. PP0172
Ibragimov, B. OP204, PP0535
Ibrahim, W. PP0185
Ibrahimli, H. PP0275
Ibsen, J. **MP044**
Ibude, O.C. PP1180
Ichikawa, Y. MP460
Ichimasa, K. OP202, PP0734, PP0738, PP0914, PP0915
Ide, Y. PP0738, PP0914, PP0915
Idrees, R. PP0434, PP0435
Iemoto, T. OP014, MP693
Ierardi, A.M. MP466, MP469, PP1018, PP1020
Ierardi, E.G. PP0269
Igel, C. OP204, PP0535
Iglesias, J. MP554
Iglesias-Flores, E. OP023, OP151, OP187, OP191, OP196, MP268, MP503, MP508, PP0364, PP0381, PP0436, PP0439
Iglesias-Garcia, J. OP016, OP198, MP537, MP640, MP643, MP647, MP649, PP0024
Ignatavicius, P. MP591
Ihara, E. PP0172
Iida, T. MP696
Iizuka, T. PP1149
Ijspeert, J.E. OP180
Ikeda, Y. PP0153, Y. PP0111, MP101, PP0152
Ikegawa, T. MP693
Ikematsu, H. OP089, OP091, PP1196
Ikeuchi, H. PP0432, PP0103
Ikeura, T. OP101, MP130, PP1124

Ikezaki, H. PP0966
Ikusaka, H. PP1038
Ilchishina, T. MP427, MP552, PP0276
Ilchishina, T.A. PP0280
Ilgü, H. PP1122
Ilham, E. MP559, PP0742, PP0905, PP1036, PP1087, PP1107, PP1114
Ilham, S. PP1140
Iliás, Á. PP0420, PP0584
Iliescu, E.L. PP0300
Illicito, M.T. PP0433
Iloro, I. OP023, PP0364, PP0381, PP0382
Im, C.-M. MP018, **PP0839**, PP0840
Im, S.-G. **MP232**
Imai, A. PP1196
Imai, K. OP089
Imai, T. **PP0385**, PP0617
Imai, T. OP028
Imamura, S. PP0114
Imamura, Y. MP475
Imene, J. PP0829
Imhann, F. OP020
Imperatore, N. PP0629, PP0670
Imura, Y. MP458, PP0683
Inaba, A. MP561, **PP1195**, PP1196
Inagaki, M. PP0601
Inatomi, O. MP187, PP0385, PP0617, PP1139, PP1151
Inatsugi, N. PP0601
Inavolu, P. OP051
Ince, M.M. PP0527
Inciuraite, R. OP022, **OP107**, MP468, PP0446, PP0366
Inczeffi, O. **PP0811**
Inderson, A. MP030
Infante, P. OP064
Innocenti, G. OP001, OP111
Innocenti, T. **OP175**
Inoue, H. MP502
Inoue, J. OP028, **PP0686**
Inoue, M. PP0216
Inoue, R. MP113, PP0011
Inoue, R. MP038, **MP040**, MP404, PP0582
Inoue, S. PP0134
Inoue, T. OP231
Intven, M. OP224
Invernizzi, P. MP511, PP0129, PP0130
Ioannidis, G. **PP0227**
Ionescu, E.M. PP1204
Iovino, P. MP261, MP491, PP0069, PP0492
Irak, K. MP416
Irfan, M. PP0314
Irie, Y. **OP028**
Irinio, T. PP0186
Iriso, P. PP0651
Irving, A. MP074
Irving, P. MP326, MP333, MP617, **MP622**, MP628, **MP680**, PP0447, PP0553, PP0588
Isayama, H. OP101, OP231, MP181, MP302, MP423
Ishibashi, F. **MP366**, PP0125
Ishibe, E. PP0216
Ishida, F. PP0432, PP0738, PP0915
Ishida, H. PP1240
Ishida, H. PP0234
Ishido, K. PP0248
Ishihara, S. PP0432
Ishii, Y. MP197
Ishikawa, A. PP0444
Ishikawa, H. PP1207, PP1240
Ishikawa, K. PP1038
Ishikawa, S. MP475
Ishikawa, T. OP101, MP696
Ishikawa, T. OP035
Ishikawa, T. PP0148, PP0328, PP0462, PP0703
Ishikawa, Y. MP404, PP0150, PP0151, **PP0160**, PP0168
Ishimaru, S. PP0574

Ishizaki, J. PP1098
Isikawa, T. PP0702
Ismaiel, A. PP0038, **PP0337**
Ismail, S.Y. PP1197
Ismail, S. MP431, PP0222
Ismaili, Z. MP405, MP418, PP0201, PP0261, PP0677, PP0972, PP0977, PP0998, PP1156, PP1167
Ismayilova, S. PP0275
Isola, J. OP002, MP655
Issa Ernesto Coelho, G. **PP1136**, PP1175, PP1178
Issa Ernesto Coelho, M. PP1136, **PP1175**, PP1178
Istvanffy, R. OP132
Iswanti, W. **PP0771**
Itabashi, M. PP0432
Itambu, J.R. PP0963
Iticovici, M. PP0399
Ito, K. PP0067
Ito, K. PP0844
Ito, M. MP323, **MP439**, PP0933
Ito, S. MP703, **PP1153**
Ito, S. OP089
Ito, Y. PP0968
Itobayashi, E. OP035
Itoh, A. PP1139
Itoh, T. OP014
Itoh, Y. MP113
Iughetti, L. MP059
Ivanič, D. PP0075
Ivanov, G. VC01
Ivanov, I. PP0338
Ivany, E. PP0746
Ivány, E. **MP158**, MP627, PP0584, PP0614, PP0675, PP0710
Ivy, M.I. OP075, PP0094, PP0095
Iwado, Y. PP0173
Iwai, T. PP1098
Iwakiri, K. MP036, PP0582
Iwakiri, K. MP038, MP040, MP404, PP0150, PP0151, PP0160, PP0168, PP0581
Iwamoto, A. PP0767
Iwamura, C. MP667
Iwamuro, M. MP321, PP0120
Iwasa, Y. MP181, MP302, MP423
Iwasaki, A. PP0913
Iwasaki, E. **OP101**
Iwasaki, S. PP0738
Iwashita, T. OP101, OP231, MP181, MP302, MP423
Iwata, K. OP231, MP181, MP302, MP423
Iwata, K. MP458, PP0683
Iwaya, M. PP0103
Iwaya, Y. **PP0103**
Iyer, K. OP159
Iyo, E. OP009, MP428, MP549
Izbéki, F. OP012, MP379, MP648, PP1130
Izquierdo, S. OP187
Izquierdo-Sanchez, L. MP530

Jabor Veiga, L. PP1136
Jacenik, D. **MP400**
Jachs, M. OP183, OP186, MP072, MP077, MP173, MP638
Jacobasch, L. MP479
Jacob-Nara, J. MP490, MP492
Jacob-Nara, J.A. PP0085
Jacob-Nara, J.A. MP487
Jacobs, I. OP008
Jacobs, R.J. PP0641
Jacobs, R.J. PP0345, PP0454
Jacobsen, H.A. MP507
Jacques, J. MP068, MP276, MP285, MP318, MP440, PP0183, PP0849, PP1100
Jaczynska, M. PP0783
Jafari, J. OP076, MP091
Jagielski, C. PP0634
Jagt, J. PP0490
Jagtap, N. OP051
Jain, A. OP085, MP680, MP681, MP684
Jain, A. PP0522
Jain, A. PP0875
Jairath, V. OP032, OP044, OP046, OP079, **OP080**, OP102, **OP131**, MP100, MP105, MP108, MP123, MP270, MP385, MP484, MP615, MP672, MP677, **PP0460**, PP0531, PP0546, **PP0550**, **PP0556**, **PP0560**, PP0565, PP0573, PP0598, PP0620, PP0627, **PP0632**, PP0706
Jakšić, M. PP0449
Jaleel, R. PP0027, PP0700, PP0795
James, M. MP132
James Lindsay, P. PP0434
Jamonneau, I. PP0374
Janakiraman, D. MP309, **MP633**, PP0959, **PP0997**
Jančiauskas, D. PP0357
Jancoriene, L. PP1031
Janelidze, D. PP0857
Jang, C. MP483
Jang, J.Y. PP0295
Jang, J. **PP0336**
Jang, K.A. PP0278
Jang, M. **PP0423**
Jankiel Miszputen, S. PP0340
Jankovic, K. MP552, MP606, PP0276
Janmaat, V.T. MP719
Jans, A. **PP0861**, PP0864
Jänsch, R. **PP0698**
Jansen, B.H. PP0379
Jansen, B.H. MP600
Jansen, B.H. OP020
Jansen, D. PP0368
Jansen, J.M. PP1197
Jansen, M. OP112
Jansen, S. OP188, PP0484
Jansen-Skoup, S. MP638
Januszewicz, W. MP374, **PP0112**
Jara, M. OP058
Jaramillo Buendía, C. **PP0980**
Jarkovsky, J. PP0116
Jarosova, J. MP192
Jarus, K. OP123
Jaspers, T. MP715, PP0167, PP1198
Jasukaitiene, A. MP591
Javid, M. PP0019
Javid, D. PP0219
Jayanthi, A. OP088
Jayasankar, B. PP1042
Jayson, C. PP0375
Jazi, K. MP240
Jaziri, H. MP215, PP0495
Jaziri, H. PP0430, PP0619, PP0987
Jazrawi, R. MP257, MP436
J. Butler, T. PP0271
Jean-Baptiste, Z. MP285, PP0849
Jearth, V. PP0394, PP0603
Jedamzik, J. OP186
Jeen, Y. OP072

- Jeen, Y.-T. OP165, MP196, **PP0848**
 Jekkel, E. PP0805
 Jekkel, É. OP117
 Jeler, R.G. MP424
 Jelsness-Jørgensen, L.-P. **PP0417**
 Jemni, I. MP234, MP525, PP0669
 Jendle, J. PP0182
 Jenkinson, P. PP0674
 Jeon, E.-b. MP551
 Jeon, S.W. **PP0121**
 Jeong, H. PP0733
 Jeong, S. MP456
 Jeppesen, P.B. **MP141**
 Jeppesen, P.B. OP158, OP159, OP161, MP140, MP146, MP148, PP0298
 Jeppsson, H. PP0808
 Jepsen, P. PP0912
 Jerez, M. MP287
 Jerotic, D. MP201
 Jess, T. OP215, PP0416
 Jess**, T. OP017, MP507
 Jharap, B. OP188
 Ji, E. MP603
 Ji, J.H. MP018
 Ji, L. PP0837
 Jia, H. **PP0949**
 Jia, S. OP120
 Jia, T. MP353, **MP597**
 Jia, Y. **PP0718**
 Jiang, B. OP120
 Jiang, H. PP0001
 Jiang, J. **PP0358**
 Jiang, Q. MP029
 Jiang, R. PP1007
 Jiang, S. PP0753, PP0875, **PP0888**, **PP0936**, **PP0937**
 Jiang, S. OP160
 Jiang, X. MP161
 Jiang, Y. OP201
 Jiang, Y. MP550
 Jiang, Y. OP120
 Jiang, Z. OP047
 Jiao, Z. MP675
 Jimenez, C. PP0421
 Jiménez-Moreno, M. MP428, MP549
 Jiménez-Rosales, R. **MP103**, **MP107**, **MP291**, **PP0016**, **PP0018**
 Jin, B.-C. PP0840
 Jin, E.H. MP232
 Jin, H. MP474, PP1051, **PP1143**, PP1144
 Jin, Z. OP068, MP641
 Jin, Z. **PP1051**
 Jinbo, N. MP368
 Jing, W. **MP372**, **PP0001**
 Jinga, M. PP0311, PP0312
 Jioua, C. MP375, **PP0938**, PP1104, PP1215
 Jiyani, R. PP0413
 J Komocsar, W. OP192
 Jlassi, H. PP0402, PP1033
 Jo, H. MP232, **MP603**
 Jo, H.H. PP0126
 Jo, J.H. MP482
 Jo, Y.W. PP0006
 Jochum, W. PP0074
 Joglekar, S. **MP139**
 Johanns, J. OP042, MP672
 Johannsen, G. PP0057, PP0058
 Johansen, I. MP341, PP0417
 Johansen, S.U. PP0475
 Johansson, M. MP451
 John, A. PP0027, PP0700
 John, J. MP534, MP704, PP1052, PP1054
 Johns, J. OP192, MP613
 Johns, J.T. MP617
 Johnsen, K.-M. PP0475
 Johnson, C. **MP253**
 Johnson, G. MP553, PP0098, PP0104, PP0240
 Johnson, M. OP038
 Johnston, E. MP326
 Johnston, M.J. PP0602
 Jójárt, B. OP015, **MP446**, **PP0520**
 Jokelainen, K. MP709
 Joly, F. OP157, OP158, **OP159**, MP141, MP146, MP148, PP0298, PP0349
 Jomni, M.T. PP0551, PP0772
 Jomni, T. MP473, PP0727, PP0871, PP1236
 Jonaitis, L. MP433, MP547, PP0271, PP0273
 Jonaitis, L.V. OP022, OP107, MP427, MP545, PP0366, PP0446
 Jonaitis, P. **PP0277**
 Jonaitis*, L.V. PP0277
 Jones, C.D. OP077
 Jones, G.R. PP0674
 Jones, G.-R. PP0579
 Jones, K. PP0438
 Jones, M.P. MP160, MP723
 Jones, W. PP1226
 Jong, M.R. MP715, MP717, PP0167, PP1198
 Jonkers, D. OP117, PP0805
 Jonkers, D.M. OP121, MP051, MP162, PP0780
 Joo, L. MP534, MP704, PP1052, PP1054
 Joo, Y.-E. MP018, PP0839, **PP0840**
 Jörgensen, E. MP682
 Jørgensen, E.M. PP0607
 Jørgensen, H.L. MP300
 Jose Arguello, R. OP027
 Josefsson, A. MP163
 Joseph, A. PP0027, PP0795
 Joseph, A.J. PP0700
 José Temido, M. PP1072
 Joshi, D. MP132
 Joshi, M. MP575
 Joshi, N. MP677
 Joshi, R. MP589
 Jouet, P. PP0804
 Jouini, R. PP0361
 Joukar, F. PP0092
 Joustra, V. MP629
 Jovanovic, I. PP0763
 Jovanovic, M. PP0763
 Jovanovic, M. MP298
 Jover, R. MP014, MP278
 Jovicic, I. PP0578
 Jovicic, Z. PP0541
 Joy, M. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211
 J. Rockwood, N. MP050
 J. Tahir, M. MP050
 Ju, K. **PP1202**
 Juan-Juan, A. PP0076
 Juanola, A. MP071
 Juanola, O. PP0945
 Juanola Juarez, O. PP0990
 Juarez, D. MP483
 Juárez Valdés, E.I. MP429, MP430
 Juglard, C. MP285
 Juhász, M.F. MP585, PP0563, PP1121, PP1125, **PP1246**
 Juif, L. PP0398
 Juillerat, P. OP128, MP339, PP0422, PP0562, PP0647, **PP0665**
 Jukema, J. MP715, PP0167, PP1198
 Jukic, A. **OP018**
 Julier, C. MP081, PP1123
 Julsgaard, M. PP0422
 Julsgaard*, M. MP339
 Jun, C. **PP0935**
 Jun, Y.K. MP551, MP603, PP0126, PP0131
 Juncu, S. MP080
 Juncu, S.Ş. **MP294**
 Jung, C.F.M. MP364
 Jung, D.H. PP0110
 Jung, J.H. MP232
 Jung, Y. **OP092**
 Jung, Y.-K. MP470
 Jung, Y. PP0765
 Jürgensen, C. OP167, MP021, PP1181
 Juri, N. **MP083**
 Jurica, J. PP0065
 Jus, A. MP330
 Juvyns, L. MP056
 Juyal, G. MP575
 Juzenas, S. OP107
 Juzėnas, S. PP0366
 J.W. Nielsen, Y. OP174
K
 K, S. **PP1034**
 K, S. PP0512
 Kaakoush, N. OP141
 Kabbaj, N. PP1047, PP1140
 Kabir, Y. OP088
 Kabrawala, M.V. OP217, PP1084
 Kaca, W. MP543
 Kaçar, S. MP416
 Kachroo, S. MP153
 Kaczmarczyk, W. PP0457
 Kader, R. **OP088**
 Kadiiri, M. MP129, PP0109, PP1028, PP1164
 Kadlecikova, K. PP1113
 Kadlečková, B. PP0679
 Kadota, T. MP561, PP1195
 Kadri, S. PP1206
 Kafetzis, I. PP0178, PP0897, PP0899, PP0900
 Kagramanova, A. MP339, PP1235
 Kahaleh, M. MP137, PP0766
 Kahl, M. MP329
 Kahlaoui, F. PP0402
 Kahlke, D.G. PP0918
 Kahn, S. MP527
 Kahrilas, P.J. PP0099
 Kaibori, M. MP467, PP1013
 Kaighobadi, T. MP285
 Kaimakliotis, I. MP149
 Kainov, D. OP134, MP035
 Kaitsas, F. MP577
 Kajári, L. MP446, PP0520
 Kakadiya, R. OP217, PP1084
 Kakiuchi, T. MP425
 Kakizaki, S. **OP035**, MP467, PP1013
 Kakkadasam Ramaswamy, P. PP0678
 Kakked, G. **PP1081**
 Kako, S. PP0103
 Kakugawa, Y. PP0844
 Kakuyama, S. MP693
 Kalabic, J. MP619, **MP620**
 Kalachnuk, T. PP0513
 Kalager, M. OP178
 Kalaitzakis, E. MP062
 Kalali, B. **MP426**
 Kalamees, P. PP0219
 Kalapala, R. OP051
 Kale, A. MP541
 Kalisvaart, K.J. PP0641
 Kalka, I.N. OP001
 Kallel, H. **MP215**, PP0430, PP0495
 Kallinikidis, S. PP0599
 Kalopitas, G. MP676, MP692, MP695, PP0568
 Kamada, H. OP231, PP1046
 Kamada, H. OP087
 Kamal, A. **PP1024**
 Kamal, S. PP0648
 Kamaldeep, K. PP0068
 Kamath, R. OP025
 Kamberoglou, D. PP0048, PP0073, PP0089
 Kamble, P. PP0415
 Kamei, T. PP0234
 Kamigaichi, Y. MP227
 Kaminski, M.F. OP123, OP126, OP178, PP0112, PP0853
 Kamiński, M. MP374
 Kamisawa, T. PP1149
 Kamiya, T. **PP0067**
 Kamm, M.A. PP0602
 Kampa, K.C. PP1188
 Kamperidis, N. PP0642
 Kamto, G. OP009, MP549, PP0271
 Kan, M. OP231
 Kanai, T. PP0683
 Kanamori, M. PP0133
 Kanamoto, A. PP0334
 Kanata, T. OP089
 Kanazawa, M. PP1196
 Kanazawa, N. OP087
 Kandemir, I. PP0948
 Kaneko, T. MP437, MP667, PP0148, PP0328, PP0462, PP0703
 Kanellopoulos, P. PP0330
 Kanemitsu, Y. PP0067
 Kang, B. MP118, MP450
 Kang, S.J. MP232
 Kang, W. OP052, MP207
 Kang, W. PP0083
 Kang, X. MP505
 Kanishev, I. PP0242
 Kanistras, I. MP676, PP0568
 Kano, Y. MP460, PP0133
 Kanodia, J. MP568
 Kantsevov, S. **PP0874**, **PP0906**
 Kanzawa, M. OP014
 Kao, D. **OP155**
 Kaosombatwattana, U. PP0872
 Kaouissi, S. **PP0658**, **PP0831**
 Kaouk, N. PP1192
 Kapila, D. PP0163
 Kaplan, J.L. OP192, MP613
 Karagianni, V.-M. OP208
 Karagiannis, T. MP695
 Karagyozov, P. MP132, PP1016, **PP1064**, **PP1090**, **PP1117**, **PP1183**
 Karakan, T. **PP0625**
 Karamanolis, G. **PP0048**, **PP0073**, **PP0089**
 Karami, R. PP1157
 Karamintziou, E. PP0568
 Karaskova, E. PP0580
 Karatas, A. PP0625
 Karatzas, P. MP676, PP0568
 Kardonsky, D. PP0513
 Kårhus, M.L. PP0717
 Karim, L. OP019
 Karimi, N. MP387
 Karimi, N. PP0256
 Karimov, M. PP0117
 Kariyama, K. OP035, MP467, PP1013
 Karki, S. MP568
 Karl, C. MP452
 Karmi, N. MP127, MP147
 Karmiris, K. OP150, PP0553
 Karnaukhov, N. PP1179
 Karpaviciute, V. **PP0699**
 Karrer, J.H. PP0535
 Karsdal, M. PP0509
 Karsdal, M.A. OP172, PP0502
 Karstensen, J.G. MP300
 Kartal, M. PP0985
 Karthaus, M. MP479
 Karunaratne, T.B. PP0049
 Kasai, T. MP242
 Kasap, E. MP416
 Kase, M. **MP506**
 Kashatnikova, D. PP0513
 Kashyap, P. PP0690
 Kasper, P. PP1048
 Kasprzak, Z. MP110, PP0762, PP0783
 Kassam, Z. PP0531
 Kasuga, K. PP0868
 Kata, D. PP0520, PP0584
 Katagiri, A. PP1196
 Kataoka, H. MP032, PP0237
 Kataoka, M. PP0125
 Katayama, M. PP0966
 Katayama, T. PP0834
 Katkits, K. OP011

Kato, J. MP437, MP667, PP0148, PP0328, PP0462, PP0702, PP0703, PP0735

Kato, M. MP458, PP0153, PP0683

Kato, N. OP087

Kato, N. MP437, MP667, PP0148, PP0328, PP0462, PP0703, PP0735

Kato, T. MP693

Kato, T. PP0844

Kato, Y. MP239, MP360

Kato, Y. PP0159

Katrevula, V.A. **OP051**

Katsanos, K. OP085

Katsanos, K.H. MP676, PP0568, PP0583

Katsara, A. MP226

Katsara, M.-A. **PP1231**

Katsoula, A. MP692, MP695

Kats-Ugurlu, G. OP065, OP071, MP147, PP0107

Katsuki, S. PP1228

Katsukura, N. OP231

Katsuyoshi, M. OP046

Katukuri, G.R. OP051

Kaung, T. MP471

Kauppinen, K. **MP308**

Kaur, S. MP351

Kaushik, V. PP0352

Kávási, S.B. MP099

K. Awad, A. MP225

Kawaguchi, S. MP238

Kawaguchi, Y. **PP1150**

Kawahara, Y. MP321

Kawai, Y. PP0120

Kawakami, T. MP366, PP0125

Kawakubo, K. OP231

Kawamura, N. MP178

Kawano, S. MP321

Kawasaki, S. MP458, PP0683

Kawashima, H. MP696

Kawashima, J. OP202, PP0914

Kawashima, Y. PP1150

Kawata, A. PP0458, PP0459, PP0460

Kaya, M. MP416

Kayali, S. **OP199, MP476**

Kayani, F. **PP0975**

Kayhan, C. OP212, PP0594

Kazeka, D. **PP0580**

Kazemier, G. MP030, MP702

Kazenaite, E. PP1031

Kchir, H. MP046, PP0318, PP0346, PP0350, PP0516, PP0525

Keating, B.J. MP600

Keating, L. PP0222, PP0737

Keating, M. PP0544

Keck, J.O. PP0602

Keco-Huerga, A. OP009, MP427, MP428, MP433, MP549, MP674, PP0271

Keefer, L. PP0471

Keely, S. MP609

Keisuke, S. PP0734

Keita, Á.V. OP021

Keitel-Anselmino, V. PP0136, PP0538

Kekic, D. MP552, PP0276

Kelber, O. MP579, **PP0009, PP0041, PP0692**

Keller, M. PP1137

Kelly, F. PP0019

Kelly, O. MP319, PP0214, PP0737

Kelsell, D. OP053, MP384

Kelsey, M. MP009

Kenarlı, K. PP0527

Kennedy, J. PP0579

Kentaro, S. MP423

Kerbazh, N. MP298

Kerkham, A. **PP0623**

Kernbauer-Hoelzl, M. MP489

Kerr, H. PP0214

Kerrison, C. MP069, MP284, MP317, MP371, MP381, PP0179, PP0769, PP0876, PP0890, PP0891, PP0892, PP1199

Kersting, J. MP453

Kesavelu, D. PP0512

Kesavelu, D. PP0887

Keshlaf, H. PP0706

Keskes, I. PP1000

Keskin, E. PP0527

Kessler, M. **MP463**

Kestler, H.A. OP062

Keszthelyi, D. OP121, MP162, **PP0052, PP0434, PP0780, PP0791, PP0792, PP0814**

Keum, B. OP072, MP196, PP0848

Kevans, D. MP570

Kevrekidou, P. PP0528, PP0599

Khadija, M. OP117, **PP0805**

Khafizov, K. PP0004

Khaity, A. PP0032, PP0925

Khalaf, K. MP298, PP0845

Khalaidzheva, K. **PP0800**

Khalatyan, A. MP580

Khaled Madeeh, A. PP0032, PP0925

Khalid, A. **MP078**

Khalid, Y. MP534, MP704, PP1052, PP1054

Khalil, E. PP1055

Khalil, F. PP0287

Khalil, M.T.-A. PP1062

Khalil, S. **MP678**

Khalili, H. OP216

Khamaki, S. MP240

Khamaysi, I. PP1043

Khan, H.N. OP031

Khan, J. PP0975

Khan, J. MP070

Khan, M. PP0824

Khan, O. PP0101

Khan, P. MP326

Khan, S. **MP295**

Khan, S.W. PP0425, **PP0443**

Khan, S. MP565

Khanchel, F. PP0361

Khanenko, V. PP1142, PP1158

Khanfour, M. MP229

Khannoussi, W. PP0885

Khara, H. PP0210

Khare, S. MP541

Kharief, M. PP1030

Kharrasse, G. MP405, MP418, PP0261, PP0677, PP0972, PP0977, PP0998, PP1156, PP1167

Khashab, M.A. MP136, PP1100

Khatkov, I. PP1179

Khayat, L. **MP234, MP525**

Khazaie, K. OP095

Khemiri, R. PP0516

Khemiri, W. MP473, **PP0543, PP0551, PP0590, PP0772**

Khilko, Y. PP1142

Khomiak, I. PP1142

Khoshiwal, A. OP113, MP367

Khosroshahi, A. MP350

Khoury, A. MP106

Khsiba, A. MP422, PP0259, PP0294, PP0981, PP0987, PP1000, PP1006

Khusnutdinova, D. MP578

Khwaja, I. PP0434, PP0435

Kibune Nagasako, C. MP102, PP0263

Kida, M. PP0248, **PP1098**

Kierkus, J. OP082, PP0556

Kierkuš, J. OP079

Kiessler, M. OP132

Kikuchi, S. PP0736

Kikuta, K. OP101

Kikuyama, M. PP1149

Kilani, K. PP1137

Kilgour, E. **OP077**

Kilic, V. PP1073

Killan, E. **PP0145**

Kim, A. PP0040

Kim, B. **PP0189**

Kim, B. MP622

Kim, C.W. PP0694

Kim, C.G. PP0215

Kim, D.H. MP096

Kim, D.H. PP0208

Kim, D.-H. MP018, PP0839, PP0840

Kim, D.H.(. **PP0877**

Kim, E.H. PP0295

Kim, E.-S. MP196, PP0765, PP0848

Kim, G.H. PP0110

Kim, G. PP0192

Kim, G.H. MP096

Kim, H.J. OP105

Kim, H.S. PP0694

Kim, H. OP166

Kim, H.-S. **OP166**, MP018, PP0839, PP0840

Kim, J.G. PP0199

Kim, J. MP599

Kim, J. **MP482**

Kim, J.-H. MP546

Kim, J.H. **PP0006**

Kim, J.-H. PP0126

Kim, J. OP149

Kim, J.W. **PP0250**

Kim, J. **PP0696**

Kim, J.H. **MP456**

Kim, J. PP0696

Kim, K. MP599, PP0696

Kim, K.O. MP456

Kim, K. PP0441

Kim, M. PP0766

Kim, M.-J. **MP546**

Kim, M. **PP0044**

Kim, M.K. MP599

Kim, M.-S. PP0199

Kim, M. PP0923

Kim, N.H. PP0250

Kim, N. MP144, **MP548**, MP551, MP603, PP0126, **PP0127**, PP0131, PP0295, PP0336

Kim, S.H. MP196, PP0848

Kim, S.-W. PP0840

Kim, S. PP0006

Kim, S.J. PP0765

Kim, S.-J. PP0840

Kim, S. MP144, MP548

Kim, S. MP599

Kim, S.H. PP0208, PP1004, **PP1045**, PP1115

Kim, S. OP149

Kim, S.-Y. OP166

Kim, T.H. PP0278, PP0694

Kim, T.I. OP165, PP0733, PP0909

Kim, T.-O. MP687

Kim, Y. MP144, **MP551**, PP0126, PP0131

Kim, Y.O. OP092

Kim, Y. MP599

Kim, Y.-I. **PP0215**

Kim, Y. **PP1038**

Kimman, M. PP0791, PP0792

Kimoto, Y. VC04, PP0133, PP0766

Kimura, H. PP0432

Kimura, K. PP0331

Kimura, K. OP089

Kimura, T. PP0133

Kinaany, F. PP0232

Kindt, S. **PP0037**

King, J. PP0969

Kinjo, T. PP0419

Kinscherf, R. PP0009

Kinugasa, H. MP461

Kinugasa, Y. PP0432

Kioroglou, D. MP116

Király, R. MP654

Kirby, D. OP159

Kirchgesner, J. MP156, MP267, PP0386, **PP0407**, PP0483, PP0596

Kirchner, M. MP479

Kirita, K. PP0150, PP0151, PP0160, PP0168

Kiriukova, M. **MP480**, PP1179

Kishida, Y. OP089

Kishikawa, T. PP1034

Kiss, A.K. **OP197**

Kiss, G. PP0022

Kiss, S. **PP1121**

Kita, Y. MP101, PP0152

Kitadai, Y. MP457

Kitagawa, H. PP0966

Kitala, D. OP123

Kitamura, H. PP0736

Kitano, R. OP231

Kitchen, H. PP0566

Kitti, H. PP0475

Kiudeliene, E. MP289

Kiudelis, G. OP107, PP0366, PP0446, PP0699

Kiudelis, V. OP022, MP182, PP0357, PP0446

Kiyohara, H. PP0683

Kjær, M.S. OP058

K. Jensen, F. OP174

Kjoller, Y. MP434

Klaassen, R.A. OP003

Klaassen, M.A.Y. PP0379

Klauff, J. OP103, MP327

Klang, E. PP0858

Klatte, D. MP082, MP245, MP697, PP1155

Klauss, S. MP298

Kleemann, T. MP280

Kleger, A. OP013, OP062, OP069, OP200, OP229, MP081, MP086, MP088, MP298, MP305, MP481, MP483, PP1123, **PP1137**, PP1152

Kleigrew, K. MP143

Klein, A. MP184, MP283, PP0876, PP1043

Klenina, I. PP0356, PP0960, PP0962

Klenske, E. PP0902

Klepsch, V. OP018

Kleynerman, A. **MP332**

Kliers, I. MP236, MP527

Kligys, K. OP083, MP614, MP677, PP0588, PP0589

Klinge, M. OP154

Klinger, A. PP0902

Klintmalm, G. MP600

Klomborg, R. **OP127**

Klompus, S. OP001

Kloor, M. MP463

Klopocka, M. PP0556

Klotz, A. MP465

Kluck, K. MP479

Kluge, A. MP720

Knabe, M. PP1063

Knight, H. PP0572, **PP1226**

Knoop, R. OP229

Knop, F.K. PP0046, PP0717

Knoph, C.S. **OP168**, OP230, MP168, **MP186**

Knowles, C. PP0821

Knowles, C.H. MP151

Knudsen, L.B. OP058

Knudsen, T. PP0360

Knutová, D. **PP1233**

Ko, B.M. OP165

Ko, C. MP136

Ko, H.H. PP0077

Ko, M.K.L. PP0851

Ko, M.T. **MP711**

Kobara, H. PP1046

Kobayashi, A. PP1195

Kobayashi, K. **PP1046**

Kobayashi, K. MP366

Kobayashi, M. MP323

Kobayashi, M. OP145, **PP0171**

Kobayashi, N. PP0736

Kobayashi, T. OP014, OP028, MP083, MP693

Kobayashi, T. OP044, OP085, MP615, MP617, PP0465

Koch, A.D. OP112

Koch, C. PP1218

Koch, S. PP0398

Kodama, Y. MP035

- Kodama, Y. OP014, OP028, MP083, MP368, MP693, PP0686
- Kodric, T. MP335
- Koelzer, V.H. MP393
- Koemdzhiev, D. PP1016
- Koenigsmann, M. MP479
- Koenitzer, J. **MP665**
- Kofinas, A. PP0583
- Koga, M. OP145, PP0171
- Koga, Y. PP0331
- Kogure, H. OP231
- Kohansal, A. PP0706
- Kohl, K. PP0390
- Kohla, M. MP409
- Kohler, K. OP193
- Köhler, N. MP143
- Kohlmann, T. OP229
- Kohl-Sobania, M. MP141
- Kohnke-Ertel, B. PP0388
- Kohoutova, D. MP587, PP0225
- Köhrer, K. MP638
- Kói, T. MP576, PP1119, PP1121
- Koizumi, E. MP404, PP0150, PP0151, PP0160, **PP0168**
- Koizumi, M. MP475
- Kojima, K. OP073
- Kojima, T. MP206
- Kojima, Y. MP032, PP0237
- Kok, K.B. MP326
- Kokkonis, G. MP676, PP0568
- Köksal, A.Ş. MP416
- Kokubu, M. MP475
- Kola, J. **MP721**
- Kolah, K. PP0375
- Kolawole, B.B. MP383, MP392, PP0479
- Kolho, K.-L. MP709
- Kolle-Casso, L. MP674
- Koller, T. PP1233
- Kölling, M.A. PP0230
- Kollmann, D. PP0094, PP0095
- Kołodziej, P. OP123
- Kolokolnikova, O. PP1235
- Kolokolnikova, O.A. PP0280
- Koloski, N.A. PP0043
- Komatsu, K. **PP0432**
- Komatsu, M. PP0465
- Komocsar, W. MP613, PP0655
- Komolibus, K. PP0499
- Komolmit, P. PP0989
- Komorí, H.K. PP0354
- Komorí, H.K. PP0355
- Komorí, K. **MP668**
- Komorí, K. PP0432
- Kon, H. PP1196
- Koňáříková, T. PP0846
- Konda, K. PP1196
- Kondo, K. PP0738, PP0914, PP0915
- Kondrashina, E. PP1035
- Kondrashova, E. **PP0322**
- Kondylis, G. MP134
- Konecny, S. **PP105**
- Kong, B. OP132, MP087, MP089
- Kong, Q. PP1202
- Kong, W. OP047
- Kono, Y. MP321
- Konstandi, M. PP0583
- Konstantinides, S. MP233
- Koo, J.-S. MP001
- Koo, S.H. PP1111
- Kooistra, E. MP362
- Koop, K. MP572
- Koot, B. PP0500
- Kop, M. MP022
- Kopchak, V. PP1142, PP1158
- Koper, J.E. PP0778
- Kopetskiy, S. PP0866
- Kopon, A. PP0556
- Koppelman, L.J.M. MP211
- Koppelman, L.J. **PP0345, PP0454**
- Kopylov, U. PP0501, PP0506, PP0869, PP1200
- Korakas, E. MP692
- Korbut, E. MP199, **MP719**
- Koreň, R. PP0846
- Korff, S. PP1025
- Korica, B. PP0985
- Korman, L. OP085
- Körner, F.J. OP167, MP021, PP1181
- Körner, J. PP0593
- Kornfehl, A. MP072
- Kormmann, M. PP0911, PP1137
- Korponay-Szabo, I. **MP654**
- Korsunskiy, E. PP0513
- Kortekaas, R.T. PP0484
- Koseki, Y. PP0134
- Koshibu, Y. PP0462, PP0702
- Kosiorowska, A. PP1145
- Košir Božič, T. PP1014
- Kosztá, G. PP1135
- Kothari, S. PP0210
- Kothari, T. PP0210
- Kotsafti, A. MP223
- Kottwitz, J. PP0428
- Kotze, P.G. MP339, MP686
- Kou, Y. PP0103
- Koukoulioti, E. PP1177
- Kouladouros, K. MP377
- Koulali, H. MP405, MP418, PP0261, PP0677, PP0972, PP0977, PP0998, PP1156, PP1167
- Kouno, H. OP087
- Koutroubakis, I. OP169, MP676, PP0568
- Koutsoumpas, A. PP0073, PP0089, PP0245
- Kouw, E. MP022
- Kouyama, Y. PP0734, PP0738, PP0914, PP0915
- Kovacic, B. MP262
- Kovacs, A. PP1125
- Kovalainen, T. PP0415
- Kovats, P. MP354
- Kowalski, M. PP0077
- Koyama, F. PP0432
- Kozakova, V. PP0513
- Kozompoli, D. PP0330
- Kraft, K. PP0041
- Kraglund, F. MP140
- Král, J. MP131
- Kralj, D. PP0541
- Kramer, G. MP077
- Kranidiotis, G. MP254
- Krarup, A.L. PP0076
- Krarup, H.B. OP017, MP507
- Krarup, N. OP060, PP0955
- Krarup, P.-M. OP190
- Krasnov, A. PP0292
- Krati, K. PP0202, PP0662, PP0682, PP1065
- Kratzer, A. PP1218
- Kraus, J. OP062
- Kravchenko, T. OP082
- Kreienbühl, A. MP264, PP0074
- Kreisel, W. **MP661**
- Kremer, A.E. **OP185**
- Krifa, N. PP0871
- Kriščiukaitis, A. PP0357
- Kristensen, V.A. MP341, PP0417
- Kristensen, V.A. OP021
- Kristiansen, M.F. OP204
- Kristo, I. PP0094, PP0095
- Kriukas, M. PP0699
- Křivinka, J. OP229
- Krogh, K. OP154, MP168, PP0046, PP0918, PP0919
- Krokošová, J. PP0689
- Krol, R. PP1041
- Kröner, P.T. PP1057, PP1058
- Kruchinina, M.V. **PP0537**
- Krug, S. PP0372
- Krugluger, W. MP638
- Krukowska, K. OP055
- Krupa, L. MP644
- Kruse, R. OP021
- Krznaric, Z. OP024, MP339
- Ksiaa, M. MP215, PP0353, PP0430, PP0495, PP0619
- Ksissa, O. PP0645
- Ku, B. MP228
- Kuan, L. MP589
- Kuban, P. PP0105
- Kubassova, O. MP393
- Kubat, M. PP0580
- Kubesch, A. **PP0624**
- Kubota, E. PP0067
- Kubota, K. OP101
- Kucerova, K. PP1113
- Kucharzik, T. OP130
- Kudlich, T. PP0221, PP0916
- Kudo, S. OP202, PP0734, **PP0738**, PP0914, **PP0915**
- Kuellmer, A. PP0221
- Kufaishi, H. PP0046
- Kui, B. PP1130
- Kuiken, S. MP022, PP1101
- Kuiken, S.D. MP030
- Kuipers, R.N. MP023
- Kujaruk, M. PP0321
- Kujawski, M. OP104
- Kukla, M. MP719
- Kulandaivelu, A. MP724
- Kulkarni, A. **PP1094**
- Kulkarni, A.V. OP051
- Küllmer, A. MP280
- Kulokiene, U. OP022
- Kumada, T. OP035, MP467, PP1013
- Kumagi, T. MP475
- Kumar, A. MP724, PP1066
- Kumar, K.K. PP0425
- Kumar, L. MP213
- Kumar, P. MP317
- Kumar, S. MP665
- Kumbaroğlu, F.B. **PP1205**
- Kunda, R. MP554
- Kunio, M. PP1195
- Kunovský, L. OP229, MP131
- Kunst, C. MP413, PP0973, PP0974
- Künstle, G. PP0047
- Kuntzen, T. PP0284
- Kunyi, B. MP292
- Kuo, B. **PP0220**
- Kuo, Y.-J. PP0113
- Kupcinskaite-Noreikiene, R. MP591
- Kupcinskas, J. OP022, OP107, OP152, MP289, MP427, MP433, MP468, MP545, MP547, PP0012, PP0271, PP0273, PP0277, PP0446, PP0699, PP1031
- Kupcinskas, L. MP289, **MP545**, PP0699, **PP1031**
- Kupčinskas, J. **PP0357**, PP0366
- Kuraoka, S. MP321
- Kurata, M. PP1149
- Kurian, R.T. PP0795
- Kuribayashi, S. PP0767, PP0868
- Kurién, R.T. PP0027, PP0700
- Kurihara, W. **PP0111**
- Kurita, Y. OP101
- Kuroda, H. MP467, PP1013
- Kurokawa, Y. MP197
- Kuroki, T. **OP202**
- Kuronuma, S. PP0465
- Kurosugi, A. **MP437, MP667**, PP0148, PP0328, PP0462, PP0703, PP0735
- Kurti, F. PP1124
- Kurt, Jara, M. MP528
- Kurup, A.K. PP0088
- Kurz, G. OP196
- Kusano, C. PP0248, PP0968, PP1098
- Kushima, R. MP368
- Küster, B. OP013
- Kusters, C. MP715, MP717, PP0167, PP1198
- Kusters, M. OP223
- Kusunoki, R. OP087
- Kutsumi, H. MP206
- Kuwabara, H. OP145, PP0171
- Kuwabara, S. PP0133
- Kuwai, T. OP087, MP227, PP0444
- Kuwatani, M. OP101, OP231
- Kuzman, M. MP298
- Kuznetsova, T. PP1035, PP1232
- Kvamme, C. PP0119
- Kvaššayová, J. PP0097
- Kwan, V. PP0184
- Kwek, B.E.A. MP218
- Kwon, J.W. PP0006
- Kwon, K.A. MP456
- Kwon, K.-S. MP581, PP0744
- Kwon, T. PP0423
- Kylänpää, L. MP132
- Kyriakos, N. MP676, PP0330, PP0568
- Kyritsi, V. MP290, PP0743, PP0991
- Kyryk, B. PP0720
- Kyziroglou, M. MP290
- L**
- Laabidi, S. PP0543, PP0590
- Laaroussi, R. PP1238
- Laatta, J. MP655
- Labidi, A. PP0590
- Labidy, A. PP0543
- Labreuche, J. PP0377
- Labriola, D. OP057, OP059, OP061, MP526
- Lackner, K. MP233
- Lacle, M.M. OP224
- Lacy, B. PP0045
- Lacy, B.E. OP119
- Lacy, E. OP193
- Lada, S. PP0306
- Ladabaum, U. MP278
- Ladrón Abia, P. PP1005
- Laferl, H. MP638
- Lagdali, N. MP129, PP0109, PP1028, PP1164
- Lagergren, J. PP0122
- Laghi, L.A. OP199, MP476
- Lago, P. MP386
- Laharie, D. **OP046**, OP105, MP002, MP156, MP616, PP0386
- Lahat, A. PP0858
- Lahav, M. MP592
- Laheru, D. OP133
- Lahner, E. OP140, MP203, MP205, MP728, PP0007, PP0129, PP0130, PP0325, PP1194
- Lahssini, H. PP0961
- Lahusen, A. **MP479**
- Laiho, J. MP248
- Lairani, F. PP0202, PP0682, PP1065
- Laiş, I. MP592, PP0869
- Laiyemo, A. PP1191
- Lakatos, L. PP0420
- Lakatos, P.L. PP0420, PP0584
- Lakhtakia, S. OP098
- Lał, S. OP159, MP140, PP0298
- Lala, V.G. PP0853
- Lam, B. MP069, **PP0769**, PP0876, PP0891, PP0892, **PP1199**
- Lam, C.P.M. PP0851
- Lam, E. PP0753
- Lam, E. OP142, PP0875, PP0936, PP0937
- Lamanda, R. PP0670
- La Mantia, A. MP152, PP0476
- La Marca, M. PP1209
- Lamaziere, A. PP0386
- Lamazza, A. PP0023
- Lamba, M. MP065
- Lambadiari, V. MP692
- Lambeck, A.J. MP600
- Lambers, T.T. MP314
- Lambert, J. MP149, MP630
- Lambert, J. PP0494
- Lambiase, C. PP0068, PP0782, **PP0793, PP0794**, PP0809
- Lammers, W.J. MP535
- Lammert, F. PP1138
- La Montagna, M. OP077

Lamouri, C. MP676
Lampertico, P. MP466, MP469, PP1018, PP1020
Lamprecht, G. PP0298
Lamprou, S. PP0466, PP0728
Lan, C. MP675
Lanari, J. MP406
Lanas, A. MP427
Lancho Munoz, A. MP103, MP107, MP291, PP0016, PP0018
Lancho-Muñoz, A. PP1131
Lanciotti, S. PP0818
Lande, R. PP0624
Landi, R. MP539
Landi, S. MP132, PP0870
Landman, C. MP267
Landry, W. MP329
Lang, A. MP592, PP0869
Lang, E. OP219
Lang, S. OP067, PP1048
Lang, S. PP0398
Lang, Y. MP370, MP459
Langdahl, B. MP140
Lange, A.H. **PP0717**
Lange, C. OP182, PP0967
Lange, J.F. OP188
Langer, F. OP186
Langhorst, J. **MP165**
Langner, J. **PP0209**
Lanka, L. MP478
Lansdorp-Vogelaar, I. MP226, PP0128, PP0711, PP1197, PP1231
Lanzillotta, M. **OP170**, MP350, PP1138
Laoun, R. **MP685**, **PP0596**
Lapeere, H. PP0494
Lapenna, L. MP295, PP1003
Lappas, I. MP254
Laquente-Saez, B. MP138
Lara, G. MP554
Laranjeira Correia, J.P. PP0050, PP0051, PP0062
Laraqui, H. PP0938
Larbi, A. OP109
Larghi, A. MP028, MP137, MP193
Lariño-Noia, J. **OP198**, **MP537**, MP640, MP643, MP647, MP649
Lario, S. MP673
Larkin, A. OP192, MP613, PP0655
Laroussi, R. PP1214, PP1215
Laroute, V. PP0778
Laroux, F.S. PP0375
Larrea, E. **OP184**
Larsen, I.M. MP168, PP0919
Larsen**, L. OP017, MP507
Larsson, K. **OP011**
Lasa, J. MP614
Lasa, J.S. MP387
Lasch, K. OP079
Laserna-Mendieta, E.J. OP211, MP664, PP0076
Lassen, A. MP195
Lastovickova, M. PP0105
Latenstein, C.S. MP705
La Terra, M.A. MP714
Laterza, L. MP269, MP577, PP0393, PP0613, PP0637, PP0654, PP0656
Latorre, G. MP429, MP430
Latour, M. PP1187
Lau, J.Y.W. MP255
Lau, L.H.-S. MP377
Lau, W. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210
Laub, H. MP446
Laudanno, O. MP429, MP430
Laukens, D. OP077
Laukkarinen, J. MP182
Laumen, H. PP1122
Laurel, L. **PP0030**
Laurenza, C. PP0139
Lauret-Braña, E. OP171
Lauri, G. OP016, **MP244**, **MP542**, **MP583**
Lauritsen, M.L. **MP300**
Lauronen, J. MP593
Laursen, S. MP104
Laursen, S.B. MP100, **MP108**
Lavelle, A. PP0386
Lawlor, G. MP681, **PP0586**
Lawrance, I. PP0630
Lázár, G. OP197
Lazaraki, G. PP0205, PP0528, PP0599
Lazaretti, C.R. **PP0709**
Lazarev, M. PP0521
Lazarevic, D. MP188
Lazin, K. MP003, MP342, PP0544
Lazou, D. PP0599
Lazzano, P. MP024
Le, C. MP133
Le, S.T.T. MP074
Leal, C. PP0050, PP0051, PP0062
Leal, T. PP0526, PP0827
Leal-Lopez, S. MP643, MP647
Leão-Moreira, P. PP0620
Learoyd, A. OP076
Le-Bagousse-Bego, G. PP0085
Le Baleur, Y. MP068, MP442
Le Berre, C. PP0377
Leblanc, S. MP068, MP318
LeBlanc, J.-F. **MP154**
Le Bourhis, L. PP0395
Lebrun-Vignes, B. MP002
Lebwohl, B. MP042, MP047, PP0308
Lechowicz, Ł. MP543
Leclercq, P. MP068, MP285, PP0849
Le Cosquer, G. MP002, MP156, PP0377
Lecuna-Muñoz, M. PP1134
Ledderman, N. MP512
Ledeboer, M. MP022
Ledent, T. OP027, OP110
Ledo, A. MP064
Lee, A. PP0220
Lee, B. **OP072**, **MP196**
Lee, C. OP155
Lee, C. PP0101
Lee, C.K. MP066, PP0143
Lee, D.H. MP232, MP603
Lee, D.-H. MP144, MP548, MP551, PP0126, PP0127, PP0131
Lee, E. MP069, MP284, MP317, MP371, MP381, MP0179, PP0184, PP0769, PP0876, PP0890, PP0891, PP0892, PP1199
Lee, F.-J. **MP713**
Lee, G.H. MP279, PP0157
Lee, G.H. PP0061
Lee, H. MP456
Lee, H.S. MP482
Lee, H.-K. PP0131
Lee, H.-k. MP551
Lee, H.-S. PP0441
Lee, H.M. PP0825
Lee, H. MP096
Lee, H.T. PP0090
Lee, J.G. MP018
Lee, J.Y. PP0441
Lee, J. MP551
Lee, J.h. **PP0131**
Lee, J.H. MP144, PP0126
Lee, J. OP149
Lee, J. **MP142**, **PP0192**
Lee, J.Y. PP0215
Lee, J.Y. **MP224**
Lee, J. OP149
Lee, J. OP149
Lee, J. PP0840
Lee, J.W. MP548
Lee, J.Y. **PP0694**
Lee, J.K. PP0696
Lee, K.M. MP279, PP0157
Lee, K. OP092
Lee, K.J. **PP0061**
Lee, M.S. PP0177
Lee, M. PP0399
Lee, O.Y. MP096
Lee, S.H. MP025, MP599
Lee, S. OP149
Lee, S.K. PP0110
Lee, S.-S. PP1004, PP1045, PP1115
Lee, S. OP085, MP617
Lee, S. OP149
Lee, S. OP149
Lee, T.S. MP025
Lee, W.M. OP165
Lee, Y.Y. OP075, PP0094, PP0095, PP0187, PP1235
Lee, Y.-C. PP0842
Lee, Y.C. PP0110
Lee, Y. MP481
Leech, T. PP0101
Leech, T. **OP053**, **MP384**
Leelakusolvong, S. PP0786
Leem, G. **OP135**, MP482
Leemreis- van Noord, D. PP0561, PP1197
Leentjens, J. OP219
Lees, C.W. MP326, PP0416, PP0579, PP0674
Lefevre, J. MP267, **MP274**
Leffler, D.A. OP002, MP042, MP043, MP047, MP050, MP250, MP252, **MP652**, **MP655**, **PP0302**, **PP0307**, PP0308
Legrain-Raspaud, S. PP0778
Legros, R. MP068, MP285, PP0849, PP1100
Leguizamo, A.M. PP1050
Lehmann, T. MP097
Lehr, K. **OP152**, PP0136
Lehr*, K. **PP0012**
Lei, L. MP397
Lei, Q. MP250, MP655
Lei, Y. MP401
Leibovitzh, H. PP0671
Leick, S. PP0993
Leidig, T. MP479
Leijonmarck, W. **PP0122**
Leila, S. PP0829
Leimbacher, A. PP0369
Leite, S. MP637, PP0761, PP0883
Leithead, J. OP032, MP100, MP105, MP108, MP123
Leitner, C. OP148
Leja, M. MP427, MP433, MP547, PP0096, PP0238, PP0271, PP0273, PP0279
Lekakis, V. PP0245
Le Magoarou, T. MP634
Lembo, A. PP0220
Lemes, K. MP048, MP251
Lemmers, A. OP126, MP317
Lemrabott, A. **PP0109**, **PP1028**
Lenarcik, M. MP374
Lenart, Z. MP251
Lénárt, Z. MP048
Lenti, M.V. OP096, MP013, PP0129, PP0130
Lenzen, H. PP0910
Leo-Carnerero, E. OP023, MP343, MP503, MP674, PP0364, PP0381, PP0557
Leonardi, G. PP1071, PP1243
Leone, R. MP027, MP188, MP536, MP540
Leone, S. MP151
Leone, S. PP0422
Leong, R.W. OP078
Leong, R.W. OP079
Lepetit, H. MP068, MP285, PP0849, PP1100
Lepilliez, V. MP068, MP318
Lera dos Santos, M.E. OP228
Lerang, F. MP427, MP433, MP547, PP0271, PP0273
Lerch, M.M. MP642
Lerchova, T. PP0580
Leroi, A.-M. PP0299, PP0799
Lerotic, I. PP0863
Leroux, J. PP0185
Leroyer, A. MP345, PP0410
Lerro, F. PP0320
Lesko, K. **PP1179**
Le Thi, G. MP143
Letizia, M. MP572
Letnar, G. MP007
Leucuta, D.-C. PP0038, PP0337
Leung, D. OP052
Leung, G. PP0766
Leung, W.K. OP010, **PP0140**, **PP0695**, PP0851
Leung, W.-K. MP396
Leung, Y. MP342, PP0564
Levartovsky, A. PP0501, PP0869
Levenick, J. OP142
Levesque, B. PP0600
Leviatan, S. OP001
Levin, E. MP629
Levine, P. MP620
Levink, I.J.M. MP131
Levitskaya, A. PP0496
Levoir, D. MP442
Levy, I. MP592, PP0869
Levy, J. MP440
Lewis, J. PP0459
Ley, D. **MP345**, PP0410
Li, B. MP349
Li, C. OP158, OP159, MP146, MP148
Li, F. MP675
Li, F. OP070, MP076, MP411
Li, G. MP500
Li, G. MP397
Li, H. OP193
Li, H. OP201, MP087, **MP089**, PP1146
Li, J.W. MP218
Li, J. **OP068**, MP641
Li, J. MP486, MP488, MP665
Li, J. MP075, PP0949
Li, J. PP0396, PP0644
Li, J. PP0405, PP0663
Li, L. PP0376
Li, N. MP401
Li, P. PP0264, PP0281, PP0282
Li, Q. **OP027**, **OP029**, OP110, MP397
Li, Q.-L. MP443, PP0922
Li, R. MP122, PP0920
Li, R. PP0920
Li, S. MP596, **PP0841**
Li, S. MP447
Li, S. MP012
Li, T. MP198, MP369
Li, T. **PP0045**
Li, T. PP0075
Li, W. OP068, **MP641**
Li, X. **MP567**
Li, X. PP1061
Li, X. OP120
Li, X. MP675
Li, X. PP0100
Li, X. **MP403**, PP0695
Li, X. PP1007
Li, Y. MP161
Li, Y. MP600, PP1061
Li, Y. PP1202
Li, Y. PP0405
Li, Y. MP026
Li, Y. PP1202
Li, Y. MP247
Li, Y. PP0140
Li, Z. PP0455
Liakos, A. MP692, MP695
Liang, C. PP0405, PP0663
Liang, J. MP500
Liang, J. OP047
Liao, A. OP120, MP675
Liao, F. **MP500**
Liao, K. MP288
Liao, S. **PP0939**
Liao, W. PP0636
Liao, Y. MP401
Liaqat, M. **MP471**
Liatsos, C. MP676, PP0330, PP0568

Libânio, D. MP365, MP373, PP0164, PP0255
 Libert, F. MP009
 Libroero-Jimenez, M. PP1134
 Li Cavoli, T.V. **PP1012**
 Lichtenstein, G. OP084, MP670
 Lichtenstein, G.R. OP102, MP681
 Licia, L. MP223
 Licon, E. PP0268
 Liebe, R. MP020
 Liebgott, C. PP0778
 Loefflerinckx, C. **OP019**, PP0622
 Liem, M.S. MP030
 Liepniece-Karele, I. PP0238
 Ligato, I. PP0007, PP0325, PP1194
 Ligresti, D. MP639
 Liguori, A. **PP0958**, PP0963
 Lillik, V. OP012, **MP303**
 Lim, A. **MP478**, **MP589**
 Lim, B. MP191
 Lim, C. **PP1099**
 Lim, C.T. **PP0464**
 Lim, J.H. MP232
 Lim, J.Y.L. PP1068
 Lim, J.M.S. MP218
 Lim, K.W. PP0161
 Lim, K. MP018
 Lim, S.H. PP0127
 Lim, S.G. MP279, PP0157
 Lima, F. MP499
 Lima, H.C. PP0050, PP0051, PP0062
 Lima, L. PP0739
 Lima, P.A. **PP0934**, PP1237
 Lima Capela, T. MP637, PP0477, PP0486, PP0883, **PP1216**
 Lima Júnior, E. PP0408
 Limam, R. **PP0430**, **PP0495**
 Limarzi, F. MP084
 Limbert, M. PP0747
 Limdi, J.K. MP326
 Limsrivilai, J. PP0872
 Lin, C.-W. PP0842
 Lin, J.-T. MP713
 Lin, J. **MP122**, PP0862, PP0920
 Lin, J. **MP348**, **PP0943**
 Lin, L. PP0678
 Lin, L. OP120
 Lin, M. OP007
 Lin, R. **MP012**
 Lin, S. OP040
 Lin, V. OP190
 Lin, W.C.K. MP218
 Lin, Y. MP687
 Lin, Z. OP131, MP618, PP0550, PP0560
 Lin, Z. PP0405, PP0663
 Linas, I. MP552, PP0276, PP0284
 Lincoff, M. MP527
 Lindenmayer, J. OP062, OP200
 Lindi, E. PP0475
 Lindner, D. PP0611
 Lindqvist, C.M. OP021
 Lindsay, J.O. **MP684**, PP0435
 Linevska, K. PP0781
 Ling, G. MP249, PP0228
 Ling, J. PP1187
 Lingvay, I. MP527
 Link, A. OP152, MP468, PP0012, PP0136, **PP0538**, PP0698
 Lionetti, P. PP0433
 Lipp, M. **OP012**, **MP648**
 Lips, D.J. MP030
 Liptak, P. **MP053**, **MP435**, PP0065, PP0097
 Liptak Ziacikova, I. PP0065
 Lira-Aguilar, A. OP171
 Lisman, J. MP127
 Lisotti, A. MP137, MP193, MP540, PP0917
 List, M. MP453
 Litke, A. PP0077
 Liu, C. MP161, MP675
 Liu, D. MP161
 Liu, E. MP050, MP252, PP0307
 Liu, G. **PP0978**
 Liu, H. PP1202
 Liu, H. OP100, PP0170
 Liu, J. **MP288**
 Liu, J. **MP401**
 Liu, J. PP0380
 Liu, J. MP348
 Liu, J. MP012, PP1007
 Liu, K. OP201, PP1146
 Liu, L. PP0083
 Liu, L. MP190
 Liu, L. PP0862
 Liu, L. MP142
 Liu, L. OP007, PP0370, PP0380
 Liu, M. **PP0368**
 Liu, Q. OP047
 Liu, R. OP210, MP660
 Liu, S. **PP0194**, **PP0224**
 Liu, S. MP198
 Liu, S. OP120, MP026
 Liu, S.H.K. PP0851
 Liu, X. PP0137, PP0283
 Liu, X. MP687
 Liu, X. MP161
 Liu, X. MP198, MP369
 Liu, Y. **PP0146**
 Liu, Y. PP0358
 Liu, Y. OP120, MP675
 Liu, Y. PP0283
 Liu, Y. MP447
 Liu, Y. PP0405
 Liu, Y. **OP041**, PP0108
 Liu, Z. PP0091
 Liu, Z.-Q. MP443, PP0922
 Liu Chen Kiow, J. OP124
 Liukkonen, V. **MP593**
 Liusina, E. PP0952
 Liverani, E. MP364
 Liviu, V. PP1124
 Livne Margolin, M. **PP0501**
 Livzan, M.A. PP0280
 Li Yim, A.Y. MP629
 Lizzul, P. MP448
 Ljubicic, N. PP1078
 Llach, J. MP031
 Llaó, J. OP187, MP334
 Llaó Guàrdia, J. PP0035
 Llerena Castro, R. MP664, PP0076
 Llewellyn, S. MP065, PP0352
 Llgoña, A. MP071
 Llorente-Barrio, M. PP0076
 Llovet Soto, L.P. OP171, MP673
 Lluch García, P. PP0008
 Lo, B. **OP204**, **PP0535**
 Lo, C.H. PP0825
 Lobaton Ortega, T. OP081, MP328, PP0494, PP0647
 Lobo Alvarez, B. MP159, PP1235
 Locci, G. PP0442
 Loebenberg, R. OP155
 Loewenberg Weisband, Y. MP512
 Loftus, E.V. OP103, OP105
 Loftus, Jr., E.V. **MP677**
 Loghmari, M.H. PP0669
 Löhr, J.-M. PP1147
 Löhr, M. OP170, MP243, MP350, MP590, MP594, PP1138
 Lohse, A.W. MP707
 Lolic, I. PP0985
 Lolli, E. PP0621
 Lolli, I. MP562
 Lolli, R. PP1053
 Lomakina, E. PP0496
 Lombardo, V. MP041
 Londoño castillo, J. PP0268
 Long, M. MP527
 Long, M. MP620, MP623, MP686, PP0547
 Long, S. MP500, PP0636
 Longcroft-Wheaton, G. OP037, MP325, PP0165, PP0768
 Longman, R. OP085
 Loomba, R. OP058
 Loomba, R. OP059, MP526
 Lopatta, P. **OP069**
 Lopes, A.I. OP208
 Lopes, C. **MP373**
 Lopes, L. MP394
 Lopes, S. PP0365
 Lopes, S. PP1220
 Lopes Cravo, M. PP0138
 Lopetuso, L.R. **MP008**, MP269, MP624, PP0393, PP0613, PP0637, PP0654, PP0656, PP1209
 Lopez, G. MP010
 Lopez-Díaz, J. PP0024
 López-Fernández, H. MP064
 López-García, A. OP187
 López-García, O.N. PP0684
 Lopez-Gonzalez, E. PP1131, PP1134
 Lopez Lazcano, A. MP071
 López Martínez, C. PP0079
 López-Pelayo, H. MP071
 López Sáez, B. **MP673**
 López Serrano, P. OP213, MP343
 Lopez Tobaruela, J.M. MP291, PP0016, PP0018
 López-Tobaruela, J.M. MP103, MP107
 López-Vico, M. MP103, MP107, **MP157**, MP291, PP0016, PP0018, **PP0606**
 Lopenen, H. PP0415
 Loras Alastruey, C. OP191
 Lorca Antón, I. PP0008
 Lorente, R. PP0382
 Lorente Montoro, J.R. PP0451
 Lorente Poyatos, R. OP151, MP268, MP510, MP674, PP0362
 Lorenzon, G. MP259, MP491
 Loreto, H. OP208
 Löscher, B.-S. MP572
 Losurdo, G. OP009, MP433, MP552, PP0017, PP0269, PP0271, PP0276, PP0285, PP0301
 Lotfi, A. MP528
 Lotte Gluud, L. MP528
 Lotz, S. MP513
 Louie, B.E. OP075, PP0094, PP0095
 Louie, T. OP155
 Louis, E. MP009, **MP306**, MP630, MP677, PP0530
 Louise Costa de Faria, C. PP1070
 Louisias, M. OP210, MP660
 Loukou, A. PP0519
 Loureiro, J.F.M. PP0725
 Loureiro, R. VC03, PP0226
 Loureiro-Veira, M. MP537, PP0615
 Lourenço, L. PP1241
 Lourenço, L.C.C. MP067, PP1212
 Lovat, L.B. OP088, PP0227
 Lovati, A.E. OP129
 Lovece, A. PP0094
 Loveikyte, R. **MP211**
 Löwbeer, C. OP164
 Lowenberg, M. OP147, MP209, **MP330**, PP0504, **PP0554**, PP0567
 Löwenberg, M. OP086
 Loy, L. OP169, MP390, MP571, PP0431
 Loza, B.-L. MP600
 Lozada Hernández, É.E. OP171
 L. P. Beales, I. MP433, PP0271
 Lu, H. PP0939
 Lu, L. PP1143
 Lu, Q. OP163, **MP515**
 Lu, S. **OP118**
 Lu, X. PP0405, **PP0663**
 Lu, Z. MP596
 Lu, Z.H. PP0399
 Lübbert, Lübbert, Lübbert, C. PP0685
 Lub-de Hooze, M.N. OP065
 Lucats, L. PP0438
 Lucchetti, D. MP390
 Lucendo, A. **OP209**
 Lucendo, A.J. OP009, OP023, OP187, OP208, OP211, OP213, MP343, MP427, MP428, MP433, MP489, MP503, MP508, MP547, MP549, MP664, **PP0076**, PP0271, PP0273, PP0364, PP0381, PP0557
 Ludvigsson, J. OP214
 Ludvigsson, J. MP505
 Ludvigsson, J.F. OP214, OP216, MP047, MP174, MP214, MP243, MP594
 Ludvik, B. **MP527**
 Lueerssen, D. PP0688
 Luglio, G. PP0670
 Lugonja, S. MP201
 Lui, T.K.L. **PP0851**
 Luis, A. PP0747
 Lujan, R. MP512
 Lukas, M. PP0575
 Lukens, F. **PP1057**, **PP1058**
 Lukic, M. PP0449
 Lukic, S. PP1235
 Lum, J.H.Y. MP681
 Lukina, P. OP003, MP657, MP658
 Lukosevicius, R. OP107
 Lukusa, L. PP0564
 Lum, J.H.Y. PP0192
 Luna-Rodriguez, D. MP138
 Lund, C. MP341, PP0417
 Lund, J. MP451
 Lund, S.R. MP044
 Lundby Høyer, K. PP0046
 Lundin, K.E. OP003, MP044, MP657, MP658, **PP0313**
 Lungaro, L. MP659, **PP0310**, PP0347
 Luo, C. PP1007
 Luo, L. **PP0376**
 Luo, W. MP012
 Luo, X. OP041
 Luo, X. OP033, MP292, PP0978, PP0979
 Luo, Y. MP565
 Luongo, C. PP1009
 Lupas, D. MP627
 Lupo, M. **MP562**
 Luppino, I.M. PP0508
 Lupu, A. MP068
 Lusetti, F. MP013
 Lust, M. PP0602
 Luthra, P. **PP0435**
 Lutsenko, I. PP0857
 Lutz, M.P. MP479
 Luu, L.D.W. OP141
 Luvero, D. MP313
 Lux, T.J. PP0900, **PP1221**
 Luz, A. MP690, MP698
 Luzzi, A.P. OP199, MP476
 Lv, W. **PP0370**
 Lv, X.-H. **OP163**, MP515
 Lv, Y. MP087, MP089, PP1146
 Lychkovska, O. PP0803
 Lykke Poulsen, J. OP170
 Lynch, E.N. OP175
 Lyons, G. PP1178
 Lysy, J. PP0796
 Lyu, T. OP010
 Lyu, Y. OP052

M

Ma, C. **OP194**, MP270, MP484, MP623, PP0546, PP0556, PP0598

Ma, K.-Y. PP0839, PP0840

Ma, L. OP218, PP0029

Ma, L. **MP443**, **PP0922**

Ma, M. MP161

Ma, Y. OP120

Ma, Z. **MP198**, **MP369**

Maamouri, N. MP046, PP0318, PP0346, PP0350, **PP0516**, PP0525, PP0867

Maaser, C. OP130

Macabodbod, L. OP088

Macaluso, F.S. **OP106**, **PP0645**

Maccioni, F. PP0491

MacDonald, K.V. OP155

Macedo, C. PP1216

Macedo, G. OP099, OP205, MP060, PP0207, PP0329, PP0828, PP0830, PP1201

Macedo, M.G. OP228

Macedo Silva, V. PP0883, PP1216

Macek, C. **PP0973**

Macenlle, R. MP064

Macey, J. PP0566

Machaira, A. MP676, PP0568

Machanov, U. PP0275

Machida, H. **MP038**, MP040

Machín Delgado, M. **PP0079**

Macías Iglesias, E.M. MP666

Maciel, J. PP0747

Macinga, P. OP170, MP192

Mackay, S. MP139

Mackenzie, H. **OP176**

Maconi, G. MP271, MP275, MP389, PP0015, PP0488, PP1235

Macrae, F. PP0389

Macri, G. OP175

Madácsy, L. MP020, MP255

Madders, G. MP431, **PP0223**, PP0266, **PP0514**

Maddux, R. MP488, MP683, PP0549

Madeira, J. MP555

Madero, L. OP043, **PP0403**

Madl, C. MP638

Madrigal, T.P. **MP635**

Madsen, G. OP174, MP149, MP336, **MP391**, PP0411, PP0535

Maeda, J. PP0966

Maeda, N. OP203

Maeda, Y. OP202, MP383, PP0457, PP0479, PP0482, PP0499, PP0505

Maemoto, A. PP0432

Maes, F. OP126, PP0861, PP0864

Maev, I.V. PP0280

Maftai, D.-M. PP1204

Magalhães, B. PP0164

Magalhães, J.L.T.M. MP171, MP637, PP0477, PP0750, PP0757, PP0761, PP1216

Magam, S.G. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211

Magam, S.R. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211

Magdy, M. PP0287

Maggio, M. PP1235

Maggiora, M. PP0942

Magierowska, K. MP719

Magierowski, M. OP055, MP199, MP719

Magnante, M. PP0325

Magnuson, F.S. PP0919

Magnusson, M.K. OP021

Magro, F. OP102, OP131, OP156, **MP615**, PP0556, PP0560, PP0573, PP0592, PP0620, PP0628

Magyar, D. PP0710, PP0746

Magyar, D. PP0713, **PP0731**, PP0732

Mahadevan, U. MP339, MP342

Mahajan, U.M. MP644

Mahapatra, A. MP143

Maharshak, N. PP0218, PP0465, PP0671, PP0675

Mahdi-Joest, D. OP030

Mahfouz, E. MP106, MP229, MP516, PP0297, PP1192

Mahfouz, M. PP1057, PP1058

Mahida, Y. PP0014

Mahmoud, A. MP225

Mahmoud, A. PP0287

Mahmoudi, M. MP422, PP1006

Mahmoudi, S. PP0660

Mahmudov, U. MP427, MP547, PP0273, PP0275

Mahrn, E. MP121

Maia, L. MP414

Maia-Gonçalves, A. MP365, PP0093, PP0255

Maibier, M. **PP0249**

Maida, M.F. **MP136**, **MP276**, PP0832, **PP0855**, **PP0856**, PP1138

Maier, S. OP044

Maiero, S. OP054, MP395, MP398, PP0132

Maieron, A. OP183, MP638, PP0020

Maimaris, S. MP013, MP653, MP656, PP0315

Mainie, I. MP485

Maino, M. PP0470

Mainou, M. MP695

Maio, R. MP690, MP698

Maiolo, K. PP0630

Maione, F. MP716

Maione, R. MP716

Maiorino, M.I. PP0452

Maipang, K. PP0872

Maiseonneuve, P. OP171

Maisonnette, P. MP480, MP590

Maisterra, S. MP138

Majano, P.L. MP664

Majcher, B. PP0060, PP0902

Majek, O. MP517, MP587

Majorova, E. PP0689

Majumder, S. PP0457, PP0482, PP0499, PP0505

Mak, L.L.Y. PP0851

Makarenko, N. PP1179

Makaro, A. **MP110**, PP0762, PP0783

Makhlouf, N. MP121

Mäki, M. OP002, OP004, MP654

Makin, H. OP0566

Makino, T. MP197

Makki, M. MP682

Makris, C. OP167, MP021, PP1181

Maksic, M. **PP0763**

Malagelada, C. MP054, **MP057**, MP159

Malagón, M. MP522

Malahieude, B. PP0651

Malamut, G. PP0386

Malandris, K. **MP692**, **MP695**

Malats, N. OP132

Malazarte, M. PP0351

Malecka-Panas, E. PP0610

Malecka-Wojcieszko, E. PP1161

Malenkovic, A. MP310

Maléth, J. OP015, OP197, MP299, MP446, PP0520, PP1120

Malezieux, E. PP0676

Malfertheiner, P. OP056, OP137, MP426, MP468, PP0698

Malham, M. MP007

Malhi, N.S. PP0025, PP0141, PP0820, PP1184

Malhotra, S. MP374

Maligaya, P. PP0222

Malik, I. PP0019

Malik, T.A. PP0425, PP0443

Maljaars, J.P. OP188, PP0454

Maljaars, P.W.J. PP0641

Maljaars, P.W.J. MP211

Malkov, V. PP0600

Mallick, B. MP541

Malone, A. **PP0077**

Maloney, J. OP210, MP660

Malovanna, A. PP0866

Malta, I. PP0827

Malta Carvalho, I. **PP0708**, **PP0774**

Maly, B. **PP0065**

Mamalis, S. PP0205, PP0599

Mamiya, Y. **PP0462**, PP0702, PP0703

Mammadov, E. MP427, MP547, PP0273, PP0275

Mamutova, E. PP0952

Mamza, J.B. OP219

Manasirisuk, W. PP1108

Mancone, R. PP0426, PP0427, **PP0621**

Mancuso, T. MP607

Mandarino, F.V. **MP069**, MP260, **MP284**, **MP317**, **MP371**, **MP381**, MP441, MP722, PP0179, **PP0183**, PP0184, PP0769, PP0876, **PP0890**, PP0891, PP0892, **PP1190**, PP1199

Mandavdhare, H. PP0394, PP0603

Mandavdhare, H.S. MP004, MP420

Mandelli, G. MP063

Mandile, R. PP0320

Mándity, I. MP446

Mandorfer, M. OP183, OP186, MP072, MP077, MP131, MP173, MP347, MP638

Maneerattapanorn, M. PP0786

Manes, G. MP013

Manfredi, C. PP0452

Manfrin, E. MP130

Mangas-Sanjuan, C. MP031, MP278

Mangia villano, B.P. MP136, MP137, MP193, PP0707, PP0917

Mangili, A. OP105

Mangla, K.K. PP0955

Manhota, M. MP287, MP608

Maniak, A. PP1081

Maniero, D. MP045, MP256, MP259, **MP491**, MP653, PP0076

Maniscalco, M. MP729, PP0086, PP0087

Mann, S. PP0416

Manna, S. PP0372

Manne, S. MP042, PP0308

Manning, S. PP0726

Manno, M. MP281, MP540

Mannucci, A. PP0135, PP0348

Mannucci, P.M. PP0414

Mañosa, M. PP0557

Mañosa Ciria, M. OP043, OP151, OP213, MP268, MP334, MP508, PP0035

Manou, D. PP0466, PP0728

Manpreet, M. PP0298

Mansilla-Vivar, R. MP429, MP430

Mansmann, U. MP298

Mansour-Ghaneaï, F. **PP0092**

Mansueto, P. MP659, PP0347

Manta, R. PP0285, PP1071, PP1243

Mantaka, A. OP169

Mantica, G. MP653, MP656

Mantovani, L.G. PP1190

Mantzaris, G.J. MP339, **MP676**, **PP0519**, PP0568

Manver, A. PP0210

Manz, Q. MP143

Manza, F. **MP659**, PP0310, PP0347

Manzione, T. PP0830

Manzoni, G. MP310, MP606

Manzoni, S. MP057

Mao, T. **PP0405**, PP0663

Mao, X. MP246, MP396, PP1169

Maqbool, K. **PP0088**

Maquet, V. MP306

Marabotto, E. OP075, OP199, MP256, MP476, PP0094, PP0095

Maraczi, F. MP297

Maradey, C. PP0501

Maradey-Romero, C. **PP0054**

Marafini, I. PP0621

Maramreddy, N. PP0600

Marasco, G. **MP059**, MP136, MP276, PP0779, **PP0797**, PP0813, PP0856, **PP1235**

Marasco, M. **MP241**, **PP1092**, PP1170, **PP1173**

Maray Mateos, I. PP0076

Marazzato, M. MP261

Marcel, K. MP285

Marchegiani, F. MP223

Marchese, M. PP0023

Marchetti, F. **PP0309**

Marchitto, S.A. PP0473

Marchuk, I. MP280

Marciano, E. MP652, MP727

Marcinkowska, M. OP055

Marcon, A. MP237

Marcos Carrasco, N. OP187

Marcos-Pinto, R. OP009, MP433, MP547, PP0271, PP0273

Marcozzi, G. PP0244

Marculescu, R. MP077

Marden, J.R. MP252, PP0307

Mares, W. PP0484

Mareš, J. PP0191

Maresca, R. MP577

Marescaux, E. MP361, MP502

Marett, S. PP0616

Maretto, I. MP223

Margalit Yehuda, R. PP0434, PP0435

Mari, A. OP221, MP491, PP0272, PP0796, PP0882

Maria, A. **PP1037**

Mariatti, M. PP0672

Marigorta, U.M. MP116

Marijnissen, F.E. **PP1197**

Mårlid, K. OP216

Marin, I. PP0755

Marin, S. PP0436, PP0439

Marina Cobreros del Caz, M. OP171

Marinescu, A. MP586

Marinho, R.T. PP0050, PP0051, PP0062

Marín-Jiménez, I. PP0557

Marin Melia, M. MP138

Marinoni, B. MP256, PP0078

Marín Pedrosa, S. OP213, MP343

Marin Serrano, E. PP1242

Marinucci, N. PP1225

Mario Rodrigues, D. MP164

Marisi, G. MP084

Maristany, E. PP0585

Maristany Bosch, E. OP191

Mark, E.B. PP0046, PP0801, **PP0918**, **PP0919**

Markelova, M. MP578

Marko, L. PP0846

Marks, J. PP0877

Markus, L. MP143

Marlicz, W. OP009, MP549, PP0271, PP0610

Marmo, C. MP455, **MP560**, PP0637

Marmo, P.L. **PP0893**

Marmo, R. MP560

Marolleau, F. MP521, PP0836

Marone, P. PP0670

Marongiu, A. PP0442

Maroto Arce, N. PP0403

Marotti, A. PP0301

Maroufizadeh, S. PP0092

Marques, D. PP0138

Marques, M. PP0207

Marqués, M. PP0493

Marques da Silva Sant'Anna, M. MP555

Marques de Sá, I. PP0093

Marqués García, P. PP0451

Márquez, J.R. MP339

Márquez Mosquera, L. OP151, MP268

Márquez-Mosquera, L. OP187, OP213, MP343, MP508, MP674

Marra, F. OP034, PP1012

Marrero, G. PP0387

Marrero, J.M. MP510
Marrocchi, E. MP625
Marrone, G. PP0958
Marshall, A. OP077
Marshall, D. OP155
Marshall, H. PP0531
Marshall, J.K. MP385, PP1187
Marta, F. MP653
Márta, K. OP012, MP648, PP1128
Martano, G. MP571
Marteau, P. PP0386
Martí-Marqués, E. OP171
Martin, A. PP1048
Martin, B. PP0398
Martin, N. MP407
Martin, V. PP0363
Martin-Alonso, M. OP134
Martin Arranz, E. PP0364
Martin-Arranz, E. OP023, MP334, MP503, PP0381, PP0469, PP1242
Martín-Arranz, M.D. OP196
Martín-Arranz, M.D. OP043, OP151, OP187, OP191, MP268, MP343, MP510, MP616, MP674, PP0469, PP0557
Martin-Cardona, A. PP0403
Martin Domínguez, V. MP664, PP0076
Martinek, J. PP0191, PP0225, PP1113
Martinekova, P. MP194
Martinelli, L. MP237, PP0139
Martinez, F. MP429
Martinez, G. PP0288
Martinez, S. PP0945, PP0990
Martinez, T. MP483
Martinez, A. MP064
Martínez, M. PP0493
Martínez, P.J. OP023, **MP503**
Martínez-Cadilla, J. MP674, PP0474
Martínez-Cara, J.G. MP103, MP107, MP291, PP0016, PP0018, PP1131, PP1134
Martínez Cuevas, C. OP043
Martínez-Domínguez, S.J. OP009, MP428, MP433, MP547, MP549, PP0271, PP0273
Martínez-Domínguez, S.J. MP427
Martínez-Guillén, M. **PP0049**
Martínez-Moreno, B. OP229
Martínez Pascual, C. OP043
Martínez Perez, T.d.J. PP0403
Martínez-Pérez, T.d.J. MP674
Martínez-Roca, A. MP014
Martínez-Seara, X. OP016, OP198, MP537, MP640, MP649, PP0424
Martínez Tirado, M.d.P. MP343
Martínez Tirado, P. MP674
Martínez Villareal, J. OP132
Martinho, M. PP0665
Martin-Holgado, D. MP428, MP433
Martino, M. MP607
Martin Rodríguez, D. OP043
Martin Rodríguez, M.M. MP157, PP0606
Martins, A. PP1212, PP1241
Martins, A.M. MP408
Martins, C. PP0489
Martins, M. OP099, **OP205**, MP060, PP0207, PP0329, PP0830, **PP1201**
Martins, O. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0986, PP0988, PP1001, PP1002, PP1023, PP1027, PP1103, PP1105, PP1106
Martins Acras, F. VC07
Martins Figueiredo, L. MP408, PP1212
Martins Pinto da Costa, A.M. OP099
Martí Romero, L. MP510
Marty, O. MP442
Marubashi, K. PP0767
Marui, K. MP475
Marulanda, H. MP429, MP430
Maruta, A. OP231, MP181, MP302, MP423
Maruyama, H. OP073
Mary, J.-Y. MP149
Maryam, S. PP0499
Masamune, A. OP101
Masamunt, M. OP026
Masaoka, S. MP242
Mascagni, P. MP502
Mascarenhas, A. **PP0050**, **PP0051**, **PP0062**, PP0934, PP1237
Mascarenhas, M. PP0329
Mascarenhas Lemos, L. MP690, MP698
Mascarenhas-Lemos, L. PP0138
Mascarenhas Saraiva, M. PP0050, PP0051, PP0062
Mascarenhas Saraiva, M.J. OP099, OP205, **OP228**, MP060, **PP0830**, PP1201
Mascarenhas-Saraiva, M. PP0329
Mascia, D. MP258
Masclee, A.A. MP162
Masedo Gonzalez, A. OP213, MP343
Maselli, R. MP276, MP281, **MP714**, PP0166, PP0244, PP0754, PP0832, PP0845, PP0877
Mashtoub, S. **PP0630**, **PP0631**, **PP0896**
Masi, L. MP624, PP0393
Masia, S. MP310, MP606
Masic, M. PP0541
Masini, G. PP0673
Masiques-Mas, M.L. PP0076
Mas Mercader, P. PP0008
Mason, J.B. MP141
Masoud, A. PP0220
Masrour, M. MP240
Massani, M. MP223
Massi, M. MP177
Massidda, M. MP310, MP606
Massimi, D. MP714, PP0244
Massimino, L. MP152, MP260, PP0431, PP0517, PP0626, PP1190
Massironi, S. **PP0129**, **PP0130**, **PP0470**, **PP0471**
Mastrorocco, E. PP0244
Masucci, L. MP577
Masuda, A. OP014, OP028, OP101, OP231, MP083, MP302, MP423, MP693
Masuda, T. MP439, PP0094, PP0095
Masuda, T. PP0767
Masuda, T. **PP0601**
Masunaga, T. MP458, PP0683
Matamoras, S. PP0815
Mata-Romero, P. MP428, MP433
Mateescu, B.R. MP538
Matejin, E. MP078
Materna, A. PP0323, PP0775, PP0777, PP0798
Máth, B. MP251
Mathews, N.V. PP0795
Mathieu, N. MP266
Mathou, N. MP676, PP0568
Mathur, K. PP0833
Mathur, W. PP0232
Mathurin, P. MP634
Mato, J. OP023, PP0364, PP0381
Mato, J.M. MP503
Matovic Zaric, V. **PP0985**
Matrai, P. MP194
Mátrai, P. MP585
Matsakyan, G. MP580
Matsubara, S. OP231, MP302, MP423
Matsuda, A. PP0168
Matsuda, K. PP0432
Matsuda, T. PP0736, PP1196
Matsueda, K. PP0144
Matsui, H. MP439
Matsui, S. **MP239**
Matsumoto, C. MP425
Matsumoto, H. PP0011, PP0158
Matsumoto, N. MP242
Matsumoto, T. PP0149
Matsumoto, T. OP028
Matsumoto, Y. PP0134
Matsumura, T. MP437, MP667, PP0148, PP0328, PP0462, PP0702, PP0703, **PP0735**
Matsuoka, K. OP105, MP616, MP672, MP684
Matsushima, M. PP0331
Matsuura, B. **PP0334**
Matsuura, M. MP178
Matsuura, N. MP458, PP0683
Matsuzaki, H. PP1196
Mattackal, J.S. PP0443
Matteo, M.V. **MP311**, MP605, PP0247
Matteucci, M.C. OP117
Matthews, T. **PP1030**
Matthias, R.M. PP0576
Matthys, C. MP145
Mattsson, F. PP0122
Matysiak-Budnik, T. MP549, MP552, PP0276
Matz, E. MP512
Maurer, J. MP173
Mauriz Barreiro, M.V. PP0424
Mauro, A. MP013, **MP540**
Mautong, H. MP078
Mawdsley, J. MP628
Maxfield, D. PP0726
Maxia, C. PP0378
Maxwell, J.R. MP655
Mayer, A. OP019
Mayer, B. MP305
Mayerle, J. OP229, MP298, MP644
Mayorga Ayala, L. PP0403
Mayr, L. OP018
Maziero, R. VC07
Mazor, Y. PP0796
Mazza, S. MP013, MP540
Mazzarella, G. MP652, PP0302
Mazzawi, F. MP283, **PP1043**
Mazzitelli, F. MP410
Mazzoni, G. OP058
M'Baye, D. MP155
M. Beyer, A. MP332
McAlindon, M. MP253, MP255, PP0333
McBride, J. OP079
McCallum, R. PP0220
McCann, E. MP490
McCarthy, J. PP0499
McCarthy, J. PP0457
McCartney, S. OP176
McClurg, D. MP058
McConville, L. MP608
McCord, M. OP037, MP325
McDonnell, A. MP003, MP342, MP686, PP0544
McDougall, C. OP155
McGinnis, K. OP044, PP0565
McGregor, C. MP629
McGuinn, N. MP078
McKee, S. PP0438
McKeever, H. OP077
McKillen, B. PP0043
McLaughlin, J. OP114, PP0701
McLaughlin, M.M. OP185
McLellan, P. MP267
Mclemán, L. PP1011
McLeod, L. MP050
McLin, V. **PP1025**
McNamara, D. MP431, PP0223, PP0266, PP0289, PP0514
McPhaul, T. OP133
McRae, B. MP563
Mcshane, C. **MP570**
Meacci, D. PP0797
Mechhor, S. PP0026, PP0028, PP0034, **PP0400**, PP0401, PP0657, PP0658, PP0681, PP0831, **PP0926**, **PP0927**, PP0971, PP1032, PP1049
Medas, R. MP069, PP0179, PP0876, PP0891
Medawar, E. **OP142**, PP0877
Medel-Jara, P. MP429, MP430
Medhioub, M. MP422, PP0259, PP0294, PP0981, PP0987, PP1000, PP1006
Medina Prados, L. PP0403
Medkour, M. OP097
Medlij, C. MP442
Medmoun, M. MP634
Meehan, E. **MP358**
Meerdink, M. MP030
Meginnis, K. MP602
Megraud, F. OP009, MP427, MP428, MP433, MP547, MP549, MP552, PP0271, PP0272, PP0273, PP0276, PP0277, PP0280, PP0285, PP0289
Mégraud, F. PP0275
Meguro, K. PP0913
Mehandru, S. MP150
Méheut, L. PP0377
Mehmedovic, A. MP588
Mehra, D. OP085, MP684
Mehrabi, M. **PP0303**, PP0947
Mehrl, A. PP1218
Mehta, A. PP0955
Mehta, K. **MP724**, **PP1066**
Mehta, M.J. MP191
Mehta, N.A. PP1081
Mehta, R. OP171
Mehtälä, J. PP0415
Meier, M. PP1222
Meijer, S.L. OP112, MP039
Mejjide-Fernandez, I. MP537
Meine, G. MP678, PP0816, PP0999
Meine, G.C. PP0709
Meine, M. MP678, **PP0816**, **PP0999**
Meine, M.C. PP0709
Meinhardt, C. OP229, MP298
Meinikheim, M. MP377, MP380
Meining, A. PP0178, PP0221, PP0899, PP0900, PP0916, PP1221
Meinzer, A. VC01
Meiring, S. OP049
Mekala, D. PP0437
Mekala, S. PP0873
Melcarne, L. MP673, PP1235
Melchior, C. PP0299, PP0799
Mele, M.C. MP645
Meleshko, T. PP0010
Melia, J. PP0521
Melina, R. PP0452
Mellor, K. PP0566
Melmed, G.Y. PP333
Melnitchouk, N. PP0866
Melón-Ardanaz, E. OP026
Melotti, L. PP0640, **PP0668**
Melzer, M.K. OP069
Men, R. MP348, MP353
Mena, R. MP508
Menard-Katcher, C. MP660
Mena Sánchez, R. PP0403
Menchén, L. MP334, MP674
Menchén Viso, L.A. MP216
Mendel, R. MP377, MP380
Mendes, F. OP099, OP205, OP228, **MP060**, **PP0207**, PP0329, **PP0828**, PP0830, PP1201
Mendes, I. PP0033
Mendes, R.R. PP0050, PP0051, PP0062, PP0934, PP1237
Mendes, S. PP0365, PP1072
Mendez, J.C. MP554
Méndez, L. MP287
Mendez Santos, S. PP0255
Mendolaro, M. PP0450
Mendoza, C. PP1225
Mendoza, J. PP0364
Mendoza Hernández, J.L. PP0079
Mendoza-Rodriguez, R. PP1131
Menendez, A. PP0387
Menéndez Ramos, A. **MP666**

Menezes, R. MP367
Meng, C. MP143
Meng, Q. MP370
Meng, Y. MP026
Menif, A. **PP0981**
Menini, M. MP714, PP0845
Menna, C. PP0621
Mennet-von Eiff, M. PP0047
Mennini, G. PP1003
Mensink, P.B. OP086
Menys, A. OP158
Mercado, J. PP0382
Mercer, C. MP351
Mercier-Bonin, M. PP0778
Merciris, D. MP112
Merenda, R. MP223
Meriam, S. PP1033
Merino, V. MP216
Merino Ochoa, O. MP334
Meriranta, L. MP506
Merli, M. MP295, PP1003
Merugu, C. OP051
Meruge, M. MP555
Merz, S. MP081, PP1123
Mescoli, C. PP0587
Meseguer, P. MP383, MP392, PP0479
Mesonero Gismero, F. OP043, OP151, OP187, MP268, MP508
Mesquita, B. PP0812
Mesquita, P. PP0827
Messmann, H. OP112, OP206, MP317, MP377, MP380
Mestivier, D. OP095
Mestre – Alagarda, C. MP037
Mestrovic, A. MP552, PP0276
Metcalfe, C. OP164
Metselaar, P.I. MP209
Metwaly, A. MP143, MP453
Meunier, P. PP0530
Meyer, A. **PP0810**
Meyer, M. PP0542, PP0555
Meyer, M. OP018
Meyer-Gerspach, A.C. OP048, MP312
Meyhöfer, S. MP527
Meys, K. PP0894, PP0898
Mezza, T. MP455, PP1165
Mezzapesa, M. **PP0269**
Mfaume, B. PP0963
M. Frankell, A. MP376
Mghyly, F.z. **PP0657**
Mghyly, F.Z. PP0026
Mhlanga, S. PP0630, PP0631, PP0896
Miceli, E. PP0129, PP0130
Michael, J.S. PP0700
Michaels, J. MP448
Michal, M. MP233
Michalopoulos, A. MP290
Michalopoulos, G. MP676, PP0568
Michalski, C. OP132
Michans, B. PP0493
Michel, M.-L. OP027, OP110
Michel, M. **MP233**
Michelon, M. PP0327
Michels, B. PP1222
Michetti, P. PP0665
Michielan, A. OP169
Michl, P. OP229
Michopoulos, S. MP676, **PP0568**
Micu, L. PP0300
Middelhoff, M. PP0388
Midenfjord, I. **OP117**, OP121, PP0802, PP0805
Midha, V. MP575
Miehlke, S. MP489
Miele, E. PP0433
Miele, L. PP0958, PP0963
Miette, V. OP060
Migliozzi, S. PP0427, PP0621
Mignini, I. PP0613
Miguel, I. PP0755
Miguel, I. PP0747
Miguel García, L. OP187
Miguez-Sanchez, P. MP640
Mihai, C. PP0536
Mihály, E. MP671
Mihaylova, C. PP1016
Miheller, P. PP0675
Mikami, Y. PP0683
Mikhael, E. **MP106, MP229, MP516**, PP0297, PP1192
Mikhael-Moussa, H. **PP0799**
Miki, M. **OP014**
Mikkelsen, S. OP154
Mikó, A. OP012, MP194, MP648, PP1124
Mikocka-Walus, A. PP1186
Mikoviny Kajzrlíkova, I. PP0209
Mikula, M. MP374
Milanez, I. **PP1014**
Milani, A. MP028
Milani, A. PP0986, PP1001, PP1002, PP1023, PP1027, PP1103
Milani, S. OP175
Milata, J. MP617
Milenkovic, S. MP625
Miler, M. MP417
Milic, A. MP523
Milic, A. PP0985
Milioli, N. PP1103
Milioli, N.J. **MP331**, MP464, **MP679**, **PP0649**, **PP0650**, PP0907, PP0982, PP0986, PP0988, **PP1001**, **PP1002**, PP1023, PP1027, PP1105, PP1106
Milito, P. PP0095
Milivojevic, V. OP009, MP433, **MP552**, PP0271, **PP0276**
Milla, M. OP175
Miller, E. PP1225
Miller, L. MP208
Millet, O. OP023, MP503, PP0364, PP0381
Milligan, J. MP118, MP450
Milne, A.N. OP115
Milosavljevic, T. MP552, PP0276
Milovanovic, T. MP201, PP0985
Milutinovic, S. PP0985
Mimori, N. PP0159
Min, M. PP0146
Minami, R. MP696
Minato, Y. VC04, PP0125, PP0133, PP0766
Mindermann, N. **MP453**
Minea, H. MP294
Minea, H.-O. **MP080**
Minegishi, Y. PP0738, PP0914, PP0915
Minerba, P. MP656
Minezaki, D. MP458, PP0683
Mingos, N. PP0533
Minguez Pérez, M. PP0008
Minguez Sabater, A. OP187
Minguez Sabater, A. **PP0404**
MINGUEZ SABATER, A. PP0403
Minieri, S. PP0473
Ministro, J. MP450
Minsart, C. OP019, PP0622
Mion, F. PP0799
Miosotis, I. MP064
Miranda, A. PP0452
Miranda, P. PP0755
Miranda Albo Cardoso, V. PP1136
Miranda Fernandes, L. **PP0263**
Mirante, V.G. MP540
Mirosevic, G. PP1078
Miruzzi, L. **PP0316**, **PP0317**
Misawa, M. OP091, OP202, PP0734, PP0738, PP0845, PP0914, PP0915
Mitchell, C. PP0631
Mitchell, W. OP215
Mitrova, K. PP0580
Mitrovic, M. **MP523**
Mittal, N. PP0210
Mittelstädt, A. MP720
Mittur, Y. **PP0933**
Miutescu, B. **PP1079**, PP1204
Miyachi, H. OP202, PP0734
Miyahara, K. PP0120
Miyakawa, A. OP087
Miyake, A. PP0966
Miyake, T. PP0334
Miyamoto, R. MP457
Miyamoto, S. PP0216
Miyaoka, D. PP0173
Miyasaka, Y. OP035
Miyazaki, K. MP458, PP0683
Miyazaki, M. PP0334
Miyoshi, J. MP178
Miyoshi, Y. PP0966
Mizokami, Y. PP0125
Mizuguchi, Y. OP091
Mizumoto, T. OP087
Mizuno, K.-I. OP073
Mizuno, M. PP0144, PP0173
Mizuno, S. PP1034
Mizuno, T. MP316
Mizuno, Y. MP425
Mizunuma, M. MP460
Mizutani, M. MP458, PP0683
Mizutani, Y. MP696
Mizuuchi, Y. PP0432
Mjones, P. PP0119
M. Leonard, M. MP250
M. Meckley, L. MP050, MP252, PP0307
M Møller, J. OP174
M Møller, J. PP0411
Mnif, L. PP0660
Moalem, R. MP283
Moalla, M. PP0660
Mocanu, I. MP149
Mocci, C. **MP438**
Mocci, G. PP0442, PP0629
Mocciaro, F. PP0645, PP0856
Mochida, K. MP366, PP0125
Mochizuki, K. PP0734, PP0914
Modesto, I. MP003
Modica, S. MP306
Modolell, I. OP038
Moeini, H. MP426
Moerk, E. PP0487
Moerkerke, M. PP0691
Moes, C. PP0940
Moffa, S. MP455
Moga, T.V. MP298
Mogyorossy, S. MP354
Mohamed, A. PP1140
Mohamed, A. OP157
Mohamed, I. **MP601**, PP0524, PP0756
Mohamed, M. PP0019
Mohamed, S.Y. PP1235
Mohamed, S. MP601
Mohamed El-sayed, M. PP0032, PP0925
Mohamed Gouse, A. PP0349
Mohamed Taieb, J. PP0453, PP0456
Mohammad Hussein, A. PP0925
Mohammadi, B. MP553, PP0098
Mohammed, N. MP322
Mohamud Osoble, N.M. PP0367
Mohanathass, K. PP0217
Mohiuddin, G. **PP0705**, **PP0740**
Mohrbacher, R. OP002, OP004, MP250
Mohsen, W. PP0678
Mok, J. MP142
Mol, B. OP031
Mol, F. **MP629**
Molander, P. MP506
Molander, P. MP339
Molayusufoglou, B. PP0205
Molina Arriero, G. OP213, MP343, PP0666
Molina-Barceló, A. MP014
Molina Fernández, M.L. PP1005
Molina-Infante, J. MP664
Molina-Jiménez, F. MP664
Mollagiusoufoglou, B. PP0528
Møller, B.L. OP204, PP0535
Mollnow, T. OP229
Molnar, G. MP424, PP1182
Molnár, A. PP0335
Molnár, R. MP576, **PP1119**
Molnár, T. OP147, MP158, MP339, MP627, PP0520, PP0584, PP0614, PP0647, PP0675, PP0710, PP0713, PP0731, PP0732, PP0746, PP0811
Molnár, T. **OP015**, PP0520
Molnes, S. **PP0115**
Molontay, R. MP379
Molontay, R. MP297
Molteni, P. PP0015
Momose, K. MP197
Monaghan, T. OP155
Monastiri, S. PP0516
Monden, S. PP0158
Mondi, I. MP223
Monfort, D. OP151
Monfort Miquel, D. OP191, MP268, MP334
Mongiat, M. MP395, MP398
Monica, F. MP604
Monnet, J. PP0595
Monno, Y. PP0149
Monostori, P. MP299
Montague, J. PP0391
Montalbano, M. MP539
Montalti, R. PP1009
Montebianco Abenavoli, L. PP0337
Monteleone, G. MP389, PP0488, PP0621
Montes, C. MP102
Montes, N. MP428
Montil Miguel, E. MP674
Montori, M. VC08, MP019, PP0730, PP0838, PP0853, PP0895
Montori, S. MP428, MP549
Montori Pina, S. MP031, MP068
Montoto-Meijide, R. MP537
Mooijart, S.P. PP0641
Mookhoek, A. PP0540
Moon, J. OP092
Moon, S. MP096
Moons, L.M. OP222, OP224, OP226, MP222
Moore, A. OP037, MP325
Moradi, A. MP303
Morais, R. PP0828, PP0832
Moral, K. PP0625
Moraleja, I. OP151, MP268
Morales Alvarado, V.J. MP508
Morales-Alvarado, V.J. PP0557
Moran, G.W. PP0556
Morão, B. VC03, MP690, MP698, PP0050, PP0051, PP0062, PP0226, PP0422
Morarasu, S. PP1204
Moravkova, P. PP0116
Moreels, T. PP009, PP1063
Moreira, L. OP009, MP428, MP433, MP547, MP549, PP0271, PP0273, PP0275, PP0277, PP0280, PP0289
Moreira, R. MP522
Moreira, T. MP365, PP0093
Moreira-Barbosa, C. PP0468
Moreira-Barbosa, C. MP005
Moreira Basto, M.J. PP1216
Moreira Ruiz, L. MP031, MP427, MP429, MP430, MP552, PP0272, PP0276, PP0284, PP0285
Morell, B. PP0080
Morelli, M. MP188
Morello, E. PP0450
Moreno, E. MP216
Moreno, M.L. PP0321
Moreno De La Vega, V. PP0755
Moreno-Indias, I. OP023, PP0364, PP0381
Moreno Loro, A. OP009, MP428, MP547, MP549, PP0273
Moreno-Monteagudo, J.A. PP0364

Moreno Sánchez, N. PP0403
Moreta, M. MP071
Moretti, C. **MP574**
Morganti, R. PP0793
Mori, G. MP390, MP571
Mori, H. PP0173
Mori, K. PP0248
Mori, T. **PP1139**
Mori, Y. OP090, OP123, OP202, PP0845, PP0903
Morimoto, S. **MP227**
Moris, M. MP131
Morisco, F. MP410, PP1009
Morishita, T. MP366
Morita, Y. MP368
Morita, Y. PP0734, PP0914
Moriyama, T. PP1207
Morkunas, E. MP468
Mörling, J. MP172
Mormone, C. MP729
Morosi, L. MP571
Morozova, L. PP0238
Morretta, C. PP0637
Morris, D. OP038, MP265, PP0217
Morris, J. MP100, MP108
Morris, J.D. MP136
Morris, N. OP131, MP618, PP0560
Mortagy, M. MP471
Mortensen, J.H. MP683
Mortensen, J.H. PP0549
Mortensen, J.H. OP024, **OP172**, MP565, PP0502, PP0509
Mortensen, M.B. OP168
Morton, A. **MP519**
Morton, D. PP0821
Moschen, A.R. OP130, OP183
Moschetta, A. PP0463, PP0480, PP0517, **PP0957**
Möschler, O. MP280
Moses, R. OP044, MP615, MP617, MP623, PP0550, PP0565
Moshiree, B. PP0220
Mosig, R. MP449
Mosko, J.D. OP142, MP317
Moss, A.C. PP0876
Moss-Morris, R. MP208
Mostafa Al-dardery, N. **PP0032**
Mostafazadeh, A. MP426
Mostaguir, K. PP1025
Moszczynski, P. PP0057, PP0058
Mota, J. OP205, MP060, PP0329, PP1201
Motam, A. PP0031
Mota Reyes, C. **OP132**
Motomura, D. MP368
Motta, R. **MP351**, PP1138
Moualif, A. PP0190
Moufida, M. PP0259, PP0294, PP0981, PP0987, PP1000
Mourad, F. OP220
Moura dos Santos, P.M. PP0592, PP0628
Mouri, H. PP0144
Mousa, S. PP0623
Mouslim, I. MP559, **PP0742**, PP0905, PP1036, **PP1087**, PP1104, PP1107, PP1114
Mousourakis, K. **PP0330**
Moussion, A. MP070
Moustafa, E. PP0287
Movérare, R. OP021
Moyer, M. OP142
Mozayani, B. OP186
Mpartsea, A. MP676, PP0568
Mpouga, G. PP0245
Mpoumponaris, A. PP0568
Mrabet, E. **PP1033**
Mrabti, S. MP559, PP0742, PP0905, PP1036, PP1087, PP1107
Mrad, J. **OP220**
Mrevlje-Simon, Z. MP485
Mroz, A. MP374, PP0610
M'solli, O. **PP0353**

Mtir, M. **PP0453**
Mucha, Š. PP0689
Muckenhuber, A. OP132
Mueller, R. OP208, MP250, MP489
Mughal, M. MP553, PP0098
Muir, A. MP483
Mujagic, Z. OP086, PP0052, PP0567
Mujahid, M. **PP0319**
Mukai, S. PP0148
Mukai, T. OP231, MP302, MP423
Mukewar, S. PP1094
Mukewar, S.V. PP1094
Mukherjee, D. OP037, MP325
Mukherjee, M. MP434
Mukherjee, S. OP185
Mukhopadhyaya, A. PP1011
Mulak, A. MP164
Mulder, D. OP117, PP0805
Mülder, D. PP0128
Mulders, E. PP0792
Mulders, L.G.M. **MP117**, **PP0523**
Mulinacci, G. PP0470
Müller, J.R. MP682
Müller, M. MP305
Müller-Schilling, M. OP229, MP413, PP0973, PP0974, PP1218, PP1222
Müller-Ziehm, J. MP682
Mullin, M. MP033
Mulvaney, W. PP0019
Mumm, M. VC01
Mummey, H.M. MP481
Munck, L.K. **PP0607**
Mundet, L. PP0049
Muñoz, J.F. MP674
Muñoz, S. OP121
Muñoz Codoceo, R. MP343
Muñoz-González, R. PP0755
Muñoz León, J.A. MP666
Muñoz Villafranca, C. MP674
Muñoz-Villafranca, C. PP0557
Munters, K. **OP116**
Münzel, T. MP233
Murakami, M. **PP0248**
Murakami, S. PP0248
Murakami, Y. MP206
Murakawa, K. **MP467**
Murano, T. OP089, **MP460**
Murashima, Y. PP1038
Murata, A. MP101, PP0152
Murata, S. MP458, PP0683
Murciano Gonzalo, M.F. MP508
Murgia, A. MP287, MP608
Murino, A. MP553, PP0098, PP0104, PP0240, PP1200
Murphy, M.F. OP032, MP105, MP123
Murray, C. OP050, MP553, PP0098, PP0104, PP0240
Murray, F. PP0080
Murray, J. MP250, MP655
Murray, P. PP0482
Murtas, D. PP0378
Murthy, B. PP0083, PP0586
Murugananthan, A. PP1219
Muscarella, S. OP106, PP0645
Muscas, A. PP0442
Muscia, R. MP013
Mushtaq, I. **PP0064**
Musina, A.-M. PP1204
Muslim, M.F. PP0314
Mussetto, A. MP540, MP653
Mussies, C. OP208
Mustacchia, P. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211
Mutalemwa, K. PP0963
Muthas, D. PP0075
Mutignani, M. MP137, MP540
Muzalyova, A. MP377, MP380
Muzica, C.M. MP080
Muzzin, S. OP054
Mwangi, L. **MP226**
Myeni, S.R. MP707
Myreliid, P. MP339

Mytych, D.T. PP0638
Myung, S.-J. PP0441

N
Na, H.Y. PP0295
Na, S.-Y. **PP0765**
Nabil, T. PP0660
Nachev, P. MP307
Nachtmann, S. PP1233
Nachury, M. MP149, MP156, MP217, PP0395
Nacir, O. **PP0202**, **PP0662**, **PP0682**, **PP1065**
Nadal, R. MP071
Nadal, S. PP0830
Nadi, A. PP0885
Nadin, M.G. OP054, MP395, MP398
Nadler, M. MP592
Naessens, D. MP153, PP0571
Nafria*, B. PP0257
Nagae, S. PP0133
Nagahara, A. MP101, PP0152
Nagai, J. MP086
Nagano, S. **MP197**
Naganuma, A. OP035, MP467, PP1013
Nagata, J. PP0331
Nagaya, T. PP0103
Nagdee, T. MP180
Nagengast, W.B. OP065, OP112, OP225, PP0107
Naghipour, M. PP0092
Nagl, S. OP206, MP377
Nago, H. MP101, PP0152
Nagtegaal, I. OP162
Nagy, R. MP303, PP1129
Nahm, J.H. MP546
Naito, Y. MP113
Najdawi, F. PP0375
Naji, N. MP225
Nakagawa, T. MP693
Nakagome, S. MP404, **PP0150**, PP0151, PP0160, PP0168
Nakaguchi, H. PP0334
Nakahara, K. OP231
Nakahata, Y. MP206
Nakahodo, J. MP696, **PP1149**
Nakai, Y. OP231, MP181, MP302, MP423, PP1034
Nakaji, S. OP231
Nakajima, A. PP0913
Nakajima, K. MP197
Nakajima, N. OP073
Nakajima, S. PP0216, PP1228
Nakajima, T. PP1240
Nakajo, K. MP561, PP1195
Nakamura, A. OP101
Nakamura, K. PP0844
Nakamura, K. PP1038
Nakanishi, H. PP0125
Nakano, M. PP0465
Nakano, R. OP014, OP231, MP302, MP423, MP693
Nakano, Y. PP0868
Nakao, S. PP0385, **PP0617**
Nakao, T. PP0601
Nakaoka, M. OP145, PP0171
Nakase, H. OP104
Nakatani, E. MP238
Nakatani, K. PP1046
Nakatani, Y. PP0736
Nakatsuka, T. PP1034
Nakayama, A. **MP458**, PP0683
Nakayama, T. PP0767
Nakazawa, H. PP0462, **PP0702**, PP0703
Nakhli, A. PP0964, PP1245
Nakos, A. MP676, PP0568
Nalivaiko, P. **PP0238**
Nam, K. **PP0441**
Nam, R.H. PP0295
Nam, S.Y. PP0121

Namiki, S. OP203
Namiki, S. MP460
Namima, D. OP231
Nanayakkara, A. PP0546
Nancey, S. OP189, MP156, MP630, PP0377, PP0386, PP0395, PP0608, **PP0676**
Nandi, N. PP0547
Nandi, N. MP041, PP0309, PP0327
Nantes-Castillejo, O. PP0557
Nantes-Castillejo, Ó. PP0076
Napoli, C. PP1194
Napolitano, C. MP073, MP632
Napolitano, D. PP0393, PP0612, PP0613
Napolitano, L. PP0452
Napolitano, M. MP729, PP0086, PP0087
Napolitano, M. MP722, PP1190
Naranjo, V. MP383, MP392, PP0479
Narayan, J. MP541
Narayanan M J, D. **PP0512**, **PP0887**
Nardone, G. PP0285, PP0452, PP0473
Nardone, O.M. MP152, PP0452, **PP0476**, **PP0481**, PP0573, PP0832
Narra Figueiredo, P. MP079, MP189, MP301, MP555, MP557, PP0236, PP0291, PP0429, PP0812, PP0819, PP1141
Narula, N. MP270, MP385, PP0546, PP0564, PP0598
Narvaez-Gonzalez, H.F. PP1116
Nascimento, C. MP284, PP0138
Nass, K.J. OP181
Nassar, R. **MP249**, PP0228
Nasser, Y. OP153
Nastasa, R. MP080
Natali, C. PP1200
Natalia, T. MP063
Natt, D. PP0253, PP0412, PP0413, PP0704, PP1208, **PP1210**, PP1211
Nau, A. PP0816, PP0999
Naughton, T. PP0524
Navabi, S. MP616
Navaneethan, U. OP227
Navani, N. MP033
Navares-Gómez, M. MP664
Navarrete, I. PP0404
Navarrete Rueda, F. PP0945
Navarro, P. MP510, PP0557
Navarro Cortés, P. MP508
Navarro-Cortés, P. OP171
Navarro Gerrard, C. PP0615
Navarro-Llavat, M. OP151, MP268, MP334, MP510, PP0557
Navarro Sánchez, M.P. OP211, MP664, PP0076
Naves, J.E. PP0076
Navoyan, I. MP580
Nawacki, L. MP298, PP1124
Nayar, M. MP186
Ncir, M. PP0871
Ndile, E. PP0963
Ndukwe, S. PP0631
Ndunguru, B. PP0963
Nedbalova, L. PP0575
Neeffes-Borst, A. OP031
Neelankavil, C. MP611
Neese, A. OP229
Neff-Baro, S. MP153
Nefzi, A. PP0964
Negreanu, L. PP1132
Negri, M. MP645
Negro, S. MP223
Neilson, L.J. OP181
Neilson, L.J. PP0019, PP0726
Neiva, F. OP208
Nemeth, J. **MP297**
Németh, B. **PP0022**
Nemoto, N. MP178
Nemoto, T. PP0734
Nennstiel, S. PP0930

Neo, C.H. PP1068
Neo, E. MP478, MP589
Neri, B. MP607, PP0426, **PP0427**, PP0621, PP0629, **PP0917**
Neri, M. MP261
Ness-Jensen, E. **OP003**, **MP657**, MP658
Neto, A. PP0164
Netzer, P. PP0074
Neu, S. PP1122
Neuberg, J. PP0651
Neufert, C. MP572
Neuhaus, H. OP112, MP324
Neuhaus, K. OP094, MP143
Neuhauser, M. MP638
Neuman, S. MP592
Neumann, H. OP126
Neumann, J. OP182
Neumayer, D. MP173
Neurath, M.F. MP462, PP0529
Neverovskiy, A. **PP0781**
Neves, J. MP286, PP0526, PP0552, PP0826, PP0827
Neville, A. PP0564
Newsome, P. MP527
Newsome, P.N. MP236, MP528
Newsome, P.N. OP058
Nezu, R. PP0432
Ng, C.W. PP1068
Ng, C.E. MP166
Ng, H.Y. OP010
Ng, J. PP1099
Ng, W.K. PP1068
Ngamchokwathana, E. **PP0872**
Nghiem, E. MP483
Ngo, O. MP517, MP587
Ngollo, M. PP0395
Ngu, N. **MP074**
Nguyen, C. MP568
Nguyen, D. MP118, MP450, PP0635, **PP0643**
Nguyen, H.T.T. MP402, PP0363
Nguyen, H. MP568
Nguyen, N.Q. MP478, MP589, PP0077
Nguyen, P.B. PP0265
Nguyen, T.H.T. PP0265
Nguyen, T.T. PP0265
Nguyen, T. PP1011
Nguyen, V.A. PP0632, PP0646
Nguyen-Cleary, T. OP207, MP493
Nguyen-Khac, E. MP185, MP634
N. Hader, S. MP332
Ni, L. OP010
Ni, P. OP047
Nicholls, S. MP527
Nicholson, B.D. MP519
Nicholson-Scott, L. MP287, MP608
Nicola, D. OP221, PP0723, PP0882, PP1095
Nicolas, I. OP043
Nicolau, A. **PP0489**, PP0653
Nicolay Maneru, J. PP0076
Nicoletti, A. MP645
Nicoletti, L. PP1053
Nicoletti, R. MP714
Nie, J. **MP143**
Nie, S. OP201, **MP087**, MP089, PP1146
Nieber, K. PP0041
Nielsen, K.R. OP017, MP507
Nielsen, L.B.J. OP168
Nielsen, S.H. MP565
Nielsen, T.S.S. OP161
Niemarkt, H.J. MP573
Nieponice, A. OP050
Nierhoff, D. PP0984, PP1048
Nieto-Garcia, L. OP043, MP640, MP649, PP0424
Nieto-García, L. PP0373
Nieto Vitoria, M.Á. PP0403
Nieuwdorp, M. OP049
Nieuwenhoven, M.A.v. PP0182
Nieuwenhuijs, V.B. MP705
Nieuwenhuijs, V.B. MP022
Nieuwenhuis, E.A. OP112
Nieuwenhuis, L. MP127, **MP600**
Niewiadomski, O. PP0602
Niezychowski, W. PP0547
Nigam, G. **OP032**, **MP100**, **MP105**, MP108, **MP123**, **PP0539**
Niida, K. PP0153
Niikawa, M. PP0150, PP0160, PP0168
Niimi, A. PP0067
Niimura, Y. **PP0734**, PP0915
Nijkamp, M. MP030
Nikawa, M. PP0151
Nikiforova, Y. MP131
Nikitina, D. MP289
Nikolic, M. MP417, MP552, PP0276, PP1078
Nikolich, A. **PP0578**
Nikolouzakis, T.K. MP062
Nimer, R. PP0341
Nimura, S. PP1207
Ning, J. OP139, **MP370**, **MP459**
Ninomiya, T. PP0158
Niño Ramirez, S.F. PP0268
Nion Iarmurier, I. MP267
Niosi, M. MP632
Nir, E. PP0604
Nishida, A. PP0385, PP0617
Nishie, H. MP032, PP0237
Nishijima, Y. MP332
Nishikawa, T. PP0407
Nishikawa, Y. MP425
Nishimata, N. PP0419
Nishimoto, T. MP036, MP038, MP040, MP404, PP0581, **PP0582**
Nishimura, N. PP0144
Nishino, K. PP0248
Nishiyama, Y. MP460
Nishizawa, T. MP017, PP0847
Nissen, L. PP0484
Nista, E.C. MP645, PP0954, PP1165
Nitcheu, J. OP195, MP689
Nitchingham, D. MP478
Nitride, C. MP652, PP0302
Nitze, L.M. OP058
Niv, Y. PP0272
Niveloni, S. MP045, PP0321
Nixdorf, L. OP186
Noble, A. MP629
Noble, C. PP0579
Nobuto, T. MP242
Noda, H. PP0150, PP0151, PP0160, PP0168
Nogami, A. PP0465
Noguchi, T. PP0432
Nogueira-Rodríguez, A. MP064
Noh, C.-K. MP279, PP0157
Nöhammer, C. MP390
Nøhr*, A.K. OP017, MP507
Nomura, S. OP054
Nomura, T. PP1046
Noorani, A. PP0229
Nopora, K. PP0593
Nordaas, I.K. **MP646**
Nordestgaard, R. OP190
Nordin, A. MP593
Nordio, F. PP0632, PP0646
Noreillie, M.-A. OP143, MP221, MP277, MP282, PP0881, PP0886, PP0889
Noriyuki, T. MP242
Norlin, J. OP058
Norman, G.L. MP045
Norsa, L. PP0433
Norton, B. **OP050**, MP553, **PP0098**, PP0104, PP0240
Norton, C. MP208, PP0434, PP0435
Nose, K. OP231
Nos Mateu, P. OP151, MP151, MP268, PP0404
Noureddin, M. OP059
Nousbaum, J.-B. MP634
Nouso, K. OP035, MP467, PP1013
Novielli, D. PP0463, PP0480
Noviello, D. **OP129**, OP150, MP010, **PP0414**, **PP0629**
Novovic, S. OP168, MP300
Nowicki-Osuch, K. MP374
Nseir, M. PP0808
Ntelis, V. MP676, PP0568
Ntuli, Y. PP0524
Nüchter, A. PP0899
Numata, Y. **MP475**
Nunes, G. PP0033
Nunes Yoshio Yoshihara, R. PP0340
Nunez, E. PP0268
Nuñez, P. PP0084
Núñez, Ó. OP009, MP428, MP433, MP547, PP0271, PP0273
Núñez, P. MP339
Núñez Martínez, O. MP427
Nuñez Ortiz, A. OP213
Núñez Ortiz, A. MP510
Núñez-Torvisco, S. PP0391
Nurcis, J. **PP0942**
Nuzzo, A. OP157, MP156, PP0349, PP0377, PP0483
Nysen, O.P. PP0275, PP0280
Nysen*, O.P. **PP0257**
Nzelu, D. OP176
O
Oakland, K. OP032, MP100, MP105, MP108, MP123, PP0706
Oba, M. OP089
Obaidi, I. MP570
Obediat, M. PP0335
Obeidat, M. MP099, **MP104**, MP194, MP303, MP304, **MP612**, PP1127, PP1129, PP1133, PP1157, PP1180
Obora, A. MP206
Ocaña, T. MP522
Occhionero, A.S. OP096
Ochoa Palominos, A. MP355
O'Connell, F. MP570
O'Connell, J. MP431
O'Connor, A. PP0597
Ocskay, K. MP576, **MP585**, PP0563, PP1119, PP1121, PP1246
Ocvirk, S. OP094
Ocvirk, S. OP030
Oczella, L. MP020
Odeh, S. PP0272
O'Donnell, M. MP651
O'Donovan, M. MP265
O'Donovan, M. MP374, MP376
O'Driscoll, E. PP0457
Oelen, R. MP147
Oeuvery, C. PP0386
Ofosu, A. MP137
Ogasawara, A. PP0114
Ogata, H. OP202
Ogata, N. OP202, PP0738, PP0914, PP0915
Ogawa, Y. OP202, PP0738, PP0914, PP0915
Ogino, T. PP0432
Ogisu, K. MP693
O'Gorman, D.B. MP484
O'Grady, G. PP0059
Ogresta-Kordej, D. PP0541
Ogura, T. OP101, OP231
Oguri, N. **MP178**
Oğuz, D. MP416
Oh, D. MP130
Oh, D.-Y. MP599
Oh, H.-H. **MP018**, PP0839, PP0840
Oh, H.-S. OP092
Oh, J. MP118, MP450, PP0635, PP0643
Oh, K. PP0441
O'Hara, F. MP431, PP0266
O'Hare, C. PP0579
Ohashi, R. MP404
Ohata, K. VC04, PP0133, PP0766
Ohgi, K. MP360
Ohgi, K. MP239
Ohkubo, A. PP0114, PP0172
Ohlsson, B. **PP0807**, **PP0808**
Ohmiya, N. **MP316**, **PP0844**
Ohn, J.H. MP603
Ohno, K. MP238
Ohno, M. PP0385, PP0617
Ohno, T. OP035
Ohta, Y. PP0148, PP0328, PP0462, PP0702, PP0703
Ohtagaki, H. MP242
Ohtsuka, H. MP242
Ohtsuka, K. OP202
Ohyama, H. OP231
Oka, P. **MP255**, **PP0333**
Oka, S. MP227, MP457, PP0432, PP0444, PP0844, PP1240
Okabayashi, K. PP0432
Okabe, Y. MP693
Okada, M. PP0153
Okamoto, H. PP0234
Okamoto, K. PP0432
Okamoto, K. PP0601
Okamura, T. PP0103
O'Kane, C. PP0545, PP0616
Okanou, S. PP0120
Okanoue, T. MP524
Okasha, H. PP0201, PP1171
Okazaki, K. MP350
Okdahl, T. MP168, PP0046, PP0918, PP0919
O'Keefe, A.-M. PP0499
Okimoto, K. MP437, MP667, **PP0148**, PP0328, PP0462, PP0702, PP0703, PP0735
Okita, Y. PP0432
Okitsu, R. PP0172
Okolicsanyi, S. **PP1053**
Okuda, A. OP231
Okuda, J. PP0432
Okuda, Y. OP087
Okujima, Y. MP475
Okumura, T. OP091, PP0914, PP0915
Okuno, M. OP231, MP181, MP302, MP423
Okusa, K. PP0125
Okutomi, M. PP0149
Okuwaki, K. PP1098
Okuwobi, K. PP0524
Okuyama, S. PP1038
Okuzono, T. **MP703**, PP1153
Olabinatan, O. OP143, MP221, MP277, MP282, PP0854, PP0879, PP0881, PP0886, PP0889
Olah, F. MP354
Olah-Varga, K. MP447
Olawuyi, D. PP0835
Oldenburg, B. PP0379
Oldenburg, L. OP147, MP390, **PP0503**
Oleas, R. MP407
Oleksiw, M. **OP124**
Olén, O. OP214
Olesen, S.S. OP230, PP0323, PP0775, PP0777
Olfati, H. PP0092
Oliferuk, N. PP1232
Oliva, S. OP210, **MP492**, PP0076, PP0491
Oliva Escudero, G. MP452, PP0399
Olivares, D. PP0684
Oliveira, A.M. PP0827, PP1212
Oliveira, B. MP690, MP698
Oliveira, E. PP0343
Oliveira, J. PP0747
Oliveira, R. OP169
Oliveira, S. MP118
Oliveira, T. OP036
Olivera Sendra, P. MP387
Oliveras Font, B. PP0755
Olivier, R. MP285
Olivieri, S. MP073

- Ollech, J. PP0553
 Ollech, J.E. MP273
 Olsen, B.C. PP0417
 Olthoff, K.M. MP600
 Oliveira Martín, A. OP184
 Om, R. MP101, PP0152
 O'Mahony, C. **MP114**
 Omar, A. PP0214
 Omary, M. PP0228
 Omatsu, T. MP206
 Omer, H. MP453
 Omichessan, H. PP0407
 O'Morain, C. MP427
 O'Morain, C. OP009, MP319, MP428, MP433, MP547, MP549, MP552, PP0271, PP0272, PP0273, PP0275, PP0276, PP0277, PP0280, PP0285, PP0289
 Omori, J. MP036, MP040, MP404, PP0150, PP0151, PP0160, PP0168, PP0582
 Omori, J. MP038
 Omori, T. MP316
 Omoto, S. OP014, OP231, MP302, MP423
 On, A. MP296, PP1067
 Onali, S. OP106, OP150, MP625, PP0378, PP0418, PP0476, PP0629
 Onana Ndong, P. MP440
 Onda, T. PP0150, PP0151, PP0160, PP0168
 O'Neill, G. PP1226
 Ong, E.J.S. PP0602
 Ong, S. PP0674
 Oniciuc, O. PP1204
 Onidi, F.M. PP0442
 Onnekink, A. MP022, **MP082**, **PP1155**
 Ono, A. MP014
 Ono, K. PP0133
 Ono, M. PP1046
 Ono, M. PP0216
 Ono, S. PP0216, **PP1228**
 Oomkens, D. **PP0567**
 Ooms, A.H.A.G. OP188
 Oortwijn, A. PP0447, PP0605
 Oosera, S. PP1196
 Oosterlinck*, B. PP0012
 Opheim, R. OP021, MP341, PP0417
 Oppong, K. MP132
 Oppová, D. PP0097
 Opuni, K. **MP524**, **MP528**, **PP0955**
 Orbosuè, F. PP0132
 Ordás, I. OP026, OP187, MP149, PP0403
 Ordell Sundelin, E. PP0805
 Ordoñez, I.T. PP1050
 O'Regan, P. PP1030
 Oregel-Aguilar, V. MP554
 Oregui, M.E. PP0321
 Orejudo, M. MP503
 Orejudo del Río, M. OP023, **PP0362**, PP0364, PP0381, PP0382
 Oresic, M. OP004
 Orfanidou, A. PP0583
 Orfanoudaki, E. MP676
 Orgler, E. MP298
 Oriol- Escudé, M. MP159
 Orlandini, B. OP175
 Orlando, A. OP106, PP0452, PP0476, PP0629, PP0645, PP0670
 Ormanns, S. MP644
 Ormos, R. PP1135
 Orobitg, J. PP0585
 Orrù, G. **PP0442**
 Orsi, G. MP480, MP583
 Ortega, G.J. PP0273
 Ortega, H. MP668
 Ortega, L. MP071
 Ortega, S.P. MP031
 Ortega-Suazo, E.J. MP103, MP107, MP291, PP0016, PP0018
 Ortiz de zarate, J. MP510
 Ortiz Fernández-Sordo, J. OP038, OP112
 Ortiz-Fernández-Sordo, J. MP494
 Ortiz Fernández-Sordo, J. PP0068
 Ortiz-Olvera, N. MP429, MP430
 Ortiz-Polo, I. OP009, MP549
 Ortonne, N. PP0321
 Oruç, N. MP416
 Orzan, R.-I. PP1182
 Orzan, R.I. MP424
 Orzeszko, Z. **OP125**
 Osagiede, O. PP1057, PP1058
 Osama Yehia Ibrahim, D. PP0032
 Osawa, M. PP0158
 Osborne, R. MP322
 Oshita, A. MP242
 Osina, O. PP0065
 Osipenko, M.F. PP0280
 Oskrochi, R. PP1191
 Osmanovic, A. PP0276
 Osmanović, A. MP552
 Oßwald, A. **OP030**, OP094
 Ostanin, D. OP025
 Osterman, M.T. OP085, MP680, MP681, MP684
 O'Sullivan, C. PP0457
 O'Sullivan, J. MP570
 O'Sullivan, T. MP284, PP0769, PP0890
 O'Sullivan, T. MP065, MP069, MP371, MP381, PP0179, PP0184, PP0876, PP0891, PP0892
 Ota, S. OP014
 Otaegui-Campos, E. **OP141**
 Otake, Y. OP089
 Otani, Y. **PP0559**, **PP0655**
 Otero, E. MP429, MP430
 Otero, L. MP429, MP430
 Otero, W. MP429, MP430
 Otero-Fraga, M.J. MP643, MP647
 Otero_iglesias, M. MP537
 Otero-Iglesias, M. PP0615
 Othmane, D. PP0201
 Otoya, G. MP429, MP430
 Otsuka, M. MP321, MP461, PP0120
 Otsuka, S. MP239, MP360
 Ou, W. PP1223
 Ouahid, S. MP375, PP1214, PP1215, PP1238
 Oualaalou, S. MP375, PP1214, PP1215
 Ouaya, H. MP131
 Oubaha, S. PP0202, PP0662, PP0682, PP1065
 Oubella, H. **PP0681**
 Oudijk, L. OP188
 Oudkerk Pool, M. OP162
 Oumrani, S. PP0185
 Ouziel, R. MP328
 Ovadia, B. PP0723
 Overbeek, K. OP170
 Overdevest, A. **MP702**
 Overwater, A. OP116
 Ovesen, P.D. OP190
 Ovidi, F. MP092, MP263, MP662, MP663, MP727
 Owada, S. PP1228
 Owen, C. OP131, PP0560
 Owen, C. PP0479
 Oyama, K. PP0686
 Oyama, T. **MP498**, MP501
 Oyama, Y. PP0462, PP0702, PP0703
 Oza, V. **PP0210**
 Ozawa, S. PP0125
 Ozawa, Y. PP0234
 Ozeki, Y. PP0462, PP0702
 Ozturk, O. PP0527
 Ö
 Öberg, L. PP0075
 öğütmen koç, D. MP416
 Öhlund, D. MP590
 Öhman, L. OP021
 Özçelik, M. **MP016**
 Özdemir, P. PP1205
 Özdoğan, O. MP416
 Özşeker, B. MP416
 Østergaard, L.H. MP236
 Østergaard, M. PP0411
 Østvik, A.E. PP0367
 Østvik, A.E. PP0445
 P
 Pabon, V. MP544
 Pabón-Carrasco, M. OP009, MP427, MP428, MP433, MP547, MP549, PP0271, PP0273
 Pacheco, N. PP0084
 Pachiadakis, I. MP676, PP0568
 Pachler, F. OP190
 Pachón Martínez, C. **PP1005**
 Padalko, E. PP0494
 Padia, G. PP1066
 Paduano, D. MP137, PP0707, PP1209
 Padulles, N. PP0585
 Paez A., M. MP191
 Paez Cumpa, C.I. MP552
 Paéz Cumpa, C. PP0276
 Pagadapelli, A.A. PP0766
 Pageaux, G.P. MP634
 Pager, S. PP1225
 Paggi, S. MP063
 Pagliaro, M. MP716
 Pagoni, A. PP0466, PP0728
 Pahomeanu, M.-R. **PP1132**
 Pai, R. OP131, PP0560
 Paiella, S. OP136
 Paik, W.H. **MP025**
 Pais, M.T.d.A.P. PP0093, PP0255
 Pajancic, L. MP465
 Pajares, R. OP043, MP508
 Pajares Villarroja, R. OP009, MP428, MP549, MP674
 Pala, V. PP0348
 Palac, H. MP333
 Palaga, A. PP0311
 Palaga, M. PP1204
 Palarasah, Y. PP0360
 Palatianou, M. MP676, PP0568
 Palau, R. PP0493
 Palinkas, D. MP379, **PP0021**
 Pallagi, P. OP015, OP197, MP446, PP0520, PP0811, PP1120
 Pallah, O. PP0010
 Pallares Manrique, H. OP023, MP503, PP0364, PP0381
 Palle, M. MP524
 Palle, M.S. OP058
 Palleschi, C.V. PP0672
 Pallotta, L. PP0324
 Palm, C. OP206, MP377, MP380
 Palma, C. PP0033
 Palma, C.S. **MP346**, MP530
 Palma, P. MP625
 Palmela, C. MP005, PP0468, PP0532, PP0751
 Palmeri, E. **VC06**
 Palmisano, C.M. **PP0463**, **PP0480**
 Palo, M. PP0013
 Palomera, E. PP0049
 Palomino, L. **MP343**
 Pålsson, O.S. OP119, MP164, PP1186, **PP1230**
 Palucci, I. PP0393
 Palumbo, C. **PP0007**, PP0325
 Palumbo, D. MP027
 Palumbo, G. PP1165
 Pan, S. MP494
 Pan, W. PP0264, PP0281, PP0282
 Pan, X. MP500
 Panaccione, R. OP042, **OP083**, OP103, **OP104**, OP212, **MP327**, MP617, MP619, MP623, MP671, MP672, MP686, PP0547, **PP0594**
 Panagaki, A. MP134
 Panait, R. MP586
 Panaitescu, A.-O. **MP182**
 Panattoni, L. PP0548
 Panceri, R. PP0470
 Pancheva, R. PP0338
 Pancieri, R. PP0433
 Panda, P. PP0394
 Pandanaboyana, S. OP168, OP229, MP186, MP298, PP1124
 Pandolfi, M. MP607
 Pandur, T. PP0420
 Panés, J. OP082, OP084, **OP102**, OP103, **MP619**, MP670, MP671
 Panés, J. OP026, MP672
 Pang, S.K. MP142
 Pani, G. PP0393
 Panic, N. MP310, MP480, MP606
 Panlilio, M.T. MP635
 Panni, T. OP212, PP0594
 Pannikodu, L. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211
 Panseri-Rodrigues, R. MP365, PP0093, PP0255
 Pantic, I. **MP201**, PP0985
 Pantzios, S. PP1015
 Panzer, M. OP183
 Panzeri, V. PP1154
 Panzini, B. OP124
 Panzuto, F. MP241, PP1092, PP1170, PP1173
 Papa, A. MP269, PP0613, PP0637, PP0654, PP0656
 Papadakis, S. PP0245
 Papadopoulos, N. MP695
 Papadopoulou, A. OP208
 Papaethymiou, A. OP050, PP0098
 Papaethymiou, A. MP553, PP0104, PP0240
 Papagiouvanni, I. PP0743
 Papamichael, K. PP0553
 Papanikolaou, I.S. **PP1177**
 Papastergiou, V. PP0330
 Papathanasiou, E. MP290
 Papathanassiou, E. MP676, PP0568
 Papatheodoridis, G. MP676, PP0048, PP0073, PP0089, PP0568
 Papaxoinis, K. PP0073, PP0089
 Pape, U.-F. MP141
 Papovic, V. MP588
 Papp, A. MP447
 Papp, M. MP179, MP354
 Papp, R. MP304, PP1129, PP1180
 Papp, V. MP048, MP251, MP433, MP552, PP0276
 Pappalardo, V. OP113, MP367
 Papparella, L.G. MP514
 Pár, G. MP048
 Paradiso, S. **OP064**
 Paranandi, B. MP296, PP1067
 Paraskeva, K.D. **MP134**, MP676, PP0568
 Paraskevopoulos, P. **MP194**
 Paraskevopoulou, A. MP134
 Paraskevopoulou, M.D. **OP025**
 Paraskevopoulou, P. MP134
 Paratore, M. **MP645**
 Parayitam, V. PP0897
 Parc, Y. MP274
 Pardi, D. MP214
 Paredes Arquiola, J.M. PP0451
 Parekh, D. **VC04**, **PP0766**
 Parent, E. PP0778
 Parente, J.M. PP0340
 Parfenov, A. PP0322
 Parfitt, H. PP0545, PP0616
 Parian, A. PP0521
 Parigi, T.L. MP152, MP388, MP511, **PP0431**, PP0517, **PP0626**
 Parihar, V. PP0222
 Parikh, R.C. PP0085
 Parisi, I.M. MP540
 Parisi, M.I. MP013

Parisio, L. MP006, MP269, PP0613, PP0637, PP0654, PP0656
 Park, B.K. MP066, PP0143
 Park, D. **OP165**
 Park, G. OP149
 Park, H. MP546
 Park, H. **MP096**
 Park, J.J. OP165, PP0733, PP0909
 Park, J.Y. **PP0199**
 Park, J. MP183
 Park, J.Y. MP482
 Park, J. PP0733, PP0909
 Park, J.H. PP0441
 Park, J. PP0623
 Park, J.H. MP279, PP0157
 Park, J.S. **MP279**, PP0157
 Park, J.C. PP0110
 Park, J.-H. MP0208, PP1004, PP1045, PP1115
 Park, M.H. MP096
 Park, S.H. PP0441
 Park, S. PP1039
 Park, S.W. PP0558
 Park, S. OP092
 Park, S.W. MP482
 Park, S.J. **PP0558**, PP0733, PP0909
 Park, S.J. MP096
 Park, S.C. PP0006
 Park, Y.S. MP603, PP0126
 Park, Y.-S. MP551, PP0131
 Park, Y. **PP0208**, **PP1004**, PP1045, **PP1115**
 Parker, J. OP177
 Parkes, G. OP103, MP327
 Parkes, M. PP0434, PP0435
 Parkman, H.P. PP0053
 Parks, M.L. MP387
 Parmentier, F. PP0651
 Parmigiani, M. PP0082
 Parmley, S. MP448
 Párnitzky, A. MP576, MP585, PP1119, PP1121, PP1246
 Parodi, A. MP540
 Parola, I. MP586
 Parola, M. PP0942
 Paroni, M. OP129
 Parra, P. OP009, MP427, MP428, MP429, MP430, MP433, MP547, MP549, MP552, PP0271, PP0272, PP0273, PP0275, PP0276, PP0277, PP0280, PP0284, PP0285, **PP0286**, PP0289
 Parra, R. PP0340
 Parra-Blanco, A. PP0165, PP0768
 Parra Izquierdo, V. PP0422
 Parry, S. PP0711
 Parsa, N. MP380
 Parshutin, S. PP0279
 Partanen, J. MP593
 Paschos, P. MP692, MP695
 Pascual, I. PP0493
 Pascual-Moreno, I. PP0008
 Pascual-Moreno, I. OP151, MP268
 Paspatis, G.A. PP1177
 Pasquali, E. MP057
 Pasquinelli, G. PP0779
 Passaretti, S. MP090, MP260, MP261
 Pasta, A. MP256, **PP0652**
 Pastore, M. PP0433
 Pastorelli, L. OP150
 Pásztor, G. MP048
 Pata, F. MP151
 Patankar, J. PP0372
 Patel, A.E. PP0680
 Patel, A.S. PP0955
 Patel, A. PP1094
 Patel, C. OP217, PP1084
 Patel, C. MP326
 Patel, F. PP0293
 Patel, H. MP183
 Patel, H. PP0845
 Patel, K.V. MP326
 Patel, K. OP038
 Patel, L. PP0700
 Patel, L. PP0369
 Patel, M. PP0879
 Patel, N. OP217, PP1084
 Patel, P. PP0784
 Patel, R. PP0437
 Patil, M. MP115, **MP177**
 Patita, M. PP0033
 Patrick, D. PP0678
 Patrón, O. MP031
 Patrón Román, G.O. MP549
 Patruno, C. PP0086
 Patterson, K.R. MP183
 Pattni, C. MP554
 Pattynama, L. **PP0162**
 Pauker, M. OP093
 Paul, S. OP189, PP0608
 Pauling, J.K. MP143
 Paulis, M. MP571
 Paulissen, J. OP046, MP623
 Paulsen, V. MP044
 Paupard, T. MP634
 Pausawasdi, N. PP0201
 Pavagada, S. OP063, MP712
 Pavan, C.R. MP102
 Pavel, V. PP1218
 Pavelcova, J. PP0580
 Pavic, T. MP417
 Pavlenko, A. PP0406
 Pavlenko, N. **MP230**
 Pavlenko, V. **PP0406**
 Pavlidi, A. **MP328**
 Pavlovic, S. PP0763
 Pavoni, M. OP009, MP427, MP433, MP549, MP552, PP0271, PP0276, PP0285
 Pawlak, K. MP298, PP0877
 Pawlewicz, K. PP0112
 Payer, J. PP1233
 Pazenko, E. **PP1035**
 Pazo Mejide, P. MP428
 Pazos, A. MP544
 Pazos, A.J. PP0290
 Pazos-Randulfe, Y. MP643, MP647
 Peaucelle, A.S. PP0608
 Pecere, S. MP011, MP514, MP714
 Pech, O. OP112, OP126, MP280, MP317, PP0845
 Peck, V. PP0077
 Pecorella, G. PP0450
 Pécsi, G. PP0022
 Pedersen, N. MP149
 Pedicelli, A. PP0706
 Pedrero Leparmentier, N. PP0403
 Pedroto, I. MP386, MP414
 Peerally, M.F. PP1206
 Peeters, K.C.M.J. PP0484
 Peeters, R. OP158
 Pegatraju, K.B. **PP0027**
 Pehrsson, M. OP024, OP172, **MP565**, PP0502, PP0509
 Peiris, M. OP053, MP384
 Peiró García, E. PP0451
 Peisl-Gunckel, M. PP0974
 Peixe, B. PP0774
 Pela, T. MP487, MP490, MP492, PP0085
 Peláez Luna, M.C. MP419
 Pelajic, S. MP417, PP0541, PP0863, PP1078
 Pelizzaro, F. PP0013, PP0880
 Pelizzo, P. PP0132
 Pellacani, A. MP057
 Pellat, A. PP0185
 Pellegatta, G. MP662, PP0076, **PP0166**
 Pellegrini, C. PP0782
 Pellegrini, E. OP034
 Pellegrini, V. MP223
 Pellegrino, S. PP0433
 Pellicano, R. PP0285
 Pellino, G. MP131, MP151
 Pellisé Urquiza, M. OP123
 Peña Aldea, A. PP0008
 Penagini, R. MP256, MP491, PP0078, PP0094, PP0095
 Peñalva Peñas, M. PP0585
 Peñarrubia, L. PP0688
 Peng, C.-Y. MP363
 Peng, C. PP0618
 Peng, L. OP100, MP626, PP0170, PP0455
 Peng, P. MP026
 Peng, S. PP0083
 Peng, Y. PP0943
 Pennant, T. MP258
 Penny, H.A. PP0304, PP0305
 Penz, D. **PP0741**, PP0902, PP0904
 Peon-Gonzalez, J. PP0424
 Peranathan, V. MP069, **PP0071**, PP0179, PP0876, PP0891, PP0892, PP1199
 Peraro, L. PP0752, PP0880
 Perbellini, R. MP466
 Perdigoto, D. OP036, MP079, MP555, PP1072
 Perée, H. OP019
 Pereira, A.C. MP373, PP0739
 Pereira, B. MP155, MP266, PP0659
 Pereira, J. PP0429
 Pereira, J. PP0826
 Pereira, J.P. PP0895
 Pereira da Costa, C. MP393
 Perelló, M.A. PP0076
 Perelló Juan, A. MP552, PP0276
 Pererva, L. **PP1142**, **PP1158**
 Peres da Costa Duarte, C. PP1136
 Peres Piva, T. PP1070, PP1136, PP1175, **PP1178**
 Peresztegi, M.Z. MP048, **MP251**, PP0306
 Perez, A. MP407
 Pérez-Aísa, Á. OP009, MP427, MP428, MP433, MP547, MP549, PP0271, PP0273
 Pérez Álvarez, J.C. PP1005
 Pérez-Calle, J.L. OP151, MP268
 Perez-Cuadrado-Robles, E. MP193, PP1100
 Pérez-Galbarro, C. MP159
 Pérez-Galindo, P. OP187
 Pérez-Guasch, M. MP071
 Pérez Ibáñez, A.A. PP0451
 Pérez-Martínez, I. OP187, OP213, MP343, PP0076
 Pérez-Roldán, F. OP191
 Pérez Torrado, V. OP151, MP268
 Perez Useche, H.M. PP0268
 Pérez Valle, I. MP428
 Perillo, F. MP010
 Perini, B. MP084
 Perk, L. OP225, MP022
 Perkhofer, L. OP062, OP200, MP088, MP481, PP1137, **PP1152**
 Perl, T. PP0230
 Perminow, G. PP0417
 Perna, F. PP0672
 Pernanathan, V. PP0769
 Perona, M. OP009, MP428, MP433, MP547, PP0273
 Perona Vincenti, M.C. MP427
 Perreault, N. PP0387
 Perretta, S. **MP361**, MP502
 Perri, V. MP539
 Perrod, G. MP068
 Pertsinidou, E. **OP021**
 Perus, O. PP0653
 Pesatori, A.C. PP0414
 Pesce, M. **MP716**, MP729, PP0086, PP0087
 Pesi, A. **OP005**
 Pessarelli, T. PP0327, PP0414, **PP1200**
 Peter, I. PP0422
 Péter, Z. PP1069
 Péterffy, A. PP0075
 Peters, D.E. PP0521
 Petersen, A. OP085, MP683, MP684, PP0549
 Peterson, K. MP487
 Petishko, O. PP0960, PP0962
 Petito, V. MP624, PP0393
 Petkevicienė, J. MP545, PP1031
 Petkova, Y. PP1064, PP1090, PP1183
 Petlenko, S. PP0292
 Petlickij, F.H. PP1126
 Petrakis, I. MP042, PP0308
 Petrella, C. PP0392
 Petreska, A. PP1183
 Petrolis, R. PP0357
 Petrone, M.C. MP024
 Petroniene, R. PP0556
 Petrov, M. PP0338
 Petrov, V. OP019
 Petrucci, L. PP0958
 Petruzzellis, C. PP1209
 Petruzzello, C. PP0621
 Pettengell, C. MP154
 Pettold, G. OP229
 Peyrin-Biroulet, L. OP045, OP079, OP082, OP083, **OP084**, OP105, OP195, **MP119**, MP152, MP387, MP388, MP393, MP511, MP617, MP618, MP622, MP630, MP670, MP688, MP689, PP0386, PP0407, PP0431, PP0517, PP0550, PP0553, PP0556, PP0565, PP0588, **PP0589**, **PP0595**, PP0605, PP0620, PP0626, **PP0646**, PP0651
 Pferschy-Wenzig, E.-M. MP579
 Pfister, A. OP018
 Pfisterer, N. MP638
 Pfuetzenreiter, V. PP0725
 P. Gisbert, J. OP009, OP046, MP151, MP339, MP343, MP428, MP429, MP430, MP433, MP547, MP549, MP552, PP0271, PP0273, PP0276
 P. Gisbert*, J. OP187, MP503, PP0277, PP0362
 Phaleng, X. MP385
 Pham, H.P. PP0395
 Pham, K.D.-C. MP137
 Pham, S.T.D. PP0360
 Phathong, C. MP231
 Philipp, V. MP298
 Philippe, A.-s. MP440
 Philippou, E. PP1235
 Philips, C. OP077
 Phillip, V. OP229
 Phillips, M. OP016
 Phillpotts, S. MP132
 Philpott, H. OP207, MP493
 Phonekeo, K. MP528
 Phull, P.S. MP433, PP0271
 Phuong Pham, H. OP110
 Piagnani, A. MP063
 Piazza, A. PP0099
 Piazza O Sed, N. OP129
 Piazzesi, A. MP624
 Piazzolla, M. PP0017, PP0269
 Pibiri, P. **OP071**
 Picard, O. MP592
 Piccioli, A. MP223
 Pieptu, A. PP1204
 Pierik, M. OP086, PP0484
 Piermarini, L. **MP415**
 Pierson, A.J. MP573
 Pietrangelo, A. PP1235
 Piggott, M. MP570
 Pignata, L. **PP0139**
 Pigò, F. MP562
 Pígoni, A. PP0471
 Píjoan Comas, E. OP191, **PP1172**
 Pilati, P. MP223
 Pilavaki, P. PP0227
 Pillay, L. MP326
 Pilonis, N. OP123, OP126, **OP178**, MP374, PP0112
 Pillozzi, E. PP0893

- Pimentel, J. MP555
Pimentel, R. MP555
Pimentel-Nunes, P. **MP365, PP0093, PP0255**
Pin, N. MP064
Pinar, I. **OP161**
Pinard, F. MP285
Pineda, J.R. MP334
Pineda, M. MP522
Pineda Chavez, S.E. **MP390**, MP571
Piñero, C. MP510
Piñero, G. **OP151, MP268, MP334**
Pineton de Chambrun, G. MP630
Pinheiro, I. MP582
Pinheiro Machado de Carvalho, S. PP1070, PP1136, PP1175
Pinho, R.T. PP0661
Pinkas, M. OP055
Pinkey, T. MP151, PP0821
Piñol, V. MP522
Pinter, M. MP465
Pintér, J. MP297, MP379
Pinto, F. MP659, PP0347
Pinto, N.A.J. **PP0725**
Pinto Marques, P. PP0033
Pinto-Pais, T. MP365
Pioche, M. MP068, MP285, MP318, MP440, PP0849, PP0877
Piqué-Borràs, M.-R. **PP0047**
Piqueras, M. OP043
Piqueras Cano, M. OP187, OP213, MP343, MP508
Pirola, L. PP0470
Pironi, L. MP141, PP0298
Pirozzolo, G. MP223
Piruzza, A. OP054, MP395, MP398, PP0132
Pisani, A. MP131
Pisani, F. MP663
Pisano Puchois, V. OP110
Piscaglia, F. OP034
Pisciotta, L. PP0652
Piscitelli, E. MP287, MP608
Piscovets, V. MP566
Piscoya, A. MP429, MP430
Pitanga-Lukashok, H. MP109, MP191, MP359, MP407, MP554, PP0204, PP1118
Pitotti, G. MP573
Pituti, H. PP1204
Pivetta, G. PP0007, PP0325
Pivorunas, V. OP129
Pizarro, M. MP429, MP430
Pizarro, T.T. MP008
Pizzicannella, M. MP502
Pizzolante, F. PP0958
Plachta-Danielzik, S. MP329
Planella, M. OP009, MP428
Planella de Rubinat, M. PP1172
Plant, E. MP556
Plastaras, L. MP002
Platt, A. PP0075
Plaza Santos, M.d.R. PP0403
Plehhova, K. **MP262**
Plevris, N. OP0579, PP0674
Plomteux, O. MP285
Płoszaj, P. MP543, PP0252
Plotogea, O.M. PP1204
Pluth, M.D. MP199
P. Nyssen, O. **OP009, MP427, MP428**, MP429, MP430, **MP433, MP547, MP549**, MP552, **PP0271**, PP0272, **PP0273**, PP0276, PP0277, PP0284, **PP0285**, PP0289
P. Nyssen*, O. PP0286
Podmanicky, D. PP0679
Pohl, D. PP1245
Pohl, H. OP124, PP0877, PP0884
Pöhler, A.-M. MP682
Pöhlmann, D. PP0369
Pohnan, R. PP0759
Poincloux, L. PP1100
Pojoga, C. MP424, PP0976, PP1182
Pojskic, N. MP035
Pokharel, A. PP0906
Polák, D. PP1113
Polaka, I. PP0096, PP0238, PP0279
Polat, M. MP416, PP1083
Polavarapu, J. **PP0700**
Poletti, V. MP584
Poletto, E. **MP395**, MP398
Poley, J.W. MP022
Poliani, L. PP0135
Policar, C. PP0395
Polishchuk, S. PP0781, PP0857, PP0866
Pollard, K.S. MP143
Polymeropoulos, C. PP0042, PP0057, PP0058
Polymeropoulos, M.H. PP0042, PP0057, PP0058
Pomej, K. MP465
Pompili, M. PP0325
Pompili, M. PP0958
Poncela, M. OP043
Ponce Romero, M. PP0008
Pone, E. PP0571, PP0572, PP1187
Ponferrada, Á. MP674
Ponferrada Díaz, Á. MP510
Ponferrada-Díaz, Á. OP043, OP151, OP187, MP268
Ponich, T. PP0627
Ponnusamy, S. MP394
Ponomarenko, V.A. PP0254
Pons, M.T. MP071
Ponsioen, C. OP031
Ponsioen, C.Y. PP0815, PP1138
Ponte, A. MP169, MP520, PP0661
Ponte, S. **MP386**, PP0827
Pontecorvi, V. MP311, MP605, PP0247
Pontillo, G. PP1009
Pontone, S. PP0023
Ponz de Leon Pisani, R. MP024, MP244, MP583
Ponziani, F.R. OP034, MP455, PP0082
Poortmans, P.J. **VC02**, VC08, MP019, **PP0730**, PP0838, **PP0850**, PP0853, PP0895
Pop, A.-V. OP117, PP0805
Popa, I.V. PP0536, PP1204
Popa, S.-L. PP0793
Popescu, A. PP1204
Popova, S. PP0338
Popovic, D. PP0578
Popp, A. PP0311, PP0312
Popp, C. MP538
Porcari, S. OP096, MP577
Porcedda, C. PP0378
Porretta, F. MP271
Portela, F. PP0365
Portincasa, P. PP1235
Porto-Silva, M.d.S. MP640, MP649, PP0373, PP0424
Portugal, M. PP0708, PP0774
Poscia, A. PP0393
Pose, E. MP071
Possemiers, S. OP081, OP156, MP582
Posteraro, B. MP577
Potjer, T. MP082, PP1155
Potts Bleakman, A. OP212, PP0594
Pouillon, L. OP169
Poulsen, A. **OP190**, OP204, PP0502, PP0607
Pourcel, G. PP0595
Pourrastegar, A. MP303
Pouw, R.E. OP112, OP116, MP039, MP317, MP717, PP0162, PP0167
Powell-Brett, S. OP016
Poyatos García, P. **PP0008**
Poza Cordon, J. PP0469
Pozo Blanco, A.B. OP009, MP428
Pozza, A. MP223
Pozza, G. MP223
Pradeep, G. PP0547
Prado, L. MP365
Prado Castro, L. PP0093, PP0255
Prager, G. OP186
Prahm, A.P. MP298
Prajapati, R. **OP217, PP1084**
Prasad, A. PP1037
Prasad, K.K. MP004
Prat, F. MP318
Prata, A. PP0986, PP1001, PP1002, PP1023, PP1027, PP1103, PP1105, PP1106
Prata, A.A. MP679
Prata, A.A. MP331, MP464, PP0649, PP0650, PP0907, PP0982, PP0988
Prata, R. OP148
Preatoni, P. MP027
Prendiville, C. PP0499
Prestel, J. PP0698
Previtera, M. MP136
Priadko, K. MP549, MP552, PP0276, PP0452
Pricci, M. PP0269
Pricope, D. PP0518
Prieto Aparicio, J.F. MP284
Primas, C. PP0390
Principi, M.R.D. PP0463, PP0480, PP0629
Prins, F. **PP0379, PP0490**
Prinsen, J. PP0691
Privitera, G. **OP150**, MP008, **PP0639**
Probst, A. OP206, MP377
Procopet, B.D. PP0976
Pronio, A. PP0023
Pronk, A.J. PP0484
Pronk, A.M.C. PP0641
Prood, N. PP0548
Prosenz, J. PP0020
Prószéky, K.G. MP379
Prothe, C. **PP0398**
Protic, M. OP128, OP131, PP0550, PP0560, PP0562, PP0565
Protopapa, N. PP0743, PP0991
Protopapas, A. **MP290**, MP676, PP0568, **PP0743, PP0991**
Protopapas, A. MP290, MP676, PP0568, PP0743, PP0991
Prueksapanich, P. PP0989
Prujt, M. MP390, PP0464, **PP0504, PP0540**
Prüß, M. PP0372
Prystaia, A. PP0866
Przepióra, A. PP0697
Pu, L.Z.C.T. PP1099
Puca, P. MP269, **PP0393**, PP0613, PP0637
Puccetti, F. MP722
Puchois, V. OP027
Puebla, R.A. PP0321
Puente Ubierna, N. OP208
Puga, M. MP064
Puga-Tejada, M. **MP109, MP191, MP359**, MP383, **MP407, MP554, MP204**, PP0457, PP0479, PP0482, PP0499, **PP0505, PP1118**
Pugliese, D. OP106, OP150, OP169, MP006, MP269, PP0393, PP0613, PP0637, PP0639, PP0654, PP0656
Pugliese, F. MP281
Puig, M. **PP0035**
Puigcerver-Mas, M. MP138
Pukacka, K. PP1145
Pukitis, A. OP169
Pulcini, G. MP645
Pulimood, A. PP0700
Pulwermacher, P. MP634
Pumpo, R. PP0508
Puncochár, M. MP659
Punčochár, M. PP0347
Punin, A. PP1232
Pupo Gomez, D. **PP0387**
Puppe, F. PP0899
Puri, A. MP724
Putignani, L. MP313, MP624, PP0393
Putoto, G. PP0963
Pützfeld, S. PP0685
Putzu, L. PP0427
Puxeddu, I. MP663
Puy Guillén, A. MP673
Puzzono, M. PP0135, PP0348

Q
Qamar, A. **PP0487**
Qarch, I. **PP1164**
Qasim, A. MP484
Qasim, A. PP0289
Qejvani, O. MP131
Qi, J. MP568
Qian, H. PP0753, PP0875
Qiang, Z. MP111
Qin, H. PP0296
Qin, M. MP026
Qin, Y. PP0083
Qiu, R. MP675
Quaglio, D. OP064
Quante, M. PP0388
Quaranta, G. MP577
Quario, L. PP1190
Quarti, L.M. PP0139
Quast, D. MP280
Queiroz, N. PP0422
Queiroz, N.S.F. PP0544
Quek, S. PP0192
Quénéhervé, L. MP285
Quera, R. PP0084
Quertinmont, E. OP019
Quickert, S. PP0984
Quigley, E. PP0220
Quintana, S. MP138
Quintini, D. MP170
Quiroga Pelaez, M. MP527
Quispel, R. MP022, PP1101
Quiñones, M. OP187
Quteineh, A. OP172
Qvigstad, G. OP134, MP085

R
R, S.K. MP633, PP0959
Rabadán Mata, A. PP0451
Rabbat, C. OP195, MP688, MP689
Rabben, H.-L. OP134, MP035, MP085
Rabiega, P. PP0407
Rabiei, M. MP710
Rabinovich-Guilatt, L. MP447
Rabinowitz, K.M. OP093, PP0354, PP0355
Racamier, I. OP209
Racca, F. PP0076
Rachart, A. PP0489
Radadiya, D. PP0845
Radaelli, F. MP063
Rademaker, E. OP226, **MP220**, MP222
Radhakrishnan, S. PP0642
Radia, C. MP326
Radin, A. OP210, MP660
Radocchia, G. MP261
Radochova, V. PP0225
Radojevic, D. PP0763
Radouane, I. PP1238
Radwan, A. MP487, MP490, MP492, PP0085
Radziszewski, W. PP0638
Rae, W. PP0075
Raes, J. MP145, MP160, PP0691
Rafael, L. MP365, PP0093, PP0255
Rafael, M.A. PP0532, PP1212
Raffals, L.E. MP684
Raftopoulos, S. MP284, PP0876
Ragab, K. PP0201
Ragab, M. **PP0388**
Ragab, M.F. MP409
Ragg, J. **MP481**
Raghunathan, N. PP0437
Ragunath, K. MP317
Rahaoui, M. **PP0972, PP0977**

Rahbari, N. PP1137
 Rahier, J.F. MP328
 Rahier, J.-F. MP009
 Rahili, M.A. PP0653
 Rahimpour, E. PP0303
 Rahlves, M. MP513
 Rahmadia Ekawidyan, K. PP0771
 Rahman, M.M. PP1235
 Rahman, T. OP037, MP325
 Rahmi, G. MP068, MP440
 Rahmouni, S. OP019
 Raho, N. MP625, PP0378
 Rai, A.A. **MP265**
 Raijman, I. MP554
 Raikhelson, K. PP1035
 Raimundo, D. MP005
 Raimundo, L. PP0255
 Raina, A.H. **VC05, MP098**
 Raine, T. MP326
 Rainteau, D. PP0386
 Raitses - Gurevich, M. MP592
 Rajani, S.Z. **PP0873**
 Rajão Saraiva, M. MP061, **PP0748**
 Rajčić, D. **OP067**, MP235
 Rajec, J. PP1113
 Rajendra, S. MP710
 Rajiah, R. **MP307**
 Raju, S. PP0304
 Raju, S.A. PP0309
 Rakonczay, Z. MP299
 Ramadan, A. PP1112
 Ramadan, W. PP0680
 Rama-Fernandez, A. MP537
 Ramai, D. MP136, MP137, PP0855, PP0856
 Ramalhosa, F. MP555
 Ramesh, J. OP227
 Rameshshanker, R. **PP0163**, PP0873
 Ramió-Pujol, S. MP522
 Ramirez, C. OP009
 Ramirez, C. OP023, PP0364
 Ramírez, C. MP503, PP0362, PP0381, PP0382
 Ramírez, C. MP674
 Ramírez de la Piscina, P. OP213, MP674
 Ramírez de la Piscina Urraca, P. MP343
 Ramírez García, J. MP429, MP430
 Ramírez-Lázaro, M.J. MP673
 Ramírez Palanca, J.J. PP0403
 Rammohan, R. **PP0253, PP0412, PP0704, PP1208, PP1210, PP1211**
 Ram mohan, R.m. **PP0413**
 Ramonaite, R. PP0446
 Ramonaitė, R. PP0357
 Ramos, J.A. MP159
 Ramos, L. OP169, MP674
 Ramos Júnior, O. PP0408
 Ramos Lopes, S. PP0033, **PP0485**, PP0859, PP0860
 Ramos Lopez, L. OP151, OP187, MP268
 Ramos-Quiroga, J.A. OP117
 Ramos-Quiroga, J.A. PP0805
 Rampal, N. MP350
 Ramser, M. PP0930
 Ramsewak, D. PP0531
 Ran, Z. MP620
 Raña-Garibay, R. MP429, MP430
 Rancatore, G. **MP170, MP639**
 Rancel-Medina, F.J. MP674
 Ranchor, A. PP0940
 Rancz, A. PP1133, PP1157, PP1166, PP1180
 Randall, M. PP0447
 Rando Munoz, F.J. OP225
 Ranieri, L. **MP410**, PP1009
 Rao, S. PP0220
 Rapaccini, G.L. PP0958
 Raphael, B. MP487, MP490
 Raphael, B.P. PP0085
 Raphael, G. MP447
 Rapposelli, I.G. MP084
 Rasch, S. MP298
 Rashad, A.M. PP1022
 Rashed, M.A. PP1112
 Rashid, H. MP221, MP277, PP0889
 Rashid, R. MP568
 Rashid, S. OP204
 Rasmussen, J. OP190
 Rasmussen, L. PP1124
 Raso, T. MP344
 Ratcliffe, E. **OP114**
 Rath, E. MP453
 Rath, S. OP130
 Råth, S. MP479
 Ratna, P. MP180
 Rato, B. MP079
 Ratone, J.P. PP1100
 Rattanachaisit, P. **PP0989**
 Rattananukrom, C. **PP1108**
 Ratziu, V. OP058
 Ratziu, V. OP059, OP061, MP236
 Rauber, D. OP206, MP380
 Raunig, D. MP655
 Rausch, A. MP339
 Ravaoli, F. MP059
 Raventós, A. PP0049
 Ravi, R. PP0161
 Ravindran, P. MP394
 Ray, S. MP326, MP628
 Raymenants, K. MP056, **MP434**, PP0039, PP0806
 Raynaud, J.-J. PP0804
 Rayner, C.K. MP478, MP589
 Rayyan, Y. OP045
 Razavi-Shearer, D. PP1031
 Ražov-Radas, M. MP552, PP0276
 Razpotnik, M. **OP167, MP021, PP1181**
 Razuka-Ebela, D. **PP0279**
 Rea, B. PP0309
 Real, F.X. OP132
 Realdon, S. OP054, MP395, MP398, PP0132
 Rebelo, A. PP0526
 Rebiai Hadjmat, S. PP0201
 Reboiro-Jato, M. MP064
 Rebours, V. OP016, PP1138
 Recchia, S. MP390
 Recordare, A. MP223
 Reddy, M. PP0101
 Rednic, V. MP424, PP1182, PP1204
 Redondo, I. OP046, MP615, MP616, PP0374
 Redondo-Cerezo, E. MP103, MP107, MP291, PP0016, PP0018, PP1131, PP1134
 Reenaers, C. MP156, PP0377, **PP0530**
 Rees, C.J. OP181
 Regel, I. MP644
 Regenber, B. MP624
 Regev, O. PP0506
 Regina Pavan, C. PP0263
 Regnat, K. MP465
 Regné, S. MP182, PP1168
 Regueiro, C. MP014, MP064
 Regueiro, M. OP128, PP0460, PP0562, PP0566
 Regueiro Expósito, C. **PP0666**, PP0929
 Reguerio, M. MP333
 Regula, J. OP178, PP0112, PP0610
 Reguła, J. MP374
 Rehfeld, J.F. OP048
 Reiberger, T. OP183, OP186, MP072, MP077, MP173, MP347, MP638, MP691, PP0993, PP0994
 Reichardt, L. **OP013**
 Reicher, R. **PP0232**, PP0233
 Reid, K. **PP0099**
 Reider, L. MP072
 Reif, A. OP117, PP0805
 Reijm, A.N. PP1197
 Reijntjes, M. PP0540
 Reims, H.M. MP044
 Reimund, J.-M. PP0386
 Reinders-Luinge, M. PP0397
 Reinecke, J. PP0230
 Reiner, J. MP329
 Reinisch, W. OP042, OP131, MP330, **MP385**, MP563, MP672, PP0390, PP0447, PP0560
 Reis, A. PP1105, PP1106
 Reis, A.M. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0988
 Reis, D. PP0934
 Reis, G. **MP102**
 Reiter, S. OP183
 Reitmeier, S. MP453
 Reivytyte, R. **PP0169**
 Rejchrt, S. PP0116
 Rekab, R. MP176
 Rellou, S. **PP0466, PP0728, PP1015**
 Relvas, L. PP0708, PP0774
 Rembacken, B. MP322
 Remedios, D. MP064, PP0929
 Remelli, F. PP0310
 Remes-Troche, J.M. MP430
 Remes-Troche, J.M. MP429, **PP0288**
 Remke, M. MP453
 Remple, V. OP103, OP104, MP327, MP619
 Ren, R. MP626, PP0455
 Renard, B.Y. MP150
 Rendle, B. PP0711
 Reni, M. MP024, MP188, MP244, MP480, MP536, MP583
 Renna, S. PP0645
 Renteria, S.C.U. MP466
 Rentsch, C. PP0389
 Repici, A. OP090, OP203, MP011, MP063, MP132, MP137, MP193, MP261, MP276, MP281, MP317, MP390, MP542, MP571, MP662, MP714, PP0166, PP0244, PP0707, PP0754, PP0845, PP0856, PP0903
 Repsilber, D. OP021
 Resál, T. MP158, **MP627**, PP0520, PP0584, PP0675, PP0710, PP0713, PP0731, PP0732, PP0746
 Resell, M. OP134, MP035, **MP085**
 Reshef, L. OP093
 Resheq, Y.J. OP062
 Restoy, D. MP159
 Réthy, L. PP1129
 Retrosi, M. MP656
 Rettura, F. **PP0782**, PP0793, PP0794, PP1071, PP1243
 Retzbach, L. PP0916
 Reuken, P.A. PP0685, PP0984
 Revés, J. MP005, MP149, PP0050, PP0051, PP0062, PP0468, PP0532, PP0751
 Rex, D.K. OP090, PP0845, PP0877, PP0884
 Reyes, V. PP0387
 Reyes-Avedaño, R. PP0908
 Reyes Moreno, J. OP191
 Reyes-Placencia, D. **MP429, MP430**
 Reyes Zermeno, M.G. MP293
 Rezus, I.I. **PP1180**
 Rezus, I.-I. PP1157
 R. Fernandes, A. MP690, MP698
 Rhiel, T. PP0399
 Riah, S. **PP0361**
 Riauka, R. **MP591**
 Riba, B. MP576
 Ribaldone, D.G. OP106, OP169, PP0629, PP0647
 Ribas, A. PP0422
 Ribeiro, H. MP394
 Ribeiro, H. MP499
 Ribeiro, R. MP149
 Ribeiro, R. MP394
 Ribeiro, T. OP099, OP205, MP060, PP0207, PP0329, PP0830, PP1201
 Ribichini, E. MP261, MP438, PP0324
 Ricanek, P. OP021, MP341, PP0417
 Ricart, E. OP026, OP043, OP151, MP268, MP330
 Riccardi, L. PP0958
 Ricchiuti, M. MP716, MP729, **PP0086, PP0087**
 Ricci, C. PP1235
 Ricci, C. MP298
 Ricci, P. PP0818
 Ricciardi, F. MP287, MP608
 Riccioni, M.E. MP455, PP0637
 Richard, N. MP345, PP0410
 Richardet, J.-P. MP634
 Richards, D. **MP563**
 Richards, M. PP0071
 Richir, M. OP224
 Richir, M.C. PP0484
 Ricke, J. MP468
 Rickert, C. PP0910
 Ricotti, L. MP390
 Riedel, J. MP280
 Rieder, F. PP0447, PP0598
 Riedl, F. MP638
 Riestra, S. OP151, MP268, MP334, MP510, MP674, PP0557
 Riestra Menendez, S. MP508
 Riezzo, G. PP0269
 Riggio, O. MP261
 Rijnders, E. **OP162**
 Rijnders, E.E.C. PP1197
 Rijpma, S.R. PP0332
 Rinaldi, P.M. MP310
 Rinckhout, S. MP051
 Rinella, M.E. MP236
 Rinja, E. PP1204
 Rinninella, E. MP645
 Rinzivillo, M. MP241, PP1170
 Rios, D. MP450, PP0635, PP0643
 Ripoll, P. PP0404
 Riquelme Pérez, A.J. MP429, MP430
 Rispo, A. OP169, MP389, PP0476, PP0488, PP0670
 Ritieni, C. MP728
 Ritter, T. MP680
 Riva, A. PP0390
 Riva, D. PP0284
 Riva, P. MP502
 Rivas, A. **MP484**
 Rivas, C. OP187
 Rivas, D. PP664
 Rivas, L. MP064
 Rivero, M. OP043, OP151, OP213, MP268, MP334, MP343, MP508, MP510, PP0362, PP0382, PP0557
 Rivero Tirado, M. MP674
 Rivory, J. MP068
 Rizk, C. OP220
 Rizkala, T. **OP090, PP0845, PP0903**
 Rizzatti, G. MP028, MP137, PP1088
 Rizzello, F. PP0640, PP0668
 Rizzi, S. PP0017
 Rizzo, G.E.M. MP170, MP639
 Rizzo, G. MP390, MP571
 Roager Madsen, G. PP0498
 Roales, V. PP0076
 Roales Gómez, V. PP0079
 Robbins, E.C. **OP179**
 Robert, M.E. MP655
 Roberts, K.J. OP016
 Robertshaw, E. PP0542, PP0555
 Robin, B. MP119
 Robinson, D.J. PP1017
 Robinson, D.J. OP065
 Robinson, P. PP0569
 Robinson, R. PP0604
 Robledo, P. OP043
 Robledo Andrés, P. OP187
 Robles Alonso, V. OP213, MP343

- Robles-Medranda, C. MP109, MP137, MP191, MP193, MP359, MP407, MP554, PP0204, PP1118
- Roblin, X. **OP189**, MP156, PP0386, PP0608
- Rocca, R. PP0450
- Rocchetto, S. **MP063**
- Rocchi, C. MP310, MP606
- Rocchi, G. **MP313**
- Rocco, A. PP0285, PP0473
- Rocco, C. OP175
- Rocha, B. PP0291
- Rocha, M. PP0093, PP0255
- Rocha, M.L. PP0910
- Rocha, M.L. MP386
- Rocha, M. PP1188
- Rocha, P. MP555, MP557, PP0429, PP0819, PP1072
- Roche, D. PP0352
- Rockenbauer, L.-M. PP0741, PP0902, PP0904
- Rockey, D. OP220
- Roden, M. **MP236**, MP524
- Rodrigo, L. OP009, MP428, MP433, MP547, MP549, MP552, PP0271, PP0273, PP0276
- Rodrigo, M. OP026
- Rodrigo Sáez, L.R. MP427
- Rodrigues, Á. PP0826
- Rodrigues, B.G. PP0934
- Rodrigues, F. PP0193
- Rodrigues, I. **PP0592, PP0628**
- Rodrigues, J. MP520
- Rodrigues, J. MP530
- Rodrigues, P.M. MP530
- Rodrigues dos Santos, C. MP102, PP0263
- Rodríguez, P.C. MP429, MP430
- Rodríguez, A. MP064
- Rodríguez, C. OP196, MP503
- Rodríguez, L. PP0688
- Rodríguez-Alcolado, L. **OP211, MP664**
- Rodríguez-Alonso, L. PP0585
- Rodríguez-Camacho, E. MP014
- Rodríguez Camarinha Loureiro, M. PP1070
- Rodríguez Carrillo, C. **MP052**
- Rodríguez Carrillo, C. PP0079
- Rodríguez-De Santiago, E. PP0755
- Rodríguez Gandía, M.Á. OP171
- Rodríguez-Girondo, M. MP211
- Rodríguez Grau, M.D.C. MP343
- Rodríguez Grunert, L. OP050
- Rodríguez Gutiérrez, C. OP023, PP0364, PP0381
- Rodríguez Insa, R. OP213
- Rodríguez-Lago, I. PP0422
- Rodríguez-Lago, I. OP023, OP150, OP213, **MP116**, MP149, **MP151**, **MP216**, MP334, MP343, MP503, MP518, MP510, PP0362, PP0364, PP0381, PP0382, PP0557
- Rodríguez-Moranta, F. OP043, PP0585
- Rodríguez-Moranta, F. PP0403
- Rodríguez-Muñoz, L.O. PP1116
- Rodríguez Oballe, J.A. PP0076
- Rodríguez-Peña, A. PP0391
- Rodríguez-Pescador, A. MP508
- Rodríguez Prada, J.I. PP0474
- Rodríguez-Sánchez, A. PP0076
- Rodríguez-Urrutia, A. OP117, PP0805
- Roedder, S. **PP0600**
- Roelandt, P. OP126, PP0861, PP0864
- Roelstraete, B. MP214, MP594
- Rogai, F. OP175
- Rogalidou, M. OP208
- Roger, E. OP062, OP200, MP088, MP481
- Rogers, B. OP075, PP0094, PP0095
- Rogic, D. MP417
- Rogler, G. OP105
- Rogoveanu, I. PP1163
- Roh, S. **PP0923**
- Rohatagi, S. MP447
- Rohde, U. PP0607
- Rohmer, N. OP157
- Röhr, J. PP0047
- Roig Ramos, C. OP187
- Rojas Campos, E. PP0980
- Rojas-Feria, M. MP157, PP0606
- Rojas Hernandez, A.K. PP1116
- Rojas-Mendoza, F. PP0908
- Rojo, E. PP0755
- Rojo, J. PP0083
- Roka, R. PP0811
- Rokkas, T. MP433
- Roldan, L. PP0268
- Rolhion, N. OP027, OP110, PP0386
- Rollet, S. OP016
- Romanczyk, M. OP123
- Romano, L. PP0452
- Romano, M. OP009, MP427, MP549, MP552, PP0276, PP0285, PP0452
- Roman Siebner, H. PP0411
- Romberg-Camps, M. OP188
- Romdhane, C. PP0651
- Romeiro, P. MP331, MP464, MP679, PP0649, PP0650, PP0907, PP0982, PP0986, PP0988, PP1001, PP1002, PP1023, PP1027, PP1103, PP1105, PP1106
- Romeo, M. MP073, **MP632**
- Romeo, S. MP063
- Romero Portales, M. OP184
- Romiti, C. MP223
- Römkens, T.E. OP086
- Rommel, N. MP434
- Römmele, C. OP206, MP377
- Rompianesi, G. PP1009
- Ron, Y. PP0796
- Roncoroni, L. MP041, MP653
- Rondinella, D. OP096, MP577
- Rondonotti, E. MP063, PP0845, PP1200
- Rong, J. MP500
- Rönnelid, J. OP021
- Rooijakkers, M.J. PP0332
- Roosterman, D. MP535
- Roque Ramos, L.M. MP005, PP0226, PP0468, PP0751
- Roques Ramos, L. PP0532
- Rosa, B. PP0477, PP0789, PP0883, PP1216
- Rosa, I. MP061, PP0747, PP0748
- Rosania, R. OP009, MP549, **PP0136**, PP0538
- Rosa Rizzotto, E. PP0752
- Rosa-Rizzotto, E. MP281, PP0880
- Rosati, R. MP722, PP0135
- Rösch, T. MP317
- Rose, M. MP450, **PP0635**
- Rösel, P. PP0230
- Rosen, M. MP681
- Rosendahl, J. OP170, OP229, PP1122
- Rosenstiel, P. PP0391
- Rosenstiel, P. MP390
- Roser, D.A. **MP380**
- Rosevics, L. **PP0408, PP1188**
- Rosewick, N. MP009
- Rosi, M. PP1012
- Rosinach, M. PP0755
- Rosolowski, M. PP0610
- Rossel, J.-B. PP0074
- Rossella, V. MP188
- Rossi, G. MP024, MP027
- Rossi, R.E. **PP0754**
- Rosso, C. PP0942
- Rostain, F. MP068
- Rostami, K. PP0040
- Rostom, Y. PP1024
- Rosu, R. PP0566
- Rotaru, A. MP080
- Roth, B. PP0807, PP0808
- Rothenberg, M.E. MP488, MP492
- Roth-Hochreutener, M. PP1224
- Rotondi Aufiero, V. MP652, PP0302
- Rotulo, S. MP344, PP0392
- Rouanet, P. MP070
- Roufael, F. MP271
- Rougemont, A.-L. PP1025
- Rouibaa, F. PP1107
- Rouibaa, F. MP559, PP0201, PP0742, PP0905, PP1036, PP1087, PP1104, PP1114
- Rousseaux, C. MP306
- Routhiaux, K. MP056, MP160, PP0039
- Roy, S. MP004, MP420
- Royo, A. OP187
- Royo, V. PP0362
- Royo Escosa, V. PP0382
- Rozera, T. OP096, **MP577**
- Rozier, R. PP0653
- Rozotte, C. PP0363
- R. Siebner, H. OP174
- Ruan, X. MP247
- Ruane, D. MP563
- Ruano-Raviña, A. PP0424
- Ruão, M. PP1141
- Rubbini, L. PP0315
- Rubin, D.T. **OP044**, OP045, OP082, OP083, OP084, OP102, OP212, MP327, **MP333, MP393**, MP621, MP670, MP671, MP672, PP0586, PP0594
- Rubín de Célix, C. PP0403, PP0557
- Rubio, A.B. MP071
- Rubio, E. PP0693
- Rubio, S. MP510
- Rubio Iturria, S. OP213
- Rubod, C. PP0377
- Rückert, T. MP380
- Rud, C.L. **MP140**
- Rudler, M. MP634
- Rudolph, C. OP105
- Rueda García, J.L. PP0469
- Rueda Soriano, J. MP128
- Ruemmele, F. OP127
- Ruesing, G. OP117, PP0805
- Ruess, D.A. MP298
- Ruffle, J. MP307
- Ruffolo, C. MP223
- Rugge, M. OP056
- Ruggiero, L. PP0069, PP0492
- Rughwani, H. OP051
- Ruigrok, R.A.A. OP020
- Ruigrok, R.A.A.A. **OP108**
- Ruiz, M. PP0693
- Ruiz Barcia, M.J. PP0666
- Ruiz Cerulla, A. MP343
- Ruiz-Cerulla, A. OP213, MP674, PP0585
- Ruiz-Clavijo, D. OP016
- Ruiz-Clavijo Garcia, D. MP298
- Ruiz Fernandez, G. PP1242
- Ruiz-Molsgaard, J. PP0535
- Ruiz-Ramírez, P. **OP191**
- Ruiz-Rebollo, M.L. MP298
- Ruiz Sánchez, L. PP0403
- Rullier, E. MP070
- Rull Murillo, N. OP151, MP268
- Rumi, G. PP0613
- Runfola, M. PP0442
- Ruotolo, M. PP0956
- Rupp, L. OP132
- Rusconi, F. MP511
- Russ, K.B. PP0611
- Russell, W. **MP451**
- Russnak, A. PP0572
- Russo, A. MP624
- Russo, C. PP0426
- Russo, F. PP0269
- Russo, F.P. MP406
- Russo, G. PP0491
- Russo, S. MP491
- Rustichelli, A. **MP051**
- Rusu, I. MP424
- Rusu, R.-I. **OP076, MP091**
- Ruszkiewicz, A. MP478, MP589
- Ruta, V. PP1154
- Rutigliano, A.G. MP410
- Rutka, M. PP0614, PP0710, PP0713, PP0746
- Rutter, M.D. MP278
- Ruttmann, K. PP1222
- Ruurda, J.P.H. MP039
- Ryan, K. MP065
- Ryan, R.D. PP0354, PP0355
- Rydell, N. OP021
- Rydzewska Wyszowska, G. PP0697
- Rydzewska-Wyszowska, G. PP0610
- Ryozawa, S. OP101
- Ryu, C.B. **PP0177**
- Ryu, J.K. PP0189
- Ryu, J.-K. MP025

S

- Saad, H. MP531
- Saad, M. MP121
- Saad, R. MP042, MP050, MP252, PP0307, PP0308
- Saad, R. PP1055
- Saadeh, L. MP223
- Sabaté, J.-M. PP0804
- Sabbah, M. PP0361
- Sabbah, M. **PP0402**
- Sabbek, A. PP0669
- Sabino, J. MP145, MP445, PP0494
- Sabrdaran, S. MP141
- Sachdeva, S. MP724, PP1066
- Sachen, K. **OP193**
- Sadeçoluk, M. PP0072, PP0270
- Sadigov, H. MP131
- Saeed, A. PP0064
- Sæterstad, S. **PP0445**
- Safaeian, R. MP148, MP589
- Safarpour, A.R. PP0303, PP0947
- Safer, L. MP234, MP525, PP0669
- Saffon, M.A. PP0268
- Safina, D. MP578
- Safonova, K. PP1232
- Safranek, P. PP0229
- Safranow, K. PP1145
- Safroneeva, E. MP264, MP685, PP0074, PP0596
- Saftoiu, A. OP227, PP1163
- Săftoiu, A. MP694
- Sagaert, X. PP0861, PP0864
- Sagami, R. MP696
- Sagami, S. PP0465
- Sagatun, L. PP1115
- Saghir, A. PP1206
- Sahai, A.V. MP191
- Sahebal, S. PP0822
- Sahin, M. **PP0948**
- Sahin-Toth, M. MP585
- Sahlin Pettersen I, H.P. PP0367
- Saibeni, S. OP106, MP013, MP389, PP0488
- Said, A. PP0515
- Saidani, K. OP097, MP176, MP533, PP1082
- Saidani, R. **MP046, PP0346, PP0350, PP0525, PP0867**
- Sainz Arnau, E. MP343, MP508
- Sair, A. PP0885
- Saito, H. **MP425**
- Saito, K. OP231
- Saito, K. PP0328, PP0703
- Saito, T. MP197
- Saito, T. **OP231, MP181**, MP302, **MP423**
- Saito, Y. OP089, OP091, PP0736, PP0844, PP0877, PP0933, PP1196
- Saiz Chumillas, R.M. MP031
- Saizu, A. PP1204
- Saka, D. OP182, PP0967
- Sakaguchi, C. PP0120
- Sakai, A. OP014, OP028, OP231, MP083, MP302, MP423, MP693

Sakai, E. PP0913
Sakaki, K. PP0159
Sakamoto, N. PP0216, PP1228
Sakamoto, N. MP206
Sakamoto, T. OP091, PP0736
Sakata, Y. PP0419
Sakatani, A. PP1228
Sakemi, R. PP0419
Saker, T. MP592
Sakhnini, E. MP592
Sakiris, A. MP284, MP381, PP0769
Sakurai, H. MP458, PP0683
Sakurai, T. PP0738, PP0914, PP0915
Salaga, M. MP110, MP131, PP0762, **PP0783**
Salah mahklouf, M. PP0032
Salame, M. MP328
Sala Miquel, N. MP278
Salas, A. **OP026**
Salas Martínez, C. PP1005
Salate Biagioni Vulcano, D. PP0343
Saldana, R. MP330
Saleh, S. PP0201
Salese, L. OP042, MP671, MP672
Salgado, M. MP386
Salgueiro, P.S. PP0827
Salha, A. PP0873
Salioun, M. PP1140
Salimgereeva, D. PP1179
Salmaso, B. MP223
Salmaso, R. MP223
Salmeri, N. PP0183, PP1190
Salmon, M. PP1203
Salmoral Luque, R. PP0403
Salomon, B. OP021
Salomon, C. OP168
Salonoja, K. MP655
Salvador Castelhano, N. PP0340
Salvatore, D. PP1009
Salvesen, Ø. PP0115
Salvi, D. PP0066
Salzberg, N. PP1030
Samaan, K. OP046, MP616
Samaan, M. MP326, PP0553
Samaan, M.A. MP628
Samad, A. **PP0180, PP0326**
Samanta, J. OP098, MP004, MP137, MP186, MP420
Sambri, V. MP084
Samrani, Z. PP0202, PP0682, PP1065
Sampietro, G.M. MP271
Samsom, J.N. MP504
Sanada, H. PP0913
Sanahuja Martínez, A. PP0008
Sanchez, E. PP0585
Sanchez, M. PP0220
Sánchez, E. MP064
Sánchez Alonso, M. MP428, MP549
Sanchez Ardila, C. MP278
Sanchez-Azofra, M. OP213, PP0469
Sánchez-Cabo, F. PP0362
Sánchez Cano, C. MP128
Sanchez Capilla, A.D. MP157, PP0606
Sanchez-Cepeda, M. MP554
Sánchez César, J. PP0079
Sánchez del Hoyo, R. MP052
Sánchez Gómez, C.A. PP0929
Sanchez Gonzalez, Y. OP103, MP619
Sánchez-Hernández, J.G. MP216
Sánchez-Marin, C. OP171
Sánchez Pardo, A.M. OP171, PP0008
Sánchez Rodríguez, E. MP510
Sánchez Sánchez, C. PP0382
Sanchiz, V. OP191
Sánchez Soler, V. PP0008
Sancho San Martín, L. OP184
Sandblom, G. PP1124
Sandblom, V. PP1124
Sandborn, W. OP149
Sandborn, W.J. PP0556
Sander, A. OP030, **OP094**
Sanders, D.S. PP0304, PP0305, PP0309
Sando, D.V. MP194
Sandø, A.D. PP0119
Sandrin, L. OP060
Sandru, V. MP480, PP1079
Sands, B.E. **OP042**, OP078, OP082, OP102, OP149, OP194, **OP195**, MP150, **MP617**, **MP618**, MP670, MP671, MP677, MP683, **MP686**, MP688, MP689, PP0549, PP0550, PP0565, PP0586
Sanduleanu-Dascalescu, S. PP1204
Sandvik, A.K. PP0367
Sandvik, A.K. OP109
Sanekommu, H. PP0314
Saner, C. MP264, PP0074
Sangiovanni, A. MP466, MP469, PP1018, PP1020
Sangnes, D.A. MP646
Sanguinetti, M. MP577, PP0958
Sani, G. MP340, PP0612
Sankaranarayanan, S. PP0512, PP0887
San Miguel, E. MP674
Sannino, M.M. MP716
Sano, Y. OP089, PP1196
Sanon, M. **MP153**, PP0571, **PP0572**
Sanromán, L. MP508
Sanromán Alvarez, L. PP0474
Sansoni, S. MP295
Santacrocce, G. MP383, **MP392**, PP0457, PP0479, PP0482, **PP0499**, PP0505
Santander, C. MP060, MP487
Santander Vaquero, C. MP664, PP0076
Santare, D. PP0096, PP0279
Santarosa, M. PP0132
Santi, G. PP0665
Santiago, N.R. OP085, MP684
Santini, F. MP527
Santo, P. PP0816, PP0999
Santonicola, A. MP045, PP0069, PP0492, **PP0956**
Santopaolo, F. OP034
Santos, A.G. MP346
Santos, D.A.R. **PP0739**
Santos, J. OP117, MP051, MP159, MP164, PP0805, PP1235
Santos, L.D. MP710
Santos, L.L. PP0739
Santos, L. **MP499**, MP555, **PP1072**
Santos, M. PP0747
Santos, M. PP0739
Santos Peixe, B.M. PP0708
Sanuki, T. MP693
Sanyal, A.J. MP236, MP527
Sanz de Pedro, M. OP184
Sanzo-Machuca, Á. OP026
Sapmaz, F. **MP558**
Sapurovs, N. PP0279
Saqib, I.-u.-d. **PP0229**
Sarabia, I. OP193
Saraiva, S. PP0195, PP0196, PP0197
Saraiva, S. PP0592, PP0628
Saraiva, S. MP690, MP698
Sarakapina, A. MP692
Saray, A. **MP588**
Sarkar, A. MP137
Sarlós, P. OP012, PP0584, PP0675
Sarnelli, G. MP716, MP729, PP0086, PP0087
Sarosiek, I. PP0220
Sarraf, B. PP1099
Sarsenbaeva, A.S. PP0280
Sarter, H. MP345, PP0410
Sartini, A. MP364
Sartoris, R. OP158
Saruç, M. MP416
Saruta, M. OP045
Sasabe, K. PP0738, PP0915
Sasahira, M. **PP0011**, PP0158
Sasaki, M. MP032, **PP0237**
Sasaki, N. MP242
Sasaki, S. PP0834
Sasaki, S. PP0432
Sasaki, T. PP0114, PP0172
Sasaki, Y. PP0237
Sasani, A. PP0603
Sassatelli, R. MP281, MP540
Saßmannshausen, Z. PP0900
Sathananthan, D. PP0576
Sato, C. PP0234
Sato, D. PP1196
Sato, H. OP073
Sato, K. PP0868
Sato, S. MP101, PP0152
Sato, S. MP101, PP0152
Sato, T. MP302, MP423
Sato, Y. MP693, PP0432
Satoh, T. **MP238**
Satsangi, J. MP629
Sattayalertyanong, O. PP0872
Sattler, C. OP080
Sauciuc, L. PP0312
Saukhat, O. PP0054
Saunders, B.P. PP0165, PP0768
Saunders, R. MP016
Saunier, M. MP440
Saur, D. MP453
Saurenbach, J. MP572
Sauvanet, P. MP402, PP0363
Savale, L. PP1025
Savari, M. PP0256
Savarino, E. PP0076
Savarino, E.V. OP075, OP150, OP169, OP199, MP010, MP092, MP256, MP259, MP260, MP263, MP476, MP491, MP662, MP663, MP727, PP0013, PP0094, PP0095, PP0476, PP0481, PP0587, PP0629, PP0633, PP0647
Savasta, S. PP0442
Savic-Radojevic, A. MP201
Savilova, I.V. PP0254
Savina, I. PP1179
Savino, F. PP0463, PP0480
Savopoulos, C. MP290, PP0743, PP0991
Savoye, G. OP189, MP002, MP345, PP0377, PP0410
Sawada, N. PP0734, PP0738, PP0915
Sawaguchi, H. PP0103
Sawyer, W. MP330
Sayed, M. MP121
Sayed-Hassen, A. MP139
Saylam, M.S. PP0970
Sazonovs**, A. **OP017**, MP507
Sbarigia, C. **MP725**, MP728, **PP0068**, **PP0809**
Scaiscia, D. MP431, PP0266
Scalamonti, S. PP0007, PP0325
Scaldeferri, F. OP081, MP006, MP269, MP340, MP577, MP624, PP0393, PP0612, PP0613, PP0629, PP0637, PP0654, PP0656
Scalese, G. MP415, MP438, **PP0324**
Scalvenzi, M. PP0086
Scalvini, D. **MP013**, **MP653**
Scanzi, J. PP0659
Scanziani, E. OP054
Scapinello, A. MP223
Scaramella, L. MP041, PP0327
Scaramuzza, G. MP662, MP663
Scardella, C. MP653, MP656
Scardino, G. MP063, PP0629
Scaringi, S. PP0672
Scarlata, G.G.M. PP0337
Scarpa, M. MP223, MP569
Scarpa, M. MP223, MP569
Scarpa, M. PP0693
Schaefer, M. MP068, MP440, PP1100
Schafer, P. MP665
Schäffer, E. MP720
Schalk, E. PP0685
Schanze, D. OP152
Scharl, M. PP0369
Scharpf, M. MP305
Scharrer, S. PP0910
Schartum, M. PP0487
Schattenberg, J. **OP057**, **OP059**, OP061, MP233, **MP526**
Schattenberg, J.M. **OP060**
Schauer, F. MP661
Schauwen, R. OP162
Schedlbauer, A. MP173
Scheepers, J. **PP0070**
Scheiner, B. MP173, MP465
Schembri, J. PP0316, PP0317
Schepis, T. MP539, PP1088
Scheppach, M. **OP206**, **MP377**
Scherer, B. PP0630
Schettino, M. MP013
Schiavello, F. PP0963
Schiavone, F.P. OP140, MP203, MP205, PP0007, **PP0325**
Schiavone, S.C. PP0426, PP0427, PP0621
Schiavoni, E. PP0393, PP0612, PP0613
Schiepatti, A. MP013, MP653, MP656, PP0315
Schiffelholz, A. MP329
Schiffman, C. OP079
Schiliro, A. PP0845
Schilling, C.P. **OP066**
Schinello, G. MP395, MP398
Schippa, S. MP261
Schirizzi, A. MP415, PP0818
Schirra, J. MP280
Schlag, C. OP112, **MP487**, PP0930
Schlager, H. PP0080
Schleinitz, N. MP350
Schlosser, S. MP131, PP1222, **PP1224**, **PP1229**
Schlosser-Hupf, S. OP229, PP1218
Schmal, A. **PP0193**
Schmelz, R. OP130
Schmelzle, M. MP298
Schmerbach, H. OP094
Schmid, D. MP638
Schmid, R.M. PP0206, PP0388, PP0852
Schmid, S. **PP1218**, PP1222
Schmidt, A. MP377, PP0221
Schmidt, C. PP0647
Schmidt, K. MP329
Schmidt, S. **MP642**
Schmidt Cerski, C.T. PP1021
Schmidtman, I. MP233
Schmidt-Wilcke, T. PP0685
Schmiedel, S. PP0685
Schmitt, J. PP0009
Schmitt-Graeff, A. MP661
Schmitz, M. OP132
Schmitz-Rode, M. PP0685
Schmulson Wasserman, M.J. MP164
Schneider, A. PP1138
Schneider, M. PP1122
Schneider, N. **MP305**
Schnierer, M. PP0065
Schoch, S. **MP720**
Schoder, M. MP072
Schoepper, A.M. MP264, MP489, PP0074
Schol, J. MP056, PP0039
Schoon, E.J. OP112, OP122
Schoonjans, C. PP0838
Schoormans, S.C. PP0332
Schoots, M.H. PP0397
Schoppmann, S. PP0094, PP0095
Schot, I. PP1197
Schou Olesen, S. OP168, MP186
Schramm, C. MP354, MP707, PP0984
Schreiber, N. PP0810
Schreiber, S. OP079, OP104, OP105, **OP149**, **OP212**, MP329, MP330, MP390, MP449, MP614, **PP0447**, **PP0459**, PP0542, **PP0548**, PP0550, PP0555, PP0565, PP0594, **PP0605**

Schreinemakers, J.M. MP705
Schreiner, P. **MP489**, PP0074, **PP0080**
Schreuder, R.-M. OP225
Schroeder, S. MP660
Schubert, S. MP682
Schug, B. PP0593
Schulberg, J.D. PP0602
Schulte, B. **MP513**
Schulte, L. OP229, MP298
Schulte, M. MP479
Schulte, N. MP479
Schultheiss, H.-P.D. PP0379
Schulz, C. OP137, MP426, MP644
Schulz, D. PP0206
Schulz, M. PP0249
Schulz, T. OP030
Schulze, C. MP280
Schumacher, A.A. MP718
Schumacher, F. OP030
Schumacher, J.C. **PP1048**
Schumann, M. MP250, **MP650**, **PP0372**
Schuppan, D. OP002, OP005, OP070, MP076, **MP250**, MP411, MP707
Schuster, A.K. MP233
Schuster, T. PP1122
Schütte, K. MP468
Schütz, A. PP0994
Schütz, A. MP572
Schütz, J. PP1152
Schwab, J. OP062
Schwab, U. MP308
Schwartz, L.K. MP141
Schwartz, M.P. OP225
Schwarz, C. OP183, **MP072**, MP638, **PP0993**, **PP0994**
Schwarz, J. PP0580
Schwarz, M. **OP183**, OP186, MP072, MP077, MP173, **MP638**
Schwarzer, A. MP479
Schwarzfischer, M. PP0369
Schwärzler, J. OP018
Schweistein, H. PP0272
Schwenter, F. PP0877
Schwerd, T. MP143
Schwind, A. MP043
Sciberras, M. PP0316, PP0317
Sciberras, N. PP0317, PP1138
Sciola, V. PP0129, PP0130
Sciorio, C. PP0452
Scognamiglio, F. MP223
Scriba, M. PP0293
Scricciolo, A. MP041
Scuderi, V. MP057
Sdonas, T. MP676, PP0466, PP0568, PP0728
Sears, L. PP0632, PP0646
Sebajang, H. PP0877
Sebastian, S. MP149, PP0556
Sebesta, C. MP638
Sebode, M. MP707
Secchettin, E. OP136
Sedano, R. PP0531, PP0556
Seddik, H. MP559, PP0742, PP0905, PP1036, PP1087, PP1104, PP1107, PP1114
Sedivy, J.M. MP009
Seelig, J. MP298
Seenan, J.P. MP330
Seewald, S. OP112
Segal, E. OP001
Segal, J. PP0389, PP0533
Segal, J.P. PP0648
Segarra Ortega, J.X. MP666
Segarra Ortega, J.X. MP549
Segata, N. MP659, PP0347
Segato, S. PP0508
Segatta, F. MP063
Segovia-Hilara, A. MP511
Sehgal, V. MP033, PP0106, PP0227
Seibold, F. MP618
Seicean, A. MP424, PP0201, PP0976, **PP1182**
Seidelin, J. OP190
Seidelin, J.B. OP174, MP007, MP336, MP391, PP0411, PP0498, PP0502
Seidita, A. MP659, PP0347
Seifert, H. OP229
Seitzinger, M. MP298
Sejling, A.-S. MP524
Sejling, A-S. OP058
Sekar, A. PP0603
Sekiguchi, M. PP0767
Sekiguchi, M. PP0736
Seksik, P. MP002, MP267, MP630, PP0377, PP0386, **PP0395**
Sekulić, O. PP0449
Selahattin Topalak, Ö. MP421
Selaru, F. PP0521
Selling Feigin, L. MP592
Sellami, W. **PP1000**
Seller, N. PP0009
Sellitti, A. PP0069
Selvanathan, P. MP317
Selvanderan, S. PP0888
Selvaraj, E. PP1176
Semba, S. OP087
Semba, S. PP0738, PP0914, PP0915
Sembera, S. PP0116
Semen, M. **PP0803**
Semen, V. PP0803
Semenova, M. MP593
Seminario, C. PP0075
Semmler, G. OP186, **MP173**
Sempoux, C. PP0074
Sendelhofert, A. MP644
Sendler, M. MP642
Sendra Rumbau, P. OP213, MP343, MP674
Sendur, I.N. PP1217
Seng, C. PP0678
Senneca, P. MP729
Senore, C. MP011
Senzolo, M. MP406
Seo, G.-S. PP0840
Seo, J. MP602
Seo, J.-y. PP0090, PP1039
Sepodes, B. MP555
Sequeira, C. PP0485
Serclova, Z. PP0575, PP0675
Serghini, M. PP0543, PP0590
Serizawa, K. PP0465
Serra, C. MP364
Serra, E. MP183
Serra, J. MP054, MP159, PP1235
Serra, K. PP0585
Serra-Pegès, M. MP522
Serrero, M. MP002, MP630, PP0377
Serrés Gómez, M. OP184
Sesé, E. OP043, OP151, OP187, MP268, MP508, PP0493
Sessa, F.M. PP1165
Sethi, A. PP0877
Sethi, S. MP252
Sethia, M. OP217, PP1084
Sethi-Arora, K. MP326
Seto, W.-K. OP010, MP246, MP396, PP1169
Setshedi, M. PP0293
Sette, C. MP024, PP1154
Seufferlein, T. OP062, OP200, MP305, MP479, MP483, PP0911, PP1137, PP1152
Severi, C. MP415, PP0324, PP0818
Severino, A. OP096, MP577
Sey, M. PP0531, PP0627, **PP0706**
Seyfried, F. PP0178
Sezer, S. MP558
Sezgin, O. MP416
Sfarti, C. MP080
Sfeir, N. MP016
Sferrazza, S. MP276, MP281, PP0832
Sgamato, C. **PP0473**
Sgambato, A. MP390
Sgambato, D. PP0452
Shaaban Abdelgalil, M. MP225
Shabbir, A. PP0192
Shabeeb, S. PP1062
Shagaleeva, O. PP0513
Shah, A. PP0043
Shah, B. MP541
Shah, E. **MP093**
Shah, I. MP333
Shah, J. PP0603
Shah, K. MP326
Shaham, D. PP0675
Shahed, Q. **PP0182**
Shaheen, H. MP118, MP450, PP0635, PP0643
Shahid, H. MP137
Shahid, Y. **PP0995**
Shahidi, N. OP142, PP0753, PP0875, PP0888, PP0936, PP0937
Shahzad, M.A. PP0678
Shaib, Y. OP220
Shaked, A. MP600
Shamsey, A.M. **PP0287**
Shamshoian, J. **PP0375**
Shamsiddinova, A. **PP0680**
Shao, L. **PP0380**
Shao, W. **OP047**
Shao, X. PP0600
Sharara, A. OP220
Sharar Fischler, T. **OP093**
Sharif, K. **PP0858**
Sharif, Y. PP0858
Sharma, A. OP134, MP085
Sharma, B.C. PP1066
Sharma, D. OP103, MP619
Sharma, E. MP628
Sharma, P. OP090, OP123, MP317, PP0845, PP0903
Sharma, V. PP0394, PP0603
Sharma, Y.P. PP0394
Shashi, A. MP393
Shastri, K. **PP0667**, **PP1185**
Shater, M. PP1024
Shaukat, A. PP0855
Shaw, C. PP0542, PP0555
Shaw, K. MP265, PP0217
Shea, R. MP033
Sheehan, T. PP0214
Shehata, N. MP225
Sheida, F. PP0092
Sheik, R. OP159
Sheikh, S. PP0413
Shen, H. PP1143
Shen, J. **PP0865**
Shen, M. MP353
Shen, P. PP1068
Shen, S. OP201, MP087, MP089, **PP1146**
Shen, W. OP047
Shen, Y. **MP353**, MP597
Sheng, J. MP401
Shenoy, S. PP0522
Sheppard, D. MP471
Sheptulina, A. **PP0952**
Sheridan, H. MP570
Sheridan, J. MP213
Sheridan, P. PP0556
Sherrill, J.D. **PP0075**
Shetty, A. PP0522
Shevchuk, V. OP196
Shi, R. OP120
Shi, T. MP247
Shi, W. **MP029**
Shi, Z. **OP201**, MP089, PP1146
Shibata, T. OP091
Shibata, Y. PP0601
Shibeika, M. MP180
Shibolet, O. PP1095
Shibui, S. **PP0465**
Shibutani, M. PP0432
Shibuya, K. OP035
Shibuya, T. PP0738, **PP0914**, PP0915
Shida, D. PP0432
Shiha, M. PP0309
Shiha, M.G. **PP0304**
Shiha, M.G. MP253, MP255, **PP0305**
Shiina, O. PP0734
Shikano, M. PP0067
Shikh, E. PP0800
Shimada, Y. **MP101**, **PP0152**
Shimamoto, F. PP0444
Shimamoto, Y. MP368
Shimazu, Y. **MP036**, MP038, MP040, MP404, PP0581, PP0582
Shimizu, A. MP242
Shimizu, D. MP457
Shimizu, T. PP0913
Shimoda, R. OP089
Shimodate, Y. OP089, **PP0144**, PP0173
Shin, C.M. MP232, MP603, PP0126
Shin, C.-M. MP551, PP0131
Shin, D.H. **PP0733**
Shin, H. **MP001**, **MP470**
Shin, J.B. **MP581**, **PP0744**
Shin, S.J. MP279, **PP0157**
Shin, S.K. PP0110
Shinagawa, K. PP0913
Shinagawa, T. PP0432
Shinmura, K. OP089, **OP091**, MP561, PP1195, PP1196
Shintani, S. **MP187**, PP0385, PP0617, PP1139, PP1151
Shiomi, A. PP0334
Shiomi, H. OP014, OP231, MP181, MP302, MP423, MP693
Shiotani, A. PP0011, PP0158
Shipitofsky, N. OP084, MP670
Shiratori, T. OP231
Shirinskaya, N. PP1124
Shiroyama, M. OP091
Shishin, K. PP0242
Shitrit, A. PP0272, PP0675
Shivaji, U.N. PP0482
Shkarban, V. PP1142, PP1158
Shnell, M. PP0233
Shnell, M. PP0232
Shoeb Patel, A. OP060
Shojaei-Zarghani, S. PP0303, **PP0947**
Shotre, A. PP0375
Shruti, S. MP004, MP420
Shu, N. PP0462, PP0702
Shu, X. MP500, PP0636
Shukla, N. MP619, MP677
Shutova, O. MP230
Siau, K. MP104
Siboni, S. **OP075**, MP092, PP0094, **PP0095**
Sibuet, I. PP1213
Sica, N. PP0492
Sicilia, B. OP043
Sicilia Aladrén, B. OP191, MP508, MP674
Sidal, S. OP034
Sidani, S. OP124
Sidhu, M. MP381, PP0179
Sidhu, R. MP253, MP255, PP0333
Sidiropoulos, O. MP131
Siebert, K. MP143
Siegel, C. OP078, OP103, MP615, PP0422
Siegel, C.A. OP046, MP387, MP617
Siegler, G. MP479
Siegmund, B. OP195, **MP449**, MP572, MP615, MP622, **MP688**, MP689, **PP0354**, **PP0355**, PP0372, PP0588, PP0589
Siegmund, K. OP018
Sieri, S. PP0348
Sierra, M. OP151, MP268, MP510
Sierra-Ausín, M. MP674
Siersema, P.D. MP023, MP030, MP317, PP1041, PP1101
Sievert, W. MP074
Siffert Pereira de Souza, H. PP0193

Sigal, M. OP167, MP021, PP0003, PP0249, PP1181
Siggens, K. **OP203**, MP553, PP0165, PP0768
Signorette, M. MP241, PP1170
Signoretto, P. PP0570, PP0664
Sikkema, M. PP0484
Sikó, B. PP0563
Sikorski, K. PP0487
Silantiev, A. PP0513
Silin, H. PP0935
Silkanovna Sarsenbaeva, A.S. MP427
Silva, A. OP036, MP189
Silva, A.E.P. PP0236
Silva, F. MP429, MP430
Silva, J.C. PP0050, PP0051, PP0062
Silva, J.R. PP0138
Silva, K. PP0469
Silva, M.R. MP555
Silva, M. OP155
Silva Portela, F. PP0429, PP0812
Silverberg, J. MP486
Silverberg, M.S. PP0556
Silverstein, J. OP172
Silvester, J. MP250
Sim, S.M. MP142
Simao, I. PP0033, PP0934, PP1237
Simão, A.L. MP346, MP530
Simas, D. PP0033
Simbrunner, B. MP072, MP077, MP173, MP691
Simeon-Aznar, C.P. MP054
Simeth, C. MP604
Simkova, D. **PP0191**
Simon, E. PP0700
Simon, E.G. PP0027
Simon, O.A. MP379, PP0021
Simonetti, S. PP0818
Simons-Linares, C.R. OP050, PP0240
Simovic, I. OP141
Simrén, M. OP117, OP119, MP051, MP163, MP164, MP574, PP0784, PP0801, PP0802, PP0805, PP0806, PP1186, PP1230, PP1235
Simsek, C. MP131, **PP1217**
Sin, C.W. MP322
Sina, C. PP0806
Sinagra, E. PP0183, PP0832
Sinakos, E. MP692, MP695
Sinan, H. **OP133**
Singeap, A.M. MP080
Singeap, A.-M. MP294
Singh, A. PP1081
Singh, A.K. PP1066
Singh, A.K. PP0394, PP0603
Singh, A. MP575
Singh, A.P. MP513
Singh, G. **PP0389**
Singh, H. PP0564, PP0706
Singh, M. PP0603
Singh, N. PP0632, PP0646
Singh, R. **MP532**
Singh, R. MP447
Singh, R. OP039, PP0876, PP1193
Singh, R.A. PP0147
Singh, R. MP483
Singh, S.K. PP0833
Singh, S. PP0598
Singh, S. MP270
Singh, V.K. **MP183**
Singhal, N. MP478, MP589
SinghMann, J. PP0616
Singh Mann, J. PP0545
Sinh, P. MP332
Sinha, S.K. MP004, MP420, PP0603
Siniagina, M. MP578
Siniscalchi, M. PP0956
Sinonquel, P. **OP126**, PP0861, PP0864
Sinopoulou, V. PP0539
Sintusek, P. **PP0823**
Sioofy Khojine, A. MP248
Sipeki, N. MP179, MP354
Sipos, Z. MP048, MP251
Siragusa, N. PP0078
Siranovic Pongrac, I. **PP0863**, PP1078
Siriwardena, A. MP186
Sirtl, S. OP229, MP298, **MP644**, PP1124
Siu, W. OP203
Siveke, J. MP479
Sjöberg Jabbar, K. MP574, PP0784
Sjöblom, N. MP308
Sjöland, W. MP574, **PP0784**
Sjölund, J. **OP119**, PP1235
Skalshøi Kjær, M. OP060, MP528
Skieceviciene, J. OP022, OP107, OP152, MP289, MP468, PP0446
Skiecevičienė, J. PP0357, PP0366
Skladany, L. PP1113
Skogaker, N.T. MP085
Skrha, J. MP587
Skybalo, S. OP196
Slim, R. PP1192
Slim Karam, R. MP106, MP229, MP516, PP0297
Sloan, S. OP195, MP688, MP689
Slobodniková, A. PP0846
Sluckin, T.C. OP223
Slusher, B. PP0521
Smaha, J. PP1233
Smania, V. PP0327
Smecuol, E.G. MP045, **PP0321**
Smed Kornum, D. OP154, **PP0046**
Smeets, S. VC02, VC08, MP019, PP0730, **PP0838**, PP0853, PP0895
Smet, A. PP0012
Smets, T. OP193
Smieszek, S. PP0042
Smith, B.J. MP143
Smith, C. MP342
Smith, E.R. MP136
Smith, E.R. PP0855
Smith, H.T. MP602
Smith, N. **PP0043**
Smith, S. MP427, **PP0289**
Smith, S.M. PP0271
Smith-Aguasca, R. **PP0688**
Smithson, G. MP655
Smits, R. MP719
Smolinska, A. MP287
Smolovic, B. PP0591
Smolović, B. **PP0449**
Smyth, C. PP0214, PP0737
Snijkers, J.T.W. PP0780
So, B.Y.J. PP0192
Soares, J.B. PP0526, PP0552
Sobhani, I. **OP095**, PP0483
Sobirova, G. **PP0117**
Socas, K. MP143
Soddu, P. MP625, PP0418
Söderholm, J.D. OP021
Sodmann, P. PP0178, PP0897, PP0900
Søe Riis Jespersen, H. OP190
Sofia, R. PP0730
Sofia Pinheiro Machado de Carvalho, S.P.M.d.C. PP1178
Sofue, K. OP014, MP693
Sogni, P. MP634
Sogos, V. PP0378
Soh, J.S. **PP0461**
Sohn, C.I. PP0044
Sokic Milutinovic, A. PP0578
Sokic-Milutinovic, A. MP339
Sokol, H. OP027, OP110, MP267, PP0386, PP0434, PP0435, PP0659
Sokolova, A.S. PP0537
Sökücü, V. PP0625
Solak, C. **VC07**
Solano, G. PP0544
Solbach, P. PP0685
Soldaini, C. **PP0069**
Soldbro, L. OP161
Soldovieri, L. PP1165
Soledad Marcos, M. OP009, MP428, MP549
Soletto, I. OP023, MP503, PP0362, PP0364, PP0381, PP0382
Solhaug, H. PP0487
Soliman, H. **PP0066**, **PP0299**
Solina, G. PP0670
Solinas, I. MP092, MP263, MP662, MP663, MP727
Solitano, V. MP270, **PP0531**, **PP0546**, **PP0598**, PP0620, PP0627
Sollid, L.M. OP003, MP657, MP658
Solodovnikchenko, I. MP230
Solymosi, D. PP1011
Somers, M. MP328
Sommella, E. MP010
Sommer, N. PP1224
Soncini, M. MP560, PP0508
Song, A. OP083, MP614
Song, C.-H. PP0295
Song, D.H. **MP228**
Song, H.-Y. PP0840
Song, Q. **PP0100**
Song, S.-Y. MP482
Song, Y. MP161
Song, Y. **MP599**
Song, Y.m. PP0044
Soni, D. MP556
Sonja, B. PP0456
Sonika, U. PP1066
Sonnenberg, E. MP339, MP342
Sonoda, M. MP437, PP0148, PP0328, PP0462, PP0702, PP0703
Sood, R. MP322
Soon, G. PP0192
Sørensen, H.G. PP0422
Sørensen, L.T. OP190
Sørensen, L.S. OP168
Sorge, A. OP106, VC02, VC08, **MP256**, MP494, **PP0327**, PP0838, PP0853, **PP0895**
Soria, A. MP071
Soria-Chacartegui, P. MP664
Soriani, P. MP281
Soriano, A. OP106, PP0476
Soriano, A. PP0693
Soriano, M. MP432
Soro, S. PP0139
Sorokina Alexdóttir, M. OP024, OP172, MP565, **PP0502**, PP0509
Soroosh, P. MP448
Sorriento, A. MP390
Sosa, R. **PP1116**
Sosnowicz, K. PP0407
Soto, P. PP0436, PP0439
Soto, S. MP064
Soto-Escribano, P. MP157, PP0606
Soto-Solis, R. PP1116
Soua, S. PP0402, PP1033
Souaid, C. MP442
Soufleris, K. MP676, PP0205, PP0528, PP0568, PP0599
Soukaina, B. **PP0190**, **PP0213**, **PP0515**
Soukup, O. PP0225
Sousa, C. PP0255
Sousa, P. MP131
Sousa-Pinto, B. PP0620
Souto, M. MP171, **MP637**, PP0750, **PP0757**, **PP0761**, **PP0883**
Souto, P. MP555, MP557, PP0050, PP0051, PP0062, PP0819
Souza, M. MP678
Souza, R. MP719
Sovran, B. MP314, MP573
Soweid, A. OP220
Soytürk, M. MP416, MP421
Sozzi, M. OP075, **PP0094**, PP0095
Spaander, M.C.W. PP1197
Spaander, M.C. OP112, OP162, OP180, PP0128
Spada, C. MP011, MP028, MP281, MP311, MP514, MP539, MP605, MP714, PP0247, PP1088, PP1154
Spadaccini, M. OP090, MP136, MP193, MP540, MP584, PP0166, PP0244, PP0845, PP0855, PP0903
Spaggiari, P. MP390, MP571, MP584
Spagnolo, G. MP340
Spagnuolo, R. PP0629
Spalinger, M.R. **PP0369**
Spandre, M. MP441
Spanogianni, A. MP134
Sparrow, M.P. PP0553
Sparrow, M.P. OP194
Spencer, A. **MP118**, MP450, PP0635, PP0643
Spencer, E. PP0422
Spencer, R. PP0545, PP0616
Sperber, A.D. OP119, MP164, PP1186, PP1230
Spergel, J.M. MP490
Sperna Weiland, C. MP023, PP1041
Spessotto, P. OP054
Spicak, J. MP192
Spicakova, K. MP510
Spiessberger, B. OP137
Spigaroli, M. **PP1003**
Spigset, O. PP0115
Spiller, R. PP0809
Spina, L. PP0324
Spindler, L. PP0830
Spinelli, A. MP571
Spinelli, I. **MP455**, **PP0082**, PP0954
Spinou, M. MP134
Spirić, J. PP0578
Spirito, L. PP0452
Spizzo, P. PP0577
Spolverato, G. MP223
Sprinzl, K. PP0624
Spyrantis, A. PP0466, PP0728
Squeo, F. **PP0301**, PP0463, PP0480
Sredharan, Y. MP485
Sridhar, A. **PP0367**
Sridhar, S. OP102
Srinivasa, A. **OP037**, **MP325**, **MP556**, **PP0155**, **PP0156**
Srinivasan, A. PP0602
Srinivasan, D. OP062, MP088, MP481
Srirajaskanthan, R. MP037
Srivastava, S. PP1066
S. Sarsenbaeva, A. MP547, PP0271, PP0273
Stachler, M. OP113, MP367
Stadlbauer, V. PP0339
Stafie, R. MP080
Stafylidou, M. PP0205
Stalla, F.M. **PP0450**
Stallmach, A. MP680
Stamou, A. PP1177
Stanciu, C. MP080
Stanghellini, V. MP057, MP659, PP0347, PP0779, PP0797, PP0813, PP1235
Stanisavljevic, I. PP0763
Stanislas, C. PP0185
Stanley, A. OP032, MP100, MP105, MP108, MP123
Staron, R. MP644
Starostin, B.D. PP0280
Starzynska, T. PP1145
Stasinios, I. PP0330
Stassek, L. PP0458, PP0459, PP0460
Stassen, L. OP188
Stassen, L.P. PP0484
Stassen, P.M.C. MP132
Stathopoulou, I. PP1015
Statovci, I. OP159
Stättermayer, A.F. OP183, MP347
Staudacher, J.J. MP131, PP1224, PP1229
Stecca, T. MP223
Stecher, B. MP453
Steele, R. OP164

- Steenholdt, C.S. OP024, PP0509
Stefanescu, C. MP156, PP0651
Stefanescu, H. PP0976
Stefanidis, G. MP254
Stefani Donati, D. MP092, MP263, MP662, MP663
Stefanini, B. OP034
Stefan-Lucian, P. PP0038, PP0337
Stefanolo, J.P. MP045, PP0321
Stefanovic, M. OP122
Steffen, T. MP280
Steidl, K. PP0080
Steiger, K. OP132, MP453, MP644
Stein, A. PP0272
Stein, J. MP682
Steinacher, D. MP691
Steinbrück, I. MP280
Steindl, C. MP413
Steiner, C. MP590
Steiner, T. OP155
Steiner-Gager, E. OP229
Steinhart, A.H. MP154
Stella, L. **OP034**
Stemmer, N. PP0422
Stendardo, G. MP205
Stenzinger, A. MP479
Stepanyan, A. **MP223, MP569**
Stephanini, G.C. PP0725
Steponaitienė, R. **PP0366**
Stergiou, E. PP0568
Stern, D. OP019
Sterpi, C. PP1071, PP1243
Steshenko, A. **PP0846**
Stevens, A. PP0098
Stevens, C.L. PP0345
Stevns Hansen, C. PP0046
Steyaert, J. PP0691
Stigliano, S. MP137, PP0917
Stillingen, T. PP0119
Stobernack, T. MP362
Stocker, A. PP0220
Stockmann, H.B. MP705
Stoerzer, S. MP298
Stoikevych, M. **PP0356**
Stojkovic Lalosevic, M. MP131, PP1138
Stoker, J. MP117, PP0523
Stokes, D. PP0726
Stolinska, H. PP0690
Stommel, M. MP030
Stommel, M.W. MP022
Stone, J.H. MP350
Stopfer, K. MP173
Storer, V. **MP259**
Stougie, P. **OP113, MP367**
Straathof, J.W.A. PP1101
Straatmijer, T. PP0567
Strachan, J. PP1113
Stradella, D. PP0450
Strande, V. MP341
Strasser, M. OP183
Strassl, R. MP638
Strati, F. MP010
Straub, B. MP233
Straumann, A. OP209, MP264, MP489, PP0074
Strobel, D. PP0529
Stubbe, H. MP298
Stückler, A. MP638
Study group, R. PP0395
Stundiene, I. PP0169
Sturkenboom, R. **PP0814**
Sturm, N. PP0911, PP1239
Stuyt, R.J.L. PP0641
Stylopoulos, N. PP0053
Su, C. OP207, MP493
Su, D. MP675
Su, M. MP675
Su, S. PP0458, PP0459, PP0460, **PP0566**
Suarez, K.E. PP0546
Suarez-Farinas, M. MP150
Suárez Ferrer, C. PP0469
Suárez González, A. PP0076
Suárez Matías, M. MP549
Suárez Solís, M. PP0079
Suarez-Trujillo, F. PP0382
Subhaharan, D. PP0678
Subhan, A. PP0995
Subhani, M. **PP0969**
Subramani, K. PP0412, PP0413
Subramaniam, S. OP122, PP0165, PP0768
Subramanian, A. MP556
Subramanian, V. PP0539
Suchanek, S. **MP517**, MP587, PP0225, PP0759
Suda, K. OP231, MP302
Suerbaum, S. OP137
Sueyoshi, T. **MP382**
Sufyan, A. **PP0314**
Suga, H. MP534, MP704, PP1054
Sugata, S. OP087
Sugihara, K. PP0432
Sugimoto, M. MP382
Sugimoto, S. OP089, PP0683
Sugimura, N. **PP1196**
Sugitani, S. OP073
Sugiura, R. OP231
Sugiura, T. MP239, **MP356**, MP360, **PP1148**
Sugrue, K. PP0457
Sui, G.P. MP091
Sujendran, V. MP494
Sujendran, V. PP0229
Sujino, T. MP458, PP0683
Sultan, S. PP0845
Sulzer, S. OP229
Sümegi, L.D. PP0584
Sumida, Y. OP087
Sumiyama, K. MP323, MP439, PP0933
Sun, D. **PP0128**
Sun, J. **OP214**, MP047, MP174, MP214, MP243, MP505
Sun, J. MP111
Sun, L. OP118
Sun, S. OP071, PP0368
Sunakawa, H. MP561, PP1195
Sunami, E. PP0432
Sund, M. MP590
Sundaram, S. MP541
Sundby-Palle, M. MP528
Sundelin, E. OP117
Sundquist, K. PP0808
Suomalainen, A. MP308
Superina, R. PP1025
Suppressa, P. PP0957
Surabattula, R. **MP707**
Suravaram, S. OP104, MP327, MP333
Surdea-Blaga, T. MP124
Sureka, B. PP0833
Suria Bolufer, C. PP0403
Surjanhata, B. PP0220
Surmont, M. **PP0822**
Surnacheva, E. OP190
Suryanarayana Reddy, C. PP1191
Susánszki, P. OP197
Sushilova, A. MP552, **PP0267**, PP0276
Suski, M. OP055, MP199
Sutherland, T. PP0602
Sutinen, J. MP308
Sutthichaimongkol, T. PP1108
Sutti, S. PP0942
Suzuki, M. PP1149
Suzuki, N. PP0165, PP0768
Suzuki, S. MP366, PP0125, PP0149
Suzuki, T. **PP0331**
Suzuki, T. PP0237
Suzuki, Y. PP1038
Svagzdys, S. PP0821
Svensson, M.K. OP134
Svetlova, I.O. PP0537
Svorcan, P. MP523
Swaid, T. PP0425
Swallow, E. PP0307
Swarte, J.C. MP127
Sweeney, K. MP608
Sweerts, K. PP0052
Sweis, R. OP076, MP033, PP0227
Swierczynski, M. MP110, **PP0762**, PP0783
Swietek, N. OP169
Swift, B. OP185
Swijnenburg, R.-J. MP702
Sydhom, P. **MP225**
Sy-Janairo, M.L. MP432
Syriha, A. PP1015
Syto, M. PP0586
Syundyukov, E. PP0238
Szabó, I. MP379
Szabó, L. PP0563
Szabó, V. OP015, MP446, PP0520, **PP1120**
Szalai, E. MP297
Szalai, E.Á. MP304, PP0335, PP1124, PP1128
Szalai, M. MP020
Szántó, K. PP0520
Szczepanek, K. PP0298
Szekeres, G. MP048
Szentési, A. OP012, MP304, MP379, MP648, PP0335, PP1128, PP1130, PP1133
Szepes, Z. MP158, PP0614, PP0710, PP0713, PP0731, PP0732, PP0746
Szetela, M. OP055, MP199
Szinay, D. MP602
Szirmay, B. MP048
Szita, I. PP0420
Szolovits, P. PP0415
Szredzki, P. MP549
Szűcs, M. PP0713
Szura, M. OP125
Szymkowski, D. MP568
Šabanias, P. PP0357
Šaltenienė, V. MP545, PP0366
Šmid, A. PP1014
Štiastny, M. PP0846
Štupar, S. PP1014
Šahan, M.A. PP0625
Šeulean, E.C. **MP424**
Śliwowski, Z. MP199
- T**
T A, S. **MP309**, MP633, PP0959, PP0997
Tababi, R. **PP0669**
Tabacelia, D. MP109, MP554
Tabata, H. PP1149
Taboada-López, S. **MP522**
Tacelli, M. MP024
Tacheci, I. PP0116
Tack, J. OP008, MP056, MP057, MP160, MP164, MP167, MP434, MP723, PP0039, **PP0053**, PP0063, PP0066, PP0070, PP0806, PP1186, PP1230
Tacke, F. OP167, MP021, PP0249, PP1181
Tada, F. OP035, MP467
Tada, N. MP323, MP439
Tada, T. OP035, MP467, PP1013
Tadano, T. PP0834
Tadikonda, A. PP0253, PP0412, PP0413, PP0704, PP1208, PP1210, PP1211
Tafciu, V. OP019
Taft, T. **MP164**, PP0634, **PP1186**
Taft, T.H. PP1230
Tag-Adeen, M. PP0201
Tagami, T. PP0736
Taghiakbari, M. OP124, OP142, PP0877, **PP0884**
Tahata, Y. PP0159
Taher Natour, R. **OP221, PP0723, PP0882, PP1095**
Tahiri, M. PP0961, PP1234
Tahiri Joutei Hassani, M. PP0190, PP0213, PP0515
Taida, T. PP0148, **PP0328**, PP0462, PP0702, PP0703, PP0735
Taj-Aldeen, W. PP0154
Tajdine, M.T. PP0938
Takabayashi, K. OP202, MP458, **PP0683**
Takada, K. OP089
Takagi, K. PP1038
Takagi, M. MP693
Takagi, T. MP113
Takahara, N. PP1034
Takahashi, A. MP498, **MP501**
Takahashi, H. **MP696**
Takahashi, K. PP0767
Takahashi, K. **OP073**
Takahashi, K. PP0432
Takahashi, K. OP231
Takahashi, K. PP0134
Takahashi, S. MP437, PP0462, PP0702, **PP0703**, PP0735
Takahashi, S. OP231, MP302, MP423
Takahashi, T. MP197
Takahashi, Y. PP1207
Takai, Y. PP0913
Takamaru, H. **OP089, PP0736**, PP0933, PP1196
Takamori, A. PP0419
Takao, T. **MP368**
Takasago, K. PP0444
Takashina, Y. PP0734
Takatori, Y. MP458, PP0683
Takayanagi, S. VC04
Takedomi, H. PP0419
Takehara, Y. MP227
Takei, D. MP242
Takemoto, S. MP696
Takenaka, K. OP202
Takenaka, M. OP014, OP101, OP231, MP181, MP302, MP423
Takenaka, R. PP0120
Takeshita, E. PP0153
Takeshita, N. PP1196
Takeuchi, K. MP327, MP460
Takeuchi, N. VC04, PP0133
Takeuchi, O. PP0465
Takeuchi, T. PP0114
Takeuchi, Y. PP0767
Takezawa, R. OP089, PP0144
Takigawa, H. MP457, PP0444
Takishima, K. OP202
Takizawa, K. PP0868
Talar-Wojnarowska, R. PP1161
Talley, N.J. MP609, PP0043
Taloumtzis, C. MP676, PP0568
Talukdar, R. MP186
Tamai, N. OP091, PP0933
Tamaki, A. PP1098
Tamandl, D. MP465
Tamaru, Y. **OP087**
Tamba, B.-I. PP1157, PP1180
Tamburrino, D. MP583
Tamim, H. OP220
Tammouch, Z. **PP1140**
Tampaki, M. PP0245
Tamponi, E. PP0442
Tamura, E. PP0738, PP0915
Tamura, H. PP0966
Tamzaourte, M. MP375, PP1214, PP1215, PP1238
Tan, A. MP478
Tan, B. MP142
Tan, C. PP0924
Tan, C.K. PP1111
Tan, H. OP207
Tan, J. OP039
Tan, J.T. OP010, **MP246**, PP1169
Tan, J.-T. MP396
Tan, J.L. PP1193
Tan, N. **MP675**
Tan, S. PP1007

Tan, W. PP1007
Tan, W.K. OP038, MP718
Tan, Y. **PP0715**
Tanabe, M. **PP0968**
Tanabe, S. PP0248
Tanaka, A. OP101
Tanaka, H. OP014
Tanaka, H. MP227, PP0444
Tanaka, H. **PP0767**
Tanaka, H. PP1196
Tanaka, K. MP197
Tanaka, M. **MP032**, PP0237
Tanaka, R. MP366
Tanaka, S. MP242, PP0844, PP1240
Tanaka, S. MP040
Tanaka, S. MP038
Tanaka, T. PP0120
Tanaka, T. OP028
Tanaka, T. **PP0574**
Tanaka, Y. MP350
Tanakaya, K. PP1240
Tandel, R. OP171
Tandon, B. PP0577
Tandon, P. **PP0571**
Tang, A. MP371
Tang, C. PP0396
Tang, C. PP0941
Tang, J. OP002
Tang, J. MP161
Tang, W. MP161
Tang, X. PP0376
Tang, Y. PP0928
Tange, K. PP0153
Tani, J. MP467, PP1013
Tani, T. PP0601
Tanida, S. MP619
Tanino, F. MP227
Tanis, P.J. OP223, OP226, MP220, MP222
Taniyama, Y. **PP0234**
Tanizawa, Y. PP0134
Tannapfel, A. MP479
Tanne, M. **PP0879**
Tantawy, E. PP1022
Tantry, B.V. PP0522
Tanzi, G. PP0139
Tappenden, K. OP159
Tarabar, D. MP671
Tarabová, K. PP1233
Tarantino, I. MP170, MP193, MP540, MP639
Tarasconi, A. PP0139
Tarasenko, Y. PP0238, PP0279
Tarasova, G. MP566, **PP0507**, **PP0510**
Tarasova, G.N. PP0280
Tarasova, L.V. PP0280
Tarasova, T. PP0356
Tarcay Marques Neto, F. PP1136
Tardillo Marín, C. OP213
Tardillo Marín, C. MP343
Tardio Duchan, M. PP592
Tarek Hasan, M. PP0925
Tarek Osman, M. MP225
Targownik, L. PP0571
Targownik, L.E. **PP1187**
Tari, E. MP297, MP379, PP0563, **PP1056**, PP1127, **PP1166**
Tarján, D. MP297, **PP1124**
Tarnowski, M. PP1145
Tarrio, I. MP394
Tashiro, K. MP316
Tasovasili, A. PP0466, PP0568, PP0728
Tassini, A. MP402
Tassovassili, A. MP676
Tatarchuk, O. PP0960, PP0962
Tate, D.J. OP126, VC02, VC08, MP019, MP284, PP0730, PP0838, PP0850, PP0853, PP0876, PP0895
Tateishi, R. PP1034
Tatiana, I. MP547, PP0273
Tatosian, D. PP0586
Tatsuguchi, A. MP036, MP038, MP040, MP404, **PP0581**, PP0582
Taub, R. OP057, OP059, OP061, MP526
Tavakoli, P. PP0888
Tavecchia Castro, M. PP1242
Taveira da Silva, A.J. PP0770
Tawfik, M. MP524
Tawfike, A. MP608
Tawn, J. **PP1206**
Taxonera, C. **PP0684**
Taxonera Samso, C. OP151, OP187, MP268, PP0595
Taylor, A. MP317
Taylor, C. PP0726
Taylor, S. MP611
Tayyab, G.U. PP0201
Teberdieva, M. PP0496
Tedeschi, R. PP0794
Tee, V. OP075, PP0094, PP0095
Tehami, N. PP0201
Tehrani, A. PP1187
Teich, N. PP0647
Teichert, C. PP0464, **PP0500**, PP0504
Teixeira, C. PP0485, PP0859, PP0860
Teixeira, M. PP0033, PP0485, **PP0859**, **PP0860**
Tejedor-Tejada, J. OP009, MP031, MP427, MP428, MP433, MP547, MP549, PP0271, PP0273, PP0755
Tejedor-Tejada, J. MP552, PP0276
Tejerizo García, L. MP666
Tejpar, S. PP0861, PP0864
Telaprolu, H. **PP0394**
Telese, A. OP050, **MP553**, PP0098, **PP0104**, **PP0240**
Telford, J. PP0888
Teller, M. OP043, MP508
Temido, M.J. **PP0429**, **PP0812**
te Morsche, R. MP023
Temprano, P. PP0321
Tenca, A. **MP709**
Tendero Peinado, C. MP291
Tendero-Peinado, C. MP103, MP107, PP0016, PP0018
ten Hove, W.R. OP225
Tenlik, I. PP1073
Teoh, A. OP098
Tepeš, B. MP427, MP433, MP547, PP0271, PP0273
Tepeš, K. MP131
Terai, S. OP073
Terai, Y. MP101, PP0152
Teramura, E. PP0331
Teran, A. PP0755
Teraoka, Y. OP087
Terasawa, T. PP0834
Terauchi, S. PP0601
ter Borg, F. OP225
Terhaar Sive Droste, J.S. OP225
te Riele, W.W. MP030
ter Kuile, M.M. PP0484
Termite, F. PP0613, PP0958
Terranova, C. MP313
Terrin, M. MP584, PP0754
Terry, N.A. OP042, MP563, MP671, MP672
Teruel Sanchez - Vegazo, C. PP0076
Teshima, C. OP142, MP317
Testa, A. MP389, PP0476, PP0488
Testa, G. MP441, **PP0647**
Testa, G. MP600
Teston Cini, B. PP1021
Teutsch, B. MP104, MP379, MP612, PP0021, PP0563, PP1125, PP1128, PP1129, PP1180
te Velde, A. MP629
te Velde, A.A. MP209
Tewes, B. OP002, OP004
Thackray, L. MP452
Thakrar, R. MP033
Thanapirom, K. MP231
Thant, A.M. PP0088
Thapa, D. **MP115**, MP177
Tharmarajah, S. MP680
Thayeswaran, T. PP1030
Theede, K. MP391, PP0535
Theis, V. PP0031
Thelma, B.K. MP575
Then*, C.K. PP0012
Theocharidou, E. MP692, MP695
Theocharis, G. MP676, PP0568
Theodorou, D. OP075, PP0094, PP0095
Theodorou, V. PP0778
Theresa Müllner-Bucsics, T. MP072
Thevenot, T. MP634
Thierens, N.D. PP0332
Thomas, A. PP0027, PP0700
Thomas, K. MP272
Thomas, M. PP0083, PP0586
Thomas, R.B. MP492, PP0085
Thomas, T. MP711
Thomas, W. MP633, PP0959, PP0997
Thomas-Gibson, S. PP0680
Thomopoulos, K. MP676, PP0568
Thompson, A.J. PP0602
Thompson, R. OP016
Thomsen, M.K. PP0912
Thomson, J.-E. MP478, MP589
Thon, C. OP152, PP0538
Thoo, M. PP0569
Thorlacius-Ussing, O. OP168
Thorpe, S. PP0227
Thoufeeq, M. PP1219
Thrumurthy, S. OP143, MP221, MP277, MP282, PP0055, PP0881, PP0886, PP0889
Thuraisingham, A. PP0102
Thurm, T. PP0218, **PP0671**
Thursby-Pelham, F. PP0165, PP0768
Tian, D. MP352
Tian, H. **PP0296**, PP0342, **PP0687**, **PP0787**
Tielbeek, J. MP117, PP0523
Tielemans, M.M. PP1197
Tieranu, C. PP1132
Tighe, R. OP037, MP325
Tikhonov, S.V. OP0254
Tilg, H. OP018, OP195, MP688, MP689
Tilindé, D. **OP022**, OP107, PP0366, PP0446
Tilton, S.T. MP490, MP492, PP0085
Timmermans, B. **MP037**
Timmis, H. OP077
Timofte, O. PP0749
Tinahones, F.J. OP023, PP0364, PP0381
Ting, L. PP0935
Tinoco, J. MP067
Tiriach, H. MP483
Tishchenko, V. PP0781
Tjora, E. MP646
Tjörnblom, H. PP0805
Tlili, A. PP1124
To, E.W.P. PP0851
To, K.F. OP052
Tocarciuc, I. PP0749
Todd, K. OP192
Todeschini, A. **PP0570**, **PP0664**, **PP0673**
Todovichin, K. PP1117
Toes-Zoutendijk, E. OP162, PP0711, PP1231
Toft Sørensen, H. PP0912
Toh, D.-E. PP1087
Tohmatsu, Y. **MP360**
Toi, M. PP1149
Toigo, M. PP0321
Tojo, A. MP458, PP0683
Tokai, Y. PP0125
Tokmak, S. MP136
Tokokdai, K. PP0234
Tokonyai, M.R. PP0539
Tokumoto, Y. MP475
Tokunaga, E. PP0686
Tolmanis, I. PP0238
Tolone, S. OP075, PP0094, PP0095
Tolsgaard, M.G. PP0535
Toman, J. MP114
Tomaru, S. OP091
Tomás, D. PP0485, PP0859, PP0860
Tomasic, V. PP0541, PP0863
Tomescu, F.A. PP1204
Tomez, S. MP638
Tomida, H. **PP0153**
Tomita, H. MP035
Tomita, N. PP0133
Tomita, N. PP1228
Tommerup, L. PP0487
Tomoaki, T. PP0103
Tomonaga, M. OP089
Tomović, A. PP0985
Tomon, G. PP0049
Tong, G. MP483
Tong, H. PP0941
Tong, Q. MP161
Tonhajzerova, I. MP435, PP0065
Tonini, G. PP0917
Tønnesen, C. MP044
Tonon, G. MP188
Tontini, G.E. PP0327, PP1200
Topa, M. MP041
Toplicanin, A. PP0578
Toppeta, A. **PP0015**
Torkington, J. OP177
Tornai, D. MP179, MP354
Tornai, I. MP354
Tornai, T. VC02, VC08, MP019, PP0730, PP0838, PP0853, PP0895
Tornatore, V. OP148
Törnblom, H. OP117, OP119, MP163, MP574, PP0784, PP0801, PP0802
Tornkvist, N. **MP163**, PP1235
Toro, B. PP0670, PP1071, PP1243
Torp, R. MP341, PP0417
Torrealba, L. OP196, MP503
Torrealba Medina, L. OP023, PP0364, PP0381
Torrella Cortes, E.A. MP510
Torrente Sánchez, J. PP0451
Torres, G. PP0493
Torres, J. **OP085**, **OP103**, MP005, MP149, MP339, MP619, PP0422, PP0468, PP0532, **PP0547**
Torres, N. PP0493
Torresano Lominchar, J.V. OP017, MP507
Torres-Herrera, C. MP407
Torres-Larrubia, M. MP664
Torres Monclús, N. PP1172
Torres Reyes, C. MP280
Torres-Vicente, G. OP191
Torrijos García, P. OP184
Tortora, A. MP455
Tosca Cuquerella, J. PP0008
Toshifumi, I. PP0133
Toth, E. PP1200
Toth, J. OP008, MP056, MP160, PP0039
Toth, K.A. MP452, PP0399
Tóth, E. MP299
Tóth, R. MP576, PP1119
Tóth, T. MP627, PP0710, PP0713, PP0731, PP0732, PP0746
Tóth, T. PP1056
Tótté, K.M. OP086
Touibi, A. PP1215, PP1238
Touloumtzi, M. MP695
Tourne-García, C. MP014
Touw, H. MP362
Tovoli, F. OP034
Toya, Y. **PP0149**
Toyama, H. OP014, MP693
Toyama, Y. PP0125
Toyoda, H. OP035, MP467, PP1013
Toyokawa, T. PP0120
Toyonaga, T. MP368

- Toyoshima, N. OP091
 Toyoshima, O. **MP017, PP0847**
 Tozlu, M. PP0072, PP0270
 Traboulsi, E. PP0759
 Trachuk, V. PP1158
 Traina, M. MP170, MP639
 Trajkovska, M. PP1235
 Tran, F. MP390
 Trandafir, A. PP1204
 Trapani-Vondran, D. PP1122
 Trapero-Martínez, A.M. MP157, PP0606
 Trasolini, R. PP0936, PP0937
 Trauner, M. OP183, OP186, MP072, MP077, MP173, MP347, MP465, MP691, PP0741, PP0902, PP0904
 Travis, S. OP032, OP212, MP100, MP105, MP123, MP623, PP0458, PP0550, PP0556, PP0565, PP0594
 Traxler, K. OP128, PP0562
 Treeprasertsuk, S. **MP231**, PP0989
 Treiber, S. MP347
 Trelle, S. PP0074
 Tremaroli, V. MP574, PP0784
 Trepo, E. MP009
 Trespalacios, A. MP429, MP430
 Tretón, X. MP630, PP0386, PP0395, PP0651
 Trevisani, F. OP034, PP1012
 Triantafyllou, K. PP1177
 Triantafyllou, T. OP075, PP0094, PP0095
 Triantopoulou, C. MP134
 Tribonias, G. MP676, PP0568
 Trifan, A. MP294
 Trifan, A.-V. MP080
 Trigo, A. MP499, MP555, **PP1141**
 Trikola, A. **MP254**, MP676, PP0568, PP1138
 Trimponias, G. PP0330
 Trindade, E. OP208, PP0207
 Trindade, I.A. OP117, PP0805
 Trinder, D. MP0630
 Tringali, A. MP539, PP1088
 Tripiana-Iglesias, T. PP1131
 Tripke, V. PP1224
 Tripodi, G. MP028
 Trivedi, R. PP0075
 Trkulja, V. MP417
 Troisi, R.I. PP1009
 Troke, P.J.F. **MP602**
 Troncone, E. MP540
 Troncone, R. PP0320
 Tropeano, F.P. PP0670
 Trotter, J. MP600
 Troya, J. PP0899, PP0900
 Trudgill, N. OP037, OP038, MP325, MP436, MP556, PP0155, PP0156, PP0497
 Truong, T. MP568
 Truys, M. PP0494
 Tsai, M.-C. MP173
 Tsai, Y.-N. MP713
 Tsankof, A. MP290
 Tsapanou Katranara, T. **OP024**, MP565
 Tsapas, A. MP692, MP695
 Tse, E. MP478, MP589
 Tseng, P.-H. MP713, PP0187
 Tshikudi, D. MP444
 Tsilkos, K. OP128, PP0550, PP0562
 Tsotsoros, R. PP0075
 Tsuboi, A. MP227, PP0444, PP0844
 Tsubokura, M. MP425
 Tsuda, M. PP1228
 Tsuda, S. PP0331
 Tsui, V.W.M. PP0851
 Tsuji, Y. PP0933
 Tsujimae, M. OP014, OP028, OP231, MP083, MP302, MP423
 Tsukamoto, T. MP316
 Tsukanov, V.V. PP0280
 Tsumura, H. OP014, MP693
 Tsuruoka, N. **PP0419**
 Tsushima, K. MP242
 Tu, M. MP401
 Tukey, R. OP094
 Tulewicz-Marti, E.M. **PP0697**
 Tümen, D. PP0973
 Tuo, B. MP198, MP369
 Turan Gökçe, D. MP590, **PP0970**
 Turchini, L. MP624, PP0393
 Turck, D. MP345, PP0410
 Turcu-Stiolica, A. PP1163
 Turina, M. PP0930
 Turkot, M. MP374
 Turnbull, C. MP257, MP436
 Turner, D. OP172, OP192, MP512, MP613
 Tüscher, O. MP233
 Tuynman, J. OP224
 Tyberg, A. MP137
 Tynninen, O. MP308
 Tziatzios, G. MP134
 Tzilver, D. PP0205, PP0528, **PP0599**
 Tzouvala, M. MP676, PP0568
 U
 Ubieto, V. OP171
 Uchida, D. MP321
 Uchida, H. PP0601
 Uchima, H. PP0755
 Uchino, M. PP0432
 Uchiyama, K. MP113
 Uchiyama, T. MP425
 Uclés Ramada, E. **MP128**
 Udd, M. MP132
 Udristoiu, A. OP227
 Uedo, N. PP1207
 Uemura, S. OP231, MP181, MP302, MP423
 Uenishi, Y. **PP0173**
 Ueno, H. PP0432
 Ueno, S. OP231
 Uesaka, K. MP239, MP360
 Ueshima, E. OP014
 Uetsuki, K. MP696
 Ueyama, H. PP0125
 Ugolini Lopes, M. MP618
 Ujita, W. PP1149
 Ukashi, O. PP0858
 Ul Haq, E. PP0434
 Ulivi, P. MP084
 Ullah, A. PP0685
 Ullah, S. **PP0181**, PP0241
 Ullah, S. PP0019, PP0577
 Ullrich, R. MP650
 Ulrich, J. PP0206, PP0852
 Umar, N. **MP257, MP436, PP0497**
 Umeda, S. PP0465
 Umegaki, E. PP0011, **PP0158**
 Umehara, H. MP350
 Ung, T. MP447
 Ungaro, F. MP010, MP152, MP260, PP0431, PP0517, PP0626
 Ungaro, R. MP149, PP0422
 Ungaro, R.C. MP150
 Unge, P. OP011
 Unger, J. OP094
 Ungureanu, B. **PP1163**
 Uniken Venema, W.T. OP071
 Uniken Venema, W.T.C. **MP147**
 Unno, M. PP0234
 Urabe, Y. MP227, MP457, PP0444, **PP1240**
 Uraoka, T. PP0767, PP0868, PP1196
 Uraushihara, K. PP0125
 Uray, K. MP721
 Urbanek, P. PP0759
 Urbaniak, M. MP543
 Urbauer, E. MP453
 Urbonas, G. PP1031
 Urbonas, T. PP0699
 Urpi, M. PP0693
 Usai, A. PP0418
 Usai Satta, P. PP0442
 Usak, J. PP1113
 Uslan, M.I. PP0072, PP0270
 Uspenskiy, Y. PP0292
 Ustaoglu, A. OP053, OP063, **MP712**
 Ustares, F. MP429, MP430
 Usui, T. MP238
 Uthaug, L. MP657
 Uzokov, J. PP0117
 Uzzan, M. OP169, MP002, MP156, PP0483
 Ünal, H. MP416
 Ünal, N.G. MP416
 V
 Vackova, Z. PP0759
 Vadalà di Prampero, S.F. **MP310**, MP606
 Vadhariya, A. OP128, PP0458, PP0459, PP0460, PP0550, PP0562, PP0565, PP0566
 Vadori, V. MP383, PP0479
 Vaia, P. MP073, MP632
 Vaiano, M.L. **MP275**
 Vaillo-Rocamora, A. OP171
 Vaira, B. PP0285
 Vaira, D. MP552, PP0276
 Valatas, V. MP062
 Valaydon, Z. MP078
 Valbuena Gómez, I. MP016
 Valdovinos-García, L.R. PP0288
 Valente, A.I. PP0592, PP0628
 Valente, R. **PP0186**
 Valente, S. PP0779
 Valibouze, C. MP306
 Valitova, E. PP0004, PP0242
 Valjevac, A. MP588
 Valldosera Gomis, G. OP213, MP343
 Valle, A.M. MP635
 Vallelonga, V. MP571
 Valluri, S. PP0437
 Valori, R. OP037, MP325, PP0853
 Valuyskikh, A.I. PP0537
 Valuyskikh, E.Y. PP0537
 Valverde-López, F. MP103, **PP1131, PP1134**
 Vámosy, K.L. PP1126
 Vámosy, L.K. PP0335
 Vanaclocha, M. MP014
 Vanasek, T. PP0575
 Vanassche, T. PP0298
 van Asseldonk, D. PP0554
 van Asselt, S.J. OP065
 van Baalen, S.M. PP1197
 van Baar, A. OP049
 van Barneveld, M. PP0554
 van Beelen Granlund, A. PP0445
 van Berge Henegouwen, M. MP039
 van Berge Henegouwen, M.I. PP0162
 Vanbiervliet, G. MP068, MP318, MP440
 van Bodegraven, A. PP0554
 van Bokhorst, Q.N. **OP181**, PP1198
 Vánca, S. MP099, PP1127, PP1166
 Van de Bruene, C. MP056, **MP723, PP0039**, PP0063, PP0066
 Vandecandelaere, P. PP0836
 van de Laar, B.C. MP222
 van Delft, F. MP023, MP030, PP1041, PP1101
 Van den Abbeele, P. PP0692
 van den Berg, D.M.N. PP0711, PP1231
 van den Berg, S. MP082, PP1155
 van den Heuvel, M.C. MP600
 van den Hoek, K. OP049
 Van den Houte, K. **MP160**, MP723, PP0039, PP0066, PP0070
 Van den Houte, M. OP117, PP0805
 Van Den Houte, M. OP121
 van de Pol, N. PP0561
 van der Bilt, J. OP188, PP0484
 van der Bilt, J.D. MP705
 van der Burgt, Y. MP245
 Van Der Heide, F. MP132, MP147
 Van der Linden, L. PP0298
 van der Marel, S. PP0641
 van der Marel, S. OP086, OP188, MP211, PP0567
 van der Merwe, S. MP137
 van der Meulen – de Jong, A.E. MP504
 van der Meulen-de Jong, A.E. PP0641
 van der Meulen-de Jong, A.E. OP086
 Van Der Meulen - De Jong, A.E. MP211, PP0345, PP0454, PP0484, PP0567
 van der Putten, J. MP715, MP717, PP0167
 van der Schee, L. **OP224**
 van der Sloot, K. PP0440, PP0448
 van der Sluis, H. OP225
 van der Sommen, F. MP715, MP717, PP0167, PP1198
 van der Spek, B.W. OP225
 Vanderstappen, J. MP145
 van der Vegt, B. OP001
 van der Vlugt, M. OP181, PP1198
 Van der Voort, V. MP285
 Van der Voort, V. MP068
 van der Waaij, A.M. **OP065, PP0107**
 van der Waaij, L.A. OP065
 Van der Wijst, M.G. OP071, MP147
 van der Woude, C.J. OP188, MP337, PP0561
 van der Zander, Q.E.W. OP122
 van der Zwaan, S. MP082, PP1155
 van de Schootbrugge-
 Vandermeer, H.J. PP0128
 van Deursen, F. PP0688
 van de Veerdonk, W. PP0128
 Van Domselaar, M. OP023, OP187, OP213, MP343, MP503, PP0364, PP0381, PP0557
 van Dongen, K. PP0484
 van Doorn, R. MP082, PP1155
 van Dop, W.A. MP337
 van Driel, L.M.J.W. MP030
 van Driel, L.M. MP535
 van Dulleman, H. MP022, MP210
 Van Dulleman, H. OP020
 van Eijck, C. OP132
 van Eijck, C.H. OP132, MP022
 van Eijck van Heslinga, R. **MP715, MP717, PP0167, PP1198**
 Vanek, P. PP1217
 Vanella, G. MP024, **MP027**, MP137, **MP188, MP536**, MP540
 Vanelslander, P. PP0518
 van Gaalen, F.A. MP504
 van Geenen, E.-J.M. PP1041
 van Geenen, E.J.M. PP0332
 Van Geenen, E.-J.M. MP023, MP030, PP1101
 van Geffen, E.G.M. OP223
 van Gennep, S. PP0554
 van Gils, T. MP574, PP0784, **PP0801, PP0802**, PP0806
 van Ginkel, Y.J. OP065, PP0107
 Vangoitsenhoven, R. MP145
 van Goor, H. PP0397, PP0511
 Van Gossuin, A. PP0298
 Van Gucht, H. MP434
 Van Haaren, S. OP083, MP622
 van Hattum, A. PP0890
 van Heijst, L.E. PP0107
 Van Hillegersberg, R. MP039
 van Hooft, J. MP022, MP082, MP245, MP697, PP1041, PP1155
 van Hulst, R. MP117, PP0523
 Vanigli, N. PP0640, PP0668
 van Kaam, A.H.L.C. MP573
 Van Laarhoven, C.J. MP705
 Van Laethem, A. PP0494
 van leerdam, M. PP1155

van Leerdam, M. OP162, MP082, MP245, MP697
van Leerdam, M.E. OP180
van Loo, M. PP0128
van Munster, S. OP116
Vanni, D. MP236
van Oostrom, J. **MP387**
Van Oudenhove, L. OP048, OP117, PP0805
Vaňová, N. PP0689
Van Rampelbergh, R. OP042, MP671, MP672
van Roermund, N.S. **OP180**
van Royen, N. PP0332
van Ruler, O. OP188, PP0484
van Santvoort, H.C. MP022, MP030
van Schaik, F.D.M. OP086
Van Schaik, F. OP188, PP0484, PP0567
van Schajik, Y. **MP573**
Vanslembrouck, R. OP158
Vanuytsel, T. OP008, OP157, OP158, OP159, MP056, MP146, MP148, MP160, MP167, MP434, MP723, PP0039, PP0063, PP0298
van Wanrooij, R.L. MP030, PP1089
van Wanrooij, R.L. MP702
Van Wanrooij, R... MP022
Van Wanrooij, R.L. PP1101
van Welden, S. OP077
van Westreenen, H.L. OP222, MP222
Van Westreenen, H.L. OP226, MP220
van Wijk, M.P. OP208
Van Workum, F. MP362
Vanzin Fernandes, M. **PP0982**
van Zon, S. MP629
Vara, K. PP0688
Varadarajulu, S. OP227
Vara Luiz, F. **PP0033**
Varanese, M. PP0023
Varela, P. MP674
Varela Trastoy, P. OP043, OP151, MP268, MP510
Varga, A. OP197, PP0520
Varga, B. PP1119
Vargas, J. **OP098**, MP355
Vargas, J.I. MP429, MP430
Vargas-Alayza, C. MP429, MP430
Vargas García, A.L. PP1172
Vargas-Madrigal, J. MP137
Vargas Olmos, I.O. **MP419**
Vargas-Rubio, R. PP1050
Varghese, C. PP0055
Varghese, J. MP541
Variola, A. OP106, OP169, PP0476, PP0570, PP0664, PP0673
Varkalaite, G. MP468
Varzaru, B. MP586
Vasant, D.H. PP0701
Vasapolli, R. OP056, **OP137**, MP280, MP549
Vasas, B. MP446, PP0713, PP0731, PP0732, PP0746
Vašátko, M. PP0191
Vass, V. OP012, MP297, MP379, MP648, PP1128, PP1130
Vassallo, R. PP0508, PP0856
Vastarella, J. **PP0492**
Vatn, S. MP341
Vaughan, R. PP1099
Vaughan, R. PP0533
Vavallo, M. OP140, **MP203**, MP205
Vayreda, E. PP0755
Vaz, R. PP0635
Vážanová, D. **PP0097**
Vázquez Gómez, D. PP0493, PP1172
Vázquez Morón, J.M. MP343
Vázquez Rey, M.T. PP0666
V D Geijn, M. OP020
Vecchi, M. OP129, MP010, MP041, MP256, PP0078, PP0129, PP0130, PP0327, PP0414, PP0629
Vecchio, F.M. PP0958
Vecchione, M. MP340
Vega, P. OP151, MP064, MP268, MP343, MP510, PP0666
Vega Villamil, P. OP213
Vegni, E.A.M. PP0471
Vehreschild, M.J.G.T. PP0685
Veiser, T. MP324
Veisman, I. PP0506
Vela, M. OP187
Vela, M. MP510
Velarde Ruiz Velasco, J.A. MP430
Velarde-Ruiz Velasco, J.A. MP429
Velasco, F. PP0708
Velasco Guardado, A.J. MP666
Velasco Rodríguez-Belvis, M. MP343
Velasquez-Rodriguez, J.G. MP138
Velayos, B. OP009, MP428, PP0271
Velazquez López, J.R. PP0980
Veldhuijzen Van Zanten, S. PP0706
Veljkovic, T. PP0763
Veloso, R.F. MP365, PP0093
Velut, G. MP440
Venâncio, J. PP0747
Venegas, J. PP0084
Venerito, M. OP009, MP549, PP0136
Venezia, G. MP540
Venglovecz, V. **MP299, PP1135**
Venkat, S. MP563
Venkatachalapathy, S.V. MP132
Venneman, N.G. MP022, MP023, MP030, PP1101
Ventimiglia, M. PP0629, PP0645
Ventura, M. MP389, PP0488
Venturi, D. **PP0020**
Venturini, I. OP096, MP577
Veny, M. OP026
Vera, I. MP510
Vera Mendoza, M.I. OP151, MP268
Vera-Mendoza, I. PP0557
Verbeke, C.S. MP085
Verbeke, J. MP145
Verbeke, K. MP051, MP145
Verbiest, A. **OP158, MP146, MP148**
Verbói, M. OP012
Verdaasdonk, E.G. PP0484
Verdi, D. MP223
Verdiyev, E. PP0275
Verdonk, F. MP104
Verdonk, R.C. MP022, MP023, MP030, PP1101
Verdu, E. OP005
Vereczkei, Z. MP048, MP251, **PP0306**
Veres, D.S. PP1180
Veres, D.S. MP099, MP612, PP0335, PP0563, PP1125, PP1157, PP1166
Verga, M.C. MP441, MP722
Vergara, A. PP0693
Vergés Aleix, L. **PP0493**
Vergnolle, N. PP0434, PP0435, PP0779
Verhagen, M.A.M.T. OP115
Verheyden, A. **MP167**
Verheyden, M. PP0822
Verhoeven, R.H.A. PP0128
Verjee, A. MP151
Verkade, H.J. MP600
Verlato, G. PP0139
Verleye, L.M.M. **OP086**
Vermeer, E. PP0490
Vermeire, S. OP026, **OP081**, OP105, OP147, **OP156**, OP195, MP009, MP112, MP145, MP327, MP330, MP445, MP449, MP564, MP582, MP617, **MP623**, MP686, MP688, **MP689**, PP0354, PP0355, PP0494, PP0556, PP0605
Vermeire, S. PP0542, **PP0555**
Vermeulen, J.L.M. MP314
Verreth, A. MP328
Verscheuren, P. PP0494
Verstappen, G.M. OP071
Verstockt, B. OP026, MP112, MP145, MP328, MP445, MP449, MP564, PP0588, PP0647
Verveer, C. OP162
Vescovo, M. OP054
Vespa, E. **MP090**, MP260, MP491, PP0183
Vesterberg, A. PP1147
Vestergaard*, M.V. OP017, **MP507**
Vetrano, S. MP390, MP571
Vetter, M. PP0529
Vetter, M. MP563
Veysel Özden, A. MP444
Vezakis, A. PP1177
Viale, E. MP441, MP722, PP1190
Viana Baptista, P. MP690, MP698
Viazis, N. MP254, PP0330
Vibeke Verstergaard, M. OP215
Viceconti, N. PP0958
Vicente, R. MP510
Vicente Lidón, R. OP213, MP031, MP343, MP508
Vich Vila, A. OP071, OP108, PP0379, PP0691
Vich Villa, A. OP020
Vico, E. OP075
Vidadi Oğlu, Q.F. MP427
Vidal, J. PP0643
Vidal, O. PP0688
Vidon, M. MP156, PP0377
Viegas, M.I. **PP0195, PP0196, PP0197**
Viel, A. PP0132
Viennot, S. OP189
Vierlinger, K. MP390
Vieth, M. OP208
Vieujean, S. OP169, MP002, MP149, MP328, PP0647
Vigano*, C. OP169, PP0629
Viganò, M. PP1018
Vignane, T. MP199, MP719
Vignolle, G. MP390
Vignotto, C. MP223
Viiri, K. **OP002**, OP004, MP248
Vij, A. PP0898
Vijayan, B. PP1011
Vikse, J. PP1138
Vila, J.J. MP132, MP193
Vilas-Boas, F. OP228
Vilchez-Vargas, R. OP152
Vilhena Alves dos Santos, M. PP1175
Villagrasa Manzano, R. PP0008
Villalvazo López, A.S. PP0980
Villanacci, V. MP045
Villarejo, G.M. PP0068
Villasanta, A. PP0693
Villas Boas Legentil, F. PP1178
Villoria Ferrer, A. MP334, MP673
Vinaixa Aunés, C. MP128
Vinasco Pacheco, K. OP141
Vincze, Á. OP012, MP104, MP379, MP1128, PP1130
Vind, I. OP204, PP0535
Vinge Holmquist, O. OP170
Vinokurova, L. PP1179
Viola, A. OP169, PP0645
Virk Hundal, N. MP660
Visaggi, P. OP075, MP092, MP256, MP259, **MP263, MP662, MP663, MP727**, PP0094, PP0095
Vishwanathan, S. OP038
Visnovcova, N. PP0065
Visnovcova, Z. MP435, PP0065
Vispo, E. MP216
Visschedijk, M.C. OP020, MP210, MP337, PP0397, PP0484, PP0567
Visser, E. **PP0561**
Visser, E. PP0540
Vissers, E. MP145, MP564
Vitale, A. PP1018
Vitale, F. MP645
Vitalis, Z. MP179, MP354
Vitek, P. PP0209
Vitello, A. PP0645, PP0856
Vitikainen, K. MP506
Vitus, E.S. **PP0416**
Viviane Sá dos Santos Rondon, M. PP0263
Vizzuso, A. MP084
Vlachogiannakos, J. PP0048, PP0073, PP0089
Vladea, R. MP327, MP620
Vladimirova, N. PP0411
Vlăduț, C. **MP590**
Vlasenko, N. PP0004
Vlckova, E. PP0580
Vleggaar, F.P. OP222, OP224, OP226, MP022, MP030, MP222, PP1101
Vlug, M.S. OP225
Vnučáková, J. PP0056
Voeller, A. PP1031
Voermans, R.P. MP022, MP030, MP702, PP1089
Vogl, T. OP001, OP111, MP210
Vogt, G. PP0221
Voigtländer, L. PP1122
Voill-Glaninger, A. MP638
Voiosu, A.M. MP131, MP538
Voiosu, T.A. MP538, PP1203
Vojnovic, M. PP0985
Vojtek, P. **PP1113**
Vojtko, M. MP053, **PP0056**
Volkers, A. PP0554
Volkov, A. MP566
Voll, D. **PP0230**
Vologzanina, L. MP427, MP547, MP552, PP0271, PP0273, PP0276
Vologzhanina, L.G. PP0280
Voloshyna, L. MP230
Volpato, S. PP0310
Volta, U. MP659, PP0310, PP0347
von Armin, U. **PP0085**, PP0538
von Hahn, T. **MP280**
von Heesen, M. PP0230
von Knebel Doeberitz, M. MP463
von Muhlenbrock, C. MP429, MP430, **PP0084**
von Renteln, D. OP124, OP142, PP0706, PP0845, PP0877, PP0884
von Weikersthal, L.F. MP479
von Widdern, J.C. OP229
Voorneveld, P. MP504
Voorneveld, P.W. MP211, PP0454
Vörhendi, N. MP379, PP0021
Vork, L. OP121, MP162
Vornhuelz, M. **MP298**
Vorobyeva, E. PP0513
Vos, J.M. PP0500
Voskuil, M. MP600
Votto, M. PP0076
Voulgaris, T. PP0048, PP0073, PP0089, PP0583, PP1177
Vovk, T. MP335
Voynovan, I. MP427, MP433, MP547, MP552, PP0271, PP0273, PP0276, PP0280
Vradelis, S. MP676, PP0568
Vrakas, S. OP169
Vrbová, P. PP1233
Vrolijk, J.M. PP1101
Vrško, M. **PP0689**
V. Sá dos Santos Rondon, M. MP102
Vu, T.U. PP0265
Vuillemoz, M. PP0665
Vuitton, L. MP156, PP0398, PP0407
Vujaninovic, M. MP243, **MP594, PP1138, PP1147**
Vuković, P. MP523
Vuksanovic, S. PP0578
Vuletici, D. PP1079
Vu Trung, K. PP1168
Vuyyuru, S.K. **MP270**, PP0531, PP0598, **PP0627**
Vyncke, V. PP0605
Vysoudil, M. PP0116
Vythilingam, D.I. **MP710**

W

- Waal, T. PP0538
 Wachter-Weizl, J. MP638
 Wacker, J. PP1025
 Wadhwa, A. MP154
 Wadhwa, N. PP1037
 Wagner, M. PP0911, PP1239
 Wahab, E. OP080
 Wai, T. OP027, OP110
 Wakabayashi, M. PP1196
 Wakai, T. PP0432
 Wakamura, K. OP202, PP0734, PP0738, PP0914, PP0915
 Wakim El-Khoury, J. **MP264, PP0074**
 Waldherr Ávila de Melo, C.M. PP0388
 Waldmann, E. PP0741, PP0902, PP0904
 Waldner, M. PP0529
 Waldschmidt, D. MP479
 Wali, A. PP0888
 Walia, A. PP0936, PP0937
 Walker, A. PP0873
 Walker, A. MP602
 Walker, C. **MP651**
 Walker, G. PP0678
 Walker, S. PP0586
 Walker-Smith, B. MP376
 Wallace, M. MP245, MP317, MP697
 Wallace, Z.S. MP183
 Wallace, Z.S. MP350
 Wallenhorst, T. MP285, MP318, MP440, PP1100
 Wallenhorst, T. MP068
 Waller-Gonzalez, L.A. PP1116
 Wallis, S. MP556
 Walsh, A. MP326, MP681, PP0548
 Walter, B. MP377, **PP0911, PP1239**
 Walter, J. OP044
 Walter, J. OP155
 Walters, T.D. OP127
 Wan, K.Y.Y. MP672
 Wan, N. **PP0576, PP0577, PP1193**
 Wang, B. OP120
 Wang, B. PP0083
 Wang, C. MP500
 Wang, C. MP370
 Wang, C. PP1061
 Wang, D. OP085, MP684
 Wang, F. PP0137, **PP0283**
 Wang, F. PP0224
 Wang, G. **OP153**
 Wang, H. PP0865
 Wang, H. PP0179
 Wang, J.-Y. PP0842
 Wang, J. PP1007
 Wang, J. **PP0124**
 Wang, J. PP0534, PP1007
 Wang, J. MP026
 Wang, J. OP120
 Wang, J. **PP0002**
 Wang, K. **PP0091**
 Wang, L.M. MP218, PP1111
 Wang, L. OP296
 Wang, L. OP201, MP087, MP089, MP401, PP1146
 Wang, L. PP0663
 Wang, M. PP0405, PP0663
 Wang, P. PP0396
 Wang, Q. MP029
 Wang, Q.-L. **MP243**
 Wang, Q. OP047
 Wang, R. OP160
 Wang, S. MP161
 Wang, S. **MP352**
 Wang, S. MP496
 Wang, T. MP333
 Wang, T. OP134, MP085
 Wang, T.C. MP035
 Wang, W. PP0534
 Wang, W. MP012
 Wang, W. OP207, MP493
 Wang, W.J. **PP0059**
 Wang, X. MP349
 Wang, X. OP120
 Wang, X. **MP550**
 Wang, X. **OP033, MP292**, PP0978, **PP0979**
 Wang, X. PP0944
 Wang, X. MP687
 Wang, X. MP089
 Wang, Y. OP160
 Wang, Y. PP0600
 Wang, Y. OP139, MP459
 Wang, Y. MP136, PP0855
 Wang, Y. **MP474, PP1144**
 Wang, Y. OP084
 Wang, Y. **OP040**
 Wang, Z. PP0405
 Wang, Z. MP217
 Wang, Z. PP0841
 Wang, Z. MP626
 Wanner, K. PP0631
 Wannhoff, A. PP0916
 Wanten, G.J. PP0298
 Ward, B. **PP1067**
 Ward, J. PP1031
 Ward, R. MP154
 Wardi, J. PP0272
 Warmbrodt, N. MP044
 Warne, L. MP115, MP177
 Warnock, I. PP0597
 Warren, D.J. OP003
 Warren, F.C. PP0969
 Wasif, A. MP037
 Wasko-Czopnik, D. PP0610
 Wasserberg, N. MP273
 Watanabe, K. PP0432
 Watanabe, M. PP1098
 Watanabe, T. MP475
 Watanabe, T. **MP561**
 Watanabe, Y. PP0234
 Waterboer, T. MP203, MP205
 Watzl, P. MP638
 Wauters, L. OP008, **OP157**, MP131
 Wawer, A.A. OP039
 Waxman, I. MP317, PP1081
 Wazeery, A. PP1062
 Webb, D.-L. **PP0219**
 Webb, M. PP0077
 Weber, A. PP0074
 Weber, M. PP0221
 Weber, R. **PP0897**, PP0899
 Weber, S. OP182, **PP0967**
 Weber Nunes, D. OP206
 Weber-Sparrow, K. **PP0040**
 Webster, G. MP132, MP350
 Wedel, P. OP080
 Wedel, T. MP513
 Wedemeyer, J. MP280
 Wedemeyer, R.-S. PP0593
 Wedershoven, V. MP426
 Wedi, E. MP280, PP0221
 Weeramange, C. MP568
 Weersma, R.K. PP0379
 Weersma, R.K. OP001, OP020, OP071, OP108, MP127, MP147, MP210, MP575, MP600, PP0368, PP0440, PP0448, PP0490
 Weerts, Z.Z. MP162
 Wegeberg, A.-M. PP0046
 Wei, B. **MP015**, PP0837, **PP0843**
 Wei, Y. MP161
 Weich, A. PP0221, **PP0916**
 Weidinger, C. **MP572**
 Weidinger, G. MP638
 Weidner, A. PP0726
 Weilert, F. MP478
 Weinberger, A. OP001
 Weismuller, T. MP280
 Weiss, F.U. MP642
 Weiss, J. MP154
 Weiß, F. PP0372
 Wellens, J. **MP145**
 Welsch, L. OP229
 Welsh, R.C. OP219
 Wen, L. PP0545, PP0616
 Wen, X. PP0138
 Weng, Z. **MP412**
 Wengström, Y. PP1147
 Wenisch, C. MP638
 Wenske, T. MP329
 Wentink-Bonnema, E.M. PP0815
 Werge, M.P. MP300
 Wertheimer, J. OP193
 Weseslindtner, L. MP638
 West, J. **MP172**, MP519, PP0912
 West, R. OP086, OP188, PP0484, PP0554, PP0561, PP0567
 Westerberg, M. OP164
 Westerhof, J. OP112
 Weston, A. MP697
 Weusten, B.L.A.M. OP115
 Weusten, B.L. OP112, OP116, OP225, MP039, MP717
 Wewer, M.D. OP190, **MP007**
 Wewer, V. MP007
 Weymar, L.M. **MP324**
 Weyrauch, S. MP165
 Wheler, J. **PP0912**
 White, C. **MP326**, MP628
 White, I. MP273
 White, J. PP0874, PP0906
 White, J. PP0165, PP0768
 White, L. PP0678
 Whiteman, M. MP719
 Whiteside, C. PP0711
 Whitfield, A. MP069, MP284, MP317, MP371, MP381, PP0179, PP0184, PP0769, PP0876, PP0890, PP0891, PP0892, PP1199
 Whitmarsh, R. MP431
 Wickramasekera, N. PP0304
 Wickramasinghe, D.G. PP0102
 Wickramasinghe, N. **PP0102**
 Widmer, J. OP099, OP228
 Wiegel, M. OP005
 Wiekowski, M. PP0390
 Wieland, J. PP0388
 Wielenga, M.C.B. PP1089
 Wieler, J. MP568
 Wiemer, H. PP0706
 Wien, L. PP0993
 Wientjes, C. OP225
 Wierdak, M. MP199, MP719
 Wiering, B. MP705
 Wiese, J.J. MP650, PP0372
 Wiese, M.L. MP642
 Wiessner, J. PP0206
 Wiessner, J.R. **PP0852**
 Wifi, M.-N. MP121
 Wiggers, J.K. OP223
 Wijsman, K. **MP697**
 Wild, P. MP233
 Wilde, J. PP0529
 Wilder-Smith, C.H. **PP0323, PP0775, PP0777, PP0798**
 Wilhelm, L. PP0564
 Wilkens, R. MP391
 Willandt, B. MP328
 Willheim, M. MP638
 Willi, N. PP0074
 Williams, D. OP176
 Williams, G. MP609
 Williams, J. PP0053
 Williams, S. MP069, MP284, MP317, MP371, PP0890
 Williams, S.J. PP1199
 Williams, S. PP0876
 Williamson, V. PP0824
 Wilmlink, J.W. PP1089
 Wilms, E. MP162
 Wilmsen, N. MP211
 Wils, P. MP345, MP630, PP0377, PP0410
 Wilson, A. PP0539, PP0701
 Wilson, R. OP084, OP102, MP670
 Win, S. PP0623
 Winata, L.S. PP0602
 Winchester, C. PP0210
 Windsor, J. MP186
 Winkens, B. PP0780
 Winkle, P. PP0638
 Winters, C. MP322
 Wirenfeldt, M. PP0360
 Wirth, D. MP153
 Wissner, S. MP479
 Witczak, K. PP0112
 Witjes, C.D. PP0484
 Witteman, B.J. MP022
 Wittmer, L. MP668
 Wium Bjerrum, J. MP391
 Wizenty, J. **PP0003**, PP0249
 Włodarczyk, B. MP182, **PP1161**
 Włodarczyk, P. PP1161
 Wohl, P. MP708
 Wohlmuth, P. MP280
 Wojciechowska, U. PP0112
 Wojtowicz, A.M. PP0611
 Wójtowicz-Popiel, M. MP374
 Wolak, A. PP0101
 Wolanski, L. PP0556
 Wolf, D. MP671
 Wolf, D.C. MP680, MP684
 Wolf, J.M. PP1021
 Wolf, L. PP0529
 Wölnerhanssen, B.K. OP048, MP312
 Wolpin, B. MP243
 Wolters, L.M.M. PP1197
 Won, D.-S. PP1115
 Won, S.Y. MP066, PP0143
 Wong, C. MP149
 Wong, E.C. MP385
 Wong, J. MP478
 Wong, K. OP155
 Wong, M.-W. MP713
 Wong, T. OP076, MP091, MP727
 Wong, T.L.M. MP255
 Wong, V.W. OP058
 Woo, M. OP153
 Woodland, P. OP053, MP384, PP0101
 Woods, R.J. PP0602
 Woodward, T.A. PP0045
 Woolcott, J.C. OP207, MP493, MP686, PP0354, PP0355
 Wooldrage, K. OP179
 Worbs, J. PP0041
 Worland, T. MP074
 Wosik, K. MP342, PP0548
 Wozny, M. MP390, MP571
 Wray, J. MP262
 Wree, A. OP167, MP021, PP0249, PP1181
 Wright, E.K. PP0602
 Wu, C. MP683, PP0549
 Wu, D. PP1124
 Wu, E. MP369
 Wu, H. MP675
 Wu, H. OP085, MP680, MP681, MP684
 Wu, H. PP1007
 Wu, J.-Y. MP113
 Wu, J. OP120
 Wu, J. MP615
 Wu, J. MP161
 Wu, J. **MP247**
 Wu, J. MP003, MP342, MP686, PP0544, PP0547
 Wu, J. OP010
 Wu, K. MP687
 Wu, L. **MP376**, MP378, PP0002
 Wu, L. **OP070, MP076**, MP126, **MP411**, PP0983
 Wu, Q. MP247
 Wu, T.-T. MP655
 Wu, X. MP029
 Wu, X. MP247
 Wu, X. OP160
 Wu, Y. MP350
 Wu, Y. PP0855
 Wu, Y. OP120, MP161
 Wuestenberghs, F. **PP0804**
 Wuhrer, M. MP245
 Wulff, M.V. MP280

Wüthrich, H. MP685, PP0596

X

Xavier, S. PP0486, PP0750, PP0757, PP0789, PP1216
Xavier de Andrade, T. PP1136
Xia, B. OP041, **PP0108**
Xia, C. MP487, MP490, MP492
Xia, G. OP025
Xia, L. OP118
Xia, M. MP675
Xia, T. **PP0928**, PP1040
Xian, F. MP453
Xiang, Q. OP007
Xiang, T. PP0978
Xiao, B. **PP1007**
Xiao, C. PP0042, PP0057, PP0058
Xiao, S. **PP1017**
Xiao, W. MP675
Xiao, X. OP218
Xiao, Y. MP096, MP675, PP0100
Xie, F. MP026
Xie, F. **OP052**
Xie, J. PP0137
Xie, L. PP0100, PP0264, PP0281, PP0282
Xie, S. MP403, PP0950
Xie, X. **PP1061**
Xing, X. **OP218**
Xing, Y. PP0663
Xinou, E. PP0528
Xinxing, T. MP012
Xiong, C. MP401
Xiong, W. MP393, PP0888, PP0936, PP0937
Xiong, Y. MP370, MP459
Xu, B. OP120
Xu, B. PP0837, PP0843
Xu, C. PP0862, PP0920, PP1040
Xu, H. PP0264, PP0281, PP0282
Xu, H. OP155
Xu, J. PP0376
Xu, M. OP120
Xu, P. MP162
Xu, S. **MP026**
Xu, W. OP109
Xu, Y. PP1144
Xu, Y. MP298
Xu, Z. OP120
Xuan, S. OP103
Xuan, W. MP710
Xue, C. **PP0083**
Xue, R. **MP595, MP598**
Xue, Z. PP0100

Y

Yaacoub, H. PP0867
Yaacoub, T. PP1192
Yablecovitch, D. **MP592**
Yabuuchi, Y. OP089
Yacoub, H. MP046, **PP0318**, PP0346, PP0350, PP0516, PP0525
Yacoub, M.-R. MP260
Yadav, D. MP186
Yadav, T. PP0833
Yadegar, A. MP426
Yafarova, A. PP0952
Yaghi, C. MP106, MP229, MP516, PP0297, PP1192
Yagi, N. MP206
Yahagi, N. MP458, PP0153, PP0683
Yakoubi, M. MP422, PP0259, PP0294, PP0981, PP1000, PP1006
Yalcin, S. OP002
Yamabe, E. PP0133
Yamada, K. PP0432
Yamada, M. OP089, PP0736
Yamada, M. PP1228
Yamada, M. MP239, MP360
Yamada, R. OP231
Yamada, T. PP1196

Yamada, T. MP040
Yamaguchi, A. OP087
Yamaguchi, D. OP089
Yamaguchi, H. MP460
Yamaguchi, K. PP1196
Yamaguchi, M. MP101, PP0152
Yamaguchi, S. PP0432
Yamaji, T. PP0736
Yamamoto, K. MP197
Yamamoto, K. PP0216
Yamamoto, K. PP0120
Yamamoto, M. PP0736
Yamamoto, N. MP227, **PP0444**
Yamamoto, S. PP0432
Yamamoto, T. PP0432
Yamamoto, Y. PP0111, PP0153
Yamamoto-Furusho, J.K. MP429, MP430
Yamanaka, K. MP693
Yamao, K. MP696
Yamashita, H. MP460, PP1195
Yamashita, K. MP227, PP0444
Yamashita, K. MP197
Yamashita, Y. MP242
Yamazaki, H. **PP0133**
Yamazaki, T. OP231, PP1038
Yan, B. OP100, PP0170
Yan, B. PP0627
Yan, H. OP218, **MP496, PP0029**
Yan, J. OP100, **MP626, PP0455**
Yan, P. OP120
Yan, Z. MP029, **MP190**
Yanai, H. OP093, OP150, MP273
Yanai, Y. **PP0125**
Yañez, F. MP054
Yang, A. MP029, MP190
Yang, B. PP0083
Yang, B. MP075
Yang, C. **MP075**, MP596, PP0841, PP0949
Yang, C. PP0837
Yang, C.-Y. MP363
Yang, D.-H. PP0441
Yang, F. MP348
Yang, H. PP0194, PP0224
Yang, H. PP1187
Yang, J. OP173, **MP631, PP0467**
Yang, J. **MP133**, MP474, **PP1044, PP1059, PP1097**, PP1143, PP1144
Yang, J. PP0184
Yang, J. PP0718
Yang, J. PP0001
Yang, J. OP029, OP041, OP218, MP288, MP372, MP496, PP0001, PP0029, PP0108, PP0715
Yang, J.-L. OP163, MP515
Yang, J. OP092
Yang, J.Y. PP0603
Yang, L. MP125, MP348, MP349, MP353, MP597, PP0718, PP0979
Yang, L. PP0935
Yang, M. PP1110, PP1223
Yang, S. OP120
Yang, S.-K. MP387, PP0441
Yang, X. PP0283
Yang, Y. OP100, PP0170
Yang, Y. **OP100**, MP626, **PP0170**, PP0455
Yang, Z. **PP0941**
Yang, Z. PP0216
Yang, Z. OP042, MP671, MP672
Yang-Bor, L. PP0935
Yannick, B. PP1215
Yano, F. MP439
Yano, H. PP0248
Yano, T. MP460, MP561, PP1195
Yao, J. OP214, **MP047**
Yao, J. MP026
Yao, K. PP1207
Yao, L. PP1007
Yao, S. PP0283
Yao, T. **PP1207**
Yao, X. PP1110

Yao, X. OP104
Yapali, S. PP1235
Yarandi, S. OP045, OP082, OP102, MP670
Yaraş, S. MP416
Yarlagadda, R. **PP1174**
Yarol, R.C. MP421
Yarur, A. OP079, MP449
Yarur, A.J. MP686, PP0547
Yaskina, M. OP155
Yassin, K. PP1043
Yasuda, I. OP101, OP231, MP181, MP302, MP423
Yasuda, T. **MP113, MP206**
Yasuda, T. **PP1151**
Yasuda, Y. MP206
Yata, Y. MP467, PP1013
Yavzori, M. MP592
Ye, B. OP120
Ye, B.D. MP387, PP0441
Ye, J. PP0921, PP1040
Ye, T. **MP701**
Ye, Y. MP012
Yeh, J.-H. **PP0842**
Yehuda Margalit, R. PP0501
Yektaei, E. OP011
Yemula, N. MP556
Yen, H.-H. MP713
Yen, M. OP078, OP194
Yeo, J.H. MP326
Yerushalmi, B. MP249, PP0228
Yetim, A. PP0948
Yi, T. PP0369
Yildirim, A.E. MP416
Yin, A. PP0534
Yin, F. MP567
Yin, M. MP403, **PP0950**
Yin, Z. PP0695
Yin, Z. MP500, PP0636
Ying, L. MP687
Yingchun, Z. PP0935
Yip, H.C. MP377
Yiu, T.H. MP078
Ylisaukko-oja, T. PP0415
Yoda, Y. PP1196
Yoi, S. PP0158
Yokoi, C. PP0125
Yokoo, T. PP0601
Yokosuka, R. PP1038
Yokota, H. MP696
Yokota, Y. PP0385, PP0617
Yoo, H. PP0423
Yoon, H. MP551, MP603, PP0126, PP0131
Yoon, J. MP599
Yoon, J.H. **PP0110**
Yordanova, R. PP0338
Yoshida, A. OP014
Yoshida, H. PP0168
Yoshida, K. OP231, MP181, MP302, MP423
Yoshida, O. MP475
Yoshida, S. OP087
Yoshida, S. MP017, PP0847
Yoshikata, K. PP0150, PP0151, PP0160, PP0168
Yoshikawa, S. PP0601
Yoshimatsu, Y. PP0683
Yoshimoto, T. MP460
Yoshimura, D. **PP0114**, PP0172
Yoshioka, M. **PP0120**
Yoshioka, S. PP0419
Yoshizaki, T. MP368
Youn, Y.H. MP546
Younis, F. OP221, PP0723, PP0882
Yousef, N. PP0341
Yousefian, N. MP483
Youssef, N.N. OP158, OP159, MP146, MP148
Yu, G. OP128, PP0562, PP0565
Yu, H. MP378, PP0002, PP1007
Yu, H. OP113, MP367
Yu, H.M. PP0521

Yu, H. MP161
Yu, J. OP207, MP493
Yu, K. PP0083, PP0586
Yu, Y. OP201, MP087, MP089, PP1146
Yu, Z. PP0935
Yuan, C. MP243
Yuan, Y. PP0405, PP0663
Yuan, Y. MP484, PP0573, PP0598
Yuang, Y. MP270
Yuanyuan, Y. MP255
Yuen, S. PP0894, PP0898
Yukie Sasaki, L. PP0340, PP0343
Yüksekyayla, O. PP1083
Yüksel, I. **PP0527**, PP1073, PP1075
Yun, C.E. PP0208
Yun, H. MP599
Yung, S. MP074
Yusko, L. PP0010
Yusuf, A. **MP315**
Yusuf, A. **MP374**
Yzet, C. OP169, MP068, **MP185, PP0518**

Z

Zabalza, L. OP043
Zabalza San Martin, L. OP151, MP268
Zabana, Y. OP150, OP151, MP268, MP334, **MP508**, PP0403
Zaccari, P. MP024
Zachäus, M. MP280
Zacho, J. MP236
Zaffalon, D. MP031
Zagaria, G. MP632
Zaghloul, M. MP121
Zaghloul, N. PP0287
Zagonel, V. MP223
Zahariev, O.J. **PP1125, PP1126**
Zahmatkeshan, M. PP0303
Zahra, W. PP0064
Zaid, A.B. PP1022
Zakaria, N. PP1080
Zakhama, M. PP0669
Zakharzhevskaya, N. **PP0513**
Zalov, Z. PP0275
Zamaray, B. OP226, MP222
Zambrano, J. OP083, MP614, MP677, PP0588, PP0589
Zammarchi, I. MP383, MP392, **PP0457**, PP0479, PP0482, PP0499, PP0505
Zamorano, J. MP664
Zampeli, E. MP676, PP0568
Zanati, S. PP0876
Zanconato, M. **PP0587**
Zanetto, A. MP131, MP406
Zang, H. OP057
Zangen, T. OP208
Zanoni, M. MP084
Zaouga, S. **PP0760**
Zapater, P. OP171, MP278
Zapater, R. PP0684
Zaplotnik, M. PP1014
Zaragoza Velasco, N. PP1172
Zarandi-Nowroozi, M. PP0877
Zarei, M. MP655
Zaremba-Pechmann, L. OP044, MP616
Zaric, D. MP523
Zarraquiños, S. MP064
Zarraquiños Martínez, S. PP0929
Zarrin, A. PP0888, PP0936, PP0937
Zaru, L. PP0632, PP0646
Zarubova, K. PP0580
Zatta, V. MP569
Zavhorodnia, N. **PP0960, PP0962**
Zavalal, M. MP517, MP587, PP0225, PP0759
Zaytsev, O. MP427, MP547, PP0273
Zaytsev, O.V. PP0280
Zazour, A. MP418, PP1156, PP1167
Zeeman, M. MP563
Zeevaert, J.-B. MP068

- Zefelippo, A. PP1020
Zeina, A.-R. OP221, PP0723, PP0882, PP1095
Zeino, Z. MP611
Zeissig, S. **OP130**
Zeißig, S. **MP682**
Zeki, S.S. OP076, MP091, MP263, MP663, MP727
Zelinkova, Z. **PP0679**
Zema, C. MP258
Zemel, M. PP0671, PP0675
Zeng, C. **PP0396**, PP0636, **PP0644**
Zenker, M. OP013, OP152
Zenovia, S. MP080, PP1079
Zerbi, A. MP584
Zerbib, F. MP440, PP0085
Zerem, M. PP0228
Zessner-Spitzenberg, J. PP0741, **PP0902**, PP0904
Zeuzem, S. PP0624
Zevit, N. OP208
Zhan, J. OP045, OP082
Zhan, Q. MP015, PP0837, PP0843
Zhang, C. PP1007
Zhang, D. OP068, MP641
Zhang, H. OP120
Zhang, H. OP045, OP082, OP084, OP102, MP670
Zhang, H. MP567, MP687
Zhang, J. OP002
Zhang, J. MP683, PP0549
Zhang, J. OP007
Zhang, J. OP139, MP012, MP370, MP459
Zhang, J. OP120
Zhang, J. OP218
Zhang, L. OP120
Zhang, M. **PP0137**
Zhang, M. OP120
Zhang, P. PP0083, PP0586
Zhang, P. MP141
Zhang, Q. MP161
Zhang, R. OP219
Zhang, S. PP0283
Zhang, S. MP029, MP190
Zhang, S. PP0002
Zhang, S. PP0949
Zhang, S. MP403, PP0950
Zhang, S. MP127
Zhang, S. PP0283
Zhang, T. MP142
Zhang, W. MP247
Zhang, W. MP350
Zhang, W. PP0663
Zhang, W. PP0405
Zhang, X. MP474, PP1051, PP1143, PP1144
Zhang, X. MP626, PP0455
Zhang, X. OP120
Zhang, X. MP675
Zhang, X. PP0618
Zhang, X. OP192, MP613, PP0559, PP0655
Zhang, X. MP397
Zhang, Y. OP083, MP614
Zhang, Y. MP029, MP190
Zhang, Y. MP401
Zhang, Z. MP675, MP687
Zhao, C.M. **OP134**, MP085
Zhao, C.-M. MP035
Zhao, F. MP308
Zhao, H. OP120
Zhao, J. OP160
Zhao, Q. MP161
Zhao, R. OP120
Zhao, Y. PP0264, PP0281, PP0282
Zhao, Y. MP198
Zhao, Y. OP027, OP110
Zhaou, F. **PP0264**
Zharkov, A. PP0267
Zharkov, A.V. PP0254
Zhecheva, I. **PP1016**, PP1117
Zhelyazkova, D. PP0338
Zhen, Y. OP120
Zheng, H. OP207, MP493
Zheng, H. **OP139**
Zheng, L. OP133
Zheng, M. MP161
Zheng, P. MP401
Zheng, Y. MP349
Zhernakova, A.P. OP001, OP108
Zhong, G. MP401
Zhong, J. MP687
Zhong, L. OP007
Zhong, X. PP0376
Zhou, F. **PP0618**
Zhou, F. **PP0281**, **PP0282**
Zhou, F. PP0706
Zhou, G. MP626
Zhou, J. PP0220
Zhou, J. **PP0533**
Zhou, J. MP012
Zhou, J. PP0600
Zhou, L. **MP349**
Zhou, P. OP040
Zhou, P.-H. MP443, PP0922
Zhou, Q. MP397
Zhou, Q. OP201, MP089, PP1146
Zhou, S. MP089, PP1146
Zhou, W. PP1007
Zhou, W. OP120
Zhou, X. PP0458, PP0459, PP0460
Zhou, X. PP0124
Zhou, X. MP500
Zhou, Z. OP120
Zhu, B. MP615, MP623
Zhu, E. MP450, PP0635
Zhu, J. MP122, PP0862, PP0920
Zhu, L. OP118
Zhu, R. OP160
Zhu, S. MP403
Zhu, S. **PP0862**, **PP0920**
Zhu, X. PP0843
Zhu, Y. OP120, MP401
Zhu, Z. MP687
Zhu, Z. MP500
Ziegler, D. PP0899
Zielinska, M. MP400
Zierke, L. MP642
Zignani, M. MP330
Zijlstra, F.A. PP0780
Zileri Dal Verme, L. MP645
Zilli, A. MP152, MP388, MP511, PP0129, PP0130, PP0431, PP0517, PP0626
Zimmer, E. MP481, MP483
Zimmerman, D. PP0484
Zimmerman, T. OP002
Zimmermann, K. PP1218
Zimmermann, L. MP329
Zimmermann, T. OP004
Zimmermann-Klemd, A. PP0810
Zinger, A. **MP621**
Zingone, F. **MP042**, **MP045**, MP653, **PP0013**, **PP0308**, PP0315, PP0347, PP0481, PP0587, PP0633
Zinober, K. MP465
Zittan, E. MP672
Zivkovic, M. MP417
Zizzo, M. MP223
Zmora, O. MP151
Zmudziński, M. MP672
Zobel, J. MP478, MP589
Zocco, M.A. MP645, PP0958
Zolcsák, Á. MP303, MP304, PP1127, PP1129, PP1133
Zolfino, T. PP0442
Zoller, H. OP183
Zoller, W.G. PP0900
Zollner, A. OP018
Zoltán, S. MP627, PP0584, PP0675
Zonderhuis, B.M. MP702
Zonneveld, R. PP0815
Zorniak, M. MP644
Zorzi, F. MP389, PP0488
Zou, D. OP120
Zou, G. PP0556
Zou, H. **OP160**
Zou, X. OP201, MP087, MP089, PP1146
Zoughlami, A. PP0546
Zougmore, H. **MP634**
Zreik, A.E. OP220
Zu, M. MP459
Zubcevic, N. MP588
Zubiaur, P. MP664
Zubova, A. MP566, PP0507, PP0510
Zucari Nogueira, E. PP0340, PP0343
Zucchini, N. PP0470
Zucconi, F. MP344, PP0392
Zuddas, A. MP606
Zuin, G. PP0470
Zuleta, J. PP0268
Zuluaga, N. PP0268
Zuluaga Aguilar, J.N. PP0268
Zundel, L. OP018
Zundler, S. PP0529
Zúñiga de Mora-Figueroa, B. OP213
Zwager, L. OP225
Zwahlen, M. PP0074
Zwolinska-Wcislo, M.M. PP0610

UEG gratefully acknowledges the support of this year's Premier Supporters:

abbvie

