Methods: A randomized, double-blinded, placebo-controlled clinical trial in otherwise healthy adult patients with untreated LDL cholesterol ≥160 mg/dL at screening and providing informed consent. Placebo or LP (10^9 cfu) capsule were taken once daily for 12 weeks. LDL, HDL, total cholesterol levels (TC) and triglycerides (TG) were measured in serum at baseline and after 12 weeks. Recruitment and intervention took place during the Covid19 pandemic in Hannover University (Germany), in three consecutive waves, March to December 2021. Thus, data was analyzed with linear model (GLM), with treatment arm as fix factor, recruitment wave as random factor, and baseline LDL, TC and TG values as covariates.
Results: 91 subjects (of 100 planned) were randomized and completed the study. Median age was 63.5 years (range: 38-76), 69% were female, and median baseline LDL and BMI were 188 mg/dL (range 149-229) and 26.3 Kg/m^2 (range 18,6-38,5), respectively. Study groups were well balanced at baseline, except for a trend difference in TG (p=0.079). LP achieved a larger reduction from baseline in LDL (p=0.036) and TC (p=0.086) than placebo. No effects were observed on HDL or TG. Adjusting for treatment wave and baseline TG increased significance of effect for both LDL and TC (p<0.001 vs placebo). Recruitment wave and baseline LDL, TC and TG values significantly modulated LDL and TC change (all p<0.05). No adverse events or liver enzyme changes were detected. Statistical assumptions of GLM were met.
Conclusion: This probiotic formulation significantly lowered LDL and TC during a 12-week intervention, compared to placebo. Recruitment waves caused by Covid19 pandemic restrictions also accounted for significant variability.
Disclosure of Interest: F. Kerlikowsky: None declared, T. Greupner: None declared, M. Müller: None declared, J. Espadala Mazo Other: statistical support, H.-J. Müller Other: Probiotic formulation was provided by SymbioPharm GmbH, Germany. The company had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the Results, A. Hahn: None declared

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EQUATIVE: QUALITY OF LIFE IN ADULT PATIENTS WITH SHORT BOWEL SYNDROME TREATED BY TEDUGLUTIDE, A FRENCH REAL-WORLD STUDY

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Rationale: Short bowel syndrome with intestinal failure (SBS-IF) requires use of parenteral support (PS) and highly impacts patients (pts) quality of life (QoL). Teduglutide (TED), a GLP-2-analog, has proven efficacy reducing the need for PS. The study aimed to compare QoL in French TED vs non-TED pts.
Methods: EQUATIVE is a multi-centric observational study, enriching the French adult cohort of the SBS-IF Registry with cross-sectional collection of QoL. Enrolled pts initiated PS at least 12mos prior inclusion (Ti) and were stable. TED initiation and the first available visit at least 6mos prior Ti defined T0 in TED and non-TED pts respectively. Pts and disease characteristics were described at T0/Ti. Pts were matched with propensity scores based on T0 characteristics. Mean SBS-QoL^{TM} and SF-12 physical (PCS) and mental (MCS) scores (±SD) were compared (Wilcoxon rank sum test). Mean difference in pair-differences (DPD) [±IC95] were calculated.
Results: Overall, 67 TED and 76 non-TED pts were enrolled and followed-up after T0 for 2.5±0.9yrs and 1.2±0.7yrs respectively. At T0, pts were 54±17yrs old, 57% females. SBS duration was 10±10yrs, after vascular (53%) or inflammatory bowel diseases (30%). Remnant small bowel length was 76±53cm. Half pts had an end-jejunostomy. History of PS pre-T0 was 9±9yrs, with volume of 10.5±6.8L/wk administered 4.8±1.6 times/wk. At Ti, on the 48 matched pairs, SBS-QoL^{TM} score was significantly higher in TED (49±37 vs 68±44, p=0.03) with DPD of -20 [-35; -5]. PCS and MCS were not different (45±9 vs 42±9, p=0.06 and 47±9 vs 44±10, p=0.17); 100% items improved in both scales.
Conclusion: This first study on QoL in SBS-IF in France showed significantly improved QoL in TED pts. Further studies are required to confirm findings. QoL scales could be more routinely used to better assess effectiveness of therapeutic strategies in SBS-IF.
Disclosure of Interest: F. Joly Grant / Research Support from: Takeda, Zealand, Vectibio, Allena Pharmaceuticals, Fresenuis-Kabi, Theradial , Consultant for: Takeda, Zealand, Vectibio, Sanofi, Speakers Bureau of: Baxter, Takeda, Fresenius-Kabi, Nestlé Health Science, BBraun, Mayoli, D. Quilliot Consultant for: Takeda, Baxter, Fresenius-Kabi, Nestlé, C. Chambrier Grant / Research Support from: Shire-Takeda, Zealand, VectivBio AG, Parexel, B Braun, Consultant for: Nutricia, Shire, Speakers Bureau of: Nutricia, Fresenius, Baxter, Theradial, Takeda, S. Schneider Grant / Research Support from: B. Braun, Takeda, VectivBio, Zealand, Consultant for: Axium mTech, Baxter, Nestlé Health Science, Takeda, Speakers Bureau of: Biocodex, Fresenius-Kabi, Laboratoires Grand Fontaine, Nestlé Heath Science, Takeda, Theradial, G. Fotsing Speakers Bureau of: Abbvie, MSD, HAC Pharma, Pfizer, Tillots Pharma, Janssen, F. Poullenot Grant / Research Support from: Takeda, Consultant for: Abbvie, Ferring, Speakers Bureau of: Takeda, Pfizer, Janssen, MSD, S. Layec: None declared, N. Flori Consultant for: Fresenius-Kabi, Speakers Bureau of: Amgen, Lilly, Takeda, R. Thibault Consultant for: Aguettant, Baxter, BBraun, Fresenius-Kabi, Nutricia, Roche, Speakers Bureau of: Astra-Zeneca, Homeperf, Lactalis, Nestlé, Shire , E. Fontaine Grant / Research Support from: Baxter, Nutricia, Fresenius Kabi, Aguettant, Consultant for: Baxter, Nutricia, E. Ressiot: None declared, V. Campana Other: Takeda employee, N. Schmidely Other: Takeda employee, D. Seguy Grant / Research Support from: Nestlé Health Care, Alliance 7, Takeda, Consultant for: Abbvie, Shire, Takeda, Speakers Bureau of: Abbvie, Shire

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EFFECT OF A NUTRITIONAL MODULATION OF THE GUT-BRAIN AXIS IN ALCOHOL-DEPENDENT PATIENTS

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Rationale: Our previous studies have shown that chronic alcohol abuse induces a leaky gut and alterations of the gut microbiota composition, which are correlated with the severity of psychological symptoms, suggesting the involvement of the gut-brain axis in the development of alcohol use disorders (AUD). The Gut2Brain study aims at supplementing AUD patients with prebiotics (inulin) in order to modulate the gut

microbiota composition and to evaluate the putative effect on metabolism, inflammation and behavior.
Methods: A randomized, double-blind, placebo-controlled study included 50 AUD patients hospitalized for a 3-week detoxification program.
The patients were assigned to inulin versus maltodextrin (placebo) daily supplementation for 17 days. Biological measurements (fecal microbial 16S rDNA sequencing, serum clinical biology), and validated questionnaires for psychological traits and gastrointestinal tolerance assessment were performed at the beginning and at the end of the study. Multiple regression analysis was used to assess the effect of inulin. Microbial data were analyzed using Mann–Whitney test and P-values were adjusted according to the Benjamini and Hochberg procedure.
Results: Prebiotic treatment was well tolerated by patients. All patients showed improvement in depression, anxiety and craving scores after 17 days regardless of the treatment group. Only patients treated with prebiotics significantly improved the sociability score. Placebo treatment lead to sporadic changes in the gut microbiome whereas inulin increased *Bifidobacterium* and decreased *Bacteroides, Dorea* and *Ruminococcus torques group* ($q < 0.1$). Neither Inulin nor placebo supplementation had beneficial effect on systemic inflammation.
Conclusion: The Gut2Brain study shows that prebiotic like inulin can modulate the social behavior in AUD patients, but does not significantly modify biological outcomes. Picrust analysis and metabolomics data are in progress in order to evaluate the potential involvement of gut microbial metabolites in the modulation of gut-brain axis in AUD patients, that could be helpful to revisit nutritional recommendations addressed to AUD patients.
Gut2Brain study, clinicaltrial.gov: NCT03803709, https://clinicaltrials.gov/ct2/show/NCT03803709
Disclosure of Interest: None declared.

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ENHANCED ANABOLIC CAPACITY, BUT UNCHANGED ANABOLIC THRESHOLD IN CLINICALLY-STABLE NORMAL WEIGHT PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Rationale: Previously we observed an enhanced anabolic response to high quality protein sip feeding in normal weight Chronic Obstructive Pulmonary Disease (COPD) on group level. To further explore this on an individual level and in a larger group of COPD patients, we used a recently developed isotope method (ClinNutr 2019;38:1833-43) to assess whether the efficiency of dietary protein to promote protein anabolism (anabolic capacity) is enhanced and the minimal amount of protein to obtain protein anabolism (anabolic threshold) is altered in COPD patients as compared to healthy controls.
Methods: We studied 23 clinically stable COPD patients (GOLD stage: 2-4, age: 70.4 [66, 74.9] yo, 12 m/11 f, BMI: 27.3 [24.3, 30.2] kg/m2) and 16 controls (age: 67.1 [63.6, 70.7] yo, 8 m/8 f, BMI: 28.0 [26.2, 29.7] kg/m2). Subjects ingested sips of a mixture of hydrolyzed casein protein and carbohydrates (2:1) every 20 min for 4 h at 2 levels of protein intake (0.12 and 0.23 g * kg lbm-1 * hr-1). We gave an IV primed continuous infusion of phenylalanine (L-ring[-D5]-PHE) and tyrosine (L-[13C9,15N]-TYR) and collected blood samples to assess net protein balance (whole body protein turnover minus PHE to TYR hydroxylation). We determined anabolic threshold (intake when net protein balance = 0) and anabolic capacity (slope) from linear regression between protein intake and net protein balance. Medical history, nutritional status (body composition by DXA), and lung function (FEV1) were assessed. Statistics by ANCOVA with covariates: age, gender, and BMI; estimate is the difference from matched-controls. Data are mean [95% CI], $\alpha<0.05$.
Results: Net protein balance had a linear relationship with protein intake ($p<0.001$). The COPD group had greater anabolic capacity in comparison to matched controls (0.9540 [0.9438, 0.9643] vs 0.9363 [0.9275, 0.9450], $p=0.0288$). The anabolic threshold was comparable ($p=0.2128$) between the groups (123 [103, 143] vs 153 [129, 178] μmol PHE * kg lbm−1 * hr−1). Anabolic capacity in COPD tended to be increased in subjects who experienced COPD exacerbations in the previous year ($p=0.099$, estimate: 0.026) and decreased by diabetes ($p=0.030$, estimate: -0.028). Nutritional status, lung function and disease severity did not affect the response to feeding in COPD group.
Conclusion: COPD patients in comparison to healthy subjects have an enhanced anabolic capacity but similar anabolic threshold in response to nutrition. However, the response to feeding in COPD is affected by comorbidities and disease severity.
Disclosure of Interest: None declared.

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MUSCLE-RELATED MIRNAS AND ITS RELATIONSHIP WITH CIRCULATING GDF-15 AND FGF-21 LEVELS IN PATIENTS WITH CARDIAC CACHEXIA

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Rationale: Cachexia is highly prevalent in patients with heart failure and we aimed to identify micro-RNA (miRNA) and cytokines likely associated with this condition
Methods: 27 patients with Heart Failure (NYHA classes II-IV) and 17 healthy controls were enrolled. Cachexia was defined as involuntary weight loss > 5% in the prior 6 months. GDF-15 and FGF-21 serum levels were assessed by ELISA. Total RNA was extracted from plasma and circulating levels of several miRNAs potentially involved in "muscle wasting" (miR15b-3p, miR21-5p, miR29a-3p, miR29b-3p, miR133a-3p, miR206, miR486-5p) were analyzed by RT-PCR
Results: Median GDF15 serum levels were higher in HF patients vs controls (1065.60 vs 418.80, $p<0.001$), whereas median FGF-21 were higher in patients with cardiac cachexia vs those without cachexia (412.30 vs 201.60, $p=0.046$). Plasma miR15b-3p median levels were lower in HF patients vs controls (0.80 vs 2.00, $p= 0.002$), whereas we found in cachectic patients vs controls lower plasma levels of miR29b-3p and higher of miR486-5p (0.94 vs 1.60, $p= 0.046$ and 0.30 vs 0.20, $p= 0.036$, respectively). miRNA15b-3p showed a negative correlation with GDF-15 levels ($R= -0.33$; $p= 0.029$)
Conclusion: GDF-15 levels were modulated in HF and FGF-21 were increased in patients with cardiac cachexia. miR29b-3p and miR486-5p seem to play a key role in cardiac cachexia and miRNA15b-3p was downregulated in HF and negatively correlated with GDF-15 levels.
Disclosure of Interest: None declared.

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GLEPAGLUTIDE PHARMACOKINETIC PROFILE AFTER SINGLE SUBCUTANEOUS INJECTION IN HUMAN SUBJECTS WITH VARYING DEGREES OF RENAL FUNCTION

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Rationale: Glepaglutide (Zealand Pharma A/S) is a potent long acting GLP-2 analogue currently in phase 3 for the treatment of short bowel syndrome.
A clinical phase 1 trial was conducted to investigate the pharmacokinetics of glepaglutide in subjects with varying degrees of renal impairment to assess if dose adjustment of glepaglutide potentially could be warranted
Methods: Sixteen Caucasian subjects were enrolled, four with end stage renal disease (ESRD) not on dialysis (eGFR <15), four with severe renal impairment (eGFR 15 to <30) and eight matching controls with normal