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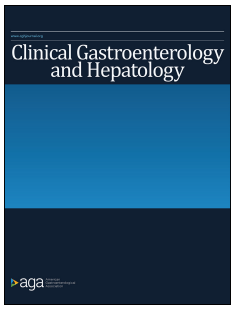

Real-world effectiveness of advanced therapies in microscopic colitis

Bram Verstockt, Thibault Taelman, Shahida Din, Stephan R. Vavricka, Andreas Blesl, Yamile Zabana, Wouter Van Moerkercke, Vytautas Kiudelis, Juan de la Revilla Negro, Michel H. Maillard, Edoardo Vincenzo Savarino, Niels Teich, Gilles Macaigne, Marie Truyens, Davide Giuseppe Ribaldone, Manuel Barreiro-de Acosta, Signe Wildt, Pauline Rivière, Mathurin Fumery, Aurélien Amiot, Jan Marsal, Gian Eugenio Tontini, Asaf Levartovsky, Sophie Vieujean, Michael Somers, Anneline Cremer, Ivan Lutakov, Nathaniel A. Cohen, Sophie Dewit, Lukas Bajer, Jean-Francois Rahier, Ann-Sofie Backman, Stephane Nancey, Tenzin Choden, Jurgen Van Dongen, Gerhard Rogler, Matthias Lenfant, Mhairi Finlayson, Andreas Münch, Mette Julsgaard

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Real-world effectiveness of advanced therapies in microscopic colitis

Bram Verstockt[1,2], Thibault Taelman[1,3], Shahida Din[4,5], Stephan R. Vavricka[6], Andreas Blesl[7], Yamile Zabana[8], Wouter Van Moerkercke[3], Vytautas Kiudelis[9], Juan de la Revilla Negro[10], Michel H. Maillard[11,12], Edoardo Vincenzo Savarino[13], Niels Teich[14], Gilles Macaigne[15], Marie Truyens[16], Davide Giuseppe Ribaldone[17], Manuel Barreiro-de Acosta[18], Signe Wildt[19], Pauline Rivière[20], Mathurin Fumery[21], Aurélien Amiot[22], Jan Marsal[23], Gian Eugenio Tontini[24,25], Asaf Levartovsky[26], Sophie Vieujean[27], Michael Somers[28], Anneline Cremer[29], Ivan Lutakov[30], Nathaniel A. Cohen[31], Sophie Dewit[32], Lukas Bajer[33,34], Jean-Francois Rahier[35], Ann-Sofie Backman[36,37], Stephane Nancey[38], Tenzin Choden[39], Jurgen Van Dongen[40], Gerhard Rogler[6], Matthias Lenfant[1,2], Mhairi Finlayson[4,5], Andreas Münch[41#], Mette Julsgaard[42,43,44#]

shared senior author

1 Department of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, Belgium.
2 Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium.
3 Department of Gastroenterology, AZ Groeninge, Kortrijk, Belgium.
4 Institute of Genetics and Cancer, University of Edinburgh, Edinburgh, United Kingdom.
5 Edinburgh Inflammatory Bowel Diseases Unit, Western General Hospital, Edinburgh, United Kingdom.
6 Department of Gastroenterology and Hepatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland.
7 Department of Internal Medicine, Division of Gastroenterology and Hepatology, Medical University of Graz, Graz, Austria.
8 Department of Gastroenterology, Hospital Universitari Mútua Terrassa and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Spain.
9 Department of Gastroenterology, Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Kaunas, Lithuania.
10 Department of Gastroenterology, Addenbrookes Hospital. Cambridge University Hospitals, Cambridge, United Kingdom.
11 Lausanne Digestive Disease Center, Lausanne, Switzerland.
12 Service of Gastroenterology and Hepatology, Lausanne University Hospital, Lausanne, Switzerland.
13 Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy.
14 Internistische Gemeinschaftspraxis, Leipzig, Germany.
15 Hepatogastroenterology Unit, Centre Hospitalier de Marne-la-Vallee, Jossigny, France.
16 Department of Gastroenterology, University Hospital Ghent, Ghent, Belgium.
17 Department of Medical Sciences, University of Turin, Turin, Italy.
18 Department of Gastroenterology- IBD Unit. University Hospital Santiago De Compostela CHUS, Spain.
19 Gastrounit, Hvidovre Hospital, University Hospital of Copenhagen, Denmark.
20 Service d'hépato-gastroentérologie et oncologie digestive, CHU de Bordeaux, France.
21 Department of gastroenterology, Amiens University Hospital, France.
22 Department of Gastroenterology, Hopitaux Universitaires Bicêtre, AP-HP, Université Paris Saclay, INSERM CESP, Le Kremlin Bicêtre, France
23 Department of Gastroenterology, Skane University Hospital, Lund University, Lund and Malmö, Sweden.
24 Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy
25 Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
26 Department of Gastroenterology, Sheba Medical Center, Ramat-Gan; Faculty of Medical and Health Sciences, Tel-Aviv University, Israel
27 Hepato-Gastroenterology and Digestive Oncology, University Hospital CHU of Liège, Liège, Belgium.
28 Department of Gastroenterology and Hepatology, University Hospital Antwerp, Antwerp, Belgium.
29 Department of Gastroenterology and Hepatology, Erasme University Hospital, Brussels, Belgium.
30 Clinical Center of Gastroenterology, University Hospital "Queen Joanna-ISUL" Sofia, Medical University Sofia, Bulgaria.
31 IBD Center, Department of Gastroenterology and Liver Diseases, Tel Aviv Medical Center, Tel Aviv, Israel.
32 Department of Gastroenterology, Noorderhart Mariaziekenhuis, Pelt, Belgium.
33 Department of Gastroenterology and Hepatology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic.
34 Department of Internal Medicine, Second Faculty of Medicine, Charles University, Prague, Czech Republic.
35 Department of Gastroenterology and Hepatology, Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium.
36 Department of Internal Medicine, Ersta Hospital, Stockholm, Sweden
37 Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden.
38 Department of Gastroenterology, Lyon-Sud hospital, Hospices Civils de Lyon, Pierre-Bénite, France.
39 Inflammatory Bowel Disease Center, University of Chicago Medicine, Chicago, IL, USA.
40 Department of Gastroenterology, AZ Sint Maarten, Mechelen, Belgium.
41 Department of Gastroenterology and Hepatology, Linköping University, Linköping, Sweden
42 Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark.
43 Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.
44 Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark.

Corresponding author

Bram Verstockt MD PhD

Department of Gastroenterology & Hepatology

University Hospitals Leuven

Leuven, Belgium

bram.verstockt@uzleuven.be

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The data underlying this article will be shared on reasonable request to the corresponding author.

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Conflicts of interest

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T Taelman declares no conflicts.

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http://orcid.org/0000-0003-2855-3400

S Vavricka has received consulting fees, speakers honorary and unrestricted research grants from Abbott, Alfasigma, Amgen, Arenapharm, BMS, Falk Pharma GmbH, Ferring Pharmaceuticals, Gilead, iQuone, Janssen, MSD, Permamed, Pfizer Inc, Sanofi-Aventis, Schwabe Pharma, Takeda, Tillotts, UCB, and Vifor.

A Blesl has served as speaker and consultant for Abbvie, Aengus, Boston Scientific, Bristol-Myers Squibb, Dr. Falk Pharma, Genericon, Gilead, Janssen, Lilly, MSD, Olympus, Pfizer, PSI, Sandoz, Takeda, Vifor.

Y Zabana has received financial support for travelling and educational activities from or has served as an advisory board member for AbbVie, Adacyte, Alfasigma, Almirall, Amgen, Boehringer Ingelheim, Dr Falk Pharma, Faes Pharma, Fresenius Kabi, Ferring, Galapagos, Janssen, Johnson&Johnson, Kern, Lilly, MSD, Otsuka, Pfizer, Sanofi, Shire, Takeda, and Tillotts Pharma.

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V Kiudelis has received financial support for travelling and educational activities from AbbVie, Takeda, Janssen, Pfizer, Ferring, Dr. Falk Pharma, MSD, and has received speaker fees from AbbVie, Ferring, Dr. Falk Pharma.

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N Teich received speaker's fees from AbbVie, Alfasigma, Biogen, Celltrion, Eli Lilly, Falk Foundation, Ferring, Galapagos, and Takeda. He has served as a consultant for AbbVie and Takeda.

G Macaigne has served as speaker or consultant for Abbvie, Jansen, Takeda, Johnson and Johnson, Tillotts Pharma. Has received congress support from Abbvie, Takeda, Dr Falk Pharma.

M Truyens has received congress support from Pfizer, AbbVie, Galápagos, Janssen-Cilag, and Takeda.

D Ribaldone declares no conflicts.

M Barreiro-de Acosta has been speaker, consultant and advisory member for or has received research funding from MSD, AbbVie, Janssen, Kern Pharma, Celltrion, Takeda, Alphasigma, Lilly, Pfizer, Sandoz, Biocon, Abivax, Fresenius, Faes Farma, Ferring, Tillots, Chiesi, Adacyte Oncostellae and SunRock

S Wildt has served as an advisory board member for AbbVie and Bristol Myers Squibb

P Rivière consultancy and speaker fees from Abbvie, Celltrion and Janssen.

M Fumery has received lecture/Consultant fees from MSD, Pfizer, AbbVie, Bristol Myers Squibb, Celltrion, Galapagos, Janssen, Ferring, Takeda, Amgen, Lilly, Alphasigma; Hospira, Arena, Sandoz, Fresenius-Kabi and Tillots.

A Amiot received consulting fees from Abbvie, Pfizer, Takeda, Tillotts Pharma, Adacyte, MSD, Janssen and Sandoz as well as lecture fees and travel accommodations from Abbvie, Ferring, Adacyte, MSD, Sandoz, Amgen, Janssen, Pfizer, Takeda, Biogen, Fresenius Kabi, Amgen and Celltrion.

J Marsal has served as a speaker, consultant or advisory board member for AbbVie, Amgen, Bayer, Biogen, BMS, Eli Lilly, Ferring, Galapagos/Alfasigma, Hospira, ITH, Janssen, Lument, MSD, Otsuka, Pfizer, Sandoz, Takeda, Tillotts and UCB; and has received grant support (not for this study) from AbbVie, BMS, Calpro AS, Carbiotix, Ferring, Fresenius Kabi, Pfizer, Svar Life Science and Takeda.

GE Tontini has received speaker's honoraria from Ferring and has served as a consultant for NTC Pharma, Fujinon, Invicro.

A Levartovsky declares no conflicts.

S Vieujean received speaker's fees from Abbvie, Celltrion, Ferring, Janssen, Takeda and has served as a consultant for AbbVie and Alfasigma

M Somers declares no conflicts.

A Cremer has received speaker's fees from AbbVie, Alfasigma, Celltrion, Eli Lilly, Galapagos, Johnson and Johnson, Pfizer, She has served as a consultant for AbbVie, Alfasigma, Galapagos, Johnson and Johnson, Takeda.

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N Cohen has served as a consultant for or received speaker's fees from Abbvie, Abivax, Bristol-Myers Squibb, Iterative Health, Rafa Pharmaceuticals, Seres Pharmaceuticals and Takeda; and received travel support from Pfizer and Takeda.

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L Bajer has received honoraria and/or speaker' fees from: Alfasigma, Celltrion, Ferring, PROMed and Takeda.

JF Rahier has received lecture fees from MSD, Pfizer, AbbVie, Bristol Myers Squibb,Celltrion, Galapagos, Janssen, Ferring, Falk, Takeda, Amgen, Lilly, Alphasigma; advisory board fees from MSD, Pfizer, AbbVie, Takeda, Hospira, Celltrion, Amgen, Mundipharma, Glaxo Smith Kline, Galapagos, Janssen; and research support from Takeda, Janssen and AbbVie.

AS Backman has received research funding from Ferring and speaker/consulting fees from Tillotts, Takeda, Ferring, Galapagos,, AlfaSigma, Meda, Johnsen&Johnsen/Janssen, Pfizer, Roche

S Nancey reports receiving research support from AbbVie, Celltrion, and Sandoz. He has received speaker's fees from AbbVie, Alfasigma, Biogen, Celltrion, Lilly, Ferring, Galapagos, Johnson and Johnson, Pfizer, Sandoz, Takeda, Fresenius Kabi. He has served as a consultant for Takeda, Lilly, Johnson and Johnson.

T Choden declares no conflicts.

J van Dongen has received consultancy fees from Galapagos and Sandoz

G Rogler has consulted to Abbvie, Arena, Augurix, BMS, Boehringer, Calypso, Celgene, FALK, Ferring, Fisher, Genentech, Gilead, Janssen, Lilly, MSD, Novartis, Pfizer, Phadia, Roche, UCB, Takeda, Tillots, Vifor, Vital Solutions and Zeller; Gerhard Rogler has received speaker's honoraria from Abbvie, Astra Zeneca, BMS, Celgene, FALK, Janssen, MSD, Pfizer, Phadia, Takeda, Tillots, UCB, Vifor and Zeller; Gerhard Rogler has received educational grants and research grants from Abbvie, Ardeypharm, Augurix, Calypso, FALK, Flamentera, Lilly, MSD, Novartis, Pfizer, Roche, Takeda, Tillots, UCB and Zeller. Gerhard Rogler is cofounder and head of the scientific advisory board of PharmaBiome.

M Lenfant has received financial support for travelling and educational activities from Dr. Falk Pharma, Takeda, Johnson and Johnson and AbbVie.

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M Julsgaard has received a research grant from Takeda; consulting/advisory board fees from Ferring, Takeda, AbbVie, PharmaCosmos, Eli Lilly and Tillots Pharma; speaker's fees from Tillotts Pharma, MSD, Ferring, Janssen and Takeda.

ABSTRACT

Background and aims

Microscopic colitis (MC) is a leading cause of chronic diarrhoea, particularly in older adults. While many patients respond to budesonide, refractory and dependent cases pose major therapeutic challenges. Although the off-label use of advanced IBD therapies is expanding, robust real-world data remain scarce.

Methods

Through the ECCO CONFER network, we conducted a multinational, retrospective study in MC patients treated with biologics or small molecules following budesonide failure or intolerance. We systematically analyzed clinical outcomes, treatment durability, and predictors of therapeutic success.

Results

Among 229 treatment cycles in 142 patients, anti-TNF agents were most frequently initiated (55.9%), followed by vedolizumab (28.8%) and JAK inhibitors (9.2%). Short-term clinical response and remission rates were highest with JAK inhibitors (95.2% and 81.0%, respectively), significantly outperforming anti-TNFs, vedolizumab, and ustekinumab ($p<0.01$). Long-term drug persistence mirrored these findings: JAK inhibitors demonstrated a markedly lower discontinuation rate (23.8%) compared to other agents (56.3%, OR 5.07, 95% CI 1.52–16.9, $p = 0.008$). Multivariate analysis confirmed drug class as the only independent predictor of therapy continuation. Despite advanced therapies, 4.2% of patients ultimately required surgical intervention.

Conclusion

This real-world study demonstrates the promising short- and long-term effectiveness of advanced therapies—particularly JAK inhibitors—in budesonide-refractory and budesonide-dependent MC. These findings pave the way for dedicated prospective trials and highlight evolving therapeutic strategies in MC.

Keywords

microscopic colitis, collagenous colitis, lymphocytic colitis, advanced therapy, small molecules, JAK inhibitor, biologics

WHAT YOU NEED TO KNOW

- **Background**

  Microscopic colitis is a chronic cause of diarrhoea, especially in older adults, with limited treatment options beyond budesonide. Some patients are dependent or refractory to budesonide.

- **Findings**

  JAK inhibitors show significantly higher short-term remission and long-term durability than other biologics in budesonide-refractory or -dependent microscopic colitis, based on the largest real-world study to date.

- **Implications for patient care**

  This study provides the most robust real-world evidence to date for using JAK inhibitors or other biological therapies in microscopic colitis, and paves the way for prospective trials and precision-guided care.

INTRODUCTION

Microscopic colitis (MC) is a chronic inflammatory disease of the colon that presents clinically with persistent, non-bloody, watery diarrhoea, despite a normal or near-normal endoscopic appearance.[1] Histologically, MC is classified into two main subtypes: lymphocytic colitis (LC), characterized by an increased number of intraepithelial lymphocytes, and collagenous colitis (CC), distinguished by a thickened subepithelial collagen band. Both subtypes share similar clinical features and have been associated to the intake of various environmental factors, including drugs,[2] but may differ slightly in pathophysiology, associated comorbidities, and therapeutic responses.[3]

The burden of MC is substantial, with patients frequently experiencing urgent bowel movements, faecal incontinence, weight loss, and nocturnal stools. Epidemiological studies estimate a lifetime risk up to almost 1% in female and 0.4% in male,[4] with an annual pooled incidence of 10.5 to 25.8 cases per 100,000 person-years.[4, 5] MC accounts for up to 20% of chronic diarrhoea cases in individuals older than 65 years, emphasizing its clinical relevance in ageing populations.[3, 6]

Therapeutic options for MC remain limited. Oral budesonide is the only agent approved by the European Medicines Agency (EMA) for induction of remission. Although initial response rates to budesonide are high, relapse rates after discontinuation exceed 50%.[7] Furthermore, a significant proportion of patients become budesonide-dependent or -refractory, facing long-term exposure to corticosteroids and their associated adverse effects.[8] Alternative therapies—including bile acid binding agents, aminosalicylates, loperamide, bismuth subsalicylate, and immunomodulators—are often used off-label but are supported only by limited or low-quality evidence.[1, 6, 9-11]

As a result, clinicians have increasingly explored the off-label use of advanced inflammatory bowel disease (IBD) therapies, such as biologics and small molecules, to manage refractory or steroid-dependent MC. However, the exact prevalence of this off-label use is unknown, and prospective trial data to guide treatment are lacking. Existing evidence stems primarily from very small retrospective series or case reports, with most reports focusing on the effectiveness of anti-TNF agents and vedolizumab.[12-14]

Considering these unmet needs, the present ECCO CONFER study aims to provide real-world evidence on the use of advanced IBD therapies, including biological agents and small molecules, for the treatment of budesonide-refractory and budesonide-dependent MC. By consolidating multinational data across expert centres, this study seeks to inform clinical practice and guide future research efforts in this challenging disease area.

METHODS

Study design

This observational, multicentre, retrospective study was conducted through the European Crohn's and Colitis Organisation (ECCO) COllaborative Network For Exceptionally Rare (CONFER) cases. The

CONFER project was established by ECCO to systematically identify and collectively report rare IBD associations that are typically underreported.[15] After the steering committee selected a specific topic, ECCO issued a global call for case submissions from IBD physicians, disseminated through announcements at the ECCO Congress, national and international IBD meetings, direct emails to ECCO members and affiliates, the ECCO website, and eNews. Collaboration was further strengthened through communication within the European Microscopic Colitis Group (EMCG). Physicians were invited to contribute cases using a standardized reporting form, ensuring consistent and comprehensive data entry into the CONFER database. This study was conducted and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational research.[16] The overarching ECCO-CONFER project was approved by the ethics committee, the Chaim Sheba Medical Center, Ministry of Health, Israel (approval no. 9545-12-SMC). The current study was approved by the Ethics Committee for Research at UZ/KU Leuven (S68207).

Included patients

Consecutive patients included in this study had a histologically confirmed diagnosis of MC, classified as either collagenous or lymphocytic colitis based on established criteria.[6] All participants had been treated with advanced therapies approved for IBD, including both biologics and small molecules.

Definitions

A treatment cycle was defined as the initiation of a new advanced therapy in a given patient. Each change to a different biologic or small molecule, regardless of prior exposure, was considered a distinct treatment cycle.

Budesonide dependency refers to the recurrence of clinical symptoms upon tapering or discontinuation of budesonide, necessitating ongoing therapy to maintain remission. Budesonide intolerance referred to the inability to continue budesonide due to adverse effects.[1] Budesonide refractiveness was defined as either a primary non-response (PNR), characterised by failure to achieve clinical response during an adequate course of induction therapy, or secondary loss of response (LOR), where patients initially responded but subsequently became refractory during the disease course.

Clinical outcomes were assessed based on stool frequency and consistency. Clinical response was defined as a ≥50% reduction in stool frequency from baseline. Clinical remission was defined according to the Hjörtswang criteria, requiring a mean of fewer than three stools per day or fewer than one watery stool per day.[17] Treatment effectiveness was assessed on short-term (at the end of therapy induction) and long-term (during maintenance). Treatment discontinuation was defined as the permanent cessation of an advanced therapy due to primary non-response (PNR), secondary loss of response (LOR), intolerance and/or adverse events (AE), or other physician- and/or patient determined reasons.

Statistical analyses

All statistical analyses were conducted using R (version 4.5.0; R Development Core Team, Vienna, Austria) and SPSS (version 29.0.2.0; IBM Corp, Armonk, NY, USA). Continuous variables are

presented as medians with interquartile ranges (IQR), and categorical variables as absolute numbers and percentages.

Descriptive clinical outcomes—such as induction response and remission rates—were reported per treatment cycle, as this reflects the real-world sequence of therapeutic decision-making. Since these outcomes were presented descriptively and not used for formal statistical comparison, no correction for within-patient clustering was applied in these instances.

However, when conducting inferential analyses that compared outcomes across treatment classes, we accounted for the fact that individual patients could contribute multiple treatment cycles. For binary outcomes (e.g., clinical response and remission), we applied generalized estimating equations (GEE) with an exchangeable correlation structure and robust standard errors, clustering on patient ID to account for intra-individual correlation. Continuous outcomes, such as changes in stool frequency, were analyzed using linear mixed-effects models, with patient ID included as a random intercept.

Time-to-event outcomes, including drug discontinuation and therapy durability, were analyzed using Cox proportional hazards models with shared frailty terms to account for within-patient clustering. As a sensitivity analysis, we also fitted marginal Cox models with robust sandwich variance estimators, clustered on patient ID, which yielded consistent results.

A last observation carried forward (LOCF) approach was applied for patients who discontinued therapy before completing induction. All statistical tests were two-tailed, and p-values <0.05 were considered statistically significant.

RESULTS

Study cohort and drug sequencing

We identified 142 unique patients with MC in 15 counties treated in 38 different centers (Supplementary Table 1), comprising 52.8% with collagenous colitis (CC) and 47.2% with lymphocytic colitis (LC) (**Table 1**) from 15 countries. As expected, the cohort exhibited a strong female predominance (85.9%), with a median [interquartile range, IQR] age at MC diagnosis of 52.6 [38.3–61.7] years. The median age at initiation of first-line advanced therapy was 56.6 [44.3–65.3] years, median 2.7 [0.9-6.2] years after diagnosis. All but one patient had previously received budesonide, which was discontinued due to PNR (n=16; 11.3%), LOR (n=50; 35.5%), intolerance (=11; 7.8%), or dependency (n=64; 45.4%). Histologically active MC was documented in 46.5% of patients before starting the first advanced therapy, and in 43.7% of all treatment cycles.

A total of 229 treatment cycles were recorded, reflecting that several patients required multiple lines of advanced therapy due to PNR or secondary LOR. First-line therapy predominantly consisted of anti-TNF agents, as well as vedolizumab, whereas use of other advanced therapies was rare (**Figure 1A**). In later lines of therapy, the use of other advanced agents increased, although anti-TNF therapies remained the most commonly prescribed across all lines (n=128; 55.9% for all anti-TNFs combined)

(**Figure 1B**). Vedolizumab was the second most frequently used agent across all treatment cycles (n=66; 28.8%), followed by JAK inhibitors, which accounted for nearly one in ten treatment cycles (n=21; 9.2%). Use of JAK inhibitors included tofacitinib (n=9; 3.9%), filgotinib (n=6; 2.6%), and upadacitinib (n=6; 2.6%), primarily in later treatment lines. Overall, the use of ustekinumab (n=11; 4.8%), anti-IL23p19 inhibitors (n=2; 0.9%), and S1PR modulators (n=1; 0.4%) remained limited.

Median drug exposure across advanced therapies was 0.9 [0.4–2.0] years for infliximab and 0.9 [0.4–2.3] years for adalimumab, while exposure was slightly shorter for vedolizumab (0.7 [0.3–1.5] years) and ustekinumab (0.6 [0.3–1.1] years). Exposure for JAK inhibitors reached 1.6 [0.4–2.2] years.

Short-term drug effectiveness

Across all treatment cycles, we observed a 65.1% clinical response and 48.9% clinical remission rate. By the end of induction, infliximab led to a marked reduction in watery stools frequency (SF), decreasing from 7.0 [5.0–10.0] episodes per 24 hours at baseline to 3.0 [2.0–5.8] ($p<0.001$), with associated clinical response and remission rates of 68.1% and 48.6%, respectively (**Figure 2**). Similarly, adalimumab significantly reduced SF from 6.0 [5.3–8.0] to 4.0 [2.0–6.0] ($p<0.001$), resulting in induction response and remission rates of 60.8% and 51.0%, respectively. Vedolizumab and ustekinumab also achieved significant reductions in SF ($p<0.001$ and $p=0.01$, respectively), with corresponding response and remission rates of 59.1% and 40.9% for vedolizumab, and 54.5% and 36.4% for ustekinumab at the end of therapy induction. Although JAK inhibitors were predominantly used in later lines of therapy (**Figure 1B**), they demonstrated a substantial reduction in SF from 7.0 [5.0–10.0] to 2.0 [1.5–2.0] ($p<0.001$), with high response and remission rates of 95.2% and 81.0%, respectively. Given the very small number of patients treated with anti-IL23 agents and ozanimod, the observed response and remission rates of 50.0% (anti-IL23) and 100.0% (ozanimod) should be interpreted with caution.

To assess differences in clinical outcomes post-induction across treatment groups, while accounting for repeated treatment cycles within individuals, we employed GEE with patient ID as the clustering variable and treatment class as a categorical predictor. In the class-wide comparison, JAK inhibitors demonstrated significantly higher odds of achieving clinical response (OR 8.71, 95% CI 1.70–44.74, $p=0.009$) and clinical remission (OR 4.39, 95% CI 1.42–13.60, $p=0.01$) compared to anti-TNF agents (reference group). Vedolizumab (response: OR 0.80, 95% CI 0.42–1.52, p=0.50; remission: OR 0.73, 95% CI 0.39–1.36, p=0.33) and ustekinumab (response: OR 0.62, 95% CI 0.17–2.21, p=0.46; remission: OR 0.59, 95% CI 0.16–2.18, p=0.43) did not show significant differences. Sparse data limited interpretation of other agents. To further validate the observed signal, we also performed a binary comparison of JAK vs non-JAK therapies. This analysis confirmed the superiority of JAK inhibitors, with significantly increased odds of both clinical response (OR 10.0, 95% CI 1.85–50.0, $p=0.008$) and remission (OR 5.0, 95% CI 1.64–14.3, $p=0.005$. None of the other clinical variables (sex, age, smoking status, histological type of MC) emerged as independent predictors of short-term response in multivariable analysis.

Long-term drug persistence

Although induction results were encouraging, discontinuation rates remained substantial (**Figure 3**), primarily due to PNR (45.9%), secondary LOR (28.7%), or adverse events (AE)/intolerance (18.0%). Discontinuation rates were comparable between patients with collagenous colitis (56.1%) and lymphocytic colitis (53.8%) (p=0.79). Only 3.3% of patients discontinued therapy following sustained long-term remission after 1.0 [0.9-1.1] years (two on infliximab, one on vedolizumab, and one on ustekinumab).

Among infliximab-treated patients, 62.5% discontinued therapy after a median of 0.8 years [IQR 0.3–1.4], mainly due to intolerance (n=15; 33.3%), secondary LOR (n=14; 31.1%), or PNR (n=13; 28.9%). Notably, 43.1% of these patients had received infliximab as monotherapy, which may have contributed to immunogenicity and subsequent LOR. A similar discontinuation pattern was observed with adalimumab, where 54.9% of patients discontinued after a median of 0.6 years [0.3–1.6], largely driven by PNR (n=16; 57.1%) and LOR (n=10; 35.7%), with intolerance being rare (n=1; 3.6%).

Vedolizumab showed a comparable profile, with 56.1% discontinuation mainly due to PNR (n=23; 62.2%) and LOR (n=10; 27.0%) after a median exposure of 0.5 years [0.2–1.0]. No discontinuations due to AEs were reported with vedolizumab. Ustekinumab demonstrated a similar trend, with discontinuations primarily related to PNR (n=4; 57.1%), followed by LOR (n=1; 14.3%) and intolerance (n=1; 14.3%) after a median of 0.3 years [0.2–0.8].

In contrast, JAK inhibitors were associated with significantly higher treatment durability, with an odds ratio of 4.76 (95% CI 1.64–14.3, *p*=0.004) for persistence compared to non-JAK therapies, exclusively due to intolerance after a median of 0.4 years [0.3–0.4]. Survival analysis using a Cox proportional hazards model with shared frailty terms confirmed the superior durability of JAK inhibitors compared to other advanced therapies (HR = 0.41, 95% CI: 0.21–0.82, p = 0.01). These results were consistent in a marginal Cox model using robust sandwich estimators clustered on patient ID (HR = 0.39, 95% CI: 0.19–0.79, p = 0.008), supporting the robustness of the findings. (**Figure 4**). In the entire cohort, no new safety signals were observed.

In multivariate analysis using GEE to account for repeated measures, drug class emerged as the sole independent predictor of therapy continuation. JAK inhibitors were associated with significantly greater persistence compared to other advanced therapies (OR 5.07, 95% CI 1.52–16.9, p = 0.008), while other clinical and demographic variables—including age, gender, smoking status and histological subtype—did not independently predict long-term use (**Figure 5A**).

In a separate model comparing individual drugs (with infliximab as the reference), JAK inhibitors again demonstrated significantly improved persistence (OR 6.35, 95% CI 1.79–22.5, p = 0.004). No other biologic therapy showed statistically significant differences in drug survival compared to infliximab (**Figure 5B**).

Ultimately, 6 patients (4.2% of the total cohort; 83.3% with CC) required colorectal surgery due to inadequately controlled disease: three underwent proctocolectomy, and three received a diverting ileostomy.

DISCUSSION

This multinational ECCO CONFER study represents the largest and most comprehensive series to date showing that all advanced IBD therapies were used off-label for budesonide refractory or dependent MC patients in real-world practice. By capturing 229 treatment cycles across 142 patients, the study exceeds the total number of cases included in prior systematic reviews (limited to 164 cycles),[14] and overcomes the sample size limitations of previous case reports and small case series.[18-30] These results define an important reference point for future research efforts and emphasize the need for prospective registries and randomized controlled trials to further refine therapeutic approaches.

Comparing our findings to the most recent meta-analyses highlights several key points. Prior pooled data suggested clinical remission rates of 63.5%, 57.8%, and 39.3% for vedolizumab, infliximab, and adalimumab, respectively.[14] Our current results largely mirror these trends, yet offer greater nuance as definitions of clinical endpoints were largely heterogeneous in the pooled studies. We observed remission rates of 40.9% for vedolizumab, 48.6% for infliximab and 51.0% for adalimumab at the end of induction, thus validating existing effectiveness signals in a much larger and more standardized cohort. Importantly, while Chehade et al. attempted to summarize maintenance outcomes, their reported long-term remission data were derived from small cohorts with short and variably defined follow-up periods—typically under 6–12 months for most agents.[14] In contrast, our study offers robust long-term data, with vedolizumab showing a discontinuation rate of 56.1% and anti-TNF agents around 60% after a median exposure of 0.5–0.9 years. This provides a more realistic and clinically meaningful view of the durability of advanced therapies in MC, highlighting both the initial promise and the limitations of long-term disease control. Our results emphasize that while anti-TNF agents and vedolizumab offer substantial short-term effectiveness, sustaining remission over time remains a significant unmet challenge, necessitating the exploration of newer therapeutic classes.

A unique aspect of our study is the inclusion of agents that had not been systematically assessed in MC before: the JAK inhibitors (tofacitinib, filgotinib, upadacitinib). While previously limited to anecdotal reports,[26-30] our cohort offers the first clearer signal of their potential short- and long-term effectiveness. Even though the exact pathophysiology of MC remains incompletely understood,[31, 32] emerging molecular data[33] suggest a possible involvement of the JAK/STAT pathway—providing a mechanistic rationale for the observed efficacy of these agents. With an 81.0% remission rate and superior drug durability compared to other advanced agents at the end of induction, JAK inhibitors may represent a paradigm shift in MC management. Although patients with MC carry an intrinsically elevated risk of venous thromboembolism (VTE),[34] and regulatory bodies such as the EMA have issued general safety warnings regarding JAK inhibitors, especially in elderly patients,[35] concerns regarding their use in MC should be carefully contextualized. Notably, patients with IBD—who similarly exhibit an increased

baseline VTE risk[36]—have not yet demonstrated any emerging safety signals in multiple clinical trials, real-world studies, or long-term extension programs with JAK inhibitors.[37-39] These data are reassuring and suggest that, with appropriate patient selection and monitoring, JAK inhibitors may represent a low risk and effective therapeutic option for refractory MC. Nevertheless, the patient's comorbidity should be considered and properly acknowledged.

Traditionally, MC is considered a '*disease of the elderly'*.[1, 3] However, multiple studies already highlighted the impact of MC also at younger age.[40] The median age at advanced therapy initiation in our cohort was 56.6 years—considerably younger than epidemiological studies suggest for the general MC population. This indicates that severe, budesonide-refractory or -dependent disease is not solely confined to older individuals with potentially higher co-morbidities, but necessitates a more dynamic, life-course approach to MC management strategies.

Several limitations merit acknowledgment. First, the retrospective design, inherently prone to selection and reporting bias. We recognize that centres contributing to CONFER are predominantly expert centres, which may limit the generalizability of our findings. However, the magnitude and consistency of the dataset likely mitigate this concern to a considerable extent. Additionally, we lacked systematic histological reassessment, which could have provided important mechanistic insights into treatment response or failure. Finally, we lacked data on therapeutic drug monitoring for anti-TNF agents, as well as data on the recently validated Microscopic Colitis Score (MCS).[41]

From a future perspective, two imperatives emerge. First, prospective cohort studies should be established to confirm and expand upon these findings, integrating not only clinical, but also histologic endpoints, to comprehensively define remission. Second, and even more crucially, there is a pressing need for randomized controlled trials in MC. The growing body of evidence—now significantly strengthened by this series—should catalyse pharmaceutical and regulatory interest in developing approved therapeutic options for this often debilitating condition. The establishment of a standardized outcome framework for MC, approved by regulatory bodies, would facilitate such trials and ultimately lead to tailored, evidence-based treatment algorithms.

In conclusion, advanced therapies, once considered experimental for MC, are increasingly being used for (refractory) MC. This large, retrospective, multicentre study demonstrates the real-world effectiveness of both biologics and small molecules, and highlights the potential of JAK inhibitors as a transformative treatment option. However, the era of small case series and anecdotal evidence must now give way to rigorous clinical trials. Future research should focus on validated endpoints, prospective designs, and the integration of MC into the broader framework of precision gastroenterology.

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TABLES AND FIGURES

Figure 1: Patterns of advanced therapy use in microscopic colitis. (**A**) First-line advanced therapies after budesonide discontinuation. Bar height represents the relative proportion of patients receiving each advanced therapy, subdivided by histologic subtype: collagenous colitis (CC, light blue) and lymphocytic colitis (LC, dark blue). Percentages above the bars indicate the overall usage within first-line. Absolute numbers are displayed within bar segments when greater than five. (**B**) Treatment sequencing across lines of therapy. Stacked bars represent the relative proportion of patients receiving each advanced therapy, segmented by treatment line (from first- to fifth-line therapy). Colours indicate the treatment line, with lighter shades denoting later lines. Absolute patient counts are shown within segments when greater than five.

Figure 2: Clinical response (**A**) and clinical remission (**B**) rates at the end of induction across advanced therapies in microscopic colitis. Results shown for the overall cohort and separated by histological subtypes (collagenous colitis and lymphocytic colitis). Data are expressed as percentages.

Figure 3: Drug discontinuation rates across advanced therapies in microscopic colitis. Bar heights represent the overall continuation rate after induction therapy, with subdivisions illustrating the relative contribution of collagenous colitis (CC) and lymphocytic colitis (LC). Data are expressed as percentages.

Figure 4: Drug survival in microscopic colitis. (**A**) Kaplan-Meier curves showing drug survival probability for each individual treatment class. (**B**) Kaplan-Meier curves comparing pooled advanced therapies against JAK inhibitors.

Figure 5: Independent predictors of treatment persistence to advanced therapies in MC. Odds ratios (ORs) and 95% confidence intervals (CIs) are displayed on a logarithmic scale. Significant predictors are indicated in colour. (**A**) Forrest plot showing the overall independent predictors. "Drug class" represents the global impact of treatment choice independent of other clinical covariates. (**B**) Forrest plot comparing treatment persistence between different advanced therapies, using infliximab as the reference.

Table 1: Baseline characteristics of all included patients

Sex, female, *n* (%)	122 (85.9)
Age at MC diagnosis, *y,* median [IQR]	52.6 [38.3-61.7]
Age at initiation of advanced therapy, *y,* median [IQR]	56.6 [44.3-65.3]
MC diagnosis, *n* (%)	
- Collagenous Colitis	75 (52.8)
- Lymphocytic colitis	67 (47.2)
Concomitant therapy at MC diagnosis, *n* (%)	
- Proton pump inhibitors	37 (26.1)
- Serotonin reuptake inhibitors	37 (26.1)
Reasons for budesonide discontinuation, *n* (%)	
- Primary non-response, PNR	16 (11.3)
- Budesonide dependency	64 (45.4)
- Secondary budesonide refractiveness, LOR	50 (35.5)
- Adverse event	11 (7.8)
Smoking status, *n* (%)	
- Active smoking	37 (26.2)
- Previous smoking	19 (13.5)
- Never smoked	85 (60.3)
Familial history of MC, *n* (%)	3 (2.1)
Concomitant immune mediated disease, *n* (%)	
- Celiac disease	4 (2.8)

- Psoriasis	9 (6.3)
- Spondyloarthropathy	7 (4.9)
- Rheumatoid arthritis	3 (2.1)
- Other	8 (5.6)

IQR, interquartile ranges; LOR, loss of response; MC, microscopic colitis; PNR, primary nonresponse.

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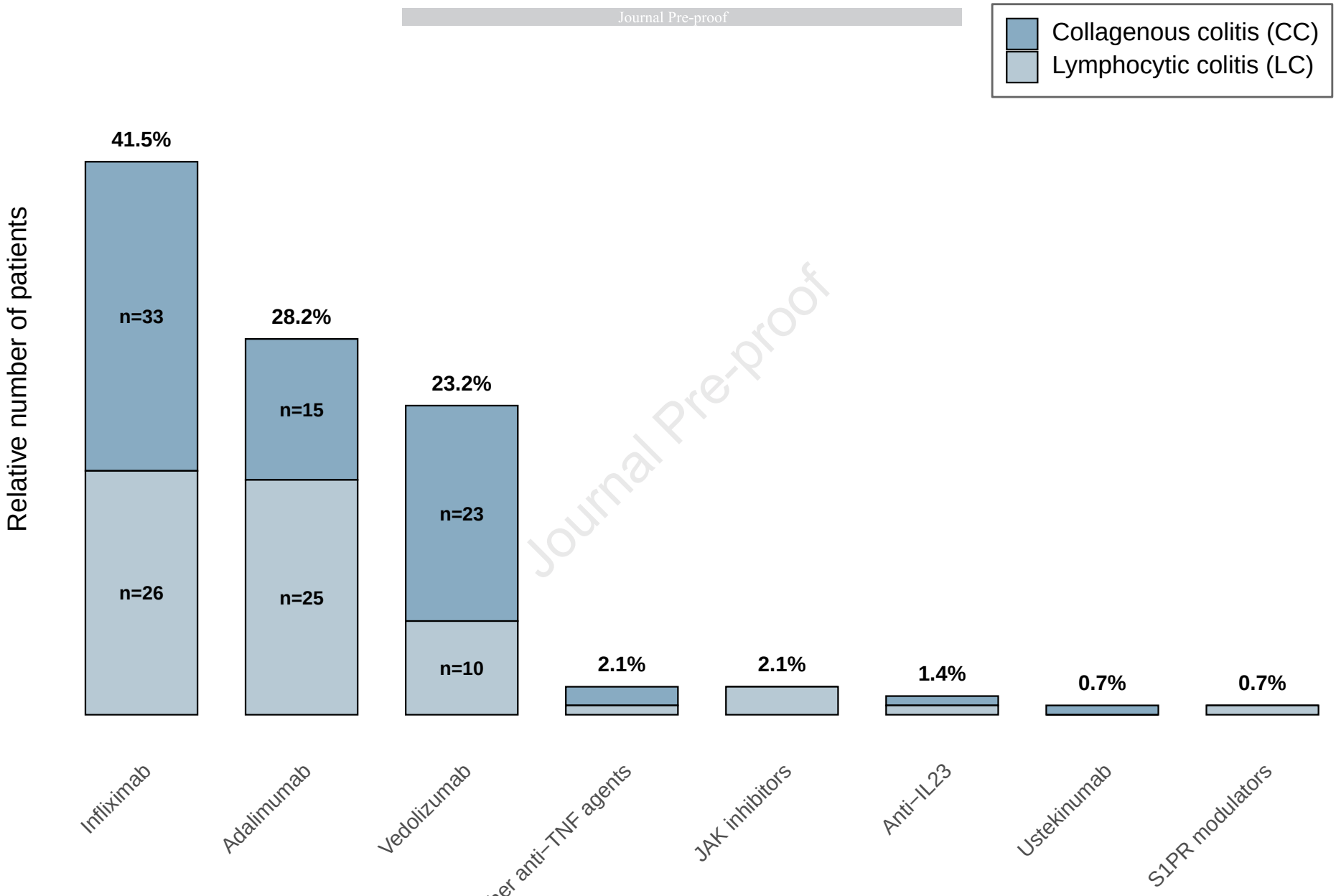

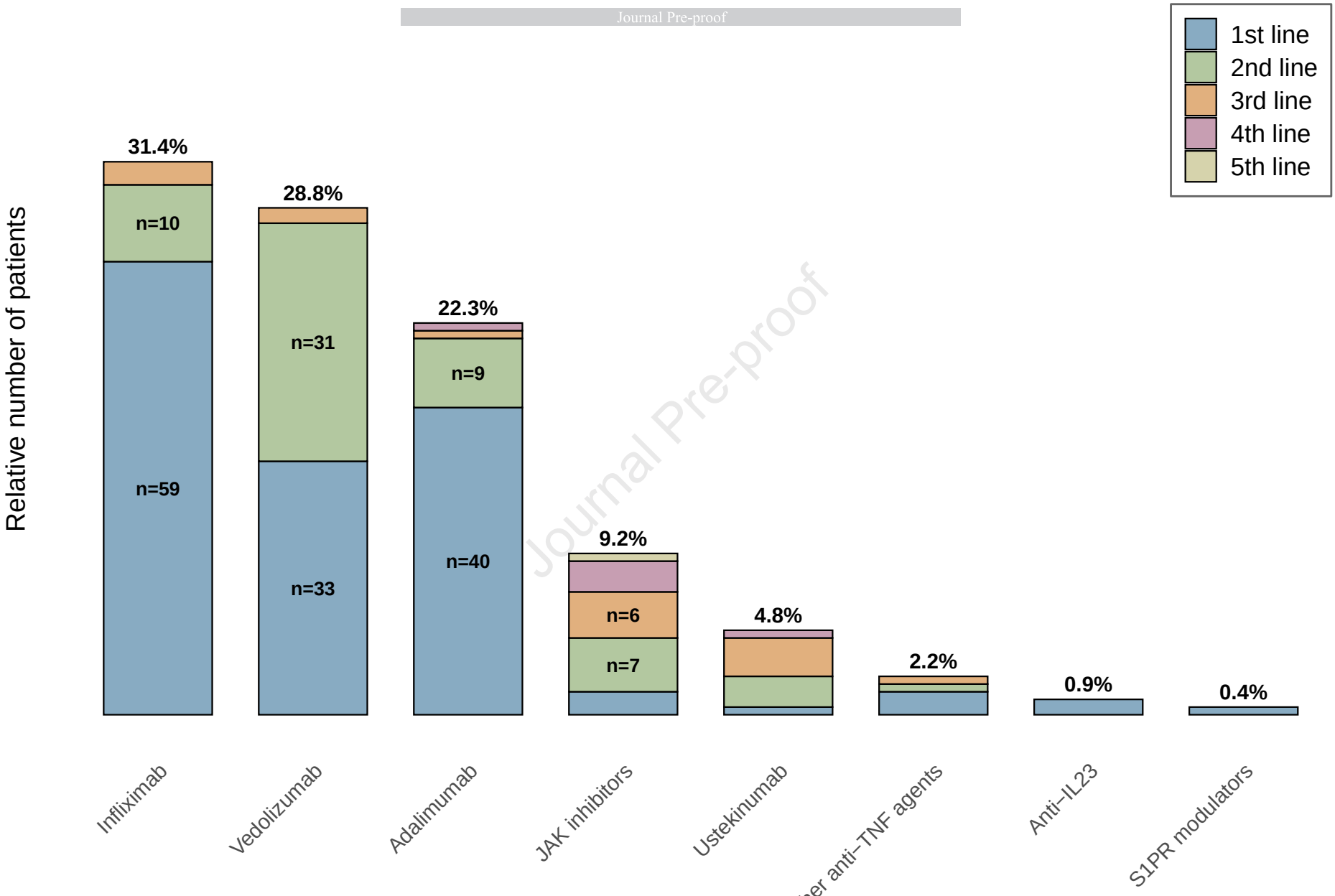

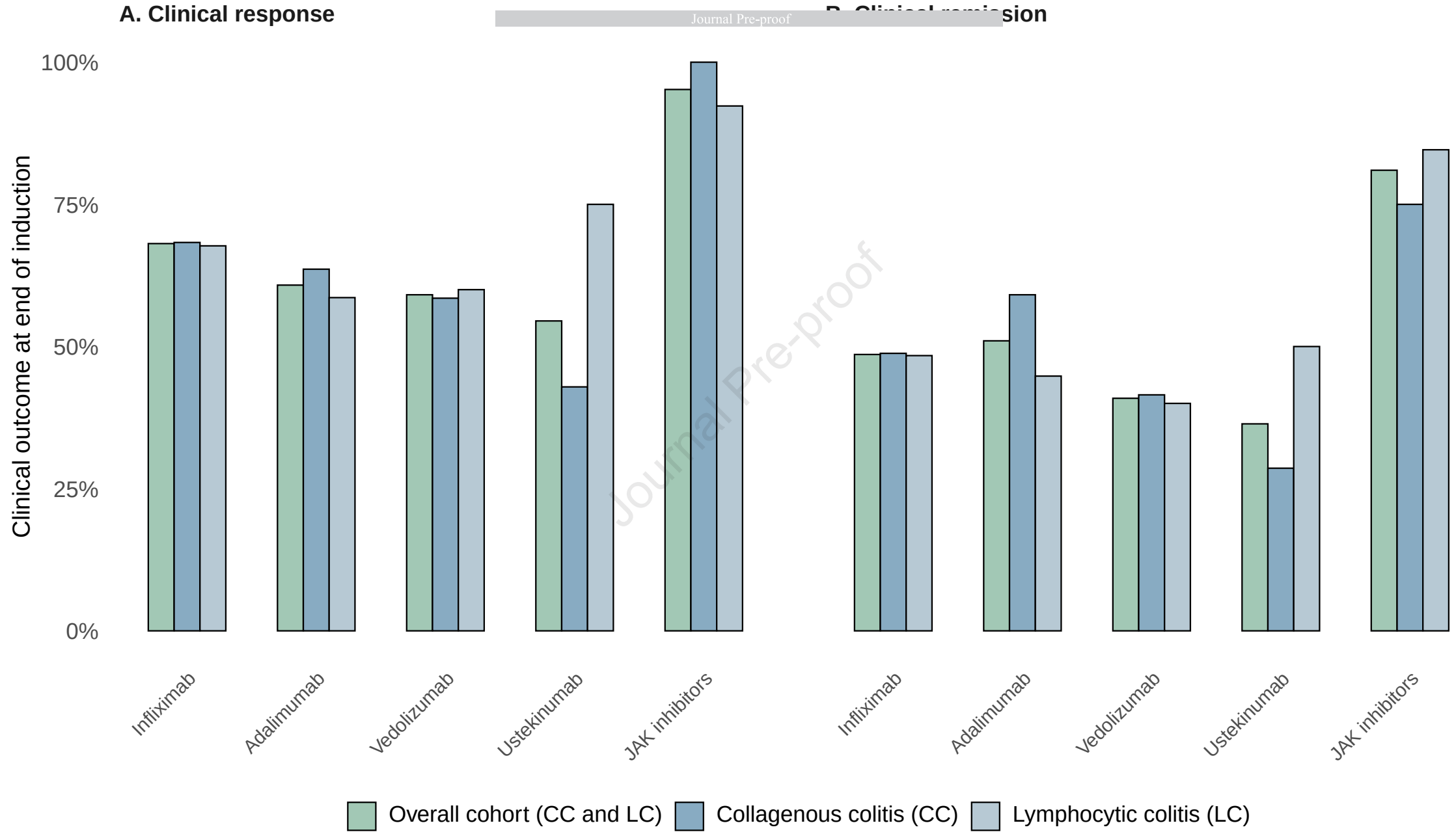

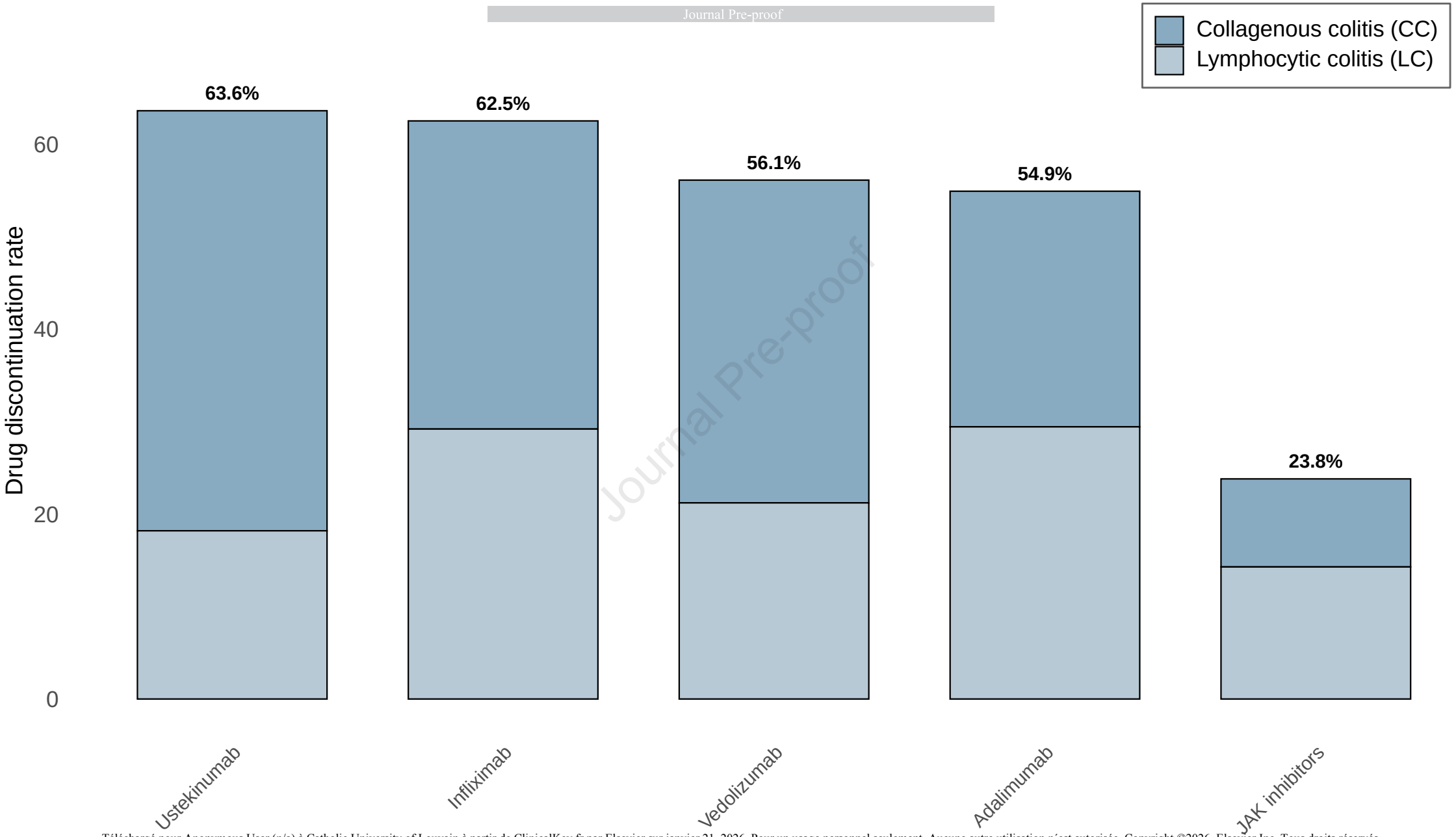

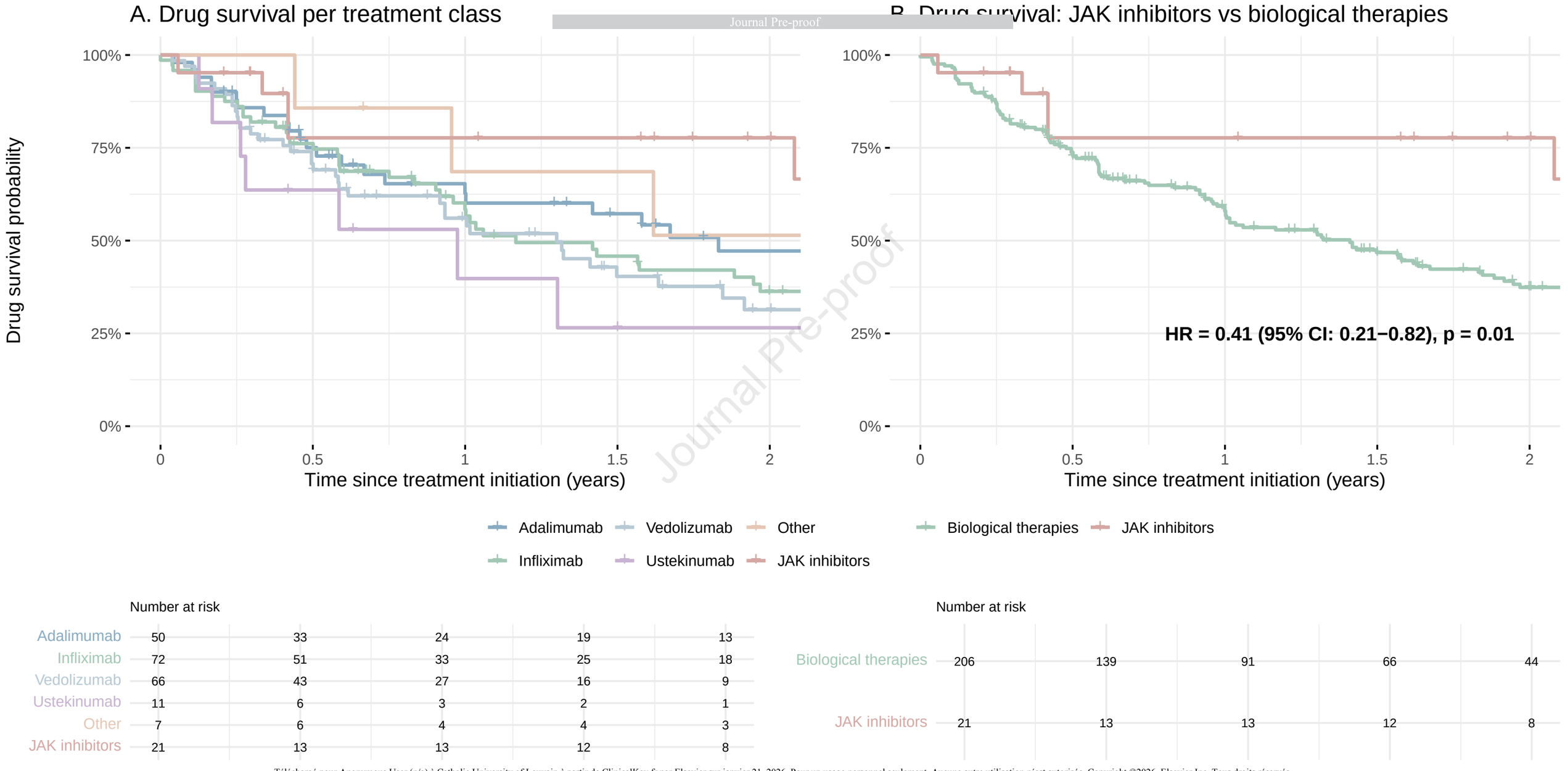

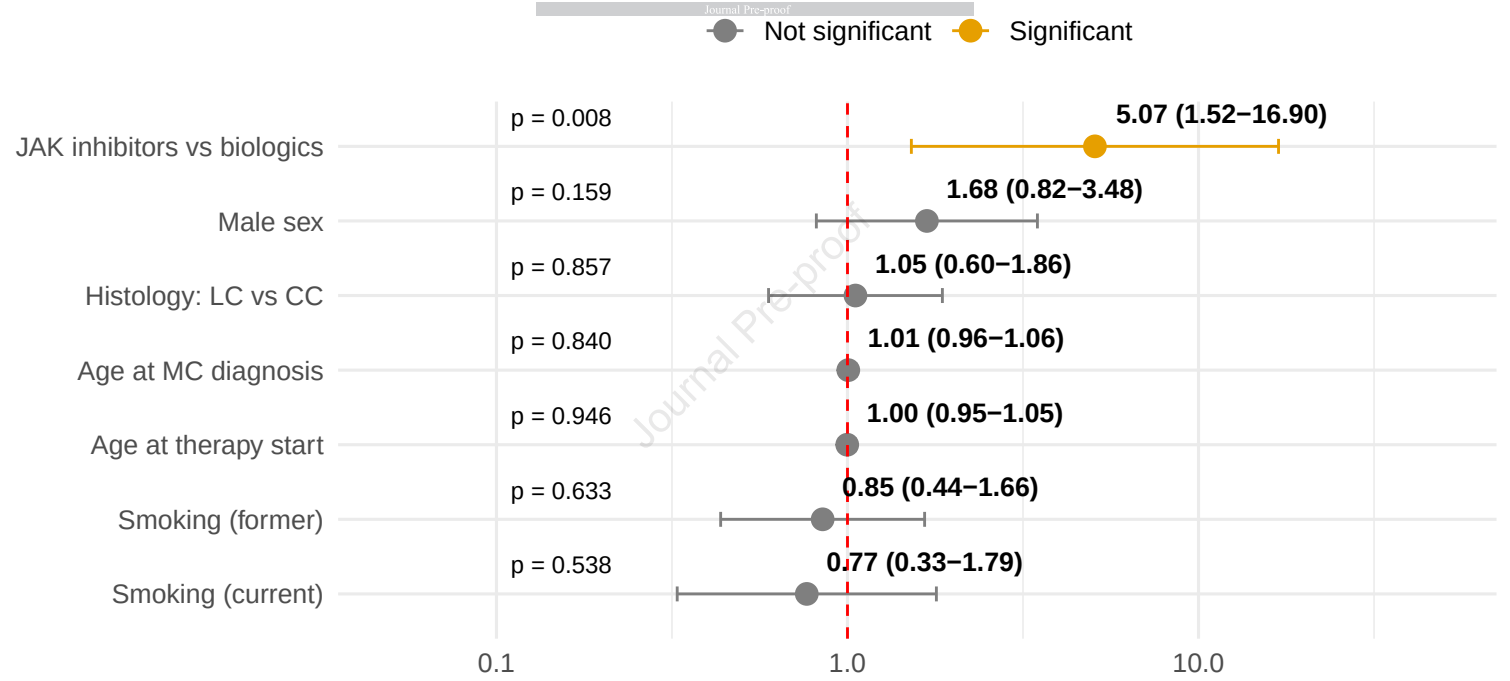

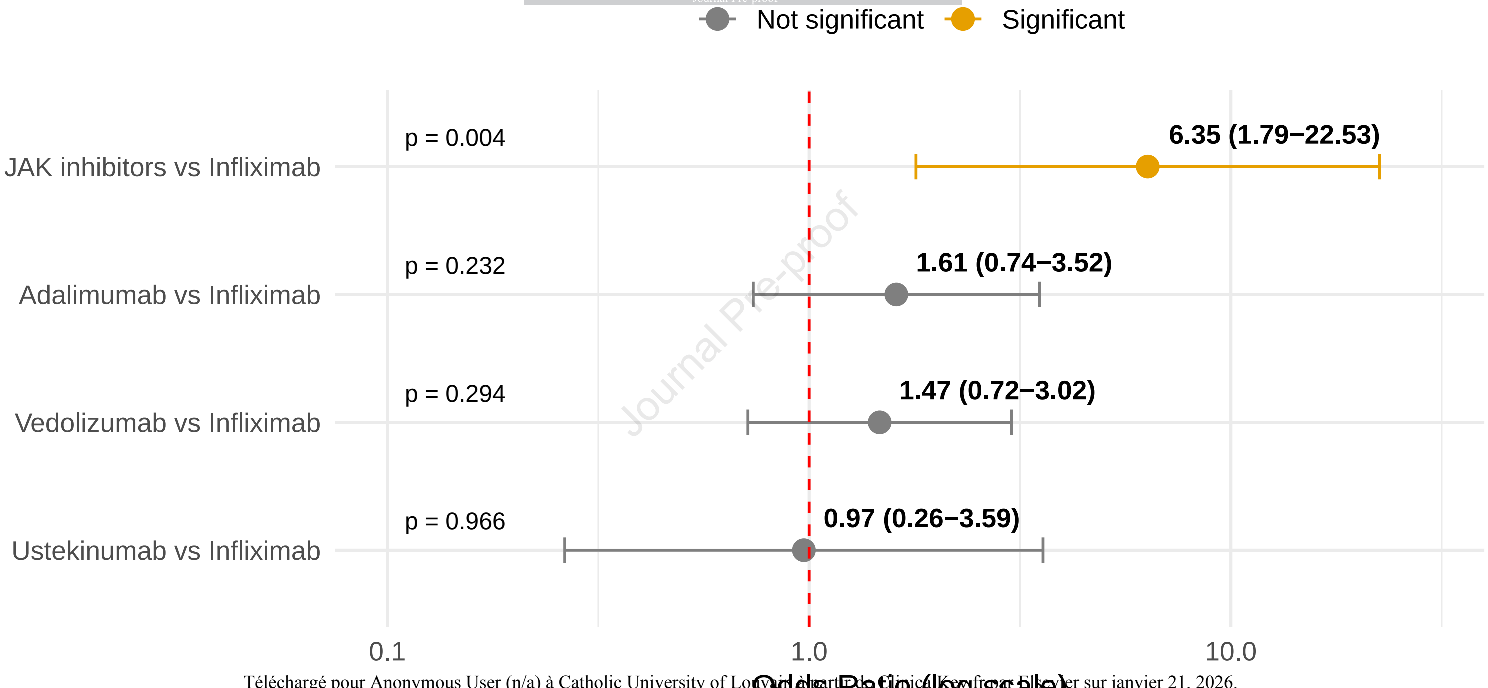

Supplementary Table 1: Representation of individual patients per country

Country	*n* (%)
Austria	8 (5.6)
Belgium	50 (35.2)
Bulgaria	1 (0.7)
Czechia	1 (0.7)
Denmark	3 (2.1)
France	10 (7.0)
Germany	4 (2.8)
Israel	2 (1.4)
Italy	7 (4.9)
Lithuania	4 (2.8)
Spain	9 (6.3)
Sweden	11 (7.7)
Swiss	12 (8.5)
United Kingdom	19 (13.4)
United States of America	1 (0.7)