DOP75

Loss-of-response and immunogenicity following immunomodulator withdrawal from anti-tumour necrosis factor alpha combination therapy: Results from a large retrospective cohort study

R. Mahmoud*[1], J. Schultheiss[1], J. Louwers[1], M. van der Kaaij[1], B. van Hellemondt[1], N. Mahmmod[2], P. van Boeckel[2], B. Jharap[3], H. Fidder[1], B. Oldenburg[1]

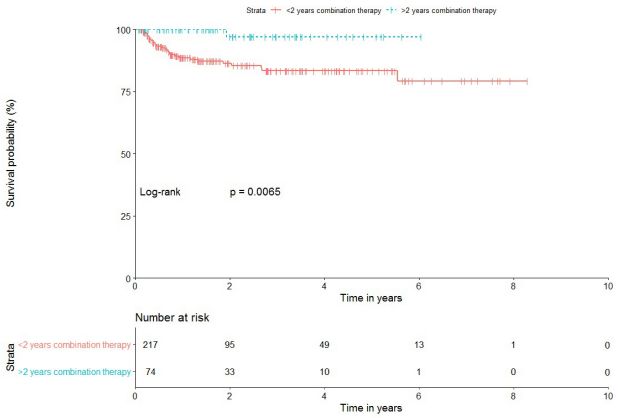
[1]*University Medical Centre Utrecht, Division of Internal Medicine and Dermatology- Department of Gastroenterology and Hepatology, Utrecht, The Netherlands,* [2]*St. Antonius Hospital, Division of Internal Medicine- Department of Gastroenterology and Hepatology, Nieuwegein, The Netherlands,* [3]*Meander Medical Center, Division of Internal Medicine- Department of Gastroenterology and Hepatology, Amersfoort, The Netherlands*

Background: Combination therapy with anti-TNF compounds and immunomodulators (IMM; thiopurine or methotrexate) is superior to IMM or anti-TNF monotherapy in patients with inflammatory bowel disease (IBD). IMMs are frequently discontinued during the maintenance phase to mitigate the risk of adverse events, but long-term consequences of this practice are not well studied. We explored the real-world outcomes after IMM discontinuation, including loss-of-response (LOR), dose escalations, immunogenicity and trough levels.

Methods: This was a multicenter, retrospective cohort study in a general hospital and a tertiary referral center. We included adult patients with IBD, treated >4 months with infliximab (IFX) or adalimumab (ADA) and an IMM at baseline between 2011–2019. The IMM had to be started within 30 days of anti-TNF initiation, or continued for >30 days in case of prior IMM monotherapy. LOR was defined as anti-TNF discontinuation due to disease activity. Adjusted hazards rates (aHR) were calculated using mixed-effects Cox regression analysis with time-varying covariates, accounting for follow-up prior to and after IMM cessation. We adjusted for sex, age, BMI, smoking, Crohn's disease (CD) vs ulcerative colitis (UC), disease duration, primary sclerosing cholangitis, rheumatological comorbidity, ADA vs IFX, and prior anti-TNF exposure.

Results: We included 615 episodes of combination therapy (543 individual patients; CD, n=382, 70%). The IMM was discontinued in 296 (48%) episodes after a median of 0.9 (IQR: 0.6 – 2.1) years, at which point 252 (85%) patients were in clinical remission. IMM withdrawal was performed as part of a de-escalation strategy (n=158, 53%), for intolerance (n=86, 29%) or for miscellaneous reasons (n=52, 18%). During a median follow-up of 1.7 (IQR 0.8 – 3.5) years after IMM withdrawal, 46 (16%) patients experienced LOR, 79 (32%) required dose-escalation and 31 (10.3%) developed anti-drug antibodies. Compared to IMM continuation, withdrawal did not significantly increase the risk of LOR (aHR 1.10, 95%CI: 0.74 – 1.64), but more patients required dose escalations (aHR 1.42, 95%CI 1.02 – 1.97) or developed anti-drug antibodies (aHR 2.22, 95%CI 1.21 – 4.08). Among patients who stopped the IMM, clinical remission at IMM withdrawal was the only predictor of LOR (aHR 0.48, 95%CI 0.23 – 0.99), while higher BMI (aHR 1.09, 95%CI 1.01 – 1.17) and shorter duration of combination therapy (Figure 1, aHR 0.57 per year, 95%CI 0.33 – 0.96) increased the risk of immunogenicity. IFX, but not ADA, trough levels decreased significantly after IMM withdrawal.

Figure 1. Immunogenicity following immunomodulator withdrawal



Conclusion: Withdrawal of immunomodulators is not associated with higher risk of LOR, but does increase the risk of dose-escalation and unfavorable pharmacokinetics.

DOP76

No durable impact of COVID-19 on disease activity and microbiome composition in patients with IBD

G. Funez-dePagnier[1], S. Lima[1], L. Duenas-Bianchi[1], D. Lai[1], W. Ahmed[1], R. Battat[1], E. Scherl[1], D. Lukin[1], R. Longman*[1]

[1]*Weill Cornell Medicine, Medicine, New York, United States*

Background: Although patients with inflammatory bowel disease (IBD) reported an increased frequency of gastrointestinal (GI) symptoms following infection, the durable impact of COVID-19 on underlying IBD is not well defined.

Methods: In 118 IBD patients with COVID-19, clinical and endoscopic IBD activity, laboratory markers (ESR, CRP, hemoglobin (Hb), fecal calprotectin(FCP)), and medication utilization was assessed up to 6 months post-infection and compared to during infection or up to 6 months prior to infection. Active disease was defined by a Harvey Bradshaw Index > 4, Mayo Score ≥2, SES-CD ≥2, Mayo endoscopic score ≥1. 16S rRNA analysis was used to evaluate microbiome composition in a subset of 12 patients before and after COVID-19.

Results: Although upper respiratory (86.6%) and new GI symptoms (39.1%) were common in patients with IBD, there was no significant change in IBD clinical disease activity (Pre vs. Post-COVID-19 HBI: 4.7 vs. 4.9; partial Mayo: 3.0 vs. 2.1), endoscopic evaluation (Pre vs. Post-COVID-19 SES-CD: 7.2 vs. 8.9, Mayo endoscopic score: 1.5 vs. 1.7), or laboratory markers (Pre vs. Post-COVID-19 CRP: 1.2 vs. 1.3; ESR: 25 vs. 26; Hb 12.8 vs. 13.2; FCP: 388 vs. 250) up to 7 months post-COVID-19 compared to the 6 months prior to infection (Table 1). Overall active disease was present in 60% of the cohort prior to COVID-19 and 55% and 59% during and post-COVID-19, respectively. More subjects (8.5%) reported a delay in medical therapy during COVID-19, but there were no differences in the need for corticosteroids, a change in medical therapy, or IBD-related surgery or hospitalization during or post-COVID-19 compared to the prior 6 months. Microbiome composition stratified by underlying IBD disease activity, but did not show significant change post-COVID-19 (Figure 1).

Conclusion: COVID-19 showed no durable impact on clinical IBD disease activity or microbiome composition supporting guidelines for continued maintenance care.

DOP77

Effect of Inflammatory Bowel Disease and Related Medications on COVID-19 Incidence, Disease Severity, and Outcome -The Israeli Experience

V. Richter*[1], A. Bermont[1], D.L. Cohen[1], E. Broide[1], H. Shirin[1]
[1]*Shamir Medical Center, Gastroenterology, Tzerifin, Israel*

Background: The COVID-19 pandemic raised concerns among IBD patients fearing an increased risk of infection and poor outcomes. We aimed to evaluate the incidence of COVID-19 among IBD patients; its influence on disease severity and outcome; its relationship to medication use; and how the pandemic affected IBD management.
Methods: An anonymous questionnaire was posted online to members of the Israel Crohn's Disease and Ulcerative Colitis Foundation (November 2020- January 2021). The questionnaire addressed the course of IBD disease and COVID-19 infection over the past year.
Results: 2152 IBD patients completed the questionnaire. 104 (4.8%) had been infected with COVID-19, significantly lower than the "expected" infected cases among the Israeli population (p=0.033). The median age of participants was 39; 60.5% were female. Most patients (75.6%) had no comorbidities other than IBD.
No correlation was found between IBD type or disease severity and COVID-19 infection. Most IBD patients reported mild COVID-19 disease, regardless of the type of IBD medications. Multivariable logistic regression analysis revealed that younger age, elevated BMI, and diabetes were independent risk factors for COVID-19 infection. IBD treatment including 5-aminosalicylic acid, smoking, and hypertension were protective factors. 25.2% of COVID-19 patients discontinued their IBD treatment, compared to 8.5% of non-COVID-19 infected patients. IBD flares were significantly higher in those who discontinued treatment (p<0.001).
Conclusion: IBD patients do not have an increased risk for COVID-19, regardless of IBD activity or treatment. Patients should be encouraged to continue effective IBD therapy, including biologics and steroids, to minimize active IBD.

DOP78

The differential diagnosis and clinicopathological spectrum of Inflammatory Bowel Disease: An interesting and informative ECCO topical review

R.M. Feakins*[1], J. Torres[2], P. Borralho-Nunes[3,4], J. Burisch[5], T. Cúrdia Gonçalves[6,7,8], L. De Ridder[9], A. Driessen[10], T. Lobatón[11], L. Menchén[12,13,14], A. Mookhoek[15], N. Noor[16], M. Svrcek[17], V. Villanacci[18], N. Zidar[19], M. Tripathi[20], TR Clinicopathological spectrum and differential diagnosis of IBD
[1]*Department of Cellular Pathology, Royal Free London NHS Trust, London, United Kingdom,* [2]*Department of Gastroenterology, Hospital Beatriz Ângelo, Loures, Portugal,* [3]*Department of Pathology, Hospital Cuf Descobertas, Lisbon, Portugal,* [4]*Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal,* [5]*Gastrounit, medical division, Hvidovre Hospital, University of Copenhagen, Denmark,* [6]*Department of Gastroenterology, Hospital da Senhora da Oliveira, Guimarães, Portugal,* [7]*School of Medicine, University of Minho, Braga/Guimarães, Portugal,* [8]*ICVS/3B's–PT Government Associate Laboratory, Braga/Guimarães, Portugal,* [9]*Department of Paediatric Gastroenterology, Erasmus MC Sophia Children's Hospital, University Medical Center Rotterdam, The Netherlands,* [10]*Department of Pathology, University Hospital Antwerp, University Antwerp, Edegem, Belgium,* [11]*Department of Gastroenterology, Ghent University Hospital, Ghent, Belgium,* [12]*Department of Digestive System Medicine, Hospital General Universitario-Insitituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain,* [13]*Department of Medicine, Universidad Complutense, Madrid, Spain,* [14]*Centro de Investigación Biomédica En Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain,* [15]*Department of Pathology, Amsterdam UMC, Amsterdam, The Netherlands,* [16]*Department of Gastroenterology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom,* [17]*Department of Pathology, Sorbonne Université, AP-HP, Saint-Antoine hospital, Paris, France,* [18]*Departments of Histopathology, Spedali Civili and University of Brescia, Brescia, Italy,* [19]*Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia,* [20]*Department of Histopathology, Cambridge Biomedical Campus, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom*

Background: A wide variety of intestinal and non-intestinal diseases can resemble chronic idiopathic inflammatory bowel disease (IBD) clinically and/or pathologically. The aim of the current Topical Review was to explore the differential diagnosis of IBD and to discuss clinical, histomorphological features and ancillary techniques that help distinguish between IBD and its mimics.
Methods: An open ECCO call led to the selection of 12 participants who formed three working groups (WG) to study the mimics of IBD. WG 1 comprised gastroenterologists, who explored mainly the clinical features. WG 2 consisted of histopathologists, who focused on macroscopic and microscopic pathological aspects. WG 3 was a mixed group of pathologists and clinicians who studied the value of additional investigative techniques such as imaging, serology and molecular markers. A systematic literature search allowed exploration of these topics and the identification of the most helpful and relevant distinguishing features. The process led to the development of Current Practice Position (CPP) statements and supporting text. Consensus meetings with voting by all participants facilitated modification and finalisation of CPP statements.
Results: The project highlighted several points. Firstly, there is a wide and sometimes overwhelming variety of potential mimics of new and established IBD, both in adults and in children.
Secondly, some mimics are more important clinically and others pathologically, meaning that the emphasis on the mimics of IBD is different for clinicians and pathologists. Thirdly, close attention to all clinical features, pathological findings and other evidence optimises accuracy. Finally, newer techniques sometimes have a role, e.g., in distinguishing monogenic IBD-like disorders from IBD in young children, and the value of many novel techniques is as yet uncertain. A practical message is that constant awareness by clinicians and pathologists of the possibility of mimics is particularly important.
Conclusion: Discussions between pathologists and clinicians were particularly useful during this process and were a reminder of the importance of clinicopathological correlation. There is a wide variety of mimics of IBD, including infections, diverticular disease, drug effect, radiation damage, immune disorders, vascular disorders and