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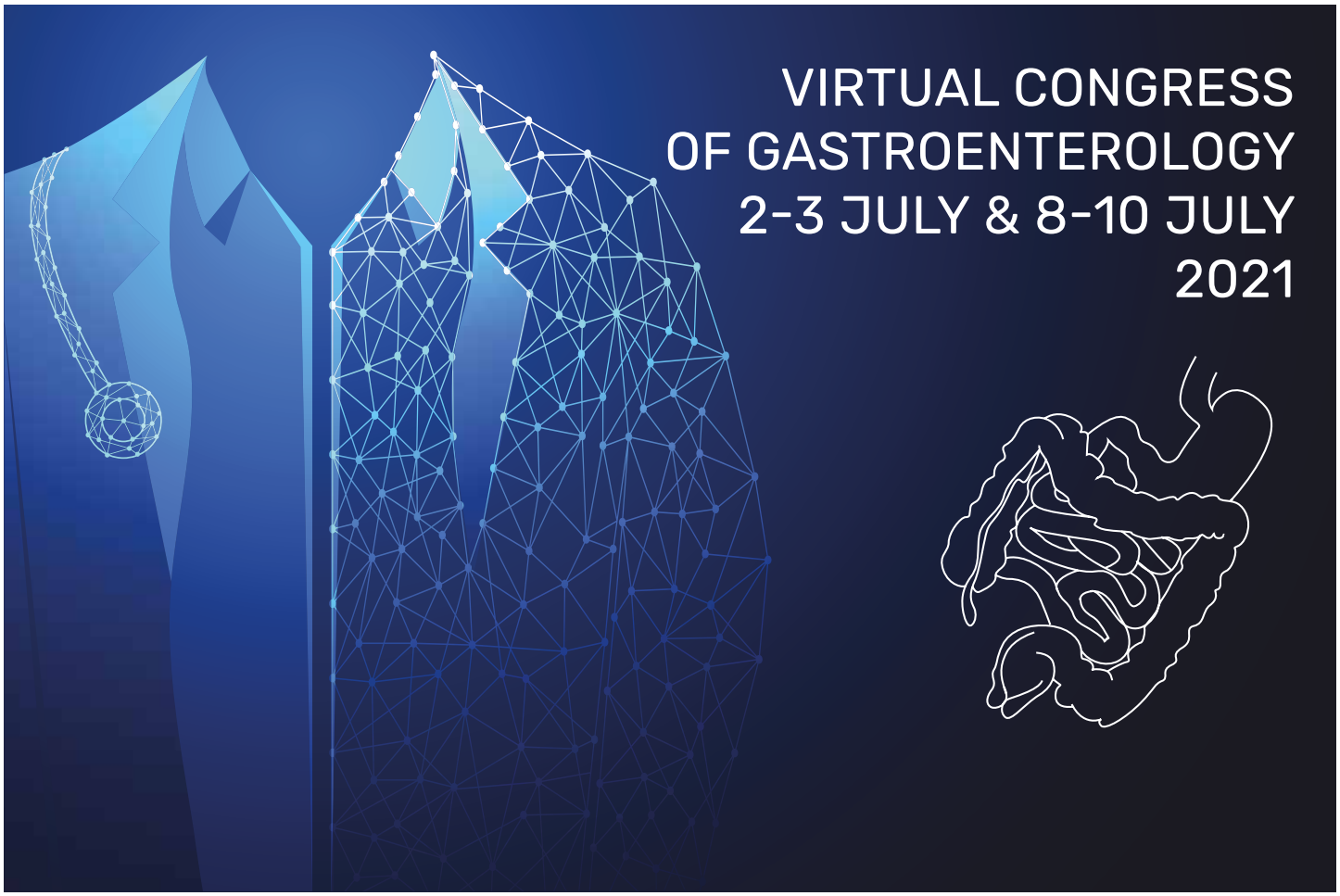

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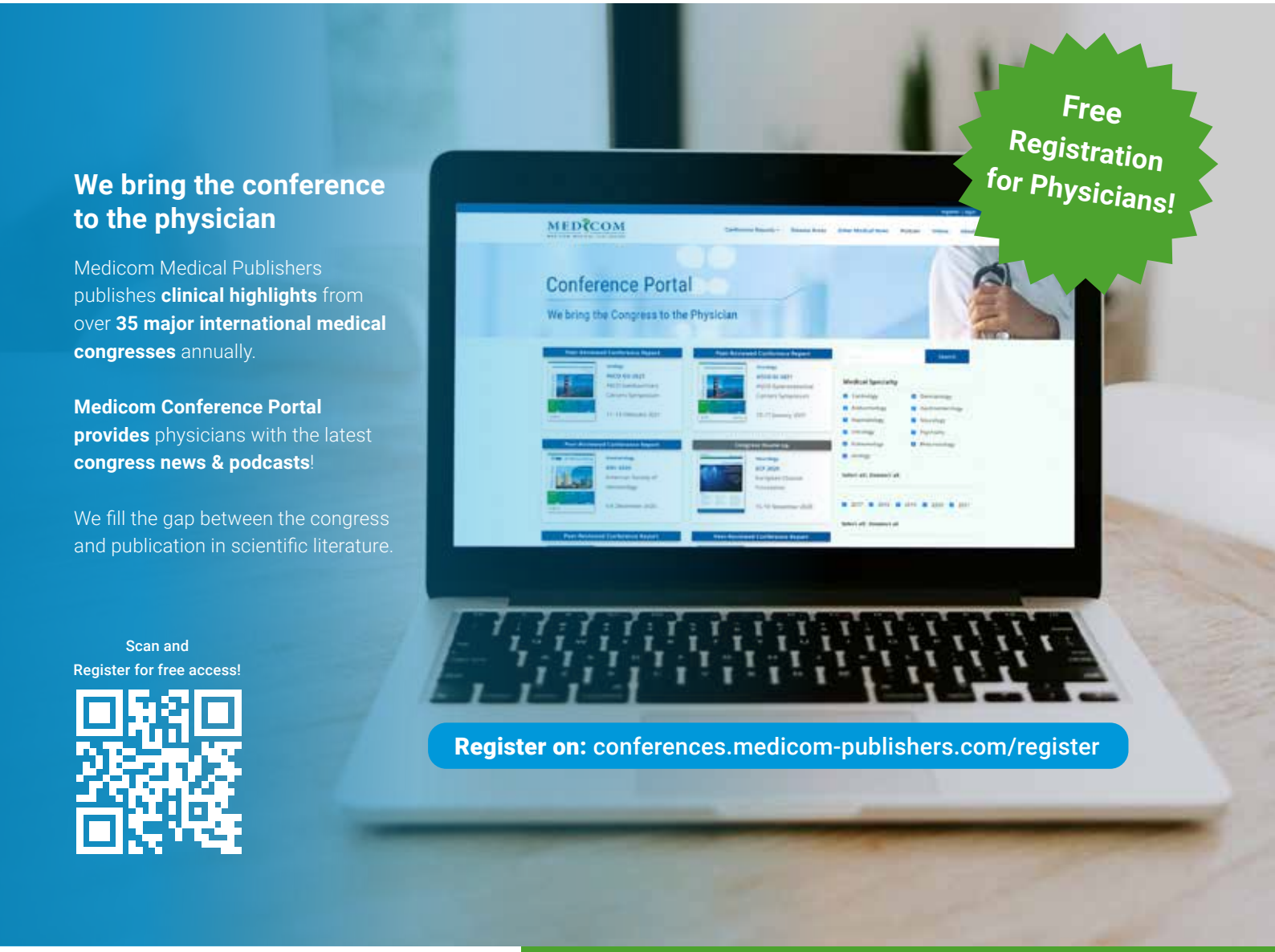

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1. Similar efficacy of ustekinumab and adalimumab for moderate-to-severe CD

Ustekinumab and adalimumab both showed high efficacy in biologic-naïve patients with moderate-to-severe Crohn's disease (CD). No significant difference in clinical remission rate was observed between the two therapies at 52 weeks of follow-up. The multicentre, randomised, blinded SEAVUE study was the first trial comparing these two biologics head-to-head in a population of CD patients.

Head-to-head studies are needed to make informed treatment decisions. In the SEAVUE study (NCT03464136), biologic-naïve moderate-to-severe CD patients (n=386) were randomised to ustekinumab, an IL-12/23(p40) antagonist, or adalimumab, a TNF antagonist. Safety and efficacy of both therapies was assessed. Patients in the ustekinumab arm received 6 mg/kg ustekinumab, intravenously injected, followed by a subcutaneous dose of 90 mg every 8 weeks. Patients in the adalimumab arm received 4 doses of 40 mg adalimumab, subcutaneously injected, in the first 2 weeks, followed by 2 doses of 40 mg in week 2-4 of the study. Hereafter, these patients were administered 40 mg of adalimumab every 2 weeks. Clinical remission, defined as a Crohn's Disease Activity Index (CDAI) score <150, was the primary endpoint of this trial. Dr Peter Irving (Guy's and St. Thomas' Hospital, UK) presented the results [1].

There was no significant difference in clinical remission rates between adalimumab and ustekinumab at 52 weeks of follow-up (61.0% vs 64.9%; P=0.417). Major secondary endpoints confirmed this result. The number of patients in corticoid-free remission at 52 weeks was similar for the 2 arms (adalimumab 57.4% vs ustekinumab 60.7%). Endoscopic remission, defined as simple endoscopic score for Crohn's disease (SES-CD) ≤3, did not show a significant difference in efficacy between adalimumab (30.7%) and ustekinumab (28.5%) in this population. Moreover, the 2 therapies demonstrated a similar pattern of increasing clinical remission rates over the course of the study.

The results of the safety analysis were consistent with prior experience for both medications. Among users of adalimumab, 77.9 % experienced at least one adverse event. Among ustekinumab recipients, adverse events were reported in 80.1%.

1. Irving P M, et al. Ustekinumab versus adalimumab for induction and maintenance therapy in Moderate-to-Severe Crohn's Disease: The SEAVUE study. OP02, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

2. Early clinical remission and response following risankizumab therapy in CD

Risankizumab was significantly more efficacious than placebo in inducing clinical remission and response 4 weeks after treatment initiation in patients with moderate-to-severe Crohn's disease (CD). Clinical remission and response rates continued to improve up to week 12. Since agents that induce an early and effective disease response are limited in CD, risankizumab adds value to the spectrum of therapy options.

The 12-week efficacy and safety data of the randomised, double-blind placebo-controlled phase 3 trials ADVANCE (NCT03105128) and MOTIVATE (NCT03104413), assessing risankizumab as induction therapy in patients with moderate-to-severe CD, have been presented earlier this year [1]. Dr Stefan Schreiber (University Hospital Schleswig-Holstein, Germany) and his colleagues further analysed the efficacy data of these trials [2]. Clinical remission, defined as Crohn's disease activity index (CDAI) scores <150, was the primary endpoint of both trials.

At week 4, CDAI scores revealed that clinical remission was achieved in a significantly greater proportion of patients receiving risankizumab compared with patients receiving placebo in both the ADVANCE trial (risankizumab 600 mg: 18.4% vs risankizumab 1,200 mg 18.9% vs placebo 10.3%) and the MOTIVATE trial (risankizumab 600 mg 20.9% vs risankizumab 1,200 mg 19.4% vs placebo 11.2%). Stool frequency/abdominal pain scores confirmed that early clinical remission could be achieved with risankizumab treatment in this population. In addition, clinical response rates showed significant benefits of risankizumab over placebo at week 4. Furthermore, ongoing improvement of risankizumab efficacy up to week 12 was observed.

1. D'Haens G, et al. DDW Virtual Conference 2021, May 21–23.
2. Schreiber S, et al. Risankizumab induces early clinical remission and response in patients with moderate-to-severe Crohn's disease: Results from the phase 3 ADVANCE and MOTIVATE studies. OP26, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

3. Ustekinumab safe and effective in elderly CD patients

The efficacy and safety profiles of ustekinumab is similar in elderly (60 years and older) and younger patients with Crohn's disease (CD). No differences were observed between age groups for clinical response rates, steroid-free remission rates, and biochemical response to the drug. These results confirm that ustekinumab is a safe and effective drug for elderly CD patients in real-life practice.

Studies investigating the effectiveness and safety profile of ustekinumab in elderly patients with CD are limited. Therefore, the authors of the current study performed a retrospective analysis of 648 patients enrolled in the ENEIDA registry to assess the safety and effectiveness of ustekinumab in an elderly CD population [1]. Based on a cut-off of 60 years, 212 elderly patients (mean age 67.0 years) and 436 young patients (mean age 41.6 years) were followed for 54 weeks.

At 54 weeks, the clinical response rate of the elderly and young patients was similar (74.0% vs 74.9%). Likewise, steroid-free remission rates, calprotectin normalisation rates, and C-reactive protein normalisation rates did not demonstrate differences throughout follow-up. The occurrence of adverse events (AEs) was also comparable between the elderly and the young patients (14.2% vs 11.2%). Furthermore, there was no difference between groups in the occurrence of severe infections, the need for surgery, or the need for hospital admission. Appearance of *de novo* neoplasms was the only AE that occurred more often in the elderly patient group (4.25% vs 0.69%, P=0.003).

1. Casas Deza D, et al. Effectiveness and safety of ustekinumab in elderly patients: Real world evidence from ENEIDA registry. P262, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

4. Risk of hospitalisation and surgery linked to IBD biological

A comparative analysis of biological therapies used in the treatment of inflammatory bowel disease (IBD) revealed that users of adalimumab as a first-line therapy for Crohn's disease (CD) were at higher risk of hospitalisation than users of infliximab. Moreover, vedolizumab as a second-line therapy for ulcerative colitis (UC) was associated with an increased risk of IBD-related surgery. Future studies should assess whether these results reflect drug efficacy and safety differences, or differences in disease state at the start of treatment.

A Danish, nationwide cohort study compared biologic treatments for CD and UC [1]. Between 2015 and 2018, bio-naïve patients (n=3,722) starting a treatment with infliximab, adalimumab, vedolizumab, golimumab, or ustekinumab were enrolled. The analysis was adjusted for health-related and socio-economic factors at baseline.

Infliximab was the prescribed first-line treatment in >90% of the patients. In addition, patients treated with infliximab were younger at the start of treatment than users of other biologics. On average, infliximab recipients were more often males, had a lower level of education, and were less likely to have been exposed to IBD surgery than users of other biological therapies. CD patients receiving adalimumab as a first-line treatment had a higher risk of all-cause hospitalisation than users of infliximab (HR 1.56; 95% CI 1.16-2.10). However, adalimumab- and infliximab treated patients did not differ on IBD hospitalisation, IBD-related surgery, or the use of corticosteroids. In comparison with adalimumab, second-line treatment with vedolizumab was associated with an increased risk of IBD-related surgery among UC patients (HR 1.94; 95% CI 1.01-3.71).

1. Bjørn Jensen C, et al. Patient characteristics and adverse effects in biologic treatment of Crohn's Disease and Ulcerative Colitis: A nationwide Danish cohort study 2015-2018. P603, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

5. Obesity increases the risk of immunogenicity to adalimumab in IBD

Obese patients with inflammatory bowel disease (IBD) who are treated with TNF inhibitor adalimumab demonstrated increased immunogenicity and lower trough levels compared with non-obese patients who were treated with this drug. Obesity was not associated with immunogenicity in patients treated with another TNF inhibitor, infliximab. These results indicate that obese IBD patients treated with adalimumab could benefit from proactive drug monitoring.

A multicentre, retrospective cohort study investigated the association between obesity and treatment response to adalimumab and infliximab in IBD patients (n=728) [1]. Treatment failure, anti-drug antibodies, and trough levels were the assessed outcome measures. Mixed-effects Cox regression analysis was used to examine the data.

In patients treated with adalimumab, obesity was significantly associated with an increased risk of developing immunogenicity (aHR 2.07; 95% CI 1.09-3.91). In addition, trough levels in obese patients on adalimumab were on average 0.20 mg/L lower than the trough levels of non-obese patients.

After adjusting for confounding factors, obesity was not significantly associated with treatment failure in patients receiving adalimumab (aHR 1.40; 95% CI 0.93-2.11). However, the results trended towards an increased risk of treatment failure in these patients. Obesity was not associated with treatment failure, immunogenicity, or trough levels in patients using infliximab.

1. Mahmoud R, et al. Obesity is associated with a higher risk of immunogenicity to adalimumab, but not infliximab, in patients with IBD. P414, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

6. Upadacitinib meets primary endpoint for moderate-to-severe UC

Induction of upadacitinib treatment in patients with moderate-to-severe ulcerative colitis (UC) led to higher clinical remission rates than placebo after 8 weeks. Moreover, all ranked secondary endpoints of the phase 3 U-ACCOMPLISH trial were met. The treatment was well tolerated and no new safety issues with upadacitinib were observed.

Upadacitinib is an oral selective and reversible JAK inhibitor. The phase 3 U-ACCOMPLISH trial (NCT03653026) randomised patients with moderate-to-severe active UC to 45 mg once daily upadacitinib (n=344) or placebo (n=177) [1]. The primary endpoint was the proportion of patients in clinical remission at week 8. Clinical remission was defined as Mayo stool frequency subscore ≤1 and not greater than baseline, rectal bleeding subscore of 0, and endoscopic subscore ≤1.

Clinical remission was achieved more frequently in the upadacitinib arm (33.4%) than in the placebo arm (4.1%). Ranked secondary endpoints also demonstrated superiority of upadacitinib over placebo: clinical response (74.5% vs 25.4%), endoscopic improvement (44.0% vs 8.3%). Moreover, the fast-acting agent upadacitinib demonstrated significantly higher clinical remission rates than placebo after 2 weeks already.

Adverse events occurred in 52.9% of the upadacitinib subjects and in 39.5% of the placebo subjects. Serious adverse events were limited (upadacitinib 3.2% vs placebo 4.5%). The most common adverse events in the upadacitinib arm were acne, increased blood creatine phosphokinase, and anaemia. These results are consistent with the known safety profile of upadacitinib.

Dr Séverine Vermeire (University hospital Leuven, Belgium), lead author of the study, concluded by arguing that safety and efficacy data of upadacitinib in this study are in line with the U-ACHIEVE study [2]. U-ACHIEVE is a second phase 3 trial presented at ECCO 2021 investigating the safety and efficacy of 45 mg upadacitinib in moderate-to-severe UC patients.

1. Vermeire S, et al. Efficacy and safety of upadacitinib as induction therapy in patients with moderately to severely active Ulcerative Colitis: Results from phase 3 U-ACCOMPLISH study. OP23, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.
2. Danese S, et al. Efficacy and safety of upadacitinib induction therapy in patients with Moderately to Severely Active Ulcerative Colitis: Results from the phase 3 U-ACHIEVE study. OP24, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

7. Promising safety and pharmacokinetic data on BT051 for UC

BT051, a drug in clinical development for the treatment of ulcerative colitis (UC), was safe and well tolerated in the healthy subject population of a phase 1, randomised, double-blind trial. Moreover, the drug demonstrated very limited systemic exposure. The results support the further development of BT051 as a potential gut-targeted therapy for patients with UC.

BT051 is an oral, non-systemic, multidrug resistance-associated protein 2 (MRP2)/formyl peptide receptor 1 (FRP1) antagonist. The drug targets gut neutrophil activity. To assess the safety, tolerability, and pharmacokinetics of BT051, healthy subjects were enrolled in five BT051 ascending single-dose cohorts (n=40) or placebo (n=10) [1]. The lowest administered dose was 100 mg, the highest dose was 3,500 mg. Participants were followed until 30 days post-dose.

Adverse events (AEs) occurred equally often in the BT051 cohorts and placebo group, with 22.5% and 20% of the subjects, respectively, experiencing at least 1 AE. No serious AEs or study discontinuations due to AEs were reported. In addition, no dose-limiting toxicities were observed for the BT051 cohorts. Moreover, systemic exposure was not quantifiable in most subjects. Only 2 subjects showed 1 quantifiable blood sample each. The mean percentage of BT051 excreted through faeces ranged between 10.2% and 23.7%. This suggests that BT051 is primarily excreted in the faeces. The mean percentage of BT051 excreted in urine was 0.01-0.03%. Importantly, concentrations of BT051 in the large intestine showed limited gut absorption after oral dosing. Immunosuppression through circulating T-cells was not observed for any dose.

1. Stevens C, et al. Safety, tolerability and pharmacokinetics of BT051, an oral inhibitor of neutrophil migration and activation in clinical development for Inflammatory Bowel Disease. P259, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

8. Surgical closure plus anti-TNF outperforms anti-TNF alone for perianal fistula

Anti-TNF treatment plus surgical closure resulted in radiological healing more frequently than anti-TNF treatment alone in Crohn's disease (CD) patients with perianal fistula. In addition, no recurrences were observed in patients with radiological healing. According to the authors of this trial, surgical closure is therefore the superior treatment option in CD patients with perianal fistula.

A patient-preference, randomised controlled trial assessed the radiological healing 18 months after anti-TNF (n=56) or anti-TNF plus surgical closure (n=38) in CD patients with high perianal fistulas with a single internal opening [1]. Radiological healing was defined as a complete fibrotic fistula observed on MRI or a magnetic resonance novel index for fistula imaging in CD (MAGNIFI-CD) score ≤5. Ms Elise Meima-van Praag (Amsterdam University Medical Centre, the Netherlands) presented the findings of the study.

In the intention-to-treat analysis, patients in the surgical closure arm demonstrated a higher rate of radiological healing than patients in the anti-TNF arm (42.1% vs 12.5%; P<0.001). Clinical closure rates were not significantly different between the surgical closure arm (68%) and the anti-TNF arm (52%) in the intention-to-treat analysis. However, in the per-protocol analysis, the difference in clinical closure between the 2 treatment arms was significant, favouring the surgical closure arm. Furthermore, the median Perianal Disease Activity Index (PDAI) scores were significantly lower in the surgical closure arm at 18 months of follow up. The occurrence of re-intervention was not significantly different between the 2 treatment arms (surgical closure 13% vs anti-TNF 29%). Recurrence rates were similar for the 2 treatment arms. Importantly, patients with observed radiological healing did not have recurrences.

1. Meima-van Praag E, et al. Treatment of perianal fistulas in Crohn's disease: anti-TNF with surgical closure versus anti-TNF alone (PISA-II), a patient preference RCT. OP18, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

9. Blood proteins predicting relapse in CD identified

Distinct patterns of blood proteins were related to short-term (e.g. high levels of circulating IL-6 and IL12RB1) and mid/long-term relapse (e.g. low circulating levels of IL-10 and HSD11B1) in Crohn's disease (CD) patients after infliximab withdrawal. These distinct sets of biomarkers showed a higher predictive capacity of relapse than C-reactive protein or faecal calprotectin.

The level of 92 different blood proteins was assessed in CD patients in corticosteroid-free remission stopping infliximab from the STORI cohort (n=102). Patients were divided in short-term relapse (6 months), and non-relapse cohorts. Mr Nicolas Pierre (University of Liège, Belgium) presented the results [1] and updated their recently published study [2].

The risk of short-term relapse was associated with high levels of circulating IL-6 and IL12RB1, two pro-inflammatory effectors. In addition, short-term relapse was linked to both high and low circulating levels of specific proteins involved in immunoregulation. Mid/long-term relapse was related to low circulating levels of IL-10 and HSD11B1, both anti-inflammatory effectors. High levels of proteins involved in lymphocyte tolerance and low levels of cellular junction proteins were also associated with the risk of mid/long-term relapse. Low levels of proteins involved in the downstream signalling of cytokine receptors were associated with short-term relapse. In contrast, high levels of these proteins were related to mid/long-term relapse in this population. The best combination of these blood protein biomarkers could predict relapse more accurately than C-reactive protein or faecal calprotectin. Therefore, these newly identified biomarker candidates have potential to improve CD management in clinical practice.

1. Pierre N, et al. Blood proteins related to immunoregulation or cellular junctions reveal distinct biological profiles associated with the risk of short-term versus mid/long-term relapse in Crohn's Disease patients stopping infliximab. OP12, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.
2. Pierre N, et al. Gut. 2020 Oct 26;gutjnl-2020-322100.

10. Extracellular RNA has potential as a non-invasive biomarker in IBD

In the development of biomarkers for inflammatory bowel disease (IBD), liquid biopsies showed promising results in a Belgian pilot study. The presence of unique extracellular RNAs accurately distinguished Crohn's disease (CD) from ulcerative colitis (UC). Future larger studies should examine the potential of this novel non-invasive tool in-depth.

Liquid biopsies have been studied in oncology as a potential tool for diagnostics and prognostics [1]. Dr Bram Verstockt (University Hospital Leuven, Belgium) and colleagues designed a pilot study to examine the value of extracellular RNA in IBD patients [2].

In the serum of 26 participants, 60,675 unique extracellular RNAs could be identified. Dr Verstockt explained that this is over 75% of all annotated intestinal transcripts specifically expressed in the gut that are known in the literature. Therefore, this method is able to capture essential extracellular RNAs in the serum of IBD patients. In addition, weighted gene co-expression analysis demonstrated that certain clusters of extracellular RNAs were associated with diagnosis of IBD disease type. After running an independent machine learning pipeline, a panel of 8 extracellular RNAs were able to differentiate between CD and UC with an accuracy of 96.2%. Dr Verstockt argued that the functional link with a known genome-wide association study supports the results of this study [3].

1. Happel C, et al. J Cancer Metastasis Treat 2020;6:32.
2. Verstockt B, et al. Extracellular RNAs as liquid biopsy non-invasive biomarker in IBD. OP14, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.
3. Mirkov MU, et al. Lancet Gastroenterol Hepatol 2017;2(3):224-234.

11. No increased risk of (severe) COVID-19 among IBD patients

An Israeli cohort study concluded that patients with inflammatory bowel disease (IBD) are not at increased risk of infection with SARS-CoV-2. In addition, medication that was used for IBD disease activity did not increase the risk of infection. The authors therefore concluded that patients with IBD should be encouraged to continue the prior management of their disease.

To assess the COVID-19 burden among IBD patients in 2020, a questionnaire was provided to members of the Israel Crohn's Disease and Ulcerative Colitis Foundation between November 2020 and January 2021. A total of 2,152 IBD patients completed the questionnaire (median age 39 years; 60.5% female). Dr Vered Richter (Tel Aviv University, Israel) presented the results of the study [1].

The incidence of SARS-CoV-2 infections among IBD patients (4.8%) was significantly lower than the infection rate in the general Israeli population (P=0.033). Logistic regression analysis demonstrated that a younger age, an elevated BMI, and diabetes were associated with an increased risk of SARS-CoV-2 infection among IBD patients. In contrast, treatment with 5-aminosalicylic acid or other IBD therapies were significantly associated with a decreased risk of SARS-CoV-2 infection. Smoking and hypertension also showed a protective effect against SARS-CoV-2 infections. Dr Richter argued that the protective effect of smoking has been discussed in the literature and that anti-hypertensive medications could explain the link between hypertension and a reduced risk of SARS-CoV-2 infection in this population. IBD disease severity was not associated with an increased risk of SARS-CoV-2 infection.

Severe COVID-19 was limited among these patients; only 3.8% was hospitalised. Furthermore, this study showed that corticosteroids and immunomodulators were not related to COVID-19 severity in this population. According to Dr Richter, this is in contrast with the existing evidence.

1. Richter V, et al. Effect of Inflammatory Bowel Disease and Related Medications on COVID-19 Incidence, Disease Severity, and Outcome - The Israeli Experience. DOP77, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

12. Artificial intelligence outperforms human classifying of endoscopic images in UC

A deep learning model exceeded human evaluation of classifying endoscopic images in patients with ulcerative colitis (UC). This result shows that artificial intelligence has potential to optimise and standardise the assessment of disease activity in this population. Moreover, the study demonstrated that artificial intelligence surpassed human evaluation with a limited number of images.

Mayo endoscopic subscores (MES) are used to identify disease activity in patients with UC. However, observer variance up to 75% has been reported. Dr Bobby Lo (Hvidovre Hospital, Denmark) and colleagues aimed to develop a deep learning model that is able to distinguish between the 4 MES scores [1].

Initially, 1,484 endoscopic images from 467 UC patients were scored independently by 2 experts. Subsequently, 85% of the images was used as a training set for the machine learning process. The other 15% was used as a test set. The developed deep learning model outperformed human evaluation of the endoscopic images, distinguishing between all MES scores with an accuracy of 84% for the test set, with a sensitivity of 88% and a specificity of 81%. In addition, the deep learning model demonstrated excellent results of distinguishing between inactive to mild (MES 0-1) and moderate to severe (MES 2-3) disease. On the other hand, the weighted kappa value between the 2 expert assessors was 0.66.

Dr Lo mentioned that the model is currently launched for local usage and that the model is under evaluation as a training tool for inexperienced physicians.

1. Lo B, et al. Artificial intelligence surpasses gastrointestinal experts in the classification of endoscopic severity among Ulcerative Colitis. OP07, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

13. Oral faecal microbiota transplant therapy efficacious in UC

Patients with ulcerative colitis (UC) who received oral administration of faecal microbiota transplant (FMT) therapy after antibiotic treatment had higher clinical remission rates and endoscopic remission/response rates, compared with patients who received antibiotic treatment alone. Clinical and endoscopic remission were preserved during FMT maintenance therapy.

FMT therapy has demonstrated patient benefits for inflammatory bowel disease (IBD) [1]. In the double-blind, randomised controlled LOTUS trial (ACTRN12619000611123), Dr Craig Haifer (University of Sydney, Australia) and colleagues investigated the effects of orally administered FMT therapy after a pre-treatment of antibiotics (n=15) versus treatment with antibiotics alone (n=20) in patients with mild-to-moderate UC [2]. Subsequently, FMT responder were re-randomised to FMT maintenance therapy (n=4) or FMT withdrawal (n=6). The primary endpoint was steroid-free clinical remission and endoscopic remission/response at week 8 and week 56 for induction therapy and maintenance therapy respectively.

The primary endpoint was met for 54% of the patients in the FMT arm versus 15% of the patients in the placebo arm. Clinical remission rates were 73% for patients receiving FMT therapy and 25% for patients receiving placebo. All patients enrolled in the maintenance FMT therapy showed clinical and endoscopic remission at week 56, whereas all patients randomised to FMT withdrawal experienced disease flare. In addition, IBD questionnaire scores demonstrated a reduced quality of life for patients in the withdrawal arm compared with patients in the maintenance arm.

Adverse events occurred in 47% of the patients in the FMT arm and in 90% of the patients in the placebo arm. There were 2 cases of severe adverse events in both arms of the trial. Dr Haifer concluded that FMT therapy was well tolerated and feasible in this population. Furthermore, he argued that the potential enhanced efficacy of FMT therapy due to pre-treatment with antibiotics should be investigated in-depth.

1. Paramsothy S, et al. J Crohns Colitis 2017;11(10):1180-1199.
2. Haifer C, et al. Lyophilised Orally administered FMT therapy in Ulcerative colitis (LOTUS) study. OP30, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

14. Increased risk of rectal cancer after colectomy in IBD

The risk of rectal cancer was 8 times higher in patients with a diverted rectum after subtotal colectomy, as compared with inflammatory bowel disease (IBD) patients without a history of subtotal colectomy. This result implies that this subgroup of patients needs a specific strategy monitoring rectal cancer.

The cumulative risk of subtotal colectomy with ileostomy and diverted rectum is ~7.5% after 5 years. The current, nationwide Danish, population-based cohort study compared the risk of rectal cancer in IBD patients with a diverted rectum following subtotal colectomy with IBD patients without surgery [1]. In addition, the results were compared with a matched background population.

Rectal cancer occurred in 42 of 4,931 IBD patients (0.9%) with a diverted rectum after subtotal colectomy. In IBD patients without colectomy, 209 of 49,251 (0.4%) received a diagnosis of rectal cancer. The background population demonstrated a similar ratio of rectal cancer (941 of 246,550 participants, 0.4%). After adjusting for IBD type and sex, the results showed that IBD patients with a diverted rectum had an increased risk of rectal cancer 10 years after surgery compared with IBD patients without colectomy (HR 7.93; 95% CI 5.48-11.48; P<0.0001). Similarly, 10 years after colectomy, IBD patients with a diverted rectum were more at risk of rectal cancer than the matched background population (HR 10.25; 95% CI 7.36-14.28; P<0.0001).

1. Akimenko E, et al. Rectal cancer risk 10 years after colectomy in patients with inflammatory bowel disease: a population-based Danish cohort study 1978-2018. P090, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

15. Risk of colorectal cancer is detected by low-pass whole genome sequencing

Low-pass whole genome sequencing was able to stratify the risk of colorectal cancer in patients with inflammatory bowel disease (IBD) undergoing endoscopic surveillance. This result indicates that patients at risk could be selected early, by detecting cancer-related DNA changes prior to neoplastic formation. Moreover, this novel technique is robust and cost-effective.

A retrospective case control study (n=119) compared left-sided biopsies from surveillance colonoscopies of IBD patients who progressed to cancer 1-5 years later with matched controls by means of low-pass whole genome sequencing [1]. This technique

is able to detect chromosomal copy number alterations (CNAs), which are associated with colorectal carcinogenesis. All evaluated biopsies were free of dysplasia or colorectal cancer. Dr Ibrahim Al Bakir (Queen Mary University of London, UK) presented the findings of the study.

Both cases (81.8%) and controls (76.2%) showed CNAs in at least 1 of the 4 biopsies that were assessed. However, case biopsies had significantly higher proportions of genome-bearing CNAs, a greater number of CNAs, and a greater mean size of CNAs, compared with control subjects. In addition, larger reductions of CNAs were almost exclusively observed in cases (P<0.05). The risk prediction of dysplasia or colorectal cancer by detection of large CNA reductions in any biopsy was analysed by Kaplan-Meier and ROC analysis. The results demonstrated a specificity of 96% and a sensitivity of 26%, with an accuracy of 73%.

Dr Al Bakir argued that low-pass whole genome sequencing is mostly feasible for high-risk patients, due to the high specificity and low sensitivity of the technique. However, fine-tuning of the technique could improve its accuracy. For example, the current study found that CNAs occur more frequently in the rectum than in the sigmoid colon or descending colon (P<0.001). Dr Al Bakir therefore mentioned that it could be interesting to evaluate rectum biopsies only in future studies.

1. Al Bakir I, et al. Developing a Cost-Effective Genomic Biomarker of Cancer Risk in Patients with Ulcerative Colitis using Low-Pass Whole Genome Sequencing of Unselected Endoscopic Biopsies: A Case-Control Study. OP38, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

16. Large variability in IBD care and education across Europe

High- and low-income countries across Europe demonstrate clear differences in inflammatory bowel disease (IBD) care and education. Physicians in high-income countries have a better access to IBD medicine. Moreover, these physicians have been exposed to specialised training for IBD care more frequently than physicians in low-income countries. In order to improve and standardise IBD care and education across Europe, these inequalities need to be addressed.

Dr Jan Král (Institute for Clinical and Experimental Medicine, Czech Republic) and colleagues investigated the differences in IBD care and education across Europe [1]. An online survey examining IBD education, IBD clinical care, and demographics was distributed across 39 European countries. In total, 1,268 participants responded. Results were compared between high- and low-income countries, based on GDP per capita.

Physicians from high-income countries reported a better access to IBD-specific training than their colleagues from low-income countries (56.4% vs 38.5% positive responses, respectively; P<0.001). Nonetheless, most physicians feel comfortable in treating IBD patients (77.2% vs 72.0%; P=0.04). More dedicated IBD units are available in high-income countries (58.5% vs 39.7%; P<0.001), and physicians in high-income countries organise more multidisciplinary meetings. In the current era, physicians in high-income countries are more inclined to make use of telemedicine. Furthermore, physicians in high-income countries have a better access to most IBD medications, especially biologics.

1. Král J, et al. Large differences in IBD care and education across Europe, first results of the pan-European VIPER study. DOP37, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

17. Ultra-processed food intake associated with IBD

A higher intake of processed food was found to increase the risk of inflammatory bowel disease (IBD). This result is consistent within the different categories of processed food that were assessed in a large international cohort study. Future studies are needed to assess which components in processed food lead to an increased risk of IBD.

Certain food additives, such as emulsifiers and detergents, have been associated with IBD [1]. The current prospective, observational cohort study (2003-2016) investigated the link between food intake and incident IBD in 116,037 participants from 21 countries [2]. At baseline, habitual food intake was assessed through food frequency questionnaires (FFQ's). The diagnosis of IBD was determined per self-report. Dr Neeraj Narula (McMaster University, UK) presented the findings of the study.

A multivariate Cox proportional hazard model revealed that the number of processed food servings per day was associated with the occurrence of incident IBD in this cohort. Participants with an intake of ≥5 servings per day had a higher risk of IBD than participants with an intake of <1 serving per day (HR 1.82; P=0.0063). This result was more pronounced in incident Crohn's disease (HR 4.50) than in incident ulcerative colitis (HR 1.46). The risk of incident IBD was increased for all 4 categories of highly processed food that were analysed in this study: processed meat intake, soft drink intake, the intake of sweets, and salty food and snacks.

1. Swidsinski A, et al. Inflamm Bowel Dis 2009;15(3):359-64
2. Narula N, et al. Association of Processed Food Intake with Risk of Inflammatory Bowel Disease: Results from the Prospective Urban Rural Epidemiology (PURE) study. OP05, ECCO 2021 Virtual Congress, 2-3 & 8-10 July.

18. Factors of coping difficulties in IBD revealed

Female gender, a higher disease activity, a deficient understanding of the disease, a reduced sense of control over the disease, and an increased perception of disease stigma were all related to coping difficulties in inflammatory bowel disease (IBD). The identification of these factors provides a starting point for the development of targeted psychological interventions. In this way, the results of this study could help to improve the psychological wellbeing of IBD patients.

A cross-sectional study, using data from a large national survey performed by Crohn's and Colitis UK, was conducted to investigate factors associated with coping in IBD patients (n=802, mean age 45.5 years) [1]. Ordinal regression analysis was performed to examine the data.

The multivariable analysis showed that females were at higher risk of reporting coping difficulties than males (OR 1.60). A higher disease activity (OR 2.64) and increased perceptions of disease-related stigma (OR 2.12) were also associated with coping difficulties in this population. A better understanding of the disease (OR 0.81) and a higher level of perceived control over the disease (OR 0.68) were related to fewer difficulties with coping.

The authors argued that interventions targeting the improvement of the psychological wellbeing of IBD patients should address the adjustable factors revealed in this study, such as illness perceptions, and sense of control over the disease. In addition, public awareness on IBD-related stigma should be raised to counter the impact of this factor on patients' psychological wellbeing. Furthermore, clinicians should take into account that females with a high disease activity are particularly at risk of experiencing difficulties in coping with their disease.

1. Marshall J, et al. Coping in Inflammatory Bowel Disease: insights from a national survey. P105, ECCO 2021 Virtual Congress, 2-3 & 8-10 July