Congress Review

Review of the 17th Congress of the European Crohn's and Colitis Organisation (ECCO)

DIVING into the virtual programme available at the 17th Congress of the European Crohn's and Colitis Organisation (ECCO) saw attendees share in the latest updates to the field of gastroenterology. Aiming to 'navigate the oceans of IBD', this shaped the various informative sessions, stretching from the depths of developing environmental recipes for inflammatory bowel disease (IBD) to future applications of telemedicine in this area.

Hosted in the Austrian capital, Vienna provided a virtual experience this time around. Instead of negotiating the historic streets of the city to attend sessions, delegates were able to access the ECCO booth and interact with congress material online. Across the 4-day event, 5,901 attendees observed the scientific programme presented at ECCO'22, voyaging 17 virtual booths to witness major breakthroughs, highlights, and trends in the field of IBD. With engagement from 105 different countries, this international gathering of leading experts consisted of 12 different academic sessions and 31 talks. The scientific programme boasted 865 abstracts, with 90 of these presented orally, in addition to several satellite symposia and 735 exhibited e-posters.

In his welcome, Laurent Peyrin-Biroulet, ECCO President, spotlighted a short list of sessions to watch out for, including a lecture delivered by Séverine Vermeire, KU Leuven, Belgium, on 'A European IBD voyage'. Other noteworthy sessions he mentioned included 'From basic science to practical approach' and 'Aiming high with treatment goals in IBD: the modern Icarus?' All these sessions remain accessible, temporarily, on the congress portal, alongside presentations on minimising malignancy risks, which highlighted interesting clinical cases and modern monitoring methods related to managing IBD in clinical practice.

As is custom at each congress, ECCO recognised the outstanding contributions made by numerous individuals; these awards highlight the global diversity that was integral to the material shared at ECCO'22. ECCO Grants, acknowledging the promotion of innovative scientific research in IBD in Europe, were awarded to Silvia Cerantola and Ferdinando D'Amico

of Italy; Celia Escudero-Hernández in Germany; Danish Urs Mörbe; Joep van Oostrom and Elsa van Wassenaer from the Netherlands; Margarita Papatheodoridi from the UK; and Australian Robert Venning Bryant. ECCO Fellowships for promoting innovative scientific research and knowledge exchange in IBD in Europe were awarded to Vittoria Bellato of Italy and Sulak Anandabaskaran from Australia. ECCO Pioneer Awards, which are awarded to congratulate visionary interdisciplinary research projects in the field of IBD, were presented to the partnerships of Salomé Pinho and Harry Sokol, of Portugal and France, respectively, as well as Annemarie de

Vries and Alison Simmons, from the Netherlands and the UK. Finally, Swiss Marianne Spalinger and Raja Atreya of Germany shared the ECCO Multi-Year Research Grant. These researchers and clinicians received their prestigious awards alongside many others to congratulate their significant work as leading gastroenterologists.

Where ECCO'22 allowed attendees to 'navigate the oceans of IBD', the 18th Congress of ECCO will encourage participants to journey north to Copenhagen, Denmark, in March 2023, where preparations for the next annual meeting have already begun. ∎

ECCO 2022 REVIEWED →

Long-Term Outcomes for Patients with Very Early Onset Inflammatory Bowel Disease

NFLAMMATORY bowel disease (IBD) is characterised by chronic inflammation of the gastrointestinal tract and is estimated to affect nearly 80,000 children in the USA alone. Very early onset IBD (VEOIBD) occurs when a patient receives an IBD diagnosis before they are 6 years old; if the patient is <2 years old, the condition is diagnosed as infantile IBD. Recently, a longitudinal, multicentre, retrospective cohort study of patients with VEOIBD was conducted using data from 21 international paediatric centres to determine the long-term outcomes for these populations, with findings shared at ECCO'22. The patients with VEOIBD included in the study were diagnosed between the years 2008 and 2018, with at least 2 years of follow-up.

The cohort was made up of 243 patients (52% male), 69 (28%) of which were diagnosed before the age of 2 years old. The median age at diagnosis was 3.3 years, with a median follow-up of 5.8 years. Of this population, IBD was classified as either Crohn's disease, ulcerative colitis, or IBD-unclassified in 30%, 59%, and 11% of patients, respectively. Within the population of patients with ulcerative colitis or IBDU, 75% presented with pancolitis, whereas in the cohort of patients with Crohn's disease, 62% presented with isolated colonic disease, 32% with ileocolonic disease, and 19% with perianal involvement. Genetic testing was performed in 96 (40%) patients, identifying a monogenic diagnosis in 23% of cases, mutations of the IL-10 receptor in 5 cases (23%), and structuring or penetrating diseases in 9 cases (4%).

First induction therapies used in the study were corticosteroids, 5-aminosalicylic acid, and nutritional therapy, which were utilised in 53%, 30%, and 11% of patients, respectively. Corticosteroids were used more commonly to treat patients with infantile rather than non-infantile IBD (64% versus 49%), and no significant differences between age groups were observed with the use of maintenance therapies.

Patients with infantile IBD presented with higher rates of IBD-unclassified, lower levels of haemoglobin and albumin, higher levels of C-reactive protein, lower weight z-scores, lower rates of response to first induction therapy, and a shorter time to hospitalisation during follow-up when compared with patients who were diagnosed after 2 years of age. A colectomy was performed in 11% of patients and diversion surgery in 4% of patients, with no significant differences observed between age groups. Furthermore, no malignancies or deaths were observed in the cohort, and 85% of patients were in corticosteroid-free clinical remission at the end of follow-up.

Overall, although patients with infantile IBD were observed as having more severe clinical features at presentation and a lower response to induction therapy than patients who were 2–6 years of age, it was found that all patients with VEOIBD had a fair long-term outcome with low rates of complications and surgical interventions. Moving forward, further steps could include replicating this study on a larger scale to confirm long-term clinical outcomes. ∎

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Inflammatory Bowel Diseases Activity Is Not Linked with Severity of COVID-19 Outcomes

POPULATION-based study carried out in Denmark, presented at ECCO'22, stated that there is no link between the disease activity of inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD) and COVID-19 severity and long-term outcomes. The severity of COVID-19 in this study was defined as requiring admission to an intensive care unit, ventilation requirement, or death. Long-term COVID-19 outcome was defined as COVID-19 infection hospitalisation.

UC disease was measured by a clinical colitis, while CD was measured by the Harvey–Bradshaw Index (HBI). Other IBD measures such as biochemical and endoscopic activity of UC and CD were also considered. Either C-reactive protein >5 mg/L or faecal calprotectin >250 µg/g were used to determine the biochemical activity of CD and UC. Additionally, a Mayo Endoscopic Subscore (MES) of ≥2 defined the endoscopic activity of UC, while a Simple Endoscopic Score (SES) of ≥3 was used for CD.

The aim of the study was to understand whether the disease activity of UC and CD is correlated with the severity of COVID-19. The researchers utilised a Danish IBD database that collates and records the course of disease in patients with UC and CD and who have confirmed COVID-19. The inclusion period of the study was between 28th January 2020 and 1st April 2021, with 319 patients diagnosed with UC and 197 patients with CD. All the patients included in the study had positive confirmation of COVID-19 and results showed that the patients with UC had clinical activity: 83.1%; biochemical activity: 100.0%; and endoscopic activity: 20.7%. Patients with CD had clinical activity: 71.1%; biochemical activity: 66.5%; and endoscopic activity: 21.3%. In this population-based study it was concluded that the clinical, biochemical, and endoscopic activity in both CD and UC were not associated with adverse or severe COVID-19 or the long-term outcomes. ∎
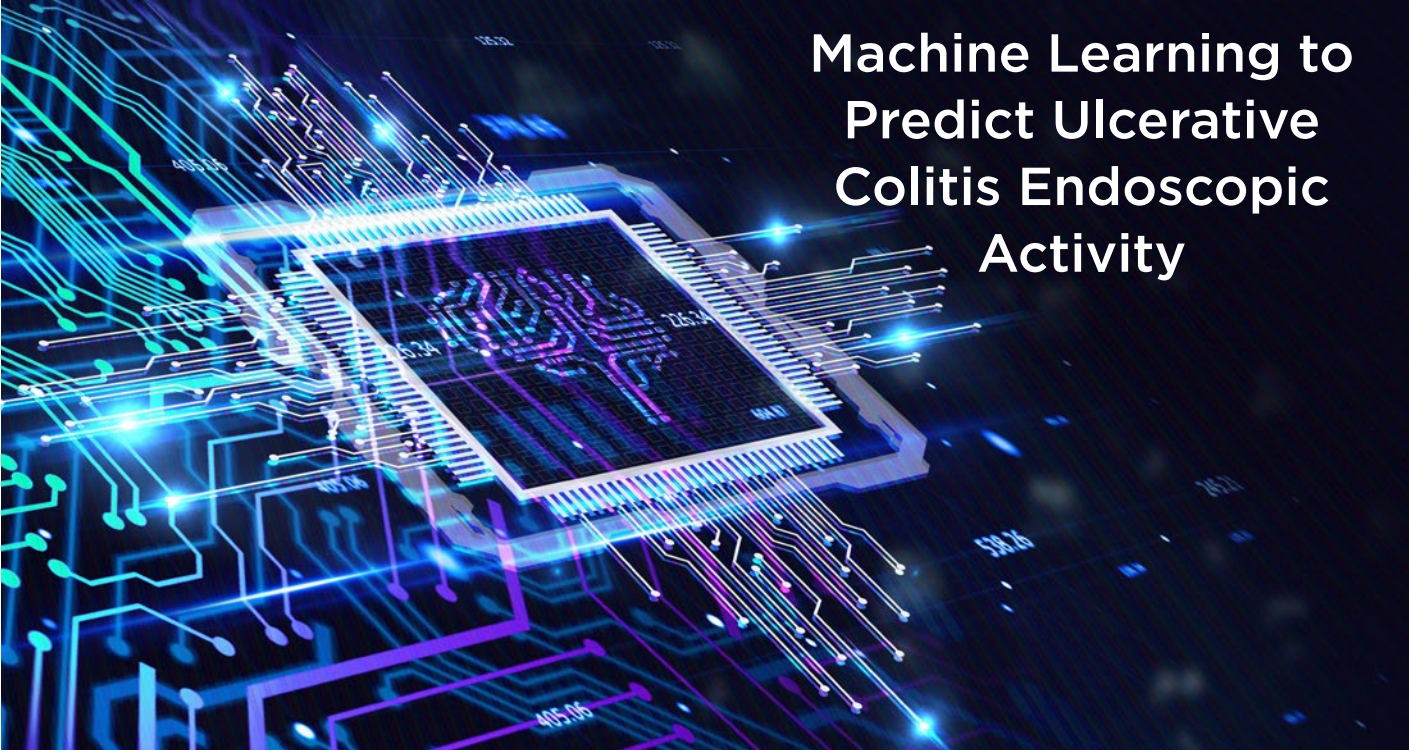
The Role of Adherent and Invasive *E. Coli* in Crohn's Disease

A STUDY presented at ECCO'22 supported the role of adherent and invasive *Escherichia coli* (AIEC) as a predictive factor in the re-occurrence ileal Crohn's disease (CD). The researchers used a post-operative recurrence model from the REMIND multicentre prospective cohort of patients with CD who had undergone an ileocolonic resection to examine rates of AIEC.

Surgical specimens were used to identify AIEC in 181 patients following the operation, whilst a colonoscopy of the neo-terminal ileum was carried out at 6 months in 119 of the 181 patients. The Rutgeerts' score, an endoscopic scoring system, was used to predict endoscopic post-operative disease recurrence, with a score ≥i2b classed as post-operative endoscopic recurrence or ≥i3 as severe recurrence. Additionally, the reappearance of the initial ileal lesions was classed as i1, from a pathophysiological point of view, and more progressive post-operative ileal recurrence was i2b+i3. Furthermore, the relative risks and/or odds ratios were modified based on potential confounding factors such as gender, smoking history, duration and phenotype of CD, preventative treatment, antibiotics, and prior bowel resection.

Of the 181 patients included in the study, 46.3% had not received any preventative treatment for endoscopic post-operative recurrence; however, 24.3% of the 181 study participants had been treated with an anti-TNF for preventative measures. According to the results, AIEC was two-fold more common in the neo-terminal ileum at Month 6 compared with the initial surgical specimen: 30.3% versus 14.9%, respectively (p<0.001). Data from this study also demonstrated that AIEC colonisation was linked to a specific microbiota signature including higher levels of Ruminococcus gnavus. Based on the post-operative recurrence model, the data from this study supported the discovery of AIEC within the surgical specimen was a predictive factor recurrence of ileal CD. ∎

Machine Learning to Predict Ulcerative Colitis Endoscopic Activity

> *"this machine learning approach to endoscopic evaluation could be used as an alternative to human central reading when conducting future clinical trials."*

MACHINE learning algorithms have been described to predict how human readers would evaluate disease activity in ulcerative colitis using the endoscopic Mayo score (eMS). Advancing this field of research further, Jean-Frederic Colombel, Icahn School of Medicine at Mount Sinai, New York City, USA, and collaborators have now developed a machine learning predictive model that is trained on eMS features using centrally read endoscopies. The results were shared in an award-winning abstract presented at ECCO'22.

In total, Colombel et al. obtained 793 full-length videos from approximately 250 patients enrolled in a Phase II study that investigated mirikizumab for moderate-to-severe ulcerative colitis. Notably, these participants had a centrally read eMS. The machine learning workflow involved annotation, segmentation, and classification. A test set of 147 videos and a consensus set of 94 videos were used to assess the model.

Regarding the primary objective, the machine learning model was shown to categorically predict inactive disease versus active disease with an accuracy, positive predictive value (PPV), and negative predictive value (NPV) of 84%, 80%, and 85%, respectively, in the test set. Moreover, in the consensus set, the model predicted inactive disease compared with active disease with an accuracy, PPV, and NPV of 89%, 87%, and 90%, respectively.

For the secondary objectives, it was revealed that, in the full test set, the model predicted endoscopic healing with an accuracy, PPV, and NPV of 90%, 44%, and 95%, respectively. In this same set, the model predicted severe disease with an accuracy of 80%, a PPV of 86%, and a NPV of 86%. In the consensus set, the model predicted endoscopic healing with an accuracy of 95%, a PPV of 86%, and an NPV of 95%. Additionally, severe disease was predicted with an accuracy, PPV, and NPV of 85%, 82%, and 87%, respectively.

Based on these results, it has been proposed that this machine learning approach to endoscopic evaluation could be used as an alternative to human central reading when conducting future clinical trials. ∎

Targeting Hedgehog Signalling Pathway to Treat Inflammatory Bowel Disease

"inhibiting the hedgehog signalling pathway with the small inhibitor vismodegib or genetic ablation of Ihh led to a significant decrease in clinical disease severity and decrease in IL-17a+ Th17 cells."

NFLAMMATORY bowel disease (IBD) affects approximately 1 in 210 people in the UK. The aetiology is poorly understood and there is no cure. Therefore, understanding what is occurring at a cellular level could be useful in discovering novel therapeutic drug targets for IBD. Hedgehog signalling has an important role in tumorigenesis, development, and tissue homeostasis and is targetable using approved small molecule inhibitors. Presenters from the University of Cambridge, UK, among other institutions, worked together to understand the role of hedgehog signalling in Th17 differentiation in an award-winning abstract and original study shared at ECCO'22.

Th17 cells play a vital role in protecting the gastrointestinal tract but are also key pathological drivers of IBD. In this study, researchers analysed the signalling pathways that regulate the differentiation of Th17. Firstly, the team created two knock-out mouse models that targeted Indian hedgehog (Ihh) and its receptor smoothened in the hedgehog signalling pathway. Using techniques such as flow cytometry and gene expression analysis, they were able to study Th17 differentiation. Other methods conducted by the researchers included *in vivo* studies such as T cell adoptive transfer colitis using knockout T cells or controls, histological analysis, colon length, and weight measurements. Bioinformatic analyses of gene expression data of human rectal biopsies was also carried out to reinforce the translational relevance of the findings from mouse models.

Results showed that hedgehog signalling, in the absence of Ihh, selectively drives differentiation of Th17 cells. Further to this, the speakers were able to show that inhibiting the hedgehog signalling pathway with the small inhibitor vismodegib or genetic ablation of Ihh led to a significant decrease in clinical disease severity and decrease in IL-17a+ Th17 cells. This study opens doors for scientists to investigate small molecules to inhibit the hedgehog pathway and consequently Th17 differentiation, which can drive the pathology of IBD. Next steps could include conducting a larger study in humans and testing approved small inhibitors of the hedgehog signalling pathway to treat IBD. ∎

Corticosteroid-Free Remission in Patients with Ulcerative Colitis

JAK inhibitor upadacitinib (UPA) has proven effective in corticosteroid (CS)-free remission in patients with moderate-to-severe active ulcerative colitis in a Phase II clinical programme. Presented at ECCO'22, this programme comprised of two induction trials and the U-ACHIEVE maintenance study.

Patients were randomised 2:1, using UPA 45 mg once daily (QD) or placebo for 8 weeks. After the initial 8 weeks, patients who achieved clinical response were randomised again 1:1:1, receiving UPA 15 mg QD, UPA 30 mg QD, or placebo for 52 weeks. Despite the CS use among patients, disease characteristics of the participants were well balanced.

Results indicate that clinical remission for patients receiving UPA 45 mg did not differ from the use of baseline CS. In fact, treatment-emergent adverse events increased in the group taking UPA 45 mg plus baseline CS, including the risk for serious and opportunistic infections, compared with the placebo and UPA without baseline CS groups. However, CS-free remission (defined by the Adapted Mayo Score as being CS-free for ≥90 days) was significantly increased with UPA 30 mg QD and UPA 15 mg QD, compared with placebo ($p<0.001$).

Rates of adverse events as a result of treatment with UPA with baseline CS versus UPA without baseline CS were 33% versus 39% and 27% versus 35% for UPA 30 mg and UPA 15 mg groups, respectively. Adverse events such as malignancy and major adverse cardiovascular events were not frequently reported by patients receiving UPA.

This clinical programme indicates that UPA is superior to placebo in conferring CS-free remission in patients with moderate-to-severe active ulcerative colitis, while baseline CS use did not have any efficacy benefit. Therefore, disease control with UPA without CS use is an optimal treatment strategy. ∎

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Online Training Platform to Improve Dysplasia Detection in Inflammatory Bowel Disease

"training using the new OPTIC-IBD learning platform improved the confidence of endoscopists to accurately diagnose dysplasia despite their previous experience."

PATIENTS with inflammatory bowel disease (IBD) are at a significantly greater risk of developing colorectal cancer. To treat patients with IBD timely and effectively, healthcare professionals conduct endoscopy to detect dysplasia. This technique helps doctors characterise legions accurately; however, the speakers of the prize-winning abstract shared at ECCO'22 discussed how there was a gap in training, particularly in ability to recognise and accurately diagnose dysplastic lesions in IBD. In their presentation, the speakers discussed how they created an online training platform called OPTIC-IBD to help overcome this issue for healthcare professionals old and new.

The team created an online multi-modality learning module, which included key aspects of detecting dysplasia in IBD from surveillance principles to classifications, examples, and optical diagnosis methods. Researchers conducted a study to test the efficacy of their new interactive training platform by recruiting 77 participants from Canada, Italy, and the UK. Participants included a mix of intermediate and experienced endoscopists who completed training that included 24 endoscopic videos of IBD colonic lesions. All those taking part in the study had to classify lesions, predict histology, provide feedback, and rate their confidence. Finally, participants were randomised to receive feedback and extra training in a 1:1 ratio and had a final assessment at 60 days.

Impressively, the online learning platform had positive results and diagnostic accuracy was improved largely for new and intermediate endoscopists. Moreover, experienced endoscopists also benefitted from using OPTIC-IBD as sensitivity for dysplasia increased from 50.3% to 59.1%. Most importantly, the speakers had succeeded in executing the aim of their learning platform as specificity and accuracy for diagnosing dysplasia was the most improved outcomes from 44.9% to 70.3% and 55.0% to 64.6%, respectively.

Optical online training using the new OPTIC-IBD learning platform improved the confidence of endoscopists to accurately diagnose dysplasia despite their previous experience. Future work for the team will include studying the training approaches to improve the platform and make it available to endoscopists treating patients with IBD. ∎

Novel Study Compares Effectiveness of Vedolizumab Versus Ustekinumab in Crohn's Disease

> *"a significant number of patients with CD following anti-TNF failure were able to maintain ustekinumab or vedolizumab on a medium–long-term basis"*

PATIENTS with Crohn's disease (CD) can maintain ustekinumab or vedolizumab in medium-to-long-term clinical practice after failure or intolerance of anti-TNF therapy, said a comparative study presented at ECCO'22. The aim of this study was to compare the retention rate, short- and long-term efficacy, and the safety of both treatments following anti-TNF failure.

A total of 755 patients with CD from the ENEIDA registry from 30 centres, following failure or intolerance of anti-TNF agents and who had received either vedolizumab or ustekinumab as an alternative, were included in the study. Clinical activity, both in short- and long-term duration, was classified based on Harvey–Bradshaw Index (HBI). The predictive factors for effectiveness and durability of both treatments were analysed by Kaplan–Meier curves, Cox regression models, inverse probability weighting, and propensity matching score. There were 195 patients in the vedolizumab cohort and 560 patients in the ustekinumab cohort.

Following a 20-month follow-up, the survival rate for vedolizumab therapy was lower than ustekinumab. Additionally, the clinical response, steroid-free remission, and short-term clinical remission proportion of patients was greater in the ustekinumab cohort compared with the vedolizumab cohort. Following a 2-year period after starting both treatments, significant differences were discovered in both cohorts. Vedolizumab and ustekinumab were discontinued due to primary non-response in 142 patients (52%) and 185 patients (58%), respectively. Adverse events were observed in 12% of patients, mainly infections and skin lesions; however, this was not distinguishable in either treatment. The results concluded that in clinical practice, a significant number of patients with CD following anti-TNF failure were able to maintain ustekinumab or vedolizumab on a medium–long-term basis; however ustekinumab had a higher retention rate in these patients compared to vedolizumab. ∎

Using Monoclonal Antibody Clearance to Predict Treatment Response in Inflammatory Bowel Disease

PREDICTING treatment outcomes in patients with inflammatory bowel disease is a long-term goal for clinicians. A recent study presented at ECCO'22 investigated the benefits of monitoring monoclonal antibody clearance in patients with Crohn's disease (CD). Using data from clinical trials, the researchers investigated two monoclonal antibodies: infliximab and ustekinumab.

The study recruited patients with moderate-to-severe CD who were treated with either infliximab (n=108) or ustekinumab (n=80). Disease was assessed at Week 12 and 24 by endoscopic remission, which was judged to be a CD Endoscopic Index Score of <3, and endoscopic response, ≥50% decrease from baseline in simple endoscopic score for CD. Predictions were made using previously built pharmacokinetic models, with faecal calprotectin, albumin, CD activity index, and antibodies towards infliximab all used to estimate infliximab clearance. Albumin and body weight were used to estimate ustekinumab clearance.

Researchers found that patients with endoscopic remission at Week 12 had lower infliximab clearance and higher infliximab serum concentration at both Week 2 and 6 of treatment. Most patients with early clearance of infliximab did not reach endoscopic endpoint. Contrastingly, the serum concentrations at Week 4 and 8 of ustekinumab treatment were similar between patients with and without endoscopic response.

The research concluded that lower infliximab and ustekinumab clearance predicted more favourable endoscopic outcomes. In patients treated with ustekinumab, the researchers further concluded that clearance monitoring may better predict endoscopic response than standard therapeutic drug monitoring. ∎
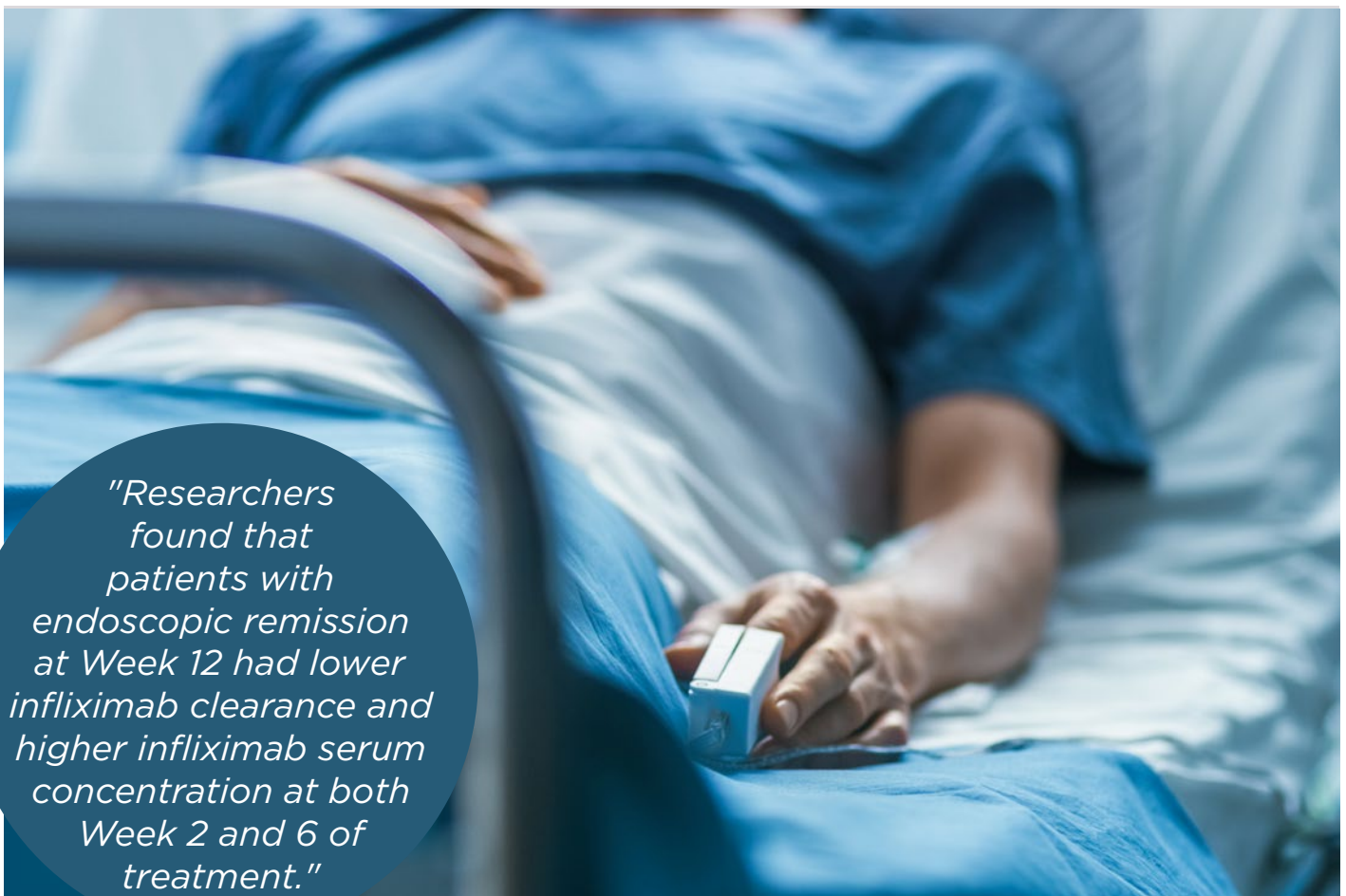
"Researchers found that patients with endoscopic remission at Week 12 had lower infliximab clearance and higher infliximab serum concentration at both Week 2 and 6 of treatment."

Contributing Factors for Chronic Abdominal Pain in Inflammatory Bowel Disease

CHRONIC abdominal pain is a common symptom in patients with inflammatory bowel disease (IBD), yet the aetiology is not well understood. Scientists believe an altered gut–brain interaction as well as persistent histologic inflammation contribute to chronic abdominal pain in IBD. In an award-winning abstract presented at ECCO'22, scientists aimed to identify lifestyle, psychosocial, and clinical factors in patients with IBD with abdominal pain to fill in gaps in the research in IBD aetiology.

Researchers conducted a multicentre study involving a real-world cohort of patients with IBD in remission between January 2020 and July 2021. Patients used 'myIBDcoach', a patient-centred app for smartphones, which monitors IBD, quality of life, and symptoms of anxiety and depression. The study monitored these outcome measures in 3-month intervals in a total of 559 patients, 76.7% of whom were in remission. Additionally, the researchers assessed chronic abdominal pain in

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patients with IBD in remission, characterised by an abdominal pain score of ≥3.

Results showed that 46.4% of those patients in remission had a pain score that met the criteria for chronic abdominal pain. Patients with IBD in remission with chronic abdominal pain had significantly greater levels of stress, fatigue, depression, difficult life events, and anxiety compared to patients in remission without chronic abdominal pain. Using a multivariable logistic regression, the research team were able to link clinical and psychosocial factors with the presence of chronical abdominal pain in patients with IBD in remission.

The authors shared their concluding remarks stating that quality-of-life, fatigue, anxiety, and psychosocial factors could contribute to the presence of abdominal pain in IBD in patients in remission and that this association could be exacerbating the abdominal pain via perceived levels of stress. ∎