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PEER-REVIEWED CONFERENCE REPORT

SEQUENCE: Risankizumab doubles remission compared with ustekinumab in CD

Among 10 trial outcomes in IBD in this report, SEQUENCE revealed that risankizumab outperformed ustekinumab in achieving endoscopic remission in participants with Crohn's disease.

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Cold snare resection safer for removal of large polyps

Cold snare endoscopic mucosal resection exhibited a lower intra-procedural bleeding rate during removal of large colorectal polyps, according to the CHRONICLE prospective, multicentre, randomised trial.

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Apraglutide benefits short bowel syndrome

The long-acting GLP-2 analogue apraglutide markedly decreased parenteral support volume needs for patients with short bowel syndrome with intestinal failure and colon-in-continuity at 52 weeks.

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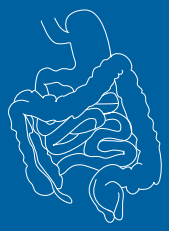

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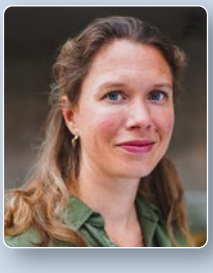
Letter from the Editor



Dear esteemed readers,

It is with great pleasure and pride that I present the Conference Report on UEG Week 2023, held from October 14 to October 17. This year's event saw an unprecedented level of international engagement, with a staggering 11,200 individuals from over 120 countries participating. The enthusiasm and dedication of the global medical community were truly commendable, showcasing the significance of UEG Week as a premier platform for exchanging knowledge and advancements in gastroenterology.

This comprehensive report delves into the cutting-edge developments presented at UEG Week 2023, offering a detailed exploration of outcomes from inflammatory bowel disease trials, breakthroughs in colorectal lesion management, advances in upper endoscopy and colonoscopy techniques, the latest in artificial intelligence applications, and various other therapeutic revelations. We fervently hope that this compilation serves as a valuable resource, not only for practitioners navigating the dynamic landscape of gastroenterology but also for researchers seeking to contribute to the ongoing evolution of medical science. UEG Week 2023 has marked a pivotal moment in the collaborative pursuit of knowledge and innovation, and we are honoured to present this report as a testament to the collective dedication of the global gastroenterological community.

Greetings,
Marjolijn Duijvestein

Biography
Marjolijn Duijvestein works as a gastroenterologist in the IBD team of the Radboudumc in Nijmegen, the Netherlands. In 2012 she obtained her PhD at Leiden University and was trained as a gastroenterologist specialised in IBD disease at the Amsterdam UMC in Amsterdam. As part of her training, she gained experience at the University of California San Diego (UCSD, USA) and performed an internship at Alimentiv (former Robarts Clinical Trials), an academic research organisation dedicated to drug development for IBD. Her clinical activity and research are focused on IBD, in particular clinical and translational research.

Conflict of Interest Statement:
She has served as an advisor for Echo pharma and Robarts Clinical Trials, reports nonfinancial support from Dr Falk Pharma, and received speaker fees from Janssen, Merck & Co., Pfizer, Takeda and Tillotts Pharma. Advisory boards Janssen, Takeda, BMS and Abbvie.

Outcomes of IBD Trials

DIVERSITY1: Filgotinib results in Crohn's disease leave investigators puzzled

Although filgotinib did not achieve its primary endpoints in the induction part of a phase 3 trial in Crohn's disease (CD), it successfully met its efficacy endpoints in the maintenance part of the study.

The preferential JAK1 inhibitor filgotinib was assessed in participants with moderately to severely active CD in the double-blind, randomised, placebo-controlled, phase 3 DIVERSITY1 study (NCT02914561). The trial comprised 2 induction studies, the first including biologic-naïve and bio-experienced participants (n=704), the second study including biologic-experienced participants only (n=659), followed by a maintenance study (n=173). In both induction studies, participants were randomised 1:1:1 to placebo, filgotinib 100 mg, or filgotinib 200 mg, once daily. At week 10, responders from the induction studies were re-randomised 2:1 to filgotinib 200 mg or to placebo and continued into the maintenance study for an additional 48 weeks. The co-primary endpoints were the 2-item patient-reported outcome (PRO2) clinical remission and endoscopic response at week 10 and week 58. Prof. Séverine Vermeire (UZ Leuven, Belgium) presented the results [1].

In the first induction study, the primary endpoints were not met, with PRO2 clinical remission rates of 32.9% in the filgotinib 200 mg group and 25.7% in the placebo group (P=0.096), and endoscopic response rates of 23.9% and 18.1% for these respective study arms (P=0.14). In the induction study that included biologic-experienced participants only, a significant difference was seen between those in the filgotinib 200 mg group and the placebo group in terms of PRO2 clinical remission (29.7% vs 17.9%; P=0.0039) but not for endoscopic response (11.9% vs 11.4%; P=0.98). At week 58, both co-primary endpoints were met: PRO2 clinical remission rates were 43.8% in the filgotinib arm versus 26.4% in the placebo group (P=0.038), while the endoscopic response was 30.4% versus 9.4% (P=0.0038), respectively.

According to Prof. Vermeire, no notable safety concerns were detected. The safety profile of filgotinib was overall consistent with previous findings of this agent in patients with ulcerative colitis or rheumatoid arthritis. The rates of adverse events, including the serious ones, were fairly balanced across the arms of the study.

Prof. Vermeire tried to explain the differences between the outcomes seen in the induction studies and the maintenance study: "For the induction studies, a higher dose would perhaps have been better to induce a response in patients with CD," she said. "If patients reach remission, the maintenance study shows that it is well sustained with filgotinib and that patients have good endoscopic responses. Next to that, the long disease duration and heavy treatment history of the patient population may explain why there was not a clear signal of efficacy in the induction studies," she highlighted.

1. Vermeire S, et al. Efficacy and safety of filgotinib as induction and maintenance therapy for Crohn's disease: results from the phase 3 randomised, double-blind, placebo-controlled DIVERSITY1 study. OP097, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

SEQUENCE: Risankizumab doubles endoscopic remission rates compared with ustekinumab in CD

Risankizumab outperformed ustekinumab in achieving endoscopic remission in participants with Crohn's disease (CD). Moreover, risankizumab was superior to ustekinumab for all secondary efficacy endpoints. The safety profiles of the 2 agents were similar, albeit participants on ustekinumab had a numerically higher rate of serious adverse events (AEs).

The phase 3, head-to-head SEQUENCE trial (NCT04524611) compared the efficacy and safety of the specific IL-23 inhibitor risankizumab with the IL-12/IL-23 inhibitor ustekinumab in participants with moderate-to-severe CD who had failed at least 1 TNF inhibitor [1]. The participants (n=520) were randomised to 1 of these agents in a 1:1 ratio. The primary endpoints were Crohn's disease activity index (CDAI) clinical remission at week 24, tested in 50% of the participants for non-inferiority, and endoscopic remission at week 48, assessed for superiority. Prof. Laurent Peyrin-Biroulet (University Hospital of Nancy, France) presented the main outcomes.

At week 24, CDAI clinical remission rates were 58.6% and 39.5% in the risankizumab and ustekinumab arms,

respectively, meeting the non-inferiority endpoint (P<0.0001). Moreover, at week 48, the endoscopic remission rate was 31.8% in the risankizumab group and 16.2% in the ustekinumab group (P<0.0001). "All secondary endpoints significantly favoured risankizumab over ustekinumab," mentioned Prof. Peyrin-Biroulet. The agents were similar concerning safety: 85.1% and 82.6% of the participants in the risankizumab arm and the ustekinumab arm, respectively, experienced treatment-emergent AEs."The serious AE rate was higher in the ustekinumab arm (17.4% vs 10.3%) due to a higher rate of CD flares," added Prof. Peyrin-Biroulet. Of note, the 2 drugs also had similar rates of malignancies (14.4% in the risankizumab arm vs 11.9% in the ustekinumab arm) and serious infections (3.9% vs 5.2%, respectively).

In the SEQUENCE trial, risankizumab met both primary endpoints of non-inferiority for clinical remission at week 24 and superiority for endoscopic remission at week 48 versus ustekinumab with a comparable safety profile. Therefore, the benefit-risk assessment favours risankizumab over ustekinumab in participants with CD who had failed at least 1 TNF inhibitor.

1. Peyrin-Biroulet L, et al. Risankizumab versus ustekinumab for patients with moderate to severe Crohn's disease: results from the phase 3b SEQUENCE study. LB01, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Guselkumab provides benefits in UC regardless of advanced therapy history

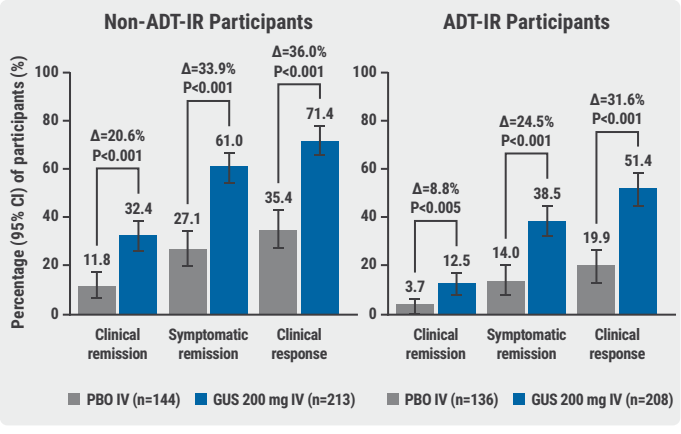
Induction therapy with guselkumab was efficacious in participants with moderately to severely active ulcerative colitis (UC), irrespective of treatment history with advanced therapies. The phase 3 QUASAR trial results demonstrated the benefits of guselkumab over placebo across clinical, symptomatic, and endoscopic endpoints.

"The IL-23 inhibitor guselkumab has been approved for the treatment of plaque psoriasis and psoriatic arthritis," said Prof. Axel Dignass (Goethe University, Germany) at the start of his presentation [1]. To further assess the potential of this agent, the phase 3 QUASAR induction study (NCT04033445) compared the efficacy of guselkumab and placebo in participants with moderately to severely active UC who had an inadequate response or intolerance to corticosteroids, immunosuppressants, and/or advanced therapies (ADT) such as TNF inhibitors, integrin receptor antagonists, or JAK inhibitors. The participants (n=701) were randomised 3:2 to guselkumab 200 mg, intravenously administered every 4 weeks, or placebo. Prof. Dignass presented the efficacy results at week 12, stratified by the history of inadequate response or intolerance to ADT.

In total, 49% (n=344) of the participants had an inadequate response or intolerance to ADT. Among them, approximately 88%, 54%, and 18% of the participants were non-responsive or intolerant to TNF inhibitors, integrin receptor antagonists, and/or JAK inhibitors, respectively. In the population with no history of inadequate response or intolerance to ADT (n=357), 32.4% of the participants on guselkumab achieved clinical remission compared with 11.8% of those on placebo (P<0.001). For symptomatic remission, the corresponding rates were 61% and 27.1% (P<0.001).

In the population with inadequate response or intolerance to ADT, clinical remission was reached by 12.5% of the participants on guselkumab and by 3.7% of those on placebo (P=0.005). For symptomatic remission, the rates were 38.5% and 14% for the guselkumab arm and placebo arm, respectively (P<0.001; see Figure). "Looking at additional endpoints, among the population without inadequate response or intolerance to ADT, endoscopic improvement was observed in 38.5% and 16.7% of the participantson guselkumab or placebo, respectively (P<0.001), and endoscopic normalisation was seen in 21.1% and 7.6% of cases, favouring the guselkumab arm over the placebo arm (P<0.001)," added Prof. Dignass. In the population with inadequate response or intolerance to ADT, the rates of endoscopic improvement were 14.9% and 5.1% (P=0.005), and the rates of endoscopic normalisation were 8.7% and 2.2% (P=0.015).

Figure: Clinical endpoints at week 12 by advanced therapy history [1]



ADT-IR, inadequate response or intolerance to advanced therapy; GUS, guselkumab; IV, intravenous; PBO, placebo.

To sum up, guselkumab induction therapy outperformed placebo across various efficacy endpoints in participants

with UC, regardless of their advanced therapy treatment history.

1. Bressler B, et al. The efficacy of induction treatment with guselkumab in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR induction study results at week 12 by prior advanced therapy history. OP019, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

INSPIRE: Risankizumab meets all efficacy endpoints in UC

Risankizumab induction therapy was superior to placebo in achieving clinical remission in participants with moderately to severely active ulcerative colitis (UC), according to the primary findings of the phase 3 INSPIRE study. The therapy was well tolerated, and the observed safety profile was similar to previous reports on this agent.

The IL-23 inhibitor risankizumab was tested in participants with moderately to severely active UC with an inadequate response or intolerance to conventional and/or advanced therapies in a double-blind, placebo-controlled, phase 3 trial called INSPIRE (NCT03398148) [1]. Participants received 1,200 mg of risankizumab intravenously every 4 weeks (n=650) or a placebo (n=325). At baseline, about 35% of the participants were on corticosteroids, 73% were on aminosalicylates, and 16.5% were on immunosuppressants. Also, over 50% of the participants had an inadequate response or were intolerant to advanced therapies. The primary endpoint was the clinical remission rate at week 12, per adapted Mayo score, defined as stool frequency subscore ≤1 and not greater than baseline, rectal bleeding subscore of 0, and endoscopic subscore ≤1 without friability. Prof. Edouard Louis (Liège University Hospital, Belgium) presented the key results.

The primary endpoint was met by 20.3% of the participants in the risankizumab arm and by 6.2% of those in the placebo arm (P<0.0001). The corresponding clinical remission rates in the advanced therapies-naïve population were 29.7% and 8.4%. In those with an inadequate response or intolerance to advanced therapies, the clinical remission rates were 11.4% and 4.3%, respectively. Furthermore, the clinical response rate per adapted Mayo score at week 12 was 64.3% in the risankizumab arm and 35.7% in the placebo arm (P<0.0001). Notably, the clinical response rates already favoured risankizumab over placebo at week 4 (52.2% vs 30.5%; P<0.0001). Prof. Louis added that endoscopic, histologic, and patient-reported endpoints significantly favoured risankizumab over placebo.

Adverse events (AEs) were reported in 49.7% of the participants on placebo and 42.1% of those on risankizumab. Finally, the rate of serious AEs appeared to be higher in the placebo arm, at 10.2%, compared with 2.3% in the active arm. Worsening of UC (10.2%), anaemia (6.5%), and COVID-19 (5.9%) were the most common AEs in the placebo arm. In the risankizumab arm, the corresponding rates for these AEs were 1.7%, 3.4%, and 4.8%. Finally, hepatic events occurred numerically more frequently in the placebo arm than in the risankizumab arm (4.3% vs 1.5%).

Induction therapy with risankizumab showed benefits over placebo in clinical, endoscopic, histologic, and patient-reported outcomes in participants with UC, and was well-tolerated in this population.

1. Louis E, et al. Risankizumab induction therapy in patients with moderately to severely active ulcerative colitis: efficacy and safety in the randomised phase 3 INSPIRE study. OP21, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Risankizumab resolves extraintestinal manifestations in CD

A pooled analysis of 3 trials investigating risankizumab in participants with Crohn's disease (CD) demonstrated that induction therapy with this agent improved the resolution of extraintestinal manifestations (EIMs) compared with placebo. Furthermore, risankizumab maintenance therapy contributed to sustaining the resolution of EIMs.

Prof. Subrata Ghosh (Cork University College, Ireland) conducted a post-hoc pooled analysis of the ADVANCE (NCT03105128) and MOTIVATE (NCT03104413) induction trials and FORTIFY (NCT03105102) maintenance study to assess the effect of risankizumab on EIMs in participants with moderate-to-severe CD as compared with placebo [1]. At baseline, 622 participants with EIMs were included. "Importantly, most participants had failed on at least 1 biologic therapy," emphasised Prof. Ghosh. The most common EIMs were peripheral arthropathy, anaemia, and axial arthropathy.

After 12 weeks of induction therapy, the percentage of participants with resolution of EIMs was 34.5% in the risankizumab group and 22.5% in the placebo group (P<0.05). Looking at specific EIMs, axial arthropathy was resolved in 50% and 30.8% of the participants in the risankizumab group and placebo group, respectively (P<0.05). Similar trends were observed for anaemia (37.4% vs 22.4%; P<0.05) and peripheral arthropathy (39.8% vs 31.2%; P>0.05), although the latter did not reach statistical significance.

In the maintenance period, at week 52, the percentage of participants with resolution of any EIM was 52.2% in the risankizumab 360 mg group, 41.7% in the risankizumab 180 mg group, and 36.3% in the placebo group. Finally, in participants who resolved EIMs following induction therapy, the corresponding rates at week 52 were 71.9%, 45.9%, and 45.0%, respectively.

The current post-hoc analysis showed that risankizumab is more efficacious than placebo in resolving EIMs and sustaining the resolution of EIMs during maintenance therapy.

1. Ghosh S, et al. Effect of risankizumab treatment on extraintestinal manifestations in patients with moderate to severe Crohn's disease: results from the ADVANCE, MOTIVATE, and FORTIFY studies. OP037, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Obefazimod takes the spotlight as promising UC treatment

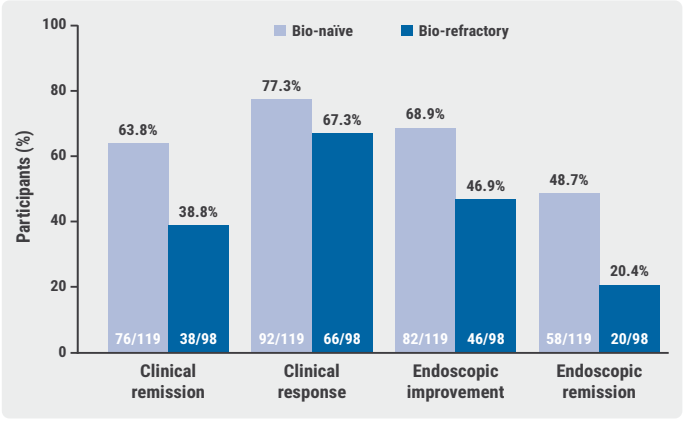
Obefazimod displayed ongoing efficacy over 2 years of treatment in participants with moderately to severely active ulcerative colitis (UC) in an open-label phase 2b study. The investigational agent was well tolerated, and no worrisome safety signals were observed.

"New oral treatments with novel mechanisms of action are needed to treat patients with UC," expressed Prof. Séverine Vermeire (UZ Leuven, Belgium). "The investigational agent obefazimod evokes an enhanced expression of miR-124, resulting in a reduction of pro-inflammatory cytokines." Obefazimod has demonstrated encouraging efficacy and safety data after 8 weeks of induction therapy in participants with UC in a phase 2b study [1]. All participants who completed the phase 2b study could then enrol in the open-label, 96-week maintenance study, irrespective of their clinical response. Prof. Vermeire presented the current findings of the open-label study [2]. Clinical remission was based on the Modified Mayo score (MMS) and defined as a stool frequency subscore ≤1, rectal bleeding subscore (RBS)=0, and an endoscopic subscore ≤1. Clinical response was defined as a decrease in the MMS ≥2 points and ≥30% from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1. Endoscopic remission and improvement were assessed as endoscopic subscores of 0 and ≤1, respectively. The 217 participants received 50 mg of obefazimod once daily, orally administered. "Over 90% of these participants had been exposed to 2 or more biologic therapies and/or JAK inhibitors," she stressed.

The clinical remission rates at weeks 48 and 96 were 54.8% and 52.5%, respectively. Other outcomes displayed promising efficacy results for obefazimod as well: at weeks 48 and 96, clinical response rates were 82% and 72.8%, respectively; endoscopic improvement rates were 61.3% and 59%; and endoscopic remission rates were 33.2% and 35.9%.

In bio-naïve participants, the corresponding rates of efficacy outcomes were 63.8% for the clinical remission rate, 77.3% for the clinical response rate, 68.9% for the endoscopic improvement rate, and 48.7% for the endoscopic remission rate. For bio-experienced participants, the rates were numerically lower but still promising, according to Prof. Vermeire, with 38.8%, 67.3%, 46.9%, and 20.4%, respectively (see Figure). She added that 48.2% of the participants who were not in clinical remission at baseline (n=168) achieved clinical remission at 2 years of therapy.

Figure: Efficacy results in bio-naïve and bio-refractory participants at 2 years [2]



Treatment-emergent adverse events (TEAEs) were reported in 68.7% of the participants over the 2-year course of the study. COVID-19 (14.3%), headache (11.5%), and UC worsening (7.8%) were the most common TEAEs. Nearly 8% of participants had TEAEs leading to study discontinuation. Finally, serious AEs occurred in 8.7% of the participants, including a wide variation of events from which no concerning pattern could be distilled.

"At week 96, obefazimod showed promising safety and efficacy results in participants with UC. The agent is currently being investigated in phase 3 trials," concluded Prof. Vermeire.

1. Vermeire S, et al. Lancet Gastroenterol Hepatol. 2022;7:1024–-1035.
2. Vermeire S, et al. Obefazimod in patients with moderate-to-severe ulcerative colitis: efficacy and safety analysis from the 96-week open-label maintenance phase 2b study. OP077, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

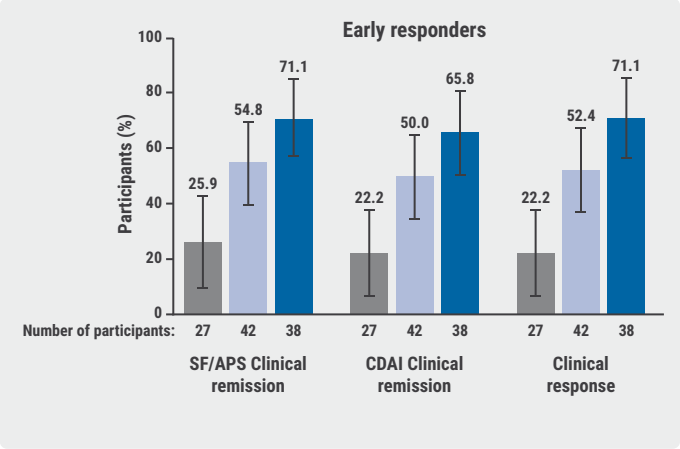
Rapid response to upadacitinib boosts outcomes in severe Crohn's disease

Upadacitinib, an oral selective JAK1 inhibitor, showed promising results in the treatment of moderate-to-severe active Crohn's disease (CD) in 2 phase 3 trials. A post-hoc analysis of these studies focused on participants who exhibited early responsiveness to upadacitinib and demonstrated improved clinical and endoscopic outcomes over time.

In the U-EXCEED (NCT03345836) and U-EXCEL (NCT03345849) studies, upadacitinib demonstrated its efficacy compared with placebo as a treatment option for participants with moderately to severely active CD. Prof. Jean-Frederic Colombel (Icahn School of Medicine at Mount Sinai, NY, USA) presented a post-hoc analysis that concentrated on participants who demonstrated early clinical improvements within the initial 15 days of treatment [1]. These early responders were monitored and evaluated for clinical and endoscopic outcomes during the 12-week induction and 52-week maintenance phases.

At week 12, early responders exhibited higher rates of stool frequency and abdominal pain score (SF/APS) clinical remission (84% vs 46%) and mucosal healing (34% vs 21%) with upadacitinib compared with the overall population. These improvements persisted through the 52-week maintenance phase, underscoring the sustained effectiveness of upadacitinib (see Figure).

Figure: Clinical outcomes for early responders and the overall population at week 52 [1]



CDAI, Crohn's Disease Activity Index; PBO, placebo; QD, once daily; SF/APS, stool frequency and abdominal pain score; UPA, upadacitinib.

"This is quite encouraging, and we should aim to look further at the predictors of response, as those patients who are responding very well to the treatment early on are doing well at weeks 12 and 52," Prof. Colombel emphasised. The findings suggest that an early response to upadacitinib therapy could be a strong indicator of sustained improvement and effectiveness in CD. This discovery could be instrumental in identifying and categorising patients more likely to benefit from upadacitinib therapy, enabling a more personalised and effective treatment approach.

1. Colombel J-F, et al. Rapid clinical response to upadacitinib therapy is associated with improved clinical and endoscopic outcomes in patients with moderate to severe Crohn's disease. OP099, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

LUCENT trials: Mirikizumab works in UC, regardless of targeted therapy history

Mirikizumab outperformed placebo for efficacy endpoints in participants with moderately to severely active ulcerative colitis (UC), irrespective of the number and types of failed prior targeted therapies. This was the key finding of research into the data of the LUCENT-1 induction study and LUCENT-2 maintenance trial.

Prof. Silvio Danese (Vita-Salute San Raffaele University, Italy) assessed the efficacy of mirikizumab, a humanised monoclonal antibody against IL-23p19, in participants with moderately to severely active UC based on the number and types of failed targeted immunomodulators [1]. The investigators examined the influence of prior use of TNF inhibitors, vedolizumab, and tofacitinib. Participants from the LUCENT-1 study (NCT03518086; n=1,162) who responded to mirikizumab induction therapy at week 12 were re-randomised to mirikizumab or placebo through week 52 in the LUCENT-2 trial (NCT03524092; n=544). Among other endpoints, clinical response was evaluated, which was defined as a decrease in the modified Mayo score of ≥30% and ≥2 points from baseline, a decrease of ≥1 point in the rectal bleeding subscore (RBS) or an RBS of 0 or 1. At baseline, 683 participants were targeted immunomodulator-naïve, 245 had failed 1 prior advanced therapy, and 234 had failed 2 or more targeted immunomodulators. In addition, 36.3% of the participants failed TNF inhibitors, 18.8% failed vedolizumab, and 15.2% failed a TNF inhibitor plus 1 other agent, either vedolizumab or tofacitinib.

At week 12, a higher percentage of immunomodulator-naïve participants achieved clinical response with mirikizumab compared with placebo (69.8% vs 50.6%; P<0.001). The same findings were observed for the other subgroups when compared with placebo, including for participants who

failed 1 prior therapy (63.9% vs 36.9%; P<0.001) and those who failed 2 or more therapies (45.3% vs 20.8%; P<0.001). Regarding the type of targeted therapy, a higher percentage of participants who previously failed TNF inhibitors achieved clinical response compared with placebo (54.2% vs 26.8%; P<0.001). The same trend was found for participants who failed vedolizumab or TNF inhibitor plus another agent.

Similar trends were observed for other efficacy endpoints, namely, symptomatic remission, clinical remission, and endoscopic remission. Importantly, these results were consistent for the maintenance population at week 52.

In short, mirikizumab outperformed placebo in participants with UC across all efficacy endpoints, as an induction or maintenance therapy, irrespective of the number and types of failed advanced therapies.

1. Navabi S, et al. Effect of mirikizumab on clinical and endoscopic outcomes based on prior advanced therapy failure in patients with moderately to severely active ulcerative colitis. OP040, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

ARTEMIS-UC: New kid in town for UC

In a phase 2 trial, induction therapy with the investigational agent MK-7240 was associated with higher clinical remission rates than placebo in participants with moderately to severely active ulcerative colitis (UC). According to the authors, a phase 3 study will be initiated to confirm these results.

MK-7240 is an investigational monoclonal antibody inhibiting tumour necrosis factor-like cytokine 1A (TL1A)-mediated signalling. TL1A is an upstream regulator of pro-inflammatory cytokines and fibrosis signals. The phase 2 ARTEMIS-UC trial (NCT04996797) randomised 135 participants with moderately to severely active UC 1:1 to placebo or MK-7240 [1]. Participants in the active arm received 1,000 mg of this agent intravenously on day 1 and 500 mg every 4 weeks, starting from week 2. The primary endpoint was clinical remission per modified Mayo score (MMS) at week 12, defined as endoscopic subscore of 0 or 1, rectal bleeding subscore (RBS) of 0, and stool frequency subscore of 0 or 1 and not greater than baseline. Secondary endpoints included clinical response (defined as a decrease from baseline in the MMS of ≥30% and ≥2 points, and a decrease of ≥1 point in the RBS or an RBS ≤1), endoscopic improvement (i.e. endoscopy subscore ≤1 with no friability), and mucosal healing (Geboes score ≤2B.1 and endoscopy subscore ≤1). Dr Bruce Sands (Icahn School of Medicine at Mount Sinai, NY, USA) presented the main findings.

The primary endpoint was met, with 26.5% and 1.5% of the participants achieving clinical remission at week 12, favouring the active arm over the placebo arm (95% CI 13.9–36.6; P<0.0001). In addition, all secondary efficacy endpoints showed improvements with MK-7240 compared with placebo, including endoscopic improvement (36.8% vs 6.0%; 95% CI 17.4–43.2; P<0.0001), clinical response (66.2% vs 22.4%; 95% CI 27.4–56.9; P<0.0001), mucosal healing (30.8% vs 3.5%; 95% CI 14.3–39.6; P<0.0001), and inflammatory bowel disease questionnaire (IBDQ) response (82.4% vs 49.3%; 95% CI 17.2–46.8; P<0.0001). Moreover, the results appeared to be consistent in advanced therapy-experienced participants.

Adverse events (AEs) were observed in 40.3% and 41.2% of the participants in the placebo arm and experimental arm, respectively. Serious AEs were reported in 7.5% and 0.0% of the participants, numerically favouring the active arm over the placebo arm. Finally, the rates of infections and infestations were comparable, with 16.4% in the placebo arm and 14.7% in the MK-7240 arm.

In conclusion, MK-7240 showed encouraging efficacy and safety results in participants with moderately to severely active UC in this phase 2 study, instigating the launch of a phase 3 trial.

1. Sands BE, et al. A phase 2, randomised, double-blind, placebo-controlled trial of PRA023 (MK-7240) as induction therapy in patients with moderately to severely active ulcerative colitis: ARTEMIS-UC, Cohort 1. OP102, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Subcutaneous infliximab shows promise in UK IBD study

A retrospective study, the largest of its kind in the UK, has unveiled promising results in the use of subcutaneous (SC) infliximab for treating inflammatory bowel disease (IBD), challenging the conventional intravenous (IV) administration of the drug. The study aimed to fill the data gap by comparing SC and IV infliximab, particularly focusing on patients who have been receiving the IV formulation for an extended period.

Although SC infliximab has been studied as an alternative to IV infliximab to maintain remission in patients with IBD, SC infliximab in high-risk patients or in those who had been treated with IV infliximab for a long period has not yet been evaluated. The current retrospective cohort study involved 306 participants in clinical remission, either high-risk patients

or patients who had been on IV infliximab for a longer duration [1]. The efficacy, pharmacokinetics, and safety of SC infliximab were analysed compared with its IV counterpart. The study assessed objective biomarkers and clinical disease activity scores, ensuring a comprehensive evaluation of the drug's performance over various periods.

The participants on SC infliximab demonstrated remarkable treatment persistence, with an 87% rate compared with 35% in the IV group (P<0.001). The SC infliximab group also exhibited a significant increase in drug levels (OR 31.77; P=0.001) and a decrease in treatment discontinuation rate due to anti-drug antibody formation (2% vs 20%, in the SC and IV groups, respectively) and side effects (3% vs 13%, respectively).

The findings advocate considering SC infliximab as a viable and effective alternative for patients in established clinical remission on IV infliximab. One of the researchers elaborated on the study's findings: "Subcutaneous switch should be considered in patients in established clinical remission on IV infliximab as offering an effective and safe alternative in IBD. Subcutaneous switch should even be considered in those high-risk patient groups." The SC route has shown favourable pharmacokinetic properties, heralding a new era in the personalised-treatment approach in IBD.

1. Mahmood T, et al. A retrospective cohort study to compare the efficacy, pharmacokinetics and safety of subcutaneous (SC) and intravenous (IV) infliximab in the treatment of inflammatory bowel disease. LB02, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Breakthroughs in Colorectal Lesions

Safer removal of large polyps with cold snare technique

Traditionally, the removal of smaller colorectal polyps, i.e. less than 10 mm in size, has been performed using cold snare endoscopic mucosal resection (CS-EMR), while larger polyps, i.e. 20 mm and above, have typically been removed using hot snare endoscopic mucosal resection (HS-EMR). This new study aimed to compare the efficacy and safety of CS-EMR with HS-EMR in removing large colorectal polyps.

The prospective, randomised, controlled trial, presented by Dr Ingo Steinbrück (Evangelisches Diakoniekrankenhaus Freiburg, Germany), enrolled 394 participants with non-pedunculated colorectal polyps measuring 20 mm or more [1]. This study primarily focused on major complications such as perforation or clinically significant post-endoscopic bleeding.

The results of this intention-to-treat analysis showed that the CS-EMR group had a significantly lower rate of major complications at 1% compared with the 8% observed in the HS-EMR group (P=0.001). These included a lower incidence of perforation (0% vs 4%; P=0.007) and post-endoscopic bleeding in the CS-EMR group (1% vs 4.5%; P=0.038).

In addition to these primary findings, the study also shed light on various secondary outcomes. For instance, the CS-EMR group exhibited a lower intraprocedural bleeding rate than the HS-EMR group (14% vs 22.9%; P=0.023). Still, the technical success rate was slightly lower in the CS-EMR group than in the HS-EMR group (92.2% vs 97.5%; P=0.017).

Dr Steinbrück concluded: "CS-EMR is superior in safety to HS-EMR, almost eliminating major adverse events. However, it presents a higher rate of residual neoplasia, necessitating careful lesion selection to mitigate recurrence risks." Further analysis is required to identify the most suitable lesions for CS-EMR and to explore technical and procedural enhancements that could bolster its effectiveness.

1. Steinbrück I, et al. Cold vs. hot snare resection of non-pedunculated polyps ≥2cm in the colorectum – first results from the prospective, randomized, controlled, multicentric CHRONICLE trial. LB06, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Higher recurrence rates with cold snare EMR than with conventional EMR

Cold snare (CS) endoscopic mucosal resection (EMR) led to a higher recurrence rate than conventional EMR in participants with large, non-pedunculated colonic lesions, according to the data of a randomised controlled trial. The effect was particularly evident in lesions with serrated histology or those larger than 30 mm.

"No randomised trials have been performed to compare CS-EMR with conventional EMR for the resection of non-pedunculated lesions without signs of invasiveness," said Dr Óscar Nogales (Hospital General Universitario Gregorio Marañón, Spain) [1]. Therefore, Dr Nogales and colleagues designed a trial (NCT04418843) to compare the efficacy of both techniques, measured as the absence of recurrence at 6 months. Participants with consecutive non-pedunculate lesions with adenoma or serrated histology with sizes ≥20 mm (n=229) were randomised to CS-EMR or conventional EMR in a 1:1 ratio.

At 6 months, the recurrence rate was significantly higher in participants in the CS-EMR arm than in those who underwent the standard treatment (33.6% vs 16.7%; P=0.007). A subgroup analysis revealed that this effect was particularly present in serrated lesions (34.4% vs 4.2%) and lesions larger than 30 mm (44% vs 19%). "Adverse events were low overall," added Dr Nogales. No significant differences were found between the 2 arms with respect to delayed bleeding, perforation, post-EMR fever, or post-polypectomy syndrome.

In conclusion, CS-EMR does not appear to be a feasible alternative to conventional EMR in patients with large, non-pedunculate colonic lesions.

1. Nogales Ó, et al. Recurrence in large non-pedunculated colonic lesions is significantly higher after cold snare endoscopic mucosal resection than after the standard technique. Results of a randomised controlled trial. LB07, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

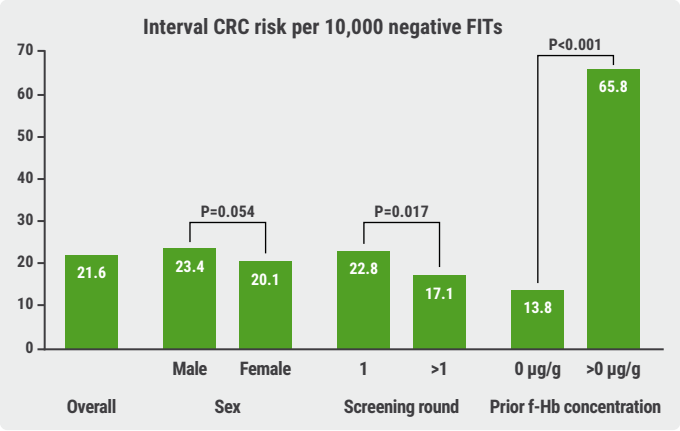
How to deal with at-risk patients above the CRC screening age limit?

Patients who had reached the upper age limit for colorectal cancer (CRC) screening with a negative faecal immunochemical test (FIT) and who displayed blood in their last screening had a much higher interval CRC risk than those who did not display blood in their last screening. This finding indicates that elderly individuals with detectable faecal-haemoglobin (f-Hb) may benefit from additional screening.

"For CRC screening, we aim to target those who are most at risk," said Dr Esther Toes-Zoutendijk (Erasmus University Medical Center, the Netherlands). "There is, however, not much data on how to deal with patients who have reached the upper age limit of screening, which is 75 years in the Netherlands." The current study assessed the interval CRC risk in patients who had reached the upper age limit of screening in relation to the f-Hb concentration of their last FIT. The research team collected data from 305,761 individuals with a last negative FIT at the upper age limit of CRC screening.

In total, 661 interval CRC cases were reported within 24 months of these patients' latest negative FIT. Individuals with any blood in their last screening (f-Hb >0 µg/g) had a much higher interval CRC risk than those without blood in their last screening, with a risk of 65.8 versus 13.8 per 10,000 negative FITs (P<0.001). Dr Toes-Zoutendijk added that interval CRC was also more likely to be diagnosed at an advanced stage in these at-risk individuals (see Figure).

Figure: Interval CRC risk per 10,000 negative FITs [1]



f-Hb, faecal-haemoglobin; FIT, faecal immunochemical test.

These findings implicate that individuals with detectable f-Hb may benefit from additional screening. "However, screening the elderly is not without harm," stressed Dr Toes-Zoutendijk. "We do not know exactly how harmful a colonoscopy is in patients above the age limit for screening. Future research should, therefore, evaluate the harm-benefit ratio of additional screening and outline the optimal screening scenario for this population."

1. Van Stigt B, et al. Risk stratification in colorectal cancer screening: interval cancer risk after the upper age limit of screening has been reached. LB08, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

European CRC screening needs to be revised

The results of a nationwide, company-based colorectal cancer (CRC) screening initiative among healthcare provider employees revealed inconsistent quality and performance and a wide variability in adenoma detection rates (ADR) and reporting standards. According to the authors, CRC prevention, screening, and quality control must be revised.

"In Europe, CRC screening is inconsistent, and participation rates vary from 1% to 73%," claimed Dr Julian Prosenz (Karl Landsteiner University of Health Sciences, Austria) [1]. "In Austria, there is opportunistic screening, but the uptake is unknown, and there is no mandatory quality assurance." Dr Prosenz and co-investigators designed a study to investigate step-wise CRC screening among public healthcare provider employees between 50 and 65 years. The step-by-step screening process included an initial stool test (faecal immunochemical test [FIT] and M2 Pyruvate Kinase [M2PK]), and, if positive, a follow-up colonoscopy carried out by unselected endoscopists across the state. The study aimed to assess the performance and quality of this screening intervention.

In total, 10,239 employees were invited to join the screening (of which 74% were women) and 3,063 stool tests were analysed. The participation rate was higher among women (25%) than men (18%). In total, 747 stool tests turned out positive, 179 with a positive FIT test and 593 with a positive M2PK test. The initial acceptance rate for performing a follow-up colonoscopy was just below 80% (n=517). Most colonoscopies were performed by office-based physicians (66%), and the remaining were performed at a hospital (34%). Internists/gastroenterologists performed 59% of the procedures, and surgeons performed 41%.

No high-grade dysplasia or CRC was detected. The ADR was 20.5%, which is lower than the standard set by the European Society of Gastrointestinal Endoscopy (ESGE) for screening colonoscopy (25%). There were also differences in detection rates between office-based endoscopists (18.5%), and hospital endoscopists (24.3%). Furthermore, quality metrics such as Boston Bowel Preparation Scale (BBPS) >5 (88%), complete colonoscopy (85%), polyp size reported (48%), and PARIS/NICE/JNET classification reported (27%) did not meet the required ESGE standards (see Figure).

Figure: Quality metrics: study results versus required standards [1]

BBPS, Boston Bowel Preparation Scale.

In short, the current corporate-based CRC screening intervention yielded a participation rate of 23%, and 72% of the employees with a positive test underwent colonoscopy. "The participation rate is low, given that there was promotion of this study and repeated invitations," added Dr Prosenz. Finally, the performance measures showed inconsistent quality and a wide variability in ADR and reporting standards.

1. Prosenz J, et al. Results of a state-wide CRC screening initiative for 10,000 eligible health-care provider employees. LB09, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Advances in Upper Endoscopy and Colonoscopy

Epinephrine boosts efficiency in gastric ESD

Epinephrine, known for its vasoconstrictive properties, is commonly used for managing haemorrhage. A recent international study explored the efficacy of an epinephrine-enhanced solution in the endoscopic submucosal dissection (ESD) of early gastric cancer treatment. The objective was to determine whether epinephrine could optimise ESD procedures by shortening operational times and reducing intra-operative bleeding.

Haemorrhage is an important adverse event of gastric ESD, potentially obscuring the view of the surgeon during

the procedure. Some operators use epinephrine during gastric ESD due to its vasoconstrictive effects. However, no evidence is available to support the use of this substance for this purpose. Dr Hon Chi Yip (The Chinese University of Hong Kong, China) presented the findings of a double-blind, multicentre, randomised-controlled trial that evaluated the efficacy of epinephrine during gastric ESD [1].

The study involved 774 adults diagnosed with gastric mucosal neoplasia, excluding those with multiple lesions or on certain anticoagulants. Participants were divided into 2 groups: 1 received an epinephrine-added solution, and the control group did not. The study's primary outcome was the duration of the procedure, from the initial mucosal incision to the completion of resection, and secondary outcomes included intra-operative haemorrhage and post-procedure adverse events.

The epinephrine-enhanced solution significantly reduced the procedure time (59.96 minutes in the epinephrine arm vs 68.06 minutes in the control arm; P=0.018) and the number of intra-operative bleeding episodes (mean 1.76 in the epinephrine arm vs 3.02 in the control arm; P<0.001). "The addition of epinephrin significantly shortened the procedural time by about 10% and reduced the need for intraoperative haemostasis," said Dr Yip.

The study advocates for the routine inclusion of epinephrine in the injection solutions used in gastric ESD procedures, representing an advancement in the field.

1. Yip HC, et al. Epinephrine added solution significantly reduced procedural time during gastric endoscopic submucosal dissection (ESD) – results from an international double blinded multi-centre randomized controlled trial. LB11, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Artificial intelligence-aided colonoscopy did not improve outcomes in Lynch syndrome

Computer-aided detection (CADe) colonoscopy was not associated with higher adenoma detection rates (ADR) compared with white light endoscopy (WLE) in participants with Lynch syndrome. Additionally, the false positive rate in the CADe group was higher than in the WLE group, according to the results of a randomised-controlled trial.

"Evidence indicates that artificial intelligence improves ADR, particularly in small non-advanced lesions," said Mr Oswaldo Ortiz (Hospital Clinic Barcelona, Spain) [1]. "In patients with Lynch syndrome, it is extra important to detect every adenoma, since these patients tend to progress faster towards adenocarcinoma" [2]. Mr Ortiz and colleagues designed a randomised-controlled trial to compare the performance of CADe colonoscopy with WLE in 430 participants with Lynch syndrome [3]. Adenoma per colonoscopy was the primary endpoint of the study.

The mean adenoma per colonoscopy was 0.64 in both study arms, showing no difference between the 2 study procedures (RR 1.00; 95% CI 0.73–1.27; P=0.42). Stratifying the outcomes by location, size, or morphology did not reveal significant differences between the 2 study arms. Also, polyp detection rates and ADR were similar for the 2 interventions. However, the rate of serrated lesions per colonoscopy was higher in the CADe arm than in the WLE arm (0.58 vs 0.46; RR 1.26; P=0.01). Finally, Mr Ortiz noted that the false positive rate was higher in the CADe arm than in the WLE arm (0.21 vs 0.08; RR 2.8; P=0.04).

1. Hassan C, et al. Ann Intern Med. 2023;176:1209–1220.
2. Ahadova A, et al. Int J. Cancer. 2021;148:800–811.
3. Ortiz O, et al. Evaluation of artificial intelligence-assisted colonoscopy for adenoma detection in Lynch syndrome: a multicentre randomized controlled trial (timely study). LB15, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Can computer technology improve our everyday colonoscopy results?

A computer-aided detection (CADe) system did not ameliorate adenoma detection rates (ADR) compared with conventional colonoscopy (CC) among high-performing endoscopists in an international, randomised-controlled trial. However, CADe did improve performance in detecting sessile serrated lesions (SSLs).

"Although colonoscopy is the golden standard with respect to detecting adenomas, up to 26% of the adenomas are missed with this procedure," stated Dr Michiel Maas (Radboud University Medical Center, the Netherlands) [1]. According to Dr Maas, CADe has shown promise for improving ADR during colonoscopy. He and his colleagues compared CADe with standard colonoscopy for diagnostics, surveillance, and non-immunochemical faecal occult blood test screening. In total, 581 individuals were randomised 1:1 to CADe or CC. The primary outcome measure was ADR.

No difference was seen between the CADe arm and the CC arm concerning ADR (38.4% vs 37.7%; P=0.86). Likewise, mean adenoma per colonoscopy was equal (0.66 for both

arms; P=0.97). The polyp detection rates were also similar, with 55.2% and 51.4%, respectively (P=0.40). A sub-analysis of colonoscopy indication, adenoma location, and adenoma size did not reveal any differences between the 2 interventions. However, SSL per colonoscopy favoured the CADe arm over the CC arm (0.30 vs 0.19; P=0.049). In addition, an almost significant effect was observed for the SSL detection rate, suggesting that CADe may be better than CC at detecting these subtle lesions (18.4% vs 12.1%; P=0.053; see Figure). Finally, Dr Maas mentioned that lower-performing endoscopists appear to benefit more from CADe than their high-performing counterparts.

Figure: Primary and secondary outcomes of the comparison of CADe with CC [1]

	CADe (n=250)	CC (n=247)	P-value
Adenoma detection rate	38.4%	37.7%	0.864
Adenoma per colonoscopy	0.66	0.66	0.971
Polyp detection rate	55.2%	51.4%	0.398
SSL per colonoscopy	0.30	0.19	0.049
SSL detection rate	18.4%	12.1%	0.053
Withdrawal time in minutes (IQR)	9.2 (8–11)	9.0 (8–11)	0.052

CADe, computer-aided detection; CC, conventional colonoscopy; IQR, interquartile range.

"CADe did not increase ADR compared with CC for diagnostic, non-immunochemical faecal occult blood test screening, and surveillance colonoscopy but did increase SSL detection by 58%," concluded Dr Maas.

1. Maas MHJ, et al. A computer-aided detection system in the everyday setting of diagnostic screening and surveillance colonoscopy: an international, randomised, controlled trial. LB14, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Is AI-assisted colonoscopy ready for clinical practice?

The 'GI Genius' artificial intelligence (AI) endoscopy module improved the adenoma detection rate (ADR) and sessile serrated polyps (SSPs) detection rate in patients undergoing colonoscopy. According to the authors, the results indicate that the 'GI Genius' system could be routinely used in most patients undergoing this procedure to improve polyp detection rates and, consequently, to reduce post-colonoscopy colorectal cancer incidence.

"Polyp detection rates are correlated with post-colonoscopy colorectal cancer rates," outlined Dr Alexander Seager (Newcastle University, UK) [1]. "Therefore, any increase in detection may result in a direct patient benefit." The current randomised-controlled trial compared the effectiveness of 'GI Genius'-assisted colonoscopy (GGC) with standard colonoscopy (SC) in routine practice. For this purpose, 2,032 participants who were scheduled for colonoscopy were randomised 1:1 to GGC or SC. The study was executed across 10 hospitals in England. The primary endpoint was mean adenomas per procedure (MAP).

The MAP rates were 1.21 for participants in the SC group and 1.56 for participants in the GGC group (IRR 1.30; 95% CI 1.15–1.47; P<0.001). The key secondary outcome also favoured the GGC arm, with ADRs of 0.48 and 0.57 for the SC and GGC arms, respectively (OR 1.47; 1.21–1.78; P<0.001). "We also saw an SSP detection rate increase of 3.3% with GGC," said Dr Seager. "If we bear in mind that a 1% increase in proximal SSP detection rate can decrease post-colonoscopy colorectal cancer rate by 7%, this is potentially a big finding."

As expected, adjusted mean polyp sizes were smaller in the GGC arm, with 5.18 mm, compared with 5.78 mm in the SC arm (P=0.016). Interestingly, the study also showed that GGC was associated with an increased detection rate of polyps of a specific morphology, namely 0-IIa polyps (34% vs 27%; P=0.002). Finally, there were no significant differences with respect to withdrawal time or safety events.

In conclusion, GGC outperformed SC in terms of overall polyp detection rate, as well as ADR and SSP detection rate, without increasing adverse events. The increased detection rate for SSPs, in particular, may strongly reduce post-colonoscopy colorectal cancer rates.

1. Seager A, et al. Colo-detect: a randomised controlled trial of polyp detection comparing colonoscopy assisted by the GI genius artificial intelligence endoscopy module with standard colonoscopy. LB18, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Should we use E-SEMS or EVT for traumatic oesophageal perforations?

Although endoscopic self-expandable metal stents (E-SEMS) and endoscopic vacuum therapy (EVT) yielded similar clinical outcomes for the treatment of traumatic oesophageal perforations in the FORTAL trial, participants who underwent E-SEMS had a shorter hospital stay than those who underwent the EVT procedure. Moreover, the costs of E-SEMS were significantly lower than for EVT.

"Oesophageal perforation may lead to mediastinitis, empyema, sepsis, and eventually, organ failure," outlined

Dr Alessandrino Terceiro de Oliveira (Federal University of Ceará, Brazil) [1]. "Surgical interventions to tackle this issue are associated with a mortality rate of up to 20%." The single-centre, randomised, double-blind, controlled FORTAL trial compared the efficacy of E-SEMS versus EVT in participants with a traumatic oesophageal perforation (n=30).

No significant differences were observed in clinical outcomes between the two arms. In the E-SEMS arm, 93.7% of the participants were discharged and 6.3% had deceased. The corresponding rates for the EVT arm were 71.4% (P=0.16) and 28.6% (P=0.16). Dr Terceiro de Oliveira added that the treatment duration was significantly longer in the E-SEMS arm than in the EVT arm (mean 45.8 days vs 24.4 days; P<0.05). In contrast, the length of hospital stay was significantly shorter among patients in the E-SEMS arm (number of days vs number of days; P=0.021). Finally, the mean cost of an E-SEMS procedure was substantially lower than the mean cost of an EVT procedure (€19,266 vs €38,453; P=0.013).

The current randomised-controlled trial provided insights into the differences between the 2 investigated surgical approaches in terms of treatment duration, length of hospital stay, and costs. Larger studies are needed to observe whether the procedures differ with regard to clinical outcomes.

1. Terceiro de Oliveira A, et al. Endoscopic self-expandable metal stent (E-SEMS) versus endoscopy vacuum therapy (EVT) for traumatic esophageal perforations: the FORTAL randomized double-blind controlled comparative effectiveness trial. LB12, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

What's New in Artificial Intelligence

Digital intervention relieves symptoms and improves QoL in IBS

A digital health application (DiGA) reduced symptoms and improved quality-of-life (QoL) for participants with irritable bowel syndrome (IBS) in a randomised-controlled trial. According to the authors, this tool may benefit patients with IBS, reducing the need for intervention from a healthcare practitioner.

"Currently, most patients with IBS do not receive adequate treatment," said Ms Linda Weißer (HiDoc Technologies GmbH, Germany) [1]. "Digital therapeutics may help close the healthcare gap by providing guided self-help for chronic conditions such as IBS." The current study randomised 378 participants with IBS (80.7% of which were women) to a DiGA intervention or to a control intervention, which comprised a modified sham app. The DiGA intervention included an in-app symptom journal and a personalised treatment plan, with nutrition therapy and various psychotherapy modalities. The investigators used the IBS Severity Scoring System (IBS-SSS), the IBS-QOL questionnaire, the Work Productivity and Activity Impairment (WPAI)-IBS questionnaire, and the European Health Literacy Survey (HLS-EU-Q16) to assess the efficacy of the intervention.

After 12 weeks of intervention, participants who used DiGA significantly improved all the assessed efficacy outcomes, including symptom severity, QoL, work productivity impairment, activity impairment, and health literacy.

Ms Weißer added that 70.2% of the participants in the experimental arm had a clinically relevant improvement of symptoms, compared with 33.2% of the participants in the control group (OR 4.87; 95% CI 3.12–7.60; P<0.001). Also, 70.8% of the participants in the active intervention arm had a clinically meaningful improvement in QoL, compared with 19% of those in the control group (OR 10.70; 95% CI 6.55–17.49; P<0.001).

"The assessed DiGA intervention was largely effective in participants with IBS, improving situations from disease symptoms to work productivity, without interference from a healthcare practitioner," concluded Ms Weißer.

1. Weißer LM, et al. The effectiveness of an App-based digital therapeutic for irritable bowel syndrome: results of a randomised controlled trial. LB17, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

GastroGPT: Successful proof-of-concept study of gastroenterology-specific large language model

A first blinded systematic comparison of a speciality-specific large language model (LLM) outperformed general LLMs such as ChatGPT across key clinical tasks. The next step would be to compare the performance of this model to human performance.

Dr Cem Şimşek (Hacettepe University, Turkey) and his research team designed a specialty-specific LLM to perform clinical tasks in gastroenterology [1]. The current proof-of-concept study compared this gastroenterology-specific model named GastroGPT against 3 general state-of-the art LLMs, being chatGPT4, Google Bard, and Anthropic's Claude. An expert panel with reviewers from varying sub-specialities across Europe compared the models' performances across 7 clinical tasks for various simulated patient cases. "The clinical tasks included assessment, collecting additional history, recommending diagnostic tests and treatment, patient education, planning follow-up visitations, and referring patients to specialists," clarified Dr Şimşek. The cases varied in complexity, rarity, and setting/urgency. The expert panel rated the accuracy, relevance, alignment with clinical guidelines, usability, interpretability, and potential clinical impact of the models' output on a 10-point Likert scale.

The experts executed 480 evaluations. GastroGPT had a higher overall score across tasks than the other models (8.05 vs 4.95, 5.63, and 6.92; P<0.001 for all) for all 10 cases that were evaluated. GastroGPT performed significantly better than all general models with respect to 'overall evaluation', 'additional history', and 'referrals', scored better than ChatGPT and Google Bard in terms of 'assessment', 'treatment', and 'patient education', and was associated with better outcomes than ChatGPT regarding 'recommended diagnostic tests' (see Figure). Furthermore, GastroGPT was more consistent than the other models across different cases, clinical tasks, complexity levels, and rarity (Levene's test<0.001). Finally, the panel scored a Cronbach's alpha of 0.76 for coherency.

Figure: Clinical task outcomes for GastroGPT and general LLMs [1]

	GastroGPT	LLM-A (OpenAI GPT4)	LLM-B (Google Bard)	LLM-C (Anthropic Claude)	P-value
Task 1 - Initial assessments	8.02 ± 1.73 [A,B]	5.83 ± 2.67	6.72 ± 2.23	7.75 ± 1.78	P<0.001
Task 2 - Additional history gathering	8.38 ± 1.96 [A,B,C]	2.90 ± 3.04	2.85 ± 3.24	2.72 ± 2.92	P<0.001
Task 3 - Diagnostic tests	7.75 ± 1.83 [A]	4.32 ± 3.32	7.33 ± 2.82	7.52 ± 1.70	P<0.001
Task 4 - Management plans	7.85 ± 2.22 [A,C]	6.27 ± 2.21	7.65 ± 2.23	6.20 ± 2.98	P<0.001
Task 5 - Follow-up planning	7.45 ± 2.04 [A,B]	5.55 ± 2.51	4.20 ± 3.47	7.82 ± 1.88 [A,B]	P<0.001
Task 6 - Multidisciplinary care, referral	8.25 ± 1.74 [A,B,C]	4.25 ± 3.36	5.12 ± 3.48	7.72 ± 1.71	P<0.001
Task 7 - Patient education and counseling	8.40 ± 1.83 [A,B]	4.97 ± 2.73	4.93 ± 3.29	7.83 ± 1.90	P<0.001
Task 8 - Overall evaluation	8.30 ± 1.28 [A,B,C]	5.58 ± 2.02	6.23 ± 2.16	7.78 ± 1.42	P<0.001

LLM, large language model.

GastroGPT outperformed general-purpose LLMs across key clinical tasks, indicating that speciality-specific LLMs have potential in medical practice. However, this approach must be tested across specialities and compared with physicians' real-world evaluations.

1. Şimşek C, et al. GastroGPT: first specialty-specific AI language model outperforms general models across key clinical tasks. LB16, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Other Therapeutics and Outcomes

Primary results from MAESTRO-NASH trial: resmetirom efficacious for NASH

Resmetirom proved efficacious in the treatment of non-alcoholic steatohaepatitis (NASH) and has shown improvement in fibrosis. Together with the agent's acceptable safety profile, resmetirom offers a useful oral therapy for patients with NASH.

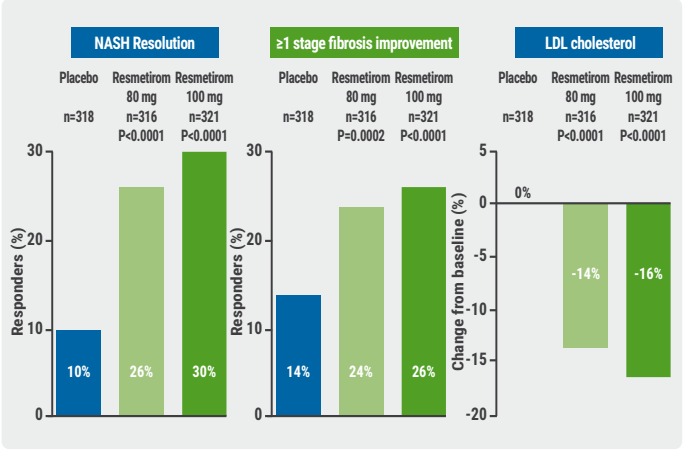
Resmetirom is an investigational, liver-targeted thyroid hormone receptor-β (THR-β) agonist. In a phase 2 trial, this agent showed promising activity in participants with NASH and fibrosis [1]. Building on these findings, the double-blind, placebo-controlled, phase 3 MAESTRO-NASH trial (NCT03900429) randomised adult participants with biopsy-confirmed NASH and fibrosis (n=966) in a 1:1:1 ratio to 3

groups: placebo, resmetirom 100 mg, or resmetirom 80 mg, once daily [2].

Prof. Jörn Schattenberg (University Medical Center Mainz, Germany) mentioned that participants needed to have at least 3 metabolic risk factors and ≥8% hepatic fat measured by magnetic resonance imaging-proton density fat fraction to be eligible for the study. The dual primary endpoint at week 52 was NASH resolution with no worsening of fibrosis or ≥1-stage improvement in fibrosis with no worsening in the non-alcoholic fatty liver disease (NALFD) activity score. According to Prof. Schattenberg, about 60% of the participants had type 3 fibrosis, and around 14% and 47% were on baseline GLP-1 receptor agonists and/or statins, respectively. Prof. Schattenberg presented the primary findings of the trial at 52 weeks.

Both the 80 mg and the 100 mg arms significantly outperformed the placebo arm in terms of NASH resolution, with 26% and 30% of the participants achieving this endpoint in the active arms compared with 10% of the participants in the latter arm (P<0.0001 for both). Similarly, a significantly larger proportion of participants in the resmetirom arms reached ≥1-stage improvement in fibrosis, with 24% in the 80 mg arm (P=0.0002) and 26% in the 100 mg arm (P<0.0001), compared with 14% of patients in the placebo arm. Prof. Schattenberg added that participants in the 80 and 100 mg arms had a mean percentage change in low-density lipoprotein (LDL) cholesterol of -14% and -16%, respectively, whereas this change was 0% in participants on placebo (see Figure).

Figure: Dual primary endpoints and key secondary endpoint at week 52 [1]



NASH, non-alcoholic steatohaepatitis; LDL, low-density lipoprotein.

The safety profile did not show any concerns. Prof. Schattenberg mentioned that the treatment-emergent adverse event-related discontinuation rate was somewhat higher in the 100 mg arm (6.8%) compared with the 80 mg arm (1.9%) or the placebo arm (2.5%), but this trend was only visible during the first 12 weeks of the study. Diarrhoea (30%) and nausea (20%) were the most common treatment-emergent adverse events in the active arms.

In conclusion, these results from the MAESTRO-NASH trial support resmetirom as a potential treatment for patients with NASH.

1. Harrison SA, et al. Lancet. 2019;394(10213):2012–2024.
2. Schattenberg J, et al. A randomized controlled phase 3 trial of resmetirom in nonalcoholic steatohepatitis: 52-week data from MAESTRO-NASH. OP001, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Apraglutide: Advancing the treatment of short bowel syndrome

A recent study has unveiled the potential of apraglutide in managing short bowel syndrome with intestinal failure and colon-in-continuity (SBS-IF-CiC). This research offers hope for patients grappling with the challenges of short bowel syndrome, a rare gastrointestinal condition marked by a high risk of developing intestinal failure.

The study, presented by Ms Astrid Verbiest (University of Leuven, Belgium), investigated the safety and efficacy of apraglutide, a novel, long-acting glucagon-like peptide-2 (GLP-2) agonist [1]. The open-label, phase 2 study was conducted across multiple centres over 52 weeks and assessed the impact of apraglutide on patients with SBS-IF-CiC. During the study, 9 participants, whose small bowel lengths varied from 0 to 50 cm and who had 43–100% of their colon preserved, received weekly subcutaneous injections of apraglutide 5 mg.

The results revealed a marked decrease in the weekly necessity for parenteral support volume from an average of 9,919 mL to 5,217 mL following 52 weeks of intervention (P=0.0004). Accordingly, a remarkable reduction in the parenteral support energy content was observed, diminishing from an average of 7,938 kcal weekly to 4,428 kcal (P=0.0006). Additionally, participants benefited from an average extra 2.1 days without needing weekly parenteral support.

These findings highlight significant clinical advancements for patients with SBS-IF-CiC. Apraglutide has a reliable safety profile and clinical efficacy, as seen by a 52% reduction in the weekly parenteral support volume post-52 weeks of treatment. "A closer examination of the metabolic balance outcomes will be essential to fully assess apraglutide's

influence on intestinal absorption and to get a better understanding of its functional mechanisms," Ms Verbiest concluded.

1. Verbiest A, et al. The long-acting GLP-2 analog apraglutide provides clinical benefit for patients with short bowel syndrome with intestinal failure and colon in continuity at 52 weeks. LB03, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

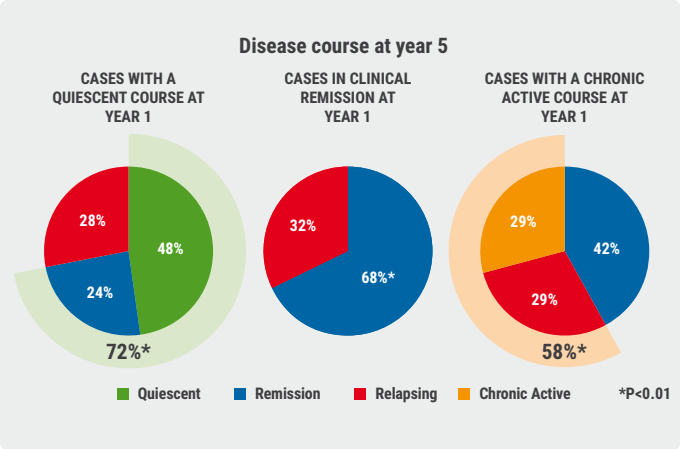
Raising awareness for microscopic colitis: disease course and predictors

A prospective cohort study demonstrated that microscopic colitis (MC) can be a relapsing or chronic disease, hampering patients' quality-of-life. In addition, the disease course at 1 year appears to be predictive of the further course of the disease. The authors hope that these results create awareness by physicians to inform and follow up patients with this condition properly.

"Not much is known about the long-term disease course of MC," said Dr Bas Verhaegh (Laurentius Hospital Roermond, the Netherlands) [1]. "Also, predictive markers for disease severity are lacking." The current PRO-MC collaboration study objectified to address these issues. A web-based registry was used to collect MC incident cases from 14 European countries, followed prospectively for 5 years. The participants were categorised according to disease course: quiescent, sustained clinical remission after treatment, relapsing, or chronically active.

At the time of the study presentation, 422 incident cases of MC had been identified, and 220 cases had completed the 5-year follow-up. The mean age of participants was 63 years, 73% were women, and there was an equal distribution between collagenous colitis and lymphocytic colitis. After 5 years of follow-up, 5% had a quiescent disease course, 55% had sustained clinical remission phenotype, 33% had the relapsing disease course, and 7% had chronically active disease. Dr Verhaegh stressed that the disease course at 1 year appeared predictive of disease course at 5 years: 72% of the participants with a quiescent disease course at 1 year had a quiescent or sustained remission disease course at 5 years. On the other hand, those with a chronic active disease at 1 year had a 58% chance to have the relapsing or chronically active disease course at 5 years (see Figure). "This is something we did not know before, and physicians should use this information in their consultations with patients," highlighted Dr Verhaegh. The findings also showed that quality of life is especially impaired in patients with a relapsing or chronically active disease course. Finally, oral budesonide was the most applied treatment (24%), followed by loperamide (21%) and bulging agents (15%). Biologic agents were used in less than 2% of the cases.

Figure: Disease course at 1 year predictive of disease course at 5 years [1]



"MC is a relapsing or chronic disease in a large proportion of patients, reducing their quality of life," concluded Dr Verhaegh. "Hopefully, this study will raise awareness for MC by physicians, health insurance companies, and pharmaceutical companies."

1. Verhaegh B, et al. The disease course of microscopic colitis: a 5-year prospective European incident cohort (PRO-MC collaboration). LB05, UEG Week 2023, 14–17 October, Copenhagen, Denmark.

Endobiliary radiofrequency ablation in pCCA: a pilot study

A pilot study demonstrated the safety and feasibility of endobiliary radiofrequency ablation (eRFA) in advance of uncovered self-expanding metal stent (uSEMS) placement in patients with perihilar cholangiocarcinoma (pCCA). Randomised-controlled trials are now needed to assess the efficacy of this intervention.

Biliary drainage is standard-of-care in the palliative treatment of patients with pCCA. Although uSEMS is preferred over plastic stents, due to the longer stent patency and fewer re-interventions, there is a risk of recurrent biliary obstruction by tumour ingrowth. As such, eRFA may be a helpful additional therapy to reduce tumour ingrowth and improve stent patency. Dr Jeska Fritzsche (Amsterdam UMC, the Netherlands) and colleagues investigated the safety and feasibility of eRFA prior to uSEMS placement in patients with pCCA [1]. Between April 2021 and March 2022, a single-centre pilot study included 10 participants with a median age of 68.5 years, a median stricture length of 30 mm, and a median serum total

bilirubin of 15 µmol/L. The outcome measures were technical success, clinical success, adverse events, stent patency, and re-interventions.

According to the authors, the procedure was technically and clinically successful in all treated participants. One of the participants had a self-limiting bleeding event of grade 2, and 7 participants experienced post-procedural abdominal discomfort. After 14 months of follow-up, the stent patency was 78%, with an estimated median stent patency of 8 months. Also, the re-intervention rate was 67%, with an estimated 2.0 re-interventions per patient-year. In addition, recurrent biliary obstruction occurred in 7 participants, with 6 cases of ingrowth and 1 case of sludge.

This pilot study showed that eRFA prior to uSEMS placement may be a safe and feasible treatment option in patients with pCCA. According to Dr Fritzsche, the risk of post-procedural pain is no reason to be reluctant to use eRFA in this population. The next step is to conduct randomised-controlled trials to assess the efficacy of the intervention.

1. Fritzsche JA, et al. Endobiliary radiofrequency ablation for malignant biliary obstruction due to perihilar cholangiocarcinoma (RACCOON-P): a prospective pilot study. MP234, UEG Week 2023, 14–17 October, Copenhagen, Denmark.