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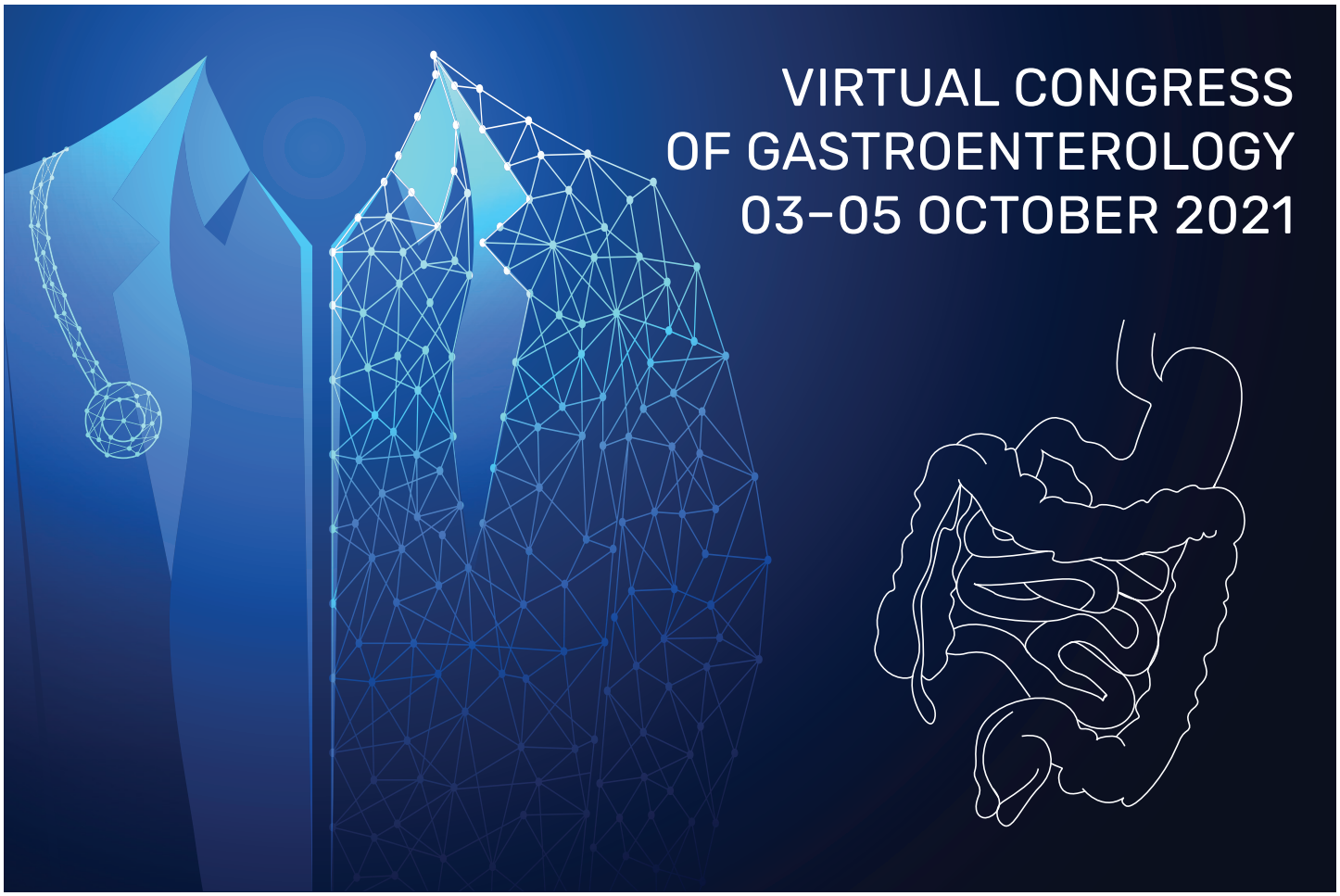

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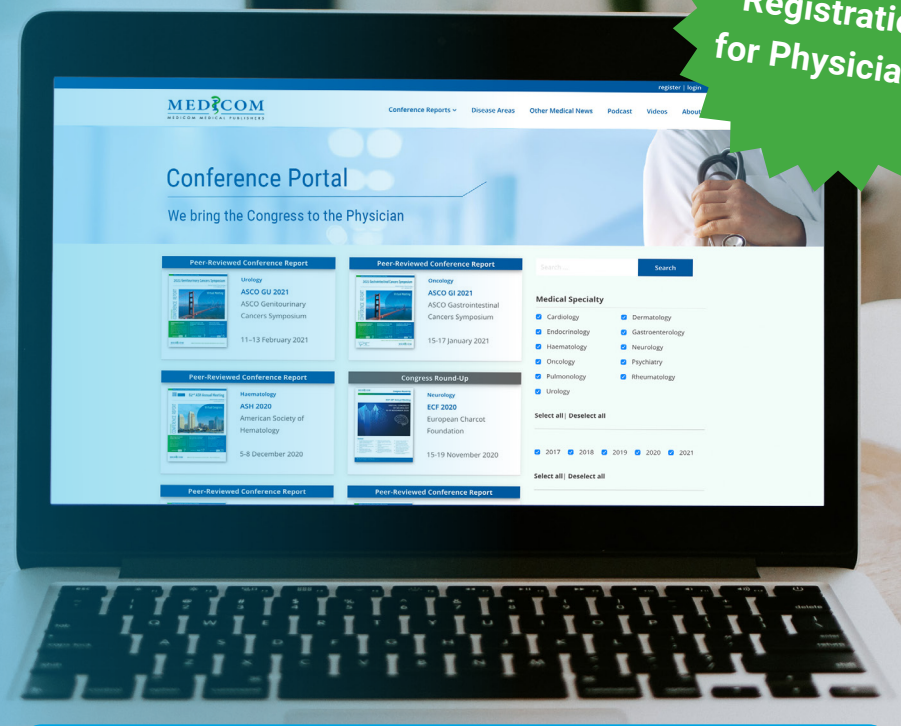

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1. Risankizumab meets primary endpoints in maintenance study for CD patients

Clinical remission was sustained throughout the 52-week FORTIFY maintenance study for patients with Crohn's disease (CD) who responded well to risankizumab induction therapy. Moreover, endoscopic remission and deep remission endpoints revealed a consistent dose-response relationship of continued risankizumab use. Risankizumab showed a favourable safety profile and was generally well tolerated.

Risankizumab is a humanised monoclonal antibody inhibiting IL-23 that has demonstrated greater efficacy than placebo in two 12-week phase 3 induction studies (ADVANCE [NCT03105128] and MOTIVATE [NCT03104413]). Patients with moderate-to-severe CD who responded well to risankizumab (600 mg or 1,200 mg intravenous injection every 4 weeks) were eligible for the FORTIFY maintenance study (NCT03105102) [1]. Participants were randomised 1:1:1 to 180 mg risankizumab (subcutaneous injection every 2 months; n=179), 360 mg risankizumab (n=184), or placebo (n=179). Approximately 70% of the participants had an inadequate response to at least 1 prior biologic therapy. Co-primary endpoints were clinical remission and endoscopic response. Prof. Marc Ferrante (University Hospital Leuven, Belgium) presented the findings of the trial.

Crohn's Disease Activity Index (CDAI) clinical remission scores showed that patients who continued risankizumab were significantly more likely to achieve clinical remission at week 52 than patients who switched to placebo in the maintenance study (risankizumab 180 mg, 55.4%; P=0.003; risankizumab 360 mg, 52.2%; P=0.005; placebo, 40.9%). However, a large proportion of placebo users achieved clinical remission as well. Prof. Ferrante argued that a carry-over effect of the risankizumab induction therapy is a possible explanation for this result. The endoscopic response, defined as a reduction of >50% in the simple endoscopic score (SES)-CD from induction baseline, showed clear benefits of risankizumab over placebo (risankizumab 180 mg, 47.1%; P<0.001; risankizumab 360 mg, 46.5%; P<0.001; placebo, 22.0%).

Adverse events (AEs) were evenly distributed across the 3 study groups. Likewise, there was no apparent difference between the number of serious AEs between the study conditions (risankizumab 180 mg, 33; risankizumab 360 mg, 35; placebo, 31). Risankizumab receivers did not show an increased risk of serious infections.

1. Ferrante M, et al. Efficacy and safety of risankizumab as maintenance therapy in patients with Crohn's disease: 52 week results from the phase 3 FORTIFY study. LB13, UEG Week 2021 Virtual Congress, 03–05 October.

2. Ustekinumab treat-to-target strategy offers long-term alternative for standard-of-care in CD

A treat-to-target (T2T) strategy of ustekinumab in a population of Crohn's disease (CD) patients was able to maintain the proportion of patients in endoscopic response in a long-term extension (LTE) of the phase 3 STARDUST trial. Moreover, the majority of patients who completed the LTE achieved the primary clinical endpoint of endoscopic response. However, the T2T strategy did not outperform the standard-of-care (SoC) therapy.

The phase 3 STARDUST trial (NCT03107793) compared a T2T strategy with ustekinumab in combination with early endoscopic assessment to a SoC regimen with ustekinumab in an adult population of CD patients. Efficacy and safety data of this trial were presented last year [1]. In total, 323 patients entered the LTE of the trial [2]. The participants followed either the T2T or the SoC regimen. Dose adjustment in the T2T strategy was based on an algorithm evaluating clinical symptoms, endoscopies, and biomarkers. Within the SoC regimen, dose adjustment was solely based on disease flare as confirmed by a physician. Hospital visits were scheduled every 8 weeks. The primary clinical endpoint was an endoscopic response of ≥50% reduction in the simple endoscopic subscore (SES)-CD in comparison with baseline at week 104. Prof. Laurent Peyrin-Biroulet (University Hospital of Nancy, France) presented the results.

Of the patients who completed the LTE until week 104, 57.2% achieved the primary endpoint (as observed). There was no apparent difference between patients in the SoC group (57.0%) and the T2T group (57.4%). In addition, the proportion of patients that reached the primary endpoint was maintained throughout the LTE (week 48, 43.7% vs week 104, 39.3%). Similarly, the proportion of patients in endoscopic remission was mostly sustained over the course of the LTE (week 48, 17.0% vs week 104, 14.6%).

In total, 20.6% of the participants who were enrolled in the LTE discontinued the study. Approximately one-third discontinued because of inadequate benefit-risk ratio treatment. There were no apparent differences in discontinuation figures between the 2 arms of the study. No new safety issues emerged during this LTE.

1. Danese S, et al. United European Gastroenterol J. 2020;8:1264-1265 (Abstract LB11)
2. Peyrin-Biroulet L, et al. Clinical and endoscopic outcomes with ustekinumab in patients with Crohn's disease: results from the long-term extension period of the STARDUST trial. LB14, UEG Week 2021 Virtual Congress, 03–05 October.

3. Long-term efficacy data of dupilumab for eosinophilic oesophagitis

Dupilumab showed maintained patient benefits in an eosinophilic oesophagitis (EoE) population. The 28-week extended treatment period of the randomised, double-blind, placebo-controlled, phase 3 LIBERTY EoE TREET trial showed sustained symptomatic, histologic, and endoscopic benefits of dupilumab. The drug was well tolerated and few severe adverse events were reported.

Dupilumab is a human monoclonal antibody inhibiting IL-4 and IL-13 signalling. Part A of the LIBERTY EoE TREET trial (NCT03633617) demonstrated that 300 mg dupilumab (subcutaneous injection, once weekly) was more efficacious than placebo after 24 weeks in a symptomatic, severely inflamed population of EoE patients. Part C of the trial investigated the long-term efficacy and safety of dupilumab in a 28-week extended treatment period [1]. All patients (n=77) who completed part A were enrolled in part C and received 300 mg dupilumab (subcutaneous injection, once weekly). Co-primary endpoints were the absolute change in Dysphagia Symptom Questionnaire (DSQ) score and the proportion of patients achieving peak oesophageal intraepithelial eosinophil count of ≤6 eosinophils/high-power field at week 52. The findings were presented by Dr Evan Dellon (University of North Carolina, NC, USA).

After 52 weeks, the reductions in DSQ scores were maintained for patients who were randomised to the dupilumab condition in part A of the trial (LS mean: -21.9 at 24 weeks; -23.4 at 52 weeks). Patients who were originally randomised to placebo showed similar changes in DSQ score at 52 weeks (LS mean: -9.6 at 24 weeks; -21.7 at 52 weeks). The intraepithelial eosinophil counts showed a comparable pattern: the proportion of patients that achieved an eosinophil count of ≤6 eosinophils/high-power field in the dupilumab arm in part A of the trial was maintained throughout part C (percentage of responders: 59.5% at 24 weeks; 55.9% at 52 weeks). Original placebo receivers showed similar response rates after 52 weeks (percentage of responders: 5.1% at 24 weeks; 60.0% at 52 weeks). Treatment-emergent adverse events (AEs) were mostly mild, injection-site reactions and injection-site erythema being the most common. Two treatment-emergent AEs led to discontinuation of the study.

1. Dellon ES, et al. Dupilumab efficacy and safety up to 52 weeks in adult and adolescent patients with eosinophilic oesophagitis: results from part A and C of a randomized, placebo-controlled, three-part, phase 3 LIBERTY EoE TREET study. LB10, UEG Week 2021, 03–05 October.

4. Upadacitinib efficacious and safe as maintenance therapy for UC

Upadacitinib outperformed placebo at all primary and secondary endpoints evaluating maintenance therapy for patients with moderately to severely active ulcerative colitis (UC). The randomised, phase 3 U-ACHIEVE maintenance study evaluated clinical, endoscopic, and histologic endpoints. The observed safety profile of upadacitinib was consistent with prior induction trials.

The oral, selective, reversible JAK inhibitor upadacitinib showed greater efficacy than placebo as induction therapy for patients with UC in two phase 3 trials (U-ACHIEVE [NCT02819635] and U-ACCOMPLISH [NCT03653026]). Clinical responders of the U-ACHIEVE and U-ACCOMPLISH trials (both 45 mg upadacitinib once daily) were enrolled in the U-ACHIEVE maintenance study (n=451). This trial examined the efficacy and safety of upadacitinib as maintenance therapy for patients with moderately to severely active UC [1]. Subjects were randomised 1:1:1 to 15 mg upadacitinib once daily, 30 mg upadacitinib once daily, or placebo. Primary endpoint was the clinical remission per adapted Mayo score at week 52. Results were presented by Dr Remo Panaccione (University of Calgary, Canada).

A significantly greater proportion of upadacitinib receivers achieved clinical remission at week 52 in comparison with placebo receivers (upadacitinib 15 mg, 42%; upadacitinib 30 mg, 52%; placebo, 12%; P<0.001). In addition, maintenance of clinical remission was observed for 59%, 70%, and 22% of the patients in the 15 mg, 30 mg, and placebo groups respectively. Similar outcomes were reported for maintenance of clinical response and maintenance of endoscopic remission.

No new safety issues of upadacitinib emerged in this trial. Adverse events (AEs) were reported in 78.6% (30 mg), 77.7% (15 mg), and 75.8% (placebo) of the patients. Serious AEs were numerically more common in the placebo group (12.8%) than in the experimental conditions (15 mg, 6.8%; 30 mg, 5.8%). The elevation of creatine phosphokinase levels was reported more frequently in upadacitinib receivers, but this did not lead to discontinuations of the trial. Finally, although severe infections were reported more often in the placebo group, herpes zoster infections were exclusively reported in the upadacitinib 15 mg (4.1%) and 30 mg (3.9%) receivers.

1. Panaccione R, et al. Efficacy and safety of upadacitinib maintenance therapy in patients with moderately to severely active ulcerative colitis: results from a randomized phase 3 study. LB11, UEG Week 2021 Virtual Congress, 03–05 October.

5. Upadacitinib outperforms placebo in UC patients with inadequate response to biologics

Superiority of upadacitinib over placebo as induction therapy for patients with moderately to severely active ulcerative colitis (UC) was observed regardless of biological-inadequate responder status. In addition, efficacy of upadacitinib was consistent in patients for whom previous biologic therapies had failed and in patients who had a prior inadequate response to conventional therapies.

Upadacitinib is an oral selective and reversible JAK inhibitor. Two phase 3 induction trials (U-ACHIEVE [NCT02819635] and U-ACCOMPLISH [NCT03653026]) have demonstrated efficacy of upadacitinib over placebo in patients with moderately to severely active UC. Yet, in patients who have had an inadequate response (IR) to a biologic or conventional therapy, data on appropriate induction therapy is lacking. The post-hoc analysis presented by Prof. Séverine Vermeire (University Hospital Leuven, Belgium) aimed to assess the efficacy of upadacitinib (45 mg once daily) in patients who showed previous IR to biologics or conventional therapies [1]. The primary endpoint was the clinical remission per adapted Mayo score at week 8 (stool frequency score ≤1 and not greater than baseline, rectal bleeding score=0, Mayo endoscopic subscore ≤1).

Upadacitinib was superior to placebo in both biologic-IR patients and non-biologic-IR patients, in both the U-ACHIEVE trial and the U-ACCOMPLISH trial. In the biologic-IR patients of the U-ACHIEVE trial, clinical remission was achieved in 18% of the upadacitinib patients (n=168) versus 0% of the placebo patients (n=78). Among the non-biologic-IR participants, 35% of the upadacitinib receivers (n=151) reached clinical remission compared with 9.2% of the placebo patients (n=76). The U-ACCOMPLISH trial showed similar rates. Moreover, secondary endpoints demonstrated a superior efficacy of upadacitinib over placebo as well. No new safety issues emerged in this subgroup analysis.

1. Vermeire S, et al. Upadacitinib induction therapy in patients with moderately to severely active ulcerative colitis by biologic inadequate responder status: results from two randomized phase 3 studies. OP017, UEG Week 2021 Virtual Congress, 03–05 October.

6. Rapid symptom control for UC patients on upadacitinib

In a population of patients with moderately to severely active ulcerative colitis (UC), control of symptoms was achieved for a significantly greater proportion of patients receiving upadacitinib than for patients receiving placebo after 2 weeks of therapy. This result was consistent for 2 phase 3 induction trials, U-ACHIEVE and U-ACCOMPLISH.

Upadacitinib is an oral, selective, and reversible JAK inhibitor. In 2 recent phase 3 trials, upadacitinib has demonstrated to outperform placebo after 8 weeks of induction therapy in patients with moderately to severely active UC. Rapid symptom control is important for UC patients, since their quality of life is reduced by gastrointestinal symptoms, such as abdominal pain, bowel urgency, and diarrhoea. Therefore, the current study investigated whether upadacitinib is more efficacious than placebo after only 2 weeks of therapy [1]. Patients were randomised 2:1 to upadacitinib (45 mg, once daily) or placebo in both the U-ACHIEVE (NCT02819635) and U-ACCOMPLISH trial (NCT03653026). Clinical remission, clinical response, stool frequency score, and rectal bleeding score were the clinical endpoints of this post-hoc analysis of these 2 trials. Dr Edward Loftus Jr (Mayo Clinic College of Medicine, MN, USA) presented the results.

In both trials, all clinical endpoints demonstrated significant patient benefits for upadacitinib over placebo after 2 weeks of therapy. In the U-ACHIEVE trial, the proportion of patients that had reached the clinical endpoints in the upadacitinib arm was 15% to 40% larger than for the placebo arm, depending on the observed endpoint. The U-ACCOMPLISH trial showed even more benefits of upadacitinib over placebo, with differences on clinical endpoints ranging from 25% to 40%. In addition, inflammatory markers faecal calprotectin and high-sensitivity C-reactive protein were significantly lower after 2 weeks among upadacitinib receivers compared with placebo receivers.

1. Loftus Jr EV, et al. Rapidity of symptom control with upadacitinib induction therapy in patients with moderately to severely active ulcerative colitis: results from two randomized phase 3 studies. OP043, UEG Week 2021 Virtual Congress, 03–05 October.

7. Filgotinib demonstrates promising results for various lines of therapy in UC

Both biologic-naïve and biologic-experienced patients with moderately to severely active ulcerative colitis (UC) achieved clinical remission more frequently when treated with filgotinib compared with placebo at weeks 10 and 58 of the phase 2b/3 SELECTION trial. In addition, the results at week 58 suggest that patients who had failed multiple biologics (of different mechanisms of action [MoA]) previously, could benefit from a treatment with high-dose filgotinib.

Filgotinib is an oral, once daily, JAK1 inhibitor that has demonstrated to induce and maintain clinical remission in UC patients with more efficacy than placebo in the phase 2b/3 SELECTION trial (NCT02914522). The current post-hoc analysis compared the efficacy of filgotinib in biologic-naïve and biologic-experienced patients with placebo at week 10 (induction) and at week 58 (maintenance) [1]. Furthermore, 4 subgroups of biologic-experienced patients were analysed, those who had not responded to: 1 biologic, ≥2 biologics, 1 MoA, or 2 agents with different MoAs. Primary endpoints were clinical remission and Mayo score response at week 10 and week 58. Prof. Iris Dotan (Rabin Medical Center, Israel) presented the findings.

At week 10, filgotinib 200 mg outperformed placebo regarding the proportion of patients in clinical remission in both biologic-naïve patients (26.1% vs 15.3%) and biologic-experienced patients (11.5% vs 4.2%). Clinical remission for patients on filgotinib 200 mg was achieved numerically more frequently in patients whose disease was not controlled after only 1 biologic (16.3%) or 1 MoA (15.1%) compared with subjects whose disease was not controlled after ≥2 biologics (7.4%) or 2 MoAs (6.7%). The Mayo score response showed a similar trend at week 10. At week 58, superior clinical remission rates were observed for filgotinib 200 mg versus placebo in both biologic-naïve patients (48.6% vs 16.7%) and biologic-experienced patients (23.9% vs 6.8%). Interestingly, filgotinib 200 mg demonstrated higher clinical remission rates than placebo in responders who had not responded to ≥2 biologics (27.9% vs 4.5%) or 2 MoAs (25.8% vs 0.0%) at the end of the maintenance study. However, this last result should be interpreted with caution due to low patient numbers.

1. Dotan I, et al. Efficacy of filgotinib in patients with ulcerative colitis by line of therapy in the phase 2b/3 SELECTION trial. OP191, UEG Week Virtual Congress 2021, 03–05 October.

8. Filgotinib demonstrates long-term corticosteroid-sparing effects in UC

Post-hoc analysis of the phase 2b/3 SELECTION trial showed that corticosteroid (CS)-free remission was reached in a greater proportion of patients receiving filgotinib in the maintenance phase than patients who were receiving placebo in the maintenance phase, in a population of patients with moderately to severely active ulcerative colitis (UC). Moreover, patients receiving filgotinib in the maintenance phase who achieved clinical remission at week 58 were mostly CS-free for at least 6 months.

Filgotinib is an oral, preferential JAK1 inhibitor in development. Efficacy of filgotinib in patients with moderately to severely active UC was demonstrated in the randomised, double-blind, placebo-controlled, phase 2b/3 SELECTION trial (NCT02914522). Since long-term use of CS is linked to significant adverse events [1], the current post-hoc analysis aimed to assess if filgotinib has CS-sparing effects [2]. For the maintenance study, responders of the original induction trial were re-randomised 2:1 to either the same dose of filgotinib they received in the induction study (100 mg or 200 mg once daily) or placebo. Prof. Séverine Vermeire (University Hospital Leuven, Belgium) presented the results.

Regarding the patients on CS at maintenance baseline, 30% of the patients who were re-randomised to the filgotinib 200 mg arm (n=202) reached CS-free remission of at least 1 month at week 58, compared with only 6% of the placebo receivers (n=99). In addition, 27% of the filgotinib 200 mg receivers showed a CS-free remission of 6 months at week 58. Similarly, daily CS dosing of CS receivers at maintenance baseline was lower in the filgotinib arm than in the placebo arm. Finally, 93% of the patients receiving filgotinib 200 mg during maintenance and reaching remission at week 58 were CS-free ≥6 months.

1. Selinger CP, et al. Aliment Pharmaco Ther. 2017; 46:964-973
2. Loftus Jr EV, et al. Corticosteroid-free remission of ulcerative colitis with filgotinib maintenance therapy: post hoc analysis of the phase 2b/3 SELECTION study. OP042, UEG Week 2021 Virtual Congress, 03–05 October.

9. Long-term benefits of tofacitinib for substantial proportion of UC patients

Maintained efficacy of tofacitinib was observed for a substantial proportion of ulcerative colitis (UC) patients in the OCTAVE open-label extension study. Although almost half of the patients discontinued the study at some point, the sustained efficacy in the patients that did continue the study demonstrated the long-term value of tofacitinib.

Tofacitinib is an oral JAK inhibitor that has shown efficacy and a favourable safety profile for the treatment of UC in three phase 3 trials (OCTAVE Induction 1 and 2: NCT01465763, NCT01458951; OCTAVE Sustain: NCT01458574). The current study aimed to assess the long-term efficacy of tofacitinib in a subpopulation including 163 patients with moderately to severely active UC who were in remission at week 52 of the OCTAVE Sustain trial [1]. Included patients received 5 mg tofacitinib twice daily at baseline of the open-label extension study. They were able to dose-escalate to 10 mg twice daily after 2 months. The median treatment duration was 1,529 days. Dr Walter Reinisch (Medical University of Vienna, Austria) presented the results.

Patients who did not discontinue the open-label extension study showed a maintained efficacy at 36 months. The sustained endoscopic improvement, clinical remission, and clinical response was irrespective of the dose that patients had received in the OCTAVE Sustain trial (5 mg or 10 mg). However, 48% of the patients that entered the open-label extension study discontinued. The main reasons for discontinuing the study were adverse events and insufficient clinical response, causing respectively 12.3% and 11.7% of patients to discontinue. The safety profile of tofacitinib users in this study was consistent with the previous OCTAVE trials.

1. Colombel JF, et al. Maintenance of remission with tofacitinib in patients with ulcerative colitis: final results of a subpopulation analysis from an open-label, long-term extension study, OCTAVE Open. OP044, UEG Week 2021 Virtual Congress, 03–05 October.

10. Ritlecitinib and brepocitinib are promising JAK inhibitors for UC

Ritlecitinib and brepocitinib showed significant patient benefits over placebo at 8 weeks of the 32-week, phase 2b, induction-maintenance VIBRATO umbrella trial in a moderately to severely active ulcerative colitis (UC) population. The safety profiles of ritlecitinib and brepocitinib were favourable, and no clinically meaningful trends for changes in vital signs, laboratory parameters, or ECGs could be detected.

According to the authors, combinations of JAK inhibitors could offer an improved benefit-risk profile for patients with various autoimmune diseases. In the phase 2b VIBRATO study (NCT02958865), ritlecitinib, an oral JAK3/TEC inhibitor, and brepocitinib, an oral TYK2/JAK1 inhibitor, are assessed for their efficacy and safety in moderately to severely active UC patients who showed an inadequate response to corticosteroids, immunosuppressants, or biologic therapies [1]. Patients (n=318) were randomised to 20 mg, 70 mg, or 200 mg of ritlecitinib (oral, once daily), 10 mg, 30 mg, or 60 mg of brepocitinib (oral, once daily), or placebo. After 8 weeks, all participants were randomised to 30 mg or 50 mg brepocitinib. The 8-week results were presented by Dr William Sandborn (University of California San Diego, CA, USA).

Clinical remission was achieved more often in participants in the ritlecitinib 70 mg (28.6%, P=0.0027) and 200 mg (34.0%, P=0.0010) conditions compared with placebo receivers (0%). Similarly, clinical remission rates were higher for patients receiving brepocitinib 30 mg (25.5%, P=0.0043) or 60 mg (23.4%, P=0.0055) than for placebo receivers (0%). Moreover, for all ritlecitinib and brepocitinib conditions, the proportions of subjects achieving modified clinical remission or endoscopic improvement were significantly higher than in the placebo condition.

The safety data showed that 4.4% of the participants discontinued the study due to adverse events (AEs). In total, 45.7% of the patients experienced AEs (placebo: 52.0%, ritlecitinib: 42.7%, brepocitinib: 47.9%) and no dose-related effects were observed in either experimental group. Most AEs were mild (n=230), or moderate (n=70), but some serious AEs (n=10) were reported. The most common AEs were infections and infestations (n=39), gastrointestinal complaints (n=30), and nervous system disorders (n=26). Infections and infestations were more frequently reported in the brepocitinib (17.6%) and ritlecitinib (8.7%) groups compared with placebo receivers (4.0%)

1. Sandborn W, et al. Oral ritlecitinib and brepocitinib in patients with moderate to severe active ulcerative colitis: data from the VIBRATO umbrella study. OP045, UEG Week 2021 Virtual Congress, 03–05 October.

11. First pharmacological therapy with clear efficacy in coeliac disease patients

The administration of ZED-1227 demonstrated clinical and histological efficacy in patients with coeliac disease. This is the first pharmacological therapy for coeliac disease patients that showed efficacy in a phase 2a trial. Moreover, no important side effects were reported. A phase 2b/3 trial will be conducted among symptomatic coeliac disease patients at the end of this year to investigate the full potential of the new agent.

A gluten-free diet is the most important therapy for coeliac disease patients. Beyond the psychological and social burden of maintaining a strict gluten-free diet, minimal gluten intake cannot be avoided. Minimal ingestion of gluten can already cause symptoms in 30% of the patients, according to Prof. Detlef Schuppan (Mainz University Medical Center, Germany). Therefore, a supportive pharmacological therapy is needed. Currently there is no effective or approved drug for coeliac disease. A phase 2a trial examined ZED-1227, an irreversible transglutaminase-2 inhibitor, among 160 coeliac patients in remission who followed a gluten-free diet [1]. All patients were to eat a standardised cookie with 3 g gluten daily for 6 weeks and were randomised to 10 mg, 50 mg, or 100 mg of ZED-1227 (oral, once daily), or placebo. Primary endpoint was histological damage, represented by villus height to crypt depth ratio.

Patients in all ZED-1227 conditions showed significantly improved villus height to crypt depth ratios compared with patients receiving placebo (P<0.001). Similarly, the intraepithelial lymphocyte (IEL) density was significantly lower in the ZED-1227 groups, compared with placebo. Other secondary endpoints, such as the Celiac Disease Questionnaire Gastrointestinal (CDQ GI) symptom subscore, transglutaminase-2 autoantibodies, and markers of inflammation showed patient benefits for the ZED-1227 subjects. To conclude, no relevant side effects were reported in this trial.

1. Schuppan D, et al. Oral inhibitor of transglutaminase 2 prevents mucosal damage in coeliac patients undergoing gluten challenge. LB06, UEG Week 2021 Virtual Congress, 03–05 October.

12. Serologic response to COVID-19 mRNA vaccine reduced in IBD patients on anti-TNFα

Patients with inflammatory bowel disease (IBD) treated with an anti-TNFα agent showed a significantly reduced immune response to COVID-19 mRNA vaccines compared with IBD patients not on anti-TNFα treatment and healthy controls. The results of this prospective, observational, multicentre study suggest that IBD patients treated with anti-TNFα could benefit from a third dose of an mRNA vaccine.

IBD patients are exposed to infections, and they need (COVID-19) vaccines. However, anti-TNFα therapy has been associated with a reduced immune response to vaccines, stated Ms Hadar Edelman-Klapper (Rabin Medical Center, Israel) [1]. The extent to which IBD patients on anti-TNFα therapy show a decreased immune response to COVID-19 mRNA vaccines has not yet been investigated. Therefore, the current study examined the immunogenicity and safety of the BNT162b2 mRNA vaccine (Pfizer-BioNTech) in IBD patients stratified by treatment type (anti-TNFα, n=67; non-anti-TNFα, n=118) and healthy controls (n=73). Primary outcome measures were seropositivity rate and magnitude of the immune response.

IBD patients treated with anti-TNFα showed a lower serological response than healthy controls and IBD patients on non-anti-TNFα therapies (P<0.001) after the second dose of the mRNA vaccine. Interestingly, after the first vaccine dose, a significantly lower number of the patients on anti-TNFα therapy had reached the seropositivity threshold of 50 Arbitrary Units/mL, compared with patients on non-anti-TNFα therapy, as well as healthy controls. Nonetheless, the infection rate after the second vaccination was less than 2% in all groups, and adverse events rates did not differ between anti-TNFα receivers, non-anti-TNFα receivers, and healthy controls. The authors did not find correlations between vaccine response and drug levels, anti-drug antibodies, or interval time between drug and vaccine administration. Consequently, modification of the timing of the vaccine will not likely change the results of this study.

1. Edelman-Klapper H, et al. Decreased serologic response to COVID-19 mRNA vaccine in patients with inflammatory bowel diseases treated with anti-TNFα: a prospective, multi-center Israeli study. OP020, UEG Week 2021 Virtual Congress, 03–05 October.

13. Serious adverse events put a stop to ASTIClite trial for CD

The ASTIClite trial, developed to analyse the efficacy of haematopoietic stem cell transplantation (HSCT) on refractory Crohn's disease (CD) patients, was halted due to unexpected serious events. Although the HSCT regimen was associated with regression of endoscopic ulcers in some patients, the adverse safety profile, including 2 deaths, rules out its future use in clinical practice.

Autologous HSCT has been associated with patient benefits in several autoimmune diseases, stated Prof. James Lindsay (Barts and The London School of Medicine, UK). He argued that there are CD patients with active disease who need non-surgical alternative therapies. Serious adverse events (AEs) that have been reported in the preceding ASTIC trial were suspected to be caused by high doses of cyclophosphamide. Therefore, the ASTIClite trial (ISRCTN17160440) aimed to investigate the efficacy and safety of and adapted low-intensity HSCT regimen compared with standard-of-care (SoC) in refractory CD patients in a 2:1 randomisation ratio [1]. The primary clinical endpoint was a simple endoscopic score (SES)-CD ulcer subscore of 0 at 48 weeks.

The trial was terminated due to unexpected serious adverse events, after 23 patients had been randomised into the study (SoC, n=10; HSCT, n=13). Only 13 patients contributed to the primary endpoint assessment. Although 3 out of 7 patients in the HSCT arm reached the primary endpoint versus 0 patients in the SoC arm, the number of serious AEs in the HSCT group (n=38) exceeded that of the SoC arm (n=16). Grade 4 serious AEs were exclusively reported in the HSCT group (n=8). Thrombotic microangiopathy resulted in several significant events in the HSCT arm. This complication was confirmed through biopsy in 3 patients who suffered from significant renal dysfunction. One patient died from refractory pulmonary hypertension secondary to pulmonary veno-occlusive disease. A second death occurred after the final endpoint of the trial, due to respiratory failure of the participant after HSCT.

1. Lindsay J. A randomised controlled clinical trial of autologous stem cell transplantation (HSCT) in patients with treatment refractory Crohn's disease (low intensity therapy evaluation): ASTIClite. OP192, UEG Week Virtual Congress 2021, 03–05 October.

14. Motorised spiral enteroscopy safe in real-life and in patients with altered anatomy

In a real-life setting, motorised spiral enteroscopy (MSE) was safe and effective to use in a large cohort of patients. Moreover, safety and feasibility of this procedure was demonstrated for the first time in post-surgical patients and patients with altered anatomy. These were the main outcomes of the prospective multicentre SAMISEN trial.

Two trials have shown the safety and efficacy of MSE for antegrade and total enteroscopy respectively [1,2]. The use of MSE in real-life settings outside MSE-expert centres and safety and effectiveness of MSE in post-surgical patients and patients with altered anatomy had not yet been investigated. The SAMISEN trial (NCT03955081) enrolled 10 European centres with a variety of MSE experience [3]. For the core analysis, 251 patients were included, and 47 patients were allocated to the training phase for novel MSE users. Primary endpoint was a non-inferior safety profile of the procedure, defined as a serious adverse event (SAE) rate <8%. Dr Torsten Beyna (Evangelic Hospital Düsseldorf, Germany) presented the results.

MSE demonstrated favourable safety outcomes. The overall SAE rate was 2.3% (95% CI 0.9-4.8). The core phase had an SAE rate of 2.0% and the training phase had an SAE rate of 4.3%. The SAEs included a perforation and a deep mucosal laceration of the oesophagus. Subgroup analysis showed that within the postsurgical/altered anatomy subgroup the SAE rate was 1.9%, representing only 1 case out of 53 participants. In 9.6% of the patients AEs occurred, mostly related to clinically asymptomatic mucosal lacerations at the level of the oesophagus, the cardia, and the small bowel. The anatomic region of interest was reached in 88% of the performed procedures, total enteroscopy was successful in >50% of the patients that were planned for this procedure (n=81). The diagnostic yield of MSE was 83% and the therapeutic yield was 60.2% in this study.

1. Beyna T, et al. Gut. 2021; 70(2):261-267.
2. Beyna T, et al. Gastrointest Endosc. 2021;93(6): 1362-1370.
3. Beyna T, et al. Motorized spiral enteroscopy: results on an international multicenter, prospective clinical trial (samisen) including patients with postsurgical/altered anatomy. LB03, UEG Week 2021 Virtual Congress, 03–05 October.

15. Novel tool can reliably exclude submucosal invasion in colorectal polyps

Endoscopists of varying experience were able to reliably exclude submucosal invasion (SMI) in large, non-pedunculated, colorectal polyps (LNPCPs) using a novel clinical decision support tool. The blink impression only was highly predictive for the absence of SMI. The tool is easy-to-use and just requires a short training intervention. Application of this tool in clinical practice could reduce the negative consequences of missing SMI during an endoscopic assessment.

The presence of SMI is decisive for the endoscopic technique used by the specialist to treat polyps and determines whether additional systemic therapy should be initiated. The detection of SMI in LNPCPs is currently poor [1]. Therefore, the current study aimed to develop an evidence-based, easy-to-use, clinical decision support tool for endoscopists to detect SMI in colorectal polyps [2].

Dr Lynn Debels (University Hospital Ghent, Belgium) and colleagues created an algorithm which used the blink impression of the endoscopist, scanning for an overt demarcated irregular area, and scoring several parameters (size, location, morphology, Paris classification of early cancer) if no overt demarcated area was present to estimate the risk of SMI. The authors prospectively selected 20 LNPCPs with help from experts. Endoscopy videos were standardised, and a 10-minute educational video was developed to explain the use of the clinical decision tool. In total, 37 endoscopists with a broad range of experience estimated the risk of SMI in all 20 selected LNPCPs, following the algorithm. Participant observations were compared with expert opinions and histopathology.

Overall, the participating endoscopists could estimate the presence of SMI with an accuracy of 75.0%, with a negative predictive value (NPV) of 93.2% and a positive predictive value (PPV) of 70.4%. The blink impression of the participants could predict SMI with an accuracy of 72.3%. The NPV of their blink impression was 97.5%, whereas the PPV was 41.8%. The presence of an overt demarcated area was detected with an accuracy of 78.6%. Again, the NPV was higher than the PPV (97.6% and 48.2%, respectively). Expert and participant observations of covert SMI parameters showed an overlap ranging between 61.8% (morphology) and 94.8% (location). In this study, 71.3% of the cases would receive the correct treatment, whereas 13.1% would receive undertreatment (mostly high-risk patients), and 15.6% would be subjected to overtreatment.

1. Tate DJ, et al. Endosc Int Open 2020; 8(3):E445-E455.
2. Debels L, et al. The accuracy of human detection of submucosal invasive cancer in large non-pedunculated colorectal polyps: analysis of 739 individual assessments of large non-pedunculated colorectal polyps using a novel clinical decision support tool. LB01, UEG Week 2021 Virtual Congress, 03–05 October.