Muirizumab for ulcerative colitis

Muirizumab—a monoclonal antibody that binds to the p19 subunit of interleukin 23—could represent a new treatment option for patients with moderate-to-severely active ulcerative colitis, according to data presented from two phase 3 trials. Bruce Sands presented data from LUCENT-1, in which patients with moderate-to-severely active ulcerative colitis who had inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressants, biologic therapies, or tofacitinib were randomly assigned in a 3:1 ratio to undergo induction with muirizumab 300 mg (n=959) or placebo (n=322) every 4 weeks for 12 weeks. Significantly more patients in the muirizumab group than in the placebo group were in clinical remission at week 12 (24·2% of 868 patients vs 13·3% of 294 patients; p=0·00006); similar results were seen for endoscopic and histological outcomes. The frequencies of treatment-emergent adverse events were similar in each group, the most common being nasopharyngitis, anemia, headache, and worsening of ulcerative colitis. There were numerically fewer serious adverse events and discontinuations due to adverse events in the muirizumab group than in the placebo group.

Marla Dubinsky presented data from the LUCENT-2 trial, in which 544 patients who had responded to induction muirizumab in the LUCENT-1 trial were randomly assigned (2:1) to receive muirizumab 200 mg or placebo every 4 weeks for 40 weeks. Significantly more patients in the muirizumab group than in the placebo group were in clinical remission after 52 weeks of treatment (ie, week 40 of maintenance; 182 [49·9%] of 365 patients vs 45 [25·1%] of 179 patients; p<0·001; 97·8% of patients treated with muirizumab in clinical remission were not on corticosteroids. As with LUCENT-1, results for endoscopic and histological endpoints were consistent with the primary outcome. Treatment-emergent adverse events occurred at similar frequencies between the two groups, with the most common being nasopharyngitis, arthralgia, and worsening of ulcerative colitis.

Optimal endoscopic resection technique for laterally spreading lesions

Endoscopic submucosal dissection should be preferred to piecemeal endoscopic mucosal resection for laterally spreading colonic lesions, according to the first head-to-head trial of the two techniques. Jérémie Jacques (Limoges, France) presented data from the RESECT-COLON trial, which compared the two techniques for large benign laterally spreading lesions of the colon. In this multicentre trial, 178 patients were randomly assigned to receive endoscopic submucosal dissection while 182 were assigned to undergo piecemeal endoscopic mucosal resection. There were no endoscopic treatment failures, and in the endoscopic submucosal dissection group, the en-bloc resection rate was 96·6%. Piecemeal endoscopic mucosal resection failed for two lesions and were managed by salvage endoscopic submucosal dissection. There were no delayed bleeding.

Treatment for coeliac disease

KAN-101—an investigational agent composed of a liver-targeting glycosylation signature conjugated to an immunodominant peptide from gliadin—was safe in patients with coeliac disease and reduced gliadin-specific T-cell responses, according to a phase 1 trial presented by Joseph Murray (Rochester, MN, USA). In an initial open-label, single ascending dose study, patients received a single dose of KAN-101 at one of five dose levels; subsequently, in the second part of the study patients were randomly assigned (3:1) to receive three administrations of KAN-101 at one of three dose levels or placebo, on days 1, 4, and 7 followed by a 3-day oral gluten challenge (9 g/day) starting on day 15.

41 patients were enrolled: 14 in part A and 27 in part B. No deaths, serious adverse events, or dose-limiting toxicities were observed at any dose level. The most common adverse events were mild-to-moderate coeliac-like reactions (eg, nausea, vomiting, abdominal pain,
diarrhoea) and resolved within hours of onset. Biomarker data suggest KAN-101 reduced gliadin-specific T-cell responses and controlled the broader immune response to gluten challenge.

**Upadacitinib for Crohn’s disease**

The oral selective JAK1 inhibitor upadacitinib was superior to placebo as induction therapy for patients with moderate-to-severely active Crohn’s disease who had had an inadequate response or intolerance to biologics, according to the results of the U-EXCEED phase 3 trial, presented by Jean-Fred Colombel (New York, NY, USA). Eligible patients were randomly assigned (2:1) to receive upadacitinib 45 mg once daily or placebo for 12 weeks. The trial had co-primary endpoints of clinical remission and endoscopic response. At 12 weeks, significantly more patients in the upadacitinib group than in the placebo group were in clinical remission (when assessed by Crohn’s Disease Activity Index, clinical remission was noted in 39% of patients in the upadacitinib group vs 21% of 171 patients [p<0·0001]; when assessed by stool frequency and abdominal pain score, clinical remission was noted in 40% of patients vs 14% of 171 patients [p<0·0001]). 35% of 324 patients in the upadacitinib group had a reduction in IBS-SSS of 50 or more (the primary endpoint).

**Optimal management of irritable bowel syndrome**

A larger benefit was seen with diet therapy than with medical treatment for patients with at least moderate irritable bowel syndrome (IBS) symptom severity, according to a randomised trial presented by Sanna Nybacka (Goteborg, Sweden). Adults with Rome IV IBS with an IBS-symptom severity score (IBS-SSS) of 175 or more were randomly assigned to receive either a diet with low total carbohydrate content, a diet combining a low FODMAP approach and traditional dietary advice, or an optimised medical treatment strategy (based on predominant symptom and previous experience with pharmacological agents for IBS) for 4 weeks. IBS symptom severity was reduced in all three groups (p<0·001 for within group changes), but the change in symptom severity was greater in the two dietary intervention groups than with medical therapy (p=0·001). 72% of 97 patients in the low carbohydrate group (p=0·042 vs medical treatment), 75% of 97 patients in the low FODMAP and traditional IBS diet group (p=0·012 vs medical treatment), and 58% of 101 patients in the medical treatment had a reduction in IBS-SSS of 50 or more (the primary endpoint).

**Etrasimod for ulcerative colitis**

Etrasimod, a once-daily, oral, selective sphingosine 1-phosphate receptor 1,4,5 modulator, was superior to placebo for the treatment of moderate-to-severely active ulcerative colitis that had an inadequate response, loss of response, or intolerance to one or more other treatments for ulcerative colitis, according to the results of the ELEVATE UC 52 and ELEVATE UC 12 trials, presented by Bill Sandborn (San Diego, CA, USA). In both trials, patients were randomly assigned to receive etrasimod 2 mg or placebo; in the treat-through ELEVATE UC 52 trial, patients received a 12 week induction period followed by a 40 week treatment period, while in ELEVATE UC 12, patients underwent a 12 week induction period only. Clinical remission at week 12 and clinical remission at week 52 were co-primary endpoints in ELEVATE UC 52. 74 (27·0%) of 274 patients in the etrasimod group and ten (7·4%) of 135 patients in the placebo group were in clinical remission at week 12, as were 88 (32·1%) patients and nine (6·7%) patients at week 52, respectively (both p<0·001). Key secondary endpoints—including symptomatic remission at week 12 and week 52, mucosal healing at week 12 and week 52, and clinical response at week 12 and week 52—were also significantly better with etrasimod than with placebo.

In ELEVATE UC 12, the primary endpoint was clinical remission at week 12; a greater proportion of patients in the etrasimod group than in the placebo group was in clinical remission at this time (55 [24·8%] of 222 patients vs 17 [15·2%] of 112 patients; p=0·0264). Key secondary endpoints—eg, endoscopic improvement, symptomatic remission, and mucosal healing—followed a similar pattern to the primary endpoint.

The most frequently reported treatment-emergent adverse events across both trials were headache, worsening of ulcerative colitis, COVID-19 infection, and dizziness. Serious infections were noted in three patients in the etrasimod group and five in the placebo group in ELEVATE UC 52; no serious infections were reported in ELEVATE UC 12.

Rob Brierley