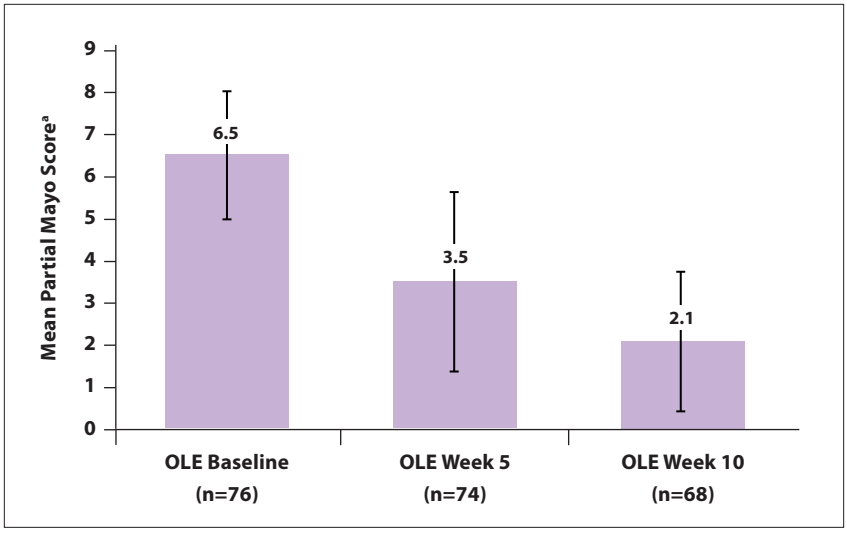

Figure 2. The mean partial Mayo score at OLE in a post hoc analysis of data from the phase 3 True North trial that focused on patients treated with ozanimod who achieved a clinical response at week 10, relapsed while receiving placebo during the maintenance period, and subsequently received reinduction therapy with open-label ozanimod. The error bars represent the standard deviation. [a]The mean partial Mayo score encompasses the sum of the rectal bleeding subscore, the stool frequency subscore, and the Physician's Global Assessment subscore. OLE, open-label extension. Adapted from Afzali A et al. DDW abstract 969. *Gastroenterology*. 2022;162(suppl 1).[5]

stool frequency subscore of 0 or 1 was reported in 80.5% of patients. A Physician's Global Assessment subscore of 0 or 1 was reported in 81.8% of patients.

In the OLE study population of 77 patients who received ozanimod for a second induction, a symptomatic clinical response was reported in 55.8% at week 5 and in 58.4% at week 10 (Figure 1).[5] Among the 38 patients who were biologic-naive at baseline, a symptomatic clinical response was reported in 63.2% at week 5 and in 52.6% at week 10. Among 38 patients with prior exposure to 1 or more biologic therapies at baseline, a symptomatic clinical response was observed in 50.0% at week 5 and 65.8% at week 10. Among 76 evaluable patients, the mean partial Mayo score decreased from 6.5 at the OLE baseline, to 3.5 at OLE week 5, to 2.1 at OLE week 10 (Figure 2). Across the same time points, the rectal bleeding score decreased from 1.5 to 0.6 to 0.2, the stool frequency subscore decreased from 2.6 to 1.6 to 1.0, and the Physician's Global Assessment subscore decreased from 2.4 to 1.4 to 0.9. Study limitations included the small sample size and the post hoc nature of the analysis.

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Efficacy and Safety of Mirikizumab as Maintenance Therapy in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 LUCENT-2 Study

Interleukin (IL) 23 is a key cytokine that mediates the inflammatory state of the intestinal mucosa in UC.[1] Mirikizumab is a humanized immunoglobulin G4 monoclonal antibody that attenuates inflammation by binding to subunit p19 of IL-23. The phase 3 LUCENT-1 study compared mirikizumab vs placebo as induction therapy in 1281 patients with UC.[2] The trial met its primary endpoint, showing a superior rate of clinical remission at week 12 with mirikizumab vs placebo (24.2% vs 13.3%; 99.875% CI, 3.2-19.1; *P*=.00006).

LUCENT-2 was a double-blind phase 3 trial that evaluated mirikizumab maintenance therapy in patients with a clinical response to mirikizumab induction therapy at week 12 in LUCENT-1.[3] Enrolled patients were randomly assigned in a 2:1 ratio to receive mirikizumab (200 mg) or placebo every 4 weeks through week 40 of LUCENT-2, for a total of 52 weeks of study treatment. Corticosteroid therapy was tapered starting at week 0 of LUCENT-2. The primary outcome was clinical remission at week 40 of maintenance therapy. Clinical remission was defined as a stool frequency score of 0, or a stool frequency score of 1 with a decrease of at least 1 point from baseline; a rectal bleeding score of 0; and an endoscopic subscore of 0 or 1, excluding friability. Secondary endpoints were also evaluated at week 40 of the trial.

The LUCENT-2 study randomly assigned 365 patients to treatment with mirikizumab and 179 to placebo. The patients' median age was 42 years, and 59% were male. The baseline characteristics were well balanced between the mirikizumab and placebo arms,

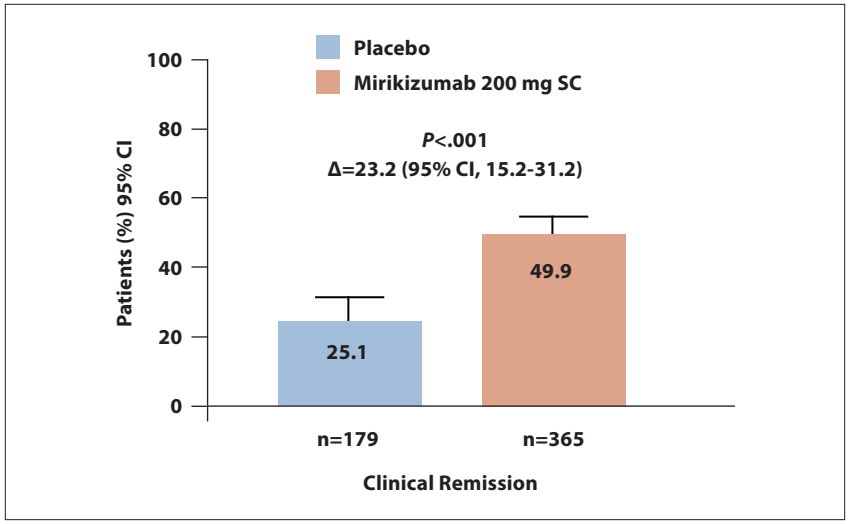

Figure 3. Clinical remission in the double-blind phase 3 LUCENT-2 trial, which evaluated mirikizumab maintenance therapy in patients with moderately to severely active ulcerative colitis who achieved a clinical response to mirikizumab induction therapy at week 12 in the LUCENT-1 trial. SC, subcutaneously. Adapted from Dubinsky MC et al. DDW abstract 867e. *Gastroenterology*. 2022;162(suppl 1).[3]

including disease duration (6.7 vs 6.9 years), median bowel urgency severity (6.0 for both arms), baseline corticosteroid use (37% vs 38%), and baseline immunomodulator use (21% vs 22%). Prior unsuccessful therapies included a biologic agent in 35% of patients and tofacitinib in 36% of patients.

The LUCENT-2 trial met its primary endpoint. Clinical remission was achieved by 49.9% of the mirikizumab arm vs 25.1% of the placebo arm (*P*<.001; Figure 3). The rate of clinical remission at week 40 was 63.6% in the mirikizumab arm vs 36.0% in the placebo arm (95% CI, 10.4%-39.2%; *P*<.001). Moreover, 97.8% of patients in the mirikizumab arm who maintained clinical remission at week 40 were no longer receiving corticosteroids. The rate of corticosteroid-free remission was higher in the mirikizumab arm compared with the placebo arm (*P*<.001). The rate of endoscopic remission was superior with mirikizumab (*P*<.001), as was the rate of histologic-endoscopic mucosal remission (*P*<.001). Treatment with mirikizumab was superior to placebo in maintaining clinical remission at week 40 among patients who were naive to biologic therapy or tofacitinib (*P*<.001) and in patients who had previously received unsuccessful treatment with these agents (*P*<.001). Similarly, mirikizumab led to better endoscopic remission vs placebo in patients without prior exposure to biologic therapy or tofacitinib (*P*<.001) and in those who had received unsuccessful treatment with these agents (*P*<.001). The safety profile of mirikizumab was similar to that observed in prior studies.

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Long-Term Cardiac Safety of Ozanimod in a Phase 3 Clinical Program of Ulcerative Colitis and Relapsing Multiple Sclerosis

Treatment with S1P receptor modulators may be associated with cardiovascular adverse events (AEs), including bradycardia and delays in atrioventricular conduction. The effects of ozanimod on long-term safety were evaluated in a retrospective analysis of UC patients from the phase 3 True North trial and in patients with relapsing multiple sclerosis from the phase 3 SUNBEAM and RADIANCE trials.[1-4]

In the True North trial, patients received treatment with ozanimod at 0.92 mg. Patients in cohort 1 were randomly assigned to receive ozanimod or placebo, whereas patients in cohort 2 received open-label ozanimod. Patients with a clinical response to ozanimod at week 10 were randomly assigned a second time to receive ozanimod or placebo. Patients underwent echocardiogram (ECG) monitoring at screening, day 1, week 10, and week 52. Heart rate was monitored at screening and day 1, and at weeks 5, 10, 18, 28, 40, and 52.

In the SUNBEAM and RADIANCE trials, patients received ozanimod at 2 doses: the standard dose of 0.92 mg and a lower dose of 0.46 mg. ECGs were performed at screening, baseline, day 15, month 12, and, in RADIANCE only, month 24. Heart rate was monitored at screening and baseline visits, on day 15, and every 3 months until the end of treatment.

Key cardiac exclusion criteria for the UC and multiple sclerosis trials included a resting heart rate of less than 55 beats per minute at screening, recent cardiovascular events, and a prolonged corrected QT interval. The trials excluded patients who were receiving concurrent therapy with QT-prolonging medications.

In all of the studies, continuous treatment with ozanimod did not lead to clinically significant changes in ECG results or heart rate. In the True North trial, the mean change in heart