Rapidity of Ozanimod-Induced Symptomatic Response and Remission in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Induction Period of True North

Ozanimod is an oral immunomodulatory agent that acts as a selective sphingosine-1-phosphate (S1P) receptor agonist. The multicenter, double-blind phase 3 True North trial evaluated ozanimod as induction and maintenance therapy in patients with moderately to severely active ulcerative colitis.[1,2] During the 10-week induction period, patients in cohort 1 were randomly assigned in a 2:1 ratio to receive daily ozanimod hydrochloride (1 mg, equivalent to 0.92 mg of ozanimod) or placebo. Patients in cohort 2 received open-label ozanimod hydrochloride (1 mg). After 10 weeks, patients who demonstrated a clinical response to ozanimod were randomly assigned in a double-blind manner to receive ozanimod or placebo during the 42 weeks of the maintenance period. The primary endpoint was the proportion of patients with clinical remission, based on the 3-component Mayo score.[3]

To assess induction therapy, the True North trial randomly assigned 429 patients to ozanimod and 216 to placebo in cohort 1. In cohort 2, open-label ozanimod was administered to 367 patients. The maintenance period of the trial included 457 patients. The study demonstrated a significant increase in the incidence of clinical remission with ozanimod vs placebo, during both induction (18.4% vs 6.0%; *P*<.001) and maintenance (37.0% vs 18.5%; *P*<.001).[1] Treatment with ozanimod also yielded a greater proportion of patients with a clinical response compared with placebo, during both induction (47.8% vs 25.9%; *P*<.001) and maintenance (60.0% vs 41.0%; *P*<.001).

Britta Siegmund, MD, presented an analysis of the True North trial that evaluated the rapidity of symptomatic response and remission among patients who received ozanimod during the 10-week induction period.[2] A symptomatic response was defined as a decrease in the adapted partial Mayo score of at least 1 point and at least 30% from baseline, as well as a decrease of at least 1 point from baseline in the rectal bleeding subscore or an absolute rectal bleeding subscore of 1 or less. Symptomatic remission was defined as a rectal bleeding subscore of 0 and a stool frequency subscore of 1 point or less, as well as a decrease from baseline of 1 or more points.

The patients' baseline characteristics were generally well balanced among the 3 cohorts. The patients' mean age was 42 years, and their mean body mass index (BMI) was 25 to 26. The mean total Mayo score was approximately 9±1.5, and the mean partial Mayo score was approximately 6.1±1.2. Across the 3 cohorts, the proportion of patients with a rectal bleeding subscore of 2 or 3 ranged from 92% to 96%, and the proportion of patients with a stool frequency subscore of 2 or 3 ranged from 42% to 47%. Prior use of anti–tumor necrosis factor (TNF) agents was reported in 30% of patients in cohort 1 and 42% in cohort 2.

A first symptomatic response to treatment with ozanimod vs placebo was evident after 2 weeks of induction therapy, in both the overall study population (difference, 9.6%; Figure 1) and among patients without prior exposure to anti-TNF therapy (difference, 9.4%). Among patients with prior anti-TNF treatment, the first response to induction therapy was observed at 4 weeks (difference, 15.8%). Symptomatic remission was observed with ozanimod vs placebo at week 5 in the overall study population (difference, 8.6%; Figure 2), at week 4 in patients without prior exposure to anti-TNF therapy (difference, 9.4%), and at week 8 in patients with prior exposure to anti-TNF therapy (difference, 11.7%).

The investigators concluded that

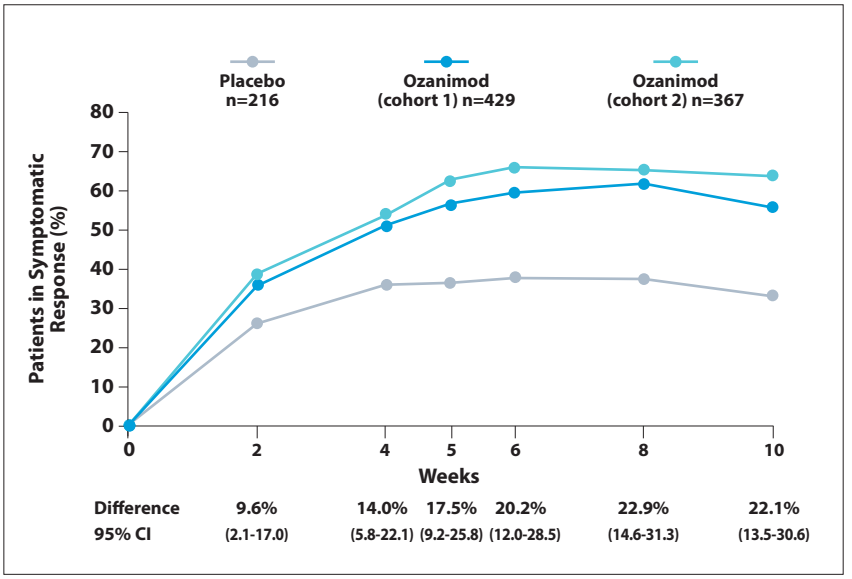

Figure 1. Symptomatic response in patients with moderately to severely active ulcerative colitis during induction treatment with ozanimod in the phase 3 True North trial. Adapted from Siegmund B et al. ECCO abstract DOP43. *J Crohns Colitis.* 2022;16(suppl 1).[2]

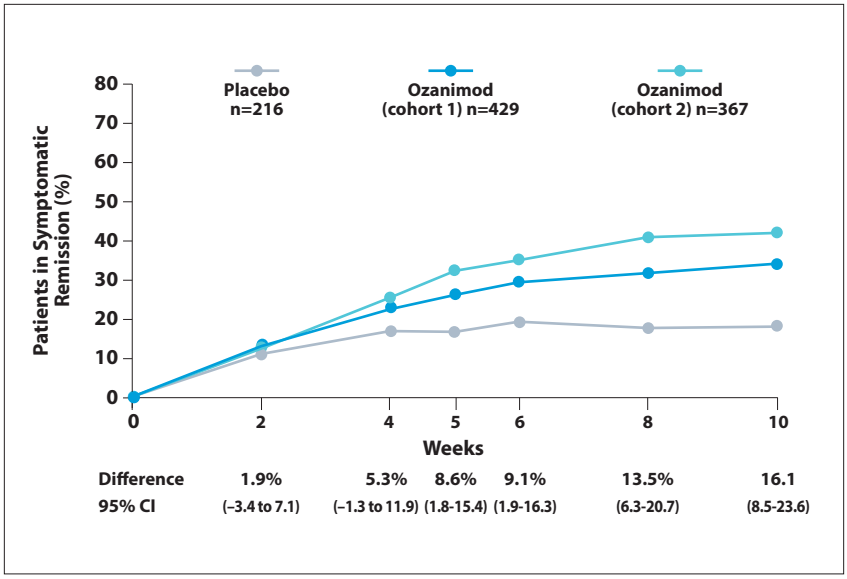

Figure 2. Symptomatic remission in patients with moderately to severely active ulcerative colitis during induction treatment with ozanimod in the phase 3 True North trial. Adapted from Siegmund B et al. ECCO abstract DOP43. *J Crohns Colitis*. 2022;16(suppl 1).[2]

treatment with ozanimod improved symptomatic response compared with placebo as early as 2 weeks after the initiation of treatment. Symptomatic remission was seen with ozanimod as early as 5 weeks after treatment began. For patients who were naive to TNF inhibitors, ozanimod led to a significant improvement in symptomatic response in as early as 2 weeks. This duration increased to 4 weeks among patients previously treated with TNF inhibitors. For symptomatic remission, ozanimod was associated with significant improvement as early as 4 weeks for patients naive to TNF inhibitors and as early as 8 weeks for those previously treated with TNF inhibitors.

References

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2. Siegmund B, Axelrad J, Osterman MT, et al. Rapidity of ozanimod-induced symptomatic response and remission in patients with moderately to severely active ulcerative colitis: results from the induction period of True North [ECCO abstract DOP43]. *J Crohns Colitis*. 2022;16(suppl 1).
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Efficacy and Safety of Extended Induction Treatment With Upadacitinib 45 mg Once Daily Followed by Maintenance Upadacitinib 15 or 30 mg Once Daily in Patients With Moderately to Severely Active Ulcerative Colitis

Phase 2b and phase 3 studies have demonstrated the safety and efficacy of upadacitinib (45 mg) when administered daily for 8 weeks as induction treatment for patients with moderately to severely active ulcerative colitis.[1-3] A study evaluated the safety and efficacy of 16 weeks of induction therapy with daily upadacitinib at 45 mg, followed by 52 weeks of maintenance therapy with daily upadacitinib administered at 15 mg or 30 mg.[4] The patient population consisted of 125 patients with ulcerative colitis without a clinical response after 8 weeks of induction therapy with upadacitinib in the U-ACHIEVE study. Clinical response was defined as a decrease in the adapted Mayo score of 2 or more points and 30% from baseline, plus a

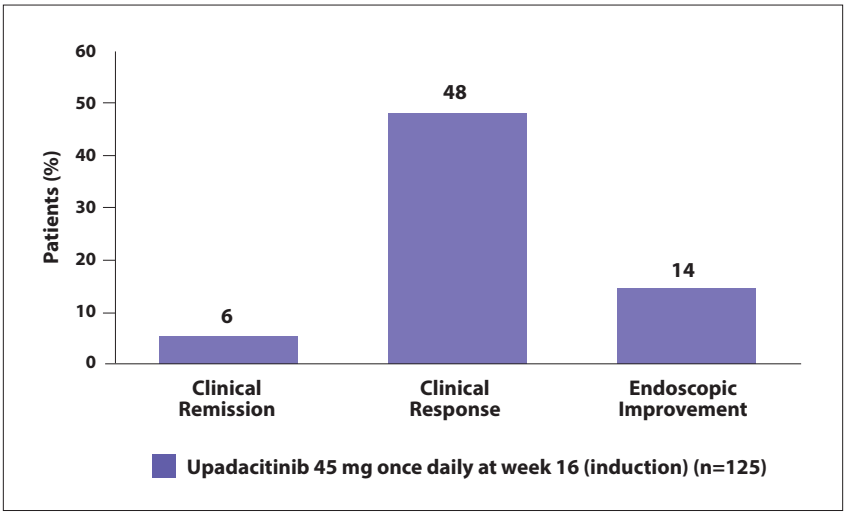

Figure 3. Efficacy after 16 weeks of extended induction treatment with upadacitinib at 45 mg/day among patients with ulcerative colitis without an initial clinical response in the U-ACHIEVE trial. Adapted from Vermeire S et al. ECCO abstract DOP41. *J Crohns Colitis*. 2022;16(suppl 1).[4]