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A SPECIAL MEETING REVIEW EDITION

Highlights in Ulcerative Colitis From the American College of Gastroenterology 2023 Annual Scientific Meeting

A Review of Selected Presentations From the ACG 2023 Annual Scientific Meeting • October 20-25, 2023 • Vancouver, Canada

Special Reporting on:

- Early Symptomatic Improvement With Guselkumab Induction Treatment in Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 QUASAR Study
- Comparative Effectiveness of Upadacitinib vs Ustekinumab for Ulcerative Colitis at 8-16 Weeks: A Multicenter Retrospective Cohort Study
- Insights From Studies on Ustekinumab: Efficacy, Long-Term Outcomes, and Treatment Persistence in Patients With Ulcerative Colitis
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PLUS Meeting Abstract Summaries

With Expert Commentary by:

Gary R. Lichtenstein, MD
Professor of Medicine
Vice Chief, Division of Gastroenterology
Development and Philanthropy
Emeritus Director, Center for Inflammatory Bowel Disease
The Raymond and Ruth Perelman School of Medicine of the University of Pennsylvania
University of Pennsylvania Health System
Hospital of the University of Pennsylvania
Gastroenterology Division, Department of Internal Medicine
Perelman Center for Advanced Medicine
Philadelphia, Pennsylvania

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Early Symptomatic Improvement With Guselkumab Induction Treatment in Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 QUASAR Study

Guselkumab is a human selective interleukin-23 (IL-23) p19 subunit antagonist approved for the treatment of moderate to severe plaque psoriasis and psoriatic arthritis, and is currently under investigation in patients with ulcerative colitis (UC).[1] The QUASAR protocol is a phase 2b/3 clinical development program evaluating the safety and efficacy of 12 weeks of guselkumab in patients with moderately to severely active UC.[2] Patients enrolled in QUASAR had an inadequate response, loss of response, or intolerance to conventional therapies (corticosteroids and immunomodulators) and/or advanced therapies (tumor necrosis factor α [TNFα] antagonists, integrin receptor antagonists [vedolizumab], and/or Janus kinase [JAK] inhibitors [tofacitinib]). The phase 2b portion of this trial was previously reported, demonstrating the activity of guselkumab at week 12 in achieving clinical response and remission.[3]

At the American College of Gastroenterology (ACG) 2023 Annual Scientific Meeting, Lichtenstein and colleagues reported results from the phase 3 QUASAR study, focusing on the early onset of symptomatic improvement with guselkumab as induction therapy.[4] Patients 18 years of age or older were enrolled in this phase 3 study. All patients had moderately to severely active UC, defined at baseline as a modified Mayo score of 5 to 9 by central review, with a Mayo rectal bleeding subscore (RBS) of at least 1 and a Mayo endoscopic subscore of at least 2. After screening, 701 patients were randomized 3:2 to treatment with either guselkumab (200 mg intravenously [IV]; n=421) or placebo (n=280) at weeks 0, 4, and 8. Concomitant treatment with conventional immunosuppressants, oral 5-aminosalicylic compounds, and corticosteroids (up to 20 mg/day prednisone or equivalent) was allowed. Randomization was stratified by a history of inadequate response or intolerance to advanced therapy, region, and concomitant use of corticosteroids at baseline. Patients underwent an endoscopy at baseline and again at week 12. Symptomatic remission at weeks 2, 4, and 12 were major secondary endpoints.

Overall, baseline characteristics were well balanced between the guselkumab and placebo arms. In the overall population, the mean age was 40.5 years (SD, 13.72), and 56.9% were male. Patients had a mean dura-

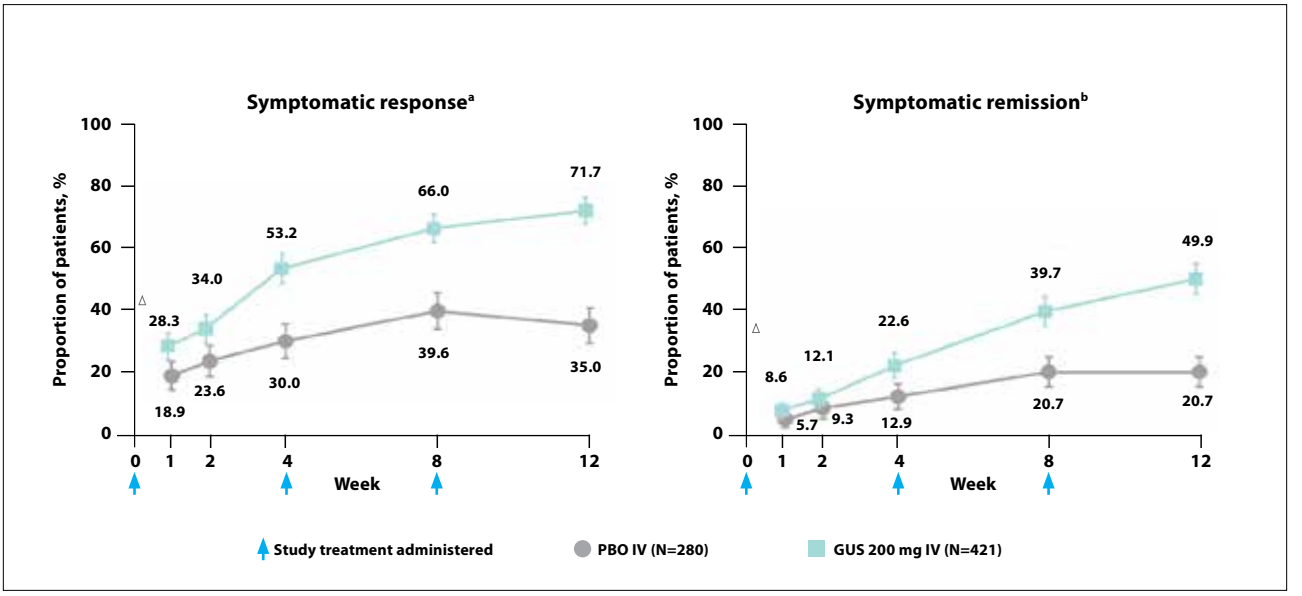

Figure 1. Symptomatic outcomes of patients with moderately to severely active ulcerative colitis who received guselkumab through week 12 from the QUASAR phase 3 induction study.

[a]A decrease from induction baseline in the symptomatic Mayo score by ≥30% and ≥1 point, with either a ≥1 point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1. The symptomatic Mayo score was defined as the sum of the stool frequency and the rectal bleeding subscores.

[b]A stool frequency subscore of 0 or 1 and not increased from baseline, and a rectal bleeding subscore of 0.

GUS, guselkumab; IV, intravenous; PBO, placebo.

Adapted from Lichtenstein et al. Abstract 34. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[4]

tion of UC disease of 7.52 years (SD, 7.282), and 47.8% had extensive disease. The mean modified Mayo score was 6.9 (SD, 1.10), and most patients (64.5%) had a severe modified Mayo score of 7 to 9; 67.9% of patients had a severe Mayo endoscopic subscore of 3. At baseline, 72.5%, 43.1%, and 20.8% were using oral aminosalicylates, oral corticosteroids, and immunosuppressants, respectively. About one-half of patients (49.1%) had a history of inadequate response or intolerance to advanced therapies. Of these 344 patients, most had a history of inadequate response or intolerance to TNFα antagonists (87.5%), followed by integrin receptor antagonists (54.1%), and JAK inhibitors (18.0%). A total of 163 patients (47.4%) had a history of inadequate response or intolerance to 2 or more advanced therapy classes.

Symptomatic response was defined as a decrease from induction baseline in the symptomatic Mayo score by at least 30% and at least 1 point, with a 1 or greater point decrease from baseline in the RBS or an RBS of 0 or 1. The symptomatic Mayo score was defined as the sum of the stool frequency and the RBS. By week 12, 71.7% of guselkumab-treated patients had achieved a symptomatic response, compared with 35.0% of placebo-treated patients (P<.001) (Figure 1). This improvement in symptomatic response was evident as early as week 1 and 2, with a statistically significant improvement with guselkumab vs placebo (week 1: 28.3% vs 18.9%, P<.01; week 2: 34.0% vs 23.6%; P<.01). Symptomatic remission was defined as a stool frequency subscore of 0 or 1 and not increased from baseline, and an RBS of 0. A statistically significant difference in the proportion of patients who achieved symptomatic remission in the guselkumab arm vs the placebo arm was observed by week 4 (22.6% vs 12.9%; P<.001) and maintained through week 12 (49.9% vs 20.7%; P<.001). Both stool frequency and rectal bleeding outcomes were improved with guselkumab compared with placebo as early as week 1 and increased over time. At week 12, significantly more patients in the guselkumab arm had achieved a stool frequency subscore (SFS) of 0 or 1 (60.1% vs 31.8%, P<.001) and there was also a significant improvement in the absolute stool number between the guselkumab and placebo arms (-3.15 vs -1.36). At week 12, significantly more patients in the guselkumab arm had achieved an RBS of 0 (64.6% vs 28.6%; P<.001), and there was also a significant improvement in the absolute RBS (-1.2 vs -0.6; P<.001).

The study investigators concluded that these outcomes were clinically relevant in this patient population, showing a relatively rapid onset of benefit with guselkumab induction therapy in patients with refractory moderately to severely active UC.

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Comparative Effectiveness of Upadacitinib vs Ustekinumab for Ulcerative Colitis at 8-16 Weeks: A Multicenter Retrospective Cohort Study

Several advanced therapies for UC are now available that include ustekinumab, an inhibitor of IL-12/23 p40, and JAK inhibitors such as upadacitinib.[1,2] However, no clinical randomized trials have directly compared these agents. Real-world data have suggested similar effectiveness of tofacitinib and ustekinumab in the treatment of UC, but the comparative effectiveness of upadacitinib to ustekinumab has not been established.[3] At the ACG 2023 Annual Scientific Meeting, Dalal and colleagues presented data from a multicenter retrospective cohort study of adults with UC who initiated treatment with either upadacitinib or ustekinumab for UC between January 2021 and February 2023.[4] This study compared both clinical and endoscopic outcomes at weeks 8 to 16 among these patients.

This cohort included 70 patients treated with upadacitinib and 148 patients treated with ustekinumab. Baseline demographics were overall similar between groups. However, an important difference was the proportion of patients with experience with advanced therapies, which was higher in the upadacitinib group (100%) than in the ustekinumab group (79.1%). A similar proportion of patients in each group were receiving prednisone or oral budesonide at baseline (54.3% and 55.4%, respectively).

The analysis utilized inverse probability of treatment-weighted logistic regression to adjust for baseline differences in the treatment groups. Covariate balance was confirmed by requiring a standardized mean difference of less than 10%. The primary endpoint was clinical response at 8 to 16 weeks; secondary endpoints included corticosteroid-free clinical remission at 8 to 16 weeks and endoscopic response and remission within 52 weeks.

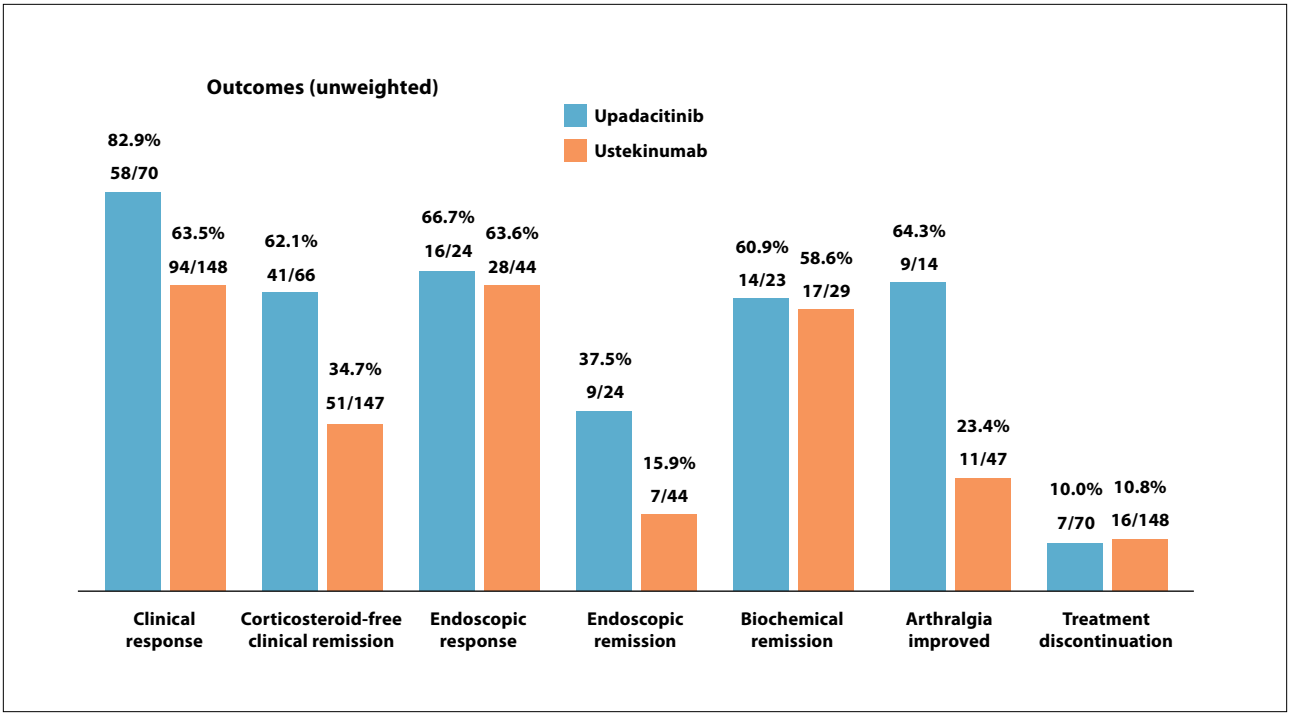

Figure 2. Outcomes from a multicenter retrospective cohort study comparing patients with ulcerative colitis treated with upadacitinib vs ustekinumab.

Adapted from Dalal et al. Abstract 72. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[4]

The unadjusted outcomes showed that a relatively higher proportion of patients in the upadacitinib group than in the ustekinumab group achieved the outcomes of clinical response (82.9% vs 63.5%, respectively), corticosteroid-free clinical remission (62.1% vs 34.7%, respectively), and endoscopic remission (37.5% vs 15.9%, respectively), as well as improved arthralgia (64.3% vs 23.4%, respectively) (Figure 2). Similar proportions of patients achieved the outcomes of endoscopic response (66.7% vs 63.6%, respectively), biochemical remission (60.9% vs 58.6%, respectively), and treatment discontinuation (10.0% vs 10.8%, respectively). Treatment discontinuation in both groups was primarily owing to nonresponse.

The results of the weighted logistic regression demonstrated a higher weighted odds ratio (OR) for clinical response (OR, 2.39; 95% CI, 1.04-5.49), corticosteroid-free clinical remission (OR, 3.17; 95% CI, 1.55-6.46), and endoscopic remission (OR, 5.10; 95% CI, 1.34-19.3), all of which favored upadacitinib over ustekinumab. There were similar odds of endoscopic response in both groups (OR, 1.49; 95% CI, 0.45-4.95).

The study investigators found higher odds of clinical response and corticosteroid-free remission at 8 to 16 weeks and endoscopic remission within 52 weeks for upadacitinib compared with ustekinumab. The main strength of the study was the successful balancing of covariates using inverse probability of treatment-weighted logistic regression, although limitations included the retrospective design. Additionally, the investigators noted there were incomplete data for certain markers of disease severity, such as C-reactive protein. Overall, these results suggest that among a largely bio-exposed population of patients with UC, upadacitinib may be more effective than ustekinumab for the induction of remission.

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Insights From Studies on Ustekinumab: Efficacy, Long-Term Outcomes, and Treatment Persistence in Patients With Ulcerative Colitis

The UNIFI study showed that patients who achieved both histologic and endoscopic improvement of the mucosa (histologic-endoscopic mucosal improvement [HEMI]) following ustekinumab induction therapy proceeded to have higher rates of 1-year clinical remission and 3-year symptomatic remission than patients with histologic or endoscopic improvement alone.[1,2] The UNIFI long-term extension study, presented by Peyrin-Biroulet and colleagues, further assessed ustekinumab as maintenance therapy over 4 years, and focused on patients who achieved symptomatic remission with or without HEMI.[3]

The proportion of patients in symptomatic remission through 200 weeks (approximately 4 years) of ustekinumab treatment was highest among those patients who achieved disease clearance following induction. A total of 73.4% of patients who showed disease clearance after induction achieved symptomatic remission at 200 weeks, compared with 53.5% of patients who achieved symptomatic remission without HEMI and 45.1% of patients who achieved neither symptomatic remission nor HEMI (Figure 3). Similar outcomes were shown for patients who achieved corticosteroid-free symptomatic remission at week 200 (70.9% of patients who achieved disease clearance compared with 52.1% of patients who achieved symptomatic remission without HEMI and 42.7% of patients who achieved neither symptomatic remission nor HEMI).

The time to treatment failure was prolonged in patients who achieved disease clearance following ustekinumab induction, which was significantly longer than in patients in symptomatic remission without HEMI (P=.043), who in turn had significantly longer time to treatment failure than patients in neither symptomatic remission nor HEMI (P=.004). Similarly, the rates of Inflammatory Bowel Disease Questionnaire (IBDQ) remission (defined as a total IBDQ score ≥170) at week 200 were highest in those patients with disease clearance after induction therapy (58.2%), compared with patients in symptomatic remission without HEMI (46.5%) and neither symptomatic remission nor HEMI (42.7%).

A separate study presented by Zhdanava and colleagues evaluated treatment persistence during the maintenance phase of therapy among patients with UC who were naive to biologic therapy when they initiated

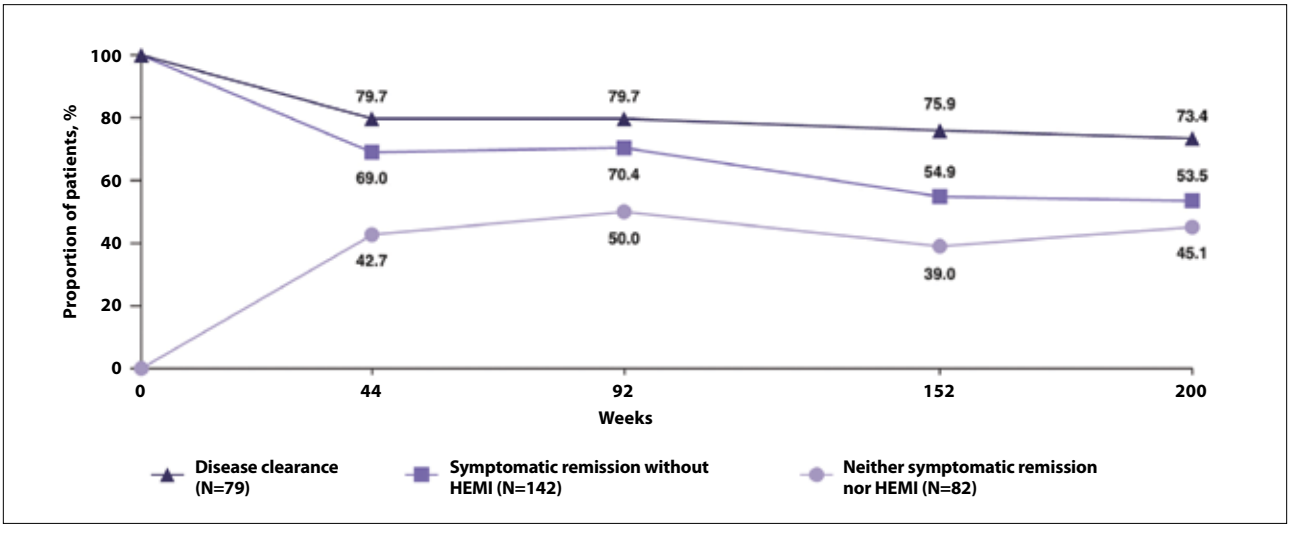

Figure 3. The proportion of patients with ulcerative colitis in symptomatic remission through week 200[a-e] of UST treatment from the UNIFI study.

[a]Included patients randomized to receive SC UST at week 0 of maintenance.
[b]Patients with insufficient data to evaluate histologic improvement status at the end of induction were excluded.
[c]Patients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.
[d]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or used a rescue medication after a clinical flare or discontinued study agent owing to lack of therapeutic effect or owing to an AE of worsening of UC before week 44 were considered not to be in symptomatic remission at week 44.
[e]Patients who had an ostomy or colectomy or discontinued study agent due to lack of therapeutic effect or owing to an AE of worsening of UC after week 44 and before the designated visit were considered not to be in symptomatic remission.
AE, adverse event; HEMI, histo-endoscopic mucosal improvement; SC, subcutaneous; UC, ulcerative colitis; UST, ustekinumab.
Adapted from Peyrin-Biroulet et al. Abstract P2203. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[3]

treatment with either ustekinumab or adalimumab (the index biologic therapy).[4] Persistence is considered an important outcome reflective of both the efficacy and safety of a biologic therapy.[5,6] This study had a retrospective cohort design and used US administrative claims data. Several measures of persistence were assessed as study outcomes.

Persistence on the index biologic was defined as the absence of index biologic therapy exposure gap between the end of supply and the date of next claim or the end of follow-up. The exposure gap was greater than 120 days for ustekinumab (based on twice the duration of the ustekinumab maintenance cycle) and greater than 60 days for adalimumab (based on a maintenance cycle of 2 weeks, with dispensing typically of 2 doses covering 4 weeks). The probability of persistence on the index biologic was significantly higher with ustekinumab compared with adalimumab (83.8% vs 57.6%; hazard ratio [HR], 3.09; 95% CI, 2.29-4.16; log-rank P<.001). Persistence while corticosteroid free was a composite outcome defined as the absence of index biologic therapy exposure gap and of corticosteroid used for at least 14 consecutive days of supply after day 90 postindex. The probability of persistence while corticosteroid free was also higher for ustekinumab than adalimumab (64.9% vs 42.4%; HR, 2.00; 95% CI, 1.63-2.45; log-rank P<.001). Persistence while on monotherapy was a composite outcome defined as the absence of index biologic therapy exposure gap and of immunomodulator (azathioprine, cyclosporine, mercaptopurine, methotrexate, or tacrolimus) and non-index advanced therapy use. Persistence while on monotherapy was significantly higher among ustekinumab-treated patients than adalimumab-treated patients (78.2% vs 50.9%; HR, 2.67; 95% CI, 2.07-3.44; log-rank P<.001).

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Symptomatic Improvement Observed Within 2 Days of Etrasimod Induction Therapy: Results From ELEVATE UC 52 and ELEVATE UC 12 Studies in Patients With Ulcerative Colitis

The time from treatment initiation to symptom relief is a key outcome for patients with UC, which can be used to guide therapeutic decisions.[1] Patient-reported outcomes of interest to assess symptom relief include rectal bleeding and stool frequency, both of which can be informed by the daily use of patient e-diaries.[2] Dubinsky and colleagues presented results from a study to evaluate the speed of onset of symptomatic improvement as measured by RBS and SFS, using these e-diaries from the ELEVATE UC program.[3] The ELEVATE UC program was designed to evaluate etrasimod, an oral, once-daily, selective sphingosine 1-phosphate (S1P) receptor modulator approved for the treatment of moderately to severely active UC.[1,4,5] The efficacy and safety of etrasimod have been shown in the ELEVATE UC 52 and ELEVATE UC 12 studies, which demonstrated that higher rates of clinical remission and response during the 12-week induction periods were achieved with etrasimod vs placebo.[4]

For this daily diary analysis, data from patients in both ELEVATE studies were pooled and used to calculate daily Mayo RBS and SFS, partial modified Mayo score (RBS + SFS), and change from baseline during the first 28 days of therapy. At baseline, each of these measures were found to be balanced across patients receiving etrasimod or placebo.

Symptomatic response was defined as 30% or greater change from baseline (decrease in partial modified Mayo score), and symptomatic remission was defined as an RBS of 0 and an SFS of 0 or 1 with at least 1-point improvement from baseline.[3] The proportions of patients achieving symptomatic response and symptomatic remission were greater among patients receiving etrasimod compared with placebo (Figure 4). Differences were based on estimated common risk difference using the Mantel-Haenszel weights and stratified by actual naive to biologic/JAK inhibitor therapy at trial entry, actual baseline corticosteroid use, and actual baseline disease activity. The differences between the 2 treatment groups became significant from day 2 for symptomatic response (difference, 5.56; 95% CI, 0.79-10.33; P=.022) and day 11 for symptomatic remission (difference, 4.69; 95% CI, 0.36-9.03; P=.034).

Rectal bleeding remission was defined as an RBS of 0, and stool frequency normalization was an SFS of 0. The proportion of patients achieving rectal bleeding remission and stool frequency normalization was increased

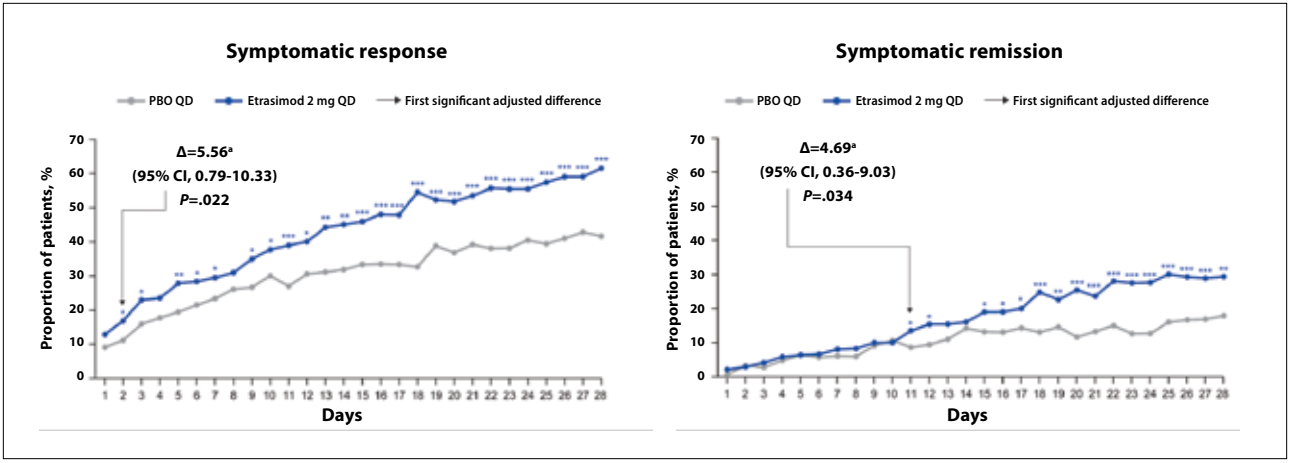

Figure 4. The proportion of patients with ulcerative colitis achieving symptomatic response and symptomatic remission from the ELEVATE UC 52 and ELEVATE UC 12 studies.

*P<.05; **P<.01; ***P<.001

ªFirst day of a significant difference from PBO.

PBO, placebo; QD, once daily.

Adapted from Dubinsky et al. Abstract 33. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[3]

in patients treated with etrasimod vs placebo. The differences between treatment groups became significant from day 15 for rectal bleeding remission (difference, 6.33; 95% CI, 0.14-12.51; *P*=.045) and day 3 for stool frequency normalization (difference, 3.51; 95% CI, 0.87-6.14; *P*=.009).

The study investigators concluded that the phase 3 ELEVATE UC trials demonstrated clinically relevant symptomatic improvements that were apparent in etrasimod-treated patients as early as day 2 of induction therapy. These findings suggested that etrasimod has a rapid treatment effect with early symptomatic response, although these results are noted to be limited owing to the nature of the post hoc analysis.

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Upadacitinib Safety and Time to Relapse: Analysis of Phase 3 Maintenance Studies, U-ACHIEVE and U-ENDURE, in Patients With Moderately to Severely Active Ulcerative Colitis

In a poster presented by Panaccione and colleagues, the safety of upadacitinib in patients with inflammatory bowel disease was analyzed through a pooled analysis of 2 phase 3 maintenance studies, U-ACHIEVE and U-ENDURE.[1] Both studies demonstrated the efficacy and safety of upadacitinib vs placebo as maintenance treatment in either moderately to severely active UC (U-ACHIEVE) or Crohn's disease (U-ENDURE).[2,3] Both trials examined 2 doses of upadacitinib maintenance therapy (15 mg once daily or 30 mg once daily), each administered for up to 52 weeks in patients who achieved a clinical response to 8 weeks of induction therapy (45 mg once-daily upadacitinib). This pooled analysis was conducted to better understand the long-term safety data available from these trials.

The integrated patient population consisted of 471 patients treated with 15 mg upadacitinib (353.1 patient-years), 480 patients treated with 30 mg upadacitinib (395.7 patient-years), and 468 patients treated with placebo (246.4 patient-years). Overall, the investigators concluded that there were no new safety signals observed in this integrated safety population. The exposure-adjusted event rate (EAER) of treatment-emergent adverse events (TEAEs), calculated as the number of events per 100 patient-years, were higher with placebo (EAER, 482.9) compared with either 15 mg upadacitinib (EAER, 330.2) or 30 mg upa-

Table. Overview of Treatment Adverse Events at Week 52 From the U-ACHIEVE and U-ENDURE Studies in Patients With Moderately to Severely Active Ulcerative Colitis or Crohn's Disease

	UC data			CD data			Integrated safety (UC + CD) data		
Parameter, n (%)	PBO n=245	UPA 15 mg QD n=250	UPA 30 mg QD n=251	PBO n=223	UPA 15 mg QD n=221	UPA 30 mg QD n=229	PBO n=468	UPA 15 mg QD n=471	UPA 30 mg QD n=480
PY	135.0	199.4	218.5	111.5	153.7	117.2	246.4	353.1	395.7
	Exposure-adjusted event rates, E (E/100 PY)								
Any AE	674 (499.4)	626 (313.9)	691 (316.2)	516 (462.8)	540 (351.3)	575 (324.5)	1190 (482.9)	1166 (330.2)	1266 (319.9)
Any serious AE	28 (20.7)	24 (12.0)	22 (10.1)	41 (36.8)	37 (24.1)	35 (19.7)	69 (28.0)	61 (17.3)	57 (14.4)
Any severe AE	29 (19.3)	18 (9.0)	23 (10.5)	39 (35.0)	38 (24.7)	31 (17.5)	56 (15.9)	56 (15.9)	54 (13.6)
Any AE leading to discontinuation of study drug	26 (19.3)	11 (5.5)	19 (8.7)	8 (7.2)	19 (12.4)	14 (7.9)	30 (8.5)	30 (8.5)	33 (8.3)
Any AE with possibility of being related to the study drug	192 (142.3)	178 (89.3)	233 (106.6)	134 (120.2)	139 (90.4)	147 (82.9)	317 (89.8)	317 (89.8)	380 (96.0)
COVID-19 infection-related AE	9 (6.7)	6 (3.0)	13 (5.9)	11 (9.9)	16 (10.4)	23 (13.0)	22 (6.2)	22 (6.2)	36 (9.1)
Any deaths	0	0	0	0	0	0	0	0	0

AE, adverse event; CD, Crohn's disease; E, events; PBO, placebo; PY, patient-years; QD, once daily PBO; UC, ulcerative colitis; UPA, upadacitinib.
Adapted from Panaccione et al. Abstract P3631. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[1]

dacitinib (EAER, 319.9) (Table). This trend was also observed for patients with a serious TEAE (placebo: EAER, 28.0; 15 mg upadacitinib: EAER, 17.3; 30 mg upadacitinib: EAER, 14.4) as well as a severe TEAE (placebo: EAER, 27.6; 15 mg upadacitinib: EAER, 15.9; 30 mg upadacitinib: EAER, 13.6). Further, the rate of TEAEs resulting in discontinuation of upadacitinib was highest with placebo (EAER, 13.8) compared with either 15 mg upadacitinib (EAER, 8.5) or 30 mg upadacitinib (EAER, 8.3). Serious infections occurred at a similar EAER. Overall, the most frequently reported infections included nasopharyngitis (EAER, 11.6-14.2), upper respiratory infection (EAER, 6.8-7.3), COVID-19 infection (EAER, 6.9-7.6), herpes zoster infection (EAER, 1.6-7.1), and urinary tract infection (EAER, 2.5-6.1).

A second poster, presented by Dubinsky and colleagues, examined the time to relapse among patients with UC who initially had a response to upadacitinib induction therapy but lost that response over the maintenance period.[4] A total of 681 patients who had an induction response entered the maintenance trial (U-ACHIEVE), of whom 618 comprised this analysis, which included 248 patients classified as induction remitters.

Among induction responders, more patients in the placebo arm (73.1%) experienced a relapse by week 52 than either the 15 mg or the 30 mg upadacitinib arms (32.8% and 20.6%, respectively). Similarly, among induction remitters, more patients in the placebo arm (68.4%) experienced a relapse by week 52 than either the 15 mg or 30 mg upadacitinib arms (23.2% and 16.7%, respectively). The median time to relapse for patients in the placebo arm was 169 days for induction responders and 210 days for induction remitters. The median time to relapse was not estimable for either upadacitinib arm. Overall, compared with placebo, patients treated with either upadacitinib dose had a lower probability of relapse. The HR for 15 mg upadacitinib was 0.30 (95% CI, 0.22-0.41) for induction responders and 0.23 (95% CI, 0.13-0.40) for induction remitters. The HR for 30 mg upadacitinib was 0.18 (95% CI, 0.13-0.25) for induction responders and 0.16 (95% CI, 0.09-0.29) for induction remitters. The investigators concluded these results demonstrated that the probability of relapse with either dose of upadacitinib was lower throughout maintenance than with placebo, for both induction responders and the subset of patients in remission after induction therapy.

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Risankizumab Induction Therapy in Patients With Moderately to Severely Active Ulcerative Colitis: Efficacy and Safety in the Randomized Phase 3 INSPIRE Study

Risankizumab is a humanized monoclonal antibody that binds to the IL-23 p19 subunit, inhibiting IL-23–mediated signaling and the related inflammatory cytokine cascade.[1] The INSPIRE study, a phase 3, double-blind, placebo-controlled trial, was designed to evaluate the efficacy and safety of risankizumab as induction therapy in patients with moderately to severely active UC. In a presentation by Loftus and colleagues, the primary efficacy and safety results at week 12 from the INSPIRE study were reported.[2]

Patients enrolled in INSPIRE had an intolerance or inadequate response to conventional and/or advanced therapies for UC. No prior exposure to ustekinumab or IL-23 inhibitors was permitted. A total of 975 patients comprised the intention-to-treat population; patients were randomized in a 2:1 fashion to either placebo or 1200 mg risankizumab IV administered at weeks 0, 4, 8, and 12. Following induction therapy, responding patients were eligible for enrollment in the COMMAND maintenance study, whereas nonresponding patients were eligible for an additional 12 weeks of induction treatment.

The primary endpoint of clinical remission at week 12 was significantly higher with risankizumab vs placebo (20.3% vs 6.2%; 95% CI, 10.0-18.0; *P*<.00001) (Figure 5). A benefit with risankizumab compared with placebo was observed in patients with an inadequate response to prior nonadvanced therapy (29.7% vs 8.4%) as well as in patients with an inadequate response to prior advanced therapy (11.4% vs 4.3%). The secondary endpoints of clinical response were also significantly improved with risankizumab vs placebo both at week 4 (52.2% vs 30.5%; 95% CI, 15.6-28.1; *P*<.00001) and week 12 (64.3% vs 35.7%; 95% CI, 22.3-34.8; *P*<.00001).

Several measures of endoscopic and histologic improvements at week 12 were also significantly improved with risankizumab compared with placebo. These included endoscopic improvement (36.5% vs 12.1%; 95% CI, 19.3-29.4; *P*<.00001), endoscopic remission (10.6% vs 3.4%; 95% CI, 4.2-10.2; *P*<.00001), HEMI (24.5% vs 7.7%; 95% CI, 12.3-21.0; *P*<.00001), and histologic-endoscopic mucosal remission (HEMR; 6.3% vs 0.6%; 95% CI, 3.5-7.7; *P*<.00001). Risankizumab was associated with improvements in a number of patient-reported outcomes, such as no bowel urgency (44.1% vs 27.7%; 95% CI, 10.3-22.4; *P*<.00001), no nocturnal bowel movements (67.3% vs 43.1%; 95% CI, 17.9-30.5; *P*<.00001), and no abdominal pain (35.8% vs 26.5%; 95% CI, 3.4-15.3; *P*<.00001).

Reported safety results were consistent with the already known toxicity profile of risankizumab across other indications. The 3 most common adverse events (reported by ≥5% in either treatment arm) were COVID-19 infection (4.8% with risankizumab vs 5.9% with placebo), anemia (3.4% vs 6.5%), and worsening of UC (1.7% vs 10.2%). There were no adjudicated cases of major cardiovascular event,

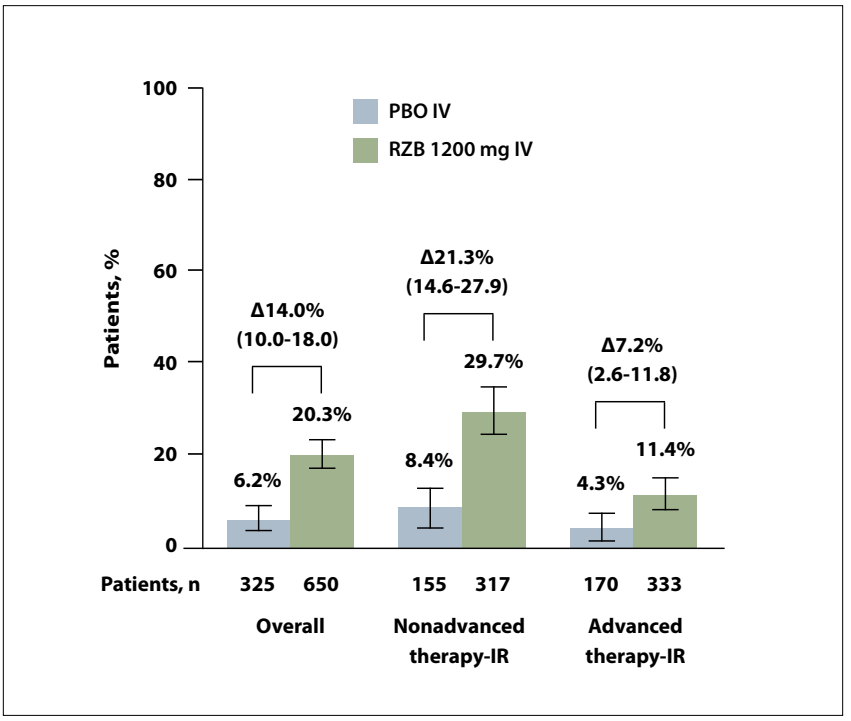

Figure 5. Clinical remission[a] at week 12 of RZB induction therapy in patients with moderately to severely active ulcerative colitis from the phase 3 INSPIRE study.

[a]Clinical remission per Adapted Mayo score: SFS ≤1 and not greater than baseline, RBS of 0, and endoscopic subscores ≤1 without friability. Results reported as adjusted treatment difference RZB vs PBO, % (95 CI) and are based on nonresponder imputation incorporating multiple imputation (NRI-MI) to handle missing data owing to COVID-19 or owing to geopolitical conflict in Ukraine or surrounding areas.

IR, inadequate response; IV, intravenous; PBO, placebo; RBS, rectal bleeding subscore; RZB, risankizumab; SFS, stool frequency subscore.

Adapted from Loftus et al. Abstract 35. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[2]

active tuberculosis, opportunistic infections (excluding tuberculosis and herpes zoster), nonmelanoma skin cancer, serious hypersensitivity reactions, or anaphylactic reactions reported in either treatment group. Overall, 9.4% of patients in the risankizumab arm and 8.0% of patients in the placebo arm experienced an adverse event that was potentially drug related. More patients in the placebo arm experienced a severe or serious adverse event (10.2% for both) vs the risankizumab arm (2.5% and 2.3%, respectively). Discontinuations owing to an adverse event occurred in 3.7% of the placebo arm and 0.6% of the risankizumab arm.

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Two-Year Efficacy and Safety of Mirikizumab Following 104 Weeks of Continuous Treatment: Interim Results From the LUCENT-3 Open-Label Extension Study (Ulcerative Colitis)

Mirikizumab is a humanized monoclonal antibody that specifically binds the p19 subunit of IL-23. The efficacy and safety of mirikizumab in patients with moderately to severely active UC were evaluated in the LUCENT-1 induction trial and LUCENT-2 52-week maintenance trial.[1] Patients with a response to mirikizumab induction therapy were permitted to enroll in LUCENT-2, then were permitted to continue in the open-label, long-term extension study LUCENT-3. Sands and colleagues reported interim results from

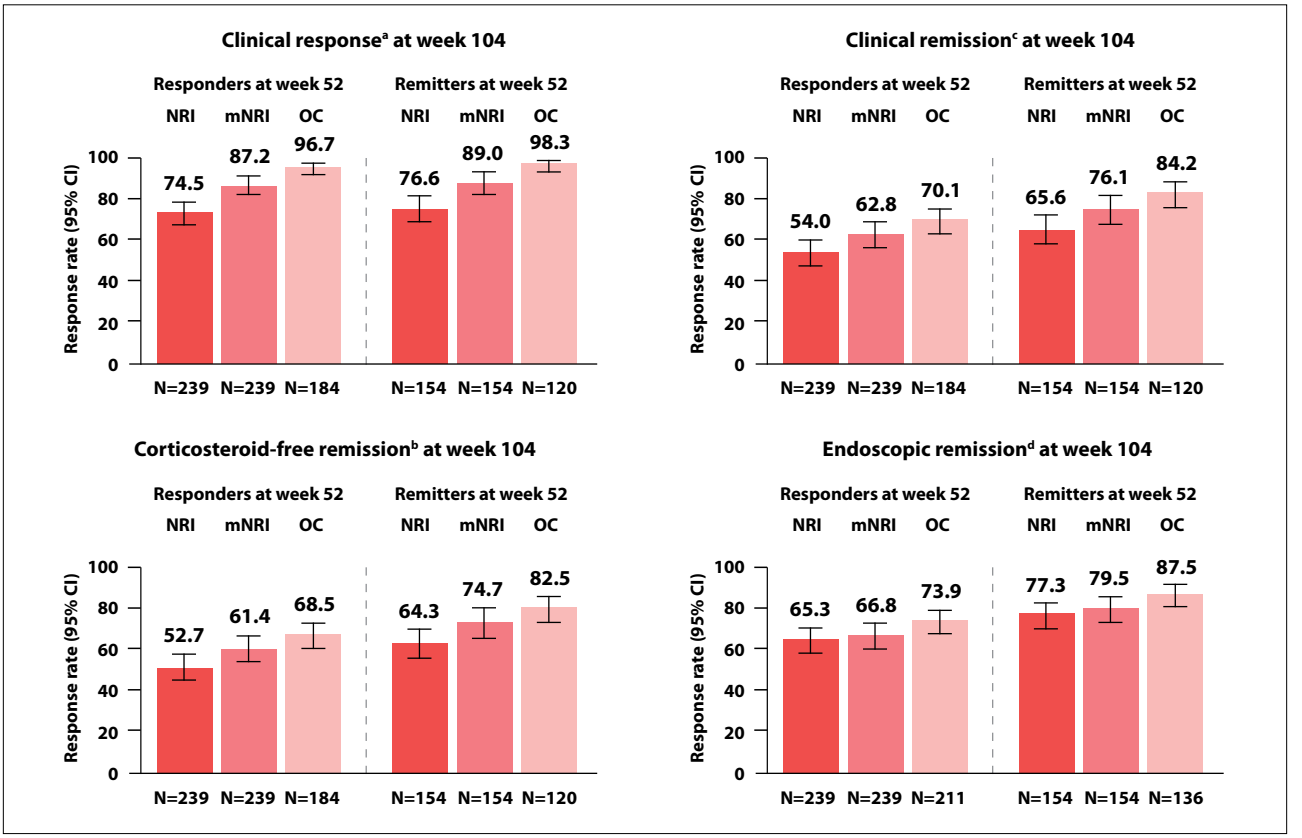

Figure 6. Response and remission rates from the LUCENT-3 trial of patients with ulcerative colitis at week 104 of continuous mirikizumab treatment in the LUCENT-2 responders and remitters, NRI, mNRI, and OC.

[a]Clinical response: ≥2-point and ≥30% decrease in MMS from baseline; RB=0 or 1 or, RB ≥1-point decrease from baseline.

[b]Corticosteroid-free remission: clinical remission at LUCENT-3 week 52 with no corticosteroid use for ≥12 weeks.

[c]Clinical remission: SF=0 or 1 with ≥1-point decrease in MMS from baseline; RB=0; and ES=0 or 1 (excluding friability).

[d]Endoscopic remission: ES=1 or 1 (excluding friability); score ranges from 0 to 4; a lower score indicates less mucosal damage.

ES, endoscopic subscore; MMS, modified Mayo score; mNRI, modified NRI; NRI, nonresponder imputation; OC, observed case; RB, rectal bleeding; SF, stool frequency.

Adapted from Sands et al. Abstract 70. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[2]

LUCENT-3 from 266 patients who had completed a total of 104 weeks of continuous treatment with mirikizumab, administered at 200 mg every 4 weeks as maintenance therapy.[2] The investigators noted that discontinuations or missing data were handled using nonresponder imputation (NRI), modified NRI, and observed case (OC) approaches. NRI is biased to show low remission rates, OC is biased to show high remission rates, and modified NRI uses multiple imputation to balance the bias of NRI and OC. The NRI strategy was primarily used and reported with this current dataset.

Among patients who had a clinical response at week 52, the rate of clinical response at week 104 was 74.5%, and was similar among patients without (77.1%) or with (68.5%) prior biologic failure (Figure 6). Among patients with a clinical remission at week 52, the rate of clinical response at week 104 was 76.6%, and was 75.7% and 78.7% among patients without and with prior biologic failure, respectively.

In patients who had a clinical response at week 52, the rate of clinical remission at week 104 was 54.0%, and was similar among patients without (56.0%) or with (49.3%) prior biologic failure. Among patients with a clinical remission at week 52, the rate of clinical remission at week 104 was 65.6%, and was 67.3% and 61.7% among patients without and with prior biologic failure, respectively.

Similar trends were noted in the outcomes of week 104 symptomatic remission (67.8% in week 52 responders and 74.0% in week 52 remitters) as well as week 104 corticosteroid-free remission (52.7% in week 52 responders and 64.3% in week 52 remitters). Outcomes of week 104 endoscopic remission (65.3% in week 52 responders and 77.3% in week 52 remitters), week 104 HEMI (53.1% in week 52 responders and 66.2% in week 52 remitters), and week 104 HEMR (47.7% in week 52 responders and 59.1% in week 52 remitters) were also reported.

At week 104, similar proportions of patients reported a clinically meaningful improvement in bowel urgency (67.0% of week 52 responders and 67.3% of week 52 remitters) as well as bowel urgency remission (50.2% of week 52 responders and 51.3% of week 52 remitters).

A mixed models for repeated measures analysis was performed to determine the mean change in certain outcomes from baseline. There was little change observed from the beginning of the LUCENT-3 open-label extension study (week 52 of mirikizumab treatment) to week 104 in stool frequency (-1.68 at week 52 to -1.79 at week 104), rectal bleeding (-1.45 to -1.45), abdominal pain (-3.74 to -3.91), and urgency (-4.03 to -4.44).

No new safety signals were reported, and there was a low rate of mirikizumab discontinuation owing to adverse events. The most frequently reported adverse events included COVID-19 infection (12.1%), UC (7.6%), arthralgia (6.2%), headache (6.2%), and nasopharyngitis (5.9%).

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Long-Term Clinical, Endoscopic, and Symptomatic Outcomes of Treatment With Ozanimod: Interim Analysis of the True North Open-Label Extension Study

Ozanimod is a selective $S1P_{1,5}$ receptor modulator that was shown to be effective and safe for the treatment of patients with moderately to severely active UC in the phase 3 True North trial.[1] Two presented posters summarized data from an interim analysis of the True North open-label extension study.

The objective of the first study, presented by Afzali and colleagues, was to evaluate the durability of ozanimod efficacy (up to week 94 in the open-label study) among patients who were clinical responders and who did and did not achieve clinical remission at week 52 in True North.[2] At the time of data cutoff, all 83 clinical responders/remitters and 43 patients who were clinical responders/nonremitters had completed week 94 of the open-label extension study or discontinued the study. This interim analysis found that, compared with clinical responders/nonremitters, more clinical responders/remitters achieved all the endpoints evaluated at weeks 46 and 94 of the open-label extension trial. This was true for both the OC and the NRI analysis. In the OC analysis at week 94, 75.9% of clinical responders/remitters had achieved clinical remission compared with 55.6% of clinical responders/nonremitters (Figure 7). Further, 94.4% of clinical responders/remitters had achieved clinical response at week 94 vs 85.2% of clinical responders/nonremitters. In addition, higher proportions of clinical responders/remitters achieved and maintained endoscopic improvement and corticosteroid-free remission for an additional 2 years compared with clinical responders/nonremitters. Discontinuations owing to TEAEs occurred in 4.8% of clinical responders/remitters and in 8.3% of clinical responders/nonremitters.

The second study, presented by

Abreu and colleagues, investigated whether achievement of increasingly objective endpoints at week 52 of True North impacted the durability of symptomatic and clinical outcomes in patients treated with continuous ozanimod throughout the open-label extension study.[3] These endpoints included clinical remission, endoscopic improvement, endoscopic remission, histologic remission, mucosal healing, and stringent mucosal healing. The investigators concluded that, in the open-label extension trial, maintenance of clinical response, clinical remission, and corticosteroid-free remission was not significantly impacted by achievement of endpoints

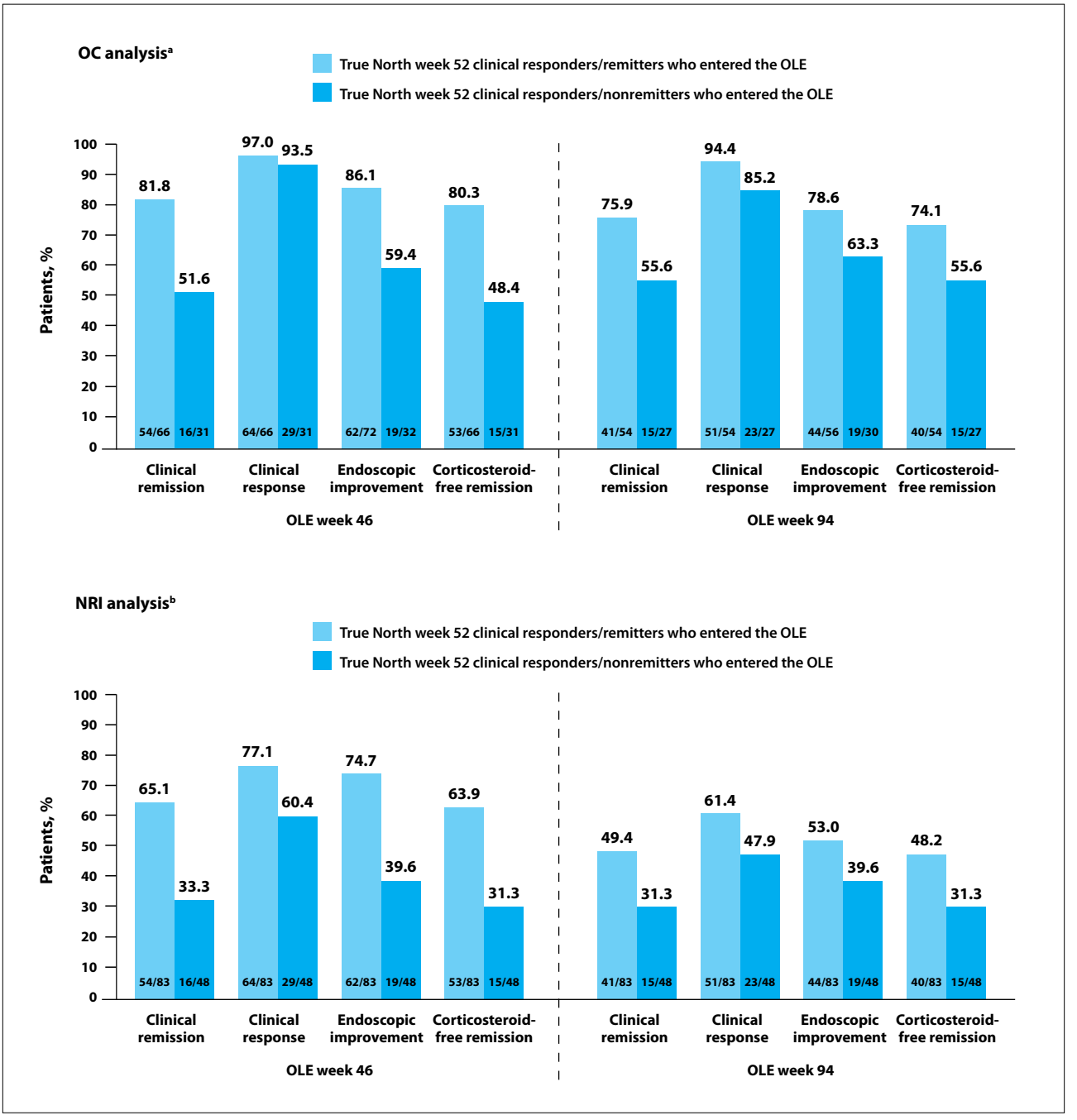

Figure 7. Remission and response rates in the OC analysis and NRI analysis of ozanimod treatment at OLE weeks 46 and 94 in patients with moderately to severely active ulcerative colitis from the phase 3 True North study.

[a]Denominators for the OC analyses were based on the numbers of patients who completed OLE week 46 or OLE week 94 and had data available for the endpoints in question.
[b]Denominators for the NRI analyses were based on the numbers of patients who completed OLE week 46, completed OLE week 94, or discontinued ozanimod treatment.
OC, observed case; OLE, open-label extension; NRI, nonresponder imputation.
Adapted from Afzali et al. Abstract P0675. Presented at: ACG 2023; October 20-25, 2023; Vancouver, Canada.[2]

of increasing objectivity. However, they found that achievement of clinical remission to warrant entry into the open-label extension trial had an incremental benefit over achievement of clinical response for the outcomes of maintenance of clinical remission and corticosteroid-free remission at both week 46 and week 94. Overall, clinical outcomes were sustained from week 46 to week 94 of the open-label extension, regardless of the endpoint achieved at study entry. Symptomatic clinical response was maintained throughout the open-label extension study, with continued response at week 94 in greater than 92% (by OC analysis) of patients in all groups at entry. Additionally, improvements in both RBS and SFS were sustained through week 94 regardless of the patient disposition at entry into the open-label extension.

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Highlights in Ulcerative Colitis From the American College of Gastroenterology 2023 Annual Scientific Meeting: Commentary

Gary R. Lichtenstein, MD
Professor of Medicine
Vice Chief, Division of Gastroenterology
Development and Philanthropy
Emeritus Director, Center for Inflammatory Bowel Disease
The Raymond and Ruth Perelman School of Medicine of the University of Pennsylvania
University of Pennsylvania Health System
Hospital of the University of Pennsylvania
Gastroenterology Division, Department of Internal Medicine
Perelman Center for Advanced Medicine
Philadelphia, Pennsylvania

The American College of Gastroenterology (ACG) 2023 Annual Scientific Meeting, held in Vancouver, Canada, in October 2023, provided valuable insights into the management of ulcerative colitis (UC). Data focused on the efficacy, safety, and utilization of treatment options among several single-agent therapies, such as guselkumab, ustekinumab, etrasimod, upadacitinib, risankizumab, mirikizumab, and ozanimod.

Guselkumab

When caring for patients with inflammatory bowel disease (IBD), it is important to keep in mind the patient's disease activity and the presence or absence of extraintestinal manifestations. The severity of the disease is as important as the rapidity with which significant clinical response or remission needs to be reached while treating a patient. Therefore, what is deemed appropriate treatment depends on the patient's clinical presentation. In general, it is preferred to use medications that are effective and have a rapid onset of efficacy. To do so, we are constantly trying to improve the way we deliver care to patients, particularly with novel therapeutics.

One such agent that was presented at the ACG meeting is guselkumab, a selective p19 inhibitor of interleukin-23 (IL-23).[1] At the ACG meeting, I presented data from the phase 3 QUASAR induction study on early symptomatic improvement with guselkumab induction in patients with moderately to severely active UC. The findings revealed that the use of guselkumab induction at 200 mg intravenously (IV) was effective in improving symptoms, starting as early as week 1 after the first dose. The symptomatic improvements increased through week 12, with the goal of therapy being rapid improvement. What we could not determine from the study is whether we could completely avoid the use of corticosteroids, given their well-known

potential side effects. Given the potential adverse events that could arise with the use of corticosteroids in patients with IBD, I envision a future study looking at a prospective randomized controlled study evaluating patients' ability to completely avoid the use of corticosteroids while being treated with placebo or active guselkumab therapy. We do have other agents that are effective and treat patients rapidly, including infliximab as salvage therapy in hospitals for patients with acute severe colitis. We also have preliminary data on the efficacy of tofacitinib with clinical response as early as day 3, and the efficacy of upadacitinib as early as day 1.[2-5] These data are exciting and potentially a game-changer for future medical therapeutic interventions.

Ustekinumab vs Upadacitinib

A multicenter, retrospective cohort study compared the effectiveness of ustekinumab, a monoclonal antibody directed against IL-12 and IL-23, with that of upadacitinib, a Janus kinase inhibitor, in patients with UC between weeks 8 to 16, evaluating endoscopic outcomes post-induction therapy.[6] Conducted at 2 centers, the primary endpoint was clinical response between week 8 and week 16, with a secondary endpoint of corticosteroid-free clinical remission within that same timeframe as well as endoscopic response and remission within 1 year. This study showed significantly higher odds of clinical response, corticosteroid-free clinical remission at weeks 8 to 16, and endoscopic remission within 52 weeks for upadacitinib vs ustekinumab. However, the study's limitations include its retrospective nature, incomplete data regarding certain disease severity markers, and a relatively short-term follow-up. Nonetheless, the study provides an initial insight into whether a signal exists, and further investigation is warranted. Recently, a network meta-analysis demonstrated that upadacitinib may prove to be more effective than ustekinumab for induction of response and remission in patients with UC.[7]

In the United States, gaining access to upadacitinib typically requires failing an antitumor necrosis factor agent, per the US Food and Drug Administration (FDA). Although upadacitinib has some issues, its efficacy is excellent and is considered a potent agent. Similarly, ustekinumab demonstrates significant effectiveness. Therefore a clinician must personally determine the most suitable approach for the clinical scenario and specific patient.

Ustekinumab Monotherapy

A presentation by Dr Sands examined the use of ustekinumab monotherapy for patients with UC from the UNIFI study, which focused on the association between efficacy and long-term outcomes.[8] In the study, patients were randomized to receive IV ustekinumab or placebo. Following the IV induction, they received subcutaneous ustekinumab at 90 mg every 12 or 8 weeks or placebo, and were then enrolled in the maintenance trial. Notably, the FDA-approved dose in the United States is the 8-week regimen, not the 12-week regimen. Observing the 4-year results, the patients who experienced the best outcomes were those who had disease clearance. This group exhibited histologic-endoscopic mucosal improvement (HEMI) and symptomatic remission shortly after induction. Patients who attained disease clearance 8 weeks after the IV induction showed greater long-term symptomatic remission outcomes and experienced a longer time before treatment failure compared with patients who achieved symptomatic remission without HEMI, or patients who had neither symptomatic remission nor HEMI after induction. Early positive responses across all factors led to more durable responses, which, although expected, is valuable to articulate and present in the literature. The beauty of the IL-23 antagonist ustekinumab lies in its exceptional and durable

ABSTRACT SUMMARY A Nationwide Comparison of Ustekinumab, Vedolizumab, and Adalimumab on Infections, Vascular Disorders, and Neuromusculoskeletal Adverse Events in Ulcerative Colitis Patients: A Pharmacovigilance Investigation

A nationwide cohort of patients with UC were evaluated in a study by Miranda and colleagues, in which the safety profiles of 3 biologic agents were examined (ustekinumab, vedolizumab, and adalimumab) (Poster 2191). The US Food and Drug Administration's Adverse Event Reports System was queried for each drug, resulting in a dataset of 34,418 reported adverse event cases among patients with UC. Patients with UC were significantly more likely to develop an infection while on ustekinumab therapy compared with adalimumab therapy (relative risk [RR], 1.20; 95% CI, 1.06-1.35; $P<.05$); a similar outcome was observed with vedolizumab (RR, 1.22; 95% CI, 1.16-1.28; $P<.001$). Significantly fewer patients treated with ustekinumab vs adalimumab experienced vascular complications (RR, 0.51; 95% CI, 0.35-0.74; $P<.001$) and musculoskeletal complications (RR, 0.52; 95% CI, 0.41-0.65; $P<.001$). Compared with adalimumab, nervous system complications were significantly reduced for ustekinumab (RR, 0.76; 95% CI, 0.63-0.91; $P<.001$) and vedolizumab (RR, 0.83; 95% CI, 0.78-0.89; $P<.001$)

ABSTRACT SUMMARY Cumulative Response to Guselkumab Through Week 24 of Induction in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 QUASAR Induction Study

The phase 3 QUASAR induction study assessed the efficacy and safety of the IL-23 p19 subunit antagonist guselkumab among patients with moderately to severely active UC who had an inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressants, and/or advanced therapies. In a poster presented by Rubin and colleagues, the cumulative response and safety results of continued treatment with guselkumab for up to 24 weeks was reported (Poster 0726). Among patients who were treated with guselkumab who did not achieve a response at week 12, more than one-half (55%) achieved a clinical response at week 24 with continued guselkumab treatment. Continued treatment with guselkumab provided a clinical benefit to patients regardless of prior exposure to advanced therapies. No new safety signals were reported in this long-term follow-up compared with the first 12 weeks of guselkumab treatment.

responses. Patients who initially respond to treatment tend to maintain that response. This is something we have seen with other IL-23 selective antagonists, including guselkumab and mirikizumab. Notably, mirikizumab recently gained regulatory approval for the treatment of UC. Patients who respond to therapy with mirikizumab within a short time can be assured of maintaining their favorable clinical state.

Ustekinumab vs Adalimumab

Evaluating therapeutic persistence in real-world scenarios is crucial to understanding the duration of drug usage after treatment begins. Presented at the ACG meeting, a study by Zhdanava and colleagues assessed the effectiveness and real-world treatment persistence among bio-naive patients with UC who were initiated with ustekinumab or adalimumab treatment.[9] The study was a retrospective analysis of the IQVIA PharMetrics Plus database, encompassing an overall assessment of 371 patients in the ustekinumab cohort and 1726 in the adalimumab cohort. The patients receiving ustekinumab were more likely to be persistent on medication, including persistence while corticosteroid free and also while on monotherapy ustekinumab, compared with patients treated with adalimumab. This durable and sustained treatment is a desirable outcome when initiating a medication. This outcome is also not surprising, considering the characteristics of the IL-12/23 inhibitors, which are known for their ability to sustain durable responses. After a patient enters a state of response or remission, they tend to maintain it over time.

Etrasimod

Dr Dubinsky presented a study showcasing symptomatic improvement within 2 days on etrasimod induction from the ELEVATE UC 52 and the ELEVATE UC 12 studies evaluating patients with UC.[10] This study underscored the desire for our medical therapies to have rapid responses from specific agents, aiming to potentially reduce corticosteroid exposure, improve patients' quality of life, and facilitate a faster recovery. Conducted as a post hoc analysis of phase 3 trials, the findings revealed early improvement among patients receiving etrasimod vs placebo, with noticeable differences starting only 2 days after treatment initiation, suggesting a rapid onset of efficacy. But what proportion of patients responded positively to this treatment within the 2-day timeframe? Answering this question will be crucial, because if most patients do not respond, the advantage of using this treatment may be limited. Further insights are eagerly awaited.

Upadacitinib

Dr Panaccione presented data on the safety profile of upadacitinib in IBD through a pooled analysis of 2 phase 3 maintenance studies: U-ACHIEVE and U-ENDURE.[11] These studies

ABSTRACT SUMMARY Endoscopic and Histologic Remission After 2 Years Treatment With Mirikizumab in Patients With Moderately-to-Severely Active Ulcerative Colitis

Magro and colleagues provided results of endoscopic and histologic remission following 2 years of treatment with mirikizumab in patients with moderately to severely active UC treated in the long-term, open-label extension trial LUCENT-3 (Poster 2204). The study authors found that several histologic and endoscopic outcomes were sustained after 2 years of mirikizumab treatment, including histologic improvement (59.4%), histologic remission (51.9%), endoscopic remission (65.3%), HEMI (53.1%), HEMR (47.7%), endoscopic normalization (28.9%), and alternate HEMR (24.7%). These outcomes were sustained regardless of prior biologic or tofacitinib failure.

ABSTRACT SUMMARY Real-World Clinical, Endoscopic, and Safety Outcomes After Upadacitinib Induction for Ulcerative Colitis: A Multicenter Retrospective Cohort Study

Dalal and colleagues reported real-world outcomes from a retrospective cohort study of 76 patients with UC who had initiated treatment with upadacitinib induction therapy between March 2022 and February 2023 at 2 large academic institutions (Poster 3556). Corticosteroid-free clinical remission, the primary outcome, was achieved in 64.0% of the cohort at a follow-up visit between 8 to 16 weeks after upadacitinib induction. Clinical response was achieved in 84.2% of patients, biochemical remission in 88.2% of patients, and improvement in arthralgia in 62.5% of patients, all of which were assessed at a follow-up visit between 8 to 16 weeks after upadacitinib induction. Endoscopic response and endoscopic remission, both assessed at a median of 34.1 weeks of follow-up, was achieved in 61.5% and 34.6% of patients, respectively. Adverse events were recorded in 14.5% of patients, and a total of 11.8% of patients discontinued treatment during the follow-up period.

included patients who had either UC or Crohn's disease (CD). Although combining data from UC and CD directly is unusual, when assessing safety, combining this data becomes important because of the rarity of safety events. The study's safety profiles were acceptable, showing no identification of new safety signals that would suggest an increased likelihood of adverse events. Infectious complications, such as herpes zoster, were higher in active treatment vs placebo. There was 1 patient in the upadacitinib cohort and 2 in the placebo cohort who experienced gastrointestinal perforation, making it challenging to establish a clear relation. Cardiovascular events occurred in 1 patient under active therapy and 1 patient taking placebo, and 2 patients had venous thromboembolic disease under active therapy. In terms of malignancies, there were 4 cases in the higher-dose group (2 cases with 15 mg, and 4 cases with 30 mg) and 1 case in the placebo group. Importantly, there were no reported cases of tuberculosis, lymphoma, or death.

Dr Dubinsky presented a study focusing on the time to relapse during treatment with upadacitinib in patients with UC who have responded to induction therapy.[12] This study evaluated 2 approved maintenance doses of upadacitinib 15 mg and 30 mg and found that the probability of relapse during maintenance was lower with low-dose upadacitinib. However, this raises the question of the safety advantages of maintaining a lower dose over a higher one. In general, when using immunosuppression, the principle of lower is better often applies. One notable advantage of upadacitinib is its lack of immunogenicity, allowing for the initial use of a lower dose while observing patient response. If a patient responds well to a lower dose, it is a positive outcome. Conversely, if they do not respond, the dose may be escalated directly to 30 mg or an intermediate approach may be attempted, starting at 15 mg and moving up to 30 mg. However, the study did not directly address this potential dosing strategy. Nonetheless, this nuanced approach to dosing may emerge as a clinical practice pattern, given the safety profile of upadacitinib.

Risankizumab

Dr Loftus presented data on the phase 3 INSPIRE study, which evaluated risankizumab—a monoclonal antibody targeting the p13 component of IL-23—induction in patients with moderate to severely active UC.[13] The findings revealed that treatment with risankizumab was superior to placebo as an inductive therapy for achieving clinical remission. Additionally, the study showcased positive outcomes across secondary endpoints, including an endoscopic-histologic improvement while maintaining a well-tolerated profile with no new safety concerns. These data are promising, as they introduce a potentially favorable and durable treatment option for UC patients, especially considering the need for more agents with favorable safety profiles. Although risankizumab is not yet FDA approved for UC, its efficacy and safety in this study could make it a valuable addition to our treatment options in the near future.

Mirikizumab

Dr Panaccione presented 2-year efficacy and safety data on mirikizumab after 104 weeks of continuous treatment in the LUCENT-3 trial, an open-label extension study.[14] Mirikizumab was recently FDA approved for UC treatment. The study focused on the sustained benefits of mirikizumab in patients, including those who previously failed biologic therapy. The study demonstrated sustained long-term benefits through week 104. Notably, patients who had experienced biologic therapy failure showed significant improvement with mirikizumab, unlike with some other agents in the IL-23 class, which might have reduced efficacy after prior biologic use. Understanding treatment response after a failed biologic is crucial in guiding future treatment choices. These findings reiterate the potential of mirikizumab as a valuable treatment option, especially for patients who have not responded to previous biologic therapies.

Ozanimod

Dr Afzali presented findings from the True North study, specifically examining the long-term outcomes of patients with UC treated with ozanimod, a selective sphingosine 1-phosphate receptor modulator, who sustained clinical remission for over 3 years (week 52) in the open-label extension.[15] Ozanimod has been approved for the treatment of moderate to severely active UC, initially based on the 52-week efficacy data. This post hoc analysis assessed patients who demonstrated clinical response at week 52 and then continued treatment in the open-label extension. The analysis revealed that most patients who had clinical remission after 1 year demonstrated sustained efficacy for an additional 2 years during continuous treatment. This finding aligns with observations in other trials, highlighting that patients who achieve positive outcomes after 1 year tend to maintain a durable response.

Dr Abreu conducted a study analyzing the durability of symptomatic and clinical outcomes in patients receiving ozanimod treatment in the open-label extension phase of the True North study.[16] The ongoing open-label study collected data over 3 years and focused on symptomatic, clinical, and mucosal endpoints in patients who were clinical responders at week 52. This highlights that patients exhibited durable symptomatic responses and sustained clinical outcomes up to week 94 with continuous treatment, emphasizing the lasting benefits of the medication. Of note, these outcomes were not influenced by achieving more objective measures of responsiveness at week 52. This suggests that patients who initially respond well to treatment tend to maintain their positive status over the long term. These promising findings offer reassurance to patients that maintaining a state of well-being over an extended period is a strong likelihood.

Disclosures

Dr Lichtenstein has consulted for AbbVie, American Regent, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Gilead, Janssen, Ortho Biotech, Kabi (Fresenius), MedEd Consultants, Merck, Morphic Therapeutics, Pfizer, Prometheus Laboratories, Romark, Sandoz, Salix Pharmaceuticals/Valeant, Shire Pharmaceuticals, Takeda, and UCB; has served on the Data Safety Monitoring Board for Eli Lilly; and has received stock options from Virgo. He has received CME honorarium from AbbVie (CME), Allergan (CME), Amgen (CME), American College of Gastroenterology (IBD Associate Editor), American Gastroenterological Association (CME), Chemed (CME), Ferring (CME), Ironwood (CME), Gastroenterology and Hepatology [Gastro-Hep Communications], Imedex (CME), Janssen (CME), American Regent (CME), Merck (CME), Physician Education Resource (CME), Pfizer (CME), Professional Communication Corporation (Book Honorarium), Romark (CME), Salix (CME), SLACK (Book Royalty), Springer Science and Business Media (Editor), University of Kentucky (CME), Up-To-Date (Wolters Kluwer), and Vindico (CME). He also has received research/funding from Bristol Meyers Squibb, Celgene, Janssen, Ortho Biotech (Research and IBD Fellowship Funding), Pfizer (IBD Fellowship Funding), Takeda (Research, IBD Fellowship Funding), and UCB.

ABSTRACT SUMMARY Efficacy and Safety of Etrasimod in Patients With and Without Concomitant Corticosteroid Treatment in the Phase 3 ELEVATE UC 52 And ELEVATE UC 12 Trials

The efficacy and safety of the oral, once-daily, selective S1P receptor modulator etrasimod was evaluated for the treatment of moderately to severely active UC in the ELEVATE UC trial (Poster 2200). Among patients with corticosteroid use at baseline, this study demonstrated that patients randomized to treatment with etrasimod were more likely to achieve corticosteroid-free clinical remission at week 52 compared with placebo. Among patients with corticosteroid use at baseline, 31.2% in the etrasimod arm and 9.5% in the placebo arm achieved clinical remission at week 52. In patients with no corticosteroid use at baseline, 33.2% in the etrasimod arm and 6.9% in the placebo arm achieved clinical remission at week 52. The clinical and endoscopic benefits observed with etrasimod were similar regardless of corticosteroid use at baseline. Additionally, safety outcomes remained consistent with etrasimod regardless of baseline corticosteroid use, with no change in the incidence of infections according to baseline corticosteroids.

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Notes


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