GASTROENTEROLOGY & HEPATOLOGY
The Independent Peer-Reviewed Journal

July 2024 Volume 20, Issue 7, Supplement 6

A SPECIAL MEETING REVIEW EDITION

Highlights in Ulcerative Colitis From Digestive Disease Week 2024

A Review of Selected Presentations From DDW 2024
May 18-21, 2024 • Washington, DC

Special Reporting on:

- Extended Induction Response Over Time in Patients With Moderately to Severely Active Ulcerative Colitis Treated With Mirikizumab in the LUCENT-1 and -2 Trials
- The Efficacy and Safety of Guselkumab as Maintenance Therapy in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 QUASAR Maintenance Study
- Clinical Relevance of Baseline and Change in Urgency Numeric Rating Scale Score for Mirikizumab Treatment for Ulcerative Colitis
- Risankizumab in Patients With Moderately to Severely Active Ulcerative Colitis in the Phase 3 INSPIRE and COMMAND Studies
- Effect of Mirikizumab on Clinical and Endoscopic Outcomes After 1 Anti-TNF Failure in Patients With Moderately to Severely Active Ulcerative Colitis
- One-Year Comparative Effectiveness of Upadacitinib Versus Tofacitinib for Ulcerative Colitis: A Multicenter Cohort Study

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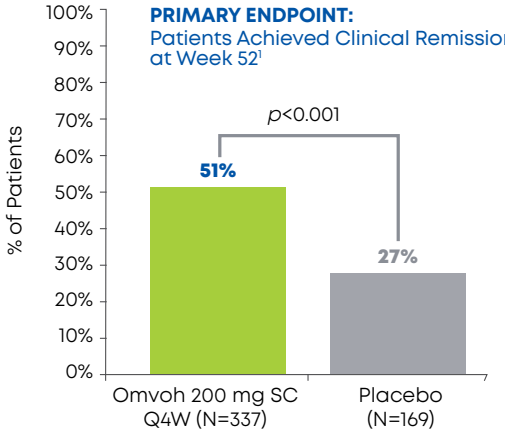
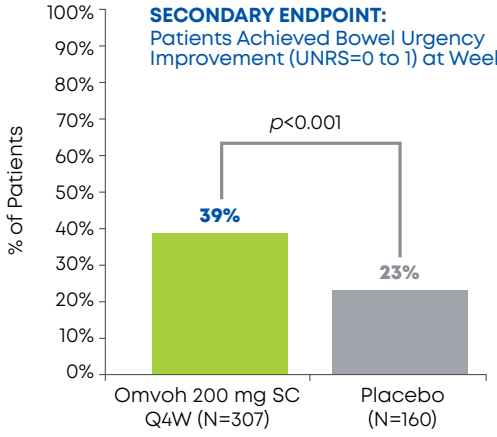
For your adult patients with moderately to severely active ulcerative colitis (UC) who had inadequate response to their current treatment[1]

MAKE THE URGENT CHANGE WITH OMVOH

AMONG PATIENTS WHO ACHIEVED CLINICAL RESPONSE WITH OMVOH AT WEEK 12[1]

Omvoh demonstrated sustained clinical remission and reduced bowel urgency at Week 52[1]





Nearly 2 in 3 patients taking Omvoh achieved clinical response at Week 12[1]

65% of patients (n=517/795) taking Omvoh achieved clinical response* after 12 weeks of induction dosing vs 43% (n=115/267) with placebo (secondary endpoint), and nearly 1 in 4 (24%, n=191/795) achieved clinical remission[a] vs 15% (n=40/267) with placebo (primary endpoint).[1]

[a]Clinical remission based on mMS is defined as: SF=0 or 1, RB=0, and centrally read ES=0 or 1 (excluding friability).[1]

*Clinical response is defined as a decrease in the mMS of ≥2 points with ≥30% decrease from baseline, and either a decrease of ≥1 point in RB from baseline or RB=0 or 1.[1]

INDICATION

Omvoh™ is an interleukin-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

Please see Important Safety Information below.

UC-1 AND UC-2 TRIAL DESIGN

Omvoh was studied in two Phase 3, randomized, double-blind, placebo-controlled clinical trials of adult patients with moderately to severely active UC. Patients (N=1279) were randomized 3:1 to receive Omvoh 300 mg IV infusion or placebo every 4 weeks (Q4W) for 12 weeks (Week 0, 4, and 8) in the induction study (UC-1). Patients who achieved clinical response with Omvoh at Week 12 in UC-1 (N=581) were re-randomized 2:1 to receive Omvoh 200 mg SC injection or placebo Q4W for 40 weeks in the maintenance study (UC-2) (52 weeks of continuous therapy). The primary endpoint was the proportion of patients in clinical remission at Week 12 in UC-1 and Week 40 in UC-2.[1]

At baseline of UC-1, all patients had inadequate response, loss of response, or intolerance to at least one corticosteroid, immunomodulator, biologic treatment (TNF blocker, vedolizumab), or tofacitinib. In UC-2, patients who were on concomitant UC therapies during UC-1 were required to continue on stable doses of oral aminosalicylates and immunomodulator agents. Corticosteroid tapering was required for patients who were receiving oral corticosteroids at baseline and achieved clinical response in UC-1.[1]

Patients with an mMS of 5 to 9 at baseline of UC-1 were included for efficacy analyses. Patients had a median mMS of 7, and 58% had severely active disease (mMS 7 to 9). Patients' baseline therapies included 41% of patients receiving oral corticosteroids, 24% receiving immunomodulators, and 75% receiving aminosalicylates. Patients' prior treatment experiences include: 57% were biologic- and JAKi-naive, 41% had failed at least one biologic, 3% had failed a JAKi, and 2% had previously received but had not failed a biologic or JAKi.[1]

Bowel urgency was assessed using an Urgency Numeric Rating Scale (UNRS) ranging from 0 (no urgency) to 10 (worst possible urgency) during UC-1 and as a secondary endpoint in UC-2. Bowel urgency improvement was evaluated as the proportion of patients with a baseline UNRS weekly average score of ≥3 achieving a weekly average score of 0 to 1 at Week 12 in UC-1 and Week 40 in UC-2.[1,2,4]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS - Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis during intravenous infusion, have been reported with Omvoh administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritus, were reported during induction. If a severe hypersensitivity reaction occurs, discontinue Omvoh immediately and initiate appropriate treatment.

Infections

Omvoh may increase the risk of infection. Do not initiate treatment with Omvoh in patients with a clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Omvoh. Instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is

not responding to standard therapy, monitor the patient closely and do not administer Omvoh until the infection resolves.

Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Omvoh. Do not administer Omvoh to patients with active TB infection. Initiate treatment of latent TB prior to administering Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after Omvoh treatment. In clinical trials, subjects were excluded if they had evidence of active TB, a history of active TB, or were diagnosed with latent TB at screening.

Hepatotoxicity
Drug-induced liver injury in conjunction with pruritus was reported in a clinical trial patient following a longer than recommended induction regimen. Omvoh was discontinued. Liver test abnormalities eventually returned to baseline. Evaluate liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter according to routine patient management. Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations
Avoid use of live vaccines in patients treated with Omvoh. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Prior to initiating therapy, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh.

ADVERSE REACTIONS

Most common adverse reactions (≥2%) associated with Omvoh treatment are upper respiratory tract infections and arthralgia during induction, and upper respiratory tract infections, injection site reactions, arthralgia, rash, headache, and herpes viral infection during maintenance.

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See Brief Summary of Prescribing Information on subsequent pages. See Instructions for Use included with the device.

ES=endoscopic subscore; IV=intravenous; mMS=modified Mayo score; Q4W=every 4 weeks; RB=rectal bleeding subscore; SC=subcutaneous; SF=stool frequency subscore; TNF=tumor necrosis factor; UC=ulcerative colitis; UNRS=Urgency Numeric Rating Scale.

References: 1. Omvoh (mirikizumab-mrkz). Prescribing Information. Lilly USA, LLC. **2.** D'Haens G, Dubinsky M, Kobayashi T, et al. Mirikizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2023;388(26):2444-2455. doi:10.1056/NEJMoa2207940 **3.** Data on File. DOF-MR-US-0018. Lilly USA, LLC. **4.** Dubinsky MC, Irving PM, Panaccione R, et al. Incorporating patient experience into drug development for ulcerative colitis: development of the Urgency Numeric Rating Scale, a patient-reported outcome measure to assess bowel urgency in adults. *J Patient Rep Outcomes*. 2022;6(1):31. doi:10.1186/s41687-022-00439-w

Omvoh™ (mirikizumab-mrkz) injection, for intravenous or subcutaneous use

Brief Summary: Consult the package insert for complete prescribing information.

INDICATIONS AND USAGE
Omvoh is an interleukin-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults.

CONTRAINDICATIONS
Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Serious hypersensitivity reactions, including anaphylaxis during intravenous infusion, have been reported with Omvoh administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritis, were reported during induction [see *Adverse Reactions*]. If a severe hypersensitivity reaction occurs, discontinue Omvoh immediately and initiate appropriate treatment.

Infections
Omvoh may increase the risk of infection *[see Adverse Reactions]*.

Do not initiate treatment with Omvoh in patients with a clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Omvoh. Instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely and do not administer Omvoh until the infection resolves.

Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Omvoh.

Do not administer Omvoh to patients with active TB infection. Initiate treatment of latent TB prior to administering Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after Omvoh treatment.

In clinical trials, subjects were excluded if they had evidence of active TB, a past history of active TB, or were diagnosed with latent TB at screening.

Hepatotoxicity
A case of drug-induced liver injury (alanine aminotransferase [ALT] 18x the upper limit of normal (ULN), aspartate aminotransferase [AST] 10x ULN, and total bilirubin 2.4x ULN) in conjunction with pruritus was reported in a clinical trial subject following a longer than recommended induction regimen. Omvoh was discontinued. Liver test abnormalities eventually returned to baseline.

Evaluate liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter according to routine patient management.

Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations
Avoid use of live vaccines in patients treated with Omvoh. Prior to initiating therapy with Omvoh, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh.

ADVERSE REACTIONS
The following topics are also discussed in detail in the Warnings and Precautions section:
Hypersensitivity Reactions
Infections
Tuberculosis
Hepatotoxicity

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Omvoh was studied up to 12 weeks in subjects with moderately to severely active ulcerative colitis in a randomized, double-blind, placebo-controlled induction study (UC-1). In subjects who responded to induction therapy in UC-1, long-term safety up to 52 weeks was evaluated in a randomized, double-blind, placebo-controlled maintenance study (UC-2) and a long-term extension study *[see Clinical Studies]*.

In the induction study (UC-1), 1279 subjects were enrolled of whom 958 received Omvoh 300 mg administered as an intravenous infusion at Weeks 0, 4, and 8. In the maintenance study (UC-2), 581 subjects were enrolled of whom 389 received Omvoh 200 mg administered as a subcutaneous injection every 4 weeks.

Table 1 summarizes the adverse reactions reported in at least 2% of subjects and at a higher frequency than placebo during UC-1.

Table 1: Adverse Reactions[a] in Subjects with Ulcerative Colitis through Week 12 in a Placebo-Controlled Induction Study (UC-1)

Adverse Reactions	OMVOH 300-mg Intravenous Infusion[b] N=958 n (%)	Placebo N=321 n (%)
Upper respiratory tract infections[c]	72 (8%)	20 (6%)
Arthralgia	20 (2%)	4 (1%)

[a] Reported in at least 2% of subjects and at a higher frequency than placebo.
[b] Omvoh 300 mg as an intravenous infusion at Weeks 0, 4, and 8.
[c] Upper respiratory tract infections includes related terms (e.g., COVID-19, nasopharyngitis, pharyngitis, rhinitis, sinusitis, and upper respiratory tract infection).

In the induction study (UC-1), infusion-related hypersensitivity reactions were reported by 4 (0.4%) subjects treated with Omvoh and 1 (0.3%) subject treated with placebo.

Table 2 summarizes the adverse reactions reported in at least 2% of subjects and at a higher frequency than placebo during the 40-week controlled period of UC-2.

Table 2: Adverse Reactions[a] in Subjects with Ulcerative Colitis through Week 40 In a Placebo-Controlled Maintenance Study (UC-2)

Adverse Reactions	OMVOH 200-mg Subcutaneous Injection[b] N=389 n (%)	Placebo N=192 n (%)
Upper respiratory tract infections[c]	53 (14%)	23 (12%)
Injection site reactions[d]	34 (9%)	8 (4%)
Arthralgia	26 (7%)	8 (4%)
Rash[e]	16 (4%)	2 (1%)
Headache	16 (4%)	2 (1%)
Herpes viral infection[f]	9 (2%)	1 (1%)

[a] Reported in at least 2% of subjects and at a higher frequency than placebo
[b] Omvoh 200 mg as a subcutaneous injection at Week 12 and every 4 weeks thereafter for up to an additional 40 weeks.
[c] Upper respiratory tract infections includes related terms (e.g., COVID-19, nasopharyngitis, pharyngitis, rhinitis, sinusitis, and upper respiratory tract infection).
[d] Injection site reactions includes related terms (e.g., erythema, hypersensitivity, pain, reaction, and urticaria at the injection site).
[e] Rash is composed of several similar terms.
[f] Herpes viral infection includes related terms (e.g., herpes zoster, herpes simplex, and oral herpes.)

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for intravenous or subcutaneous use MR HCP BS UC APP

Infections
In UC-1 through Week 12, infections were reported by 145 (15%) subjects treated with Omvoh 300 mg and 45 (14%) subjects treated with placebo. Serious infections were reported by less than 1% in both groups. Serious infections in the Omvoh group included intestinal sepsis, listeria sepsis, and pneumonia.

In the maintenance study (UC-2) through Week 40 (a total of 52 weeks of treatment), infections were reported by 93 (24%) subjects treated with Omvoh 200 mg and 44 (23%) subjects treated with placebo. A case of COVID-19 pneumonia was reported as a serious infection in the Omvoh group.

Hepatic Enzyme Elevations
In UC-1 through Week 12, alanine aminotransferase (ALT) ≥5X ULN was reported by 1 (0.1%) subject treated with Omvoh 300 mg and 1 (0.3%) subject treated with placebo. Aspartate aminotransferase (AST) ≥5X ULN was reported by 2 (0.2%) subjects treated with Omvoh 300 mg and no subject treated with placebo. These elevations have been noted with and without concomitant elevations in total bilirubin.

In the maintenance study (UC-2) through Week 40 (a total of 52 weeks of treatment), 3 (0.8%) subjects treated with Omvoh 200 mg reported ALT ≥5X ULN and 3 (0.8%) subjects reported AST ≥5X ULN; with or without concomitant elevations in total bilirubin. No subjects treated with placebo experienced similar elevations *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry
There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Omvoh during pregnancy. Pregnant women exposed to Omvoh and healthcare providers are encouraged to call Eli Lilly and Company at 1-800-Lilly-Rx (1-800-545-5979).

Risk Summary
Available data from case reports of mirikizumab-mrkz use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Although there are no data on mirikizumab-mrkz, monoclonal antibodies can be actively transported across the placenta, and mirikizumab-mrkz may cause immunosuppression in the in utero-exposed infant. An enhanced pre- and post-natal development study conducted in pregnant monkeys at a dose 69 times the maximum recommended human dose (MRHD) revealed no adverse developmental effects to the developing fetus, or harm to infant monkeys from birth through 6 months of age. There are risks of adverse pregnancy outcomes associated with increased disease activity in women with inflammatory bowel disease *(see Clinical Considerations)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-Associated Maternal and Embryo/Fetal Risk
Published data suggest that the risk of adverse pregnancy outcomes in women with inflammatory bowel disease (IBD) is associated with increased disease activity. Adverse pregnancy outcomes include preterm delivery (before 37 weeks gestation), low birth weight (less than 2500 g) infants, and small for gestational age at birth.

Fetal/Neonatal Adverse Reactions
Transport of endogenous IgG antibodies across the placenta increases as pregnancy progresses, and peaks during the third trimester. Because mirikizumab-mrkz may interfere with immune response to infections, risks and benefits should be considered prior to administering live vaccines to infants exposed to Omvoh in utero. There are no data regarding infant serum levels of mirikizumab-mrkz at birth and the duration of persistence of mirikizumab-mrkz in infant serum after birth. Although a specific timeframe to delay live virus immunizations in infants exposed in utero is unknown, a minimum of 2 months after birth should be considered because of the half-life of the product.

Data
Animal Data
An enhanced pre- and postnatal development study was conducted in cynomolgus monkeys administered mirikizumab-mrkz by intravenous injection during organogenesis to parturition at a dose of 300 mg/kg twice weekly (69 times the MRHD based on exposure comparisons). Mirikizumab-mrkz crossed the placenta in monkeys. No maternal toxicity was noted in this study. No mirikizumab-mrkz-related effects on morphological, functional, or immunological development were observed in infant monkeys from birth through 6 months of age. However, incidences of embryo/fetal loss were higher in the treated groups compared to control (6.7% [1 of 15] in controls vs 26.7% [4 of 15] at 300 mg/kg (69 times the MRHD, based on exposure comparisons) but were within the range of historical control data. Following delivery, most adult female cynomolgus monkeys and all infants from the mirikizumab-mrkz-treated group had measurable serum concentrations up to 28 days postpartum. In the infant monkeys, mean serum concentrations were approximately 4.8 times the respective mean maternal concentrations.

Lactation

Risk Summary
There are no data on the presence of mirikizumab-mrkz in human milk, the effects on the breastfed infant, or the effects on milk production. Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to mirikizumab-mrkz are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Omvoh and any potential adverse effects on the breastfed infant from Omvoh or from the underlying maternal condition.

Pediatric Use
The safety and effectiveness of Omvoh have not been established in pediatric patients.

Geriatric Use
Of the 795 Omvoh-treated subjects in the two clinical trials, 64 subjects (8%) were 65 years of age and older, while 10 subjects (1%) were 75 years of age and older. These clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger adult subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects. No clinically meaningful differences in the pharmacokinetics of mirikizumab-mrkz were observed in subjects 65 years of age and older compared to younger adult subjects *[see Clinical Pharmacology]*.

DOSING

Recommended Dosage

Induction Dosage
The recommended induction dosage of Omvoh is 300 mg administered by intravenous infusion over at least 30 minutes at Week 0, Week 4, and Week 8 *[see Dosage and Administration]*.

Maintenance Dosage
The recommended maintenance dosage of Omvoh is 200 mg administered by subcutaneous injection (given as two consecutive injections of 100 mg each) at Week 12, and every 4 weeks thereafter *[see Dosage and Administration]*.

PATIENT COUNSELING INFORMATION
Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Hypersensitivity Reactions
Advise patients to discontinue Omvoh and seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions]*.

Infections
Advise patients that Omvoh may lower the ability of their immune system to fight infections and to contact their healthcare provider immediately if they develop any symptoms of infection *[see Warnings and Precautions]*.

Tuberculosis
Advise patients to contact their healthcare provider if they experience symptoms suggestive of TB (e.g., unexplained fever, cough, or difficulty breathing) *[see Warnings and Precautions]*.

Hepatotoxicity
Inform patients that Omvoh may cause liver injury. Advise patients to seek immediate medical attention if they experience symptoms suggestive of liver dysfunction (e.g., unexplained rash, nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine) *[see Warnings and Precautions]*.

Immunizations
Advise patients that vaccination with live vaccines is not recommended during Omvoh treatment and immediately prior to or after Omvoh treatment. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Instruct patients to inform their healthcare provider that they are taking Omvoh prior to receiving a vaccination *[see Warnings and Precautions]*.

Pregnancy
Advise patients who are exposed to Omvoh during pregnancy to contact Eli Lilly and Company *[see Use in Specific Populations]*.

Administration
Instruct patients in preparation and administration of Omvoh, including choosing anatomical sites for subcutaneous administration, and proper subcutaneous injection technique. Instruct patients in the technique of pen disposal *[see Instructions for Use]*.

Instruct patients or caregivers to administer two 100-mg prefilled pens to achieve the full 200-mg dose of Omvoh.

Additional information can be found at www.Omvoh.com

See Instructions for Use accompanying the product device.

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Extended Induction Response Over Time in Patients With Moderately to Severely Active Ulcerative Colitis Treated With Mirikizumab in the LUCENT-1 and -2 Trials

Mirikizumab is a monoclonal antibody directed against the p19 subunit of interleukin 23 (IL-23) that is approved for the treatment of moderately to severely active ulcerative colitis (UC).[1,2] The double-blind phase 3 LUCENT-1 and LUCENT-2 trials evaluated mirikizumab vs placebo as therapy for patients with moderately to severely active UC.[3] In the LUCENT-1 trial, 1281 patients were randomized 3:1 to receive mirikizumab (300 mg) vs placebo administered every 4 weeks for 12 weeks. After the induction phase, 544 patients exhibited a response and 272 patients were nonresponders. In LUCENT-2, patients with a response to mirikizumab induction treatment were randomized 2:1 to receive mirikizumab (200 mg) vs placebo administered every 4 weeks for 40 weeks. In addition, the 272 patients who failed to respond to 3 doses of induction therapy entered the LUCENT-2 open-label extension study, in which patients received 3 additional doses of mirikizumab (300 mg) at weeks 12, 16, and 20.

Clinical response was defined as a decrease of at least 2 points and 30% in modified Mayo score vs baseline and either a decrease in rectal bleeding subscore of at least 1 point from baseline or a rectal bleeding subscore of 0. Symptomatic response was defined as a 30% decrease in the composite clinical endpoint comprising the stool frequency and rectal bleeding subscores. Symptomatic remission was defined as having a rectal bleeding subscore of 0 plus having either a

> Incorporation of an extended induction therapy with mirikizumab induced a clinical response in 53.7% of patients at week 24; adding the benefit of extended induction, a total of 80.3% of patients treated with mirikizumab achieved first clinical response by week 24. The results of this study using an extended induction treatment highlight that there is continued symptomatic improvement in induction nonresponders treated with extended induction mirikizumab, and support the concept of introducing an extended induction treatment into clinical practice.
>
> – Gary R. Lichtenstein, MD

Table. An Increasing Proportion of Induction Nonresponders Improved in Outcomes During an Additional 12 Weeks of Mirikizumab Induction Treatment

Outcomes for mirikizumab IV extended induction	W12 (W0 extended induction)[a] (N=272)	W16 (W4 extended induction)[a] (N=272)	W20 (W8 extended induction)[a] (N=272)	W24 (W12 extended induction)[a] (N=272)
Clinical response	0	N/A	N/A	146 (53.7)
Symptomatic response	83 (30.5)	144 (52.9)	169 (62.1)	197 (72.4)
Symptomatic remission	13 (4.8)	53 (19.5)	73 (26.8)	101 (37.1)
BU change from baseline (mBOCF; mean [SD])	-1.2 (2.2)	-1.8 (2.4)	-2.1 (2.5)	-2.5 (2.7)
BU remission (Nx=256)	18 (7.0)	28 (10.9)	38 (14.8)	51 (19.9)

BU, bowel urgency; IV, intravenous; mBOCF, modified baseline observation carried forward; N/A, not available; Nx, number of patients with Urgency Numeric Rating Scale ≥3 at induction baseline; q4w, every 4 weeks; W, week.

[a]The mirikizumab induction nonresponder population received 300 mg mirikizumab IV q4w during induction and only included patients who continued to the maintenance trial (LUCENT-2).

Data are n (%) unless stated otherwise.

Adapted from Rubin DT et al. DDW abstract Su1802. *Gastroenterology*. 2024;166(6)(suppl 1).[5]

stool frequency subscore of 0 or a stool frequency subscore of 1 with a 1-point or greater decrease vs baseline. The Urgency Numeric Rating Scale (NRS) was used to assess bowel urgency, and a lower score reflected a decrease in bowel urgency. Bowel urgency remission was defined by an Urgency NRS score of 0 or 1.

At baseline in LUCENT-1, the 272 patients who eventually entered the extension study had a median age of 44.0±14.2 years and 67% were male.[4,5] The median duration of disease was 7.6±6.8 years, and 56.6% of patients had left-sided colitis while 42.6% had pancolitis. The mean modified Mayo score was 6.5±1.4, and over one-half of patients (56.6%) had a severe modified Mayo score of 7, 8, or 9. The mean Urgency NRS score was 6.2±2.2, and 72.4% of patients had a Mayo endoscopic subscore of 3, indicating severe disease in nearly two-thirds of patients. Over one-half of the patients (54.0%) had failed prior therapy with tofacitinib or a biologic agent. Corticosteroid use was noted in 43.4% of patients and immunomodulator use in 28.3%.

At week 24 of the extension study, after receiving a total of 6 doses of mirikizumab, 53.7% of patients demonstrated a clinical response (Table). At weeks 12, 16, 20, and 24, the rate of symptomatic response was 30.5%, 52.9%, 62.1%, and 72.4%, and the rate of symptomatic remission was 4.8%, 19.5%, 26.8%, and 37.1%, respectively, reflecting meaningful improvements in the population of patients who failed 12 weeks of induction treatment. Improvements were also observed across the 12 weeks of extended induction therapy in terms of bowel urgency change from baseline, which improved from -1.2±2.2 at week 12 to -2.5±2.7 at week 24. The proportion of patients experiencing bowel urgency remission improved from 7.0% at week 12 to 19.9% at week 24.

References

1. Choi D, Sheridan H, Bhat S. Mirikizumab: a new therapeutic option for the treatment of ulcerative colitis [published online February 12, 2024]. *Ann Pharmacother*. doi:10.1177/10600280241229742.
2. Omvoh [package insert]. Indianapolis, IN: Eli Lilly and Company; 2023.
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The Efficacy and Safety of Guselkumab as Maintenance Therapy in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 QUASAR Maintenance Study

Guselkumab is a fully human monoclonal antibody that binds to the p19 subunit of IL-23, preventing binding to and activation of the IL-23 receptor and release of proinflammatory cytokines. The phase 3 QUASAR maintenance study evaluated the safety and efficacy of guselkumab subcutaneous (SC) maintenance treatment in patients with moderately to severely active UC who responded to induction treatment with intravenous (IV) guselkumab.[1-3] Patients who had demonstrated a response in the phase 2b or phase 3 QUASAR induction study were enrolled.[1,3] Prior to entering the QUASAR induction study, eligible patients had a baseline modified Mayo score of 5 to 9, with a rectal bleeding subscore of 1 or greater, and a Mayo endoscopic subscore of at least 2 based on central review. The phase 2b induction study randomized 313 patients evenly across 3 arms to receive guselkumab 400 mg IV, guselkumab 200 mg IV, or placebo, administered every 4 weeks for a total of 3 doses. The phase 3 QUASAR induction study enrolled 701 patients who were randomized 3:2 to receive IV guselkumab (200 mg, every 4 weeks) vs placebo at weeks 0, 4, and 8. Patients who responded to guselkumab induction therapy and entered the QUASAR maintenance study were evenly randomized into 3 arms. Patients in Arm 1 received guselkumab SC (200 mg, every 4 weeks); patients in Arm 2 received guselkumab SC (100 mg, every 8 weeks); and patients in Arm 3 received placebo. Patients in Arm 3 experienced guselkumab withdrawal. The study continued through week 44. Tapering of corticosteroid therapy was mandatory during the maintenance portion of the study.

The QUASAR maintenance study enrolled 568 patients. Characteristics at induction baseline were well balanced across the 3 arms in the maintenance study.[2] The median age was 40.7±13.75 years, and 55% of patients were male. Sixty-four percent of patients had a modified Mayo score of 7, 8, or 9, and 66% had a Mayo endoscopic subscore of 3, reflecting severe disease in the majority of patients prior to induction therapy. The median level of C-reactive protein (CRP) was 3.9 mg/L (interquartile range [IQR], 1.5-9.2 mg/L), and the median level of fecal calprotectin was 1605.0 mg/kg (IQR, 669.0-3337.0 mg/kg). Forty percent of patients were using corticosteroids, and 42% of patients had a history of inadequate response or intolerance to biologic and/or Janus kinase (JAK) inhibitor therapy.

Prior to entering the QUASAR

maintenance study, 34% of the 568 patients were in clinical remission, 39% exhibited endoscopic improvement, and 22% were in endoscopic remission. The mean modified Mayo score was 2.5±1.53. Levels of inflammatory markers had decreased from the induction baseline: the mean level of CRP was 1.5 mg/L (IQR, 0.6-3.8 mg/L), and the mean level of fecal calprotectin was 303.5 mg/kg (IQR, 79.5-1194.0 mg/kg). Through week 44, the rate of discontinuation was low, at 12.0% (range, 10.6%-13.7%). The majority of patients who discontinued study therapy did so owing to an adverse event (AE; 5.1%).

The QUASAR maintenance study met its primary endpoint, demonstrating clinical remission rates at week 44 of 50.0% with the higher dose of guselkumab (*P*<.001 vs placebo), 45.2% with the lower dose of guselkumab (*P*<.001 vs placebo), and 18.9% with placebo (Figure 1). Sixty-nine percent of patients in Arm 1 or Arm 2 were also in endoscopic remission. The study also met its major secondary endpoints with statistical significance at week 44 for both Arm 1 and Arm 2 vs Arm 3, including corticosteroid-free clinical remission (*P*<.001 for both), maintenance of clinical remission (*P*<.005 for both), maintenance of clinical response (*P*<.001 for both), and symptomatic remission (*P*<.001 for both). The trial met its secondary endoscopic and histologic endpoints, including endoscopic improvement, histologic-endoscopic mucosal improvement, and endoscopic remission (*P*<.001 for each comparison of Arm 1 or Arm 2 vs Arm 3). Patient-reported endpoints were also significantly improved with maintenance guselkumab compared with placebo. Guselkumab treatment was generally well tolerated, with no new safety signals.

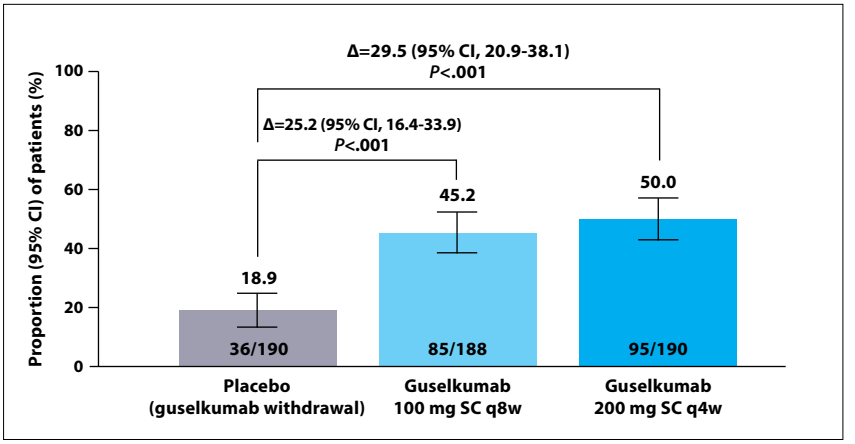

Figure 1. Primary endpoint of clinical remission at week 44. Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and Mayo endoscopic subscore of 0 or 1 with no friability present. Randomized full analysis set. 69% of guselkumab-treated patients in clinical remission were also in endoscopic remission (Mayo endoscopic subscore=0).

q4w, every 4 weeks; q8w, every 8 weeks; SC, subcutaneous.

Adapted from Rubin DT et al. DDW abstract 759. *Gastroenterology*. 2024;166(6)(suppl 1).[2]

Overall, 50% of patients with moderately to severely active UC receiving guselkumab SC 200 mg every 4 weeks and 45.2% of patients receiving guselkumab SC 100 mg every 8 weeks achieved the primary endpoint of clinical remission at week 44 compared with placebo (18.9%). In additional analyses of patients in clinical remission, 67% and 71%, respectively, were also in endoscopic remission at week 44. This study highlights the potential of guselkumab to enable patients with moderately to severely active UC to achieve durable, clinical remission and achieve important clinical endpoints, such as endoscopic remission to the point of normalization and histologic remission, which represents the level of progress needed in new treatments for IBD.

– Gary R. Lichtenstein, MD

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Clinical Relevance of Baseline and Change in Urgency Numeric Rating Scale Score for Mirikizumab Treatment for Ulcerative Colitis

In the phase 3 LUCENT-1 induction and LUCENT-2 maintenance trials, mirikizumab demonstrated efficacy and safety vs placebo in patients with moderately to severely active UC.[1,2] Patients in LUCENT-1 were randomized 3:1 to receive mirikizumab (300 mg) vs placebo every 4 weeks for a total of 3 doses. Patients with a response in LUCENT-1 were enrolled into LUCENT-2 and were randomized 2:1 to receive mirikizumab (200 mg) vs placebo every 4 weeks through week 40, for a total of 52 weeks of study therapy. A study was conducted to evaluate efficacy endpoints among patients in the LUCENT-1 and -2 trials based on bowel urgency severity at induction baseline.[3] Bowel urgency was characterized by the Urgency NRS score, with patients grouped into categories based on scores of 0 to 3 (low), 4 to 6 (moderate), and 7 to 10 (severe).

The analysis included 1162 patients from LUCENT-1 and 544 from LUCENT-2. At baseline, the LUCENT-1 population included 149 patients with a low Urgency NRS score, 437 patients with a moderate score, and 576 with a severe score, whereas the LUCENT-2 population included 70 patients with a low score, 215 with a moderate score, and 259 with a severe score. In general, mirikizumab yielded superior results compared with placebo, regardless of baseline bowel urgency status. At week 12, a greater proportion of patients showed a clinical response with mirikizumab vs placebo in the low, moderate, and severe cohorts (P<.001; Figure 2). Also at week 12, mirikizumab was superior to placebo in terms of endoscopic remission (low, P<.001; moderate, P<.01; severe, P<.05), clinical remission (low, P<.01; moderate, P<.05; severe, P<.05), and symptomatic remission (low, P<.05; moderate, P<.01; severe, P<.001).

At week 52, the rate of clinical response was significantly improved with mirikizumab compared with placebo (low, P<.01; moderate, P<.001; severe, P<.001), as was the rate of endoscopic remission (low, P<.05; moderate, P<.01; severe, P<.001) and the rate of symptomatic remission (low, P<.01; moderate, P<.001; severe, P<.001). The rate of clinical remission was not significantly different between mirikizumab and placebo among patients in the low cohort at week 52; however, the rate of clinical remission was superior with mirikizumab vs placebo among patients in the moderate (P<.01) and severe (P<.001) cohorts.

In general, Urgency NRS scores were more likely to improve among patients treated with mirikizumab vs

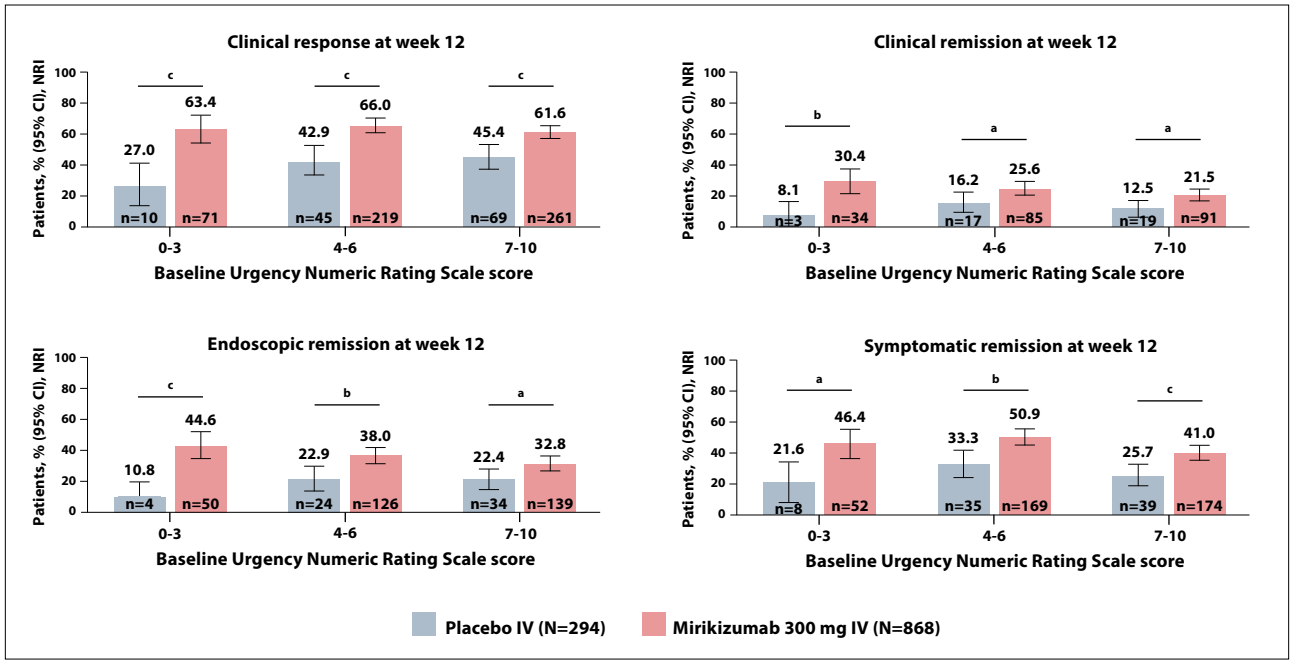

Figure 2. At week 12, a greater proportion of patients achieved clinical response, clinical remission, endoscopic remission, and symptomatic remission with mirikizumab vs placebo, regardless of Urgency Numeric Rating Scale score at induction baseline.

IV, intravenous; NRI, nonresponder imputation.

[a]P<.05; [b]P<.01; [c]P<.001 vs placebo.

Note: Data are % responder (95% CI) with NRI. CIs were constructed using the asymptotic method, without continuity correction.

Adapted from Clemow D et al. DDW abstract Su1814. *Gastroenterology*. 2024;166(6)(suppl 1).[3]

placebo at weeks 12 and 52; however, improvement in NRS score was less likely among patients who did not achieve the clinical endpoints. Individual Urgency NRS scores were also analyzed. Among patients who had a baseline NRS score of 6 and who achieved remission at week 52, the NRS score at week 52 had shifted to a lower value from baseline in most patients, with nearly one-half of patients (47.6%) achieving an Urgency NRS score of 0. Greater improvements in Urgency NRS score were observed with mirikizumab compared with placebo among patients who did achieve the clinical endpoints as well as in patients who did not achieve the clinical endpoints.

The mechanism of bowel urgency may be multifactorial; thus, patients with different bowel urgency severity may have different phenotypes, which may influence treatment outcomes. In this study, mirikizumab was efficacious in achieving symptomatic, endoscopic, and clinical endpoints in patients with moderately to severely active UC, regardless of baseline bowel urgency severity. Also, mirikizumab improved bowel urgency severity vs placebo, even among patients who did not achieve clinical endpoints. These findings are important for patients' well-being and suggest that mirikizumab effectively reduces bowel urgency severity in patients with UC, leading to better clinical outcomes. Further evaluation of the diverse etiologies that induce bowel urgency in patients with UC is needed to better predict who will respond to therapy.

– Gary R. Lichtenstein, MD

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Risankizumab in Patients With Moderately to Severely Active Ulcerative Colitis in the Phase 3 INSPIRE and COMMAND Studies

Risankizumab is a humanized monoclonal antibody directed at the p19 subunit of IL-23.[1] The phase 3 INSPIRE study investigated the safety and efficacy of 12 weeks of risankizumab vs placebo as induction therapy in patients with moderately to severely active UC.[2] Patients were randomized 2:1 to receive risankizumab (1200 mg, IV) vs placebo at weeks 0, 4, 8, and 12. The double-blind study yielded a significant improvement with risankizumab vs placebo in the primary endpoint of clinical remission at week 12 (20.3% vs 6.2%; $P<.00001$). Risankizumab therapy was superior to placebo for all secondary endpoints and was generally well tolerated.

Patients with a response at week 12 in the INSPIRE study were eligible for enrollment in the COMMAND maintenance study.[3] Patients in this study were evenly randomized to receive risankizumab (360 mg, SC; n=195), risankizumab (180 mg, SC; n=193), or placebo (n=196) every 8 weeks. The primary endpoint was the rate of clinical remission based on the adapted Mayo score at week 52. Baseline characteristics were well balanced across the 3 arms. The mean disease duration ranged from 7.1 to 7.4 years, and the proportion of patients with an adapted Mayo score of greater than 7 ranged from 41.4% to 49.7%. One-fourth of patients had no prior failure to advanced therapies, whereas approximately 22% (range, 19.7%-25.3%) had failed more than 2 prior advanced therapies. The proportion of patients in clinical remission at baseline based on the adapted Mayo score ranged from 21.6% to 29.3%.

The COMMAND study met its primary endpoint. The rate of clinical remission at week 52 was 37.6% with the higher dose of risankizumab ($P\leq.01$) and was 40.2% with the lower dose ($P\leq.001$) vs 25.1% with placebo (Figure 3). Among patients who had shown an inadequate response to prior therapies such as aminosalicylates, corticosteroids, and immunomodulators, the rate of clinical remission at week 52 was 61.7% with the higher dose of risankizumab ($P\leq.01$) and was 50.9% with the lower dose ($P>.05$) vs 31.1% with placebo. Among patients with an inadequate response to advanced therapies, the rate of clinical remission at week 52 was significantly improved with the lower dose of risankizumab (36.6% vs 23.2%; $P\leq.05$) but the

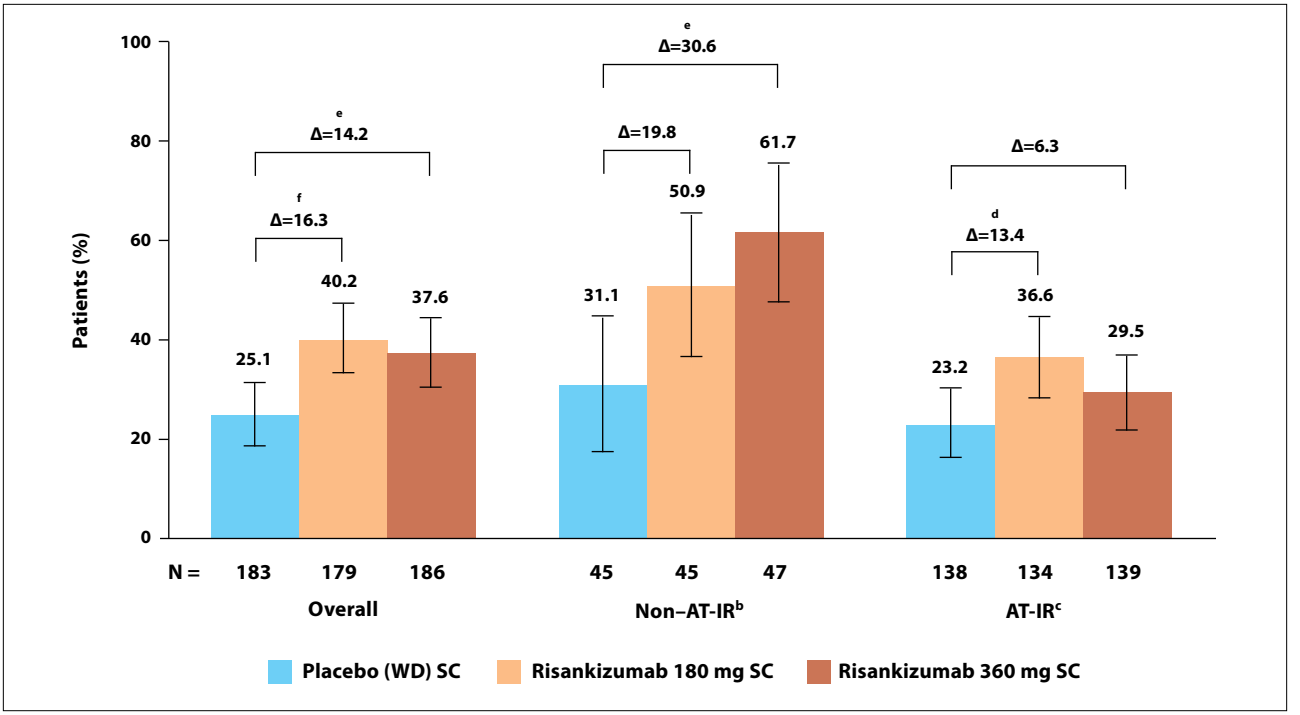

Figure 3. Primary endpoint of clinical remission[a] at week 52. Results reported as adjusted treatment difference risankizumab vs placebo (WD) SC, % (95% CI) and are based on NRI-MI to handle missing data owing to COVID-19 or owing to geopolitical conflict in Ukraine or surrounding areas. *P* values for treatment difference between risankizumab and placebo were calculated using the Cochran-Mantel-Haenszel test for categoric endpoints, controlling for stratification factors. Multiplicity-adjusted *P* values for treatment differences between risankizumab and placebo were reported for the overall population, whereas nominal *P* values were reported for non–AT-IR and AT-IR subgroups. Error bars are 95% CI.

AT-IR, advanced therapy–inadequate response; JAK, Janus kinase; non–AT-IR, nonadvanced therapy–inadequate response; NRI-MI, nonresponding multiple imputation; RBS, rectal bleeding subscore; SC, subcutaneous; SFS, stool frequency subscore; S1P, sphingosine-1 phosphate; WD, withdrawal.

[a]Clinical remission per adapted Mayo score: SFS ≤1 and not greater than baseline, RBS of 0, and endoscopic subscore ≤1 without friability. [b]Non–AT-IR: defined as patients who demonstrated an IR to conventional therapies (aminosalicylates, corticosteroids, and/or immunomodulators). [c]AT-IR: defined as patients who demonstrated an IR to at least 1 biologic approved for ulcerative colitis, JAK inhibitor, or S1P receptor modulator. [d]$P \leq .05$; [e]$P \leq .01$; [f]$P \leq .001$ vs placebo (WD) SC.

Adapted from Schreiber S et al. DDW abstract 984. *Gastroenterology*. 2024;166(6)(suppl 1).[3]

It is of interest and very clinically relevant to recognize that patients who receive IV risankizumab with moderately to severely active UC who do not respond can receive an additional 12 weeks of therapy, and more than 50% of these patients will respond and have similar long-term outcomes as patients who initially respond at 12 weeks. This clearly lays the foundation to justify introduction of an additional 12 weeks of therapy in initial nonresponders.

– Gary R. Lichtenstein, MD

difference did not reach significance with the higher dose. Both dose levels of risankizumab were significantly better vs placebo based on endoscopic improvement, histologic-endoscopic mucosal improvement, and endoscopic remission, as well as maintenance of clinical remission and corticosteroid-free clinical remission. Patient-reported outcomes were also superior with risankizumab compared with placebo. Maintenance treatment with SC risankizumab was generally well tolerated, and no new safety concerns were raised.

Patients with an inadequate response to 12 weeks of induction therapy in the INSPIRE study were enrolled in the extended treatment

period.[4] These patients were evenly randomized to receive risankizumab (1200 mg or 1800 mg, IV), risankizumab (360 mg, SC), or risankizumab (180 mg, SC), administered every 8 weeks. Patients in a fourth arm received placebo. After 12 weeks of additional treatment with risankizumab, the rate of clinical response ranged from 50.0% to 57.1% and the rate of clinical remission ranged from 8.8% to 15.7% across the 3 arms. Among patients who demonstrated a response to 12 additional weeks of risankizumab SC induction therapy, the proportion of patients with a clinical response at week 52 ranged from 45.3% to 46.4% and the proportion of patients who achieved clinical remission ranged from 17.9% to 22.8%. No new safety signals arose.

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Effect of Mirikizumab on Clinical and Endoscopic Outcomes After 1 Anti-TNF Failure in Patients With Moderately to Severely Active Ulcerative Colitis

The phase 3 LUCENT-1 induction and LUCENT-2 maintenance trials enrolled patients who had received prior therapy for their moderately to severely active UC.[1] Among the 1281 patients enrolled in LUCENT-1, 41% had experienced failure to a biologic or tofacitinib at baseline, and 36.3% had experienced at least 1 failure to an anti–tumor necrosis factor (TNF) agent. A post hoc analysis investigated the clinical efficacy of mirikizumab vs placebo as induction or maintenance therapy, as well as the efficacy of mirikizumab in extended induction, among patients who had failed a single anti-TNF therapy at baseline.[2] Of the 190 included patients, 146 received mirikizumab and 44 received placebo as induction therapy in LUCENT-1. *P* values were determined using the Cochran-Mantel-Haenszel test. Adjustments included baseline corticosteroid use, baseline disease activity, and region for LUCENT-1, and corticosteroid use, region, and clinical remission status at week 12 for LUCENT-2.

Mirikizumab was numerically superior to placebo based on most clinical endpoints in this patient subgroup; however, the number of patients in most groups was small, precluding robust analysis of statistical significance. At week 12, with mirikizumab vs placebo, the rate of clinical response was 64.4% vs 34.1% (*P*<.01), the rate of clinical remission was 18.5% vs 13.6%, the rate of symptomatic remission was 43.8% vs 27.3%, and the rate of endoscopic remission was 30.1% vs 15.9%, respectively (Figure 4). At week 52, with mirikizumab vs placebo, the rate of

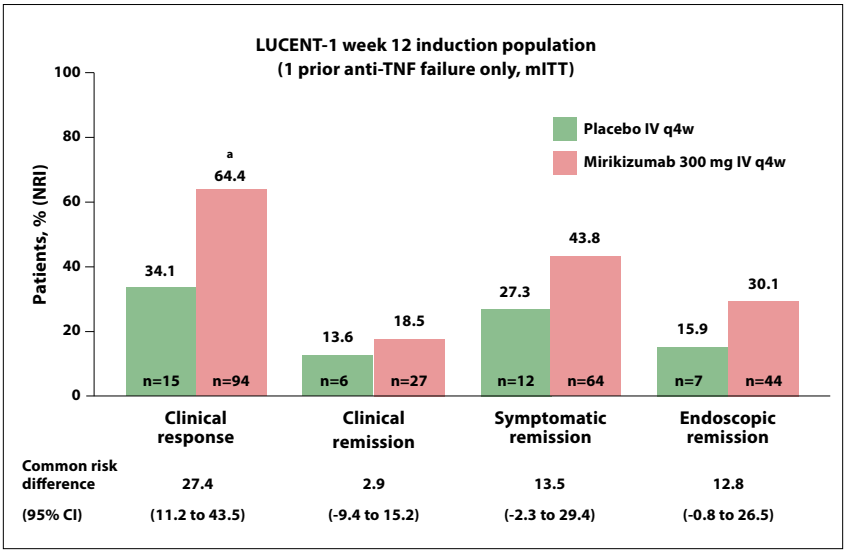

Figure 4. Efficacy outcomes for mirikizumab vs placebo at week 12 in patients with 1 prior anti-TNF failure. Clinical response defined as ≥2-point and ≥30% decrease in modified Mayo score from baseline and RBS=0 or 1, or ≥1-point decrease in RBS from baseline; clinical remission defined as SFS=0, or SFS=1 with ≥1-point decrease in SFS from baseline and RBS=0 and ES=0 or 1 (excluding friability); symptomatic remission defined as SFS=0, or SFS=1 with ≥1-point decrease from induction baseline and RBS=0; endoscopic remission defined as ES=0 or 1 (excluding friability).

ES, endoscopic Mayo subscore; IV, intravenous; mITT, modified intention-to-treat; NRI, nonresponder imputation; q4w, every 4 weeks; RBS, rectal bleeding subscore; SFS, stool frequency subscore; TNF, tumor necrosis factor.

[a]*P*<.01 vs placebo.

Adapted from Hart A et al. DDW abstract Su1818. *Gastroenterology*. 2024;166(6)(suppl 1).[2]

Notably, patients who had experienced anti-TNF therapy failure (45% of the initial patient population in the LUCENT-1 study) showed significant improvement with mirikizumab, specifically in clinical response, clinical remission, and symptomatic remission, but not endoscopic remission or corticosteroid-free remission at week 52 compared with placebo. Mirikizumab is thus unlike some other biologic agents. In contrast to mirikizumab, other biologic agents might have reduced efficacy with insignificant benefit after prior anti-TNF therapy 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.

– Gary R. Lichtenstein, MD

clinical response was 67.2% vs 44.8% (P<.05), the rate of clinical remission was 44.3% vs 17.2% (P<.05), and the rate of symptomatic remission was 63.9% vs 34.5% (P<.01), respectively. Mirikizumab was superior to placebo for other endpoints examined, but the comparison did not reach statistical significance, including for endoscopic remission (47.5% vs 27.6%), corticosteroid-free remission (37.7% vs 17.2%), and histologic-endoscopic mucosal remission (32.8% vs 17.2%).

Among 46 patients who had failed a single prior anti-TNF therapy and entered the extended induction portion of the LUCENT-2 trial, response rates to mirikizumab (300 mg, every 4 weeks) at week 24 were 45.7% for clinical response, 4.3% for clinical remission, 28.3% for symptomatic remission, and 10.9% for endoscopic remission. In the same subgroup of 46 patients, outcomes at week 52 were promising, based on rates of clinical response (75.0%), clinical remission (30.0%), symptomatic remission (55.0%), endoscopic remission (40.0%), corticosteroid-free remission (30.0%), and histologic-endoscopic mucosal remission (30.0%).

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One-Year Comparative Effectiveness of Upadacitinib Versus Tofacitinib for Ulcerative Colitis: A Multicenter Cohort Study

Two JAK inhibitors are approved for the treatment of patients with UC.[1-4] Upadacitinib selectively inhibits JAK1, whereas tofacitinib inhibits both JAK1 and JAK3. The 2 JAK inhibitors have not been directly compared in a clinical trial setting, and comparative real-world outcomes have not been well described. To address this gap, a retrospective real-world cohort study was conducted to evaluate efficacy and safety outcomes in patients with UC after 52 weeks of therapy with upadacitinib vs tofacitinib.[5] The study included patients from 2 sites who initiated treatment with tofacitinib or upadacitinib for UC between January 1, 2020 and February 1, 2023. The primary outcome was corticosteroid-free clinical remission at 52±4 weeks. In addition to no corticosteroid use, corticosteroid-free clinical remission was defined by 3 criteria, based on data availability: (1) A Simple Clinical Colitis Activity Index score of 2 points or less; (2) a partial Mayo score of 2 points or less; and (3) the physician global assessment of clinical remission.

Included in the comparative analysis were 74 patients treated with tofacitinib (58% female) and 81 treated with upadacitinib (47% female). The median age at initiation of treatment was 39 to 40 years, and the median disease duration was 7 to 9 years. Eighty-eight percent of patients in each cohort were White. The median body mass index ranged from 24.2 to 25.0. Patients in both cohorts had received similar numbers of prior lines of anti-TNF therapy (P=.69). However, more patients in the upadacitinib cohort had received prior vedolizumab (74% vs 59%; P=.05)

or prior ustekinumab (31% vs 8%; *P*<.01). In the upadacitinib cohort, 30% of patients had received prior tofacitinib. Over one-half of patients (53%-56%) were using prednisone or budesonide at baseline. Measures of disease activity were similar in the 2 cohorts at baseline.

After 12 weeks of therapy, a greater proportion of patients treated with upadacitinib experienced corticosteroid-free clinical remission (61% vs 47%), but the difference was not significant (Figure 5). However, a significant difference was observed at 52 weeks, with 72% of patients treated with upadacitinib achieving corticosteroid-free clinical remission vs 48% of patients treated with tofacitinib (*P*<.05). Treatment persistence at 52 weeks was also superior with upadacitinib compared with tofacitinib (86% vs 64%; *P*<.05). Other comparisons at 52 weeks that did not reach significance included endoscopic response (70% vs 73%) and endoscopic remission (52% vs 34%) with upadacitinib vs tofacitinib, respectively.

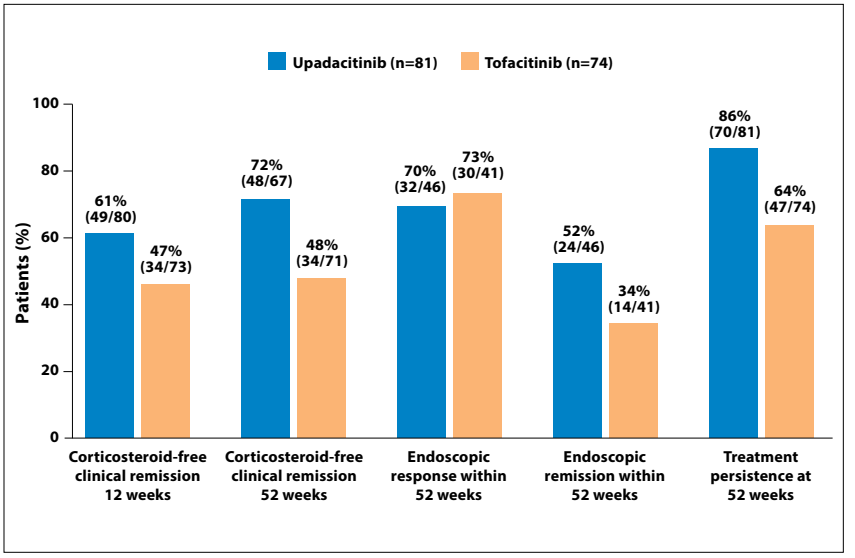

Figure 5. Unadjusted outcomes. There is variability in fraction denominators owing to missing data.

Adapted from Dalal RS et al. DDW abstract 247. *Gastroenterology*. 2024;166(6)(suppl 1).[5]

Covariates were successfully balanced to adjust for confounding. Upadacitinib was associated with a superior likelihood of achieving corticosteroid-free clinical remission at both 12 weeks (odds ratio, 2.28; 95% CI, 1.13-4.59) and at 52 weeks (odds ratio, 3.01; 95% CI, 1.39-6.55). A sensitivity analysis showed that upadacitinib was still superior to tofacitinib in achieving corticosteroid-free clinical remission at both 12 and 52 weeks when patients with prior exposure to tofacitinib in the upadacitinib cohort were excluded. With upadacitinib vs tofacitinib, the most common reasons for discontinuation were a lack of response (64% vs 89%), AEs (18% vs 7%), colectomy for dysplasia (9% vs 0%), and adherence or cost (9% vs 4%). AEs with both JAK inhibitors were consistent with descriptions in published reports.

The numbers of patients treated with upadacitinib and tofacitinib were small—81 and 74 patients, respectively, with 24 of the 81 patients (30%) treated with upadacitinib having received prior tofacitinib therapy. Overall, the results suggest that upadacitinib was superior to tofacitinib for corticosteroid-free clinical remission as well as persistence on drug at week 52. Endoscopic response and remission were not statistically different between the 2 groups. Given the small number of patients in each arm of the study and the fact that there are missing endoscopic data, the results should be considered preliminary and not conclusive. Further larger studies will be required to confirm these preliminary results.

– Gary R. Lichtenstein, MD

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