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A Fully Subcutaneous Guselkumab Regimen is Efficacious and Durable for Moderately to Severely Active Ulcerative Colitis


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This summary reviews Long M, Allegretti JR, Danese S, et al. Efficacy and safety of subcutaneous guselkumab induction therapy in participants with moderately to severely active ulcerative colitis (ASTRO): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Gastroenterol Hepatol. 2026; 11 (4): 284-298.

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STRUCTURED ABSTRACT

Question: Is subcutaneous (SC) guselkumab induction safe and efficacious for adults with moderately to severely active ulcerative colitis (UC)?

Design: The ASTRO study is a phase 3, double-blind, treat-through, randomized, placebo-controlled trial.

Setting: The study was made in 153 sites, including community centers and hospitals, across 25 countries.

Patients: Adults ≥18 years with moderately to severely active UC (modified Mayo score 5–9, Mayo endoscopic subscore [MES] ≥2, and rectal bleeding subscore ≥1) with current or prior inadequate response or intolerance to corticosteroids, immunosuppressants, biologics, Janus kinase inhibitors, or sphingosine-1-phosphate receptor modulators, or a history of corticosteroid dependence.

Intervention: Participants were randomly assigned (1:1:1) to SC guselkumab 400 mg at weeks 0, 4, and 8 followed by 100 mg every 8 weeks (400/100 mg group); SC guselkumab 400 mg at weeks 0, 4, and 8 followed by 200 mg every 4 weeks (400/200 mg group); or matched placebo. Participants meeting rescue criteria at week 16 received guselkumab 400 mg at weeks 16, 20, and 24 followed by 100 mg every 8 weeks, while guselkumab-treated participants underwent sham rescue.

Outcomes: The primary outcome was clinical remission at week 12, defined as stool frequency subscore of 0 or 1 (not increased from baseline), rectal bleeding subscore of 0, and MES of 0 or 1 with no friability. Secondary outcomes included clinical remission at week 24, endoscopic improvement, histologic-endoscopic mucosal improvement, symptomatic remission, and safety.

Data Analysis: Efficacy analyses were conducted in the modified intention-to-treat population (all randomized participants who received at least 1 dose of study drug). Adjusted treatment differences between pooled guselkumab groups and placebo were estimated using a Cochran–Mantel–Haenszel method stratified by prior advanced therapy failure and baseline MES.

Funding: Johnson & Johnson (Janssen Research and Development).

Results: Between September 2022 and April 2024, 418 participants were randomized: 139 to the 400/100 mg group, 140 to the 400/200 mg group, and 139 to placebo. Mean age was 41.7 years, 61% were men, mean disease duration was 7.6 years, and mean modified Mayo score was 6.7.

At week 12, guselkumab achieved significantly higher rates of all primary and secondary endpoints compared to placebo, including clinical remission (28% vs 6%; adjusted difference 21 percentage points; P <0.001), clinical response (66% vs 35%; P <0.001), symptomatic remission (51% vs 21%; P <0.001), endoscopic improvement (37% vs 13%; P <0.001), and histologic-endoscopic mucosal improvement (31% vs 11%; P <0.001). Efficacy was consistent across advanced therapy–naïve and advanced therapy–experienced subgroups.

At week 48, among advanced therapy–naïve participants, clinical remission rates were 50.6% and 48.1% in the 400/200 and 400/100 mg groups, respectively, compared to 7.6% with placebo; among advanced therapy–experienced participants, rates were 32.7%, 21.1%, and 7.1%, respectively.

Adverse event rates were comparable between guselkumab and placebo groups, with no treatment-related deaths and no new safety signals identified through 48 weeks.

COMMENTARY

Why Is This Important?

Guselkumab was approved by the FDA in September 2024 for intravenous (IV) induction in UC. The subsequent approval of subcutaneous induction in September 2025, supported by the phase 3 ASTRO trial, represents an important shift in the IL-23 inhibitor landscape. While risankizumab and mirikizumab currently require IV induction for UC, guselkumab is now the first in its class to offer a fully subcutaneous induction and maintenance option.

For clinicians, ASTRO provides the data needed to determine which patients may reasonably avoid infusion-based therapy and begin treatment entirely at home.

Key Study Findings

ASTRO was a phase 3, randomized, placebo-controlled trial of 418 patients with moderate-to-severe UC. Patients received subcutaneous guselkumab 400 mg in weeks 0, 4, and 8, followed by maintenance dosing. The higher induction dose reflects the lower (~50%) bioavailability of subcutaneous administration compared to IV.

At week 12, the primary endpoint of clinical remission was achieved in 28% of patients receiving guselkumab compared to 6% with placebo (P <0.0001). Secondary endpoints, including clinical response and endoscopic improvement, were also significantly improved.

Symptomatic improvement in stool frequency and rectal bleeding was observed as early as week 2–4, an important consideration for patients with active disease.

By week 24, clinical remission rates were maintained at approximately 35%–36%. Approximately 40% of participants had prior exposure to biologics, Janus kinase inhibitors, or sphingosine-1-phosphate modulators. Efficacy in this treatment-experienced population was consistent with the overall cohort, supporting use in later-line settings.

Caution

While the 28% remission rate at week 12 is numerically similar to IV induction data from the QUASAR trial[1], no direct head-to-head comparison exists. The inverse probability weighting analysis performed by the authors suggests comparable efficacy between SC and IV induction, but this remains indirect and hypothesis-generating.

Additionally, 56% of participants had severe endoscopic disease (Mayo endoscopic subscore 3) at baseline, which may limit generalizability to patients with milder disease.

The treat-through design further complicates interpretation of longer-term outcomes. At week 16, placebo non-responders were rescued with active

therapy, which limits the strength of placebo comparisons at later time points.

Finally, the study was industry-funded, which should be acknowledged, although the trial design was rigorous.

Our Practice

In our practice, ASTRO does not make subcutaneous induction the default for all patients, but it clearly establishes it as a viable option.

We are most likely to prioritize a fully subcutaneous approach in patients with logistical barriers to infusion centers, including long travel distances or inflexible work schedules, as well as in those who strongly prefer self-administered therapy.

At the same time, we still consider IV induction in select situations. For patients with more severe disease, particularly those who were recently hospitalized or have markedly elevated inflammatory markers, we may favor IV induction to ensure immediate and reliable drug exposure, recognizing that direct comparative data are lacking.

More broadly, ASTRO reinforces the importance of not only selecting the appropriate therapeutic agent but also individualizing the delivery strategy to align with each patient's clinical needs and preferences.

Future Research

A key unanswered question is whether subcutaneous and intravenous induction strategies are truly equivalent in higher-risk populations. A prospective head-to-head trial would be particularly valuable.

In addition, as more IL-23 inhibitors and subcutaneous options become available, understanding the cost-effectiveness of avoiding infusion-related care will be increasingly important for both clinicians and health systems.

Conflict of Interest

The authors of the summary declare no conflicts of interest.

REFERENCE

1. Rubin DT, Allegretti JR, Panés J, et al. Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. Lancet. 2025 Jan 4;405(10472):33-49.