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Subcutaneous Guselkumab Is Effective for Both Induction and Maintenance of Crohn's Disease

Dr. Rahul Dalal
Associate Editor

Rahul Dalal, MD, MPH

Instructor, Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

IBD

This summary reviews Hart A, Panaccione R, Steinwurz F, et al. Efficacy and safety of guselkumab subcutaneous induction and maintenance in participants with moderately to severely active Crohn's disease: Results from the phase 3 GRAVITI Study. *Gastroenterology*. 2025:S0016-5085(25)00522-0.

Correspondence to Rahul Dalal, MD, MPH, Associate Editor. Email: EBGI@gi.org

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STRUCTURED ABSTRACT

Question: Is subcutaneous (SC) guselkumab safe and effect for moderate-to-severe Crohn's disease (CD) for both induction and maintenance?

Design: Phase 3, randomized, double-blind, placebo-controlled treat-through trial.

Setting: One hundred forty-three centers across 23 countries or territories.

Patients: Three hundred forty-seven adults of age ≥18 years with moderately to severely active CD and prior exposure to one or more biologic or conventional therapies

Interventions: Patients were randomized in a 1:1:1 ratio to receive either a placebo, guselkumab 400 mg SC every 4 weeks (q4w) for induction followed by 100 mg SC q8w for maintenance (standard dose maintenance), or 400 mg SC q4w for induction followed by 200 mg SC q4w for maintenance (high dose maintenance).

Outcomes: Co-primary endpoints were the clinical remission (Crohn's Disease Activity Score <150) and endoscopic response (≥50% reduction of baseline Simple Endoscopic Score for Crohn's Disease) score), both at week 12. Other endpoints included Patient-Reported Outcome-2 remission (abdominal pain score ≤1 and stool frequency score ≤3) at week 12, clinical response at week 12, clinical remission at weeks 24 and 48, change in C-reactive protein and fecal calprotectin, and adverse events.

Data Analysis: Common Risk Differences were calculated using Mantel-Haenszel stratum weights at a significance level of 0.05. Efficacy analyses were performed for participants who received ≥1 dose of study agent.

Funding: Johnson & Johnson.

Results: At week 12, guselkumab was superior to placebo for clinical remission (56.1% vs 21.4%, $P < 0.01$) and endoscopic response (41.3% vs 21.4%, $P < 0.01$). Similar findings were observed at week 48 for clinical remission (60.0% standard dose, 66.1% high dose, 17.1% placebo, $P < 0.01$) and endoscopic response (44.3%, 51.3%, 6.8%, $P < 0.01$) (**Figure 1**). Guselkumab was effective for both bio-naïve and bio-exposed patients. Median C-reactive protein and fecal calprotectin concentrations decreased through week 48 with guselkumab compared to placebo. Adverse events were similar between guselkumab (327.2 per 100 participant years [PY] high dose maintenance, 307.2 per 100 PYs standard dose maintenance) and placebo (413.0 per 100 PYs).

COMMENTARY

Why Is This Important?

The GALAXI trials have previously established the efficacy of guselkumab for induction and maintenance of moderate-to-severe CD.[1,2] Guselkumab is now the third approved anti-interleukin (IL) 23 therapy approved for this indication.[3,4] However, the GRAVITI trial is the first to evaluate an IL-23 therapy with a SC induction option. Efficacy results for both induction and maintenance in GRAVITI were overall similar to the findings from the GALAXI trials, which only included IV induction of guselkumab. Importantly, both trials utilized treat-through designs to better represent real-world clinical practice. SC induction offers patients greater convenience and less resource utilization but without sacrificing clinical efficacy through at least 48 weeks of therapy.

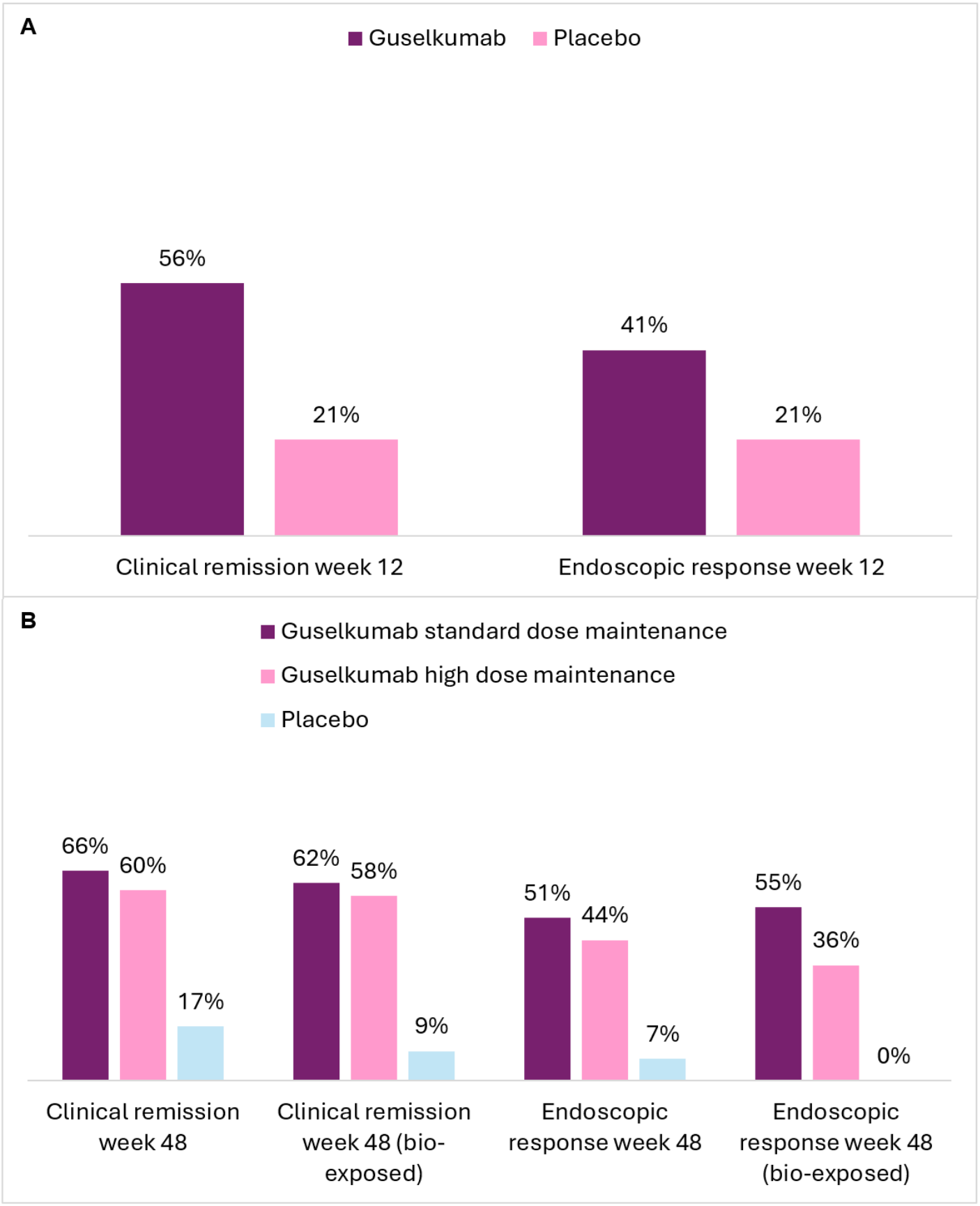

Figure 1. **A**. Coprimary endpoints for subcutaneous guselkumab vs placebo. **B**. Selected 48-week endpoints. All comparisons vs placebo are statistically significant at $P = 0.05$.

Key Study Findings

The study found that SC guselkumab for both induction and maintenance resulted in superior clinical and endoscopic outcomes through 48 weeks compared to placebo.

Efficacy was maintained for both bio-naïve and bio-exposed populations. These findings were consistent with results from the GALAXI trials that utilized IV guselkumab induction. Adverse events were similar between both dosing regimens of SC guselkumab maintenance and placebo, and the most commonly reported AEs being upper respiratory tract infections, abdominal pain, and COVID-19. No new safety signals were identified in this study when compared to other indications for guselkumab, including ulcerative colitis. Anti-guselkumab antibodies were detected in 8.8% of participants, however there was no impact on serum guselkumab concentrations, efficacy, or safety.

Caution

The study was not designed to detect differences in efficacy and safety between SC maintenance regimens, nor were there statistical comparisons to intravenous induction regimens. Maintenance dose escalation from 100 mg q8w to 200 mg q4w was not assessed in cases of loss of response, which should be the subject of future research. The long-term efficacy, safety, and durability of SC guselkumab maintenance therapy are also unknown.

My Practice

In my practice, I commonly prescribe IL-23 antagonists as both first and second-line therapies for both CD and ulcerative colitis. Now with a SC induction option, I will likely utilize guselkumab therapy more often than other IL-23 antagonists for Crohn's disease. The majority of my patients appreciate and prefer the convenience of SC therapies over intravenous infusions for both induction and maintenance. Furthermore, the option of having 2 maintenance dosing regimens allows me to tailor my therapy to a patient's disease severity.

For Future Research

Because of the rapid growth of advanced therapies for inflammatory bowel disease, there is an increasing need for head-to-head trials and comparative effectiveness studies to guide therapy selection. Additionally, we require large, prospective studies to evaluate and compare the effectiveness of IL-23 antagonists across the various disease locations and phenotypes of CD (e.g. ileal and fistulizing disease).

Conflict of Interest

Dr. Dalal has research grant support from Janssen and Pfizer and has served as a consultant for Janssen, Takeda, and Centaur Labs.

Abbreviations

CD, Crohn's disease; COVID-19, coronavirus disease-2019; q4w, Every 4 weeks; q8w, every 8 weeks; PY, participant year; SC, subcutaneous.

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