

Benefit-Risk of guselkumab compared to placebo in the treatment of moderately to severely active ulcerative colitis

Ellen Janssen, Thomas Baker, Jacqueline Yee, Hewei Li, Ye Miao, Matthew Germinaro
Johnson & Johnson, Titusville, NJ/ Springhouse, PA

Introduction

An informed judgement on whether the benefits of a drug outweigh the potential risks is an integral component to the drug approval decisions by regulatory agencies (US Food and Drug Administration, 2023)

- Structured Benefit-Risk Frameworks aid in the analysis and communication of the benefit-risk assessment throughout the development of medicines and increase transparency of these decisions (Pignatti et al., 2015)

Guselkumab (GUS) is a selective dual-acting interleukin (IL)-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23 (Sachen et al., 2025)

GUS was recently approved to treat moderately to severely active ulcerative colitis (UC) and Crohn's disease. QUASAR and ASTRO are Phase 3, double-blind, randomized controlled studies evaluating the efficacy and safety of guselkumab compared to placebo in the treatment of moderately-to-severely active UC (Rubin et al, 2024; L Peyrin-Biroulet et al., 2025).

Objective

This post hoc analysis of the QUASAR and ASTRO trials assessed the benefit-risk profile of guselkumab IV or SC induction and SC maintenance treatment for participants with moderately-to-severely active ulcerative colitis (UC).

Methods

- The Benefit-Risk Action Team (BRAT) framework was used to structure the B-R analysis (Leviton et al., 2011)
- Included outcomes
 - Efficacy: the primary endpoint of clinical remission and other guideline-endorsed UC treatment targets.
 - Safety: risks or potential risks of guselkumab or other biologic treatments approved for IBD.
- Risk differences per 100 treated participants were calculated between the guselkumab groups and the placebo group.
 - This value can be interpreted as the additional number of participants among 100 participants who would experience a particular outcome when treated with guselkumab compared to placebo.
- The B-R assessment was conducted for
 - Induction Week 12:
 - QUASAR: 200 mg IV q4w
 - ASTRO: 400 mg SC q4w
 - Maintenance Week 44:
 - QUASAR:
 - 100 mg SC q8w;
 - 200 mg SC q4w
 - Populations:
 - The overall population
 - Clinically relevant subgroups based on UC treatment history (advanced therapy naïve (ADT-naïve) and advanced therapy failure (ADT-failure)).

Key Findings

- For each induction and maintenance dose regimen, guselkumab treatment resulted in clinical benefits compared with placebo at induction week 12 and maintenance week 44.
- AEs of interest were reported infrequently (Figure 1, 2, 3). The incidence rates of treatment-emergent AEs, including but not limited to serious infections, MACE, VTE, malignancy, and clinically important hepatic disorders, among participants treated with guselkumab were comparable with those treated with placebo (no clinically meaningful risk differences observed) through the reporting period across the populations studied.

Conclusion

- These findings support a favorable benefit-risk profile for guselkumab induction (200 mg IV q4w or 400mg SC q4w) and maintenance (200 mg SC q4w or 100 mg SC q8w) treatment in participants with moderately to severely active UC.
- The favorable benefit-risk profile was consistently demonstrated across the populations studied, including ADT-naïve and ADT-IR participants.

Results

- For induction treatment regimens compared to placebo, if 100 participants were treated (Figure 1):
 - QUASAR: 14.9 more (95% CI: 9.9, 19.9) in the guselkumab 200 mg IV q4w induction group would achieve clinical remission at induction Week 12
 - ASTRO: 21.1 more participants (95% CI: 14.5, 27.6) in the guselkumab 400 mg SC q4w induction group would achieve clinical remission at Week 12.

- For the maintenance dose regimens evaluated in QUASAR compared to placebo, if 100 participants were treated (Figure 2):
 - 200mg SC q4w group: 29.5 more (95% CI: 20.9, 38.1) would achieve clinical remission at maintenance week 44.
 - 100 mg SC q8w group: 25.2 more participants (95% CI: 16.4, 33.9) would achieve clinical remission at maintenance week 44.

Figure 1. Benefit-Risk Comparison of Guselkumab Induction Compared to Placebo at Week 1–12, Overall Population

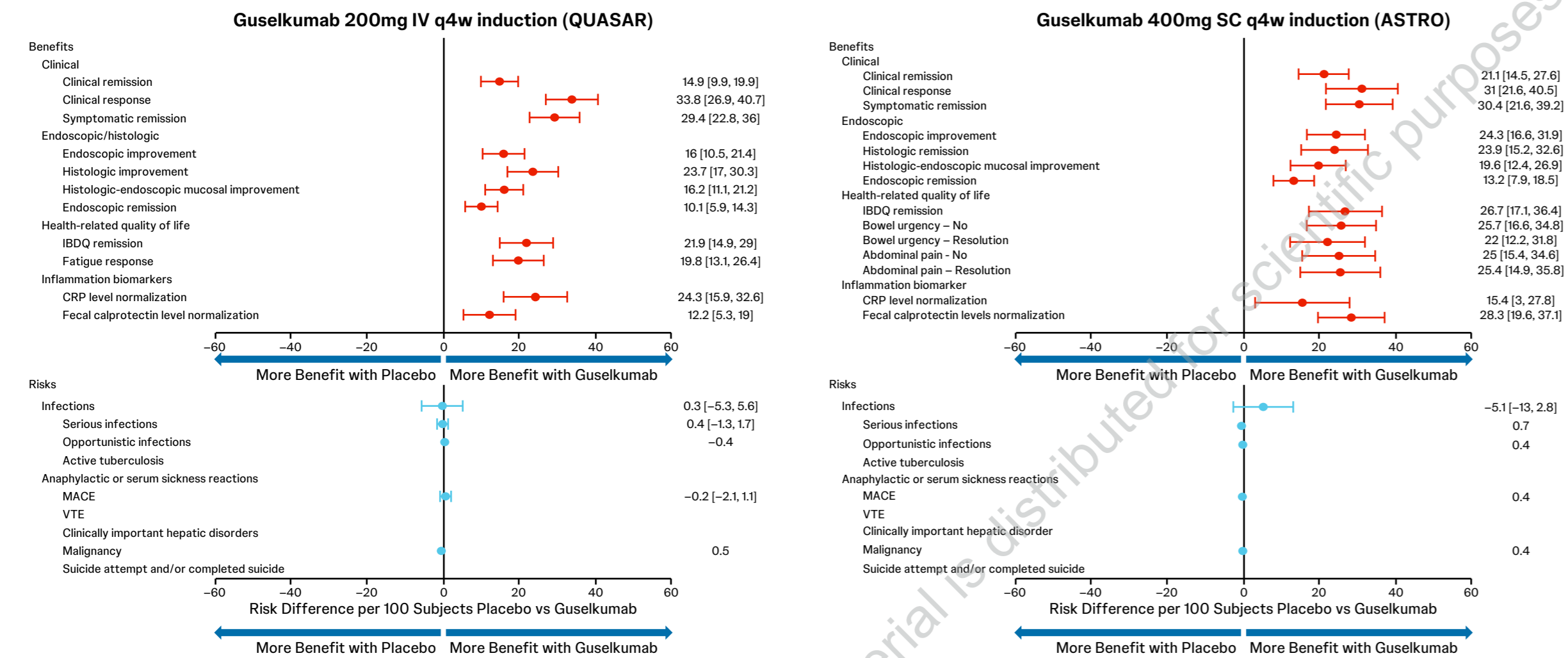
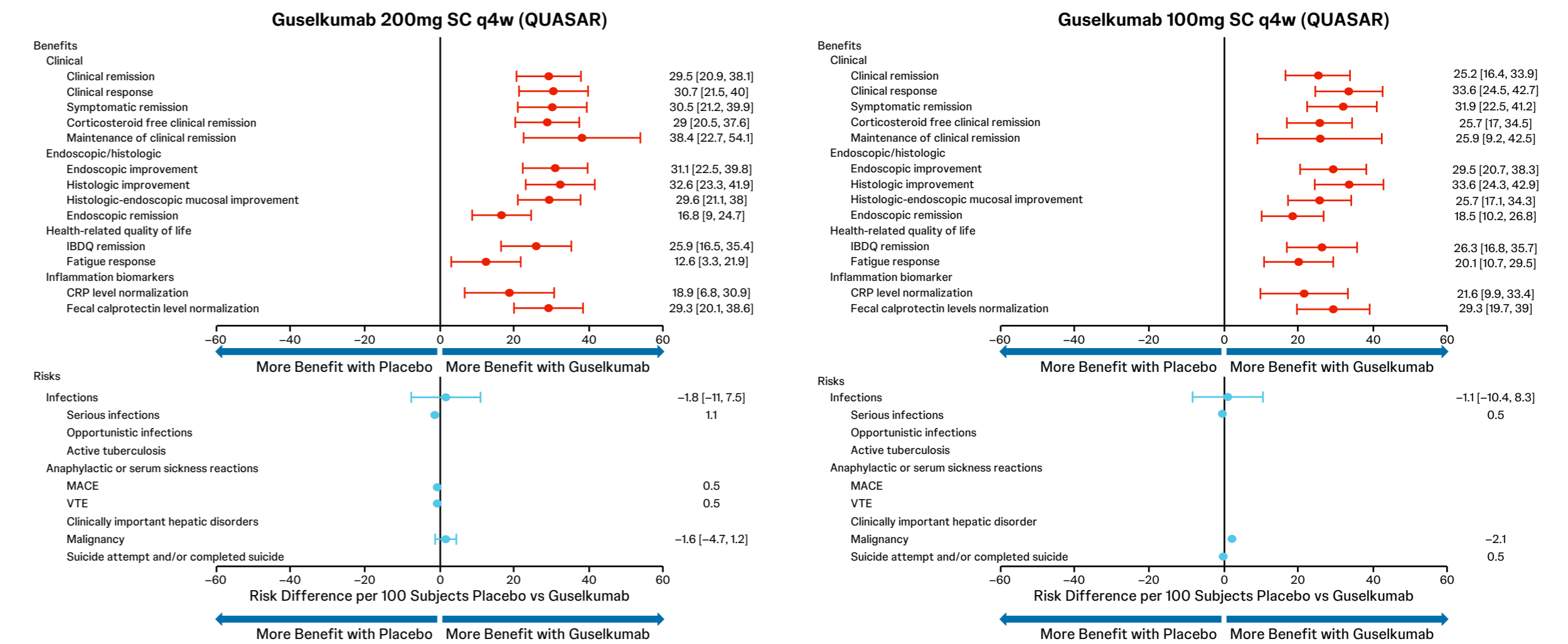


Figure 2. Benefit-Risk Comparison of Guselkumab Maintenance Dose Regimen Compared to Placebo at Week M–44, Overall Population



Clinically important hepatic disorders were defined as hepatic disorder SAEs or AEs leading to discontinuation. For efficacy, the adjusted treatment difference(s) and CI(s) were based on the Wald statistic with Cochran-Mantel-Haenszel weight. For safety, empty rows indicate no events were observed in either treatment group; the CIs for risk difference were based on Newcombe method; No CI was tabulated when there were 0 or 1 event in either group

Maintenance of clinical remission was only measured for those participants who achieved clinical remission at maintenance baseline. Clinically important hepatic disorders were defined as hepatic disorder SAEs or AEs leading to discontinuation. For efficacy, the adjusted treatment difference(s) and CI(s) were based on the Wald statistic with Cochran-Mantel-Haenszel weight. For safety, empty rows indicate no events were observed in either treatment group; the CIs for risk difference were based on Newcombe method; No CI was tabulated when there were 0 or 1 event in either group