

Guselkumab versus risankizumab as maintenance treatment for moderately to severely active ulcerative colitis: Network meta-analyses of clinical and endoscopic outcomes

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Background

Ulcerative colitis (UC) is a chronic inflammatory condition characterized by persistent inflammation of the colon and rectal mucosal lining, leading to formation of ulcers in the large intestine.¹ It presents through various gastrointestinal symptoms, including urgency of bowel movements, fatigue, abdominal pain, and bloody stools.²

Key treatments for UC include interleukin (IL)-23 inhibitors, which prevent the p-19 subunit of the IL-23 molecule from binding to leukocytes, thus preventing the transformation of undifferentiated T-helper cells into Th17 cells which are known to be primary drivers of the inflammatory response seen in UC.³

Guselkumab and risankizumab are IL-23 inhibitors approved for the treatment of moderately to severely active UC in the United States (US) Food and Drug Administration (FDA), as well as the European Medicines Agency (EMA). These agents have not been directly compared in an interventional trial.

Objective

The objective of this study was to conduct network meta-analyses (NMAs) of randomized controlled trials (RCTs) to compare clinical and endoscopic outcomes during maintenance therapy with guselkumab versus risankizumab, informed by a systematic literature review (SLR)

Methods

SLR of RCTs

- Trials of interest for NMA were identified through a rigorous systematic literature review (SLR) and feasibility assessment.
- Of the 5,638 records identified across broad database and supplemental searches, 188 records were included in the SLR, which reported on 45 unique randomized controlled trials (RCTs) investigating twelve interventions for UC.
- In general, trials from the SLR were found to be of good quality based on the NICE Single Technology Appraisal Checklist.⁴

Feasibility assessment

- Of the 45 RCTs, two trials were considered in the NMA feasibility assessment, as they reported on guselkumab or risankizumab.
- Study designs, key population characteristics such as treatment experience, as well as the definitions of outcomes were considered comparable between the four trials.
- As such, NMAs comparing guselkumab and risankizumab in the maintenance phase of treatment for moderately to severely active UC were considered feasible.

NMAs comparing guselkumab and risankizumab

- Network meta-analyses (NMAs) were conducted to compare guselkumab and risankizumab as maintenance therapy for moderately to severely active UC, based on key outcomes from pivotal Phase 3 RCTs, that were identified in the SLR:
 - QUASAR trial of guselkumab
 - COMMAND trial of risankizumab
- Data from these re-randomized RCTs (QUASAR, COMMAND) were used directly, as both trials were similarly designed.
- Frequentist, fixed-effect NMAs were conducted for key efficacy endpoints at the end of maintenance (44 weeks in QUASAR and 52 weeks in COMMAND) as reported by the trials, including: clinical remission, endoscopic improvement, endoscopic remission, histologic endoscopic mucosal improvement (HEMI).
 - Analysis results are reported as odds ratios (OR).
 - Analyses included population with varied advanced therapy [ADT] failure status.

Key Takeaways

Results of NMAs suggest that guselkumab regimens are superior to risankizumab 360 mg Q8W for maintenance treatment of moderately to severely active UC.

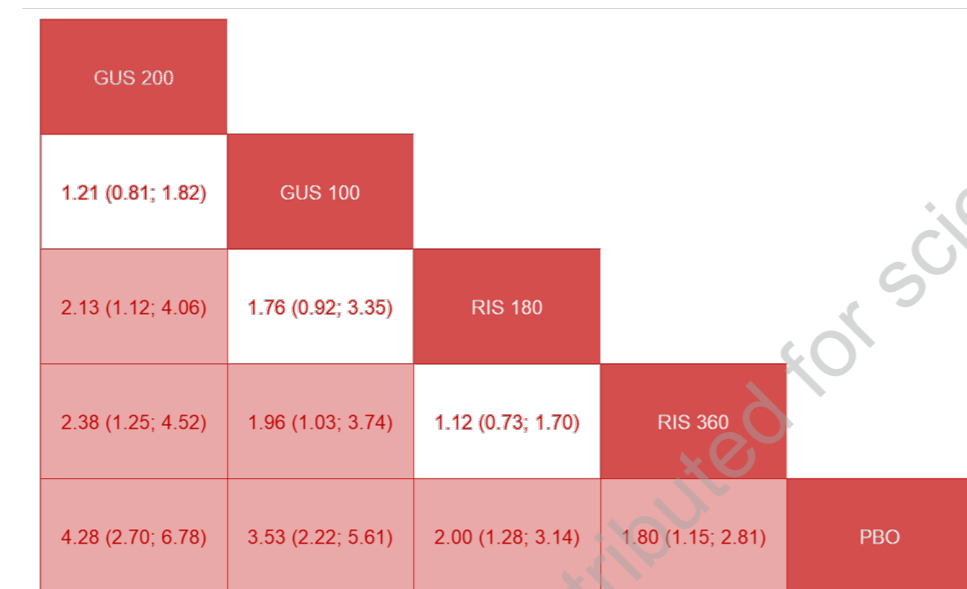
This benefit of guselkumab exists across multiple efficacy endpoints, with significant effect estimates noted for endoscopic improvement and clinical remission.

Results

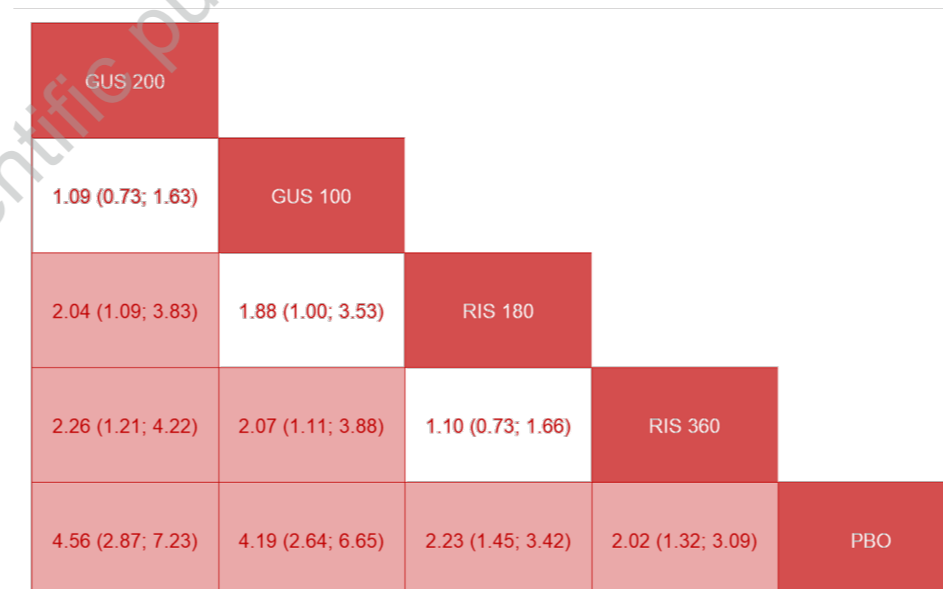
Table 1. Summary of results for NMAs comparing efficacy of guselkumab and risankizumab regimens at the end of maintenance (OR [95% CI])

	RIS 180 mg Q8W	RIS 360 mg Q8W	PBO
Clinical remission			
GUS 100 mg Q8W	1.76 (0.92, 3.35)	1.96 (1.03, 3.74)	3.53 (2.22, 5.61)
GUS 200 mg Q4W	2.13 (1.12, 4.06)	2.38 (1.25, 4.52)	4.28 (2.70, 6.78)
Endoscopic improvement			
GUS 100 mg Q8W	1.88 (1.00, 3.53)	2.07 (1.11, 3.88)	4.19 (2.64, 6.65)
GUS 200 mg Q4W	2.04 (1.09, 3.83)	2.26 (1.21, 4.22)	4.56 (2.87, 7.23)
Endoscopic remission			
GUS 100 mg Q8W	1.71 (0.82, 3.55)	1.59 (0.77, 3.29)	2.93 (1.79, 4.82)
GUS 200 mg Q4W	1.64 (0.79, 3.41)	1.53 (0.74, 3.16)	2.82 (1.72, 4.63)
HEMI			
GUS 100 mg Q8W	1.55 (0.81, 3.00)	1.59 (0.83, 3.06)	3.82 (2.37, 6.15)
GUS 200 mg Q4W	1.85 (0.96, 3.56)	1.89 (0.98, 3.63)	4.54 (2.82, 7.30)

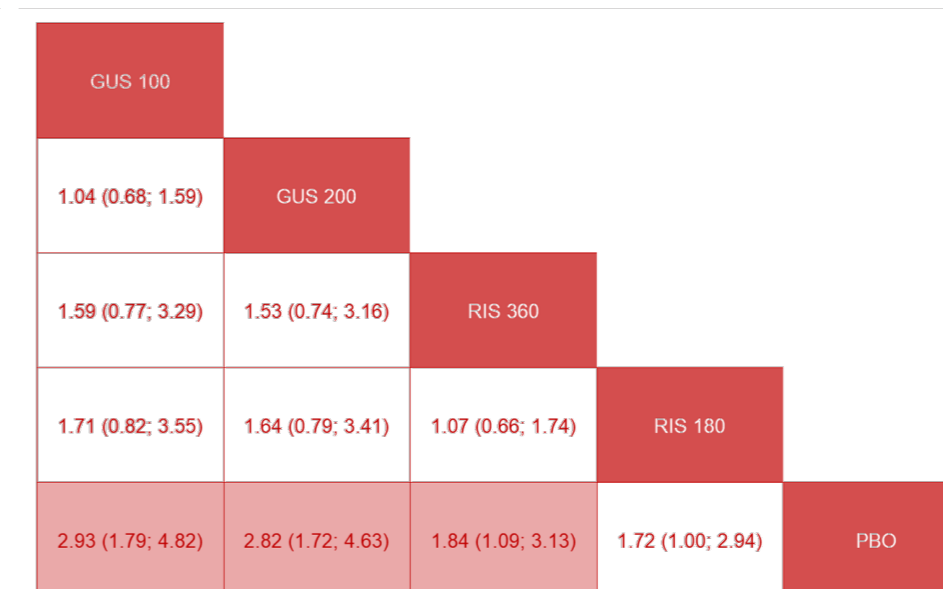
Figure 1. NMA results at the end of maintenance for (A) Clinical remission, (B) Endoscopic improvement, (C) Endoscopic remission, and (D) HEMI



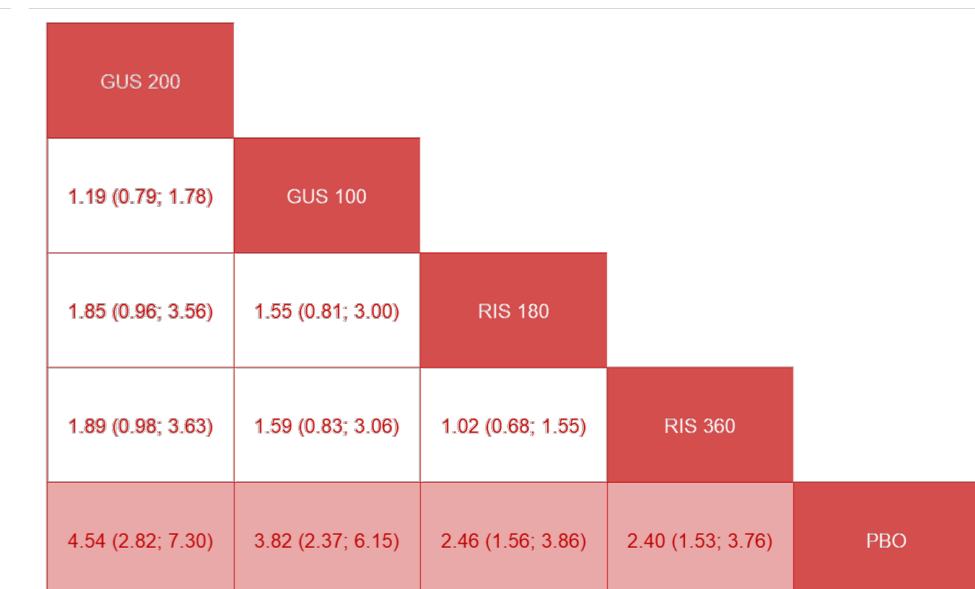
(A) NMA of clinical remission found significantly higher odds of remission for guselkumab 200 mg Q4W compared to both doses of risankizumab (360 mg Q8W, 180 mg Q8W). Guselkumab 100 mg Q8W had significantly higher odds of clinical remission versus risankizumab 360 mg Q8W.



(B) NMA of endoscopic improvement found significantly higher odds of improvement for guselkumab 200 mg Q4W compared to both doses of risankizumab (360 mg Q8W, 180 mg Q8W). Guselkumab 100 mg Q8W had significantly higher odds of endoscopic improvement compared to risankizumab 360 mg Q8W.



(C) NMA of endoscopic remission found no significant differences between included treatments. Only risankizumab 180 mg Q8W was not significantly more effective than placebo.



(D) NMA of HEMI found no significant differences between included treatments.

All cells present on OR and present the corresponding 95% CI in brackets. **Red text** denotes significantly benefit of a GUS regimen over RIS regimen (ie, confidence interval does not include 1). **Blue text** denotes significantly benefit of a RIS regimen over PBO (ie, confidence interval does not include 1). **Grey text** denotes no significant difference between GUS and RIS regimens (ie, confidence interval includes 1) or between RIS and PBO (ie, confidence interval includes 1). **Abbreviations:** CI, confidence interval; GUS, guselkumab; HEMI, histologic endoscopic mucosal improvement; NMA, network meta-analysis; OR, odds ratio; PBO, placebo; Q4W, every four weeks; Q8W, every 8 weeks; RIS, risankizumab; UC, ulcerative colitis.