

# Comparative Efficacy of Guselkumab vs. Risankizumab in Induction Phase for moderate to severe Crohn's Disease: An Anchored MAIC Analysis

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## Introduction

- Guselkumab (GUS) and Risankizumab (RIS) are monoclonal antibodies approved for the treatment of moderate to severe Crohn's disease.
- There are no direct head-to-head clinical trials available investigating the efficacy of these treatments.
- The aim of this study was to evaluate the relative efficacy of GUS and RIS at the end of induction treatment across a set of endpoints.

The following characteristics, which were considered the most relevant treatment effect modifiers (TEMs), were used in the matching process as base case analysis: Age, Sex, BMI, CDAI, disease location, prior biologic treatment failure, disease severity, disease duration, CRP, SES-CD, fCal, concomitant immunomodulator and/or corticosteroid use. Matching on all available characteristics was explored in a sensitivity analysis (see table 1).

## Bucher Indirect Treatment Comparison

The matching-adjusted ORs were calculated based on the reweighted GUS data and compared to the reported ORs from the RIS trials. The indirect treatment effect of GUS versus RIS was then estimated using a Bucher ITC (4,5) with placebo as the common comparator across both studies. For all endpoints, ORs with 95% confidence intervals (CI) are reported.

## Analyses conducted

The base case focused on a core set of treatment effect modifiers, while in a sensitivity analysis we included all available baseline characteristic to evaluate the impact of matching these additional characteristics.

The primary analysis focusses on a mixed population consisting of bio-naïve and failure CD patients. However, since the MOTIVATE trial reported outcomes for bio-failure patients separately, a secondary analysis was performed including only these patients from the Gus and RIS cohorts.

Finally, since the GRAVITI trial involved patients receiving subcutaneous induction only -whereas the GALAXI 2/3 trials used intravenous induction- a sensitivity analysis was performed using only the GRAVITI data to explore whether subcutaneous induction would produce different results.

## Data and Method selection

- Five phase 3 placebo-controlled, blinded clinical trials have been identified: GUS has been compared vs. placebo in the GRAVITI, GALAXI 2, GALAXI 3 trials (1,2), and RIS has been compared to placebo in ADVANCE and MOTIVATE trials (3).
- During induction, patients received GUS 200 mg intravenous or 400 mg subcutaneous at weeks 0, 4, and 8 or RIS 600 mg intravenous at weeks 0, 4, and 8. The endpoints of interest for this analysis are clinical remission, PRO-2 remission, clinical response, abdominal pain and stool frequency remission, as well as endoscopic response at week 12, which marks the end of the induction period.
- As all studies had different inclusion/exclusion criteria and the populations differ on baseline characteristics, which may impact the relative treatment effect, an anchored MAIC was performed.
- Individual patient level data were available for trials of GUS, whereas for RIS trials aggregated level data were used.

## Matching

All study baseline characteristics which could potentially affect the relative treatment effect and that were reported in ADVANCE and MOTIVATE were matched using inverse probability weighting. The weights were estimated using the method of moments as described by Signorovitch et al. (4).

## Results

The combined GUS cohort consisted of 1077 patients. Since the main eligibility criteria between all trials were similar, no patients needed to be excluded from the analyses. After matching, cohorts' characteristics were balanced. The effective sample size in the base case analysis was 585 (table 1).

Table 1: Baseline characteristics of pooled GUS trials before and after adjustment to the pooled RIS trials

	ADVANCE and MOTIVATE (3)	GRAVITI and GALAXI 2-3(1,2)		
	Observed N = 899	Observed N =1077	Base case adjusted N=1070 ESS=585	All variables adjusted (sensitivity) N=1002 ESS=383
% Bio-failure = Yes	75	50	75	75
% Failed >1 anti TNFs	31	11	31	31
mean Disease duration (yrs)	10	7	10	10
% Disease location: Ileal only	15	23	15	15
% Disease location: Colonic only	37	38	37	37
% Disease location: Ileal-Colonic	48	39	48	48
mean CDAI	314.4	296	314.4	314.4
med hs-CRP (mg/L)	8.4	6.4	8.4	8.4
mean SES-CD	14.5	12.6	14.5	14.5
med Fecal calprotectin (mg/kg)	1100.5	900	1100	1100
% Immunomodular use	23	30	23	23
% Corticosteroid use	32	34	32	32
mean Age	38.7	36.6	38.7	38.7
% Female	47	42	47	47
mean Average daily abdominal pain	1.9	2.1	2.1	1.9
mean Average daily stool frequency	6.1	4.7	5.4	6.1
mean Weight	71.2	68.6	68.4	71.2
% Race: White	82	75	73	82
% Race: Asian	14	23	25	14
% Race: Other	4	2	2	4
% Ethnicity: Hispanic/Latino	6	6	8	6
% Ethnicity: Non-Hispanic/Latino	94	94	92	94

Footnotes: grey cells in base case are variables which had not been used in the matching process

In a mixed population of bio-naïve and bio-failure CD patients, GUS demonstrated statistically significant results in favor of GUS compared to RIS for PRO-2 remission and clinical response (table 2). Clinical remission and abdominal pain remission showed a trend in favor of GUS. Endoscopic response and stool frequency remission were comparable to RIS.

When only focusing on the CD patients with biologic treatment failure from the MOTIVATE trial, GUS demonstrated statistically significant improved outcomes compared to RIS for PRO-2 remission. For all other endpoints, results were numerically in favor of GUS vs. RIS, as seen for the mixed population.

Results of the analysis with only data from the GUS GRAVITI trial included are presented in table 3. In the mixed population, GUS demonstrated statistically significant better results compared to RIS for clinical response, PRO-2 remission and abdominal pain remission. For clinical remission GUS was numerically better than RIS. Stool frequency remission was comparable to RIS, while for endoscopic response a trend in favor of RIS was observed that was not statistically significant. When only focusing on the CD patients with biologic treatment failure from the MOTIVATE trial, GUS demonstrated statistically significant improved outcomes compared to RIS for clinical response and abdominal pain. For all other endpoints, results were numerically in favor of GUS vs. RIS with high odds ratios.

## Disclosures

All authors are employees of Johnson & Johnson and may hold stock in the company.

Table 2: Results of GUS from pooled GRAVITI, GALAXI 2/3 vs. RIS for induction period at week 12

Endpoint	Mixed population (ADVANCE & MOTIVATE)		Bio-failure population (MOTIVATE)	
	BC	SA	BC	SA
Analysis				
N(ESS)	1070 (585)	1002 (383)	534 (342)	487 (218)
Clinical response	1.78* [1.06; 2.99]	1.42 [0.76; 2.64]	1.71 [0.82; 3.57]	1.23 [0.49; 3.04]
Endoscopic response	1.05 [0.56; 1.97]	1.05 [0.53; 2.09]	1.57 [0.59; 4.18]	1.56 [0.49; 5.01]
Clinical remission	1.51 [0.84; 2.70]	1.22 [0.60; 2.46]	1.52 [0.65; 3.51]	1.08 [0.39; 3.01]
PRO-2 clinical remission	1.96* [1.13; 3.38]	1.85* [1.03; 3.33]	2.89* [1.29; 6.49]	2.97* [1.11; 7.94]
Abdominal pain score remission	1.68 [1.00; 2.82]	1.37 [0.75; 2.52]	2.02 [0.97; 4.20]	1.68 [0.69; 4.09]
Stool frequency score remission	0.99 [0.62; 1.59]	0.93 [0.55; 1.58]	1.14 [0.59; 2.19]	1.04 [0.48; 2.26]

Table 3: Results of GUS from GRAVITI vs. RIS for induction period at week 12

Endpoint	Mixed population (ADVANCE & MOTIVATE)		Bio-failure population (MOTIVATE)	
	BC	SA	BC	SA
Analysis				
N(ESS)	346 (167)	304 (94)	160 (94)	134 (44)
Clinical response	2.22* [1.04; 4.73]	1.84 [0.74; 4.57]	3.04* [1.03; 8.97]	3.03 [0.68; 13.53]
Endoscopic response	0.74 [0.30; 1.84]	0.56 [0.22; 1.47]	0.97 [0.23; 4.11]	0.84 [0.17; 4.28]
Clinical remission	2.27 [0.99; 5.22]	1.64 [0.70; 3.85]	3.22 [0.88; 11.74]	1.87 [0.43; 8.07]
PRO-2 clinical remission	2.79* [1.06; 7.34]	2.17 [0.90; 5.23]	4.36 [0.99; 19.20]	4.01 [0.89; 18.12]
Abdominal pain score remission	2.73* [1.23; 6.06]	1.98 [0.78; 5.04]	3.87* [1.25; 11.93]	1.98 [0.50; 7.92]
Stool frequency score remission	0.93 [0.47; 1.88]	0.71 [0.31; 1.67]	1.21 [0.46; 3.17]	0.95 [0.26; 3.39]

Footnotes for tables 2 & 3: BC=base case adjusted analysis; SA=sensitivity analysis; \*p<0,05  
Dark green: stat. sign. in favor of GUS, Light green: trend in favor of GUS, Orange: trend in favor of comparator, Yellow: similar (ORs between 0.95 and 1.05)

## Discussion and Conclusion

This anchored MAIC demonstrates Guselkumab efficacy was comparable, or even superior to Risankizumab in inducing symptomatic improvements in Crohn's disease patients. Similar findings had been observed in a recent Bayesian NMA (6).

This MAIC also seems to suggest that subcutaneous induction of Gus vs. Ris is showing favorable results, based on analyses using only the GRAVITI trial dataset.

## References

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