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Efficacy and safety of guselkumab for ulcerative colitis through week 92 of the QUASAR long-term extension study

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Key Takeaways

- Both GUS maintenance dose regimens sustained symptomatic, endoscopic, and histologic efficacy in participants with UC through week 92 of the LTE
- Efficacy was sustained regardless of prior biologic and/or JAK inhibitor treatment history
- No new safety concerns were identified

Background

- 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[1]
- GUS was recently approved in the United States to treat moderately to severely active ulcerative colitis (UC) and Crohn's disease
- QUASAR long-term extension (LTE) is an ongoing, multicenter study of the efficacy and safety of GUS in participants with moderately to severely active UC[2,3]

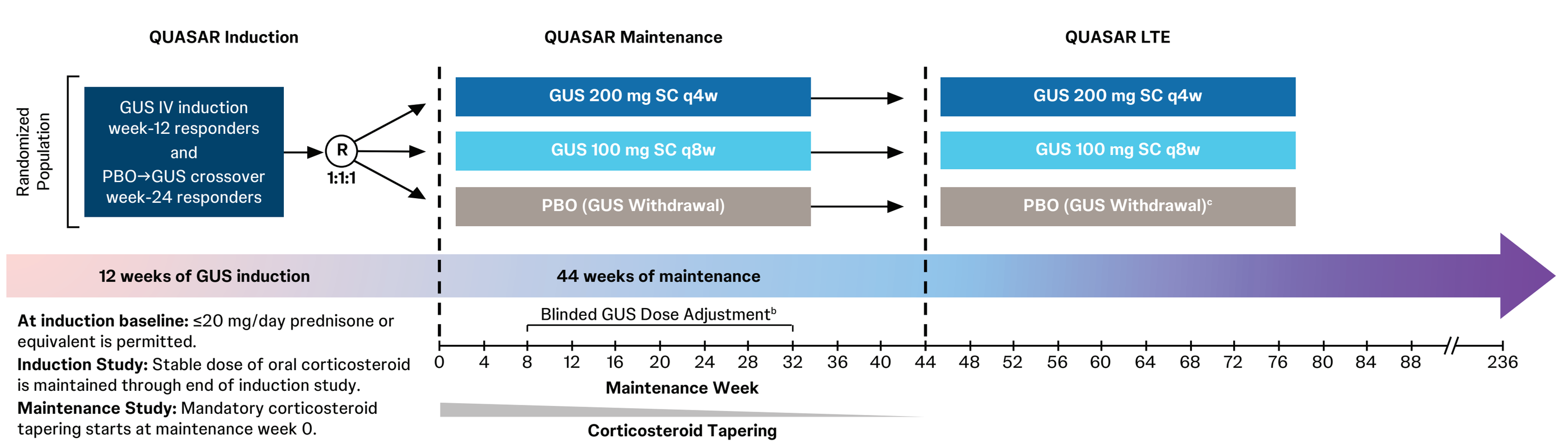
Objectives

- To understand the long-term efficacy and safety of GUS in patients with UC
- Here, we report efficacy and safety results of the ongoing QUASAR LTE study through week 92

Methods

Phase 3 QUASAR Maintenance Study Design

Target Participant Population: Adults with moderately to severely active UC[a] who were in clinical response 12 weeks following GUS IV induction



[a]Defined as induction baseline modified Mayo score of 5 to 9 with a Mayo rectal bleeding subscore ≥ 1 and a Mayo endoscopic subscore ≥ 2 based on central review. [b]Between maintenance weeks 8 and 32, randomized participants meeting loss of clinical response criteria (based on the modified Mayo score and required an endoscopic assessment) were eligible for a blinded dose adjustment as follows: PBO SC → GUS 200 mg SC q4w; GUS 100 mg SC q8w → GUS 200 mg SC q4w; GUS 200 mg SC q4w → GUS 200 mg SC q4w (sham adjustment). [c]The study blind was maintained during the LTE until the last participant in the Maintenance Study completed the maintenance week 44 visit. After the Maintenance Study was unblinded to the investigative sites, participants receiving PBO were terminated from study participation. **IV**=Intravenous, **PBO**=Placebo, **q4w**=Every 4 weeks, **q8w**=Every 8 weeks, **R**=Randomization, **SC**=Subcutaneous

- Participants completing the maintenance study week 44 visit who, in the opinion of the investigator, could benefit from continued study intervention, had the opportunity to participate in the LTE and continue their current treatment regimen
- Participants receiving PBO discontinued after study unblinding and were not included in efficacy analyses
- Efficacy was evaluated among participants with an induction baseline modified Mayo score of 5 to 9 randomized to GUS at maintenance week 0 who continued to receive GUS treatment in the LTE (LTE randomized GUS-treated population)
- Safety was evaluated among all participants regardless of modified Mayo score at induction baseline in the maintenance study (randomized and nonrandomized) who received any treatment in the LTE (LTE all treated population)

Outcomes Evaluated

- **Clinical remission:** stool frequency subscore of 0 or 1 and not increased from induction baseline, rectal bleeding subscore of 0, and endoscopic subscore of 0 or 1
- **Maintenance of clinical remission:** achievement of clinical remission at week 92 among participants who achieved clinical remission at maintenance baseline
- **Symptomatic remission:** stool frequency subscore of 0 or 1 and not increased from induction baseline, and rectal bleeding subscore of 0
- **Endoscopic improvement:** endoscopic subscore of 0 or 1
- **Endoscopic remission (normalization):** endoscopic subscore of 0
- **Histo-endoscopic mucosal improvement (HEMI):** achievement of a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations, or granulation tissue according to the Geboes grading system) and endoscopic improvement

Statistical Analysis and Data Handling

- Data were analyzed using 2 methods: 1) nonresponder imputation (NRI) accounting for treatment failure and missing data rules, and 2) "as observed" based on data as observed without applying any rules
- For NRI analyses:
  - Participants who had an ostomy or colectomy or discontinued study agent due to lack of therapeutic effect or due to an adverse event (AE) of worsening of UC before LTE week 92 were considered not to have achieved efficacy endpoints
  - After accounting for the above rules, participants who were missing ≥1 of the components pertaining to an endpoint were considered not to have achieved that endpoint

Results

Overall, 87% of participants randomized to GUS at maintenance week 0 entered the LTE, and approximately 95% of participants in the LTE randomized GUS-treated population completed treatment through LTE week 92

	GUS	
	100 mg SC q8w (N=155)	200 mg SC q4w (N=148)
Participants who discontinued study treatment prior to week 92, n (%)	7 (4.5)	9 (6.1)
Reason for discontinuation, n (%)		
Adverse event	2 (1.3)	2 (1.4)
Worsening of UC	1 (0.6)	1 (0.7)
Other than worsening of UC	1 (0.6)	1 (0.7)
Lack of efficacy	1 (0.6)	2 (1.4)
Any other reason	4 (2.6)	5 (3.4)
Withdrawal by participant	2 (1.3)	3 (2.0)
Other	2 (1.3)	2 (1.4)

Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from week 8 through week 32

Demographic and disease characteristics at induction baseline in the LTE randomized GUS-treated population

	GUS	
	100 mg SC q8w (N=155)	200 mg SC q4w (N=148)
Demographics		
Age, yrs, mean (SD)	40.2 (12.8)	40.6 (15.1)
Male, n (%)	83 (54%)	75 (51%)
Disease Characteristics		
UC disease duration, mean in years (SD)	8.2 (9.0)	8.2 (8.5)
Modified Mayo score (0-9), mean (SD)	6.8 (1.2)	6.9 (1.1)
Modified Mayo score 7-9 (severe), n (%)	94 (61%)	97 (66%)
Mayo endoscopic subscore of 3 (severe), n (%)	103 (66%)	95 (64%)
Extensive UC, n (%)	66 (43%)	69 (47%)
CRP, median in mg/L (IQR)[a]	4.0 (1.4; 10.4)	3.9 (1.5; 9.5)
Fecal calprotectin, median in mg/kg (IQR)[b]	1709.0 (815.0; 3607.0)	1605.5 (596.0; 3253.0)
Oral corticosteroid use, n (%)	56 (36%)	54 (36%)
Immunosuppressant use, n (%)[c]	38 (25%)	36 (24%)

Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from week 8 through week 32. [a]Based on N=153 for GUS SC 100 mg q8w and N=145 for GUS SC 200 mg q4w. [b]Based on N=133 for GUS SC 100 mg q8w, and N=134 for GUS SC 200 mg q4w. [c]6-mercaptopurine, azathioprine, and methotrexate. **CRP**=C-reactive protein, **IQR**=Interquartile range, **SD**=Standard deviation.

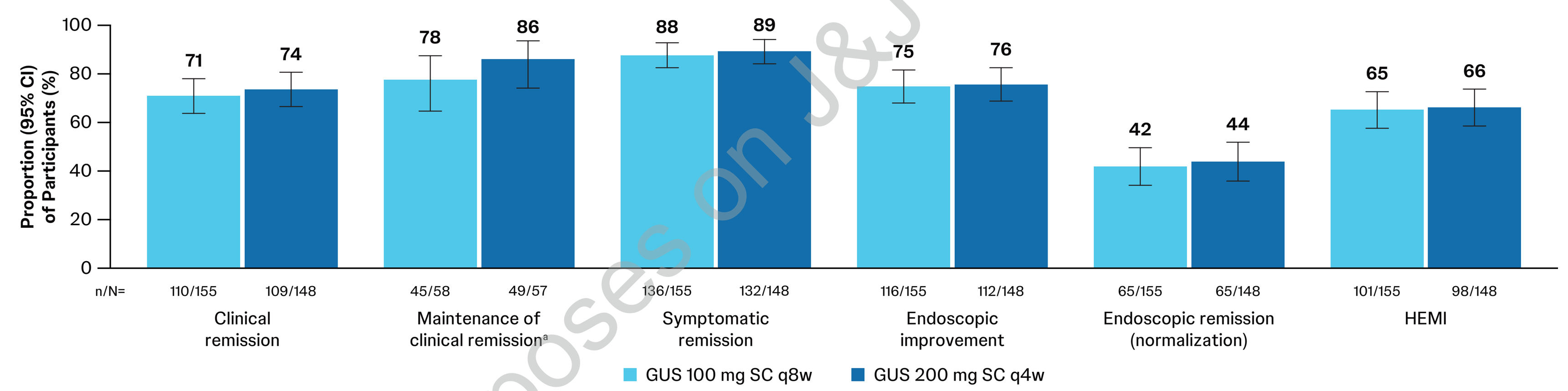
UC-related biologic and/or JAK inhibitor history at induction baseline in the LTE randomized GUS-treated population

	GUS	
	100 mg SC q8w (N=155)	200 mg SC q4w (N=148)
No history of inadequate response or intolerance to biologic and/or JAK inhibitor therapy,[a] n (%)	**95 (61%)**	**86 (58%)**
Biologic/JAK inhibitor naïve[b]	90 (95%)	81 (94%)
Biologic/JAK inhibitor experienced, without documented failure[b]	5 (5%)	5 (6%)
History of inadequate response or intolerance to biologic and/or JAK inhibitor therapy,[a] n (%)	**60 (39%)**	**62 (42%)**
One biologic or JAK inhibitor[c]	33 (55%)	41 (66%)
Two or more biologics and/or JAK inhibitor[c]	27 (45%)	21 (34%)
Any anti-TNF (regardless of vedolizumab or tofacitinib)[c]	54 (90%)	52 (84%)
Vedolizumab (regardless of anti-TNF or tofacitinib)[c]	31 (52%)	26 (42%)
Tofacitinib (regardless of anti-TNF or vedolizumab)[c]	14 (23%)	7 (11%)

Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from week 8 through week 32. [a]Tumor necrosis factor α antagonists, vedolizumab, and/or tofacitinib. [b]Denominator is participants without a history of biologic or JAK inhibitor inadequate response or intolerance. [c]Denominator is participants with a history of biologic or JAK inhibitor inadequate response or intolerance. **JAK**=Janus kinase, **TNF**=Tumor necrosis factor

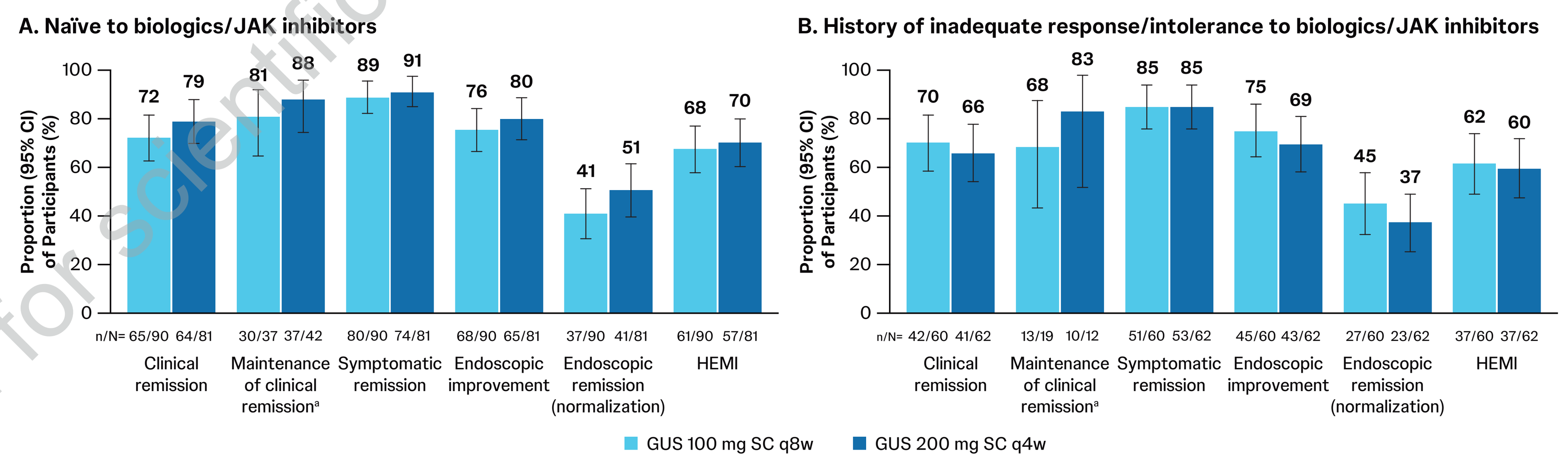
Efficacy outcomes were sustained at week 92 in the LTE randomized GUS-treated population (NRI analysis)

- 218 of 219 (99.5%) participants in clinical remission at week 92 were corticosteroid free ≥8 weeks before week 92



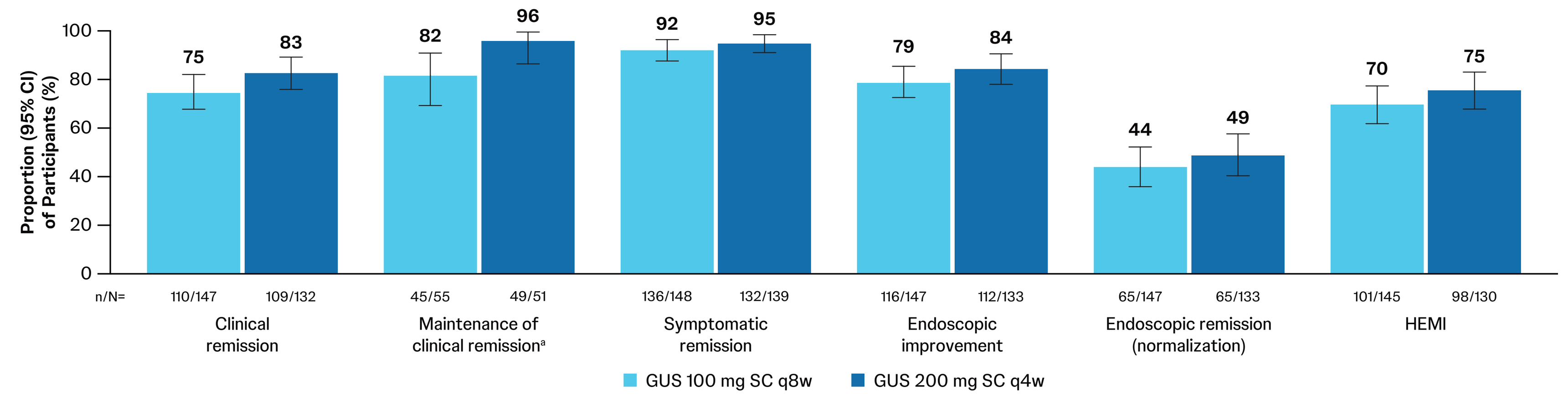
Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32. [a]Clinical remission at LTE week 92 among participants in clinical remission at maintenance week 0. **CI**=Confidence interval

Efficacy at LTE week 92 among GUS-treated participants naïve to biologic and JAK inhibitor treatment (A) or with a history of inadequate response or intolerance to biologics and/or JAK inhibitors (B) was consistent with efficacy in the overall population



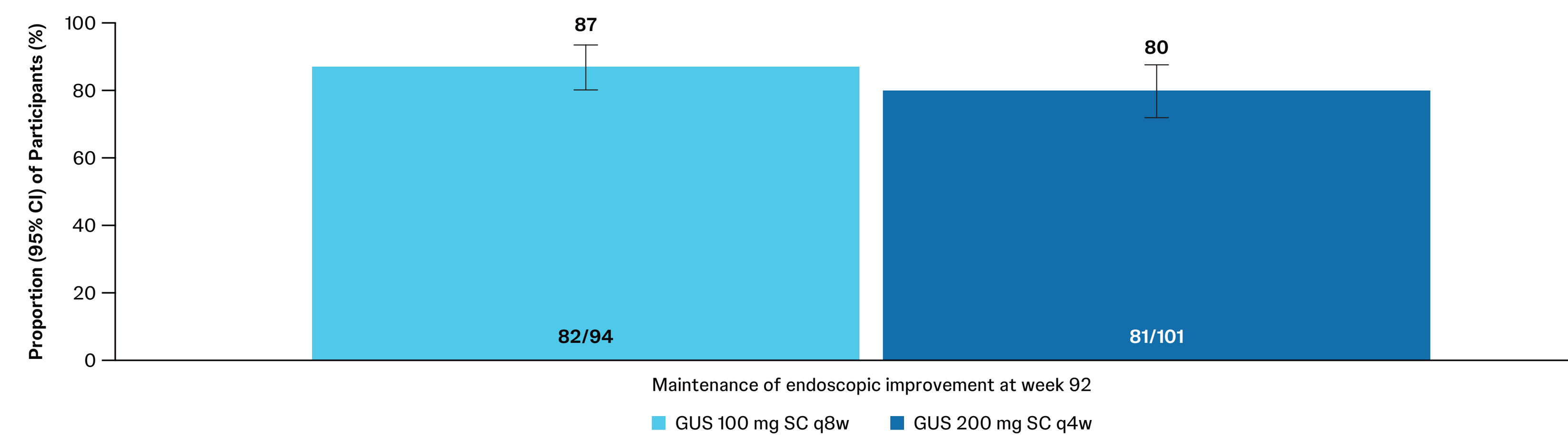
Based on NRI analysis. Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32. [a]Clinical remission at LTE week 92 among participants in clinical remission at maintenance week 0

As-observed results at week 92 in the LTE randomized GUS-treated population were consistent with those based on NRI



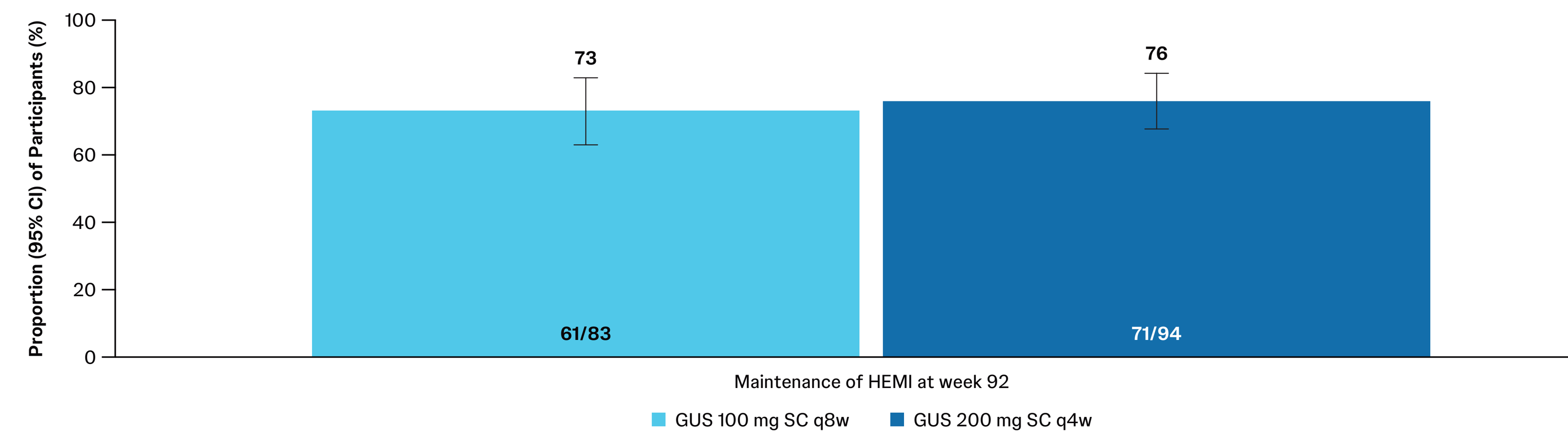
Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32. [a]Clinical remission at LTE week 92 among participants in clinical remission at maintenance week 0

Among GUS-treated participants who achieved endoscopic improvement at maintenance week 44, ≥80% maintained endoscopic improvement at LTE week 92



Based on NRI analysis. Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32.

Among GUS-treated participants who achieved HEMI at maintenance week 44, ≥73% maintained HEMI at LTE week 92



Based on NRI analysis. Includes only participants with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32.

The number of participants with ≥1 AEs per 100 patient-years from maintenance week 44 through LTE week 92 was not higher in the GUS treatment groups compared with the PBO group

- No cases of death, active tuberculosis, opportunistic infection, anaphylaxis, or serum sickness were reported in GUS-treated participants
- Serious infections were infrequent and similar across treatment groups (2 [1.1%] in the PBO group [1 chronic tonsillitis, 1 UTI], 2 [1.2%] in the GUS 100 mg group [1 epididymitis, 1 pneumonia], 3 [0.9%] in the GUS 200 mg group [1 pneumonia, 1 appendicitis, 1 C. *diff* infection])

		GUS	
	PBO (N=189)	100 mg SC q8w (N=162)	200 mg SC q4w (N=349)
Average duration of follow-up, weeks	40.8	46.9	46.5
Average exposure, weeks	9.4	10.9	11.4
Participants with event/100 patient-years of follow-up (95% CI)			
AEs	81.8 (67.9–97.8)	71.5 (58.4–86.6)	75.9 (66.5–86.2)
SAEs	10.8 (6.2–17.6)	2.8 (0.8–7.0)	6.1 (3.7–9.5)
AEs leading to discontinuation of study agent	14.9 (9.3–22.5)	3.4 (1.1–8.0)	4.8 (2.7–8.0)
Infection[a]	41.2 (31.6–53.0)	37.1 (27.9–48.4)	40.5 (33.7–48.2)
Serious infection[a]	1.4 (0.2–4.9)	1.4 (0.2–5.0)	1.0 (0.2–2.8)

Includes all participants regardless of modified Mayo score at induction baseline who participated in the maintenance study and received any treatment in the LTE (LTE all treated population). Data were summarized based on the study treatment participants were receiving upon entering the LTE. [a]Infections were defined as any AE coded to the MedDRA system organ class 'Infections and infestations'. **SAE**=Serious adverse event, **UTI**=urinary tract infection

PRESENTED BY: GR Lichtenstein at Digestive Disease Week (DDW); May 3-6, 2025; San Diego, CA.

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