Efficacy and Safety of Guselkumab for Ulcerative Colitis Through Week 140 of the QUASAR Long-term Extension Study

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Disclosure of Conflicts of Interest

I, Laurent Peyrin-Biroulet, herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

I report consulting fees from AbbVie, Abivax, Adacyte, Alfasigma, Alimentiv, Amgen, Apini, Banook, Bristol Myers Squibb, Celltrion, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Iterative Health, Johnson & Johnson, Lilly, LifeMine, Medac, Morphic, MSD, Nordic Pharma, Novartis, Oncodesign Precision Medicine, ONO Pharma, OSE Immunotherapeutics, Par' Immune, Pfizer, Prometheus, Roche, Roivant, Samsung, Sandoz, Sanofi, Sorriso, Spyre, Takeda, Teva, ThirtyfiveBio, Tillots, Vectivbio, Vedanta, and Ventyx and lecture fees from AbbVie, Alfasigma, Amgen, Biogen, Celltrion, Ferring, Galapagos, Genentech, Gilead, Iterative Health, Johnson & Johnson, Lilly, Medac, MSD, Nordic Pharma, Pfizer, Sandoz, Takeda, and Tillots.

Background and Objective

QUASAR

QUASAR (NCT04033445) is a phase 2b/3 program evaluating guselkumab in participants with moderately to severely active UC[1,2]

Guselkumab

Guselkumab is a selective dual-acting IL-23p19 subunit inhibitor that potently neutralises IL-23 and binds to CD64, a receptor on cells that produce IL-23[3]

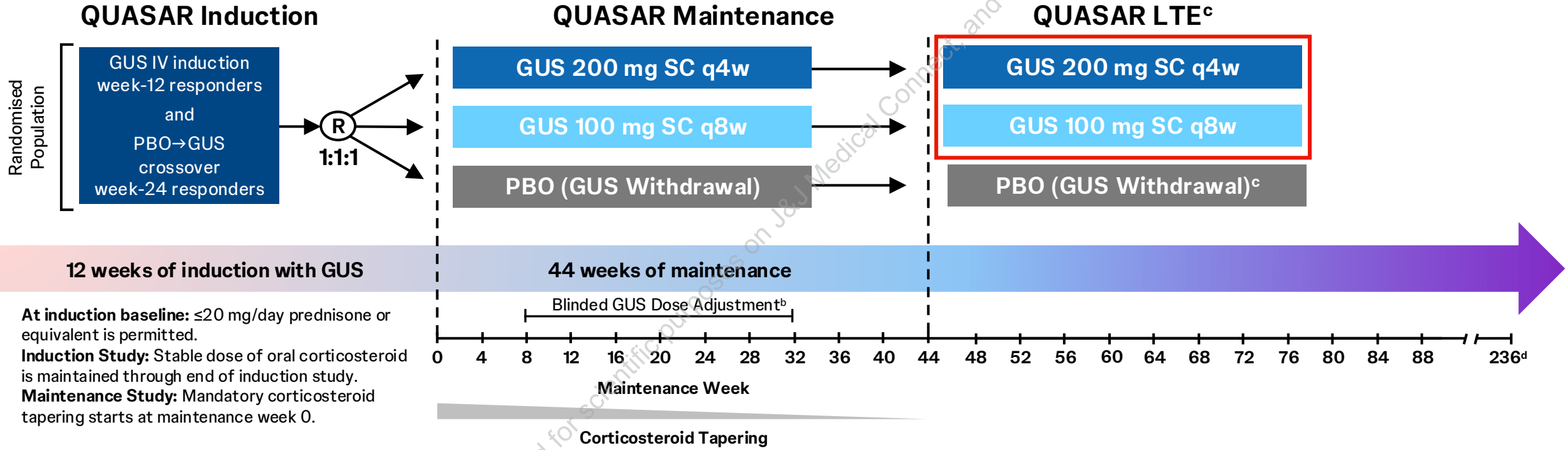
Objective

Here, we report QUASAR LTE efficacy and safety results through week 140

1. Peyrin-Biroulet L, et al. *Gastroenterology*. 2023;165:1443-57. 2. Rubin DT, et al. *Lancet*. 2025;405:33-49. 3. Sachen KL, et al. *Front Immunol*. 2025;16:1532852. **IL**=interleukin. **LTE**=long-term extension. **UC**=ulcerative colitis.

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



At induction baseline: ≤20 mg/day prednisone or equivalent is permitted.
Induction Study: Stable dose of oral corticosteroid is maintained through end of induction study.
Maintenance Study: Mandatory corticosteroid tapering starts at maintenance week 0.

Overall, 87% of participants randomised to guselkumab at maintenance week 0 entered the LTE, and approximately 89% of the LTE randomised guselkumab-treated population completed treatment through LTE week 140
- Reasons for discontinuation were AE, lack of efficacy, lost to follow-up, death, withdrawal by participant, physician decision, pregnancy, and other

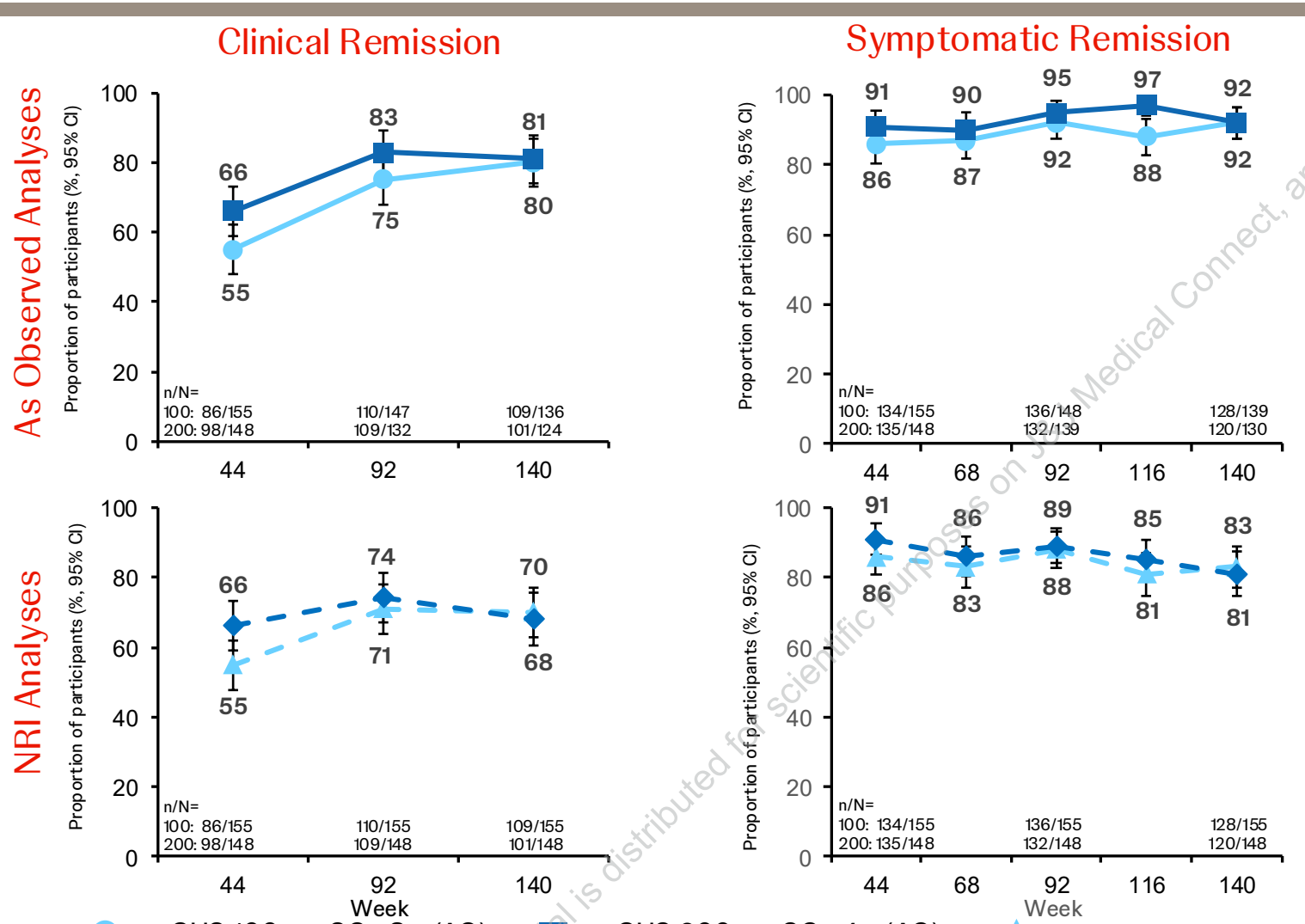
[a]Defined as induction baseline modified Mayo score of 5 to 9 with a Mayo RBS ≥ 1 and an MES≥ 2 based on central review. [b]Between maintenance weeks 8 and 32, randomised pts meeting loss of clinical response criteria (based on the modified Mayo score and required an endoscopic assessment) were eligible 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 pt in the Maintenance Study completed the maintenance week 44 visit. After the Maintenance Study was unblinded to the investigative sites, pts receiving PBO were terminated from study participation. [d]Week 236 is the final efficacy visit; the final safety visit is 12 weeks from the last GUS dose (approximately week 244). **AE**=adverse event, **GUS**=guselkumab, **IV**=intravenous, **MES**=Mayo endoscopy score, **PBO**=placebo, **pt**=participant, **q4w**=every 4 weeks, **q8w**=every 8 weeks, **R**=randomisation, **RBS**=rectal bleeding subscore, **SC**=subcutaneous.

Demographics and Disease Characteristics at Induction Baseline Among Participants Who Entered the LTE

Characteristics		Guselkumab 100 mg SC q8w (N = 155)	Guselkumab 200 mg SC q4w (N = 148)
Demographics			
	Age, yrs	40.2 (12.8)	40.6 (15.1)
	Male	54%	51%
Disease Characteristics			
	UC disease duration, yrs	8.2 (9.0)	8.2 (8.5)
	Modified Mayo score (0-9)	6.8 (1.2)	6.9 (1.1)
	Modified Mayo score 7-9 (severe)	61%	66%
	Mayo endoscopic subscore of 3 (severe)	66%	64%
	Extensive UC	43%	47%
	CRP, mg/L, median (IQR)[a]	4.0 (1.4; 10.4)	3.9 (1.5; 9.5)
	Faecal calprotectin, mg/kg, median (IQR)[b]	1709.0 (815.0; 3607.0)	1605.5 (596.0; 3253.0)
	Oral corticosteroid use	36%	36%
	Immunomodulatory drug use[c]	25%	24%
UC-related Biologic/JAK inhibitor Medication History[d]			
	Biologic and JAK inhibitor naïve[e]	58%	55%
	History of inadequate response or intolerance to biologic and/or JAK inhibitor therapy	39%	42%

Data shown are mean (SD) unless otherwise noted. Includes only pts with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomised 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, or methotrexate. [d]Includes TNF α antagonists, vedolizumab, and/or tofacitinib. [e]3% of pts in each group were biologic/JAK inhibitor experienced without documented inadequate response/intolerance. **CRP**=C-reactive protein, **IQR**=interquartile range, **JAK**=Janus kinase, **SD**=standard deviation, **TNF**=tumor necrosis factor.

Clinical remission and Symptomatic Remission Were Sustained From Week 44 Through Week 140 Among LTE Participants

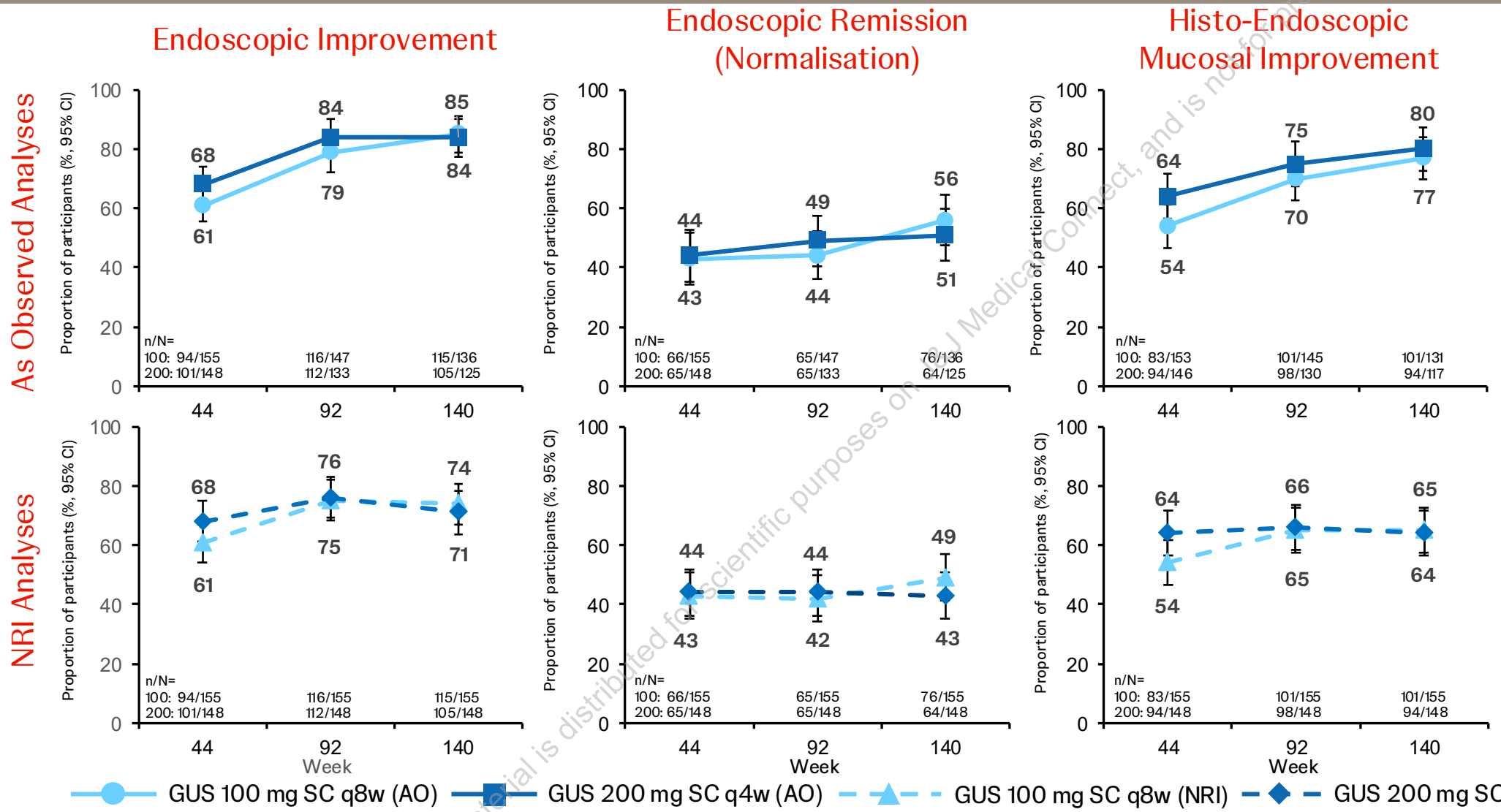


- 205 of 210 (98%) participants in clinical remission at week 140 were corticosteroid free ≥8 weeks before week 140
- Results were similar with as observed and NRI analyses

Clinical remission: SFS of 0 or 1 and not increased from induction baseline, RBS of 0, MES of 0 or 1
Symptomatic remission: SFS of 0 or 1 and not increased from induction baseline, RBS of 0

Includes only pts with modified Mayo score 5-9 at induction baseline in clinical response to GUS IV induction and randomised to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32 and continued to receive GUS treatment in the LTE (LTE randomised GUS-treated population). "as observed" analyses were based on data available at analysis timepoint. For NRI analyses, pts who had an ostomy or colectomy or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC before a timepoint were considered not to have achieved binary endpoints, and for pts who discontinued study agent due to COVID-19-related reasons (excluding infection), regional crises, or reasons other than those previously stated, observed values (if available) were used; after accounting for the above rules, pts missing ≥1 of the components pertaining to an endpoint were considered not to have achieved that endpoint. **AO**=as observed, **CI**=confidence interval, **NRI**=nonresponder imputation. **SFS**=stool frequency subscore.

Endoscopic and Histologic Outcomes Were Sustained From Week 44 Through Week 140 Among LTE Participants

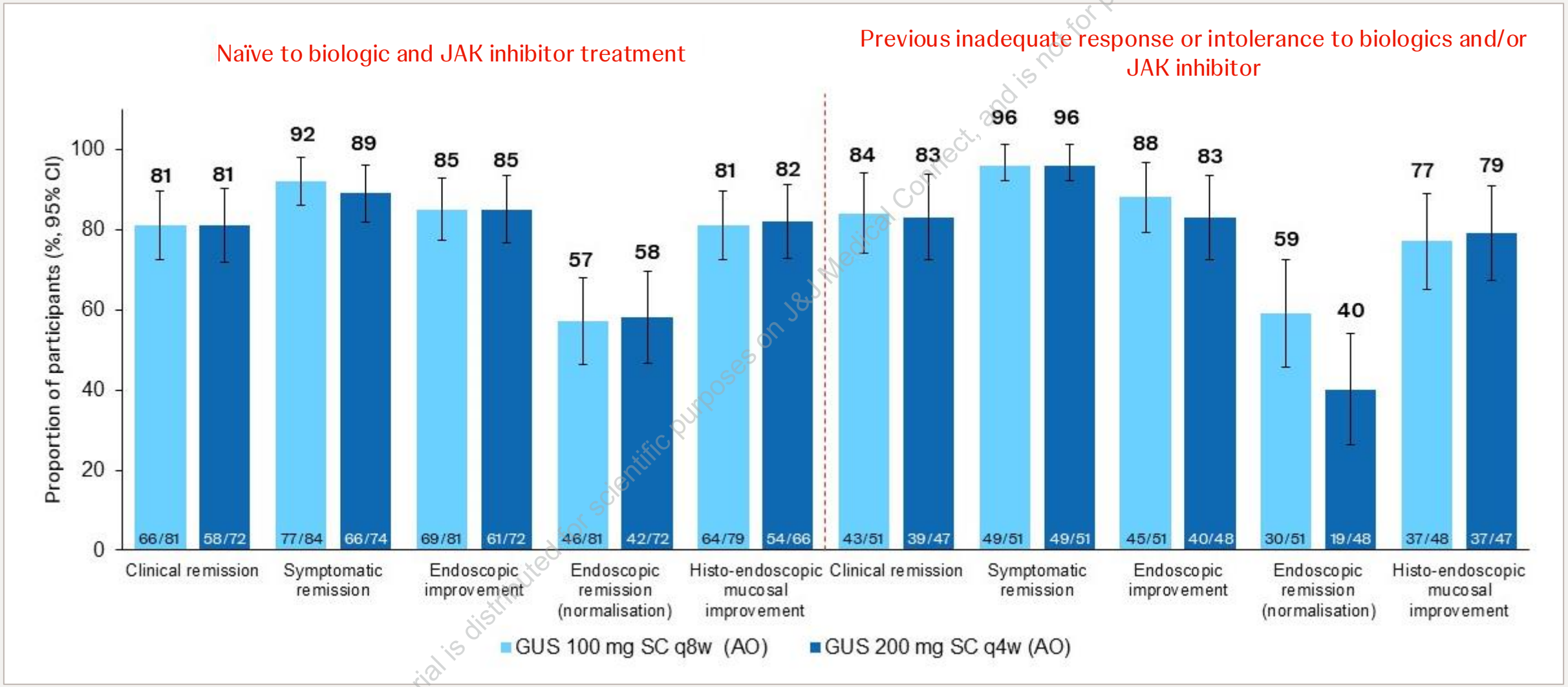


Results were similar with as observed and NRI analyses

Endoscopic improvement: MES of 0 or 1
Endoscopic remission (normalisation): MES of 0
Histo-endoscopic mucosal improvement: 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

Includes only pts with modified Mayo score 5-9 at induction baseline in clinical response to GUS IV induction and randomised to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32 and continued to receive GUS treatment in the LTE (LTE randomised GUS-treated population). "as observed" analyses were based on data available at analysis timepoint. For NRI analyses, pts who had an ostomy or colectomy or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC before a timepoint were considered not to have achieved binary endpoints, and for pts who discontinued study agent due to COVID-19-related reasons (excluding infection), regional crises, or reasons other than those previously stated, observed values (if available) were used; after accounting for the above rules, pts missing ≥1 of the components pertaining to an endpoint were considered not to have achieved that endpoint.

Outcomes at LTE Week 140 Were Consistent in Biologic and JAK Inhibitor Medication History Subpopulations (As Observed)



Includes only participants with modified Mayo score 5-9 at induction baseline in clinical response to GUS IV induction and randomised to receive GUS maintenance treatment and did not experience a dose adjustment from maintenance weeks 8 through 32 and continued to receive GUS treatment in the LTE (LTE randomised GUS-treated population). “as observed” analyses were based on data available at analysis timepoint.

Adverse Events From Week 44 Through Week 140

		Guselkumab		
	PBO[a] (N=178)	100 mg SC q8w[b] (N=155)	200 mg SC q4w[c] (N=332)	Combined (N=487)
Mean weeks of follow-up	55.0	91.3	88.8	89.6
Deaths, n (%)	1 (0.5%)[d]	0	1 (0.3%)[e]	1 (0.2%)
Participants with events/100 patient-years (95% CI)				
AEs	66.1 (55.0; 78.8)	45.0 (37.3; 53.7)	48.0 (42.4; 54.0)	47.0 (42.5, 51.9)
SAEs	10.7 (6.5; 16.5)	4.1 (2.0; 7.2)	6.6 (4.6; 9.0)	5.7 (4.2, 7.6)
AEs leading to discontinuation of study agent	12.8 (8.2; 19.0)	2.2 (0.8; 4.8)	4.1 (2.6; 6.1)	3.5 (2.3, 5.0)
Infection[f]	35.2 (27.2; 44.8)	25.1 (19.5; 31.8)	29.7 (25.4; 34.6)	28.2 (24.7, 32.1)
Serious infection[f]	1.1 (0.1; 3.8)	0.7 (0.1; 2.7)	1.4 (0.6; 2.8)	1.2 (0.6, 2.2)

Among guselkumab-treated participants
- 1 death (aortic dissection in a participant with history of hypertension and ischemia, deemed unrelated to guselkumab) was reported
- No active tuberculosis, opportunistic infection, anaphylaxis, serum sickness, or Hy's law cases were reported

Safety was evaluated only among participants modified Mayo score of 5 to 9 at induction baseline. [a]Pts in clinical response to IV GUS induction randomised to PBO and did not have a dose adjustment and pts in clinical response to PBO induction and received PBO in maintenance study. [b]Pts in clinical response to IV GUS induction randomised to SC GUS 100 mg q8w and did not have a dose adjustment. [c]Pts in clinical response to IV GUS induction randomised to SC GUS 200 mg q4w, pts randomised to PBO or SC GUS 100 mg q8w who had a dose adjustment, pts not in clinical response to IV GUS induction at induction week 12 but in clinical response at induction week 24 after receiving SC GUS. Data were summarised based on the study treatment participants were receiving upon entering the LTE. [d]No further information. [e]Aortic dissection. [f]Infections were defined as any AE coded to the MedDRA system organ class 'Infections and infestations'. **SAE**=serious adverse event.

Key Takeaways

- Both guselkumab maintenance dose regimens demonstrated sustained clinical, endoscopic, and histologic efficacy in participants with UC through week 140 of the LTE
- Although NRI results were numerically lower than as observed results, the overall trends were consistent due to the high retention rate throughout the LTE
- Efficacy was sustained regardless of biologic and/or JAK inhibitor treatment history
- Results show a favorable long-term benefit-risk profile
- No new safety concerns were observed

Acknowledgments

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