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Key Takeaways

- Both GUS maintenance dose regimens demonstrated sustained clinical, endoscopic, and histologic efficacy in pts with UC through week M-140
- 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 GUS long-term benefit-risk profile
- No new safety concerns were identified

EFFICACY AND SAFETY OF GUSELKUMAB FOR ULCERATIVE COLITIS THROUGH WEEK 140 OF THE QUASAR LONG-TERM EXTENSION STUDY

Laurent Peyrin-Biroulet,¹ Brian Bressler,² Axel Dignass,³ Tadakazu Hisamatsu,⁴ Bruce E. Sands,⁵ Yelina Alvarez,⁶ Thomas Baker,⁶ Nicole Shipitofsky,⁶ Ye Miao,⁶ Hongyan Zhang,⁶ Gary R. Lichtenstein,⁷ David T. Rubin,⁸ Jessica R. Allegretti⁹

¹Northwestern Medicine Digestive Health Institute, Chicago, IL, USA; ²University of British Columbia, Vancouver, BC, Canada; ³Department of Medicine, Agaplesion Markus Hospital, Goethe University, Frankfurt, Germany; ⁴Department of Gastroenterology and Hepatology, Kyorin University School of Medicine, Tokyo, Japan; ⁵Icahn School of Medicine at Mount Sinai, New York, NY, USA; ⁶Johnson & Johnson, Spring House, PA, USA; ⁷University of Pennsylvania School of Medicine, Philadelphia, PA, USA; ⁸University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA; ⁹Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Background

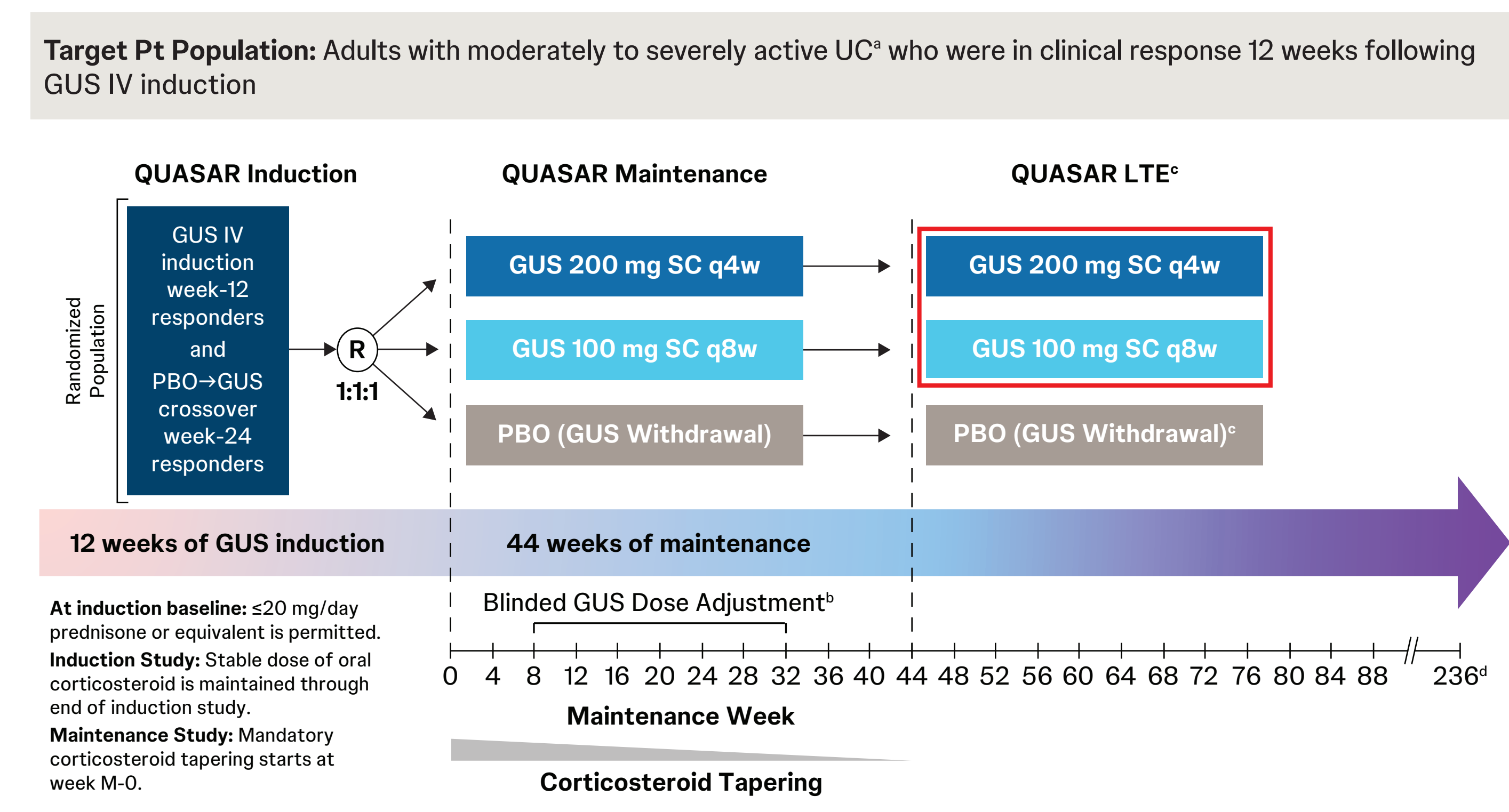
QUASAR (NCT04033445) is a phase 2b/3 program evaluating guselkumab (GUS) in participants (pts) with moderately to severely active ulcerative colitis (UC)^{1,2}

GUS is a selective dual-acting interleukin (IL)-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23³

Objective

Here, we report QUASAR long-term extension (LTE) efficacy and safety results through maintenance week 140 (M-140)

Phase 3 QUASAR Program Design



^aDefined as induction baseline modified Mayo score of 0 to 9 with a Mayo RBS ≥ 1 and an MES ≥ 2 based on central review. ^bBetween weeks M-8 and M-32, randomized 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 50 → GUS 200 mg SC q4w; GUS 100 mg SC q8w → GUS 200 mg SC q4w; GUS 200 mg SC q4w → GUS 100 mg SC q8w (upon assessment). ^cThe study blind was maintained during the LTE until the last pt in the Maintenance Study completed the week M-44 visit. After the Maintenance Study was unblinded to the investigator sites, pts receiving PBO were terminated from study participation. ^dWeek M-208 is the final safety visit in 12 weeks from the last GUS dose (approximately week M-244). ^eAE=adverse event; GUS=guselkumab; IV=intravenous; MES=Mayo endoscopic score; PBO=placebo; q4w=every 4 weeks; q8w=every 8 weeks; R=randomization; RBS=rectal bleeding subscore; SC=subcutaneous.

Methods

- Pts completing the week M-44 visit who, in the opinion of the investigator, could benefit from continued study intervention, had the opportunity to enter the LTE and continue their then-current treatment regimen
- Pts receiving PBO discontinued after study unblinding
- Efficacy was evaluated among pts with an induction baseline modified Mayo score of 5 to 9 randomized to GUS at week M-0 who did not receive a dose adjustment and continued to receive GUS treatment in the LTE (LTE randomized GUS-treated population)
- Safety was evaluated among pts with an induction baseline modified Mayo score of 5 to 9 who completed the maintenance study (randomized and nonrandomized) and received any treatment in the LTE (LTE safety population)

Outcomes Evaluated

- Clinical remission:** Mayo stool frequency subscore (SFS) of 0 or 1 and not increased from induction baseline, RBS of 0, and MES of 0 or 1
- Symptomatic remission:** SFS of 0 or 1 and not increased from induction baseline, RBS of 0
- Endoscopic improvement:** MES of 0 or 1
- Endoscopic remission (normalization):** MES of 0
- Histo-endoscopic mucosal improvement:** 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) "as observed" based on data available at the designated timepoint, and 2) nonresponder imputation (NRI) accounting for treatment failure and missing data rules
- For NRI, pts who had an ostomy/colectomy or study agent discontinuation due to lack of therapeutic effect/adverse event (AE) of worsening of UC prior to the designated timepoint were considered nonresponders; observed values were used, if available, if study agent discontinuation prior to the designated timepoint was due to COVID-19-related reasons (excluding infection), regional crises, or reasons other than those previously stated
- After accounting for the above rules, pts missing ≥1 outcome component were considered nonresponders

Results

Overall, 87% of Pts Randomized to GUS at Week M-0 Entered the LTE, and Approximately 89% of the LTE Randomized GUS-Treated Population Completed Treatment Through Week M-140

Reason for discontinuation	GUS	
	100 mg SC q8w (N=155)	200 mg SC q4w (N=148)
Pts who discontinued study treatment prior to week M-140	10%	12%
Adverse event	3%	3%
Worsening of UC	2%	2%
Other than worsening of UC	1%	1%
Lack of efficacy	3%	3%
Lost to follow-up	1%	1%
Death	0	1%
Any other reason	5%	5%
Withdrawal by pt	1%	3%
Physician decision	0	1%
Pregnancy	1%	0
Other	2%	2%

Includes only pts with modified Mayo score 5-9 at induction baseline in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from weeks M-8 through M-32 (LTE randomized GUS-treated population).

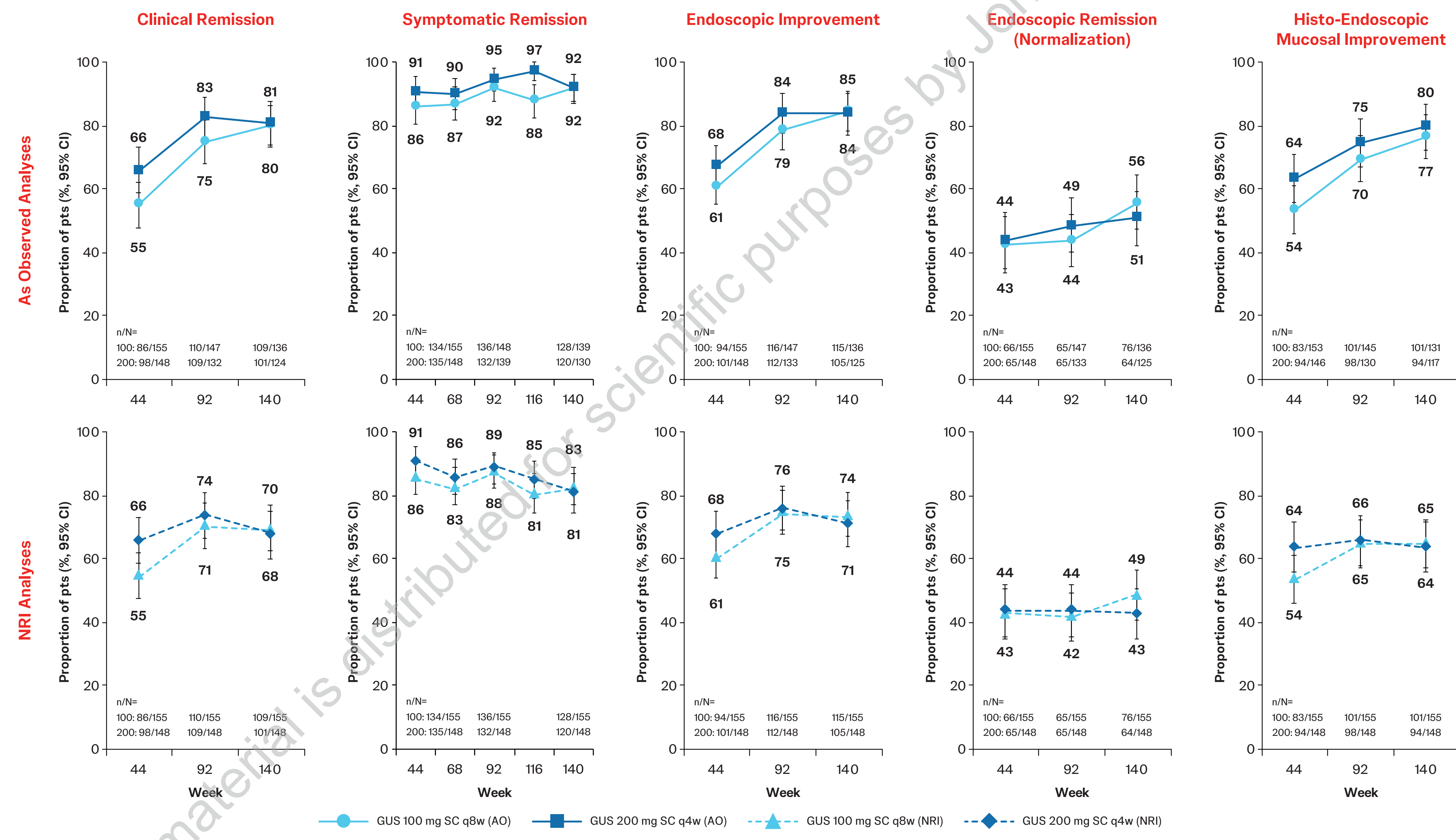
Demographics and Disease Characteristics at Induction Baseline Among Pts Who Entered the LTE

Characteristics	GUS	
	100 mg SC q8w (N = 155)	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 (8.0)	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%
MES 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)
Fecal 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%

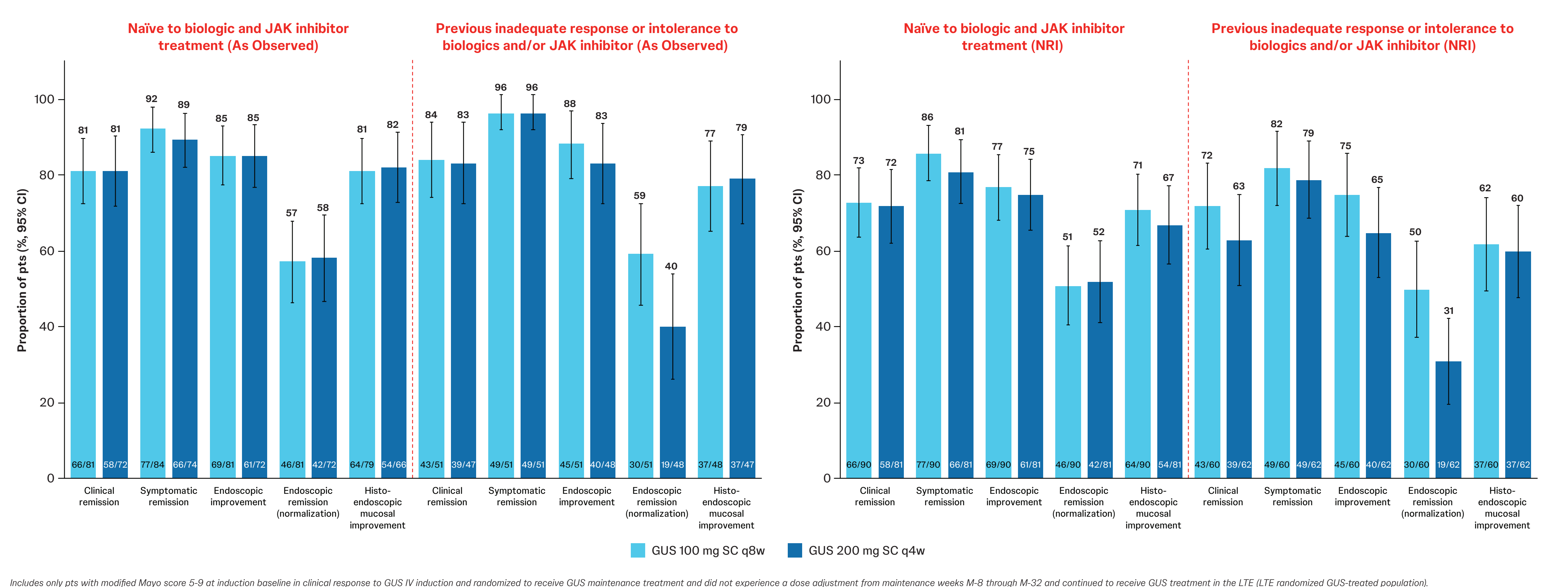
Data shown are mean (SD) unless otherwise noted. Includes only pts with modified Mayo score 5-9 at induction baseline who were in clinical response to GUS IV induction and randomized to receive GUS maintenance treatment and did not experience a dose adjustment from weeks M-8 through M-32. ^aBased on NRI03 for GUS 100 mg SC q8w and NRI04 for GUS 200 mg SC q4w. ^bBased on NRI03 for GUS 100 mg SC q8w and NRI04 for GUS 200 mg SC q4w. ^cIncludes TNF-α antagonists, vedolizumab, and/or tofacitinib. ^d3% of pts in each group were biologic/JAK inhibitor experienced without documented inadequate response/intolerance. ^eCRP=C-reactive protein; IQR=interquartile range; JAK=Janus kinase; SD=standard deviation; TNF=tumour necrosis factor.

Clinical Remission, Symptomatic Remission, and Endoscopic and Histologic Outcomes Were Sustained From Week M-44 Through Week M-140 Among LTE Pts

- 205 of 210 (98%) pts in clinical remission at week 140 were corticosteroid free ≥8 weeks before week M-140
- For all outcomes, results were similar with as observed and NRI analyses



Outcomes at Week M-140 Were Consistent in Biologic and JAK Inhibitor Medication History Subpopulations With As Observed and NRI Analyses



Adverse Events From Week M-44 Through Week M-140

Mean weeks of follow-up	GUS			Combined (N=487)
	PBO ^a (N=178)	100 mg SC q8w ^b (N=155)	200 mg SC q4w ^c (N=322)	
Deaths	0.5%	0	0.3%	0.2%
Pts with events/100 patient-years (95% CI)				
AEs	661 (55.0; 78.8)	45.0 (37.3; 53.7)	48.0 (42.4; 54.0)	47.0 (42.5; 51.9)
SAEs	107 (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 (6.2; 19.0)	2.2 (0.8; 4.8)	4.1 (2.6; 6.1)	3.5 (2.3; 5.0)
Infection ^d	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 ^e	11 (0; 3.8)	07 (0; 2.7)	14 (0.6; 8.2)	12 (0.6; 2.2)

Safety was evaluated only among pts with a modified Mayo score of 5 to 9 at induction baseline. ^aPts in clinical response to IV GUS induction randomized to PBO who did not have a dose adjustment and pts in clinical response to PBO induction who received PBO in maintenance study. ^bPts in clinical response to IV GUS induction randomized to SC GUS 100 mg q8w who had a dose adjustment, and pts in clinical response to IV GUS induction randomized to SC GUS 200 mg q4w who had a dose adjustment. ^cPts in clinical response to IV GUS induction randomized to SC GUS 100 mg q8w who did not have a dose adjustment. ^dPts in clinical response to IV GUS induction randomized to SC GUS 100 mg q8w who did not have a dose adjustment. ^ePts in clinical response to IV GUS induction randomized to SC GUS 100 mg q8w who did not have a dose adjustment. ^fIncludes bacterial, viral, and fungal infections. ^gIncludes pneumonia, tuberculosis, and other serious infections. ^hIncludes serious infections. ⁱIncludes 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