

Symptomatic and Biomarker Outcomes Among Participants Treated With Guselkumab Not in Clinical Response at Week 12: Results From the Phase 3 QUASAR Induction Study

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Background and Objective

Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potentially blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23,¹ and is approved for the treatment of moderately to severely active ulcerative colitis

In the phase 3 QUASAR induction study, clinical responders to guselkumab IV induction at Week 12 entered the randomized-withdrawal maintenance study, and clinical nonresponders received guselkumab 200 mg SC q4w and were evaluated through Week 24

Here, we present a post hoc analysis evaluating clinical characteristics, symptomatic response, and biomarkers according to Week 24 response status in the phase 3 QUASAR induction study

Phase 3 QUASAR Induction Study Design Through Week 24

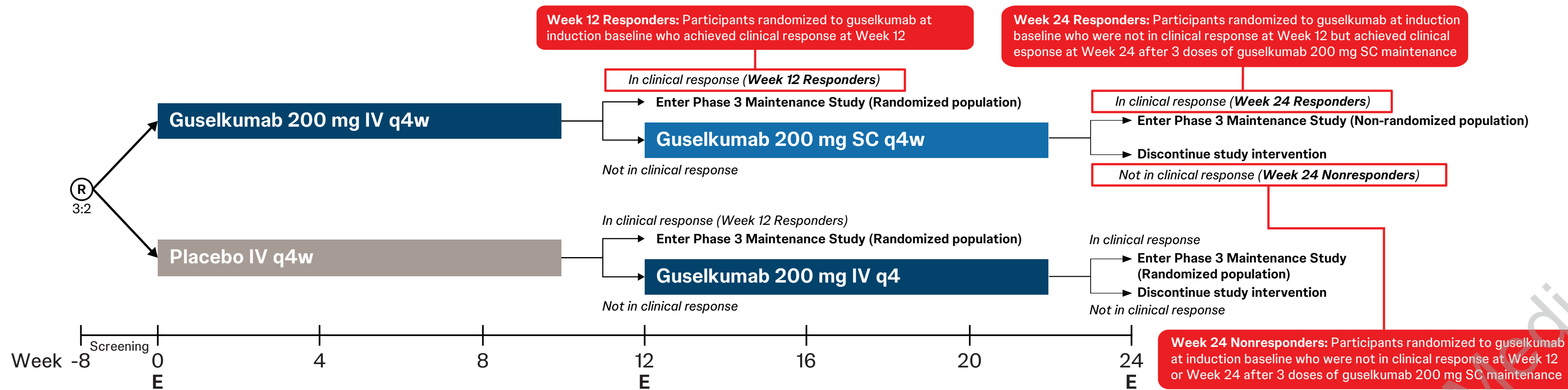
Key eligibility criteria

- Baseline modified Mayo score of 5 to 9
- Induction baseline Mayo rectal bleeding subscore ≥ 1 , Mayo endoscopic subscore ≥ 2 (centrally reviewed)
- Inadequate response/intolerance to oral corticosteroids, 6-MP/AZA, biologics,^a or JAKi

Randomization stratified by:

- Prior BIO/JAKi-IR status (Yes/No)
- Region (Eastern Europe, Asia, or rest of world)
- Concomitant corticosteroid use at baseline (Yes/No)

^a6-MP=6-mercaptopurine, AZA=azathioprine, BIO=biologic, E=endoscopy, IR inadequate response/intolerance, JAKi=Janus kinase inhibitor, q4w=every 4 weeks, R=randomization.
^bBiologic therapies: TNF antagonists or vedolizumab.
Note: Clinical response was defined as a ≤ 3.0 and ≥ 2 -point decrease from baseline in the modified Mayo score, with either a ± 1 -point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.



Outcomes and Assessments

- Symptomatic response:** A decrease from induction baseline in the symptomatic Mayo score by $\geq 30\%$ and ≥ 1 point, with either a ≥ 1 point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1; the symptomatic Mayo score is defined as the sum of the stool frequency and the rectal bleeding subscores
- Reduction from baseline in inflammatory biomarkers (ie, C-reactive protein [CRP] and fecal calprotectin [FeCal]) analyzed on the natural log scale

Results

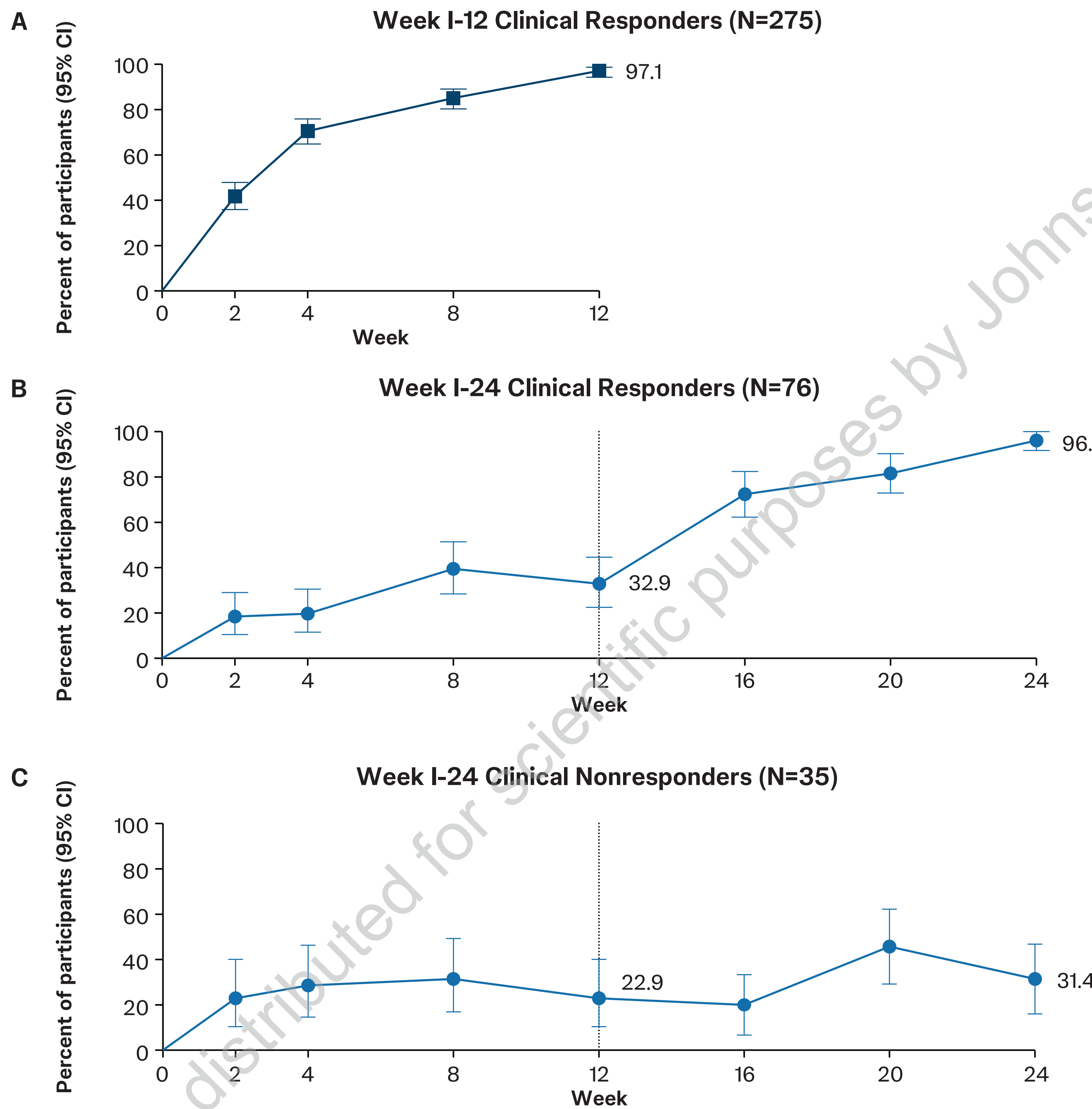
Baseline Demographics and Disease Characteristics

	GUS 200 mg IV Week 12 Clinical Responder* (N=275)	GUS 200 mg IV → 200 mg SC q4w Week 24 Clinical Responder* (N=76)	GUS 200 mg IV → 200 mg SC q4w Week 24 Clinical Nonresponder* (N=35)
Demographics			
Age in years, mean (SD)	41.2 (14.01)	40.3 (14.13)	38.9 (11.71)
Male, n (%)	146 (53.1%)	47 (61.8%)	22 (62.9%)
Disease characteristics			
UC duration in years, mean (SD)	7.90 (8.21)	6.91 (5.53)	8.99 (8.91)
Modified Mayo score (0–9), mean (SD)	6.9 (1.18)	6.9 (0.95)	6.9 (1.04)
Modified Mayo score of 7–9 (severe), n (%)	169 (61.5%)	56 (73.7%)	23 (65.7%)
Mayo endoscopic subscore of 3 (severe), n (%)	182 (66.2%)	60 (78.9%)	27 (77.1%)
Extensive UC, n (%)	122 (44.4%)	31 (40.8%)	20 (57.1%)
Biomarkers			
C-reactive protein in mg/L, N	272	76	34
Median (IQR)	3.94 (1.39; 9.11)	5.39 (1.51; 15.45)	6.46 (2.54; 9.54)
Fecal calprotectin in mg/kg, N	243	68	28
Median (IQR)	1641.0 (590.0; 3741.0)	1920.0 (807.5; 3723.5)	1624.0 (1336.0; 4382.0)
Concomitant UC medications at baseline, n (%)			
6-mercaptopurine/azathioprine	60 (21.8%)	17 (22.4%)	8 (22.9%)
Methotrexate	2 (0.7%)	0	0
Oral corticosteroids	108 (39.3%)	37 (48.7%)	21 (60.0%)
Biologic history, n (%)			
BIO/JAKi naïve	152 (55.3%)	30 (39.5%)	11 (31.4%)
BIO/JAKi-IR ^b	114 (41.5%)	45 (59.2%)	23 (65.7%)

BIO=biologic, GUS=guselkumab, IQR=interquartile range, IR=inadequate response/intolerance, IWRS=interactive web response system, IV=intravenous, JAKi=Janus kinase inhibitor, SC=subcutaneous, SD=standard deviation, UC=ulcerative colitis.
^aClinical responses/nonresponders were determined by IWRS using data observed at the designated visit (Week 12 or Week 24). ^bPrimary nonresponse, secondary nonresponse, or intolerance. Note: Includes only participants with modified Mayo score 5–9 at induction baseline. Response groups were defined sequentially using observed IWRS data. Among 421 GUS-randomized participants, 21 discontinued before Week 12, leaving 400 classified as either Week 12 Responders (N=275) or Week 12 Nonresponders (N=125). Among 125 Week 12 Nonresponders, 14 discontinued before Week 24, leaving 111 classified as Week 24 Responders (N=76) or Week 24 Nonresponders (N=35).

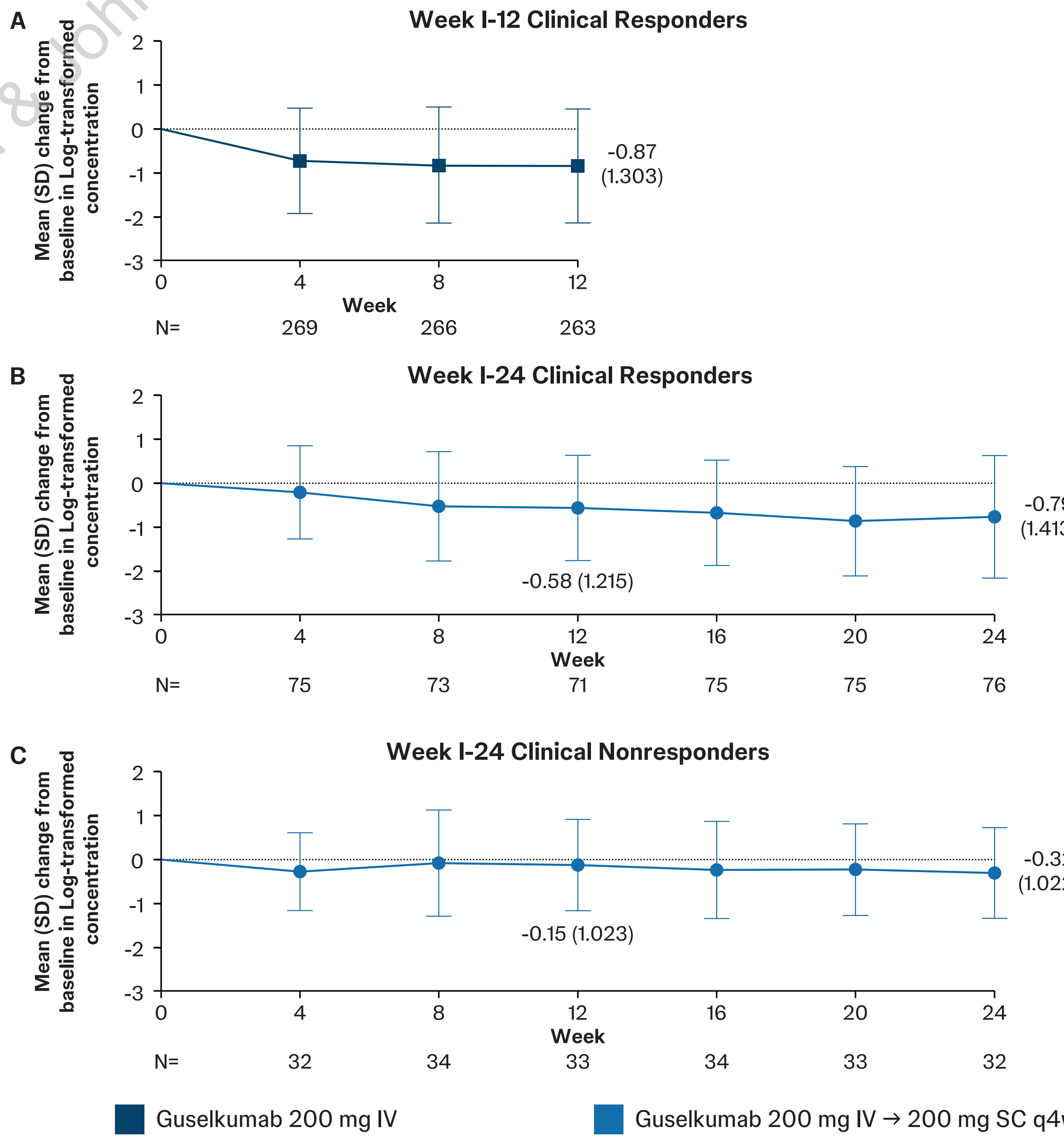
Symptomatic Response

Figure 1. Symptomatic response over time in Week 12 Responders (A), Week 24 Responders (B), and Week 24 Nonresponders (C)



CRP Concentration (mg/L)

Figure 2. Change from baseline in log-transformed CRP concentration (mg/L) over time in Week 12 Responders (A), Week 24 Responders (B), and Week 24 Nonresponders (C)



Key Takeaways

Among participants with moderately to severely active ulcerative colitis without clinical response at Week 12 after guselkumab IV induction, a subset benefited after three additional guselkumab 200 mg SC q4w injections

Baseline clinical characteristics did not distinguish Week 12 or Week 24 clinical response status

However, Week 24 Responders showed numerically greater reductions in log-transformed CRP and FeCal by Week 12 than Week 24 Nonresponders, suggesting that early biomarker improvement may help identify pts likely to respond with continued treatment