QUASAR INDUCTION STUDY 1 CUMULATIVE RESPONSE TO GUSELKUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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BACKGROUND/OBJECTIVE

Guselkumab (GUS), an interleukin-23 p19 subunit antagonist, is currently being investigated in inflammatory bowel disease

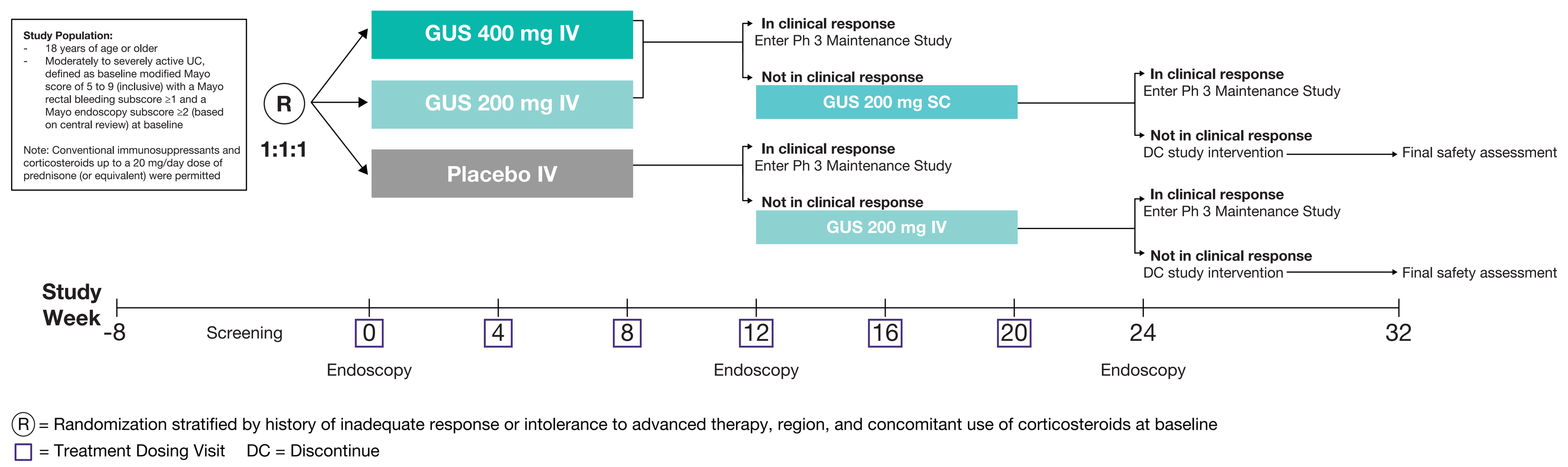
The QUASAR Induction Study 1 is a Phase 2b study of GUS as induction therapy in patients with moderately to severely active ulcerative colitis (UC) who had an inadequate response or intolerance to:

- Conventional therapy (ie, thiopurines or corticosteroids) or
- Advanced therapy (ie, tumor necrosis factor alpha antagonists, vedolizumab, or tofacitinib)

Here we report cumulative response and safety results for GUS in the QUASAR Phase 2b Induction Study

METHODS

QUASAR Induction Study 1: Study Design



Ⓡ = Randomization stratified by history of inadequate response or intolerance to advanced therapy, region, and concomitant use of corticosteroids at baseline
☐ = Treatment Dosing Visit DC = Discontinue

Endpoint Definitions

- **Clinical response:** A decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1
- **Clinical remission:** A stool frequency subscore of 0 or 1 that has not increased from baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability present on the endoscopy
- **Symptomatic remission:** A stool frequency subscore of 0 or 1 that has not increased from baseline and a rectal bleeding subscore of 0
- **Endoscopic improvement:** An endoscopy subscore of 0 or 1 with no friability present on the endoscopy
- **Histo-endoscopic mucosal improvement:** Achieving 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
- **Endoscopic normalization:** An endoscopy subscore of 0

Data Handling

- The primary analysis population included all randomized patients with a modified Mayo score of 5 to 9 who received at least 1 (partial or complete) dose of study intervention
- Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an adverse event of worsening of UC prior to the Week 12 or 24 visit were considered not to have achieved that endpoint
- Data after a discontinuation of study agent due to COVID-19 related reasons (excluding COVID-19 infection) were not used
- Patients who were missing one or more component pertaining to a specified endpoint at Week 12 or 24 were considered not to have achieved that endpoint
- Type 1 error was controlled at the 0.05 significance level for the primary endpoint; no other endpoints were controlled for multiplicity

CONCLUSIONS

- **Overall, approximately 80% of patients with moderately to severely active UC randomized to GUS treatment achieved clinical response at Week 12 or 24 of Induction Study 1**
- **Continued treatment with SC GUS allowed 50-54.3% of IV GUS Week 12 clinical nonresponders to achieve clinical response at Week 24**
- **Patients with or without history of inadequate response or intolerance to advanced therapy benefited from continued treatment with GUS through Week 24**
- **The clinical benefit of continued GUS treatment through Week 24 among Week 12 GUS clinical nonresponders was similar regardless of the IV GUS induction regimen (200 mg or 400 mg) received through Week 12, suggesting that there was no carryover effect**
- **No new safety concerns were identified for GUS**

RESULTS

Baseline Demographics and Disease Characteristics: Primary Analysis Population

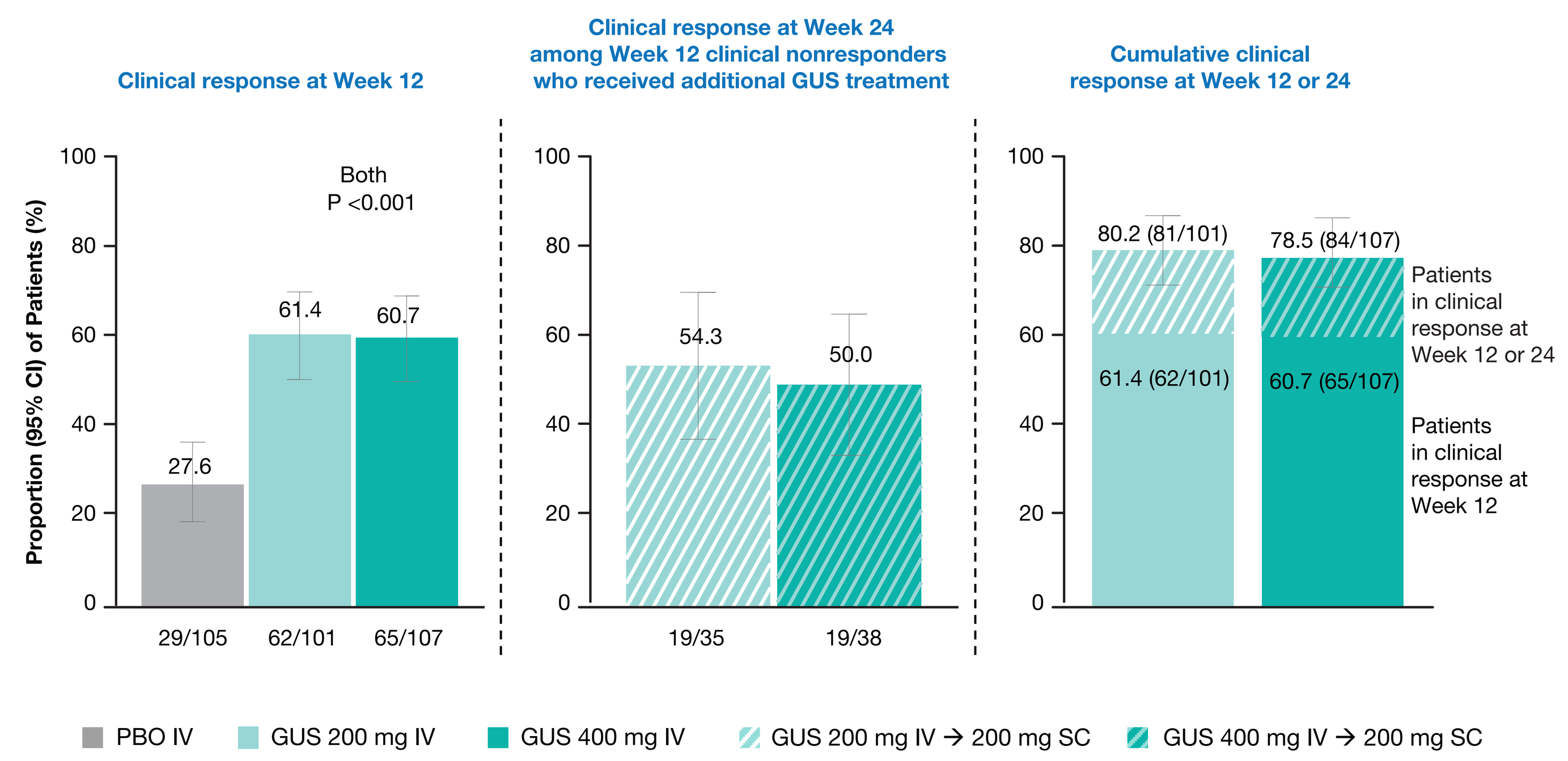
		Guselkumab		
	Placebo IV	200 mg IV	400 mg IV	Total
Primary analysis set, n	105	101	107	313
Age in years, mean (SD)	41.2 (15.05)	43.3 (14.28)	40.4 (13.84)	41.6 (14.40)
Male, n (%)	66 (62.9)	60 (59.4)	59 (55.1)	185 (59.1)
UC duration (years), mean (SD)	7.72 (7.157)	7.03 (5.996)	7.86 (7.147)	7.55 (6.789)
Mayo score, mean (SD)	9.0 (1.31)	9.2 (1.29)	9.3 (1.35)	9.2 (1.32)
Modified Mayo score, mean (SD)	6.9 (1.06)	7.0 (1.06)	7.0 (0.99)	7.0 (1.04)
Modified Mayo score of 7-9, n (%)	69 (65.7)	71 (70.3)	78 (72.9)	218 (69.6)
Mayo endoscopy subscore of 3 (severe), n (%)	75 (71.4)	66 (65.3)	78 (72.9)	219 (70.0)
Extensive UC, n (%)	46 (43.8)	48 (47.5)	59 (55.1)	153 (48.9)
Extraintestinal manifestations present, n (%)	13 (12.4)	15 (14.9)	22 (20.6%)	50 (16.0)
C-reactive protein concentration (mg/L), median (IQR)	4.9 (1.4; 10.8)	4.3 (1.6; 17.8)	4.4 (1.9; 8.8)	4.6 (1.6; 11.3)
Fecal calprotectin concentration (mg/kg), median (IQR)	1457.0 (749.0; 3054.0)	1667.0 (771.0; 2859.0)	1578.0 (811.0; 2860.0)	1564.0 (767.0; 2860.0)

UC Medications: Primary Analysis Population

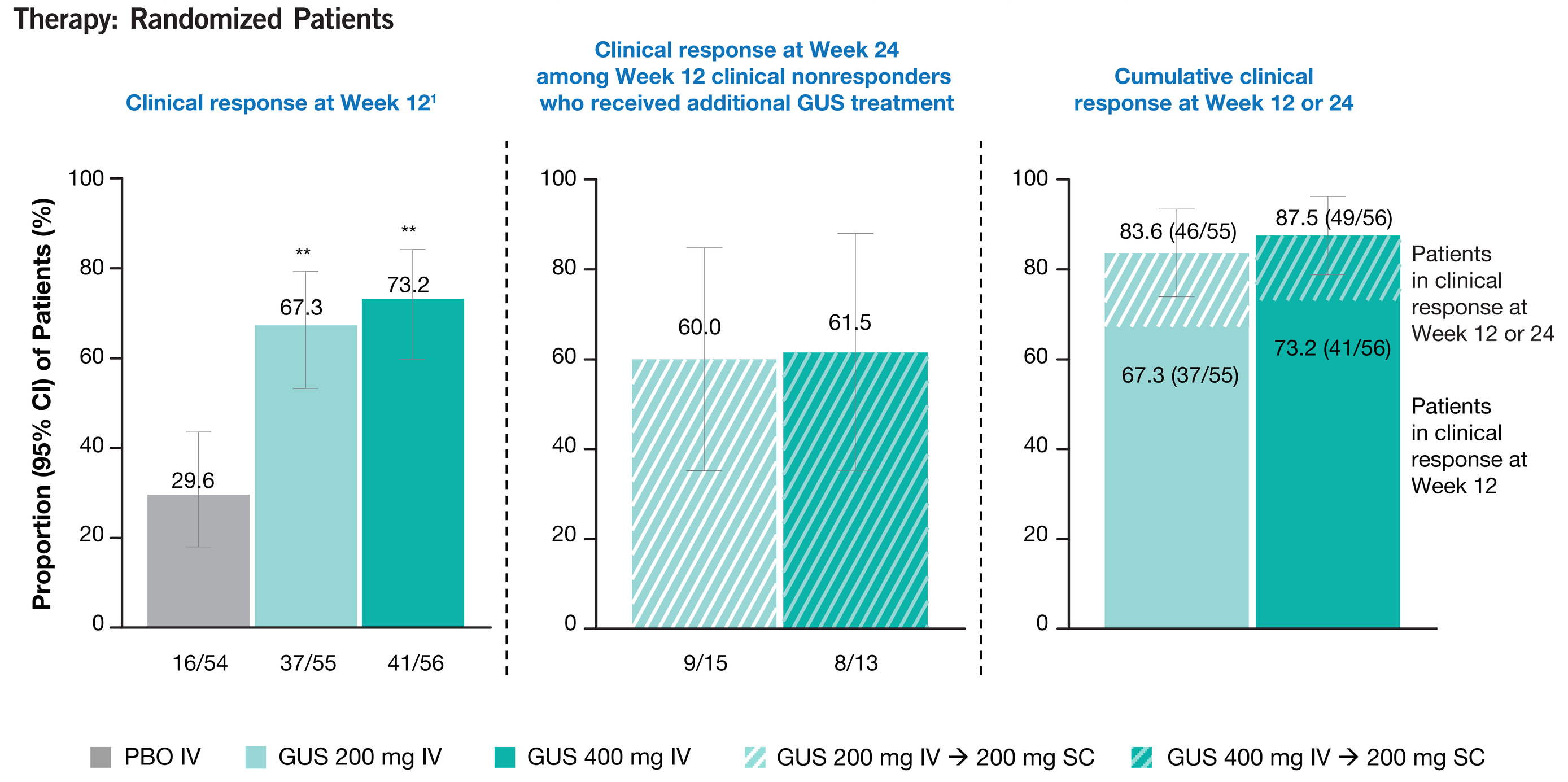
		Guselkumab		
	Placebo IV	200 mg IV	400 mg IV	Total
Primary analysis set, n	105	101	107	313
Receiving any of the following conventional therapy for UC at baseline, n (%)	95 (90.5)	92 (91.1)	96 (89.7)	283 (90.4)
Oral corticosteroids	40 (38.1)	41 (40.6)	44 (41.1)	125 (39.9)
Immunosuppressant drugs	17 (16.2)	25 (24.8)	27 (25.2)	69 (22.0)
Oral aminosalicylates	79 (75.2)	74 (73.3)	89 (83.2)	242 (77.3)
History of inadequate response or intolerance to 1 or more advanced therapies for UC, n (%)	51 (48.6)	46 (45.5)	51 (47.7)	148 (47.3)
1 advanced therapy class	23 (21.9)	27 (26.7)	25 (23.4)	75 (24.0)
2 or more advanced therapy classes	28 (26.7)	19 (18.8)	26 (24.3)	73 (23.3)
No history of inadequate response or intolerance to advanced therapy n (%)	54 (51.4)	55 (54.5)	56 (52.3)	165 (52.7)
Advanced therapy naïve	51 (48.6)	52 (51.5)	51 (47.7)	154 (49.2)
Advanced therapy experienced, but no documented failure	3 (2.9)	3 (3.0)	5 (4.7)	11 (3.5)

Advanced therapy indicates approved tumor necrosis factor alpha antagonists, vedolizumab, or tofacitinib

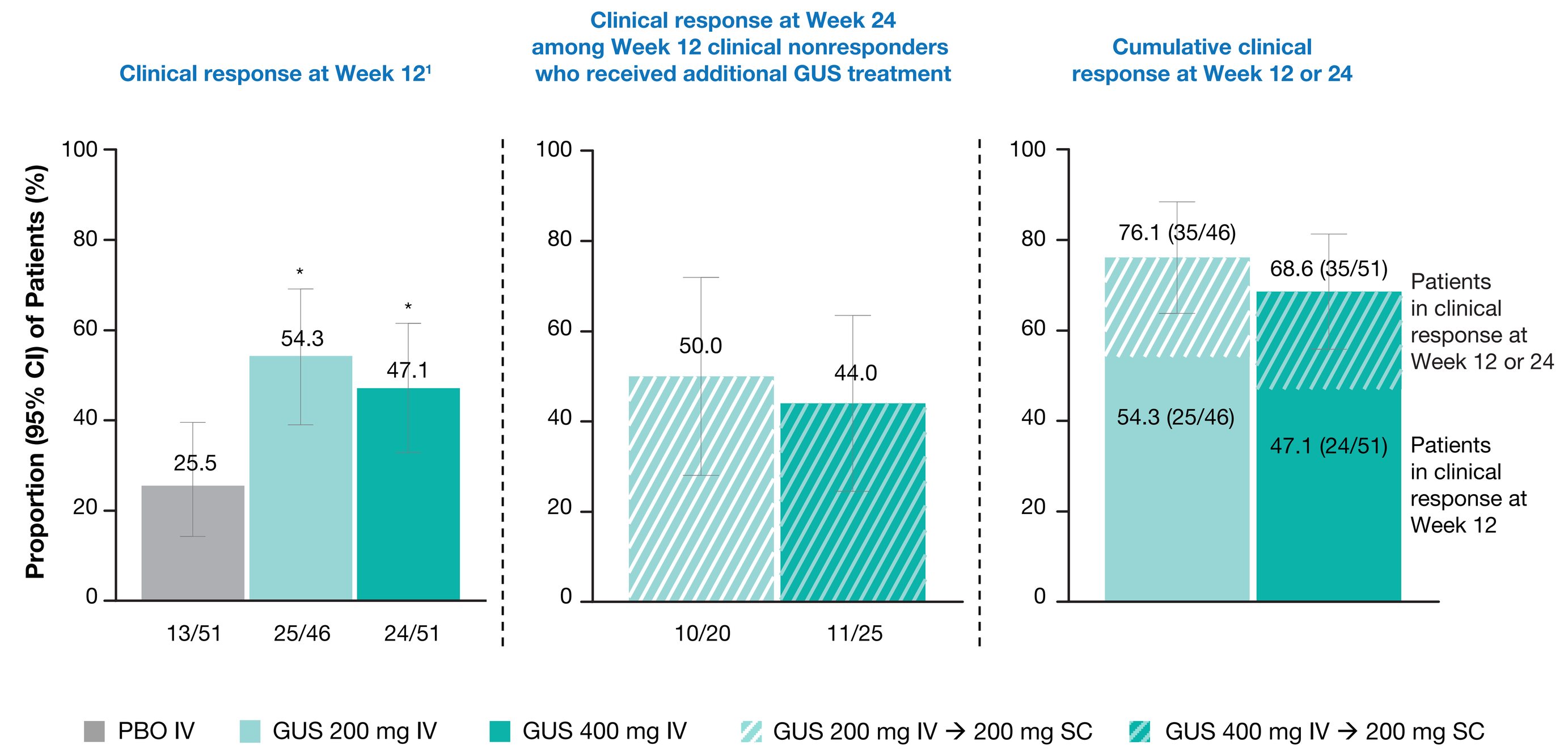
Clinical Response at Week 12 or 24: Randomized Patients



Clinical Response at Week 12 or 24 Among Patients With No History of Inadequate Response or Intolerance to Advanced Therapy: Randomized Patients

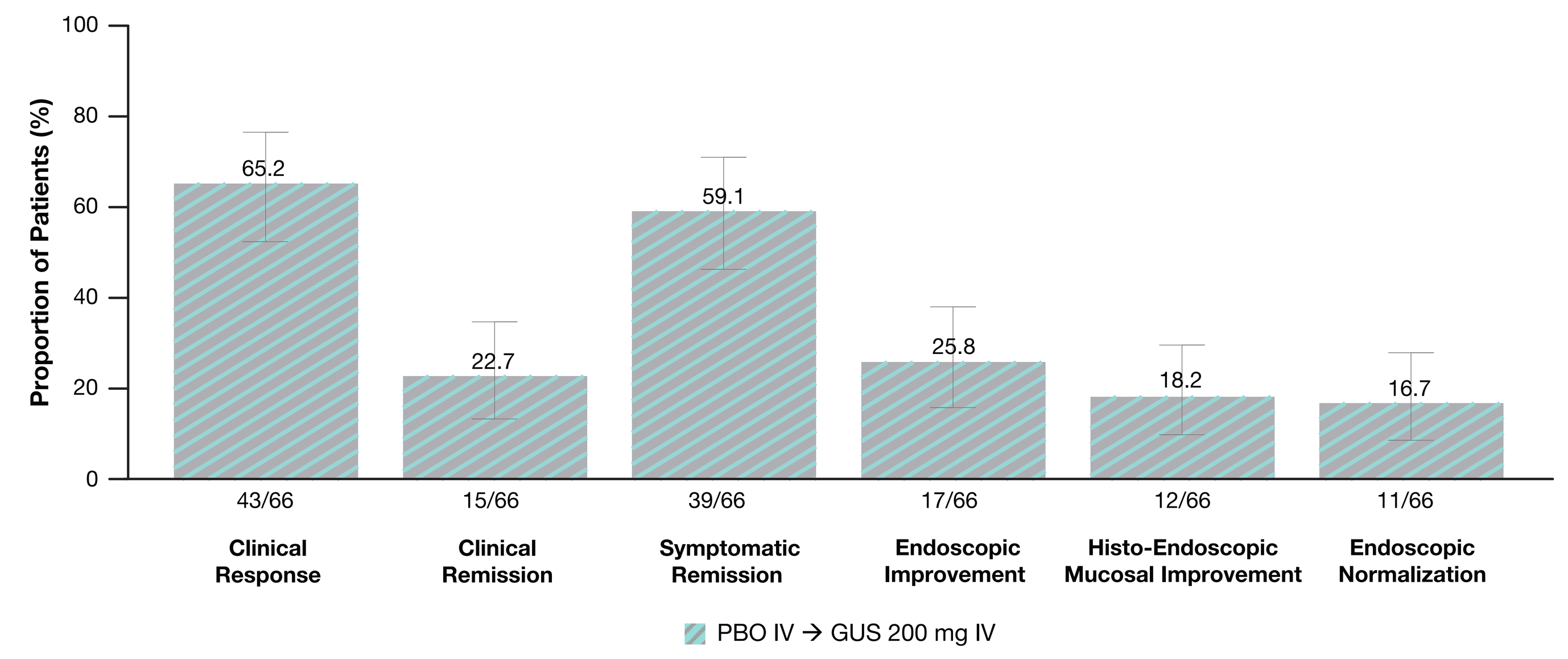


Clinical Response at Week 12 or 24 Among Patients With History of Inadequate Response or Intolerance to Advanced Therapy: Randomized Patients



*Nominal p-value <0.05. **Nominal p-value <0.001. Includes only treated patients with modified Mayo score 5-9 at induction baseline. Advanced therapy indicates approved tumor necrosis factor alpha antagonists, vedolizumab, or tofacitinib.

Key Endpoints at Week 24: Placebo Nonresponders Who Crossed Over to GUS Induction Treatment



- Baseline demographic and disease characteristics were similar among treatment groups
- At Week 12, clinical response was achieved by 61.4% and 60.7% of patients randomized to GUS 200 mg and GUS 400 mg IV vs 27.6 % of patients randomized to PBO IV (both p<0.001)
- Of the GUS-treated patients who were not in clinical response at Week 12, 54.3% in the GUS 200 mg IV→200 mg SC group and 50.0% in the GUS 400 mg IV→200 mg SC group achieved clinical response at Week 24
- Cumulative clinical response at Week 12 or 24 was achieved by 80.2% of patients who were randomized to GUS 200 mg IV and 78.5% of patients who were randomized to GUS 400 mg IV
- Among patients with no history of inadequate response or intolerance to advanced therapy, cumulative clinical response at Week 12 or 24 was achieved by 83.6% randomized to GUS 200 mg IV and 87.5% randomized to GUS 400 mg IV
- Among patients with history of inadequate response or intolerance to advanced therapy, cumulative clinical response at Week 12 or 24 was achieved by 76.1% randomized to GUS 200 mg IV and 68.6% randomized to GUS 400 mg IV
- For patients who received PBO IV→GUS 200 mg IV, clinical response at Week 24 (65.2%) was similar to Week 12 clinical response following GUS 200 mg IV induction (61.4%). Other key clinical endpoints at Week 24 for PBO cross-over patients were generally similar to those previously reported following GUS 200 mg IV induction at Week 12.[2]

Summary of Treatment-emergent Adverse Events Through Final Safety Visit

		Guselkumab[a]						
	Placebo IV[a]	200 mg IV	400 mg IV	Comb	PBO IV→GUS 200 mg IV[b]	GUS IV→GUS 200 mg SC[b]	Comb GUS IV[c]	All GUS[d]
Safety analysis set, N	105	101	107	208	66	78	274	274
Avg. duration of follow-up, weeks	12.3	12.1	12.3	12.2	13.9	14.6	12.6	16.7
Avg. exposure, number of administrations	2.9	3.0	3.0	3.0	2.9	2.9	3.0	3.8
Patients with 1 or more:								
Adverse event, n (%)	59 (56.2)	45 (44.6)	53 (49.5)	98 (47.1)	34 (51.5)	33 (42.3)	132 (48.2)	143 (52.2)
Serious adverse event, n (%)	7 (6.7)	1 (1.0)	3 (2.8)	4 (1.9)	2 (3.0)	3 (3.8)	6 (2.2)	8 (2.9)
Adverse event leading to discontinuation, n (%)	3 (2.9)	1 (1.0)	0	1 (0.5)	2 (3.0)	2 (2.6)	3 (1.1)	5 (1.8)
Reasonably-related adverse event, n (%)[e]	20 (19.0)	13 (12.9)	12 (11.2)	25 (12.0)	9 (13.6)	11 (14.1)	34 (12.4)	43 (15.7)
Infection, n (%)[f]	13 (12.4)	14 (13.9)	10 (9.3)	24 (11.5)	10 (15.2)	6 (7.7)	34 (12.4)	39 (14.2)
Serious infection, n (%)	2 (1.9)	0	0	0	1 (1.5)	0	1 (0.4)	1 (0.4)
Adverse event leading to death	0	0	0	0	0	0	0	0

- The most frequent adverse events among all GUS-treated patients were anemia (7.7%), headache (5.1%), worsening UC (4.4%), COVID-19 (3.6%), arthralgia (2.9%) and abdominal pain (2.6%) which are consistent with Week 12 results

Includes only treated patients with modified Mayo score 5-9 at induction baseline. [a]Includes data up to Week 12 for patients who received treatment at Week 12. Includes all data through final safety visit for patients who did not receive treatment at Week 12. [b]Includes data from Week 12 onward. [c]From the first GUS IV dose onward; for patients who received GUS 200 mg SC at Week 12, includes data up to Week 12. [d]From the first GUS dose onward. [e]An AE that is assessed by the investigator as possibly, probably, or very likely related to study agent or if the relationship to study agent is missing. [f]As assessed by the investigator.

References

1. Rubin DT et al. OP41. ACG 2022. Charlotte, NC; October 21-25, 2022.
2. Dignass A et al. OP23. ECCO 2022. Virtual; February 16-19, 2022.

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Disclosures

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