OP800

Efficacy and Safety of Subcutaneous Guselkumab Induction Therapy in Patients with Ulcerative Colitis: Results Through Week 24 from the Phase 3 ASTRO Study

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Disclosure information

Millie Long

I disclose the following financial relationship(s) with a commercial interest

Research support from Takeda, Pfizer, and Lilly

Consulting for Pfizer, Bristol-Myers Squibb, Roivant, Johnson & Johnson, Takeda, Prometheus, Lilly, Intercept, Target RWE, Celltrion, and Sanofi

Background and Objective

Guselkumab is a selective, dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23[1]

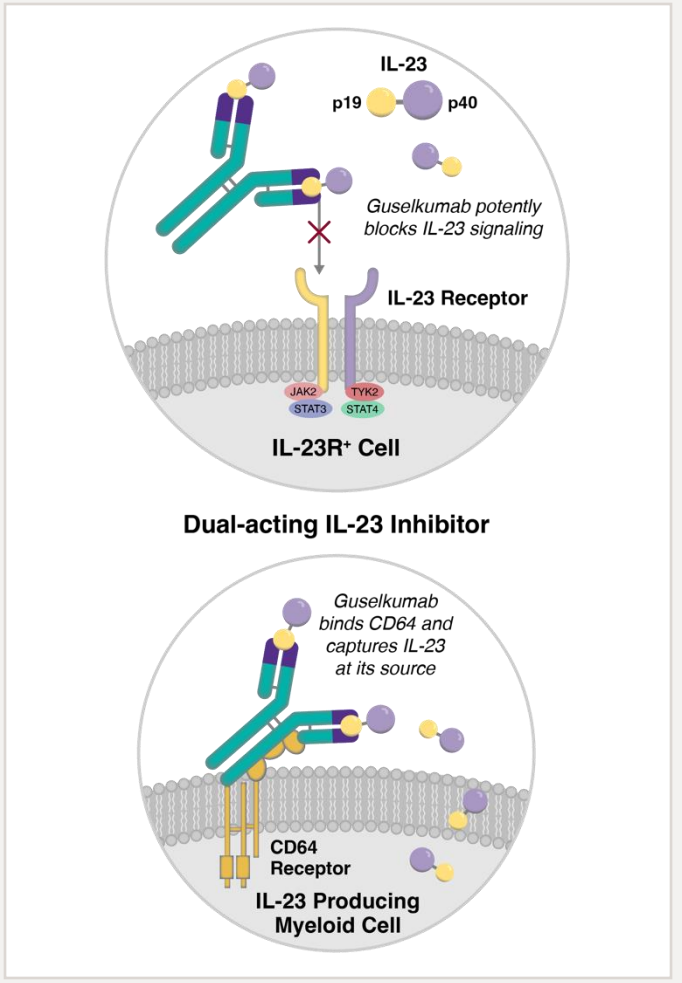
Intravenous (IV) and subcutaneous (SC) induction with guselkumab were recently approved in the United States for Crohn's disease

At present, only IV induction with guselkumab is approved for ulcerative colitis (UC)

- QUASAR established the efficacy and safety of IV induction in patients with moderately to severely active UC[2]

The SC route of administration is a simple alternative to IV and preferred by many patients and healthcare providers[3]

Objective: The ASTRO study (NCT05528510) evaluated the efficacy and safety of guselkumab SC induction in participants with moderately to severely active UC



1. Sachen KL, et al. *Front Immunol*. 2025;16:1532852. doi: 10.3389/fimmu.2025.1532852
2. Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.
3. Jonaitis L, et al. *BMC Proc.* 2021;15(suppl 17):25. doi: 10.1186/s12919-021-00230-7

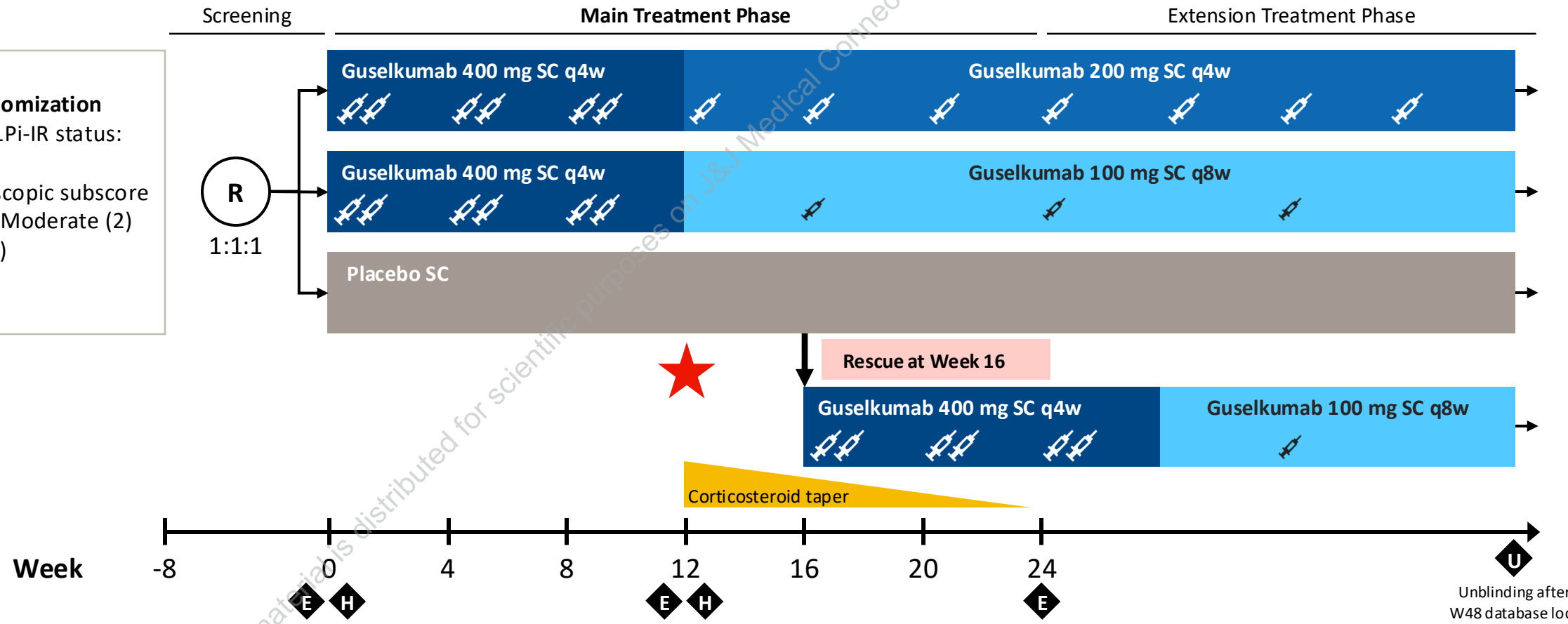
Phase 3, Randomized, Double-blind, Placebo-controlled, Treat-through Design: ASTRO

Key Eligibility Criteria:

- Baseline (week 0) modified Mayo score of 5 to 9
- Baseline Mayo rectal bleeding subscore ≥ 1, Mayo endoscopic subscore ≥ 2 (centrally reviewed)
- Inadequate response/intolerance (IR) to TNFα blockers, vedolizumab, JAK inhibitors, or S1P inhibitors (BIO/JAKi/S1Pi-IR) **OR** naïve to BIO/JAKi/S1Pi (or exposed to BIO/JAKi/S1Pi without IR) and IR to corticosteroids, 6-MP, or AZA

Stratified randomization

- BIO/JAKi/S1Pi-IR status: Yes or No
- Mayo endoscopic subscore at baseline: Moderate (2) or Severe (3)



★ Primary Endpoint (Clinical Remission at W12) | Guselkumab 200 mg | Guselkumab 100 mg | E Endoscopy | H Histology

Demographics and Baseline Disease Characteristics

	Placebo	GUS 400 mg SC → 100 mg SC q8w	GUS 400 mg SC → 200 mg SC q4w
Full analysis set, N	139	139	140
Age in years, mean (SD)	39.5 (13.58)	42.1 (14.59)	43.6 (14.27)
Male, n (%)	90 (64.7%)	79 (56.8%)	87 (62.1%)
UC disease duration in years, mean (SD)	6.61 (6.228)	8.39 (7.317)	7.69 (6.352)
Modified Mayo score[a] (0-9), mean (SD)	6.8 (1.09)[b]	6.8 (1.20)	6.6 (1.15)
Modified Mayo score of 7-9 (severe), n (%)	87 (63.0%)[b]	95 (68.3%)	77 (55.0%)
Mayo endoscopic subscore of 3 (severe), n (%)	78 (56.1%)	78 (56.1%)	78 (55.7%)
Extensive UC, n (%)	73 (52.5%)	69 (49.6%)	82 (58.6%)
C-reactive protein,[c] median in mg/L (IQR)	3.8 (1.2; 10.9)	3.7 (1.3; 7.2)	4.7 (1.7; 9.1)
C-reactive protein[c] >3 mg/L	77 (55.8%)	75 (55.1%)	86 (61.4%)
Fecal calprotectin,[d] median in mg/kg (IQR)	1749.0 (617.0; 3202.0)	1351.5 (609.0; 2805.0)	1594.0 (838.0; 3336.0)
Fecal calprotectin[d] >250 mg/kg	119 (90.8%)	107 (84.9%)	119 (93.0%)

a. Modified Mayo score: 3-component (stool frequency, rectal bleeding, and endoscopy subscores) Mayo score without the physician's global assessment.
b. Based on N=138.
c. Based on N=138 for Placebo, N=136 for GUS 400 mg SC→100 mg SC q8w, N=140 for GUS 400 mg SC→200 mg SC q4w.
d. Based on N=131 for Placebo, N=126 for GUS 400 mg SC→100 mg SC q8w, N=128 for GUS 400 mg SC→200 mg SC q4w.

UC-related Medication History and Baseline UC Medications

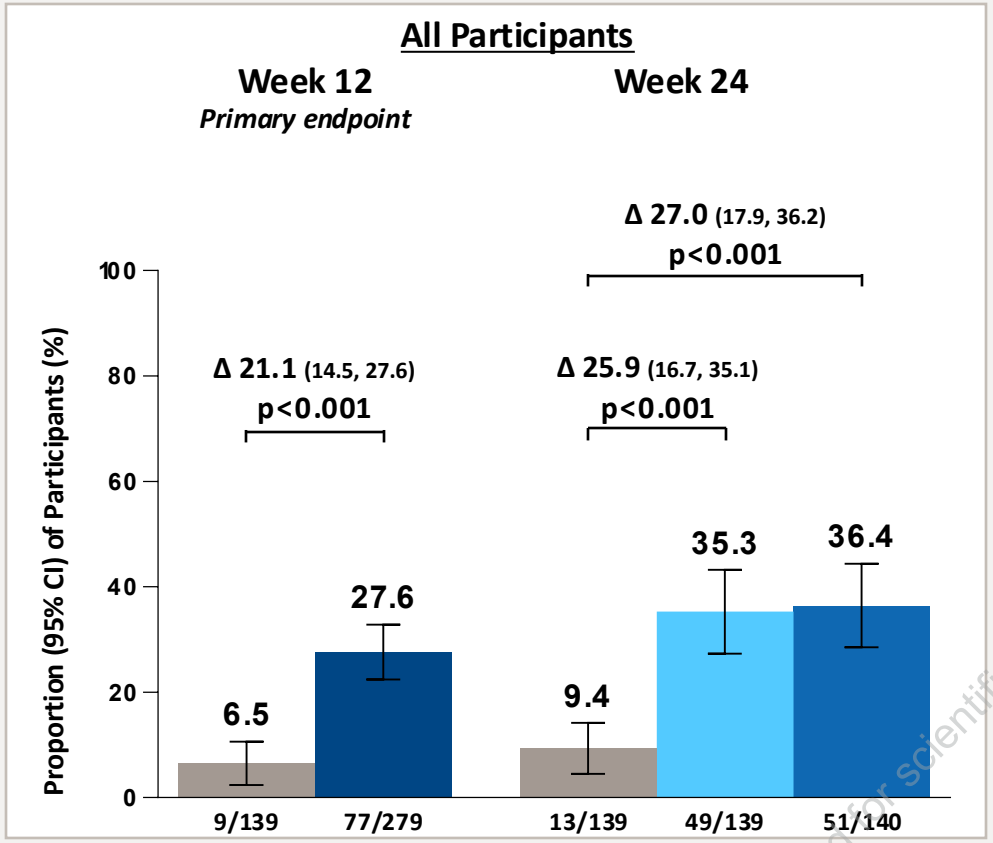
	Placebo	GUS 400 mg SC → 100 mg SC q8w	GUS 400 mg SC → 200 mg SC q4w
Full analysis set, N	139	139	140
Naïve to BIO/JAKi/S1Pi, n (%)	79 (56.8%)	81 (58.3%)	83 (59.3%)
BIO/JAKi/S1Pi-IR, n (%)	56 (40.3%)	57 (41.0%)	55 (39.3%)
One class[a]	39 (69.6%)	40 (70.2%)	38 (69.1%)
Two classes[a]	13 (23.2%)	10 (17.5%)	11 (20.0%)
Three or more classes[a]	4 (7.1%)	7 (12.3%)	6 (10.9%)
At least one anti-TNF[a] (regardless of other BIO/JAKi/S1Pi)	39 (69.6%)	42 (73.7%)	46 (83.6%)
Vedolizumab[a] (regardless of other BIO/JAKi/S1Pi)	25 (44.6%)	30 (52.6%)	19 (34.5%)
JAK inhibitors[a] (regardless of other BIO/S1Pi)	11 (19.6%)	9 (15.8%)	10 (18.2%)
Ozanimod[a] (regardless of other BIO/JAKi)	2 (3.6%)	0	3 (5.5%)
History of IR or dependence to corticosteroids, n (%)	104 (74.8%)	108 (77.7%)	100 (71.4%)
History of IR to 6-MP or AZA, n (%)	56 (40.3%)	50 (36.0%)	58 (41.4%)
Baseline oral corticosteroid use, n (%)	46 (33.1%)	50 (36.0%)	41 (29.3%)
Baseline use of 6-MP, AZA, or MTX, n (%)	28 (20.1%)	26 (18.7%)	30 (21.4%)

a. Denominator is participants who were BIO/JAKi/S1Pi-IR.

Treatment Disposition Prior to Week 24

	Placebo	GUS 400 mg SC → 100 mg SC q8w	GUS 400 mg SC → 200 mg SC q4w
Full analysis set, N	139	139	140
Discontinued study agent prior to Week 24, n (%)	22 (15.8)	5 (3.6)	11 (7.9)
Reason for discontinuation, n (%)			
Withdrawal by participant	4 (2.9)	2 (1.4)	3 (2.1)
Adverse event – worsening of UC	7 (5.0)	0	1 (0.7)
Lack of efficacy	4 (2.9)	1 (0.7)	3 (2.1)
Adverse event – other	4 (2.9)	0	2 (1.4)
Death	1 (0.7)	0	0
Initiated prohibited medication	1 (0.7)	0	0
Protocol deviation	0	1 (0.7)	0
Other	1 (0.7)	1 (0.7)	2 (1.4)

Clinical Remission

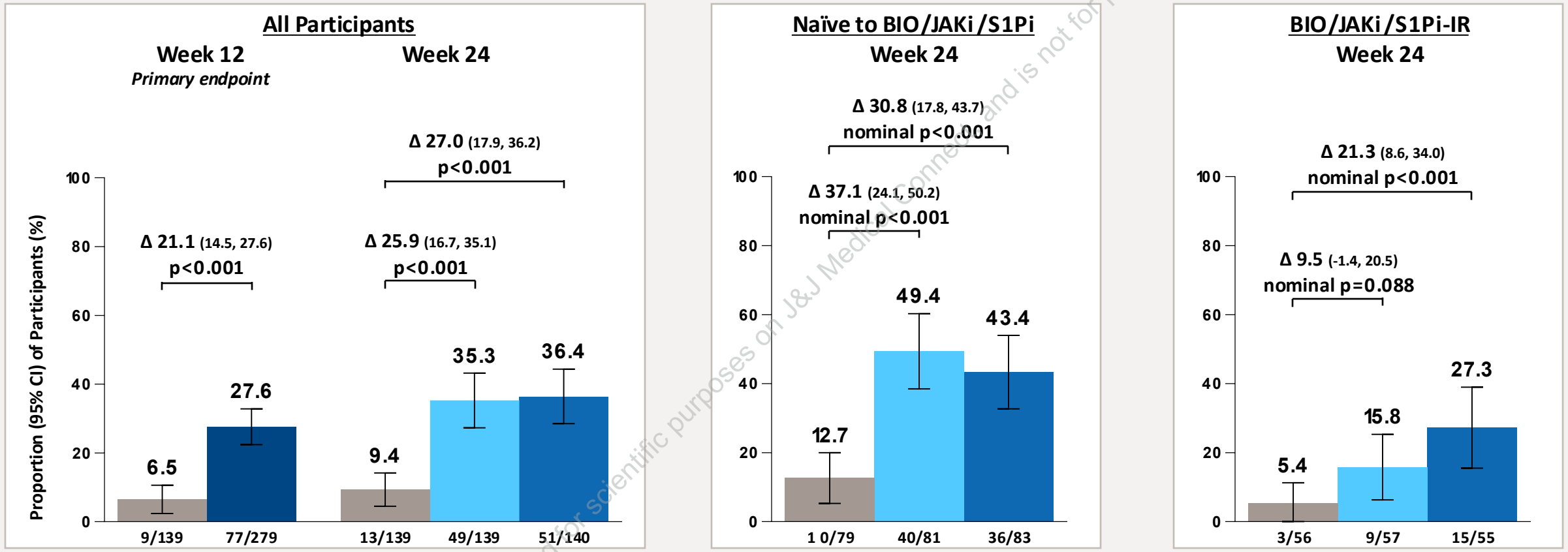


Placebo | GUS 400 mg SC induction | GUS 400 mg SC induction → 100 mg SC q8w | GUS 400 mg SC induction → 200 mg SC q4w

Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0, or 1 with no friability

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo.
Participants who, prior to the assessment timepoint, had an ostomy or colectomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC, or met rescue criteria per IWRS if applicable were considered not to meet the endpoint criteria. Participants who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Participants who discontinued study agent for other reasons prior to the assessment timepoint were considered not to meet the endpoint criteria.
After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Clinical Remission



Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0, or 1 with no friability

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Subpopulation analyses were not multiplicity controlled.
Participants who, prior to the assessment timepoint, had an ostomy or colectomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC, or met rescue criteria per IWRS if applicable were considered not to meet the endpoint criteria. Participants who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Participants who discontinued study agent for other reasons prior to the assessment timepoint were considered not to meet the endpoint criteria.
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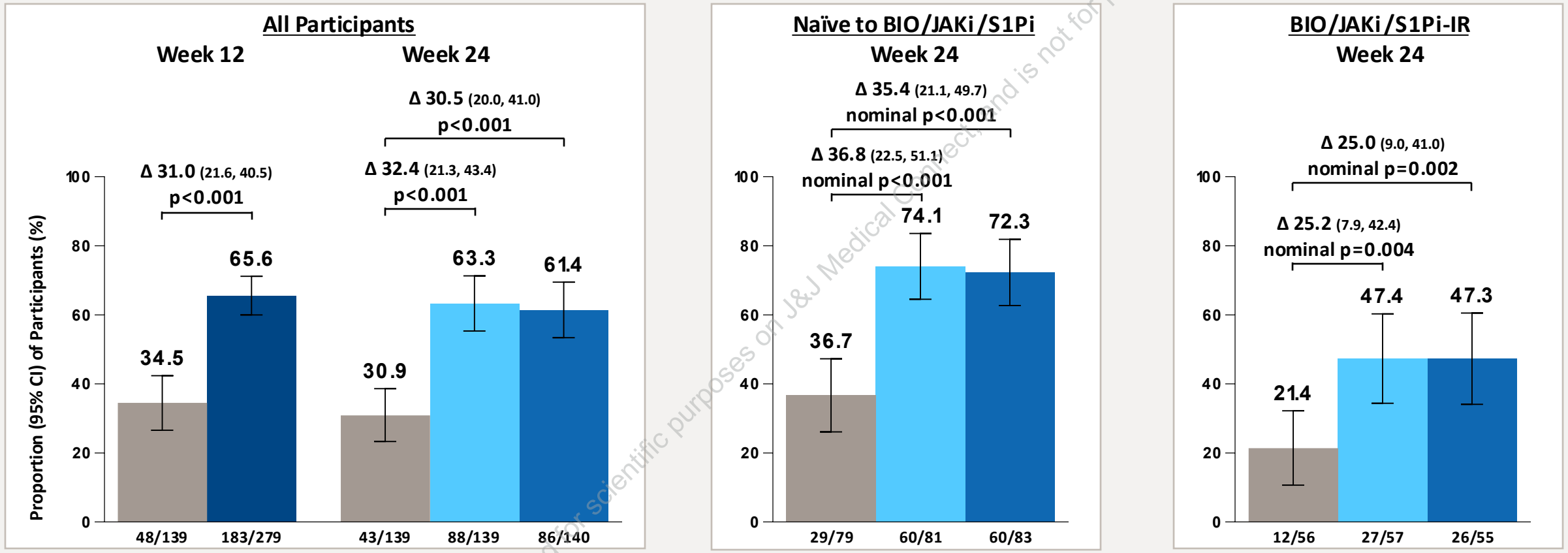
Clinical Response



Placebo | GUS 400 mg SC induction | GUS 400 mg SC induction → 100 mg SC q8w | GUS 400 mg SC induction → 200 mg SC q4w

Clinical response: A decrease from 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

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Subpopulation analyses were not multiplicity controlled.
Participants who, prior to the assessment timepoint, had an ostomy or colectomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC, or met rescue criteria per IWRS if applicable were considered not to meet the endpoint criteria. Participants who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Participants who discontinued study agent for other reasons prior to the assessment timepoint were considered not to meet the endpoint criteria.
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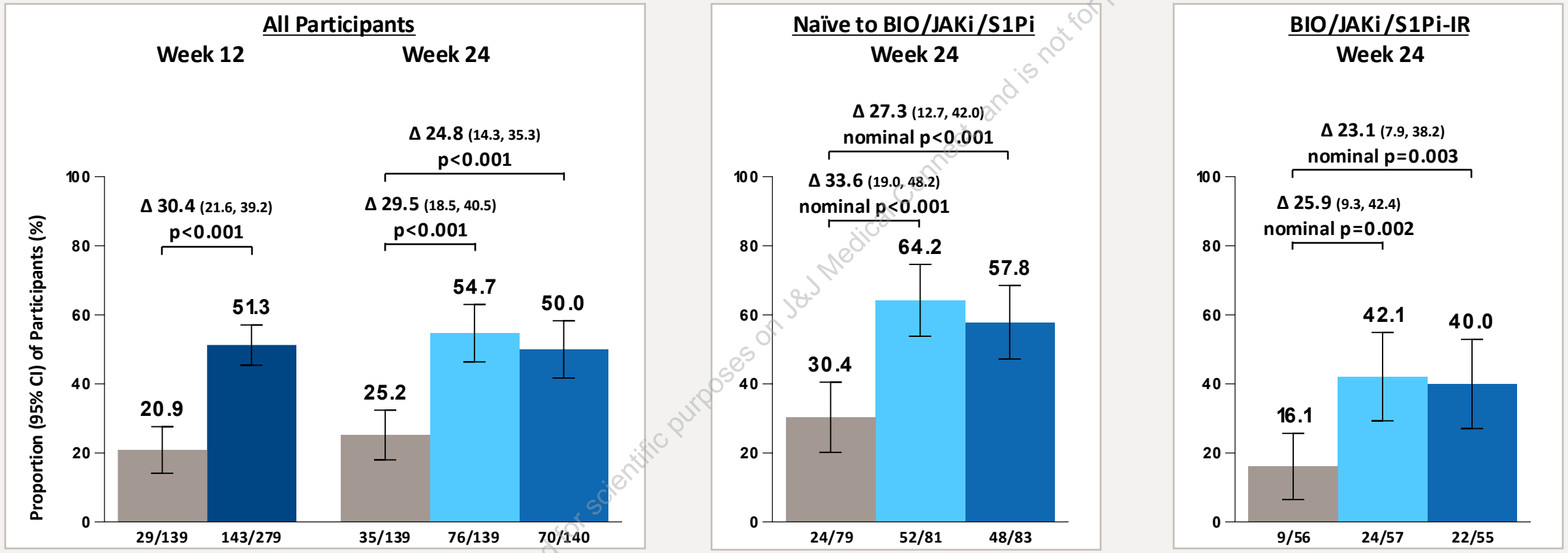
Symptomatic Remission



Symptomatic remission: A stool frequency subscore of 0 or 1 and not increased from baseline, and a rectal bleeding subscore of 0

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Subpopulation analyses were not multiplicity controlled.
Participants who, prior to the assessment timepoint, had an ostomy or colectomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC, or met rescue criteria per IWRS if applicable were considered not to meet the endpoint criteria. Participants who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Participants who discontinued study agent for other reasons prior to the assessment timepoint were considered not to meet the endpoint criteria.
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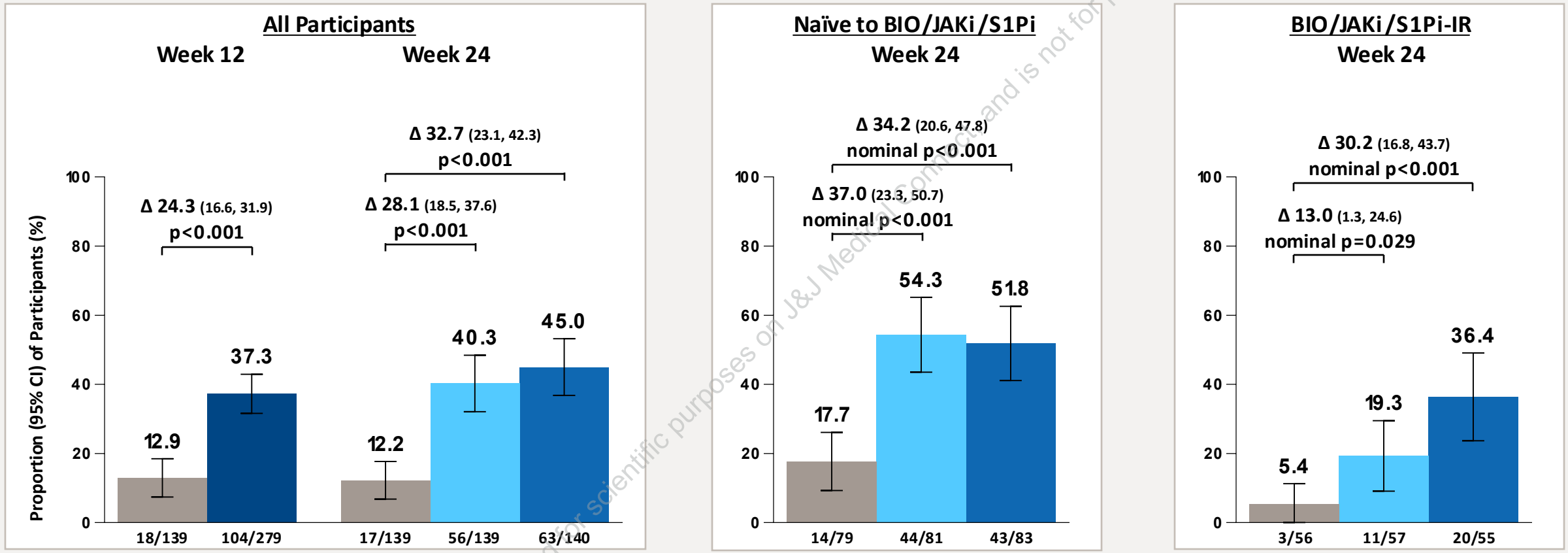
Endoscopic Improvement



Endoscopic improvement: An endoscopic subscore of 0, or 1 with no friability

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Subpopulation analyses were not multiplicity controlled.
Participants who, prior to the assessment timepoint, had an ostomy or colectomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC, or met rescue criteria per IWRS if applicable were considered not to meet the endpoint criteria. Participants who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Participants who discontinued study agent for other reasons prior to the assessment timepoint were considered not to meet the endpoint criteria.
After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Summary of Adverse Events Through Week 24

	Placebo[a]	GUS 400 mg SC → 100 mg SC q8w	GUS 400 mg SC → 200 mg SC q4w
Safety analysis set, N	139	139	140
Average duration of follow-up, weeks	20.7	24.0	24.2
Deaths, n (%)	1 (0.7%)	0	0
Participants with 1 or more:			
AEs, n (%)	91 (65.5%)	74 (53.2%)	85 (60.7%)
AEs by severity,[b] n (%)			
Mild	49 (35.3%)	42 (30.2%)	48 (34.3%)
Moderate	30 (21.6%)	27 (19.4%)	30 (21.4%)
Severe	12 (8.6%)	5 (3.6%)	7 (5.0%)
Serious AEs, n (%)	17 (12.2%)	5 (3.6%)	6 (4.3%)
AEs leading to discontinuation of study agent, n (%)	12 (8.6%)	3 (2.2%)	4 (2.9%)
Infections,[c] n (%)	36 (25.9%)	33 (23.7%)	32 (22.9%)
Serious infections	1 (0.7%)	1 (0.7%)	3 (2.1%)
Most common AEs (incidence >5% in either GUS group), n (%)			
Worsening of ulcerative colitis	29 (20.9%)	14 (10.1%)	9 (6.4%)
Arthralgia	3 (2.2%)	11 (7.9%)	7 (5.0%)
Upper respiratory tract infection	9 (6.5%)	10 (7.2%)	5 (3.6%)

- Serious infections reported with GUS were **appendicitis** (n=2), **pilonidal disease** (n=1) and **gastroenteritis** (n=1); 1 case of **pneumonia** occurred with PBO

a. Includes all PBO participants, excluding data after a participant is rescued with guselkumab.
b. The worst severity event experienced by the participant is used.
c. Infections were defined as any adverse event coded to the MedDRA system organ class 'Infections and infestations'.

Adverse Events of Interest Through Week 24

	Placebo[a]	GUS 400 mg SC → 100 mg SC q8w	GUS 400 mg SC → 200 mg SC q4w
Safety analysis set, N	139	139	140
Average duration of follow-up, weeks	20.7	24.0	24.2
Participants with 1 or more AEs, n (%)			
Active tuberculosis	0	0	0
Malignancies	1 (0.7%)	0	1 (0.7%)
Anaphylactic or serum sickness reactions	0	0	0
Opportunistic infections[b]	0	0	1 (0.7%)
Major adverse cardiovascular events (MACE)	0	1 (0.7%)	0
Venous thromboembolism (VTE)	0	0	0

- All participants reporting AEs of interest had pertinent risk factors
  - Breast cancer and lymphoma were reported in 1 GUS participant; adenocarcinoma of the colon was reported in 1 PBO participant
  - CMV colitis was reported in the GUS participant
  - Cerebral infarction was reported in the GUS participant

a. Includes all PBO participants, excluding data after a participant is rescued with guselkumab.
b. Infections were defined as any adverse event coded to the MedDRA system organ class 'Infections and infestations'.

Conclusions

- ASTRO results showed the efficacy of a fully SC induction and maintenance regimen through Week 24 with guselkumab in ulcerative colitis
- Clinically meaningful benefit was observed both in participants naïve to BIO/JAKi/S1Pi and in those with prior inadequate response or intolerance to BIO/JAKi/S1Pi
- The safety of a fully SC treatment regimen was consistent with the well-characterized and favorable safety profile of guselkumab
- These results complement the QUASAR[1] data in UC and guselkumab data in Crohn's disease,[2,3] demonstrating that both IV and SC induction with guselkumab are efficacious therapeutic options in IBD, providing simplicity for patients and healthcare providers

1. Rubin DT, et al. Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. *Lancet.* 2025;405(10472):33-49.
2. Hart A, et al. Efficacy and Safety of Guselkumab Subcutaneous Induction and Maintenance in Participants With Moderately to Severely Active Crohn's Disease: Results From the Phase 3 GRAVITI Study. *Gastroenterology* 2025; doi: 10.1053/j.gastro.2025.02.033
3. Panaccione R, et al. Efficacy and safety of guselkumab therapy in patients with moderately to severely active Crohn's disease: results of the GALAXI 2 & 3 phase 3 studies. *Gastroenterology* 2024;166(5 suppl):1057b-1057b2.

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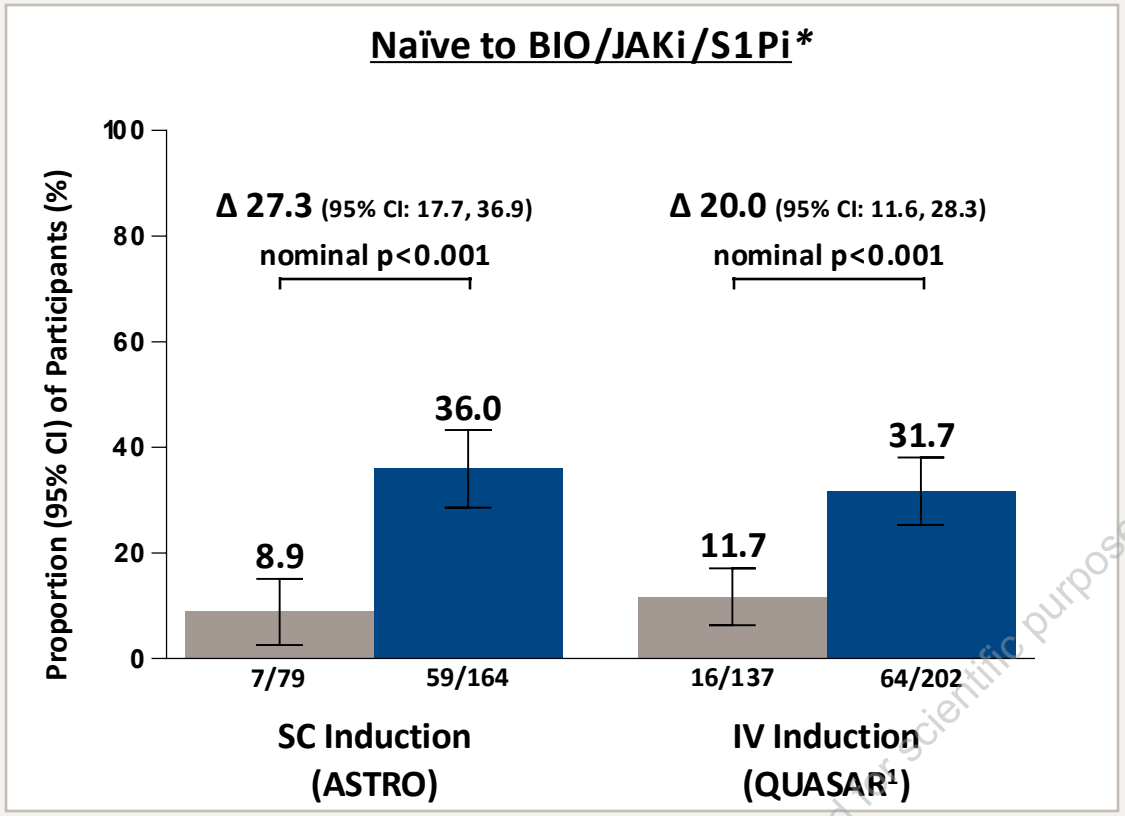
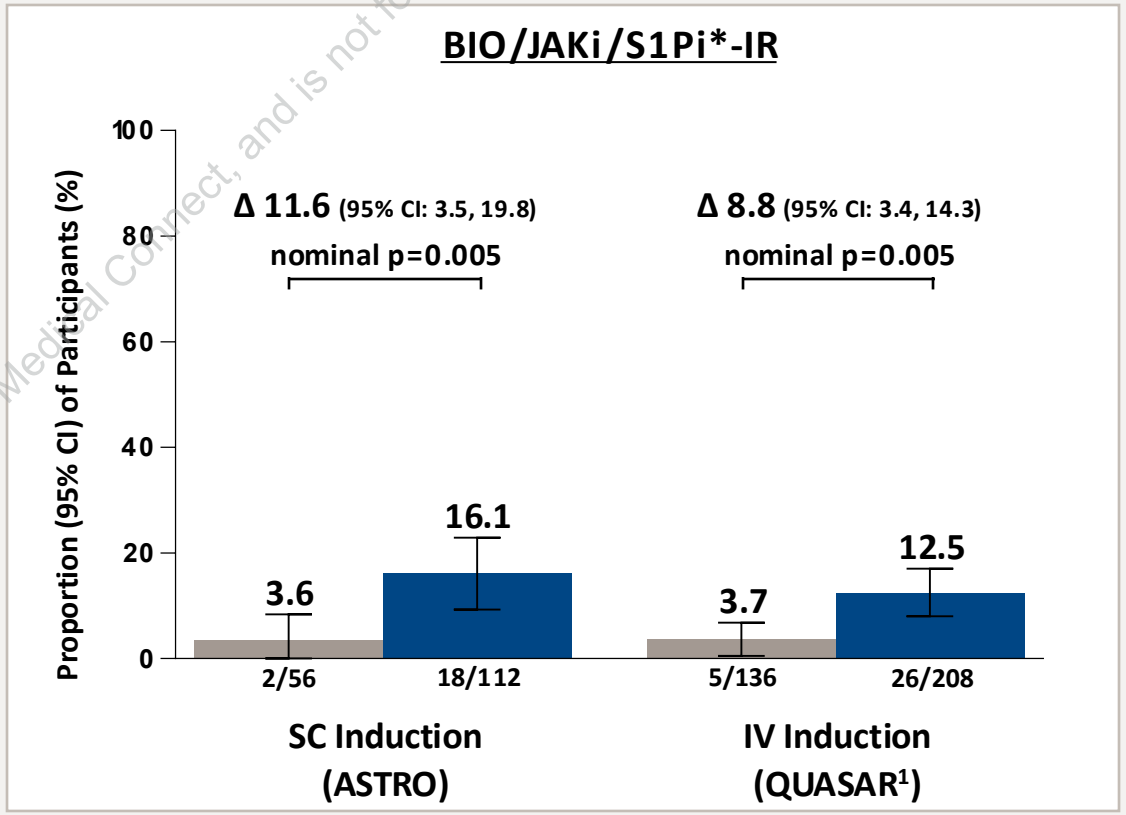
- This work was supported by Johnson & Johnson

Clinical Remission at Week 12: SC or IV Guselkumab Induction





Placebo Induction

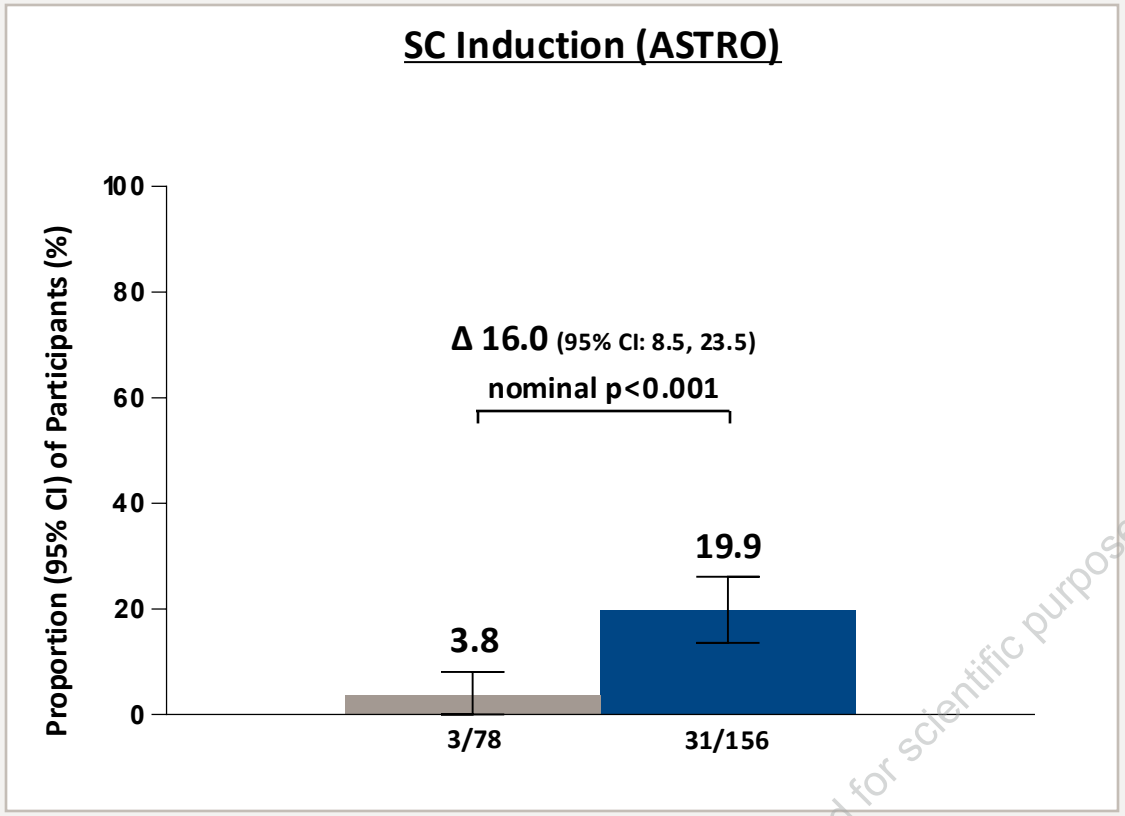
GUS Induction (400 mg SC or 200 mg IV)

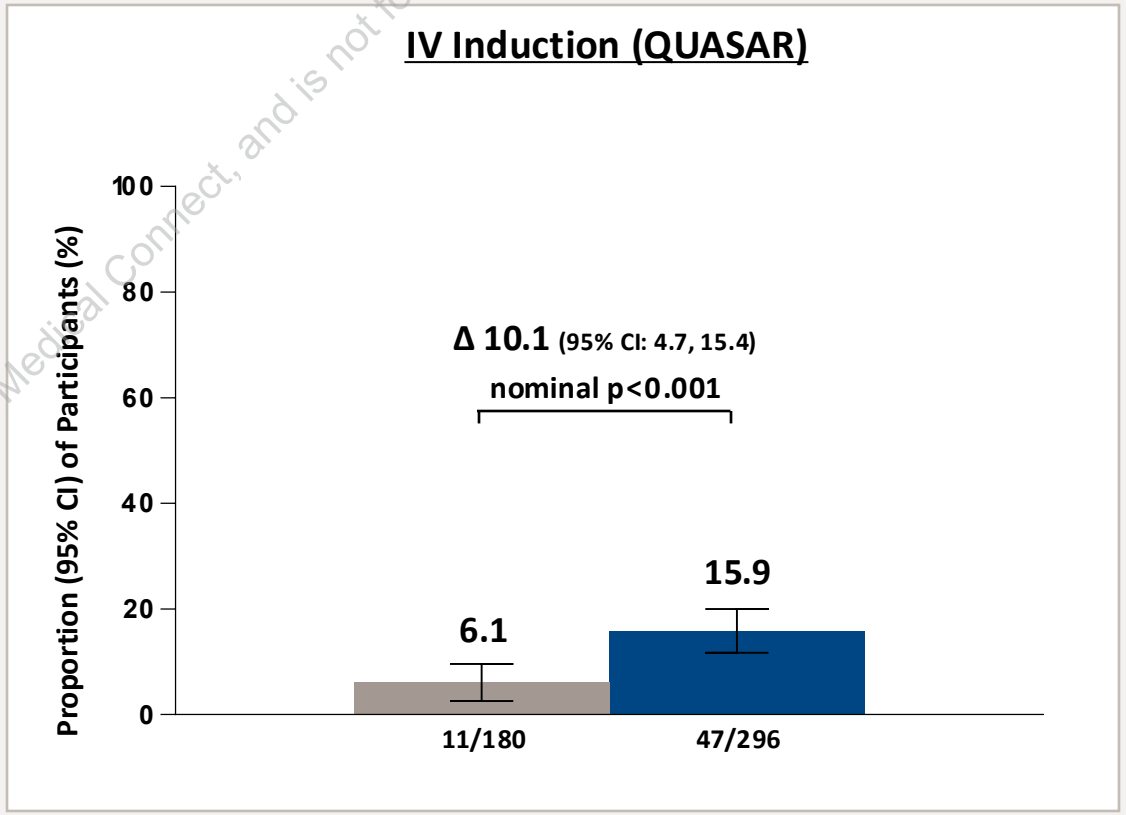
Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0, or 1 with no friability

* Participants in QUASAR had no prior exposure to S1P inhibitors

1. Rubin DT, et al. Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. *Lancet*. 2025;405(10472):33-49.

Clinical Remission at Week 12: MES=3 at Baseline





Placebo Induction

GUS Induction (400 mg SC or 200 mg IV)

Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0, or 1 with no friability