Efficacy and safety of subcutaneous guselkumab induction and maintenance therapy in participants with ulcerative colitis: Results through Week 48 from the Phase 3 ASTRO study

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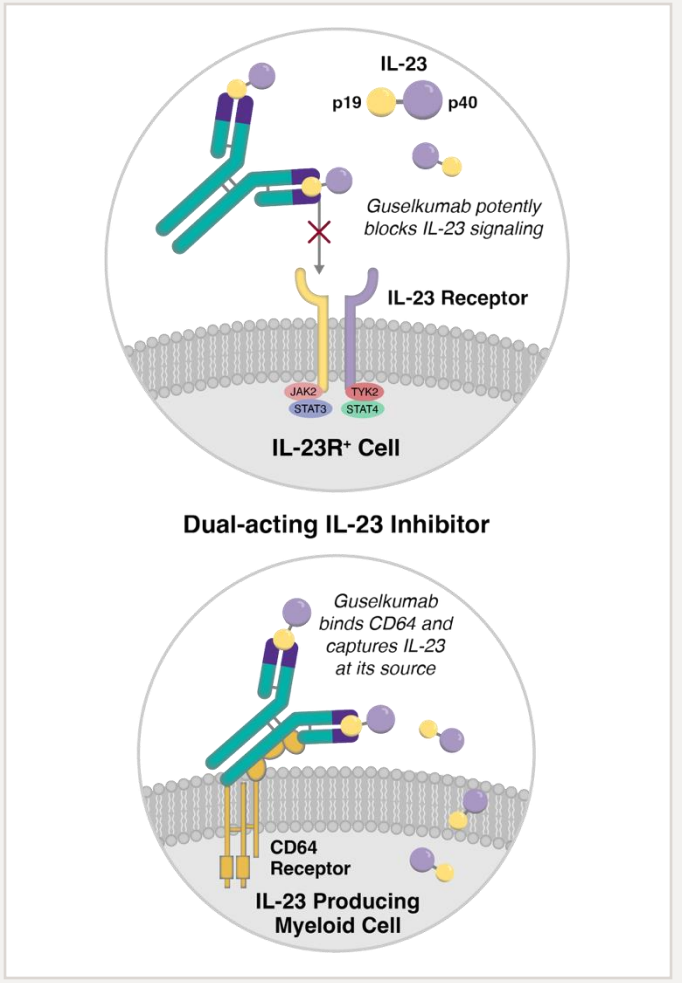
Background and Objective

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

Studies of intravenous (IV) and subcutaneous (SC) induction with guselkumab have demonstrated efficacy in both Crohn's disease[2,3] and ulcerative colitis[4] (UC)

Previous evaluation of guselkumab SC maintenance following SC induction in UC was limited to 12 weeks of follow-up during maintenance[5]

Objective: Here we report the efficacy and safety results of guselkumab SC induction followed by SC maintenance through Week 48 from the treat-through ASTRO study (NCT05528510) in participants with UC



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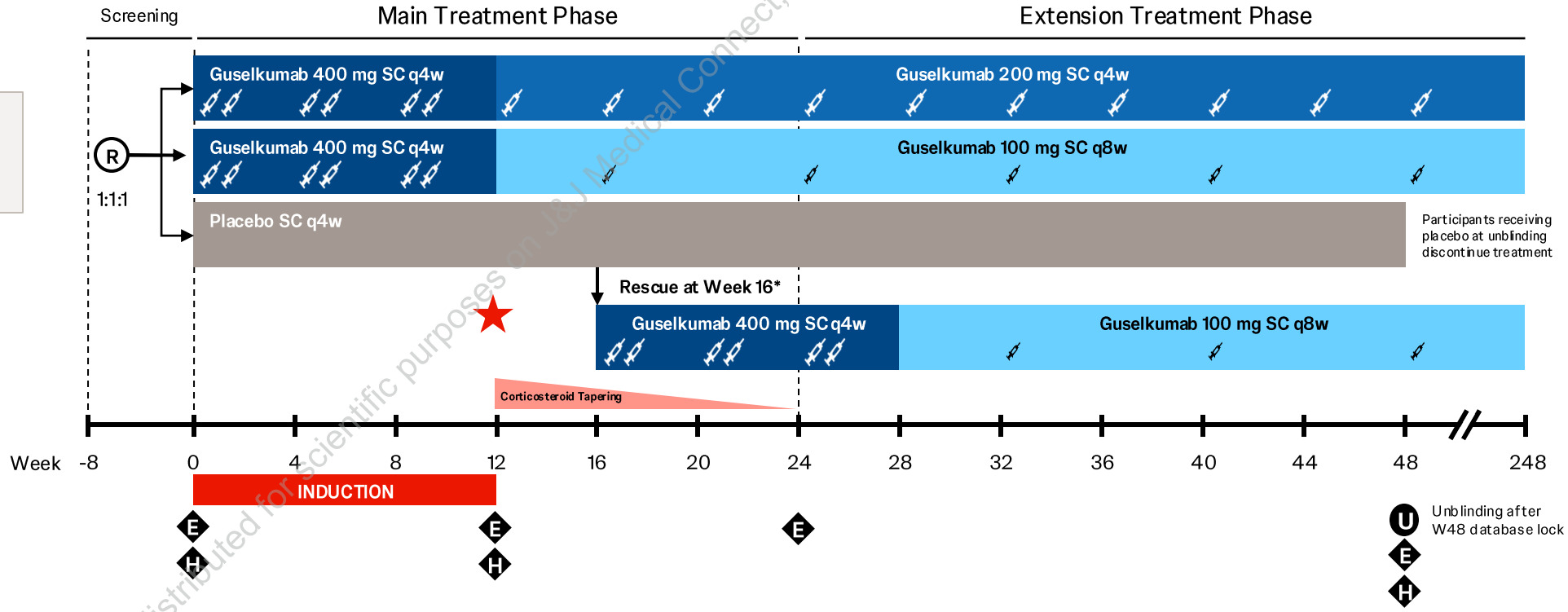
1. Sachen KL, et al. *Front Immunol*. 2025;16:1532852. doi: 10.3389/fimmu.2025.1532852
2. Panaccione R, et al. *Lancet*. 2025;406:358-75.
3. Hart A, et al. *Gastroenterology*. 2025;169:308-25.
4. Rubin DT, et al. *Lancet*. 2025;405:33-49.
5. Long MD, et al. *Gastroenterology*. 2025;169(suppl):S-190.

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

Key Inclusion 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 tumor necrosis factor alpha (TNFα) blockers, vedolizumab, Janus Kinase (JAK) inhibitors, or Sphingosine-1-phosphate (S1P) inhibitors (biologics [BIO] / JAKi / S1Pi-IR)
  OR naïve to BIO / JAKi / S1Pi (or exposed to BIO / JAKi / S1Pi without IR) and IR to corticosteroids, mercaptopurine (6-MP), or azathioprine (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 Week 12) | R Randomization | H Histology | E Endoscopy | U Study unblinding

***Rescue treatment criteria:**
No improvement in Mayo endoscopic subscore at Week 12 compared with baseline **AND**
<2 point improvement in partial Mayo score at Week 12 and Week 16 compared with baseline
***Rescue treatment for guselkumab arms:** Sham matching placebo SC to maintain the blind at Weeks 16, 20, and 24

q4w=every 4 weeks; q8w=every 8 weeks

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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 (interquartile range [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, n (%)	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, n (%)	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.

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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 or more classes[a]	17 (30.4%)	17 (29.8%)	17 (30.9%)
At least 1 anti-tumor necrosis factor (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/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 methotrexate (MTX), n (%)	28 (20.1%)	26 (18.7%)	30 (21.4%)

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

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Treatment Disposition Prior to Week 48

	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 48, n (%)	47 (33.8%)	15 (10.8%)	22 (15.7%)
Reason for discontinuation, n (%)			
Lack of efficacy	14 (10.1%)	6 (4.3%)	10 (7.1%)
Adverse event – worsening of UC	11 (7.9%)	4 (2.9%)	2 (1.4%)
Withdrawal by participant	9 (6.5%)	2 (1.4%)	5 (3.6%)
Adverse event – other	4 (2.9%)	0	2 (1.4%)
Week 24 nonresponder	4 (2.9%)	0	0
Death	1 (0.7%)	1 (0.7%)	0
Initiated prohibited medication	2 (1.4%)	0	0
Protocol deviation	0	1 (0.7%)	0
Other	2 (1.4%)	1 (0.7%)	3 (2.1%)

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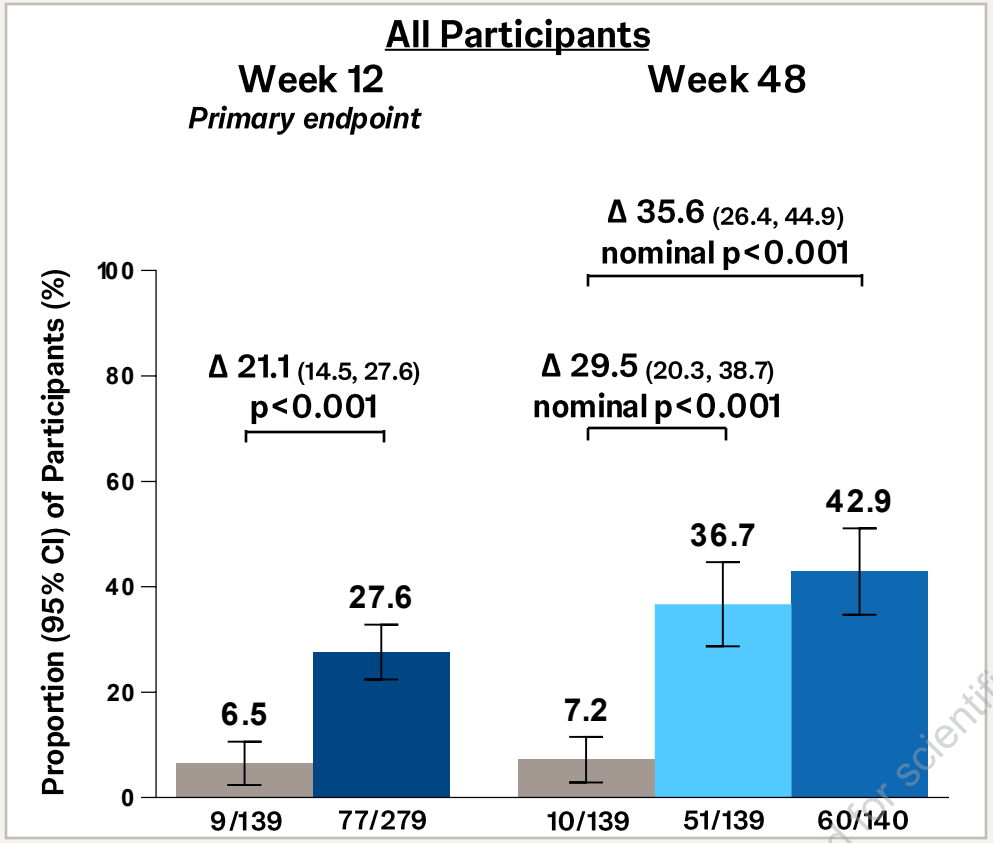
Clinical Remission



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 with no increase 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 (p-values are nominal for all Week 48 assessments).
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 adverse event (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.

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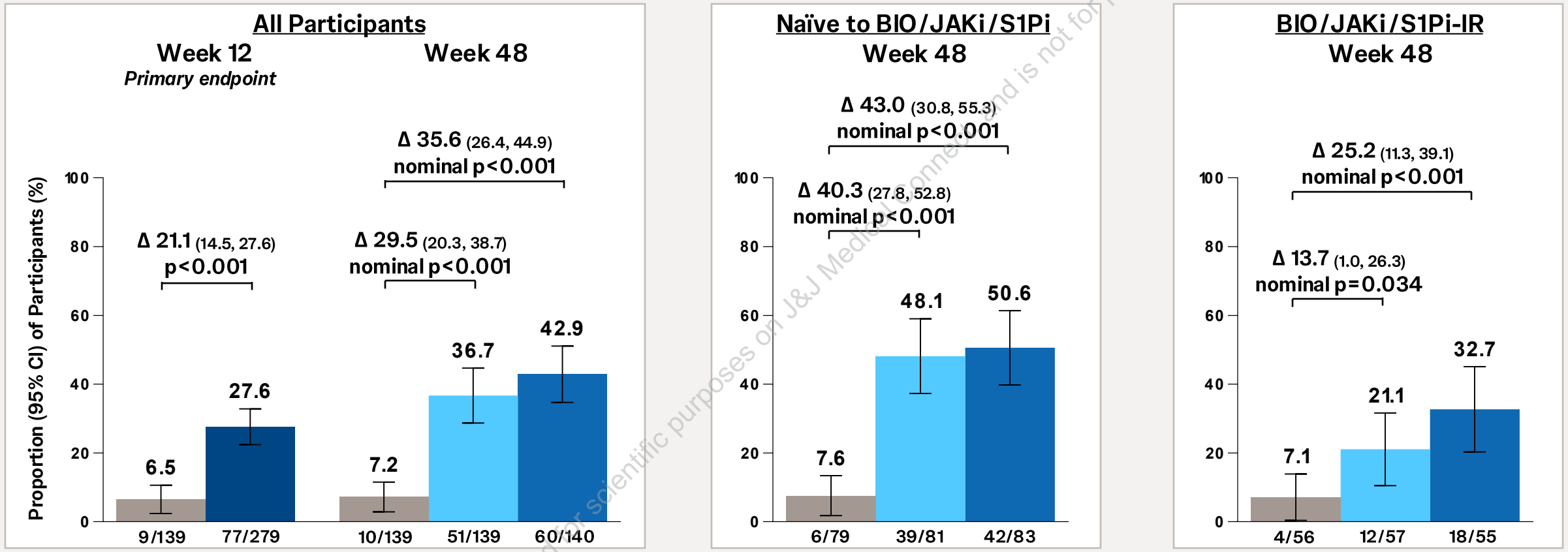
Clinical Remission



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 with no increase from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0 or 1 with no friability

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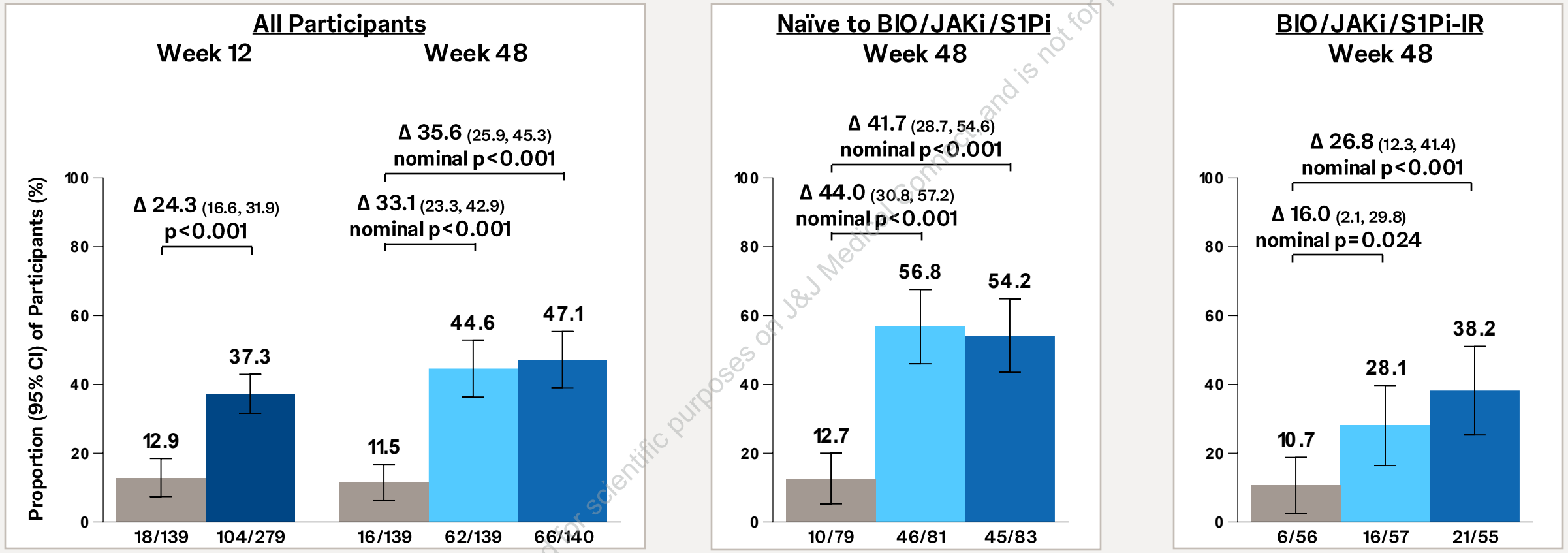
Endoscopic Improvement



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

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all Week 48 assessments).
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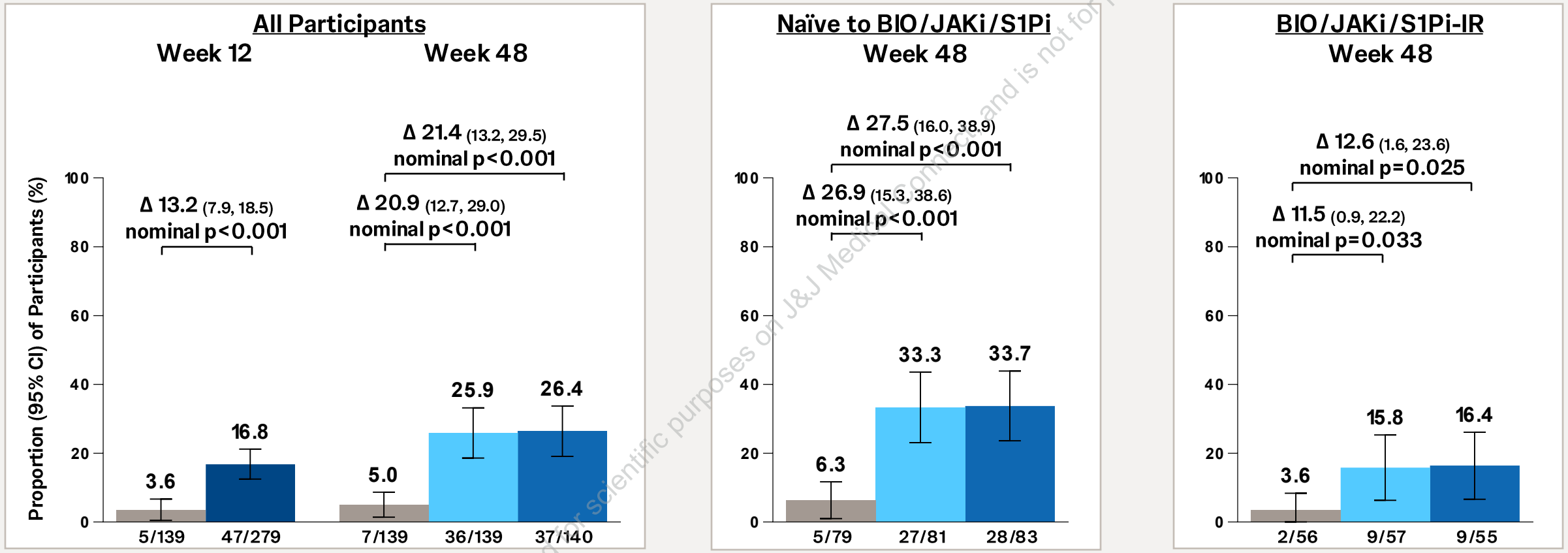
Endoscopic Remission



Endoscopic remission: A Mayo endoscopic subscore of 0

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all Week 48 assessments).
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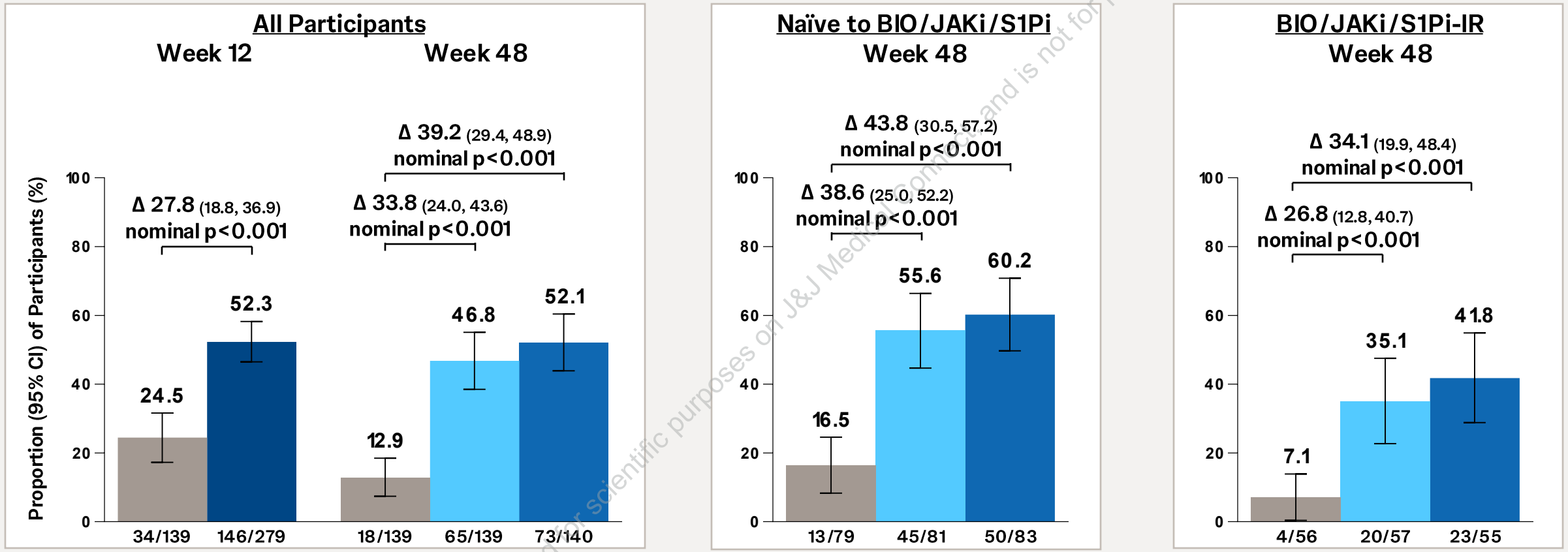
Histologic Improvement



Histologic improvement: Neutrophil infiltration in < 5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all Week 48 assessments).
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 adverse event (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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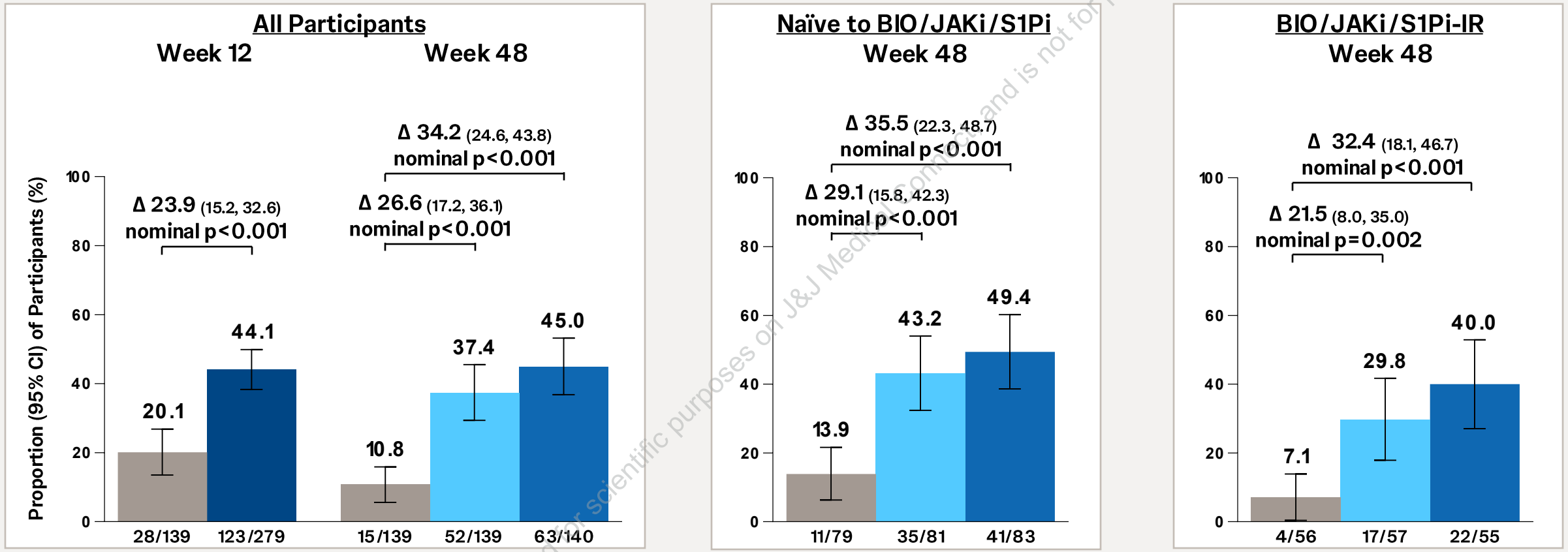
Histologic Remission



Histologic remission: Absence of neutrophils from mucosa (both lamina propria and epithelium), no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all Week 48 assessments).
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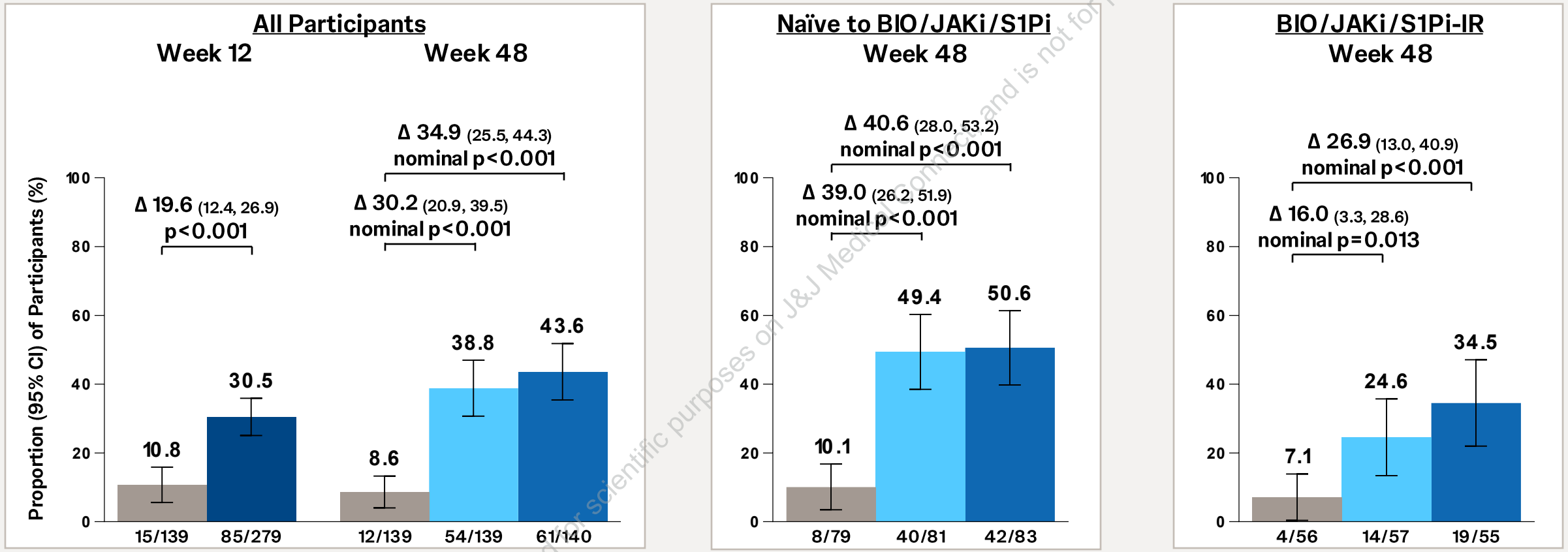
Histologic-Endoscopic Mucosal Improvement



Histologic-endoscopic mucosal improvement: Achieving a combination of histologic improvement and endoscopic improvement

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all Week 48 assessments).
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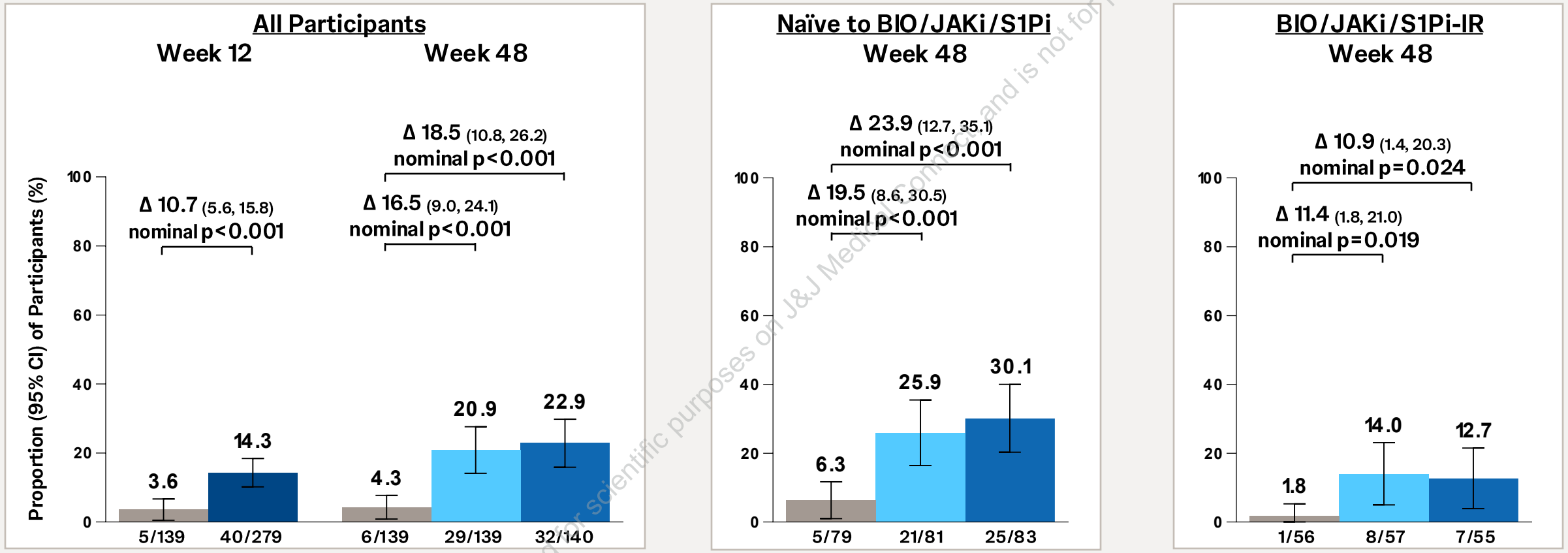
Histologic-Endoscopic Mucosal Remission



Histologic-endoscopic mucosal remission: Achieving a combination of histologic remission and endoscopic remission (MES=0)

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Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo (p-values are nominal for all assessments of histologic-endoscopic mucosal remission).
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 adverse event (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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Summary of Adverse Events Through Week 48

	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	30.3	46.3	45.3
Deaths, n (%)	1 (0.7%)	1 (0.7%)	0
Events per 100 participant-years			
Adverse events (AEs)	357.1	308.3	310.7
Serious AEs	38.4	6.5	8.2
AEs leading to discontinuation of study agent	19.8	4.9	4.1
Infections[b]	81.8	77.9	69.9
Serious infections	3.7	0.8	2.5
Most common AEs (incidence >10% in either GUS group), n (%)			
Worsening of ulcerative colitis	42 (30.2%)	26 (18.7%)	14 (10.0%)
Upper respiratory tract infection	11 (7.9%)	16 (11.5%)	13 (9.3%)
Arthralgia	5 (3.6%)	14 (10.1%)	10 (7.1%)

1.7% of guselkumab injections (61/3690) were associated with injection-site reactions

a. Includes all placebo participants, excluding data after a participant is rescued with guselkumab.
b. Infections were defined as any adverse event coded to the Medical Dictionary for Regulatory Activities (MedDRA) system organ class "Infections and infestations".

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Adverse Events of Interest Through Week 48

	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
Participants with 1 or more AEs of interest, n (%)			
Opportunistic infections[b]	0	1 (0.7%)	1 (0.7%)
Active tuberculosis	0	0	0
Malignancies	1 (0.7%)	0	2 (1.4%)
Major adverse cardiovascular events (MACE)	1 (0.7%)	2 (1.4%)	0
Anaphylactic or serum sickness reactions	0	0	0
Venous thromboembolism (VTE)	0	0	0
Clinically important hepatic disorders	0	0	0

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a. Includes all placebo participants, excluding data after a participant is rescued with guselkumab.
b. Opportunistic Infections adverse events are defined as the narrow terms in the MedDRA SMQ of "Opportunistic infections".

Conclusions

- ASTRO results demonstrate the efficacy of a fully SC induction and maintenance regimen through Week 48 with guselkumab in UC
- Clinically meaningful benefit was observed both in participants naïve to or 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
- SC induction and maintenance with guselkumab was safe and effective in UC[1,2] and Crohn's disease,[3,4] providing simplicity for patients and flexibility for healthcare providers

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1. Rubin DT, et al. *Lancet*. 2025;405:33-49.
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- This work was supported by Johnson & Johnson

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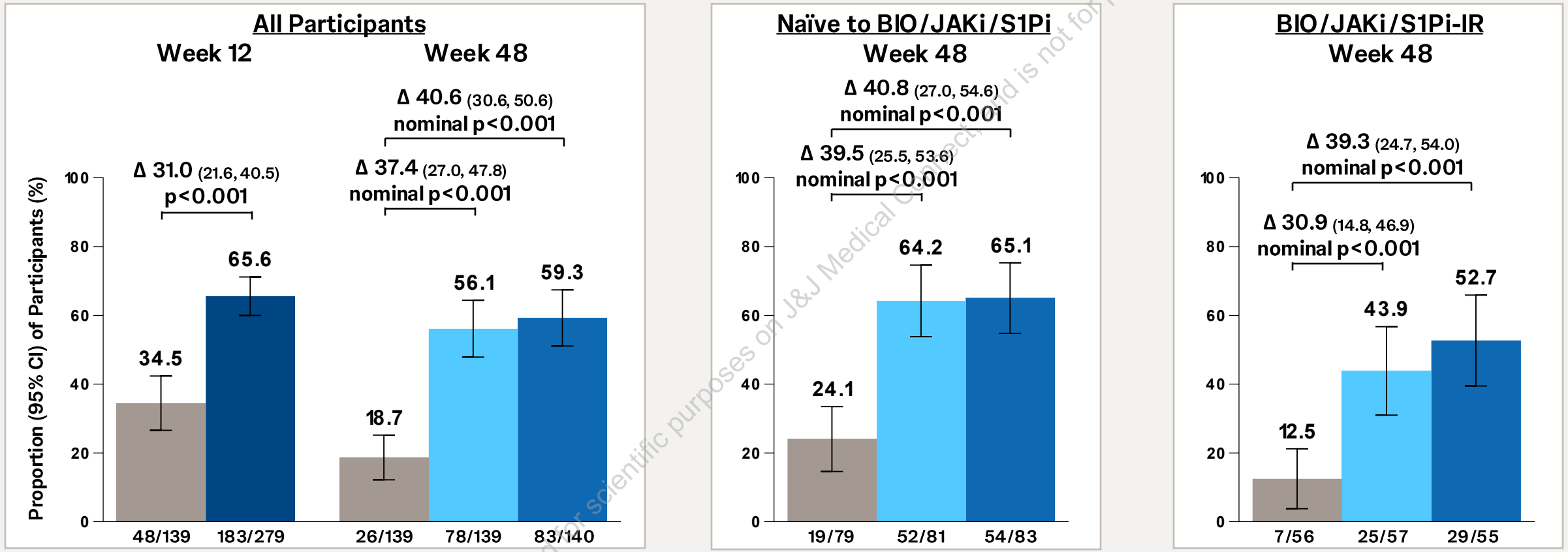
Clinical Response



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 (p-values are nominal for all Week 48 assessments).
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