OP10

Efficacy and safety of subcutaneous guselkumab induction therapy in patients with Ulcerative Colitis: Results through week 12 from the phase 3 ASTRO study

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Disclosure of Conflicts of Interest

I, Laurent Peyrin-Biroulet, herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

Grants or contracts from Celltrion, Fresenius Kabi, Medac, MSD, and Takeda; consulting and/or payment or honoraria and/or data safety monitoring board or advisory board participation for AbbVie, Abivax, Adacyte, Alfasigma, Alimentiv, Amgen, Applied Molecular Transport, Arena, Banook, Biogen, Bristol Myers Squibb, Celltrion, Connect Biopharm, Cytoki Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GlaxoSmithKline, IAG Image Analysis, Index Pharmaceuticals, Inotrem, Johnson & Johnson, Kern Pharma, Lilly, Medac, Mopac, Morphic, MSD, Nordic Pharma, Novartis, Oncodesign Precision Medicine, ONO Pharma, OSE Immunotherapeutics, Pandion Therapeutics, Par' Immune, Pfizer, Prometheus, Protagonist, Roche, Samsung, Sandoz, Sanofi, Satisfay, Takeda, Telavant, Theravance, Thermo Fischer, Tigenix, Tillots, Viatris, Vectivbio, Ventyx, and Ysopia; and meeting attendance/travel support from Abbvie, Alfasigma, Amgen, Celltrion, Connect Biopharm, Ferring, Galapagos, Genentech, Gilead, Gossamer Bio, Johnson & Johnson, Lilly, Medac, Morphic, MSD, Pfizer, Sandoz, Takeda, Thermo Fischer, and Tillots.

Background and Objective

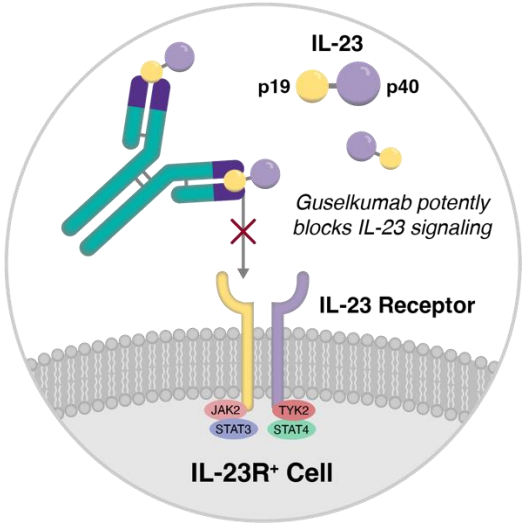
Guselkumab is a selective, dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23[1]

Intravenous (IV) induction followed by subcutaneous (SC) maintenance was efficacious and safe in participants with moderately to severely active ulcerative colitis (UC) in the QUASAR Phase 3 studies,[2]

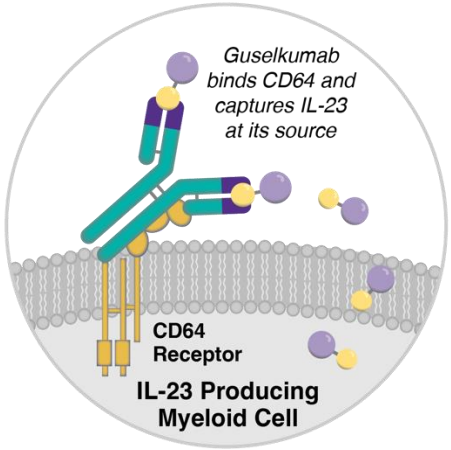
- Guselkumab is approved in some countries for UC, including the United States

SC induction provides patients and healthcare providers with greater flexibility and requires less time compared to IV

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



Dual-acting IL-23 Inhibitor

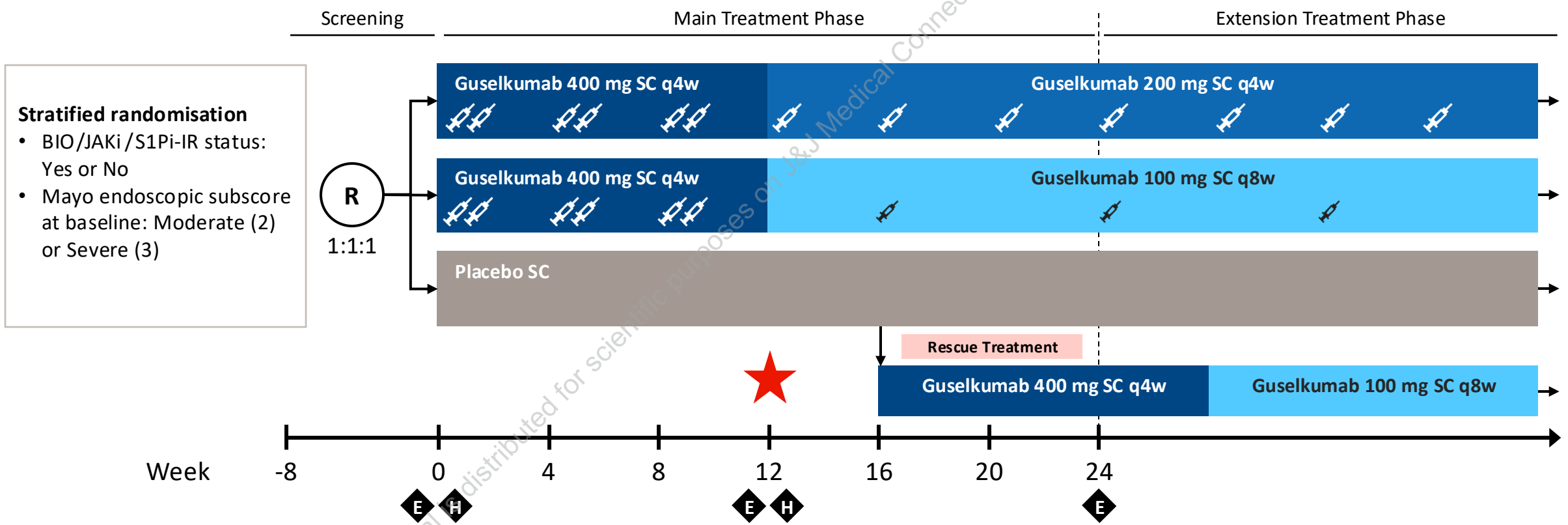


1. Atreya R, et al. Guselkumab binding to CD64⁺ IL-23–producing myeloid cells enhances potency for neutralizing IL-23 signaling. *J Crohns Colitis*. 2024;18(suppl):S470.
2. Rubin DT, et al. Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. *Lancet*. 2025;405(10472):33-49.

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

Key Eligibility Criteria:

- Baseline (week 0) modified Mayo score of 5 to 9, inclusive
- 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



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

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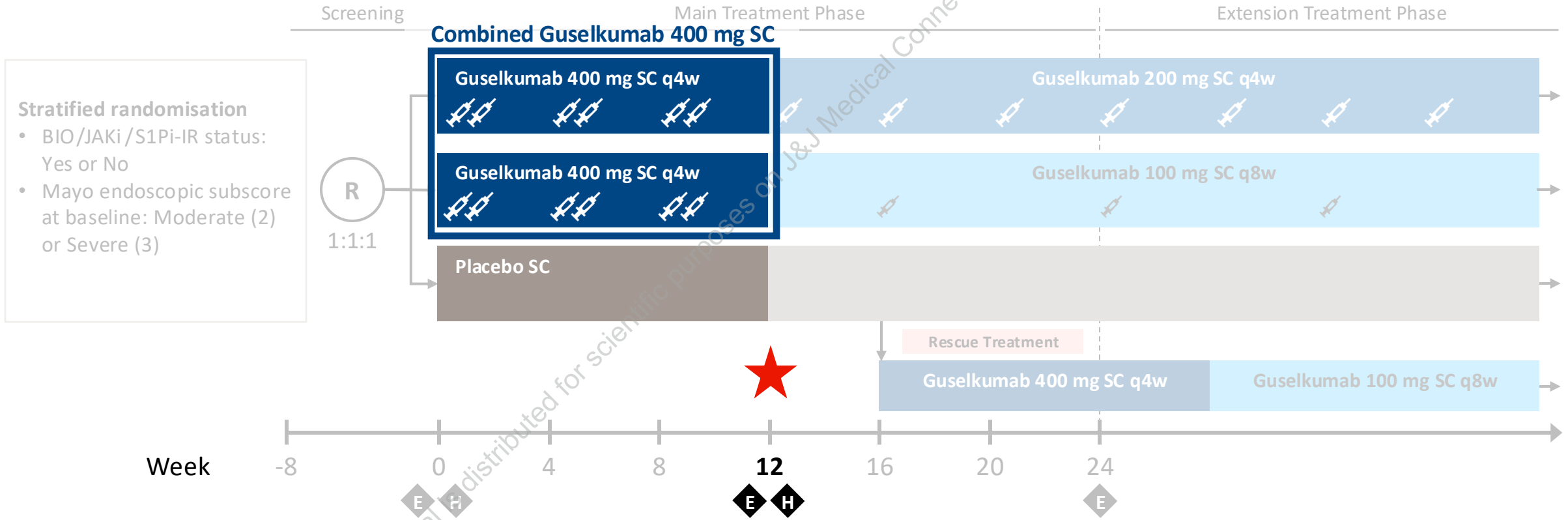


★ **Primary Endpoint (Clinical Remission)** | **Guselkumab 200 mg** | **Guselkumab 100 mg** | **E Endoscopy** | **H Histology**

Demographics and Baseline Disease Characteristics

	Placebo SC	Combined GUS 400 mg SC q4w
Full analysis set, N	139	279
Age in years, mean (SD)	39.5 (13.58)	42.9 (14.43)
Male, n (%)	90 (64.7%)	166 (59.5%)
UC disease duration in years, mean (SD)	6.61 (6.228)	8.04 (6.847)
Modified Mayo score[a] (0-9), mean (SD)	6.8 (1.09)	6.7 (1.18)
Modified Mayo score of 7-9 (severe), n (%)	87 (63.0%)	172 (61.6%)
Mayo endoscopic subscore of 3 (severe), n (%)	78 (56.1%)	156 (55.9%)
Extensive UC, n (%)	73 (52.5%)	151 (54.1%)
C-reactive protein,[b] median in mg/L (IQR)	3.8 (1.2; 10.9)	4.1 (1.5; 8.2)
C-reactive protein[b] >3 mg/L	77 (55.8%)	161 (58.3%)
Fecal calprotectin,[c] median in mg/kg (IQR)	1749.0 (617.0; 3202.0)	1494.5 (678.0; 2963.0)
Fecal calprotectin[c] >250 mg/kg	119 (90.8%)	226 (89.0%)

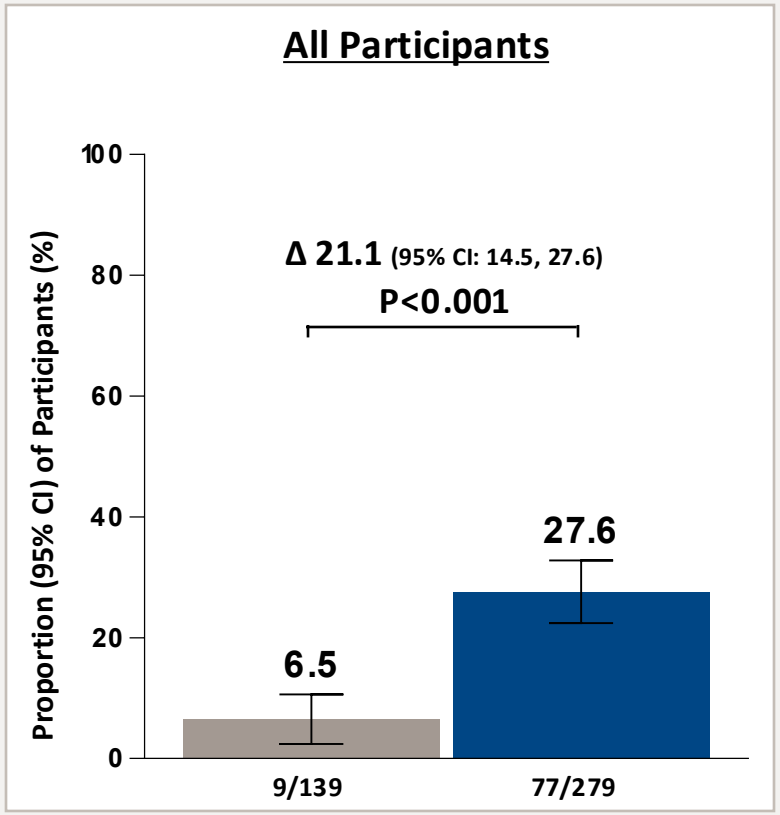
[a] Modified Mayo score: 3-component (stool frequency, rectal bleeding, and endoscopy subscores) Mayo score without the physician's global assessment.
[b] Based on N=138 for Placebo SC, N=276 for Combined GUS 400 mg SC q4w.
[c] Based on N=131 for Placebo SC, N=254 for Combined GUS 400 mg SC q4w.

UC-related Medication History and Baseline UC Medications

	Placebo SC	Combined GUS 400 mg SC q4w
Full analysis set, N	139	279
Naïve to BIO/JAKi/S1Pi, n (%)	79 (56.8%)	164 (58.8%)
BIO/JAKi/S1Pi-IR, n (%)	56 (40.3%)	112 (40.1%)
One class[a]	39 (69.6%)	78 (69.6%)
Two classes[a]	13 (23.2%)	21 (18.8%)
Three or more classes[a]	4 (7.1%)	13 (11.6%)
At least one anti-TNF[a] (regardless of other BIO/JAKi/S1Pi)	39 (69.6%)	88 (78.6%)
Vedolizumab[a] (regardless of other BIO/JAKi/S1Pi)	25 (44.6%)	49 (43.8%)
JAK inhibitors[a] (regardless of other BIO/S1Pi)	11 (19.6%)	19 (17.0%)
Ozanimod[a] (regardless of other BIO/JAKi)	2 (3.6%)	3 (2.7%)
History of IR or dependence to corticosteroids, n (%)	104 (74.8%)	208 (74.6%)
History of IR to 6-MP or AZA, n (%)	56 (40.3%)	108 (38.7%)
Baseline oral corticosteroid use, n (%)	46 (33.1%)	91 (32.6%)
Baseline use of 6-MP, AZA, or MTX, n (%)	28 (20.1%)	56 (20.1%)

[a] Denominator is patients who were BIO/JAKi/S1Pi-IR.

Primary Endpoint: Clinical Remission at Week 12



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

Data presented as n (%); Δ (adjusted treatment difference) vs placebo. Subpopulation analyses were not multiplicity controlled. Patients who, prior to Week 12, had an ostomy or colesctomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC were considered not to meet the endpoint criteria at Week 12. Patients who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Patients who discontinued study agent for other reasons prior to Week 12 were considered not to meet the endpoint criteria at Week 12. After accounting for these scenarios, patients who were missing data necessary for calculation of the outcome measure at Week 12 were considered not to have achieved that endpoint at Week 12.

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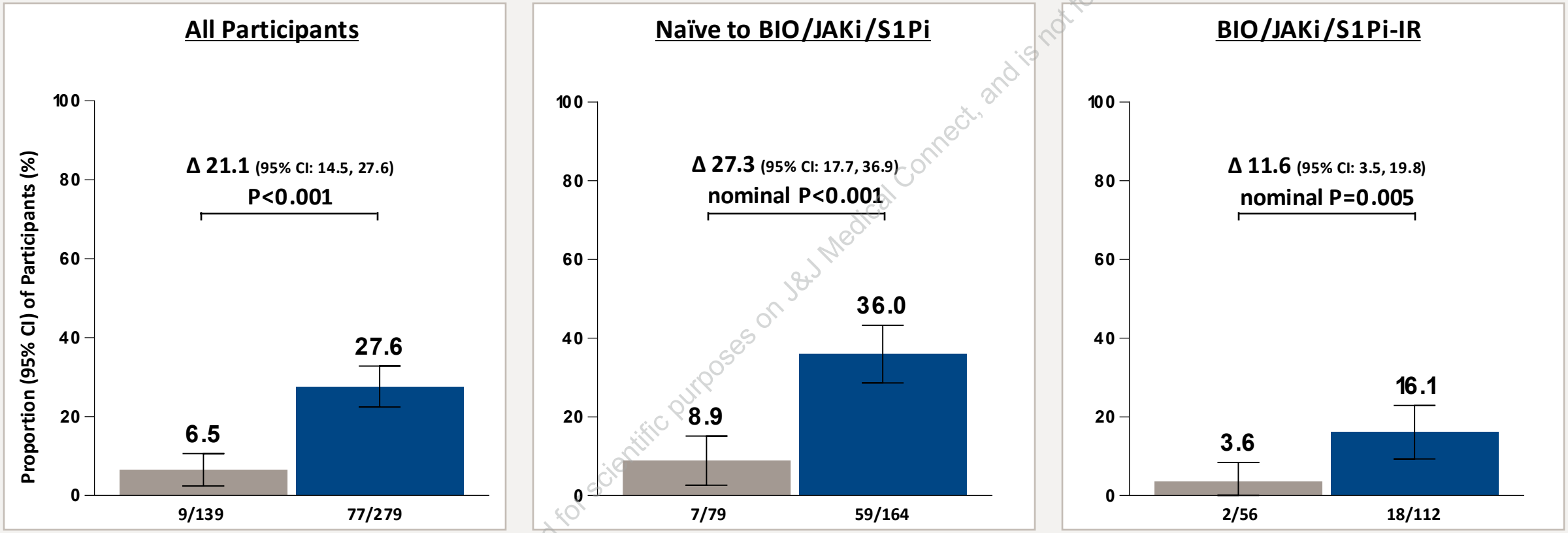

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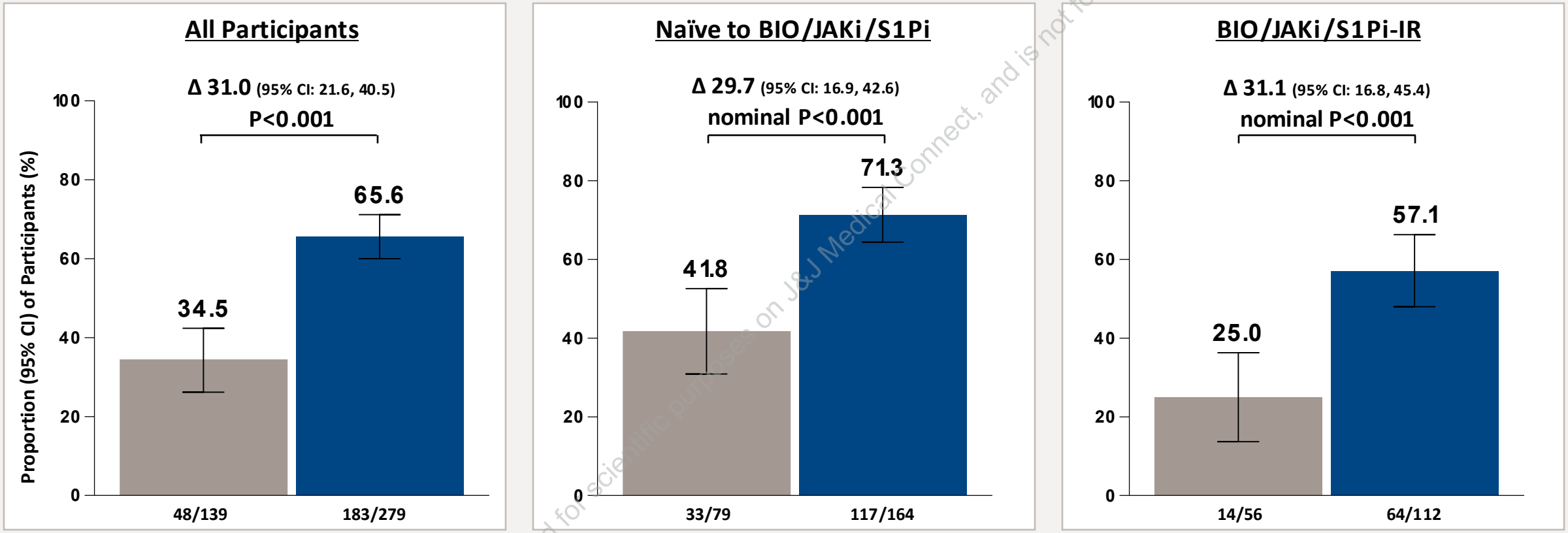
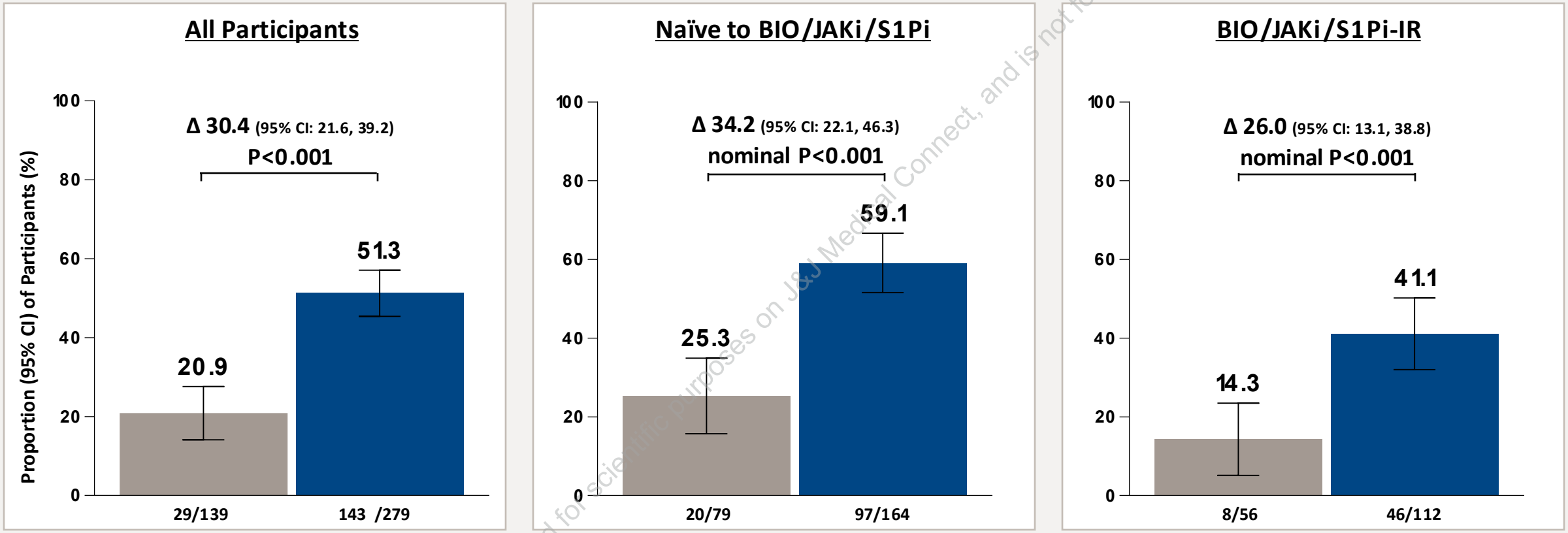
Clinical Response at Week 12



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

Data presented as n (%); Δ (adjusted treatment difference) vs placebo. Subpopulation analyses were not multiplicity controlled. Patients who, prior to Week 12, had an ostomy or colesctomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC were considered not to meet the endpoint criteria at Week 12. Patients who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Patients who discontinued study agent for other reasons prior to Week 12 were considered not to meet the endpoint criteria at Week 12. After accounting for these scenarios, patients who were missing data necessary for calculation of the outcome measure at Week 12 were considered not to have achieved that endpoint at Week 12.

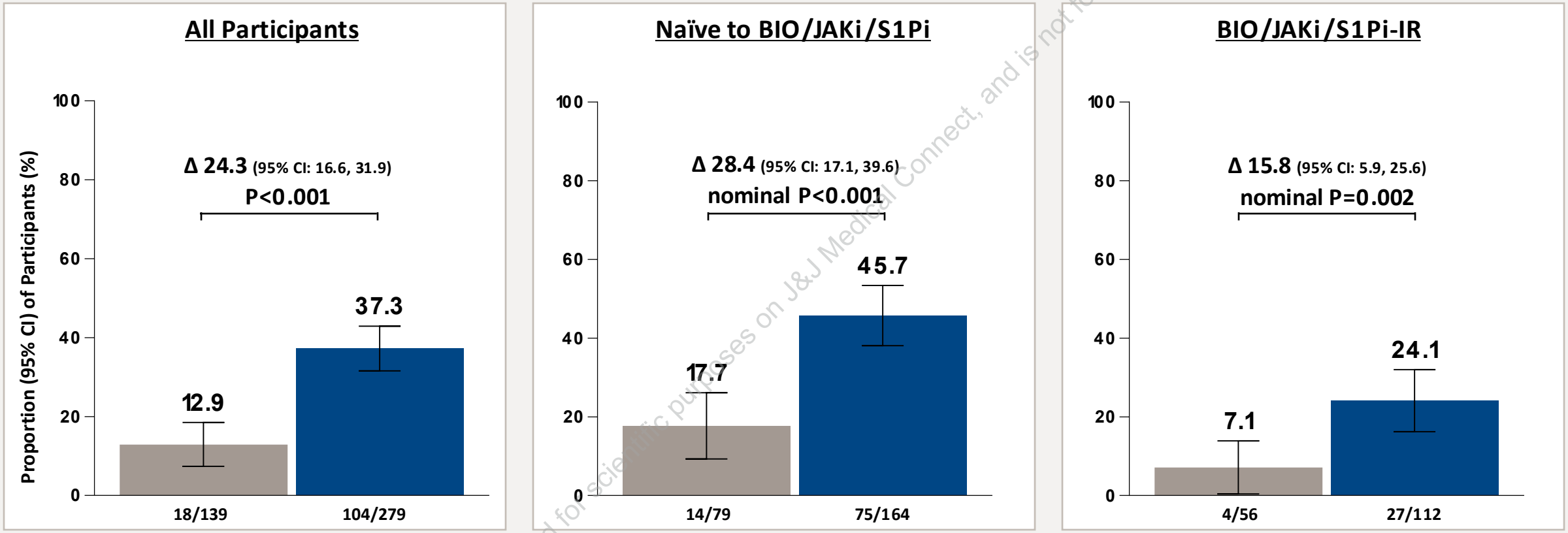
Symptomatic Remission at Week 12



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

Data presented as n (%); Δ (adjusted treatment difference) vs placebo. Subpopulation analyses were not multiplicity controlled. Patients who, prior to Week 12, had an ostomy or colesctomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC were considered not to meet the endpoint criteria at Week 12. Patients who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Patients who discontinued study agent for other reasons prior to Week 12 were considered not to meet the endpoint criteria at Week 12. After accounting for these scenarios, patients who were missing data necessary for calculation of the outcome measure at Week 12 were considered not to have achieved that endpoint at Week 12.

Endoscopic Improvement at Week 12



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

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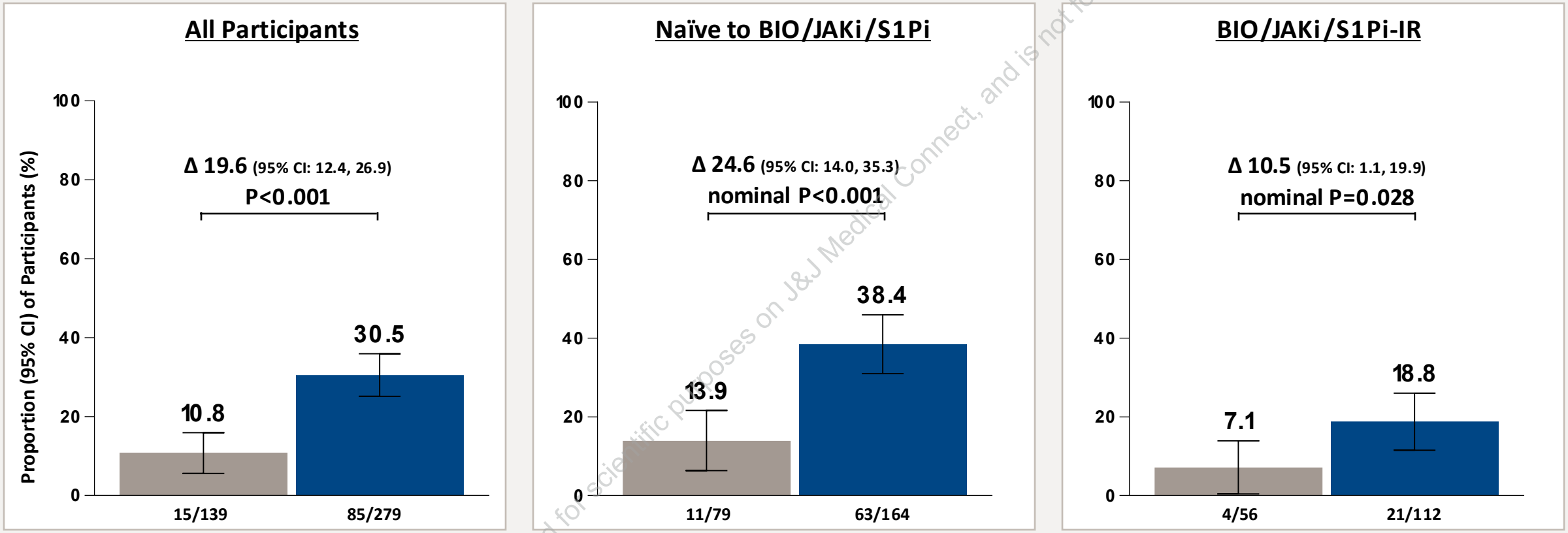
Histo-endoscopic Mucosal Improvement at Week 12



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 per Geboes grading system) and endoscopic improvement

Data presented as n (%); Δ (adjusted treatment difference) vs placebo. Subpopulation analyses were not multiplicity controlled. Patients who, prior to Week 12, had an ostomy or colesctomy, a prohibited change in concomitant UC medications, discontinued study agent due to lack of efficacy or an AE of worsening UC were considered not to meet the endpoint criteria at Week 12. Patients who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. Patients who discontinued study agent for other reasons prior to Week 12 were considered not to meet the endpoint criteria at Week 12. After accounting for these scenarios, patients who were missing data necessary for calculation of the outcome measure at Week 12, including an unevaluable biopsy, were considered not to have achieved those endpoints at Week 12.

Summary of Adverse Events Through Week 12

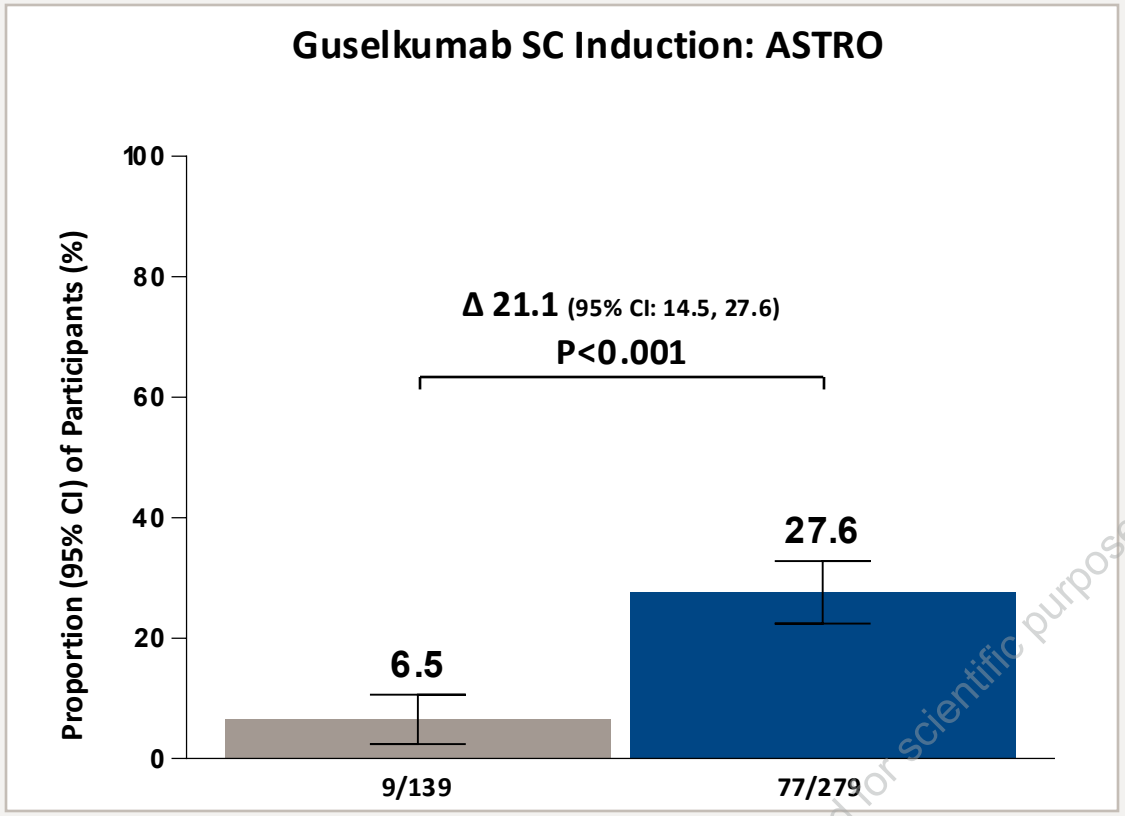
	Placebo SC	Combined GUS 400 mg SC q4w
Safety analysis set, N	139	279
Average duration of follow-up, weeks	12.2	12.3
Average exposure, number of administrations	3.0	3.0
Deaths, n (%)	1 (0.7%)	0
Patients with 1 or more:		
AEs, n (%)	73 (52.5%)	110 (39.4%)
AEs by severity, n (%)		
Mild	42 (30.2%)	62 (22.2%)
Moderate	24 (17.3%)	43 (15.4%)
Severe	7 (5.0%)	5 (1.8%)
Serious AEs, n (%)	11 (7.9%)	7 (2.5%)
AEs leading to discontinuation of study agent, n (%)	8 (5.8%)	3 (1.1%)
Infections,[a] n (%)	28 (20.1%)	42 (15.1%)
Serious infections[a]	0	2 (0.7%)

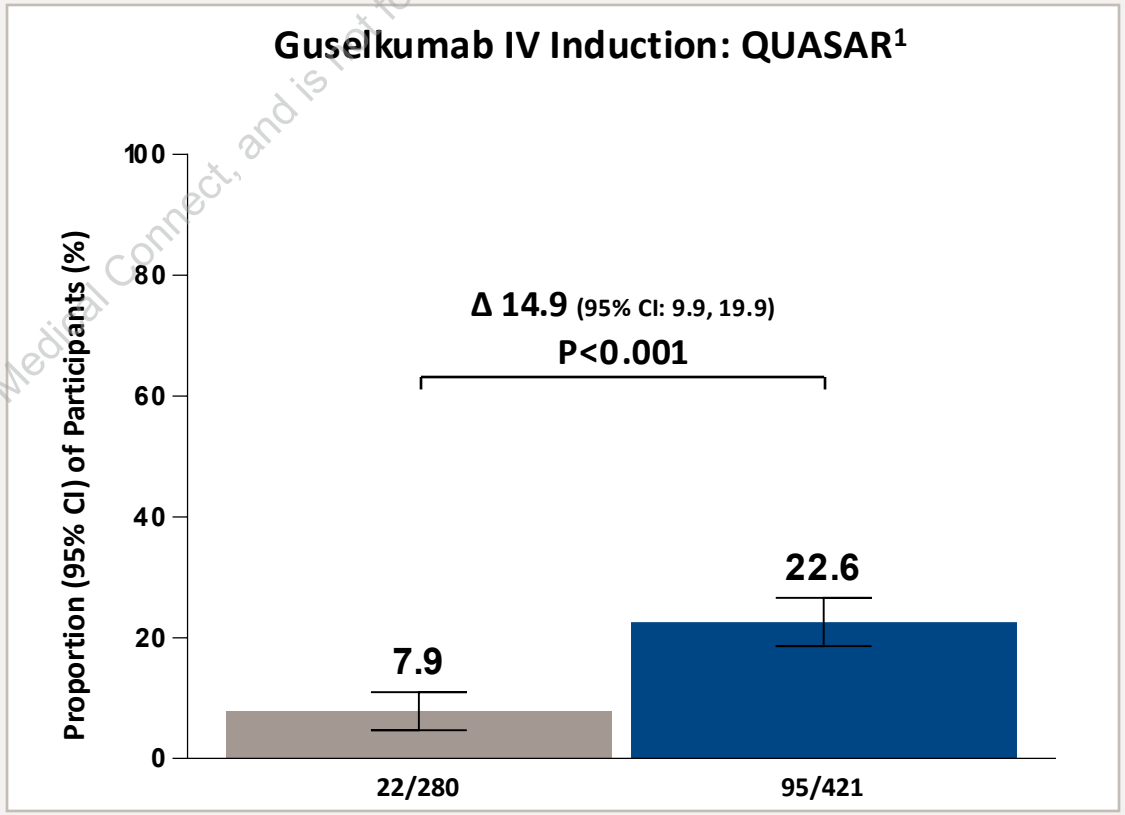
- Two serious infections reported in the combined guselkumab group were **pilonidal disease** and **gastroenteritis**
  - Both were moderate in intensity, did not interrupt study drug administration, and resolved

Most common AEs among combined GUS 400 SC group:	**Worsening of Ulcerative Colitis**	**Arthralgia**	**Headache**
	4.7% Combined GUS 12.2% PBO	3.9% Combined GUS 0.7% PBO	3.6% Combined GUS 1.4% PBO

[a] Infections were defined as any adverse event coded to the MedDRA system organ class 'Infections and infestations'.

Clinical Remission at Week 12: SC or IV Guselkumab Induction





Placebo Induction

GUS Induction (400 mg SC or 200 mg IV)

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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.

Conclusions

- Week 12 results from ASTRO establish the efficacy of SC induction therapy with guselkumab in ulcerative colitis
- Clinically meaningful benefit was also observed in patients naïve to BIO/JAKi/S1Pi and in those with BIO/JAKi/S1Pi-IR
- The safety of SC induction therapy was consistent with the well-characterized and favourable safety profile of guselkumab in approved indications
- These results complement the QUASAR[1] data, demonstrating that both IV and SC induction with guselkumab are efficacious therapeutic options, thus providing patients and healthcare providers the flexibility to choose the induction route of administration that aligns with their preferences

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.

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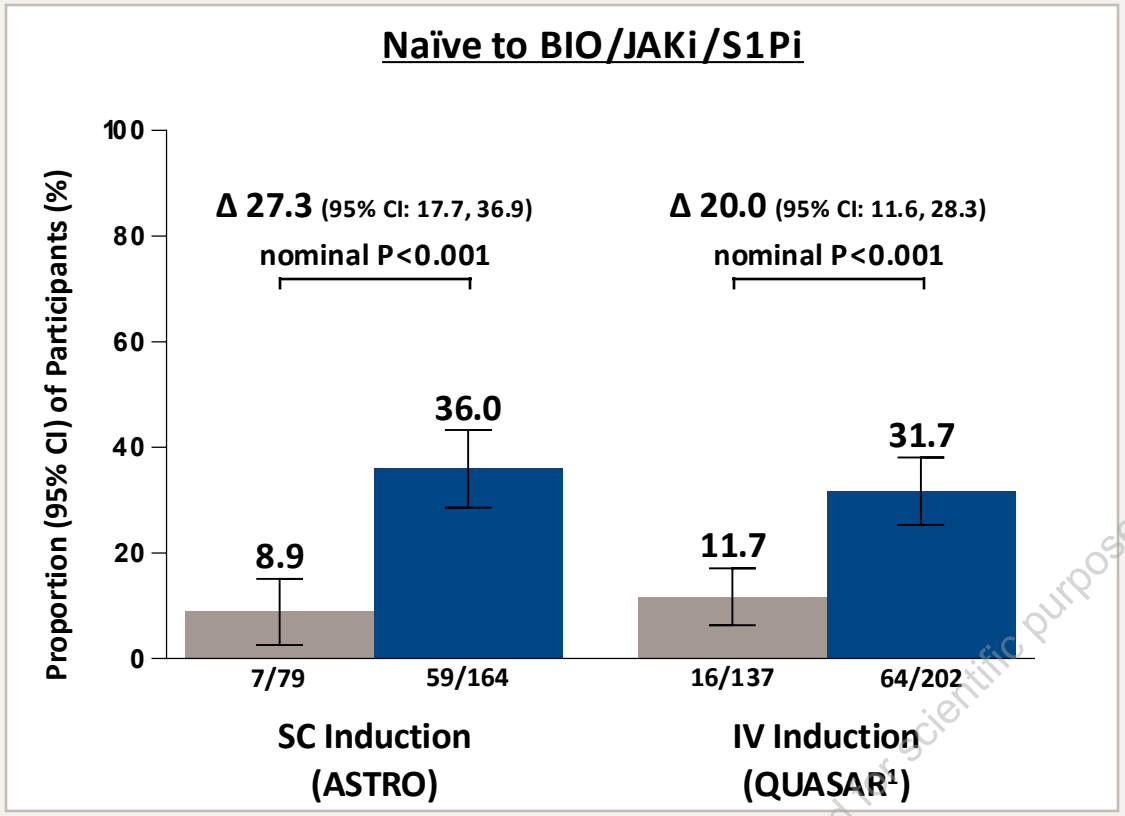
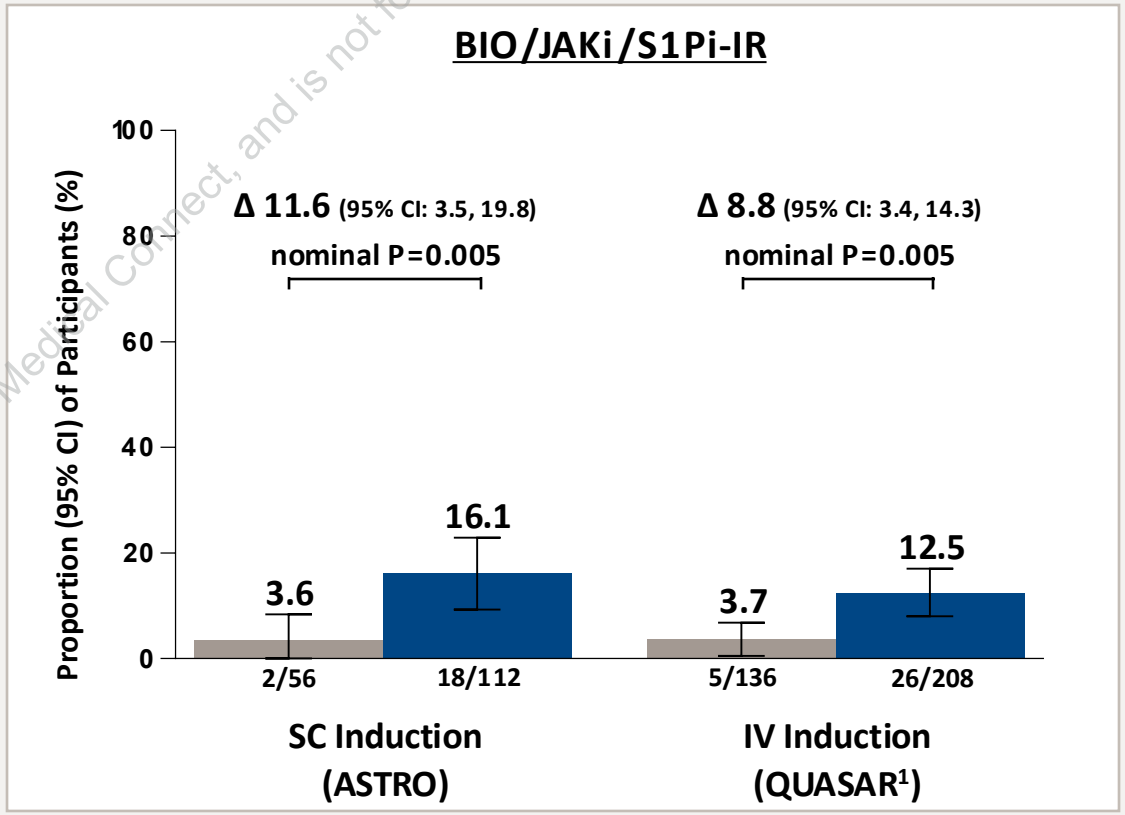
BACKUP SLIDE

Clinical Remission at Week 12: SC or IV Guselkumab Induction





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