OP73

Week 48 Efficacy of Guselkumab and Ustekinumab in Crohn's Disease Based On Prior Response/Exposure to Biologic Therapy: Results from the GALAXI 2 & 3 Phase 3 Studies

Silvio Danese,[1] Anita Afzali,[2] Remo Panaccione,[3] Julián Panés,[4] Walter Reinisch,[5] Natalie A. Terry,[6] Leonardo Salese,[6] Rian Van Rampelbergh,[7] Kitty Yuen Yi Wan,[8] Zijiang Yang,[6] Jewel Johanns,[6] Marcin Zmudziński,[9] Eran Zittan,[10] Katsuyoshi Matsuoka,[11] Vipul Jairath,[12] David T. Rubin[13]

[1]Gastroenterology and Endoscopy, IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Milan, Italy; [2]Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, OH, USA; [3]Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada; [4]Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; [5]Division of Gastroenterology & Hepatology, Medical University of Vienna, Vienna, Austria; [6]Janssen Research & Development, LLC, Spring House, PA, USA; [7]Janssen Research & Development, Antwerp, Belgium; [8]Janssen Research & Development, Basel, Switzerland; [9]Gastromed, Gastrology and Endoscopy Center, Toruń, Poland; [10]The Abraham and Sonia Rochlin IBD Unit, Department of Gastroenterology and Liver Diseases, Emek Medical Center, Afula, Israel; [11]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Sakura Medical Center, Chiba, Japan; [12]Schulich School of Medicine & Dentistry, Western University, London, ON, Canada; [13]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA

Sponsored by Janssen Research & Development, LLC, a Johnson & Johnson Company

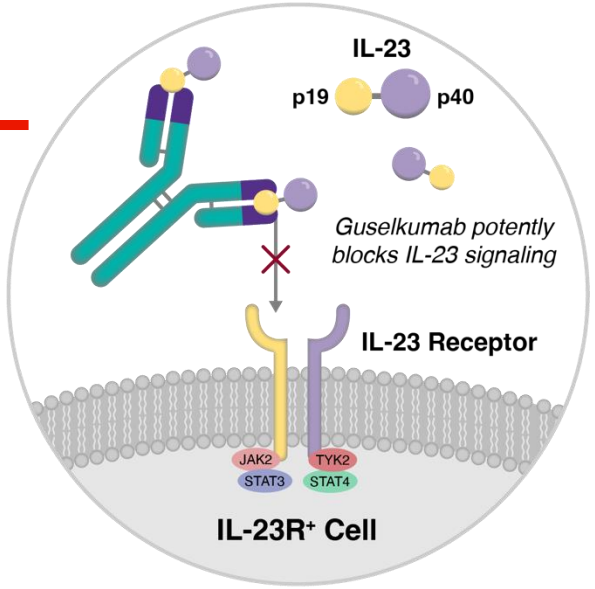
Background and Objective

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

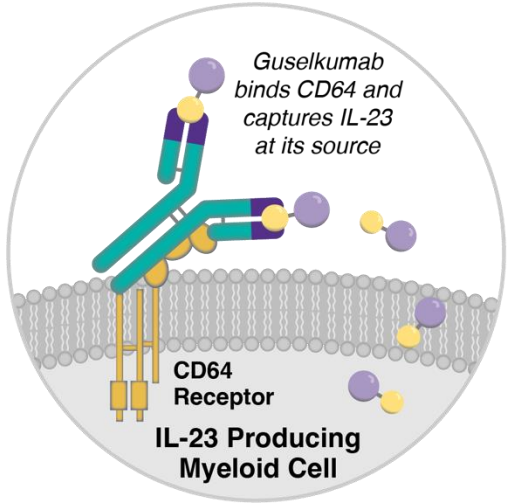
GALAXI 2 & 3 are identically-designed, 48-week, randomized, double-blind, placebo-controlled and active-comparator (head-to-head) registrational trials assessing the efficacy and safety of guselkumab in participants with moderately to severely active Crohn's disease[2]

- Co-primary efficacy endpoints were met in both studies for both guselkumab dose regimens versus placebo
- Both guselkumab regimens also demonstrated superiority to ustekinumab across all endoscopic-based endpoints (including endoscopic remission and deep remission) at Week 48
  in prespecified, multiplicity-controlled analyses based on pooled data from GALAXI 2 & 3

Here we compare efficacy outcomes with guselkumab versus ustekinumab in the BIO-naïve and BIO-IR (inadequate response/intolerance) subpopulations using the pooled GALAXI 2 & 3 dataset



Dual-acting IL-23 Inhibitor



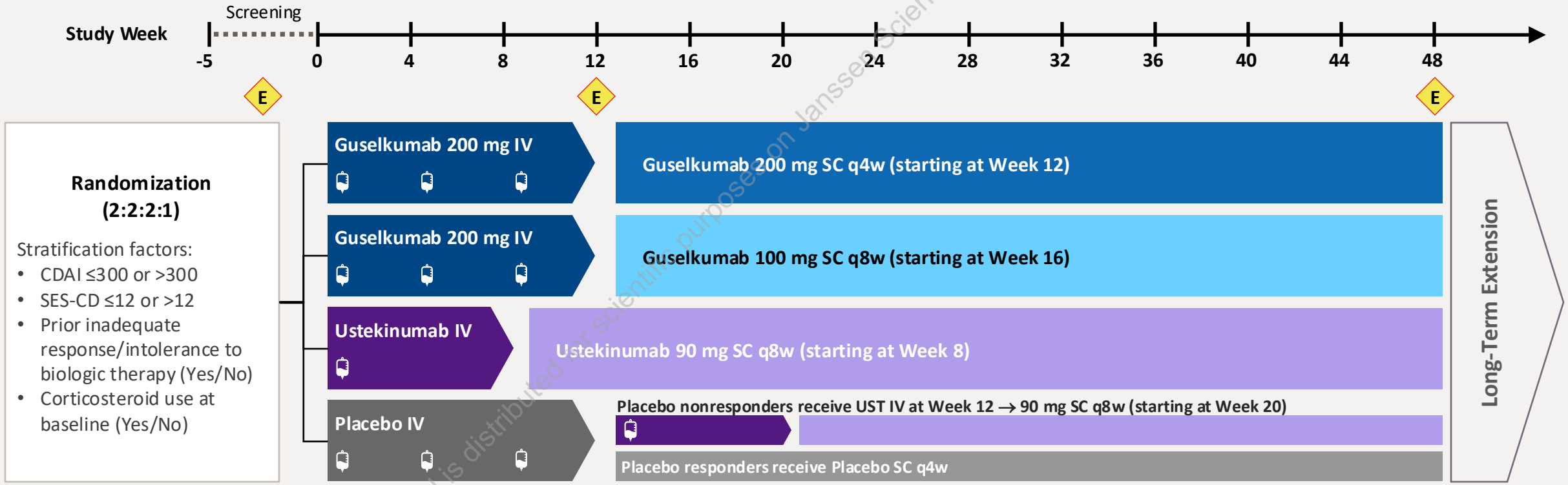
1. Atreya R, et al. Guselkumab binding to CD64+ IL-23–producing myeloid cells enhances potency for neutralizing IL-23 signaling. *J Crohns Colitis*. 2024;18(suppl):S470.
2. Panaccione R, et al. Efficacy and safety of guselkumab therapy in patients with moderately to severely active Crohn's disease: results of the GALAXI 2 & 3 Phase 3 studies. *Gastroenterology*. 2024;166(5 suppl):1057b.

ACG 2024
October 25-30, Philadelphia, PA

Identically-Designed, Head-to-head, Double-Blind Studies: GALAXI 2 & 3

Primary analysis set
- GALAXI 2: N=508
- GALAXI 3: N=513

Key eligibility criteria
- Moderately to severely active CD: CDAI score 220–450 and mean daily SF count >3 or AP score >1 and SES-CD score ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/intolerance to oral corticosteroids or 6-MP/AZA/MTX, or biologic therapies (TNF antagonists and vedolizumab)[a]



a. Biologic therapies: TNF antagonists or vedolizumab; participants with inadequate response/intolerance to ustekinumab were excluded.
E = Endoscopy
Note: To maintain treatment masking, all participants received active and/or placebo IV q4w through Week 12 and active and/or placebo SC q4w through Week 48.

Endpoints and Statistical Considerations

Comparisons of guselkumab and ustekinumab at Week 48 using the pooled GALAXI 2 & 3 dataset were prespecified and multiplicity-controlled for the following major secondary endpoints

- Endoscopic response
- Endoscopic remission
- Clinical remission **AND** endoscopic response
- Deep remission (clinical remission **AND** endoscopic remission)
- Clinical remission

Analyses in participants without prior exposure to biologic therapy (BIO-naïve) and with history of inadequate response or intolerance to biologic therapy (BIO-IR) were prespecified but not multiplicity controlled

Adjusted treatment differences (Δ) were based on the common risk difference by use of Mantel-Haenszel stratum weights (based on the stratification variables) and the Sato variance estimator

Participants with treatment failure or missing data were considered to not have met the endpoint

Baseline CD Medication History

Pooled GALAXI 2 & 3

	Guselkumab		
	200 mg IV q4w → 100 mg SC q8w	200 mg IV q4w → 200 mg SC q4w	Ustekinumab IV → SC
Primary analysis set[a], N	286	296	291
No history of inadequate response/intolerance[b] to biologic therapy, n (%)	133 (46.5%)	149 (50.3%)	135 (46.4%)
Biologic naïve (BIO-naïve)	116 (40.6%)	128 (43.2%)	121 (41.6%)
Biologic experienced, but no documented nonresponse/intolerance	17 (5.9%)	21 (7.1%)	14 (4.8%)
History of inadequate response/intolerance[b] to biologic therapy (BIO-IR), n (%)	153 (53.5%)	147 (49.7%)	156 (53.6%)
At least one anti-TNF	149 (97.4%)	143 (97.3%)	147 (94.2%)
Two or more anti-TNFs	31 (20.3%)	31 (21.1%)	46 (29.5%)
Vedolizumab	25 (16.3%)	18 (12.2%)	31 (19.9%)

a. All randomized participants who received at least 1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for participants with isolated ileal disease).
b. Primary nonresponse, secondary nonresponse, or intolerance.
Note: Participants with history of inadequate response or intolerance to ustekinumab were excluded from GALAXI 2 & 3.

Baseline Characteristics: BIO-naïve and BIO-IR Subpopulations

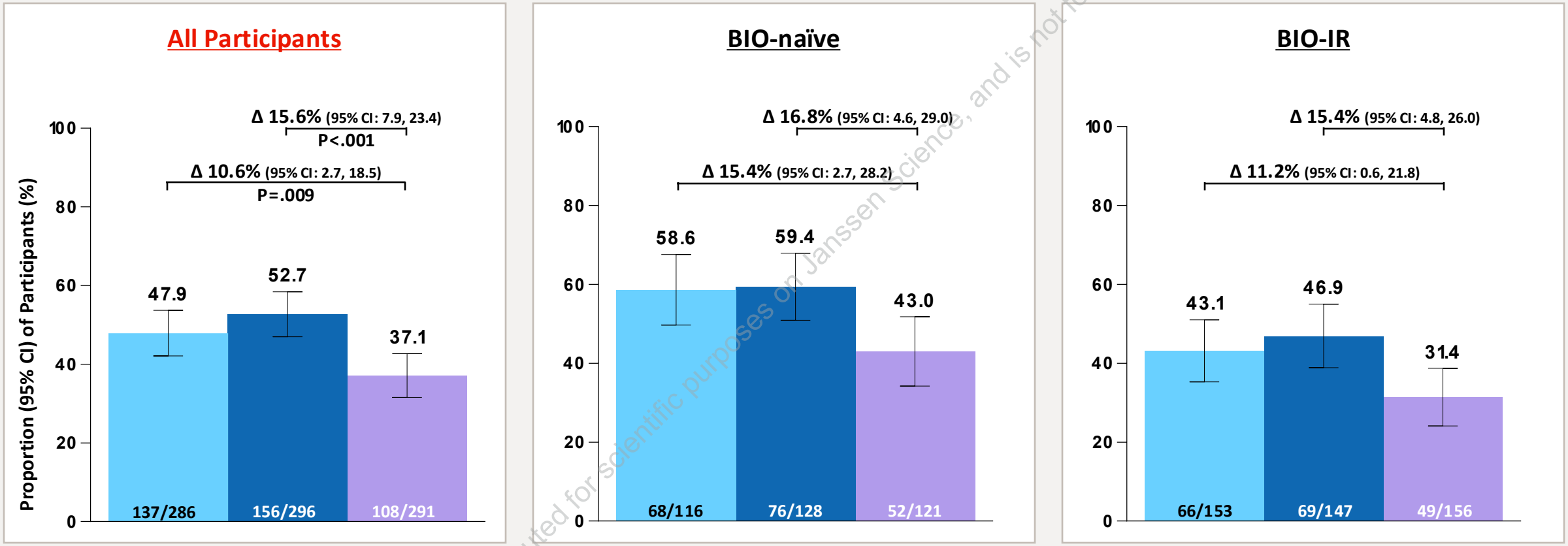
Pooled GALAXI 2 & 3

	BIO-naïve N = 426[a]	BIO-IR N = 534[a]
Age (years), mean (SD)	36.3 (13.16)	36.9 (12.79)
Female sex	44.6%	41.8%
Crohn's disease duration (years), mean (SD)	5.04 (6.058)	8.54 (7.585)
CDAI score, mean (SD)	292.9 (51.73)	294.9 (52.95)
SES-CD score, mean (SD)	11.9 (6.72)	13.7 (7.54)
Endoscopic disease severity (SES-CD score), n (%)		
Moderate (7–16)	231 (54.2%)	284 (53.2%)
Severe (>16)	98 (23.0%)	162 (30.3%)
Involved GI areas by central reader, n (%)		
Ileum only	108 (25.4%)	104 (19.5%)
Colon only	169 (39.7%)	213 (39.9%)
Ileum and Colon	149 (35.0%)	217 (40.6%)
CRP (mg/L), median (IQR)	4.8 (1.7; 13.0)	8.4 (3.1; 24.7)
>3 mg/L	272 (63.8%)	402 (75.3%)
Fecal calprotectin (µg/g), median (IQR)	728.0 (244.0; 1612.0)	1225.0 (445.0; 2494.0)
>250 µg/g	314 (74.6%)	445 (84.6%)
Concomitant CD medications at baseline		
6-MP/AZA	127 (29.8%)	136 (25.5%)
MTX	1 (0.2%)	15 (2.8%)
Oral corticosteroids	192 (45.1%)	158 (29.6%)

a. Includes all participants (including those assigned to placebo) in the BIO-naïve or BIO-IR subpopulation of the primary analysis set (all randomized participants who received at least 1 partial or complete dose of study intervention and had a screening SES-CD score ≥6 [or ≥4 for participants with isolated ileal disease]).

Endoscopic Response at Week 48

Pooled GALAXI 2 & 3



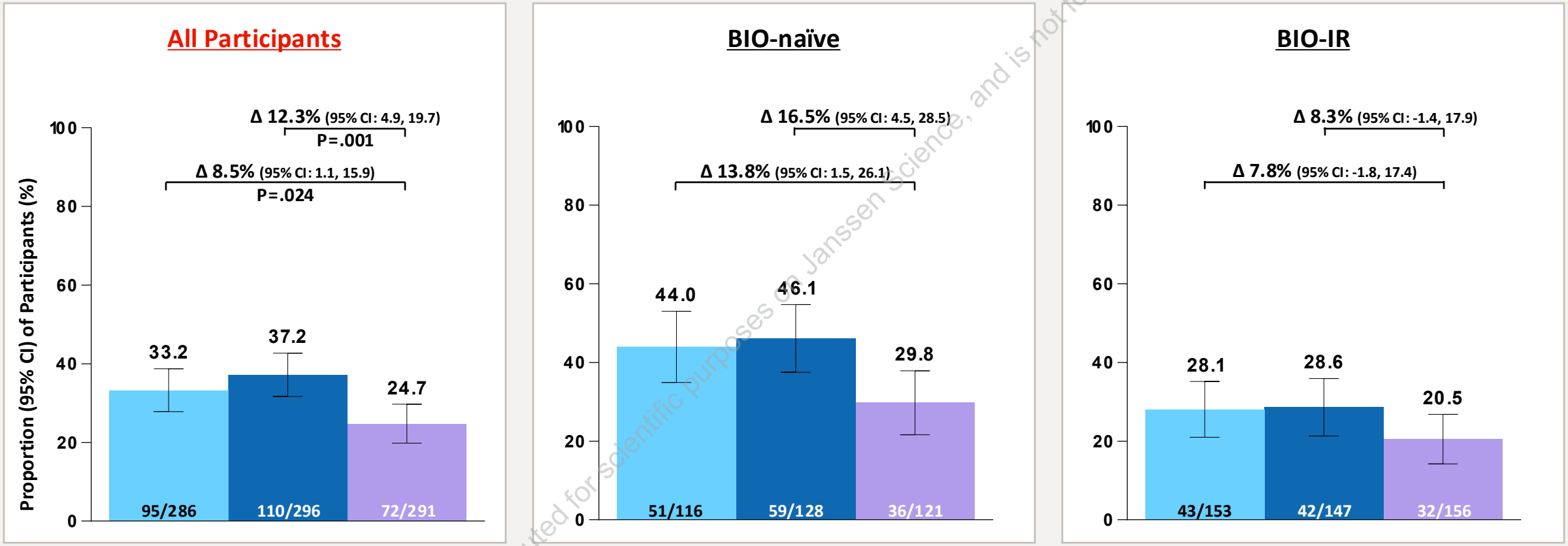
Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2

Data presented as n (%); Δ% (adjusted treatment difference) vs ustekinumab. Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Participants who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. After accounting for these scenarios, participants with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

ACG 2024
October 25-30, Philadelphia, PA

Endoscopic Remission at Week 48

Pooled GALAXI 2 & 3



Guselkumab 200 mg IV q4w → 100 mg SC q8w

Guselkumab 200 mg IV q4w → 200 mg SC q4w

Ustekinumab ~6 mg/kg IV → 90 mg SC q8w

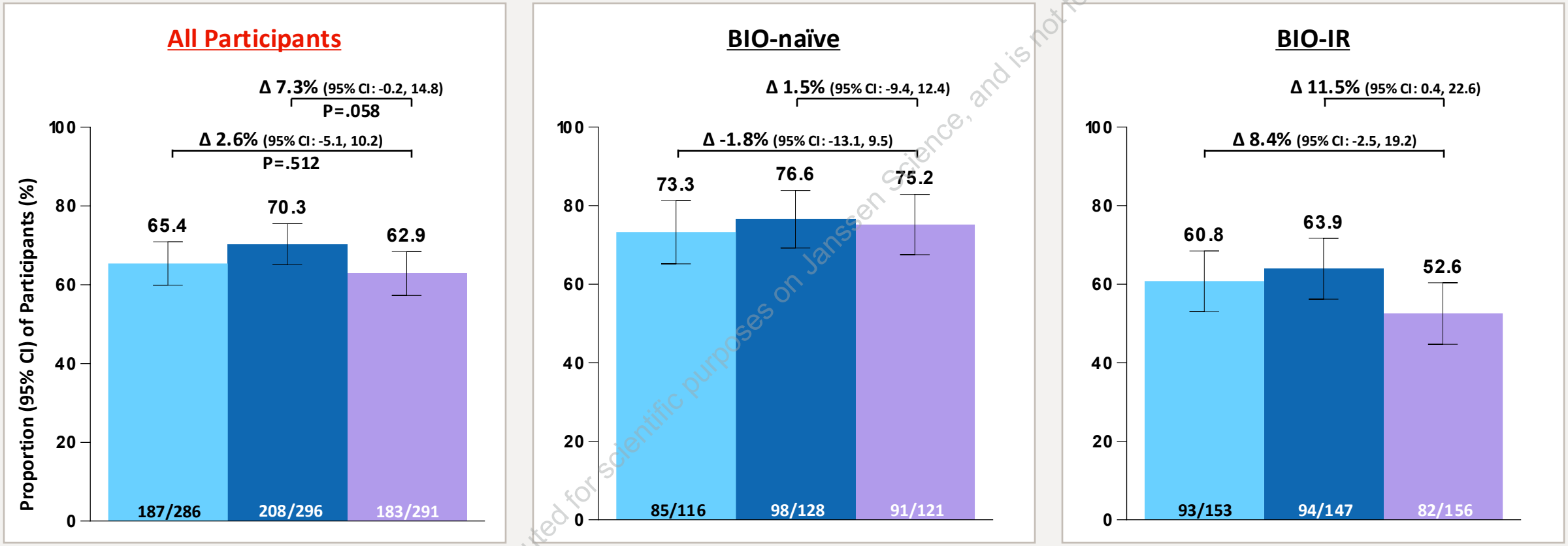
Endoscopic remission: SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component

Data presented as n (%); Δ% (adjusted treatment difference) vs ustekinumab. Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Participants who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. After accounting for these scenarios, participants with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

ACG 2024
October 25-30, Philadelphia, PA

Clinical Remission at Week 48

Pooled GALAXI 2 & 3



Guselkumab 200 mg IV q4w → 100 mg SC q8w

Guselkumab 200 mg IV q4w → 200 mg SC q4w

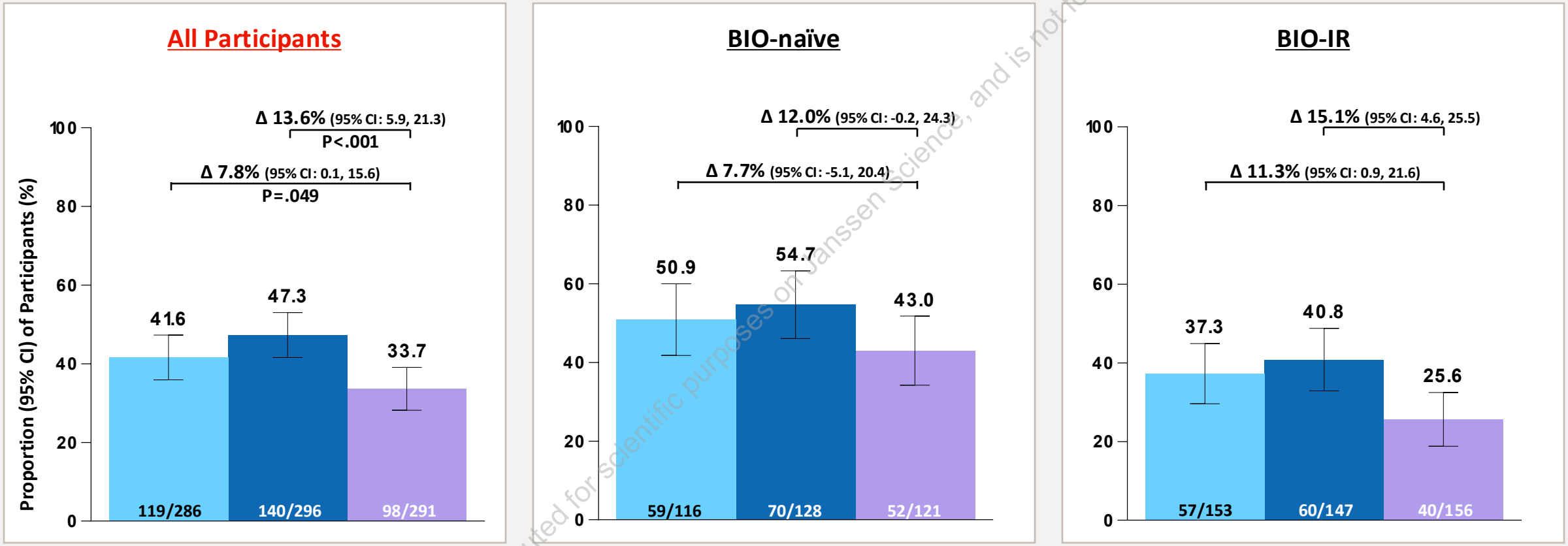
Ustekinumab ~6 mg/kg IV → 90 mg SC q8w

Clinical remission: CDAI < 150

Data presented as n (%); Δ% (adjusted treatment difference) vs ustekinumab. Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Participants who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. After accounting for these scenarios, participants with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

Clinical Remission at Week 48 AND Endoscopic Response at Week 48

Pooled GALAXI 2 & 3



Guselkumab 200 mg IV q4w → 100 mg SC q8w

Guselkumab 200 mg IV q4w → 200 mg SC q4w

Ustekinumab ~6 mg/kg IV → 90 mg SC q8w

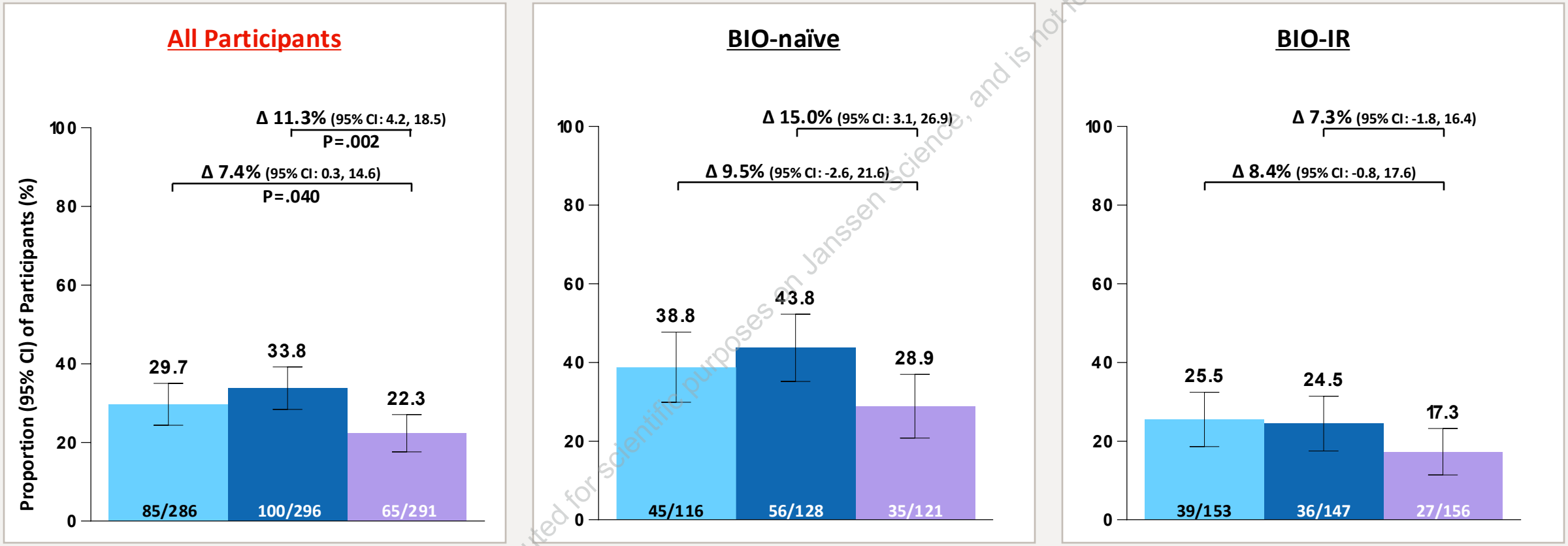
Clinical remission: CDAI < 150

Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2

Data presented as n (%); Δ% (adjusted treatment difference) vs ustekinumab. Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Participants who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. After accounting for these scenarios, participants with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

Deep Remission (Clinical Remission AND Endoscopic Remission) at Week 48

Pooled GALAXI 2 & 3



Deep remission: Clinical remission **AND** endoscopic remission

Data presented as n (%); Δ% (adjusted treatment difference) vs ustekinumab. Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with CD-related surgery; prohibited change in concomitant CD medication; or who discontinued study agent due to lack of efficacy, AE of worsening CD or Week 20/24 nonresponse, or discontinued study agent for any other reason other than COVID-19-related reasons or regional crisis prior to the analysis timepoint were considered not to have met the endpoint criteria. Participants who had discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder and non-responder status from that timepoint onwards. After accounting for these scenarios, participants with insufficient data to calculate the outcome measure at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

Conclusions

In analyses of data pooled across the double-blind GALAXI 2 & 3 trials, guselkumab was efficacious versus ustekinumab for multiple endoscopic-based endpoints at Week 48

Clinically meaningful benefit was observed for guselkumab versus ustekinumab in both the BIO-naïve and BIO-IR subpopulations for endoscopic endpoints and in the more refractory BIO-IR subpopulation for both clinical and endoscopic endpoints

These analyses show that guselkumab achieved greater clinical and endoscopic long-term efficacy versus ustekinumab in participants with Crohn's disease with and without prior inadequate response or intolerance to biologic therapy

Acknowledgements

The authors thank the participants, investigators, and study personnel who made the GALAXI 2 & 3 studies possible

This work was supported by Janssen Research & Development, LLC, a Johnson & Johnson Company

Under the direction of the authors and in accordance with Good Publication Practices, Charles Miller of Janssen Global Services, LLC provided writing and editorial assistance