AIBD REGIONALS

Improving our Gut Instinct: Evaluating the Role and Utility of IL-23 Inhibitors for IBD

David T. Rubin, MD, FACG

Joseph B. Kirsner Professor of Medicine
Chief, Section of Gastroenterology, Hepatology, and Nutrition
Director, Inflammatory Bowel Disease Center
University of Chicago

Supported by an educational grant from Johnson & Johnson.

Disclosures

- **David T. Rubin, MD, FACG:** Consultant/Advisor – AbbVie, Abivax SA, AltruBio, Athos Therapeutics, Bristol Myers Squibb, Celltrion, Connect BioPharma, Eli Lilly, Genentech (Roche), Iterative Health, Janssen Pharmaceuticals, Johnson & Johnson, Merck, Odyssey Therapeutics, Pfizer, Sanofi, Spyre, Takeda, Vedanta Biosciences, Ventyx; Grant Support – Gastro-Intestinal Research Foundation, Helmsley Charitable Trust, NIH P30 DK42086, Takeda; Board of Trustees/Directors – Cornerstones Health

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Learning Objectives

- Assess the role of interleukins in the pathogenesis of IBD and the potential therapeutic implications of targeting IL-23 and CD64 in IBD

- Evaluate the safety/efficacy data and mechanisms of action of available and emerging IL inhibitors for the treatment of IBD, with a focus on agents targeting IL-23

IBD = inflammatory bowel disease; IL = interleukin; CD = cluster of differentiation.

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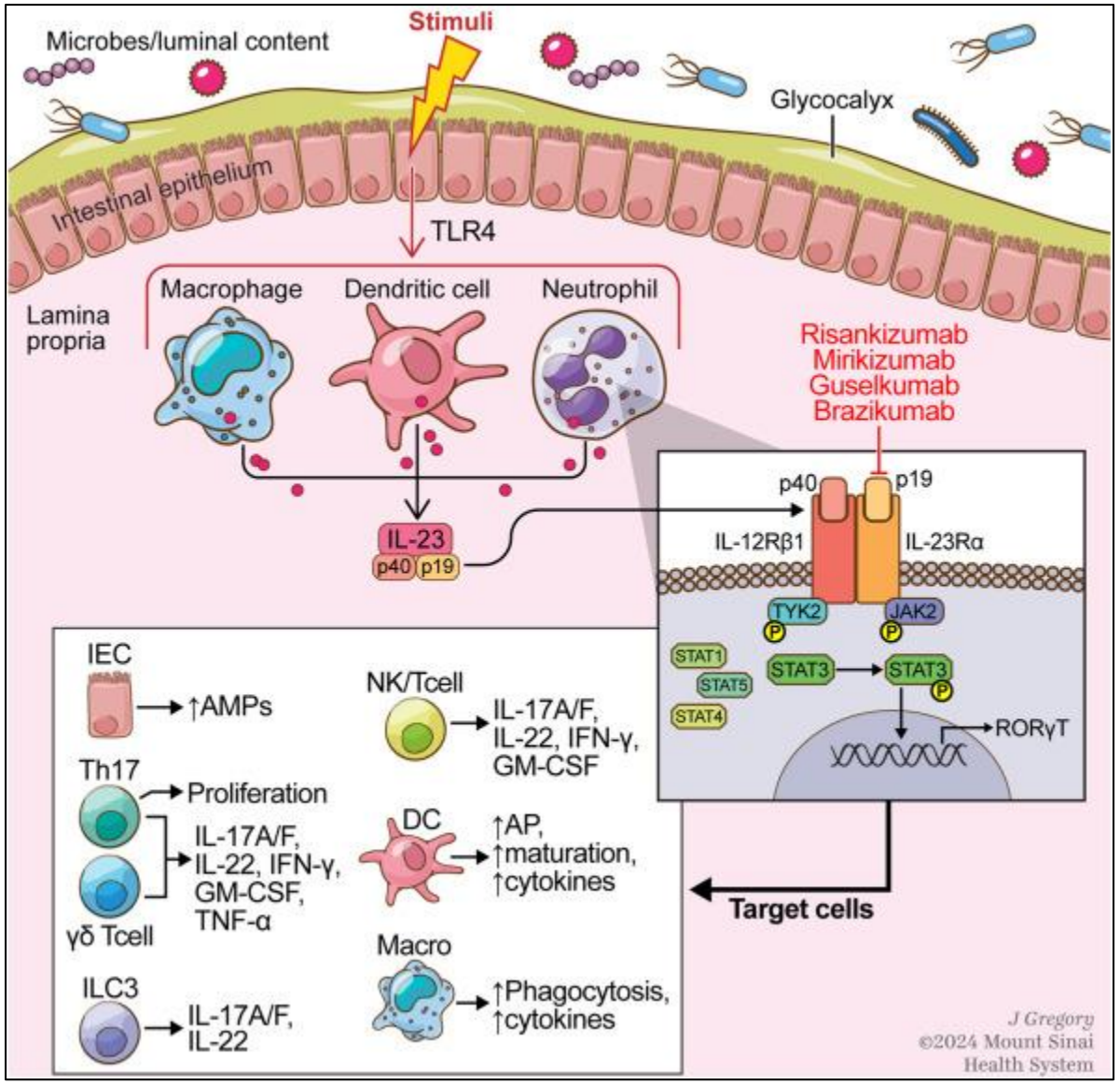
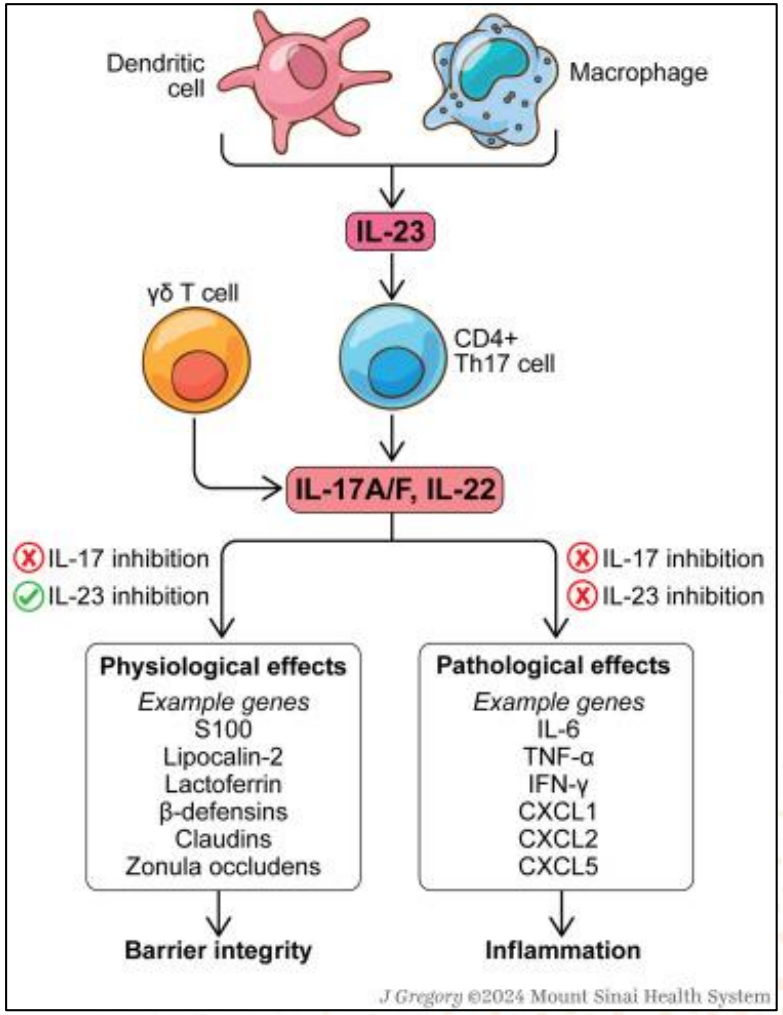
IL-23 Signaling in the Intestinal Mucosa and the Immune Impact of IL-23





Bourgonje AR, et al. *Gastroenterology*. 2025;168(1):29-52.e3.

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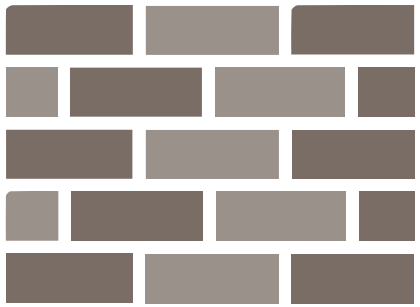
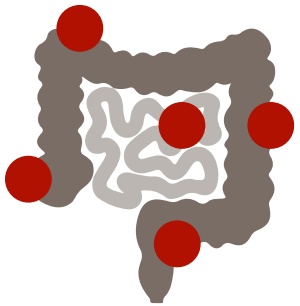
Why Target IL-23 in IBD?

Inhibition of IL-23

- Decreases mucosal inflammation and improves epithelial barrier integrity
- Suppresses gut inflammation in T-cell-mediated colitis
- Preserves protective IL-17 gut functions





Hohenberger M, et al. *J Dermatolog Treat*. 2018;29(1):13-18. Vuyyuru SK, et al. *Drugs*. 2023;83(10):873-891. Wallace KL, et al. *World J Gastroenterol*. 2014;20(1):6-21.

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Ustekinumab Biosimilars Approved for IBD

Treatment	FDA Approval for IBD	Clinical Trial (Moderate to Severe Plaque Psoriasis)
Ustekinumab-auub	October 2023	NCT04607980
Ustekinumab-ttwe	July 2024	NCT04967508
Ustekinumab-aauz	September 2024	NCT04595409
Ustekinumab-aekn	October 2024	NCT04930042
Ustekinumab-srlf	October 2024	NCT04785326
Ustekinumab-kfce	November 2024	NCT05335356
Ustekinumab-stba	December 2024	NCT04673786

Induction IV
≤55 kg: 260 mg ≤85 kg: 390 mg ≥85 kg: 520 mg
Maintenance SC
Week 8: 90 mg q8wks

ClinicalTrials.gov. Accessed June 17, 2025. https://clinicaltrials.gov.
FDA. Accessed June 17, 2025. https://www.accessdata.fda.gov/scripts/cder/daf/.

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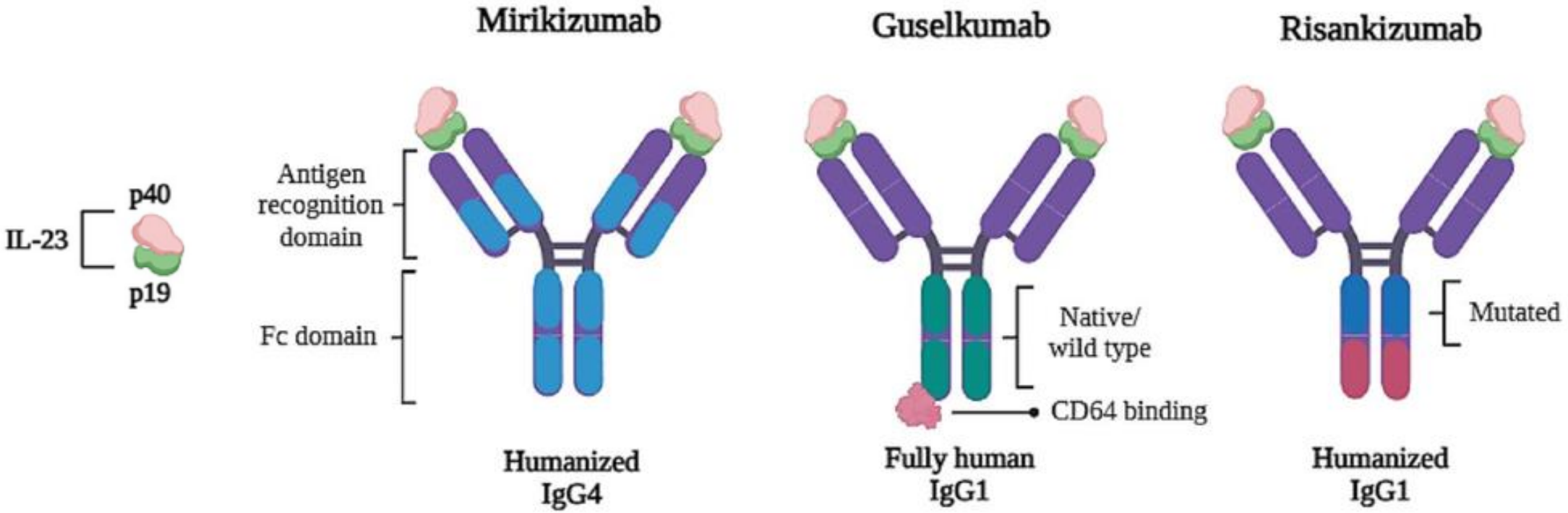
IL-23p19 Inhibitors



Binds to CD64, a glycoprotein expressed on IL-23-producing immune cells

Bezzio C, et al. *Therap Adv Gastroenterol*. 2024;17:1-22.

IL-23 Therapies for IBD

	Induction		SC Maintenance	
Treatment	**CD**	**UC**	**CD**	**UC**
Guselkumab (p19/CD64: IL-23)	IV: 200 mg wks 0, 4, 8 SC: 400 mg wks 0, 4, 8	IV: 200 mg wks 0, 4, 8	Wk 12: 200 mg q4wks Wk 16: 100 mg q8wks	
Mirikizumab (p19: IL-23)	IV: 900 mg wks 0, 4, 8	IV: 300 mg wks 0, 4, 8	Wk 12: 300 mg q4wks	Wk 12: 200 mg q4wks
Risankizumab (p19: IL-23)	IV: 600 mg wks 0, 4, 8	IV: 1200 mg wks 0, 4, 8	Wk 12: 180 mg/1.2 mL or 360 mg/2.4 mL q8wks	
Ustekinumab (p40: IL-12/23)	IV: ≤55 kg: 260 mg at wk 0 ≤85 kg: 390 mg at wk 0 ≥85 kg: 520 mg at wk 0		Wk 8: 90 mg q8wks	

FDA. Accessed June 17, 2025. https://www.accessdata.fda.gov/scripts/cder/daf/.

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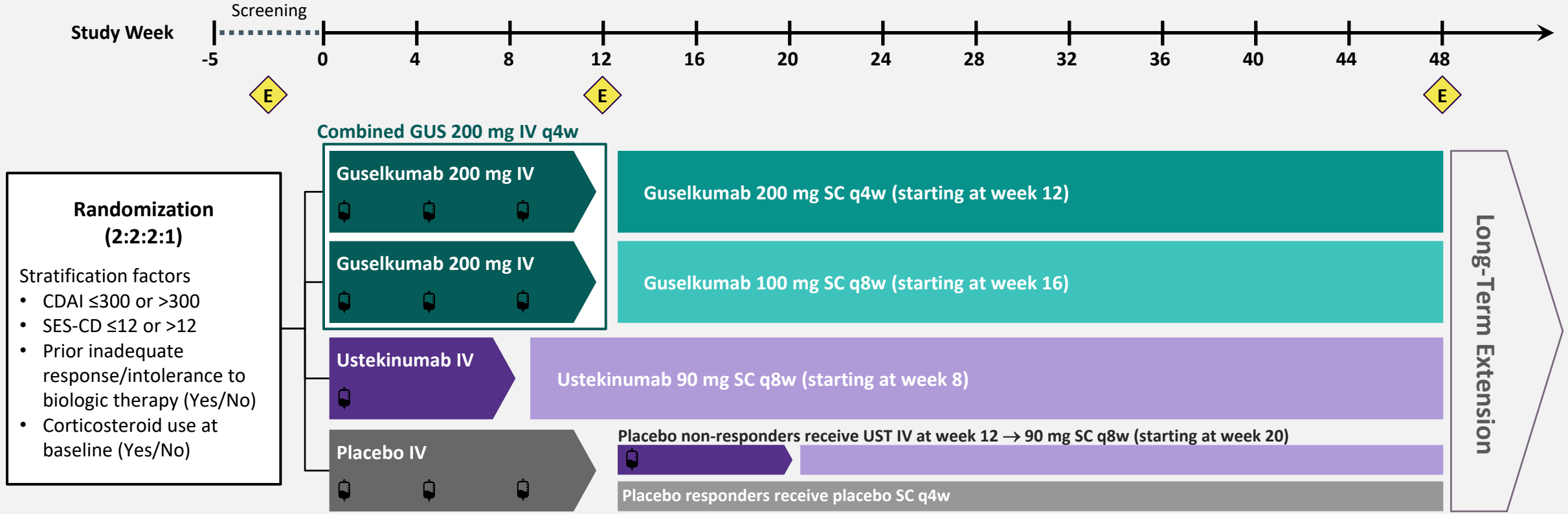
Crohn’s Disease

GALAXI 2 & 3: Guselkumab for Crohn's Disease

Primary analysis set
- **GALAXI 2: 508 participants**
- **GALAXI 3: 513 participants**

Key eligibility criteria
- Moderately to severely active CD (CDAI score 220-450 + mean daily stool frequency count >3 OR abdominal pain score >1) and SES-CD score[a] ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/intolerance to oral corticosteroids or 6-MP/AZA/MTX, or biologic therapies[b]



[a]Scored at screening by central reader with minimum scores of 1 for "size of ulcer" and "ulcerated surface"; [b]Biologic therapies: Tumor necrosis factor (TNF) antagonists or vedolizumab.
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.
E = endoscopy; SES = simple endoscopic score; MP = mercaptopurine; AZA = azathioprine; MTX = methotrexate; GUS = guselkumab.
Panaccione R, et al. Presented at: Digestive Disease Week (DDW); May 18-21, 2024; Washington, DC.

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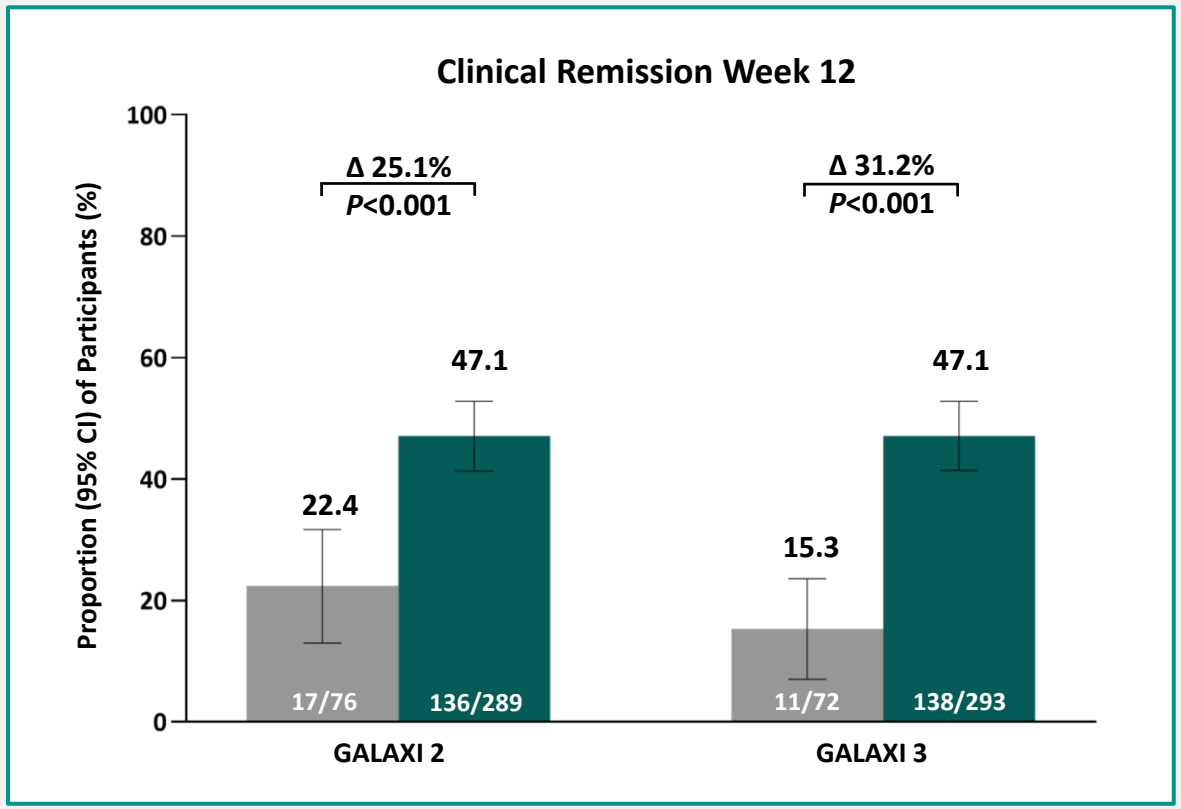
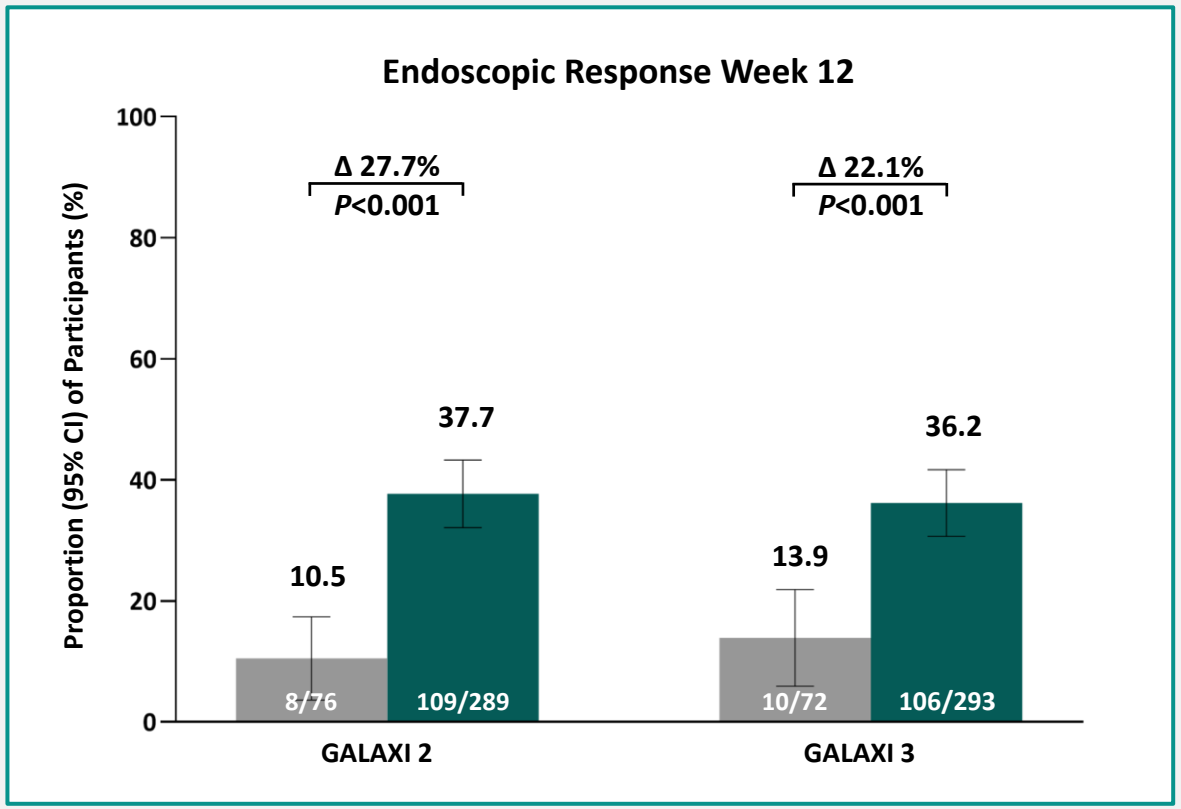
GALAXI 2 & 3: Efficacy of Guselkumab IV Induction

Major Secondary Endpoints





Placebo IV Combined GUS 200 mg IV

Clinical remission: CDAI <150.
Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤2.
CI = confidence interval.
Panaccione R, et al. Presented at: DDW; May 18-21, 2024; Washington, DC.

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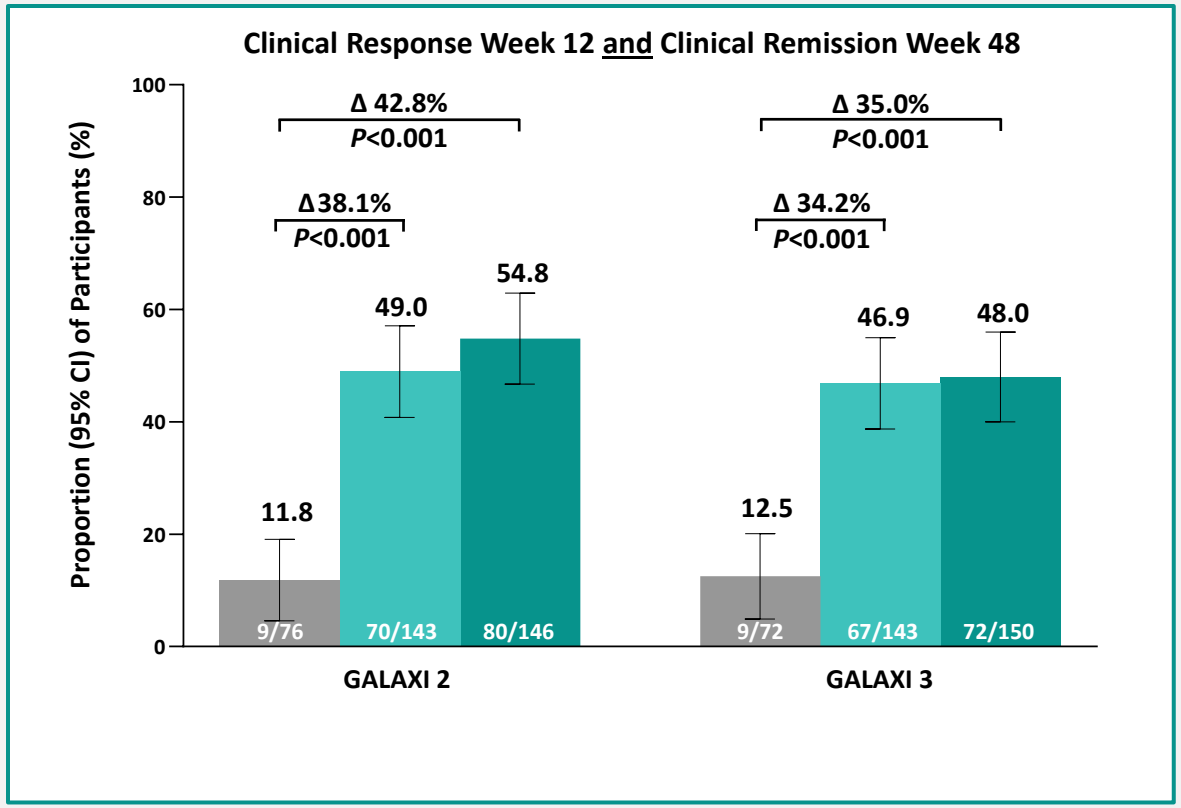
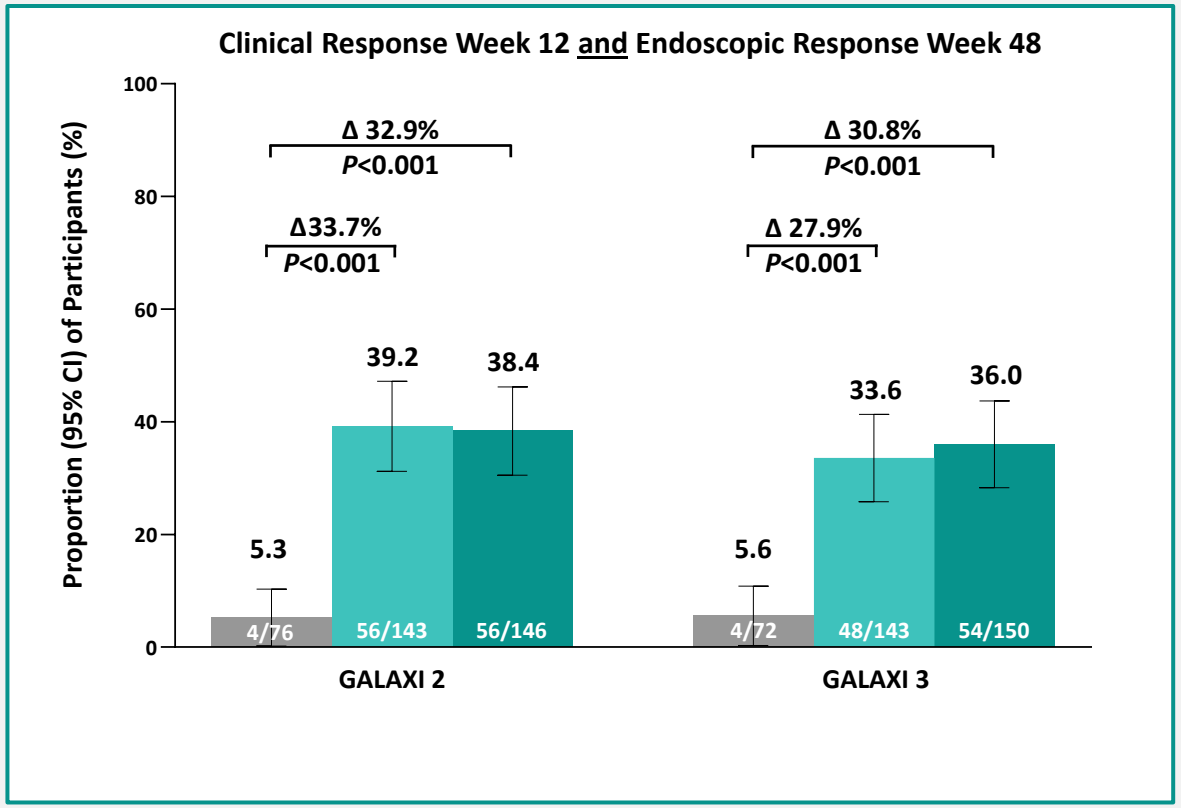
GALAXI 2 & 3: Composite Co-Primary Endpoints





Placebo

GUS 200 mg IV q4w → 100 mg SC q8w

GUS 200 mg IV q4w → 200 mg SC q4w

Clinical response: ≥100-point reduction from baseline in CDAI or CDAI <150.
Clinical remission: CDAI <150.
Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤2.
Panaccione R, et al. Presented at: DDW; May 18-21, 2024; Washington, DC.

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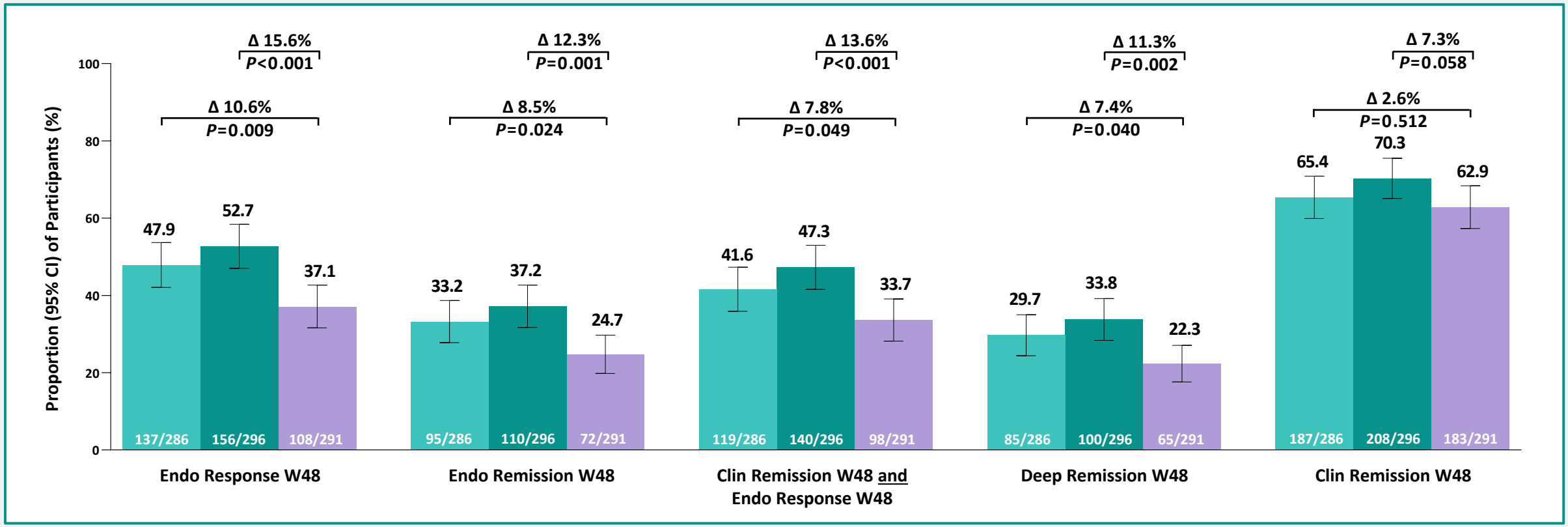
GALAXI 2 & 3: Guselkumab vs Ustekinumab: Efficacy at Week 48

Pooled GALAXI 2 & 3: Major Secondary Endpoints

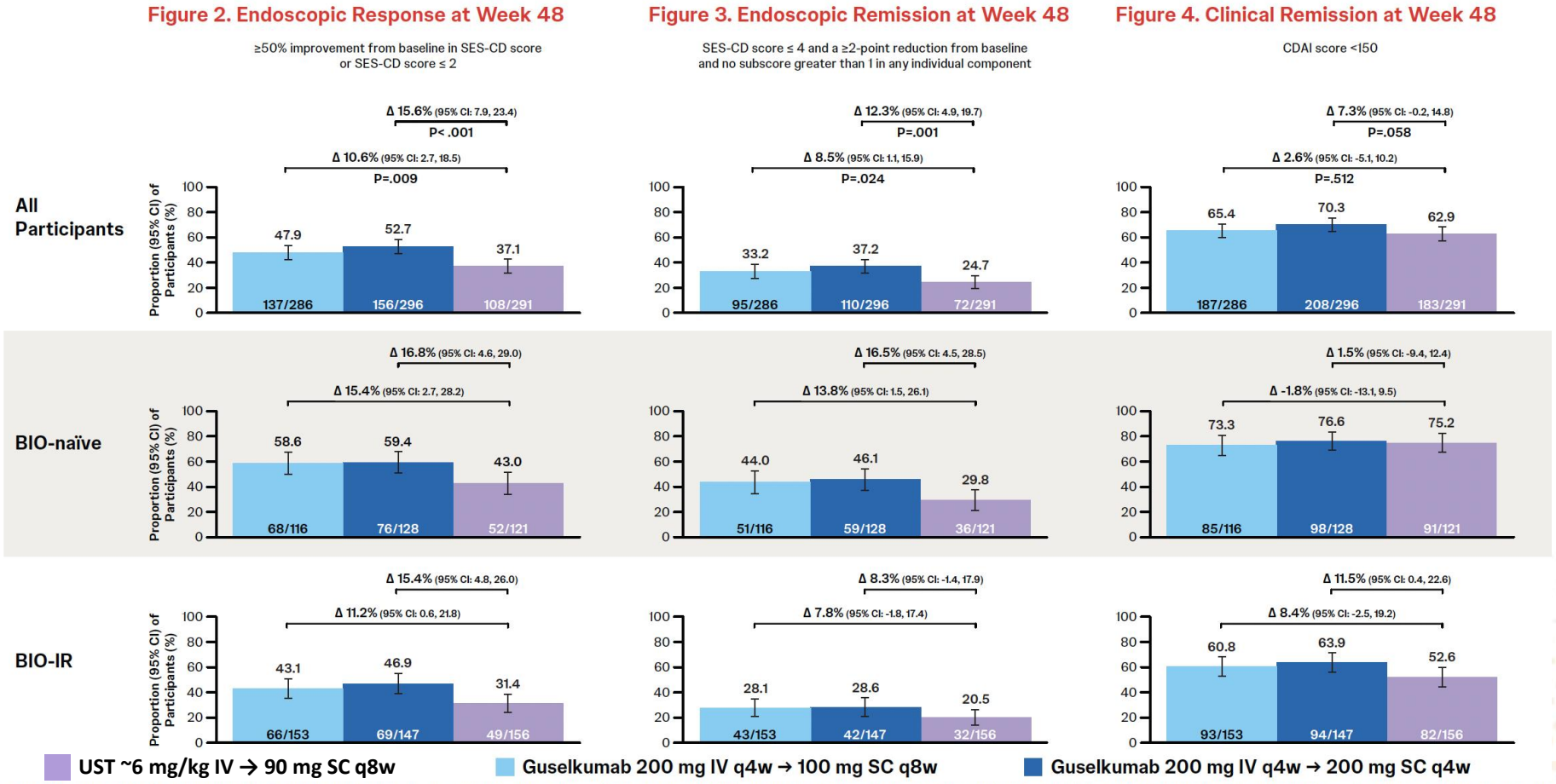


Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤2. Endoscopic remission: SES-CD ≤4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component. Clinical remission: CDAI <150. Deep remission: Clinical remission and endoscopic remission.

Panaccione R, et al. Presented at: DDW; May 18-21, 2024; Washington, DC.

AIBD REGIONALS

Guselkumab Is More Effective Than Ustekinumab in BIO-IR Patients with CD



Results from the pooled GALAXI 2 & 3 dataset presented as n (%); Δ% (adjusted treatment difference vs ustekinumab based on the common risk difference by use of Mantel-Haenszel stratum weights [based on the stratification variables] and the Sato variance estimator). Subpopulation analyses were not multiplicity controlled (p-values not shown). Participants with C 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 achieved the endpoint at that timepoint.

BIO = biologic therapy; IR = inadequate response.

Danese S, et al. Presented at: UEGW; October 12-15, 2024; Vienna, Austria.

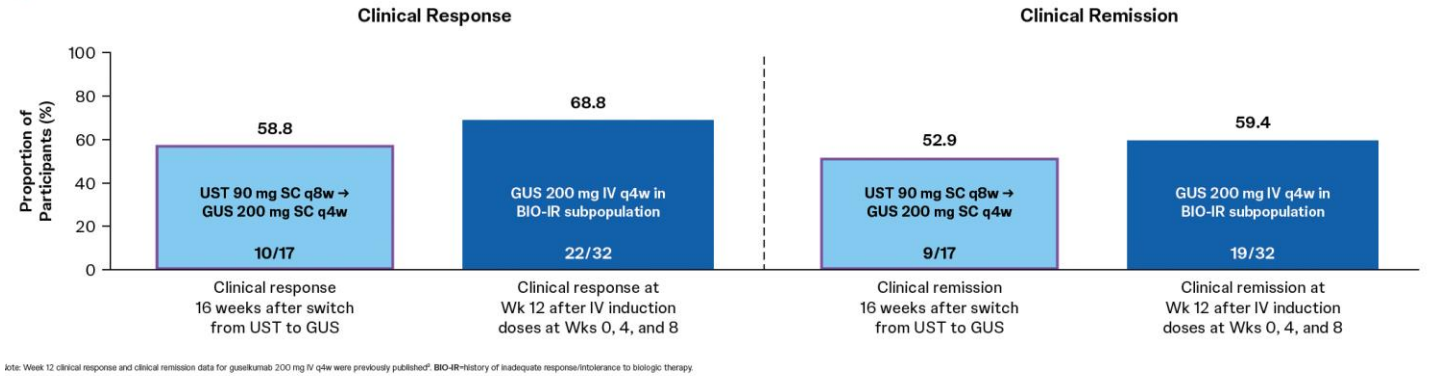
AIBD REGIONALS

Does Guselkumab Work after Loss of Response to Ustekinumab? (GALAXI 1)

A total of 17 participants treated with ustekinumab during the LTE had inadequate response and switched to guselkumab 200 mg SC q4w without IV induction

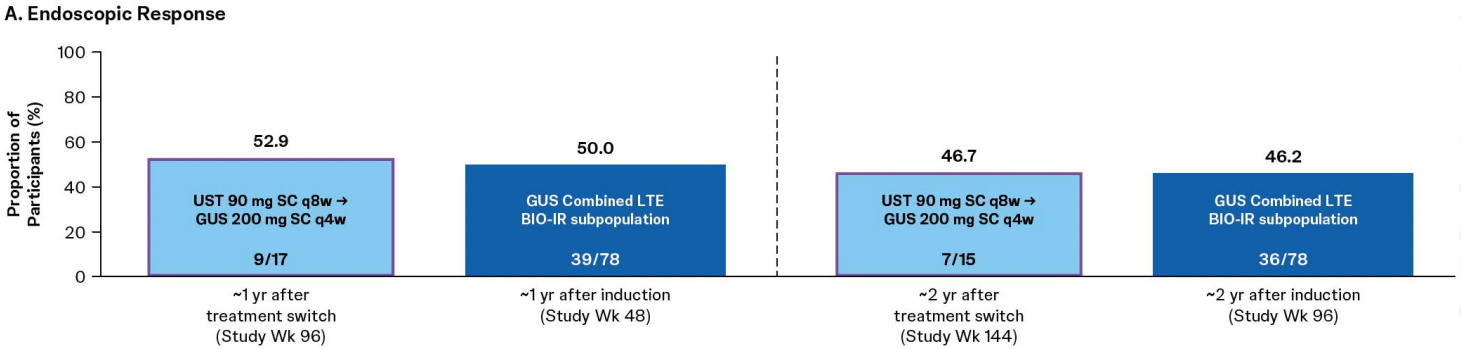
Clinical outcomes 16 weeks after treatment switch in participants who switched from ustekinumab to guselkumab 200 mg SC q4w were consistent with those in the BIO-IR subpopulation 12 weeks after IV induction with guselkumab 200 mg IV q4w

Figure 2. Clinical Outcomes 16 Weeks After Treatment Switch



Note: Week 12 clinical response and clinical remission data for guselkumab 200 mg IV q4w were previously published[2]. BIO-IR=history of inadequate response/intolerance to biologic therapy.

Figure 3. Endoscopic Outcomes by Years Treated With Guselkumab



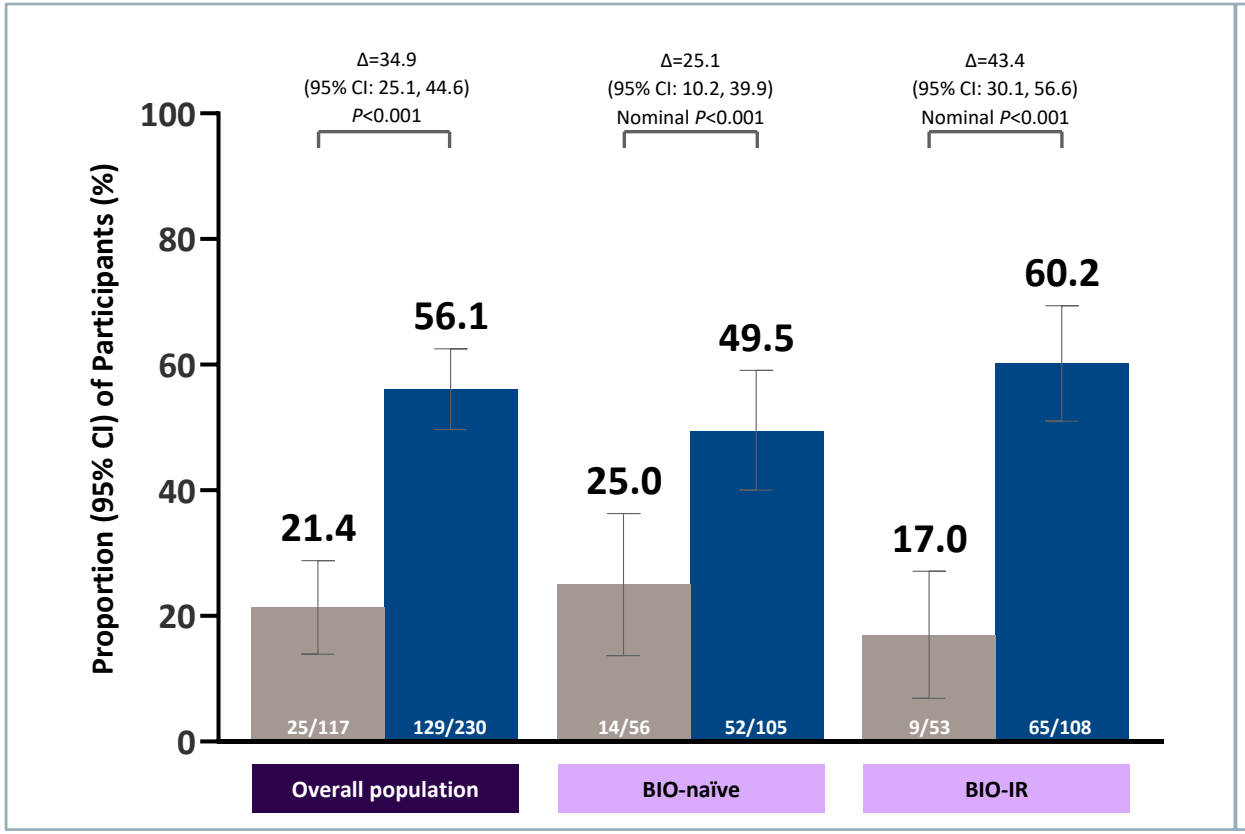
LTE = long-term extension.

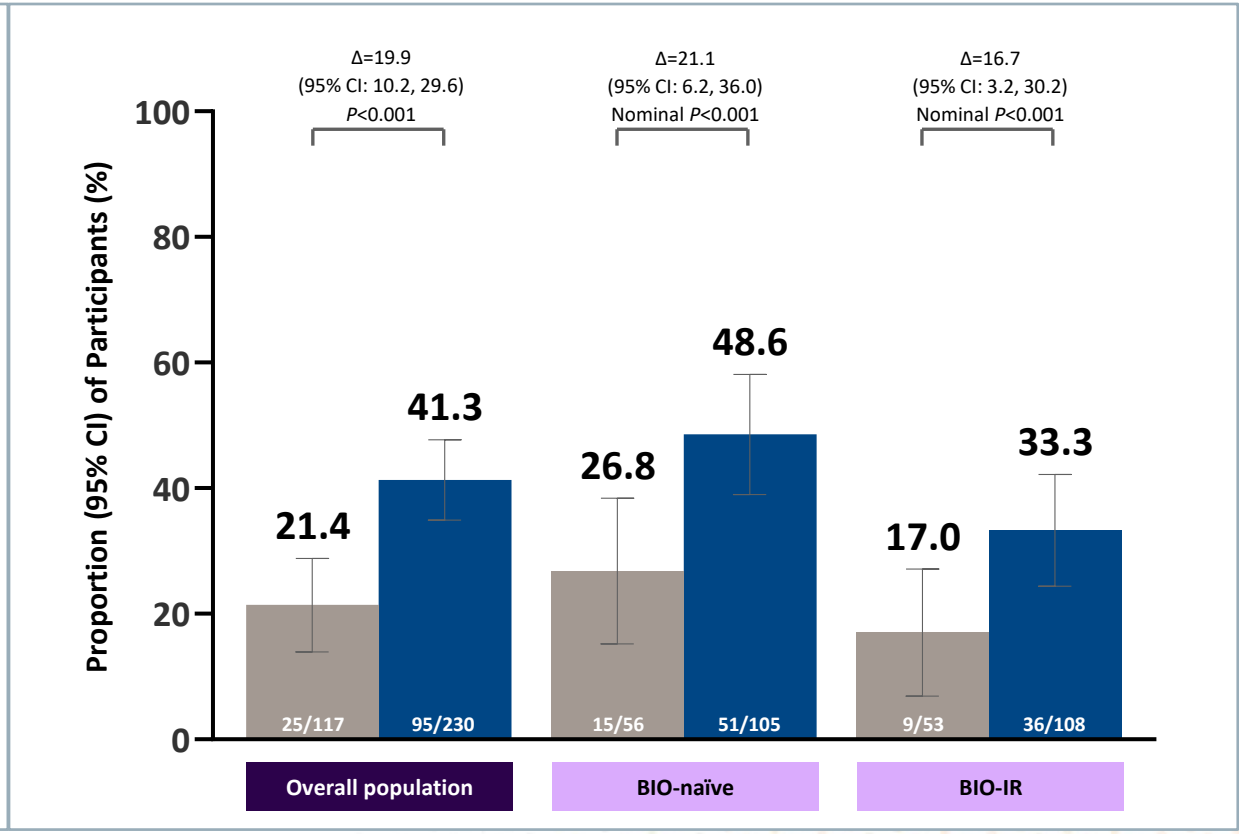
Afzali A, et al. Presented at: ACG Annual Scientific Meeting; October 25-30, 2024; Philadelphia, PA.

AIBD REGIONALS

GRAVITI: SC Induction for CD

Clinical Remission and Endoscopic Response at Week 12





Placebo SC GUS 400 mg SC q4w

Clinical remission: CDAI score <150

Placebo SC GUS 400 mg SC q4w

Endoscopic response: ≥50% improvement from baseline in SES-CD score

Note: Clinical remission at week 12 was multiplicity-controlled for the overall population, not the BIO-naïve and BIO-IR subpopulations.

Panaccione R, et al. Presented at: American College of Gastroenterology (ACG) Annual Scientific Meeting; October 25-30, 2024; Philadelphia, PA.

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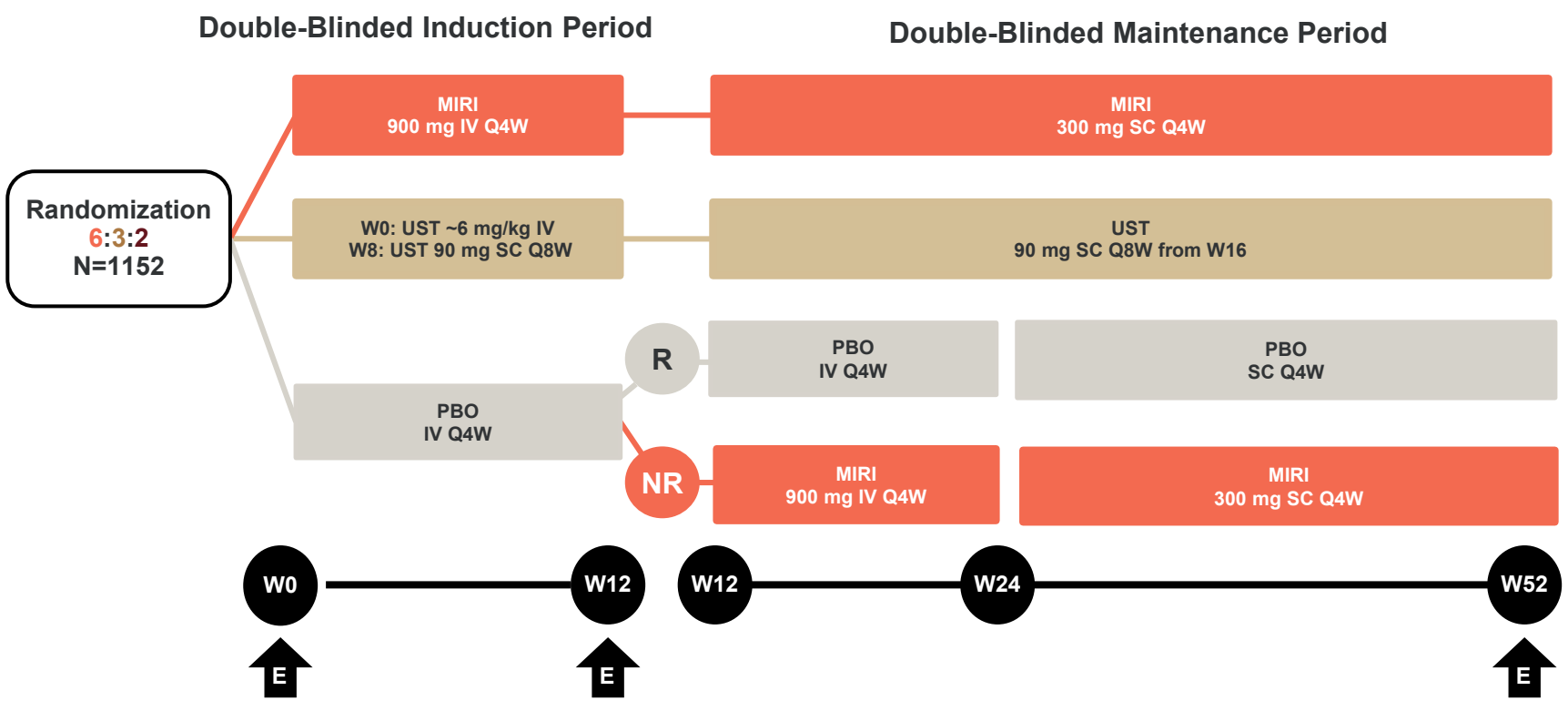
VIVID-1 Trial Design: Assessments of Mirikizumab and Ustekinumab on Histologic Inflammation in 5 Segments in Crohn's Disease

VIVID-1



Key Eligibility Criteria

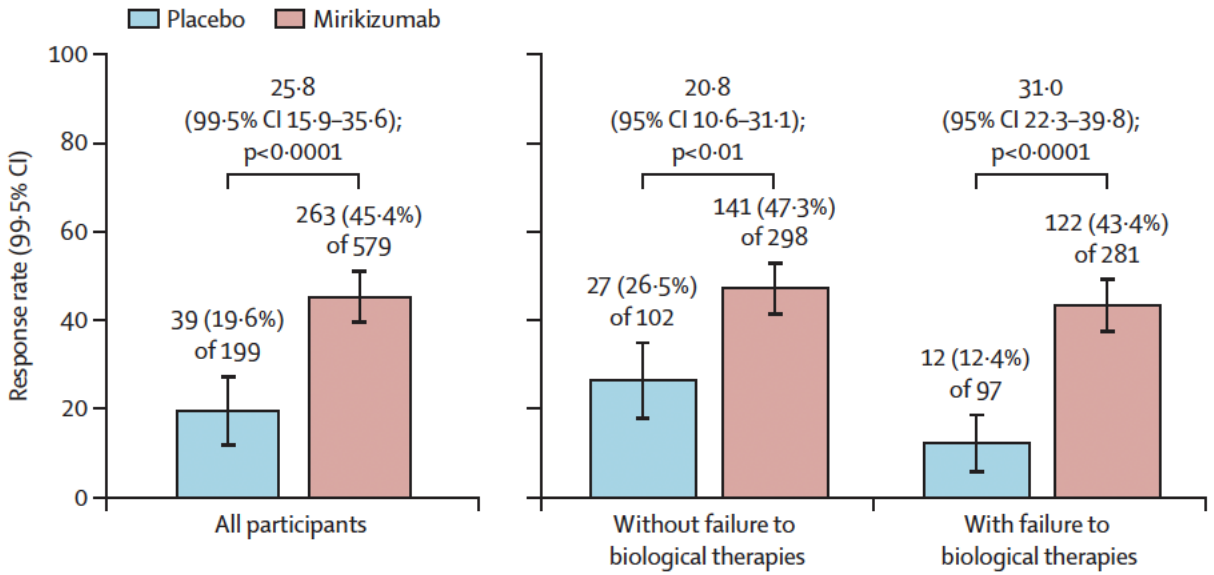
- Age ≥18 to ≤80 years
- Moderately to severely active CD as defined as unweighted daily average stool frequency (SF) ≥4 and/or unweighted daily average abdominal pain (AP) ≥2 at baseline
- SES-CD ≥7 (or ≥4 for isolated ileal disease) within 21 days before randomization
- Inadequate response, loss of response, or intolerance to ≥1 drugs, including corticosteroid, immunomodulator, or approved biologic therapy for CD

Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

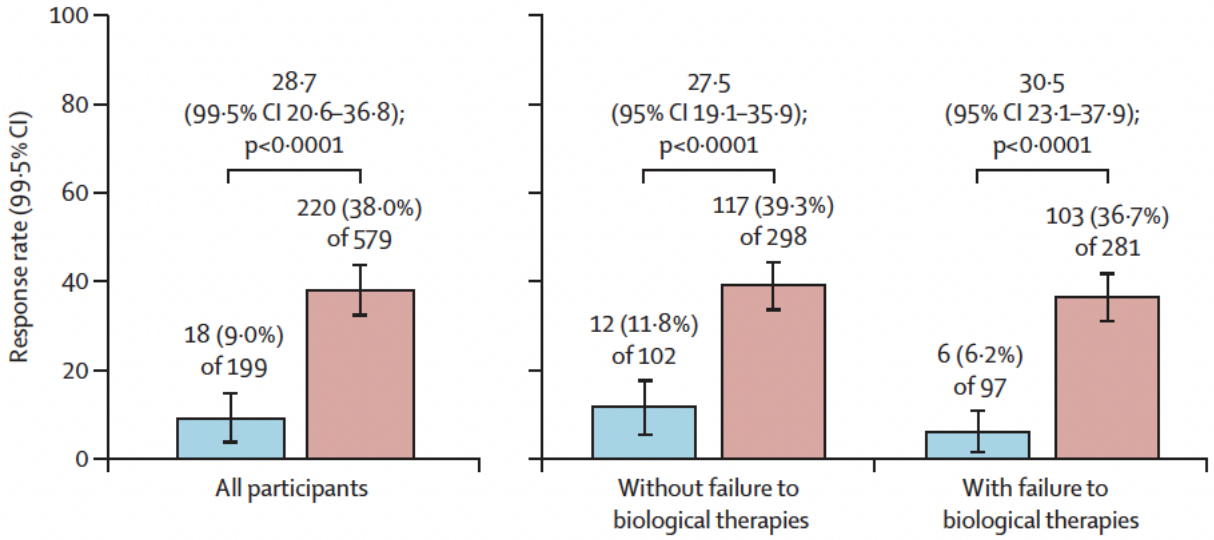
AIBD REGIONALS

VIVID: Mirikizumab vs Placebo in CD

Co-Primary Endpoints: Clinical Response by PRO at Week 12 and Clinical Remission by CDAI at Week 52 (NRI)



Co-Primary Endpoints: Clinical Response by PRO at Week 12 and Endoscopic Response at Week 52 (NRI)

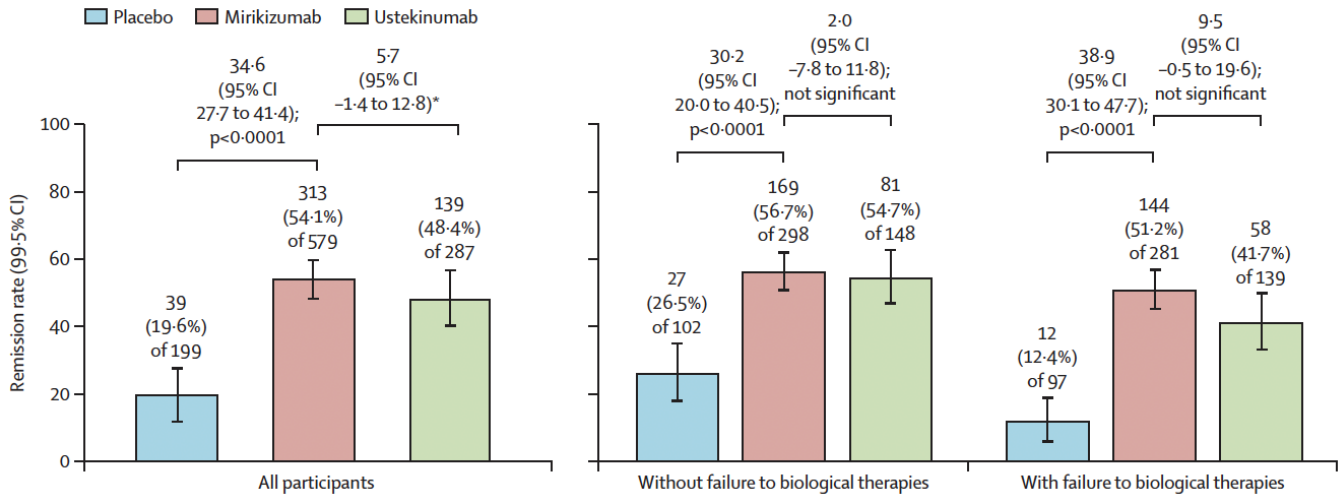


PRO = patient-reported outcome; NRI = non-responder imputation.
Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

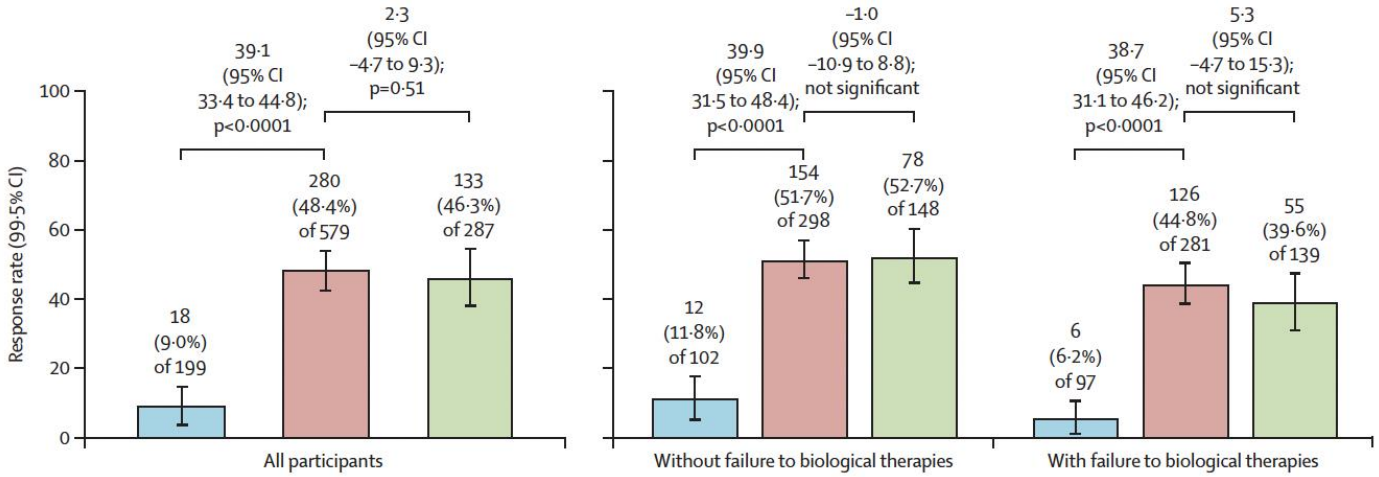
AIBD REGIONALS

VIVID: Mirikizumab vs Ustekinumab in CD

Clinical Remission by CDAI (NRI) at Week 52



Endoscopic Response (NRI) at Week 52



***Non-inferiority met after accounting for multiplicity.**

Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

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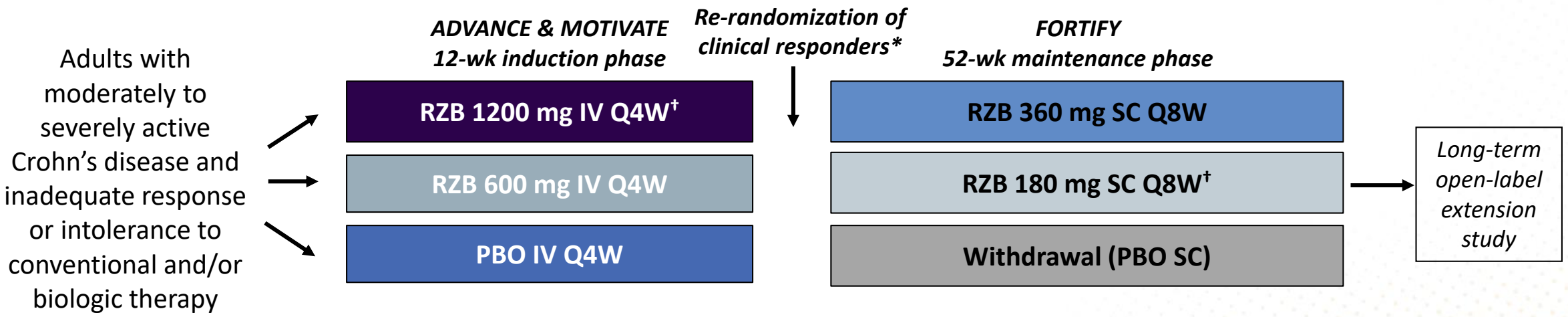
ADVANCE, MOTIVATE, FORTIFY: Risankizumab in Patients with Moderate to Severe CD Phase 3 Program



***Clinical responders defined as ≥30% decrease in average daily stool frequency or APS and not worse than baseline;**
†Data not reported in this analysis.
CD = Crohn's disease; APS = abdominal pain score; PBO = placebo; RZB = risankizumab.
D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030.

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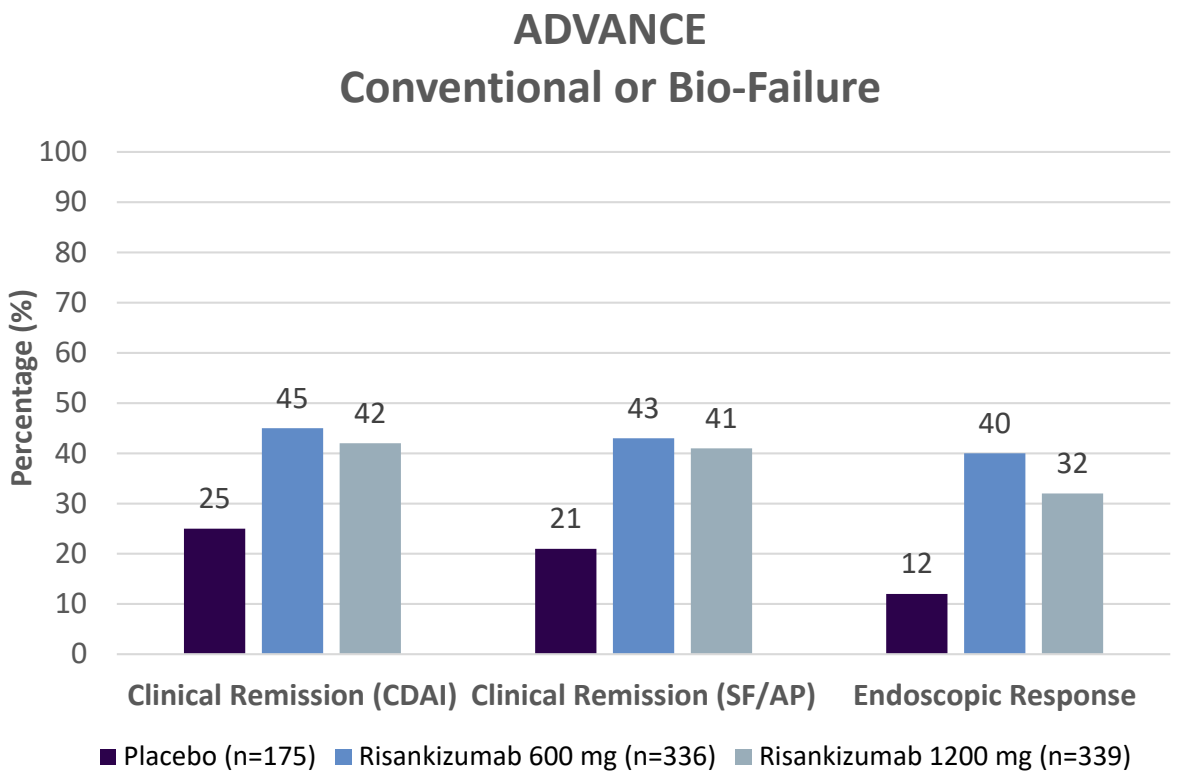
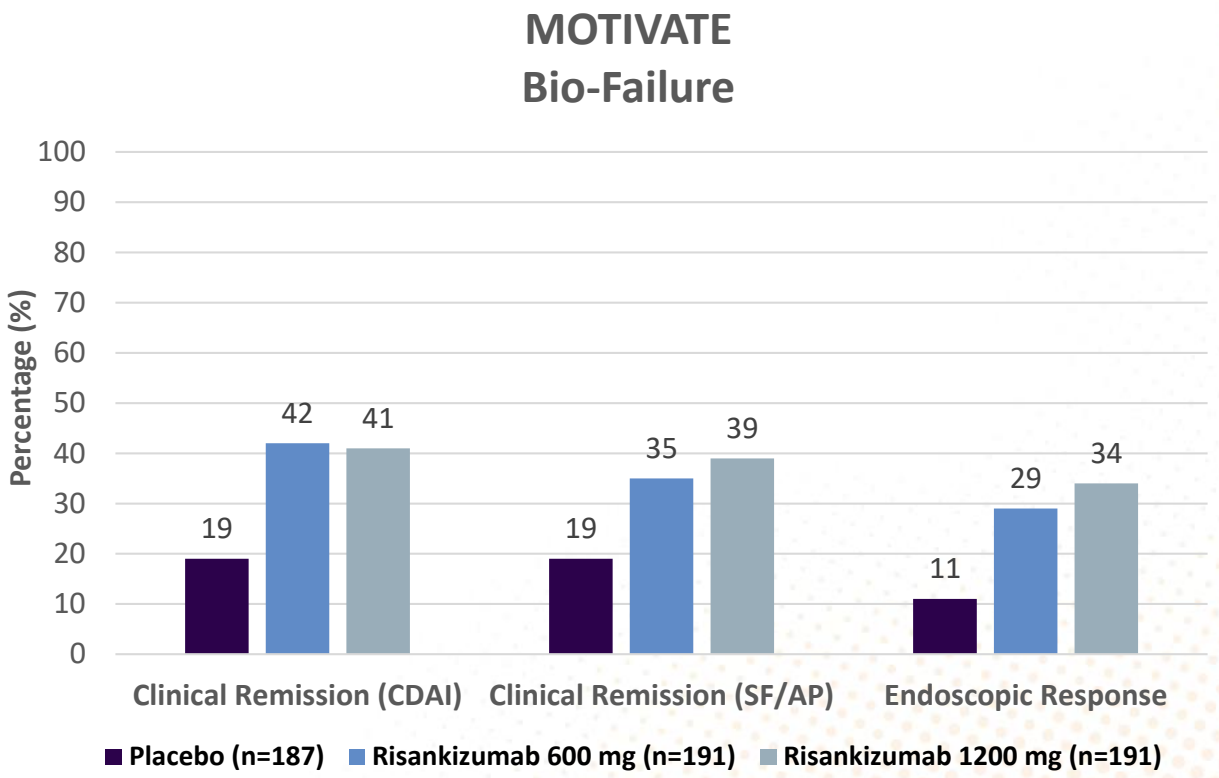
ADVANCE and MOTIVATE: Risankizumab in Crohn's Disease Phase 3 Week 12 Induction



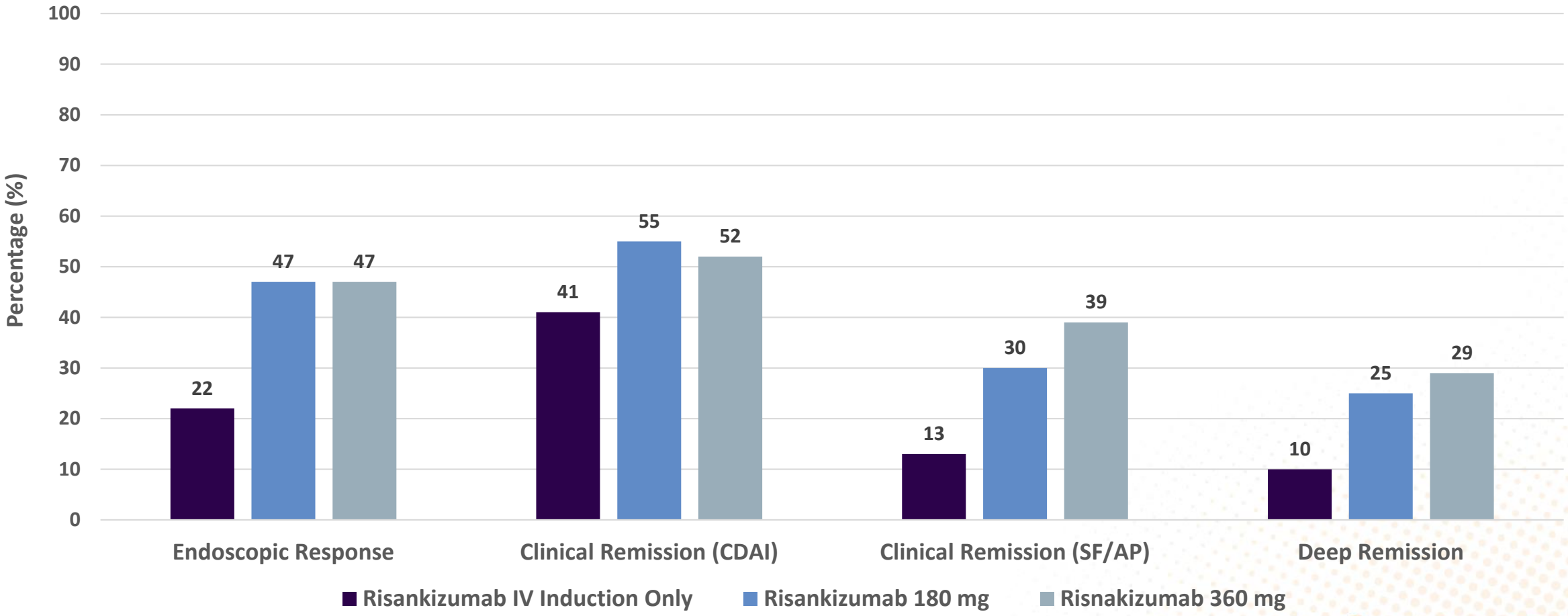


CDAI = CD activity index; SF = stool frequency.

D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

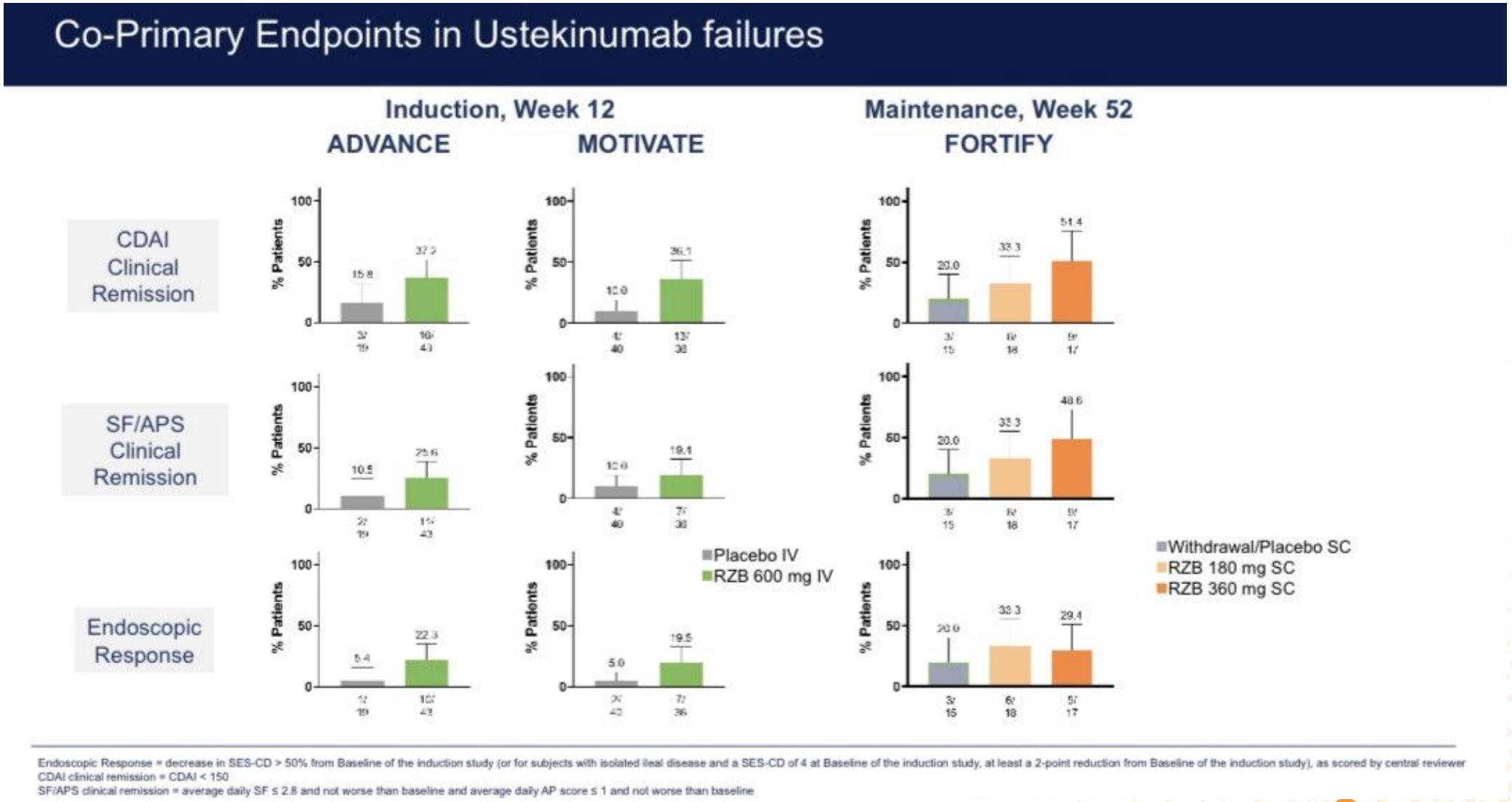
AIBD REGIONALS

FORTIFY: Risankizumab in Crohn's Disease (Phase 3) Week 52 Maintenance



Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

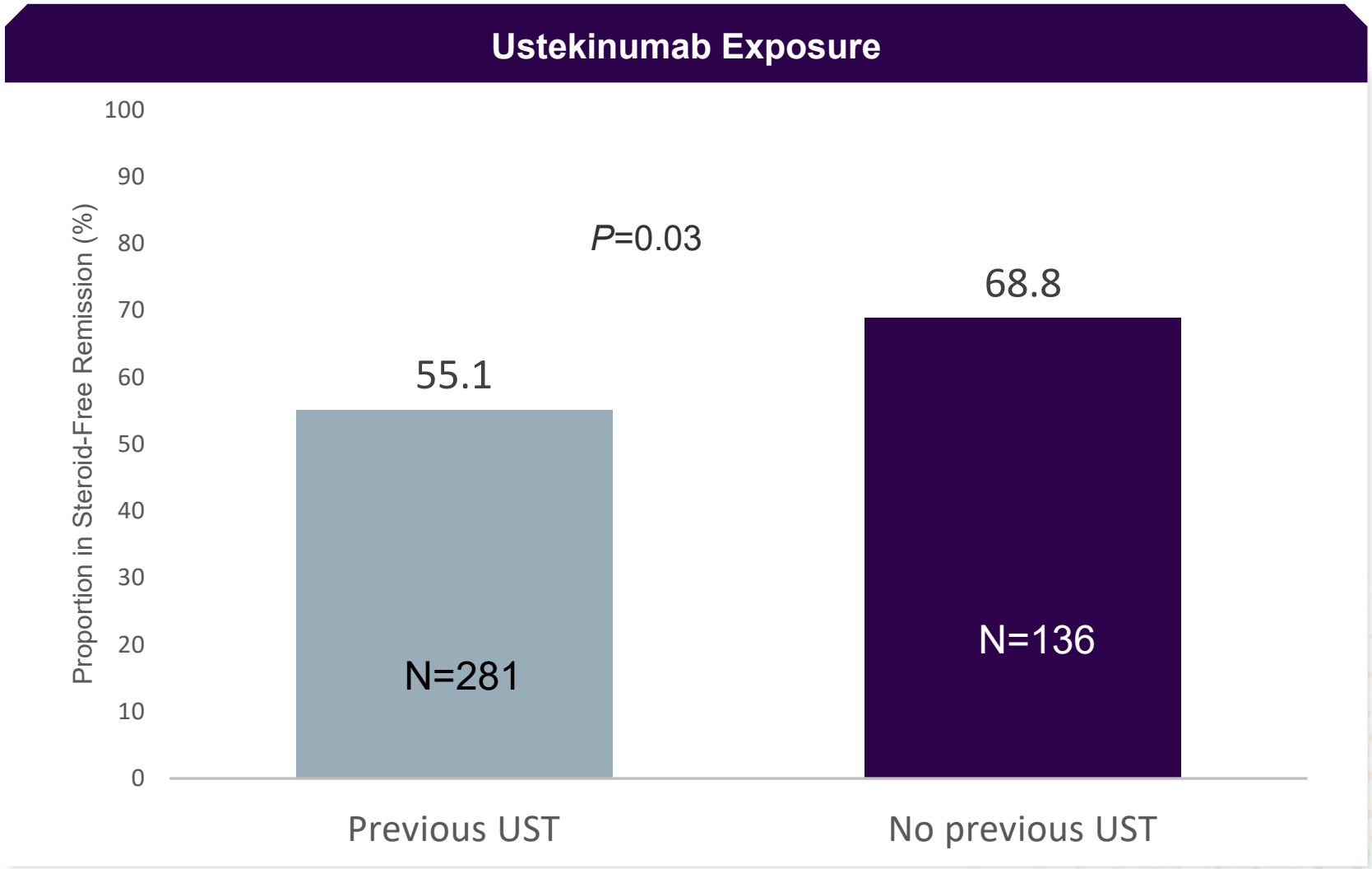
Risankizumab in Patients with Prior Failure of Ustekinumab



Ferrante M, et al. Presented at: ACG Annual Scientific Meeting; October 21-26, 2022; Charlotte, NC.

AIBD REGIONALS

Impact of Prior Ustekinumab Exposure on Steroid-Free Remission with Risankizumab: RISANCROHN Spanish Multicenter Study (N=417)

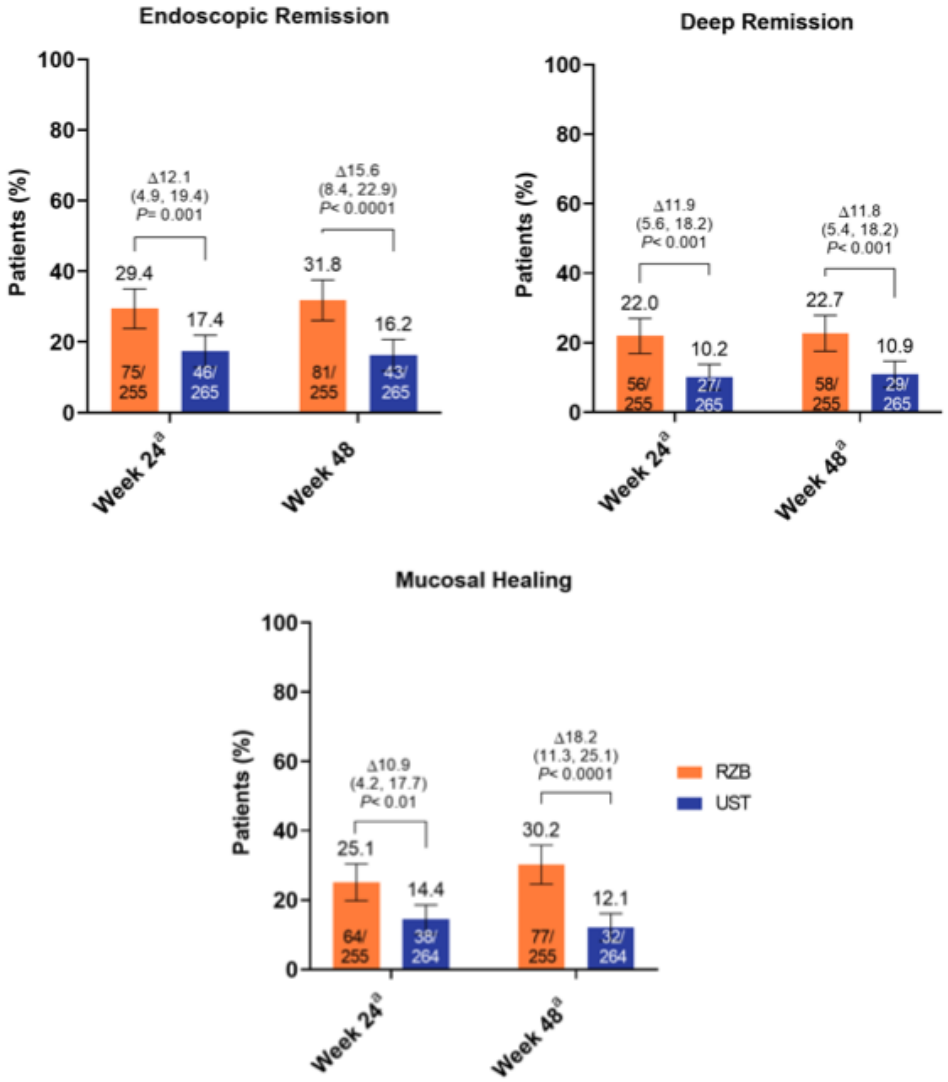


UST = ustekinumab

Barreiro de Acosta M, et al. Presented at United European Gastroenterology Week (UEGW); October 12-15, 2024; Vienna, Austria.

AIBD REGIONALS

SEQUENCE: Risankizumab vs Ustekinumab Phase 3b Head-to-Head RCT



[a]*P*-values are nominal.
RCT = randomized controlled trial.
Peyrin-Biroulet L, et al. *N Engl J Med*. 2024;391(3):213-223.

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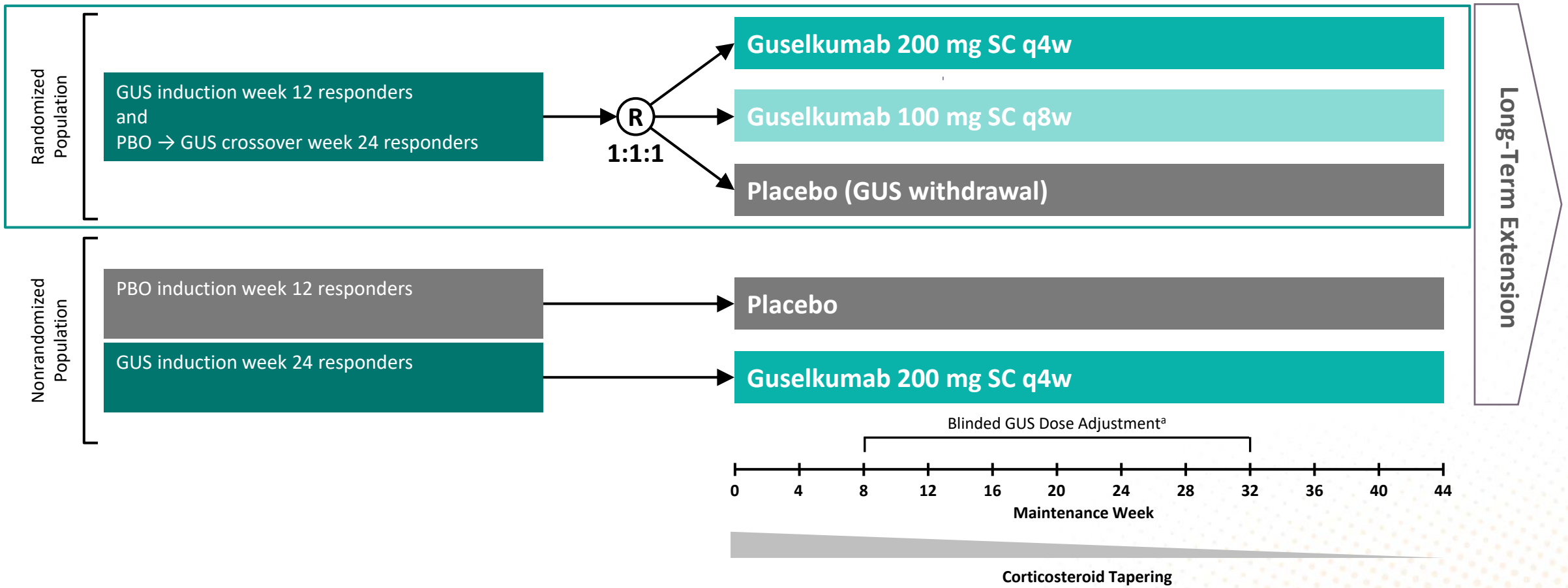
Ulcerative Colitis

QUASAR (Guselkumab in UC) Maintenance Study Design

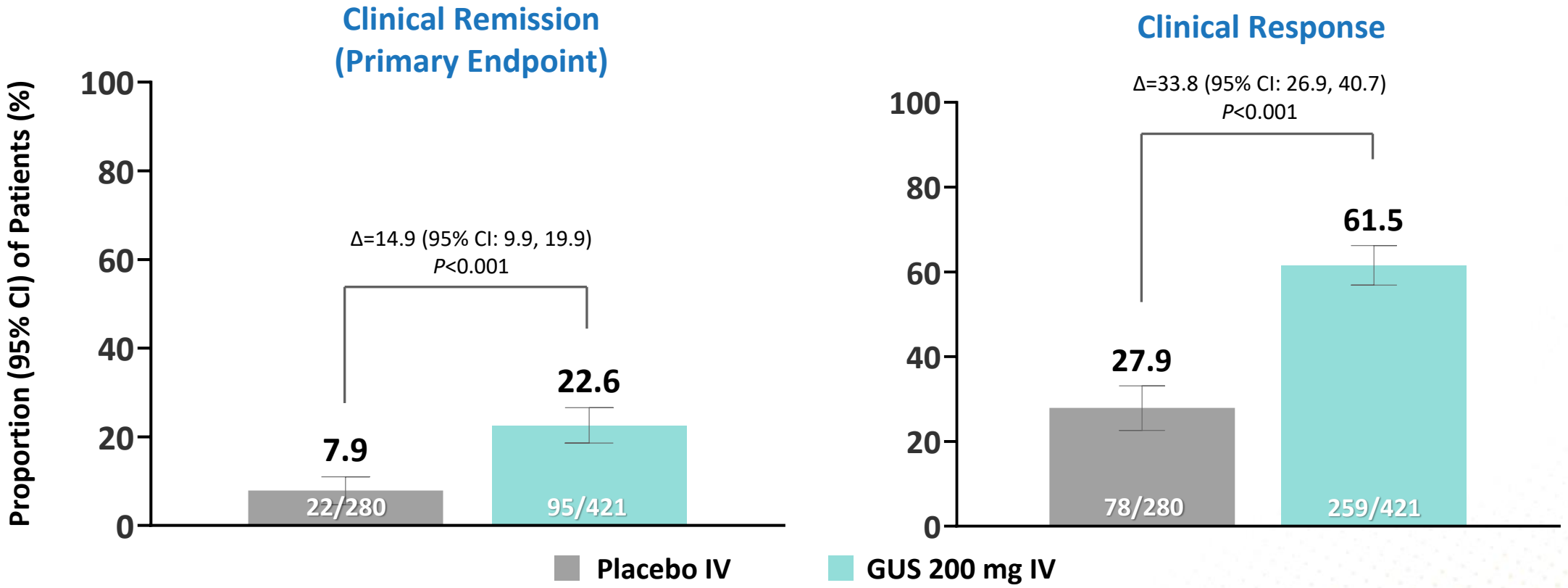


[a]Between week 8 and week 32, randomized patients meeting loss of clinical response criteria (based on the modified Mayo score and required an endoscopic assessment) were eligible for a blinded dose adjustment as follows: Placebo SC → GUS 200 mg SC q4w; GUS 100 mg SC q8w → GUS 200 mg SC q4w; GUS 200 mg SC q4w → GUS 200 mg SC q4w (sham adjustment).
R = randomization.
Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.

AIBD REGIONALS

QUASAR: Guselkumab for UC – Phase 3, Induction

Clinical Outcomes at Week 12



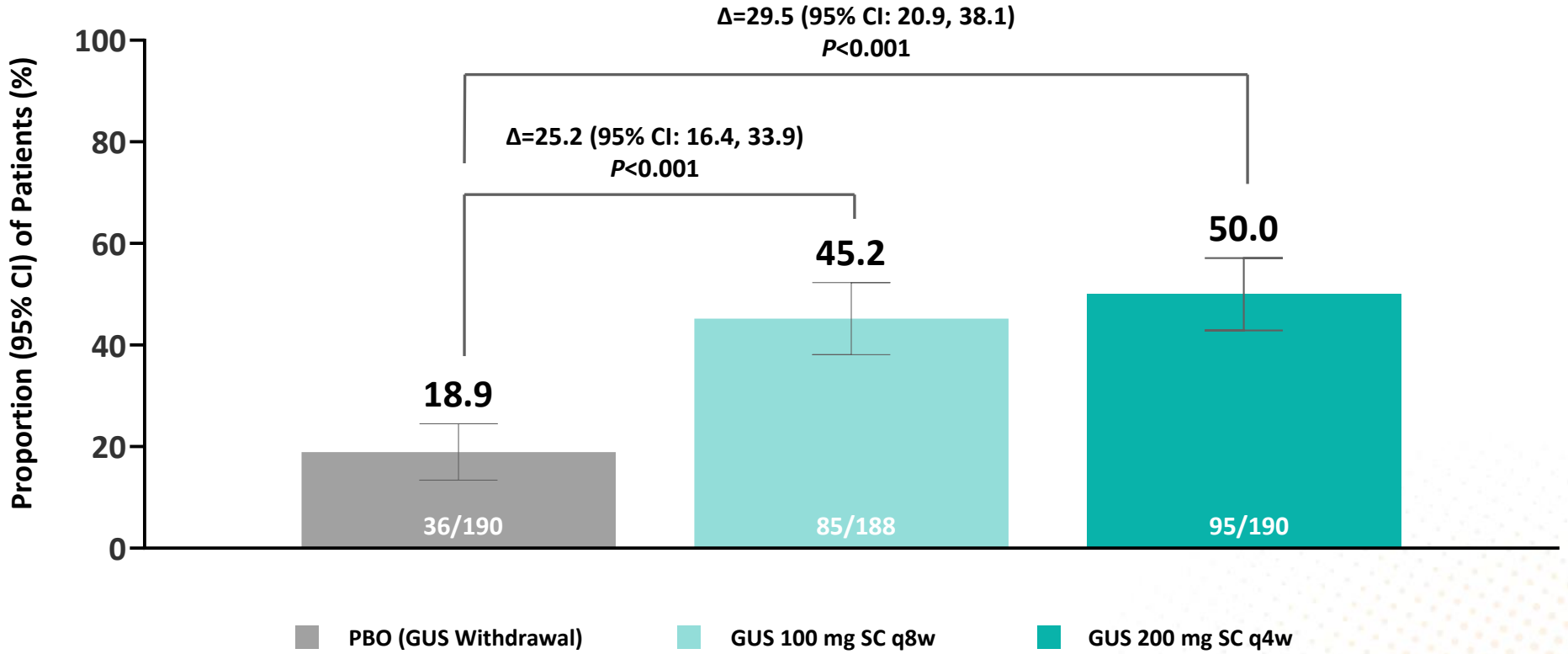
Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy
Clinical response: A decrease from baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1

Primary analysis population: Treated patients with modified Mayo score 5-9 at induction baseline.
Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.

AIBD REGIONALS

QUASAR: Guselkumab for UC – Phase 3, Maintenance

Primary Endpoint: Clinical Remission at Week 44

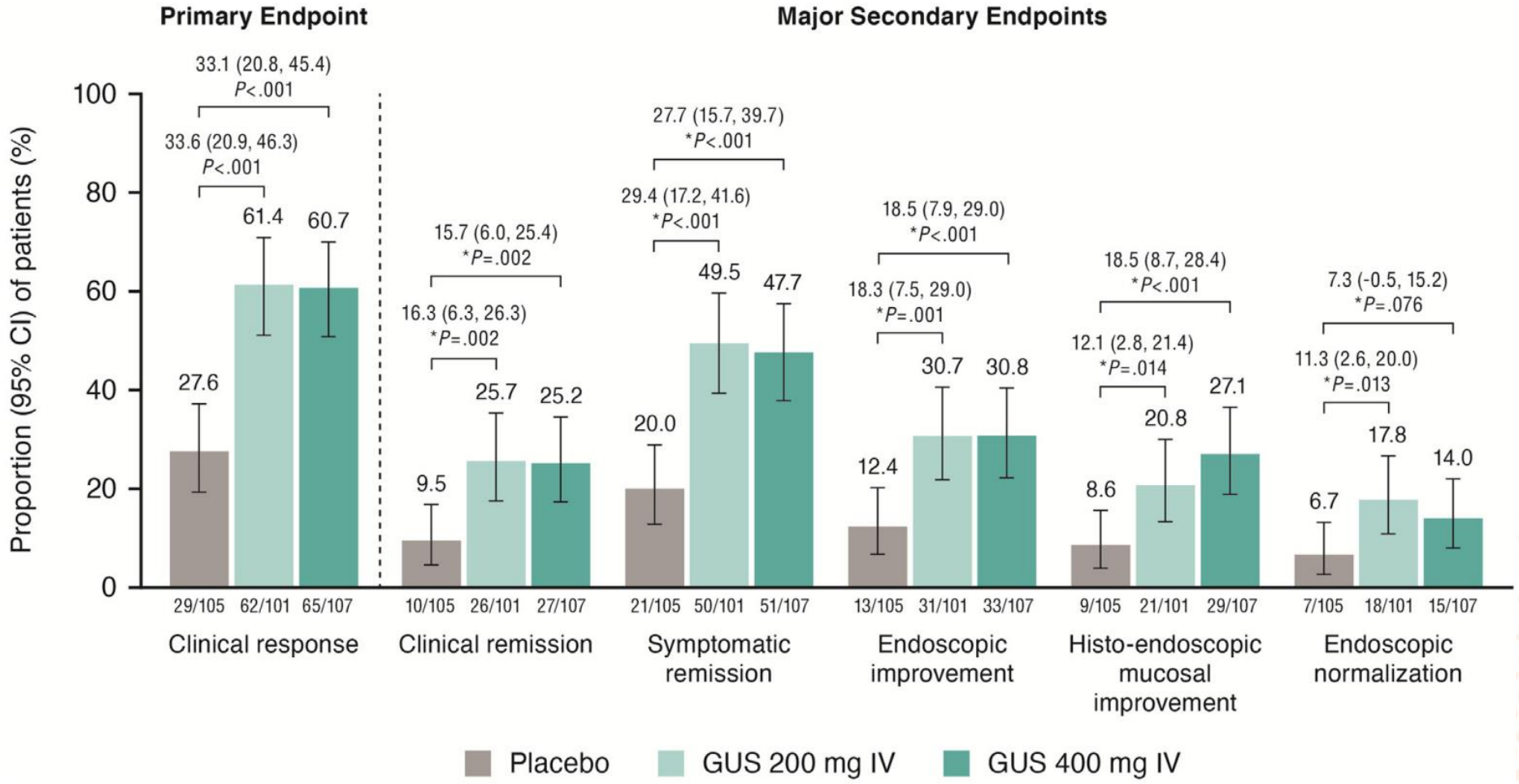


69% of GUS-treated patients in clinical remission were also in endoscopic remission (MES=0)

Randomized full analysis set.
Clinical remission: A Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and Mayo endoscopic subscore (MES) of 0 or 1 with no friability present.
Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.

AIBD REGIONALS

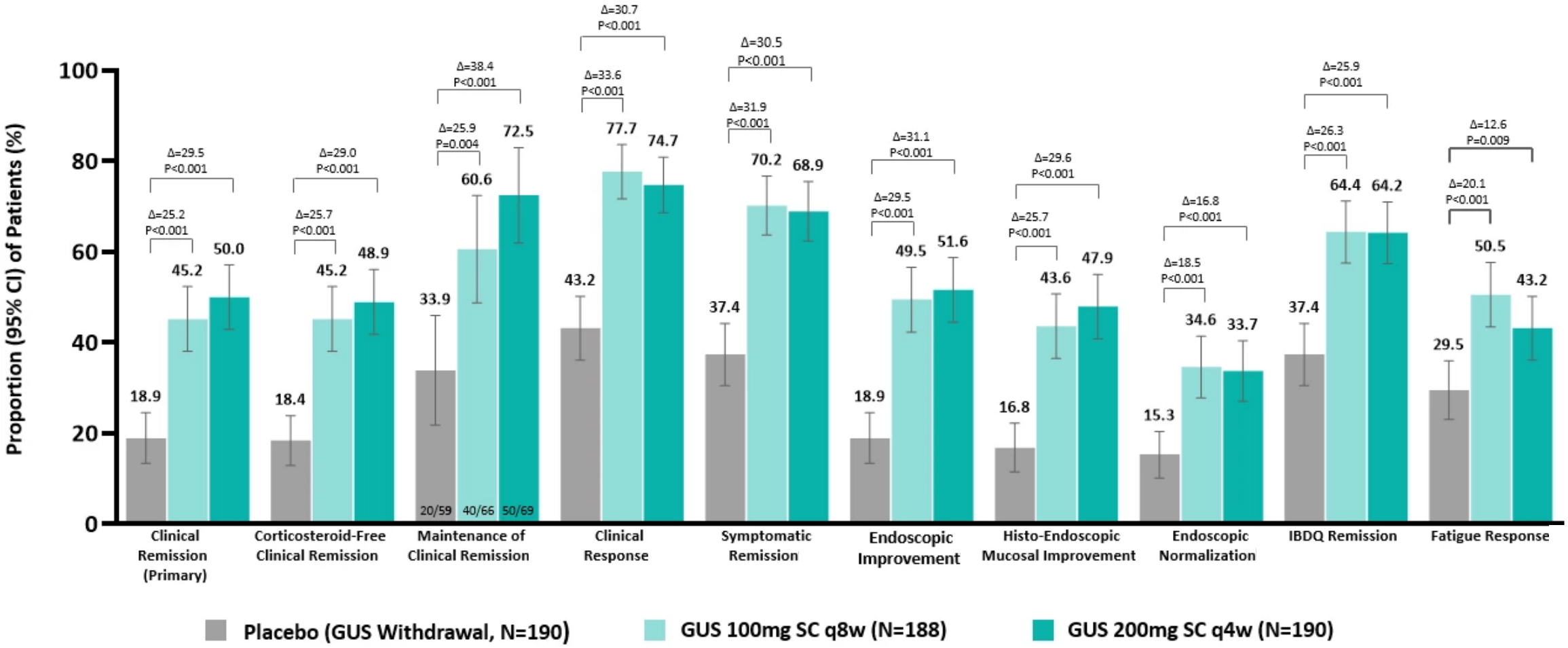
Guselkumab in UC Induction: QUASAR Week 12 Endpoints



***P*-values are nominal.**
GUS is indicated for adult patients with moderately to severely active UC.
Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.

AIBD REGIONALS

Guselkumab in UC Maintenance: QUASAR Week 44 Endpoints



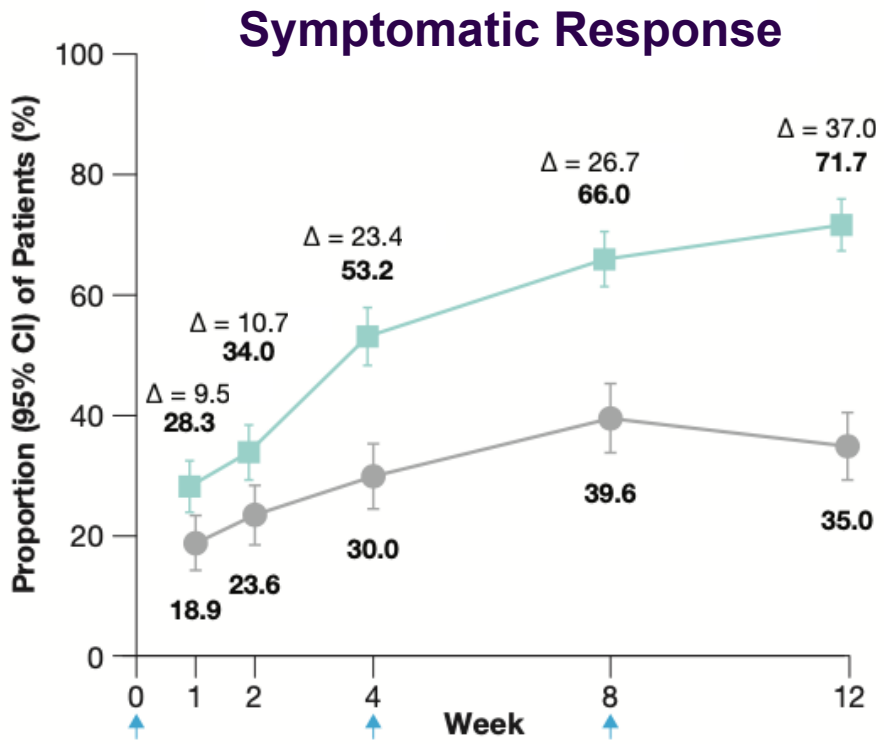
Primary Analysis Population: Randomized patients with a modified Mayo score of 5-9 at induction baseline who received at least 1 maintenance study treatment dose.

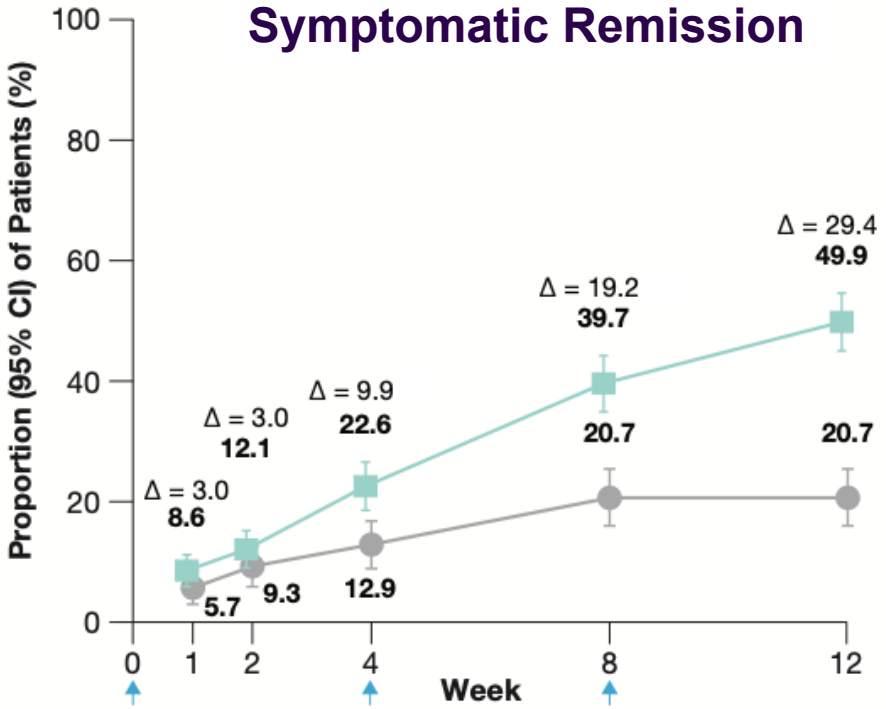
GUS is indicated for adult patients with moderately to severely active UC.

Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.

AIBD REGIONALS

Symptomatic Improvement as Early as Week 1 with Guselkumab Induction in Moderate to Severely Active UC



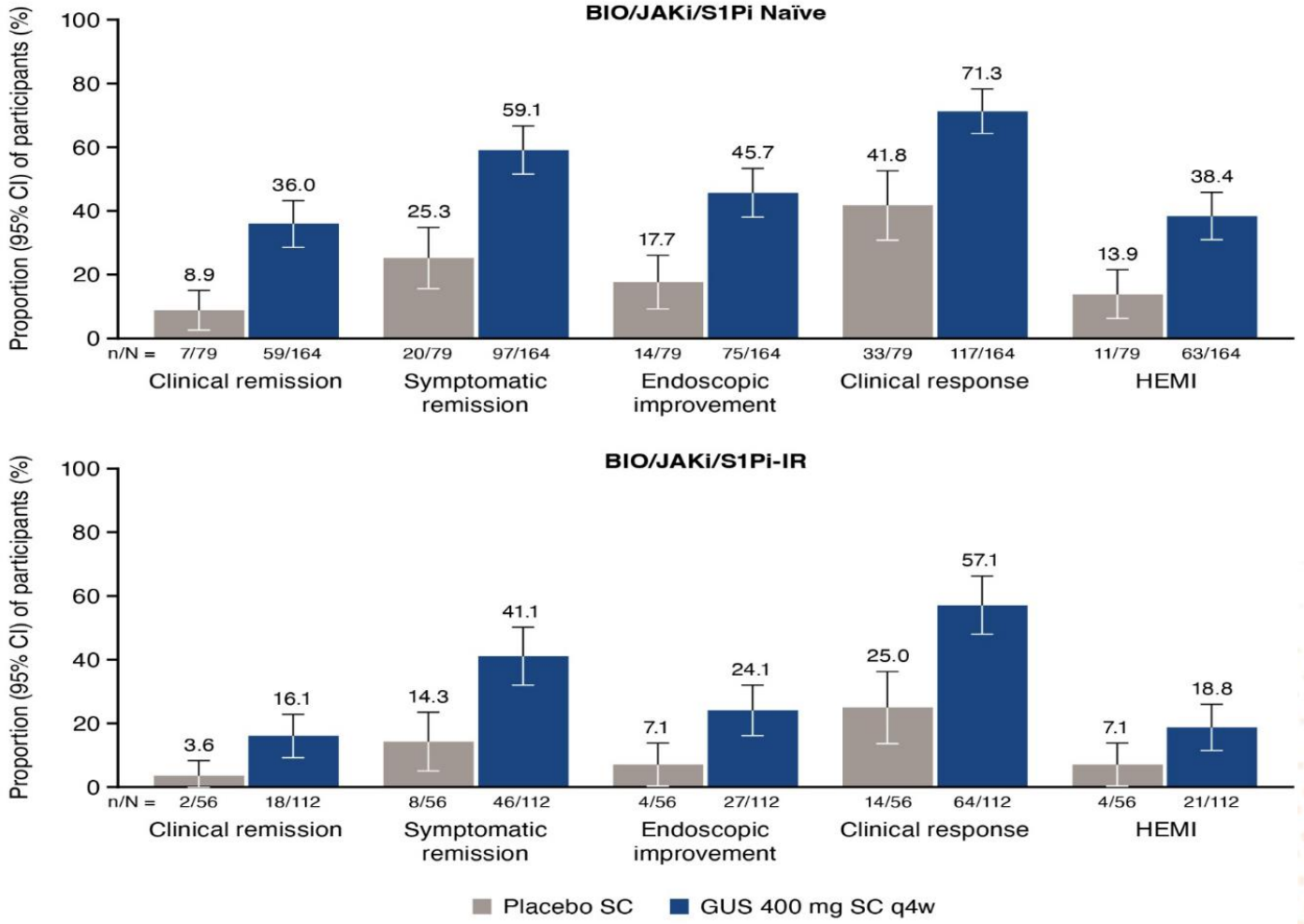


- In patients with moderately to severely active UC, guselkumab 200 mg IV induction was effective in improving symptoms as early as 1 week after the first dose
- Symptomatic improvements continued to increase through week 12 with guselkumab treatment

AIBD REGIONALS

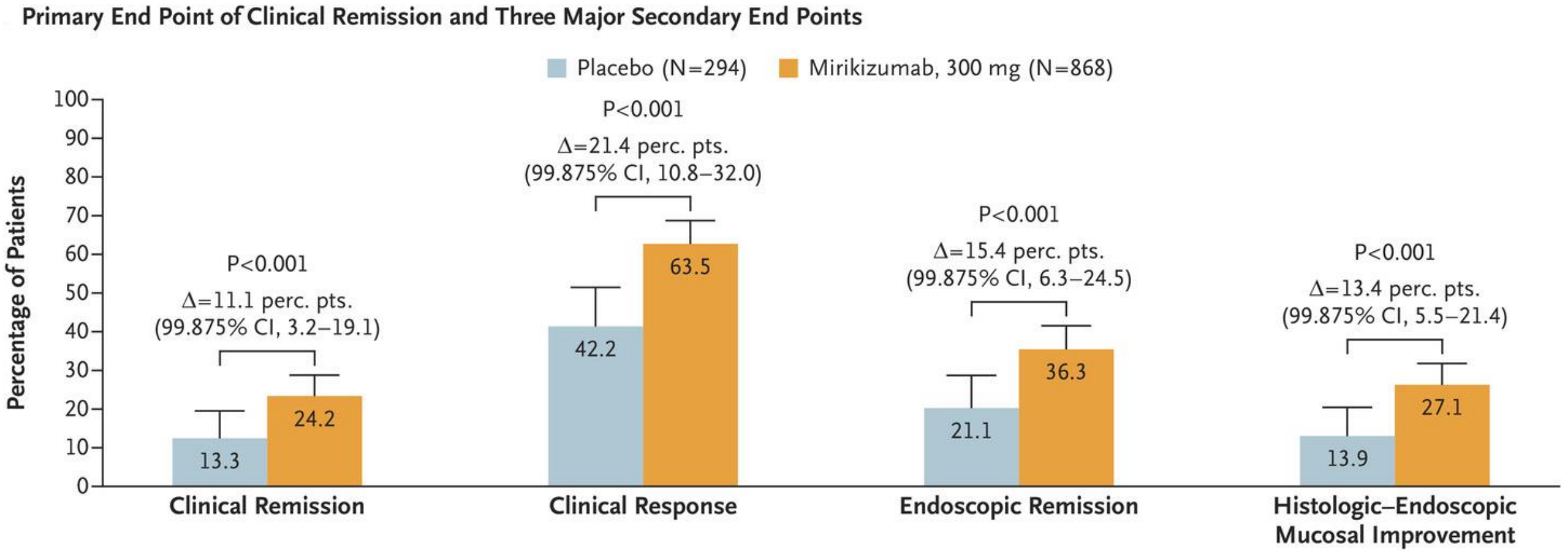
Lichtenstein GR, et al. Presented at: UEGW; October 14-17, 2023; Copenhagen, Denmark.

Guselkumab Subcutaneous Induction: ASTRO Week 12 Endpoints



Peyrin-Biroulet L, et al. Presented at: ECCO Congress; February 19-22, 2025; Berlin, Germany.

Mirikizumab in UC Induction: LUCENT-1

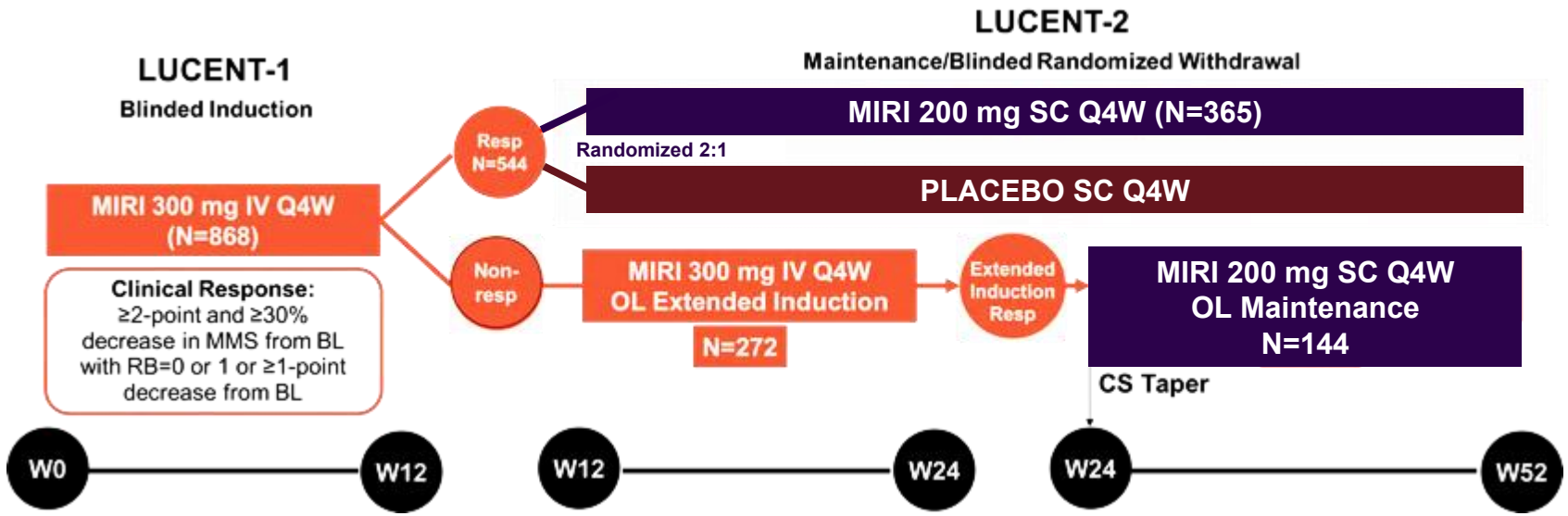


Mirikizumab is indicated for the treatment of moderately to severely active ulcerative colitis in adult patients.

D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

AIBD REGIONALS

LUCENT Trial Design (Mirikizumab in UC)



- MIRI responders in LUCENT-1= 551/868 (63.5%); 544 entered LUCENT-2
- MIRI extended induction responders who achieved clinical response at W24 in LUCENT-2=146; 144 continued with SC maintenance

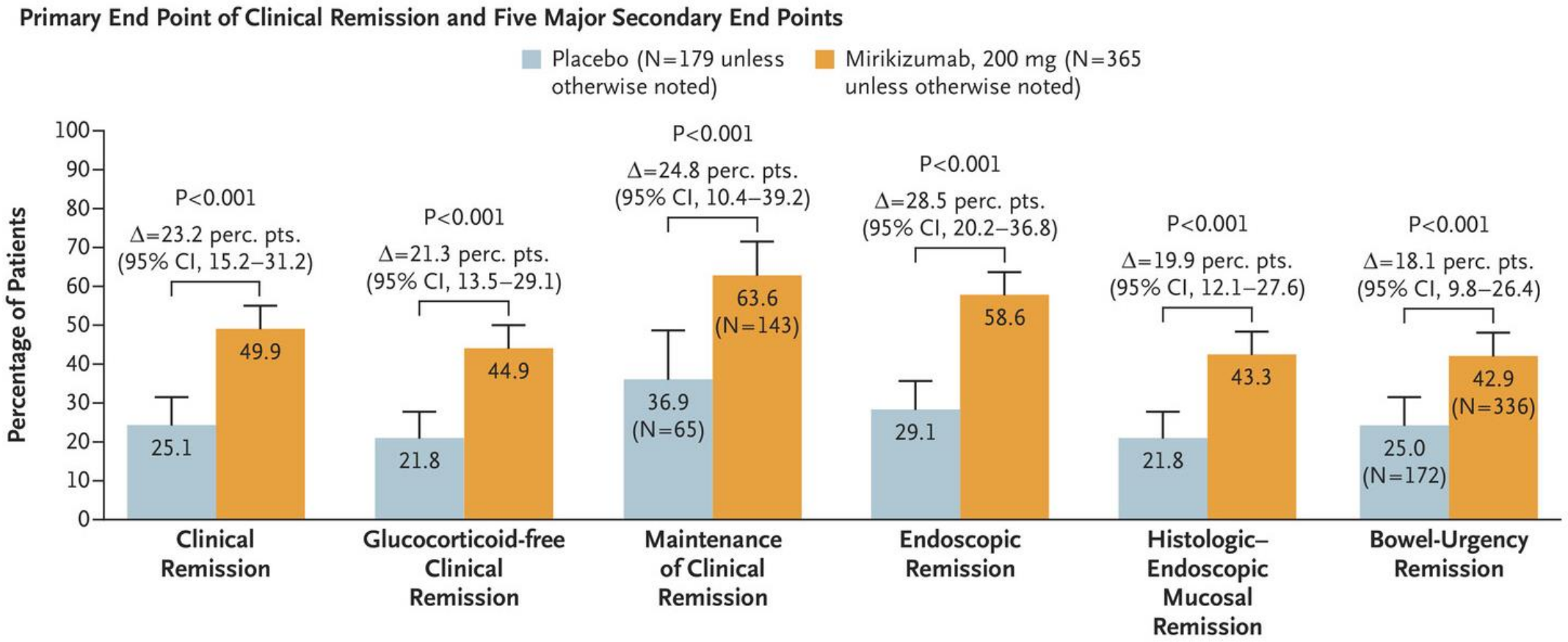
- To assess response over time during extended induction among clinical non-responders who received extended induction with mirikizumab for an additional 12 weeks
- In LUCENT-1, patients (N=1281) were randomly assigned 3:1 to receive mirikizumab 300 mg or placebo IV at W0, W4, and W8
- Patients not achieving clinical response with mirikizumab 300 mg IV at W12 of LUCENT-1 (n=272) received extended induction treatment with open-label mirikizumab 300 mg IV at W12, W16, and W20 (LUCENT-2)

BL = baseline; OL = open-label; CS = corticosteroid.

Rubin DT, et al. Presented at: UEGW; October 12-15, 2024; Vienna, Austria. Laharie D, et al. Presented at: UEGW; October 12-15, 2024; Vienna, Austria.

AIBD REGIONALS

Mirikizumab in UC Maintenance: LUCENT-2 Week 40 Endpoints



Clinical remission: Stool frequency (SF) = 0, or SF = 1 with a ≥1-point decrease from baseline; rectal bleeding (RB) = 0; endoscopic subscore (ES) = 0 or 1 (excluding friability), endoscopic remission: ES = 0 or 1 (excluding friability), clinical remission at week 40, remission of symptoms at week 28, and no glucocorticoid use for ≥12 weeks before week 40. Mirikizumab is indicated for the treatment of moderately to severely active ulcerative colitis in adult patients.

D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

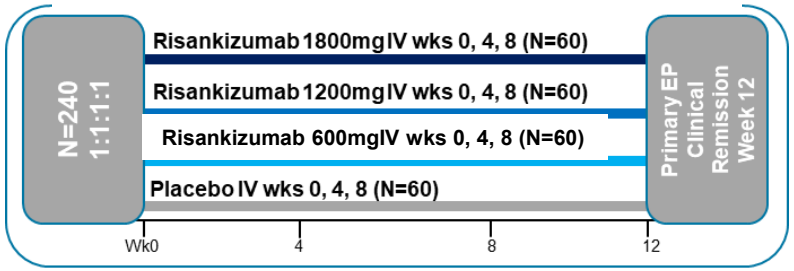
AIBD REGIONALS

Risankizumab UC Phase 3 Registrational Program
Single Induction and Re-Randomized Responder Maintenance

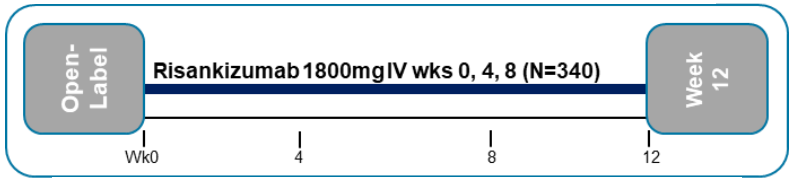
Operationally Seamless Ph 2b/3 Induction Study Enrolled Sequentially

Enrollment

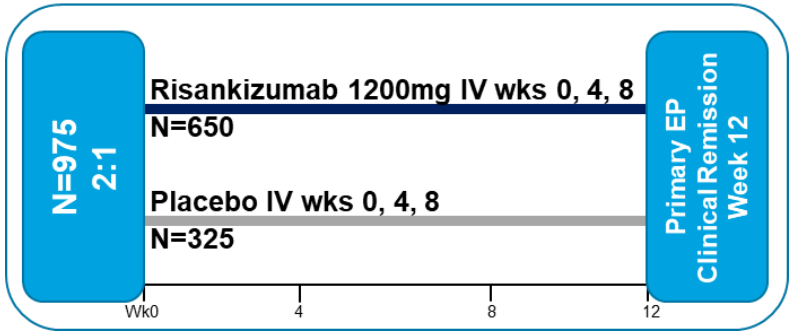
INSPIRE Ph2b Dose Ranging



INSPIRE Ph2b OL Induction

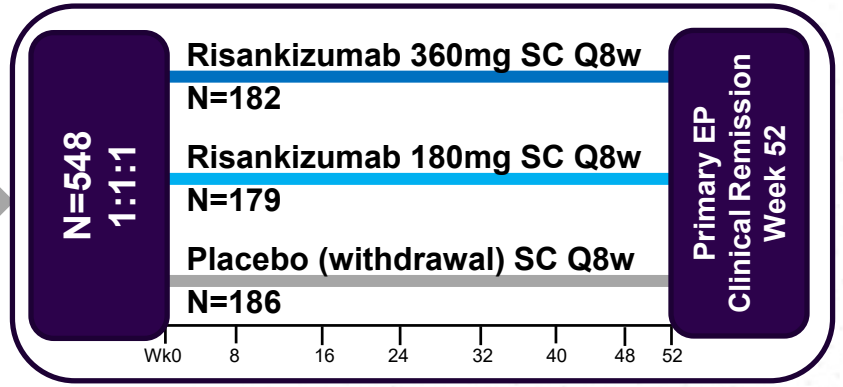


INSPIRE Ph3 Induction



Clinical response to 12 weeks risankizumab IV

COMMAND Ph3 Maintenance

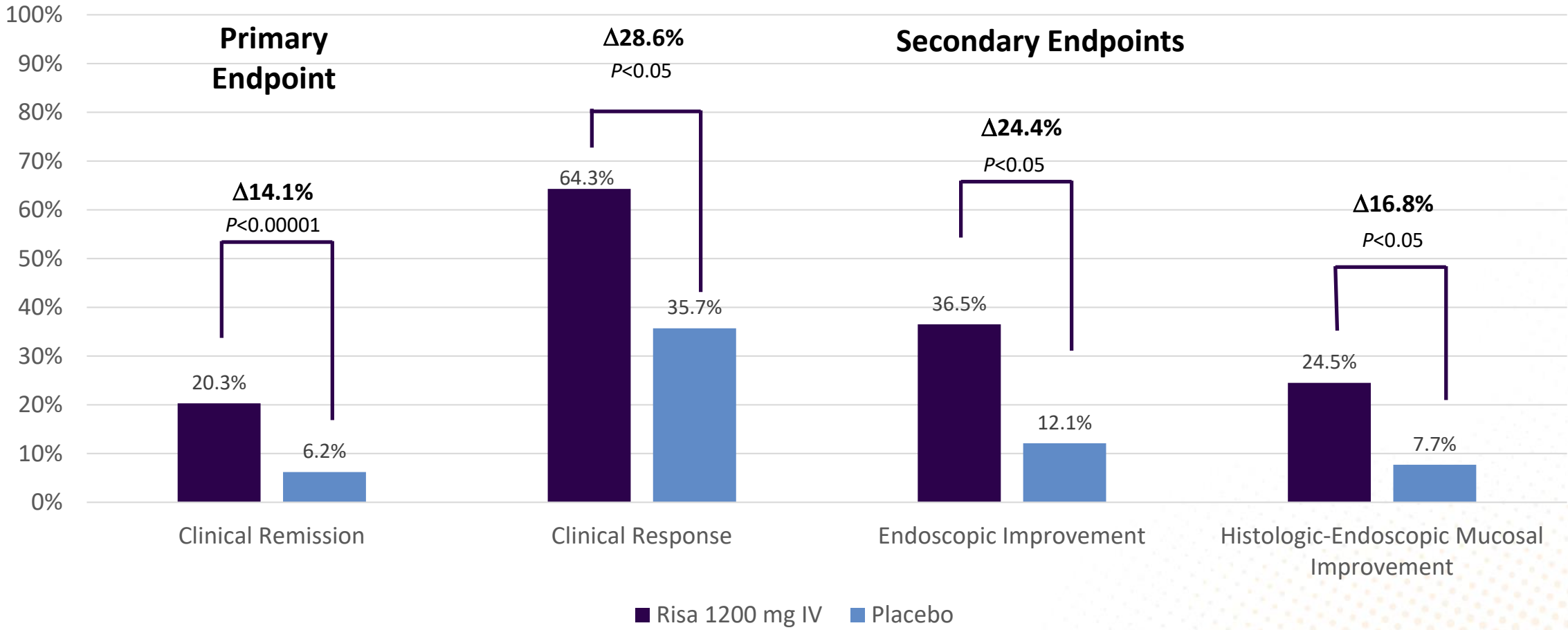


UC = ulcerative colitis.

Louis E, et al. *JAMA*. 2024;332(11):881-897.

AIBD REGIONALS

Risankizumab for Ulcerative Colitis: INSPIRE (Phase 3) Week 12 Induction

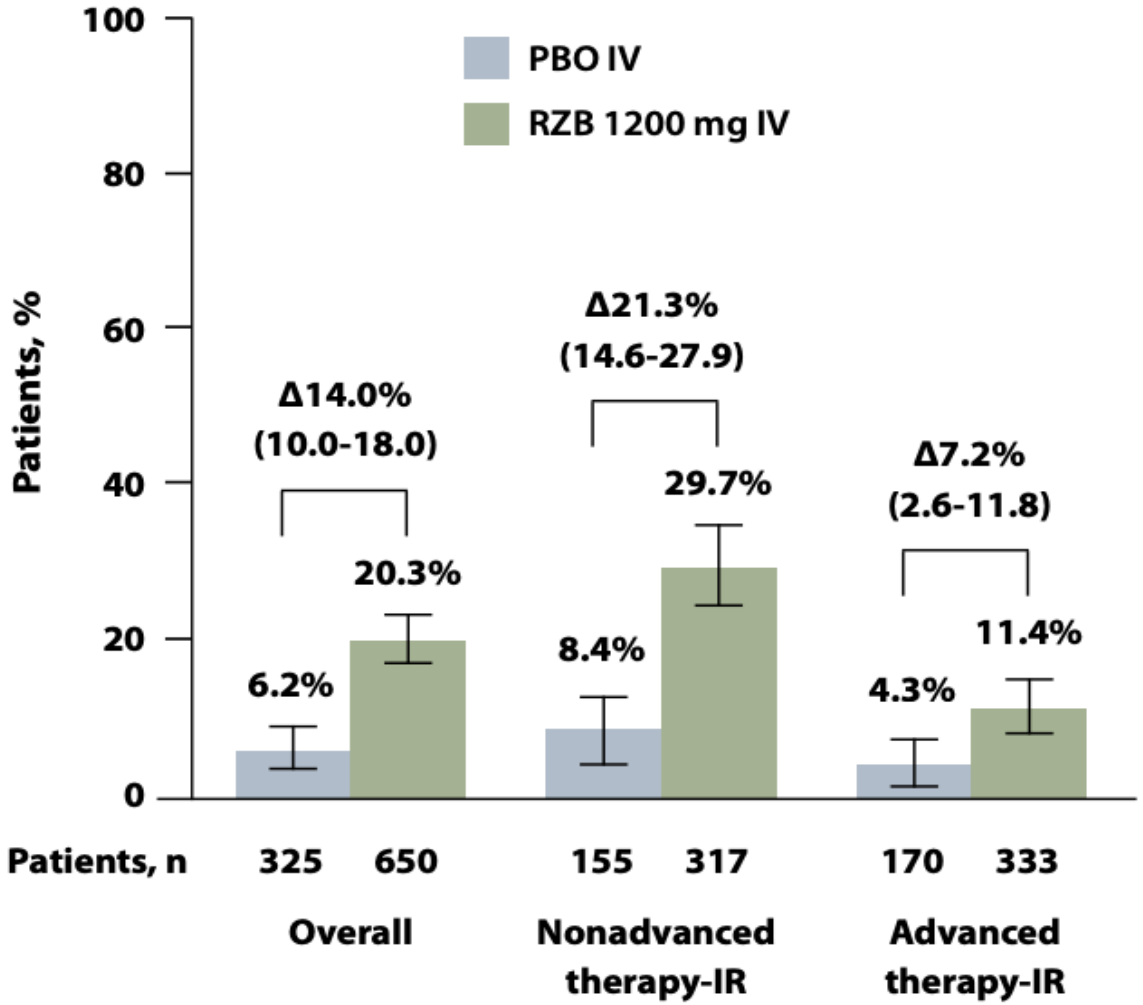


[a]Clinical remission per adapted Mayo score is defined as stool frequency subscore (SFS) ≤1 and not greater than baseline, rectal bleeding subscore (RBS) of 0, and endoscopic subscore ≤1 without friability; [b]Clinical response per adapted Mayo score is defined as a decrease from baseline in the adapted Mayo score ≥2 points and ≥30% from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1; [c]Endoscopic improvement is defined as endoscopic subscore ≤1 without friability; [d]Histologic-endoscopic mucosal improvement is defined as Geboes score ≤3.1 and endoscopic subscore ≤1 without friability.

Louis E, et al. *JAMA*. 2024;332(11):881-897.

AIBD REGIONALS

Risankizumab Induction in UC – INSPIRE
Clinical Remission at Week 12: Based on Advanced Therapy Exposure

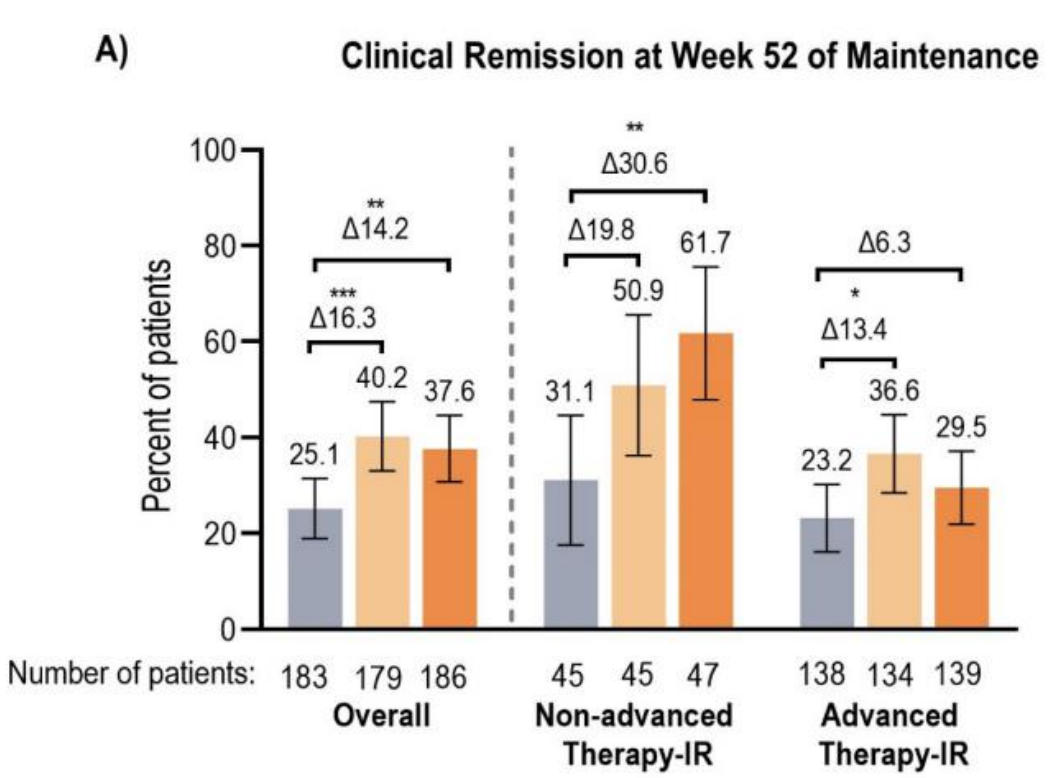


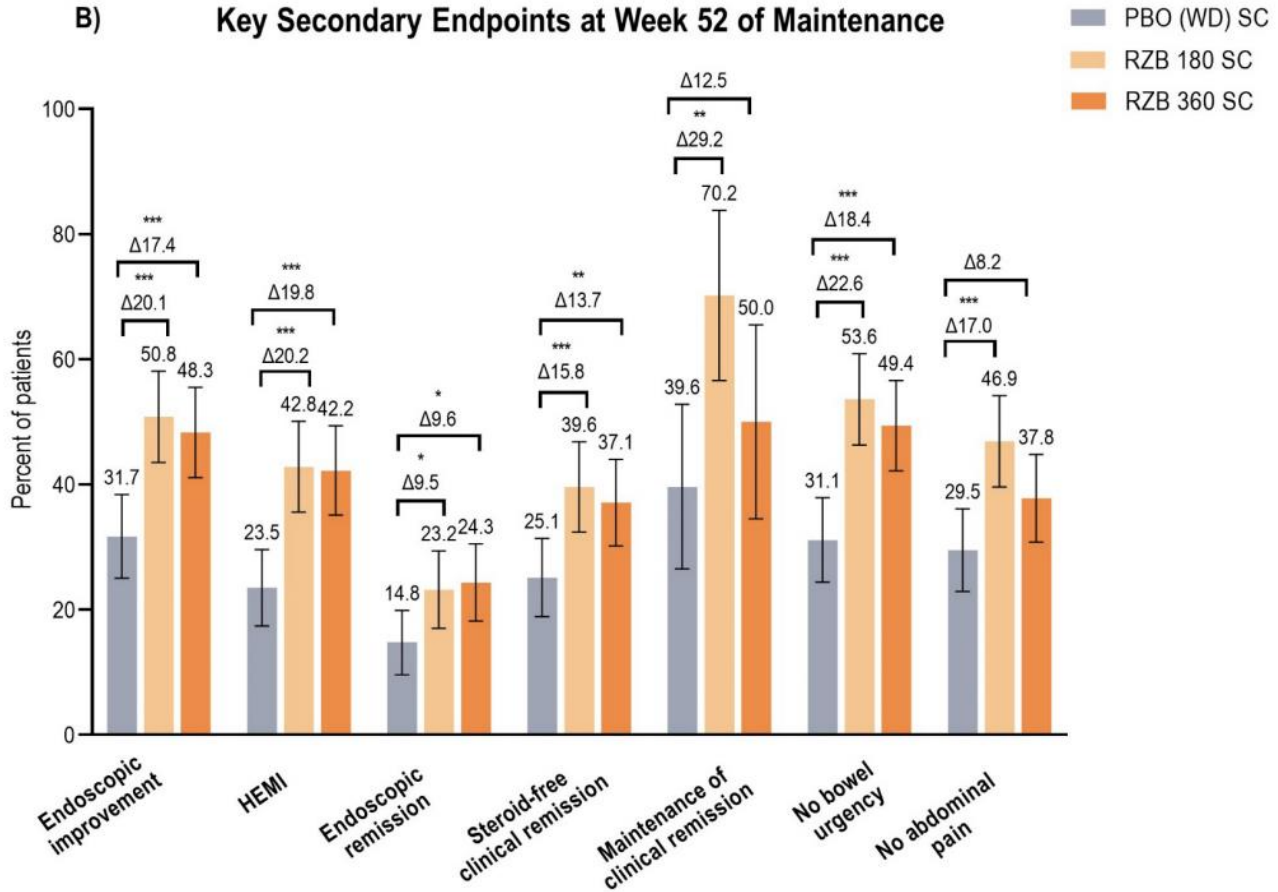
Risankizumab is indicated for the treatment of moderately to severely active UC and CD in adult patients.
Clinical remission in UC is defined as stool frequency subscore ≤1 and not greater than baseline, rectal bleeding subscore of 0, and endoscopic subscore ≤1 without friability.

Gastroenterol Hepatol (NY). 2023;19(12 Suppl 9):9-10.

AIBD REGIONALS

Risankizumab Maintenance in UC – COMMAND





***P≤0.05; **P≤0.01; ***P≤0.001 vs PBO (WD).**
Risankizumab is indicated for the treatment of moderately to severely active UC and CD in adult patients.
WD = withdrawal; HEMI = histologic-endoscopic mucosal improvement.
Louis E, et al. *JAMA*. 2024;332(11):881-897.

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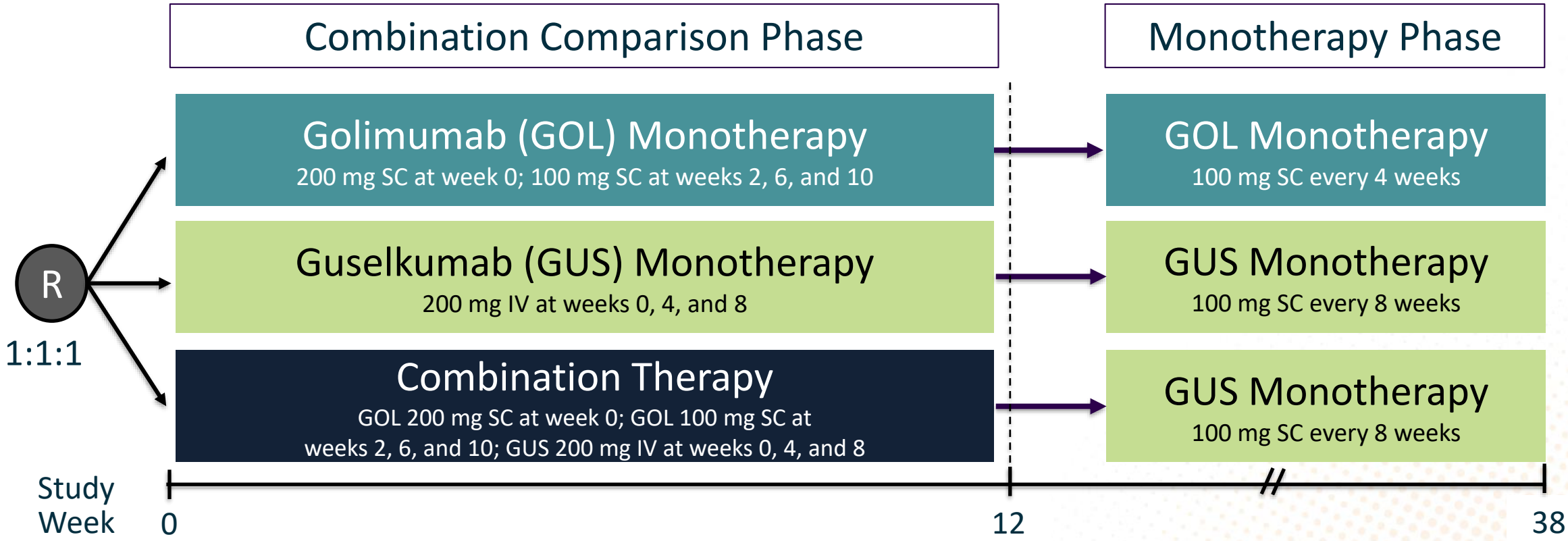
Combination Therapies

VEGA: Golimumab, Guselkumab, or Combination Therapy in UC

- Included TNF-naïve patients refractory to conventional therapy (eg, immunomodulators, corticosteroids)

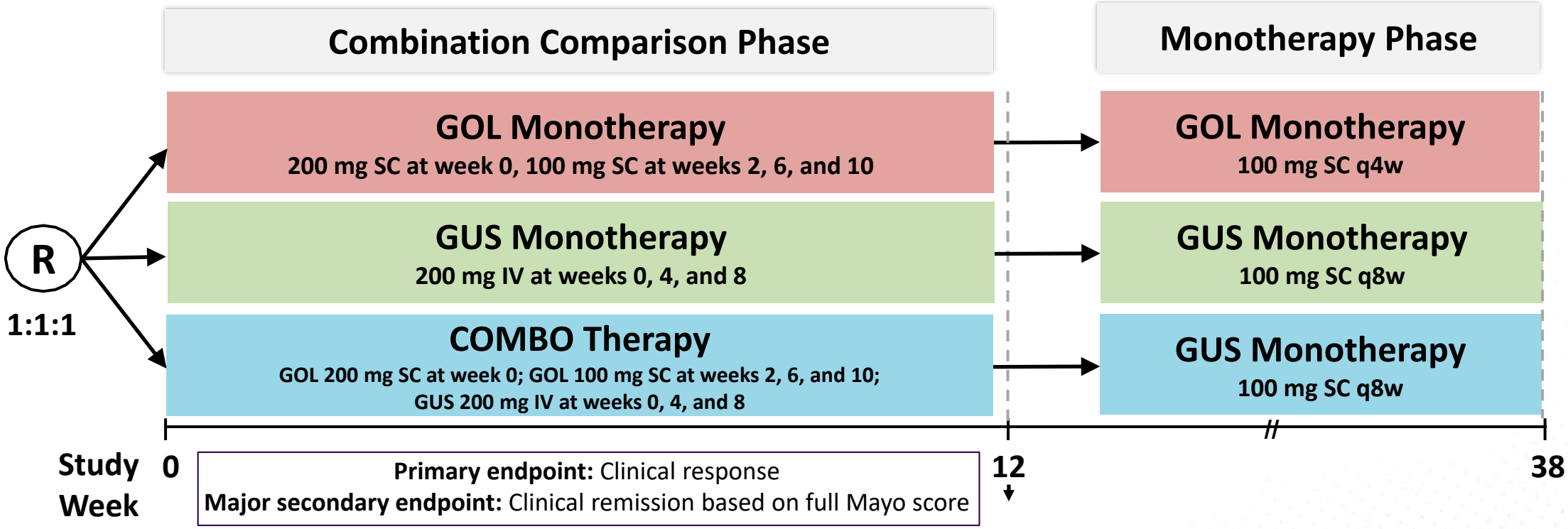


***Guselkumab is not FDA-approved for the treatment of UC.**

Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

AIBD REGIONALS

VEGA: GUS + GOL vs GUS vs GOL in Moderate to Severely Active Ulcerative Colitis



Patient Population

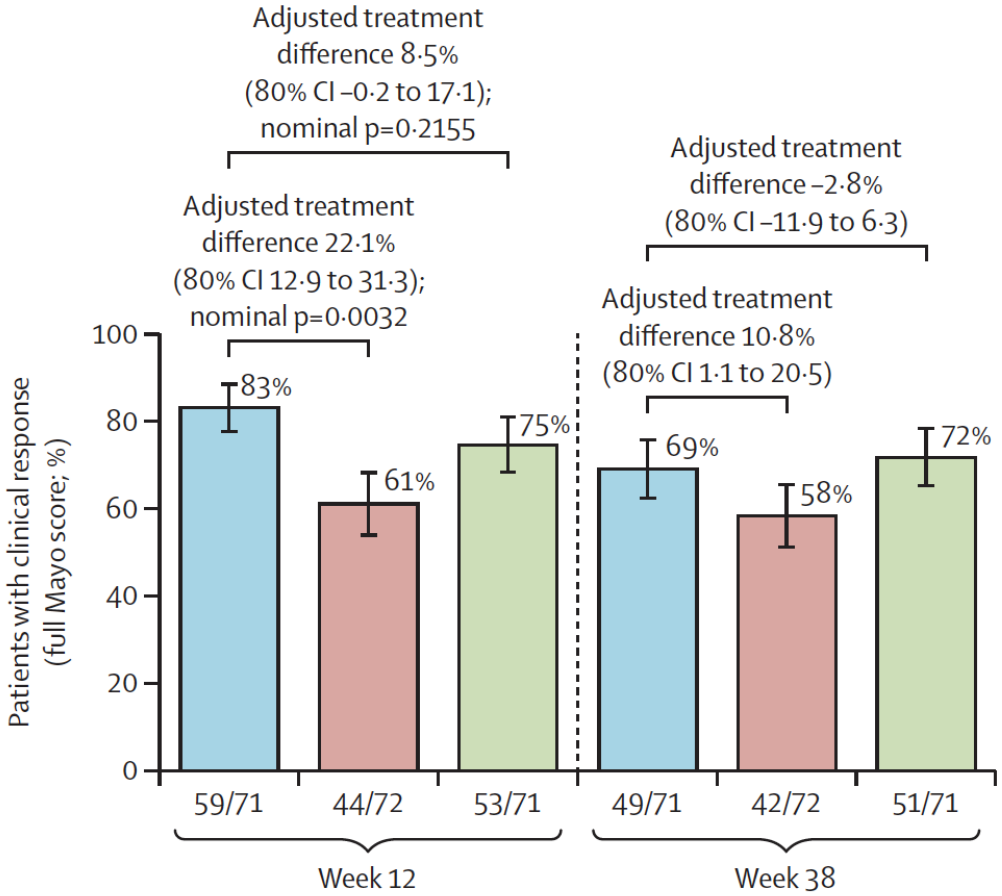
- Moderately-to-severely active UC (Mayo score 6-12, inclusive, and an endoscopy subscore ≥2 by central review)
- Naïve to TNFα antagonists and have had an inadequate response or intolerance to conventional therapy (immunosuppressants [AZA, 6-MP] and/or corticosteroids)
- Immunosuppressants must have been discontinued prior to randomization
- Corticosteroids up to a dose of prednisone (or equivalent) of 20 mg/day permitted with mandatory tapering beginning at week 6

Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

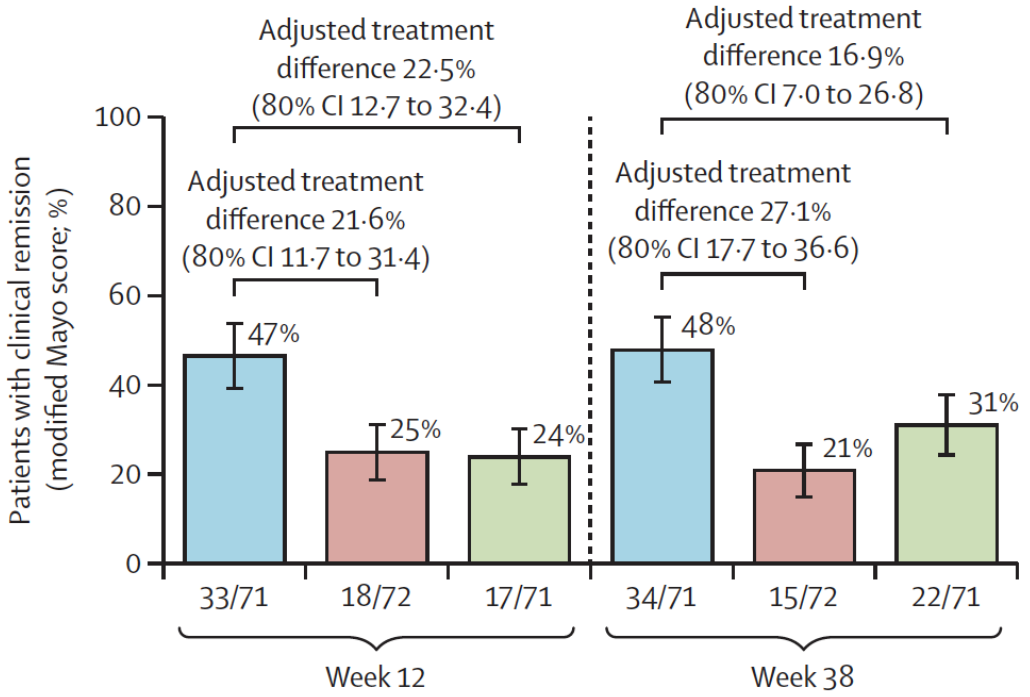
AIBD REGIONALS

Guselkumab plus Golimumab vs Guselkumab or Golimumab Monotherapy in Moderate to Severe UC

Primary Endpoint
Clinical Response



Major Secondary Endpoints
Clinical Remission (Modified Mayo Score)



Combination therapy | Golimumab monotherapy | Guselkumab monotherapy

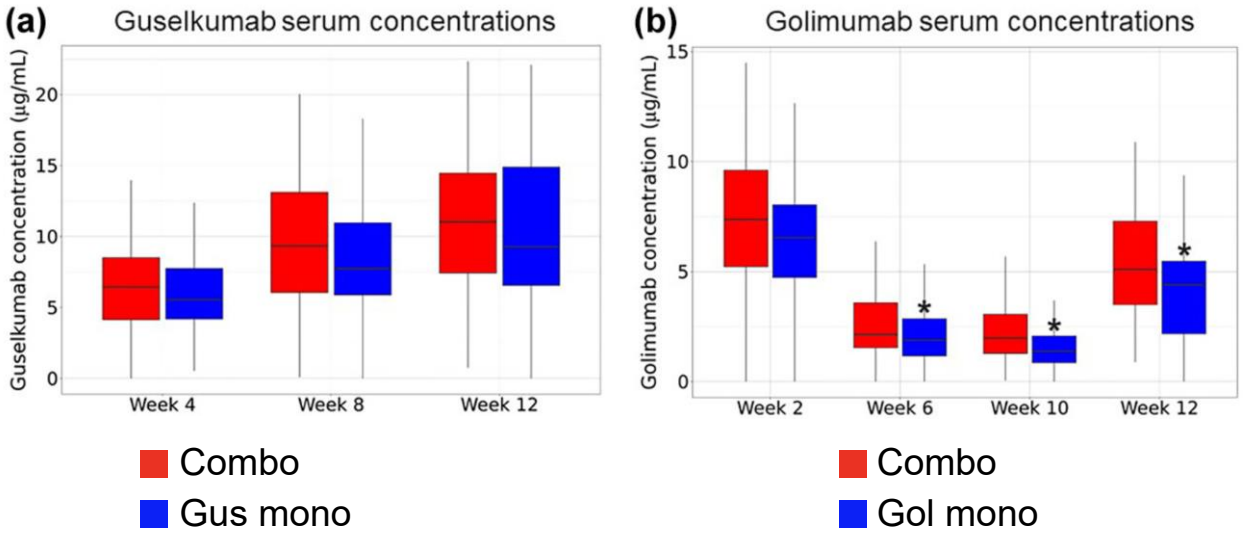
Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

AIBD REGIONALS

Post-Hoc Analysis of Immunogenicity of Guselkumab and Golimumab in Combination Therapy and Individual Monotherapies in Patients with UC (VEGA)

Serum golimumab concentrations with combination therapy were higher than with golimumab monotherapy, likely due to lower immunogenicity

Serum concentrations of guselkumab (a) and golimumab (b) at trough and primary endpoint visits in monotherapy and combination therapy



	Anti-Guselkumab Antibodies n (%)		Anti-Golimumab Antibodies n (%)	
Treatment Groups	**Guselkumab Monotherapy**	**Combination → Guselkumab Monotherapy**	**Golimumab Monotherapy**	**Combination → Guselkumab Monotherapy**
Through Week 12	0 (0)	5 (7.0)	18 (25.4)	4 (5.6)
Through Week 38	5 (7.1)	8 (11.3)	30 (42.3)	46 (64.8)

Shao J, et al. *Clin Pharmacol Ther*. 2024;115(6):1418-1427.

AIBD REGIONALS

Combination Ustekinumab and Upadacitinib in Refractory Crohn's Disease and for Patients with Co-Existing EIMs

Case Series (U Chicago)

Baseline characteristics of included patients with Crohn's disease, n=10

Case	Age	Sex	Montreal classification	Surgical history	Previous biologics exposure	EIM
1	40	F	A2L3B1	No	IFX, ADA, CER, UST	Joint pain
2	57	M	A2L1B2,3p	Yes	IFX, ADA, NAT, UST, VDZ	Joint pain
3	35	F	A2L3B2,3p	Yes (ileostomy)	IFX, ADA, NAT, UST, VDZ	No
4	45	F	A2L3B3	Yes (ileostomy)	IFX, ADA, UST	No
5	35	F	A1L3B2,3p	Yes	IFX, ADA, UST, VDZ	No
6	36	F	A1L3,4B2p	Yes	IFX, ADA, CER, NAT, UST, VDZ	No
7	20	M	A1L3B1	No	IFX, ADA, UST, VDZ	PsA
8	23	F	A2L3B1	No	IFX, ADA, UST, VDZ	No
9	26	M	A1L3B1p	Yes	IFX, ADA, GLM, NAT, UST, VDZ	SpA
10	52	M	A2L14B2,3p	Yes	IFX, ADA, NAT, UST	Joint pain

Efficacy and safety outcomes of combination therapy with ustekinumab and upadacitinib

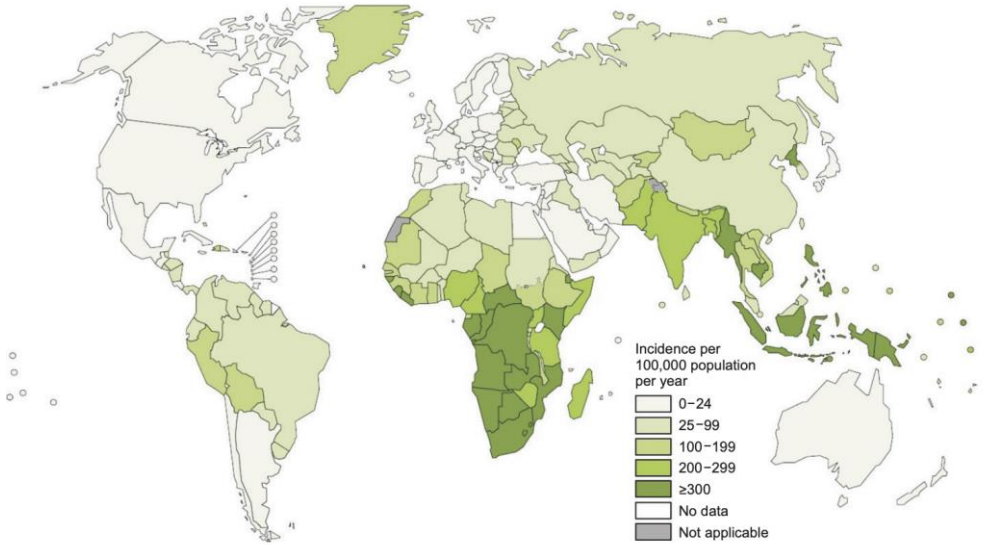
Case	Outcome at 3–6 months	Steroid-Free after DTT	Adverse effect	Follow-up period (months)	Continue DTT
1	Joint pain improved	Yes	None	12	Yes
2	Joint pain improved	N.A	Nausea	2	Yes[†]
3	Clinical remission	N.A	None	12	Yes
4	Clinical remission	Yes	SBO	4	Yes
5	Perianal fistula closed	N.A	Sinusitis	17	Yes
6	Clinical response	N.A	URI	7	Yes
7	Clinical remission, Joint pain improved	N.A	URI	9	Yes
8	Clinical remission	N.A	Acne	11	Yes
9	Clinical remission	Yes	None	17	Yes
10	N.A.[*]	No	Nausea, cutaneous fungal infection	8	No

EIMs = extraintestinal manifestations; DTT = dual-targeted therapy; SBO = small bowel obstruction; URI = upper respiratory infection.

Miyatani Y, et al. *Dig Dis Sci*. 2024;69(2):355-359.

AIBD REGIONALS

Safety



No Risk of TB Reactivation with Ustekinumab

Table 2: Non-anti-TNF-targeted biologics: reported TB cases from national registries and postmarketing surveillance.

Biologic	Country; patient N°	TB cases	IR	Expected IR/100/year (WHO)	Reference
Tocilizumab	Japan; 3881	4	0.22	15–100	[116]
	Japan; 302	0	0	15–100	[115]
Rituximab	France; 1303	0	0	10–24	[142]
	Germany; 370	0	0	10–24	[143]
	Germany; 2484	1	0.12	10–24	[145]
	Greece; 234	0	0	10–24	[144]
	Taiwan; 763	2	0.38	15–100	[140]
Abatacept	France; 682	0	0	10–24	[171]
	Japan; 231	0	0	15–100	[172]
Ustekinumab	Worldwide; 3474	0	0	NA	[180]
Secukinumab	Unavailable data	NA	NA	NA	NA

WHO: World Health Organization-estimated incidence of TB, 2016; NA: not applicable.

TB = tuberculosis; IR = immune response.

Banerjee R, et al. *Gut Liver*. 2020;14(6):685-698. Cantini F, et al. *Mediators Inflamm*. 2017;2017:8909834.

AIBD REGIONALS

Safety Summary for IL-23: Meta-Analysis in UC

- Targeting IL-23 was linked with a reduced risk of any adverse events during both induction [RR: 0.94, 95% CI (0.86-1.02)] and maintenance phases [RR: 0.93, 95% CI (0.86-0.99)]
- Any serious AE during the induction phase [RR: 0.53, 95% CI (0.36-0.78)]
- Withdrawal due to AEs compared to patients receiving placebo during induction [RR: 0.24, 95% CI (0.14, 0.43)]

RR = risk ratio.

Jaber F, et al. *Am J Ther*. 2025;32(1):e17-e29.

AIBD REGIONALS

Key Learning Points: The IL-23 Revolution

- **Guselkumab (UC and CD)**
  - SC and IV induction for CD, superior to UST
  - SC induction for UC to come
- **Mirikizumab (UC and CD)**
  - Note different dosing for UC and CD: Induction dose UC 300 mg vs CD 900 mg
  - Mirikizumab not superior to UST as it relates to endoscopic outcomes in CD
- **Risankizumab (UC and CD)**
  - Note different dosing for UC and CD: Induction dose UC 1200 mg vs CD 600 mg
  - SEQUENCE demonstrated superiority to UST after anti-TNF
- **Combination IL-23**
  - TNF or Janus kinase (JAK) 1 promising as future options
- **All 3 comparable safety profiles**

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