

Efficacy and Safety of Guselkumab Maintenance Therapy in Patients With Moderately to Severely Active Crohn's Disease: Results Through Week 144 From the Phase 3 GALAXI 2 & 3 Studies

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Disclosure of Conflicts of Interest

I, Silvio Danese, declare the following activities: consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Entera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity, Takeda, TiGenix, UCB and Vifor; and lecture fees from AbbVie, Amgen, Ferring, Gilead, Janssen, Mylan, Pfizer and Takeda.

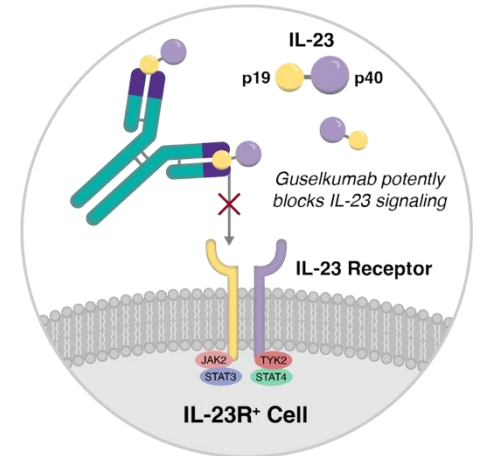
Background and Objective

Guselkumab is a dual-acting IL-23p19 subunit inhibitor that is approved for the treatment of moderately to severely active Crohn's disease

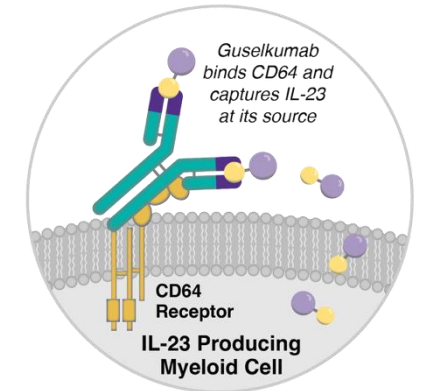
Guselkumab potentially blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23¹

The phase 3 GALAXI 2 & 3 (NCT03466411) studies evaluated guselkumab in participants with moderately to severely active Crohn's disease²

Objective: Here, we present the long-term efficacy and safety of guselkumab through Week 144 from the pooled GALAXI 2 & 3 long-term extension (LTE)



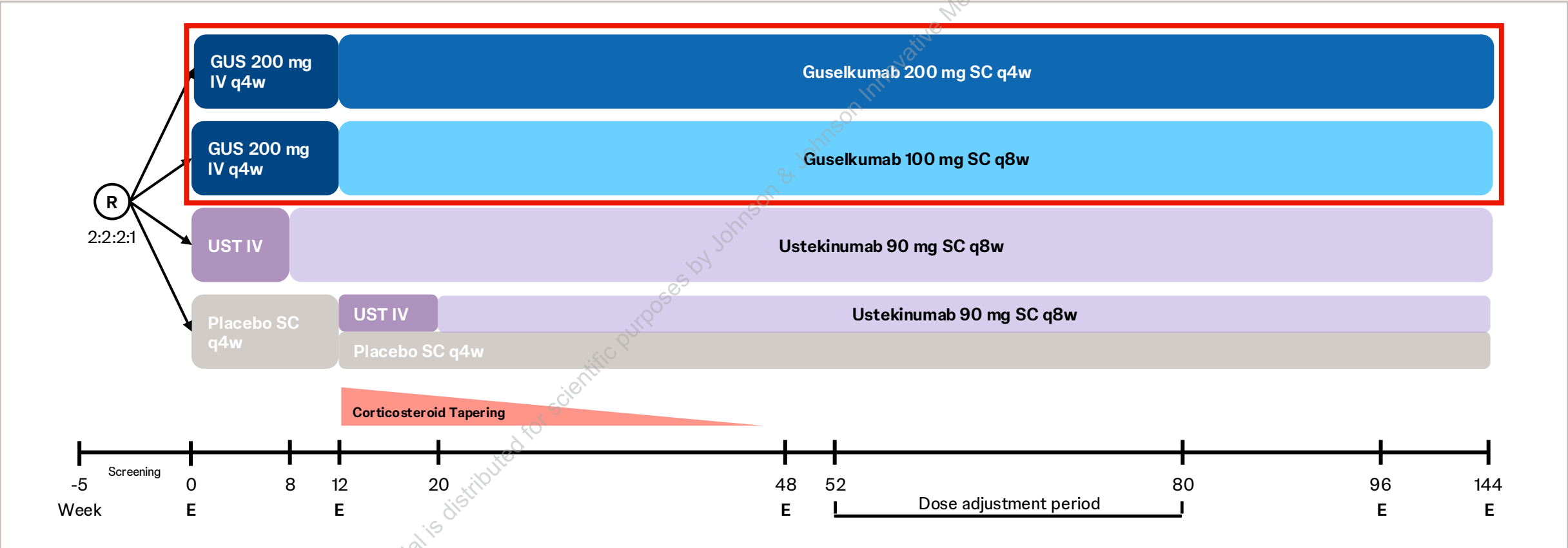
Dual-acting IL-23 Inhibitor



GALAXI 2 & 3 Study Designs Through Week 144

Key eligibility criteria: Moderately to severely active Crohn's disease (CDAI score 220–450 AND either mean daily SF >3 OR AP >1) and SES-CD score ≥6 (or ≥4 for isolated ileal disease), and inadequate response/intolerance to oral corticosteroids, 6-MP/AZA/MTX, or biologic therapies^a

Randomization stratified by: CDAI score (≤300 or >300), SES-CD (≤12 or >12), prior BIO-IR status (Yes/No), and corticosteroid use at baseline (Yes/No)



AP= abdominal pain; BIO= biologic; CDAI= Crohn's disease activity index; E= endoscopy; GUS= guselkumab; IR= inadequate response/intolerance; IV= intravenous; R= randomization; SC= subcutaneous; SES-CD= simple endoscopic score for Crohn's disease; SF= stool frequency; TNF= tumor necrosis factor; UST= ustekinumab.

^a Biologic therapies: TNF antagonists or vedolizumab.

Note: GALAXI 2 & 3 were not designed to compare guselkumab with ustekinumab beyond Week 48; blinding held through the Week 48 analysis and database lock. Participants treated with placebo during the LTE were discontinued after study unblinding. The full study designs can be found in primary trial publication.

Endpoints and Analysis Populations

Endpoints

Clinical endpoints

- **Clinical remission:** CDAI score <150
- **90-day corticosteroid-free clinical remission**

Endoscopic endpoints

- **Endoscopic response:** ≥50% improvement from baseline in SES-CD or SES-CD score ≤2
- **Endoscopic remission:** SES-CD score ≤4 and at least a 2-point reduction from baseline, with no subscore greater than 1 in any individual component

Analysis populations

- **Primary efficacy analysis set:** All participants randomized at baseline who received ≥1 dose of guselkumab evaluated by randomized group
- **LTE As Observed analysis:** Included participants who received ≥1 dose in the long-term extension. For participants who underwent dose adjustment, data from the day after dose adjustment onward were excluded
- **All treated safety analysis set:** All participants who received ≥1 dose of guselkumab from induction baseline through Week 144, pooled by actual treatment received

Statistical considerations

- **Primary Efficacy Analysis (non-responder imputation [NRI]):**
 - Participants with prohibited CD medication changes before Week 48, dose adjustment (including “sham”) during Weeks 52–80, or CD-related surgery or discontinuation of study intervention at any time were considered not to have met the endpoint at the designated timepoint from the point of intercurrent event
 - Missing endpoint data were imputed as non-response
- **LTE, As Observed Analysis:** no nonresponder imputation; only participants with available data and on treatment at the assessment timepoint were included in the analysis

Baseline Demographics and Disease Characteristics

Primary Efficacy Analysis Set

Primary efficacy analysis set	Guselkumab 200 mg IV → 100 mg SC q8w (N=286)	Guselkumab 200 mg IV → 200 mg SC q4w (N=296)
Demographics		
Age in years, mean (SD)	36.0 (12.24)	36.9 (13.27)
Male, n (%)	154 (53.8%)	178 (60.1%)
Characteristics		
CD duration in years, mean (SD)	7.12 (6.72)	7.07 (7.24)
CDAI score, mean (SD)	296.3 (54.27)	295.9 (52.74)
SES-CD score, mean (SD)	13.2 (7.43)	12.5 (7.24)
Endoscopic disease severity (SES-CD score), n (%)		
Moderate (7–16)	164 (57.3%)	147 (49.7%)
Severe (>16)	81 (28.3%)	79 (26.7%)
Involved disease location by central reader, n (%)		
Colon only	113 (39.5%)	112 (37.8%)
Ileum only	59 (20.6%)	80 (27.0%)
Ileum and Colon	114 (39.9%)	104 (35.1%)
Biomarkers		
C-reactive protein in mg/L, median (IQR)	7.7 (2.6; 21.8)	6.2 (2.7; 21.3)
Fecal calprotectin in µg/g, ^a median (IQR)	969.0 (404.0; 2085.0)	1045.5 (323.0; 2006.0)
Biologic medication history, n (%)		
Bonaïve	116 (40.6%)	128 (43.2%)
History of inadequate response/intolerance to biologic therapy, ^b n (%)	153 (53.5%)	147 (49.7%)
Concomitant CD medications at baseline, n (%)		
6-MP/AZA	85 (29.7%)	89 (30.1%)
MTX	2 (0.7%)	7 (2.4%)
Oral corticosteroids	109 (38.1%)	106 (35.8%)

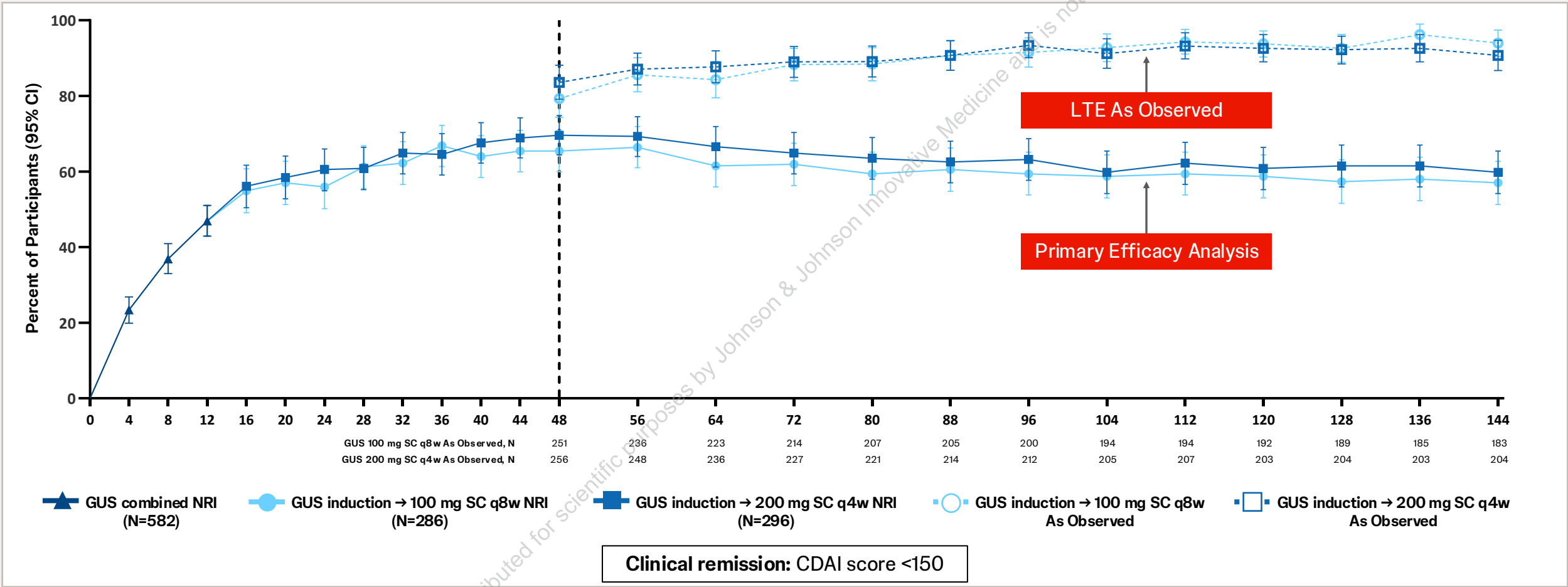
Of 582 participants who received guselkumab IV induction, 432 (74%) continued treatment through Week 144

6-MP= 6-mercaptopurine; AZA= azathioprine; CD= Crohn's disease; CDAI= Crohn's disease activity index; IQR= interquartile range; IV= intravenous; MTX= methotrexate; NRI= nonresponder imputation; SC= subcutaneous; SD= standard deviation; SES-CD= simple endoscopic score for Crohn's disease.

^aBased on N=283 for GUS 100 mg and N=294 for GUS 200 mg. ^bPrimary nonresponse, secondary nonresponse, or intolerance.

Note: Baseline demographics and disease characteristics are shown for the primary efficacy analysis set (NRI).

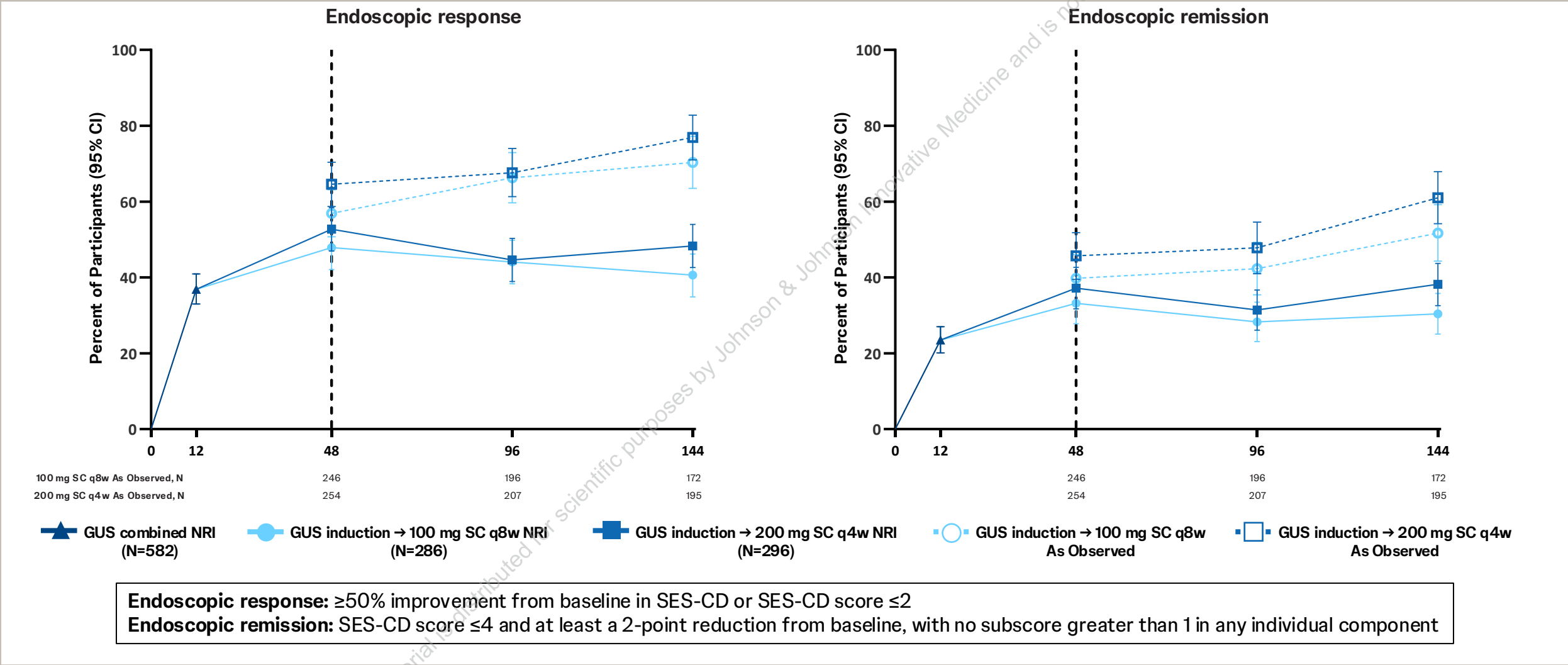
Clinical Remission



Among participants in clinical remission at Week 144, 94.5% (100 mg SC q8w) and 96.6% (200 mg SC q4w) had been corticosteroid-free for ≥90 days; primary efficacy analysis set (NRI)

CDAI=Crohn's disease activity index; CI= confidence interval; GUS=guselkumab; IV= intravenous; LTE= long-term extension; NRI= participants who met treatment failure criteria or had missing data were considered non-responders; SC= subcutaneous.
Note: Participants who were not in clinical response (≥100-point reduction in CDAI score from baseline or CDAI <150) and had CDAI ≥220 were eligible for dose adjustment (ie, guselkumab 100mg SC q8w → 200mg SC q4w or "sham" for participants treated with guselkumab 200mg SC q4w) between Weeks 52-80.
Participants in the LTE As Observed analysis who had a dose adjustment from guselkumab 100 mg SC q8w to guselkumab 200 mg SC q4w are not included from the day after the date of dose adjustment.

Endoscopic Outcomes



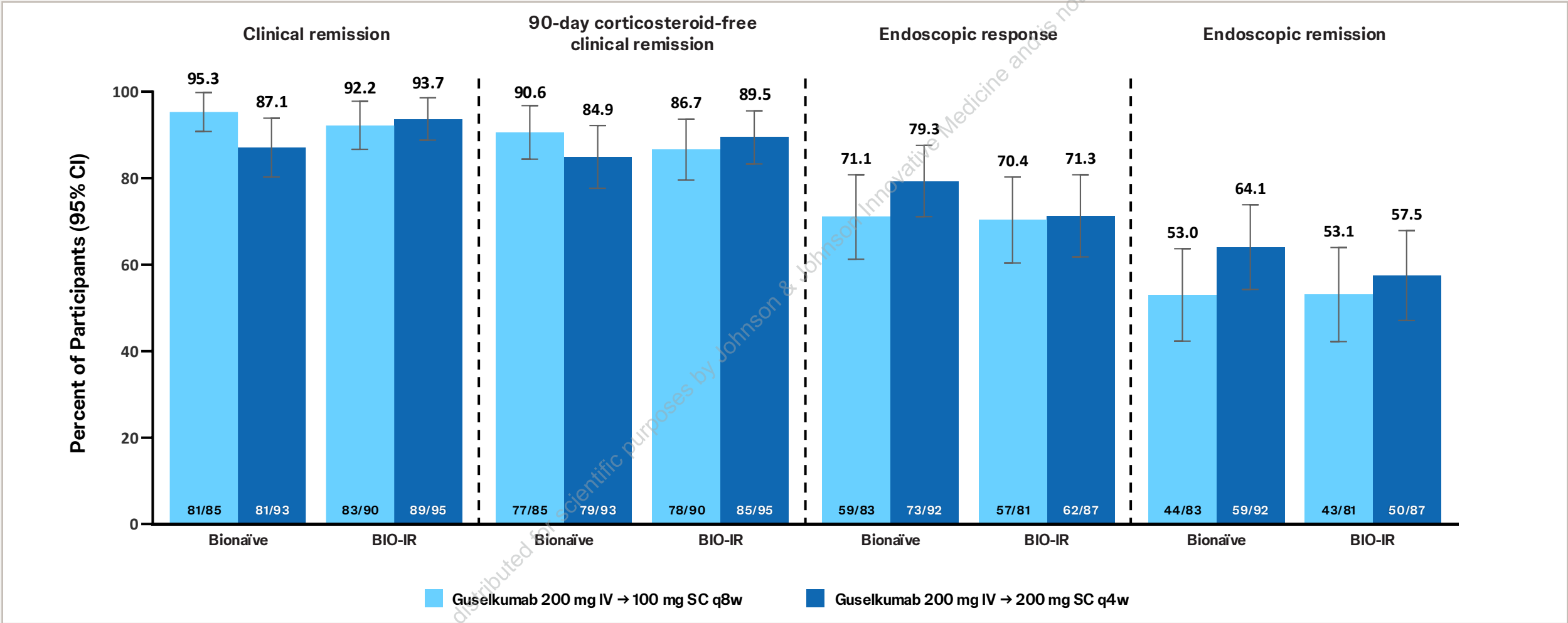
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Participants in the LTE As Observed analysis who had a dose adjustment from guselkumab 100 mg SC q8w to guselkumab 200 mg SC q4w are not included from the day after the date of dose adjustment.

Outcomes by Biologic History at Week 144

LTE As Observed



BIO= biologic; CD=Crohn's disease; CDAI=Crohn's disease activity index; CI= confidence interval; IR= inadequate response/intolerance; IV= intravenous; LTE= long-term extension; SC= subcutaneous.
Note: Participants who were not in clinical response (≥ 100 -point reduction in CDAI score from baseline or CDAI < 150) and had CDAI ≥ 220 were eligible for dose adjustment (ie, guselkumab 100mg SC q8w → 200mg SC q4w or "sham" for participants treated with guselkumab 200mg SC q4w) between Weeks 52-80.
Participants in the LTE As Observed analysis who had a dose adjustment from guselkumab 100 mg SC q8w to guselkumab 200 mg SC q4w are not included from the day after the date of dose adjustment.

Safety Summary From Week 0 Through Week 144

All treated safety analysis set	Placebo ^{a,b} (N=153)	GUS 100 mg SC q8w ^a (N=296)	All GUS 200 mg SC q4w ^c (N=407)
Exposure			
Mean duration of follow-up, weeks	30.0	113.5	111.6
Total participant-years (py) of follow-up	88.0	644.1	870.2
Events per 100 py of follow-up (95% CI)			
Adverse events	422.8 (380.92, 468.02)	274.2 (261.54, 287.28)	295.8 (284.47, 307.44)
Serious adverse events	27.3 (17.48, 40.59)	11.6 (9.16, 14.60)	10.7 (8.63, 13.09)
AEs leading to discontinuation of study agent	19.3 (11.26, 30.94)	5.1 (3.53, 7.20)	5.1 (3.67, 6.79)
Infections ^d	79.6 (62.02, 100.52)	74.4 (67.86, 81.34)	76.2 (70.50, 82.21)
Serious infections ^d	4.5 (1.24, 11.64)	0.9 (0.34, 2.03)	1.6 (0.88, 2.70)
Adverse events of interest per 100 py of follow-up (95% CI)			
Active tuberculosis	0.0 (0.00, 3.40)	0.2 (0.00, 0.87)	0.1 (0.00, 0.64)
Malignancies	0.0 (0.00, 3.40)	0.2 (0.00, 0.87)	0.3 (0.07, 1.01)
Anaphylactic or serum sickness reactions	1.1 (0.03, 6.33)	0.0 (0.00, 0.47)	0.0 (0.00, 0.34)
Opportunistic infections	2.3 (0.28, 8.21)	0.2 (0.00, 0.87)	1.3 (0.63, 2.26)
Major adverse cardiovascular events	0.0 (0.00, 3.40)	0.2 (0.00, 0.87)	0.0 (0.00, 0.34)
Venous thromboembolism	0.0 (0.00, 3.40)	0.0 (0.00, 0.47)	0.2 (0.03, 0.83)
Clinically important hepatic disorder AEs	0.0 (0.00, 3.40)	0.5 (0.10, 1.36)	0.7 (0.25, 1.50)

AE= adverse event; CI= confidence interval; GUS= guselkumab; IV= intravenous; MedDRA= Medical Dictionary for Regulatory Activities; py= participant-years; q4w= every 4 weeks; q8w= every 8 weeks; SAE= serious adverse event; SC= subcutaneous.
^a Up to dose adjustment. ^b Participants treated with placebo during the LTE were discontinued after study unblinding. ^c Participants who were randomized to receive guselkumab 200 mg SC q4w maintenance dosing, or had a dose adjustment (including “sham”) to guselkumab 200 mg SC q4w dosing from all treatment groups (including those randomized to placebo and ustekinumab); for participants who had a dose adjustment, only data after their first guselkumab 200 mg dose are included. ^d Infections are based on MedDRA system organ class “Infections and Infestations”.
 Note: Adverse events are coded using MedDRA Version 28.0. Occurrences of major adverse cardiovascular events were identified by clinical review. Terms for venous thromboembolism are based on customized MedDRA query. Clinically important hepatic disorders are defined as hepatic disorder AEs reported as SAEs or AEs leading to discontinuation of study intervention. The all-treated safety analysis set includes all participants who received ≥1 dose and differs from the primary efficacy analysis set (NRI) used for the baseline characteristics table.

Key Takeaways

- Guselkumab-treated participants with moderately to severely active Crohn's disease maintained clinical and endoscopic efficacy through Week 144 across both maintenance regimens
- Efficacy was consistent in bionative and BIO-IR participants, supporting durability irrespective of prior biologic exposure
- The 3-year safety profile was consistent with the known profile of guselkumab, and no new safety signals were identified
- The treat-through study design enabled long-term efficacy and safety evaluation of all patients initially randomized to guselkumab induction, regardless of their response status after induction or upon entry into the long-term extension

Acknowledgments

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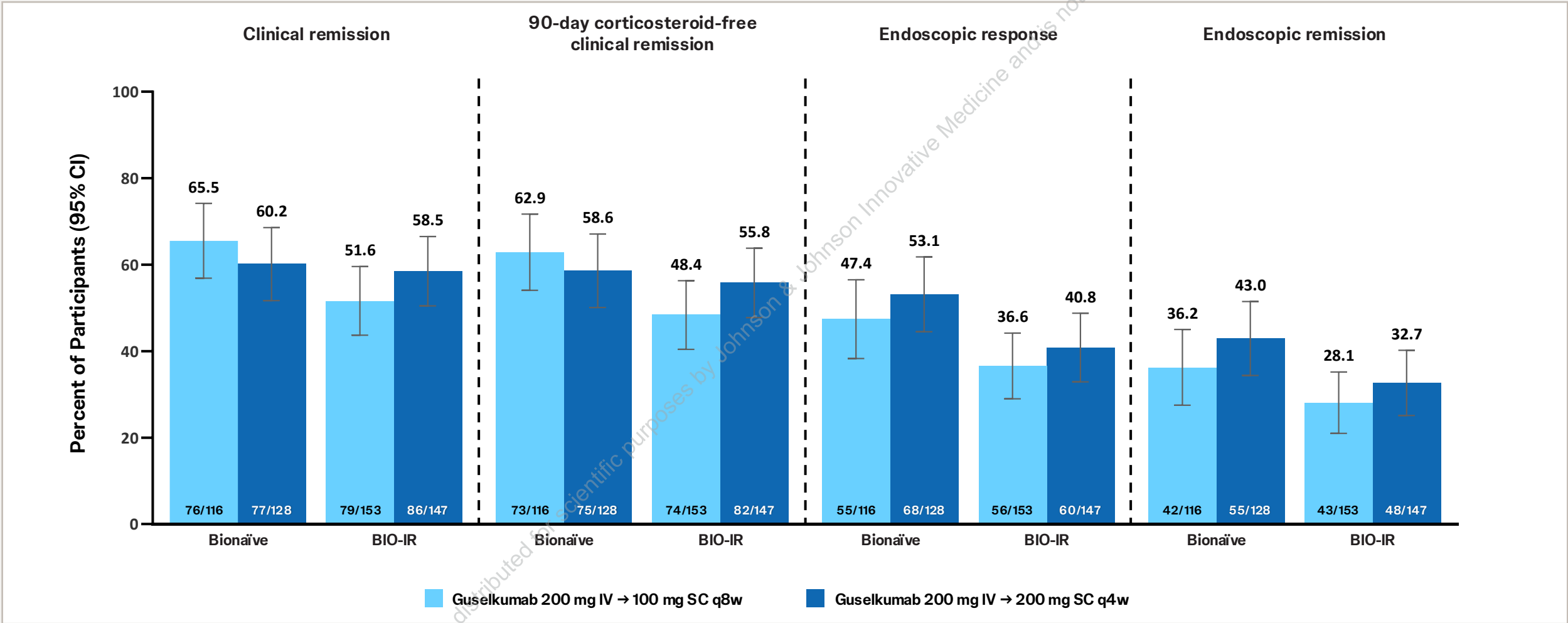
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Outcomes by Biologic History at Week 144

Primary Efficacy Analysis Set



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Note: Participants who were not in clinical response (≥ 100 -point reduction in CDAI score from baseline or CDAI < 150) and had CDAI ≥ 220 were eligible for dose adjustment (ie, guselkumab 100mg SC q8w $\rightarrow$ 200mg SC q4w or "sham" for participants treated with guselkumab 200mg SC q4w) between Weeks 52-80.