OP70

Efficacy and Safety of Subcutaneous Guselkumab Rescue Therapy in Patients with Moderately to Severely Active Crohn's Disease and Inadequate Response to Ustekinumab: Results From GALAXI 1, 2, & 3 Long-term Extension

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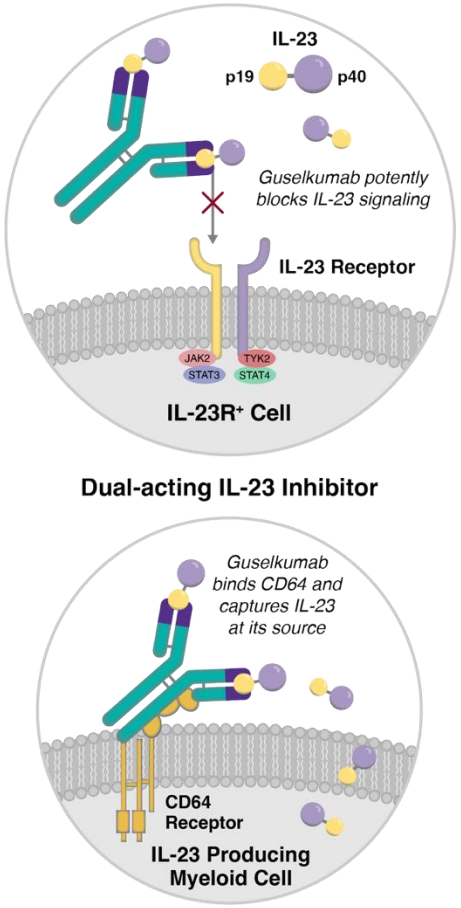
Background and Objective

- Guselkumab is a 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]
- The phase 2 GALAXI 1 and phase 3 GALAXI 2 & 3 (NCT03466411) studies evaluated guselkumab in participants with moderately to severely active Crohn's disease
  - Individuals with a history of inadequate response or intolerance to ustekinumab were excluded from GALAXI
  - Participants treated with ustekinumab in the GALAXI studies who met inadequate response criteria during the long-term extension (LTE) could cross over to guselkumab
- Here, we present efficacy and safety results in participants who received guselkumab after experiencing an inadequate response to ustekinumab in the GALAXI long-term extension



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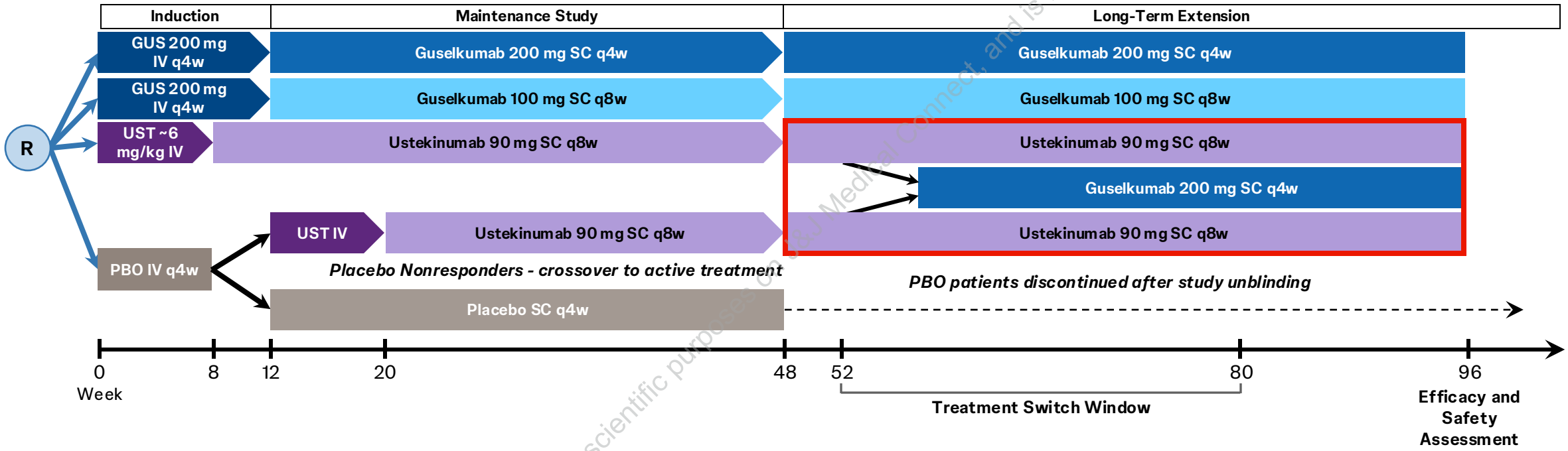
1. Atreya R, Abreu MT, Krueger JG, et al. *J Crohns Colitis*. 2024;18(suppl):S470.

GALAXI 2 & 3: Ustekinumab to Guselkumab Switch



Treatment Switch Criteria

- From Weeks 52 through 80, patients who were NOT in clinical response (≥100-point reduction in CDAI score from baseline or CDAI <150) and had CDAI ≥220 were eligible for treatment switch to guselkumab 200 mg SC q4w **without induction**
- Outcomes following treatment switch were compared with those of the BIO-IR subpopulation of participants in the pooled GALAXI 2 & 3 studies who received guselkumab 200 mg IV → 200 mg SC q4w

BIO= biologic; CDAI=Crohn's disease activity index; GUS=guselkumab; IR= inadequate response or intolerance; IV=intravenous; R=randomization; SES-CD= simple endoscopic score for Crohn's disease; SC=subcutaneous; UST=ustekinumab.
Note: Treatment switch criteria were identical in the GALAXI 1, 2, and 3 studies.

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Panaccione et al. *Lancet* 2025;406:358-75

Demographics and Disease Characteristics at LTE Baseline (Week 48): Pooled Phase 2b/3 GALAXI

Participants treatment-switched in LTE	Ustekinumab 90 mg SC q8w → Guselkumab 200 mg SC q4w (N=75) [a]
Demographics	
Age in years,[b] mean (SD)	35.2 (12.02)
Male,[b] n (%)	48 (64.0%)
Characteristics	
CD duration in years,[b] mean (SD)	8.21 (8.18)
CDAI score, mean (SD)	164.0 (82.12)
Participants in clinical remission, n (%)	29 (38.7%)
SES-CD score,[c] mean (SD)	9.2 (6.05)
Participants in endoscopic remission, n (%)	9 (12.0%)
Endoscopic disease severity (SES-CD score),[c] n (%)	
Moderate (7–16)	35 (47.9%)
Severe (>16)	11 (15.1%)
Involved GI areas by central reader,[b] n (%)	
Ileum only	16 (21.3%)
Colon only	25 (33.3%)
Ileum and Colon	34 (45.3%)
C-reactive protein in mg/L,[d] median (IQR)	3.9 (0.9; 10.0)
Fecal calprotectin in µg/g,[e] median (IQR)	427.0 (114.0; 1839.0)
History of inadequate response/intolerance[f] **to biologic therapy,** n (%)	45 (60.0%)

CD=Crohn's disease; CDAI=Crohn's disease activity index; GI= gastrointestinal; IQR=interquartile range; LTE=long-term extension; q4w= every 4 weeks; q8w= every 8 weeks; SC=subcutaneous; SD=standard deviation; SES-CD=simple endoscopic score for Crohn's disease.

[a] Includes the 75 participants who were included in the efficacy analyses. [b] Data at study baseline (ie, Week 0). [c] Based on N=73. [d] Based on N=72. [e] Based on N=65. [f] Primary nonresponse, secondary nonresponse, or intolerance.

Note: Clinical remission was defined as a CDAI score <150. Endoscopic remission was defined as an SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component. Participants who had a CD-related surgery, a prohibited change in CD medication, or discontinued study agent due to lack of efficacy, an AE of worsening CD or Week 20/24 non-responder or discontinued study agent for any reason (other than COVID-19 related reasons [excluding COVID-19 infection] or regional crisis) were considered not to have met the endpoint at the designated timepoint. Participants who discontinued study intervention due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. After accounting for the aforementioned data handling rules, participants who were missing data pertaining to an endpoint at a designated timepoint were considered not to have achieved the endpoint. Participants in GALAXI 2/3 with a Crohn's disease-related surgery (with the exception of minor procedures) prior to Week 48 or a prohibited change in CD medications prior to Week 48 who remained on treatment and subsequently entered the LTE are excluded.

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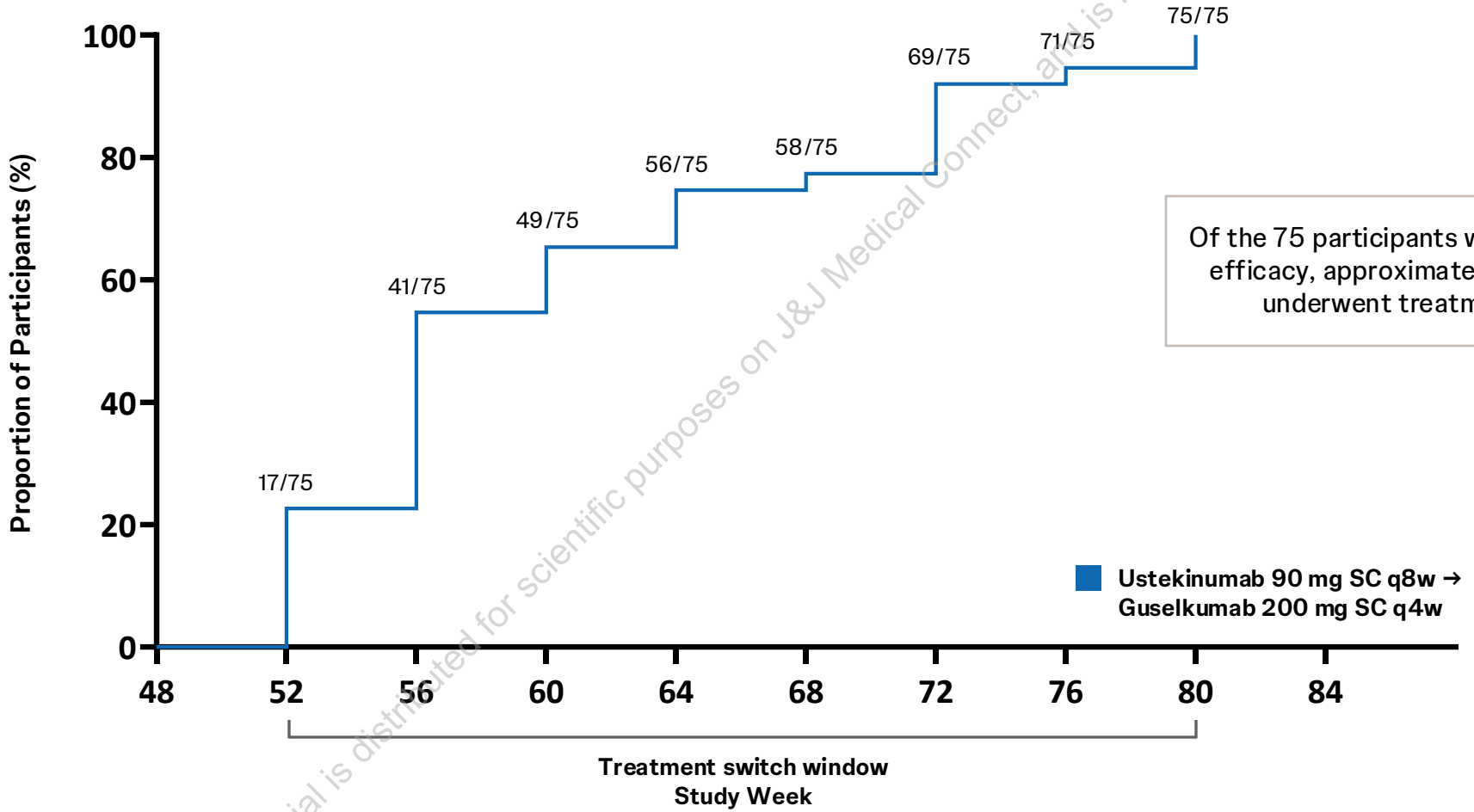
Time to Treatment Switch: Pooled Phase 2b/3 GALAXI



Of the 75 participants who were evaluated for efficacy, approximately two-thirds (65.3%) underwent treatment by Week 60

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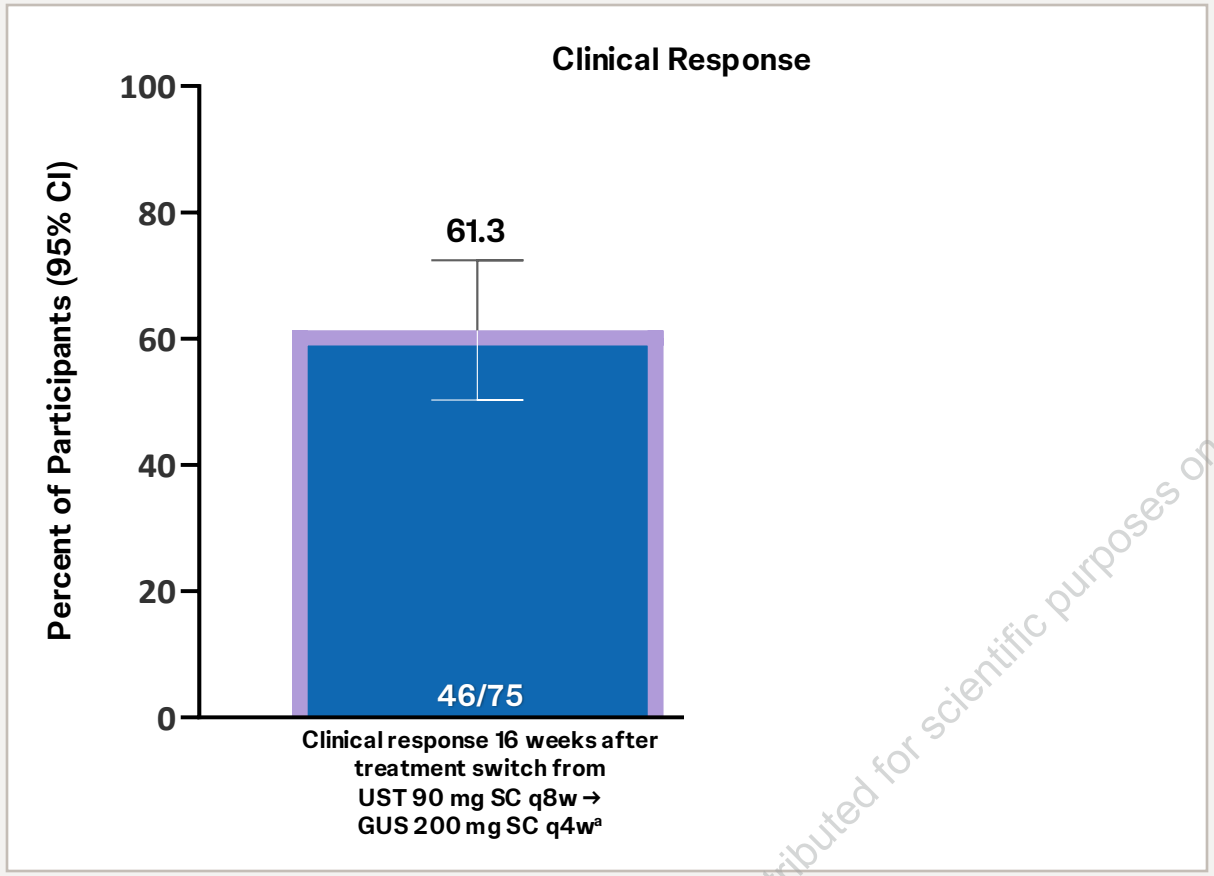
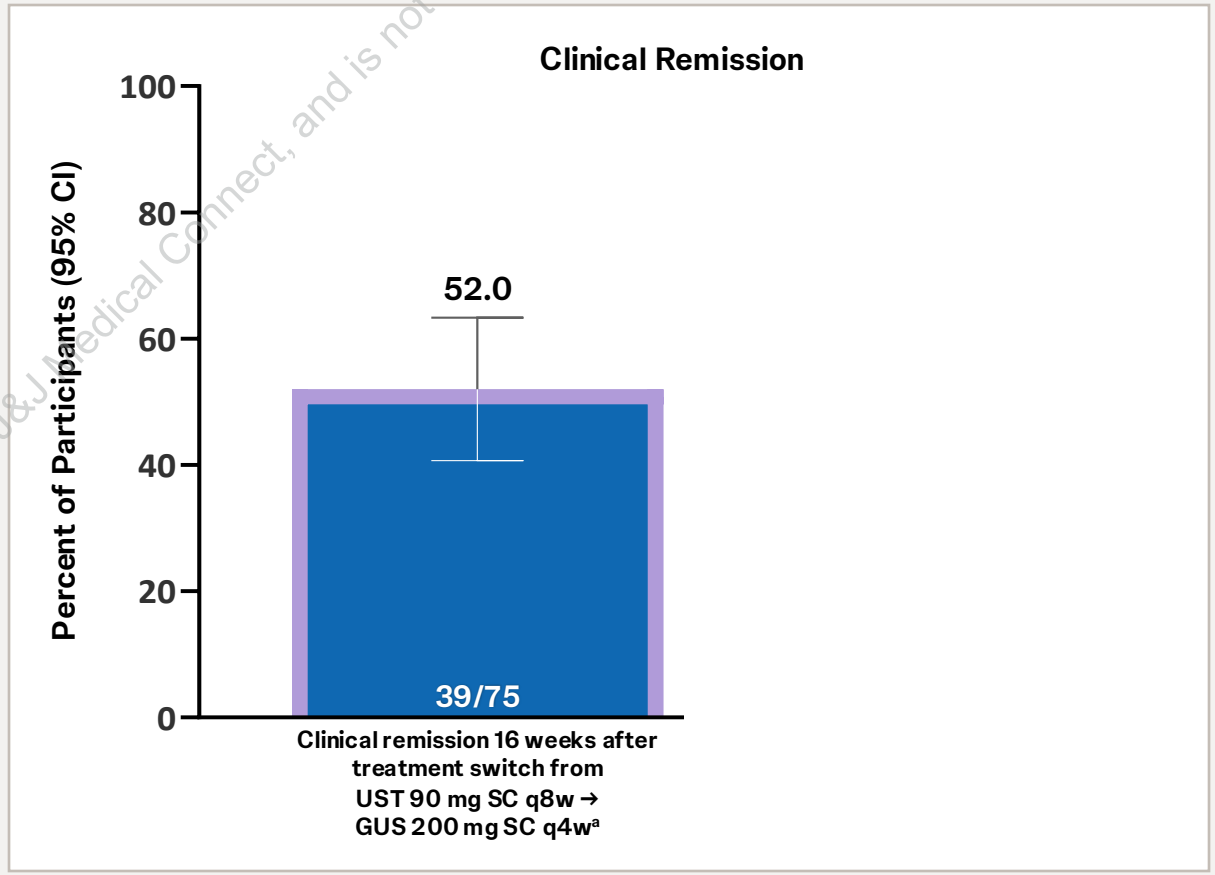
CD= Crohn's disease; LTE= long-term extension; q4w= every 4 weeks; q8w= every 8 weeks; SC=subcutaneous.

Note: Participants in GALAXI 2/3 with a Crohn's disease-related surgery (with the exception of minor procedures) prior to Week 48 or a prohibited change in CD medications prior to Week 48 who remained on treatment and subsequently entered the LTE are excluded.

Clinical Outcomes 16 Weeks After Treatment Switch





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Clinical response: ≥100-point reduction from time of treatment switch/baseline in CDAI score or CDAI score <150
Clinical remission: CDAI score <150

BIO= biologic; CD= Crohn's disease; CDAI= Crohn's disease activity index; CI= confidence interval; GUS= guselkumab; IR= inadequate response or intolerance; IV=intravenous; LTE= long-term extension; q4w= every 4 weeks; q8w= every 8 weeks; SC= subcutaneous; UST= ustekinumab.

[a] Includes participants who switched from ustekinumab 90 mg SC q8w to guselkumab 200 mg SC q4w in GALAXI 1, 2, and 3 LTE. [b] Includes participants who had a history of inadequate response or intolerance to biologic therapy in GALAXI 2 and 3.

Note: Participants were randomized to ustekinumab at Week 0 or switched from placebo to ustekinumab at Week 12 and continued SC maintenance dosing of ustekinumab in the maintenance period and treatment-adjusted to guselkumab 200 mg SC q4w dosing during the long-term extension. Participants who had a CD-related surgery (with the exception of minor procedures such as drainage of a superficial abscess or seton placement, etc.), a prohibited change in CD medication, or discontinued study intervention for any reason (other than COVID-19 related reasons [excluding COVID-19 infection] or regional crisis) were considered not to have met the endpoint at the designated timepoint. Participants who discontinued study intervention due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available. After accounting for the aforementioned data handling rules, participants who were missing data pertaining to an endpoint at a designated timepoint were considered not to have achieved the endpoint. Participants in GALAXI 2/3 with a Crohn's disease-related surgery (with the exception of minor procedures) prior to Week 48 or a prohibited change in CD medications prior to Week 48 who remained on treatment and subsequently entered the LTE are excluded.

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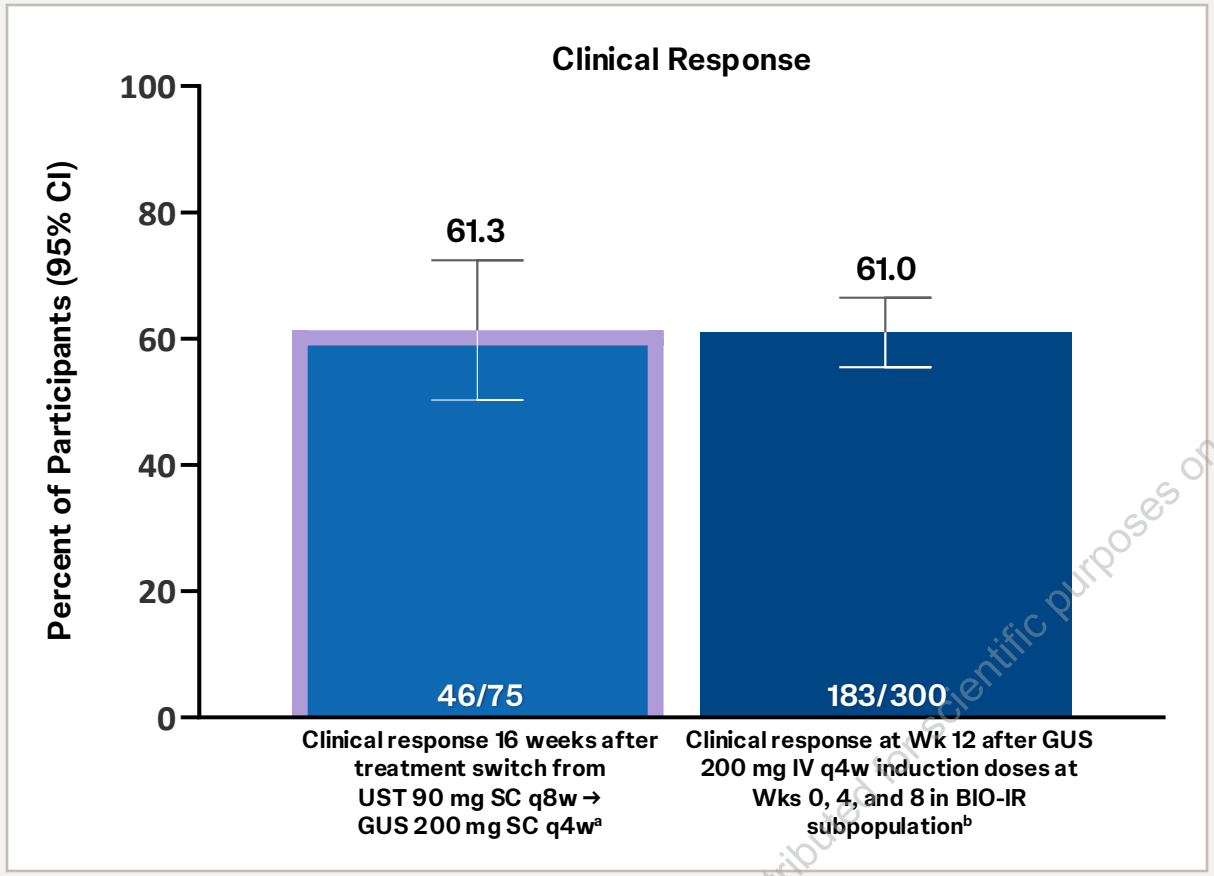

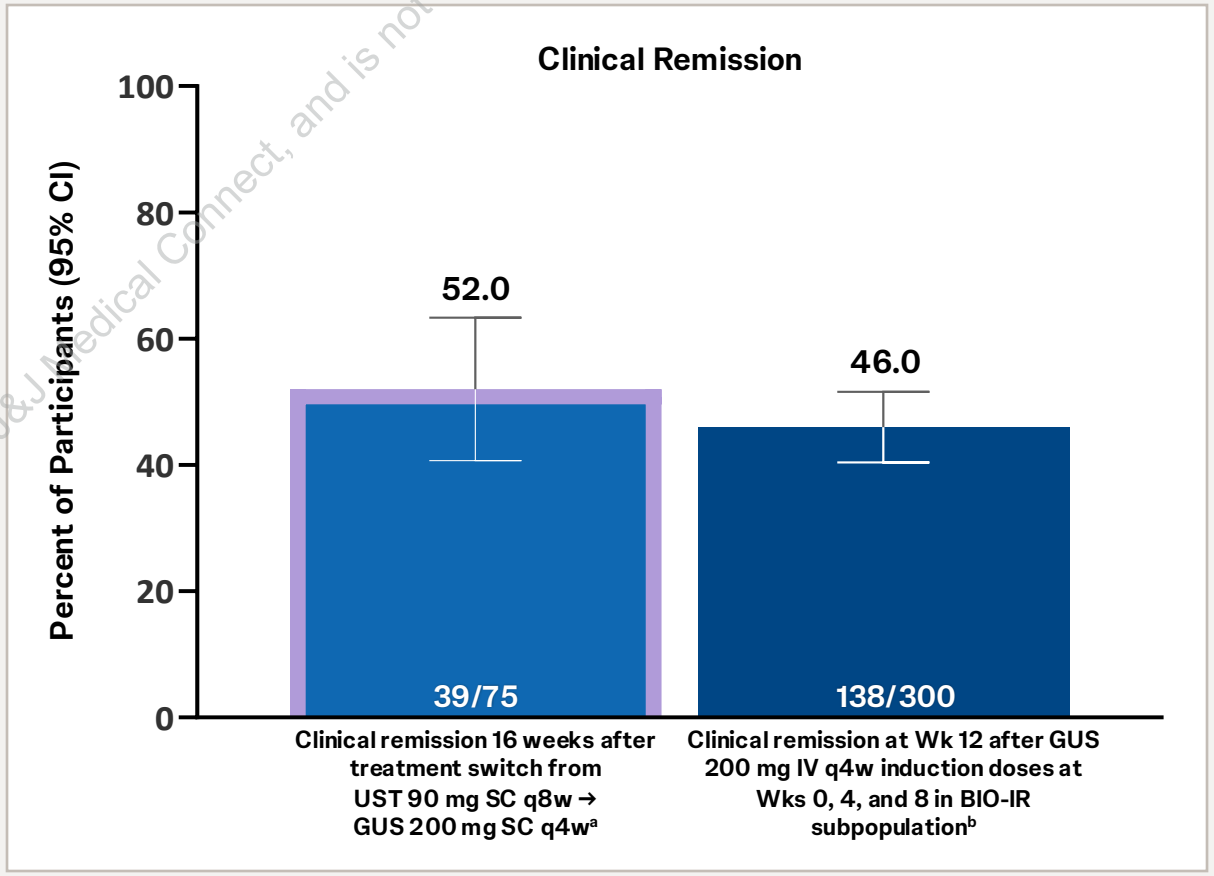

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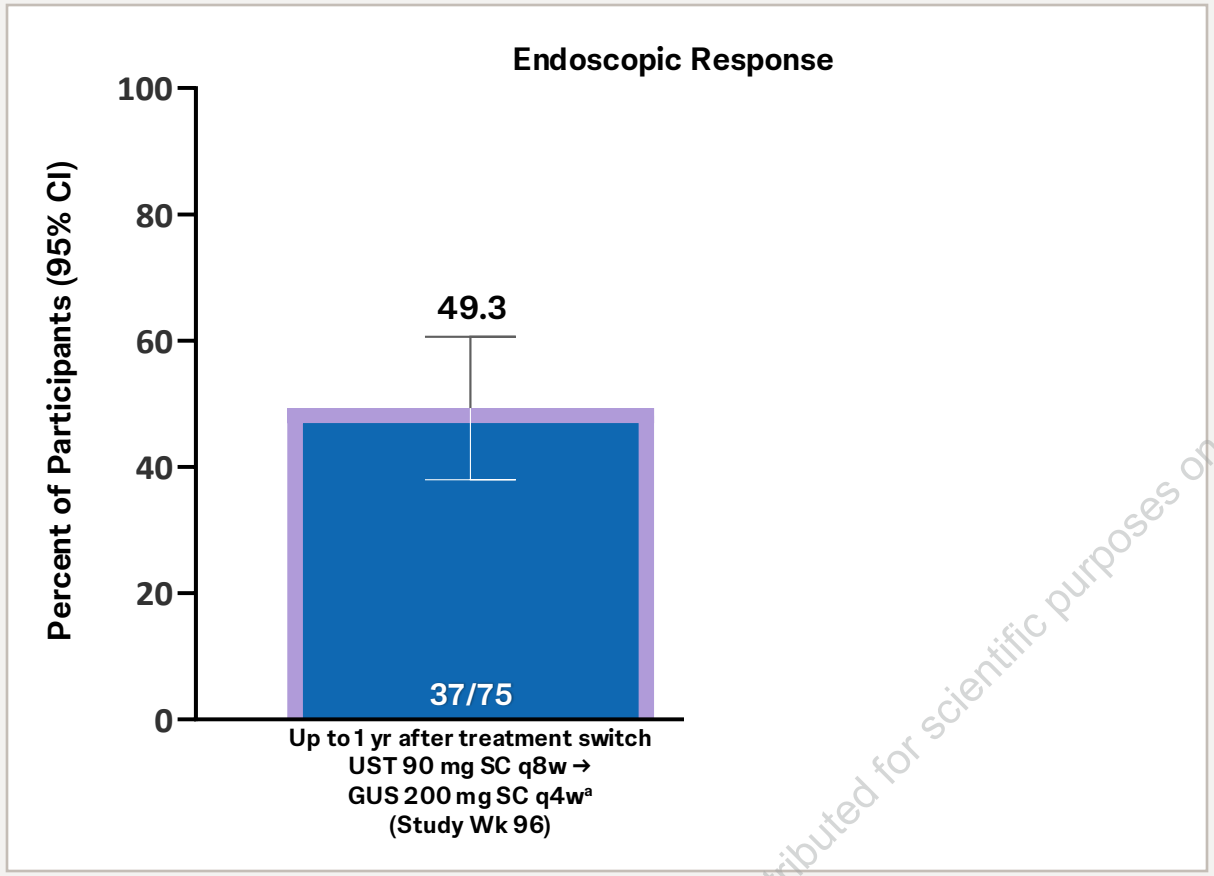
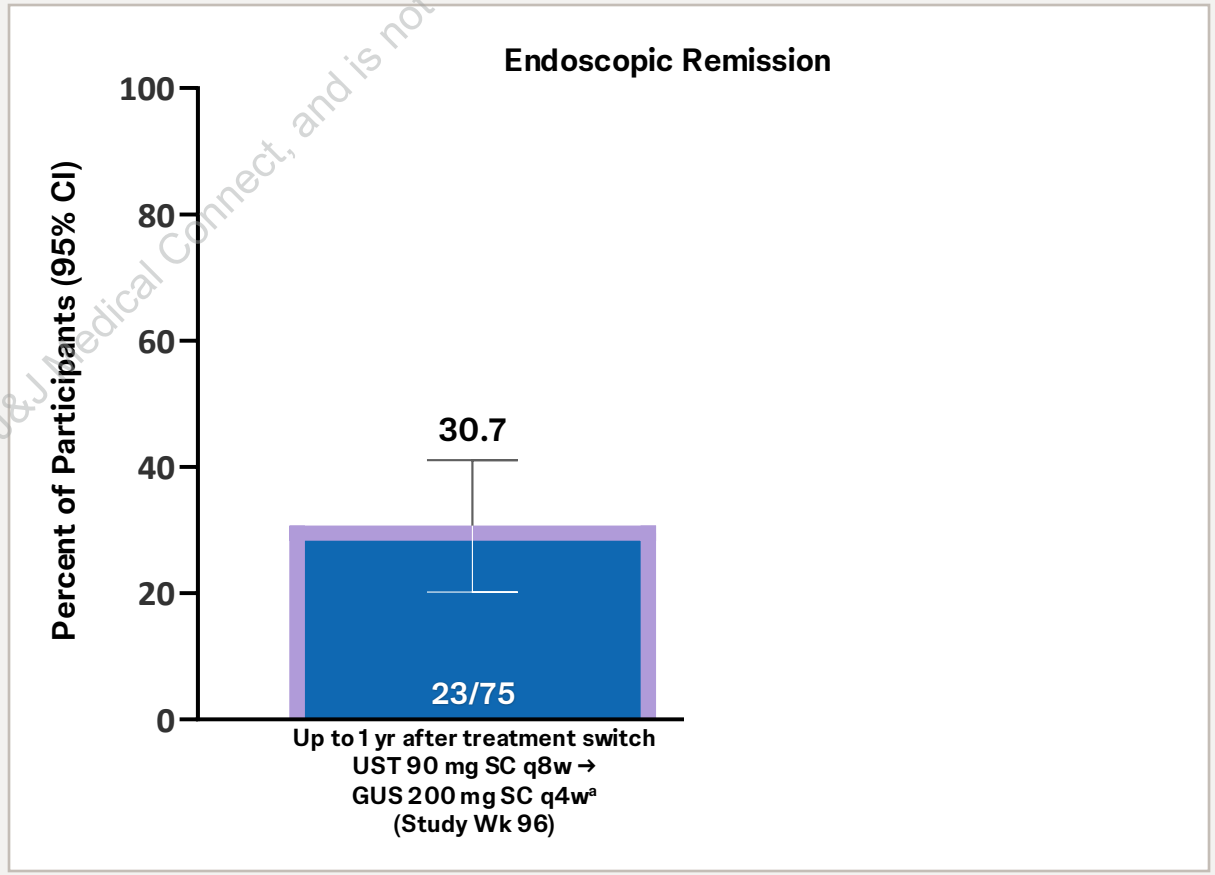
Endoscopic Outcomes at Study Week 96





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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

BIO= biologic; CD= Crohn's disease; CDAI= Crohn's disease activity index; CI= confidence interval; GUS= guselkumab; IR= inadequate response or intolerance; LTE= long-term extension; q4w= every 4 weeks; q8w= every 8 weeks; SC= subcutaneous; UST= ustekinumab.

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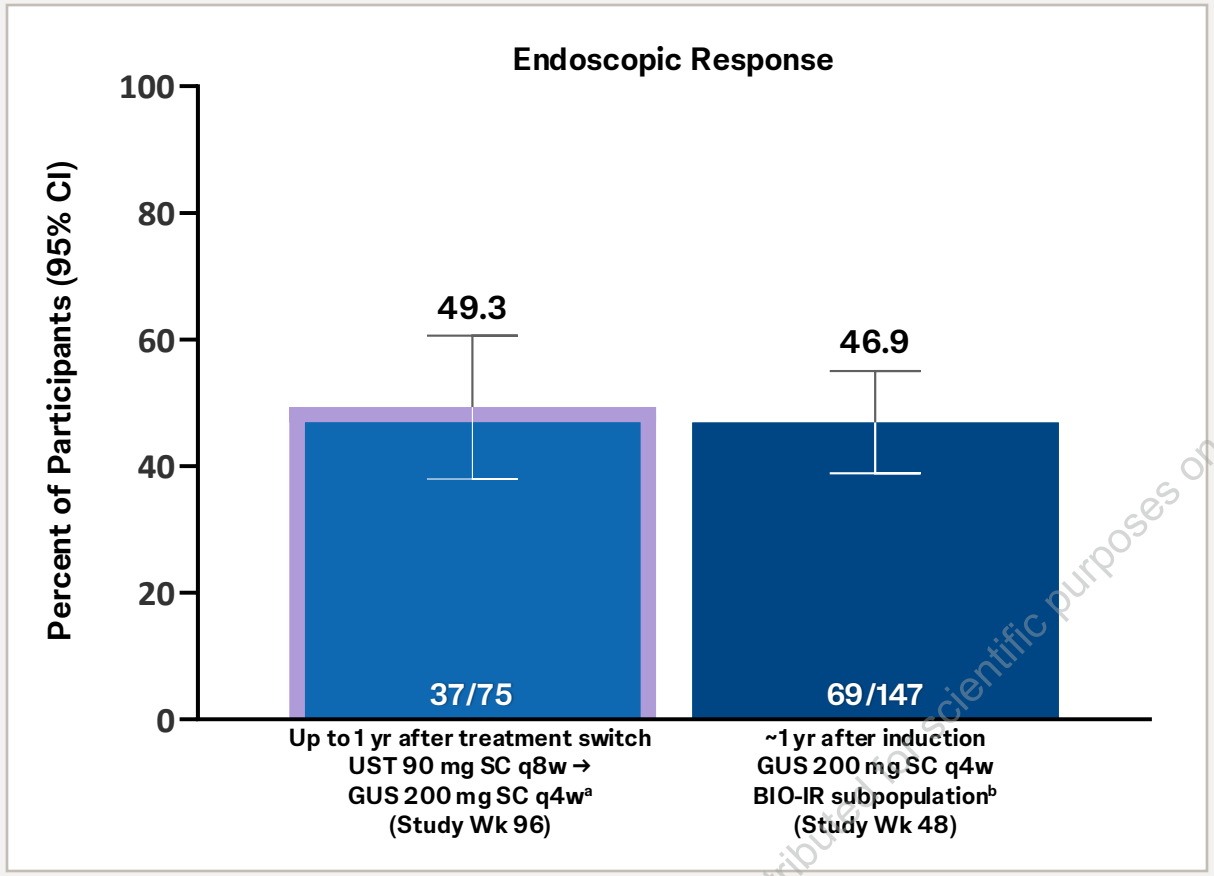

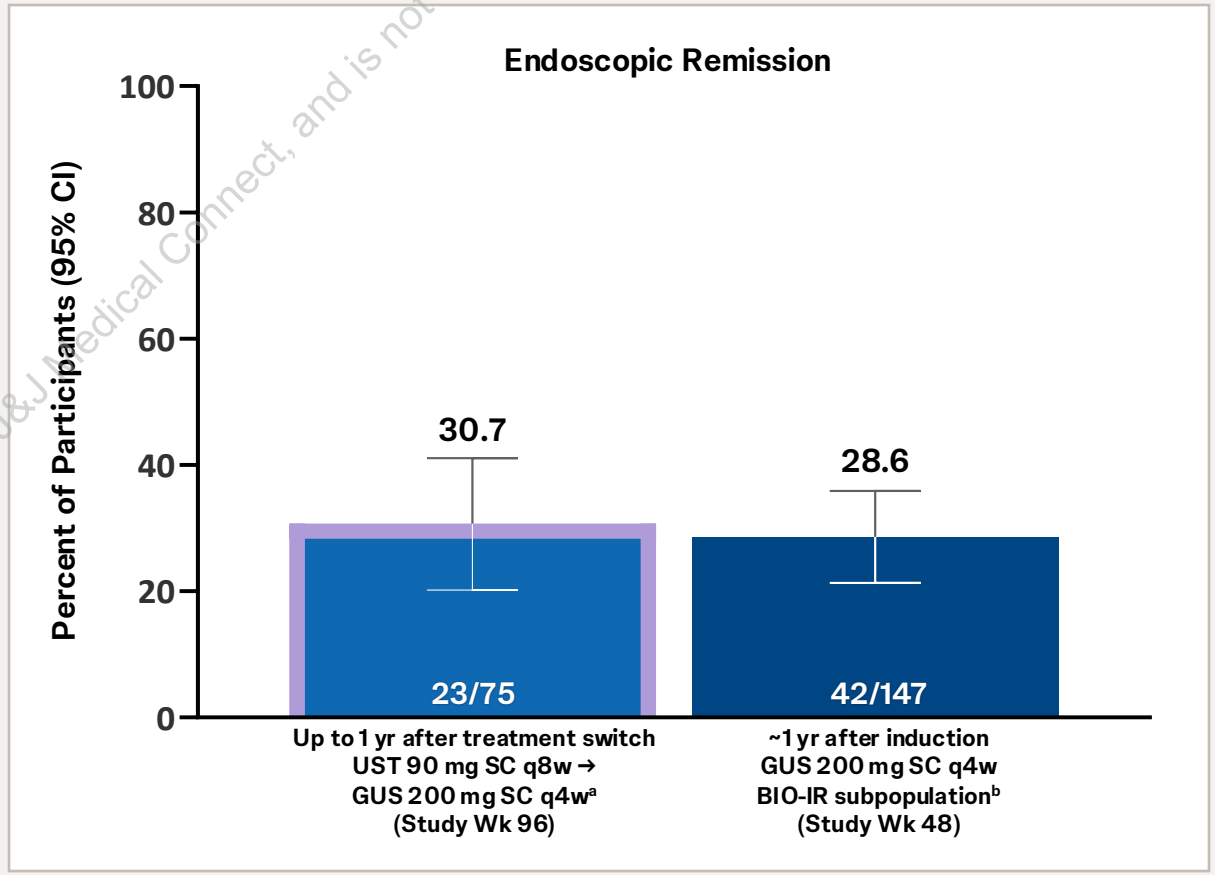

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Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2
Endoscopic remission: SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component

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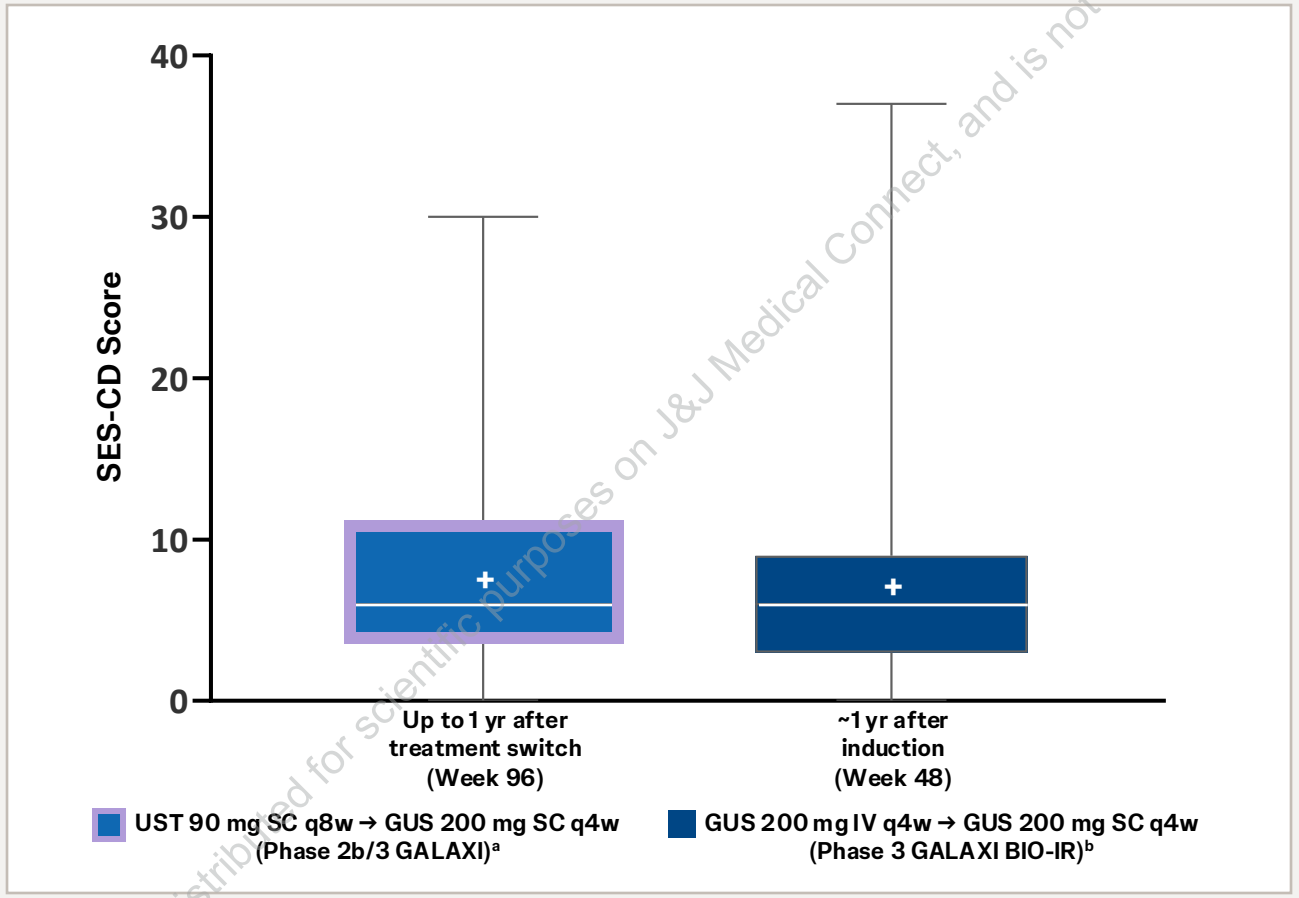
SES-CD Scores



Box = Interquartile range
Whiskers = Range
Line = Median
+ = Mean

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Safety Summary From Time of Treatment Switch Through Week 96

Participants treatment-switched in LTE	Ustekinumab 90 mg SC q8w → Guselkumab 200 mg SC q4w[a] (N=80)
Average duration of follow-up, weeks	34.8
Average exposure, number of administrations	8.4
Participants with 1 or more:	
AEs, n (%)	50 (62.5%)
SAEs, n (%)	6 (7.5%)
AEs leading to DC of study agent, n (%)	2 (2.5%)
Serious infections,[b] n (%)	0
Malignancies, n (%)	1 (1.3%)
Injection site reactions, n (%)	5 (6.3%)

AE= adverse event; DC= discontinuation; q4w= every 4 weeks; q8w= every 8 weeks; SAE= serious adverse event; SC= subcutaneous.

[a] Participants who were randomized to ustekinumab at Week 0 or who switched from placebo to ustekinumab at Week 12 and continued SC maintenance dosing of ustekinumab in the maintenance period and switched to guselkumab 200 mg SC q4w dosing during the long-term extension.

[b] Infections are based on MedDRA system organ class "Infections and Infestations".

Note: Safety analyses included all 80 participants who underwent treatment switch in the GALAXI 1, 2, and 3 LTE (ie, including the 5 participants who were excluded from the efficacy analyses due to CD-related surgery or prohibited change in CD medications before week 48). Participants are counted only once for any given event, regardless of the number of times they actually experienced the event.

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Key Takeaways

Among participants who experienced inadequate response to ustekinumab in the phase 2/3 GALAXI LTE, more than half achieved clinical remission 16 weeks after treatment switch to guselkumab 200 mg SC q4w, and ~50% were in endoscopic response up to 1 year after treatment switch

These data suggest patients with an inadequate treatment response to ustekinumab may benefit from switching to guselkumab therapy

Even though participants switched directly from ustekinumab to guselkumab 200 mg SC q4w without IV or SC induction, their results were similar to the overall BIO-IR subpopulation that received guselkumab IV induction and SC maintenance

Key safety event rates were consistent with the known safety profile of guselkumab in approved indications

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Acknowledgments

The authors thank the participants, investigators, and study personnel who made the GALAXI study possible

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Under the direction of the authors and in accordance with Good Publication Practices, Rick Mearhoff of Johnson & Johnson provided writing and editorial assistance

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Back up

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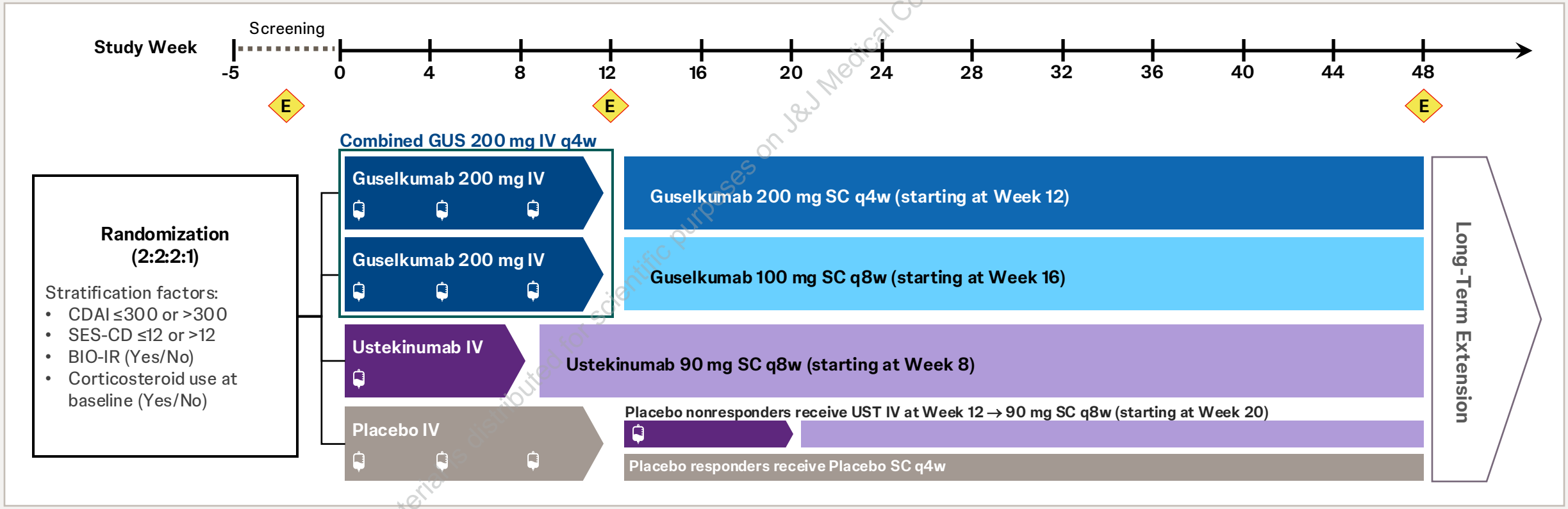
Double-Blind, Treat-Through Design: GALAXI 2 & 3

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: TNF antagonists or vedolizumab
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

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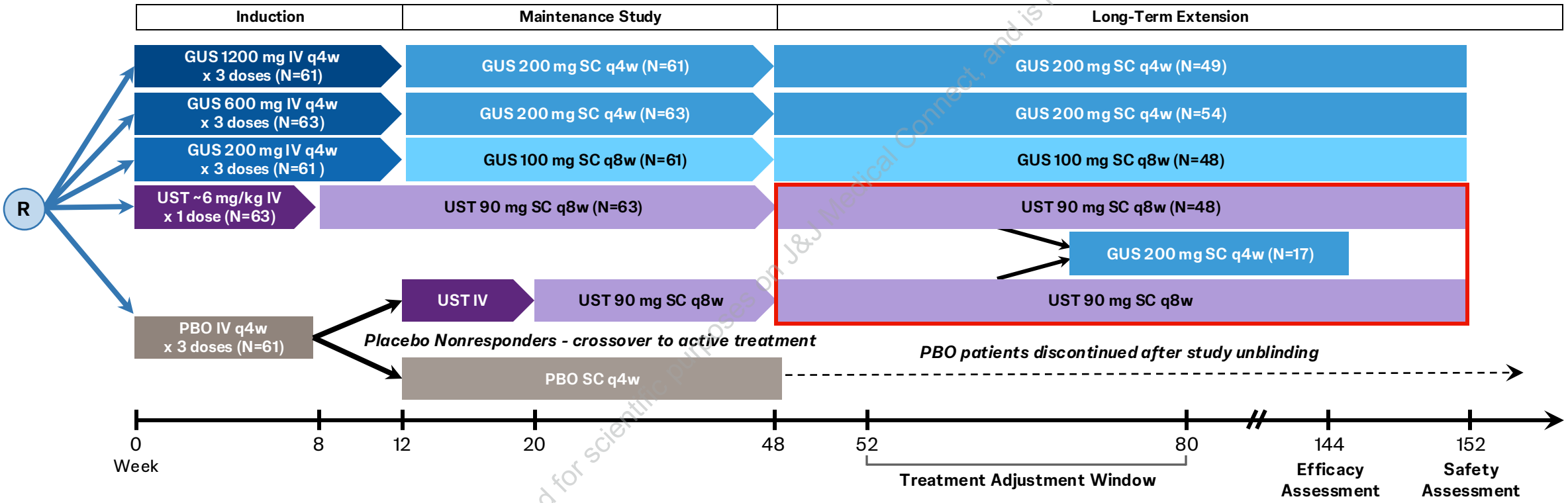
GALAXI-1 Long-Term Extension Study Design



Treatment Adjustment During LTE

- From Weeks 52 through 80, patients with an inadequate treatment response (not in clinical response [≥100-point reduction in CDAI score from baseline or CDAI <150] AND CDAI ≥220) were eligible for a treatment switch to SC guselkumab 200 mg q4w maintenance **without induction**

CDAI=Crohn's disease activity index; GUS=guselkumab; IV=intravenous; LTE=long-term extension; q4w=every 4 weeks; q8w=every 8 weeks; R=randomization; SC=subcutaneous; UST=ustekinumab.

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