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# 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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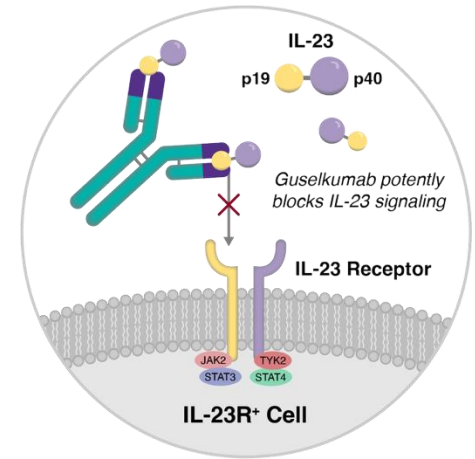
## Disclosure of Conflicts of Interest

I, **Anita Afzali**, 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:

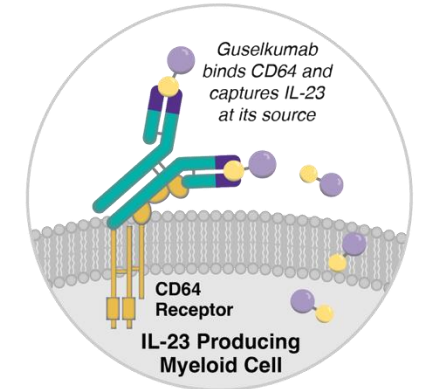
Potential conflicts of interest with AbbVie, Bristol Myers Squibb/Celgene, DiaSorin, Eli Lilly, Gilead, IBD Horizons, Johnson & Johnson, Pfizer, Takeda, and TLL Pharmaceuticals.

# Background and Objective

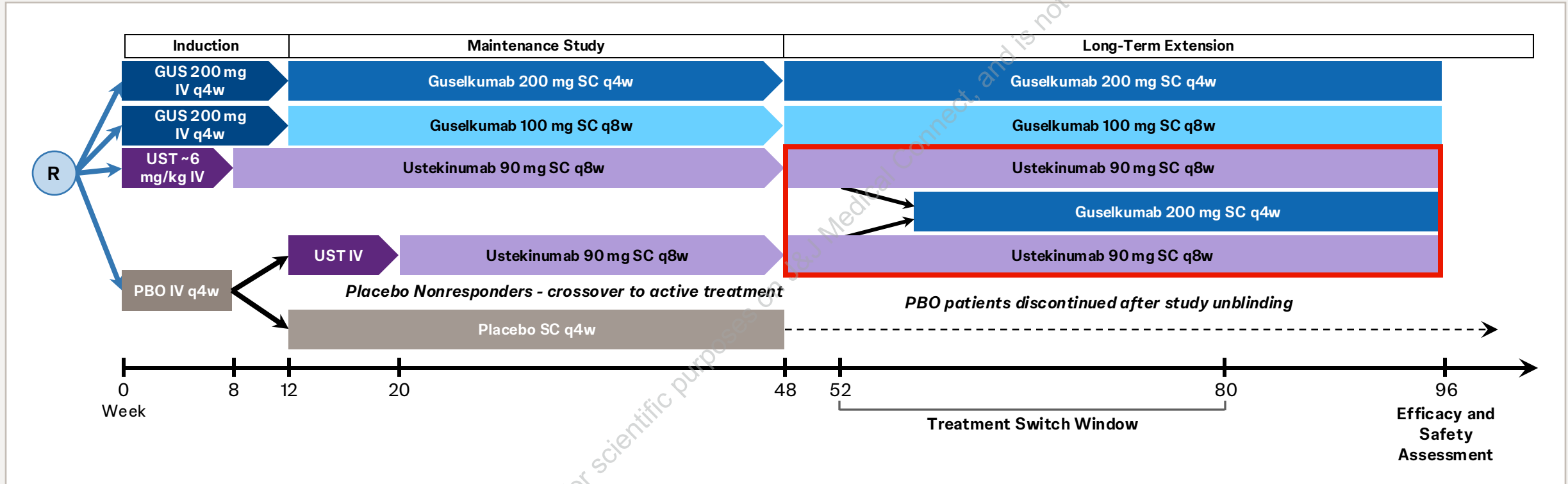
- Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23<sup>1</sup>
- The phase 2 GALAXI 1 and phase 3 GALAXI 2 & 3 (NCT03466411) studies evaluated guselkumab in participants with moderately to severely active 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



Dual-acting IL-23 Inhibitor



# GALAXI 2 & 3: Ustekinumab to Guselkumab Switch



## Treatment Switch Criteria

- From Weeks 52 through 80, patients who were NOT in clinical response ( $\geq 100$ -point reduction in CDAI score from baseline or CDAI  $< 150$ ) and had CDAI  $\geq 220$  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  $\rightarrow$  200 mg SC q4w

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

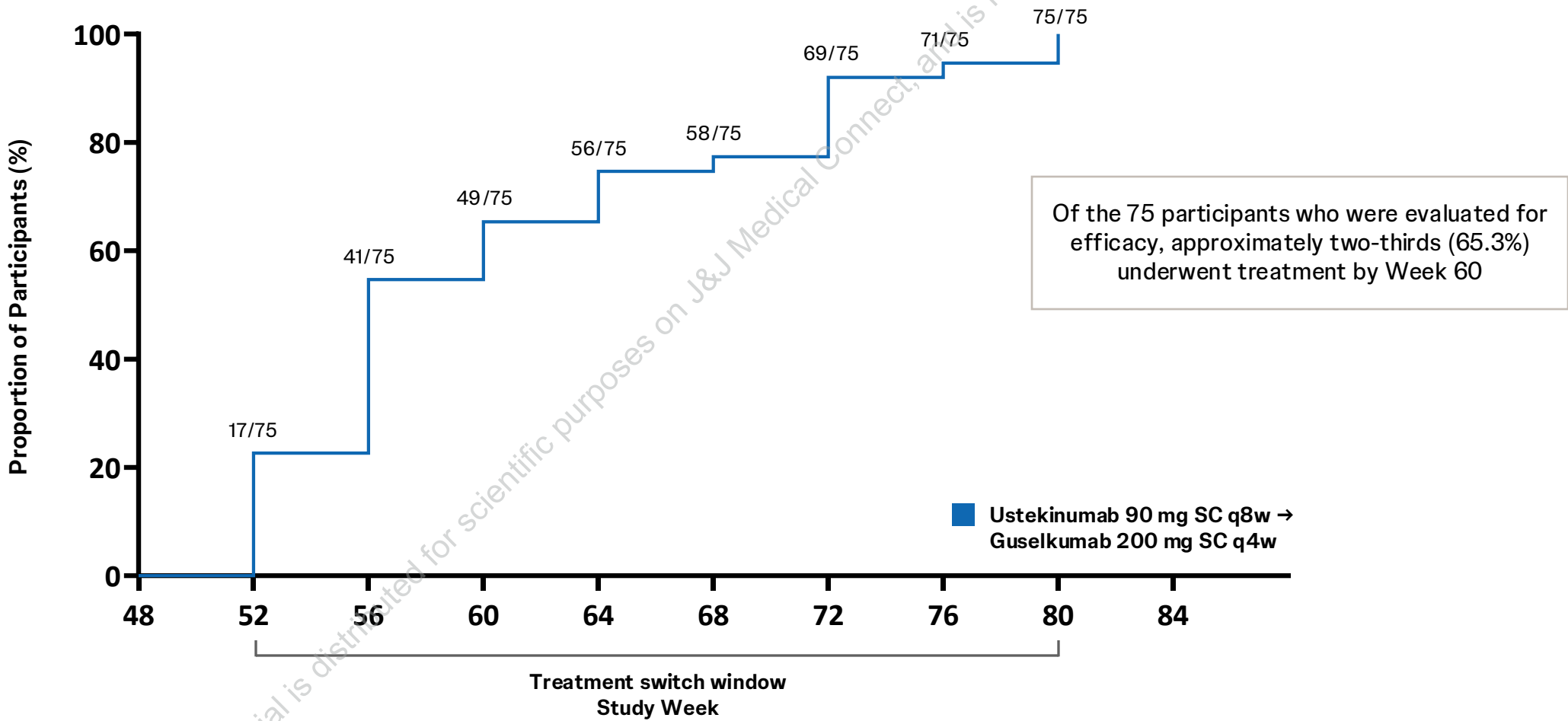
Participants treatment-switched in LTE	Ustekinumab 90 mg SC q8w → Guselkumab 200 mg SC q4w (N=75) <sup>a</sup>
<b>Demographics</b>	
Age in years, <sup>b</sup> mean (SD)	35.2 (12.02)
Male, <sup>b</sup> n (%)	48 (64.0%)
<b>Characteristics</b>	
CD duration in years, <sup>b</sup> mean (SD)	8.21 (8.18)
CDAI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

<sup>a</sup> Includes the 75 participants who were included in the efficacy analyses. <sup>b</sup> Data at study baseline (ie, Week 0). <sup>c</sup> Based on N=73. <sup>d</sup> Based on N=72. <sup>e</sup> Based on N=65. <sup>f</sup> 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 min or 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.

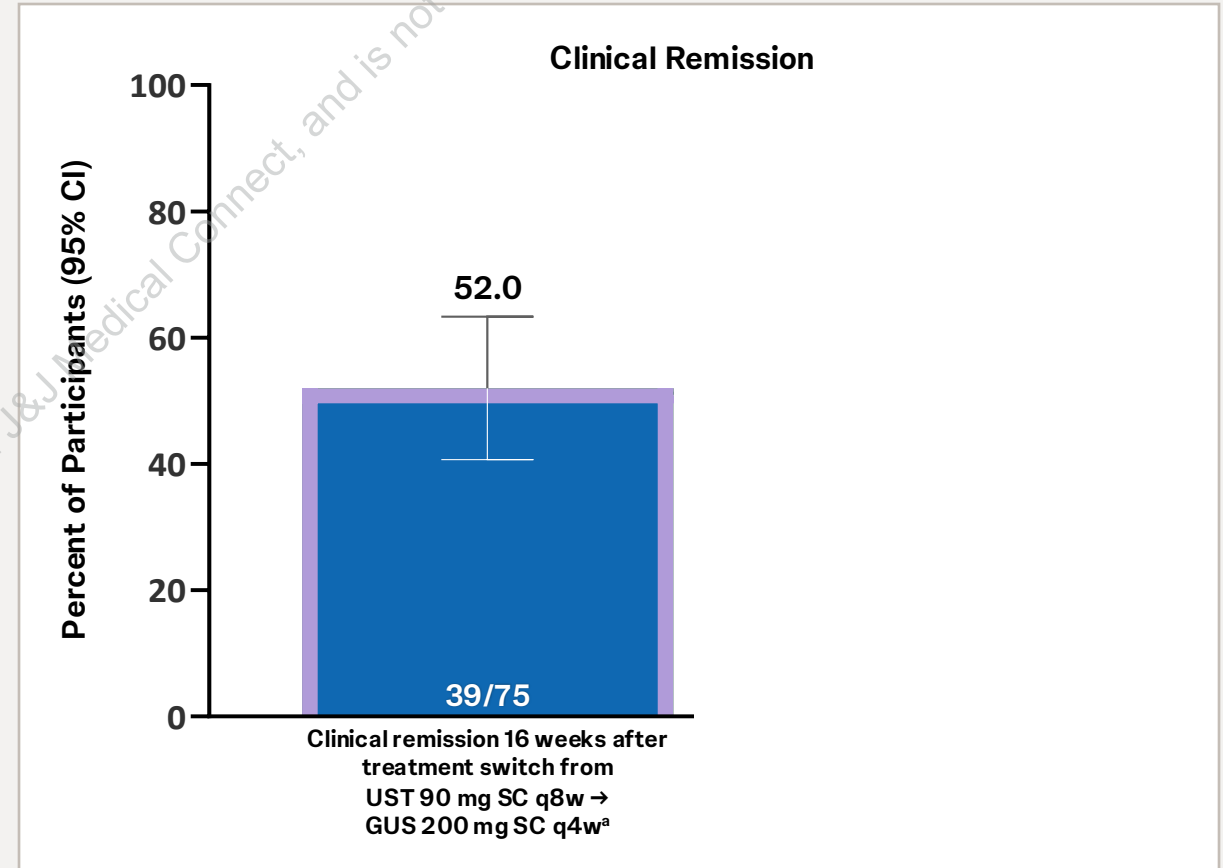
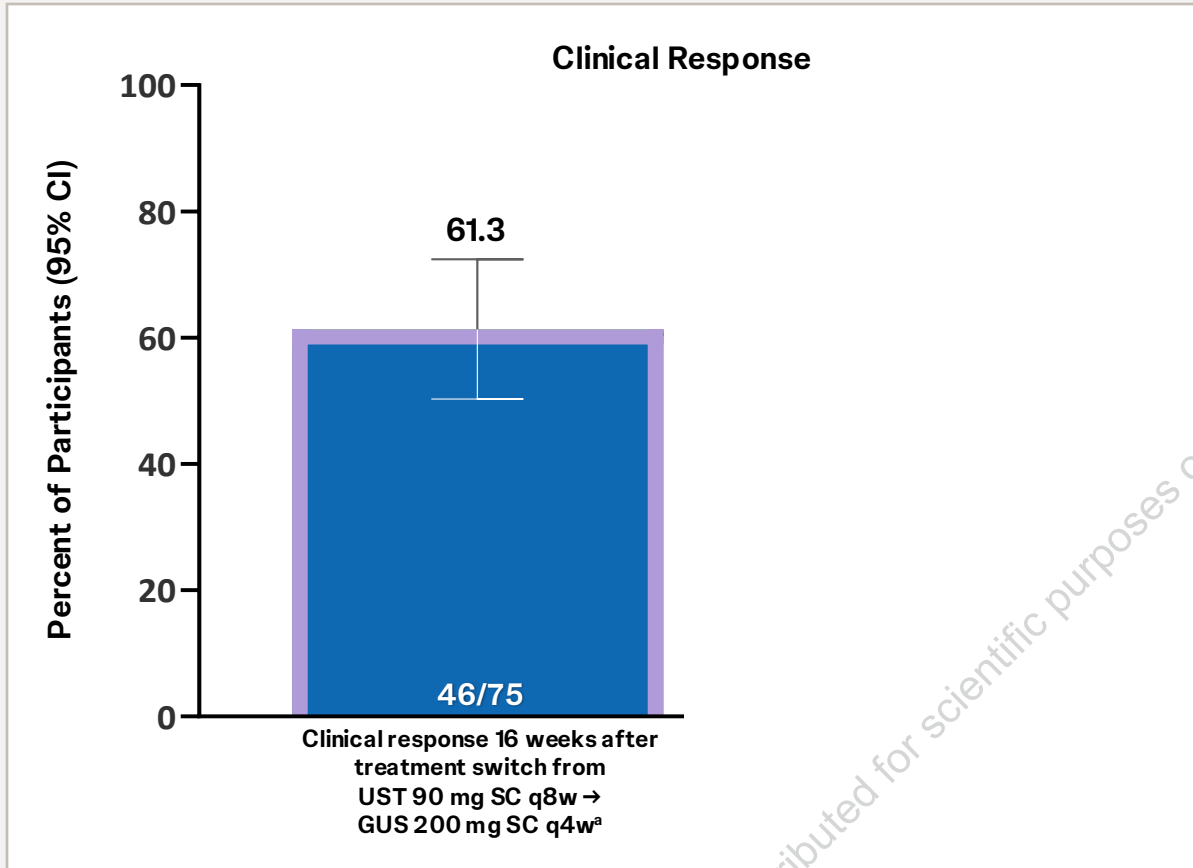
# Time to Treatment Switch: Pooled Phase 2b/3 GALAXI



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



**Clinical response:**  $\geq 100$ -point reduction from time of treatment switch/baseline in CDAI score or CDAI score  $< 150$

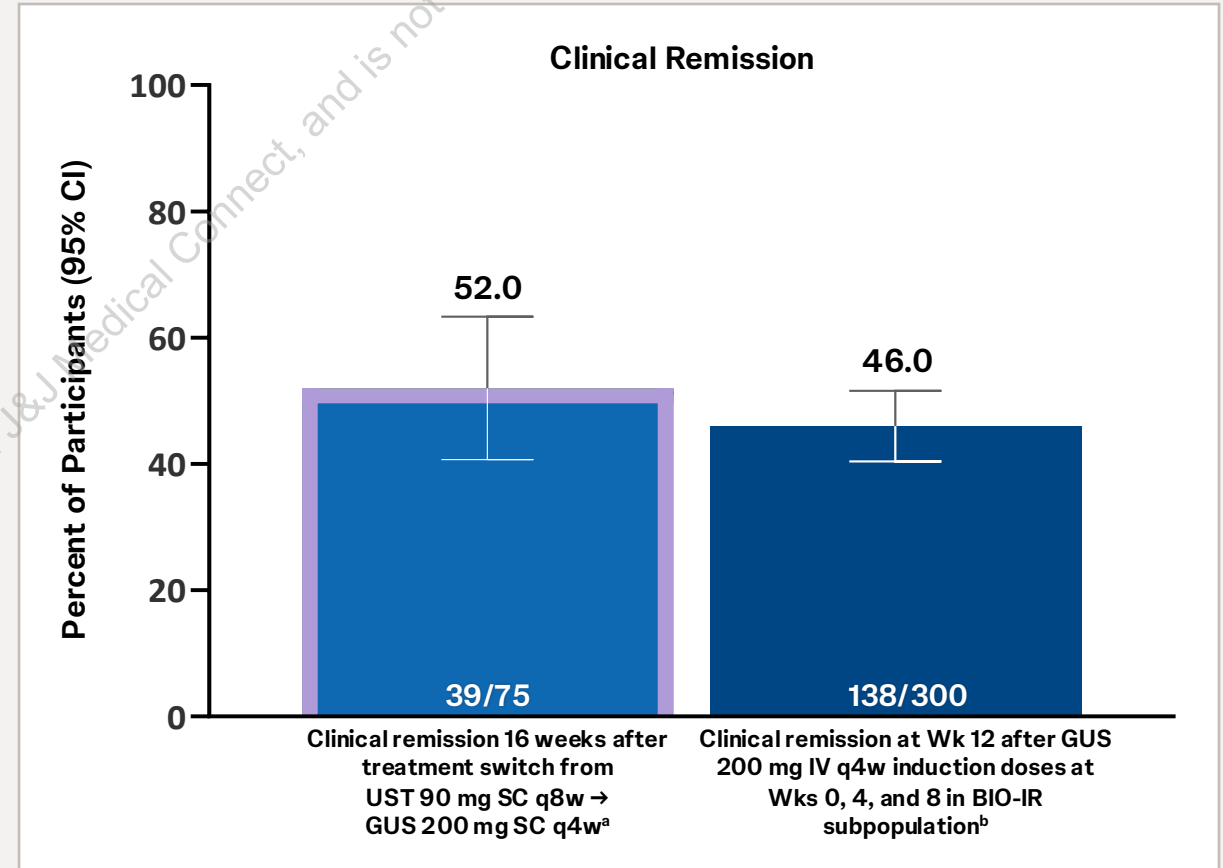
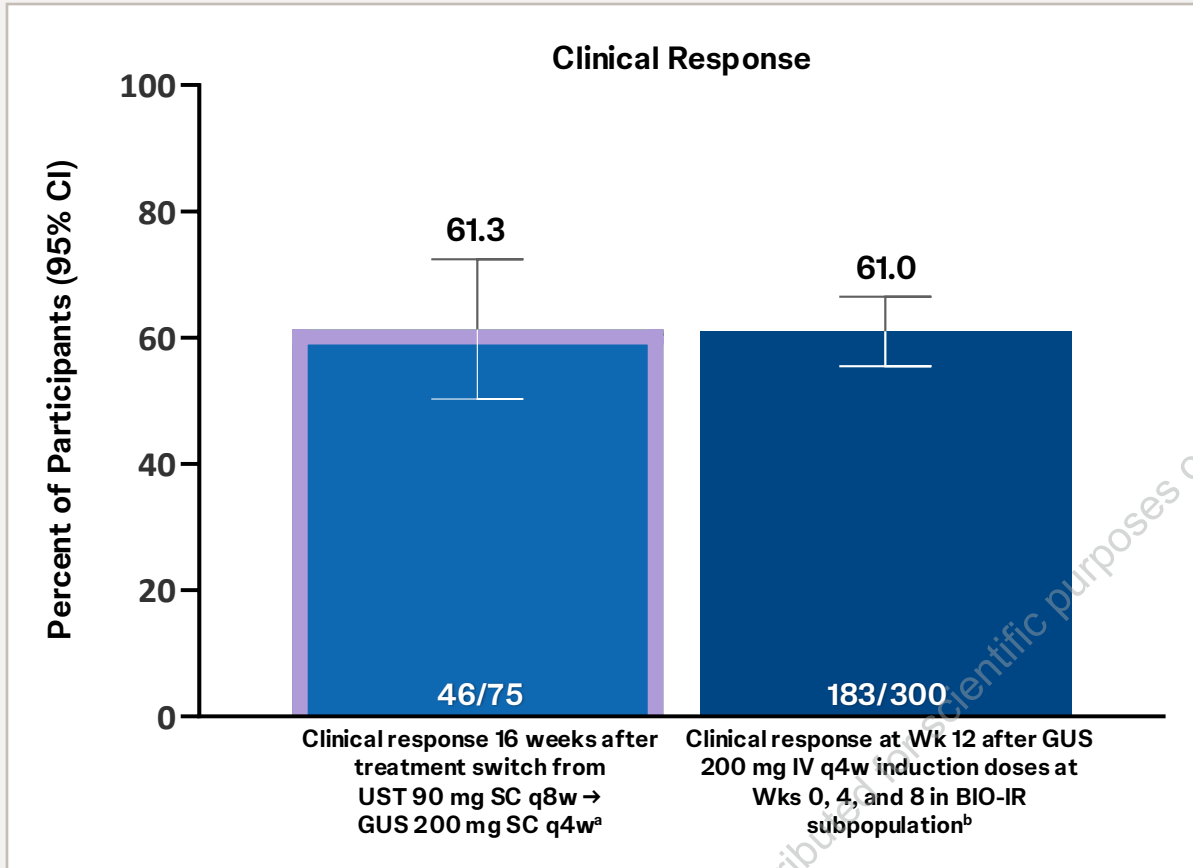
**Clinical remission:** CDAI score  $< 150$

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. º 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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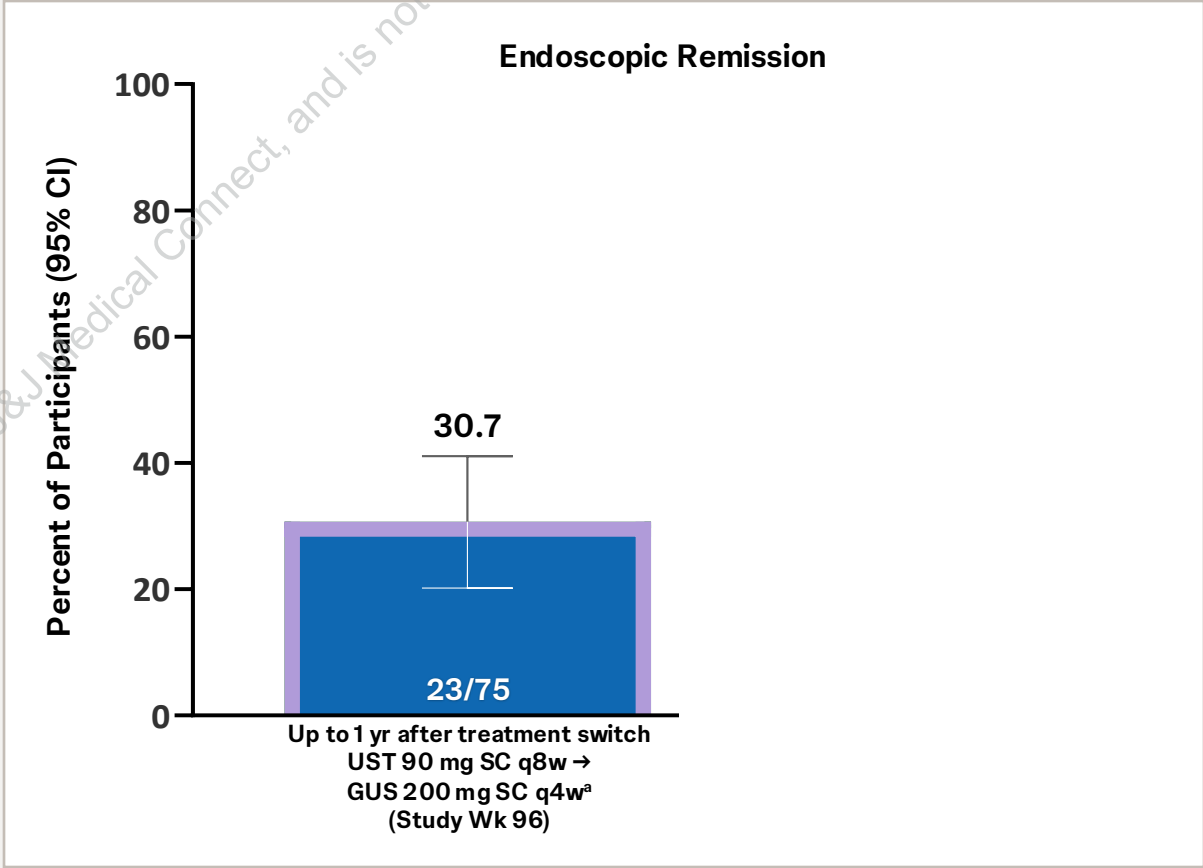
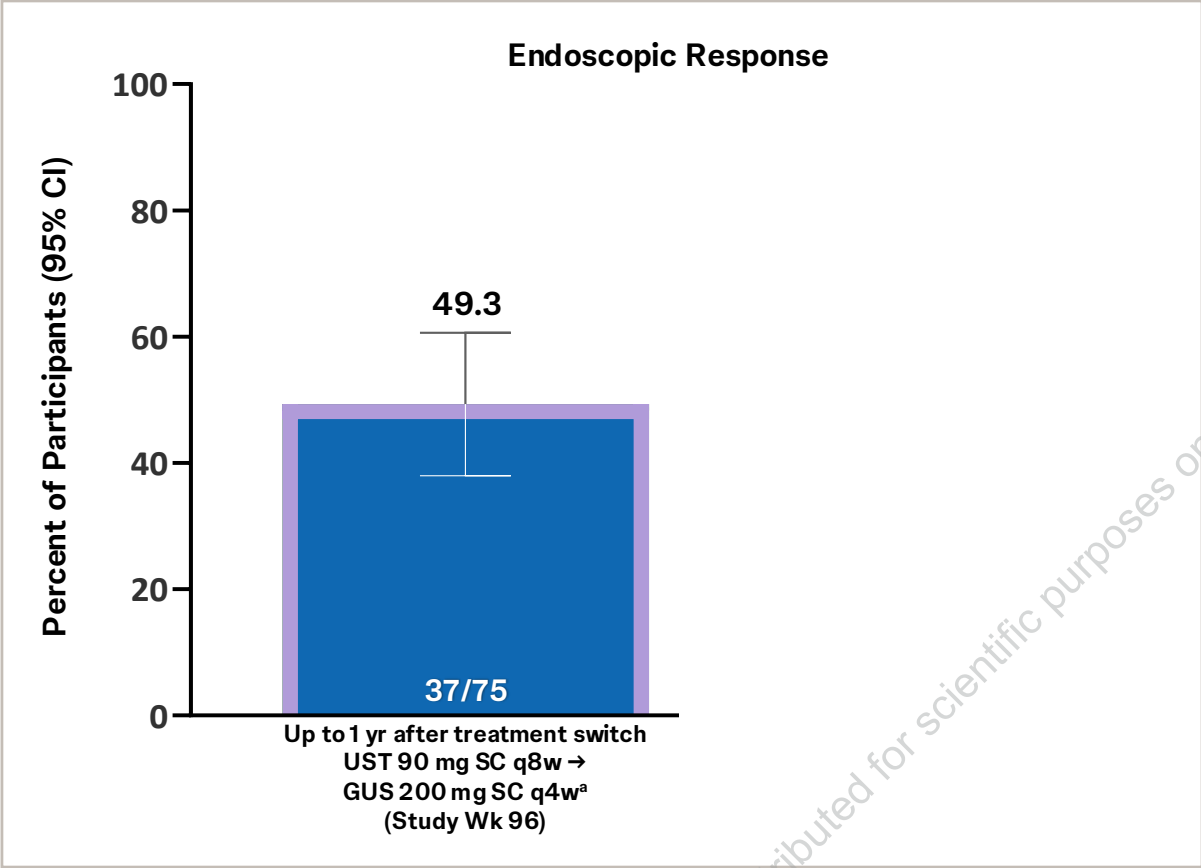
**Clinical remission:** CDAI score  $< 150$

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# Endoscopic Outcomes at Study Week 96

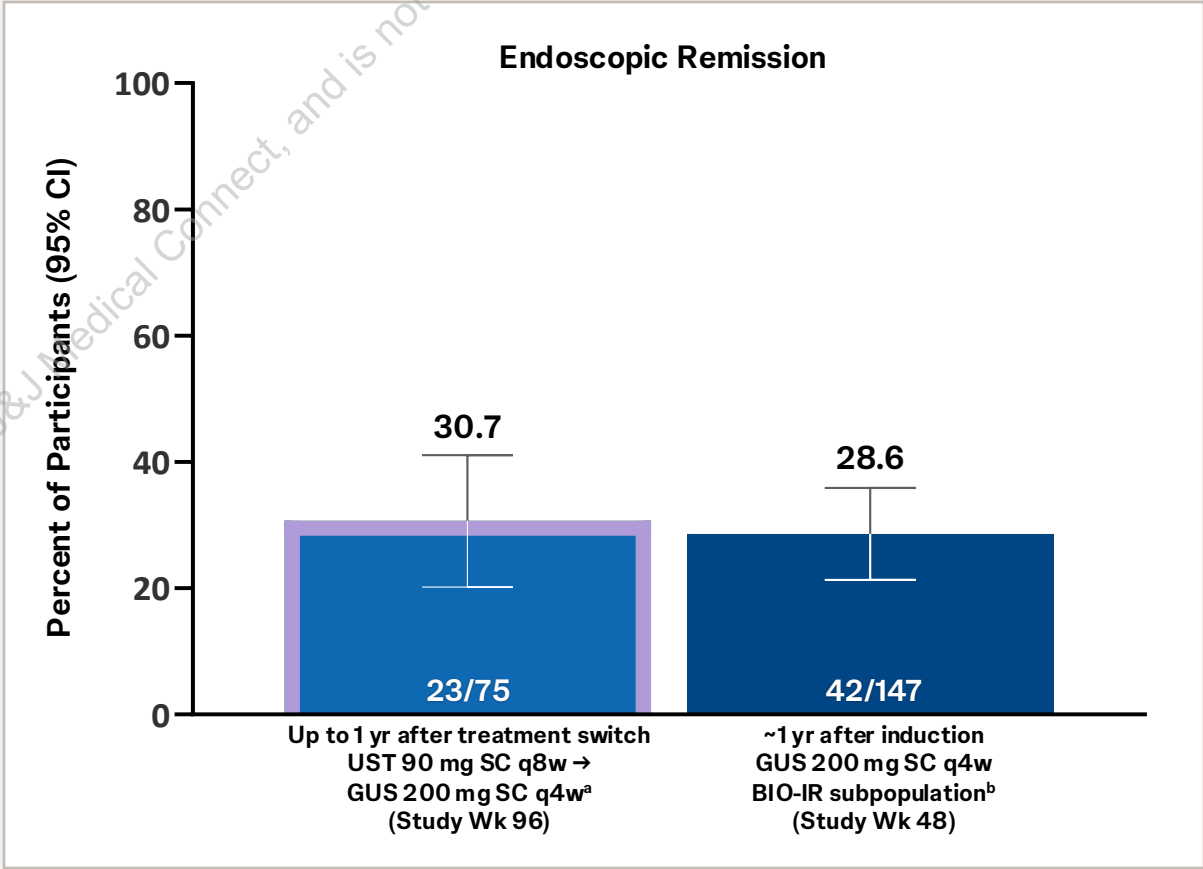
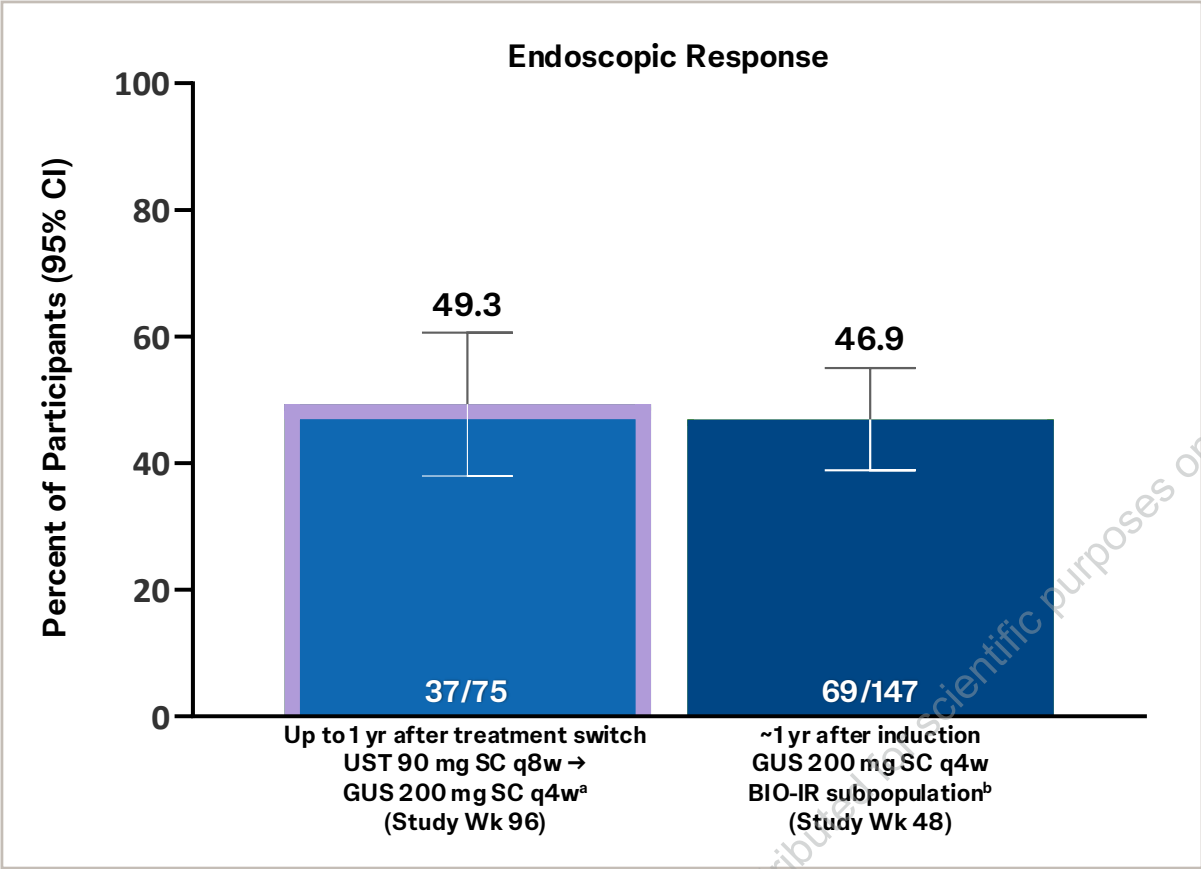


**Endoscopic response:**  $\geq 50\%$  improvement from baseline in SES-CD or SES-CD  $\leq 2$

**Endoscopic remission:** SES-CD  $\leq 4$  and a  $\geq 2$ -point reduction from baseline and no subscore greater than 1 in any individual component

BIO= biologic; CD= Crohn's disease; CDAl= 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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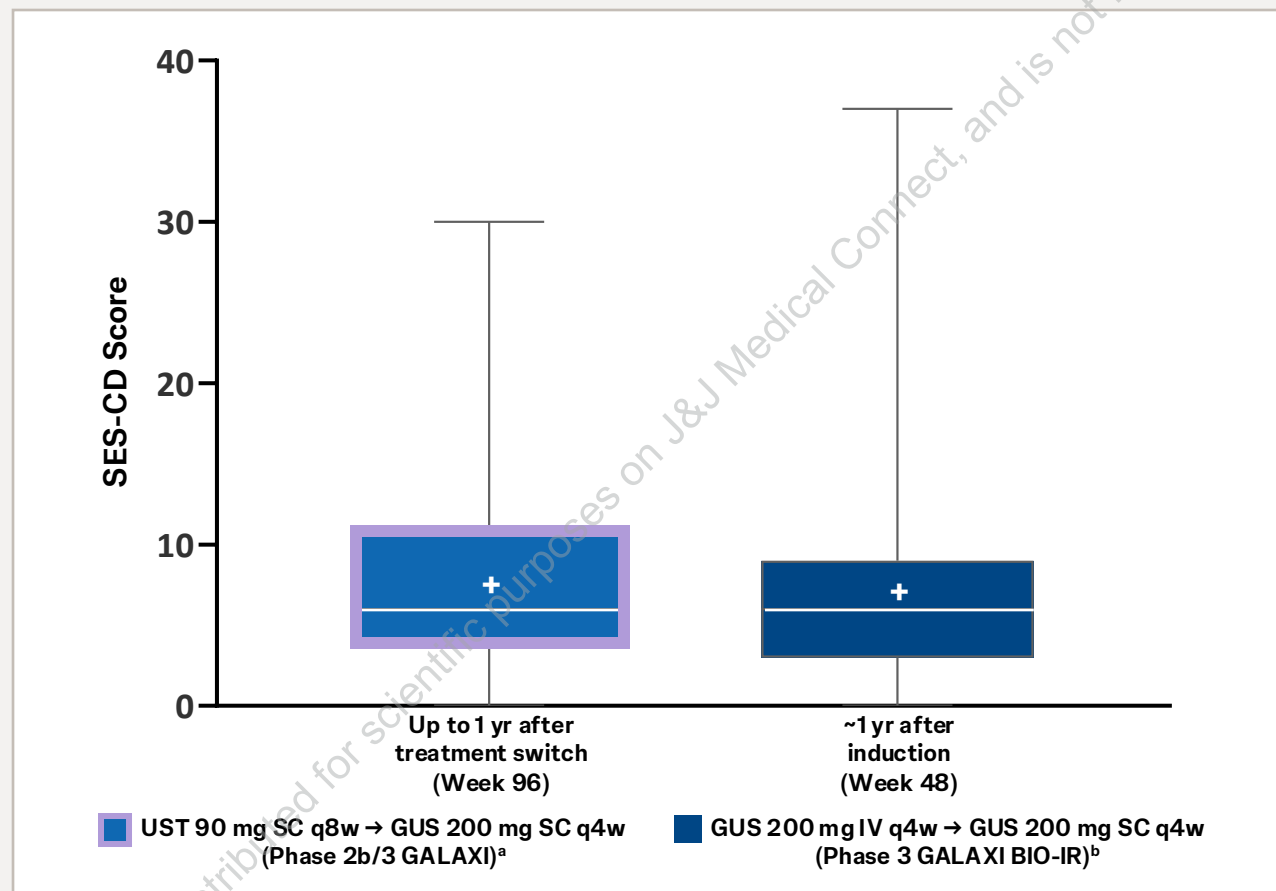


**Endoscopic response:**  $\geq 50\%$  improvement from baseline in SES-CD or  $SES-CD \leq 2$

**Endoscopic remission:**  $SES-CD \leq 4$  and a  $\geq 2$ -point reduction from baseline and no subscore greater than 1 in any individual component

BIO= biologic; CD= Crohn's disease; CDAl= 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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# SES-CD Scores



BIO= biologic; CD= Crohn's disease; GUS= guselkumab; IR= inadequate response or intolerance; IV=intravenous; LTE= long-term extension; q4w= every 4 weeks; q8w= every 8 weeks; SC= subcutaneous; SES-CD= simple endoscopic score for Crohn's disease; UST= ustekinumab.

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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 <sup>a</sup> (N=80)
Average duration of follow-up, weeks	34.8
Average exposure, number of administrations	8.4
<b>Participants with 1 or more:</b>	
AEs, n (%)	50 (62.5%)
SAEs, n (%)	6 (7.5%)
AEs leading to DC of study agent, n (%)	2 (2.5%)
Serious infections, <sup>b</sup> 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.

<sup>a</sup> 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.

<sup>b</sup> Infections are based on MedDRA system organ class "Infections and Infestations".

Note: Safety analyses included all 80 participants who underwent treatment switch in the GALAXI1, 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.

# 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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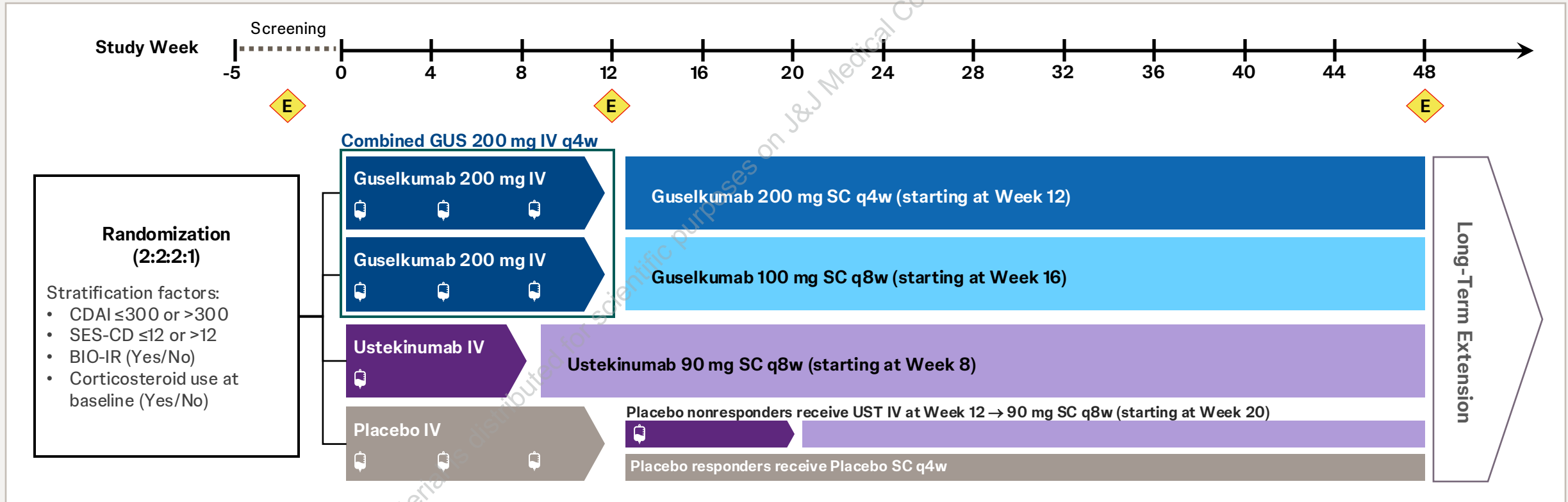
# Back up

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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<sup>a</sup> ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/intolerance to oral corticosteroids or 6-MP/AZA/MTX, or biologic therapies<sup>b</sup>



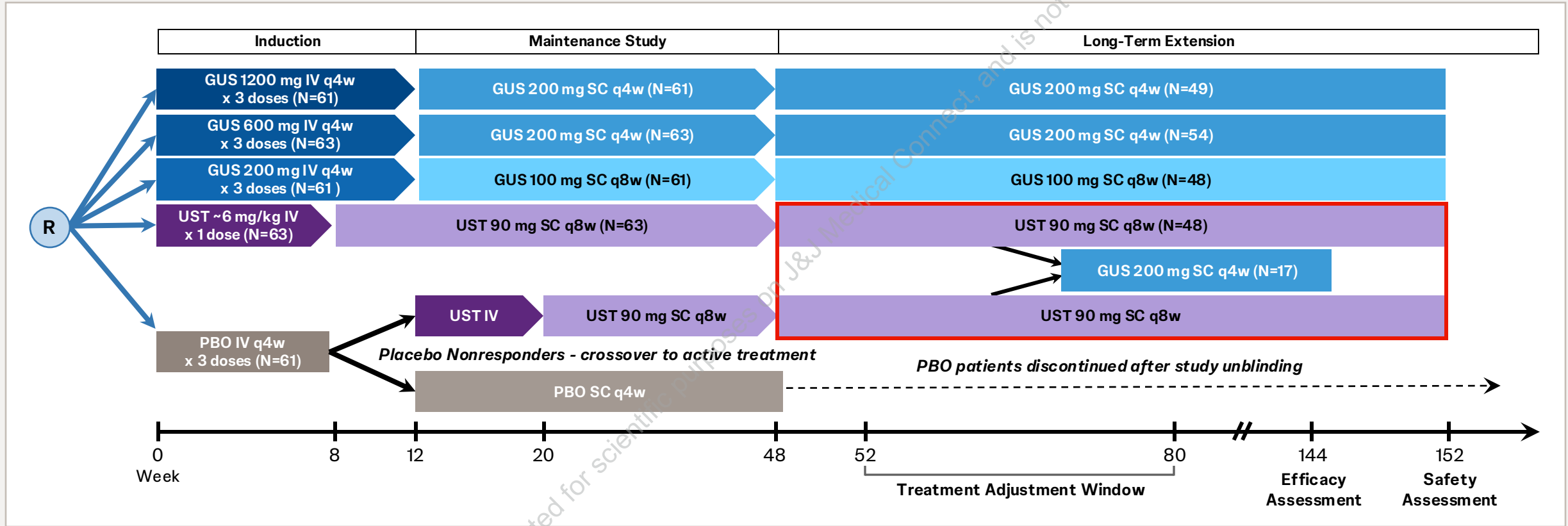
a. Scored at screening by central reader with minimum scores of 1 for “size of ulcer” and “ulcerated surface”

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

# 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 [ $\geq 100$ -point reduction in CDAI score from baseline or CDAI  $< 150$ ] AND CDAI  $\geq 220$ ) were eligible for a treatment switch to SC guselkumab 200 mg q4w maintenance **without induction**